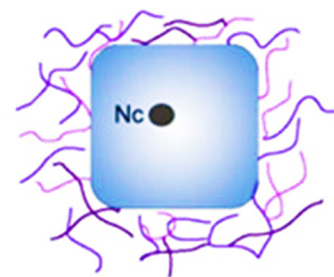
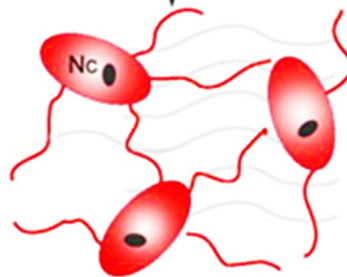
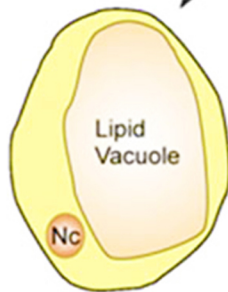
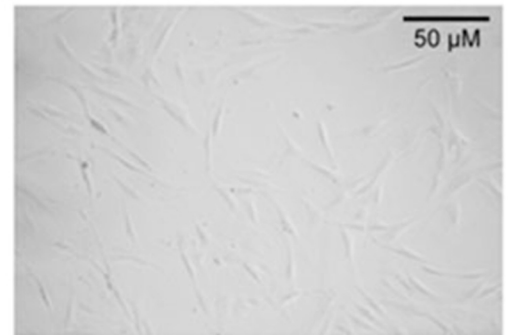
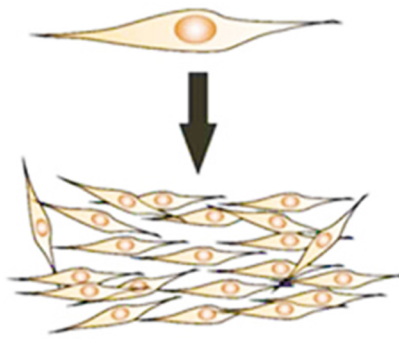


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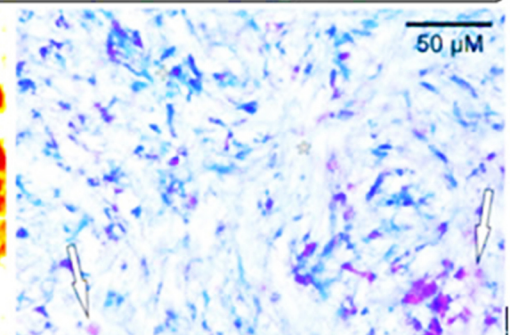
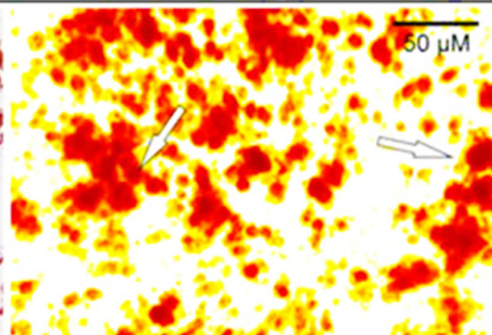
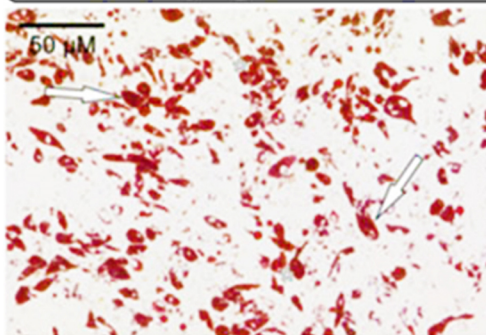
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Case Report

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# Management of the recalcitrant upper lip

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## Abstract

The aim of this study was to present our experience in the management of the recalcitrant upper lip and describe the surgical technique. We took a retrospective chart review of all patients who underwent reconstruction of the recalcitrant upper lip after maxillectomy and radiation therapy. Three female patients were identified. All patients had a history of malignant maxillary tumors, mucoepidermoid carcinoma ( $n = 1$ ), verrucous carcinoma ( $n = 1$ ), squamous cell carcinoma ( $n = 1$ ). Tumor extirpation was carried out through total maxillectomy ( $n = 2$ ), and bilateral subtotal maxillectomy ( $n = 1$ ). Primary reconstruction was accomplished with scapula free flap ( $n = 1$ ), fibula free flap ( $n = 1$ ), and nonvascularized iliac crest bone graft ( $n = 1$ ). Two patients underwent adjuvant radiotherapy. All patients developed recalcitrant upper lip. All patients had secondary reconstruction to correct of the recalcitrant upper lip using radial forearm free flap. All patients had successful dental rehabilitation. The mean follow-up was 5 years (range 3-7 years). Subjective functional and aesthetic outcome was assessed in all patients at the last follow up visit. All patients reported subjective improvement in speech, mastication and aesthetics. Free tissue transfer provides an ideal method to reconstruct the recalcitrant upper lip. Favorable functional and aesthetic outcomes can be successfully achieved using the technique described in this series.

**Keywords:** Recalcitrant upper lip, upper lip reconstruction, maxillectomy, radiation therapy

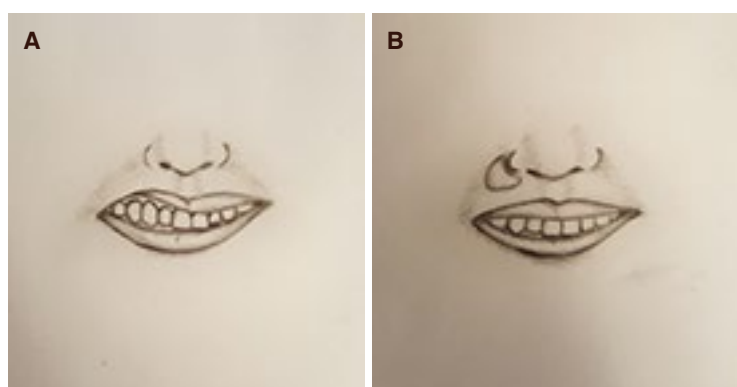
## INTRODUCTION

Complex post-ablative reconstruction often requires secondary refinements to improve the aesthetic and functional outcome. A challenging problem encountered after post-ablative maxillary reconstruction and adjuvant radiotherapy is the recalcitrant upper lip. Patients with recalcitrant upper lip present with retracted and shortened upper lip, thin vermilion and intractable vestibule [Figure 1]. This results in lip



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**Figure 1.** (A) The classic appearance of the recalcitrant upper lip; (B) inset of the radial forearm free flap at the base of the nose and the depth of the oral vestibule improves the lip, vermilion and vestibule

**Table 1. Summary of patients**

Patient	Age	Gender	Diagnosis	Ablative treatment	Adjuvant treatment	Primary reconstruction	Secondary reconstruction	Follow up	Dental rehabilitation
1	68 years	Female	Intermediate grade MEC	Left total maxillectomy	Yes	Scapulaosteocutaneous free flap Orbital floor reconstruction	Trismus release Fat grafting Canthopexy and tarsorrhaphy RFFF Flap debulking RFFF Flap debulking	7 years	Yes
2	60 years	Female	Verrucous carcinoma	Bilateral subtotal maxillectomy Bilateral neck dissection	No	Iliac crest bone graft	Flap debulking RFFF Flap debulking	3 years	Yes
3	57 years	Female	Stage 4 SCC	Right total maxillectomy Right neck dissection	Yes	Fibular free flap Orbital floor reconstruction	Zygomatic implants Fat grafting Vestibuloplasty RFFF Flap debulking	6 years	Yes

MEC: mucoepidermoid carcinoma; SCC: squamous cell carcinoma; RFFF: radial forearm free flap

incompetency, difficulty in controlling the food bolus, speech intelligibility and difficulty in prosthetic rehabilitation.

There is paucity of reports in the surgical literature on the management of the recalcitrant upper lip. In this report, we present our experience with three patients [Table 1] using the radial forearm free flap (RFFF) and describe the surgical technique in details.

## CASE REPORT

### Case 1

This is a 68-year-old female with a history of mucoepidermoid carcinoma of the left maxillary sinus. She underwent left total maxillectomy and adjuvant radiotherapy. She subsequently underwent scapula osteocutaneous free flap reconstruction. Multiple secondary procedures were performed to improve her facial symmetry and function including trismus release, fat grafting, canthopexy and tarsorrhaphy. She continued to have the classic appearance of the retracted and shortened upper lip on the affected side with intractable maxillary vestibule [Figure 2A]. RFFF reconstruction was performed to reconstruct the recalcitrant upper lip and oral vestibule [Figure 2B]. The postoperative course was unremarkable. Flap debulking was done to achieve improved symmetry. She was able to wear dental prosthesis and had improved speech and mastication [Figure 2C]. She was followed up for 7 years.





**Figure 2.** (A) The classic appearance of the shortened and retracted upper lip after primary reconstruction and adjuvant radiation therapy; (B) inset of the radial forearm free flap lengthens the lip and vestibule; and (C) allows placement of dental prosthesis with improved lip-to-tooth relationship



**Figure 3.** (A) Significant shortening of the upper lip and loss of vestibule after subtotal maxillectomy; (B) inset of the radial forearm free flap at the depth of the neo-vestibule; (C) final appearance with improved lip-to-tooth relationship

## Case 2

This is a 60-year-old female with a history of verrucous carcinoma of the anterior maxilla. She underwent subtotal maxillectomy and bilateral neck dissection. She developed a shortened and retracted upper lip with intractable vestibule [Figure 3A]. She was unable to wear a dental prosthesis. Subsequently she underwent iliac crest bone graft and radial forearm free flap to reconstruct the recalcitrant upper lip and oral vestibule [Figure 3B]. The postoperative course was unremarkable. Flap debulking was performed at a later stage. She was able to wear dental prosthesis and had improved speech and mastication [Figure 3C]. She was followed up for 3 years.

## Case 3

This is a 57-year-old female with a history of squamous cell carcinoma of the right maxilla. She underwent subtotal maxillectomy, neck dissection, fibula free flap reconstruction and adjuvant radiotherapy. She had zygomatic implants. However, due to the loss of vestibule, dental rehabilitation was difficult. She underwent multiple secondary procedures including fat grafting and vestibuloplasty. She continued to have the classic appearance of the retracted and shortened upper lip on the affected side with intractable maxillary vestibule [Figure 4A]. RFFF reconstruction was done to reconstruct the recalcitrant upper lip and oral vestibule. The postoperative course was unremarkable. She subsequently had flap debulking to achieve improved symmetry. She was able to wear dental prosthesis and had improved speech and mastication [Figure 4B]. She was followed up for 6 years.

## DISCUSSION

Ablative surgery disrupts the elegant anatomy of maxilla and the overlying soft tissue. Reconstructive techniques in the primary setting are geared toward achieving bony and mucosal continuity [Figure 5]. Adjuvant radiotherapy leads to soft tissue atrophy and fibrosis. This results in upper lip retraction and shortening, thinning of the vermilion and loss of the intraoral vestibule [Figure 1A].



**Figure 4.** (A) The classic appearance of the shortened and retracted upper lip after primary reconstruction and adjuvant radiation therapy; (B) inset of the radial forearm free flap lengthens the lip and vestibule and improves the lip-to-tooth relationship

Numerous techniques of vestibuloplasty are available to lengthen the vestibule such as submucosal vestibuloplasty, open vestibuloplasty with secondary re-epithelialization, transpositional vestibuloplasty and skin grafting<sup>[1]</sup>. In the irradiated patient, these techniques have a limited role due to the poor vascular supply, scarring and fibrosis and limited tissue laxity. The unpredictable outcome of these procedures also carries a significant risk for hardware exposure, poor healing and wound dehiscence. Pedicled flaps using the facial artery myomucosal flap and the nasolabial flap have been used in the past<sup>[2,3]</sup>. However, in the post-ablative irradiated patient, these flaps have limited role due to the limited amount of tissue available for transfer, the need for intact facial artery which is often compromised after ablative surgery, and the presence within the zone of external beam radiation<sup>[4]</sup>.

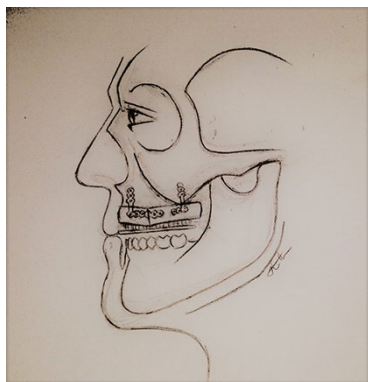
The deformity of the recalcitrant upper lip results from skin, muscle and mucosal tissue loss and fibrosis. Therefore, full-thickness reconstruction is essential to restore the length and thickness of the upper lip and re-establish the maxillary vestibule. Vascularized free tissue provides the best method of reconstruction in these patients.

St-Hilaire *et al.*<sup>[4]</sup> described 13 patients with intractable vestibules secondary to tumor extirpation, traumatic injuries and infections. They used the ulnar and anterolateral thigh flap to reconstruct the oral vestibule. In our case series, the patients had lip and vestibular deformity secondary to tumor extirpation and/or radiotherapy. In two patients, the deficiency of soft tissue was full thickness, and required tissue augmentation to the mucosal and cutaneous surfaces to allow lengthening of the lip and vestibule. We chose the RFFF which was ideal to provide thin and pliable tissue with a long vascular pedicle. It also allowed complex design of the skin to resurface the mucosal and cutaneous linings.

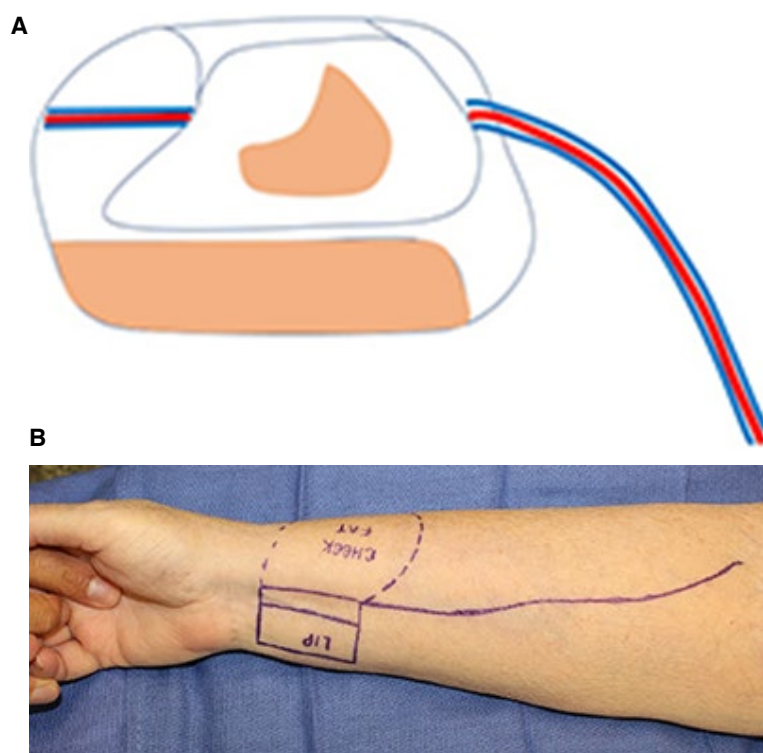
The flap is harvested in the standard technique. The skin is de-epithelialized in the middle segment [Figure 6]. The recipient site is prepared by making an incision at the depth of the vestibule to release the upper lip. Another incision is made at the base of the nose to allow lip lengthening. The two incisions are connected and the area is widely undermined to allow the flap inset. The de-epithelialized segment is tunneled and the epithelialized segments are inset at the base of the nose to lengthen the lip, and the depth of the vestibule to lengthen the neo-vestibule [Figure 1B].

Subjective outcome assessment was performed in all patients. All patients were satisfied with final aesthetic improvement. All patients were able to wear dental prosthesis and had improved lip competence, speech, mastication and bolus control.

We recognize the limitations of this study which include the retrospective case series design and the subjective outcome assessment. The purpose of this study was to demonstrate a surgical technique which is useful in a challenging clinical problem. This case series highlights the importance of secondary refinements after primary reconstruction and radiation therapy to improve the aesthetic and functional



**Figure 5.** Loss of the vestibule after primary reconstruction when the skin paddle is sutured to the labial mucosa



**Figure 6.** The skin is de-epithelialized in the middle segment leaving cutaneous and mucosal epithelized surfaces (A and B)

outcome. The RFFF provides an ideal method of reconstruction for the recalcitrant upper lip.

## DECLARATIONS

### Authors' contributions

Conception and design, data acquisition, drafting the article, revising and final approval: Al Shetawi AH  
Conception and design, drafting the article, revising and final approval: Fernandes R

### Financial support and sponsorship

None.

### Conflicts of interest

There are no conflicts of interest.

**Patient consent**

All patients were consented per the University protocol.

**Ethics approval**

Not required for case reports per the University protocol.

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Original Article

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# Transpalpebral eyebrow lift: the mini eyebrow lift

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## Abstract

**Aim:** This paper focus is to describe and evaluate the authors' personal technique for a simplified transpalpebral eyebrow lift.

**Methods:** We performed surgery in 179 patients (95% females and 5% males) between years of 2008 and 2009. Initially, a thorough assessment of brow stability and symmetry was performed. To achieve desirable aesthetic we agreed upon the consensus that the eyebrow lateral third should be 0.3 to 1 cm above the supraorbital rim in women and just above or at supraorbital rim in men. Hence the surgery consisted of the removal of excess skin, treatment for bags if they were present and a transpalpebral lateral eyebrow lift.

**Results:** There were only 5 cases in which patients reported episodes of pain on the temporal undermined area related with the suture with the evidence of pain subsiding over time and disappearing all together within 3 months. No patients required revision surgery and no patients presented lagophthalmos or any eyelid closure difficulties.

**Conclusion:** This paper presents a simplified version of an eyebrow lift technique that is easy to reproduce and effective.

**Keywords:** Eyebrow lift, blepharoplasty, transpalpebral

## INTRODUCTION

Indubitably, the upper blepharoplasty is the introductory procedure that allows surgeons from the most diverse specialties to adventure on facial cosmetic surgery. It is a procedure known to be uncomplicated,



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**Figure 1.** (A) preoperative picture: patient 67 years old, male, presenting ptosis of the lateral third of the eyebrow (identified with the white arrow), not diagnosed at the time; (B) postoperative picture: 6 months after, the remaining excess skin on the lateral third of the eyebrow (identified with the white arrow) is a common cause of complaint from various patients

effective, quick and with high success rate. The nature of the procedure therefore sets high expectations with less understanding of the need for any potential revision surgery.

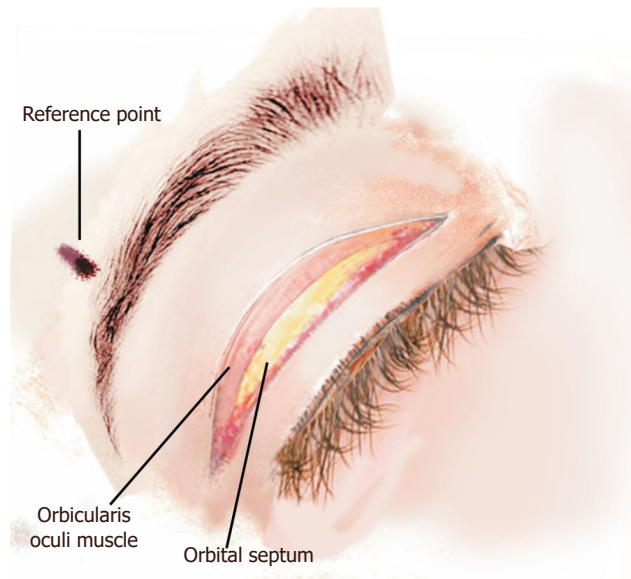
Residual fat on the medial compartment and remaining excess skin on the lateral third of the upper eyelid are probably the most common causes of patient dissatisfaction. This excess skin most of the times is not related to a conservative removal or a technique failure. Otherwise, it is caused by an undiagnosed ptosis of the lateral eyebrow [Figure 1].

Generally, eyebrows are just above the superior orbital rim in men and slightly higher in women. Many patients asking for an upper blepharoplasty complain about excessive skin on the eyelid<sup>[4]</sup>. When asked to demonstrate how they would like the final result to be, patients instinctively use their hands to raise the lateral third of the eyebrow as a sign of a youthful desired result. This clearly illustrates that the problem cannot be merely a redundancy of the eyelid skin.

In this paper, the authors discuss the eyebrow position and this experience with a simple technique to be associated with the upper blepharoplasty. The authors have performed a clinical audit of 179 patients who underwent this procedure between the years of 2008 and 2009. The detailed content of the paper will also allow other surgeons to reproduce every step of the technique.

## METHODS

Preoperative identification of patients presenting ptosis of the lateral eyebrow is very important. In this retrospective analysis, it was confirmed that the evaluation of the position of the eyebrows was present in all preoperative consultation forms. Patients with lacrimal gland prolapse were not included in the study and can be considered a contraindication for this procedure until the prolapse is investigated and corrected. The patients were 95% female ( $n = 170$ ) and 5% male ( $n = 9$ ), with ages ranged between 43 and 63 years old. All patients had their surgical procedure performed with the same surgical team. They had upper blepharoplasty associated or not with other procedures (lower blepharoplasties and/or facelifts). This clinical audit followed the Declaration of Helsinki guidelines and a written consent for the outlined procedure was obtained from all patients.

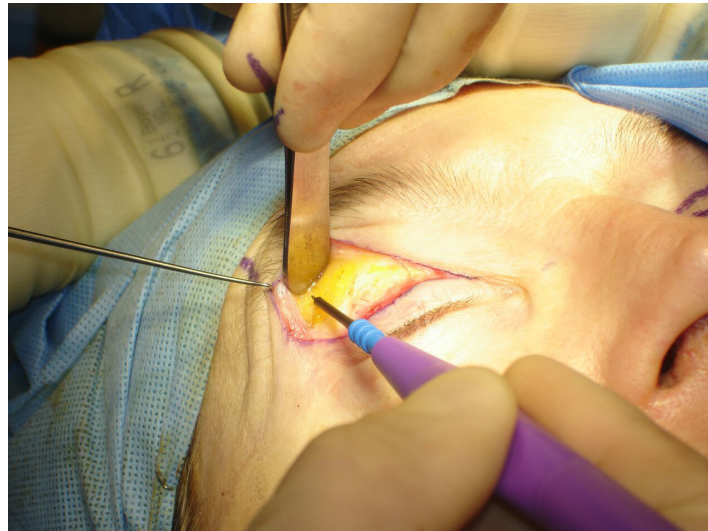


**Figure 2.** Artistic image of the upper eyelid after the excision of the skin and the small strip of orbicularis muscle

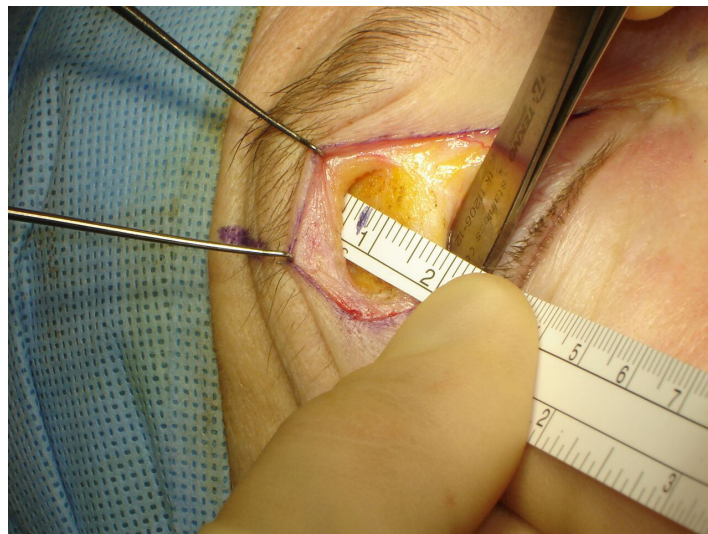
An assessment of brow stability and symmetry was performed and noted in all files. Achieving a good aesthetic result begins with a careful preoperative assessment of the patient's anatomy and desires. Nevertheless, the eyebrow lateral third should be 0.5 to 1 cm above the supraorbital rim in women<sup>[2-4]</sup>. In men, a good eyebrow position is just above or at the supraorbital rim. While performing this technique the authors aimed to achieve these reference landmarks and different fixation levels were used when asymmetric eyebrows position was diagnosed.

The surgery performed on the upper eyelid was a conventional blepharoplasty with removal of excess skin, treatment for the bags when they were present and a transpalpebral lateral eyebrow lift. During the intraoperative design of the excess skin to be resected, the surgeons marked what they would normally remove and then reduced the amount of skin to be excised on the lateral third in 2 to 4 mm, depending on the extension of lift proposed. This maneuver is paramount in order to avoid distortions on the scars positions and ultimately lagophthalmos of the lateral third of the eye. The projection of the lateral canthus is also identified as a landmark to the position of our future suture. Following marking the excess of skin to be removed, an infiltration of 20 mL lidocaine 2% associated epinephrine 1:200,000 and hyaluronidase 1500 units is performed (Hyalase, CP Pharmaceuticals, UK). The average volume of local anesthesia used is 7-10 mL for both sides and it was injected on the subcutaneous plan. Initially, only a skin flap is removed with subsequent Hemostasis, followed by a small removal of the orbicularis oculi muscle, mainly on its lateral portion. The resection of a small strip of the orbicularis muscle on its lateral portion was always performed, as it was considered to be easier to expose the orbital septum this way [Figure 2]. The surgery proceeded with the removal of the excess of fat bags when present and finally the browplasty was performed.

With the assistance of two skin hooks lifting the upper flap (with the orbicularis muscle included), it is rather easy to see the orbital rim. On the projection of the lateral corner, the surgeon initiated the dissection using a Colorado needle (Utah Medical Products, USA). The dissection is extended in the submuscular plane [Figure 3]. The dissection of a 1.5-cm semicircle cannot be too anterior, otherwise it will invade the retro-orbicularis fat (ROOF) area that is extreme vascularized and could result in excessive bleeding. On the other hand, the dissection plane cannot be too posterior as the connective tissue should be left to be used as an anchoring base for the fixation suture [Figure 4].



**Figure 3.** Picture of the initial dissection of the retro orbicularis space



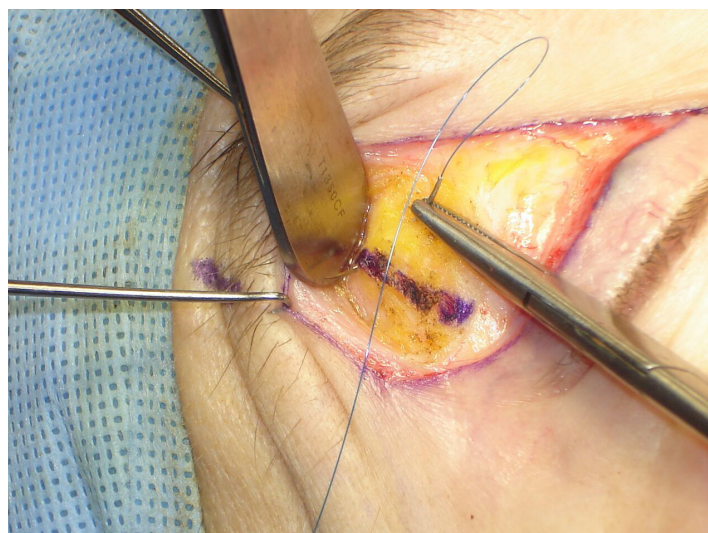
**Figure 4.** Picture of the retro-orbicularis space where we can measure with a simple ruler, the amount of tissue to be dissected

A Prolene 5.0 suture is inserted grabbing the periosteum with the curve of the needle parallel to the orbital rim [Figure 5]. The distance from the orbital rim is approximately 10 to 15 mm, depending on the degree of elevation desired. The degree of elevation was previously decided according to the patient's original desire of elevation (more or less). The surgeon uses the assistance of a forceps to find the second entrance point, by pulling the skin on the junction of the projection of the lateral canthus and the lower portion of the eyebrow's hairline. On that protrude area the suture grabs just halfway through the orbicularis muscle [Figure 6]. At this moment, prior to completing the knot, the surgeon also must verify if the suture was not too superficial and created dimples on the skin. If there were no signs of dents on the skin, the knot was completed [Figure 7]. The effect could be immediately noticed with the creation of some creases on top of the eyebrow, which will fade in 2-4 weeks [Figure 8]. The skin was closed with Nylon 6.0 continuous suture [Video 1].

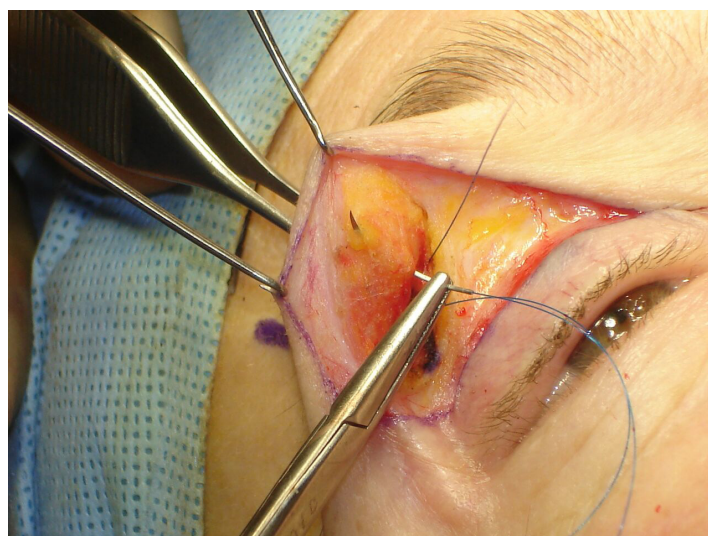
## RESULTS

Reviewing the present clinical audit revealed only five cases in which persistent pain was reported on the temporal undermined area related perhaps with the suture, however with the disappearing of the symptom





**Figure 5.** Picture showing the insertion of a needle capturing all the suprapariosteal tissue

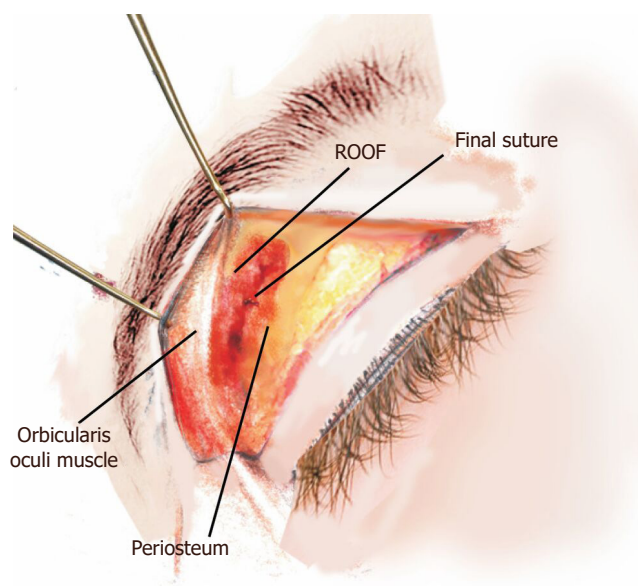


**Figure 6.** Picture showing the needle including only half of the thickness of the orbicularis muscle avoiding dimples on the skin

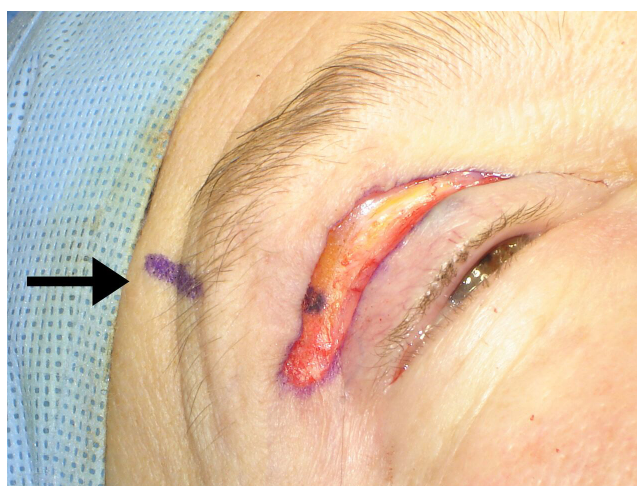
in 2 to 3 months. No patients needed any potential revision surgery for this procedure. No patients presented lagophthalmos or any eyelid closure difficulties. Hence, a favorable result could also be confirmed with the absence of revisions as no patients returned with the complaints that the eyebrow has dropped to the original position [Figures 9 and 10]. The patients were followed up for a period of 3 months to 2 years. Additional information about patient demographics, types of procedures and complications can be found in Table 1.

## DISCUSSION

Blepharoplasty is one of the top 5 cosmetic procedures performed in the United States with over 209,000 cases in the year of 2016<sup>[5]</sup>. Notwithstanding it's considered a very simple procedure, there are two very common unfavorable results: remaining lateral excess of skin and medial fat bags. In the majority of upper blepharoplasties cases, the remaining excess of lateral skin is not provenient of a limited skin removal, but from an undiagnosed ptosis of the lateral portion of the eyebrow.



**Figure 7.** Artistic image of the final aspect of the suture. All the anatomical structures remain easily identifiable. ROOF: retro-orbicularis fat

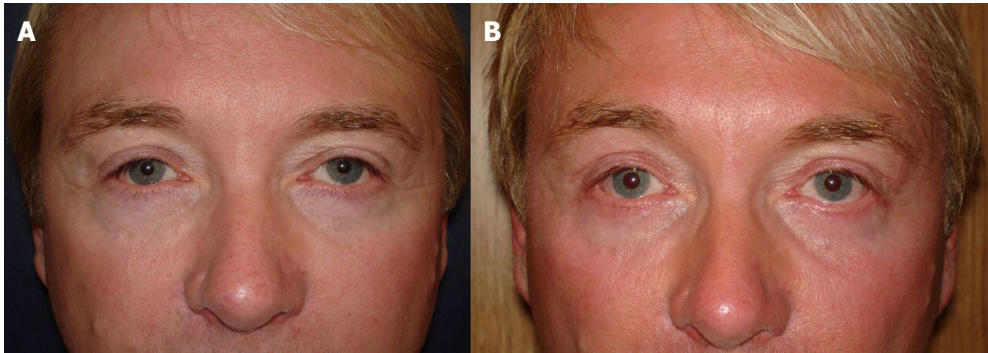


**Figure 8.** Picture of the final aspect of the suture with the eyelid returned to its anatomical position. The evidence of lift is clear and identified with a black arrow on the picture

**Table 1. Demographic and complications information for all patients**

Characteristics	Data
Number of patients	179
Age range (years)	28-63
Age average with SD (years)	42.2 4 8.28
Gender	Female: 170 (95%), male: 9 (5%)
Postoperationpain (transient)	5 (2.79%)
Seroma	0 (%)
Hematoma	0 (0%)
Infections	0 (0%)
Wound dehiscence	0 (0%)

The desired characteristics of the eyebrows are influenced by several factors including age, gender, culture, ethnic origin and even fashion trends. However, the eyebrow's change of position with ageing is common



**Figure 9.** (A) preoperative picture: patient 52 years old, male, presenting ptosis of the lateral third of the eyebrow; (B) postoperative picture: 3 months after upper blepharoplasty with mini eyebrow lift, where we can see the satisfactory effect that the lift gives to the overall rejuvenation of the eyelid



**Figure 10.** (A) preoperative picture: same patient with an oblique view; (B) postoperative picture: 3 months after, we can confirm the effective outcome of the mini eyebrow lift

to all these groups. The stretching of the scalp and the laxity of the connective tissue of the frontal region is known produce a ptosis on the lateral segment before than the medial.

The first technique for eyebrow lift could possibly be attributed to Passot in 1919. Subsequently, many techniques using the coronal approach were used to correct the eyebrow ptosis. Nevertheless, it was Castañares<sup>[6]</sup> in 1964 who introduced an isolate eyebrow lift technique with world repercussion. In 1975, Hinderer<sup>[7]</sup> using a similar procedure presented the importance of the correction of the position of the eyebrow together with the upper blepharoplasty. Unfortunately, all Castañares' like techniques lead to noticeable scars and have limited use in plastic surgeons' practices lately.

Since 1996, Knize<sup>[8]</sup> is probably one of the few surgeons who dedicated great amount of research to the ideal eyebrow position. He also developed the first isolate eyebrow lift technique with scars hidden in the scalp, which made this procedure tremendously popular on the 90's amongst all plastic surgeons.

Many other surgeons also emphasized the importance of the eyebrow position and several studies can be cited on the subject<sup>[9,10]</sup>. The reference measurements that were used in this technique are the result of an informal consensus found in these papers<sup>[11]</sup>.

Knize's surgery still has its important stance on the arsenal of techniques to enhance eyebrow lift. However, on the beginning of the millennium, the advances with endoscopic forehead lift could not only address the



eyebrow ptosis but also could promote a full fronto-temporal rejuvenation. The complexity of endoscopic lifts still limits this procedure to a select group of surgeons and the strong market presence of toxin botulinic and fillers in the market immensely reduced the request for a surgical approach to the forehead. However, these non-surgical procedures are not very effective on the eyebrow ptosis.

Sokol and Sokol<sup>[12]</sup> in 1982 was the first to propose a transpalpebral browlift, eliminating forehead scars. They used a complicated interposition of flaps (muscle and periosteum) that inevitably made this technique to fall in oblivion.

In the future, papers comparing the ROOF resection with the eyebrow lift are necessary to expand the benefits of both techniques.

Albeit, McCord and Doxanas<sup>[13]</sup> in 1990 presented his transpalpebral eyebrow lift, called browplasty. His procedure consisted of a wider dissection of the sub-brow space and a muscle plication with two to three mattress sutures to fixate the brow at the desired position. This very successful procedure is easily adjunct to the conventional upper blepharoplasty and doesn't add any extra scars to the patient. Nowadays, McCord's procedure is probably one of the most used worldwide. In his series, it is related a prolonged brow anesthesia and paresthesia up to 6 months and also some incidence of hematoma. The authors believe that through reducing the undermined area, they could limit these complications, as no causes of permanent anesthesia or hematoma was detected.

Thereupon, many techniques have been described to promote eyebrow lift; the presented procedure is as easy to reproduce as effective. In recent years, techniques have evolved not only to improve aesthetic results but also to minimize complications. Hence, 20 years later after McCord's original work, this paper presents a simplified version of his technique.

## **DECLARATIONS**

### **Authors' contributions**

Concept and design: Sforza M

Data collection and analysis: Sforza M, Zaccheddu R

Write up: Sforza M, Sforza D

Review and final approval: Sforza M, Zaccheddu R, Sforza D

### **Data source and availability**

Data was collected by the both senior authors' personal series.

### **Financial support and sponsorship**

None.

### **Conflicts of interest**

This work was presented by the first author as a Lecture at the ISAPS Course (International Society of Aesthetic Plastic Surgery), Almaty, 2011.

### **Patient consent**

A written consent for the outlined procedure was obtained from all patients.

### **Ethics approval**

This clinical audit followed the Declaration of Helsinki guidelines.

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Review

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# Complex reconstruction of the lower extremity following sarcoma resection: a literature review

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## Abstract

While amputation was traditionally the only option available for patients with sarcomas of the extremities, chemotherapy, radiation, and advances in microsurgical technique have allowed many patients to undergo limb-salvaging procedures. Given the low incidence and heterogeneity of these tumors, there is currently no standard treatment algorithm for limb reconstruction after large sarcoma resection. Thus, we systematically reviewed the various types of free tissue transfer used for the reconstruction of lower limbs after sarcoma resection. Techniques were described based on anatomic location. This literature review supports free tissue transfer as a safe and acceptable modality for reconstruction after sarcoma resection of the lower limb. It allows for the application of healthy vascularized tissue to the defect while also providing freedom of flap positioning. Flap choice is dependent on tumor and defect size, tissue type and function, as well as donor site availability.

**Keywords:** Lower extremity, sarcoma, reconstruction

## INTRODUCTION

Soft tissue and bone sarcomas represent about 1% of all adult tumors<sup>[1]</sup>, affecting 1.8-5 out of every 100,000 people annually<sup>[2]</sup>. The lower limb is the most common site of sarcoma occurrence, representing 29%-40% of all cases<sup>[3,4]</sup>. Although amputation was traditionally the only option available for patients with sarcoma of the extremities, recent implementation of a multimodal treatment approach along with advancements in chemotherapy and microsurgical techniques has led to the influx of limb salvage therapy for these cancers<sup>[5,6]</sup>. Currently, wide tumor excision combined with adjuvant and or neo-adjuvant therapy is the standard of care for the successful treatment of sarcoma of the lower limbs<sup>[2]</sup>.



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Quite often, sarcoma excision results in large anatomical soft tissue deficits with resultant exposure of vital structures such as bones, tendons, and neurovascular bundles, necessitating complex soft tissue reconstruction with vascularized soft tissue transfer thus facilitating further treatments as well as maintaining or regaining structural function and integrity of the limb in question. To this end both pedicled and free tissue transfers have become a central component of lower extremity salvage after resection and chemo-radiation therapy. Recent data has shown that these complex reconstructions have provided faster recovery with adequate soft tissue reconstruction and maintenance of functionality of the limb<sup>[2,6-11]</sup>.

Currently there is no standard treatment algorithm for limb reconstruction after large sarcoma resection. In part this due to the low incidence of these tumors as well as the heterogeneity of extremity sarcoma. This problem is further compounded by the multitude of neo-adjuvant modalities that are used to treat these tumors as well as the timing of the oncological resection. Hence a comprehensive reconstructive approach that maximizes the maintenance of function and aesthetics depends primarily on the location and size of the defects as well as the muscles, tendon, blood vessels and nerves that were extirpated. The goal of this literature review is to therefore outline various author reports published in the current literature describing the various types of free tissue transfer used for the reconstruction of the lower limbs after sarcoma resection.

## METHODS

The PubMed database was used to review literature describing free tissue coverage of the lower extremity following soft tissue sarcoma resection. The entire PubMed library was used dating to 2016. The following search terms were used: “Neoplasms, Connective and Soft Tissue” [Mesh] OR (“sarcoma” [MeSH Terms] OR “sarcoma” [All Fields]) AND (“lower extremity” [MeSH Terms] OR (“lower” [All Fields] AND “extremity” [All Fields]) OR “lower extremity” [All Fields]) AND (“free tissue flaps” [MeSH Terms] OR (“free” [All Fields] AND “tissue” [All Fields] AND “flaps” [All Fields]) OR “free tissue flaps” [All Fields]). All studies published in the English language were included. Articles were excluded if they met the following criteria: exclusively pediatric patients, cadaver subjects, pathology of the pelvic girdle, exclusively pathology related to trauma, pathology related to skin neoplasms, and studies exclusively describing pedicled flaps. Table 1 lists the studies included in this review. Table 2 describes the types of flaps used for lower extremity reconstruction by region.

## RECONSTRUCTION BASED ON TUMOR LOCATION

### Thigh

Several factors must be taken into consideration when approaching reconstruction of the thigh. Primarily, malignant sarcomas of the femur are generally challenging to treat because radical resection of the tumor often requires simultaneous resection and reconstruction of the major femoral vessels. Tumor proximity to critical neurovascular structures is particularly of concern in the adductor compartment, where outcomes are generally poor, with high local recurrence rate, high complication rates and short long-term survival<sup>[12]</sup>.

The first report of reconstruction of major vessels was by Fortner *et al.*<sup>[13]</sup> for the treatment of seven patients with sarcoma involving the iliac and femoral vessels. In their study, 3 out of 7 patients underwent vascular reconstruction with polyester or vein grafts, resulting in less postoperative complications and edema compared to the remaining 4 patients who did not undergo vascular reconstruction. In a series by Muramatsu *et al.*<sup>[14]</sup>, 12 out of 14 patients requiring arterial reconstruction underwent femoropopliteal reconstruction using a contralateral greater saphenous vein (GSV) graft ranging from 12-30 cm, while the 2 who required femoroinguinal reconstruction received expanded polytetrafluoroethylene (ePTFE). Twelve of their 15 patients additionally required venous reconstruction of the superficial vein, deep femoral vein, and greater saphenous vein, which was also done using a GSV or ePTFE graft. Of these patients, 6 had received

**Table 1. Studies included**

Author	Year	Study describes
Abramson <i>et al.</i> <sup>[15]</sup>	1997	Free tissue transfer + radiotherapy
Cordeiro <i>et al.</i> <sup>[16]</sup>	1994	Free tissue transfer + bone reconstruction
Serletti <i>et al.</i> <sup>[7]</sup>	1998	Free tissue transfer
Heiner <i>et al.</i> <sup>[8]</sup>	1993	Free tissue transfer
Barner-Rasmussen <i>et al.</i> <sup>[9]</sup>	2009	Free tissue transfer
Leow <i>et al.</i> <sup>[10]</sup>	2005	Free tissue transfer + bone reconstruction
Momeni <i>et al.</i> <sup>[11]</sup>	2011	Free tissue transfer
Muramatsu <i>et al.</i> <sup>[14]</sup>	2011	Free tissue transfer
Ng <i>et al.</i> <sup>[15]</sup>	2008	Free tissue transfer
Zbucnea <sup>[16]</sup>	2016	Free tissue transfer
Nahabedian <i>et al.</i> <sup>[17]</sup>	1999	Free tissue transfer
Vaienti <i>et al.</i> <sup>[18]</sup>	2013	Free tissue transfer
Cadenelli <i>et al.</i> <sup>[19]</sup>	2015	Free tissue transfer
Baxter <i>et al.</i> <sup>[20]</sup>	2007	Free tissue transfer
Miyamoto <i>et al.</i> <sup>[21]</sup>	2014	Free tissue transfer
Lee <i>et al.</i> <sup>[22]</sup>	2004	Free tissue transfer + radiotherapy
Choudry <i>et al.</i> <sup>[23]</sup>	2008	Free tissue transfer
Saito <i>et al.</i> <sup>[24]</sup>	2010	Free tissue transfer + bone reconstruction
Zweifel-Schlatter <i>et al.</i> <sup>[25]</sup>	2006	Free tissue transfer
Hong <i>et al.</i> <sup>[26]</sup>	2005	Free tissue transfer
Weichman <i>et al.</i> <sup>[27]</sup>	2015	Free tissue transfer
Agostini and Agostini <sup>[28]</sup>	2009	Free tissue transfer
Cribb <i>et al.</i> <sup>[29]</sup>	2010	Free tissue transfer
Brenner and Rammelt <sup>[30]</sup>	2002	Free tissue transfer
Medina <i>et al.</i> <sup>[31]</sup>	2014	Free tissue transfer
Struckmann <i>et al.</i> <sup>[32]</sup>	2014	Free tissue transfer
Zaretski <i>et al.</i> <sup>[33]</sup>	2004	Bone reconstruction
Capanna <i>et al.</i> <sup>[34]</sup>	1993	Bone reconstruction
Beris <i>et al.</i> <sup>[35]</sup>	2011	Bone reconstruction
Yajima and Tamai <sup>[36]</sup>	1994	Bone reconstruction
Duffy <i>et al.</i> <sup>[37]</sup>	2000	Bone reconstruction
Ruch and Koman <sup>[38]</sup>	1997	Bone reconstruction
Mastorakos <i>et al.</i> <sup>[39]</sup>	2002	Bone reconstruction
Enneking <i>et al.</i> <sup>[40]</sup>	1993	Nerve reconstruction
Doi <i>et al.</i> <sup>[41]</sup>	1998	Nerve reconstruction
Doi <i>et al.</i> <sup>[42]</sup>	1999	Nerve reconstruction
Fortner <i>et al.</i> <sup>[13]</sup>	1977	Vascular reconstruction
Tsukushi <i>et al.</i> <sup>[43]</sup>	2008	Vascular reconstruction
Nishinari <i>et al.</i> <sup>[44]</sup>	2015	Vascular reconstruction
Wortmann <i>et al.</i> <sup>[45]</sup>	2017	Vascular reconstruction
Rosenthal <i>et al.</i> <sup>[46]</sup>	1993	Radiotherapy
O'Sullivan <i>et al.</i> <sup>[47]</sup>	2004	Radiotherapy
Baldini <i>et al.</i> <sup>[48]</sup>	2013	Radiotherapy
Arbeit <i>et al.</i> <sup>[49]</sup>	1987	Radiotherapy
Shiu <i>et al.</i> <sup>[50]</sup>	1984	Radiotherapy
O'Sullivan <i>et al.</i> <sup>[51]</sup>	2002	Radiotherapy
Cheng <i>et al.</i> <sup>[52]</sup>	1996	Radiotherapy
Kunisada <i>et al.</i> <sup>[53]</sup>	2002	Radiotherapy
Davis <i>et al.</i> <sup>[54]</sup>	2005	Radiotherapy
Townley <i>et al.</i> <sup>[55]</sup>	2013	Radiotherapy
Chao <i>et al.</i> <sup>[56]</sup>	2012	Radiotherapy
Hidalgo <i>et al.</i> <sup>[57]</sup>	1992	Radiotherapy
Brennan <i>et al.</i> <sup>[58]</sup>	1987	Radiotherapy
Ormsby <i>et al.</i> <sup>[59]</sup>	1989	Radiotherapy
Hidalgo and Carrasquillo <sup>[60]</sup>	1992	Radiotherapy
Spierer <i>et al.</i> <sup>[61]</sup>	2003	Radiotherapy
Sadrian <i>et al.</i> <sup>[62]</sup>	2002	Radiotherapy
Pisters <i>et al.</i> <sup>[63]</sup>	1996	Outcomes
Popov <i>et al.</i> <sup>[64]</sup>	2000	Outcomes
Penna <i>et al.</i> <sup>[65]</sup>	2011	Outcomes
Lopez <i>et al.</i> <sup>[2]</sup>	2015	Outcomes

**Table 2. Types of flaps used for lower extremity reconstruction based on region**

Author	Year	Regions described	Flaps described
Cordeiro <i>et al.</i> <sup>[6]</sup>	1994	Thigh	LD RA Fibula
		Knee and proximal leg	LD RA Scapula
		Mid and distal leg	RA LD Scapula Fibula
		Foot	Radial forearm Lateral arm RA LD
Barner-Rasmussen <i>et al.</i> <sup>[9]</sup>	2009	Foot	ALT
		Ankle	Radial forearm
		Lower Leg	Gracilis
		Knee	TFL
		Thigh	Fibula
		Inguinal	RA
		Trochanteric	
		Gluteal	
Leow <i>et al.</i> <sup>[10]</sup>	2005	Thigh	LD
		Gluteal	Fibula
		Knee	RA (free + pedicled)
		Popliteal fossa	
		Middle third of the leg	
		Ankle	
Momeni <i>et al.</i> <sup>[11]</sup>	2011	Lower leg	ALT
Muramatsu <i>et al.</i> <sup>[14]</sup>	2011	Thigh	LD Pedicled RA Pedicled medial gastrocnemius TFL ALT
Ng <i>et al.</i> <sup>[15]</sup>	2008	Lateral Posterior Thigh	ALT
Zbucnea <i>et al.</i> <sup>[16]</sup>	2016	Knee	Lateral genicular artery flap
Cadenelli <i>et al.</i> <sup>[19]</sup>	2015	Knee	Advancement propeller perforator ALT
Baxter <i>et al.</i> <sup>[20]</sup>	2007	Knee	Gastrocnemius
Miyamoto <i>et al.</i> <sup>[21]</sup>	2014	Knee	Deep inferior epigastric artery perforator flap
Lee <i>et al.</i> <sup>[22]</sup>	2004	Thigh	RA
		Knee	Gastrocnemius
		Leg	Gastrocnemius
		Foot	RA
Choudry <i>et al.</i> <sup>[23]</sup>	2008	Lower leg	Soleus
Saito <i>et al.</i> <sup>[24]</sup>	2009	Ankle	LD Composite LD + scapular bone Scapular-parascapular flap Free scapular flap ALT
Zweifel-Schlatter <i>et al.</i> <sup>[25]</sup>	2006	Tibia	Lateral arm fasciocutaneous flap Scapular fasciocutaneous flap Scapular/parascapular fasciocutaneous ALT fasciocutaneous
Hong <i>et al.</i> <sup>[26]</sup>	2005	Lower leg	ALT
Weichman <i>et al.</i> <sup>[27]</sup>	2015	Foot	Adipofascial ALT
Cribb <i>et al.</i> <sup>[29]</sup>	2010	Ankle	Radial forearm
		Foot	LD Gracilis Fasciocutaneous radial forearm
Brenner <i>et al.</i> <sup>[30]</sup>	2002	Foot	Modified radial forearm fascial flap
Medina <i>et al.</i> <sup>[31]</sup>	2014	Foot	Gracilis
Struckmann <i>et al.</i> <sup>[32]</sup>	2014	Foot	Sural Medial plantar artery ALT Parascapular LD Lateral arm

Zaretski <i>et al.</i> <sup>[33]</sup>	2004	Femur Tibia	Free vascularized fibula flap 4 allograft Free double-barreled fibula
Capanna <i>et al.</i> <sup>[34]</sup>	1993	Femur Tibia	Free vascularized fibula flap + allograft
Beris <i>et al.</i> <sup>[35]</sup>	2011	Femur Tibia	Free vascularized fibula 4 allograft Free double-barreled fibula
Yajima and Tamai <sup>[36]</sup>	1994	Femur Tibia Ankle	Twin-barrelled vascularized fibular graft
Duffy <i>et al.</i> <sup>[37]</sup>	2000	Femur Tibia	Free vascularized fibula
Rush and Koman <sup>[38]</sup>	1997	Tibia	Fibula-flexor hallucis longus osteomuscular flap
Mastorakos <i>et al.</i> <sup>[39]</sup>	2002	Tibia	LD RA Gastrocnemius-Soleus Gastrocnemius-RA Gracilis + motor nerve
Doi <i>et al.</i> <sup>[41]</sup>	1998	Lower leg	LD + motor nerve
Doi <i>et al.</i> <sup>[42]</sup>	1999	Thigh Lower leg	Gracilis + motor nerve

LD: latissimus dorsi; RA: rectus abdominis; ALT: anterior lateral thigh

free latissimus dorsi flaps, while the remaining patients received pedicled flaps. In the patients who were reconstructed using free flaps, the only complications were leg edema and mild lymphedema, which the authors attributed to ischemic reperfusion or venous/lymphatic insufficiency. The use of a myocutaneous flap in combination with an autologous vein graft also results in decreased postoperative infection rates, treatment of lymphedema and fistula, and increased graft patency rates<sup>[14]</sup>.

Aesthetically, reconstruction of the thigh requires a large flap with muscle bulk that can eliminate dead space while providing adequate contour<sup>[10]</sup>. The use of a free rectus abdominis flap has been reported to be particularly successful for this purpose<sup>[6,10]</sup>. The latissimus dorsi flap, which is thin, large with a long vascular pedicle, ± neurotization has also been used for large defects of the thigh<sup>[6,10]</sup>. The use of the anterior lateral thigh (ALT) flap for large thigh defects, particularly of the posterior thigh, has also been reported<sup>[15]</sup>.

## Knee

Obtaining adequate soft tissue coverage of the knee remains challenging for many plastic surgeons, not only because of the biomechanics of the knee, but also due to exposure of vital structures as well as the joint space<sup>[16-18]</sup>. Rotational muscle flaps or myocutaneous flaps such as gastrocnemius or reverse anterior lateral thigh flaps have been the mainstay for the reconstruction of tumors in this location. These flaps usually have low donor - site morbidity. However more complex defects may require the use of free tissue transfer. In these cases the deep-seated recipient popliteal vessels of the knee can make microvascular anastomosis difficult<sup>[19]</sup>, an autologous vein graft loop can be used and the distal SFA and SFV can be used as recipient vessels if there is an extended field of neoadjuvant radiation<sup>[14]</sup>.

Multiple donor sites have been successful used in free flap coverage of knee defects. These include latissimus dorsi, rectus abdominis, and scapula flaps<sup>[6]</sup>. When there is a large contour defect in the popliteal fossa that does not require much filling of the muscular space, Leow *et al.*<sup>[10]</sup> have also described the use of a free mini-transverse rectus abdominis (TRAM) myocutaneous flap.

In many cases where complex reconstruction of the knee region is needed, salvage of the popliteal artery, which can often be involved in the disease process, becomes critical. This has traditionally been accomplished using a combination of a local gastrocnemius flap with an interpositional vein graft<sup>[20]</sup>. However, Miyamoto *et al.*<sup>[21]</sup> described two cases of successful one-stage reconstruction of complex knee defects including the popliteal artery using a free flow-through ALT flap. Although the use of a deep

epigastric artery perforator flap has also been used for these situations, this flap is often too bulky and provides a less aesthetic option.

### **Below knee**

In the distal leg, dead-space obliteration is generally not a concern and the use of bulky musculocutaneous flaps, such as TRAM flaps, can result in significant contour deformities. As a solution, several authors describe the ALT flap as a preferred method for distal lower extremity defects following sarcoma resection, given the easy ability to reshape the flap<sup>[11,22]</sup>. In a series by Barner-Rasmussen *et al.*<sup>[9]</sup>, 73 patients with soft tissue tumors located predominantly in the distal leg received 75 free-flap procedures with a 95% flap survival rate and a 97% limb salvage rate. A majority of the flaps used were latissimus dorsi flaps (72%) and ALT flaps (12%). The rectus abdominis and latissimus dorsi flaps as well as free scapula flaps have been described for this region by Cordeiro *et al.*<sup>[6]</sup> with an overall success rate close to 90%. Other flaps commonly used in the lower leg are the radial forearm flap, gracilis flap, tensor fascia lata flap, and fibula flap<sup>[9]</sup>.

### **Ankle/foot**

Several factors must be taken into account when reconstructing oncologic defects of the ankle and foot. In addition to considering the need for adjuvant radiotherapy, the soft tissue of this area is very thin and must provide a smooth surface for the tendons underneath. Traditional flaps used to cover defects of the distal third of the foot have included the rectus abdominis, latissimus dorsi, gracilis, and rectus femoris flaps<sup>[23]</sup>. Free scapular and ALT flaps have also been used with adequate results<sup>[24]</sup>. Muscle flaps provide excellent coverage, and while they are initially quite bulky for this region, they flatten significantly with time as they atrophy. Thus fasciocutaneous flaps have been described as a successful alternative with superior contouring<sup>[25,26]</sup>.

Although the versatile ALT flap has also been used in the past, the amount of adipose deposit in this flap can be addressed by primary thinning via a supra-fascial dissection or secondary procedure using mechanical lipectomy. A third approach was described by Weichman *et al.*<sup>[27]</sup> where they reported a series using an adipofascial ALT flap with a split thickness skin graft to cover dorsal foot defects on three patients after sarcoma resection. In addition to its superior contour, the fascial plexus of the adipofascial flap is stronger than that of the thinned ALT, and the extra fascia can be used to reconstruct local tendons<sup>[28]</sup>.

The fasciocutaneous radial forearm flap has also been reported to have good results in reconstruction of the foot and ankle, providing normal contour and durable stability<sup>[29,30]</sup>. Unfortunately however, it can result in significant donor-site morbidity and occasional bulkiness. Thus, Medina *et al.*<sup>[31]</sup> proposed a using a radial forearm fascial free flap for dorsal foot defects and reported its use in a patient with wound dehiscence following sarcoma resection and radiation therapy, with no resulting complications or contour defects. Another flap that can provide excellent results in the ankle if the size of the defect permits is the temporalis fascia free flap<sup>[6]</sup>.

In contrast to the dorsum of the foot, reconstruction of the weight-bearing sole of the foot requires strong soft tissue that is resistant to pressure, weight, and stress. Struckmann *et al.*<sup>[32]</sup> covered heel defects in 12 patients with a variety of free flaps including latissimus dorsi, gracilis, lateral arm, ALT, and parascapular free flaps. They found that myofasciocutaneous flaps had the best functional results, followed by adipocutaneous and muscle flaps with split-thickness skin grafts, while fasciocutaneous flaps had the lowest outcomes. However there was no significant difference between specific flap type.

## **ADDITIONAL CONSIDERATIONS: COMPROMISED STRUCTURES**

### **Bone involvement**

For bone reconstruction, the flap is chosen based on specific patient needs including location of the lesion, level of activity of the individual, need for adjuvant therapy, and growth potential. The most commonly

harvested bone flap is the free fibula flap, which can be used in three major reconstructive ways: traditional vascularized fibula flap, vascularized fibula flap combined with an allograft, and vascularized double-barreled fibula<sup>[33]</sup>.

The traditional vascularized fibula flap as a bony replacement is indicated in areas that endure lighter loads or when reinforcement of weak areas is needed. The free fibula flap with an allograft, which was first described by Capanna *et al.*<sup>[34]</sup> in 1993, involves the insertion of the vascularized fibular graft into the intramedullary canal of an allograft, which is then used to fill the bony defect. This flap provides strength and stability early on, making it ideal for anatomical locations where high forces are applied. For areas that must withstand intermediate stress loads, the free double-barreled fibula flap is typically chosen. This flap allows for twice the volume of the fibula to be substituted with the same number of microvascular anastomoses<sup>[33]</sup>. It is generally indicated for femur and proximal tibia reconstruction as well as reconstruction of the tibia of younger patients who are physically active<sup>[35,36]</sup>. Additionally for radiation-induced long-bone fractures, the vascularized fibula can also be osteotomized longitudinally and used as an onlay graft<sup>[37]</sup>. The fibula can also be harvested as a combined osteocutaneous flap for composite defects of the lower extremity<sup>[6,10]</sup>.

An additional osteomuscular flap that has been reported to have good outcomes for coverage after distal tibial osteosarcoma resection is the fibula-flexor hallucis longus osteomuscular flap<sup>[38]</sup>. Saito *et al.*<sup>[24]</sup> also describe adequate aesthetic and functional outcomes with the use of a free composite graft of latissimus dorsi and scapular bone as well as a free osteocutaneous scapular-parascapular flap. Finally, in cases of allograft bone reconstruction of the lower extremities, soft tissue flap coverage using latissimus dorsi and rectus abdominis flaps has been shown to maximize limb salvage<sup>[39]</sup>.

### Nerve reconstruction

Radical sarcoma resection often leads not only to extensive soft tissue defects, but also suboptimal degrees of functionality secondary to damage to surrounding nerves. Functional outcomes following conventional limb-sparing procedures reported in the literature have been close to 75%<sup>[40]</sup>.

Reinnervated muscle transfer, which has been extremely valuable in a number of reconstructive procedures, may also become necessary in patients with sarcoma resection. Doi *et al.*<sup>[41]</sup> describe a patient with synovial sarcoma of the anterior compartment of the lower leg who received a gracilis flap to cover the defect. The motor nerve of the gracilis was sutured to the motor branch of the tibialis anterior muscle from the peroneal nerve, resulting in gradual increase in power and range of toe and ankle extension postoperatively. In a second series by Doi *et al.*<sup>[42]</sup>, reinnervated latissimus dorsi transfer was used to improve or supplement knee flexion or extension by connecting to the sciatic or femoral nerve at the time of reconstruction.

### Vascular reconstruction

While arterial reconstruction is always indicated after limb-sparing surgery to prevent ischemia, the need for venous reconstruction is not as well-established, as venous ligation compromise the limb. Studies showing high occlusion rates have led to debates regarding the benefits of venous revascularization<sup>[43]</sup>. Additionally, there have been reports of symptoms of severe venous insufficiency such as edema, claudication, and hyperpigmentation after reconstruction<sup>[44]</sup>.

A large series of lower limb soft tissue sarcoma resection with arterial and venous reconstruction was conducted by Nishinari *et al.*<sup>[44]</sup> in 25 patients. Graft occlusion rates were found to be significantly greater in patients who received synthetic grafts *vs.* those who received saphenous vein grafts ( $P = 0.02$ ), which is consistent with the results of other studies<sup>[14]</sup>. However occlusion rates were not different between arterial and venous reconstruction and there was no association between prior radiotherapy and graft occlusion<sup>[44]</sup>. Wortman *et al.*<sup>[45]</sup> reported one-year patency rates of venous bypass grafts to be 65%, with high numbers of



overall bypass-related complications including thrombosis and emboli as well as infections. Common wound complications that occur are wound healing difficulties, infections, and lymphatic fistulas.

## NEOADJUVANT AND ADJUVANT THERAPY

Surgery with wide margins alone can be implemented to treat sarcoma of the extremities that is subcutaneous or intramuscular, small in size, or low in grade. However, if the resected margin is close, or if there is extramuscular involvement, surgery must be combined with adjuvant radiotherapy. For those that are high-grade or large in size, neoadjuvant chemotherapy must also be considered<sup>[46]</sup>. The need for additional therapy is often a determining factor in flap selection, as wound-healing difficulties can delay the onset of adjuvant therapy and negatively affect long-term survival.

Radiotherapy may be administered either pre- or postoperatively with similar local control and overall survival rates<sup>[47]</sup>. The concern with radiation therapy is the complications it causes with wound healing. Reported complications have ranged from 33%-44% in the past, with severe morbidity in 22%-27% of patients<sup>[48-50]</sup>. Abramson *et al.*<sup>[5]</sup> however only reported a 12.5% wound complication rate, including a patient who developed radiation necrosis and required a second free tissue transfer months after his initial treatment.

While preoperative radiotherapy results in higher rates of wound complications<sup>[51-53]</sup>, patients treated with postoperative radiotherapy experience more long-term fibrosis, edema and joint stiffness<sup>[54]</sup>. The National Cancer Institute of Canada (NCI Canada) conducted a randomized control trial comparing wound complications in patients who received preoperative vs. those postoperative radiotherapy and found that 35% of those in the preoperative group had major wound complications compared to 17% of those in the postoperative group<sup>[51]</sup>. O'Sullivan *et al.*<sup>[51]</sup> found higher rates of wound complications and reoperations in patients who received preoperative radiation. However a larger percentage of patients with wound complications in the postoperative radiation group required other invasive procedures.

Townley *et al.*<sup>[55]</sup> compared patients with preoperative irradiation to a control group who received no radiation and found similar microvascular complication rates such as those requiring intra-operative revision or flap reexploration or loss. Though wound healing complications were more common in the group who received radiation, the ultimate outcomes were similar between both groups. Some factors associated with wound complications in sarcoma patients who receive preoperative radiation are tumor size > 10 cm, tumor proximity to skin surface < 3 mm, and current smoking status<sup>[48]</sup>.

Chao and associates compared complication rates between patients receiving neoadjuvant and adjuvant irradiation and found no significant difference in perioperative complication rates or rates of salvaged pedicle thrombosis between the two groups. However, the rate of total free flap loss was lower in patients receiving neoadjuvant radiation, suggesting that the introduction of new, well-vascularized tissue counteracts the effects of the radiation. The authors also attributed this finding to the fact that higher doses and larger fields of irradiation are involved with adjuvant therapy, and with neoadjuvant therapy, irradiated tissue may be excised during tumor resection. Additionally, they found that late recipient-site complications (occurring > 30 days after surgery) occurred more frequently in patients who received adjuvant radiation (26.1% vs. 6.8%,  $P = 0.0006$ ), although the reoperation rate following these complications was similar between the groups<sup>[56]</sup>. Because wound complications are generally treatable without resulting in permanent damage, preoperative radiotherapy is preferred by many practitioners<sup>[48]</sup>.

Brachytherapy, another form of adjuvant therapy, is a method of administering radioisotopes directly into a surgical wound to treat residual tumor<sup>[57]</sup>. Addition of brachytherapy to surgical excision has been shown to reduce tumor recurrence rates from 14% to 4%<sup>[58]</sup>. Brachytherapy was initially administered during

the immediate postoperative period and resulted in high rates of wound complications<sup>[49]</sup>. Waiting until at least the 5th postoperative day is associated with significantly lower rates<sup>[59]</sup>. In a study by Lee *et al.*<sup>[22]</sup>, brachytherapy was initiated about 7 days after free tissue transfer and resulted in a 29% complication rate, including partial-thickness skin necrosis, venous thrombosis necessitating flap exploration, kinking of the brachytherapy catheters, and partial flap skin loss. Hidalgo *et al.*<sup>[60]</sup> described 3 patients who were treated with adjuvant brachytherapy 7-10 days postoperatively with no wound-healing complications. Although considered typically safe, the number of wound complications requiring reoperation has been shown to be higher with brachytherapy than with external beam radiation therapy<sup>[61]</sup>. Preoperative intraarterial chemotherapy is another option and has been shown to have no effect on free flap results<sup>[62]</sup>.

## OUTCOMES AND RECURRENCE

Because of the prolonged surgical time and extensive periods of bed rest combined with immunosuppressive therapy following sarcoma resection, surgical treatment of these tumors is generally associated with high numbers of postoperative complications. Lopez *et al.*<sup>[2]</sup> found that patients who received combined pedicled + free flaps after sarcoma resection had significantly higher wound complications rates compared to patients who received just one, although systemic complications were distributed equally between all groups.

Recurrence rates are generally high following flap reconstruction after resection of advanced, high-grade sarcomas<sup>[63]</sup>. Popov *et al.*<sup>[64]</sup> found a statistically significant correlation between recurrence and extracompartmental tumor location ( $P < 0.01$ ) and large tumor size ( $> 4$  cm) ( $P < 0.01$ ). Postoperative wound complications can also lead to amputation following tumor resection and flap reconstruction.

## CONCLUSION

As wide local excision has become the most commonly accepted approach to the surgical treatment of sarcomas, reconstructive surgical techniques become crucial to the success of this line of therapy. Although pedicled flaps have been traditionally preferred for oncologic resections, their use is sometimes precluded by the use of neoadjuvant radiation as well as the size of the defect left after the resection. The need to re-establish function also makes the use of a pedicle/local flap less optimal. Several recent studies have reported successful functional and aesthetic results using free tissue transfer as the main modality for reconstruction after sarcoma resection of the limb<sup>[6,7,56]</sup>. Free tissue transfer allows for the application of healthy vascularized tissue to the defect while also providing freedom of flap positioning as well as avoidance of stretching or kinking of the vasculature<sup>[2]</sup>. Studies of sarcoma resection and free tissue reconstruction have reported high success rates, with complication rates ranging between 2%-22%<sup>[7,64,65]</sup> and limb salvage rates close to 100%<sup>[6,57,64,65]</sup>. Flap choice is dependent on tumor and defect size, tissue type and function, as well as donor site availability, thus resulting in numerous different treatment options. Given the low incidence and prevalence of lower extremity sarcomas as well as the heterogeneity of the sarcomas and their respective neo-adjuvant treatments, there are currently no clear treatment guidelines or specific algorithms for the reconstruction of soft tissue defects following oncologic resection. The lack of significant case volume makes it difficult for any single institution to conduct a study comparing the success rates of various flaps, and although a systematic review would be helpful, the innate nature of the pathology also leads to a paucity of literature consisting largely of studies describing small numbers of isolated cases. This descriptive review however attempts to provide an overview of the various reconstructive options that are available, as well as the considerations that must be taken into account when treating patients with soft tissue defects of the lower limb following sarcoma resection.

## DECLARATIONS

### Authors' contributions

Performed the literature search and reviewed the articles: Azadgoli B, Perrault DP

Drafted the manuscript: Azadgoli B

Revised the manuscript: Carre AL, Wong AK

Reviewed the manuscript and approved its final version: all authors

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There are no conflicts of interest.

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Original Article

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# The labio-mandibular flap for upper lip and peri-commissural defects

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## Abstract

**Aim:** Peri-commissural defect reconstruction using the Abbe or Estlander flaps tend to pilfer tissue from the lower lip, contributing to microstomia, with its attendant problems. In this study, we aim to design a flap for more superficial defects, in which the underlying orbicularis oris muscle can be preserved when resecting peri-commissural skin malignancies whilst also ensuring completeness of excision.

**Methods:** In a retrospective case review of 7 cases at our institution over a 12-month period (2016-2017), we conceptually designed a perforator-plus fascio-cutaneous flap from within the labio-mandibular fold with a 6-month follow-up in terms of oncological clearance and aesthetic outcome. The cohort was composed of patients with skin cancers e.g. basal and squamous cell carcinomas, presenting to a tertiary care facial plastic surgery centre. The technique involved raising a flap from within the peri-oral area, with a scar disguised along the labio-mandibular and naso-labial folds which allows for both an aesthetic reconstruction and the preservation of the oral sphincter mechanism, by avoiding microstomia. The outcomes measured were (1) to ascertain whether this procedure is oncologically safe, (2) there were instances of microstomia and (3) aesthetic appearance.

**Results:** All oncological lesions were completely excised in all cases and at up to six months' follow-up, there were no instances of recurrence. Functionally, oral sphincter function was preserved in all instances as was aesthetic appearance.

**Conclusion:** The labio-mandibular flap is an oncologically safe procedure for skin cancers whilst preserving oral sphincter function and maintaining aesthetics. It is hence, a superior alternative to Abbe and Estlander flaps, for more superficial defects, not requiring mucosal excision.



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**Keywords:** Peri-commisural reconstruction, Abbe flap, Estlander flap, labio-mandibular flap

## INTRODUCTION

Upper lip reconstruction is a surgical challenge due to the high level of lip anatomy detail. This has led to the development of a “like for like” reconstruction using the “Abbe” or “Estlander” flap for upper lip and commissural defects respectively. The latter flap has the disadvantage of causing microstomia, while the Abbe flap has the additional hassle of being a two-stage lip-switch technique. In the vast majority of these cases, the primary indication is post-oncological reconstruction e.g. following skin cancer excisions. This brings to bear the next question, i.e. do these tumours necessitate full-thickness lip excisions, as they rarely involve oral mucosa.

An alternative reconstructive option here would be the use of perforator flaps for partial-thickness defects. One option to consider here would be the superior labial artery perforator flap for upper lip defects<sup>[1]</sup>. However, as with islanded flaps, they tend to develop lymphoedema and patients are often left with an unaesthetic appearance. Leaving a small skin bridge should reduce this risk but this cannot be done in a conventional manner as the length:width ratio philosophy will not allow for it. However, with the application of the perforator-plus concept<sup>[2]</sup>, such a combination is possible.

In this article, we describe the use of flaps based on a combination of traditional aesthetic sub-units; the labio-mandibular fold (LMF) and the naso-labial fold but tempered with the perforator-plus concept for an ideal blend of “beauty and blood supply”.

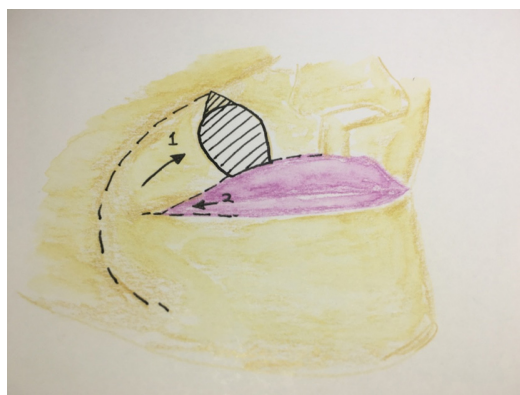
## METHODS

In a retrospective case review over 12 months at our institution (2016-2017), we performed seven cases of upper lip reconstruction ( $n = 7$ ), all as part of post-oncological reconstruction. These defects were reconstructed using a rotation-advancement flap in the supra-muscular plane, raised from within the skin of the LMF with sparing of the vermillion border of the lip. Just lateral to the oral commissure, a musculo-cutaneous perforator, arising from the modiolus is consistently found and preserved. Once this modiolar perforator is identified, the entire flap is advanced into the defect to close the primary defect first. As the flap then overlaps the oral commissure, a Y-V advancement of the oral commissure is performed, just proximal to the modiolar perforator, to translate the angle of the mouth laterally and re-establish the aesthetics of the oral commissure. This corrects microstomia and re-establishes lip aesthetics as graphically illustrated in [Figure 1](#).

### Case illustrations

An 80-year old lady presented with a 15 mm × 10 mm superficial basal cell carcinoma of the right upper lip [[Figure 2](#)], which was excised with part of the orbicularis oris and preservation of the oral mucosa. This resulted in a 23 mm × 18 mm defect over the upper lip, which was reconstructed with a labio-mandibular flap. As shown in [Figure 3](#), the outer border of the flap is along the LMF whilst the inner margin is at the vermillion border of the lip. The “length:width” ratio of the flap is approximately 4:1 and once inset, sets in seamlessly along the aesthetic lines of the lip and the LMF. Once healed, the scars are hardly discernible as they sit along the wrinkle lines of the upper lip and the LMF, as shown in [Figure 4](#).

The usefulness of the labio-mandibular flap is illustrated once more in another case wherein a large skin tumour, as is shown in [Figure 5](#), involved 40% of the upper lip with infiltration of the orbicularis oris beneath the tumour. Conventionally, this would have required a wedge excision and reconstruction with an Abbe flap, in two stages. Following excision of the lesion with a smaller section of the orbicularis oris, a labio-mandibular flap was raised and advanced into the defect [[Figure 6](#)]. Postoperative images [[Figure 7](#)] show



**Figure 1.** A graphical illustration of the labio-mandibular flap raised from the peri-oral and lower lip areas, along the LMF and vermilion border, illustrated by "1". Note also the Y-V advancement of the oral commissure into the flap itself (illustrated as "2"). The presence of the orbicularis oris musculocutaneous perforator within the distal flap ensures its continued perfusion while the narrow cutaneous bridge at the oral commissure suffices for venous and lymphatic return



**Figure 2.** A large superficial basal cell carcinoma over the upper lip/commissural area

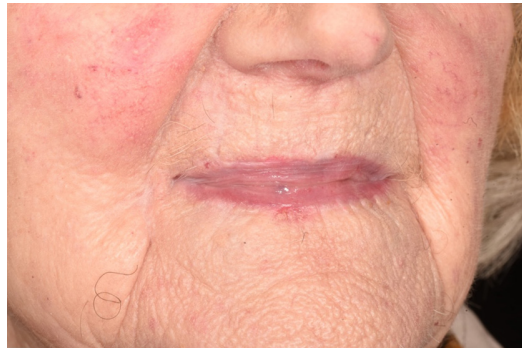


**Figure 3.** Final post-operative results of the labio-mandibular flap on the patient

the excellent lip symmetry at rest with a completely normal functioning orbicularis oris. Note the normal dimensions of the oral aperture, the absence of microstomia as well as the seamless healing.

## RESULTS

There were 7 patients' in our cohort with 6 females and 1 male patient. All patients were over the age of 60 years. The mean defect size was 23 mm × 22 mm, following oncological resections of skin cancers. On reconstructing with the LMF flap, all flaps survived completely, with healing achieved within a week at the



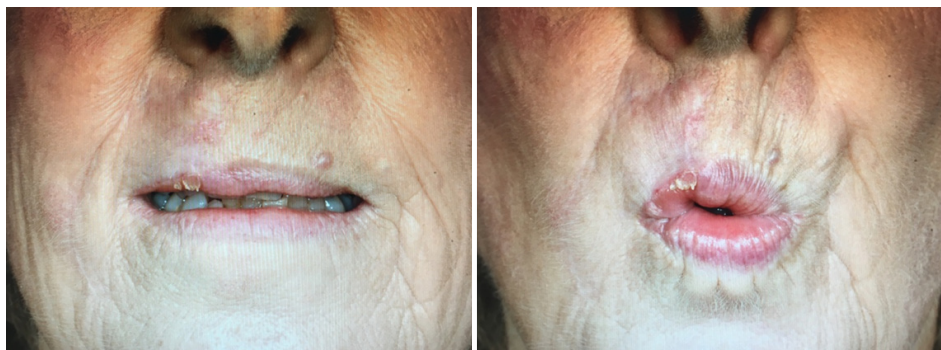
**Figure 4.** An image of the same patient, showing a seamless aesthetic appearance, at 3 months' postoperation



**Figure 5.** Preoperative image of a large skin cancer involving 40% of the width of the upper lip and extending past the vermillion border, onto the lip itself



**Figure 6.** Intra-operative image of labio-mandibular flap being advanced into the defect



**Figure 7.** Images of the labio-mandibular flap at 6-months' postoperation showing excellent lip symmetry and orbicularis oris function. Note the seamless functional and aesthetic outcome

time of suture removal with no acute or sub-acute complications. Longer-term, there were no instances of microstomia while oral sphincter function was maintained in all cases. Lip symmetry was perfect in all but one case where there was slight in-curling of the lip, requiring minor secondary revision. In spite of this, all patients were satisfied with the seamless reconstruction following tumour removal. As regards completeness of oncological resection, 100% of the tumours were completely excised with follow-up at 6 months showing no signs of local recurrence.

## DISCUSSION

Lip-based flap reconstructions have long been the primary like for like choice for lip defects, post-excision of skin cancers but given their associated drawbacks viz. microstomia and the need for a two-stage procedure, alternatives have been looked at. These include those based on the classical principles of local flaps e.g. the double rhomboid flaps<sup>[3]</sup> and variants of the Webster-Barnard flap<sup>[4]</sup>. The former option is designed for commissural defects while choice of the latter would still subject the patient to difficult mouth opening.

The advent of perforator flap know-how has provided a plethora of potential perforator flaps<sup>[5]</sup>. One such example is the modiolus perforator flap described by Gunnarsson and Thomsen<sup>[6]</sup> wherein they describe the use of a musculocutaneous perforator in a window of soft tissue bounded superiorly by the zygomaticus major, inferiorly by the risorius, medially by the oral commissure and laterally, by the facial artery. This consistent perforating vessel has been described by other studies<sup>[7]</sup> and is the source perforator used for the perforator-plus labio-mandibular flap. However, one of the issues with the use of propeller or islanded flaps is the later onset of lymphoedema; an unaesthetic feature.

In order to overcome this, we have combined the best elements of the perforator concept and placed them within the confines of traditional aesthetic sub-unit, which in this case, refers to the labio-mandibular area. Placing the flap margins within these anatomical boundaries allows for the appearance of a scarless technique. In addition, the preservation of a cutaneous bridge preserves lymphatic channels and minimises lymphoedema. However, as the flap is rotated and advanced into the defect, the oral commissure is blunted. A “Y-V” advancement of the oral commissure is then performed and advanced into the labio-mandibular flap at its middle third. Partially dividing the flap here does not reduce its distal perfusion as the modiolus perforator is preserved just distal to the Y-V advancement. This allows for an aesthetic reconstruction as illustrated earlier in [Figure 1](#).

Excising these tumours with a cuff of orbicularis oris muscle allows for completeness of cancer resection while the remaining orbicularis oris muscle is sufficient to achieve an oral sphincter seal for functional purposes. This also helps maintain the dimensions of the oral aperture, negating the microstomia effect. All of these small steps contribute to an excellent functional and aesthetic outcome.

In summary, for partial-thickness defects of upper lip and peri-commissural areas, following oncological resection, where the underlying oral mucosa is uninvolved by tumour, the perforator-plus labio-mandibular flap offers a safe and single-stage aesthetic reconstructive option with preservation of the oral sphincter and perfect lip symmetry. It must be noted that this technique is specifically suited for more superficial defects, not involving sacrifice of the lip mucosa and in particular, those in the geriatric population group.

## DECLARATIONS

### Authors' contributions

Manuscript writing: Kannan RY

Help in manuscript writing and editing: Nduka C

### Data source and availability

Case records (Queen Victoria Hospital, East Grinstead, UK).

### Financial support and sponsorship

None.

### Conflicts of interest

There are no conflicts of interest.

### Patient consent

Obtained.

### Ethics approval

Not applicable, as this technique is based on an extension of the Labbe procedure modification (Hallam *et al.*, 2012), developed at QVH, East Grinstead.

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Technical Note

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# Safe and easy hair transplantation utilizing KD spreader

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## Abstract

**Aim:** An atraumatic insertion of graft is key to successful outcomes in this procedure but there is a definite learning curve in available techniques. Many physicians do not continue hair restoration practice because of the repeated initial failures. The goal of any technique or instrument in follicular unit extraction (FUE) is to extract an individual follicular unit without transaction and implanting it in recipient area without producing physical trauma to the follicular unit. This article describes a novel technique in which an innovative instrument, the KD spreader, that addresses all the problems faced by novice physicians during FUE hair transplantation. More importantly unique design of the instrument also solves the problem of fatigue of the operator's hands while performing the hair transplantation procedure.

**Methods:** In this technique, the KD spreader, comprised of a shaft and a hook connected to the shaft are configured to allow the user to work efficiently. Two finger grip of the device provides efficient gripping for fatigue free operation. While performing FUE, the KD spreader provides sufficient traction at the time of scoring. During implantation of the grafts in premade coronal slits, this device provides adequate dilation and maximum visualization of the slit. Attachment of the graft holding plate reduces the chances of dehydration of the graft.

**Results:** In this study, we have observed use of KD spreader definitely showed advantages over the conventional technique forceps. The KD spreader provides efficient gripping, maximum visualization of slit and better stretching force for the dilatation of the slit to adjust even bigger size follicular unit grafts.

**Conclusion:** The KD spreader may improve ability of the beginners to perform FUE extraction and implantation smoothly.

**Keywords:** KD spreader, follicular unit extraction hair transplant, coronal slits graft implantation, graft extraction, hydration of graft



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## INTRODUCTION

Follicular unit extraction (FUE) is a minimally invasive hair transplantation procedure, where each hair follicular unit is individually harvested from the donor area on the scalp or from other parts of the body and then implanted directly into the recipient area. FUE hair transplant surgery has gained popularity in the last few years among patients due to its simplicity and ability to produce less visible scarring, allowing the patients to wear their hair short. The technique of the FUE procedure not only attracts patients who have fear of knives, stitches and linear scarring over the donor site but also physicians who wish to start hair restoration procedures at their clinics. With the evolution of the FUE method, this hair restoration surgery is gaining popularity all over the world.

After working in the field of hair transplantation for more than a decade, the authors have realized there is a definite learning curve in this field of medicine. Many physicians do not continue hair restoration practice because of the repeated initial failures.

Repeated improvement in technique and instrumentation may improve ability of beginners to perform FUE extraction and implantation smoothly. The goal of any technique or instrument in FUE is to extract an individual follicular unit without transection and implant it in the recipient site without producing physical trauma to the follicular unit. As hair transplant is a time-consuming procedure, your technique and instruments should also give you opportunity to work without fatigue and exhaustion. To fulfill these goals, this author created an instrument which can address the existing limitations of the FUE hair restoration procedure.

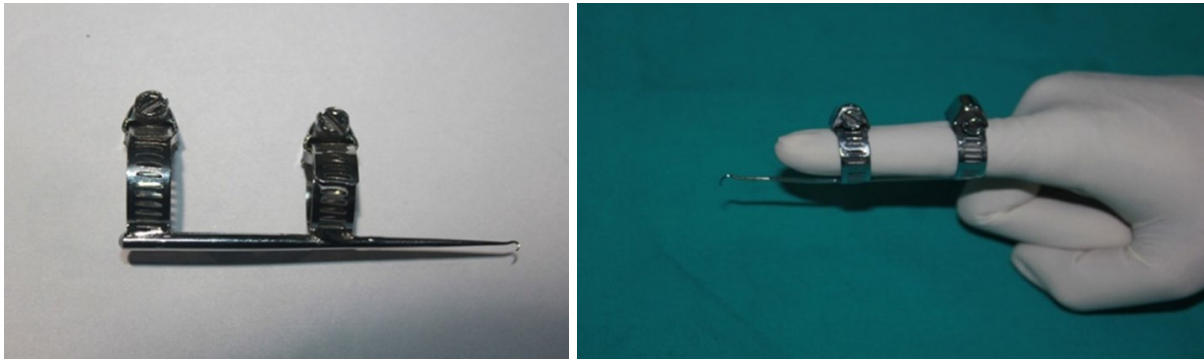
## EXISTING INSTRUMENTS AND ITS LIMITATIONS

- Manual stretching does not provide sufficient traction for scoring.
- Manual traction can cause operator fatigue especially during procedures which can last for several hours.
- Tough scalp requires extra stretching of tissue that cannot be achieved by available methods.
- Conventional skin hooks do not provide efficient gripping for desired stretching force.
- FUE over lower occipital region require maximum scalp stretch near the FUE site that is not possible by current available methods.
- While performing body hair transplant, skin is extremely pliable and tensioners or spreaders are needed to stabilized flexibility of the tissue.

Looking at these hurdles, the authors desired to develop a user - friendly instrument that can provide donor tension or traction without producing operator fatigue, specifically their hands.

I have developed a unique instrument - the KD' spreader - in response to this problem [Figure 1]<sup>[1]</sup>. This device is comprised of a shaft and a hook connected to the shaft that are configured to allow the user to work efficiently. The device uses two finger grips which are positioned on the surface of the shaft for providing efficient grip so that the desired stretching force may be applied without much fatigue to the operator muscles. This device is extremely useful while FUE is performed on tough scalp where manual stretching does not provide sufficient traction for scoring.

While performing FUE extraction, we start with a circular incision with average rotational force in which our power machine is set. We adjust rotational force as per our requirement. When scalp is tough we have to increase rotational force while when the scalp is soft, we have to decrease rotational force. When we increase rotational force to initiate circular incision on tight scalp, an opposing friction or resistance force is generated. If the applied force exceeds the friction force, chances of transection of grafts greatly increases. KD spreader provides desired stretching exactly at the site of FUE [Figure 2]<sup>[2]</sup>.



**Figure 1.** The KD spreader, a modified skin spreader



**Figure 2.** Stretching with tensioner above the extraction site

During graft harvesting, the KD spreader provides the following advantages:

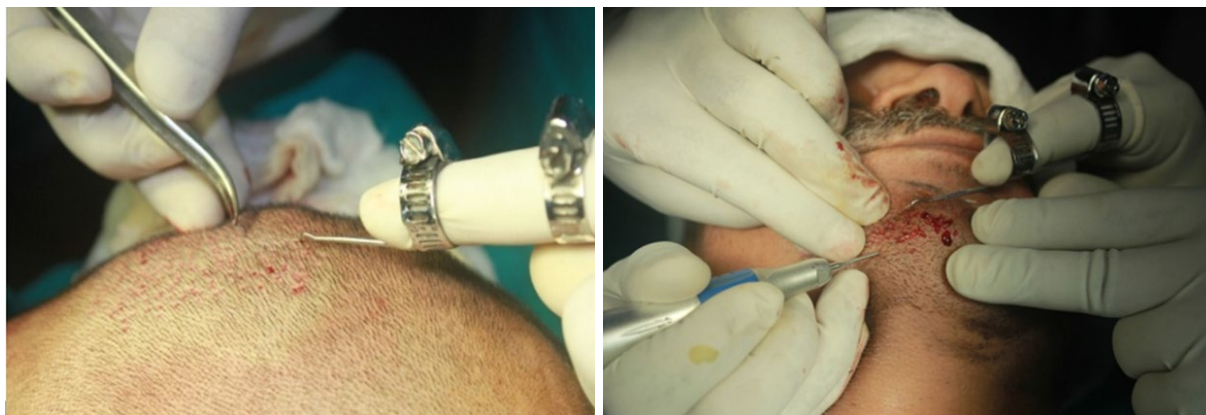
- It fits the index finger of the non-dominant hand of the user.
- Terminal portion of the device gently lifts and stretches the donor area just above the extraction site.
- Desired stretch can be achieved by pulling force at the time of scoring.
- While wearing the device, the assistant's hand is free to hold other objects without keeping the device on the surface, thus reducing the procedure time.

### **HASSLE FREE SMOOTH EXTRACTION**

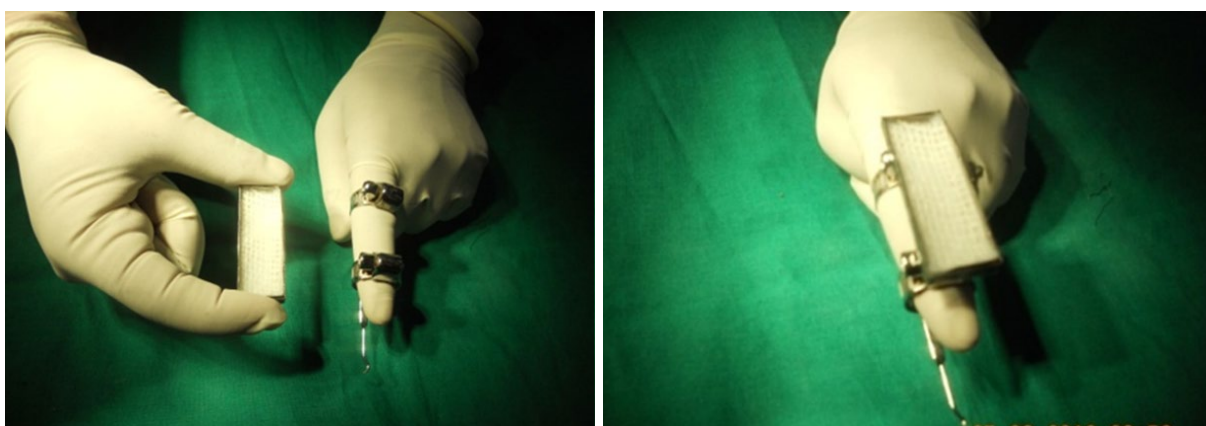
Lateral or upward traction is used for removal of the grafts after it has been punched.

This often is the most difficult part, particularly in a tight scalp or if the unit has hairs with divergent angles of emergence. Upward and lateral manual traction or pressure just near the FUE site can smoothen extraction, and the graft may be pulled out easily with forceps in one hand. The author questions when you have to extract 1500 or 2000 grafts with this manual technique, if there increases the likelihood of fatigue to the operator's hand muscles.

Secondly, desired traction cannot be achieved by using manual stretching force. While I was exploring my technique of extraction by using KD spreader, I found that use of KD spreader above the FUE site releases the grafts smoothly, thereby increasing the speed and reducing the chances of decapping of grafts. More importantly, this author has not personally experienced fatigue or pain in his fingers or hand. Even during extraction in tight scalp, we have also found that this technique works exceptionally well [Figure 3].



**Figure 3.** Skin stretching during removal of graft (left) and during beard follicular unit extraction (right)



**Figure 4.** The graft holding plate with KD spreader uses magnets for easy attachment

### NOVICE-FRIENDLY IMPLANTATION OF FUE GRAFTS

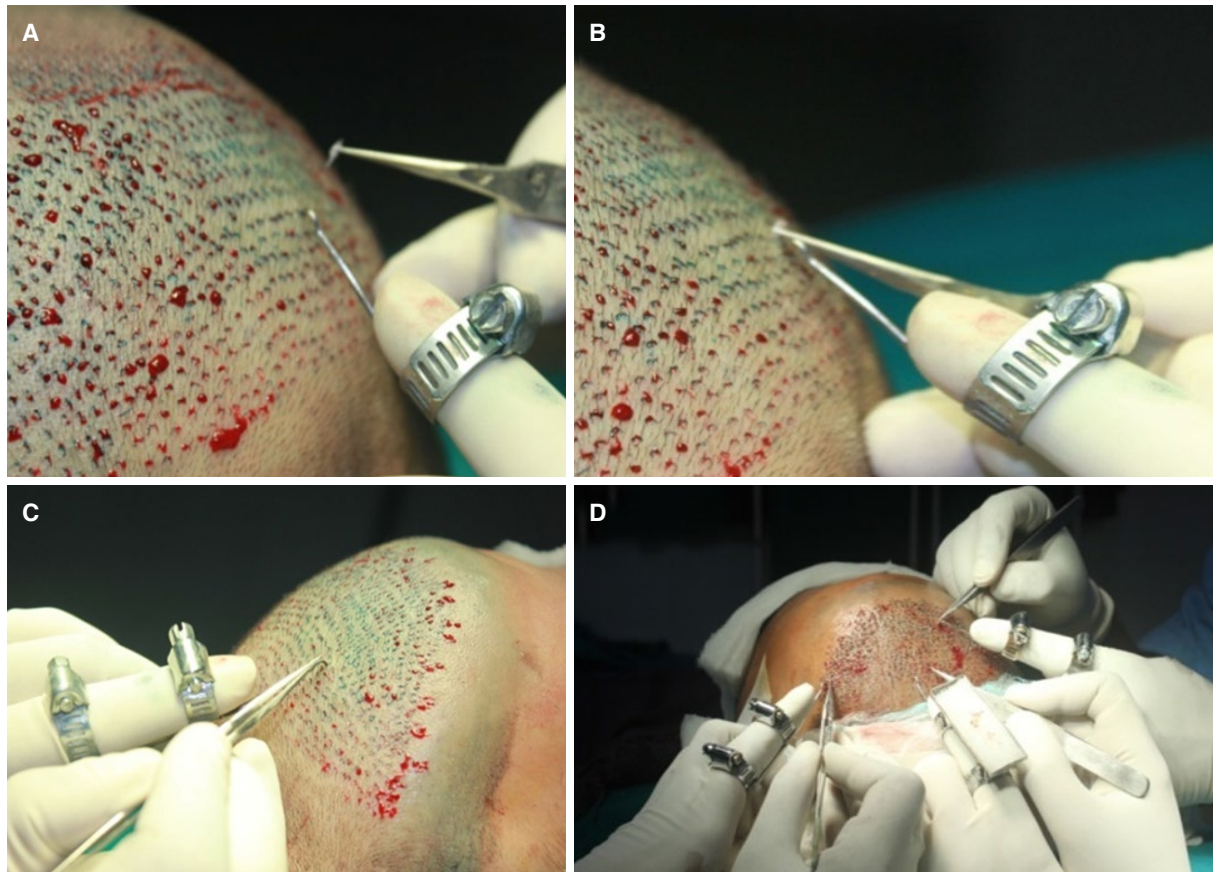
Past research and my personal experience suggests that implantation in coronal slits gives more coverage than sagittal slits but there is a long learning curve in this technique when we use forceps<sup>[3,4]</sup>.

Unlike follicular unit transplant graft, where extra fat is obtained for insulation, FUE grafts require extra care during implantation. Several attempts for inserting the graft into a small hole can permanently damage the graft. Experienced assistants and hair transplant experts can perform implantation without any problem but novice operators struggle during implantation.

I have been an advocate of properly hydrated and atraumatic insertion of FUE grafts. While exploring why some assistants or doctors struggle with the learning curve of implantation, I observed several important hurdles that beginners face, which include the following:

- Dilatation of the premade slit and visualization of hole is insufficient to insert graft.
- Gripping the forceps for dilating the premade slit was not comfortable because non-dominant hand grip was not efficient.
- Graft manipulation during graft insertion reduces their confidence.
- There is greater risk of graft dehydration due to prolonged time out of the hydrating solution for beginners compared to trained experts.
- There is an overcrowding of hands when more than one person is performing implantation simultaneously.





**Figure 5.** (A) Terminal portion skin hook gently lifts and spreads the most superficial part of skin while another hand grasps the graft using forceps; (B) graft gently slides inside slit while slit is elevated and dilated by the KD spreader; (C) the KD spreader is released and the graft positioned in place; (D) three people performing implantation without overcrowding

After discovering these issues, I concluded that to clear the learning curve, beginners would benefit from a user-friendly device that they would provide maximum visualization<sup>[5]</sup>. In addition, grafts need to be kept in hydrating solution as much as possible and during implantation there should not be overcrowding of hands.

I also noticed that fine motor skills for gentle insertion of the graft develop with time and many beginners are discouraged after failure during initial attempts.

The KD spreader gives beginners the opportunity to exert tissue spreading force as per tissue requirement. It enables them to dilate the slit and get maximum visualization before graft implantation. Since the KD spreader is worn on the index finger, it also avoids overcrowding of the hands in the transplantation site when working simultaneously with another implanter<sup>[6]</sup>.

The upper surface of the KD spreader has a shielded magnet that allows for attachment and detachment of the plates [Figure 4]. This device has another unique feature: at the time of implantation, it provides an opportunity to pick follicular units of your choice as grafts immersed in graft holding solution and placed in a row. This also increases the speed and precision of repetitive graft transfer and placement because grafts and incisions are in the same field of view.

During implantation, the KD spreader works as follows [Figure 5]:

- The implanting operator, who wears the device on the index finger of the non-dominant hand, can adjust the grip.

- The recipient area is prepared and coronal slits are made.
- The terminal portion of the device gently lifts and spreads the most superficial part of the slit.
- Another hand grasps the graft using forceps.
- The graft gently slides inside the slit while the slit is adequately dilated by the spreader.
- The spreader releases and the graft is positioned in place, thus allowing as many as 3-4 implanters to work together in an organized manner.

### **ADVANTAGE OF THE KD SPREADER**

There are many advantages to the KD spreader:

- There is lower risk of physical trauma to the graft even in a beginner's hands.
- It improves the ability of beginners to perform FUE.
- It can be used to train inexperienced assistants without jeopardizing quality control.
- It allows 3 or 4 implanters to work in the same field, so a procedure finishes faster.
- It is a low-cost instrument that can be used repeatedly.
- The operator has a reduced risk of fatigue.
- Grafts stay immersed in holding solution, thus limiting the chance of dehydration.

### **CONCLUSION**

After working in the field of hair transplantation for the last 15 years, I have realized there is a definite learning curve for this procedure. Some physicians and assistants may develop skills very fast while others struggle in clearing the steep learning curve of the FUE procedure. We introduce a novel instrument and technique that may help facilitate this procedure.

The KD spreader may improve the ability of novice operators to perform FUE extraction and implantation smoothly. A reduced learning curve may be necessary to train inexperienced assistants without sacrificing the quality of their FUE transplantation.

### **DECLARATIONS**

#### **Authors' contributions**

Saxena K contributed solely to the paper.

#### **Financial support and sponsorship**

None.

#### **Conflicts of interest**

There are no conflicts of interest.

#### **Patient consent**

Not applicable.

#### **Ethics approval**

Not applicable.

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Meeting Abstracts

Open Access



# The 3rd Annual Meeting of The Mountain West Society of Plastic Surgeons

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## 1. Pedicled omentum for coverage of extra-abdominal vascular bypass graft in the groin: a case-report

Neal Moores, Christopher Pannucci

*University of Utah*

Salvage of infected vascular bypass grafts continues to present one of the most complex reconstructive algorithms for both vascular, and plastic surgeons. Graft infection necessitates graft explantation and extra-anatomic bypass, most often with additional synthetic material. These multiply comorbid patients suffer long periods of convalescence in the ICU with attendant bed-rest, ventilator dependency and sepsis. The omentum is an established and effective source of intra-abdominal coverage for gastrointestinal and urological anastomoses, as well as vascular graft coverage. The omentum is also an established method for coverage of extra-abdominal pathology and as a free flap it may be used in any location. However, its use as a pedicled flap for extra-abdominal reconstruction has hitherto been largely limited to chest wall reconstruction.

## 2. Reconstructive phalloplasty aesthetic ideals

Julia Cook

*Indiana University Division of Plastic & Reconstructive Surgery*

**Aim:** Aesthetic ideals are often described to guide reconstruction. The number of phalloplasties performed in the United States is steadily increasing; however, there is a paucity of published literature describing the



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reconstructive ideals of the phallus. The purpose of this study was to determine the preferred aesthetics of phalloplasties.

**Methods:** Phalloplasty aesthetic subunits were defined, and subunit measurements and ratios were examined. A split-testing questionnaire was distributed to medical personnel and online forum users to determine the preferred aesthetic ideals based on phallic subunits. Digitally altered photos focusing on varying ratios of the shaft, glans, corona, and frenulum were presented to participants who were instructed to choose the image that was most aesthetically pleasing. Respondent demographics were collected, including age, sex, medical background, and sexual orientation.

**Results:** One hundred thirty-nine people completed the survey. The overall preferred aesthetic ratios are as follows: 74.8% ( $n = 104$ ) preferred a corona length to width ratio of 20:1, 95.7% ( $n = 133$ ) preferred a shaft length to width ratio of 2.5:1, 51.1% ( $n = 71$ ) preferred a unilateral taper to the glans, 79.9% ( $n = 111$ ) preferred no degree of shaft angulation, 69.1% ( $n = 96$ ) preferred a length to width ratio of 1:1, 56.1% ( $n = 78$ ) preferred angulation at the glans corona junction, 57.6% ( $n = 80$ ) preferred a curved curvature to the corona, and 66.2% ( $n = 92$ ) preferred a straight frenulum.

**Conclusion:** The preferred aesthetics of the reconstructed phallus varies by individual; however, this study can be a guide for both patients and reconstructive surgeons during surgical planning.

### 3. The impact of traumatic dog bite injuries necessitating surgical treatment in elderly

Tyler Evans

*Indiana University Division of Plastic & Reconstructive Surgery*

**Aim:** Traumatic dog bite injuries are a common reason for emergency department visits and hospital admissions. Most literature targets dog bite injuries in pediatric patients, but minimal studies are dedicated to the elderly. This study was designed to investigate the epidemiology and overall healthcare burden of dog bites in the elderly population.

**Methods:** Data was obtained using the Nationwide Emergency Department Sample (NEDS) database. Inclusion criteria included patients 65 years or older with ICD-9 E90.60=dog bite. Site of injury and cellulitis incidence were obtained. Types of procedures were categorized into two groups: minor and major therapeutic. Inpatient length of stay and total charges were also collected.

**Results:** A total of 318,161 dog bite ED visits were identified, of which 24,541 were 65 years and older. Over 95% of patients had only a single injury site, most commonly the upper extremity (72.5%). The incidence of cellulitis was 7.9%. Admitted elderly patients often had subsequent therapeutic procedures (minor 40.9%, major 26.3%, flap/graft 3.6%). Average inpatient length of stay was 4 days. The average total charge for ED services only was \$1094 per patient and combined ED and inpatient services was \$24,551.

**Conclusion:** Dog bite-related injuries are a significant source of trauma presenting to ED and often requiring surgical treatment and hospital admissions, especially in elderly. The impact of dog bite injuries poses a substantial burden on public health both medically and financially. Increased vigilance in prevention of these injuries and their associated complications is crucial to reduce overall morbidity and medical costs.

#### **4. When free tissue transfer is not an option: complex traumatic lower extremity reconstruction using perforator flaps**

**Ryan Kunkel, Christopher Demas**

*University of New Mexico Hospital*

Perforator flaps have changed the approach to reconstructive dilemmas since their emergence on the plastic surgery scene. This additional rung on the reconstructive ladder has led to new methods of closing complicated lower extremity wounds. While arguably more versatile than traditional methods of lower extremity reconstruction, they require tedious dissection and microsurgical techniques. It is important for the plastic surgeon to be familiar with the application of perforator flaps, particularly when more traditional methods of reconstruction are not viable or safe options. We present three cases of complicated lower extremity wounds that were reconstructed with perforator flaps. The first case was a Grade IIIB tibia with a 22-cm soft tissue defect involving all three zones of the lower extremity. Renal and hepatic failure precluded a prolonged microsurgical procedure. This was covered with a distally based posterior tibial perforator flap and a gastrocnemius flap. The second case was a Grade IIIB tibia with open wound in the proximal and middle third of the leg. The patient failed gastrocnemius and reverse sural flap by another surgeon and was not a candidate for a free flap because of a recent STEMI. He was successfully reconstructed with two flaps based on one posterior tibial perforator cluster. The third case was a grade IIIC tibia with 12-cm segmental bone loss. Free tissue transfer was too risky because of a femoral vein thrombosis, which, if propagated, would cause flap failure. Double opposing peroneal and posterior tibial perforator flaps were used to successfully close the defect.

#### **5. Oncoplastic nipple sparing mastectomy with immediate, implant-based reconstruction: technique and outcomes**

**Sarah E. Sasor, Julia A. Cook, Tyler A. Evans, William A. Wooden, Sunil S.Tholpady, Michael W. Chu, Juan Socas**

*Indiana University Division of Plastic & Reconstructive Surgery*

**Aim:** Nipple sparing mastectomy (NSM) is a popular option for women with small, peripherally located breast tumors. The procedure is oncologically safe in select patients but can be technically challenging in large, ptotic breasts. In this study, we examine our experience with NSM using a Wise-pattern skin reduction and nipple areola complex (NAC) preservation on an inferiorly based adipo-dermal pedicle.

**Methods:** A retrospective study of patients undergoing NSM at our institution over a six month period was performed. All patients undergoing NSM with a Wise-pattern skin reduction, NAC repositioning, and immediate, implant-based breast reconstruction were included. Variables collected included patient demographics, smoking status, medical comorbidities and indication for mastectomy. Post-operative outcomes were analyzed with respect to patient and tumor characteristics.

**Results:** Eight NSM's were performed on five patients during the study period. Mean age and BMI were 49 years and 29.1, respectively. No patients were current smokers. All breasts had grade 2 or 3 ptosis. Mean mastectomy weight was 878 grams. All patients had immediate reconstruction with

tissue expander (6) or implant (2) placement. One patient required take-back to the operating room for hematoma evacuation. Three NAC's demonstrated partial necrosis; all were successfully treated with local wound care. No NAC loss, T-junction breakdown, wound dehiscence, infection or implant extrusion/exposure was noted.

**Conclusion:** Wise-pattern skin incision with NAC repositioning and immediate, implant-based reconstruction is a safe and useful technique for managing large, ptotic breasts during NSM. In carefully selected patients, it has a high success rate and provides optimal aesthetic results.

## 6. Cherubism in a 4-year-old boy managed with tumor debulking and mandibular osteotomies and repositioning

Rhett Willis, Jared Garlick, Daniel Donato, Barbu Gociman

*The University of Utah*

Cherubism is a hereditary, disfiguring growth of the mandibles/maxilla in young children. It is characterized by significant loss of medullary bone which is replaced by excessive amounts of fibrous tissue. It is an extremely rare (300 reported cases), autosomal dominant disease. Although generally self-limiting, when severe, can cause significant functional and psychosocial impairment for the patient. Current literature advocates a "wait and watch approach", as majority of these will partially or completely remit after puberty. A 4-year old boy presented with rapidly enlarging mandible and maxilla causing significant change in the facial contour, malocclusion and phonation difficulties. He was treated with aggressive tumor debulking. In addition, using a piezo-electric saw, the lateral cortexes of the mandibular rami, angles and bodies were osteotomized and repositioned bilaterally. This allowed the obliteration of the grotesquely enlarge medullary spaces and restoration of a normal mandibular anatomy. At 8 months postoperatively, the patient had significant improvement in facial contouring and a normal outward appearance and stable dentition. A CT scan showed significant ossification around the molars at the site of mandibular bone repositioning. Although in the majority of cherubism cases there is spontaneous regression after puberty, the sequela of this disfiguring condition in the patient's formative years can cause a lifetime of psychological and physical stress in addition to permanent soft tissue and dental abnormalities. Based on our experience, we recommend that early surgical intervention in severe cherubism cases be strongly considered.

## 7. Beauty and the bull: traumatic rupture of a breast implant in Pamplona, Spain

Nicole Kurnik, Alanna Rebecca, Lyndsey Bryant

*Mayo Clinic - Arizona*

**Aim:** Bullhorn injuries are more common in Ibero-American countries where bulls are involved in sport. There is a lack of information in the literature regarding these injuries. The purpose of this study is to present a case of a bullhorn injury to the thorax causing a ruptured and infected breast implant and a review the literature.

**Methods:** A pub-med literature search was performed and all available English-language publications pertaining to bull injuries during sport were included.

**Results:** A 54 year-old female sustained a penetrating bullhorn injury to her thorax causing breast-implant rupture and resulting infection presented to our institution. She was treated with broad-spectrum intravenous antibiotics, removal of bilateral breast implants and wound debridement. Intraoperative cultures grew methicillin resistant coagulase-negative staphylococcus. After treatment with Bactrim, her implants were replaced; fat grafting of the contour deformity and pectoralis repair was performed. Upon review of the literature, emergency assistance is required during bull-related sports approximately 9% of the time. Body parts most commonly affected are the extremities (66%), inguinal/perineal regions (19%-54%) thorax (3%-10%) and head and neck (10%-19%). Infection occurs in up to 60% of those injured, yet there is minimal reported on what bacteria is cultured. Staphylococcus epidermidis has been reported and also occurred in our patient.

**Conclusion:** Bullhorn injuries can result in devastating injuries with high infection risk which go beyond typical penetrating trauma. To our knowledge this is the first reported case of a breast implant rupture with subsequent infection due to a bullhorn injury.

## 8. Transparency of provider education and board certification among cosmetic surgeons

**Jared Garlick, Kristofor Olson, Madison Hunt, Daniel Donato, Christopher Pannucci, Courtney Crombie**

*University of Utah*

**Aim:** The number of non-plastic surgery trained providers offering cosmetic procedures in the U.S. is increasing. Utah's Division of Occupational & Professional Licensing currently has no way of tracking the number of providers offering cosmetic procedures. The purpose of this study was to analyze providers throughout Utah who offer cosmetic procedures.

**Methods:** Providers in Utah who offered at least one of three cosmetic procedures (breast augmentation, liposuction, and Botox) were included in the study. Formal medical training, board certifications, marketing practices, and procedures offered outside of scope of practice were extracted from publicly available provider websites. All data was analyzed by specialty and Chi-square analyses were performed comparing the categorical data.

**Results:** Nineteen different medical specialties throughout Utah were identified. Nearly one in five providers offering breast augmentation are non-plastic surgery trained providers. Only 50% of providers offering liposuction are trained plastic surgeons, and 75% of Botox providers are not plastic surgeons. Regarding breast augmentation, liposuction, and Botox, plastic surgeons are more likely than non-plastic surgery providers to list their education (93% vs. 42%,  $P = 0.037$ ; 93% vs. 53%,  $P < 0.001$ ; 97% vs. 55%,  $P < 0.001$ ; respectively) and board certifications (90% vs. 25%,  $P = 0.007$ ; 90% vs. 40%,  $P < 0.001$ ; 95% vs. 48%,  $P < 0.001$ ; respectively) on their website.

**Conclusion:** We draw attention to this disparity in provider training and marketing practices, while highlighting a need for increased transparency of cosmetic provider credentials as a way to educate and potentially increase patient safety.

## 9. Alloplastic cranioplasty reconstruction: a systematic review comparing outcomes with titanium mesh, polymethyl methacrylate, polyether ether ketone, and norion implants

Jeremie Oliver, Joseph Banuelos Mancilla, Krishna Vyas, Basel Sharaf

*Mayo Clinic - MN*

**Aim:** Alloplastic cranioplasty has evolved significantly over the years with the development of different materials to serve as a medium of repair to the defect, such as titanium mesh (Ti), polymethyl methacrylate (PMMA), polyether ether ketone (PEEK), and norion implants. There has yet to be published a systematic review of such outcomes among the alloplastic materials we have compared in this study. Our objective in this study was to compare postoperative rates of infection, local complications and allograft failures following cranioplasty reconstruction using Ti, PMMA, PEEK, and norion implants.

**Methods:** Newcastle-Ottawa Quality Assessment Scale guidelines were used for article identification, screening, eligibility and inclusion. The electronic literature search included Medline/Pubmed, Scopus and Cochrane Database.

**Results:** Eighty-three studies and 5320 patients (mean age = 40.6 years) were included in our review (Ti = 2383, PMMA = 2116, PEEK = 487, norion = 334). Overall, Ti was associated with the lowest post-operative infection rate (4.91%,  $P = 0.0026$ , Pearson's Exact Test) compared to all other sub-groups. PMMA implants were associated with the highest infection rate (7.23%,  $P = 0.0021$ , Pearson's Exact Test). Norion implants were associated with the highest local complication rate (15.27%) but this was not statistically significant. PEEK implants were associated with the highest graft failure rate (6.78%) although this was only slightly higher than other implant types and did not show statistical significance.

**Conclusion:** This preliminary analysis begins to address the knowledge gap in determining the infection, local surgical complication and failure rates in alloplastic cranioplasty procedures, although longer-term and randomized trials are warranted to validate any association found in this study.

## 10. A single center retrospective evaluation of a surgical strategy to battle biofilm utilizing absorbable antibiotic beads

Joseph Gorvetzian, Christopher Demas, Ryan Kunkel

*University of New Mexico School of Medicine*

**Aim:** The implications of surgical site infections are undeniable. Increasingly, biofilms are being recognized as potent adversaries that promote wound infection, complicate healing, and resist attempts at treatment. Targeted delivery of ultrahigh concentrations of antibiotics following wound debridement may present a means of mitigating biofilm establishment while simultaneously minimizing the unsavory side effects of high dose systemic antibiotics. This study aimed to present a case series evaluating an antibiotic bead-based method for addressing these problematic wounds.

**Methods:** A retrospective analysis of 83 surgeries on 60 patients with high susceptibility to biofilm infection utilizing a strategy of debridement and absorbable antibiotic-laden calcium sulfate bead placement was



conducted. The surgeries consisted of complex wound and breast reconstruction performed by the senior author (C.P.D.) over 4 years at a single institution. Rates of infection, readmission, and reoperation in the 30-day postoperative period were collected.

**Results:** Of the 83 cases, there were two instances of subsequent surgical site infection (2.4%). A total of 16 reoperations were performed (19%), but in only one case was reoperation required for infectious etiology (1.2%). Readmission rate following the 83 surgeries was 2.4%. None of the 21 breast-related cases necessitated reoperation or readmission.

**Conclusion:** These results lend support to the efficacy of absorbable antibiotic-laden beads in delivering supratherapeutic and sustained levels of antibiotics to local areas. Their use in complex and infection-prone wounds may present a valuable addition to the arsenal of plastic and reconstructive surgeons in managing problematic wounds recalcitrant to standard strategies of debridement and systemic antibiotics.

## 11. A case report of breast reconstruction with a DCIA-based SIEA free flap

**Jonathan Cook, Savannah Moon, Alexander Earle, Miguel Medina**

*Cleveland Clinic Florida*

The superficial inferior epigastric artery (SIEA) flap can be used for autologous breast reconstruction when a muscle sparing operation is desired. Although the deep circumflex iliac artery (DCIA) flap is one of the most commonly used flaps for mandibular reconstruction, to our knowledge, this is the first reported case of a DCIA-based SIEA flap used for breast reconstruction. We report a unique anatomic variant of the origin of a superficially supplied abdominal flap. The patient was a 66-year-old female, with invasive ductal carcinoma of the left breast, and lobular carcinoma in situ of the right breast who underwent bilateral skin sparing mastectomies and immediate autologous reconstruction. The left sided flap demonstrated poor DIEP perforators on pre-operative CTA and was planned as a likely SIEA flap for the left hemi-abdomen. On elevation of the left flap the presumed SIE vessels were identified and traced to the left DCIA system. Clinical perfusion testing and intraoperative ICG fluorescence imaging revealed that the flap was well perfused, and it was used to support the abdominal flap. The flap was transferred with a good vessel size match and no complications. On retrospective analysis this vessel was noted to originate from the DCI system on pre-operative CTA. Although the SIEA usually arises from the circumflex femoral artery, its origin from the DCIA represents an unusual anatomical variant, which may have been otherwise overlooked as a dominant perforator. Awareness of this anatomical variant can enable future surgeons to recognize this versatile muscle-sparing alternative.

## 12. Work-related physical discomfort in ASCFS and ASMS members: a survey

**Ashley L. Howarth, Susan Hallbeck, Valerie Lemaine, Davinder J. Singh, Shelley S. Noland**

*Mayo Clinic - AZ*

**Aim:** Risks of physical discomfort and injury are high in cranio/maxillofacial surgeons (CMS), who perform surgeries with headlights and magnification. Identifying the prevalence and impact of work-

related physical discomfort (WRPD) will guide strategies to prolong surgeon well-being, job satisfaction, and career duration.

**Methods:** After IRB approval, a 30-question survey was administered to the American Society of Craniofacial Surgery and the American Society of Maxillofacial Surgery members to evaluate surgeons' current physical discomfort. Responses were collected by the Mayo Clinic Survey Center.

**Results:** Ninety-five respondents, 75% male, 56% aged 31-50 years old, 73% in academic practice. On a scale of 0-10 (0 no pain, 10 worst pain), WRPD had a median of 3 (surgery without loupes/microscope), 4 (loupe surgery), and 5 (microscope surgery). Pain during, immediately after, and day after surgery was most common in the neck. Pain within 4 h of surgery was present in 55%. Thirty-eight percent had pain influencing future surgical performance. Operating time was > 6 h per day (68%) and > 3 days per week (72%). Surgeon discomfort affects posture (72%), stamina (32%), sleep (28%), surgical speed (24%), relationships (18%), and concentration (17%). Twenty-two percent sought medical treatment for discomfort while 9% took time off work for treatment.

**Conclusion:** WRPD is a critical issue amongst CMS. Nearly all surveyed experience physical discomfort regularly. This negatively impacts daily life and often requires medical treatment. Thirty-eight percent of respondents felt that WRPD would limit their future careers, perhaps the most concerning finding. It is imperative that CMS employ preventive strategies to combat WRPD.

### 13. A2 pulley reconstruction - a novel approach using allograft

**Andrew Peredo, Ashley Ignatiuk**

*University of Colorado - Denver*

Flexor tendon pulley injuries are most commonly seen in rock climbers, but reports of ruptures in non-climbers have been increasing. It is common belief that A2 and A4 pulleys are important in preventing bowstringing of the tendon which is associated with loss of flexion, flexion contracture and altering the kinematics of the tendon. We present a 24-year-old male who underwent reconstruction of his Left index finger A2 pulley using allograft. The patient sustained a zone II flexor tendon injury to his left index finger. He had a complete laceration of his FDS and FDP tendons, and underwent repair of both. Postoperatively he regained full finger active and passive range of motion. However, 4 months postoperatively he suffered a rupture of his A2 pulley with bowstringing. Based on his age, post-operative course and presentation, and discussion of different treatment options. His A2 pulley was reconstructed with dermal allograft (Flex HD Structural-2 cm × 4 cm × 0.3 mm). The allograft was passed through a bone tunnel made within the midportion of proximal phalanx. The allograft was wrapped in a one and a half loop fashion encircling only the flexor tendons and avoiding the extensor mechanism and neurovascular bundles. The patient is currently doing well and the reconstruction of the A2 pulley is still intact. Will start occupational therapy soon. Flexor tendon pulley injuries and ruptures can lead to pain, decreased range of motion, loss of strength, bowstringing and fixed flexion contractures. Although different methods have been described with success, each method has potential drawbacks.

#### 14. Predictors of complications following breast reduction surgery: A National Surgical Quality Improvement Program study of 16,812 cases

Daniel P. Donato, Andrew M. Simpson, Alvin C. Kwok, Jayant P. Agarwal

*University of Utah*

**Aim:** Breast reduction is one of the most common procedures performed by plastic surgeons. Despite good outcomes and high patient satisfaction, there is little national data examining the predictors leading to complications in this patient population. We accessed a national outcomes database to examine these factors.

**Methods:** This is a retrospective study examining the National Surgical Quality Improvement Program database from 2006 through 2015. Patients undergoing primary breast reduction were identified. Patients undergoing any cancer-related procedures were excluded. We identified patient-related and procedure related factors for analysis. Univariate and multivariate logistic regression analysis were used to identify independent predictors of complications.

**Results:** In total 16,812 individual cases were identified. The overall complication rate for the cohort was 6.2% and the major complication rate was 3.0%. Diabetes, bleeding disorder, hypertension, obesity, smoking, steroid use and prolonged operative time were associated with increased risk of complications ( $P < 0.05$ ). Concurrent body contouring was a predictor of increased major complications, however liposuction was not.

**Conclusion:** Common surgical risk factors are associated with complications in breast reduction surgery. Although liposuction is not an independent risk factor, concurrent body contouring is associated with increased complications. Surgeons should be aware of these associations when discussing breast reduction with patients.

#### 15. Minimizing length of stay, narcotic use, operative times and complications combining an ERAS protocol to a two team approach in microsurgical breast reconstruction

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**Aim:** Enhanced recovery after surgery (ERAS) pathways are being adopted to shorten postoperative length of stay (LOS) and decrease narcotic use. A two-team approach in microsurgical breast reconstruction has been shown to decrease operative times and complications. The authors sought to compare outcomes in microsurgical breast reconstruction using a two-team approach before and after the institution of an ERAS protocol.

**Methods:** Retrospective review of 44 consecutive patients undergoing free DIEP reconstruction with a continuous two team approach undergoing DIEP flap breast reconstruction. Twenty-one patients had an ERAS protocol consisting of intraoperative TAP block, intraoperative Ketorolac that is continued on a standing basis for 48 h and Q6h scheduled Tylenol.

**Results:** The cohort was composed of 23 and 21 consecutive patients who underwent DIEP flap breast reconstruction before and after the institution of an ERAS protocol respectively. A total of 73 flaps were performed (37 and 36 flaps before and after ERAS respectively). LOS decreased from  $4.82 \pm 0.77$  to  $3 \pm 0$  after the institution of the ERAS protocol. Of the ERAS patients, 42 % did not take narcotics after discharge; the remainder of the group was on narcotics for 5.3 days on average (range 2-14 days). Operative times were on average 4.67 and 7.4 h for unilateral and bilateral procedures. Complications were similar in both cohorts.

**Conclusion:** The addition of an ERAS protocol to a two-team approach leads to a significant decrease in LOS and minimizes postoperative narcotic use after microsurgical breast reconstruction.

## 16. An evaluation of infection related readmissions after breast reconstructive surgery using the Nationwide Readmissions Database

Willem Collier, Melody Scheefer, Jaewhan Kim, Alvin Kwok

*University of Utah*

**Aim:** Hospital readmissions are costly. Thirty-day postoperative readmission rates are a common quality metric with associated financial consequences. Little is known about readmission rates for infection after implant-based breast reconstruction. We used the Nationwide Readmissions Database (NRD) to determine the rate and predictors of early and late hospital readmissions associated with infection after implant-based breast reconstruction.

**Methods:** Using the 2013-2014 NRD, we identified breast cancer patients undergoing implant-based breast reconstruction who had an infectious readmission with ICD-9 diagnosis and procedure codes. We used univariate and multivariate logistic regression models to identify patient demographic, comorbidity, and hospital predictors of infectious readmission within the early (0-30 day) and late (31-90 day) postoperative time-periods.

**Results:** In a weighted sample of the NRD, we identified 18,338 patients who underwent implant-based breast reconstruction. The overall infectious readmission rate for this group was 5.3%. Only 38.4% of such readmissions occurred within the initial 30 days after surgery, and 39.5% occurred 31-90 days after surgery. Medicaid patients (OR 1.45,  $P = 0.035$ ), median annual household income < \$40,000 (OR 1.41,  $P = 0.023$ ), diabetes (OR 1.52,  $P = 0.030$ ), and obesity (OR 1.54,  $P = 0.021$ ) were independent predictors of overall infectious readmission. Only diabetes (OR 1.74,  $P = 0.041$ ) was an independent predictor of early infectious readmissions. Medicaid (OR 1.74,  $P = 0.033$ ), median annual household income < \$40,000 (OR 1.66,  $P = 0.030$ ), obesity (OR 1.94,  $P = 0.007$ ), and length of hospital stay during the index procedure (OR 1.09,  $P = 0.028$ ) were independent predictors of late infectious readmission.

**Conclusion:** Readmissions for infectious reasons after implant-based breast reconstruction occur more frequently beyond the initial 30-day postoperative period. Traditional thirty-day readmission rates may not be an adequate quality metric for breast reconstruction given the number of late postoperative readmissions. Early and late infectious readmissions have different predictors. Interventions targeting these predictors may decrease the number of readmissions.

## 17. Predicting success in breast augmentation: sizes, shapes and subjectivity

**Hunter Moyer**

*Regional Health, Rapid City*

**Aim:** It remains difficult to define what women desire for breast augmentation. Accepted re-operation rates after primary breast augmentation remain over 20% in large studies, and implant exchange is one of the leading causes.

**Methods:** This study is a computer-generated, visual survey of eight female models with Vectra simulated augmentations using varying sizes of round and anatomic implants. A total of 314 females and 137 males rated the augmentations from best to worst for a total 1967 individual ratings.

**Results:** Natural, conservative and full are words associated positively with a successful breast augmentation. A review of current literature estimates the average breast implant volume in the United States between 350 and 374 mL. In this study, the highest rated implant was a 457 mL round device. A normal distribution simulating the best ratings has an average of 416 mL (standard deviation = 48 mL) ( $P = 0.00000001$  vs. current literature average augmentation volume). Round implants were rated better than anatomic over the entire volume range (3.47 vs. 3.54,  $P = 0.00002$ ), and within the central portion of higher rated volumes (2.67 vs. 3.01,  $P = 1.6e-12$ ). There was no difference in preference of shape or volume between men and women or between respondents of varying ages, socioeconomic status or geographic location.

**Conclusion:** While patients describe the ideal breast augmentation as natural and conservative, they universally choose an implant that is 20% greater than bio-dimensional planning. Round implants were rated better, and there is no difference in preference between men and women.

## 18. The use of bilateral paraspinous muscle flaps and bilateral composite latissimus dorsi and gluteus maximus flaps for closure of lumbosacral myelomeningocele defects in infants

**Kathleen Holoyda, John Kestle, Barbu Gociman, Faizi Siddiqi**

*University of Utah*

**Aim:** Robust, reliable and reproducible closure of lumbosacral myelomeningocele defects remains a challenge. Closure of spinal defects following neurosurgical procedures with well-vascularized flaps in high-risk patients has been shown to reduce complications in the adult population. In infants with lumbosacral myelomeningocele, in addition to the relatively standard neurosurgical repair that consists of placode tubularization and dural repair, multiple methods of soft tissue coverage have been described. These include various cutaneous, fascial and muscle flaps and grafts. We present here our closure technique with well-vascularized flaps following lumbosacral myelomeningocele repair.

**Methods:** After the neurosurgical repair of lumbosacral myelomeningocele is completed bilateral composite latissimus dorsi muscleocutaneous and gluteus maximus fasciocutaneous flaps are elevated. The paraspinous muscle flaps are then elevated and medialized based on the lateral row arterial perforators to provide

complete muscular coverage of the dural repair. The bilateral composite latissimus dorsi muscleocutaneous and gluteus maximus fasciocutaneous flaps are medialized and closed over the paraspinous muscle flap repair. Demographic and outcomes data of 7 patients from June 2014 to present were retrospectively reviewed.

**Results:** Of the 7 patients that underwent the above technique for closure of myelomeningocele defects, there have been no episodes of dehiscence with a median follow-up of 51 weeks (7-161 weeks). One patient experienced an area of small, superficial skin necrosis requiring surgical excision and reclosure.

**Conclusion:** Use of bilateral paraspinous muscle flaps and bilateral composite latissimus dorsi and gluteus maximus flaps provides robust coverage of lumbosacral defects following myelomeningocele repair in infants.

## 19. Outpatient bilateral mastectomies with immediate pre-pectoral breast reconstruction

Sara L. Struve, Barbara A. Pockaj, Raman C. Mahabir

*Mayo Clinic Phoenix, Arizona*

In the setting of breast cancer, ductal carcinoma *in-situ*, and other high risk patients, breast reconstruction can be offered in the immediate stage, at the same time as mastectomy. Immediate breast reconstruction has historically been done as an inpatient surgery, with at least one overnight stay in the hospital. Recently, we switched to performing these procedures in the outpatient setting. This case series documents ten bilateral mastectomies with immediate pre-pectoral direct-to-implant breast reconstruction patients, who were discharged home on post-operative day zero. To be able to achieve this outcome in an outpatient setting, there were several aspects we implemented prior to the transition. These included: pre-operative education and counseling, intra-operative measures, post-operative measures, and a discussion of the expected post-operative outcomes with patients and their families. Patient education and counseling was most important for setting expectations during and after surgery. Intra-operative measures included: IV Tylenol, Toradol, and steroids, as well as Exparel rib blocks, field blocks, and pectoralis major muscle blocks. Post-operatively, the patients were given scheduled analgesics for the first two post-operative days, then switching to prn medications thereafter. These factors all contributed to patients and families feeling comfortable enough for the patient to be discharged home the same day as their procedure.

## 20. Use of social media in plastic surgery resident recruitment. A perspective from the applicants

Lacey Pflibsen, Nicole Kurnik, Ashley Howarth, Anthony Smith, Shelley Noland

*Mayo Clinic - AZ*

**Aim:** There has been plenty of publications looking at how residency programs use social media websites of applicants to help with ranking; however, no such study has looked at the reverse, how social media websites of residency programs recruit applicants. This study aimed to investigate if plastic surgery residency programs are using social media platforms in resident recruitment.



**Methods:** We sent out an eight question survey (SurveyMonkey) that is distributed to integrated plastic surgery PGY-1 residents via contacting the program coordinators. The questions were aimed at investigating which platforms were being viewed (Facebook, Instagram, Twitter), what images and information was important, and how it influenced applicants (to interview, rankings, etc&).

**Results:** Preliminary data shows that although 90% of residents themselves have a personal Facebook (70% Instagram, 40% Twitter); the majority did not look at the social media page of residency programs prior to choosing to interview or ranking (90% and 70% respectively). It appears 60% of those that responded did not have a social media page at their institution; however, interestingly 87% of the respondents felt that portraying pictures of residents was influential and others commented that seeing resident-attending interaction was important.

**Conclusion:** It appears at this time social media platforms do not influence resident recruitment. With many programs starting either department or residency specific social media platforms, it will be interesting to see if increased awareness of social media platforms of programs will increase the importance of social media in resident recruitment.

## 21. The scroll suspension suture in open septorhinoplasty

**Leland Webb, Kevin Kalwerisky, Craig Czyz, Scott McCusker**

*United States Air Force*

**Aim:** The scroll area between the upper and lower lateral cartilages is often neglected during septorhinoplasty. A simple suture technique to address this area is presented as an adjunct to existing septorhinoplasty methods for improvement of form and function.

**Methods:** A single fine prolene suture is placed between the lower lateral cartilage and the soft tissue of the scroll area. By altering the vector of this suture, the tip position can be readily controlled, as can the shape of the lateral nasal wall.

**Results:** Thirty-six consecutive septorhinoplasty surgeries by a single surgeon were analyzed, and the scroll suspension suture was used in twenty-eight. All patients reported excellent subjective postoperative nasal breathing and revision surgery was performed in one, for reasons unrelated to the scroll suspension suture.

**Conclusion:** The scroll suspension suture is a useful technique to add to the rhinoplasty surgeon's toolbox and has positive aesthetic and functional characteristics.

## 22. Successful reconstruction of bilateral oral commissure fusion post Stevens Johnson syndrome

**Dino Maglic, Ray Hosein, Barbu Gociman, Neal Moores, Shadia Flores, Faizi Siddiqi**

*University of Utah Health Care*

**Aim:** Stevens Johnson Syndrome (SJS) is a type IV hypersensitivity reaction commonly triggered by drugs which results in the uncontrolled destruction of keratinocytes with both cutaneous and mucosal involvement. A rare and often life threatening disease, SJS has an incidence of approximately 1 to 2 cases per 1 million. When involvement of the skin surpasses 10% of the body surface area, it is designated as Stevens Johnson/ Toxic Epidermal Necrolysis Syndrome (SJS/TEN). A 19-year-old Hispanic female presented to the pediatric plastic surgery clinic with severe microstomia caused by bilateral oral commissure fusion post SJS/TEN after taking sulfamethoxazole/trimethoprim for the treatment of severe chronic acne vulgaris. Here, we report her successful reconstruction.

**Methods:** Triangular scar excision and mucosal Y-V advancement commissuroplasty were performed bilaterally under general anesthesia. The incisions were carefully design to avoid overlapping suture lines during the healing process.

**Results:** Our reconstruction commissuroplasty using triangular scar excision and mucosal Y-V advancement successfully resulted in normalization of the oral opening, and recreation of an esthetically pleasant mouth contour.

**Conclusion:** Although non-life threatening, microstomia can limit functionality and cause undue stress to the patients and their families. Triangular scar excision and mucosal Y-V advancement commissuroplasty proved to be an effective treatment modality of microstomia secondary to SJS/TEN.

## 23. Indications and outcomes of single-pedicle versus two-pedicle and multiple simultaneous thigh free flaps in head and neck reconstruction

Becky B. T. King, Ivan E. Rodriguez, Frederic W.B. Deleyiannis

*University of Colorado*

**Aim:** The anterolateral thigh (ALT) free flap is one of the most commonly used flaps for head and neck reconstruction. Given that perforators of an ALT flap routinely arise sequentially from the descending branch of the lateral circumflex artery as it descends down the thigh, a long ALT flap can be more reliably harvested than a wide ALT flap. The purpose of this study is to demonstrate indications and outcomes for single-pedicle ALT free flaps compared to double-pedicle ALT flaps as well as multiple simultaneous thigh (MST) flaps.

**Methods:** Our series of 81 consecutive patients undergoing head and neck reconstruction with an ALT flap was retrospectively reviewed. Receiver operating characteristics curve analysis was performed to determine our cut-off values for width and length of single-pedicle versus double-pedicle ALT flaps.

**Results:** Fifty-seven and 18 patients were reconstructed with an ALT flap with one or two pedicles, respectively. Six patients underwent MST flaps. Defect size (width 12 cm, length 17 cm) for cutaneous defects ( $P < 0.05$ ), the presence of divergent mucosal defects, and through-and-through oral cavity or pharyngeal defects were associated with the use of two pedicles. While operative time was increased for the groups of double-pedicle ALT flaps and MST flaps, there were no flap complications including partial flap loss, venous congestion, or wound healing issues from poor flap perfusion.

**Conclusion:** Harvesting an ALT flap with two pedicles has the potential to reduce flap complications and should be considered for divergent and extremely wide or long defects.

## 24. Combined TUG PAP using SPY as an aid in perineum reconstruction

Karen Lo, David Mathes, Tae Chong

*University of Colorado*

In perineal reconstruction, the goals are to provide coverage and eliminated dead space in an area prone to wound problems. The VRAM flap has traditionally been used due to its bulk and ease of transfer at the time as the oncologic surgery. However, when the abdomen is not available, other flaps are considered. We present the case of perineal reconstruction using combined TUG and PAP, with SPY angiography as an aid. KM a 59 yo F with h/o stage 3c invasive rectal adenocarcinoma s/p neoadjuvant chemoradiation. We planned a VRAM at the time of oncologic resection. However, she had positive margins; thus, underwent an APR, omental flap, mesh placement, hysterectomy and partial vaginectomy by her cancer surgeons. They placed a WV stating they did not want flap closure. A week later we were re-consulted for flap closure. As the VRAM was no longer an option, we decided on a thigh based flap. A doppler was used to identify the locations of the perforator for the TUG, ascending branch of the medial circumflex femoral artery, and the PAP, profunda artery. The PAP was clamped and we used SPY angiography to evaluate the perfusion based on the TUG alone. We noted poor perfusion of the distal skin paddle, which we intended to use to recreate the vagina. Under SPY, we released the clamp and saw immediate perfusion of the distal skin paddle and thus used both the PAP and the TUG in the reconstruction. The pt was discharged home without issues.

## 25. Delayed DIEP flap loss: a complication of microvascular progress and earlier discharge

Alicia Heelan Gladden, Becky B. T. King, Alexandra Kovar, Kristen Ohe, Colleen Murphy, Joyce Aycock, David Mathes, Tae Chong

*University of Colorado*

**Aim:** Traditional teaching is that microvascular complications most frequently occur in the early post-operative period, typically within 48 h. The purpose of this study was to investigate deep inferior epigastric perforator (DIEP) total flap loss at our institution.

**Methods:** A retrospective analysis of patients who underwent DIEP flap breast reconstruction at a single institution was performed. Pre-operative demographic data and post-operative complications were recorded. Delayed flap loss was defined as non-salvageable flap presenting greater than 48 h after surgery.

**Results:** Eighty-eight patients underwent 137 DIEP flaps during the study period. Five patients (3.6%) had threatened flaps in the first 48 h post-operatively and three of these were salvaged with emergent operative intervention. Five patients suffered total flap loss (3.6%). Sixty percent (3/5) of flap losses occurred after patient discharge, with all three patients returning the day after discharge with a non-salvageable flap. When patients with early microvascular complications were compared to the delayed flap loss group, there were no significant differences in age, BMI, smoking status, diagnosis of diabetes or hypertension, radiation, or timing of reconstruction (all  $P > 0.05$ ).

**Conclusion:** Over half of our institutions flap losses were delayed, occurring after discharge. This finding contradicts the notion that most flap losses occur in the immediate post-operative period. The advancement of microsurgical techniques is reducing the frequency of flap loss during this early period, when flaps are

closely monitored and prompt revision is possible. With greater emphasis on early patient discharge, perhaps more detailed patient education on return precautions is indicated.

## **26. Pedicled latissimus dorsi myocutaneous flap for posterior thoracic reconstruction following eloesser flap takedown: a case series**

**David Hill**

*Rush University Medical Center*

Pedicled latissimus flaps as the basis for thoracic reconstruction have been utilized for more than a century. While Dr. Abrashanoff described use of the flap as treatment for complicated bronchopleural fistula in 1911, its use in remedying iatrogenic chest wall defects resulting from external drainage procedures is less well-documented. Once medically stabilized, patients surviving chronic empyemas with Eloesser Flaps require reconstruction of the associated thoracic defect to restore quality of life, which may become of paramount importance. As the largest extrathoracic muscle flap which may be harvested on a single vascular pedicle, the latissimus dorsi serves as an ideal myocutaneous flap for obliterating Eloesser Flap defects. Its broad surface area and arc of rotation lend to coverage with minimal tension while avoiding exacerbation of respiratory mechanics. Although the latissimus dorsi muscle extends, adducts, and internally rotates the humerus, there are a number of other shoulder girdle muscles which combine to serve redundant functions, allowing for the muscle to be sacrificed with minimal loss of strength or form. We present a case series of pedicled latissimus dorsi myocutaneous flaps utilized for Eloesser Flap reconstruction with excellent aesthetic and functional results.

## **27. Indocyanine green lymphangiography optimizes the identification and management of lymphatic leaks in the groin**

**William Casey, Alanna Rebecca, Raman Mahabir, Lacey Pflibsen, Nadine Hillberg, Claire Jensen**

*Mayo Clinic - AZ*

**Aim:** The treatment of lymphatic leaks and lymphoceles in the groin can be quite challenging with no optimal management determined to date. We postulate that ICG lymphangiography improves visualization of the site of a lymphatic leak and can optimize its management.

**Methods:** A retrospective review was conducted of all cases in which ICG lymphangiography was used in the management of lymphatic leaks in the groin over an 18-month span. The inciting surgical procedure resulting in the leak was determined. Following thorough debridement, ICG was injected intradermally in the distal extremity and the site of the lymphatic leak was documented (superficial or deep) and oversewn. Outcomes were reported with regards to healing, infection, time to drain removal, and adjunctive procedures.

**Results:** Fifteen patients underwent ICG lymphangiography during the surgical treatment of a lymphatic leak in the groin during the study period. In all cases, the site of the lymphatic leak was accurately identified and oversewn. In 8 cases, the site of the lymphatic leak was in the subcutaneous tissue superficial to the femoral vessels rather than medial to the femoral vessels in the area of the lymph node basin. A local muscle flap was used in 10 cases simultaneously. All wounds healed primarily without an associated wound or infection.

**Conclusion:** ICG lymphangiography facilitated the identification of lymphatic leaks in the groin and optimized their management in these challenging cases, many of which may have been missed if the area around the inguinal lymph node basin was treated exclusively.

## 28. Geometry of wound epithelialization

**Michael Gordon**

*University of Colorado*

A mathematical computer model was created to test simple aspects of wound epithelialization. Assumptions of the model included constant production of growth factors from the edge of the wound that diffused across the open area with a  $1/r^2$  gradient from the cells at the edge of the wound. New cell growth was determined to occur when an adequate amount of growth factor had accumulated at a point in the open wound area. This model was then able to predict various characteristics of wound closure: speed of wound closure, effect of size of the wound on wound closure, shape of wound closure, effect of debridements on wound closure. These predictions were then tested in the laboratory setting using epithelial cell growth in a petri dish. Excellent agreement between the mathematical model and the laboratory model was noted. Even the often-noted, but mysterious, slowing down of wound healing as it approaches closure was observed and explained mathematically.

## 29. Lumbar artery perforator flap breast reconstruction: achieving good aesthetic results at both donor and recipient sites

**David Greenspun**

*Greenwich Hospital, Greenwich, Connecticut*

The lower abdominal wall is the most commonly used donor site for autologous breast reconstruction. The thighs and gluteal region are established alternative donor sites for breast reconstruction (PAP, TUG, GAP flaps) when the abdominal wall does not provide sufficient tissue or is otherwise unsuitable as a result of prior surgery. Flaps harvested from the buttock or thigh can produce good cosmetic results for the reconstructed breast, but this is frequently at the expense of unfavorable contour at the donor site. Harvest of the aforementioned flaps tends to flatten, or make concave, naturally convex surfaces of the body, thus producing unsatisfactory changes at their respective donor sites. In contradistinction, harvest of lumbar artery perforator (LAP) flaps, slightly superior to the iliac crest, accentuates the normal lordotic curvature of the lower back, and therefore produces favorable changes to the donor site contour whilst yielding excellent tissue for breast reconstruction. Harvest of the LAP flap pedicle is technically demanding and carries high stakes for donor site morbidity owing to the proximity of the spinal nerves to the vascular pedicle, however, these flaps can be performed safely and reliably. The routine use of arterial and venous grafts facilitates safe and efficient flap harvest as well as recipient site microsurgery and flap inseting. A retrospective series will be presented. With increased experience and good aesthetic results at both the donor and recipient sites, the LAP flap has emerged as an excellent second-choice flap for breast reconstruction when the abdomen is not suitable.



Original Article

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# Permanent volumizing and contouring of the lower face using 350 centistokes injectable silicone

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## Abstract

**Aim:** An ideal injectable material would be biocompatible with long-lasting effects. The relative polymerization and chain length of the compound determines its viscosity, as measured by centistokes (cp). It is available in 350, 1000 and 5000 cp - the higher the number, the more viscous the oil. Most of the reports used 1000-cp silicone oil for filling purposes and due to high viscosity, only microdroplet injection technique is recommended to avoid complications. This is the first report of patient series using liquid silicone with a 350-cp viscosity. The objective of this study was to explore the reliability and efficacy of low viscosity liquid silicone for lower face contour correction.

**Methods:** Lower facial region of 43 patients including chin, nasolabial and melolabial regions were treated by low viscosity (350 cp) liquid silicone. Instead of microdroplet technique, retrograde linear threading technique was used. Total injection volume was  $6.0 \pm 3.9$  mL. At least two sessions were required for complete correction which are spaced one month apart. Overcorrection was avoided. The treated areas had a soft and natural feeling with no lumpiness and stiffness.

**Results:** Mean follow-up period was  $16.8 \pm 14.3$  months. The mean aesthetic satisfaction score was 4.51. No migration of the material was seen which is revealed by palpation and no major complication was encountered. None of the patients had any complaints regarding late facial deformity due to silicone migration.

**Conclusion:** Low viscosity liquid silicone is effective, well-tolerated and easy to use. It can be used as an alternative to higher viscosity silicones to avoid technical errors and complications.

**Keywords:** Liquid silicone, injection, filler, lower face, augmentation, deep wrinkles, face contour, face volume



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## INTRODUCTION

Age-specific changes in facial soft tissues and their effects on facial morphology has been clearly described elsewhere<sup>[1-3]</sup>. Restoration of soft tissue through augmentation, modify facial contours, correct tissue loss associated with normal aging. For over five decades, liquid injectable silicone has been used for soft-tissue augmentation<sup>[4-6]</sup>. It is believed that the historical complications and delayed type hypersensitivity reactions were due to the impurities of silicone products<sup>[7]</sup>. Modern highly purified silicone products are available in the current practice which allow safer applications. Highly purified liquid silicone is chemically pure, free of particulate matter, clear, colorless, odorless, tasteless, nonvolatile, viscosity-constant within the range of human body temperatures<sup>[8]</sup>. Silicone fluids range in viscosity from 0.65 cSt (thinner than water) to more than 20,000,000 cSt (thicker than chewing gum)<sup>[9]</sup>. The longer the polymer, the higher the viscosity. Viscosity does affect flow behavior and solubility. The higher the viscosity, the more slowly the polymer will flow and less soluble in some solvents<sup>[9]</sup>. Currently various silicone brands with different viscosities are available such as Biopolimero-350, Silikon-1000, AdatoSi 1-500, and Bioplastique. Usually liquid silicone with a 1000-centistokes (cp) viscosity has been used as a tissue filler<sup>[10-15]</sup>. Microdroplet serial puncture technique is currently considered to be a safe and efficacious tissue-biocompatible material for permanent intra- and subdermal implantation within the human body<sup>[10]</sup>.

There can be impressive results and significant complications associated with injectable silicone. Clark *et al.*<sup>[7]</sup> in 1989 reviewed the safety of silicone injections and concluded that these complications are related primarily to the use of impure product, excess volumes, or inappropriate location.

## METHODS

Forty-three patients were treated with liquid silicone (Biopolimero-350 cp, ZNK, Spain) between the years 2011 and 2016. An informed consent was obtained from each patient. Prior to treatment, the patients were fully informed of the precautions, method of administration, likely treatment responses, and potential adverse reactions. The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation.

All patients were female and mean age was  $46 \pm 8$  years. No anesthetic or epinephrine was used. Before commencing injection, the skin was inspected for the presence of any dermatologic diseases, inflammation or infection (active acne, herpes simplex, *etc.*). All makeup were removed and the area was cleansed with an antiseptic. The areas to be augmented are marked with a pen with patients in a seated position under optimal lighting. No test for hypersensitivity was performed.

All injections were done subcutaneously through a 22-G needle. Nasolabial, chin, cheek and melolabial areas were treated [Table 1]. The needle is inserted into the subcutaneous plane with a 30-degree angle. The plunger of the syringe was pulled back and wait for a few seconds to see if the needle is in a blood vessels. The area to be treated is filled with liquid silicone by retrograde linear threading technique. While injecting the material, manual moderate pressure is applied with the the non-dominant hand index finger to control the depth of injection, to provide evenness and equal distribution of the liquid silicone. The injections were slowly performed and the needle is always moved to prevent embolic complications that could lead to tissue loss or blindness. The contour defects were deliberately undercorrected at the first session. Gradual augmentation was performed and at least 2 sessions were required for complete correction which are spaced 1 month apart. Optimal correction usually required 2 to 3 treatments. Usually the required volume for correction is reduced at the following sessions. No overcorrection was done. Cool compresses were recommended for 15 min immediately after the treatment to reduce redness, bruise and swelling. Topical ibuprofen (Dolgit<sup>TM</sup> cream %5, ADEKA) was commenced twice daily and continued for 1 week. Cosmetics were avoided for 24 h.

**Table 1. Treated patients' demographics, treated regions, injected volume and follow-up periods**

No.	Age (year)	Treated region	Injection volume (mL)	Total injected volume (mL)	Follow up (month)
1	51	NL	3/side	6	8
2	46	NL	2/side	4	2
3	36	NL	1/side	2	53
4	48	NL	2/side	4	13
5	58	NL	3/side	6	18
6	53	NL	2.5/side	5	5
7	46	NL/cheek	2.5/3.5/side	12	4
8	64	NL/melolabial	3/2.5/side	11	5
9	56	NL/chin	2/1.5/side	7	45
10	34	NL	1.5/side	3	51
11	48	NL	2/side	4	8
12	63	NL/cheek	2.5/3/side	11.5	12
13	67	NL	3.5/side	7	16
14	44	NL	1.5/side	3	38
15	65	NL/melolabial	3/4/side	14	7
16	56	NL/melolabial/cheek	2/2/3/side	14	2
17	47	NL/cheek	1.5/4/side	11	9
18	45	NL	2/side	4	14
19	42	NL/cheek	2/2/side	8	4
20	59	NL/ML/cheek	2.5/2.5/3/side	16	9
21	41	NL	2/side	4	6
22	33	Cheek (local)	2	2	6
23	40	NL	1.5/side	3	19
24	36	NL	1/side	2	9
25	39	NL	2/side	4	25
26	35	Cheek (one side)	2	2	13
27	39	NL	2/side	4	5
28	43	NL	2/side	4	21
29	41	NL/cheek	1/2/side	5	34
30	45	NL	2/side	4	17
31	44	Cheek	2/side	4	49
32	54	NL/cheek	2/4/side	12	22
33	36	NL	1/side	2	2
34	45	NL/cheek	1.5/3/side	9.5	42
35	41	NL	2/side	4	24
36	57	NL/cheek	3/3/side	12	22
37	38	NL	1/side	2	30
38	49	NL/cheek	2.5/3/side	11	7
39		NL	1/side	2	11
40	42	NL	1.5/side	3	12
41	44	NL/cheek	1.5/1/side	5	12
42	47	NL	1.5/side	3	10
43	48	NL	2/side	4	3

NL: nasolabial

Patients were photographed before the injection and at each visit. Before submission of this article, all patients were reached by phone and asked to rate their cosmetic and functional satisfaction on a 5-point scale: 1 - very dissatisfied; 2 - dissatisfied; 3 - neither satisfied nor dissatisfied; 4 - satisfied; 5 - very satisfied.

## RESULTS

Mean follow-up period was  $16.8 \pm 14.3$  months. The mean satisfaction score was 4.51. Total injection volume was  $6.0 \pm 3.9$  mL. No major complication was encountered. Only mild bruise was seen in 2 cases which faded within 1 week. Effective correction of the facial creases and smile lines were obtained [Figure 1]. Tissues remained



**Figure 1.** Effective correction of the facial creases and smile lines was achieved

soft, smooth and plump during the entire follow-up period [Figure 2]. None of the patients experienced late facial deformity, lump or other complications due to silicone migration. At the marionette and nasolabial creases, despite the ongoing process of aging, the results remained satisfactory for at least 1 year [Figure 3]. In patients with longer-term follow up (> 30 months), the deformity relapsed to an extent but no additional injections were demanded.

Since no overcorrection is done, the texture of soft tissue augmented with liquid silicone is usually natural with no irregularities, rubbery feeling or lumpiness.

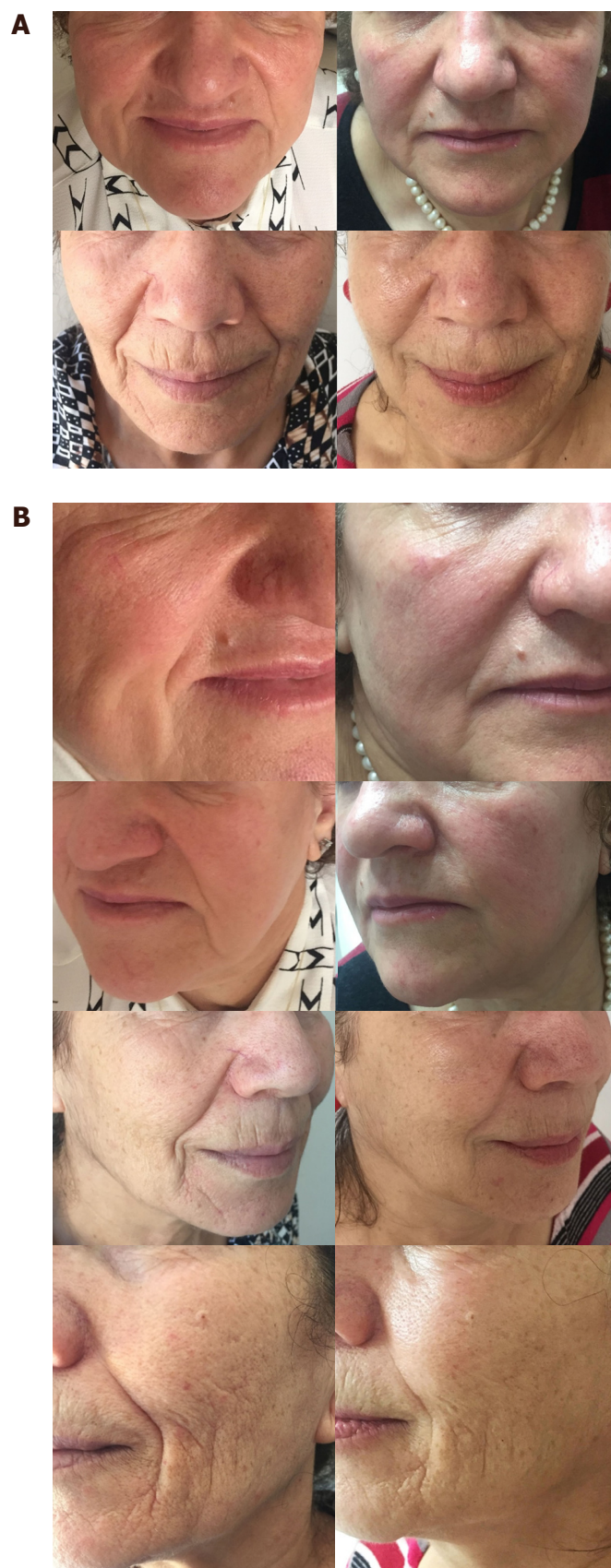
## DISCUSSION

Aging is not limited to the skin but also to its supporting structures. Atrophy of the subcutaneous adipose tissue, sagging skin due to loss of skin collagen lead to a loss of volume and change in facial contours. Facial creases (nasolabial, melolabial) progressively deepen, smile lines and periorbital lines become visible in the lower face<sup>[1-3]</sup>. In a young face superficial and deep fat is distributed evenly with smooth primary arcs and convexities. With age, the distribution of fat becomes altered by fat atrophy and hypertrophy producing hills and valleys with demarcations between the cosmetic units<sup>[16]</sup>.

Dermal and subcutaneous fillers, used either alone or as an adjunct to surgical and nonsurgical facial rejuvenation techniques, are a logical and effective treatment choice for “lifting and filling” the facial soft tissues<sup>[17]</sup>. The aesthetic goal is to create a smooth transition between the units and to restore the ample, balanced distribution of facial fullness that exemplifies the youthful face<sup>[18]</sup>. The hills and valleys should be smoothed over and the former primary arcs and convexities of youth, rebuilt<sup>[19]</sup>.

Currently fat transfer, silicone and artefill are the choices for permanent facial augmentation, enhancement and rejuvenation. In my practice, I have been performing fat injection for the last 12 years. The outcomes depend on the number of the survived fat cells and this is partly technique and partly patient dependent; therefore usually the results are unpredictable. The operation takes time, requires at least 2 sessions, expensive and should be performed under strict sterile conditions. In the last 5 years, upon patients’ demand, I have started using liquid silicone since I feel quite comfortable and skilled for filler applications. This alternative offers a rapid, practical and an effective way for patients who demand “permanent” facial volumizing and contour restoration.

Injectable liquid silicone has many qualities that could make it a suitable material for long-term soft-tissue augmentation. At the same time, there are still many unanswered questions pertaining to potential complications that need to be addressed before it can be considered for this purpose.



**Figure 2.** Restoration of smooth and soft facial contours, effective volumizing of the lower face. (A) Anterior view; (B) lateral view





**Figure 3.** The improvement of the facial creases at 1 year

Currently, Food and Drug Administration-approved clinical trials are reported to be in progress for a liquid silicone product specifically for treatment of human immunodeficiency virus-associated facial lipoatrophy and for use in cosmetic indications<sup>[20]</sup>.

Little is known about the study except that it involves the use of a microdroplet serial puncture technique, as described by Orentreich<sup>[14]</sup> and Orentreich<sup>[15]</sup>. This injection technique was reported in the late 1970s. It consists of depositing minute droplets of liquid silicone 0.01 mL or smaller into the subdermal tissues at 2 to 10 mm intervals. Injection of these microdroplets has been shown to produce a mild inflammatory reaction, resulting in a fibroblastic response. It is believed that this neocollagen synthesis is complete after approximately 3 months. The resulting fibrosis is responsible for the apparent soft-tissue augmentation. By contrast, injections of larger doses (greater than 0.05 mL) has been shown to produce granulomas and foreign body reaction<sup>[7,14]</sup>.

In 1971, Ashley *et al.*<sup>[21]</sup> presented hundreds of animal studies and followed 90 patients for 3 months, with excellent results. They did mention that it was important to use small volumes at each session. Their average volume per injection was 4 mL, which was considered a small volume in the early 1970s. They also were the first to use higher viscosity silicones up to 1000 cS, noting that large volumes of low-viscosity silicones tended to migrate where the higher viscosity silicones did not migrate. As oppose to Ashley's report, we have not encountered migration even in a single case. The filler remained stable during the entire follow-up period. It may be the injection technique (linear line versus microdroplet) that prevented migration. New histological studies are required to reveal and compare the fibroblastic responses between the two techniques.

In linear threading technique, there are fewer needle punctures, and potentially a smoother result since it is easier to produce contiguous layering. A smooth and even deposition of the filler could be attained in our series. None of the patients complained of granuloma formation of filler beads.

In conclusion, lower viscosity of liquid silicone (350 cp) is effective and safe for correction of deep facial lines and contouring. It provides soft and smooth facial contours and effectively volumize the face. Retrograde linear threading technique seems a safe technique and migration is not a concern using silicone with 350 cp viscosity.

However since there are concerns about delayed hypersensitivity and late complications, in order to accept it as a universally safe method, further studies with longer follow-up periods are required.

## DECLARATIONS

### Authors' contributions

Ulusal BG contributed solely to the paper.

### Financial support and sponsorship

None.

### Conflicts of interest

There are no conflicts of interest.

### Patient consent

An informed consent was obtained from each patient.

### Ethics approval

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation.

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Case Report

Open Access



# Reverse bilateral latissimus dorsi flap reconstruction after extensive mid back dermatofibrosarcoma protuberans excision: a case report

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## Abstract

Surgical resection of soft tissue sarcoma of the trunk can result in large defects requiring complex reconstruction for coverage of vital neurovascular structures and tissue defect. Large defects of the back could be reconstructed with multiple random pattern or local pedicled flaps. We present the case of a 48-year-old patient with a locally advanced dermatofibrosarcoma protuberans of the back. Wide local excision of the lesion was performed. The soft tissue defect measured 22 cm × 20 cm × 4 cm and was reconstructed with bilateral reverse latissimus dorsi myocutaneous (RLDM) flap. Each RLDM flap measured 24 cm × 10 cm. The donor site on the back was closed directly on both sides. The patient recovered well and the two flaps healed uneventfully. Twelve months after surgery the patient is disease-free. The use of a RLDM flap in mid-back reconstructions provided wide well-vascularized soft tissue, minimized risk of infection, and maximized back coverage. This flap is an excellent choice for reconstruction of large defects of the mid-back.

**Keywords:** Reverse latissimus dorsi myocutaneous flap, trunk reconstruction, posterior trunk defect, sarcoma, dermatofibrosarcoma protuberans

## INTRODUCTION

Soft tissue sarcomas (STS) represent less than 1% of all malignant tumors. STS can occur anywhere in the body but 75% are located in the extremities, 10% in the trunk and 10% in the retroperitoneum<sup>[1]</sup>. The mainstay



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of treatment of localized STS is the complete surgical resection of the tumor with adequate margins. Both the width and quality of the surgical margins are crucial in determining patients prognosis. Low-risk tumors are typically managed with a wide surgical resection alone. Patients with high-risk tumors may be treated with adjuvant/neoadjuvant radiotherapy and/or chemotherapy to minimize respectively the local and systemic risk of failure.

Dermatofibrosarcoma protuberans (DFSP) is a low-grade, locally aggressive, STS of the cutis. Typically, DFSP arises within the dermis as a slow-growing plaque or nodule and subsequently spread to the subcutaneous tissues. The pathogenetic driver of this tumor is the t(17;22)(q22;q13) translocation which leads to the formation of COL1A1-platelet-derived growth factor (PDGF) beta fusion transcripts. The overproduction of the PDGF beta-chain stimulates tumor cells growth with an autocrine loop<sup>[2]</sup>.

DFSP are managed with wide excision of the tumor en-bloc with surrounding soft tissues. The Mohs micrographic surgery is an option to minimize the amount of tissue resected, especially in critical areas<sup>[3]</sup>. The risk of local recurrence is in the range of 1%-4% at 10 years after wide surgery and the metastatic risk is about 2% at 10 years in major series<sup>[4,5]</sup>. The risk of local failure increases significantly in case of marginal or microscopically positive resection, thus the quality of surgery is critical. In a minority of patients, the tumor may harbour a fibrosarcomatous transformation which is associated with a much higher systemic risk. The most common site of DFSP occurrence is the trunk (72%). Here, the extensive removal of tissue often requires reconstructive surgery because primary closure is not possible. Furthermore, in case of local recurrences, the re-resections of superficial soft tissues further deplete the nearby tissues of redundancy and the transferring of healthy tissue from areas of excess becomes necessary<sup>[6]</sup>. Indeed, the complexity of the defects following soft tissue sarcoma resection has increased, as more patients now receive preoperative radiotherapy. Radiation decreases the chance for a successful skin graft, and it also renders the wound edges ischemic. Therefore, well-vascularized tissues are required for reconstruction<sup>[7,8]</sup>.

Reconstruction of soft-tissue defects of the posterior trunk can constitute a challenge for plastic surgeons. Reliable axial pattern flaps for local tissue transfer and recipient vessels for microsurgical reconstruction are scant<sup>[9]</sup>, the wound is often deep and with irregular three-dimensional contour<sup>[10]</sup>. Inadequate amounts of soft tissue can lead to contracture during the healing process, compromising trunk and upper extremity function. Moreover, the exposure of spinous processes may lead to ulceration or pressure sores after soft tissue coverage, so they should be readily removed in order to avoid such complications.

Due to the rich random vascular network multiple local flaps are possible; fasciocutaneous flaps may be raised based on septal and fascial perforators of the axillary subscapular trunks and the posterior intercostals arteries. These flaps provide missing soft tissue for upper-back moderate size defects. Nevertheless, the dorsal trunk hosts several muscles that may be transferred as pedicled flaps such as the latissimus dorsi or the trapezius. Moreover, in selected cases free flaps with vein graft or loops may be used<sup>[5-11]</sup>.

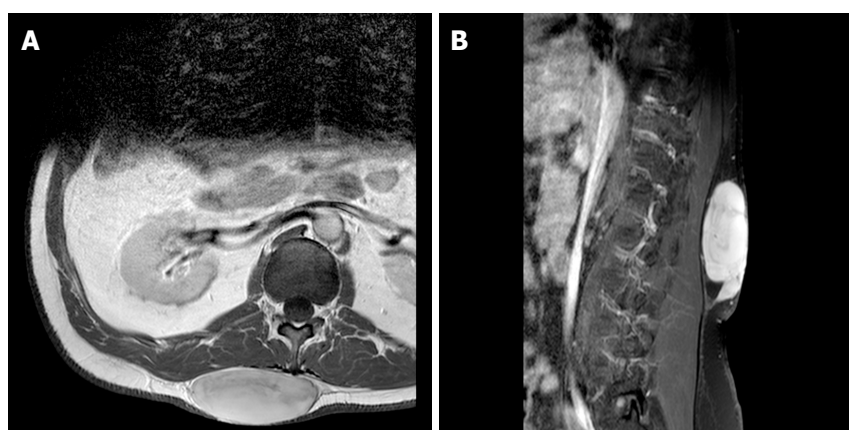
Here we present the case of a patient undergoing bilateral reverse latissimus dorsi myocutaneous (RLDM) flap reconstruction after wide excision of a primary DFSP of the middle back.

## CASE REPORT

A 48-year-old man presented with a painless superficial lesion of the mid-back that had been slowly enlarging for the previous 3 years [Figure 1]. He had no family history of cancer and the past medical history was unremarkable except for hypertension. He had never been a smoker. The clinical examination revealed a large raised lesion, measuring 16 cm × 14 cm × 6 cm in the middle of the back, extended from the scapula tip to the iliac crest edge (T12-L3). The lesion was barely mobile and hard. A pink plaque-like thickening was



**Figure 1.** A 48-year-old man with a dermatofibrosarcoma protuberans measuring 16 cm × 14 cm × 6 cm was present on the mid back



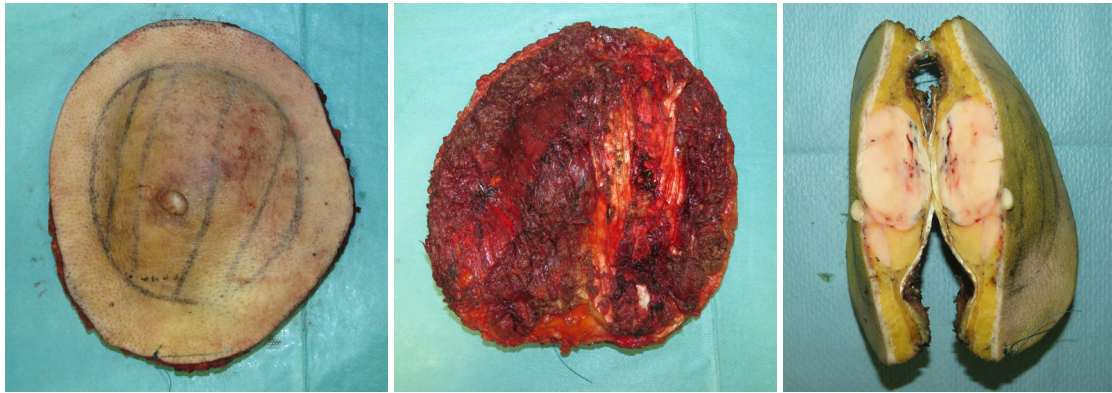
**Figure 2.** Magnetic resonance imaging showing lesion extent

present in the middle of the lesion. Contrast-enhanced magnetic resonance imaging showed an expansive subcutaneous lesion with no infiltration of deep soft tissues [Figure 2]. The thoracoabdominal computed tomography-scan did not show any other lesion. The patient underwent a percutaneous punch biopsy which revealed a neoplasia composed of CD34-positive spindle cells without atypia or necrosis and with scant mitosis. A diagnosis of DFSP was made.

The flaps were drawn with the patient in a standing position. The resection area measuring 22 cm × 20 cm was outlined on the back region (lesion: 16 cm × 14 cm, 3 cm oncologically safe distal resection margins). A bilateral RLDM flap was marked, each measuring 24 cm × 10 cm, with its long axis drawn horizontally.

During surgery, the patient was placed in the prone position. First, the tumor was resected with wide margins [Figure 3], encompassing the fascia and superficial layer of the corresponding underlying muscles: the middle and lower part of the right and left latissimus dorsi muscle, and part of the sacrospinalis muscles bilaterally were partially resected. Also the apex of T10-L2 spinous processes were removed. After the excision, a full-thickness defect measuring 22 cm × 20 cm remained in the middle-lumbar back region [Figure 4]. The size of the two RLDM flaps were reassessed according to the size and shape of the defect. The musculocutaneous flaps, measuring 24 cm × 10 cm, were designed on the superolateral part of the back, between T8-T11 in both sides. The skin and subcutaneous tissue were cut down to the latissimus dorsi





**Figure 3.** The tumor was widely resected. Intraoperative specimen



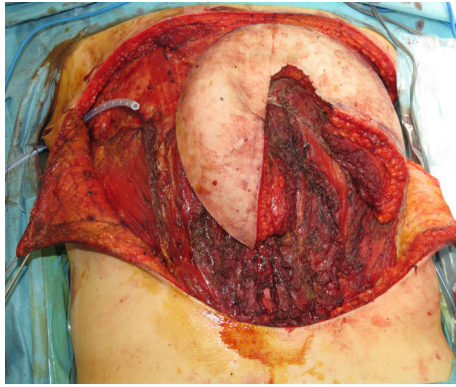
**Figure 4.** Wound defect after wide local excision of dermatofibrosarcoma protuberans that measured 22 cm × 20 cm in diameter

muscle, and the flaps were harvested between the latissimus dorsi and the serratus anterior muscles. The thoracodorsal neurovascular bundle was identified, ligated and divided with preservation of the vessels and nerve distributing to the serratus anterior muscle. The myocutaneous flaps were freed from the underlying chest wall along the superior and lower borders of the muscle, preserving dorsal intercostal perforating vessels. When the harvesting was close to the paraspinal region, multiple paraspinal perforators of the posterior intercostal arteries could be seen entering the deep surface of the muscle. We based the two flaps on the 9th and 10th intercostals perforators, in order to allow flap transfer without restriction. The two flaps were transposed to the defect and sutured together [Figures 5 and 6]. The donor sites were closed directly. Four drain tubes were placed (2 for the flap donor sites and 2 for the lumbar region).

The patient was kept in a prone position in bed to reduce the tension of the flaps for 2 days. Peri-operative antibiotics were given. He was discharged after 7 days. Drain tubes were removed on the 15th day after the operation. The final pathology showed a completely excised DFSP with clear margins all around. No further therapies were needed. Twelve months after surgery the patient has no evidence of disease recurrence [Figure 7]. The range of motion of shoulder joints and arms were not impaired after surgery. The initial flaps bulging gradually resolved.

## DISCUSSION

The thoraco-lumbar superficial tissues are relatively thick, strongly adherent to the underlying layers, and relatively inelastic. Depending on the extent of the defect and adjacent structures involvement, a variety of



**Figure 5.** A bilateral reverse myocutaneous latissimus dorsi flap measuring 24 cm × 10 cm has been raised after tumor resection. Flaps ready to be rotated



**Figure 6.** Immediate postoperative result



**Figure 7.** Postoperative picture 12 months after surgery with stable and durable coverage of the wound

options can be considered for closure of posterior trunk defects. For small wounds that can be closed tension-free, it may be possible to bring wound edges together for primary closure. This is particularly true when resection is superficial and no vital structures are exposed. Once a large area of tissue has been harvested, however, direct closure becomes more difficult. When underlying vessels, nerves, tendons, ligaments, or even bone have been removed, primary closure is not advisable. Not only it could be impossible to advance flaps far enough to achieve closure, but even if the near tissue might be undermined to allow wound edges to close, the lack of elasticity in the resulting scar tissue is at high risk of causing problems. Furthermore, STS surgery may often result in large composite tissue defects, in which functional structures are frequently exposed and susceptible to infection and mechanical trauma. Therefore, reconstruction of complex defects requires durable and stable coverage of vital neurovascular and bony structures. The posterior trunk soft-tissue defects can be reconstructed by local skin flaps, fasciocutaneous flaps, perforator flaps, muscle or musculocutaneous flaps and free flaps. Each option has its own advantages and disadvantages.

The abundance of perforating vessels in the posterior trunk offers multiple options for random pattern perforator reconstruction<sup>[12]</sup>; however the use of these flaps is highly dependent on the quality of the surrounding tissue that might be compromised due to radiation and scarring. Compared with myocutaneous flap, there is no muscle composition in perforator flap. Moreover, these flaps are usually thin and not suitable to fill dead spaces. Meanwhile, tedious dissection of the perforators and possible herniation after surgery can sometimes hinder the wide use of perforator flap in lumbar defect reconstruction<sup>[13]</sup>. In these cases the use of muscle or musculocutaneous flaps is advisable.

Myocutaneous flaps are a reliable source of tissue for coverage. The major advantages of myocutaneous flaps are successful wound healing, closure of dead space, and the use of well-vascularized tissue<sup>[14]</sup>.

In the trunk, the pedicled latissimus dorsi flap is usually used for neck, upper back, and thoracic wall reconstructions. The reverse latissimus dorsi flap was indicated for mid/lower back and upper buttock reconstructions.

In 1906, the Italian surgeon Tansini<sup>[15]</sup> firstly described the utility of the pedicled latissimus dorsi flap for chest wall defects reconstruction after radical breast amputation. The latissimus dorsi muscle flaps offers great variety and options to cover large defects in the mid-thoracic and upper-thoracic posterior trunk. It can be raised up to 30 cm × 40 cm in size and may be transferred as a muscular (eventually with additional skin grafts) or myocutaneous flap. The latter option makes postoperative monitoring considerably easier. It originates at the thoracal spinous processes, inferior ribs, and iliac crest. The latissimus dorsi muscle inserts at the intertubercular groove of the humerus. Its dominant vascular pedicle is the thoracodorsal artery, which is part of the scapular vascular system, whereas the non-dominant pedicles origin from intercostal and lumbar arteries. It is therefore a class V muscle according to the popular classification of Mathes and Nahai<sup>[16]</sup>; thus, survival of the flap may also be based on the non-dominant pedicles<sup>[17]</sup>, which would allow utilization of this flap as a “reverse” flap in order to cover contralateral or more caudal defects<sup>[9]</sup>.

The RLDM flap receives its blood supply from the perforating branches of the intercostal and lumbar arteries<sup>[17,18]</sup>. During flap elevation, all medial muscle origin from the spinous processes of the vertebrae can be released, facilitating inferior transposition of the flap. The function of the muscle part in the RLDM flap is the enhancement of bulkiness of the flap in obliterating the dead space. Moreover, multiple perforators of the medial branches of the posterior intercostal vessels and lumbar arteries can be visualized in the midline of the back. Stevenson *et al.*<sup>[17]</sup> have demonstrated, that the RLDM flap is mainly nourished by 3 vessels originating from the 9th, 10th, and 11th intercostal arteries and veins located 5 cm from the midline of the back. These perforators can be preserved if they do not limitate flap transfer, otherwise they can also be dissected. Meanwhile, Maruyama and Iwahira<sup>[19]</sup> reported that the dorsal perforating pedicle from the 9th

intercostal vessels can be divided so as to obtain sufficient pedicle length and found that flap survival was not altered. If the flap vascularity is found to be adequate, then perforators can be divided, facilitating further caudal and medial transposition of the flap. During the tumor resection, the surgical oncologist should always be reminded to preserve the integrity of the perforators of the intercostal arteries whenever possible from an oncological point of view.

The bilateral RLDM flap is suitable to cover thoraco-lumbar defect, until L2-L3 but not the sacral region; as matter-of-fact longer flaps could have distal viability and ischemic problems. On the other hand it is not possible to cover defect wider than 25 cm because larger flaps could have rotational problems.

In our opinion the bilateral RLDM flap is the more reliable surgical option to close a large and deep defect of the mid-low back as in the case described.

## DECLARATIONS

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### Authors' contributions

Acted on the demolition surgical step and subsequent patient oncological follow-up, deepened the oncological issue of the paper: Gronchi A, Callegaro D

Played a major role in the reconstructive surgical and scientific field: Bonomi S, Sala L, Cortinovis U

Planned the operation, the writing and the final review of the manuscript: all authors

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None.

### Conflicts of interest

There are no conflicts of interest.

### Patient consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

### Ethics approval

Ethical approval was not needed for this case report.

### Copyright

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Original Article

Open Access



# Evolution of hair transplantation

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## Abstract

**Aim:** Numerous non-surgical methods and surgical options are available for the solution of baldness in the practice. Technology provides mighty weapons in this field. Thus, individualized solutions are best carried out with well-trained and qualified practitioners. Here, a modification of follicular unit extraction, direct hair implantation is introduced with previously licensed unique pens.

**Methods:** Follicular unit extraction and direct hair implantation methods were carried out in 207 hair transplantations between January and December of 2014. The nests for the grafts were created via pieces of hand-cut razor blade in follicular unit extraction. In addition, a new modification of follicular unit extraction, direct hair implantation, is done via pens that are produced for this purpose.

**Results:** Thirty-eight direct hair implantations were performed in addition with 169 follicular unit extractions. An average number of 2973 grafts were transplanted. Mean operation time was calculated as 385 min.

**Conclusion:** Hair transplantation is still the best solution for hair loss. In conjunction with the surgery, the addition of non-surgical interventions may give a better result to the patient. On the other hand, the promising results in the field of regenerative medicine with cell-based solutions may alter hair transplantation and change the options solely into this field.

**Keywords:** Hair transplantation, direct implantation, razor, nest



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## INTRODUCTION

Hair transplantation has gone through a big revolution with the pioneers in this field<sup>[1-5]</sup>. To achieve a good cosmetic result in hair transplantation, a natural-looking hairline with adequate density shall be established. There are numerous modifications of defined techniques with each one explaining and suggesting verified solutions.

This note describes the available options in hair loss surgery and the concepts of non-surgical approaches, and an experience is shared with a few patients grafted via direct hair implantation (DHI) method. Moreover, to us, this is the only study demonstrating the opening of the nests with sliced razor blade just before the implantation of the hair follicles. Thus, the evolution with the future of hair transplantation is summarized as well. Moreover, this article focuses on the surgical techniques. The medical management of hair loss is out-of-scope.

## METHODS

Between January and December 2014, hair transplantation was carried out in 207 patients. The patients with beard and/or moustache transplantation, multisession transplantations and female patients were excluded. The harvested grafts out of the scalp were also not evaluated.

All the procedures were carried out under local anesthesia. The hair was cut 1-2 mm in length. Micromotor system was used in the harvesting of the hair follicles<sup>[6]</sup>. This system consists of punches attached to the hand-piece of the micromotor system (1500-3000 rpm). Punches were chosen according to the diameter of the follicles ranging between 0.8 and 1.2 mm. Harvesting of the follicles was handled in supine position. With the aid of the sharp punch attached to the motorized system, the follicle was detached from the surrounding tissue (approximately 3-4 mm in depth=deep dermis layer). Later on, it is released manually with fine-curved microforceps produced for this purpose. Temporooccipital region was used as donor site.

The harvested grafts were aligned in Petri dishes with cooled saline (4 °C). A dressing is made with sterile saline coated gauze to the donor area and the patient was turned to the supine position.

In follicular unit extraction (FUE) technique, razor blade that was cut into pieces was used to open the nests in vertically-oriented fashion that are to be grafted [Figure 1]. With this, we aimed to diminish the incarceration of the implanted follicles. However, in DHI technique, the grafts were loaded to the DHI pens with one charged staff for this purpose [Video 1]. The implantation of the follicles was carried out in accordance with the natural hair angles by the author under loupe magnification [Videos 2 and 3].

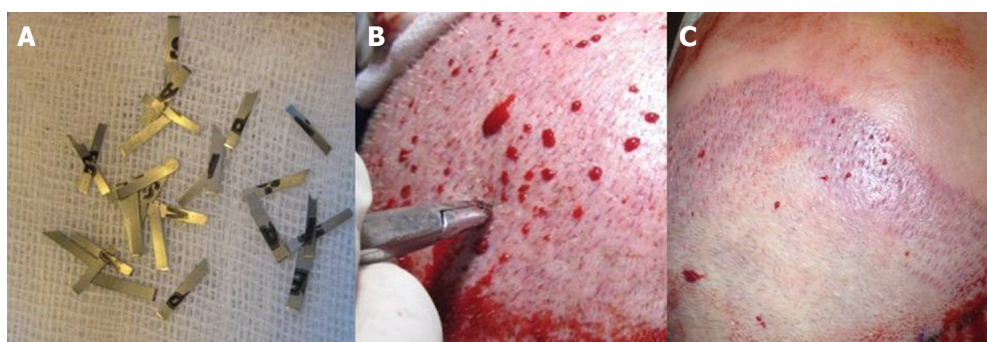
After the entire implantation was established, the patient was dressed with antibiotic coated, moisturized gauze to both donor and recipient areas that were removed 3 days later at which the first hair washing would also be carried out. The patients were recommended to have their first hair-cut 15 days later.

## RESULTS

A total number of 615,400 grafts were transplanted in 207 patients. Of these, 38 were DHI (19%) and 169 had FUE (81%).

Patients were classified as Norwood III, IV and V in 1 (0.5%), 30 (14.5%) and 176 (85%) patients, respectively. The main reasons of hair loss were androgenetic alopecia and cicatricial alopecia in our patients.

An average number of 2973 grafts were transplanted. Mean graft numbers transplanted in FUE and DHI methods were 2982 and 2934, respectively. The mean density was observed around 75 units/cm<sup>2</sup> for DHI technique and 50 units/cm<sup>2</sup> for FUE method.



**Figure 1.** (A) The razor blade is cut into pieces with 1-2 mm sharp edges; (B) perforation is carried out with these pieces held by clamps; (C) these nests are in a vertically-oriented fashion that are ready now for grafting

**Table 1. The distribution of the patients**

Month of 2014	Number	FUE	DHI	Norwood			Time (min)	Graft
				III	IV	V		
January	11	11			5	6	359.2	2904.5
February	15	15			1	14	353.7	2733.3
March	15	15		1	2	12	346.3	2693.3
April	15	14	1		7	8	354.0	2793.3
May	14	13	1			14	369.6	2842.8
June	19	17	2			19	357.1	2784.2
July	21	20	1			21	349.8	2845.2
August	20	12	8		3	17	422.0	3145.0
September	15	10	5		2	13	441.3	3306.6
October	19	12	7		1	18	392.1	3173.7
November	21	16	5		3	18	407.6	3157.1
December	22	14	8		5	17	437.7	3118.2
Mean	17.25	81%	19%	0.5%	14.5%	85%	385.0	2973.0
Total	207	169	38	1	29	177		615,400

FUE: follicular unit extraction; DHI: direct hair implantation

Mean operation time was noted as 385 min in which mean FUE and DHI times were calculated as 373 and 437 min, respectively. The patients were followed-up between 1 and 5 years. Table 1 describes the distribution of the patients.

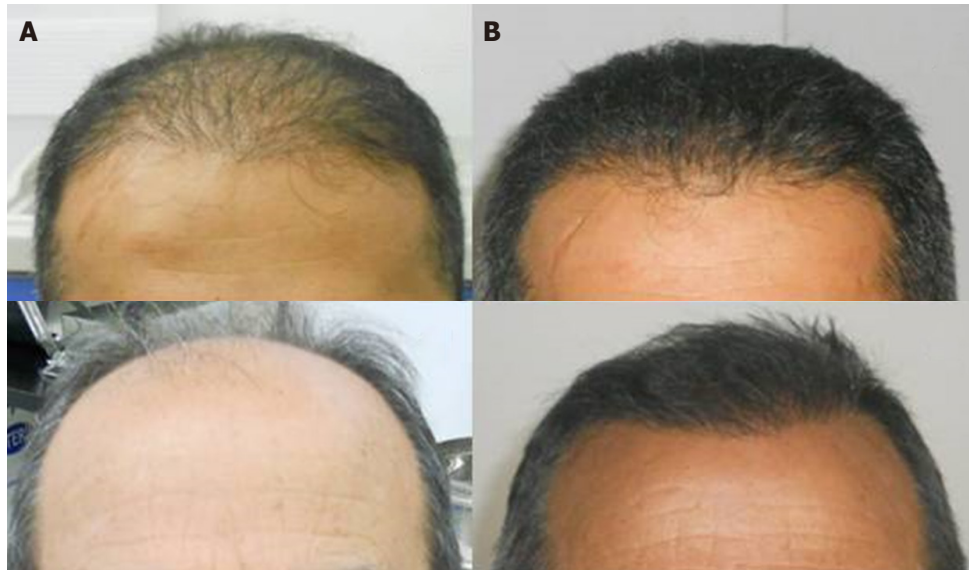
None of the patients had infection. Inclusion cyst formation was observed in 4 patients who were treated successfully.

A few results with DHI technique are presented in Figures 2 and 3.

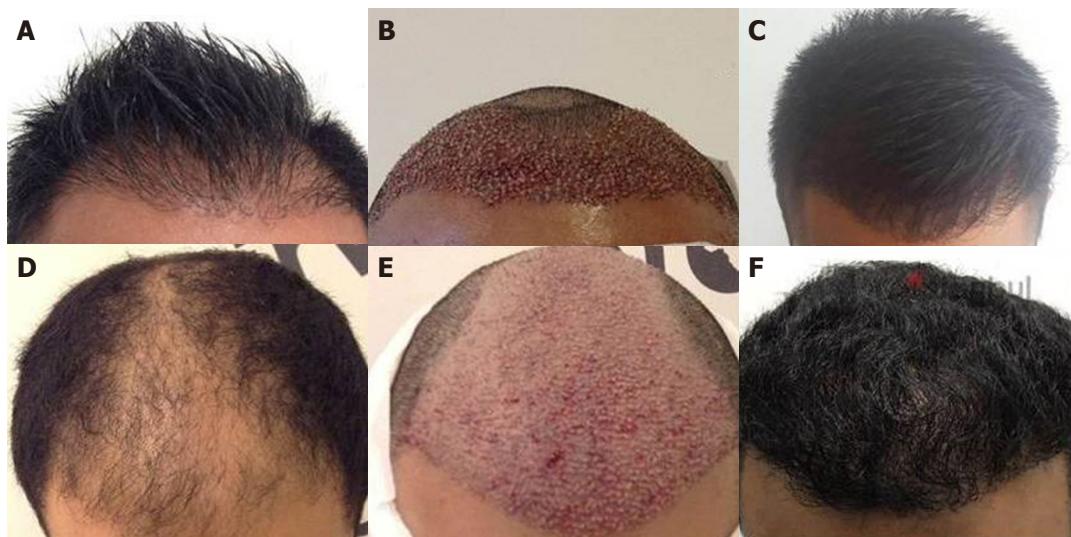
## DISCUSSION

Male type baldness may cause a negative effect on individual's self-esteem. Hair transplantation gives a unique permanent solution for those patients.

Non-surgical therapies for hair loss can be used mainly in early phases. Minoxidil, finasteride, dutasteride, spironolactone or cyproterone acetate can be prescribed in selected patients with temporary actions<sup>[7-10]</sup>. Moreover, low-level light or laser therapy can be utilized in patients with early-phase hair loss where the practitioner may choose home-use and/or in-office systems. It is known that prostaglandin analogues such as prostaglandin F2a and prostaglandin E2 promote hair growth in both mice and human follicles<sup>[11]</sup>. In practice, latanoprost (a prostaglandin F2a analogue) is a solution that provides a significant increase in hair



**Figure 2.** (A, B) A 44-year-old male patient with Norwood type III patient. (A) Preoperative appearance; (B) postoperative 1-year appearance. (C, D) A 51-year-old with Norwood type IV patient. (C) Preoperative appearance; (D) postoperative 1-year appearance



**Figure 3.** (A-C) A 32-year-old male patient with Norwood type III patient. (A) Preoperative appearance; (B) immediate appearance of the patient after transplantation; (C) postoperative 1-year appearance. (D-F) A 38-year-old with Norwood type V patient. (D) Preoperative appearance; (E) immediate appearance of the patient after transplantation; (F) postoperative 1-year appearance

growth<sup>[12]</sup>. Mesotherapy and platelet-rich plasma can be utilized in patients needing additional therapies in the enhancement of hair growth. Mesotherapy consists of superficial injections of pharmaceuticals and vitamin compounds to the follicles. Platelet-rich plasma (PRP) is used in almost every section of the medicine and includes several platelet-derived factors<sup>[13]</sup>. It is proven that PRP injections enhance hair growth in transplanted follicles<sup>[14-16]</sup>. Nevertheless, more studies are needed to evaluate PRP as a hair loss therapy.

Since the concept of “donor dominance” in male pattern hair loss was first published in 1959, it is still not clear why the occipital hair is spared<sup>[2]</sup>. The most accepted reason seems that occipital scalp is not androgen dependent<sup>[2]</sup>. Whatever the reason is, it is the feature that occipital hairs have permanent serves for hair transplantation in both female and male pattern hair loss<sup>[2]</sup>.

The permanent solution for hair loss can be achieved with hair transplantation. The grafts harvested from the donor area are transplanted to the recipient area in qualified, well-trained hands and at optimum conditions. Nevertheless, graft viability depends on several factors determined by the hair type, delicate technique, physical trauma, vascular factors, biochemical injury, infection, patient disruption, and idiopathic reasons<sup>[17]</sup>.

Hair transplantation is comprised of consecutive steps: planning, preparation, anesthesia, graft harvesting, secure of the harvested grafts, graft transplantation, and dressing. Each step may be individualized in practice. Planning of the patient consists of some blood tests, a thorough history of medical situation, and marking. After shortening of the hair if needed and preparation with antiseptic solutions, anesthesia is carried out. Mostly, local anesthesia is preferred; however, regional anesthesia or local anesthesia with sedation can be chosen. When an entire anesthesia is established, a tumescent solution is injected both to the donor and recipient area. This enables an expansion to harvest the follicles in donor area and graft them easily. The survival of the harvested graft is dependable on temperature, hydration, infection, and trauma<sup>[18]</sup>. The surgeon and staff shall not transect or crush and dehydrate the follicles during the procedure. This meticulous technique will ensure the best outcome. It is also advised to maintain the follicles that are to be transferred in a cold solution in order to reduce the ischemia and reperfusion injury. Some holding solutions exist such as intravenous holding solutions (e.g. normal saline, lactated Ringer), cell culture media (e.g. Dulbecco's Modified Eagle Medium, Williams E) and hypothermic holding solutions (e.g. HypoThermosol, BioLife Solutions, Bothell, WA)<sup>[17]</sup>. Nevertheless, stored grafts are mostly kept cold in ice blocks or cold solutions with the temperature rate between 4 °C and 10 °C. Harvesting of the follicles can be done via manually or motorized systems. The practitioner can choose sharp or dull tipped punches with a wide variety of diameter and bevel type. Eventually, the follicles are transplanted delicately into the recipient area with appropriate angle to establish similar grow pattern with the normal hair. Nests for the grafts that are to be implanted can be created via a sharp-punch and needles or scalpels in selected sizes<sup>[6,19-21]</sup>. On the front line, we prefer to make the transplantations in a zig-zag fashion to achieve a natural-looking frontal hairline design<sup>[19]</sup>. The number of hair units required for the recipient size can be calculated by the formulas defined for both frontal and vertex regions<sup>[22,23]</sup>. The normal hair density is around 100 units/cm<sup>2</sup><sup>[24]</sup>. In general, the density achieved with hair transplantation is approximately 30-40 units/cm<sup>2</sup>. Higher density called as dense packing (up to 60 units/cm<sup>2</sup>) can be achieved with high viability rates<sup>[21,25]</sup>.

Follicular unit transplantation (FUT) is a widely accepted technique in hair transplantation<sup>[26]</sup>. In this method, the donor area is shaved and an elliptical excision is made for hair follicle harvesting. The dimensions of the ellipse are calculated up to the recipient area that is to be grafted. The donor area is closed meticulously to reduce the scar formation. The collected hair-bearing skin is dissected under magnification and the extra tissues of the hair root as well as the epithelium around are removed as much as possible. The grafts containing clusters of one, two and three follicles are put into Petri dishes containing cooled saline. Later on, the grafts are inserted appropriately to the recipient area.

In contrast to FUT, FUE is a technique with the extraction of follicular units with one or two roots using circular punches. Okuda was the first that used self-made sharp circular punches in various diameters (1-4 mm)<sup>[27]</sup>. He proposed to use 2-4 mm punches with regard to 1 mm because, according to him, the transection rate was interestingly high in 1 mm harvests. In the market, there are several FUE donor harvesting devices available; of which some are hand-held punches, some are motorized and some are single user-directed robotic system which is also known as Surgically Advanced Follicular Extraction and ARTAS robotic systems<sup>[28-32]</sup>. Success with FUE depends on being able to predictably dissect excellent-quality grafts with minimum transection rates from the donor region<sup>[5,29,33,34]</sup>.

Ominigraft (Mecicamat S.A., Malakoff, France) has been introduced to optimize mini and micrograft transplantation<sup>[29]</sup>. This device consists of three major parts: hairtome; a hand-held pneumatic graft



implanter; and a hollow-shafted micromotor handpiece with a punch blade in 0.8-1.25 mm. The transection rates and the operation time are significantly lower with this device.

There are some advantages and disadvantages of FUE over FUT which was very well discussed previously<sup>[30]</sup>. FUE needs longer learning curve and operation time, excellent hand-eye coordination, patience, stamina and hair must be short enough for appropriate harvesting. Moreover, the practitioner may be a candidate for potential repetitive motion disorder in time<sup>[30]</sup>. Besides, the outcomes of FUE may be better and the number of follicles transferred may be higher when compared with FUT. In addition, FUE gives a scarless solution for the patients insisting on not accepting an incision.

Another hair transplantation method, direct hair transplantation, is presented to attenuate the transit time which may reduce the graft survival<sup>[8]</sup>. Here, follicles are implanted as soon as they are harvested. This technique was found a simple and feasible modification of FUE.

An automated FUE technique, Neograft<sup>®</sup>, enables a suction-based follicle harvesting with one or two-step extraction technique. The follicles are collected in a suction canister in which they are transplanted later by using a hand-piece with 0.8, 1 and 1.2 mm punches that are produced specifically for this purpose. The motor is silent and vibration free; however the steep learning curve and the cost of the machine are the disadvantages<sup>[35]</sup>.

Microrefined microfollicular hair transplantation is a recently described method in which anterior hairline is constructed with FUE whereas the bald area is transplanted with FUT including strip harvesting (with beveled incisions) and slivering of the strip under magnification. The author proposes the graft transection rate to nearly 0%<sup>[19]</sup>.

DHI, a modified version of FUE, has similarities with FUE in hair follicle harvesting, whereas the implantation of the follicles is carried out with unique instruments that is licensed by Konstantinos (US 8,801,743 B2) and produced specifically for this purpose. The needle of the pen may vary in size; since there are 0.40-2 mm oblique-cut needles in the market. After follicle harvesting, each pen is loaded with a micrograft containing 1 to 3 hair follicles and subsequently implanted to the recipient area that was not previously perforated. This technique allows the practitioner graft the recipient area denser and gives less trauma and bloodless field when compared with FUE. Moreover, this procedure lacks additional punching for grafting as noted in other transplantation techniques. On the contrary, the learning curve is high meaning that this surgery needs more qualified personnel per patient. In addition, the procedure is carried out with 3 or 4 personnel, because every stage is assigned to a unique staff which means that the room is more crowded than the other techniques. The pens and so this procedure are relatively expensive when compared to FUT or FUE. Nevertheless, follicle harvesting is significantly cheaper than robotic systems.

Complications after hair transplantation can be placed in the following categories: (1) standard surgical risks; (2) physician planning errors; (3) physician technical errors; (4) patient compliance factors; (5) patient physiology factors; and (6) miscellaneous causes<sup>[36]</sup>. In addition, we may observe some site-specific complications after all including donor and recipient site problems<sup>[36]</sup>. Donor site complications include wide variety of unwanted scar formation, donor-site depletion, wound dehiscence, necrosis, effluvium (shock-loss), hypoesthesia, neuralgia and neuroma and hematoma. Recipient site complications may be comprised of hairline location or shape error, progression error, graft type error, graft placement error, hypopigmentation, hair color mismatch, chronic folliculitis, necrosis, effluvium, ingrown hairs, cysts and low graft yield.

Animal studies reveal creation of human follicles from cultured dermal and epidermal cells in a mouse model<sup>[37]</sup>. A revolutionary breakthrough in this field is the discovery of induced pluripotent stem cells enabling

to reprogram differentiated fibroblasts into an embryonic stem cell state<sup>[38,39]</sup>. A recent study exhibits the creation of a bioengineered hair follicle germ using embryonic skin-derived epithelium and mesenchymal donor cells where the transplanted germ integrate to the host epithelium producing a complete functional hair<sup>[40]</sup>. A recent study revealed the generation of folliculogenic human epithelial stem cells from induced pluripotent stem cells<sup>[41]</sup>. The regenerated hair follicles possessed a KRT15+ stem cell population and produced hair shafts expressing hair specific keratins. These results suggest an approach for generating large numbers of human epithelial stem cells for tissue engineering and new treatments for hair loss, wound healing and other degenerative skin disorders.

Forthcoming studies will ensure better results. As the technology contributes to the medicine, it is possible that the whole process will be carried out entirely with robotic and automated systems. Indeed, the future may give the solutions by solely cell-based applications enabling hair growth without a surgery. Up-to-date, I believe that the combination of the surgical methods with the help of additional options may give the best option for the patients to re-gain their natural-looking hair with adequate density.

## DECLARATIONS

### Authors' contributions

Concept, design, resource, data collection and processing, and manuscript writing: Kayiran O, Cihandide E  
Supervision, literature search, analysis and interpretation: Kayiran O

### Data source and availability

Data in this study were derived from searches of the PubMed database.

### Financial support and sponsorship

None.

### Conflicts of interest

There are no conflicts of interest.

### Patient consent

Consents from all of the patients were established prior to submission.

### Ethics approval

Local Committee of Ethics approved this study with SAH-17-214.

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Review

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# Reviewing immunosuppressive regimens in animal models for vascularized composite allotransplantation

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## Abstract

The development of vascularized composite allotransplantation (VCA) and its clinical need has led to the need for more animal models to study and perform the research required to further this specialty in terms of functional recovery and immunomodulatory improvements. Much of the animal models are reported in individual series in the literature but there has not been a review as such of these models. Here we present a compilation of the animal models reported in the literature thus far in VCA. A comprehensive review of the literature was performed for any studies which involved the use of animal models in various aspects of VCA research. The models were organized according to the type of VCA transplant, whether they were orthotopic or heterotopic, immunosuppressive regimen each study used and investigation purpose. Twenty-one facial transplant models were reported, 3 abdominal wall transplants, 4 penile transplantations, 21 uterus transplantations, 12 hindlimb transplantations and 4 myocutaneous flap transplantation animal models were reported. Primates, swine, rats, mice, rabbits, sheep and dog animal models in VCA were also reported. The most used immunosuppressive drugs are calcineurin inhibitor such as cyclosporin A and tacrolimus in these VCA animal models. They can significantly suppress lymphocyte function by blocking the phosphatase activity of calcineurin of lymphocytes. They are sometimes used combined with mycophenolate mofetil or steroids or antilymphocyte serum. The review of existing animal models will allow further research to be focused in other areas of VCA where there is a current paucity of literature. The immunosuppressive regimens used in each animal model can also be reviewed to determine which regimen works in which type of animal model which will save time and resources for future research.

**Keywords:** Animal models, vascularized composite allotransplantation, immunosuppressive regimens



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## INTRODUCTION

Vascularized composite allotransplantation (VCA) is an up and coming clinical modality in the realm of reconstructive microsurgery. Being able to replace tissues like for like *en bloc* is absolutely crucial and empowers the surgeon to achieve the most optimal outcome. However, the greater goal of VCA is the ability of the reconstructive surgeon to not only restore form but also function. Functional restoration could arguably be the epitome of reconstruction where the quality of lives are improved not only from external appearance but rather also allow the patients to get back to their activities of daily living.

Trauma remains a significant burden in today's society with many resulting in soft tissue defects. Other causes of soft tissue defects include congenital deformities and neoplastic conditions. Much of the previous methods for reconstruction include prosthesis or sequential flaps that obliterate and attempted to restore the form of a tissue defect. However, this is often inadequate and is lacking in function. VCA differs from solid organ transplantation (SOT) where tissues of varying antigenicity are transplanted *en bloc*. This results in issues of varying rejection rates. In particular, skin which is often a component of VCA transplants such as the hand and face has the highest antigenicity of all body tissue types<sup>[1]</sup>. As such, rejection faced by skin component is high and the recipient or patient is dependent on a high constant level of immunosuppression. Skin contains dendritic cells such as Langerhans cells that have strong immunogenic properties and it has been shown that some of these cells of donor origin reside in the epidermis decades after the transplantation<sup>[2]</sup>.

Chronic immunosuppression itself carries deleterious effects in the long run. Patients face opportunistic infections and an increased risk of malignancy from the decreased immunity that is usually present to prevent and take on a surveillance role. As such, one has to carefully weigh up the pro and cons when deciding the perform VCA on a patient. The patient should also be able to finance a lifelong requirement of immunosuppressive drugs which are often costly and have a high dropout rate due to the side effects.

Much of the research at present in VCA is on better improving the safety profile of such procedures, especially with the need for the improvement in immunosuppressive regimens. By decreasing our reliance on immunosuppressive drugs, we increase the acceptability of such a procedure as the downside of immunosuppression can be deleterious. The ultimate goal in transplant science would be to achieve allograft tolerance. Tolerance to an allograft is a phenomenon where the recipient body does not recognize the foreign antigens from the donor and hence will accept the graft. Immunosuppressive drugs can hence be reduced or even omitted. In order for this process to occur, immunological manipulation and re-education of the recipient's immune system has to occur. Several strategies already show promise in this respect and will be discussed in this article. Varying tissue types also have varying levels of inducibility with regards to tolerance formation. In particular, due to the varying tissue types of differing antigenicity in VCA, tolerance is often difficult to achieve.

### A brief history of VCA

VCA has come a long way since its first conception back in AD 348. It has always been a goal of mankind to be able to replace like with like where allograft transplantation *en bloc* of a gangrenous leg of an elder church sacristan was performed by two brothers known as the miracle of Cosmas and Damian<sup>[3]</sup>. Previously known as composite tissue allotransplantation (CTA), VCA in the past started off with transplantation between identical twins which obviated the need for immunosuppression, which is the bane of VCA and is a focus of intense research at present.

The first-hand allotransplantation was performed in 1964 in Ecuador where a first generation drug regimen was provided. This included steroids and azathioprine initially. However, the hand allograft still was rejected 2 weeks later. Allografted tendons had been performed using non-vascularized techniques to replace lost or nonfunctional upper extremity flexor tendons but end results were unacceptable due to the lack of viability

of the grafts resulting in rupture as well. With the limited knowledge in immunological manipulation and the adverse effects that happened, further VCA cases were put on hold. It was not until the discovery and development of cyclosporin A during kidney transplantation that it was applied to VCA in the 1980s where immunosuppression finally became more effective. The first successful hand transplant then was carried out in 1998 in France. However, the patient refused to adhere to the immunosuppressive regimen due to personal reasons and compliance issues and hence the arm was again amputated almost 3 years after surgery. The first vascularized tendons were performed by Guimberteau *et al.*<sup>[4]</sup> where two allotransplantations of digital flexor tendon apparatus were collected from a living nonrelated donor and from a deceased donor. The tendons were then revascularized using the recipient's ulna vessels and ultimately received acceptable using multiple doses of cyclosporin A<sup>[5]</sup>. The first successful face transplant occurred in 2005<sup>[6]</sup> and since then, several countries have followed suit.

### **An overview of clinical VCA cases to date**

Only a few specialized centers in the world with the capability and infrastructure for performing a VCA procedure. As such, an important source of data is the International Registry on Hand and Composite Tissue Transplantation (IRHCTT), which is a voluntary registry that collects clinical information on VCAs. The most recent report of the IRHCTT was published in 2010 and provides follow-up data on 49 hand transplants in 33 patients. Thus far, there have been 89 hand transplants performed since 1998. The United States currently has the largest number of cases, followed by China and Poland.

## **TYPES OF VCA ANIMAL MODELS REPORTED**

### **Face transplant models**

A variety of animal models have been used in VCA experiments with the majority being orthotopic face transplants. The animal models were performed in animals such as primates, swine, sheep, canine, rabbit, rats and mice. Different compositions of face allograft comprising of bone, nerve and soft tissue in each animal model have been reported in the literature which has varying levels of antigenicity. As such, each report has used varying types of immunosuppression, which is also dependent on the response of each animal type and to the type of immunosuppressive drug. The transplantation of each allograft can be considered orthotopic if the graft replaces the original site of the donor, i.e., the face, or heterotopic if the allograft is placed in a distant site different from the original area. Orthotopic transplants in these animal models are mostly for assessing not only the rejection process but also the functional restoration of the allograft. Heterotopic allografts, however, are used more for assessing the degree of rejection but normally do not carry an assessment of functional recovery.

In a primate model, heterotopic transfer of a facial transplant including the mandible was transferred from MHC mismatched M fascicularis monkeys. Anti-thymocyte globulin (ATG) was used as an induction regimen with tacrolimus and rapamycin in combination as a maintenance regimen.

Two reports using swine and sheep models were used with facial allografts including bone. However, no immunosuppression was used in these models and was more for the surgical technique of producing such models.

Four canine models were used in mismatched donors to beagle dog recipients. All reports were orthotopic and involved a hemifacial transplantation. With these reports, 2 reports utilized cyclosporine and steroids as maintenance immunosuppression. Two other reports used tacrolimus as maintenance immunosuppression and with 1 report using tacrolimus only for 7 days. One report in a rabbit model used a face and scalp transplantation model with no immunosuppression.

Eleven rat animal models for face transplant were reported in the literature. Nine of the reports were allografts and 2 were syngeneic. Ten reports were orthotopically transferred and 1 with heterogenic transplantation. Various face transplant components were reported ranging from ear, scalp, face, mystacial pad or mandible with tongue transplantation. A combination of cyclosporin A or tacrolimus was used in these animal models. Four of these reports had nerve coaptation which looked at the functional recovery in allograft especially using mystacial pad transplantation.

Two reports of murine orthotopic face transplant were reported with either a hemiface or ear allograft. No immunosuppressive regimens were used in these reports with more focus on the surgical technique of transferring an ear or hemiface. The information is presented in [Table 1](#).

### **Abdominal wall transplantation models**

Abdominal wall transplantation comprising of various tissue types also constitutes a vascularized composite allotransplantation model. All reported models thus far have been carried out in rats across MHC mismatched rats from Brown-Norway to Lewis rats. The abdominal wall transplants were orthotopic with 2 hemi-abdominal wall transplants and 1 with the inclusion of a hindlimb transplant. One report had a total abdominal wall allograft transplanted. Anti-lymphocyte serum was used in 2 of the reports for induction therapy. Two reports utilized cyclosporine and 1 in combination with adipocyte derived stem cells intravenously. The models do not include all nerve anastomoses and mixed chimerism all at once. The information is presented in [Table 2](#).

### **Penile transplantation models**

Penile allograft transplantation models have been described in four articles, all of which have been performed in rats. Two studies were syngeneic rats, 1 of which was orthotopic and 1 heterotopic. These studies were focused on the surgical model and being syngeneic grafts, no immunosuppression was used. Anastomosis of the penile artery and vein was key in each model and ensuring the conduit of the urethra was restored. The other 2 studies used allografts and heterotopically transplanted penile grafts. One of the studies used tacrolimus and the other cyclosporin A. The information is presented in [Table 3](#).

### **Uterus transplantation models**

Uterus transplantation has been touted as a method of restoring fertility but functionally must perform as required. Three articles report uterus transplantations in primates, 7 in sheep, 2 in rabbits, 6 in rats and 3 in murine models. The function of the transplanted uterus was tested in rabbits, rats and mice which were successful in 3 of the studies. In primate uterus transplantation, various types of immunosuppressive regimens were used including tacrolimus, mycophenolate mofetil and methylprednisolone as maintenance regimes. Another protocol utilized ATG as an induction agent followed by tacrolimus and corticosteroids as maintenance. The information is presented in [Table 4](#).

### **Hindlimb transplantation models**

Hindlimb transplantation has been a model to mimic hand transplantation where components of bone, muscle, nerve, fat and skin are included in a hindlimb. The animal models demonstrated here to explore the feasibility of modulating the immunosuppressive regimen in improving the viability of hindlimb transplants. When transplanted orthotopically, they also serve as a model to assess the functional recovery of the hindlimb when used for gait. The nerve recovery is crucial in improving the function of the transplanted allograft. The information is presented in [Table 5](#).

### **Myocutaneous tissue transplantation models**

Soft tissue alone with varying tissue types including fat, connective tissue and muscle are collectively known as myocutaneous flaps in free flap transplantation. The varying antigenicity of the tissue types is what constitutes

**Table 1. Facial animal models**

	Allo-transplantation	Approach	Graft	Regimen	References
Primate	Mismatched donor to recipient M. fascicularis monkey	Heterotopic	Mandibular OMC	ATG (10 to 20 mg/kg/day) induction with tacrolimus (0.2 to 0.1 mg/kg/day) and rapamycin (0.05 increased to 0.2 mg/kg/day) maintenance	[7]
Swine	Pig autotransplant	Orthotopic	Le-Fort-based maxilloface	No immunosuppression	[8]
Sheep	N/A	N/A	Hemifacial and auricle	N/A	[9]
Canine	Mongrel to Beagle dog	Orthotopic	Hemiface and scalp	CSA (6-18 mg/kg/day) and steroid methylprednisolone (4-8 mg/kg/day)	[10]
Canine	Mismatched donor to recipient Beagle dog	Orthotopic	Hemiface and scalp	Tacrolimus 2 mg/kg/day for 7 days	[11]
Canine	Mismatched donor to recipient Beagle dog	Orthotopic	Hemiface	CSA (4 mg/kg/day)	[12]
Canine	Mismatched donor to recipient Beagle dog	Orthotopic	Mandibular hemijoint	Tacrolimus 1 mg/kg/day maintenance	[13]
Rabbit	NZB to NZW	Orthotopic	Facial and scalp	No immunosuppression	[14]
Rat	BN to LEW	Orthotopic	Mystacial pad	CSA 16 mg/kg on POD 1-14, 13 mg/kg on POD 15-80, then 10 mg/kg maintenance	[15]
Rat	BN to LEW	Orthotopic	Face and scalp	CSA 16 mg/kg/day, tapered to 2 mg/kg in 4 weeks and maintained	[16]
Rat	LEW syngeneic	Heterotopic	Hemiface with mandible and Tongue	No immunosuppression	[17]
Rat	BN to LEW	Orthotopic	Auricle	CSA 16 mg/kg/day for 2 weeks and tapered to 8 mg/kg/day for 2 weeks	[18]
Rat	BN to LEW	Orthotopic	Hemifacial with mystacial region	Tacrolimus 8 mg/kg/day, tapered to 2 mg/kg/day in 4 weeks	[19]
Rat	BN to Wistar	Orthotopic	Hemiface	CSA 16 mg/kg/day for 7 days, tapered to 2 mg/kg/day for 23 days	[20]
Rat	BN to LEW	Orthotopic	Auricle	CSA 16 mg/kg/day in first week, tapered to 8 mg/kg/day and maintained for 2 weeks, then 4 mg/kg maintained	[21]
Rat	LEW syngeneic	Orthotopic	Ear	No immunosuppression	[22]
Rat	Lew-BN to Wistar-Lew	Orthotopic	Mystacial pad	Tacrolimus 6 mg/kg/day in first week, tapered to 4 mg/kg/day in second week, then 2 mg/kg/day maintained	[23]
Rat	Lew-BN to LEW	Orthotopic	Hemiface with ear and scalp	CSA 16 mg/kg/day in first week, tapered to 2 mg/kg/day over 4 weeks and maintained	[24]
Rat	BN to LEW	Orthotopic and heterotopic	Hemiface and scalp	CSA 8 mg/kg on POD 1-2, 6 mg/kg on POD 3-6, 4 mg/kg on POD 7-30, 2 mg/kg on POD 31-42	[25]
Murine	BALB/c to B6	Orthotopic	Myocutaneous hemiface	No immunosuppression	[26]
Murine	BALB/c to B6	Orthotopic	Ear	No immunosuppression	[27]

NZW: New Zealand White; NZB: New Zealand Black; BN: Brown Norway; LEW: Lewis; B6: C57BL/6; CSA: cyclosporin A; ATG: anti-thymocyte globulin; OMC: osteomyocutaneous; POD: postoperative day; N/A: not available

**Table 2. Abdominal wall animal models**

	Allo-transplantation	Approach	Graft	Regimen	References
Rat	BN to LEW	Orthotopic	Hemi-abdominal	ALS 2.5 mg induction, each CSA 16, 10 and 5 mg/kg/day for 10 days	[28]
Rat	BN to LEW	Orthotopic	Total abdominal wall	Tacrolimus 0.5 mg/kg/day maintained	[29]
Rat	BN to LEW	Orthotopic and heterotopic	Hemi-abdominal with hindlimb	ALS 2.5 mg induction, CSA 16 mg/kg/day for 10 days and 3 doses of ADSC ( $2 \times 10^6$ )	[30]

BN: Brown Norway; LEW: Lewis; CSA: cyclosporin A; ALS: antilymphocyte serum; ADSC: adipose-derived stem cell

the unique response directed against vascularized composite allotransplantations. Two swine models were reported with the use of gracilis myocutaneous flaps and fasciocutaneous flap transfers. One study had no immunosuppression and another had total body radiation with cyclosporin A maintenance therapy. One study utilized the transfer of the rectus abdominus myocutaneous flaps in syngeneic beagles without any immunosuppression as a model. One study utilized a combination of heart transplantation with an abdominal



**Table 3. Penile animal models**

	<b>Allo-transplantation</b>	<b>Approach</b>	<b>Graft</b>	<b>Regimen</b>	<b>References</b>
Rat	SD19 autotransplant	Original region	Penis	No immunosuppression	[31]
Rat	SD19 autotransplant	Transferred to groin region	Penis	No immunosuppression	[32]
Rat	BN to LEW	Heterotopic	Penis	Tacrolimus 0.6 mg/kg/day maintained	[33]
Rat	Lew-BN to LEW	Heterotopic	Penis	CSA 16 mg/kg/day tapered to 2 mg/kg/day in 4 weeks, then maintained	[34]

BN: Brown Norway; LEW: Lewis; CSA: cyclosporin A; SD 19: Sprague-Dawley rats

**Table 4. Uterus animal models**

	<b>Allo-transplantation</b>	<b>Approach</b>	<b>Graft</b>	<b>Regimen</b>	<b>References</b>
Primate	M. fascicularis monkey autotransplant		Uterus	No immunosuppression	[35]
Primate	Mismatched M. fascicularis monkey	Orthotopic	Uterus	Tacrolimus 0.3 mg/kg/day, MMF 20-10 mg/kg/day, and methylprednisolone 10-2 mg/day maintained	[36]
Primate	Mismatched olive baboons	Orthotopic	Uterus	ATG 10 mg/kg induction, followed by tacrolimus 0.1 mg/kg/day, Corticosteroids 60-5 mg/kg and MMF 50 mg/kg	[37]
Sheep	Swedish wool sheep autotransplant	Orthotopic	Uterus	No immunosuppression	[38]
Sheep	Sheep autotransplant		Uterus	No immunosuppression	[39]
Sheep	Sheep autotransplant	Orthotopic	Uterus	No immunosuppression	
Sheep	Mismatched sheep	Heterotopic	Whole uterus	No immunosuppression	[40]
Sheep	Mismatched Romney marsh sheep	Orthotopic	Uterus	CSA 2-5 mg/kg/day maintained and prednisone 2 mg/kg/day for 2 weeks	[41]
Sheep	Mismatched sheep	Orthotopic	Uterus	ATG 50 mg induction, followed by tacrolimus 0.02 mg/kg/day, methylprednisolone 40 mg/day and MMF 1.5 g/day	[42]
Sheep	Mismatched limousine sheep	Orthotopic	Uterus	CSA 10 mg/kg/day and MMF 3 g/day, both on POD 7, 14, 28, 42, 56, methylprednisolone 40 mg on POD 1-7	[43]
Rabbit	NZW allotransplant	Orthotopic	Uterus	Prednisolone 10 mg was given for 3 days following the "spikes" alongside an increase in tacrolimus dose from 500 to 1 g twice/day	[39]
Rabbit	Mismatched NZW	Orthotopic	Uterus	Tacrolimus 500 $\times$ g twice daily postoperatively; embryo transfer	[44]
Rat	LEW syngeneic	Heterotopic	Uterus	No immunosuppression	[45]
Rat	LEW syngeneic	Orthotopic	Uterus	No immunosuppression	[46]
Rat	BN to DA	Heterotopic	Whole uterus and ovaries	No immunosuppression	[47]
Rat	BN to LEW	Orthotopic	Uterus	CSA 10 mg/kg/day maintained	[48]
Rat	BN to LEW	Orthotopic	Uterus	Tacrolimus 0.5 mg/kg/day pump maintained	[49]
Rat	Virgin Dark Agouti to virgin LEW	Orthotopic	Uterus	Tacrolimus 0.5 mg/kg/day maintained; male SD rats of proven fertility were used for mating	[50]
Murine	F1-hybrids of inbred female C57BL/6 $\times$ CBA/ca syngeneic	Heterotopic	Right uterine horn and the cervix	No immunosuppression; embryo transfer	[51]
Murine	B6 syngeneic	Orthotopic	Ovarian	No immunosuppression	[52]
Murine	F1-hybrids of C57BL/6 $\times$ CBA/ca to B6	Heterotopic	Right uterine horn and the cervix	CSA 20 mg/kg/day	[53]

BN: Brown Norway; LEW: Lewis; CSA: cyclosporin A; DA: Sprague-Dawley; MMF: mycophenolate mofetil; NZW: New Zealand White

musculocutaneous flap. The combination of two models is particularly interesting which confers a high degree of morbidity in the animal. In the rat study, maintenance was carried out with cyclosporin A after the inclusion of the heart transplantation. The information is presented in [Table 6](#).

## CONCLUSION

The summary of the findings in this article demonstrates the various VCA models reported in the literature before. In order to carry out further experiments and determine the future of allotransplantation, animal models summarized in this article will hopefully shed light on the future directions for research and where

**Table 5. Hindlimb animal models**

	<b>Allo-transplantation</b>	<b>Approach</b>	<b>Graft</b>	<b>Regimen</b>	<b>References</b>
Primate	Mismatched donor to recipient M. fascicularis monkey	Orthotopic	Sensate osteomyocutaneous radial forearm flap	Tacrolimus 1 mg/kg and mycophenolate mofetil 20 mg/kg; both every 12 hour, methylprednisolone 15 mg/kg for 3 days followed by 7.5 mg/kg for 2 days and a 50% reduction every 2 days until the dose was 1 mg/kg	[54]
Swine	White pig autotransplant	Heterotopic	Whole forelimb	No immunosuppression	[55]
Swine	Mismatched newborn swine	Heterotopic	Newborn knee	No immunosuppression	[56]
Swine	Mismatched donor to recipient pigs	Heterotopic	Skeletal graft consisting of the tibia, fibula, knee joint, distal femur, and surrounding muscles	No immunosuppression	[57]
Swine	Mismatched donor to recipient pigs	Orthotopic	Osteomyocutaneous forearm flap	No immunosuppression	[58]
Swine	Mismatched donor to recipient pigs	Orthotopic	Radial forelimb osteomyocutaneous flap	No immunosuppression	[59]
Rabbit	NZW autotransplant	Orthotopic	Whole knee joint	No immunosuppression	[60]
Rat	N/A	N/A	Cremaster muscle and pubic bone flap	N/A	[61]
Rat	ACI to WF	Heterotopic	Hindlimb osteomyocutaneous	TBI 600 cGy prior to 1 dose of BMC $100 \times 10^6$ cells/kg with tacrolimus 1 mg/kg/day for 10 days and ALS 5 mg on POD10	[62]
Rat	WF to LEW	Orthotopic	Simultaneous dual-surgeon hindlimb	No immunosuppression	[63]
Rat	BN to LEW	Orthotopic	Vascularized elbow	CSA 16 mg/kg/day for first week, tapered to 2 mg/kg/day, then maintenance	[64]
Rat	Lewis-BN to LEW	Orthotopic	IBOMC flap	CSA 16 mg/kg/day in 1st week, tapered to 8 mg/kg/day in 2nd week, to 4 mg/kg/day in 3rd week and to 2 mg/kg/day in 4th week and maintained	[65]

NZW: New Zealand White; BN: Brown Norway; LEW: Lewis; CSA: cyclosporin A; POD: postoperative day; N/A: not available; WF: Wistar-Furth; BMC: bone marrow cells; IBOMC: iliac bone osteomusculocutaneous

**Table 6. Myofasciocutaneous animal models**

	<b>Allo-transplantation</b>	<b>Approach</b>	<b>Graft</b>	<b>Regimen</b>	<b>References</b>
Swine	Mismatched donor to recipient MGH miniature swine	Heterotopic	Gracilis myocutaneous flap	No immunosuppression	[66]
Swine	Mismatched donor to recipient MGH miniature swine	Heterotopic	Fasciocutaneous flap	TBI 100 cGy and CD3-IT conditioning prior to 3 doses of HCT $15 \times 10^9$ cells/kg with CSA (target trough 400-800 ng/mL) for 45 days	[67]
Canine	Beagles autotransplant	Transferred to groin region	Myocutaneous rectus flap	No immunosuppression	[68]
Rat	WKY heart and LEW VCA to F344	Heterotopic heart and orthotopic VCA	Heart and abdominal musculocutaneous flap	CSA 5 mg/kg/day every other day for 10 days after heart transplant	[69]

LEW: Lewis; CSA: cyclosporin A; TBI: total body irradiation; CD3-IT: CD3-immunotoxin; HCT: hematopoietic cell transplantation; F344: Fischer 344; WKY: Wistar Kyoto

further focus can be emphasized. Experimental animal surgical models can be difficult to perform and such research in VCA should be best collaborated with both clinicians and surgeons who can perform the difficult animal models, as well as basic scientists to further developments in this specialty.

Many of the immunosuppressive regimens used thus far involve an induction agent such as anti-thymocyte globulin or total body radiation which preconditions the host's immune system in preparation for a chance of engraftment of donor antigens. In particular, the phenomenon of chimerism is particularly seen in VCA research where the transfer of vascularized bone marrow, in long bones in particular, mediates a constant exchange of cells such as regulatory T cells which serve to protect the allograft. A particular preference for cyclosporin A, tacrolimus and steroids were seen across each animal model - quite so due to their widespread

availability and immunosuppressive capabilities. They mediate and protect the allograft from being attacked by host defense mechanisms which would destroy the graft otherwise.

## DECLARATIONS

### Authors' contributions

Wang AYL and Loh CYY were both involved in data collection, drafting of the manuscript, analysis of data, the second review of data, statistical analysis, ensuring data fidelity and manuscript review.

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None.

### Conflicts of interest

There are no conflicts of interest.

### Patient consent

Not applicable.

### Ethics approval

Not applicable.

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Case Report

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# Clinical applications of the jugal lipectomy technique: case reports

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## Abstract

The adipose body of cheek is the tissue located in the buccal space. In the past, the partial removal of this tissue, called jugal lipectomy, was indicated to fill defects resulting from buccosinus communications and/or maxillary resections. Recently, such technique became popular in facial aesthetics as it gives patients the feel of a more delicate face, in which the zygomatic bone appears to be more prominent due to the reduction in the volume of the cheeks. However, many professionals are unaware of how to establish the correct diagnosis of facial volume alterations, as well as in performing and treating the complications that may arise from jugal lipectomy. The aim of this paper is to present three clinical cases with different applications of jugal lipectomy, discussing some relevant aspects of surgical planning that involve the request for imaging exams and a previous study of this tissue's anatomical features.

**Keywords:** Face, lipectomy, adipose tissue, aesthetics

## INTRODUCTION

Although previous studies on adipose body of cheek (ABC) have been brief and scarce in the literature, there is currently a greater interest by researchers in studying the anatomy of this support tissue, considered as an important factor influencing facial aesthetics<sup>[1]</sup>.

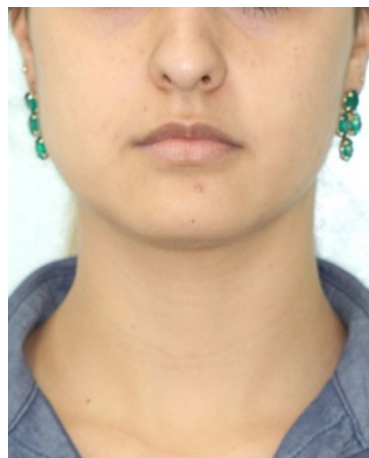
The ABC, also known as the “Bichat ball”, was described in 1802 by French physiologist and anatomist



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**Figure 1.** Front view

Marie François Xavier Bichat, father of modern histology. Histologically, the tissue is composed of the same type of fat present in other parts of the human body and is one of the last reserves to be consumed during weight loss<sup>[2]</sup>.

This adipose tissue is wrapped by a thin fibrous capsule that isolates it from other structures, divided into anterior, intermediate, and posterior lobes, fixed by six ligaments inserted in the maxilla, posterior region of zygoma, inner and outer rim of infraorbital fissure, temporal tendon, and buccal membrane. The anatomy of the ABC extension is complex and fills the space between the masticatory muscles (masseter, medial pterygoid, lateral pterygoid, and temporal). The posterior lobe presents four processes (buccal, pterygoid, pterygopalatine, and temporal), keeping a close relationship with blood vessels, branches of facial nerve, and the parotid duct. The parotid duct and zygomatic and buccal branches of the facial nerve cross the anterior and lateral surfaces of the ABC. The anterior surface of the ABC is covered by buccal branches of the facial nerve, while the lateral border is covered by zygomatic branches in almost all patients<sup>[3]</sup>.

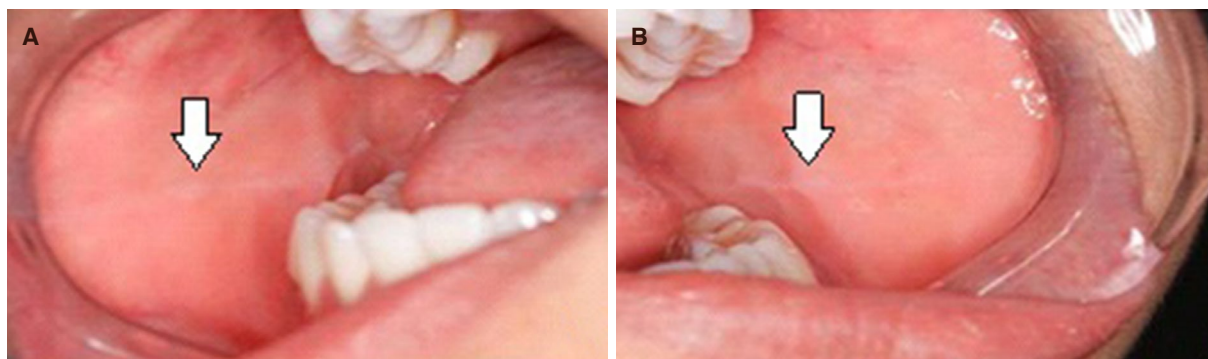
Currently, the partial removal of this tissue is no longer restricted to functional indications for the correction of buccal defects, representing one of the most desired surgical procedures by patients in aesthetic clinics. However, many professionals are unaware of how to establish the correct diagnosis of facial volume alterations, as well as in performing and treating the complications that may arise from jugal lipectomy.

Clinical evaluation has been used as the sole method to indicate the surgical procedure. However, it is known that complementary exams such as computed tomography, magnetic resonance imaging, and ultrasonography can improve the diagnosis, avoiding unnecessary surgeries. They may be employed alone or in association, and there is no consensus about the best imaging modality. Thus, the aim of this paper is to present three cases with different clinical applications, highlighting the importance of anatomical and imaging knowledge for better planning and execution of the surgical technique.

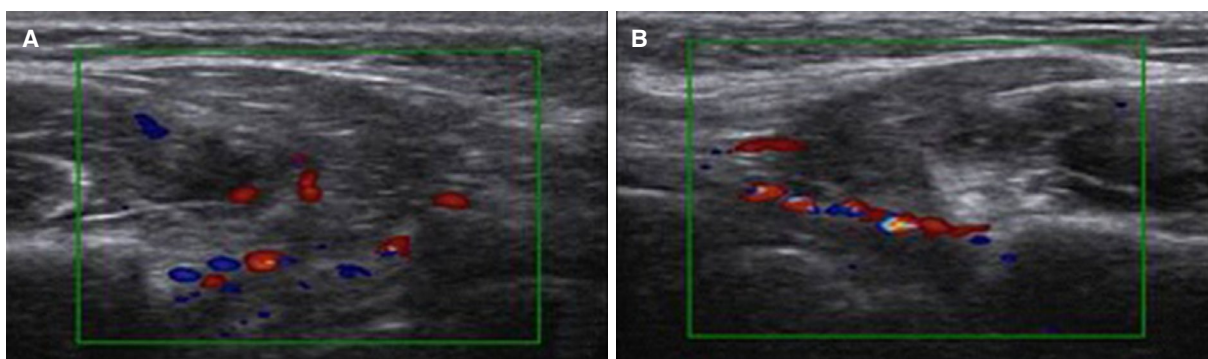
## CASE REPORT

### Case 1

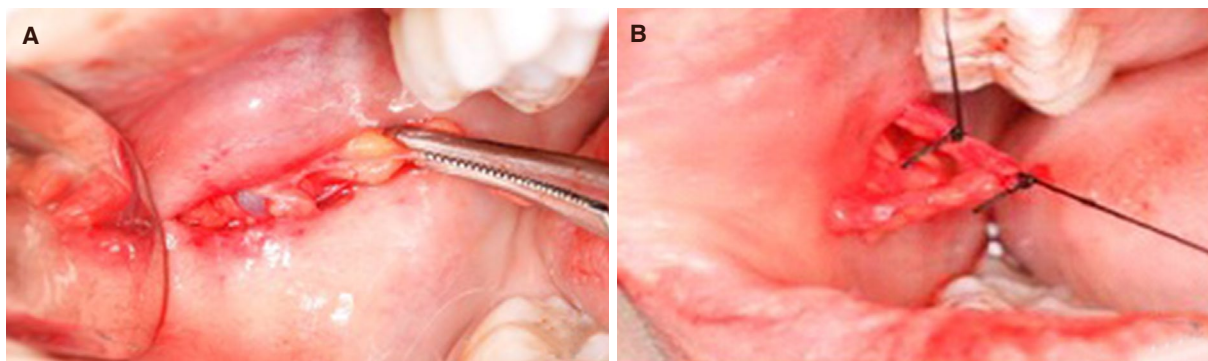
A female patient, 24 years old, sought the service of maxillofacial surgery complaining of a chronic bite of the bilateral jugal mucosa and aesthetic dissatisfaction with excessive cheek volume. She reported good health status and absence of systemic alterations. A facial examination revealed a rounded face [Figure 1] associated with the suspicion of masseter hypertrophy, which was discarded after palpation of the



**Figure 2.** Intraoral photographs on the right (A) and left (B) sides showing keratinization lines



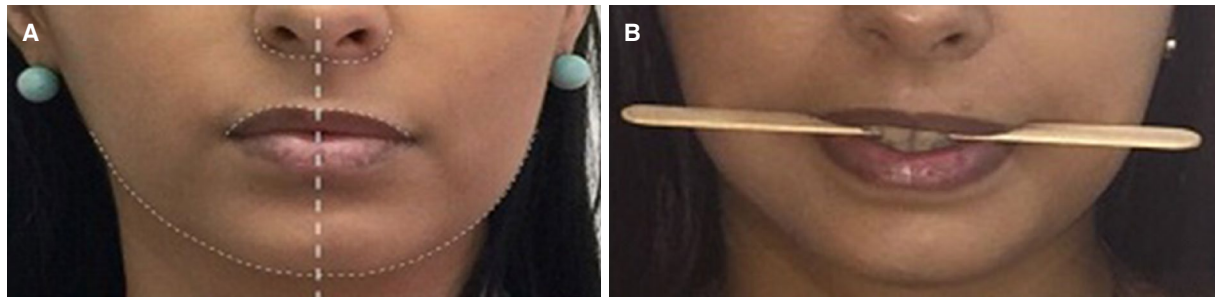
**Figure 3.** Doppler ultrasonography on the right (A) and left (B) sides, showing blood vessels over the surgical area



**Figure 4.** Intraoral photographs from the right side showing the adipose body of cheek identification (A) and link of blood vessels (B)

musculature and request for imaging exams. An intraoral examination revealed the presence of a white line of keratinization, asymptomatic, parallel to the occlusion line, suggestive of an alba line [Figure 2]. Doppler ultrasound revealed symmetry of the ABC on the right and left sides and a very close relationship of the branches of arteries and buccal veins on both sides [Figure 3].

Jugal lipectomy was performed under local anesthesia, using 2% lidocaine and 1:100,000 epinephrine, and a parallel incision was made immediately adjacent to the mucosal bite line. The access distance was at least 1 cm below the parotid caruncle and could have been extended up to 2 cm. It is recommended to start the incision 1 cm behind the caruncle, avoiding trauma in the masseter muscle. After submucous divulsion, a portion of the ABC was identified along with blood vessels, which were linked with 4-0 silk thread [Figure 4]. Next, part of the buccal extension of the ABC was pulled by rotating movements by a Halstead forceps to remove the tissue and the mucosa was sutured with 3-0 silk thread. To prevent edema, 8 mg of



**Figure 5.** Preoperative front view showing facial asymmetry (A) and occlusal unevenness (B)

dexamethasone was prescribed 1 h before surgery. After surgery, 750 mg of paracetamol every 6 h and 100 mg of nimesulide every 12 h were prescribed for three days for pain control.

Patient is in the second postoperative year with no complaint of biting jugal mucosa.

### Case 2

A female patient, 29 years old, sought the service of maxillofacial surgery complaining of facial asymmetry and reporting good health status and absence of systemic alterations. Facial examination revealed a slight increase in volume in the cheek region on the left side. Intraoral examination showed an unevenness of the occlusal plane and class I occlusion [Figure 5]. Magnetic resonance imaging did not identify alterations in bone tissue, such as condylar hyperplasia, and/or changes in soft tissue, such as masseter hypertrophy and/or temporomandibular joint disorders [Figure 6]. The surgical technique was the same used in the first reported case, removing 2.8 mL of fat from the buccal extension of the left ABC. In addition to the pre- and postoperative medications, a compressive dressing was performed to better control edema. After four months of follow-up, the patient is satisfied with the facial contour and better symmetry in the region of upper lip and the wing of the nose [Figure 7].

### Case 3

A male patient, 22 years old, sought the service of maxillofacial surgery complaining of passage of liquid from the oral cavity to the nasal cavity during feeding. In the anamnesis, he reported good health, absence of systemic alterations, and a history of tooth extraction 3 months ago. Facial examination showed palpation sensitivity in the region of the right maxillary sinus associated with a buccosinus fistula with active drainage of purulent secretion [Figure 8]. Waters view radiography identified a suggestive image of generalized thickening of maxillary sinus mucosa, which was confirmed by nasal endoscopy and lead to the diagnosis of maxillary sinusitis on the right side [Figure 9].

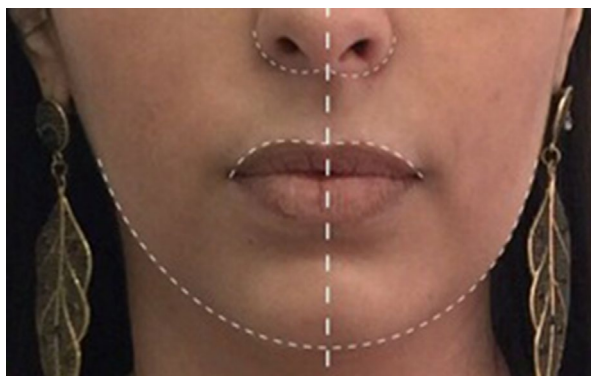
After remission of chronic sinusitis and treatment with hydration, systemic antibiotic therapy, and nasal decongestant, the surgery was scheduled to close the fistula [Figure 10]. Given that it required a small amount of adipose tissue, a 1-cm gingivobuccal incision was performed, located 1 cm above the parotid caruncle. After divulsion, a non-pedicated portion of the ABC was removed, transferred, and sutured over prior fistulectomy surgery. The sliding palatal flap was then positioned and sutured onto the ABC. After four months of follow-up, a healthy mucosa was observed and there were no signs suggesting maxillary sinusitis.

## DISCUSSION

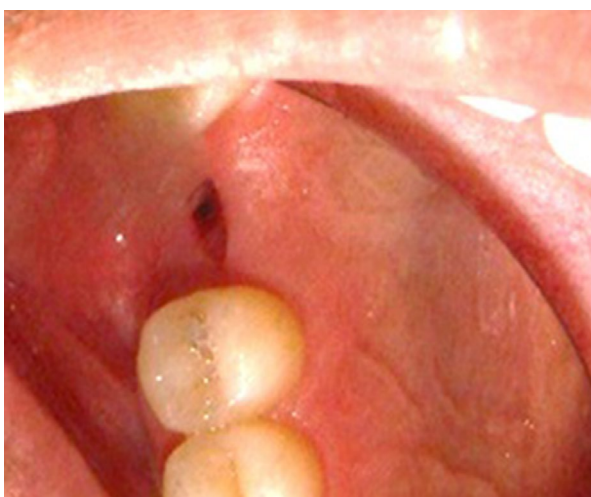
The anatomy of ABC has been investigated by several authors, and few studies have made a careful analysis of tissue dimensions and volumes with the aid of imaging exams<sup>[4-6]</sup>. Loukas *et al.*<sup>[7]</sup> (2006) measured the ABC of 20 cadavers through computed tomography (CT) and magnetic resonance imaging



**Figure 6.** Magnetic resonance imaging identifying normal mandibular condyle and chewing muscles



**Figure 7.** Postoperative front view showing correction in the facial contour



**Figure 8.** Intraoral photographs showing the buccosinus fistula

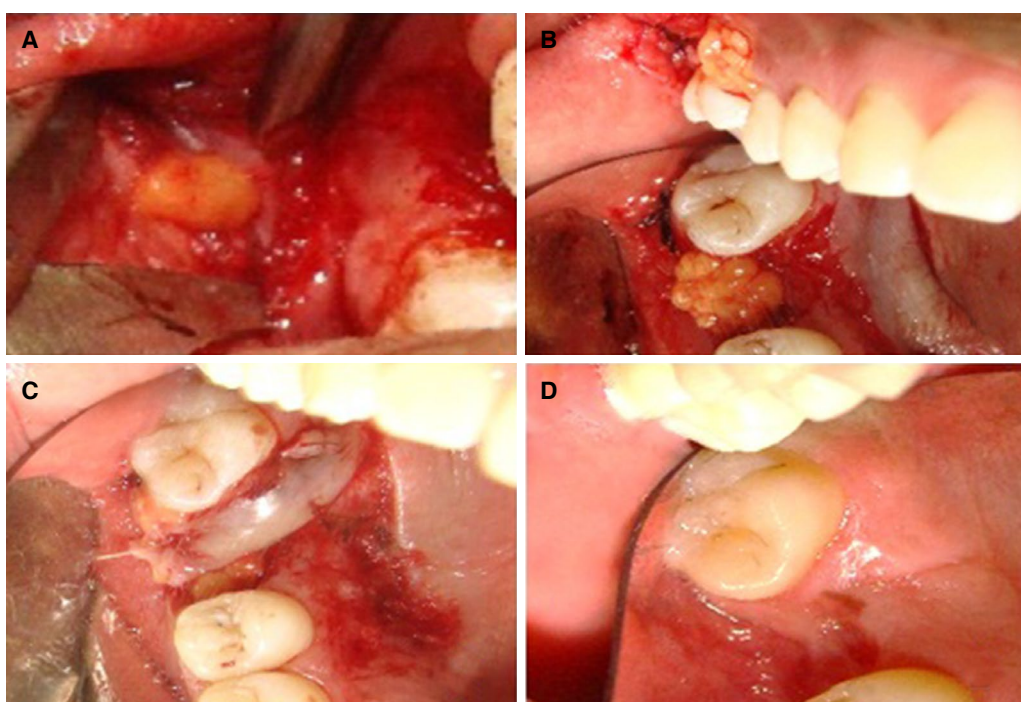
(MRI), concluding that the mean volume in men was 10.2 and 8.9 mL in women, weighing approximately 9.7 g. No significant differences between genders was observed.

As reported in the first case, a third imaging examination may be required for the study of ABC anatomy: ultrasonography (USG). This exam is based on the transmission of sound waves and reflection of these waves when they reach an interface between tissues of different densities. It is an easy-to-perform, non-





**Figure 9.** Waters view radiography showing opacification of the right maxillary sinus



**Figure 10.** (A) Gingivobuccal access and adipose body of cheek (ABC) identification; (B) transposition of part of ABC for the region of buccosinus fistula; (C) rotation and suturing of palatal flap for tissue nutrition; (D) clinical aspect after four months of follow-up

invasive exam with no image superimposition, does not use ionizing radiation, and has a relatively low cost compared to CT and MRI<sup>[8]</sup>. Because it is less widespread in maxillofacial surgery, there is a shortage of qualified professionals to perform the exam and interpret the images.

In attempt to improve such imaging findings, Jaeger *et al.*<sup>[9]</sup> (2016) presented a protocol for predicting the anatomy of buccal extension of ABC using USG. It was possible to identify tissues of small, or even the absence of, buccal extension, contraindicating jugal lipectomy and avoiding unnecessary surgeries. In the first reported case, we used the USG exam similarly to these authors, finding a symmetry of buccal extensions of ABC on both sides, with a volume of 2.4 mL on the right side and 2.2 mL on the left side. In the second case, the ABC volume calculated from MRI showed a difference of 1.5 mL. In this context, it is important to highlight the importance of preoperative imaging exams to study the symmetries or asymmetries of this tissue for surgical planning.

Each imaging exam has a contribution to make in the study of the anatomy of the ABC, and should be requested after the clinical exam according to the diagnostic hypothesis. CT is more accurate for hard tissues analysis, while USG and MRI provide more detail for soft tissues. Due to a greater detailing provided by images, CT and MRI can be useful for the study of face volumetric alterations that occur with aging<sup>[5]</sup> and the identification of pathologies in the hard or soft tissues of the maxillofacial region, such as masseter hypertrophy and condylar hyperplasias, as was suspected in the first and second reported cases, respectively.

Jugal lipectomy also presents applications other than those described in the three clinical cases<sup>[10]</sup>. Bansal *et al.*<sup>[11]</sup> (2015) evaluated the viability of ABC as interposition material after arthroplasty and concluded that the volume of 1.1 mL of fat is efficient and stable as a barrier for preventing temporomandibular ankylosis. Recently, the literature discusses the ability of ABC to be an important source of mesenchymal stem cells, promising to produce bone tissue, muscle, cartilage, and fat. However, such information is not yet accurate and further studies are needed<sup>[12,13]</sup>.

Correction of oral defects, including closure of buccosinus fistulae with ABC pedicled graft, is the most common indication found in the literature for jugal lipectomy<sup>[14]</sup>. The success of this grafting can be attributed to the rich vascularization of adipose tissue, an important condition for the long healing period<sup>[15]</sup>. However, even when a non-pedicled graft was used, as reported in the third clinical case, there was excellent tissue stability, and local vascularization was also provided by the palatal flap. Satisfactory results were also found in free grafts for treatment of patients with cleft lip and palate in the anterior region of maxilla<sup>[16]</sup>.

Three surgical accesses for jugal lipectomy are described in the literature: (1) 1 cm below the opening of parotid duct (Matarasso method), (2) behind the parotid papilla (Stuzin method), and (3) incision superior to the gingivobuccal sulcus<sup>[17]</sup>. In the first and second reported cases, the Matarasso method was used to provide wide and direct access to the buccal space, allowing the removal of a larger volume of ABC and its buccal extension, directly related to the contour of the cheek. In the third clinical case, jugal lipectomy did not present an aesthetic indication. Therefore, the gingivobuccal access was chosen since the aesthetic repercussion is almost insignificant. Upon performing an intraoral approach carefully to not pull the ABC and resecting only that which easily protrudes with gentle pressure, complications of excision for lipodystrophy or a pseudo herniated buccal fat pad are rare. The most likely complication would be over resection.

Although complications are infrequent<sup>[18]</sup>, lesions in the parotid gland, vascular plexus (branches of facial artery, maxillary artery, and transverse artery of the face), and the buccal branch of facial nerve may occur<sup>[19]</sup>. While the parotid duct presents a more lateral path in relation to the ABC, the vessels and buccal branches have a more superficial path and can go through the ABC extension<sup>[20]</sup>. Lesions of these structures can cause dry mouth sensation, the formation of large bruises, and even facial paralysis. Treatments include surgical repair of the duct, drainage of bruises and linking of blood vessels, anastomosis or grafting of neural tissue, and may be associated with laser therapy and corticosteroids. There were no hospitalizations, accidents, or complications in the three cases presented, and the procedure was performed at the dental office under local anesthesia. Superselective microcatheter angiography and embolization has been shown to be an effective modality for prompt treatment of bleeding from traumatic facial injury and refractory epistaxis when local methods fail to achieve hemostasis<sup>[21]</sup>. Trismus, infection, asymmetries, or cheek depressions may also occur, resulting from inadequate and lopsided removal of adipose tissue.

Despite these complications, it is important to highlight that jugal lipectomy is a simple technique with few variations, fast execution, and low morbidity. It is essential to know the ABC anatomy of each patient through clinical examination and complementary imaging exams.



## DECLARATIONS

### Authors' contributions

Literature search, manuscript preparation, manuscript editing: Antunes BA  
 Clinical studies, manuscript preparation: Schmitt ARM, Neto MA, Jaeguer F  
 Design, definition of intellectual content, and manuscript review: Naclério-Homem MG  
 Concept, definition of intellectual content, literature search, clinical studies, manuscript editing, and manuscript review: Carvalho MF

### Financial support and sponsorship

None.

### Conflicts of interest

There are no conflicts of interest.

### Patient consent

The proper consent of the patients was taken for carrying out all the treatment.

### Ethics approval

The procedures followed were in accordance with ethical standards of the responsible committee on human experimentation by Federal University of Juiz de Fora (CAAE 74413617.6.0000.5147).

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Letter to Editor

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## Use of “tent-pole” graft for setting columella-lip angle in rhinoplasty

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Sir,

In patients of rhinoplasty, columella-labial angle (CLA) is an important parameter to be evaluated if a pleasant aesthetic result is desired. An increase in this angle results in an upward tilt of the base of the nose with a concomitant decrease in nasal length. Owing to the wide anatomic variability, it is often times missed, thereby leading to sub-optimal surgical results.

The relationship between the columella and upper lip is complex. Trying to maintain a particular angle in patients of rhinoplasty is difficult and entails use of various manoeuvres like suturing techniques, cartilage grafts and nasal cartilage modifications. The caudal septum, nasal spine and medial crura of the lower lateral cartilages help shape the columella and thus contribute to the determination of the CLA<sup>[1]</sup>. On profile view, the desired columella-labial angle is 95° to 100° in men and 100° to 110° in women<sup>[2]</sup>. The normal columellar show ranges from 2 to 4 mm. A long or hanging columella can significantly disturb the aesthetic effect of the nose. Here the authors describe ‘the tent pole graft’, an innovative technique used to set and maintain the columellar lip angle.

The “tent-pole graft” works in a manner similar to the septo-columellar interpositional grafts but here there is no need to dissect or separate upper lateral cartilages from septum to fix the grafts. This graft is akin to fixing a bamboo of a tent in position. It is used in difficult secondary noses and cases where tip projection is increased significantly by putting long columellar strut, which tends to fall back (as in Binder’s syndrome).

In this technique, a piece of cartilage is fixed to columellar strut in a desired position and then the optimal angle is chosen by fixing the posterior end of graft temporarily with a needle to supratip cartilaginous

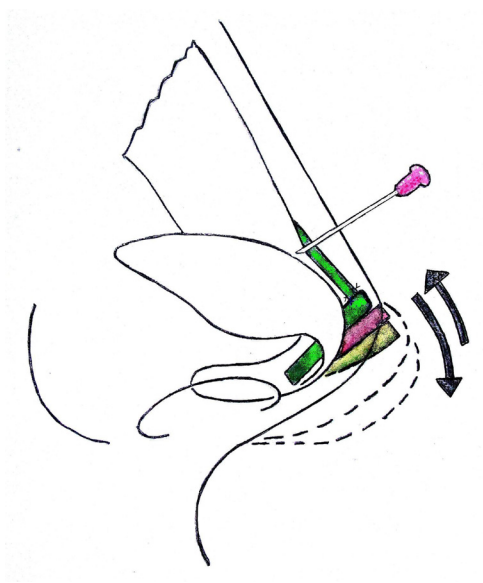


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**Figure 1.** Picture in lateral view of a patient who underwent rhinoplasty, showing temporary fixation of the tent pole graft to set the columella labial angle using needle

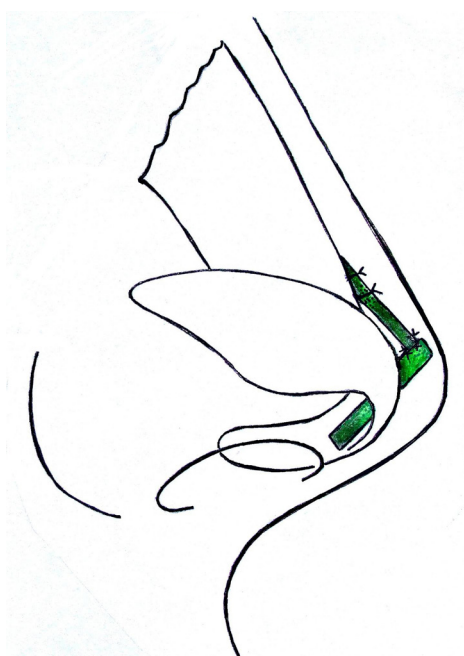


**Figure 2.** Schematic diagram corresponding to Figure 1, showing temporary cartilage graft fixation using needle so that it can be increased or decreased easily by sliding

dorsum [Figures 1 and 2]. Once sure of the angle, the graft is sutured to the dorsum [Figures 3 and 4]. Tent pole graft keeps long columellar strut stable and doesn't allow the tip to fall back. It not only helps in maintaining but gives a liberty to create a CLA of choice. Authors usually use it whenever tip support is needed in secondary rhinoplasties and cases where lengthening of tip or columella is done, to maintain the desired columellar-labial angle, and to maintain the nasal length in patients with short noses. This graft can be moved serially to easily adjust the nasolabial or columella-labial angle. To avoid supratip show of the graft the dorsal limb of the graft is placed and fixed to columellar strut 3-4 mm lower than the actual tip height. The tent pole graft is a variant of L-strut. An L-strut can be used to serve the same purpose of creating and maintaining a CLA of choice, but tent pole graft, which is fixed in supratip region, provides the liberty to



**Figure 3.** Picture in lateral view. Once the required columella labial angle is set, the tent pole graft is sutured to the dorsum to fix it



**Figure 4.** Schematic diagram corresponding to Figure 3, showing final suturing of the cartilage graft to the dorsum once the angle is set

design a natural and soft looking dorsum. The authors have used this technique in more than 25 patients of rhinoplasty with satisfactory results. A representative case is shown in [Figure 5](#).

Based on various modifications of lateral crural cartilages, Webster *et al.*<sup>[3]</sup> were the first to describe options for tip rotation. Ozmen *et al.*<sup>[4]</sup> described the sliding alar cartilage technique for nasal tip modification in which lower lateral cartilage is used. Bohluli *et al.*<sup>[5]</sup> have described lateral crural anchorage flaps in which excessive parts of the lateral crural cartilages are used as anchorage flaps and fixed with needle to the septum to set the nasal tip position. Honrado and Pearlman<sup>[1]</sup> have reviewed in detail various techniques for adjustment of naso-labial angle in rhinoplasty.





**Figure 5.** Clinical photograph of a patient who underwent cosmetic rhinoplasty for Binder's Syndrome. (A) Preoperative photograph, lateral view; (B) postoperative photograph after the use of "tent pole" graft, lateral view; (C) preoperative photograph, basal view; (D) postoperative photograph after the use of "tent pole" graft, basal view

Indian noses have peculiar combination of thick skin and weak alar cartilages. Tip refinement by suturing technique is possible only in select cases. Most of the Indian noses and especially secondary noses need add on grafts to build and refine the tip. The major techniques used to rotate the tip caudally, are septal extension graft, a columellar strut supported with extended spreader grafts and structured columellar strut. Both caudal septal extension and extended spreader grafts are the techniques of choice when either septal work is needed or in a severely short nose.

Tent pole graft is particularly helpful in cases where septal extension graft is either not feasible or very difficult to put, e.g., Binders, mild to moderate short nose, secondary noses. In cases where the noses need augmentation and tip pasty, the tent pole graft comes as a useful tool for rhinoplasty surgeons to provide mild to moderate increase in the length of nose without the need of dissection and septal extension graft, to support columellar strut and to set and maintain nasolabial angle. Thus, the "tent pole graft" technique may be used in difficult secondary nasal tip, cleft lip rhinoplasty and in noses with depressed tip (Binder's Syndrome) to prop the columella strut graft and provide optimal results to tip modification in patients undergoing rhinoplasty.



## DECLARATIONS

### Authors' contributions

Concept, design, definition of intellectual content, clinical studies, data acquisition, manuscript preparation, manuscript editing, and manuscript review: Agrawal K

Literature search, data acquisition, data analysis, statistical analysis, manuscript preparation: Shrotriya R

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### Conflicts of interest

There are no conflicts of interest.

### Patient consent

Consent has been taken.

### Ethics approval

Not applicable.

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Original Article

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# A novel highly specialized functional flap: omohyoid inferior belly muscle

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## Abstract

**Aim:** There is no previous description on the anatomy of the inferior belly of the omohyoid muscle. This muscle has specific morphological characteristic that make it appealing when solving specialized reconstructive problems. Our objective is to describe the microsurgical anatomy of the inferior belly from the omohyoid muscle.

**Methods:** Supraclavicular bilateral dissection in 5 anatomic models (fresh human cadavers). Measurements were taken with a millimetric caliper. Statistical analysis was performed with measures of central tendency.

**Results:** Eight muscles were dissected in 5 anatomic models. Average dimensions were: 93 mm long, 12 mm wide, and 7.5 mm thickness. The vascular pedicles showed great anatomical variability. In 2 flaps (1 model) irrigation came exclusively from transverse cervical vessels, in the remaining models the pedicles came directly from the subclavian vessels; 2 flaps had an accessory minor pedicle from the transverse cervical vessels. The diameter of all vascular pedicles was less than 0.8 mm, with an average length of 22.3 mm. The nerve pedicle came from ansa cervicalis in all flaps, with an average length of 27.8 mm.

**Conclusion:** Based on the findings we conclude that omohyoid muscle could be a reconstructive option when small functional flaps are required, such as facial reanimation surgery, sphincters, ptosis and vocal cord reconstruction, and blink restoration surgery although more anatomical studies are required to determine the microsurgical feasibility, excursion and strength of the muscle, and axonal load in this new myofunctional flap.

**Keywords:** Neck muscles, free tissue flaps, cadaver, models, anatomic, supermicrosurgery, infrahyoid muscles, omohyoid muscle



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## INTRODUCTION

The infrahyoid muscles are a group of paired strap-like muscles that include the thyrohyoid, sternothyroid, sternohyoid and the omohyoid. The omohyoid muscle is a digastric structure with an inferior belly originated in the scapula, a central tendon and a superior belly that inserts in the inferior border of the hyoid bone. Previous authors have described the gross and microsurgical anatomy of the infrahyoid muscles at length, however, the inferior belly of the omohyoid has remained largely ignored<sup>[1-8]</sup>.

The infrahyoid muscles' blood supply has been found to arise from the superior and inferior thyroid arteries, and the sternal branch of the internal thoracic artery; nevertheless, most authors have limited their investigations to the omohyoid's superior belly<sup>[1-3]</sup>. The ansa cervicalis has been found to present many variants in the terminal branches that innervate the strap muscles, but as of today there is no description on the branches directed to the inferior belly of the omohyoid muscle<sup>[4]</sup>.

Several descriptions on the use of the infrahyoid muscles for reconstruction of the tongue, larynx, esophagus and the vocal cords have been published, however it should be noted that most surgeons avoid the inclusion of the inferior belly of the omohyoid muscle in their flaps due to its distance from the site to be reconstructed<sup>[5-10]</sup>.

The inferior belly of the omohyoid muscle possesses appealing characteristics that may allow it to serve as a specialized functional flap, such as serving a noncritical function (easily performed by the rest of the infrahyoid muscles), and possessing small dimensions that allow for functional reconstruction in small areas; however, its potential use as a free flap has never been studied.

The objective of this work is to describe the surgical morphology of the inferior belly of the omohyoid muscle.

## METHODS

Fresh human cadavers were used for this study; standardized dissections were conducted to establish the anatomical characteristics of the inferior belly of the omohyoid muscle.

Approval by the institutional ethics board was received. Data recorded included patients' demographic characteristics; history for trauma, or surgical procedures on the neck; muscle belly dimensions from its origin in the scapula to the central tendon; length of the vascular and nerve pedicle from its proximal dissection to the point of its emergence in the muscle fibers.

### Statistical analysis

Descriptive analyses of patient demographic and clinical characteristics were performed. Continuous variables are expressed in central tendency measures, categorical values are presented as percentages.

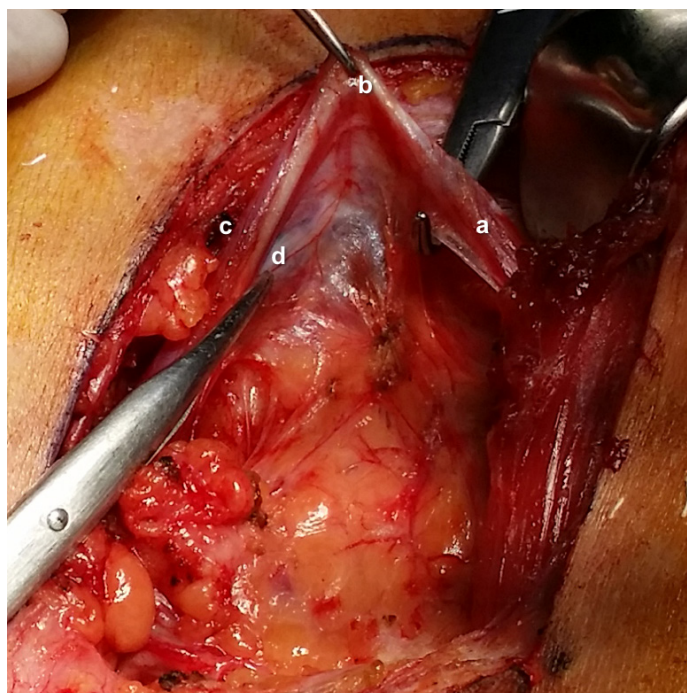
### Cadaveric dissection

A supraclavicular incision was performed following the contour of the sternocleidomastoid muscle. Subplatysmal flaps were elevated to expose the strap muscles and the sternocleidomastoid muscle. The sternocleidomastoid muscle is retracted laterally to expose of the omohyoid muscle.

The ansa cervicalis and the vascular pedicles were identified and dissected from their origin to the point of entry of the muscle belly; finally, the inferior muscle belly was extracted by disinserting it from the scapular surface and transecting the central tendon.

## RESULTS

Five male anatomic models were studied (range 18 to 65 years), 2 muscles were discarded due to previous



**Figure 1.** Anatomic dissection of the inferior belly of the omohyoid muscle. a: superior belly; b: central tendon; c: inferior belly; d: vascular pedicle



**Figure 2.** Muscle appearance after extraction

surgical procedures in 2 heminecks, resulting in a total of 8 muscle bellies studied. [Figure 1](#) shows an example of the dissection area.

Average dimensions for the muscle belly were 93 mm long (range 67-110), 12 mm wide (range 6-20), and 7.5 mm thickness (range 6-12). The vascular pedicle had a mean length of 22.3 mm and a diameter of 0.8 mm, the distance between the central tendon and the point where the pedicle entered the muscle fibers was 27.2 mm; the ansa cervicalis' branch to inferior belly had a mean length of 27.8 mm, it ran parallel to the muscle belly in all cases [[Table 1](#)]. [Figure 2](#) shows an example of the muscles dissected.

Several anatomical variations were found: a minor vascular pedicle from the transverse cervical vessels in 2 flaps; in 1 model the artery arose from the transverse cervical vessels, while in the rest of the cases it derived from the subclavian vessels; 1 model lacked a central tendon.

**Table 1. Anatomic characteristics of the inferior belly of the omohyoid muscle**

Model	# 1		# 2		# 3		# 4		# 5		Mean
	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	
Vascular pedicle length	15	17	28	-	13	21	23	-	20	42	22.3
Nerve length	46	17	37	-	26	21	31	-	25	20	27.8
Flap length	67	90	85	-	110	100	84	-	100	110	93.2
Flap width	20	16	16	-	6	11	11	-	12	11	12.8
Flap thickness	8	7	6	-	6	7	7	-	9	12	7.7
Tendon-Pedicle distance	19	19	27	-	No central tendon		25	-	75	53	27.2
Source vessel	SC	SC	SC	-	SC	SC	SC	-	TC	TC	
Main nerve	AC	AC	AC	-	AC	AC	AC	-	AC	AC	

All measurements are expressed in millimeters (mm). SC: subclavian artery; TC: transverse cervical artery; AC: ansa cervicalis

## DISCUSSION

Our work represents the first time an anatomical study focused on the morphology of the inferior belly of the omohyoid muscle and its potential use as a free flap has been performed.

Our results show that the inferior belly is a small and thin muscle, with average measures of 93 mm × 12 mm × 7.5 mm, a trait that could prove to be advantageous, especially in facial reconstruction. The short length of the muscle's belly might raise concern about its contractile capacity and usefulness as a functional flap; however the senior author of this paper has observed that the muscle presents a nice range of motion when subjected to transoperative neurostimulation during procedures for brachial plexus injury [Video 1].

Previous anatomical studies have described that the strap muscles present high morphological variability<sup>[2]</sup>, and we found that the inferior belly of the omohyoid muscle is no exception: a minor pedicle from the transverse cervical vessels was found in 2 cases, and 1 case in which the main pedicle came from the transverse cervical artery, in lieu of the subclavian artery.

The vascular pedicle of the inferior belly presents anatomical characteristics that may hinder its widespread use, mainly the presence of a short and narrow pedicle (22.3 mm × 0.8 mm), nevertheless, the use of vein grafts and supermicrosurgery might help overcome the problem. Our results show that the inferior belly of the omohyoid muscle is innervated by the ansa cervicalis, and that it is relatively short as well, with a mean length of 27.8 mm, however this limitation could be solved in a simple manner by using nerve autografts.

In conclusion, as microsurgical techniques and anatomical understanding of our body have expanded in the last decade, multiple new flaps have been described; the use of supermicrosurgery has further pushed boundaries and now vascular anastomosis in structures with a diameter minor to 0.8 mm are possible. This anatomical study of the inferior belly of the omohyoid muscle proposes its use in reconstructive procedures that require a small myofunctional flap such as facial reanimation surgery, sphincter reconstruction, vocal cord reconstruction, and blink restoration surgery.

## DECLARATIONS

### Authors' contributions

Anatomical model dissection, data acquisition and analysis: Muñoz-Jimenez G

Data analysis, paper writing, editing and translation: Telich-Tarriba JE, Palafox-Vidal D

Project supervisor and anatomical model dissection: Cardenas-Mejia A

### Data source and availability

Anatomical models were obtained from the "Institute de Ciencias Forenses" in Mexico City. Raw data on measurements can be obtained by contacting Dr. Alexander Cardenas-Mejia directly.

### Financial support and sponsorship

None.

### Conflicts of interest

Part of the work was presented at the 13th International Facial Nerve Symposium, August 3/6th 2017, Los Angeles CA, USA. The authors have no conflicts of interest to disclose.

### Patient consent

Not applicable.

### Ethics approval

This work received approval by the institutional ethics board.

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Systematic Review

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# A systematic literature review of the management of chronic venous ulcers with autologous fibrin matrix with or without growth factors

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## Abstract

**Aim:** To evaluate available evidence for the effective management of venous leg ulcers with fibrin matrix with or without growth factors.

**Methods:** A systematic review of the literature was performed to evaluate the use of fibrin matrices with or without growth factors for the management of chronic venous ulcers in lower limbs. Article searches were performed in MEDLINE, EMBASE, COCHRANE, LILACS and ongoing clinical trials at ClinicalTrial.gov.

**Results:** The search in MEDLINE and EMBASE identified three articles; one was a pilot study evaluating the use of fibrin matrix and autologous growth factors that included patients with chronic ulcers of different etiology. The second article was a description of the product used in the previous study, and the third consisted of a series case reports of patient treated with cultured keratinocytes in a fibrin matrix. A COCHRANE searched resulted in one study assessing the cost effectiveness of using different fibrin matrices. The search in ClinicalTrial.gov and LILACS did not result in any findings.

**Conclusion:** The study did not provide a conclusive evidence for the use of fibrin matrices in patients with venous leg ulcers.

**Keywords:** Venous ulcers, legs, fibrin matrix, growth factors



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## INTRODUCTION

Venous disease is a pathological chronic condition that causes significant morbidity and decreases quality of life in affected patients. The incidence of chronic venous insufficiency (CVI) varies within a range of 1% to 40% in women and 1% to 17% in men<sup>[1]</sup> with a higher prevalence in western industrialized countries. However, there is a low registration of cases due to the lack of reporting<sup>[2]</sup>. Patients with chronic peripheral vascular disease of venous origin exhibit secondary ulcer complications in skin and soft tissues of the lower limbs, with recurrence rates of 45% to 70% per year during the course of the patient's disease, which makes it difficult to manage<sup>[2]</sup>.

The pathophysiology of the venous ulcers is explained by the venous hypertension which lead to increased pressure in the distal veins of the leg; fibrin cuff theory in which the fibrin gets excessively deposited around capillary beds leading to elevated intravascular pressure causing enlargement of endothelial pores resulting in a further interstitial fibrinogen deposition increase. There is also an inflammatory trap theory in which various growth factors and inflammatory cells are trapped in the fibrin cuff promoting severe uncontrolled inflammation in surrounding tissue, thus preventing proper regeneration of wounds. Finally, the dysregulation of various pro-inflammatory cytokines and growth factors like tumor necrosis factor-alpha, transforming growth factor (TGF) beta and matrix metalloproteinases lead to chronicity of the ulcers.

In order to determine the type of ulcer, it is very important to rule out arterial etiology. The clinical history may suggest the venous etiology. Additionally, the physical examination should describe the location, the measure of the size, the characteristics of the ulcer, the amount and type of exudate, the appearance of the ulcer bed, the odor of the ulcer and the pain associated with the ulcer.

Ankle brachial pressure index (ABPI) is a noninvasive test to determine the origin of the ulcer, which is evidence level B. This test uses the handheld doppler ultrasound, which identifies peripheral arterial disease in the leg. Systolic BP is measured at the brachial artery and at the ankle level.

ABPI = highest systolic foot pressure (dorsalis pedis/posterior tibial artery)/highest systolic brachial BP

- a. ABPI 0.8-1.2: indicative of good arterial flow. Suggestive of venous etiology if an ulcer is present
- b. ABPI < 0.8: with the clinical picture of arterial disease-arterial insufficiency
- c. ABPI > 1.2: suggestive of possible arterial calcification

A meta-analysis study of venous ulcers in an adult population reported a prevalence of 0.12% to 1.1%<sup>[1]</sup>. In the USA, seven million people suffer from CVI, which may be the underlying cause of 70% to 90% of ulcers in lower limbs<sup>[1]</sup>. The overall incidence of venous ulcers is considered to increase with age. In this regard, Evans *et al.*<sup>[3]</sup> reported a prevalence of venous ulcers of 56% in patients from 55 to 64 years of age, in comparison to 12% in patients from 18 to 24 years old.

Venous ulcers in lower limbs are one of the 10 most common medical problems in western countries with a substantial socioeconomic impact due to frequent disabilities<sup>[2]</sup>. In 1992, The American Venous Forum estimated that, in the USA at any point in time, one person/1000 has an unhealed venous ulcer<sup>[4]</sup> that becomes a disability factor in multiple aspects of daily life, including the number of work days on the job. Ulcers in lower limbs not only affects older people but it also affects actively working people<sup>[5]</sup>, resulting in two million working days lost in USA<sup>[6]</sup>. Ulcers also diminish the quality of life since they can cause health consequences to the patient<sup>[3]</sup> and to the social security health system as well. The treatment cost to patients with chronic venous ulcers in the USA is about three billion dollars per year, therefore it becomes a significant public health problem<sup>[7,8]</sup>. The elevated costs for treating this pathology has resulted in the development of new treatments with the objectives of reducing healing time, morbidity and associated costs.

Current treatment of venous ulcers involves the application of compression therapy, with bandages or hosiery, along with different dressing types applied beneath the compression bandage or hosiery to enhance healing, create a humid environment and control exudates. However, several studies have reported non-significant differences when applying dressing types regarding time of healing and numbers of healed ulcers<sup>[2]</sup>.

The advancement of new biotechnologies has focused on the development of alternative therapies such as growing tissue *in vitro*, production of recombinant growth factors and tissue engineering. The use of autologous-derived products from the patient's blood, along with collagen or fibrin matrices, with or without cultured cells and autologous growth factors, has been suggested as an alternative therapy for treatment of chronic ulcers<sup>[9]</sup>. *In vitro* studies with animal models have reported a beneficial effect of growth factors, specifically platelet-derived growth factor (PDGF), fibroblast growth factor and granulocyte-macrophage colony-stimulating factor, on the proportion of healed ulcers<sup>[10-12]</sup>.

Fibrin matrices are a cost-effective option for ulcer management. Their source is from the blood of the same patient and they provide scaffolding for tissue growth, migration and cell regeneration. The beneficial effects of the fibrin matrix may be enhanced when it is used in conjunction with growth factors that stimulates cell proliferation.

The objective of the present review is to evaluate the available evidence for effective management of venous leg ulcers with autologous fibrin matrix with or without growth factors.

## METHODS

We did a systematic review of studies evaluating the use of fibrin matrices with or without growth factors for the management of chronic venous ulcers in lower limbs. All studies were included without date restrictions. Articles searched in MEDLINE and EMBASE databases were performed in English. Available systematic reviews were searched in COCHRANE, and preliminary results and ongoing clinical trials were searched at ClinicalTrial.gov. The MESH terms corresponding to “fibrin” and “matrix”, and “venous ulcer” were used in the search. The article searched was restricted to human reports. The LILACS database was used for searches in Spanish and Portuguese languages. Intervention was defined as the application of any autologous fibrin matrix (from the same patient with or without growth factors, for the treatment of venous ulcers in lower limbs).

### Criteria for inclusion

The criteria for inclusion were studies evaluating patients with peripheral vascular disease of venous origin, who exhibited venous ulcers in lower limbs and received treatment with fibrin matrices with or without growth factors. Patients with chronic venous ulcers unhealed after 8 weeks of standard medical treatment.

### Criteria for exclusion

Studies involving patients with ulcers of arterial origin or “mixed etiology” (defined as: ulcers from a combination of arterial and venous origin, venous insufficiency in pregnant women), patients with chronic osteomyelitis, diabetes with ulcers in the lower limbs, Marjolin's ulcers (ulcerating squamous cell carcinoma), malignant or terminal disease with an incidence of  $\geq 5$  years, thermic, electric or radiation burns on the ulcerated area, vasculitis, chronic liver diseases, autoimmune diseases treated with immunosuppressant's, chemotherapy or radiotherapy, and diseases that affect wound healing, such as kidney insufficiency (patients in dialysis or receiving therapy following a kidney transplant), were excluded.

Also, studies of patients with concomitant use of others substances or products different than those evaluated in the present review, and those focused on compression instead of dressing therapy for the treatment of venous ulcers<sup>[13]</sup> were excluded from the present literature review.

The risk of bias was examined with the SIGN data analysis strategy, which assesses the internal validity and the quality assurance for each clinical study. A descriptive analysis was performed on the effective granulation in patients treated with fibrin matrix and with and without growth factors. The incidence of effective granulation was defined as those ulcers that healed completely or formed granulation tissue on  $\geq 75\%$  of the initial ulcer size. The mean time to healing or formation of granulation tissue was analyzed by using the Kaplan-Meier estimator. Absolute and relative frequencies were used to analyze the numbers of fibrin matrix applications required for effective granulation and its secondary consequences.

## RESULTS

The literature searched in MEDLINE by using the MESH term, restricted to human reports and without restrictions to dates or types of study, identified 14 articles [Table 1]. Of these, five were selected by title, which fulfilled the objective of the present study, but only three were relevant to our study<sup>[9,14,15]</sup>. Analysis of abstracts from 12 articles, showed that management of venous ulcers were performed with different products, such as platelet-derived, platelet-enriched plasma or non-fibrin matrices. Since those 12 articles did not focus in fibrin matrix with autologous growth factors, they were excluded from the review.

From the three relevant articles found in MEDLINE<sup>[9,14,15]</sup>, the O'Connell *et al.*<sup>[9]</sup> study was a pilot study, assessing the use of fibrin matrix and autologous growth factors for a period of 16 weeks, in 21 patients with chronic ulcers on lower limbs of different etiologies, including venous, arterial or a combination of both. Patients with ulcers of diabetic origin were included also, which was one of our exclusion criteria. In their pilot study, 66.7% of patients with venous ulcers showed completed ulcer healing within 7.1 weeks (median = 6 weeks). The second article, from the same group as the pilot study, was a description of the Cascade® product that they used in the original study<sup>[14]</sup>. The third article, from Hartmann *et al.*<sup>[15]</sup>, primarily assessed a series of cases of seven patients with chronic venous ulcers treated with cultured keratinocytes transplanted in fibrin matrix. Results showed complete ulcer healing in 4 of 7 ulcers, with a mean healing time of 14.5 weeks; however, it was not possible to conclude that completed ulcer healing was a consequence of the presence of fibrin matrix or cultured keratinocytes.

The search in EMBASE database identified 35 articles, from which 4 were selected by title [Table 1]. The remaining 31 articles did not meet the search criteria and did not evaluate the intervention objective of the present systematic literature review. From 4 of the articles identified by their title, 3 were relevant and were the same articles found in the MEDLINE database search<sup>[9,14,15]</sup>. The search in COCHRANE (Central Register of Controlled Trials) identified 1 review of 3 randomized controlled trials assessing the cost effectiveness of using different fibrin matrices, such as bovine collagen matrix with neonatal keratinocytes, acellular matrix and poly-n-acetyl glucosamine matrices, on venous ulcers in lower limbs<sup>[16]</sup>.

The search of protocols and ongoing clinical trials at ClinicalTrial.gov database by using the MESH terms did find any reports [Table 2]. Similarly, the search in Spanish and Portuguese at the LILACS database did not find studies reported in either of the two languages [Table 1].

None of the four relevant articles selected by their summary met the criteria for inclusion as described in the material and methods section, and did not evaluate the intervention objective projected for our study [Table 3]; therefore, these articles were excluded from the review.

## DISCUSSION

The primary treatment for venous ulcers involves application of compression therapy using bandages or compression hosiery<sup>[13]</sup>. In addition to compression therapy, different dressing types are applied beneath the compression bandage or hosiery, to enhance ulcer healing by creating a humid environment and controlling

**Table 1. Results of literature search in medical databases**

Database	Search terms	Search results	Articles selected	Abstracts selected	Downloaded articles	Articles included in the review
MEDLINE	Fibrin AND matrix AND venous ulcers AND venous leg ulcers	14	5	3	3	0
EMBASE	Fibrin AND matrix AND venous ulcers AND venous leg ulcers	35	4	3	3	0
Cochrane	Fibrin AND matrix AND venous ulcers AND venous leg ulcers	1	1	1	1	0
LILACS	Matrix de fibrina Y ulcera venosa	0	0	0	0	0

General results from search in MEDLINE, EMBASE, Cochrane and LILACS databases by using search terms. The total numbers of search results, articles selected by the title associated with the objective of the present review, articles selected by summary and downloaded, and articles included in the review after evaluating the inclusion and exclusion criteria

**Table 2. Search results of protocols and ongoing trials in ClinicalTrials.gov**

Search terms	Search results	Titles selected	Protocols selected	Protocols included in the review
Fibrin AND matrix AND venous ulcer	0	0	0	0

The search of protocols and ongoing clinical trials at ClinicalTrial.gov database did not show any results

**Table 3. Criteria for exclusion of relevant articles selected by abstract and excluded from the review**

Relevant articles	Exclusion criteria
O'Connell <i>et al.</i> <sup>[9]</sup>	Included 21 patients with chronic ulcers in lower limbs of differing etiology: venous, arterial or a combination of both
O'Connell <i>et al.</i> <sup>[14]</sup>	A description of the fibrin matrix product used in the article listed above
Hartmann <i>et al.</i> <sup>[15]</sup>	Included a second intervention of cultured keratinocytes in a fibrin matrix
Hankin <i>et al.</i> <sup>[16]</sup>	Included bovine collagen matrix with neonatal keratinocytes, acellular matrix and poly-n-acetyl glucosamine matrices

Four relevant articles selected by summary during the search in MEDLINE and EMBASE were excluded from the review. (1) O'Connell *et al.*<sup>[9]</sup> is a pilot study and not a clinical trial; (2) O'Connell *et al.*<sup>[14]</sup> described a commercial product Cascade®, but it is not a clinical trial; (3) Hartmann *et al.*<sup>[15]</sup> is a series of case reports of seven patients and did not conclude if the ulcer healing was a consequence of the presence of fibrin matrix or cultured keratinocytes; and (4) Hankin *et al.*<sup>[16]</sup> is an analysis of the cost effectiveness of using different products as compared to that of fibrin matrix

exudates. However, several studies have reported no significant differences when applying dressing types regarding time of healing and numbers of healed ulcers<sup>[2]</sup>.

A systematic review of randomized controlled trials assessing the effectiveness of wound dressings indicated that certain dressing types used for the management of chronic venous ulcers, could in fact, not only enhance the rate of ulcers cured but also their healing time<sup>[17]</sup>. In contrast, a meta-analysis study of dressing types for venous ulcers published in 2011, reported non-significant differences in the numbers of ulcers cured or the healing rate between different dressing types<sup>[2]</sup>.

Wound dressings can be divided into non-occlusive or occlusive types and the latter further subdivided into three subcategories: semi-occlusive/occlusive, growth factors and human skin equivalents<sup>[17]</sup>. The function of non-occlusive and semi-occlusive dressings is prevention of loss of water vapor from the wound and acting as a thermal insulator, which are factors that promote the incidence and time of wound healing<sup>[18]</sup>. The growth factors dressings directly provide a specific growth factor to the wound, or indirectly enhance

cellular growth and release of important substances for wound healing, while the human skin equivalents cover the wound and may also provide growth factors<sup>[17]</sup>.

Hydrocolloid dressings formed part of the occlusive dressing types and are usually composed of a matrix of sodium carboxymethyl cellulose with an adhesive elastomeric substance attached to a polymer base<sup>[19]</sup>. The hydrocolloid matrix absorbs exudates away from the wound surface ensuring a humid environment and promoting wound healing<sup>[20]</sup>.

In a systematic literature review of 20 randomized controlled trials evaluating whether complex wound dressings enhanced healing of venous ulcers, the author's reported that only 25% of the trials, and less than 10% of the overall studies, showed a significant proportion of healed ulcers by using these complex wound dressings<sup>[17]</sup>. Also, the use of hydrocolloid dressings did not enhance the proportion of ulcers healed in comparison to that of other dressing types, including growth factors. Similarly, a meta-analysis study from COCHRANE identified that hydrocolloid is the most evaluated dressing type, and an analysis of 27 (60%) studies, indicated that there was no evidence that the use of hydrocolloid dressings for the treatment of chronic venous ulcers was more effective than other dressing types, and concluded that ulcer healing rates were not affected by the type of dressing used beneath compression<sup>[21]</sup>. Even though there was not enough data for most of dressing types to provide significant evidence of which type was more effective for healing venous ulcers, hydrocolloid dressings were more effective than low adherence dressings<sup>[21]</sup>. Nonetheless, none of these studies included growth factors dressing types or products with fibrin matrices, platelet-enriched-plasma or autologous growth factors in their analysis.

Regardless of the availability of new complex dressing types, the gauze is the dressing that is still most frequently used worldwide. Gauze is economical, easily available, absorbent and well known by health personal. Petrolatum or Vaseline impregnated gauzes commonly are used to provide a moist environment, and avoid desiccation that is conducive to wound healing<sup>[22]</sup>.

The advancement of new biotechnologies has focused on development of alternative therapies by growing tissue *in vitro*, producing recombinant growth factors and tissue engineering. *In vitro* studies with animal models have reported a beneficial effect of growth factors, specifically, PDGF, fibroblast growth factor and granulocyte-macrophage colony-stimulating factor, on the proportion of healed ulcers<sup>[9,11]</sup>. The practice of using growth factors for the treatment of chronic ulcers was the consequence of research results that demonstrated a significant reduction of localized growth factors in chronic wounds, resulting in cell cycle arrest and senescence of the wound bedding cells<sup>[10]</sup>.

Fibrin matrix and autologous growth factors became a cost-effective option for the management of patients with venous ulcers in the lower limbs. These biological products can be obtained from the same patient's blood, and provides scaffolding for tissue growth, migration and cell regeneration. The beneficial effects of the fibrin matrix may be enhanced when it is used with growth factors that stimulate cell proliferation. Currently, the challenge is producing an improved system for releasing high concentrations of growth factors to the bedding wound and establishing a close relationship between the bedding wound and Diana cells.

In our literature search we found little evidence for the efficacy of treating chronic venous ulcers with products containing fibrin matrix, platelet-enriched- plasma and autologous growth factors. In fact, we found only one pilot study that included patients with venous ulcers, but it also included patients with arterial ulcers and from other etiologies. The 12 patients with venous ulcers were treated with a product containing fibrin matrix, platelet-enriched- plasma and autologous growth factors, of which 8 (66.7%; 64.7% of the treated ulcers) showed completed ulcer healing within 7.1 weeks (median = 6 weeks) after a mean of



two applications per patient. The incidence of effective granulation  $\geq 75\%$  of the ulcer size was observed in 76.5% of the patients at 5 weeks of treatment initiation<sup>[9]</sup>. Also, we found a report case of seven patients with chronic venous ulcers treated with cultured keratinocytes which were transplanted in a fibrin matrix. Results showed complete ulcer healing in four of seven ulcers treated, with a mean healing time of 14.5 weeks<sup>[15]</sup>. However, it was not possible to conclude that completed ulcer healing was a consequence of the presence of fibrin matrix or cultured keratinocytes. The authors suggest, based on *in vitro* and *in vivo* studies, that the fibrin residue in cultured keratinocytes may inhibit complete wound healing after the transplantation. Therefore, the use of low density fibrin, instead of high density, to enhance grafting, keratinocytes survival and epithelialization was recommended.

### **Study limitations**

The major limitation of the present study is the few studies available evaluating the management of venous ulcer with fibrin matrix and with or without growth factors. Most studies evaluated ulcers from different etiologies and ulcer management was done with a combination of fibrin matrix with different products or non-fibrin matrices. Therefore, it was not possible to perform a meaningful analysis of this type of intervention.

### **Conclusions**

This review has not identified conclusive evidence for the use of fibrin matrices with or without growth factors in patients with venous leg ulcers. We found only a few studies that evaluated the results of this intervention.

### **DECLARATIONS**

#### **Authors' contributions**

Study conception and design, critical revision: García Botero A

Acquisition of data, critical revision: Cantini Ardila JE

Analysis and Interpretation of data, critical revision: Devos Borja LD

Drafting of manuscript, critical revision: Gómez-Ortega V

#### **Data source and availability**

Article searches were performed in MEDLINE, EMBASE, COCHRANE, LILACS and ongoing clinical trials at ClinicalTrial.gov.

#### **Financial support and sponsorship**

None.

#### **Conflicts of interest**

There are no conflicts of interest.

#### **Patient consent**

Not applicable.

#### **Ethics approval**

Not applicable.

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Original Article

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# A simple classification and a simplified treatment's algorithm for ptotic breasts

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## Abstract

**Aim:** Many classifications have been described in the literature for ptotic breasts, focusing on the nipple areola complex position compared to the inframammary fold. These use centimeters and lateral views to illustrate their various grades in a manner always insufficient to propose a clear treatment plan aimed at achieving natural results. We discuss a new dynamic approach to breast ptosis with a complete treatment algorithm.

**Methods:** Patients were examined in a standing position first with hands down then with hands up. We observed the elevation of the inter-nipple line called the "BK-line" and its relationship to a sternal benchmark that we call the "BK-Point". The "hands-up test" was positive when the line crossed the landmark. The algorithm defines the indication according to this clinical examination and to the patient's wishes. An angle between the nipple, the "BK-point" and the body meridian (called the "BK angle") was appreciated before and after surgery. This angle should become 90° or more after ptosis treatment.

**Results:** Three hundred patients were treated for ptotic breasts, including breast reductions, from January 2010 to September 2017. The definitions of "normal" non-ptotic and ptotic breast and the "ideal" breast were reconsidered. The surgical indications were adjusted to the clinical situation and to the patient's wishes, refining the final version of the algorithm.

**Conclusion:** This new classification is easy, reproducible and efficient. We propose an appropriate algorithm to treat every situation that takes care to consider patient's wishes and expectations.

**Keywords:** Breast ptosis, mammoplasty, vertical lift, mastopexy, breast reduction, breast implant, ptosis classification



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## INTRODUCTION

The female breast is one of the rare anatomical organs that has no bony or cartilaginous supports. Suspended to the trunk by its soft structures, the final shape is substantially influenced during growth by the bone, cartilage and muscle elements that surround the breast's bases. For an adult woman, the "perfect" match of a glandular tissue, fat, skin and connective tissue that hold everything in place may theoretically give rise to a "perfect breast". The natural or pathologic excess of one of these anatomical tissues may lead to breast sagging, or what we call breast ptosis.

Time and gravity also affect the breast and induce glandular and skin stretching, especially in the peri-areolar area and in the lower pole where weight is maximal. In addition to the anatomical comprehension of this auto-suspended organ, the aesthetic and social representation of the sexual organ defined over centuries, including through artwork, provided guidelines for ideal measurements of the "perfect breast", as well as various classifications for ptotic breasts.

In this paper we will revisit the primary classifications we were taught during training, to ascertain their inadequacies and to propose a new simple classification with a treatment algorithm that also takes the patient's wishes into account.

## METHODS

We consider two important landmarks:

1. The sternal landmark is a single point on the sternum where the inframammary folds, or their extensions, cross the midline. We call it the Breast Key point or "BK-Point" [Video 1].
2. The inter-nipple line or Breast Key line: "BK-line" is a virtual line joining the nipples for which we have to restore the horizontality in case of an asymmetry, and make it cross the BK-point after treating the ptosis [Video 2].

We examine the patient in a standing position hands down along the body in frontal, oblique and lateral views and take photos for preoperative analysis and as a reference for the post-operative check.

We ask the patient to put her hands up and note the BK-line ascent and its eventual crossing of the BK-point.

Photos are also taken as a reference and are saved in the patient's file.

The second examination was completed on the screen with an oblique view photo. We appreciated the angle between the ipsilateral nipple to body rotation (right nipple to right oblique view and vice-versa), and the BK-point and body meridian usually parallels the dorsal spine. We call this angle the Breast Key (BK) angle, and we roughly appreciate its value compared to a right angle.

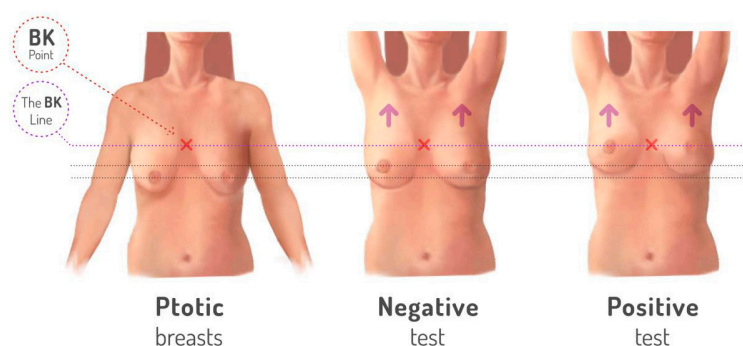
Our approach is simple:

With a patient's hands down, there is no ptosis if the BK-line crosses the BK-point.

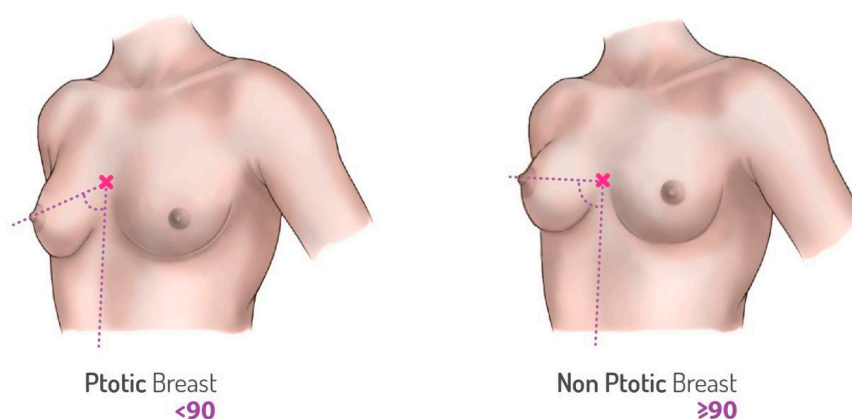
A "natural ptosis" exists when this match occurs after asking a patient to put her hands up. We call this maneuver a "hands up test" positive.

A "confirmed ptosis" is defined when the BK-line remains under the BK-point with a hands-up maneuver. We call this a negative "hands-up test" [Figure 1] [Videos 3 and 4].

## Hands' up test



**Figure 1.** The “hands-up test” maneuver



**Figure 2.** The BK angle appreciation

The BK-angle is less than  $90^\circ$  in case of a ptotic breast and becomes  $90^\circ$  or more after successful ptosis treatment [Figure 2].

## RESULTS

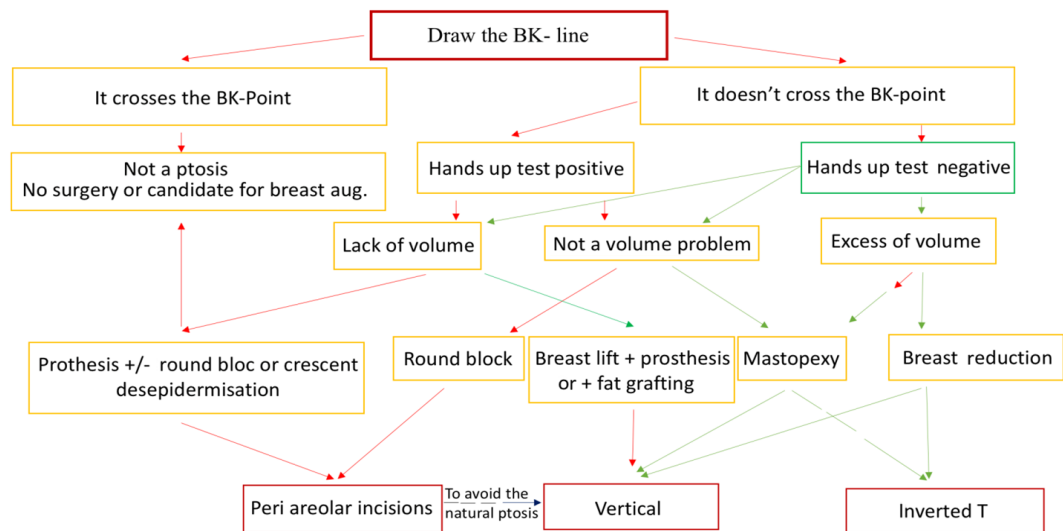
From January 2010 to September 2017, 300 patients presenting for breast lift, mastopexy or breast reduction were analyzed and treated with various surgical techniques. The first aim was ptosis treatment and the second was to satisfy the patient's wishes; at the surgeon's suggestion, augmentation or reduction of the volume, or sometimes the redefinition of the breast shape was undertaken. Gigantomastia and important asymmetries including Poland's syndrome, oncologic breast surgery and tuberous breasts were excluded from this study.

From this experience and from various clinical observations, an algorithm was proposed for every situation in our classification [Figure 3] and some representative cases were illustrated [Figures 4-7].

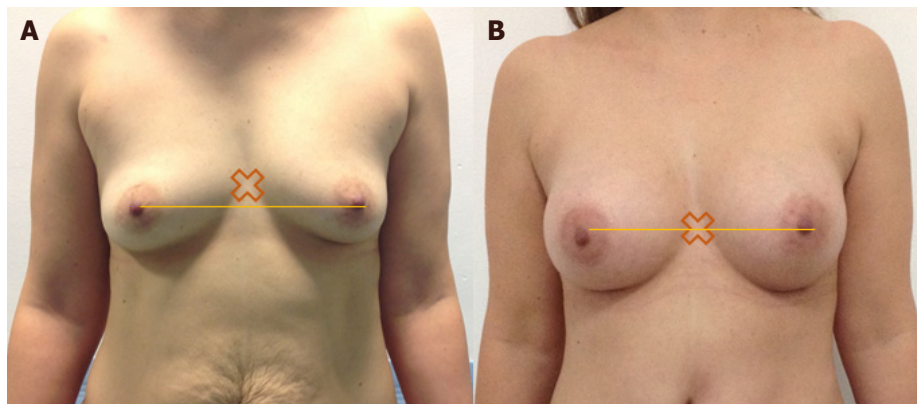
## DISCUSSION

A quick look at two mythic Venuses throughout the history of art: the Venus of Willendorf [Figure 8] and the Venus de Milo [Figure 9], shows us substantial evidence of the evolution of the criteria for aesthetic beauty

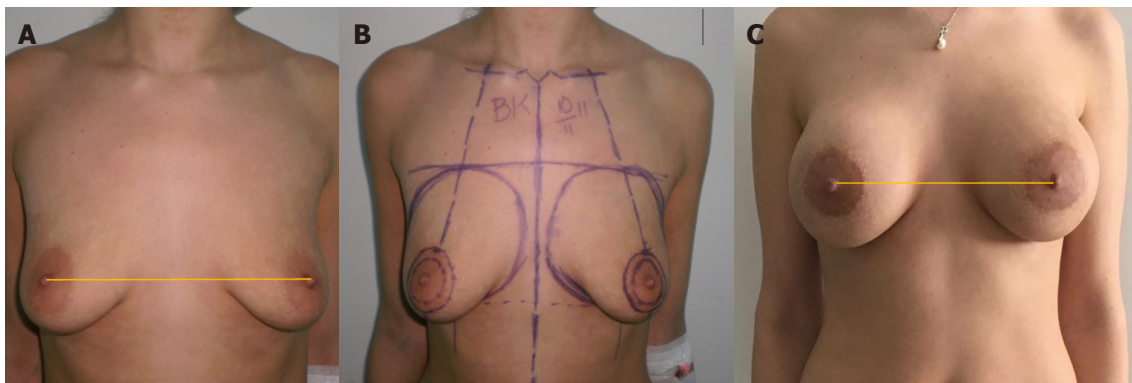




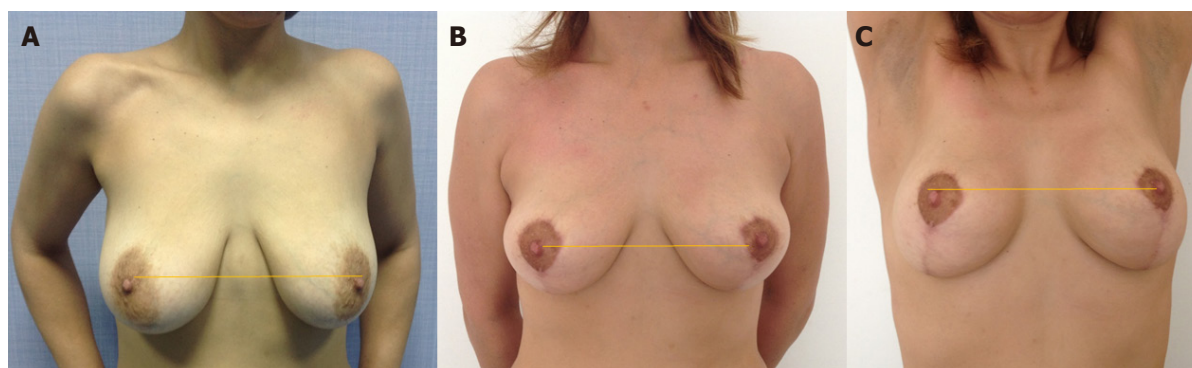
**Figure 3.** Algorithm for the ptotic breasts' treatment



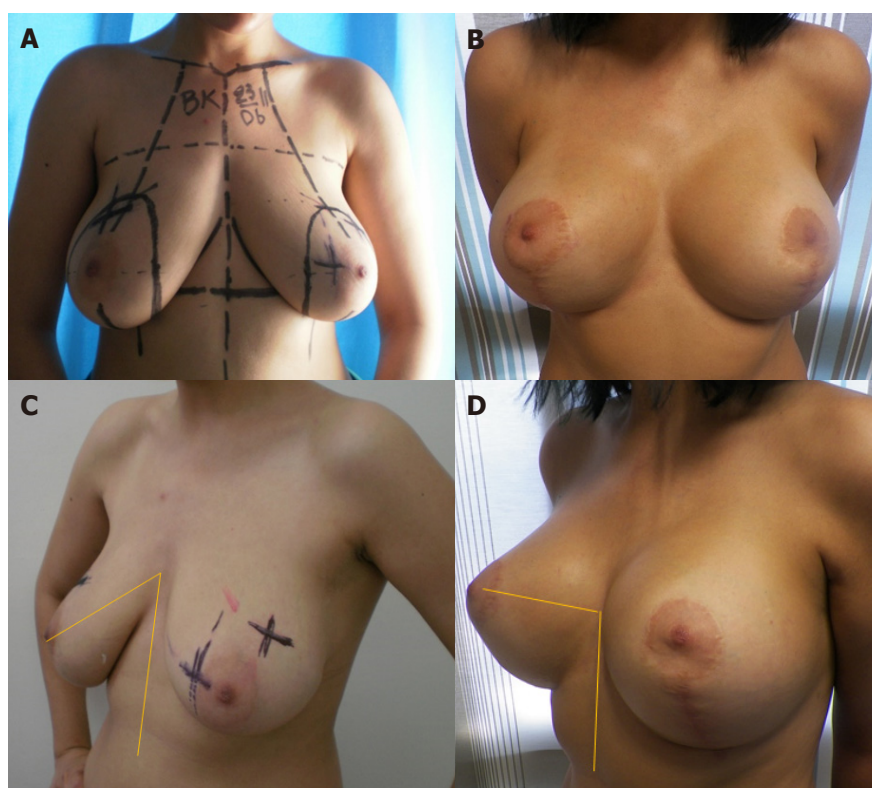
**Figure 4.** (A) Small ptosis after breast feeding with a hands up test positif; (B) a simple breast augmentation can restore the lost volume during a mommy makeover procedure and allows the ptosis treatment



**Figure 5.** (A) A 25-year-old woman asking for a breast augmentation. The distribution of the glandular tissue and the apparent "dysmastia" with an external position to the midline of the IMF may explain the eventual ptosis effect. The BK line is still crossing the BK point; (B) a round block approach with a 450 mL round silicone implants in a dual plane were performed; (C) a stable result after 4 years and 2 pregnancies



**Figure 6.** (A) A 35-year-old woman asking for a breast ptosis treatment with a natural look. Implants and fat grafting were discussed and rejected by the patient insisting to have a natural result; (B) a “chignon mastopexy” was performed keeping, after a year, a minor ptosis for a natural effect; (C) this ptosis is giving, according to our approach, a natural breast look and of course this ptosis is corrected with a hands up test



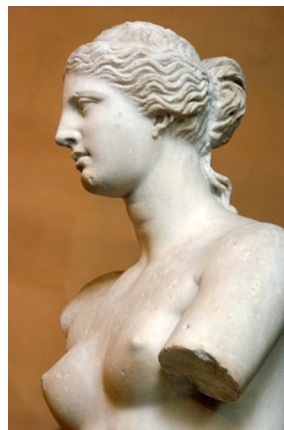
**Figure 7.** (A) A 30-year-old woman with an important ptosis and multiple nodules asking for a breast lift and a minor volume augmentation as well as a “push-up effect”; (B) a vertical breast lift approach was performed with multiple fibroadenomas resections. A 320 round and moderate profile silicone implants were added before the final cutaneous lift. Here, we did not opt for a natural breast ptosis effect and directly restored the BK line to the BK point level; (C) and (D) note also that the BK angle is deliberately pulled up to more than 90° to confirm this “push up effect”

of the female body; from enlarged and ptotic breasts symbolizing good health and perhaps breastfeeding in a mother goddess, to a small, non-ptotic and athletic breast symbolizing femininity (as well as good health) in a goddess of love and beauty<sup>[1,2]</sup>. Breast ptosis is no longer in vogue.

The definition of a ptotic breast remains controversial even if currently the standards are more or less common among continents, societies and tribes. The complexity of this task, especially for proposing



**Figure 8.** Venus of Willendorf



**Figure 9.** Venus of Milo

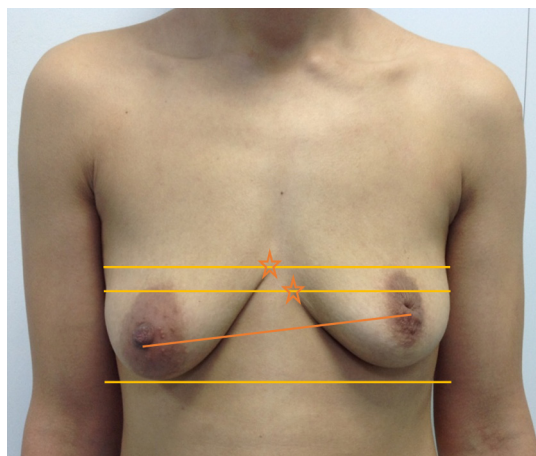
surgical treatments, has been exposed by a number of publications and classifications of ptotic breasts since Dufourmentel and Mouly's book in 1959<sup>[3]</sup>.

Dufourmentel and Mouly defined ptosis by the dropping of the nipple down and out using "5 cm" as a level unit to switch from a grade to another<sup>[3]</sup>, while Lalardrie and Jouglaire chose the inframammary fold (IMF) as a benchmark to measure the fall of the lowest point of the breast using 2 and then 4-10 cm as the levels at which grades switch<sup>[4,5]</sup>. They also reported a change in the form of segment II, normally convex according to their interpretation and becoming straight and then concave with ptosis.

A normal natural breast in our observations will never have a spontaneously convex segment 2; this remains an effect of a push-up or a surgical procedure.

Regnault<sup>[6]</sup> proposed one of the most common classifications to date, using a combination of these two former classifications while taking the nipple, the IMF and the lowest point on the breast as landmarks to define various grades as well as the "normal breast", "pseudo ptosis" and "parenchymal maldistribution".

By avoiding the use of numbers and centimeters and the individualization of two extra different types involving the glandular distribution during the breast development, Regnault<sup>[6]</sup> proposed a wide and wise clinical observation of the various types of breasts, explaining the popularity of this classification worldwide.



**Figure 10.** Example of an asymmetry with an offset definition of the Inframammary fold: The stars show different positions of the inframammary folds reaching the midline; the BK point in this case will be the upper one and the ptosis treatment will aim to horizontalize the BK line and make it crossing the BK point

Even if we totally adhere to Regnault<sup>[6]</sup> to individualize “parenchymal maldistribution” that we also excluded from our classification, we do not agree with the definitions of “normal breast”, “true” or “pseudo-ptosis”. In fact, what is “normal” for Regnault<sup>[6]</sup> is a “perfect breast” for us, as we consider that a normal breast may also have a small ptosis regressing with a “hands up test” positive. Conversely, this small ptosis may express desirable femininity in some cultures; many Asian women, in order to prove their mature femininity, waged a hashtag campaign called #carrypenunderbreast that went viral on social media, demonstrating that a glandular parenchymal distribution under the IMF is, for the majority of people, a desired target in the Eastern hemisphere and also a normal shape in Western countries.

“Pseudo-ptosis” considers the sagging of the parenchyma despite the nipple position remaining above the IMF without taking regard to the high or low position of the IMF. Indeed, this crease is a curved line, usually starting from the anterior axillary line to the sternal area with a different attachment and a different direction from one patient to another, and sometimes from one breast to another for the same woman [Figure 10]. Using it as a landmark is a shortcoming of the Regnault<sup>[6]</sup> classification, as well as the one proposed a year later by Vandebussche<sup>[7,8]</sup> and even later reconfirmed in the literature by including a physiological approach to each of the four new grades described by the same author.

Robert Brink confirmed this physiological necessity to explain ptosis one year after Vandebussche’s paper<sup>[7,8]</sup> by proposing a different classification in his work, and a variation of the “Round Block” periareolar mastopexy approach to the “true ptosis concept”<sup>[9]</sup>.

In our approach, we always analyze the physiology of breast sagging for each patient but never nest it within a treatment diagram. We believe that defining a true and a pseudo-ptosis is unfit for a decision-making process as confirmed by Kirwan’s vision<sup>[10]</sup>.

Nevertheless, despite the detailed and pragmatic algorithm proposed by this author, we do not agree with the use of centimeters as a way of measurement to differentiate one proposed alphabetic grade from another. In fact, we believe that “1 cm” on the breast is different from one woman to another according to the skeleton and to the phenotype of each body, and that the classification of the breast and the diagnosis of the ptosis have to be defined in an overview and designed in a frontal view (never on a lateral view).

In Figure 5 we elaborated an algorithm that respects the surgeon’s training and preferred technique in order to globalize the clinical and surgical approach to the primary task of breast ptosis treatment. Even if we



usually prefer a less-invasive approach to each case with as few scars as possible, by privileging the round block technique as described by Benelli<sup>[11]</sup> or by Brink<sup>[9]</sup> (with unfortunate rapid limitation of its use<sup>[12]</sup>), deliberately or not, there would be preservation of “natural ptosis” corrected with a “hands up test” positive or enlargement of the round scar. Therefore, we prefer the vertical approach for a breast lift, as described by Lassus<sup>[13]</sup>, or mastopexy using the chignon technique as described by Kotti<sup>[14]</sup> instead of the inverted T approach. However, as we believe that our algorithm must respect the patient’s wishes as to final volume, the final scars and the respect of the presence or absence of a natural ptosis, we also believe that it must respect the surgeon’s training and the diversity of the effective surgical procedures described in the literature to find final balance that serves the cause of the ptosis treatment and respects a universal beauty criterion.

We propose a classification that is:

- Simple: without measurements,
- Reproducible: with a simple clinical maneuver without the use of any special devices and,
- Efficient: the breast is analysed in a frontal view, not lateral views, as it is seen in daily social life.

We also propose an appropriate treatment algorithm for every situation that takes the patient’s wishes and expectations into account and obeys plastic surgery principles without excluding any surgical technique in order to adapt to the various surgeons’ approaches and preferable procedures.

## DECLARATIONS

### Authors’ contributions

The author contributed solely to the paper.

### Data source and availability

The data presented is original and obtained in our laboratory. It is available with the authors and can be made available if required.

### Financial support and sponsorship

None.

### Conflicts of interest

There are no conflicts of interest.

### Patient consent

Consents from all of the patients were established prior to submission.

### Ethics approval

All treatment and study were performed in compliance with our institutional standard and the Declaration of Helsinki.

### Copyright

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Original Article

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# Key rheological properties of hyaluronic acid fillers: from tissue integration to product degradation

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## Abstract

**Aim:** Over the last 15 years, hyaluronic acid (HA) fillers have become the most popular injectable biomaterial for soft tissue correction. With the increasing number of available HA fillers and the multiplication of facial treatments all over the world, there has been a need from physicians to better understand the HA fillers science. There is especially a growing interest in the science-based evaluation of rheological characteristics which represents an essential tool to guide physicians in the selection of the most appropriate HA fillers, administration techniques and depths of injection for their clinical applications.

**Methods:** Four key rheological parameters (viscosity  $\eta$ , elasticity  $G'$ , normal force  $F_N$  and elasticity  $E'$ ) are measured and discussed on five HA fillers.

**Results:** These four key rheological parameters are demonstrated to play a pivotal role, in combination with the cohesivity, for better predicting the clinical behavior of HA fillers at different stages of their lifetime.

**Conclusion:** This article discusses the importance of four key rheological parameters during the main steps of the clinical HA fillers' lifetime, from the product injection to the loss of clinical effects. A better knowledge of these HA fillers' rheological parameters can help the physicians to optimize their aesthetic outcomes, safety and patient satisfaction.

**Keywords:** Hyaluronic acid fillers, rheological properties, product lifetime, tissue integration, clinical effects



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## INTRODUCTION

Injectable hydrogels known as fillers are commonly used in aesthetic medicine to shape the face or to treat signs of facial ageing, e.g., to smooth superficial wrinkles or to palliate age-related atrophy and ptosis by remodeling some parts of the face. Among these injectable hydrogels, hyaluronic acid (HA) fillers have a dominant and unchallenged position<sup>[1]</sup>. In 2016, according to the American Society for Aesthetic Plastic Surgery (ASAPS), 2.49 million HA filler treatments were performed only in the USA with a high growth of 16.1% versus the previous year<sup>[2]</sup>. With the rising interest in the HA treatments and the increasing number of available HA fillers on the worldwide market, there is a strong demand from the medical community to better understand the science behind these products in order to optimize aesthetic outcomes and safety. Available HA fillers are designed with different manufacturing technologies<sup>[3,4]</sup>, different HA concentrations<sup>[5]</sup>, different crosslinked three-dimensional network structures<sup>[6]</sup>, different pore size distributions of the fibrous HA networks<sup>[6]</sup>, and different cohesivity levels<sup>[7]</sup> and rheological properties<sup>[8,9]</sup>. Among the proprietary manufacturing technologies, which all allow obtaining specific rheological properties, we can mention the VYCROSS™ (Allergan Inc., Irvine, CA, USA), the NASHA™ (Galderma Pharma S.A., Lausanne, Switzerland) and the CPM™ (Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany) technologies. The VYCROSS™ technology uses a combination of low and high molecular weight of HA during the crosslinking to improve the efficacy of the chemical reaction. The NASHA™ technology uses a step of controlled particle sizing, after the crosslinking reaction, to obtain specific HA gel textures. The CPM™ technology uses a two-step process during the crosslinking reaction for obtaining a cohesive gel with different crosslinking densities of the HA network. Recently, a novel proprietary manufacturing technology for the production of innovative HA fillers has been discovered. It is the OXIFREE™ technology (Kylane Laboratoires S.A., Plan-les-Ouates, Switzerland) which is characterized by the extraction of destructive oxygen during the manufacturing process, including during the crosslinking step, for significantly preserving the intrinsic properties of the long molecular weight of HA chains. This new technology provides HA fillers with advanced rheological properties which enable to exhibit strong projection capacities and therefore a high ability to volumize the facial skin tissues. All the fillers available on the market are designed by the manufacturers with the aim to be injected by the physicians into the dermal layer, for the superficial ones or into the subcutaneous tissues, for the products with a higher projection capacity. Due to their clinical applications and the major importance of their mechanical behavior features to achieve safe and good results, the rheological properties of the HA fillers are naturally considered key in the field and it is the reason why many articles have been published on this topic over the past few years<sup>[8-12]</sup>. Some of these articles emphasize the importance of the science-based evaluation of HA fillers and more specifically the rheologic tailoring for guiding physicians to identify the HA fillers that they want to use and to select the most appropriate administration technique and depth of injection<sup>[9]</sup>. Nevertheless, to the best of our knowledge, no published article has evaluated the relevance of the key rheological parameters of a HA filler during its whole clinical lifetime, i.e., from injection of the HA gel into skin tissues to its *in vivo* degradation over the months, as it is the case in this article. In the light of the assessment of these key rheological parameters, this article also analyzes the mechanical behavior of a novel HA fillers range, benefiting from the OXIFREE™ technology, in order to better understand the safety and the performance of these new products from the injection into skin tissues up to the loss of the clinical effects. Notably, the projection capacity of these new HA fillers is compared to that of the market leader in the volumizing segment, Juvéderm Voluma™ (Allergan Inc., Irvine, CA, USA), a device produced according to the VYCROSS™ technology.

## METHODS

### Materials

Five crosslinked HA fillers intended for facial injection in aesthetic medicine were subjected to flow, oscillatory shear-stress and compression tests with a DHR-1 rheometer (TA Instruments, New Castle, PA, USA). Among these 5 HA fillers, four are manufactured according to the novel OXIFREE™ technology [Table 1], and one is Juvéderm Voluma™, manufactured according to the VYCROSS™ technology.

**Table 1. Description of a novel range of HA fillers produced according to the OXIFREE™ technology**

Product reference	Manufacturer	Manufacturing technology	Crosslinked HA content (mg/mL)	Clinical indications
A	Kylane Laboratoires SA (Plan-les-Ouates, Switzerland)	OXIFREE™	15	Injection in the dermis or the lips mucosa Treatment of fine lines, medium-sized skin depressions of the face area and lips definition or enhancement
B			18	Injection in the deep dermis or the lips mucosa Treatment of deep skin depressions of the face area and lips enhancement
C			21	Injection in the fat tissue or into the supraperiostic zone Restoration of the volume of the face with a high projection capacity
D			24	Injection in the fat tissue or into the supraperiostic zone Restoration of the volume of the face with a higher projection capacity than product C

### Flow test

The flow test enables to measure the viscosity  $\eta$  of the gel. It was performed at a temperature of 25 °C under shear rate from 0.001 to 1000 s<sup>-1</sup> with a cone/plate aluminium geometry of 40 mm 2 degrees and a 50- $\mu$ m gap between the cone and the plate of the rheometer. The value of the viscosity  $\eta$  is measured at the shear rate of 1 s<sup>-1</sup>.

### Oscillatory shear stress test

The oscillatory shear stress test enables to measure the elastic modulus  $G'$ . It was performed at a temperature of 25 °C in shear stress oscillation mode at 1.0% of strain, within the linear viscoelastic region, with a cone/plate aluminium geometry of 40 mm 2 degrees and a 50- $\mu$ m gap between the cone and the plate of the rheometer. The measurements were carried out over a frequency range of 0.1-5 Hz. The value of the elastic modulus  $G'$  was measured at the physiologically oscillation frequency of 1 Hz.

### Compression test in static mode

The compression test in static mode enables to measure the normal force  $F_N$ . It was performed at a temperature of 25 °C in normal force mode, with a cone/plate aluminium geometry of 40 mm 2 degrees: 1.0 g of gel was placed between the cone and the plate and the cone was set in contact with the gel and lowered toward the bottom plate, thus compressing the gel. The normal force ( $F_N$ ) was measured for a gap between the cone and the plate of 1.11 mm (inverse gap = 0.9 mm<sup>-1</sup>).

### Compression test in dynamic mode

The compression test in dynamic mode enables to measure the elastic modulus  $E'$ . It was performed at a temperature of 25 °C in compression oscillation mode at 1.0% of strain, within the linear viscoelastic region, with a 40-mm plate/plate aluminium geometry and a 0.5-mm gap between the parallel rheometer plates. The measurements were carried out over a frequency range of 0.1-5 Hz. The value of the elastic modulus  $E'$  was measured at the physiologically oscillation frequency of 1 Hz.

### Data analysis

All measurements were carried out in triplicate. Data were expressed as the mean  $\pm$  standard deviation (SD). Coefficients of variation lower than 10% were considered as satisfactory. Results were evaluated statistically using Student's *t*-test with a level of significance fixed at  $\alpha = 0.05$ .

## RESULTS

The key rheological properties viscosity  $\eta$ , static compression  $F_N$ , elastic modulus in shear stress  $G'$  and elastic modulus in compression  $E'$  were measured on the novel range of HA fillers benefiting from the OXIFREE™ technology and on the market leader device Juvéderm Voluma™. The results are summarized in Table 2.

**Table 2. Key rheological properties of a novel HA fillers range produced according to the OXIFREE™ technology and Juvéderm Voluma™**

Product reference	Viscosity $\eta$ at $1 \text{ s}^{-1}$ (Pa.s)	Normal force $F_N$ of compression at $0.9 \text{ mm}^{-1}$ (cN)	Elastic modulus $G'$ in shear stress at 1 Hz (Pa)	Elastic modulus $E'$ in compression at 1 Hz (Pa)
A	$58 \pm 0$	$12 \pm 1$	$137 \pm 1$	$36,080 \pm 1050$
B	$95 \pm 2$	$21 \pm 2$	$192 \pm 3$	$50,130 \pm 1330$
C	$158 \pm 11$	$43 \pm 4$	$248 \pm 3$	$67,021 \pm 1569$
D	$204 \pm 12$	$71 \pm 7$	$310 \pm 4$	$85,765 \pm 1701$
Juvéderm Voluma™	$65 \pm 1$	$15 \pm 2$	$318 \pm 3$	$59,000 \pm 1440$

## DISCUSSION

Injectable HA fillers are provided in sterile syringes to the physicians. The HA fillers lifetime begins by the injection of the product into skin tissues and it concludes by the *in vivo* degradation of the HA biopolymer.

The main steps of the HA fillers lifetime after tissue implantation can therefore be defined as:

### Step 1: injection & integration

This step corresponds to the extrusion of the HA filler through the needle by the physician followed by the *in vivo* distribution and integration of the HA gel into the skin, after the injection. Based on the clinical experience, this step is considered to last from few hours to 2 weeks after the injection procedure.

### Step 2: projection

This step corresponds to the phase of skin projection for which the HA filler pull up the tissues thanks to its specific rheological properties. It lasts generally from few months to 2 years, depending on the product formulation, the treated area, the depth of injection and the patient's metabolism.

### Step 3: dynamic facial expression

This step corresponds to the phase of facial expression, e.g., when the patient speaks, smiles or eats, for which the gel firmness of the HA filler must be appropriate, i.e., as close as possible of its *in vivo* environment, to move as one with the skin tissues for offering natural clinical outcomes. This step 3, which is concomitant to step 2, lasts generally from few months to 2 years.

### Step 4: degradation

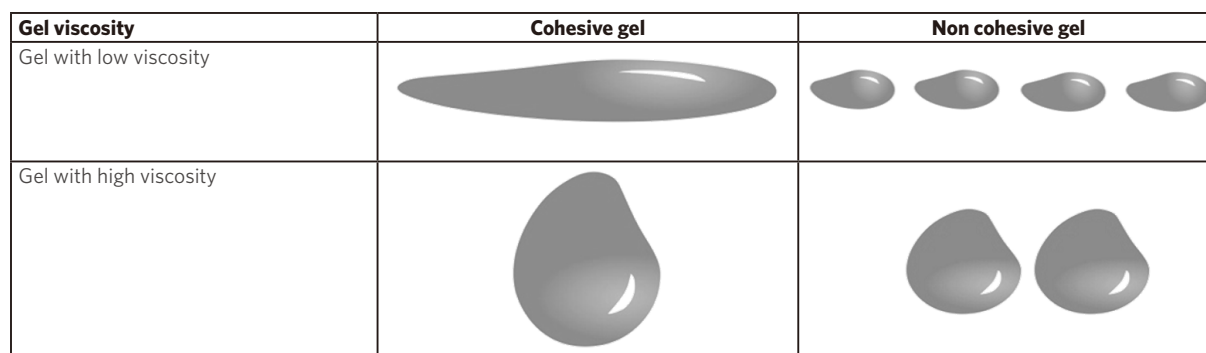
This step corresponds to the *in vivo* HA filler degradation, with the consequence of the loss of clinical effects. It corresponds to the decrease of the clinical outcomes over time due to the *in vivo* HA gel degradation in the treated area. The main factors of HA filler degradation are the free radicals, the hyaluronidases, the thermal hydrolysis and the mechanical stress. This step ends generally in the 2 years following the injection procedure.

### Step 1 of HA fillers' lifetime: injection & integration

Crosslinked hyaluronic acid, even more than the native hyaluronan, is a viscous biomaterial. Nonetheless, manufacturers produce HA fillers which are most of the time considered by physicians as easy to inject through a thin needle of 30 G or 27 G. To achieve this challenge, manufacturers develop specific technologies and product formulations to develop HA gels with a low viscosity at high shear rate when they are extruded through a thin needle. The lower this viscosity at high shear rate, the easier is the extrusion force for the physician to push the gel through the needle. Consequently, the viscosity  $\eta$  is a key parameter of the injection procedure for a HA filler, affecting its extrusion force.

When the HA gel goes out of the needle, it is distributed into the skin tissues depending on the rheological properties and cohesivity of the gel and the specific physico-mechanical properties of the receiving tissues<sup>[4,13]</sup>. The cohesivity, defined as the capacity of a material not to dissociate, because of the affinity of its molecules





**Figure 1.** Schematic representation of the cohesivity and viscosity of a HA gel. Impact of the cohesivity and viscosity on the shape and behavior of the gel

for each other, is naturally important during the product distribution into the tissues of the treated area<sup>[7]</sup>. However, the rheological properties have also a substantial role at this beginning of the *in vivo* HA filler lifetime. More specifically, among the rheological properties, the viscosity  $\eta$  is the key parameter at this step of the treatment. The viscosity level of the HA filler, combined with its cohesivity profile [Figure 1], define its capacity to remain at the injection site or to spread into the tissues. Thus, a HA gel with a poor viscosity has a higher ability to flow and spread in the tissues in comparison to a gel with a high viscosity. Appropriate viscosity and cohesivity of the HA filler provide the capacity to be easily moldable after injection during massage, allowing the product to be adequately placed, distributed and homogenized within the tissues, without fragmentation of the gel.

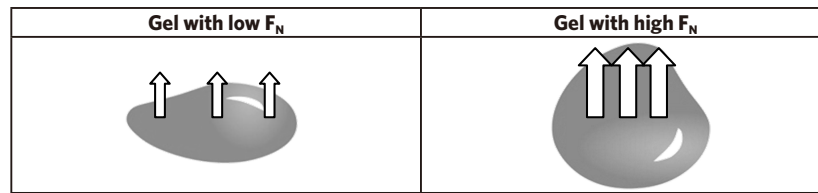
The consideration of the viscosity as a key rheological parameter for product distribution, and therefore for tissue integration, is consistent with the clinical uses of the HA fillers by the physicians. Indeed, on the contrary to high viscosity HA fillers, the products with low viscosity are often used to treat superficial indications, where nice and homogeneous tissue integration is especially desired, as for instance for the treatment of fine lines. These products spread easily or quite easily in the skin tissues, sometimes with the implementation of a smooth massage by the physicians, and there are commonly injected in the dermis, sometimes even in the superficial dermis with the “blanching injection technique”, without high risk of nodules formation<sup>[14]</sup>.

### Step 2 of HA fillers' lifetime: projection

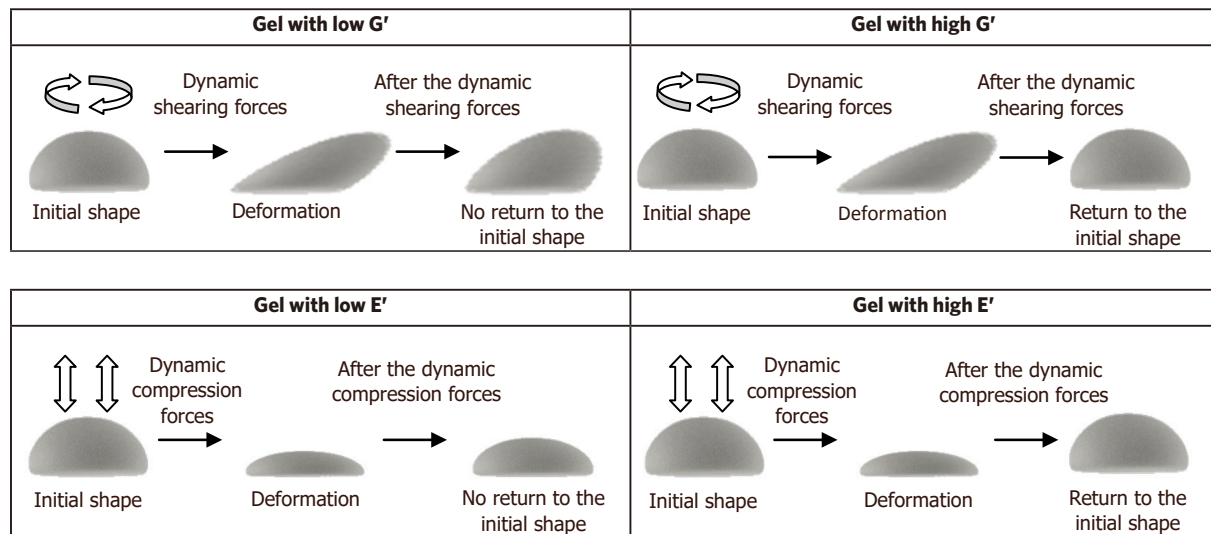
The normal force  $F_N$  of the HA filler plays a preponderant role during all the implantation phase with an essential effect on the tissues projection capacity<sup>[8]</sup>. The rheological parameter  $F_N$  is defined as the force applied by the gel perpendicularly to its surface when it is compressed. The force  $F_N$  allows the gel to push over the surrounding tissues and to counter the deformation and flattening of the product due to the pressure caused by skin tissues. Therefore, this force reflects the ability of the HA filler to project the skin tissues all along the implantation period. The higher is the normal force  $F_N$  of the filler and higher is the capacity to push the skin tissues to project them [Figure 2].

### Step 3 of HA fillers' lifetime: dynamic facial expression

As a HA filler is commonly administered in the face, it is essential for the patients and the physicians to have a product with a high capacity to smoothly and naturally accompany the mechanical motions of the face due to the dynamic facial expression. In this regard, the dynamic parameters  $G'$  (elastic modulus in shear stress) and  $E'$  (elastic modulus in compression), representative of the gel firmness in dynamic conditions, are extremely important rheological parameters during this step of the HA filler lifetime<sup>[8]</sup>. The elastic modulus  $G'$  represents the ability of the HA filler to resist to dynamic shearing forces (i.e., behavior of the gel for recovering its shape after shear deformation) while the elastic modulus  $E'$  represents the ability of the



**Figure 2.** Schematic representation of the level of normal force  $F_N$  for a HA gel. Impact on the shape and behavior of the gel for a product with a low  $F_N$  and a high  $F_N$



**Figure 3.** Schematic representation of the level of elasticity  $G'$  and  $E'$  for a HA gel. Impact of the dynamic shearing and compression forces on the deformation and return to the initial shape of the gel

product to resist to dynamic compression (i.e., behavior of the gel for recovering its shape after compression) [Figure 3]. Because a HA filler is subjected to very high levels of dynamic shear stress but also of dynamic compression stress at each moment of its *in vivo* life, when for instance, the patient speaks, smiles or eats, the  $G'$  and  $E'$  properties of the gel implant are key parameters to demonstrate its ability to respond to the mechanical constraints imposed by the dynamic facial expression. Thus, balanced  $G'$  and  $E'$  dynamic moduli confer a better capacity of the product to well respond to the muscular forces of the skin and to benefit of a better natural effect of the gel implanted in the tissues. Nevertheless, it is important to remember that this natural effect can be fully obtained only if the HA filler has an appropriate position and integration.

#### Step 4 of HA fillers' lifetime: degradation

Over time, the HA fillers are degraded by the human body due to the actions of the free radicals, the hyaluronidases, the thermal hydrolysis and the mechanical stress<sup>[15]</sup>. It is important to note that mechanical stress should play a very important role in the loss of the clinical effect. Indeed, as the hyaluronic acid is little by little cut into smaller pieces by the endogenous actors of the skin, the perpetual action of the mechanical expression of the face fosters the loss of implant cohesivity and rheological properties, and especially the normal force  $F_N$  (which enables to maintain the tissues projection) and the viscosity (which enables to resist to flow and spreading). The decrease over time of these key implant properties of the gel is fundamental to understand and explain the progressive disappearance of their clinical efficacy.

#### Summary

Following the discussion above, the Table 3 summarizes the key rheological properties for a HA filler, all along its clinical lifetime, from tissue integration to product degradation.

**Table 3. Key rheological properties of HA fillers all along their clinical lifetime. Influence of viscosity  $\eta$ , normal force  $F_N$ , elastic modulus  $G'$ , elastic modulus  $E'$  and cohesivity at each step of the HA fillers' clinical lifetime**

	Viscosity $\eta$	Normal force of compression $F_N$	Elastic modulus in shear-stress $G'$	Elastic modulus in compression $E'$	Cohesivity
Step 1: injection & integration	Major				Major
Step 2: projection		Major			
Step 3: dynamic facial expression			Major	Major	
Step 4: degradation	Major	Major			Major

### Illustration of the key rheological properties with a novel range of HA fillers

The novel range of HA fillers obtained according to the OXIFREE™ technology was designed with the aim to offer optimized cohesivity and rheological properties for clinical indications covered by each product. Two of these HA fillers (A and B), designed for dermal injection, i.e., superficial administration, have lower viscosities to obtain optimal injection and HA distribution/integration in this skin layer. The normal forces of compression have been selected to deliver an efficient intradermal projection to treat superficial to medium indications of the face, e.g., to treat fine lines or medium to deep-sized depressions of the skin. The 2 other HA fillers of this range (C and D), were designed for subcutaneous injection and to that end, they have high viscosities and high normal forces of compression to procure an optimal capacity of tissues projection in the treatment of the facial contours. Especially, it is notable to observe that product D, intended for the restoration of the volume of the face, has a very strong ability to project the skin tissues thanks to its very high normal force of compression and its high viscosity, even in front of Juvéderm Voluma™, the worldwide market leader in the segment of the volumizing HA products. Finally, it is important to outline that all HA fillers of this range have both high elastic moduli  $G'$  and  $E'$ , which give a powerful capacity to all the gel implants of this range for withstanding to the mechanical stress in shearing and compression, with the essential purpose to move as one with the skin tissues and therefore to provide natural clinical outcomes, particularly throughout the dynamic expression of the face.

### Conclusion

HA fillers play an increasingly important role in minimally invasive aesthetic procedures and a broad palette of products is now available to the physicians. Science-based evaluation of the HA fillers and especially the analysis of their rheological characteristics was emphasized to be a very useful tool for the physicians to guide them in the selection and usage of the most relevant products, administration techniques and depths of injection for the intended treatments.

The present article highlights the importance of the 4 key rheological properties viscosity  $\eta$ , elasticity  $G'$ , normal force  $F_N$  and elasticity  $E'$  for better understanding and predicting the behavior of HA fillers during their whole lifetime in the skin tissues, i.e., from their injection in dermal layer or subcutaneous tissues, to their *in vivo* degradation and therefore, their loss of clinical effects. The purpose of this article is to provide valuable scientific rationale for better explaining the products' behavior during their tissue integration after injection, their capacity to project the skin tissues, their ability to respond to the dynamic facial expression for generating a treatment natural effect, and the gradual disappearance of the clinical benefits.

On the other hand, this article provides a scientific evaluation of a novel range of HA fillers with advanced rheological features with the aim to better predict its clinical behavior. The highlighted findings illustrate how the study of key rheological properties can help the physicians to select the most appropriate product to be administered for the intended use, the volume of product to be injected and the most relevant injection technique to be applied for optimizing aesthetic outcomes, safety and patient satisfaction.

## DECLARATIONS

### Authors' contributions

Design of the concept and writing of the article: all authors

Obtain all the experimental data: Gavard Molliard S, Bon Bétemps J

### Data source and availability

Experimental data were obtained by Kylane Laboratoires SA

### Financial support and sponsorship

Kylane Laboratoires SA provided the logistical and financial support for the execution of this study.

### Conflicts of interest

Gavard Molliard S is employed by Kylane Laboratories SA, Hadjab B and Bon Bétemps J serve as consultant of Kylane Laboratoires SA.

### Patient consent

Not applicable.

### Ethics approval

Not applicable.

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Original Article

Open Access



# Fat grafting as adjuvant to reduce scars in arm

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## Abstract

**Aim:** Brachioplasty in patients who are normal weight, with moderate skin excess and who are not accepting long scars, remains a challenge for plastic surgeons.

**Methods:** We present our experience in 47 patients with short scar brachioplasty in combination with posterolateral liposuction, fascia anchoring and fat grafting in the inferomedial arm in order to improve skin quality and correct minor irregularities. Patients' satisfaction rates were evaluated after 3 and 6 months following the procedure.

**Results:** Patients (groups IIa, IIb and IIIa according to Rohrich classification) showed high satisfaction rates with the result both after 3 and 6 months after the procedure. The results were maintained. There were 2 cases (4.2%) of isolated wound dehiscence occurred, which were all resolved conservatively with dressings and antibiotics.

**Conclusion:** The technique presented in this paper has shown to be an easy and effective solution for a diverse selection of patients suffering brachial lipodystrophy. Limited scar brachioplasty only has specific applications, and should not be considered a replacement for traditional brachioplasty.

**Keywords:** Arm lift, brachioplasty, fat grafting, lipodystrophy

## INTRODUCTION

Sagging brachial-shaped deformities are a major concern among women. At the same time it is a challenge



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for plastic surgeons as the extension of scars limits the indications for brachioplasty and reduces patients' acceptance.

Since Correa-Iturraspe and Fernandez<sup>[1]</sup> first described aesthetic brachioplasty in the 1950s, the procedure has become an established division of upper extremity contouring for plastic surgeons. The dramatic rise in bariatric procedures has correlated to an exponential rise in patients seeking aesthetic brachioplasty. There were 15,183 brachioplasties performed in 2010, a 4392% increase compared to the figures for 2000<sup>[2]</sup>. At the same time it is associated with significant complication rates from 25%-40% and revision rates between 3%-25%. Most of these complications are due to the patients' dissatisfaction with the appearance of the scar<sup>[2,3]</sup>. This dissatisfaction has prompted members of the plastic surgery community to evaluate and refine current procedures, seeking a more aesthetically pleasing outcome. Using this impetus, the authors of this paper describe their current practice using fat grafting as an adjuvant to limited brachioplasty.

The majority of our patients seeking brachioplasty have typically had major weight loss after bariatric surgery or either diet and/or exercise. Yet there is still a significant portion of patients who are normal weighted but are still presenting with loose skin in the arm region due to the process of aging. These patients suffer from senile skin elastosis, but even after conventional brachioplasty, their skin still appears loose. This sub-group of brachioplasty patients always refer to a procedure with long scars as a matter of great concern. Considering this, it is a challenging task to offer those patients a satisfactory result. These patients are a minority in global brachioplasty statistics. This is probably the principal reason for a paucity of published techniques and options for these patients. However, changes in the position of incisions in continuity with the development of limited brachioplasty has demonstrated a reduced risk of idiopathic nerve and vascular damage, and improved scarring<sup>[4,5]</sup>.

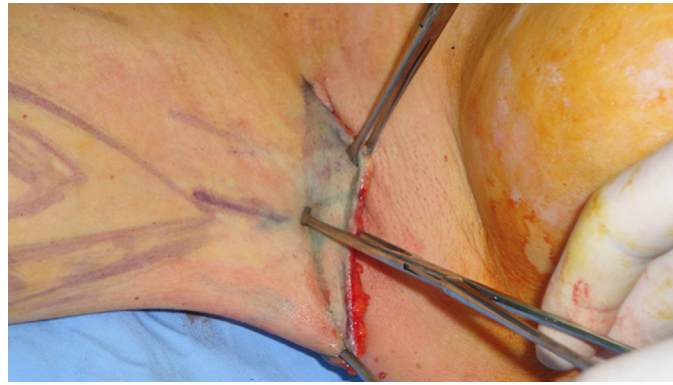
We present a more conservative aesthetic procedure in order to correct only mild to moderate sagging skin, improve the skin quality, and to reduce scarring. The authors believe surgical approaches should differ depending on the amount of skin laxity and fat excess. The purpose of this paper is to demonstrate an improvement in the current short scar brachioplasty surgery, to analyse patients' satisfaction rate and to propose an option for "border line" patients that do not accept extensive scars.

## METHODS

In this article we present our experience with short scar brachioplasty in combination with posterolateral liposuction, fascia anchoring and fat grafting in the inferomedial arm in order to improve skin quality and correct minor irregularities.

The patients were all normal weighted at time of operation, and did not change weight significantly pre- or post-operatively. All patients were in opposition of major scars, but still sought for contour improvement of the arm region. The limitations of the suggested technique were explained in comparison with traditional skin excision and the consent forms were signed. All patients were examined and carefully evaluated for both the amount of fat present and the amount of skin laxity in the arm region. Determination of excess was made by the pinch test. Patients with greater than 1.5 cm of fat detectable with the pinch test were candidates for liposuction. However, skin laxity was assessed also pinching the excess skin between the fingers, but in the different manner, and measuring the length of excess skin as described by Sacks<sup>[6]</sup>.

After physical examination, classification of upper arm deformity was determined for each patient according to the modified Rohrich classification system<sup>[4]</sup>. There were 3 groups of patients in our study: IIa, moderate skin excess and minimal fat excess, proximal location of skin excess; IIb, moderate skin excess and minimal fat excess, entire arm skin excess; IIIa, moderate skin and fat excess, proximal location of skin excess.



**Figure 1.** The redundant flap is marked using a Pitanguy marking clamp

All patients fulfilled questionnaires evaluating their satisfaction with the final result 3 and 6 months post-operatively. For those who were unable to attend the 6-month consultation, the questionnaire was completed via email or telephone call.

The amount of redundant skin and proposed areas for fat grafting were marked. The skin pattern for short scar brachioplasty typically removes skin in the longitudinal direction, with the scar well camouflaged in an axillary crease for an improved aesthetic result.

The marked areas were infiltrated with saline solution of 1:200,000 epinephrine. A decision to perform liposuction before skin excision was patient specific, depending on quantity of fat deposit (pinch test > 1.5 cm) and amount of skin laxity<sup>[4]</sup>. This was found to be necessary in the majority of cases classified as IIIa and sometimes in IIa. Liposuction was performed in the deeper planes of the subcutaneous tissue at the anterior and posterolateral parts of arm using Tulip® 3.0 cannulas (Tulip Medical Products, San Diego, USA), and fat was processed using Puregraft® system (Bimini Technologies LLC, San Diego, USA). After purification, an average amount of 40 mL per arm is injected into the anteromedial aspect of the upper arm using Tulip injectors 1.2 mm. Fat grafting was performed in several layers, both superficial and deep; with the aim to promote an expansion effect and encourage skin regeneration in the local region.

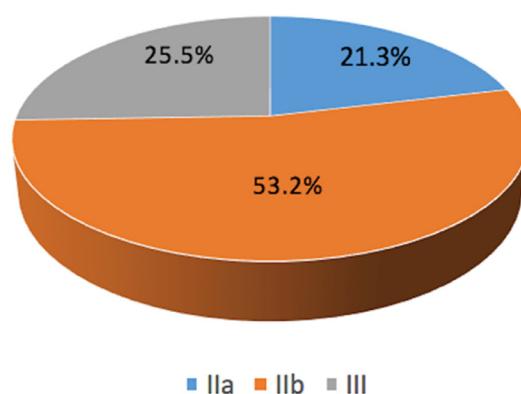
The demarcated flap is undermined and elevated superficially to the brachial aponeurosis and an axillary fascial anchoring technique was performed as described by Lockwood<sup>[5]</sup>. The use of fascial anchoring is advantageous, ensuring the axilla maintains its contour. The redundant flap is marked using a Pitanguy marking clamp, and a subsequent skin excision is performed as shown in the [Figure 1](#).

For all patients we compiled information regarding their age, upper arm classification system and their satisfaction rate 3 and 6 months post-operatively (graded as excellent, good and as fair result). Statistical analysis of the data was performed using SPSS software and modern statistical methods.

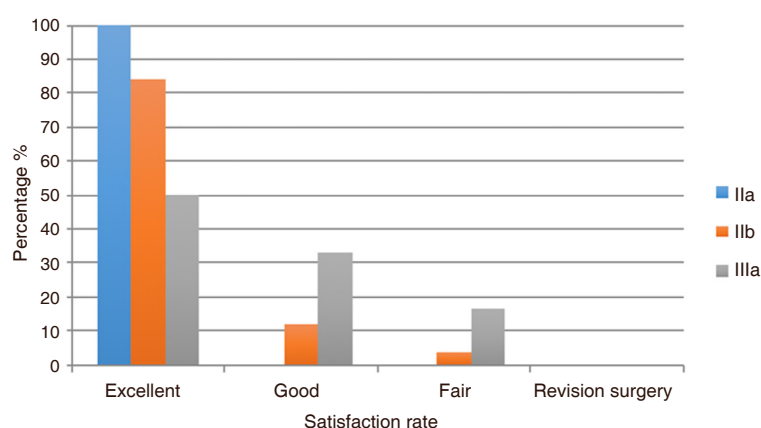
## RESULTS

In a course of 7 years (2009-2016) we treated 47 patients with this technique. All patients were female. Age ranged between 45 and 65 years (average  $55.2 \pm 5.2$ ). The surgical indication for all patients was senile elastosis, or lipodystrophy of the upper arms. There was no significant statistical difference in the age distribution of patients in the group, and also in number of patients in each group ( $P = 0.212$ ), which shows homogenous grouping when observing the age and upper arm deformity.

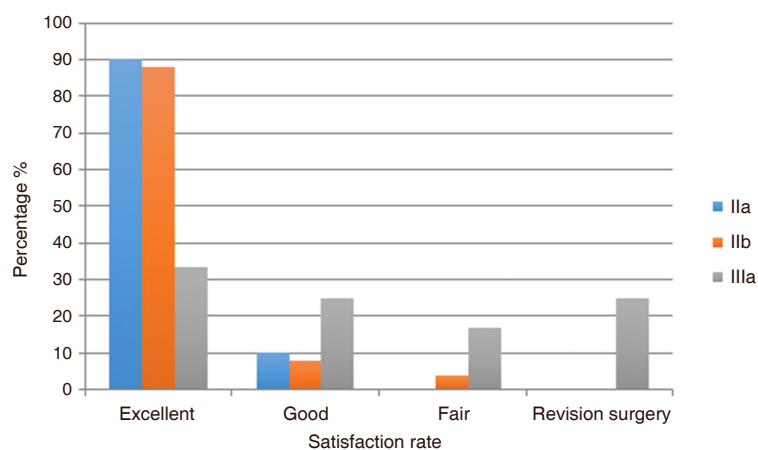
Our patient population according to the upper arm lipodystrophy classification is presented in [Figure 2](#). The satisfaction rates after 3 and 6 months after the surgery and their distribution depending on the upper arm



**Figure 2.** Patients' classification of upper arm skin and fat excess according to the Rohrich classification system



**Figure 3.** Patients' satisfaction rates with the result 3 months after the surgery



**Figure 4.** Patients' satisfaction rates with the result 6 months after the surgery

classification are presented in [Figures 3 and 4](#). There was high statistically significant negative correlation in between grade and patients' satisfaction with the final result ( $P < 0.001$ ). The higher the grade, the lower the satisfaction rate was.

After comparing satisfaction rates 3 and 6 months after the surgery, there was no significant difference in patients' satisfaction with final result ( $P = 0.096$ ), which is very encouraging since it demonstrates that results

are maintained.

In groups IIa and IIb the final surgical result 6 months after the surgery was considered good or excellent by more than 88% of patients, and no revision surgeries required. Patients were satisfied with the whole aspect of upper arm contouring, specifically with the hidden scar and improvement of the skin quality in areas where the fat grafting was performed. Satisfaction of the final surgical result for group III was graded as either good or excellent in 58.3% after 6 months.

There were no significant complications. Two cases (4.2%) of isolated wound dehiscence occurred, which were all resolved conservatively with dressings and antibiotics.

## DISCUSSION

The increased number of post-bariatric patients has popularised a whole range of body contouring procedures. Great weight loss is coupled with increased overall body skin laxity. When considering brachioplasty for this group of patients, the usual findings of severe brachial ptosis and skin laxity, with relatively little amount of adipose tissue are observed. The only suitable technique for these patients is traditional brachioplasty with or without extension depending on the quantity of excess chest skin<sup>[7-9]</sup>. There is no doubt among surgeons in the required treatment of this group of patients classified as group IIc and III by Rohrich Classification System, or group III and IV by Teimourian and Malekzadeh<sup>[10]</sup>.

Also there is unique opinion when good skin quality is present with moderate amount of fat excess. Solely liposuction of the upper arm is the treatment choice of this group, known as group I<sup>[7]</sup>.

However, when it comes to classification and treatment of patients in-between these two extreme groups, there are certain differences in approach. Surgical treatment ranges from limited incision, limited incision with liposuction to the traditional brachioplasty<sup>[7,11]</sup>. Furthermore, there are several methods described in literature that address the moderate skin laxity in upper arms with reduced scars such as laser-assisted liposuction in order to provoke skin retraction<sup>[12]</sup>. The idea of augmentation brachioplasty using small silicone implants has also been preconized by some plastic surgeons<sup>[13]</sup>. Importantly, the use of concomitant procedures does not significantly increase complication rates, and we believe our proposed use of fat grafting preserves this opinion<sup>[2,9,13]</sup>.

The regional anatomy favours our proposed operation, since there are no vascular or nerve structures in the trajectory of the incision, nor are these structures localised under or over the muscle; that could be impaired by compression exerted by the inclusion<sup>[13]</sup>. This technique can be used in selected cases of biceps brachii hypoplasia associated or not with a low degree of skin flaccidity in the posterior region of the arm. The volume augmentation in the anterior direction submits the posterior skin to traction.

Fat has well known filling and regenerative properties. It aids in the correction of sagging skin and improves skin quality, with only a minimal scar requirement. Furthermore, advantages of low complication rates, minimal surgical and recovery downtime, and in addition to good satisfaction and acceptance rate among patients have been reported. The described technique of harvesting, processing and injecting the fat provided predictable results that were maintained along the first year after small incision brachioplasty. This technique ensures an even contour is maintained, promoting patient satisfaction with the final result.

Three cases (6.4%) of revision surgery after 6 months were required in our patient population, all of whom belonged to group III. For all revision cases we performed traditional brachioplasty in order to remove the remaining excess skin. In consideration of treating those patients classified as group III, it is imperative to analyse the skin elasticity. Limited brachioplasty procedures only address skin excess in the longitudinal



**Figure 5.** A 67-year-old patient, before (A) and 1 year after (B) short scar arm lift in combination with fat grafting

direction, whereas as those procedures extending across the brachial sulcus towards the elbow can address skin excess in both a longitudinal and transverse plane<sup>[14]</sup>. Therefore this discussed technique can falter in accommodating patients with high skin excess. This emphasises the importance of patient selection.

Relatively high satisfaction rate after 6 months for the group III confirms the use of this surgical procedure as an option for selected cases within this group, especially when patients do not accept long scars.

In addition to the importance of patient selection in the success of this procedure, careful pre-operative assessment and appropriate skin markings are decisive<sup>[11]</sup>. With appropriate attention to these factors, the final aesthetic result should satisfy patient demands [Figure 5].

Major weight-loss patients are not good candidates for this surgery because of poor skin contraction potential. That is why they were not included in this study.

In conclusion, this modified short scar brachioplasty technique, as proposed by the authors, has demonstrated its invaluable place among upper extremity contouring armaentarium. The technique has shown to be an easy and effective solution for a diverse selection of patients suffering brachial lipodystrophy (IIa, IIb, IIIa). Patients classified in groups IIa and IIb reported high acceptance and satisfaction rates. When considering its application to a group IIIa patients, it is necessary to explain in detail its limited application in achieving satisfactory reduced brachial sagging. The technique discussed offers further refinement in the development of upper extremity contouring. Limited scar brachioplasty only has specific applications, and should not be considered a replacement for traditional brachioplasty<sup>[14,15]</sup>.

## DECLARATIONS

### Authors' contributions

Principal surgeon and the first author of the paper: Andjelkov K

Participated in data research, writing and processing the data: Atkinson CJ

### Data source and availability

This is a retrospective study. Patients' data were collected from their protocols. All patients were operated in "Hospital Colic", Belgrade, Serbia.

### Financial support and sponsorship

None.

### Conflicts of interest

The part of this work was presented at 11th Annual Meeting IFATS New York, November 21-23, 2013. Authors declare that they have no conflicts of interest that could inappropriately influence this work.

### Patient consent

All patients signed consent form prior to the surgery and were informed in detail about the whole procedure.

### Ethics approval

The ethical approval was obtained by the Ethical Committee in the Hospital “Colic” issued under number 021/14.

### Copyright

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Original Article

Open Access



# Projection capacity assessment of hyaluronic acid fillers

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## Abstract

**Aim:** Hyaluronic acid (HA) is considered as the gold standard biomaterial for facial soft tissue correction. Over the last 8 years, there has been a strong demand from physicians for HA products with high projection capacity to restore facial volume loss at the level of the cheeks, cheekbones, chin, temples and jawlines. The projection capacity is thus an essential property for HA fillers especially for the products dedicated to the restoration of the volume of the face.

**Methods:** In this publication, a new skin model assay for evaluating the projection capacity of HA fillers is presented, applied and discussed.

**Results:** This skin model assay enables to efficiently assess the projection capacity of a HA filler product. The comparative evaluation of a product benefiting from the novel OXIFREE technology and Juvéderm Voluma shows a higher projection capacity for the OXIFREE product than for Juvéderm Voluma.

**Conclusion:** This assay is demonstrated to be a key tool to guide physicians in the selection of products with high ability of tissue projection to optimize their aesthetic outcomes when they need to create facial volume.

**Keywords:** Hyaluronic acid fillers, projection capacity, skin model assay, facial volume



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## INTRODUCTION

Hyaluronic acid (HA) fillers are recognized as the gold standard in aesthetic medicine to treat signs of facial ageing; i.e. for filling wrinkles and skin depressions, and to shape the volume of the face<sup>[1]</sup>. In 2016, according to the American Society for Aesthetic Plastic Surgery (ASAPS), 2.49 million HA filler treatments were performed in the United States of America only with a high growth of 16.1% versus the previous year<sup>[2]</sup>. Since the market launch of Juvéderm Voluma (Allergan, Pringy, France) in 2010, the first HA volumizer and current world market leader in this segment, there has been a growing interest from physicians for HA fillers with a high ability to project the skin tissues<sup>[3]</sup>. Juvéderm Voluma is produced thanks to the VYCROSS proprietary technology<sup>[4]</sup>. This technology uses a combination of low and high molecular weights of HA during the crosslinking to improve the efficacy of the chemical reaction. Recently, a novel proprietary manufacturing technology for the production of innovative HA fillers has been discovered. It is the OXIFREE technology (Kylane Laboratoires, Geneva, Switzerland) which is characterized by the extraction of destructive oxygen during the manufacturing process, including during the crosslinking step, to significantly preserve the intrinsic properties of the high molecular weight of HA chains. This new technology provides HA fillers with advanced rheological properties which makes it possible to exhibit strong projection capacities and therefore a high ability to restore the volume of the facial skin tissues. Volumizer products such as Juvéderm Voluma or the HA fillers benefiting from the OXIFREE technology are designed by the manufacturers to be injected into the subcutaneous tissues and the supraperiostic zone. For these products, high projection capacity is thus required to efficiently treat the areas of the face for which the creation of volume is necessary such as the cheeks, cheekbones, chin, temples and jawlines. Rheological properties are also naturally considered by the manufacturers to design their products because these properties have an essential importance on the mechanical behavior of the HA gel in the tissues<sup>[5-7]</sup>. Many publications have been published on this topic over the past few years and some of them have highlighted the key role of the normal force  $F_N$  for the tissue projection of the HA fillers<sup>[8-11]</sup>. In this publication, a new skin model assay is proposed to assess the projection capacity of the HA fillers. This assay is applied on Juvéderm Voluma, the market leader in the segment of the volumizers, and a new HA filler benefiting from the OXIFREE technology, to compare the projection capacities of these products. The results obtained with this skin model assay are then discussed, with special consideration of the key rheological characteristics of these two products.

## METHODS

Two crosslinked HA fillers intended for facial injection in aesthetic medicine were subjected to flow, oscillatory shear-stress and compression tests with a DHR-1 rheometer (TA Instruments, New Castle, USA). Among these two HA fillers presented in Table 1, one is manufactured according to the novel OXIFREE technology and one is Juvéderm Voluma (Allergan, Pringy, France), manufactured according to the VYCROSS technology.

The two crosslinked HA fillers are studied in terms of rheological properties and also with the new skin model assay.

### Rheological characterization

#### *Flow test*

The flow test enables the measurement of the viscosity  $\eta$  of the gel. It was performed at a temperature of 25 °C under shear rate from 0.001 to 1000 s<sup>-1</sup> with a cone/plate aluminium geometry of 40 mm 2 degrees and a 50- $\mu$ m gap between the cone and the plate of the rheometer. The value of the viscosity  $\eta$  is measured at the shear rate of 1 s<sup>-1</sup>.

#### *Oscillatory shear stress test*

The oscillatory shear stress test enables the measurement of the elastic modulus  $G'$ . It was performed at a temperature of 25 °C in shear stress oscillation mode at 1.0% of strain, within the linear viscoelastic region, with a cone/plate aluminium geometry of 40 mm 2 degrees and a 50- $\mu$ m gap between the cone and the plate

**Table 1. Description of Juvéderm Voluma and one HA volumizer benefiting from the OXIFREE technology**

Product reference	Manufacturer	Manufacturing technology	Crosslinked HA content (mg/mL)	Clinical indications	Comment
Gel D	Kylane Laboratoires (Geneva, Switzerland)	OXIFREE	24	- Injection in the fat tissue or into the suprapariosteal zone - Restoration of the volume of the face	Product with the highest projection capacity of the HA filler range
Juvéderm Voluma	Allergan (Pringy, France)	VYCROSS	20	- Injection in the fat tissue or into the suprapariosteal zone - Restoration of the volume of the face	/

of the rheometer. The measurements were carried out over a frequency range of 0.1-5 Hz. The value of the elastic modulus  $G'$  was measured at the physiologically oscillation frequency of 1 Hz.

#### *Compression test in static mode*

The compression test in static mode enables the measurement of the normal force  $F_N$ . It was performed at a temperature of 25 °C in normal force mode, with a cone/plate aluminium geometry of 40 mm 2 degrees: 1.0 g of gel was placed between the cone and the plate and the cone was set in contact with the gel and lowered toward the bottom plate, thus compressing the gel. The normal force ( $F_N$ ) was measured for a gap between the cone and the plate of 1.11 mm (inverse gap = 0.9 mm<sup>-1</sup>).

#### *Compression test in dynamic mode*

The compression test in dynamic mode enables the measurement of the elastic modulus  $E'$ . It was performed at a temperature of 25 °C in compression oscillation mode at 1.0% of strain, within the linear viscoelastic region, with a 40 mm plate/plate aluminium geometry and a 0.5-mm gap between the parallel rheometer plates. The measurements were carried out over a frequency range of 0.1-5 Hz. The value of the elastic modulus  $E'$  was measured at the physiologically oscillation frequency of 1 Hz.

#### *Data analysis*

All measurements were carried out in triplicate. Data were expressed as the mean  $\pm$  standard deviation. Coefficients of variation lower than 10% were considered as satisfactory. Results were evaluated statistically using Student's *t*-test with a level of significance fixed at  $\alpha = 0.05$ .

### **Skin model assay**

#### *Skin model assay description*

The skin model "Injection trainer" (Limbs and things, Bristol, UK) used to assess the projection capacity is composed of multiple tissue layers: epidermis, dermis, fat and muscle. This artificial skin model could be used for training in order to practice intradermal, subcutaneous and intramuscular tissue injection techniques. The skin layers can be peeled back.

The following protocol is applied to evaluate the projection capacity of the two tested HA fillers, i.e. Juvéderm Voluma and the OXIFREE product (gel D), with this artificial skin model:

- After peeling back the upper skin layer, exactly 0.80 g of each HA gel is deposited on the top of the intermediate skin layer;
- The two HA gels are overlaid by the upper skin layer;
- Standardized pictures at a distance of 30 cm are taken (front view, with camera Nikon D5000 equipped with a lens Nikon AF-S DX VR II 18-200 mm f/3.5 - 5.6 ED);
- The projection height induced by each HA gel's bolus is measured in millimeter [difference between the top and the baseline of the ellipse (baseline is plotted between the two bending points of the ellipse)].

One test is performed with Juvéderm Voluma on the left of the skin model and gel D on the right and a second test is performed with Juvéderm Voluma on the right of the skin model and gel D on the left.

**Table 2. Key rheological properties of two HA volumizers**

Product reference	Viscosity $\eta$ at $1 \text{ s}^{-1}$ (Pa.s)	Normal force $F_N$ of compression at $0.9 \text{ mm}^{-1}$ (cN)	Elastic modulus $G'$ in shear stress at 1 Hz (Pa)	Elastic modulus $E'$ in compression at 1 Hz (Pa)
Gel D	$204 \pm 12$	$71 \pm 7$	$310 \pm 4$	$85,765 \pm 1701$
Juvéderm Voluma	$65 \pm 1$	$15 \pm 2$	$318 \pm 3$	$59,000 \pm 1440$

### Data analysis

Each test was carried out in triplicate. Data (projection heights) were expressed as the mean  $\pm$  standard deviation.

A statistical test is used to compare averages between the six projection heights of Juvéderm Voluma and the six projection heights of gel D (OXIFREE technology).

In this bilateral test (comparison of the difference of two averages at a given value), the difference of the averages (Juvéderm Voluma and gel D) is compared to the  $D_0$  value.  $D_0$  value is fixed as equal to zero, allowing to test the equality of the two averages.

## RESULTS

### Comparative rheological results measured on two HA volumizers

The key rheological properties viscosity  $\eta$ , static compression  $F_N$ , elastic modulus in dynamic shear stress  $G'$  and elastic modulus in dynamic compression  $E'$  were measured on Juvéderm Voluma and a new HA filler (gel D) benefiting from the OXIFREE technology. The results are summarized in Table 2.

### Comparative results measured with the skin model assay on two HA volumizers

The projection heights measured with the skin model assay are illustrated in the Figure 1 and the overall results are summarized in Table 3.

By statistically comparing averages between the six projection heights of Juvéderm Voluma and the six projection heights of gel D (OXIFREE technology), the two averages (Juvéderm Voluma and gel D) are statistically different.

The novel OXIFREE product gel D exhibits 34% more projection height compared to Juvéderm Voluma.

## DISCUSSION

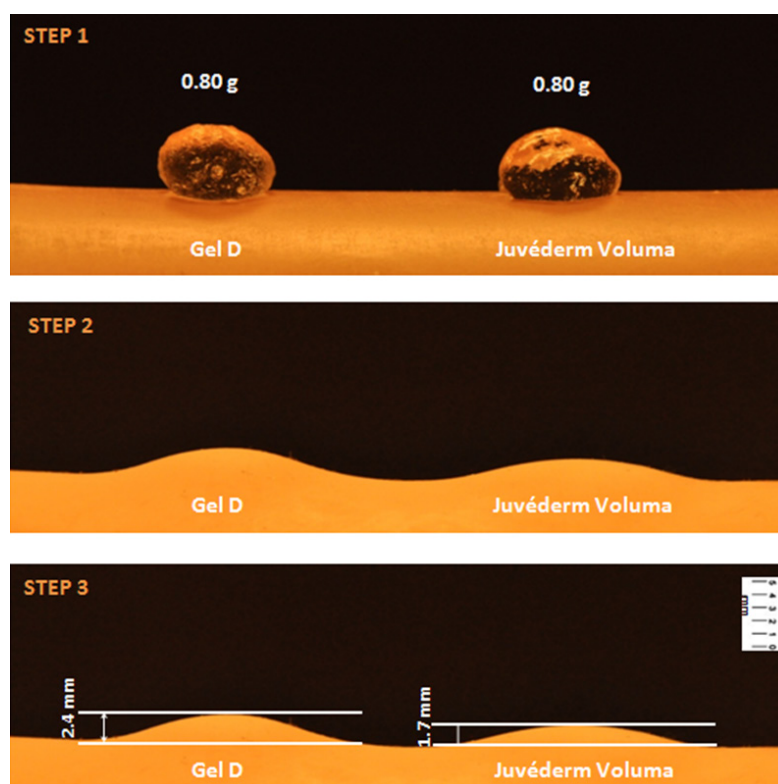
With the new skin model assay presented in this publication and applied on two HA volumizers, including the market leader Juvéderm Voluma, the projection heights are reproducible and significantly different for the two tested products.

This new assay is thus efficient and reliable to assess the ability of a HA filler to project and create volume. The projection height measured with the assay can be assimilated to the capacity of the tested gel to push the skin tissues and therefore to project them for facial volume restoration. Consequently, the assay is very useful for comparing the projection capacity of HA fillers, especially among HA volumizers.

In the case of the two HA volumizers studied in this publication, the projection height measured with the skin model assay is significantly and statistically higher for the novel OXIFREE product than Juvéderm Voluma. The projection capacity obtained with the OXIFREE product is therefore higher than Juvéderm Voluma.

**Table 3. Projection heights of two HA volumizers obtained with the skin model assay**

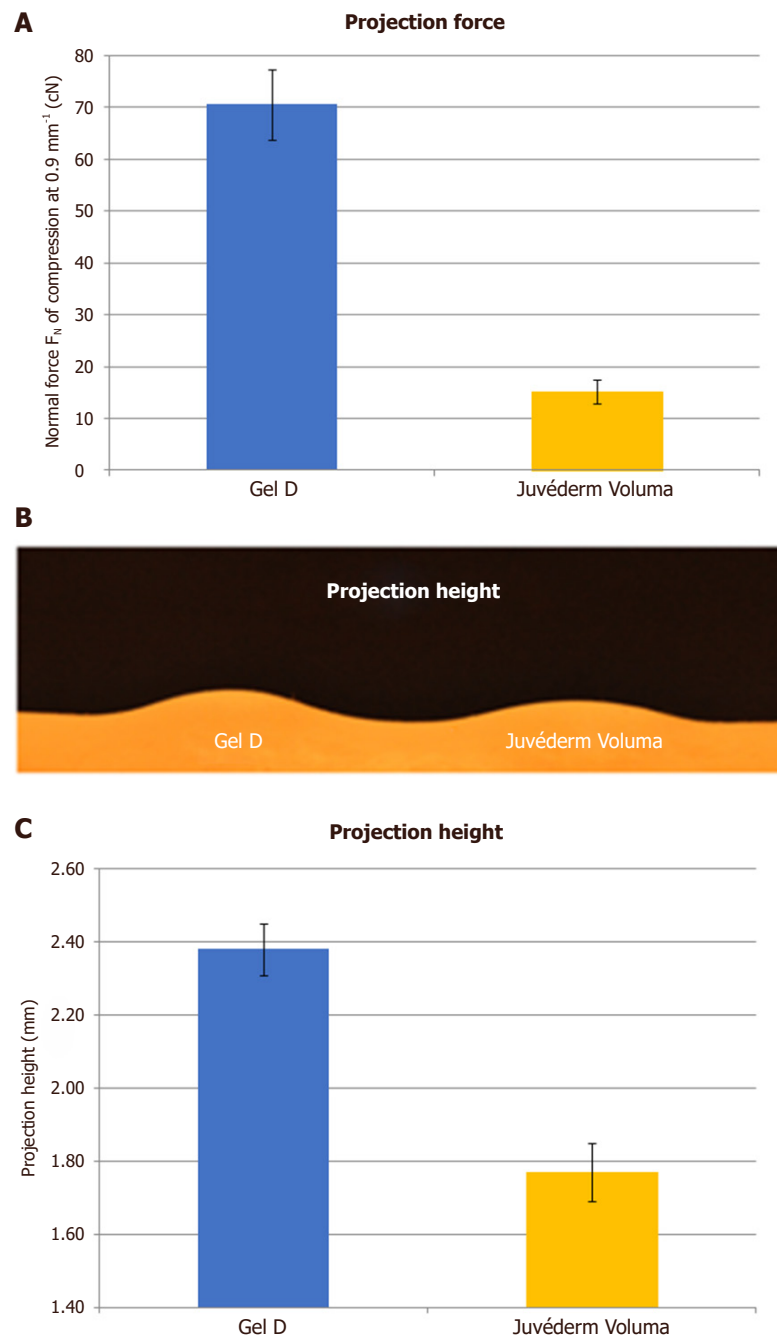
Product reference	Projection heights (mm)
Gel D	$2.38 \pm 0.07$
Juvéderm Voluma	$1.77 \pm 0.08$

**Figure 1.** Illustration of projection heights measured with the skin model assay. Step 1: deposit of the tested HA gels; step 2: HA gels are overlaid by the upper skin layer; step 3: measurement of the projection heights induced by each HA gel

This finding is consistent and in correlation with the rheological properties of the two studied HA volumizing products. As described in previous publications on the key rheological features of HA fillers, the normal force of compression  $F_N$  plays a key role in the projection capacity of the HA fillers: a high  $F_N$  enables the HA product to project more skin tissues. In this regard, the normal force  $F_N$  of compression can also be called the projection force to highlight its importance in the ability of tissue projection and volume creation. In the case of the OXIFREE product and Juvéderm Voluma, as illustrated in Figure 2, the projection force  $F_N$  and the projection height are considerably higher for the OXIFREE product in comparison to Juvéderm Voluma, which explains the much higher projection capacity of the OXIFREE product observed with the skin model assay.

The measurement of the projection capacity with the skin model assay is hence a new relevant tool for the medical community, in addition to and in correlation with the rheological property  $F_N$ , to assess and compare the projection capacities of HA fillers. For the physicians, it makes it possible to select the HA volumizers with the highest projection capacities to treat facial indications which require important volume restoration such as the cheeks, cheekbones, chin, temples and jawlines. This selection enables the optimization of the aesthetic outcomes and a better patient satisfaction.

In addition to the ability to demonstrate the projection capacity of the HA fillers, this new skin model assay is easy and quick to perform, which makes it possible to visually observe the projection capacity of the products on an applied model.



**Figure 2.** Rheological properties and projection heights of two HA volumizers. A: graph of projection forces for the 2 HA gels; B: picture of the projection heights with the 2 HA gels; C: graph of the projection heights for the 2 HA gels

In conclusion, volumizing products play an increasingly important role in the minimally invasive aesthetic procedures and they significantly contribute to the growth of the HA filler market on the world scale. HA volumizers have been demonstrated to be the gold standard solution to restore facial volume loss, especially for the correction of the midface with key clinical indications for the rejuvenation of the face such as the treatment of the cheeks, cheekbones, chin and jawlines.

Rheological characteristics analysis was demonstrated to be very useful for the physicians in order to guide them in the selection and usage of the most relevant products, administration techniques and depths of injection for the intended treatment.



This publication presents a new skin model assay to evaluate the projection capacity of HA fillers. This skin model assay was proven to be reliable and reproducible with two HA volumizers, including the market leader Juvéderm Voluma. It allows easy highlight of the ability of a HA filler to project the tissue and to create volume. It also enables a comparison of the projection capacity levels of different volumizing HA products. This model is therefore considered as a new key tool, complementary to the rheological property of projection force  $F_N$ , to assess the projection capacity of the HA fillers.

The additional acquired knowledge obtained with this new skin model assay contributes to a better characterization of the HA fillers which could be selected and used by the physicians for optimizing their aesthetic outcomes, as well as patient safety and satisfaction.

## DECLARATIONS

### Authors' contributions

Design of the concept and writing of the article: all authors

Obtaining all the experimental data: Bon Betemps J, Gavard Molliard S

### Availability of data and materials

Data in this study were derived from searches of the PubMed database. Experimental data were obtained by Kylane Laboratoires S.A.

### Financial support and sponsorship

Kylane Laboratoires S.A. provided the logistical and financial support for the execution of this study.

### Conflicts of interest

Mr. Samuel Gavard Molliard is employed by Kylane Laboratoires S.A., Mr. Basste Hadjab and Mr. Jérémie Bon Betemps serve as consultant of Kylane Laboratoires S.A.

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

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Case Report

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# Role of newer technologies in wound bed preparation in Fournier's gangrene

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## Abstract

Fournier's gangrene or necrotizing fasciitis of the perineum scrotum and penis is a highly debilitating condition with a high mortality rate of 20% to 88% reported in the literature. Management is multimodal, and the importance of aggressive debridement, broad-spectrum antibiotics and intensive supportive care cannot be emphasised. The addition of newer modalities of ulcer/wound management like low level laser therapy, hydrojet debridement and platelet rich plasma can be used to augment the existing principles of management and reduce the morbidity and mortality associated with the condition. This article is the authors' experience with the condition and the above stated newer modalities in the management while staying true to the principles of management.

**Keywords:** Fournier's gangrene, low level laser therapy, platelet rich plasma, jet force technology, hydrojet debridement, wound bed preparation, insulin therapy

## INTRODUCTION

Fournier's gangrene (FG) is a synergistic polymicrobial necrotizing fasciitis of the perineum, scrotum and penis which is characterized by obliterative endarteritis of the subcutaneous arteries, resulting in gangrene of the subcutaneous tissue and the overlying skin<sup>[1]</sup>. Jean Alfred Fournier<sup>[2]</sup>, a French dermatologist in 1883 was the first to describe a "fulminant gangrene" of the penis and scrotum that: (1) developed suddenly in previously healthy young men, (2) progressed rapidly, and (3) was idiopathic. The disease is no longer restricted to young men but may affect a wide age range from neonates to the very elderly. Since then this



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**Figure 1.** Swollen scrotum with necrotic patch on presentation

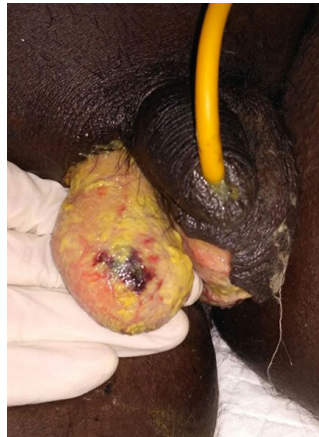
disease has been described in various nomenclatures in medical literature. Meleney<sup>[3]</sup>, a pioneer surgeon-bacteriologist described a more generalized form of the disease and named it “streptococcus gangrene”. In 1952, Wilson<sup>[4]</sup> coined the term “necrotizing fasciitis”.

FG extensively spreads to surrounding tissue and fascial layers, frequently resulting in septic shock and multiorgan failure. Standard treatment mainly includes surgical debridement of necrotic tissue and broad-spectrum antibiotics. Several earlier studies have reported a mortality rate of 20%-88% in FG<sup>[5-7]</sup>. But recent studies suggest significantly lower mortality rates of 10% or less, likely due to better understanding of pathophysiology, availability of higher antibiotics and improved processes of care for these patients<sup>[8-11]</sup>. Despite lower mortality, patients with FG suffer from increased morbidity, including multi-organ system dysfunction, complex wound care, prolonged hospitalization and ongoing care needs beyond hospital discharge<sup>[12-14]</sup>.

We present here a case of 35-year-old male diagnosed with FG with extensive spread to the abdominal wall, septic shock requiring prolonged intensive care - a multidisciplinary management experience over 6 months with experiences of some newer investigational modalities of advanced wound management in the Department of Plastic Surgery like low level laser therapy, debridement with hydrojet, application of autologous platelet rich plasma, topical application of insulin on wound bed, phenytoin topical use on wound bed and use of collagen dressings. These modalities have been studied widely for improving the wound bed preparation of chronic wounds and are specifically useful in reducing the time needed for optimal wound bed preparation in a chronic illness like FG.

## CASE REPORT

A 35-year-old married gentleman, resident of Tamil Nadu, a known alcoholic and tobacco chewer with no other known comorbid conditions, presented in surgical emergency of JIPMER on 26th of September 2017 with complaints of gradually progressive scrotal swelling for 3 days associated with redness, severe pain, and high-grade fever with chills and no history of any trauma. He had a history of perianal abscess for which incision and drainage was done in some other hospital one week back. On examination, he had an anxious look, dehydrated, with a temperature of 102.6 F, tachycardia and hypotension. There was significant scrotal wall edema, erythema and blackish necrotic patches over the right hemi-scrotum [Figure 1]. The perineal region had the evidence of previous incision and drainage (I&D) site which was unhealthy and filled with slough. The clinical findings were supplemented with an urgent ultrasonography of the perineal region and a diagnosis of FG was made and was planned for urgent debridement and exploration. Arterial blood gas (ABG) analysis showed a picture of compensated metabolic acidosis. Fournier's gangrene severity index (FGSI) score was 10 at the initial presentation, which inferred a mortality risk of more than 75%<sup>[15]</sup>.



**Figure 2.** Right hemi testis after surgical debridement on day 17



**Figure 3.** Raw area on abdomen after surgical debridement on day 17

The patient underwent debridement of the necrotic scrotal slough; exploration of the previous I&D site and diversion sigmoid colostomy (to aid the healing of the perineal ulcer). Both the testis were healthy, and no extension of the infection was noted into other spaces. Immediate postoperative period was uneventful, and he was started on broad-spectrum antibiotics, and changed to culture based sensitive antibiotics subsequently.

On 7th post-operative day, he again developed fever spikes, with rapidly deteriorating ABG values. On further evaluation he was found to be in sepsis and was shifted to the Critical care unit of our institution. He was intubated and put under mechanical ventilation and administered noradrenaline support in view of falling blood pressures. Subsequently, he was found to be having tense abdominal wall and was suspected to be having spread of the Necrotizing soft tissue infection. On 10th post-operative day, he was taken to a repeat surgery, where three horizontal incisions were given on the right side of the abdominal wall. Thorough debridement was done, washes were given, and corrugated drains kept in place [Figures 2 and 3]. For the next two months, he underwent multiple debridements with daily washes followed by vacuum assisted closure in CCU along with sepsis management. During the critical care stay, he also underwent percutaneous endoscopic gastrostomy for improving the enteral nutrition and tracheostomy for prolonged



**Figure 4.** Bed sore after surgical debridement on day 17



**Figure 5.** Bed sore debridement using hydrojet technology

ventilatory support. In the mean time, he developed a pressure ulcer on the sacral part [Figure 4], for which serial debridement and occlusive biological dressings and vacuum assisted closure were done. Gradually he recovered from sepsis and was weaned off from ventilator.

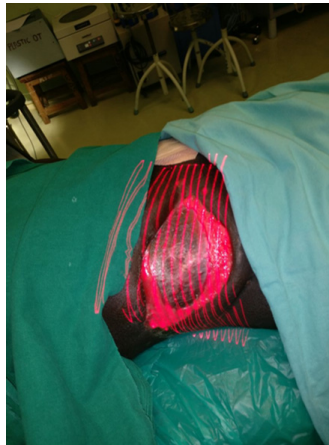
On day 25 the tracheostomy was closed and the patient was shifted to the Department of Plastic Surgery for advanced wound management for the raw areas that had developed after extensive debridement.

In the Department of Plastic Surgery, he underwent rigorous treatment of the FG and the bed sore with the novel techniques mentioned above.

Following surgical debridement, the patient was managed with debridement by hydrojet [Figure 5] every 2 to 3 days under local anesthesia plus low level laser therapy [Figure 6]. He also underwent regular autologous platelet rich plasma injections [Figure 7] and collagen dressings on the same days in the operating room. Topical insulin and phenytoin were used every time the dressing was done. Injection phenytoin (50 mg/mL) solution was diluted using normal saline (0.9% NaCl) to prepare a phenytoin solution (5 mg/mL). Serum phenytoin concentration was monitored regularly in the Department of Clinical Pharmacology, JIPMER, and it was always below 0.4 µg/mL, indicating only minuscule absorption of phenytoin following topical application. The patient did not report any local or systemic adverse event due to phenytoin during the treatment period.

Over a period of 20 days, patient condition improved drastically, and split skin grafting was done on day 21 following which patient improved and all post-surgical raw areas healed completely by day 49 [Figures 8-10].





**Figure 6.** Low level laser therapy being given to abdomen raw area



**Figure 7.** Autologous platelet rich plasma being injected in grafted raw area

## DISCUSSION

The understanding of the aetiology and pathogenesis of FG has significantly become more evident since the condition was first described by Jean Alfred Fournier. Though the basis of good management is aggressive debridement, broad-spectrum antibiotics and intensive supportive care, there is significant amount of morbidity and increased hospital stay leading to skyrocketing treatment costs. Here comes the rationale of trying novel techniques like Low level laser therapy, hydrojet irrigation and autologous platelet rich plasma, which in our experience and opinion have significantly contributed in hastening the wound healing with decreased morbidity.

Low level laser therapy (LLLT) is a proven modality in the management of chronic infected wounds. Efficacy of LLLT in wound bed preparation was discovered by Mester *et al.*<sup>[16]</sup> by application of a low-energy ( $1 \text{ J/cm}^2$ ) ruby laser. Unlike other medical lasers, LLLT does not have an ablative or thermal mechanism, but rather a photochemical effect in which the light is absorbed causing a chemical change<sup>[17]</sup>. Multiple studies have proven LLLT to be very efficacious in improvement in chronic wounds, mostly diabetic foot ulcers<sup>[18-20]</sup>. But to the best of our knowledge, no studies or case reports on the use of LLLT in Fournier's Gangrene have been reported yet.

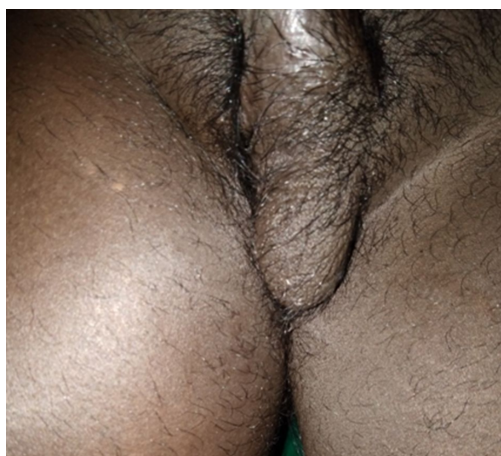
Autologous platelet rich plasma (APRP) has been reported to help in wound bed preparation in various aspects of medicine<sup>[21]</sup>. Platelets are known to express around 30 growth factors. They are chemotactic and



**Figure 8.** Healed abdomen wound



**Figure 9.** Healed sacral bed sore on day 49



**Figure 10.** Healed groin wound

induce proliferation of fibroblasts, endothelial cells and similar precursor cells<sup>[22]</sup>, thus regulating the wound healing process. In various studies in our institute, APRP has been shown to be an effective tool to enhance healing in wound bed preparation of diabetic foot<sup>[23]</sup>, in chronic wound healing<sup>[24]</sup> and many other similar indications. We have used our previous experience of using APRP in this case.

Hydrosurgical debridement is a novel modality, which enables the surgeon to precisely cut and remove nonviable tissue without causing collateral damage to healthy surrounding tissue using highly pressurized

saline solution emitted from the tip of a hand-held instrument<sup>[25]</sup>. The jet travels through the nozzle of the instrument generating a Venturi effect which is an increase in the fluid's velocity and a decrease in its static pressure due to its passage through a constricted area<sup>[26]</sup>. Here, in this case, we have used jet force technology (JFT), which is a type of hydrotherapy previously studied extensively in our department and shown to be an effective means to debride the wounds without the mess of traditional methods and hasten wound healing<sup>[27]</sup>. It uses a disposable cannula, saline and oxygen under high pressure to mechanically remove the debris and bacteria, with addition of giving positive pressure oxygen therapy to the wound. Utilizing a unique triple nozzle, JFT is one of the simplest, most efficient and effective methods to do fast and virtually painless debridement when compared to other mechanical debridement methods.

Role of topical phenytoin in dental socket healing had been established since 1958<sup>[28]</sup>. Further studies have proven its efficacy in foot venous ulcers and diabetic foot wounds. The mechanism of action of topical phenytoin is still one of the mysteries of medical science. It has been postulated to cause a proliferation of human fibroblasts and keratinocytes while reducing the incidence of gram negative bacterial growth on the wound. Local pain relief has also been observed with topical phenytoin therapy, which can be explained by its membrane-stabilizing action. Systemic effects are not yet been reported with topical phenytoin application.

Topical Insulin therapy exerts its effects via IGF 1 receptor. Use of topical insulin in diabetic foot has shown to produce faster epithelization rates. Insulin has been known to stimulate keratinocytes and the rate of endothelial proliferation leading to faster neovascularization and formation of granulation tissue<sup>[29]</sup>.

These novel modalities are some very efficacious additives in this situation which can drastically reduce the burden and morbidity of a severely debilitating condition like FG with a very high rate of mortality. Efficacy of these modalities individually has been proven in modalities like burns, chronic wounds, diabetic foot ulcers in various studies.

As it is seen in this case report, the results achieved with these interventions together were astounding and further studies with a large sample size are needed to prove the same. The benefits of these interventions are that these are cost effective, innovative and easy to do in most centers around the world.

Hope our experience with this condition will promote innovation among the medical fraternity all over the world and efforts for more such novel modalities to get desired results.

In conclusion, FG is a serious surgical disease with a high mortality and morbidity. Early rehabilitation of a patient with Fournier's gangrene involves aggressive surgical intervention together with fluid, hemodynamic and nutritional support and broad-spectrum/targeted antibiotics, but a majority of the burden of hospital stay is wasted in wound bed preparation. This case emphasizes the importance of these simple, cost effective novel adjuncts like LLLT, APRP, hydrojet debridement, topical insulin and phenytoin therapy and the use of collagen dressing in accelerating wound bed preparation and decreasing the overall hospital stay and treatment costs.

## DECLARATIONS

### Authors' contributions

Concept and design: Dutta S, Chittoria RK

Data acquisition and analysis, manuscript preparation: Dutta S, Aggarwal A

Critical revision and finalizing of the manuscript: Chittoria RK, Subbarayan E, Chavan V, Reddy KS, Gupta S, Reddy CL

### Availability of data and materials

The data were strictly obtained from medical records according to the privacy policy and ethics code of our institute.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Due consent was taken from the patient to participate in the study and separately for the photography. Ethical approval was done according to the hospital and department policy.

### Consent for publication

Not applicable.

### Copyright

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Original Article

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# Early experiences with the use of Earfold™ for correction of prominent ears

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## Abstract

**Aim:** This paper describes the author's personal experience with using the minimally-invasive Earfold™ implant.

**Methods:** The author inserted the Earfold™ implant into 19 patients (5 men, 14 women) between November 2016 and June 2018. Bilateral implantation was performed in 14 patients. In 5 cases, implantation was limited to one ear. The author's main indication for treatment was a helical-mastoid distance of more than 20 mm. Additional antihelixplasty of the upper ear was performed in 4 patients (2 primarily and 2 after explantation). One patient underwent simultaneous treatment of protruding ear lobes.

**Results:** The overall satisfaction rate was high, with 16 patients (84%) being satisfied or very satisfied. The procedure proved to be rapid with little down-time in the recovery phase. The demand for, and acceptance of the procedure was high. Although surgical otoplasty was always discussed as an alternative, no patient who presented for consultation chose standard otoplasty surgery. Complications occurred in 6 patients and implants were removed in 5 patients, 1 of them completely.

**Conclusion:** The Earfold™ procedure is an interesting, minimally-invasive alternative to surgical otoplasty which produces results which patients are pleased with. However, in this early series, the complication rate was high. A hybrid technique might reduce the complications observed.

**Keywords:** Otoplasty, minimally-invasive surgery, Earfold™ procedure



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## INTRODUCTION

The demand for non-surgical or minimally-invasive procedures in aesthetic surgery continues to increase. To date, the only minimally-invasive otoplasty procedure that has been described is the incisionless thread technique described by Fritsch<sup>[1]</sup> and modified by Haytoglu *et al.*<sup>[2]</sup>. The Earfold procedure, introduced by Kang and Kerstein<sup>[3]</sup>, offers a new approach to minimally-invasive prominent ear correction and uses a metal clip to reshape the antihelical fold. In this article, the author reported his early experiences with this new implant.

## METHODS

The Earfold™ implant was inserted into the ears of 19 patients between November 2016 and February 2018.

Earfold clips (Earfold, Allergan, Clonsaugh Business and Technology Park, Coolock, Dublin, D17 E400, Ireland) are made from thin strips of nitinol (nickel-titanium alloy) which are heat-treated and coated with 24-carat gold. The ends of the implant are fitted with tiny teeth. Once deployed, the super-elastic properties of the material ensure that the implant returns to its predetermined form<sup>[4]</sup> forcing the cartilage of the antihelix to adopt a new shape.

According to the instructions for use (IFU), the specific indication for use of the implant is an absence or poor definition of the antihelical fold in a patient who perceives that their ears are prominent. The likely outcome is first demonstrated to the patient by using non-sterile Prefold™ positioners. These are identical in shape, size and elasticity to Earfold™ but do not have the tiny teeth and can therefore be easily placed onto the ear in the region of the antihelical fold - simulating the probable outcome for the patient. Assessment of patients with Prefold™ is an important first step to determining whether a patient is suitable for treatment with Earfold™. If it proves difficult or impossible to produce a satisfactory aesthetic outcome for the patient, and/or if the implant is unlikely to end up lying flush with the cartilage, the IFU advises that an alternative to Earfold™ should be used. Once the assessment with Prefold™ is complete, the outline of the positioner is marked on the skin. This then determines the specific site for implantation of the Earfold™ implant.

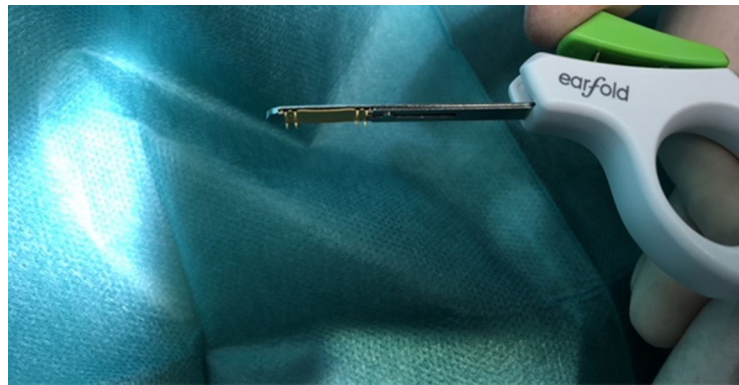
After meticulously disinfecting the skin with Octenisept (0.1 g octenidine hydrochloride, 2.0 g phenoxyethanol/100 g), the site was anesthetized with xylocaine 2% and epinephrine 1:200,000. The author used a vertical incision between the outer margin of the ear and the antihelical fold, and performed a subcutaneous and subperichondrial dissection of the previously marked area. The author then scored the cartilage to weaken its bending force using either a needle or scalpel.

The implant was then released subcutaneously (and hopefully sub-perichondrially) flat against the anterior cartilage in the position of the previously marked area. Once deployed with the introducer [Figure 1], the Earfold™ implant returned to its predetermined shape and grasped the cartilage, forcing the antihelix to adopt a new shape, thereby correcting any associated prominence of the ear [Figure 2].

The author then closed the skin with 6-0 Prolene or skin glue such as Dermabond (Ethicon Inc., Route 22, West Somerville, NJ, 08876, USA).

Post-operative pain and bruising was managed with a combination of ibuprofen 600 mg three times a day and bromelain 3 tablets a day. Antibiotic prophylactic treatment was commenced one day before the procedure with cefuroxime 500 mg twice a day. No dressing was used.

Post-operatively, the author advised patients to refrain from swimming or engaging in contact sports for the 3-4 weeks following surgery. The author also advised them to avoid any contact with water during this time. To further prevent accidental infection, any items in contact to the ear (cell phones, earplugs helmets,



**Figure 1.** EarFold™ introducer



**Figure 2.** Single Earfold™ implant in left ear [appearance before (left) and after (right) insertion]

earrings) should not be used, or only with extreme caution and held away from the incisions. Patients with a history of recurrent otitis externa were also excluded from surgery or were followed up closely after the procedure.

## RESULTS

The author inserted Earfold™ into the ears of 19 patients between November 2016 and June 2018. Unilateral implantation was performed in 5 cases; 3 were treated with 1 implant, 2 with 2 implants in each ear. Bilateral implantation was performed in 14 patients; 2 patients had 2 implants inserted into each ear. The principal motive for all patients was to avoid standard otoplasty surgery. Many patients had additional reservations about the need for bulky and visible dressings after standard otoplasty - that might make it obvious that an otoplasty had been performed.

Fifty-one patients underwent pre-operative assessment with Prefold™: 42 women/girls and 9 men. In 6 patients, the author advised that they should not undergo the Earfold™ procedure because of a deep conchal bowl. Moreover, every patient was explicitly advised of the pros and the cons of Earfold™ compared to standard surgical otoplasty (especially using the Mustardé technique<sup>[5]</sup>). Importantly, Prefold™ positioners were used to simulate the likely outcome in every case, including those patients with a deep conchal bowl. Interestingly, for some of these patients, even when it was pointed out that they might have to accept an aesthetic compromise, this was mostly accepted.

Nineteen of the 51 patients who underwent a Prefold™ assessment decided to undergo the Earfold™ proce-



**Figure 3.** Skin erosion of the upper edge of an implant placed over the superior crus of the antihelical fold

dure. Interestingly, of those who declined to go ahead with treatment using Earfold™, none went on to opt for a standard surgical alternative suggesting that this is a group of patients who would not otherwise come forward for treatment of their prominent ears.

Implants were placed at the inferior part of the antihelical fold in 5 patients. In 19 cases, the implant was placed at the superior part of the antihelical fold (11 proximal to the bifurcation, 8 distal to the bifurcation). In addition, surgery to reduce the size of the anti-tragus was performed bilaterally in 1 patient. In further 4 patients, Earfold™ was used in combination with Mustardé sutures.

Building familiarity with the introducer in the weeks before surgery is performed is critical for eventual correct deployment of the implant. In 2 cases, the implants had to be discarded as the implants were noted to be sitting proud of the cartilage. In those cases, the cartilage had not been kept flat in relation to the cartilage during release of the implant.

The author did not use a validated method of assessment of patient satisfaction and the average duration of follow-up in this series was short (6 months). However, anecdotally, 16 out of 19 patients were satisfied or very satisfied with the aesthetic result. Three patients were dissatisfied with the outcome of treatment due to issues with persistent pain and sensitivity, which were resolved after removal of the implants and the performance of a Mustardé otoplasty.

In total, the author removed 8 implants from 5 patients. Removal was necessary because of erosion of the skin over the implant in 2 patients [Figures 3 and 4] and because of continuing pain and inflammation around the implant in 2 cases. In one case, the positioning of the implant was aesthetically unsatisfying, inducing an excessive folding. Removals were performed within 2 to 15 months after implantation.

Careful examination of the cases with skin erosion [Figure 3] showed that the implant was not flush with the cartilage resulting in a sharp edge of the implant sitting proud and eventually eroding through the skin. Although every effort was made to ensure that the implants were completely flush with the cartilage at the time of deployment, it is entirely possible that minor mispositioning of the implant was not detected due to soft-tissue swelling at the time of surgery. Alternatively, the implants may have moved due to patient factors during the first 3-4 weeks after surgery (i.e., before encapsulation of the implant occurred preventing any further movement).



**Figure 4.** Skin erosion of the lower edge of an implant placed over the superior crus of the antihelical fold at 15 months after implantation

In the second case with skin erosion [Figure 4] the reason is unclear as the problem became evident 15 months after implantation. Primary insufficient positioning is unlikely, or the symptoms must have started earlier. In this case, the author did no scratching to the cartilage; the unweakened strength of the cartilage might have forced the implant out of its position.

## DISCUSSION

The author acknowledges that the limited number of patients treated in this series means that this report probably reflects a very preliminary impression of the potential of this new technique. However, as there are few independent reports of outcomes using the Earfold™ implant, the author believes that providing surgeons with additional information on his outcomes is important.

The procedure is promoted as being fast and minimally invasive with an acceptable rate of complications. The author accepts that the technique is fast and minimally invasive. However, the rate of complications in this series was higher than that reported in the “first-in-human” pilot study by Kang and Kerstein<sup>[3]</sup> who reported 7 cases of skin erosion (13% of patients) with complications affecting 20.5% of patients. The higher rate in the present series occurred despite the fact that the author applied the same care to the Earfold™ technique as to surgical otoplasty. Therefore, the author has concluded that the Earfold™ technique is different to standard otoplasty, with a different learning curve and different technical requirements - even for an experienced otoplasty surgeon.

Though the complication rate reported by Kang and Kerstein<sup>[3]</sup> is lower, it is not neglectable-especially compared to the rates of revision with the classic Mustardé technique of 2.9% reported by Olivier *et al.*<sup>[6]</sup>. This leads to the question if the complications encountered are purely surgery-related or if additional immanent factors might add to them. Possible mechanical irritation of the implant in combination with the bradytrophy of the cartilage might predispose to local infections.

The author observed complications in 6 out of 19 patients [Table 1]. Four patients developed pain and discomfort at the implantation site and went on to develop an infection forcing us to explant the clips in 2 cases; in 2 patients the clip induced an excessive folding. In total, 5 patients had to have their implants removed. Two patients only had 1 of 2 implants removed - from the superior crus. After removal of the implant, patients developed a recurrence of their prominence and so the author performed an upper antihelixplasty in 4 patients using the Mustardé technique, leading to an aesthetically and functionally satisfactory result without complications.

**Table 1. Complications (more than one event can occur in one patient)**

<b>Patients (n = 19)</b>	<b>Perichondritis subcutaneous infection, neuralgia</b>	<b>Abscess</b>	<b>Perforation + neuralgia</b>	<b>Neuralgia</b>	<b>Insufficient aesthetic result</b>	<b>Explantation, revision, reposition</b>
Implant superior anthelixfold distal to bifurcation (n = 8)	2	2	1	3	3	4
Implant superior anthelixfold proximal to bifurcation (n = 11)	-	-	-	2	1	1
Implant inferior anthelixfold (n = 5)	-	-	-	-	-	-
Anthelixplasty (Mustardé) (n = 4)	-	-	-	-	-	-
Correction of protruded lobula (n = 1)	-	-	-	-	-	-

In 3 of the 4 patients who developed an infection, the author did not provide prophylactic antibiotic cover. However, in view of the infections, the author now covers every case with oral antibiotics (cefuroxime), beginning one day prior to the procedure. The author suggests starting prophylactic antibiotic coverage the day before the procedure using 2× cefuroxime 500 mg/day and continuing this for 1 week. In the author's opinion, mechanical irritation of the cartilage predisposes to infection. However, the author accepts that other surgeons might disagree with this opinion. For example, Kang and Kerstein<sup>[3]</sup> suggest that infection is more likely if non-absorbable sutures are used because of the additional trauma involved in their removal. Moreover, Kang and Kerstein<sup>[3]</sup> suggested that the use of earrings, mobile phones or direct trauma to the area during the first 3-4 weeks after implantation were also important aetiological factors for infection.

Skin erosions affected 2 patients and occurred exclusively for implants placed over the superior crus. Therefore, the author suggests that placement of implants at this site should be avoided altogether. Alternatively, the implant could be used in combination with Mustardé sutures for the upper pole - as a hybrid procedure. In the author's opinion, a hybrid approach would neither significantly prolong the duration of the procedure nor have any major impact on down-time. If the Mustardé sutures were to be placed solely in the upper pole of the ear, then there would be no need to use an ear/head bandage - which is so disliked by patients [Figure 5].

One patient complained that their implants were too visible under the skin. The 24-carat gold coating of the Earfold™ implant is intended to make them less visible under the skin. However, the author has noted that even when the implants are flush with the cartilage, the contour of the implants is mostly detectable as a slightly raised area and patients should be warned of this before treatment.

The author encountered a problem of a “Spock-ear” in two cases [Figure 6]. The author has noted that this was the result of creating an antihelical fold that was too vertical in patient where the cartilage was relatively soft. Therefore, there was a degree of overcorrection of the prominence. From this and other experiences with using Earfold™, the author has concluded that although the technique seems simple in principle, it is critical to:

- Perform careful patient selection in advance of treatment - using Prefold™;
- Ensure that the implant is flat in relation to the cartilage before and after deployment;
- Consider (weakening) of the cartilage - either through needle perforation or scoring with a scalpel - before placement of the implant, especially in patients with very thick and inelastic cartilage;
- Consider antibiotic coverage;
- Observe careful post-operative management.

All of these factors are of course detailed in the IFU for the implant and surgeons are strongly advised to read this material carefully before proceeding to use the implant.

Although the author did not perform a formal assessment of satisfaction using a validated assessment score (e.g., Ear-Q), anecdotally, patients reported a high level of satisfaction with treatment [Table 2]. This cor-





**Figure 5.** Earfold™ - hybrid technique: Earfold™ implant inferior antihelical fold, Mustardé technique upper antihelical fold [before (left) and after implantation (right)]. In this case, there was additional reduction of the antitragus



**Figure 6.** Excessive folding and “Spock”-ear deformity. This was not anticipated during the Prefold™ assessment and was probably the result of creating an antihelical fold which was too vertical in an ear with relatively weak cartilage. After removal of the upper implants, an aesthetically satisfying result was achieved

**Table 2. Self-reported satisfaction with the aesthetic result (n = 19)**

Very dissatisfied	Dissatisfied	No change	Satisfied	Very satisfied
1	2		3	13

relates with the experience of Kang and Kerstein<sup>[3]</sup> in their pilot study of Earfold™. In our series, a total of three patients were dissatisfied with the aesthetic result and insisted on explantation. These patients also complained of pain and sensitivity related to the clips, so it is difficult to know whether it was the pain and sensitivity or dissatisfaction with the appearance that motivated them to have their implants removed. In 1 patient, we removed only the upper implant, leading to a much more pleasing result. Total explantation due to aesthetic dissatisfaction was performed in 2 patients (4 implants).

In conclusion, the minimally invasive Earfold™ technique for antihelixplasty by implantation of nitinol clips is a fast and aesthetically satisfactory procedure (16 out of 19 patients satisfied). The author can confirm that the postoperative recovery is very short and in general only limited by a small degree of localised swelling at the implantation site. Importantly, no ear/head bandage or headband was necessary and the author’s patients were able to return to normal social interactions almost immediately - an important factor in deciding to



proceed with treatment.

Although the complication rate in this series was high, the author accepts that this probably might partially reflect the learning curve with the technique which is very different to standard otoplasty. The actual study of Kang *et al.*<sup>[7]</sup> presents 403 patients with a complication rate requiring intervention of 9.7%. This is still high compared to revision rates of 2.9% in surgical otoplasty as reported by Olivier *et al.*<sup>[6]</sup> and it reflects that beside surgery-related complication, immanent factors might have to be considered like mechanical irritation. Further long term observations have to show that the safety and efficacy of an Earfold™ otoplasty is equivalent to that of surgical otoplasty. Surgeons should be familiar with the complication management and standard otoplasty manoeuvres if they decide to offer treatment with Earfold™. In the case of explantation they should be able to convert patients to standard otoplasty (e.g., Mustardé) without difficulty.

The overall aesthetic results were very satisfying and the procedure meets the demands of many patients for a fast and minimal invasive otoplasty. Despite the reported problems, the author believes therefore that this technique offers a promising alternative to surgical otoplasty and might eventually be combined with a modified surgical approach.

Indeed, it is the author's opinion that Earfold™ is most effective and secure when used as part of a hybrid approach where the implant is placed at the middle third of the ear and used in combination with other surgical manoeuvres for correction of prominent ears (e.g., Mustardé sutures).

Further studies should be performed to see if there are ways to shorten the learning curve and reduce the complication rate. Moreover, increasing the range of angles of the clips would help expand the number of patients who may benefit from this new treatment option.

## **DECLARATIONS**

### **Authors' contributions**

Schuster BW contributed solely to the paper.

### **Availability of data and materials**

The data presented is original and obtained in the author's clinic. It can be made available if required.

### **Financial support and sponsorship**

None.

### **Conflicts of interest**

There are no conflicts of interest.

### **Ethical approval and consent to participate**

As a retrospective study, no ethical approval was necessary. All photographs have been anonymized, even though written consent was obtained from all patients.

### **Consent for publication**

Not applicable.

### **Copyright**

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Review

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# Rejuvenation of the centre of the face: a new paradigm. Endoscopic lifting with fat grafting

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## Abstract

The ageing process starts in the centre of the face in the periocular region and around the mouth, with a combination of volume loss and tissue descent. It is a logical approach to assess all these problems at once. The combination of minimal incisions vertical endoscopic lifting combined with superficial enhanced fluid fat injection can be an integral approach to facial rejuvenation.

**Keywords:** Minimal incisions vertical endoscopic lifting, superficial enhanced fluid fat injection, endoscopic lifting, fat grafting

## INTRODUCTION

Scientific studies have proven the central role of the eyes in aesthetic facial rejuvenation. Nguyen *et al.*<sup>[1]</sup> used an eye-tracking system to demonstrate that age and fatigue judgments are related to preferential attention toward the eye region. Consequently, aesthetic surgery to the eye region may be one of the most effective interventions in enhancing the overall appearance of an individual<sup>[1]</sup>. A recent prospective study on 72 female patients with an average age of 48 years, showed that 74.6% of these patients felt that their first sign of ageing occurred in the eyes, 26.7% in the neck and only 12.6% in the cheeks<sup>[2]</sup>. Among this female group, 78.8% of patients expressed interest in improving the appearance of their eyes, 28.8% the cheeks and lips only 15%<sup>[2]</sup>.



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The ageing process that occurs in this age group affects the centre of the face, represented by the periocular region and the mouth. Therefore, surgeons dedicated to the periocular region should look beyond the eyelids. In a previous publication, Bernardini *et al.*<sup>[3]</sup> defined the periocular aesthetic unit as being formed by the superior complex (SC), which includes the forehead, brow and upper eyelid, the inferior complex (IC), which includes the lower eyelid and the cheek, and the lateral complex (LC) which includes the temple, the malar mound and the lateral canthus. If we expand our focus to the peri-oral unit we can assess the whole centre of the face.

In the past, aesthetic surgeons dedicated their efforts to the rejuvenation of the contour of the face, offering variably satisfying results at the cost of long scar lines, extensive dissection and strong horizontal traction with unnatural effects. Vertically repositioning the descended tissue seems to be the correct way to assess the gravitational ageing vector. This is especially true in the SC and in a lesser proportion in the IC. Minimal incision vertical endoscopic lifting (MIVEL) can obtain such results with invisible scars and fast postoperative recovery. However, as much as we lift tissue, there is no natural, three-dimensional way to achieve rejuvenation without volume restoration to the deflated areas. Superficial enhanced fluid fat injection (SEFFI) is a novel technique, which not only provides the volume restoration of autologous fat, but also aids in skin regeneration.

The authors attempt to review the literature on this two novel procedures as well as present their individual techniques and results.

## **MIVEL**

There are a few specific surgical instruments, but the single most important one is the endoscopic elevator which slides on the fiberoptic and allows the surgeon to elevate the tissue while viewing with one hand.

### **Blind dissection**

After a Klein-type of local anesthesia and with the patient under intravenous sedation the intervention requires initial dissection in preparation for the endoscopic view. Three vertical 1.5-cm long incisions are placed in the scalp, right behind the hairline: the central one in the midline and two paramedian incisions, one on each side, 5 cm from the midline, to give access to the frontal area up to the temporal crest. Two 3-cm long incisions are performed in the temporal region, one on each side, to provide access to the temporal, malar, and zygomatic regions. In the frontal area, blind dissection is performed under the periosteum up to a 2-cm safety line above the superior orbital rim. Special care needs to be taken in order not to elevate the conjoint tendon at this time. The lateral extension will be up to the temporal crest laterally and 2-3 cm posterior to the hair line. In the temporalis area an optical pocket is created blindly and the dissection plane lies above the superficial plane of the deep temporal fascia. From the temporal dissection the conjoint tendon can be safely elevated, joining both pockets.

### **Endoscopic dissection**

After the blind dissection is completed and a single optical pocket formed in the frontal and temporal areas, it is then time to enter with the endoscope. In the temporal region, the dissection is carried out on the surface of the temporal fascia past the sentinel vein to expose the zygomatic temporal and zygomatic facial bundles laterally and the lateral retinaculum and lateral canthal tendon medially. In the forehead region, subperiosteal direction is carried up to the superior orbital rim. At this level, periosteum will be elevated from lateral to medial, around the supraorbital nerve, and past it towards the glabellar region, elevating the corrugator and procerus muscles.

### **Fixation**

Fixation was achieved with Endotine devices in more than 300 cases, encountering device related complica-

tions in almost 10% of the cases (exposure, infection, visibility, rupture of the device during implantation, trephination hemorrhage), even having to remove the device in three cases<sup>[3]</sup>. One of the authors, A.G., developed a stitch for paramedian fixation with the Reverdin needle, which will be referred to as the Gennai stitch henceforth. The Gennai stitch has successfully been used for paramedian fixation in over 200 patients without complications. Two stab wounds are performed in the forehead at a certain distance from the paramedian incision. The Reverdin needle is passed through the stab incision and exits at the paramedian incision, and the suture is loaded and brought back to the stab incision, where only one of the branches is brought back with the Reverdin needle through the subcutaneous tissue back to the paramedian incision, where it is freed and tied to the other branch, thus grasping the tissue and elevating the eyebrow. This stitch will cause a characteristic bulging that will disappear in the postoperative period.

Temporal fixation of the deep subcutaneous tissue of the elevated flap to the deep temporal fascia is simply performed with a 3/0 Vicryl suture. Due to the extensive dissection, the inferior complex and the lateral complex will be elevated as a whole with this fixation.

Bicoronal fixation can be used in 50% of the cases to enhance the elevation of the eyebrows.

## SEFFI

### Harvesting

For the preparation of the tissue for harvesting a solution of lidocaine (400 mg), sodium bicarbonate (5 mEq) and epinephrine (1 mg), is prepared in a cold Ringer's lactate solution (500 mL) and it is infiltrated into the autologous collection site(s); most frequently the supra pubic region (55%), hips (22%), prethrocantalic area (18%), inner thigh (3%), and inner knee (2%)<sup>[4]</sup>. For SEFFI, manual aspiration of fat is performed with the use of a 20 cm-long multi perforated cannula (with other 0.5-mm or 0.8-mm ports) mounted in a 10-mL syringe; for micro-SEFFI, with a 15-cm long multi perforated cannula with 0.3-mm ports. Manual aspiration is begun 15 min after infiltration of the preparation solution.

The aspirated material (0.6 mL per syringe) is cleaned with Ringer's solution (0.4 mL) and left to decant in vertical position for about 2 min. The liquid part collected at the bottom of the syringe is discarded. This procedure is repeated once again to ensure that most of the blood and the anesthetic solution is eliminated from the fat<sup>[5]</sup>. The syringes are kept capped under a sterile cloth.

Autologous blood is drawn from the patient to obtain platelet rich plasma (PRP). It is poured into 4.5 mL citrated Vacutainer and centrifuged at 2000 rpm for 4 min. The fat and PRP are mixed so that PRP is 20% of the total harvested tissue<sup>[6]</sup>.

### Injection

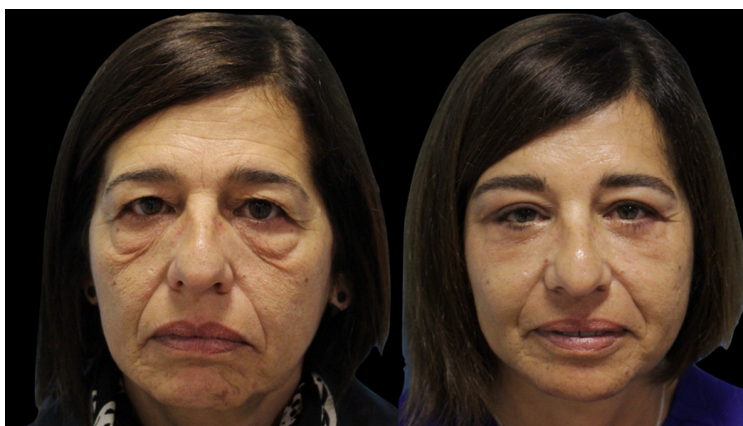
The solution is then injected according to a comprehensive study of the facial arterial system, using a linear retrograde injection technique. The M-SEFFI technique complements the SEFFI technique; SEFFI performed with cannula with distal ports of 0.8 mm is indicated for the larger volume defects in the cheek, temple, forehead, chin and jaw line, and SEFFI performed with cannula with distal ports of 0.5 mm is indicated for brow and lip volume restoration. M-SEFFI is best for the upper sulcus and infra orbital hollows and the fine wrinkles in the periocular area, such as the smile lines that form in the lower eyelid, and the perioral fine lines of the lips<sup>[4]</sup>.

## DISCUSSION

In the past, surgeons have focused on the rejuvenation of the frame of the face through extensive facelifts and the periocular structures individually, correcting brow ptosis, dermatochalasis, eyelid bags, tear trough



**Figure 1.** Pre-treatment and 6 months post-treatment views of a 53-year-old woman treated with MIVEL and SEFFI in her cheeks, periocular and perioral regions combined with four-lid blepharoplasty



**Figure 2.** Pre-treatment and 6 months post-treatment views of a 51-year-old woman treated with MIVEL and SEFFI in her cheeks, periocular and perioral regions combined with four-lid blepharoplasty

deformities and fat pads descent or atrophy in variable combinations without a systematical approach. The knowledge of the events taking place in the ageing process has evolved and the authors believe that a paradigm change in the approach of the ageing of the periocular region as a single aesthetic unit is in order. Liew and Nguyen<sup>[7]</sup> recognised two types of patients, those showing signs of tissue descent and those showing signs of volume depletion. The authors believe that, as surgeons, we should consider this two aspects of ageing as both present in a certain degree and analyze the effect of both in the different complexes of the periocular region in the preoperative evaluation of our patients, in order to offer a systematic and global solution to our patients demands. In the periocular unit, the SC is affected by both descent and deflation, the IC is affected by deflation and descent in a lesser degree and the LC is predominantly affected by deflation. A systematic approach to the aesthetic unit carries a high satisfaction rate<sup>[8,9]</sup>. MIVEL is a scarless technique that assesses the vertical vector of tissue descent that occurs in the SC. However, for as much as tissue can be lifted, a 3-dimensional rejuvenation of the periocular esthetic unit can be only achieved if associated with volume restoration<sup>[10,11]</sup>. SEFFI and M-SEFFI allow for the correction of volume depletion in the finer and more superficial areas closer to the eyes and lips as well as the deeper areas of the forehead, eyebrows, temples and cheeks, assessing not only volume depletion, but also adding skin rejuvenation due to its content of adipose-derived stem cells, with a lower rate of complications compared to traditional fat grafting techniques<sup>[12-14]</sup>. The authors believe that the main advantage of these techniques used in combination is that they assess the mayor consequences of aging in one integral surgical act, thus achieving more natural results than the previous horizontal tightening procedures.



Skin removal and fat removal-repositioning techniques can be effectively associated to these procedures when indicated. Clinical examples in [Figures 1 and 2](#).

## CONCLUSIONS

A systematic approach to aesthetic units carries a high satisfaction rate. With the goal of rejuvenating the periocular region, the authors advocate approaching this area as a unit rather than with individual isolated techniques that can achieve only limited improvements. MIVEL is a scarless technique that respects the vertical vector of tissue descent. As much as tissue can be lifted, a 3-dimensional rejuvenation of the periocular aesthetic unit can only be achieved if associated with volume restoration. SEFFI and M-SEFFI techniques assess this issue with a high satisfaction and a low complication rate.

## DECLARATIONS

### Authors' contributions

Assistant surgeon in part of the cases, research and writing: Pignata G

Surgeon in charge of part of the cases: Gennai A

Original idea, surgeon in charge of part of the cases, and processing pictures: Bernardini F

### Availability of data and materials

The data were strictly obtained from medical records according to the privacy policy and ethics code of our institute.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Informed consent was obtained for each procedure and the review adhered to the tenets of the Declaration of Helsinki.

### Consent for publication

Informed consent was obtained for publication.

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Case Report

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# Successful reconstruction of bilateral oral commissure fusion secondary to Stevens Johnson syndrome

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## Abstract

Stevens Johnson syndrome (SJS) is a rare and often fatal hypersensitivity reaction commonly triggered by drugs which results in the uncontrolled destruction of keratinocytes with both cutaneous and mucosal involvement. Fusion of the oral commissures, although reported in burn victims, is a very uncommon complication of SJS. The successful reconstruction of oral commissures fusion using a modified commissuroplasty technique in a 19-year-old Hispanic female with severe microstomia secondary to SJS is presented here. Re-establishment of normal speech, oral intake, as well as aesthetic appearance were achieved.

**Keywords:** Steven Johnson syndrome, commissuroplasty, microstomia

## INTRODUCTION

Stevens Johnson syndrome (SJS) is a type IV hypersensitivity reaction commonly triggered by drugs which results in the uncontrolled destruction of keratinocytes with both cutaneous and mucosal involvement. As a rare and often life-threatening disease, SJS has an annual incidence of approximately 1 to 6 cases per 1 million<sup>[1]</sup>. Reportedly, ophthalmologic complications are among the most severe sequelae of SJS along with cutaneous and gastrointestinal manifestations<sup>[2]</sup>. Fusion of the oral commissures, although commonly reported in burn victims, is a very uncommon complication of SJS. Incomplete fusion of the oral commissures (bands connecting the lateral aspect of upper and lower lips but sparing the very corner of the mouth) in



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**Figure 1.** (A) Stevens Johnson syndrome manifested by generalized swelling and full thickness epidermal necrosis of the skin of face and the mucosa of the lips; (B) oral commissures fusion (arrows) resulting in impairment of normal speech, oral intake, as well as a compromised aesthetic appearance

the setting of SJS has only been reported four times with this being the first report of complete fusion<sup>[3-6]</sup> (fusion of the upper to lower lip extending all the way to the corner of the mouth).

## CASE REPORT

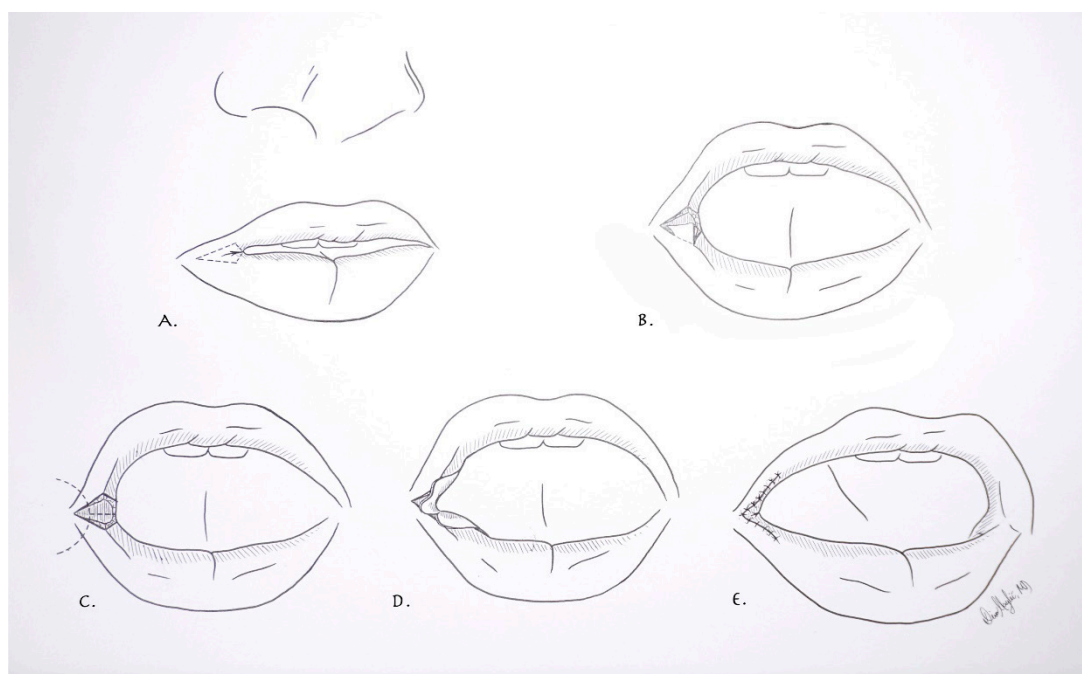
A 19-year-old Hispanic female was referred to the pediatric plastic surgery clinic for severe microstomia caused by bilateral oral commissure fusion post SJS. The SJS developed as a complication to oral sulfamethoxazole/trimethoprim used by the patient for the treatment of severe chronic acne vulgaris. This reaction to the medication resulted in generalized swelling and full thickness epidermal necrosis of the skin with involvement of face and the mucosa of the lips [Figure 1A]. Once the patient's condition stabilized re-epithelization of the affected areas commenced. During the re-epithelization process patient's oral commissures fused resulting in impairment of normal speech, oral intake, and compromised aesthetic appearance [Figure 1B]. Despite the fusion, the involved tissue remained relatively supple, in contrast to the usual thick and rigid scar associated with thermal or chemical burns).

We report here the successful functional and aesthetic reconstruction using a modified commissuroplasty technique. The procedure was performed under general anesthesia on outpatient basis. Incisions were performed at the level of the commissures in the shape of a 4-sided polygons with the long diagonal of 1.5 cm and the short diagonal of 1 cm [Figure 2A]. Full thickness excision of the scar present was performed preserving only the deep mucosal lining [Figure 2B]. The exposed mucosa was then divided in a Mercedes-sign pattern. This generated three separate mucosal flaps [Figure 2C]. The lateral flap was used to resurface the corner of the mouth, while preventing overlapping sutures lines and re-fusion during the healing process. The superior flap was used to resurface the upper lip wound and the inferior flap to resurface the lower lip wound [Figure 2D]. The flaps were secured in place with interrupted deep dermal PDS sutures. The superficial lip mucosa was closed with a running 6-0 fast absorbing suture [Figure 2E].

The patient was discharged home in stable condition and had an uneventful postoperative course. Upon the postoperative visit at 6 weeks, the patient showed complete healing with a normalized oral opening, excellent function and an esthetically pleasant mouth contour [Figure 3].

## DISCUSSION

Microstomia has various etiologies. It can be a congenital deformity or an oral manifestation of connective tissue disorders. Furthermore, it can be secondary to electrical, thermal and caustic injury, or the result of oncologic resection<sup>[7]</sup>.



**Figure 2.** (A) Modified commissuroplasty technique. Incisions performed at the level of the commissures in the shape of a 4-sided polygons; (B) excision of the scar with preservation of the deep mucosal lining; (C) development of three separate mucosal flaps; (D) resurfacing of the corner of the mouth, upper and lower lip with individual flaps; (E) final closure with re-establishment of normal lip anatomy



**Figure 3.** The 6-week postoperative image showing complete healing with a normalized oral opening and esthetically pleasant mouth contour

Microstomia is a challenging condition to treat. Its surgical reconstruction usually involves three steps: re-establishing the intended location of the commissure, excision of the existing scar and resurfacing of the resulting defect. While maintaining continuity of the orbicularis oris, the resurfacing can be achieved by primary closure, split or full thickness skin grafting, or local tissue re-arrangement<sup>[8,9]</sup>.

First employed by Dieffenbach in 1831, modified by Converse and later by Friedlander & Millard, the Y-V advancement technique is a popular choice for treatment of commissural microstomia in burn patients<sup>[9,10]</sup>. The procedure described in the present report represents a slight modification of the technique. As the dry vermillion of the commissures was not affected by the scar tissue, it was not resected in our patient. The three mucosal flaps used to reconstruct each commissure were used to resurface the wet vermillion only. They were advanced and sutured to the intact dry vermillion at the level of the red line, replacing only similar tissue.

In conclusion, although non-life threatening, microstomia can limit functionality and cause undue stress to the patients and their families. Using a modified commissuroplasty technique involving scar excision and mucosal advancement proved to be an effective treatment modality of microstomia secondary to SJS.

## DECLARATIONS

### Authors' contributions

Studied concept and designed the manuscript: Flores S, Gociman B

Drafted the manuscript: Flores S, Hosein R, Gociman B

Illustrated technique: Maglic D

Revised the manuscript: Gociman B

Supported clinical: Maglic D, Moores N, Hosein R, Siddiqi F, Gociman B

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

The authors declare that there are no conflicts of interest.

### Ethical approval and consent to participate

Ethics/Review board approval not applicable. The proper consent of the patient was taken for carrying out all the treatment and photographs.

### Consent for publication

Patient's consent obtained.

### Copyright

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Technical Note

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# Global facial rejuvenation, new technique

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## Abstract

Facial aging is the combination of multiple effects such as sun exposure, tobacco, environmental stress and smog, reflecting the cumulative and dynamic effects of time on the skin, soft tissues and the deep structural components of the face that show an important change structural features of the skin and loss of facial volume. There are many different techniques currently used to perform face lifting, the ultimate goal is to get good results with respect for patient safety. This article describes a new approach to facial rejuvenation combining superficial musculoaponeurotic system (SMAS) plication elements on four vectors, with a blepharoplasty to achieve a lasting improvement in facial aging. The plication of the SMAS on the suture provides three vectors of elevation under the skin in the middle rhytidectomy, linked to the Lorè fascia and to the third platys elevation vector behind the ear. The blepharoplasty technique is often unavoidable in the execution of the global facial rejuvenation. This allows obtaining excellent results both in terms of aesthetic and of a good patient empowerment. This new surgical technique, called "KORU technique", was used on 31 patients between October 2010 and October 2012, producing lasting results, reducing injuries and respecting anatomical planes. This approach can be safely and easily performed under local anesthesia as an isolated midface procedure, respecting and safeguarding the facial nerve. This type of chiropractic technique can be used by young surgeons.

**Keywords:** Facial aging, rejuvenation, smas, surgical technique, anatomical planes, midface, blepharoplasty

## INTRODUCTION

The aging of the face can produce the following effects: elongation of the lower eyelid, flattery of the malignant eminences, volumetric loss in the undersea area of the cheek, prominence of the cheeks and deepening of the nasolabial fold. The facial support ligaments support the soft tissue of the face in a normal ana-



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tomical position, resisting the gravitational change. In 1976, Mitz and Peyronie<sup>[1]</sup> described the superficial musculoaponeurotic system (SMAS) and after this date multiple surgical procedures were improved. These techniques produce excellent results, but require a thorough dissection and have the potential for greater morbidity. The anatomical distribution of the facial nerve has been studied by various authors<sup>[2]</sup> and during the surgical dissection the most dangerous area of the face, the most worried one, must be considered. The frontal branch is one of the most commonly damaged nerves in plastic surgery. The path of the frontal branch can be drawn on the skin by two divergent lines that start from the region of the earlobe and go<sup>[3]</sup> to the lateral extremity of the eyebrow<sup>[4]</sup> and to the highest front fold. To locate the frontal branches it is useful to look for the superficial temporal artery. The branches of the buccal and zygomatic nerve have a deep position and in the nasolabial fold there is an excess of skin and fat which provides greater protection to the underlying nerve. The mandibular branch<sup>[5]</sup> is located above the lower margin of the mandible in 80% of the cases, in the remaining 20% it forms an arch under the lower edge of this bone and always flows inside or in depth of the muscle fibers of the platysma so in this area there is almost no danger of injuring the nerve. In this study, the authors, Colombo and Ruvolo, describe a new simple and safe face lifting technique, the KORU technique, designed for their patients and to guide the young surgeons in a first approach to this surgical procedure.

## METHODS

Between October 2010 and October 2012, 31 patients were operated using the facial lifting surgical technique, called KORu, conceived by the authors Colombo and Ruvolo. There were 25 women and 6 men. The age of the patients ranged between 35 and 64 years. All patients underwent the primary facelift.

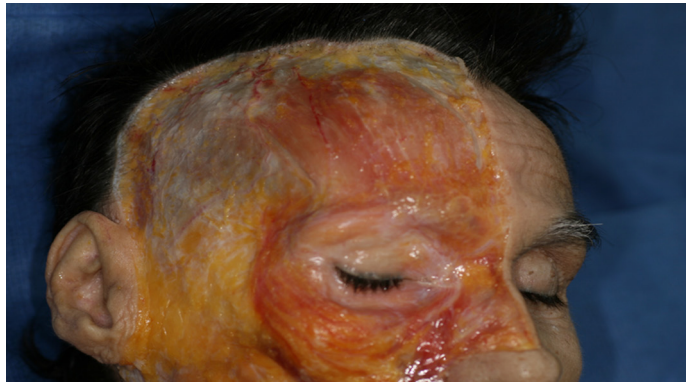
## TECHNICAL DESCRIPTION

The skin incision is performed along the temporal hairline and extends into the conventional position of the facelift in the postural auricular groove, posteriorly extending on the mastoid following an external auditory canal line. The skin flap is elevated in a subcutaneous plane and the dissection extends up to 2 cm from the labial commissure to respect the buccal branches of the facial nerve. Inferiorly the dissection is carried out to expose the neck and the mandibular edge, externally extending up to the orbital edge and beyond the upper edge of the zygoma. The authors suggest that the dissection is safer and it's less difficult to find the right dissection plan if the surgeon started from the temporal region. All face-lift procedures were associated with a blepharoplasty using the technique of Adamson *et al.*<sup>[6]</sup> and Mendelson<sup>[7]</sup>. The SMAS plications are performed on four vectors: the first vector passes from the external cantus to the tragus and gives a vertical direction; the second vector goes from Darwin to the tragus and gives a vertical/oblique direction; the third vector goes from the angle of the jaw to the Lore band; the fourth vector that goes from the back/subauric platysma to the mastoid. The last two vectors give a vertical direction and an angle definition of the jaw that draws a U around the earlobe [Figures 1-3].

The choice of these traction points was according to the area of the face where the branches of the facial nerve are deeper to work safely. A plication suture performed between cantus and tragus was made to create a spindle to restore the cheek volume [Figure 4]. The suture [Figures 5 and 6] takes less tissue on the marginal area in the direction of cantus and tragus and takes more tissue in the central zone of placcation, in this way the author restores the loss of volume at a point of greater projection of the face and gives an all-round look 3D topography that is delineated by series of arcs and convexities<sup>[8-18]</sup> [Figure 2].

## RESULTS

The authors performed 31 interventions, using the KORU technique, from October 2010 to October 2012. In no case there were infections, there was minimal tension on the suture line. There is minimal postoperative



**Figure 1.** Temporoparietal fascial



**Figure 2.** Traction points



**Figure 3.** Superficial musculoaponeurotic system

edema, as well as minimal postoperative bruising. This technique produces effective results, supports a volume of midface without causing injury to the facial nerve. This study showed a new, safe approach to facial rejuvenation combining the elements of the SMAS placenta with a blepharoplasty to achieve long-term improvement of middle-aged aging and a more natural effect. The low incidence of morbidity was accompanied by rapid convalescence and most patients were able to return to work and social activities very early with



**Figure 4.** Emplicature superficial musculoaponeurotic system



**Figure 5.** Cute positioning for sutures



**Figure 6.** Cut of the skin flaps on the delimited line

excellent satisfaction.

After a follow-up of the treated patients, the authors saw that there were no errors, but experiences described by the patients related to the feeling of tension in the tissue fixation points.

Like all the techniques, at the beginning the authors had slightly longer intervention times than traditional techniques, but the results were excellent.



During the execution of this new technique there were no errors with important post-operative aesthetic consequences.

There were initial difficulties in finding the plans despite the reference points mentioned above.

## DISCUSSION

After the description of SMAS in 1976<sup>[1]</sup>, surgical attempts to correct aging were directed towards stiffening techniques of SMAS. The introduction of Hamra<sup>[19]</sup> of deep-plane rhytidectomy in 1990 focused attention on a completely new concept of rejuvenation through the composite repositioning of facial tissues. The peripheral anatomy of the facial nerve has been intensively studied by various authors; they analyzed the anatomical distribution of the branches and the different types of nerve connections that exist between them. This document describes a new safe lifting technique that preserves the facial nerve and may be easier. This procedure has opened up the chances of further morbidity in lifting the median face. The dissection of the skin flap initiated with temporal region incision, the SMAS placcation was performed by three sutures describing three vectors. The superior suture that goes from the external cantus to the tragus is made to produce an even more sickly increase. While the platysma suture on the mastioid minimizes tension on the suture line. The authors, Colombo and Ruvolo, always associate SMAS plication with Adamson blepharoplasty and a fat sliding on Mendelson. An additional technique is performed for blepharoplasty with a lower lid. This operative procedure uses the principle of anchoring the upper edge of the lower lid by suturing a triangular flap of the muscle from it to the upper lateral part of the orbital rim. This more effective support for the lower edge of the lid allows the redundant fabric to be removed without obtaining an ectropion<sup>[20]</sup>. The concept of replacing the protruding fat of the lower lid in the orbit and keeping it there by strengthening the orbital septum is tempting because it embodies the goal of cosmetic surgery to restore the juvenile ideal by reversing the structural changes of aging. This concept is in contrast to that of standard blepharoplasty procedures that use a simple excision and narrowing approach to obtain a superficial improvement. Based on their experience, the authors believe that SMAS plication and SMAS staining provide similar results 5-10, so they only choose the blepharoplasty plication procedure, obtaining the important result as an excellent aesthetic result with a high level of patient satisfaction. The KORU face lifting technique that affects the central area, the orbital area and the neck gives a global refreshing appearance to the face, giving a natural look.

This new technique is a possibility to replace the face-lift.

## DECLARATIONS

### Authors' contributions

Concept and design: Colombo G, Ruvolo V

Manuscript preparation: Colombo G, Ruvolo V

Critical revision and finalizing of the manuscript: Colombo G, Ruvolo V

### Availability of data and materials

The data were strictly obtained from medical records according to the privacy policy and ethics code of our institute.

### Financial support and sponsorship

None.

### Conflicts of interest

Both authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

The study is approved and patients have agreed to participate

### Consent for publication

The patients gave their consent to the use of the photos shown in the article

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Original Article

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# When free flaps are not the first choice: is the distally based peroneus brevis still an option for foot and ankle reconstruction in the era of microsurgery?

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## Abstract

**Aim:** Soft tissue defects with or without exposed bones in the lower extremity, ankle and the foot-with or without bone defects or exposed hardware-often require coverage with vascularized flaps. Free flaps, which add healthy tissue especially to the lower extremity instead of further injuring a limb, are the first choice in high volume microsurgical centres. Nevertheless, in some instances pedicled flaps may have indications when free flaps are not suitable.

**Methods:** The distally based peroneus brevis flap is harvested from the lateral compartment of the leg based on the distal perforating arterial supply and covered with split skin.

**Results:** We performed a total of 69 peroneus flaps between 2003 and 2017. Minor flap necroses at the distal tip were noted in 8% of the peroneus brevis reconstructions. Total flap loss occurred in 1 peroneus flap. Defect etiology and patient age were not associated with surgical outcome.

**Conclusion:** While nowadays the first choice of lower extremity reconstruction is an appropriate free flap solution,



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the peroneus brevis muscle flap can also be seen as a valuable tool to reconstruct small to medium sized defects at the ankle, distal tibia, and the heel with an acceptable donor site morbidity. Despite the easily available variety of free flaps to achieve this purpose, still proper indications remain where a local flap can be a viable option in the hand of experienced plastic surgeons. However, caution is advisable in patients with peripheral arterial occlusive disease or venous insufficiency.

**Keywords:** Free flaps, peroneus brevis, muscle flap, lower extremity reconstruction

## INTRODUCTION

Soft tissue defects-with or without bone defects or exposed hardware-in the lower extremity, ankle and the foot often require coverage with vascularized flaps. Due to the anatomically given thin layer of soft tissue to cover vital structures and the oftentimes limited blood supply, the amount of locally available skin is very limited.

Free flaps have become a routine procedure and are a superb option in many cases, especially when large and complex defects need to be addressed. A variety of available options have been described for this problem zone<sup>[1-15]</sup>. However, when either the local conditions or other obstacles including systemic diseases, that limit an extended operation time or missing microsurgical expertise are hindrances to closure, local flaps may be a solid option. Proximally based pedicled local flaps have a limited arc of rotation and therefore are no good candidates to reconstruct defects in the lower third of the leg, ankle or foot. We describe the use of a distally based peroneus brevis flap for indications where free flaps were not suitable or not deemed the first priority.

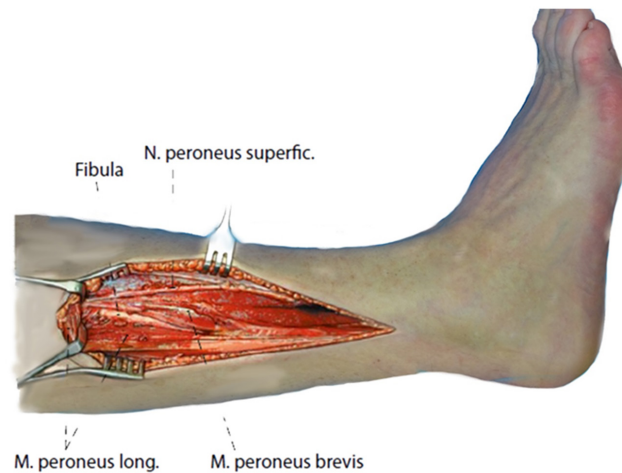
In such cases distally based muscle and fasciocutaneous flaps have constantly remained an interesting alternative to free flap surgery. While the distally based peroneus brevis muscle flap (PBF) was first reported by Donski and Fodgestan<sup>[16]</sup>, it became more popular when Masquelet described the surgical procedure in detail based on of his anatomical findings<sup>[17]</sup> and by Lyle and Colborn<sup>[18]</sup>. In our clinical routine it has been implemented as a workhorse for reconstructing small full thickness defects in the distal lower leg, ankle and heel<sup>[19-24]</sup>. Later papers added their experiences and highlighted the key points that need to be taken into account McHenry *et al.*<sup>[25]</sup> and Eren *et al.*<sup>[26]</sup>.

Because the anatomy is relatively constant this flap can be quickly and reliably harvested and the donor site poses no relevant clinical or functional problem. This flap has therefore been successfully applied by various authors to reconstruct the distal lower leg, ankle and Achilles region<sup>[4,27-29]</sup>. We discuss the peroneus brevis flap as a part of the surgical armamentarium and hence its specific technical aspects in this paper.

## METHODS

According to the description of Nahai and Mathes<sup>[30]</sup> who had first reported the peroneus brevis flap as a proximally based tool in 1974 later on described a distally based version in 1997, we performed the distally based turnover muscle flap. Modifications and standardization of this flap<sup>[18]</sup> were popularized by Eren *et al.*<sup>[26]</sup> and further propagated by others as a useful muscle flap to reconstruct small defects in the lateral distal third of the leg<sup>[4,31-34]</sup>.

In our series the peroneus brevis flap was raised as a reversed muscle flap and, following transfer into the defect, covered with a split thickness skin graft. Donor sites were closed directly in all flaps<sup>[35]</sup>. Similar to patients with sural flaps, wounds were preconditioned using topical negative pressure with or without instillation until the wound was deemed clean enough for closure. Dissection of the flap was performed under general anaesthesia with the patient supine on the operative table and a tourniquet was applied. The incision was performed straight or slightly curved depending on the localization of the defect. Preserving



**Figure 1.** Anatomy of the lateral lower leg with marked peroneus brevis muscle

the distal perforating vessel, which is approximately 5 cm above the malleolus has allowed the flap to become adopted as a standard technique of limb reconstruction in our unit with 1 case of total PBF flap loss so far, requiring secondary surgery.

Skin flaps were raised with the deep fascia, and care was taken to protect the superficial branch of the peroneal nerve, which can be dissected deep to the deep fascia in the proximal calf. It pierces the deep fascia approximately 15 cm proximal to the lateral malleolus. The peroneus longus tendon is found more posterior and superficial than its brevis counterpart. The tendons were followed up to the attachments of the muscle bellies and brevis and longus tendon were identified and separated, revealing the lateral surface of the fibula between them. Any branches of the peroneal vessels that run posterior to the fibula and segmentally pierce the muscle should be protected. In our series we found usually one larger proximal vessel and another smaller one more distally. The peroneus muscle was then detached from the anterior intermuscular septum to the anterior surface of the fibula. The muscle was elevated en bloc starting from the periosteum proximally down to the pivot point, where the dissection stopped. Two thirds of the flap can usually be elevated until the perforating vascular branch enters the muscle belly. After opening the tourniquet and hemostasis the flap was turned over and was sutured into place with a drainage underneath and split skin grafts on top. If necessary near infrared fluorescent angiography with indocyanine green was performed intraoperatively to determine flap perfusion and to eventually trim the tip of the flap. Eventually the most distal tip of the peroneus flap is prone to undergo venous congestion and may necessitate secondary skin regrafting, which usually leads to complete healing [Figures 1-5].

In a previous historic comparison of reverse flow lower extremity flaps Kneser *et al.*<sup>[36]</sup> analyzed the morbidity of the donor site and stated that equally to a reversed sural island flap (which was used historically and is no longer a routine surgical option in our hands since free flaps have become the method of choice) the peroneus brevis flap showed appropriate to successfully close full thickness defects in the lower extremity.

## RESULTS

We performed a total of 69 peroneus flaps between 2003 and 2017. Minor flap necroses at the distal tip were noted in 8% of the peroneus brevis reconstructions. Total flap loss occurred in 1 peroneus flap. Defect etiology and patient age was not associated with surgical outcome.

In a physical examination at time points with a minimum of at least 12 months after flap surgery all wounds



**Figure 2.** The 75-year-old patient with intraoperative raised distally based peroneus brevis muscle with flap turned and flipped over to 180 degrees into defect zone of a chronic wound after open reduction and internal fixation of calcaneal fracture



**Figure 3.** Primary closure of donor site with distally based peroneus brevis muscle flap sutured into place before skin grafting



**Figure 4.** Dorsal aspect of the reconstructed heel region 6 months after surgical therapy





**Figure 5.** Lateral aspect of the lower leg and foot 6 months after reconstruction with the distally based peroneus brevis muscle flap and split-thickness skin graft. The distal part of the flap needed secondary skin re-grafting and hence healed unevenly

were completely healed without any evidence of instable scars, chronic infections or fistulae. Patients reported a high level of satisfaction regarding the outcome of surgery without any significant statistical difference between the compared flaps. The active total range of motion was comparable in both groups without significant differences [extension/flexion  $78.5\% \pm 20.0\%$  (PBF peroneus flap),  $66.6\% \pm 23.1\%$  (DSF distal sural flap) and pronation/supination  $70.9\% \pm 27.7\%$  (PBF),  $61.1\% \pm 33.3\%$  (DSF)]. No instability of the ankle joint was observed in patients from both groups. Circumference of the lower leg 15 cm below the knee joint and above the ankle joint was comparable in both groups. No significant postoperative lymphedema was observed. Hypaesthesia in the lower leg or foot region, except for the flap itself and the skin-grafted regions at the donor site, was reported by 21% of patients from the PBF and 58% of patients from the DSF group<sup>[36]</sup>. Patients did not report significant functional impairment due to these hypoaesthetic zones. Neuromas were neither observed at the donor nor at the recipient sites in this series<sup>[36]</sup>.

## DISCUSSION

Soft tissue defects in the distal lower leg as well as in the foot and ankle region are not infrequent and remain challenging for plastic surgery. Methods of tissue engineering and regenerative medicine<sup>[37-51]</sup> to circumvent the use of autologous tissue and their inherent donor site morbidity seem promising but are not clinically available for these problems yet. Although a considerable number of local or free flaps has been successfully described to surgically reconstruct these defects<sup>[7,52-58]</sup> each individual case needs the optimal indication for the most suitable flap procedure. Free flap transfer has become a routine method in high volume centers and allow free tissue transfer even to the distal lower extremity with a successful closure in more than 90%-95%, depending on the comorbidities and local and systemic conditions. This does not preclude the remaining interest in local flaps to solve the problem of small to medium-sized defects in this critical anatomical region<sup>[59,60]</sup>.

Especially the advent of perforator based flaps, such as propeller flaps, have augmented the armamentarium of problem solving techniques in the lower extremity<sup>[52]</sup>. Other than in the proximal knee region and the upper and middle third of the lower leg, where a variety of proximally based local pedicled flaps are available, the lower third and foot and ankle region demand either free flaps or reversed pedicled flaps<sup>[11,61,62]</sup>. Various modifications of the sural and peroneusbrevis flaps have been described to optimize the outcome and minimize complications<sup>[63-67]</sup>. The distally based peroneus brevis flap has been described as an efficient tool for the reconstruction of the distal lower leg, ankle, Achilles tendon and proximal foot region<sup>[4,65,68-73]</sup>. This flap can be indicated to cover exposed vessels, bones, tendons, and internal fixation hardware.

The surgical procedure is comparatively straight forward and basically safe, when anatomical landmarks and precautions are taken into account. Although we no longer use the distally based sural fasciocutaneous flap our group has compared the efficacy and donor site morbidity following use PBF (when compared to a sural flap) which had not been studied earlier<sup>[32]</sup>. Using the foot and ankle outcome score (FAOS) a direct comparison between the sural flap and the peroneus flap group did not show significant differences in any of the FOAS subscales<sup>[36]</sup>. Interestingly, the general quality of life (QOL) in patients with distally based flaps was more reduced in both groups than the actual function in daily living (ADL). In an attempt to exclude the influence of initial defect-related problems on ankle stability and function, subgroups of patients with defects caused by open fractures, osteomyelitis or Achilles tendon-related defects were compared with defects secondary to tumor resection or ulcers<sup>[36]</sup>. The results from the patient-administered FOAS questionnaire were confirmed by the physical examination which did not identify any significant differences in terms of ankle joint stability or range of motion<sup>[36]</sup>.

Ultrasonic investigation may further enhance the safety of the procedure. As with other meta-analyses it is a commonly known problem in studying outcomes in reconstructive surgery, that most series comprise only small numbers of patients and lack randomized trials, which is a classical scenario in plastic surgery. This holds especially true for studies comparing different types of flaps, where personal experience and preferences as well as local conditions significantly influence decision-making and prevent randomization<sup>[9,36]</sup>. The use of near infrared laser angiography with indocyanine green intraoperatively might help further optimize the design and flap survival, as has been shown previously in other flaps<sup>[14,74]</sup>.

In conclusion, distally based peroneus brevis flaps remain valuable options for the reconstruction of full thickness defects in the distal lower leg when the routine use of free flaps is not indicated. Vascular integrity of the affected leg is a prerequisite, and if local perfusion is compromised by peripheral vascular disease, failure rates are higher. In such cases we strongly advocate the use of free flaps with vascular reconstructions and optimization of blood flow. Studies have shown that harvesting of PBF does not affect stability and ROM of the ankle joint.

Whenever free flaps are not the first choice in distal lower leg reconstructions we therefore would recommend the peroneus brevis muscle flap as an alternative procedure to close small to medium sized defects at the distal tibia, fibula, ankle and heel.

## **DECLARATIONS**

### **Acknowledgments**

Some of the results have been part of Silke Brockmann's doctoral thesis and have been published previously<sup>[36]</sup>.

### **Authors' contributions**

Performed operations, wrote the manuscript draft, literature research, and corrected versions: Horch RE  
Performed operations, helped analyze results and worked on the manuscript: Ludolph I, Schmitz M, Boos AM, Kneser U, Beier JP, Arkudas A

### **Availability of data and materials**

Results are reported in the manuscript, patient's individual data are not available to the public for the sake of data protection laws.

### **Financial support and sponsorship**

None.

### **Conflicts of interest**

All authors declare that there are no conflicts of interest.



### Ethical approval and consent to participate

Ethical approval is not applicable. Each patient has signed an informed consent that his data may be anonymously utilized for scientific reasons.

### Consent for publication

Not applicable.

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Retraction

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# Retraction: Optimization of tissue anchoring performance and mechanical properties of barbed sutures for flexor tendons repair

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1. Bakhach J, Oneissi A, Bakhach E, Karamah R, Hantouche M, Shammass E. Optimization of tissue anchoring performance and mechanical properties of barbed sutures for flexor tendons repair. *Plast Aesthet Res* 2018;5:12.



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## Retraction

## Open Access



# Retraction: Optimization of the design of a barbed suture for flexor tendon repair using extended finite element analysis

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Case Report

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# Cherubism in a 4-year-old boy managed with tumor curettage, mandibular osteotomies and repositioning

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## Abstract

Cherubism is a rare disease characterized by significant loss of medullary bone which is replaced by excessive amounts of fibrous tissue growth within the mandible and maxilla. We present a case of a 4-year-old boy with a rapidly enlarging mandible and maxilla, causing significant change in the facial contour, malocclusion and phonation difficulties. He was treated with aggressive tumor curettage, lateral mandibular cortex osteotomies with medial repositioning. This allowed obliteration of the enlarged medullary space and restoration of the normal mandibular anatomy. At 12 months postoperatively, the patient had significant improvement in facial contour, normal outward appearance, and stable dentition.

**Keywords:** Cherubism, mandibular osteotomy, tumor curettage, Piezo Electric bone cutter, surgical treatment for cherubism

## INTRODUCTION

Cherubism is a rare, autosomal-dominant, non-neoplastic fibro-osseous condition predominantly affecting the mandible and maxillary bones. It was first described as “familial multilocular cystic disease of the jaws” by William Jones in 1933<sup>[1]</sup>. The name “cherubism” later became standard nomenclature used to describe the condition due to the marked fullness of the cheeks and jaws with a slight upward tilting of the eyes, resembling cherubs from Renaissance paintings<sup>[2,3]</sup>. Cherubism usually presents as symmetric bilateral expansion of the mandible and/or the maxilla, however mandibular involvement is more common<sup>[4]</sup>. Orbital involvement can occur in more severe cases, causing scleral show and eyes towards heaven appearance that is commonly



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described<sup>[2,3,5]</sup>. The spectrum of cases ranges from clinically undetectable to severely disfiguring. This rare disease is usually clinically noticed within the first few years of life and will continue to progress through childhood until puberty, after which, many cases will spontaneously regress<sup>[6]</sup>. Dental abnormalities, such as malocclusion and congenitally missing deciduous and permanent teeth along with delayed eruption are common<sup>[5,6]</sup>. Treatment for these dental problems yield no satisfactory solutions<sup>[7]</sup>.

Cherubism is usually inherited in an autosomal-dominant fashion with variable penetrance (100% in males and 50%-70% in females) and expressivity. However, there are a few reported nonfamilial inheritance cases<sup>[8,9]</sup>. Mutations in the gene SH3BP2 have been identified as causal of cherubism in most patients<sup>[10]</sup>.

Radiographically, cherubism is commonly described as bilateral, well-defined, multilocular radiolucent areas located commonly at the level of the angle and ramus of the mandible<sup>[11]</sup>. The histopathology of the tissue involved in relation to cherubism demonstrates multinucleated osteoclast-like giant cells near bone and within the soft fibrous stroma. Although these findings are characteristic, the diagnosis of cherubism cannot be made from the histology alone<sup>[7]</sup>.

The current recommended approach to the management of most cases of cherubism is to “wait and watch” into late adolescence, with the hope of spontaneous disease remission and therefore avoidance of early surgery. Early surgical intervention is usually advocated only for severe cases<sup>[7,11-14]</sup>.

We present herein a cherubism case of an 4-year-old boy with moderate but rapidly expanding burden of disease. He underwent surgical management with curettage of the tumor, lateral cortex mandibular osteotomies and repositioning with an excellent outcome.

## CASE REPORT

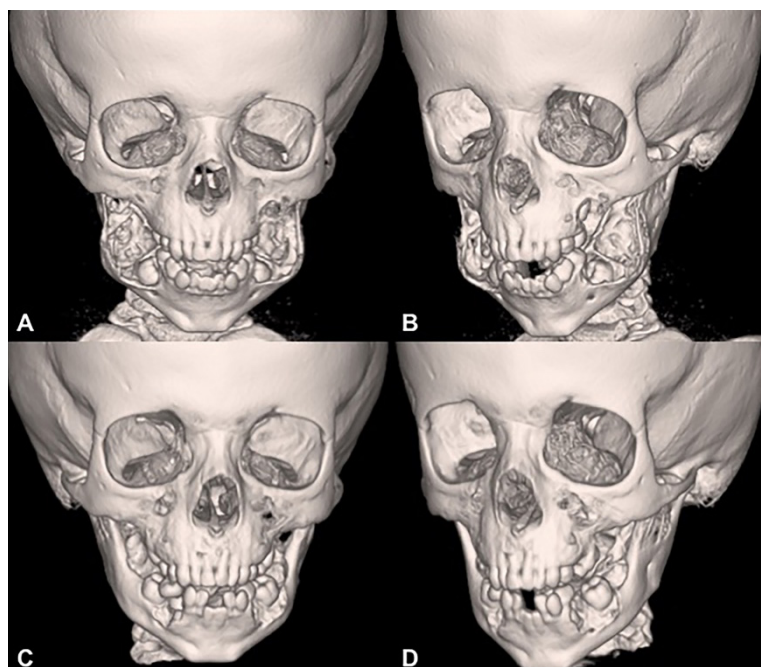
An otherwise healthy 4-year-old boy presented with progressive swelling of the cheeks. The patient's father had a history of cherubism which required multiple operations. The family's awareness of the disease allowed early recognition of the condition. On clinical evaluation the child had obvious deformity of his lower face, significant malocclusion, a narrow V-shaped palate and phonation difficulties [Figure 1A-C]. According to the family, these findings had progressively worsened over time, but particularly accelerated in the few months prior to presentation.

Given the rapid expansion of the boy's jaw and the functional and psychosocial impairment that the child was beginning to experience, the decision was made to forego observation and recommend surgical curettage with mandibular repositioning. A facial CT scan with 3D reconstruction was obtained to aid in the surgical planning [Figure 2A and B].

Under general anesthesia, the mandible was approached through bilateral lower buccal sulcus incisions. The tumor was encountered under the soft tissue, as it had eroded through the bony cortex at the level of the mandibular angle. Given the friable nature of the tumor and the clear delineation between diseased and healthy tissue, it was easily curetted from the surrounding normal bony cortex without injury to the infra-alveolar nerve, intra-medullary molars, and surrounding bony cortex. With the tumor removed, the displaced buccal mandibular cortex was osteotomized. Using a Piezo Electric bone cutter (DePuy Synthes), anterior, inferior and posterior osteotomies were performed, protecting the surrounding soft tissue that remained attached to the buccal mandibular cortex through intact periosteum. The mobilized buccal mandibular cortex was then infractured and completely medialized, obliterating the enlarged intramedullary space. The procedure was replicated on the contralateral side.



**Figure 1.** Clinical presentation of a 4-year-old boy affected by cherubism. A-C: Note the preoperative swelling of the cheeks with the obvious deformity of his lower face; D-F: eight months post-operative with normalization of the outward appearance and contour of mandible following surgical intervention



**Figure 2.** Facial CT scan with 3D reconstruction. A and B: preoperative images showing the large tumor burden displacing the mandibular cortices and dentition; C and D: CT scan, at 12 months post-operative, showing normalization of the mandibular anatomy and significant ossification around the molars providing dental stability at the site of the mandibular bone repositioning

The patient's left maxilla had a significant deformity as well. Using a left upper buccal sulcus incision, the tumor was identified eroding through the anterior wall of the maxillary sinus and protruding into the soft tissue. The tumor was removed in similar piecemeal fashion by curettage. There were no intra-operative complications.

The postoperative course was uncomplicated and at 6, 8, and 12 months follow-ups, the patient had significant improvement in facial contour with a normal outward appearance and much improved occlusion [Figure 1D-F]. Repeat CT scan examination showed normalization of the mandibular anatomy and significant ossification around the molars providing dental stability at the site of the mandibular bone repositioning [Figure 2C and D].

## DISCUSSION

Cherubism is a rare disease with just over 300 reported cases in the literature documenting the disease process and management. However, there is no consensus in regards to treatment guidelines. The variability of presentation makes it difficult to establish a "one size fits all" treatment modality. There is little argument that patients who present with minimal involvement should be followed on a regular basis, and those with severe disfigurement should be strongly considered for surgery. Yet, there is no accepted approach for the majority of patients who fall into the "grey zone" between these two extremes of presentations, as was our patient's case.

From a psychological standpoint, early surgical intervention can have a very positive impact by preventing social ridicule and promote acceptance in the child's formative developmental years<sup>[7]</sup>. Furthermore, early tumor removal in the disease process, as advocated by the current report, could prevent any long-term sequelae requiring significantly more complex reconstructive surgery. Additionally, it has also been shown that early operation, with curettage during the growth phase can arrest the tumor growth, and not prompt rapid regrowth, thereby making it a favorable option in preventing further bony deformities<sup>[7,13,15,16]</sup>. Our report further strengthens this group of patients who have good outcomes with arrested tumor growth and excellent facial contouring following early surgical intervention. With careful review of the literature it becomes apparent that the majority of patients within the "grey-zone" who opted for observation are at high risk of suffering complete tooth loss in their late twenties and early thirties and additionally require eventual surgical interventions or at a minimum extensive dental work<sup>[7]</sup>. In our view, this negates the argument that a "wait and watch" approach evades any eventual surgery. We should mention that we did not find any published review of these cases that looked at the number of these patients which require surgical interventions later following observation alone, but we feel this knowledge would be valuable for future investigation.

Surgical treatment modalities used in the management of patients with cherubism range from tooth extractions in the lesioned areas<sup>[16]</sup>, orthodontics, fixed and removable prosthetic implants<sup>[17]</sup>, osteoplastic surgery<sup>[13]</sup> to intraosseous curettage of lesions and bone grafting<sup>[13]</sup>. Taking advantage of the qualities of the Piezo Electric bone cutter, our surgical approach was achieved through minimal soft tissue disruption, but allowed for aggressive tumor removal, as well as mandibular cortical repositioning. Our technique restored the normal anatomy of the mandible without damage to the deciduous teeth, the permanent teeth, or the buccal soft tissue.

We hope that the current report will aid surgeons who manage cherubism patients discern more clearly the reasons why early surgical intervention should be considered and add the minimally invasive technique presented herein to their surgical armamentarium.

## DECLARATIONS

### Authors' contributions

Design, manuscript writing, editing and revision: Garlick JW, Willis RN, Donato DP, Gociman B  
Literature Research: Garlick JW

### Availability of data and materials

Not applicable.

### Conflicts of interest

All authors declare that there are no conflicts of interest.

### Financial support and sponsorship

None.

### Ethical approval and consent to participate

This study's need for IRB approval was waived by the University of Utah IRB, due to nature of case report and patient's parental written consent. Written consent was obtained from the patient's parents. It is available upon request.

### Consent for publication

Written consent was obtained from the patient's parents.

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Review

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# Wound healing in postbariatric body contouring surgery

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## Abstract

Due to the continuous development in the field of bariatric surgery, there is an increasing need for postbariatric body contouring surgery. The morbidity of postbariatric patients predisposes them to develop wound healing complications. In this article we describe the preoperative, intraoperative and surgical factors influencing the wound healing and therefore the final outcome. The most common postbariatric body contouring procedures, including brachioplasty, breast contouring surgery, abdominoplasty/circumferential body lift and medial thigh lift are being discussed in terms of wound healing characteristics and subsequent complications. The preoperative preparing as well as special operative techniques are described in order to achieve a low rate of wound healing complications.

**Keywords:** Body contouring, postbariatric surgery, wound healing

## INTRODUCTION

According to the World Health Organization (WHO) in 2016, 39% of the world population was overweight and 13% of this group were obese. Overweight is defined by a body mass index (BMI,  $\text{kg/m}^2$ )  $\geq 25$  and obesity is defined by a BMI  $\geq 30$ <sup>[1]</sup>. In order to reduce the comorbidities associated with overweight like diabetes mellitus type 2 and certain types of cancer and cardiovascular diseases<sup>[2]</sup>, the current guidelines for obesity recommend a weight loss of at least five percent body weight in patients with a BMI  $\leq 35$  and a weight loss of at least ten percent body weight in patients with a BMI  $\leq 35$ . The therapeutical change of life style, diet re-



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strictions and physical activity as well as pharmacotherapy are the first choices in reducing the body weight. In advanced cases the bariatric surgery comes into play, especially the laparoscopic procedures being able to provide weight loss with reduced complication rates<sup>[3]</sup>. According to the German guideline for Adiposity and Metabolic Disease Surgery, 2018, the surgical therapy is recommended in patients with a BMI  $\geq 40$ , in patients with a BMI between 35 and 40 and comorbidities associated with obesity and in patients with a BMI between 30 and 35 and type 2 diabetes mellitus<sup>[4]</sup>. In 2013 there were about half million bariatric surgical interventions<sup>[3]</sup> performed worldwide, which implements the need for these procedures.

After a long process of reducing the BMI and achieving the ideal body weight, patients still have to face the next challenge. Regardless of the methods used to successfully reduce the weight, massive weight loss patients often develop redundant, hanging skin and fat depots which cannot be removed by diet, physical exercise or medication. Functional handicaps, rashes, skin infections, difficult body hygiene, self-confidence or daily problems finding appropriate clothing motivate the patient to go to the plastic surgeon. Although the successful weight loss reduces some of the medical risks, the psychosocial and functional problems often remain a problem for these patients<sup>[5]</sup>. Up to 89% of the postbariatric patients complain of problems with the redundant skin and up to half of these patients find this condition to be worse than the initial obesity<sup>[6]</sup>. In the era of bariatric surgery, the body contouring surgery (BCS) plays a key role in achieving the final result for the obese patients.

The postbariatric BCS uses reconstructive procedures to improve the physical and psychological status of the patient and by having a medical indication, it distinguishes itself from the sheer aesthetic interventions. Up to 74% of patients who underwent bariatric surgery opt for a body contouring procedure<sup>[7]</sup>. Although it has a medical indication, the health insurances only cover a fraction of the treatment of these patients and therefore the demand for postbariatric body contouring remains higher than the actual performed interventions. In a large populational study, Lazzati *et al.*<sup>[8]</sup> found that only 21% of bariatric patients undergo BCS.

Several studies have proven that BCS in postbariatric patients is prone to more complications than in patients who did not receive weight loss surgery<sup>[9,10]</sup>. The overall early complication rate in the literature varies from 45% to 70% and includes hematoma, seroma, wound dehiscence, infection, deep vein thrombosis and pulmonary embolism, whereas wound healing disorders and seroma formation appear to be by far the most common<sup>[10,11]</sup>. Several factors seem to be involved in the development of these wound complications, including preoperative factors, intraoperative factors and surgical procedure factors.

## PREOPERATIVE FACTORS

Patients losing weight after a bariatric procedure are known to have nutritional deficiencies. Patients undergoing postbariatric body contouring have been proven to have low prealbumin and hemoglobin, vitamin A, C, B complex, iron, zinc and selenium deficiencies as well hyperhomocystinemia<sup>[12,13]</sup>. These factors are known to be essential for wound healing and therefore leave the postbariatric patient at risk for wound healing disorders. There is evidence that the perioperative nutritional supplementation can improve the wound healing process in these patients and decrease the complication rate. Some authors even recommend an extended nutritional evaluation before beginning the body contouring procedures<sup>[14]</sup>.

One of the most significant risk factors for the BCS appears to be the BMI at the time of surgery. In spite of weight loss surgery, physical exercise and strict diets, the BMI in some patients reaches a stationary level, which cannot be improved anymore. The existence of large abdominal aprons, excessive medial thigh skin and fatty tissue as well as macromastia prevent the patient from performing daily activities and exercise and result in a vicious circle, where further weight loss is not possible. Most studies have proven a high BMI to be an important risk factor for developing complications after BCS<sup>[10]</sup>. As a matter of consequence, the amount of tissue removed is also correlated with increased wound complications<sup>[14]</sup>. The combination of large opera-



tive wounds and poorly vascularized, excessive fatty tissue will most probably lead to fat necrosis, development of seromas and cellulitis as well as wound dehiscence. Certain operative techniques have been developed in order to approach this problem.

Smoking can also have an important impact on wound healing. Some studies describe that in smokers the relative risks of developing a wound infection after contouring breast surgery are 3.8 times higher and after medial thigh lift 7.74 times higher respectively<sup>[15,16]</sup>. These studies suggest that patients should be advised to quit smoking six weeks before the BCS.

The season in which the BCS takes place can also be an influential factor on wound healing. In a study on 602 patients after postbariatric BCS, Duscher *et al.*<sup>[17]</sup> found a statistically significant difference in the development of wound infections between patients operated in the warm seasons compared to those operated in the cold seasons (10.29% vs. 4.08%,  $P = 0.0071$ ). Although the frequency of BCS appears to be higher in the cold seasons, the patients operated in spring and summer seem to develop more wound complications. This could be attributed to a higher bacterial load at the surgical site as well as to deficient hygiene.

### INTRAOPERATIVE FACTORS

The intraoperative administration of higher volumes of fluids has been associated with the formation of seroma, hematoma and wound healing problems<sup>[18]</sup>. Longer periods of oxygen desaturation ( $\leq 92\%$ ) have also been associated with wound complications, while longer periods of low ( $35.6^\circ$ ) intraoperative core temperature, seem to increase the rate of hematomas and bleeding<sup>[19]</sup>. Transfusion of blood products has also been associated with the development of wound complications<sup>[20]</sup>.

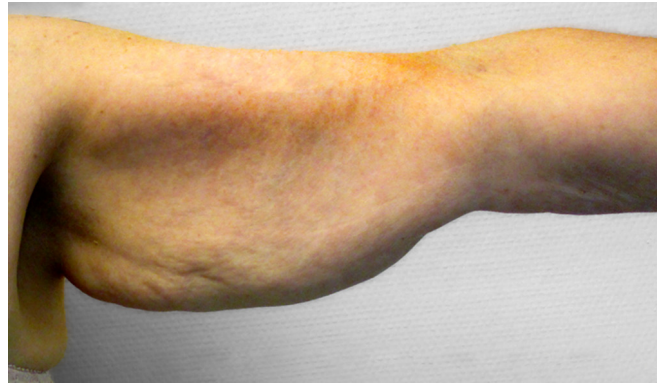
Keeping a warm environment during surgery and a constant core temperature of  $37^\circ$ , accurate surgery without bleeding and precise administration of fluids during surgery can significantly influence the outcome of the operation and favour the uncomplicated, primary wound healing.

### SURGICAL FACTORS

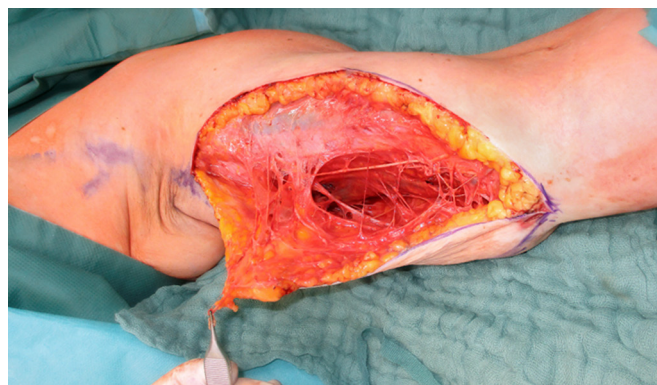
Brachioplasty, breast reduction/mastopexy, abdominoplasty/circumferential body lift and thigh lift are the most common postbariatric BCS<sup>[7,8]</sup>. Although the general patient features are the same, each body region and intervention has different characteristics and different rates of wound complications. In our practice we avoid addressing more than one body region per procedure. Studies have shown that multi-stage procedures reduce the risk of postoperative complications in comparison to long one-stage procedures. Especially, in the context of “pay for performance” probably future reimbursement from the health insurance will be reduced in treated cases with high revision operations due to postoperative complications in single-step procedures.

In the following we will address each procedure separately, analyzing the probability of wound complications and the techniques to avoid them.

Brachioplasty is one of the least frequent postbariatric BCS and has a rather low rate of postoperative complications compared to other forms of BCS. In a review on 1065 brachioplasties, there were 29.8% complications, whereby hematoma and seroma were found to be the most common early postoperative complication and poor scarring the most common late complication<sup>[21,22]</sup>. In our experience, the use of liposuction in the same procedure before performing the skin resection ensures a safe layer of dissection, without jeopardizing the superficial and deep veins as well as the lymph collectors, while ensuring the best aesthetical result [Figures 1-4]. The approach of the axillary fold is best done by a M-Y axilloplasty, which ensures an optimal aesthetic result while avoiding the postoperative wound complications and scar contractures<sup>[23]</sup>.



**Figure 1.** Redundant arm skin after bariatric surgery



**Figure 2.** Medial upper arm region after liposuction prior to resection. The superficial fat layer as well as the blood vessels, nerves and lymph collectors are preserved



**Figure 3.** Postoperative result with simultaneous liposuction and M-Y axilloplasty



**Figure 4.** Result 6 weeks postoperative after brachioplasty with simultaneous liposuction and M-Y axilloplasty

Breast contouring surgery after massive weight loss encompasses a wide spectrum of operations, including breast reduction techniques, mastopexy as well as autologous and implant augmentation. Most of these techniques use the Wise pattern skin incision, which results in an inversed-T scar. The majority of the postoperative wound complications appear in the inverted T-junction area [Figure 5], resulting from poor vascularization of the two pillars and excessive suture tension. Fatty tissue necrosis from rearrangement of tissue can also appear, causing delayed wound healing, infection and increased surgical revision rates. The nipple-areola complex (NAC) represents a special issue in breast contouring. Breasts after massive weight loss are characterized by advanced ptosis and subsequent extra-long NAC pedicles. This often causes deficient NAC vascularization followed necrosis and delayed wound healing. The overall complication rate for postbariatric breast contouring surgery is reported to be between 35.7% and 57%, mostly consisting of surgical wound problems<sup>[15,20]</sup>. We prefer the use of autoaugmentation with a lateral and medial flap for breast reshaping, as this means killing two birds with one stone: achieving the breast augmentation without foreign matter while performing a lateral lift at the same time.

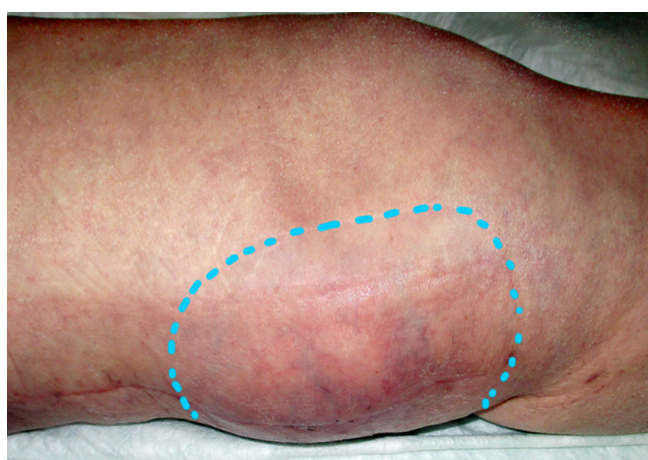
Abdominoplasty is the most frequent performed BCS. The presence of an abdominal apron represents the most common complaint of patients after massive weight loss. Skin macerations, intertrigo, rashes, difficult hygiene cause a great amount of discomfort for the patient, even more than before the weight loss. The addition of the hypertrophy of mons pubis renders this as a high symptomatic area which has to be addressed primarily, in order to improve the patient's life quality. These patients usually associate redundant fat tissue and skin in the epigastric, flank and back areas. The anterior abdominal wall can be addressed in one procedure, associating the abdominoplasty with a mons pubis lift. The epigastric and the flank regions can be approached either by a fleur-de-lis procedure or by performing a liposuction of the upper and lateral quadrants and the flanks before performing the panniculectomy, in a lipoabdominoplasty procedure. The fleur-de-lis procedure offers the largest amount of tissue excision in exchange for the longest scars. In this case the reduced vascularity of the skin flaps around the T-scar, the suture tension and the patient specific risk factors represent a hot spot for wound complications. The lipoabdominoplasty removes the excessive fat remaining in the abdominal wall while preserving the innervation and blood supply. The upper flap can be then caudally mobilized without extended undermining while preserving the vascularization of zones I and III while resecting zone II. The umbilicus can be repositioned by dissecting a narrow cranial tunnel and the skin can finally be tensioned and repositioned in order to achieve a tight, aesthetical result, while lifting the mons pubis at the same time. By maintaining the flap vascularity and removing the troublesome excessive fat tissue at the same time, this technique provides improved wound healing rates<sup>[24]</sup>. We prefer the lift of the lower back in a secondary procedure in a prone position, as the circumferential body lift provides enhanced wound complications while being economically disadvantageous<sup>[25]</sup>.

The incidence of postoperative complications after abdominoplasty is estimated around 57%, mostly consisting of seromas, wound healing problems and hematomas. Avoiding these problems requires good patient selection and operative planning, the placement of the operative incision below the contaminated infraabdominal fold, preserving the scarpa fascia, using liposuction when possible, using progressive tension sutures to reduce the dead space and seroma formation<sup>[26,27]</sup> and ensuring a tensionless wound closure.

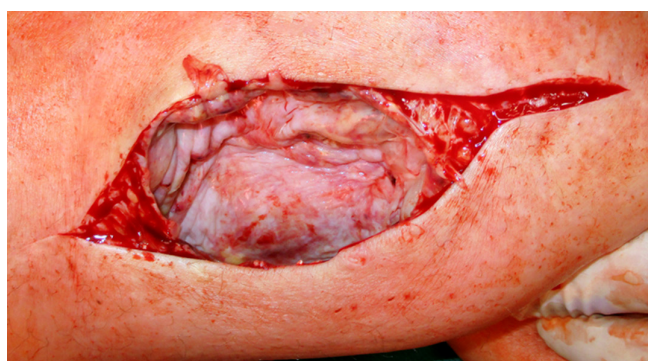
The medial thigh lift may be considered the “problem child” of the postbariatric BCS. Although the operative indication is strongly motivated by the patient discomforts, including friction, rashes and difficulty with ambulation, this intervention is marked by the high rate of postoperative complications. Complication rates as high as 69% to 78%<sup>[16,20]</sup> have been reported. The troublesome anatomical area, with superficial veins and lymph collectors running in the subcutaneous tissue predispose the patient to development of seromas, lymphoceles [Figures 6 and 7], hematomas and delayed wound healing. The use of the horizontal inguinal excision with the resulting T-scar adds more risk for wound dehiscence in this area. The use of liposuction



**Figure 5.** Wound dehiscence of the inverted T-scar after breast autoaugmentation with a lateral and medial flap



**Figure 6.** Postoperative lymphocele in the distal third of the scar after medial thigh lift on the left leg



**Figure 7.** Postoperative lymphocele with typical pseudocapsule after medial thigh lift - intraoperative view before complete capsulectomy

in thigh lift is crucial in reducing the morbidity. Serial liposuctions before paniculectomy are prerequisite, in order to reduce the excessive fatty tissue remaining around the thigh. We find the use of a concomitant liposuction with the thigh lift to be of special importance. The liposuction provides a clear dissection plane, sparing the superficial veins and especially the lymph collectors lying above the deep fascia while reducing the residual fatty tissue and reducing complications<sup>[28]</sup>.



## CONCLUSION

Obesity is considered by many to be a world epidemic. With the continuous growth of bariatric surgery, the number of patients addressing the Plastic Surgeon after massive weight loss continues to grow. Although BCS provides a high improvement in quality of life, the incidence of postoperative complications and especially wound healing problems remains high. Patient selection, thorough preoperative preparation, atraumatic surgery with use of adjunctive techniques like liposuction and preservation of important anatomical structures can lead to improved wound healing rates and less complications. Further research needs to be done in order to reduce the large amount of dead space resulting after these operations and hence reduce the morbidity.

## DECLARATIONS

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### Authors' contributions

Conception and design of the study, performed data collecting and analysis as well as manuscript editing: Bota O, Schreiber M, Bönke F, Teather D, Dragu A

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declare that there are no conflicts of interest.

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

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Review

Open Access



# Adipose-derived stem cells in cutaneous wound repair

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## Abstract

Growing interest in regenerative medicine and advances in adipose tissue research have led to the identification of mesenchymal stem cells in adipose tissue, so called adipose tissue-derived stem cells (ASCs). Due to the simple and safe harvest technique as well as high regenerative capacity, ASCs are regarded as a potential source for various indications including cutaneous wound repair. This review provides a short overview over mechanisms of ASC action in cutaneous wound repair and data regarding its clinical application. Mostly experimental data provide accruing evidence for the supportive effect of ASCs in cutaneous wound healing by secretion of soluble factors, differentiation into keratinocyte and fibroblasts, neovascularization and interaction with myofibroblasts. A number of *in vivo* experiments also support a positive effect of ASCs in different wound healing models. Furthermore, first clinical data evaluated the feasibility of ASCs in the treatment of different wound healing pathologies, e.g., chronic ulcers and burn wounds. Although the majority of currently available data indicate a beneficial role of ASCs in cutaneous wound repair, additional detailed experimental studies and larger, high-quality clinical trials are required to provide a reliable statement on the true value of ASCs in this context.

**Keywords:** Cutaneous wound healing, adipose-derived stem cells, fat grafting, regenerative medicine, cell-based therapy

## FAT GRAFTING AND ADIPOSE-DERIVED STEM CELLS

Ever since the German surgeon Gustav Neuber documented the first autologous fat transfer at the 23rd Congress of the German Surgical Society in 1893 by treating an infrorbital scar by a piece of autologous fat harvested from the upper arm, the interest in adipose tissue as a reservoir for graft material rose<sup>[1]</sup>. Czerny used



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a lipoma for autologous breast augmentation in 1895 and documented further cases of autologous fat transfer<sup>[2,3]</sup>. Case reports by Czerny, Bartlett, Lexer, Passot, Gurney, Peer, May, Miller and more were soon backed by a scientific evaluation of fat grafting with investigators examining the high rate of fat resorption. Marchand performed a histological analysis on transplanted fat and found resorption and necrosis while Neuhof hypothesized that transplanted fat tissue may necrotize and eventually be replaced by a mix of fibrous and adipose tissue<sup>[4,5]</sup>.

Contrary to the general perception that adipose tissue primarily acts as an energy storage with other rather passive functions such as mechanical padding and thermal insulation, investigators revealed its complex structure and its diverse cell composition<sup>[6]</sup>. The liposuction technique, invented by the Italian gynecologists Arpad and Giorgio Fischer, was soon popularized by Yves-Gerard Illouz<sup>[7]</sup>. While Sydney Coleman defined fat grafting protocol then established the era of lipofilling, it was the characterization of mesenchymal stem cells within adipose tissue that lay the foundation to adipose-derived stem cell (ASC) therapy<sup>[8,9]</sup>. ASC therapy is a modern approach in regenerative medicine that utilizes isolated ASCs for various indications including wound repair. In this review, the most fundamental characteristics of ASCs, and insights into their role in cutaneous wound repair based on recent experimental and clinical data will be presented.

## CHARACTERISTICS OF ASCS

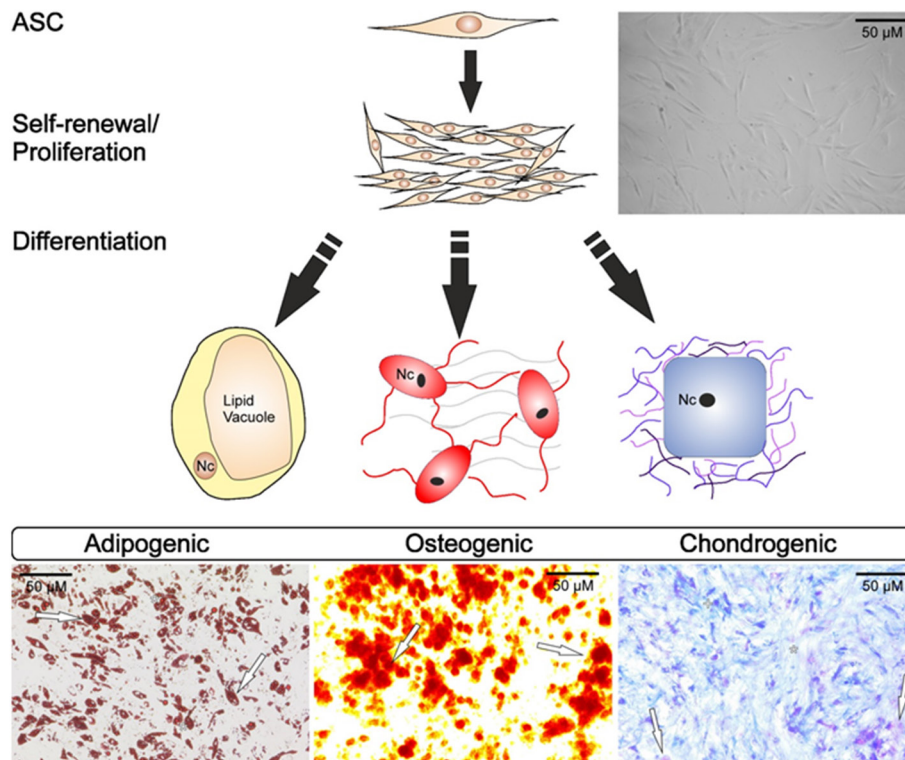
Enzymatic digestion of harvested fat tissue by collagenase separates adipose tissue into two fractions: a top layer of floating mature adipocytes and a bottom layer of cells, that are collectively called the stromal vascular fraction (SVF). The SVF represents a heterogeneous cell mixture including adipose tissue macrophages, smooth muscle cells, T- and B-lymphocytes, endothelial cells, pericytes, myocytes, fibroblasts and importantly ASCs.

ASCs are mesenchymal stem cells of mesodermal origin with low oxygen consumption and a considerable proliferation rate that differentiate into mesodermal, ectodermal and endodermal cell lines<sup>[9]</sup> [Figure 1]. In recent years, they have evolved as a serious alternative to bone marrow-derived stem cells (BMSC), the major source for mesenchymal stem cells so far<sup>[10]</sup>. In contrast to BMSCs, the harvest of ASCs is easier, and excitingly, the relative yield of ASCs is reported to be substantially higher when compared to BMSCs<sup>[11]</sup>. One milliliter of human lipoaspirate will yield approximately  $(2.5-3.75) \times 10^5$  ASCs within a timeframe of 4-6 days<sup>[12]</sup>.

The increasing interest in ASC and its applications have led to a non-transparent nomenclature that was addressed by the International Federation for Adipose Therapeutics and Science and the International Society for Cellular Therapy (ISCT). As any other mesenchymal stem cell population, ASCs have to meet the minimal criteria defined by the ISCT which encompass: plastic adherence, differentiation into the adipogenic, chondrogenic, and osteogenic line as well as expression of specific surface genes<sup>[13]</sup>. In addition, ASCs may be distinguished from SVF cells and BMSCs by other distinct surface markers. ASCs consistently express cluster of differentiation (CD) 73, CD90, CD105, CD44 and are negative for the endothelial markers CD31 and hematopoietic cell marker CD45; the population doubling capacity should be determined by the colony forming unit fibroblast (CFU-F) assay<sup>[14]</sup>.

## ISOLATION OF ASCS

The regenerative potential of ASCs has rapidly attracted worldwide attention as their isolation and utilization are easy and do not underlie the same legislative and ethical concerns as applicable to pluripotent embryonic stem cells. In the first step, fat tissue is commonly harvested by lipectomy or liposuction procedures. Although ASCs are not as vulnerable to high negative pressure as mature adipocytes (which tend to rupture), higher suction pressure may significantly decrease ASC yield<sup>[15]</sup>. Next, the aspirated adipose tissue may undergo washing steps, e.g., with phosphate-buffered saline and collagenase digestion followed by colla-



**Figure 1.** Proliferation and differentiation capacity of adipose tissue-derived stem cells (ASCs). ASCs display a fibroblast like phenotype. Their morphology is characterized by a small cell body, containing a large round nucleus, with long and thin extensions. ASC have have high proliferation and self-renewal potential *in vitro*. Upon induction by specific medium, ASCs are able to differentiate into different cell lines including the adipogenic, chondrogenic and osteogenic line. According to their cell fate, ASC change their morphology by activation of certain molecular processes during the differentiation processes. This may lead to increased fat synthesis resulting in the generation of lipid droplets (white arrows; adipogenic differentiation is indicated by red droplets upon *Oil-Red O* staining), which will increase during adipogenesis (white asterisks), and finally merge into one large fat vacuole. During osteogenesis, ASCs secrete a collagen I-rich extracellular matrix that calcifies during the later stages of differentiation. One indicator of osteogenesis is the formation of calcification appearing red after *Alizarin red* staining (arrow). Chondrogenic differentiation leads to the generation of cell nodules associated with a well-organized extracellular matrix rich in collagen II and sulfated proteoglycans. These proteoglycans can be specifically detected using the stain *Alcian Blue* under acidic conditions (white asterisk; cross marks nuclei; arrows denote acidic mucosubstances)

genase inactivation, further filtering and washing steps. The resulting SVF, by many authors commonly but inadequately and misleadingly referred to as the ASCs, is expanded in culture.

Commercial suppliers such as Celution® (Cytosol Therapeutics, San Diego, CA, USA) and many others offer manual, semi- and fully-automated systems for alternative progenitor cell/cell fraction isolation/enrichment<sup>[16]</sup>. The cell fractions isolated by pre-manufactured systems generally follow proprietary protocols and are immediately re-injected in the same procedure. As these protocols do not include an *in vitro* cell cultivation step and it is unclear whether these cell fractions do meet the ISCT minimal criteria, we do not recommend labelling cell fractions isolated by such as pure ASCs.

## MECHANISMS OF ACTION - HOW DO ASCS IMPROVE CUTANEOUS WOUND REPAIR

Cutaneous wound healing comprises four stages termed as the hemostasis, inflammatory, proliferative and remodeling phase<sup>[17]</sup>. Upon reduction of blood loss by vascular constriction, platelet aggregation and fibrin clot formation (hemostasis phase), the inflammatory phase, characterized by invasion of cells such as neutrophils/monocytes, immunomodulation by release of pro-inflammatory and chemotactic cytokines, sets in. The proliferative phase covers neoangiogenesis, re-epithelialization and reorganization of the underlying dermal layers. During this phase, invading fibroblasts in particular secrete extracellular matrix (ECM) pro-

teins, enzymes and various cytokines that jointly facilitate dermis restoration. Finally, the fibroblasts adopt a contractile myofibroblast phenotype during the remodeling phase which *inter alia* replaces immature collagen III into contractile collagen I fibres forming the ultimate scar.

ASCs are a natural component of the subcutaneous adipose tissue that lies in immediate proximity to cutaneous wounds and takes part in the delicate physiological course of wound healing. Due to their migratory ability ASCs also are believed to infiltrate the wound and thereby additionally foster wound repair<sup>[18]</sup>.

First of all, the abundant secretome of ASCs may orchestrate wound healing in a paracrine fashion. Nearly all growth factors that participate in cutaneous wound healing including keratinocyte growth factor, hepatocyte growth factor, epidermal growth factor, members of the vascular endothelial growth factor (VEGF) family, basic fibroblast growth factor (bFGF), platelet-derived growth factor-BB, insulin-like growth factor-1 and key enzymes such as matrix metalloproteinase-9 (MMP-9) and many more are secreted by ASCs<sup>[19-21]</sup>. Without going into detail, the mentioned soluble factors instigate fibroblast and keratinocyte migration, proliferation and differentiation. The literature also suggests ASCs to attenuate inflammation by secretion of soluble factors such as interleukin-10 and other cytokines implicated in leukocyte action<sup>[22]</sup>. Thereby, ASCs also may exert beneficial effects on cutaneous diseases or wounds such as non-healing ulcers that involve a pathologically pro-longed inflammatory state.

In addition to their remarkable secretome, ASCs are known to directly differentiate into keratinocytes and fibroblasts to regenerate epidermal and dermal layers that further promote cutaneous wound repair *in vitro*<sup>[23,24]</sup>. However, until the afore-mentioned experimental *in vitro* studies are supported by further investigation in a proper *in vivo* model, there is no firm evidence for a physiological differentiation of ASCs into keratinocytes that would allow a translation into the clinical context. ASCs also appear to have an impact on fibroblasts although the evidence is scarce. *In vitro* studies indicated an increase in fibroblast proliferation by direct cell-to-cell contact with ASCs but also by soluble factors released by ASCs<sup>[25]</sup>. The authors observed up-regulation of fibronectin, collagen I, collagen III as well as a down-regulation of MMP-1. The same authors supported their *in vitro* findings by additional *in vivo* experiments, where they found accelerated wound healing in mice by ASC treatment. However, those *in vivo* observations were of pure descriptive nature and did not look into the molecular or cellular effect (e.g., ASC-fibroblast interaction) in more detail.

Proper vascularization is of paramount importance to wound healing. Mounting evidence portrays the pro-angiogenic effect of ASCs, predominantly by release of prominent vasculogenic factors such as VEGF-A and bFGF, and differentiation into endothelial cells<sup>[26]</sup>.

Eventually, through differentiation into myofibroblasts and paracrine modulation of myofibroblast function ASCs dynamically influence wound maturation during the remodeling phase<sup>[27]</sup>.

## EXPERIMENTAL DATA ON THE EFFECT OF ASCS IN CUTANEOUS WOUND REPAIR

Particularly in non-healing wounds that experience a depletion of ASCs/impairment of ASC function, the transplantation of “fresh” ASCs from distant donor sites by fat grafting or stem cell therapy appears to be invaluable<sup>[28]</sup>. But also physiological cutaneous wounds appear to benefit from ASC treatment.

*In vitro* experiments with simple co-cultures or ASC-derived supernatants have shown that human lipoaspirates and ASCs enhance keratinocyte proliferation, stratification and migration<sup>[29,30]</sup>. Comparable experimental settings show enhanced fibroblast proliferation with beneficial effects on collagen synthesis and ECM remodeling<sup>[31]</sup>.

Plenty of *in vivo* studies investigated the role of ASCs in either normal or pathological wound healing in more detail. In normal wound healing, where ASCs were transferred into wounds by local injection, seeded on scaffolds (fibrin, collagen, acellular dermal matrix, *etc.*), as cell sheets or even systemically, the vast majority suggests a beneficial ASC effect on wound healing<sup>[21]</sup>. However, due to the limited clinical relevance of ASC treatment in physiologically healing wounds and considering the increase of patients with wounds not responding to conventional treatment paradigms, animal models focusing on pathological wound healing attract more attention.

As type 2 diabetes is undoubtedly the greatest trigger for delayed wound repair, it also covers the largest body of evidence. Maharlooei *et al.*<sup>[32]</sup> for instance locally injected excisional wounds in diabetic rats with ASCs and found wound healing rates almost comparable to those of normal rats. Similar observations were made in many other diabetic mice and rat models that saw ASC-induced keratinocyte and fibroblast regeneration as well as improved wound vascularization. Among these, the study of Nambu *et al.*<sup>[33]</sup> specifically used ASCs isolated from diabetic mice whereas all other authors used ASCs from either healthy human patients or healthy animals. Importantly, the authors found that even ASCs from diabetic mice significantly accelerated healing of excisional wounds. In the same way, ASCs appear to promote wound healing under ischemia. Steinberg *et al.*<sup>[34]</sup> reported enhanced wound granulation in rabbit ears under ischemic conditions (wounding after ligating two of three main arteries of the ear) upon ASC treatment and comparable observations were made in other animal models. Chronic wounds are frequently found in irradiated area and thus are subject to intense investigation. ASCs administered directly into the irradiated wound, intramuscularly *e.g.*, into the irradiated limbs or even intravenously led to markedly increased cutaneous wound repair in rats and mice, respectively<sup>[35-37]</sup>.

Taken together, existing experimental data mostly support the positive effect of ASCs on cutaneous wound repair while there is no consensus on the exact protocol of ASC transfer to the wound side.

## CLINICAL APPLICATION OF ASCS IN CUTANEOUS WOUND REPAIR

For cutaneous wound repair in the clinical setting, ASCs may be transplanted to the wound by different ways: fat grafts, fat grafts enriched by cell fractions/SVF/ASCs or pure ASCs via stem cell therapy. While fat grafts and enriched fat grafts surely contain ASCs to a certain extent, only the transplantation of purely *in vitro* expanded and characterized ASCs as mostly done in animal studies permits to draw definite conclusions of the genuine ASC effect on cutaneous wound repair. However, only few clinical studies follow exact ASC isolation protocols due to regulatory issues and use SVF/cell fraction enriched fat grafts instead in different critical wounds (diabetic foot ulcers, radiation injury, peripheral artery disease (PAD), venous leg ulcers and burn scars).

In 2010, Akita *et al.*<sup>[38]</sup> reported healing of radiation wounds without adverse effects by applying ASCs seeded on an artificial dermis (Terudermis®). At a closer look, however, ASCs were isolated by Celution® rather than according to precise ASC isolation protocols with an unclear number of patients. Bura *et al.*<sup>[39]</sup> performed a phase 1 study on the effect of *in vitro* expanded ASCs on ulcers due to critical limb ischemia. The authors found increased oxygen pressure in the affected limbs, improved ulcer healing with no adverse effects. Although the authors used proper ASC isolation protocols, the small number of merely seven patients with no control group did not allow a statistical evaluation of the results. In 2015, Liu *et al.*<sup>[40]</sup> summarized existing data on mesenchymal stem cells including ASCs on PAD in a total of 527 patients divided in 13 clinical studies. Stem cells were applied intramuscularly, intravenously or intraarterially. Although no difference in the all-cause mortality was found, a significant improvement of ulcer healing, amputation rate and the ankle-brachial-index were observed. In a review of the feasibility of ASCs in venous leg ulcers, Zollino *et al.*<sup>[41]</sup> concluded that ASCs induce new well-vascularized tissue formation at the transplanted site with only minor complications. Conde-Green *et al.*<sup>[42]</sup> reviewed twelve studies that addressed the clinical application fat



grafts and fat grafts enriched by progenitor cells via various techniques in burn scars. Despite the fact that improvements in scar size/texture, enhancement of angiogenesis, alleviation of inflammation/pain and improved function were observed, no clear and statistical significant conclusions could be made and ASC isolation protocols varied. On the contrary, Gal *et al.*<sup>[43]</sup> examined the use of fat grafts in pediatric burn scars in a prospective, randomized, double-blinded, placebo-controlled pilot study in eight patients and found no evidence for scar improvement. Of course, the number of patients in Meng *et al.*<sup>[44]</sup>'s study is low, but its scientifically sound study design, when compared to most other hitherto published clinical trials, adds to the strength of the work. Although several preclinical studies analyzed the value of ASCs in diabetic wounds, most of the clinical trials are still ongoing with no definite results provided by now.

In summary, most of the studies indicate a positive effect of ASCs/fat grafting/cell enriched fat grafts on various cutaneous wound conditions with no obvious complications, all authors of the afore-mentioned studies unanimously complain the lack of randomized high quality studies with a sufficient number of patients.

## CONCLUSION

Accruing experimental data indicate that ASCs are conducive to normal and pathological cutaneous wound repair by release of soluble factors, differentiation into various cell lines and facilitating angiogenesis. However, due to a lack of high quality clinical studies, no conclusive statement is yet possible on the true benefits of ASCs in the clinical setting.

## DECLARATIONS

### Authors' contributions

Conception, design, wrote, revised, final manuscript version: Kim BS, Debye B, Beier JP

Performed literature review: Kim BS

Assisted in literature review: Debye B

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

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Original Article

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# Extended sternoclavicular joint infections in cirrhotic patients: staged interdisciplinary approach with thoracic and plastic surgery

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## Abstract

**Aim:** Sternoclavicular joint infection associated with liver cirrhosis is an uncommon condition and the optimal surgical treatment is undefined.

**Methods:** Patients and methods: we retrospectively analysed data from six patients with sternoclavicular joint infections and liver cirrhosis underwent between February 2008 and May 2018 a staged therapy using negative pressure therapy followed by secondary "en bloc" joint resection and a pectoralis muscle flap (PMF) obliteration of the thoracic wall defect.

**Results:** Four patients successfully underwent a transfer of the PMF. The surgical revision was required for relevant bleeding in one and a tracheostomy was performed due to the prolonged intubation in another case. One patient died on the fifth day after surgery due to a cerebral septic embolic ischemia and aortic endocarditis.

**Conclusion:** The presence of liver insufficiency and coagulopathy was associated with an extensive blood product demand and required a well-balanced interdisciplinary management. During the follow-up only a minimal restriction in the shoulder mobility was observed.

**Keywords:** Liver cirrhosis, negative pressure therapy, pectoralis muscle flap, sternoclavicular joint infection



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## INTRODUCTION

Sternoclavicular joint (SCJ) infections represent 1% of all septic joints in the general population and less than 4% of them occur in patients with liver cirrhosis<sup>[1]</sup>. The surgical treatment ranges from simple joint incision and drainage to radical joint resection. However, there are no clearly defined surgical principles of the SCJ infections management. The liver cirrhosis has been identified as a risk factor for severe SCJ infections that significantly increases perioperative mortality<sup>[2]</sup>. Therefore, in patients with liver insufficiency, the choice of the surgery must be adjusted to the reduced patient condition, expected higher perioperative morbidity and advanced stage of the disease. However, it should consequently follow the principles of the septic surgery. We present our multidisciplinary experience with the staged surgical management of severe SCJ in high-risk patients, performed by the thoracic and plastic-reconstructive surgeons.

## METHODS

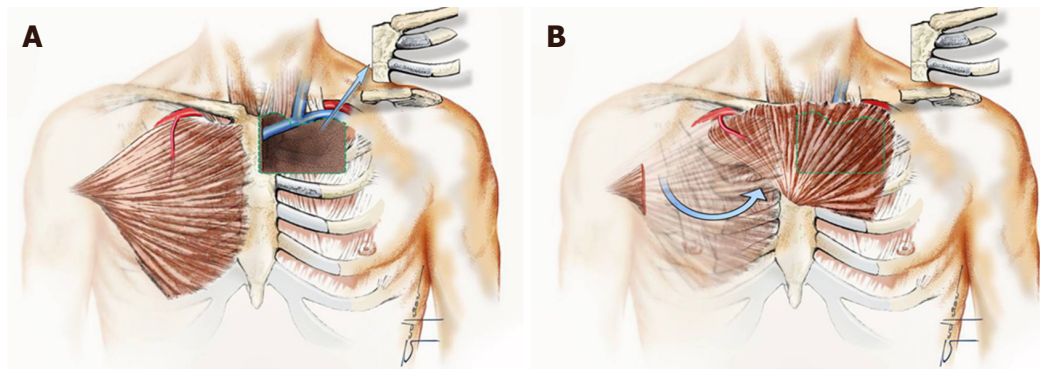
From February 2008 to May 2018 six patients with liver insufficiency were admitted to our hospital due to SCJ infections manifested by erythema and swelling over the SCJ area as well as shoulder pain aggravated by movement. Initial diagnostics included the joint aspiration, chest and neck computed tomography (CT) and standard blood tests. The first stage surgery included a J-shaped incision from the medial supraclavicular region, through the SCJ, to the median sternal line at the level of the second intercostal space. After extended debridement and necrectomy the negative pressure therapy (NPT) was started with 75 mmHg and gradually increased to 125 mmHg. During subsequent operations, the bone viability and the extent of osteomyelitis were assessed and tissue biopsies for microbiological analysis were taken regularly until definitive wound closure. The intravenous antibiotic therapy was commenced due to the general anaesthesiology after taking the blood culture probes, modified according to the antibiogram and continued for 4 weeks after the hospital discharge.

Thanks to thoracic surgeons, “*en bloc*” resection of the SCJ including the hemi-manubrium, the middle 1/3 of the clavicle as well as affected first and/or second rib was performed. Thereafter the NPT was continued for 2-3 weeks and the vacuum system exchanged every 3-5 days until wound granulation of tissue was formed. Afterwards, the chest wall defects were covered due to the plastic surgeons with the pedicled muscle or musculocutaneous flap involving chest wall musculature from the contralateral side [Figure 1].

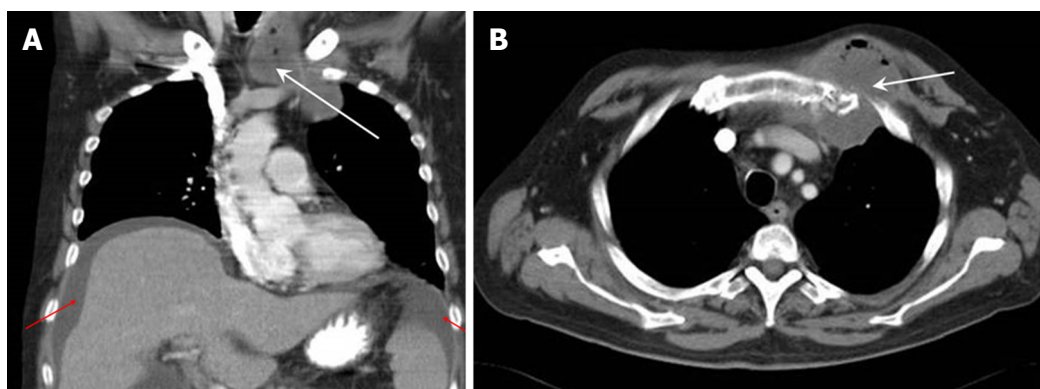
## RESULTS

The patient characteristics and clinical features are summarized in Table 1. All 6 patients were male at the age of  $58 \pm 10$  years [range 45-72] suffering from alcohol related Child B or Child C liver cirrhosis with the median model of end stage liver disease score of 11.5 [range 9-16]<sup>[3]</sup>. The chest-CT showed the destruction of the SCJ and the neighbouring ribs with the soft tissue gangrene in 5 patients, and the chest wall abscess in all patients. Inflammatory mediastinal mass and chest wall phlegmon was noted in 4 and 3 patients, respectively. Osteomyelitis was histologically proven in all patients [Figure 2]. According to the SCJI classification of Abu Arab *et al.*<sup>[4]</sup>, grade IV and V extent was noted in 2 and 4 patients, respectively. One patient died on the 5th postoperative day due to cerebral septic embolism and aortic endocarditis. Four patients underwent successful chest wall defect coverage with the contralateral PMF [Figure 3], in 1 patient delayed wound closure was possible without PMF transposition. The surgical revision was necessary in 1 patient due to severe bleeding and 1 patient required tracheotomy for prolonged ventilation case. The intraoperative blood loss at the initial operation was  $350 \pm 180$  mL. During the postoperative course  $18 \pm 14.8$  erythrocyte concentrates,  $16.3 \pm 18.1$  fresh frozen plasma concentrates and  $1.5 \pm 0.7$  thrombocyte concentrates were transfused. The average NPT duration was  $22 \pm 9$  days and the average length of hospital stay was  $35 \pm 21$  days. The average follow-up time and disease-free interval were in 5 survivors  $24 \pm 18$  months.

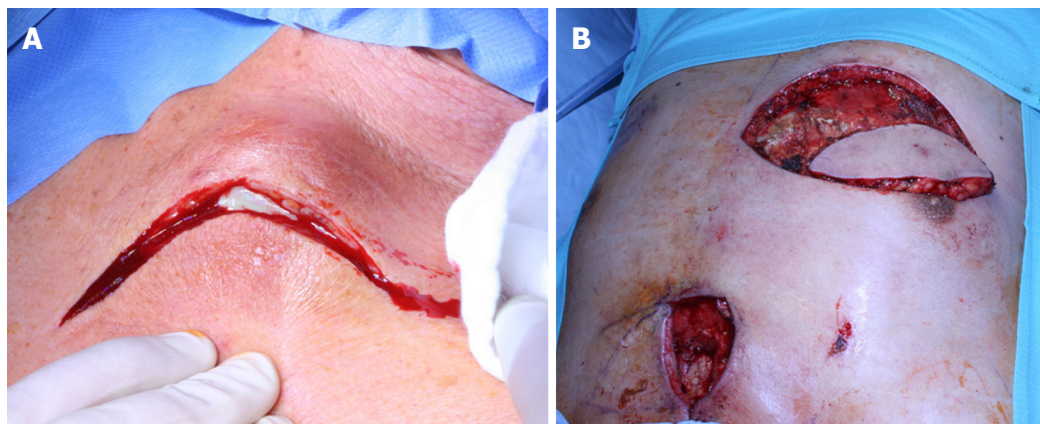




**Figure 1.** A: The scheme of "en bloc" SCJ resection involving the median third of clavicle; B: first and second rib and partial resection of manubrium combined with defect closure by contralateral pectoral muscle flap. SCJ: sternoclavicular joint



**Figure 2.** Rib osteolysis and mediastinitis extending to the neck on computed tomography scan (white arrow) and ascites according to liver insufficiency (red arrows)



**Figure 3.** A: "J-shape" incision over sternal notch for extended debridement and necrectomy; B: well granulated wound after NPT in the left sternoclavicular joint and delayed defect closure with contralateral pectoral muscle flap. NPT: negative pressure therapy

## DISCUSSION

There is only a little published evidence on SCJ infection in association with the liver insufficiency. Only one study and a case report describing in total 6 cirrhotic patients managed with open drainage and a packing are available to date<sup>[2,5]</sup>. The SCJ infections in the cirrhotic patients are debilitating and associated with surgical morbidity rate of up to 40%<sup>[5]</sup>. Compromised immunity in the liver cirrhotic patients contributes to

**Table 1. Perioperative patient characteristics**

Pat.	Age	Sex	Child class of cirrhosis	MELD-score (points)	Bact. cultures	NPT duration (day)	Bact. cultures after NPT	PMF	Complications	30-day mortality	Follow up
					Before NPT						
1	58	M	Child C	12	<i>E. coli</i>	22	No	Yes	Revision for bleeding	No	43
2	68	M	Child C	7	<i>E. coli</i>	3	<i>E. coli</i>	No	Septic cerebral embolism	Yes	
3	50	M	Child B	10	<i>Staph. aureus</i>	24	No	No		No	32
4	45	M	Child B	9	<i>E. coli</i>	32	No	Yes	Respiratory insufficiency and tracheostomy	No	30
5	58	M	Child B	15	<i>Streptococcus pneumoniae</i>	25	No	Yes		No	36
6	72	M	Child C	16	<i>Staph. aureus</i>	24	No	Yes		No	2

MELD: model of end stage liver disease; NPT: negative pressure therapy; PMF: pectoralis muscle flap

the extensive spread of infection to the surrounding mediastinal structures at the time of diagnosis, which is usually delayed<sup>[2,5]</sup>. There is no standardized treatment strategy for septic SCJ arthritis. Various surgical options including intravenous antibiotic therapy, SCJ incision with open drainage and secondary wound healing, radical joint resection with or without NPT combined with muscle flap transposition have been reported. The open drainage requires prolonged wound care up to 3 months and is associated with the failure rate of up to 80%<sup>[6]</sup>. Therefore, simple incision and drainage appears insufficient in those patients with a severe septic arthritis, sternal and clavicular osteomyelitis with mediastinal involvement. On the other hand, the complication rates of the radical joint resection and immediate obliteration of the chest wall defect with pectoralis flap have been reported even as high as 50%<sup>[7]</sup>. This aggressive surgery in the acute infection phase can further increase the perioperative morbidity in patients with liver dysfunction associated immunosuppression and coagulopathy. In our opinion, the surgery has to be adapted to the patient condition and estimated perioperative risk, tissue quality and systemic infection control. The favoured surgical management has to reduce the operative trauma in compliance with the traditional principles of the wound management<sup>[8]</sup>. We recommend the NPT as an effective addition for the surgical wound debridement. The NPT application has been widely used in acute, subacute and chronic wounds. It enables better infection control by improving the blood flow, accelerating the tissue granulation and reducing bacterial colonization in the wound<sup>[8,9]</sup>. The accelerated bacterial clearance is, in our opinion, the main advantage in the acute infection phase in patients with compromised liver function. In our patient group the chest wall resection was adapted to the extent of bone destruction, extent of the osteomyelitis and included the hemimanubrium ( $n = 6$ ), first ( $n = 5$ ) and second rib ( $n = 3$ ). Our radical SCJ resections resulted in a large chest wall defect according to classification of Joethy et al, reflecting a regularly wide infection in patients with liver insufficiency<sup>[10]</sup>. Subsequent radical joint resection has been reported adequate for the patients with extended disease<sup>[11,12]</sup>. In our opinion, the adequate assessment of the bone viability and the osteomyelitis extent is of key relevance in the treatment of SCJ infections. The postponed bone resection thanks to NPT allows to better assess the bone viability and to define the resection extent, particularly in severe infections<sup>[13]</sup>.

Chest wall defect coverage with the pedicled muscle or musculocutaneous flap has been the preferred technique. For the complete filling of the residual space, protective coverage of the exposed brachiocephalic vessels and preservation of neurovascular integrity in the upper extremity the pectoral muscle has commonly been accepted<sup>[11]</sup>. Some authors provided the vascularized muscle flap an additional anti-inflammatory effect due to the direct antibiotic delivery to the infection site once the flap is in place<sup>[13]</sup>. The novel technique of the large bone defect obliteration with engineered bone tissue is a challenge in the reconstructive surgery<sup>[14]</sup>.

Extended SCJ infection and associated massive inflammatory process usually affect the ipsilateral chest wall musculature precluding its application as the defect coverage. The transposition of the unimpaired contra-

lateral pectoralis major muscle has therefore been preferred in our patients. The chest wall reconstruction using the pectoral PMF enabling successful long-term infection control within the SCJ has already been described<sup>[6,15,16]</sup>. In addition to the described technique, other clinically important issues have to be taken into consideration. Firstly, the higher perioperative risk associated with the liver impairment has to be expected. Therefore, staged procedure adapted to the reduced patient status is recommended. Secondly, a wide involvement of the neighbouring structures and mediastinum was present in all our cases. Finally, the aggressive one stage approach with the SCJ resection and simultaneous muscle transposition is associated with higher complication rate and can be replaced by the presented staged strategy.

In conclusion, the staged NPT based surgical therapy of the acute SCJ infections in patients with hepatic impairment is feasible. It helps reduce the high perioperative morbidity, maintaining the principles of wound management. The presence of liver dysfunction and consequent coagulopathy is associated with increased blood product demand and requires a well-balanced interdisciplinary approach.

## DECLARATIONS

### Authors' contributions

Study design: Schreiner W, Horch RE, Sirbu H

Sequence alignment and manuscript drafting: Schreiner W, Dudek W, Trufa DI

Statistical analysis: Schreiner W

Coordination of the study: Horch RE, Sirbu H

Read and approved the final manuscript: all authors

### Availability of data and materials

Results are reported in the manuscript, patient's individual data are not available to the public for the sake of data protection laws.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

There are no ethical concerns over the study.

### Consent for publication

Not applicable.

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Review

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# State of the art in enzymatic debridement

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## Abstract

Surgical treatment of deep partial thickness to full thickness burn wounds by knife has been the undisputed standard of care and was one key point in surgical burn medicine for decades. Recently, it gets more and more challenged by Bromelain-based enzymatic burn wound debridement (ED) as technique for non-surgical, selective eschar removal. Although the literature on ED is increasing constantly it cannot comprise the rapid progress that is made in clinical application of ED. To outline the current state of art in ED, recent literature as well as clinical experience is summarized and the main steps in clinical application including indications, wound preparation, application of the enzyme, wound bed assessment and further treatment after ED are discussed. Initial indications and limitations in application of ED could be gradually extended to increase versatility of ED as tool in burn surgery. Several randomized controlled trials compared ED to standard of care (SOC). They could show significant shorter time to complete burn wound debridement and wound closure, reduced need for surgery, reduced blood loss, reduced area of burns that needed surgical excision and need for autograft as well as an improved scar quality. Further research is necessary to justify an extensive use of ED as tool for burn eschar removal. Especially a robust comparison to surgical burn wound excision by knife as SOC is required to facilitate evidence-based burn surgery.

**Keywords:** State of the art, enzymatic debridement, Nexobrid, eschar removal, burns

## INTRODUCTION

Effective removal of necrotic burned tissue is a key step in the treatment of all deep partial thickness and full thickness burn wounds. It aims to promote wound healing, reduce bacterial colonization and infection, is the



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basis for optimal wound bed conditioning, and thus prevents devastating scarring. Especially in severely injured patients with a high extent of burned surface, early eschar removal is as important as optimal intensive care treatment to optimize outcomes and reduce complications<sup>[1]</sup>.

To date the conventional method of tangential excision by knife as introduced 50 years ago<sup>[2]</sup> is still the most applied technique of eschar removal worldwide. Nevertheless, several further techniques have been developed and became popular in the past decades. Hydrosurgery as most established additional technique for example enables the surgeon to achieve a more selective debridement of the burn wound by an adjustable water jet<sup>[3]</sup>.

In the last decade, most progress has been achieved in enzymatic burn wound debridement (ED)<sup>[4]</sup>. This technique promises the effective eschar removal and uses bromelain-based enzymes extracted from pineapple stems in the most frequently applied medication (Nexobrid®). After preparation of the burn wound by pre-soaking the eschar, the product promotes selective eschar removal from burn wounds within 4 h even in full thickness burns, while viable dermal tissue is preserved. Due to encouraging reports and growing evidence in literature, including benefits like lower blood loss and fewer need for consecutive skin grafting<sup>[5]</sup>, ED continues to increase in popularity. While the group of users is growing continuously, indications are widened and the technique of application is constantly refined.

To catch up with these developments, this article tries to give an overview on the current state of art on indications, implementation and post-treatment in the use of ED with Bromelain-based Nexobrid®.

## INDICATIONS

According to its approval, ED can be used on all burn wounds up to 15% total burned surface area (TBSA) in adult patients per application. Effective and safe treatment of children has been reported and is practiced in pediatric surgery<sup>[5]</sup>, but has to be considered as off-label use until further approval studies are evaluated. Likewise, the treatment of a TBSA up to 30% per session can be performed with reasonable risks although it is also regarded as off-label. Treatment of more than 30% TBSA in one session of ED cannot be recommended due to risks of increasing blood loss and hemodynamic instability. In addition, further systemic effects of ED in extra-large surfaces > 30% remain unknown.

The advantages in preserving more viable dermis compared to conventional excision is most important in delicate regions with high function and relatively thin subcutaneous tissue, like on the hands, feet, genitals, perineum, axilla or in the face. Application in these regions revealed good results and can be further encouraged<sup>[6-9]</sup>.

In deep circumferential burns at the extremities, the early application of ED can release tissue pressure by timely removing the constrictive eschar, reduce inflammation-associated edema and thus may prevent patients from the need for surgical escharotomy and its possible complications and invasiveness. Despite the successful implementation in specialized burn centers, it is mandatory to re-evaluate the wound frequently and verify entire tissue release thoroughly and be prepared to perform additional surgical escharotomy or even fasciotomy if necessary in case of burn induced compartment syndrome<sup>[10-12]</sup>.

As a bedside procedure, ED has the potential to shift early eschar removal to the patient ward and thus can spare valuable resources in the operating room. In that way ED can be especially advantageous in mass casualty incidents where a higher patient count can benefit from optimal and timely treatment<sup>[13]</sup>.

## PREPARATION

Prior to the application of ED, a sufficient analgesia must be ensured. For treatment of single extremities,

regional anesthesia (e.g., plexus anesthesia) has been used successfully and is favorable due to its little side effects<sup>[7]</sup>. To perform treatment of large surfaces including the trunk or the head, general anesthesia in an intensive care setting is recommended.

Because the enzymes can only process moist tissue, a wound condition have to be prepared by pre-soaking with crystalloid or anti-infective fluids for at least 2 h, and even longer in burns with delayed application of ED<sup>[10]</sup>. Some users report better outcomes of ED after prolonged pre-soaking for up to 12 h, but there is yet no evidence to support this approach - nevertheless it might help overcome logistical deficiencies at the burn center if being more flexible in the time of post-soaking. On the other hand, when a patient is presented immediately after burn trauma, the burn wounds should be still moist enough to skip pre-soaking phase and start with ED immediately - which is mandatory for emergency ED to prevent surgical escharotomy in circumferential burns

## APPLICATION

For ED procedure itself, the prepared enzyme gel is calculated with 2 g of enzyme powder per treated % BSA, which is applied on the wound after rehydration. Unburned skin, mucosa and especially cornea and tympanic membrane must be protected thoroughly from contact with the gel by stoma paste or vaseline gauze. The active gel for ED is fixed with an occlusive dressing in order to increase the contact surface. To ensure removal of entire eschar, the gel should be placed on the wound for at least 4 h. In the absence of adverse effects of longer contact time, the enzyme can be safely left on the wound beyond the 4 h recommended by the producer<sup>[10]</sup>.

After removal of the enzyme gel including debris and mechanical cleaning, wound bed evaluation is necessary with regard to the bleeding pattern, followed by a post-soaking phase to remove further remnants of debris and enzyme gel. Post-soaking again can be performed with saline or anti-infective solutions while a superiority could not be shown by now for any agent. Duration of post-soaking should be at least 2 h, but some users report superior results with a prolonged post-soaking of up to 12 h.

## WOUND BED ASSESSMENT

One key point in treating burn wounds with ED is the postprocedural wound bed assessment. It should be performed prior to the post-soaking phase and after mechanical removal of gel remnants and debris. Photography of the wound is recommended to archive the results and as basis for further professional decision in case of late-night application. At this time, depth of the burn injury and the need for further surgical procedures should be estimated by assessment of wound bed color and bleeding patterns. A uniform pink wound bed or a uniform white wound bed with pin-point, small and dense, punctate bleeding pattern represent a high chance for spontaneous healing of the debrided burn wound putting the patient on a track for healing in-between 21 days. On the other hand, a wound bed with large diameter red circles or oval patterns, distant from each other, indicates a prolonged healing time with increased risk for necessary grafting. Exposure of subdermal tissue like fat or blood vessels indicate a full thickness burn injury and requires grafting<sup>[10]</sup>.

Figure 1 shows an exemplary case of a deep partial thickness burn wound treated with ED that healed without split-thickness skin grafting.

## POST TREATMENT

After ED, the burn wound is vulnerable and needs to be protected against wound infection and desiccation by a suitable dressing. Some authors report the use of epidermal substitutes like Suprathel or even allografts to cover the wound bed after ED in order to promote spontaneous reepithelization without instable scar-



**Figure 1.** The case of a 27-year-old male patient suffering a deep partial thickness burn due to flame burn at his right hand is shown. A: After admission to hospital right after trauma; B: two days after ED; C: two weeks after ED; D: one year after ED

ring<sup>[14]</sup>, while other authors prefer conventional antiadhesive wound dressings with polyhexanide gel<sup>[7]</sup>. If wound bed assessment indicates a deep dermal wound with expected prolonged healing time or instable scarring, early surgical coverage - eventually accompanied by additional debridement - by split-thickness skin grafting (STSG) should be considered. As in every burn wound, development of hypergranulation tissue prevents primary wound healing and can lead to hypertrophic scarring. Topical administration of potent steroids (e.g., clobetasol) can be recommended to treat occurring hypergranulation tissue in the wound management phase<sup>[15]</sup>. If spontaneous healing is absent 21 days after ED or a sticky layer, called pseudo-eschar, which does not peel off after 14 days, surgical intervention and STSG should also be taken into account<sup>[10]</sup>.

## DISCUSSION

Bromelain-based ED is more than a new technique, it includes a new concept of selective eschar removal without the necessity to schedule OR for this initial step. Due to encouraging results, the technique and its concept behind has been implemented in the leading burn centers in Europe since 2013. With experience of treating many hundreds of burn victims with ED, results could even be improved and are stable enough to use ED in routine patient treatment<sup>[10]</sup>. Despite the growing experience, the literature offers seven publications on studies with a high level of evidence proving ED's advantages with certain issues over standard of care (SOC), which is remarkable for literature in burns. Loo *et al.*<sup>[16]</sup> investigated literature on ED from 1986 to 2017 and reported seven prospective studies including four randomized controlled trials in a recent review. The largest available randomized-control trial by Rosenberg *et al.*<sup>[5]</sup> compared 74 cases of ED with 81 cases treated by SOC and could show a significant shorter time to complete eschar removal, a lower number of wounds requiring surgical excision and STSG as well as a significant lower blood loss in the ED group. No significant difference could be shown in time to wound closure and scar quality. While these results could be confirmed by other authors<sup>[6,7]</sup> one group even reported a reduced time to wound closure and an improved scar quality in comparison to historical control groups<sup>[8,9]</sup>. Further encouraging results could be

**Table 1. Overview of literature**

Study	Patients (IG/CG)	Intervention	Comparison	Outcomes (IG/CG)	Study type	Country/setting	LoE
Rosenberg <i>et al.</i> <sup>[15]</sup>	Deep burns Age (mean): 32.4/29.3 Female: 23.8%/24.7% TBSA: 11.3%/11.0%	<i>n</i> = 74 Enzymatic debridement with NexoBrid	<i>n</i> = 81 Excisional debridement followed by autografting	<ul style="list-style-type: none"> <li>Time to complete eschar (mean, days): 2.2/8.7 (<math>P &lt; 0.0001</math>)</li> <li>Wounds requiring surgical excision 24.5%/70.0% (<math>P &lt; 0.0001</math>)</li> <li>Autograft: 17.9%/34.1% (<math>P = 0.0099</math>)</li> <li>Time to complete wound closure (days): 32.8/29.2 (<math>P = 0.1197</math>)</li> <li>Blood loss-change in hemoglobinc (mean, mmol/L): 0.52/1.04 (<math>P = 0.0061</math>)</li> <li>Scar quality (mean, Modified Vancouver Scar Scale, 2-4years): 3.12/ 3.38 (<math>P = 0.88</math>)</li> <li>Scar revision/reconstructive surgery (2-4years): 3.7%/8.6% (<math>P = 0.6547</math>)</li> <li>General health (mean SF-36, 2-4years) - physical score (patients) 51.1/51.3 (<math>P = 0.68</math>)</li> <li>Adverse events: ns differences</li> </ul>	RCT	Israel	2
Schulz <i>et al.</i> <sup>[19]</sup>	Partial thickness and deep dermal burn wounds of the face age (mean): 39/48 years male: 84.6%/76.9% TBSA: 16%/34%	<i>n</i> = 13 Enzymatic debridement with NexoBrid	<i>n</i> = 13 historic control group treated with SOC	<ul style="list-style-type: none"> <li>Time of initial debridement (days after admission): 0.92/4.92</li> <li>Autografting (wounds): 15%/77%</li> <li>Time to complete healing after first debridement (days): 18.92/35.62</li> </ul>	Prospective trial with historic control	Germany, burn center	3
Schulz <i>et al.</i> <sup>[18]</sup>	Partial thickness and deep dermal burn wounds of the hands age (mean): 41/45.5y. male: 95/85% TBSA: 10.1/31%	<i>n</i> = 26 Enzymatic debridement with NexoBrid	<i>n</i> = 20 historic control group treated with SOC	<ul style="list-style-type: none"> <li>Autografting (wounds): 15%/95%</li> <li>Time to complete healing after admission (days): 24.2/35.8</li> <li>Number of surgeries until complete wound closure (includes debridement): 1.15/1.7</li> </ul>	Prospective trial with historic control	Germany, burn center	3
Cordts <i>et al.</i> <sup>[7]</sup>	Full-thickness upper extremity burns Age (mean): 47.8 Females: 31.2 % TBSA: 20.1%	<i>n</i> = 16 Enzymatic debridement	NA	<ul style="list-style-type: none"> <li>Pain (3 months, patient-related)</li> <li>Wrist Evaluation Score: 23/100</li> <li>Disabilities of the shoulder, arm and hand: 22/100</li> <li>Scar quality (3 months, Vancouver Scar Scale): 6/14</li> <li>Side effects (during hospital stay): 0</li> <li>Wound infections (during hospital stay): 0</li> </ul>	Case series	Germany, burn intensive care unit	4
Schulz <i>et al.</i> <sup>[14]</sup>	Partial thickness and deep dermal burn wounds of the hands age (mean): 43y. male: 85% TBSA: 15.67%	<i>n</i> = 20 Enzymatic debridement with NexoBrid	NA	<ul style="list-style-type: none"> <li>Time to complete healing after admission (days): 29.15</li> <li>Efficiency of debridement (%): 90%</li> <li>Autografting (wounds): 30%</li> </ul>	Case series	Germany, burn center	4
Krieger <i>et al.</i> <sup>[6]</sup>	<i>n</i> = 69 Deeply burned hand TBSA: 1.4%	Selective enzymatic debridement	NA	<ul style="list-style-type: none"> <li>Complete wound closure (mean, days): 17 (surgery), 23 (no surgery)</li> <li>Surgical escharotomy: 0</li> <li>Permanent damage: 0</li> </ul>	Case series	Israel, hospital (burn unit)	4
Rosenberg <i>et al.</i> <sup>[4]</sup>	<i>n</i> = 130 Deep second degree and third degree burns Age (mean): 18.6 Female: 48.5% TBSA < 10%: 66%	Enzymatic debridement with Bromelain-derived debriding agent	NA	<ul style="list-style-type: none"> <li>Significant adverse events: 0</li> </ul>	Case series	Israel, hospital	4

shown by Osinga *et al.*<sup>[17]</sup> who presented a series of 12 cases. While ED is most commonly used within 72 h after trauma the group of Osinga treated their patients with ED up to 19 days after burn trauma and still reported to avoid STSG even in deep burns in the majority of their cases<sup>[17]</sup>. Edmondson *et al.*<sup>[18]</sup> recently reviewed the literature from 1946 to 2017 for comparison of different tools of eschar removal. While sharp excision by knife was found to be the predominantly used technique, a robust comparison to newer tools like ED or Hydrosurgery (VersaJet®) is lacking<sup>[18]</sup>. Table 1 summarizes the latest literature on ED with given outcomes and level of evidence.

To provide detailed user-orientated guidelines and recommendations based on available literature as well as on the growing amount of experience with ED in Europe, a European Consensus Workshop was held in January 2017. As a result, 68 consensus statements based on the combined experience of > 500 patients treated by the panelists from 10 European burn centers could be generated. Various aspects of ED were discussed including indications, timing of application, preparations and application technique, pain management, blood loss, post ED wound diagnosis and management including skin grafting, scar prevention, training strategies and areas of future research. The degree of consensus was remarkably high, with a consentaneous agreement on 60 of the 68 statements (88.2%). The consensus statements contain detailed recommendations aiming to align current and future users and prevent unnecessary pitfalls. and may serve as preliminary user-orientated recommendations for the use of ED until further evidence is available<sup>[10]</sup>.

## CONCLUSION

Although the number of patients in analogue with the experience increases in literature, further research is necessary to prove further issues of superiority of ED in comparison with SOC, especially in the field of cost-efficiency to justify the progressive use of the technique in large surfaces > 15% TBSA. In addition, for large-surface areas, the potential systemic impact of ED in the severely burned patients should be addressed. Nonetheless, Bromelain-based ED is a valuable tool, technique and concept in the armamentarium of burn surgery.

## DECLARATIONS

### Authors' contributions

Conception and design: Ziegler B, Kneser U, Hirche C

Data analysis and interpretation: Ziegler B, Hundeshagen G, Cordts T

Data acquisition: Hundeshagen G, Cordts T

Administration, technic, material, and revision: Kneser U, Hirche C

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

Ziegler B is a speaker for Mediowound, Germany. Hundeshagen G and Cordts T reports no disclosures. Kneser U is a consultant and speaker for Mediowound, Germany. Hirche C is a consultant and speaker for Mediowound, Germany and member of the advisory board, KCI, Acelity, Wiesbaden, Germany.

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Copyright

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Original Article

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# Technical refinements of the modified central mound breast reduction

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## Abstract

**Aim:** Common pitfalls with existing breast reduction techniques include poor aesthetic outcome, such as development of a “boxy” breast shape, and pseudoptosis. Presented here are a series of modifications to the technique of central mound breast reduction, based on previous work, aimed at ensuring consistent aesthetic results which are maintained in the long-term.

**Methods:** All patients undergoing bilateral breast reduction by the senior author over a 7-year period were included, with outcome data collected prospectively. A detailed description of the technique is offered.

**Results:** One hundred and sixteen patients underwent bilateral breast reduction over the study period. Mean follow-up was 20.6 months. There were no cases of nipple necrosis or infection requiring antibiotics. There was one post-operative haematoma which required surgical evacuation. Three patients developed a degree of fat necrosis which was managed conservatively in two, but required surgical debridement for liquefactive necrosis in one. Results of these breast reductions at the second post-operative year and beyond are presented.

**Conclusion:** The technique described offers benefits of improved predictability, consistency and longevity of aesthetic results over existing techniques. Development of pseudoptosis in particular is effectively delayed. The modifications described have not been shown to increase the rates of surgical complications.

**Keywords:** Central, mound, breast, reduction, mastopexy, technique, technical, refinement, modification



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## INTRODUCTION

Breast reduction has been described and modified by over 30 authors over more than 100 years<sup>[1]</sup>, and most techniques share the common pitfalls of pseudoptosis (bottoming out), difficulty ensuring an aesthetically pleasing shape, and failure to maintain aesthetic results in the long-term.

Central mound breast reduction, in which the gland with the nipple at its apex contains the pedicle of blood supply to the nipple, is reported to maintain nipple sensation well<sup>[2]</sup>. In addition it maintains a reliable blood supply and allows good visualisation of the whole gland for shaping and removal of tissue.

We describe a series of refinements to the technique of central mound breast reduction, designed to optimise the aesthetic outcome and maintain longevity of results. This technique can be applied to reductions of large or small breast volumes, or of simple mastopexy without reduction.

### Principles of this technique are as follows

A smooth conical breast shape is obtained by carefully contouring the gland during the reduction, suspending and wrapping the gland from below using a dermal sling, before re-draping the widely undermined skin envelope.

A wider breast base is created by elevating the gland beyond the normal superior limit.

To reduce pseudoptosis the gland is plicated inferiorly using part of the dermal sling, which acts to shorten the distance between the areola and the inframammary fold (IMF), such that the skin envelope is not relied upon for support of the gland.

The gland is maintained in its new elevated position on the chest wall by a series of anchor points between the inferior dermal sling, an additional superior dermal strip, and the rib periosteum.

The IMF is secured to the chest wall in order to maintain lower pole definition, further reduce tension on the skin envelope, and further reduce the effects of gravity on recurrent ptosis.

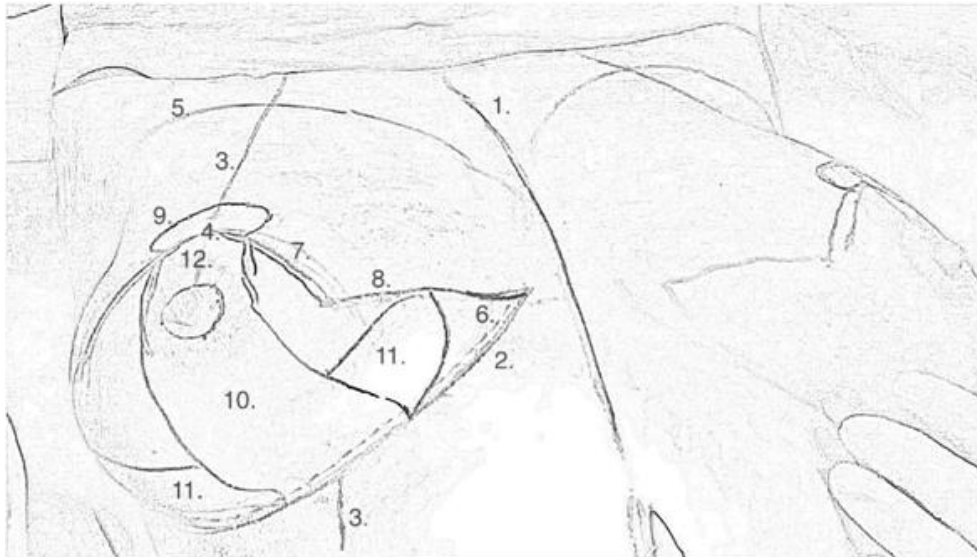
The latter three points ensure no additional tension on the skin envelope, beyond that necessary for closure, when the patient is upright. The effect of gravity on the skin is therefore diminished.

In large heavy breasts the footprint or base of the breast is narrow, so it is necessary to elevate the skin envelope beyond the normal superior limit of existing breast base & extend it close to the clavicle. This creates a reduced breast with a wider base which “takes off” more superiorly than the usual point where a ptotic breast starts.

In breast ptosis, the IMF can “slide” down the chest wall along with the rest of the base of the breast, independently of any increase in IMF to nipple-areola-complex (NAC) distance. An incision parallel and 2-3 mm superior to the IMF line bevelled in a superior direction aims to preserve and protect the IMF ligament. If this ligament is secure already, it should be kept intact. If it has become attenuated and the IMF separates from the chest wall, as is the case in patients who lose large volumes of weight, it is often readily noticeable and should be identified and addressed during the procedure.

## METHODS

All patients undergoing bilateral breast reduction by the senior author (M.R.) in both public and private practices over a 7-year period were included. Data on patient demographics, tissue mass excised, and post-



**Figure 1.** Skin markings. See body of text for number key

operative complications was collected prospectively and stored by the senior author in a secure database. All those included in the study received a minimum of 6-month follow-up. The surgical technique evolved gradually over the preceding decade, including incorporation of previous authors' work and is detailed as follows. The case examples shown have given consent for publication of their anonymised images.

Preliminary skin markings are made with the patient upright and are later re-drawn with the patient supine, after the operative field is prepared and draped [Figure 1]. Markings are similar to those for an inferior pedicle wise pattern technique, but with the addition of medial, lateral and superior dermal wings. Markings therefore consist of: (1) vertical midline from suprasternal notch to xiphoid process; (2) IMFs; (3) breast meridians (usually using a tape measure draped around the patient's neck) continuing through the areola and onto the inframammary chest wall; (4) intended height of the new nipple based on Pitanguy's point; and (5) the superior margin of the breast mound. The new nipple height is measured bilaterally to confirm symmetry.

Another line is drawn parallel and 2-3 mm superior to the IMF mark (6), which represents the line of full-thickness dermal incision. The narrow strip between here and the IMF is de-epithelialised, to which the IMF retaining sutures are later anchored.

The vertical edges of the skin envelope are marked as lines running 7.5 cm from the centre of the new nipple position in a caudal direction (7), while rotating and displacing the gland clockwise and anticlockwise. The lower limits of these lines are then turned 90° towards the ends of the IMF mark (8). The angle the vertical lines make where they meet at the new nipple position is determined by measuring the length of the IMF<sup>[2]</sup> and the corresponding lines of the skin envelope (8) to ensure the overall length is the same. If the IMF is longer than the combined length of the horizontal parts of the skin envelope, the angle at which the vertical lines meet is narrowed. A broken circle (9), greater in width than height, of around 4.5 cm diameter is marked, centred on the intended new nipple position. The exact diameter can be determined by patient preference.

A vertical dermal strip roughly 7 cm in width is marked, equivalent to that of an inferior pedicle breast reduction (10). Near the base of this strip, a wing-like projection is also marked on each side, with about 5 cm



**Figure 2.** De-epithelialised dermal strip including one superior and two lateral wing-like extensions

base width and a length sufficient to wrap around the side of the glandular mound to create a conical shape in later steps (11). A third dermal wing arises from the superior aspect of the vertical dermal strip, above the nipple, within the broken circle at the top of the markings (12). The length of the vertical dermal strip below the nipple is often much longer (and variable between individuals) than the distance from the nipple to the IMF when the skin envelope is closed. This strip will be plicated to reduce its length, by an amount that varies from person to person, and help prevent pseudoptosis in the long term.

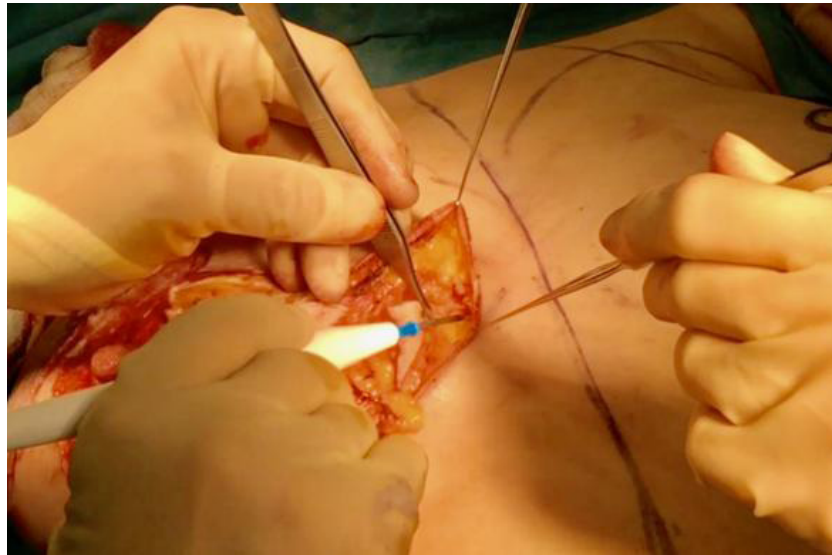
The skin envelope is infiltrated with a solution containing local anaesthetic and adrenaline, with emphasis laterally and superiorly, to block intercostal nerve sensory branches and constrict the intercostal perforator vessels. The smaller breast is reduced first. All of the marks are scored. Without the use of a breast tourniquet, the vertical dermal strip, along with the 3 dermal “wings”, are de-epithelialised using handswitch monopolar, sparing the nipple [Figure 2]. The incision parallel to the IMF is beveled superiorly to keep the ligamentous attachment of IMF intact, and prevent the gland descending postoperatively.

Full thickness incisions into the underlying subcutaneous tissue commence with elevation of the medial dermal wing at a thickness of around 1 cm. The skin at the medial end of the IMF scar is undermined while an assistant provides elevation with skin hooks [Figure 3]; the volume from this area is reduced to avoid a dog-ear. The same is then done laterally.

Laterally the tissue to be excised is raised, leaving fibrofatty tissue on the chest wall of a thickness corresponding to the layer of subcutaneous fat. This avoids injury to neurovascular structures and contour irregularity when the skin envelope is closed.

Skin flaps are raised starting medially. The assistant uses skin hooks in the breast tissue (not dermis) and lifts the tissue vertically away from the chest [Figure 4]. Dissection with handswitch monopolar proceeds in the plane of fascia is often referred to as the mastectomy plane, or sometimes deeper; the desired thickness of flaps is around 2 cm. One hand is used to keep checking the thickness of the flap. The medial skin flap is not fully raised at this time.





**Figure 3.** Undermining of the skin at the medial end of the inframammary fold (IMF), to allow tension-free re-draping of the skin at closure and prevent standing cone deformity



**Figure 4.** Elevation of the medial flap of the skin envelope, with assistant retracting away from the chest using skin hooks

The lateral flap is raised in the same way and at the same thickness, again not completely. The superior part of the skin envelope is elevated beyond the existing superior border of the breast base to create a pocket almost close to the clavicle, as planned preoperatively, to widen the base and to create fullness of upper pole. Adequacy of undermining is checked by placing a hand in the pocket formed by the skin envelope. The superior part is then connected to the medial and lateral parts of the skin envelope flap.

The reduction is then performed. Tissue that is not part of the skin flaps or the central mound, as defined by the dermal strip and lateral wings, is excised. This usually corresponds to the tissue beneath the small triangles of skin remaining around the already dissected parts. Tissue is preserved on the chest wall at the lower medial and lateral quadrants and at the superior pole to ensure good contour. Meticulous attention is paid to haemostasis with the patient at normotension.



**Figure 5.** Creation of a conical breast mound and hitching the gland to an elevated position on the chest wall by suturing dermal wings to rib periosteum in a superior direction

The essential dermoglandular suspension consists of a 2-0 prolene suture from the chest wall - either rib periosteum or the pectoralis fascia at the upper aspect of the undermined skin flap - to the superior aspect of the central mound, roughly half way from the base to the superior edge of the de-epithelialised vertical strip. It is tied loosely to avoid tissue ischaemia. With the same suture, a further bite is taken at the superior part of the de-epithelialised dermal strip and tied just tight enough to elevate the nipple to its new height. Thus the mound is sutured to a new higher position on the chest wall. Again, this is not tied tightly so as to avoid restricting the plication of the inferior part of the dermal strip later.

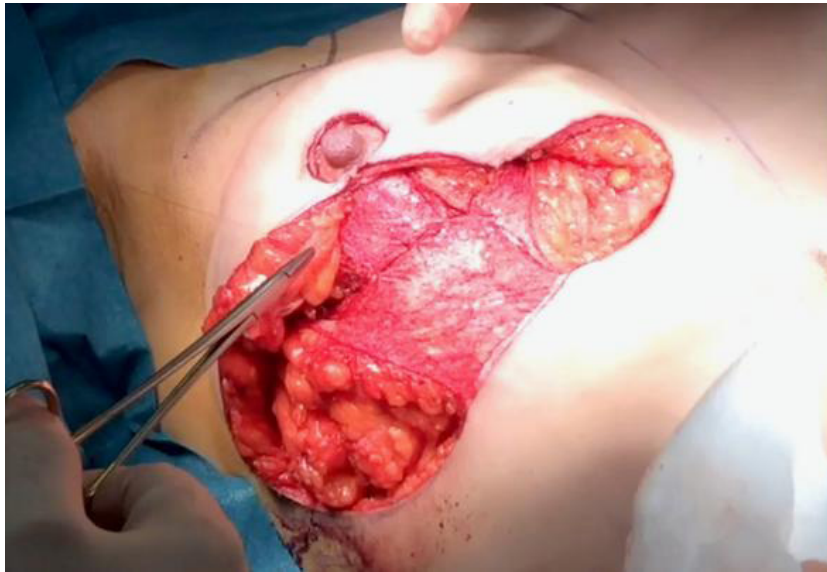
The dermal wings are sutured to the chest wall in a superior direction, wrapping partly around the central mound with 2-0 prolene [Figure 5]. If sutured at an adequate height on the chest, the IMF is lifted slightly, and the overall effect of wrapping the dermal wings around the gland is to create a youthful cone-shaped breast mound for the skin envelope to be re-draped over.

To enhance this cone shape, the supero-medial aspect of the medial and lateral dermal wings are sutured to the sides of the NAC, and the infero-lateral aspect of the wings are sutured to the chest wall.

The nipple is then partially inset using 3-0 vicryl, with a suture superiorly, inferiorly, then medially and laterally.

The necessary plication of the inferior dermal strip is performed using 3-0 Polydioxanone [Figure 6]. The distance from the nipple to IMF along the dermal strip is reduced to a length that corresponds to the vertical edge of the skin envelope and the desired nipple-to-IMF distance.

If required, the IMF ligament is reinforced or reconstructed by suturing the dermis at the IMF, particularly at the corner of the vertical dermal strip, to the chest wall using 2-0 ethibond. Latterly we have used additional de-epithelialised dermal flaps based inferiorly at the IMF incision as anchors for strength of the sutures between the IMF and chest wall. Suturing between dermis and periosteum or pectoralis fascia is more robust than suturing into the fibrofatty tissue around the IMF.



**Figure 6.** Plication of the inferior dermal strip to shorten the distance between the nipple and the inframammary fold

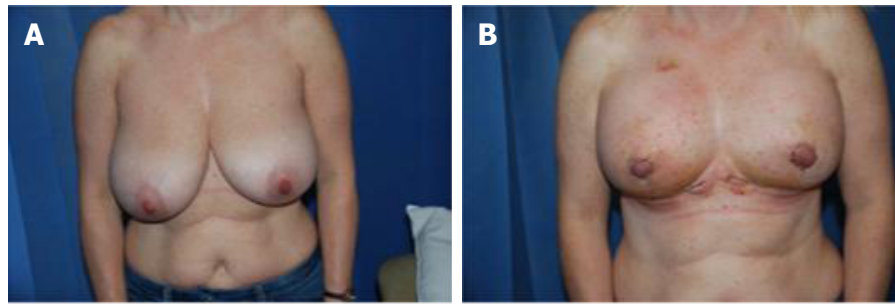
When closing the skin envelope, 2-0 prolene sutures are placed from the fascial layer to near the IMF to occlude the lateral space at the side of the gland, to prevent the tissue from lateralising and a boxy appearance of the breast. These sutures are also key to shaping the breast base, and some may be used at the medial aspect as well. The skin envelope is closed in the usual way without drains. Occasionally, volume may need to be removed from the ends of the IMF wound before final closure to prevent standing cone deformities. No formal wound drainage is required. Dressings are applied and a sports bra is provided for the patient to wear for 2 months.

## RESULTS

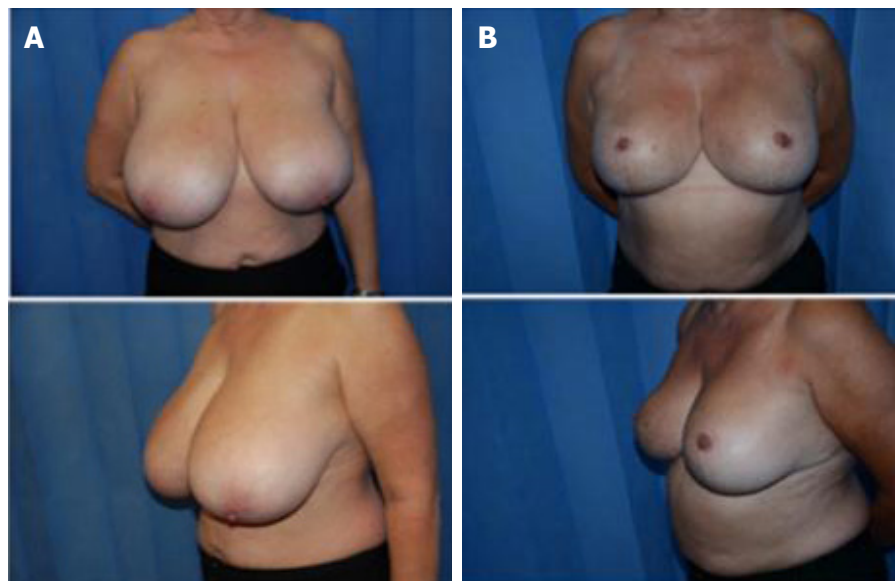
Our series consists of 116 patients, of mean age 40 years (range 19-65). Patients were from a range of racial backgrounds and exhibited broad differences in breast history including previous breastfeeding and breast surgery. The mean tissue mass excised was 865 g (range: skin only-2175 g) per breast. There were no cases of nipple necrosis or infection requiring antibiotics. There was one post-operative haematoma which required surgical evacuation. Three patients developed a degree of fat necrosis which was managed conservatively in two, but required surgical debridement for liquefactive necrosis in one. Four patients experienced superficial wound dehiscence at the T-junction which was managed successfully with dressings.

Mean follow up was 20.6 months. Several patients treated with this technique are now at post-operative year seven, and none have required revision surgery for correction of pseudoptosis or other recurrent deformities. We did not note any apparent differences in scar quality with this technique compared to those obtained before we began using the technique, though this was not formally assessed. There was no notable difference in breast firmness after surgery with this technique. The effects on lactation were not assessed, though we do not expect these technical modifications to have more of an impact than other breast reduction techniques, and it is possible that the impact may be smaller due to this being a central mound technique.

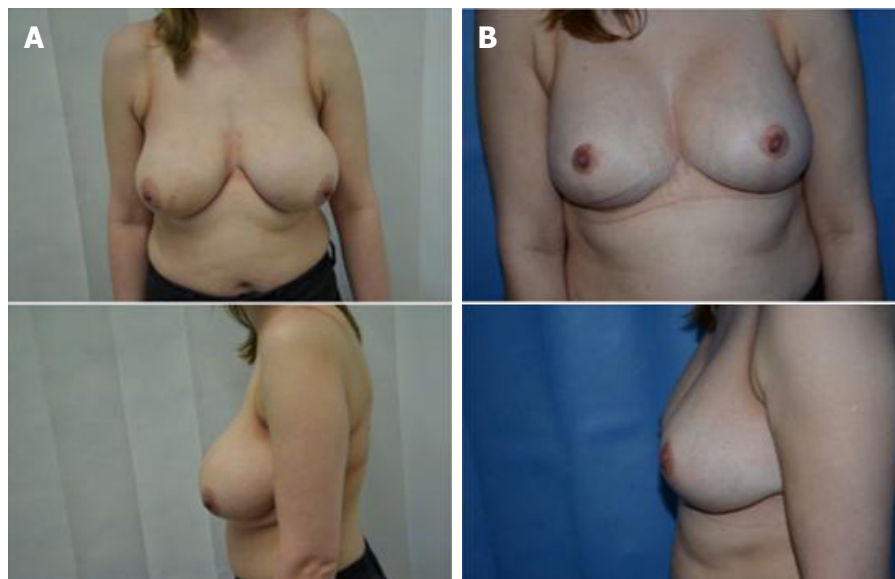
Typical cases are shown in [Figures 7-9](#). Note the fullness at the upper poles shortly after surgery in [Figure 7](#). By three months this fullness has now descended along with the rest of the breast, including the IMF to a natural non-ptotic shape. The effects of surgery are well-maintained at discharge at 2 and 3 years post-op.



**Figure 7.** A: Pre-operative; B: ten-day post-operative



**Figure 8.** A: Pre-operative; B: three-year post-operative



**Figure 9.** A: Pre-operative; B: two-year post-operative



## DISCUSSION

Kankaya *et al.*<sup>[3]</sup> state that “it is generally accepted that bottoming out deformity starts to develop at approximately six months postoperative”, and can be noticed easily at the end of the first postoperative year. Taking this into consideration, our follow-up interval seems appropriate given that many patients do not want unnecessary routine follow-up appointments once their treatment has ended. Our technique reliably reduces the appearance of the bottomingout deformity at postoperative year one and beyond. Although not as extensive as some other studies<sup>[4]</sup>, the number of patients in this series was adequate to demonstrate the consistency of results as seen in the photographs.

Aydin *et al.*<sup>[5]</sup> describe creating an internal bra effect by the use of dermoglandular suspension beneath the separate skin envelope. Several variants on this technique exist, which include using alloplastic or allogenic materials<sup>[6]</sup>. Our technique is another variant on similar pre-existing descriptions<sup>[7,8]</sup> wherein we rely solely on the patient’s autologous tissue, which has benefits of not increasing cost, and eliminating the risks associated with implanted materials.

Rubin’s paper on mastopexy in the massive weight loss patient<sup>[9]</sup> refers to plication of the dermis at the lower pole, so as to reduce the distance between the nipple and IMF with the aim of taking tension off the skin envelope at closure and improving projection. Kankaya *et al.*<sup>[3]</sup> believe the superior dermo-glandular hitching is sufficient and that inferior dermal plication is not required. We make use of inferior dermal plication in the present technique in the belief that it reduces the propensity for bottomingout. Another purpose of it is to reduce wound healing complications by reducing tension on the skin at closure.

Rubin<sup>[9]</sup> also makes use of dermo-glandular flaps to create a precisely shaped conical breast mound and suspend the breast tissue on the chest wall. He continues dissection of the skin envelope superiorly beyond the superior limit of the gland up as high as the clavicle. We create a similar pocket but just above the second rib.

Kankaya *et al.*<sup>[3]</sup> assert that fixation of the dermal flaps to the costal periosteum in-stead of pectoral fascia can decrease tissue descent over the long term, and Rubin<sup>[9]</sup> advocates this also. We favour fixation to rib periosteum in our technique wherever possible.

A factor often overlooked in studies of breast reduction is the stability of the IMF. Interference with the normal anatomy of the IMF by surgery can result in the fold being displaced in any direction, including away from the chest wall. If this occurs there is loss of the natural definition of the lower breast pole, and the parenchyma can more readily descend on the chest wall resulting in pseudoptosis or an inferior “double bubble” deformity<sup>[10]</sup>. As part of our technique we place emphasis on dissection superior to the IMF ligament, as defined by Bayati and Seckel<sup>[10]</sup>, to maintain stability of the IMF. The fold may be moved slightly in a superior direction as part of the dermal suspension element of the procedure, but this adds to its definition and does not interfere with the IMF ligament itself. Recently we have also begun to augment the definition of the IMF by adding extra non-absorbable sutures between the dermis and the chest wall with promising initial results. This, we believe, also stabilises the IMF to the chest wall to prevent it from separating or descending.

With ageing, the normal footprint of the breast becomes narrowed due to a combination of ptosis and tissue atrophy. The heavier a breast, the greater the descent due to gravity. Restoration of a youthful breast appearance should involve correction of this senescent narrowing, in addition to correcting ptosis. Our technique creates a dermoglandular cone which, on hitching upward and stabilising to the pectoralis fascia to maintain the mound above the IMF, broadens the footprint of the breast leading to a smooth, round pleasing breast appearance.



Drawbacks to our technique mainly pertain to the dissection of the skin envelope and the suspension elements: the series of modifications we use in combination add time to the breast reduction overall, of the order of around 30%, but we believe the benefits of improved aesthetics and longevity make this a worthwhile trade-off.

The large skin envelope is widely undermined and relatively thin compared to other techniques. Logically, this introduces a hypothetically increased risk of skin flap necrosis or wound healing complications such as dehiscence or poor scars, particularly at the t-junction. So far we have not yet seen this borne out in practice. Our rates of wound healing complications are comparable to those previously reported elsewhere. Meticulous attention to flap thickness and tissue handling, plus patient selection, may help ameliorate these risks. The skin flap dissection, among other elements of the technique, produces a learning curve that may deter others from incorporating these modifications into their breast reduction repertoire.

Most of our patients wish to keep good proportionate volume ranging from C to F cup. As always, we aim to match the breast volume to the body structure of each individual patient in our population. However those wishing to keep a large proportion of initial volume but obtain good breast shape and correction of ptosis, as is possible with this technique, are the challenging patients in the long run due to the rate of recurrent ptosis or pseudoptosis.

The case that developed fat necrosis requiring surgical washout and debridement had a reduction in nipple-to-IMF distance of 19 cm. Other cases in our series have had reductions in nipple-to-IMF distance of 17 cm done safely without complications. We therefore feel it is safe to reduce the pre-operative nipple-to-IMF distance by up to 17 cm without free nipple graft, assuming intrinsic patient factors are optimal.

In conclusion, the technique herein described offers a range of benefits over existing techniques, aimed at improving predictability, consistency and longevity of aesthetic results. Development of pseudoptosis in particular, which is a common pitfall with existing breast reduction techniques, is effectively delayed. We believe the learning curve and extra time required to complete the procedure, with its series of additional steps, is a very worthwhile trade-off for patients who receive a more lasting improvement in breast shape and lift. The modifications described have not been shown to increase the rates of surgical complications.

## **DECLARATIONS**

### **Authors' contributions**

Concept, design and data analysis: Riaz M, Nicholson S

Data acquisition: Riaz M, Khan MAA

Manuscript preparation, critical revision and finalizing of the manuscript: Nicholson S, Riaz M, Khan MAA

### **Availability of data and materials**

The data were strictly obtained from medical records according to the privacy policy and ethics code of our institute.

### **Financial support and sponsorship**

None.

### **Conflicts of interest**

All authors declared that there are no conflicts of interest.

### **Ethical approval and consent to participate**

Approval from hospital trust audit department. Full consent from all patients obtained.

### Consent for publication

Not applicable.

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Original Article

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# One-stage reconstruction of neck burns with single-layer dermal matrix

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## Abstract

**Aim:** The aim of the study was to describe the applicability of a single-layer acellular dermal matrix, in combination with split-thickness skin graft (STSG) in one-stage surgical procedure in patients with deep neck second - and third - degree burns.

**Methods:** A descriptive longitudinal study was conducted at the Burn Unit of the Health Services Unit of Simón Bolívar North Subnetwork E.S.E. of the Secretariat of Health in Bogotá, Colombia, from January 1 2016 to December 31 2017 in which we describe the applicability of a single-layer acellular dermal matrix in combination with STSG in one-stage surgical procedure in patients with deep neck second and third degree burns.

**Results:** A total of 9 patients were treated. Exposed areas required definitive coverage using a single-layer dermal regeneration matrix and autografts in a one-stage procedure, following excision of keloid scars and scar retractions ( $n = 7$ ), and in the case of acute-phase deep burn wounds, following complete necrotic tissue removal ( $n = 2$ ). No patient presented infection during postoperative follow-up. At 2 months postoperatively, stability of treated area and adequate resistance of the skin substitute and autografts could be observed. They appeared normal in color, with no degree of contractures or functional limitations.

**Conclusion:** This is the first study demonstrating that the use of a single-layer acellular dermal matrix template for one stage reconstruction of post-burn full thickness neck defects is an effective, safe and excellent reconstructive option. The use of an artificial dermal matrix in one-step surgical approach, allows rapid healing and early mobilization of the neck, and in selective cases, it may reduce the need for local-regional or free flap coverage; moreover, it is associated with excellent skin formation, good functional and esthetic results and minimal donor site morbidity.



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**Keywords:** Neck, burns, matrix, template, reconstruction

## INTRODUCTION

Modern burn care is based on operative wound management. There is clear evidence that immediate excision and closure are lifesaving for patients.

Significant reconstructive and rehabilitative challenges associated with neck burns must be addressed in aesthetic units. Acute care will greatly influence the succeeding scarring, reconstructive needs, and long-term outcomes. In most cases, reconstruction will encompass the restoration of both form and function of soft tissue. The procedures used will highly depend on the level of local scarring<sup>[1]</sup>.

The neck is a difficult area to reconstruct because of its cylinder-like dynamic structure. Severe neck burns are followed by various expected deformities: neck contracture with limited range of motion, problems with oral ability, and chin contracture with eversion of the lower lip, affecting both eating and speech. Thus, the initial reconstruction method selected by the surgeon will determine the functional and final aesthetic result<sup>[2]</sup>.

Neck reconstruction techniques are conditional on the extent of the release and type of defect, as well as on the institution's financial resources. In small areas having no exposed deep structures, full-thickness skin grafts are a good option, whereas for larger defects with no exposed deep structures, split-thickness skin grafts (STSGs) are indicated. Regional skin expansion is also described, along with free flaps, including the anterolateral thigh flap and the thoracodorsal artery perforator flap in the case of exposed deep structures. Normally, reconstruction following neck contracture release with STSGs produces poor results due to an elevated rate of reconstrictures. Greenwood and Mackie<sup>[3]</sup> attribute this phenomenon to natural graft contractile tendency, to pain precluding mobility, and to platysma contraction. Better results have been reported with full-thickness skin grafts, with the drawback of limited donor sites, particularly in young and lean patients.

Skin substitutes are another alternative for neck reconstruction. They have the advantage of being simpler procedures, compared to free flaps, exhibiting less secondary contracture than STSGs, and offering usability in large neck reconstruction areas<sup>[4]</sup>.

The implementation of dermal templates to effectively treat wounds is based on an appropriate debridement and a well-vascularized host bed. Applying dermal templates on contaminated wounds entails a high risk of infection, since dermal templates have a limited ability to fight infection. Once it has been applied, fibroblasts, endothelial cells, and inflammatory cells migrate into and repopulate the dermal template, ultimately replacing the scaffold. A thin STSG may be applied for wound coverage after template take in large wounds. The dermal template may be grafted at the time of its application in a well-vascularized wound if a thin scaffold is used<sup>[5]</sup>.

There are only a few published studies that have used a dermal matrix with a skin autograft in a one-stage repair. In 2011, Greenwood and Mackie<sup>[3]</sup> reported 1 case, in which Matriderm collagen/elastin dermal matrix plus STSGs were used in a one-stage repair after a neck contracture release, yielding positive results. Other substitutes, such as Glyaderm, based on glycerinized donor skin, Integra® bilayer, and biodegradable polyurethane dermal substitute, have been used for neck reconstruction. However, all of them require two surgical procedures, where a skin graft is placed 3 weeks following take of dermal matrix<sup>[6-8]</sup>.

Another study published by Seo *et al.*<sup>[9]</sup> in 2014 describes a retrospective analysis of 28 patients with post-burn severe cervical contractures, which were reconstructed in a single-stage procedure with skin substi-

tutes and STSGs, yielding an overall take rate of 95.9%, with only 1 patient showing recontracture. Nevertheless, all patients from this study underwent late reconstruction, considering that the contracture was already present as a burn sequela. To date there are no reports in the international literature demonstrating this type of management in patients with acute burns, achieving positive results. In this regard, the present study reports such management not only in 7 patients with irregular scarring but also in 2 patients exhibiting acute burns.

The aim of this prospective, single-center, observational study was to describe the application of a single-layer acellular dermal matrix, in combination with STSGs, in a one-stage surgical procedure in patients with deep partial- and full-thickness neck burns, and sequelae.

## METHODS

We report the use of a single-layer acellular dermal matrix (Integra®) for one-stage reconstruction of neck defects following a full-thickness burn.

A descriptive longitudinal study was conducted at the Burn Unit of the Health Services Unit of Simón Bolívar North Subnetwork E.S.E. of the Secretariat of Health in Bogotá, Colombia, from January 1 2016 to December 31 2017. The study was approved by the Institution's Ethics Committee, and it was based on the ethical principles contained in the Declaration of Helsinki.

The study included 9 patients with deep partial- or full-thickness burns of any etiology and extension, involving the neck either partially or totally, as well as patients who presented abnormal scarring on the neck with or without retraction, who required definitive coverage with skin grafts after complete excision of the scar lesion.

Patients were requested to sign an informed consent form to be able to participate in the study and have their pictures taken. Patients showing additional comorbidities, including malnutrition, high blood pressure, diabetes mellitus, and coagulation disorders, were excluded. Patients having severe mental disorders or exposed areas not suitable for graft coverage were also excluded.

### Surgical procedure

The dermabrasion or complete eschar removal was performed under general anesthesia in deep partial- and full-thickness burns. After obtaining a clean wound free of necrotic tissue, the host area was rinsed with isotonic saline solution, and electrocautery was used for hemostasis. Once the burn area was prepared and ready, the single-layer acellular dermal matrix template was applied to the wound bed to achieve a complete substitute of the full-thickness dermis. The single-layer acellular dermal matrix template (Integra®) was placed, allowing 1 cm to extend beyond the wound edges. Next, the template was checked to ensure there were no bubbles or hematomas. Immediately after this step, a STSG of 0.010" was obtained from the dorsolateral thigh with the use of an electric dermatome and fixed in place with surgical staples. Specialized dressings were applied to the grafts in order to stabilize them and close the dead space, thereby lowering complication rates.

Wound dressings were first uncovered on the 5th day and changed every 5 days until complete take of the dermal matrix and skin autograft. Blisters, small hematomas or seromas were drained during dressing change. In case of partial graft loss, the site was regrafted or closure was done by applying cultured autologous keratinocytes, thus, avoiding healing by secondary intention. Monitoring was conducted at 1, 2, 3, 6, 9, and 12 months, and evolution was recorded through photography.



An admission assessment was performed for each patient, and based on these findings, a physical and occupational therapy plan was designed with the aim of decreasing pain and edema, improving ranges of motion, and controlling positioning and functionality for neck rotation and extension. Both the physical and occupational therapies were suspended during the first 5 postoperative days and resumed with physical reconditioning activities and orthotic management with splints in extension (110°), acupressure on the scar, and the use of Lycra garments, silicone, lubricants, and moisturizers. Additionally, hypertrophic, red, inflexible, firm, and raised scars were treated with steroid injections.

### Statistical analysis

The socio-demographic variables age and sex were registered. Other clinical characteristics were registered as well, including total burned body surface area using the Lund and Browder chart, burn depth, size of the defect following complete necrotic tissue removal or total scar excision, amount of dermal matrix used in square centimetres, autograft take percentage, and complications. Scars were assessed at month 1 and month 12. For qualitative variables, frequencies and percentages were used, whereas for quantitative variables, mean and range were preferred. Microsoft Excel® was used.

## RESULTS

A total of 9 patients were treated. Exposed areas required definitive coverage using a single-layer dermal regeneration matrix and autografts in a one-stage procedure, following excision of keloid scars and scar retractions ( $n = 7$ ), and in the case of acute-phase deep burn wounds, following complete necrotic tissue removal ( $n = 2$ ). In this group, 5 patients were 1 woman and 4 men, with a mean age of 29.6 years (range 13-48 years).

Mean total body surface area affected was 30% (range 8%-70%). Most patients showed additional burns involving the face, anterior chest and upper extremities, exhibiting deep partial- and full-thickness burns.

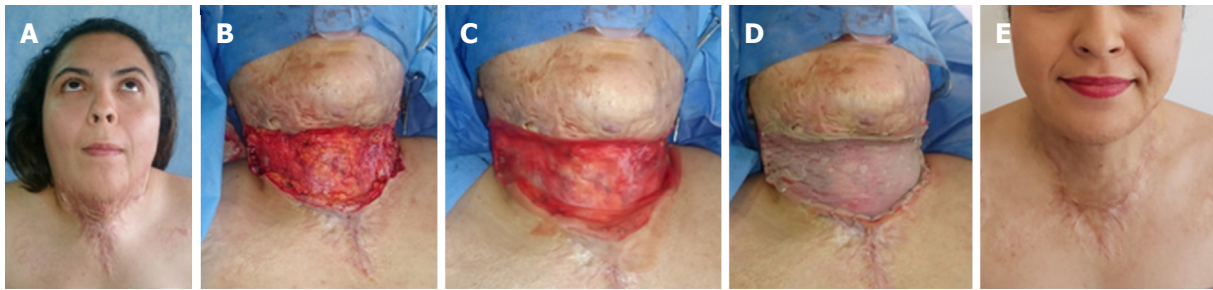
Mean treated area was 144 cm<sup>2</sup>. No patient presented infection during postoperative follow-up. At 2 months postoperatively, stability of treated area and adequate resistance of the skin substitute and autografts could be observed. They appeared normal in color, with no degree of contractures or functional limitations. The graft was smooth, flat, non-indurated, and elastic, and its color was very similar to the surrounding area. Such characteristics improved over time [Figures 1 and 2].

Four of the nine patients showed signs of hypertrophic scarring at the edges of the graft, particularly in the junction between the dermal matrix and normal skin, consisting of hyperemic, raised, and slightly indurated scars having a width of less than 5 mm. They responded adequately to management with steroid injections and the use of Lycra garments, silicone gel, and acupressure.

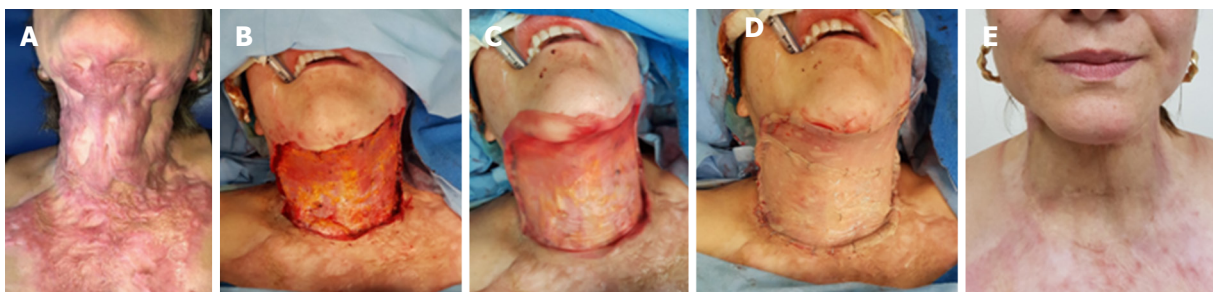
One patient presented autograft loss of 5 cm<sup>2</sup> at immediate postoperative follow-up, which was successfully managed by applying cultured autologous keratinocytes [Figure 3].

## DISCUSSION

Neck burns are difficult to reconstruct because of the cylinder-like structure and constant movement of the neck. Among the most common challenges associated with deep neck burns is the high frequency of contractures and functional impairments. Such deformities cause prolonged disabilities and social rejection. Although multiple procedures have been described, including Z-plasty, W-plasty, local flaps, and free flaps, STSGs continue to be recognized as the standard treatment, particularly for deep and extensive burns. Skin substitutes have improved the quality of STSGs significantly, reducing and preventing recontractures<sup>[5]</sup>. Additionally, they are a good alternative for this area.



**Figure 1.** A: A 25-year-old woman, who suffered thermal burn caused by alcohol, with a deep partial- and full-thickness burn covering 30% TBSA. There were injuries to the face, neck, anterior chest, and upper limbs. She presented severe mentocervical contracture; B: the photograph shows the area following excision of the scar; C: the single-layer dermal matrix is shown in place; D: the split-thickness skin graft may be observed over the template; E: outcome at 12 months postoperatively after reconstruction with 135 cm<sup>2</sup> of acellular dermal matrix and autografts in a single-step procedure, without functional limitations; F: pinch test exhibiting pliability of the reconstructed skin. TBSA: total body surface area



**Figure 2.** A: A 38-year-old woman, who suffered thermal burn caused by mineral spirits, with full-thickness burns that developed in multiple keloid scars in the mentocervical region; B: defect after excision of keloid scars; C: the photograph shows the application of the single-layer dermal matrix over the defect; D: result after placing 206 cm<sup>2</sup> of dermal regeneration matrix and autografts in a single-step procedure; E: Appearance at 10 months postoperatively. She did not present any functional limitations



**Figure 3.** A: A 38-year-old woman, who suffered thermal burn caused by alcohol, with a full-thickness burn covering 30% TBSA; B: injured area after eschar removal; C: reconstruction with 210 cm<sup>2</sup> of dermal matrix and autografts. She presented 5-cm<sup>2</sup> graft loss that was treated with autologous keratinocyte cultures; D: the picture shows the appearance at 9 months postoperatively. TBSA: total body surface area

Recently, there has been an increased number of reports describing the use of several skin substitutes as a good reconstruction alternative. Some of them, such as Glyaderm, Integra® bilayer, and biodegradable polyurethane dermal substitute, require a two-stage procedure consisting initially of a dermal matrix implantation and subsequently of skin grafting once there is complete take of the matrix. Seo *et al.*<sup>[9]</sup> show a report of 24 neck reconstructions with a 95.9% take rate, under the use of AlloDerm and Matriderm, by placing the skin graft immediately after the dermal matrix implantation in a single-stage procedure.

Even though this study is a preliminary report of a short series of 9 cases, the results obtained allow the development of comparative studies encompassing the different techniques used for post-burn neck reconstructions, comparing them with STSGs or other skin substitutes. It is worth noting that this is the first case series demonstrating that the use of a single-layer acellular dermal matrix (Integra®) in a one-stage reconstruction of neck defects following a full-thickness burn is an effective, safe and excellent reconstructive option in managing both acute burns and sequelae.

Along the same lines of the results described by Seo *et al.*<sup>[9]</sup> with AlloDerm and Matriderm, the use of Integra Single Layer in this study yielded comparable results, including the following: short operating room times, with no complications and excellent functional and cosmetic results in such a difficult-to-treat area. As may be observed from the photographs presented, there is good color match in the grafted area. The use of skin substitutes offers alternative solutions aimed at successfully treating complex soft-tissue defects, optimizing the quality of the reconstructed skin<sup>[10-12]</sup>.

In Colombia, the other skin substitute available is the Integra® bilaminar dermal regeneration matrix within the framework of current practice regarding skin substitutes, consisting of a two-stage surgical procedure: application of the dermal regeneration template to the wound and, following a 2-4 weeks' interval, the replacement of the silicone pseudoepidermal layer of the template with a thin-thickness skin autograft. The increased number of surgeries, a prolonged hospitalization and the need of additional immobilization are patent disadvantages of this two-step repair. Furthermore, the time required for the dermal matrix to fully integrate causes prolongation of the inflammatory phase, increasing the possibility of fibrosis and scar retraction<sup>[13-15]</sup>. The Integra® bilaminar dermal matrix has proven to entail a higher risk of infection, as a 3-week interval is required to allow take before placing skin autografts. Lohana *et al.*<sup>[16]</sup> report that the risk of infection is higher in such cases.

In the case of deep and extensive neck burns, where insufficient donor skin is available for full-thickness skin grafts, which require coverage with STSGs, we consider that the use of dermal matrices may be contemplated as a first surgical option to improve STSG outcomes. This would decrease the high postoperative contracture rate and poor functional results observed in these areas.

A parameter that we consider to be important for the success of this procedure is the preparation of a well-vascularized, non-infected wound bed, before applying the dermal matrix and skin graft. Adequate surgical debridement is crucial and mandatory. Stabilizing the single-layer acellular dermal matrix and the skin graft through the use of pressure dressings is also essential for a successful outcome.

No unstable or keloid scars were recorded; pliable skin and excellent elasticity of grafted areas was documented, without scar contractures or serious functional limitations. Cosmetic appearance of grafted sites was equally acceptable.

In conclusion, our efforts were centered on choosing the appropriate techniques that will provide good functional and cosmetic results. The use of an artificial dermal matrix in a one-step surgical approach allows rapid healing and early mobilization of the neck, and in some cases, it may reduce the need for local or regional flap or free flap coverage. Moreover, it is associated with excellent skin formation, good functional and aesthetic results, and low donor-site morbidity. Therefore, it should be considered as an alternative to other reconstruction techniques, particularly when covering highly demanding areas, such as the neck.

## DECLARATIONS

### Authors' contributions

Concept and design, data analysis, manuscript preparation, critical revision and finalizing of the manuscript:

Gaviria JL, Gómez-Ortega V

Data acquisition: Gaviria JL

### Availability of data and materials

We confirm that the data were strictly obtained from medical records according to the privacy policy and ethics code of our institute.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

The study was approved by the Institution's Ethics Committee. Ethical approval number UI-18-15. All participants were adults, and they all signed an informed consent form before participating in the study.

### Consent for publication

Patients were requested to sign an informed consent form to be able to participate in the study and have their pictures taken.

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Original Article

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# Negative pressure wound therapy with instillation: effects on healing of category 4 pressure ulcers

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## Abstract

**Aim:** The use of negative pressure wound therapy (NPWT) is well established in the treatment of chronic wounds. NPWT with instillation (NPWTi) combines traditional NPWT with the application of a topical irrigation solution (in this case octenidine based octenilin® wound irrigation solution) within the wound bed. The purpose of the study was to investigate the impact of NPWTi on pressure ulcers (PUs).

**Methods:** In total 13 patients with PUs in different locations were treated with negative pressure therapy combined with octenidine based instillation fluid after first surgical debridement. After 6 days the dressing was removed and wound closure using different local flaps was performed.

**Results:** Normal wound healing without irritation was found 30 days post-debridement and after 90 days the wounds showed complete healing. No adverse incidents occurred and no toxic tissue reactions were documented. During the follow up period, there was no recurrence of the PU in any of the treated patients.

**Conclusion:** It is generally recognised that for chronic wounds to heal, optimum wound bed preparation is of paramount importance. This helps prepare for secondary healing, skin grafting or coverage with flaps. Tests were performed *in vitro* simulating real clinical conditions using PU vacuum exudates. These tests quantified the antiseptic efficacy of octenilin® wound irrigation solution in the eradication of microorganisms. Further research is needed to establish the role of NPWTi with octenilin® in the management of category 4 PUs, but these initial results on 13 patients lead in the



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direction of developing an enhanced protocol for the treatment of chronic wounds.

**Keywords:** Negative pressure wound therapy with instillation, octenilin® wound irrigation solution, chronic wounds, pressure ulcer, wound bed preparation

## INTRODUCTION

Wound healing is a highly complex process which is critical in maintaining the barrier function of the skin. Chronic, non-healing wounds subject a patient to significant discomfort and distress while also using a considerable amount of costly healthcare resources<sup>[1]</sup>.

A pressure ulcer (PU) is a localised area of tissue destruction which occurs when soft tissue is compressed over bony prominences for a prolonged length of time. The tissue destruction occurs when the compressed tissue is deprived of oxygen.

PUs are estimated to affect 18% of patients in hospitals and care facilities in Europe. This prevalence is projected to rise due to an increasingly aging population<sup>[2]</sup>. Patients at particular risk of developing PUs include older patients and those with paraplegia<sup>[3]</sup>. Around 21% of paraplegic patients develop a PU, usually caused by continual skin pressure inhibiting the adequate circulation of blood to the skin and underlying tissue<sup>[4]</sup>. This frequently leads to chronic complications meaning that on average a patient with paraplegia will be hospitalised every three years as a direct result of a PU<sup>[5]</sup>.

The European Pressure Ulcer Advisory Panel (EPUAP) has categorised PUs into four categories based on severity of the lesions. These are defined below and provide a useful starting point for the management of category 4 PUs. Category 1: intact skin with non-blanchable redness of a localized area usually over a bony prominence. The area may be painful, firm, soft, warmer or cooler as compared to adjacent tissue. Category 2: partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. May also present as an intact or open/ruptured serum filled blister. Category 3: full thickness tissue loss. Subcutaneous fat may be visible but bone, tendon or muscle are not exposed. May include undermining and tunnelling. The depth of a category/stage III PU varies by anatomical location. Category 4: full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present on some parts of the wound bed. Often includes undermining and tunneling<sup>[6]</sup>.

There are many forms of management depending on the category and severity of the PU. A conservative, non-surgical approach may be appropriate for categories 1 and 2. However, categories 3 and 4 PUs usually require surgical management. Optimum pre- and post-operative care plays a key role in avoiding recurrences. Surgery may be undertaken to perform skin grafts and flap coverage, which can provide efficient and rapid methods to close wounds with good functional and aesthetic results.

There are various wound closure techniques available to the reconstructive surgeon and the reconstructive ladder is a spectrum of closure options from simple primary wound closure to more sophisticated flap reconstructive techniques. Where possible closure should be achieved by the simplest effective technique. In terms of increasing complexity, the ladder goes from healing by secondary intention, healing by primary intention, delayed primary closure, split thickness skin grafts, full thickness skin grafts, tissue expansion, random flaps, axial flaps and free flaps.

Unlike skin grafts, flaps have their own blood supply and good results have been demonstrated in the

treatment of complex wounds using this technique<sup>[7]</sup>. When select a flap for the reconstruction of a pressure wound, several factors must be considered including the site of the pressure sore, the flap design and the location of the flap relative to the site of coverage<sup>[7]</sup>.

Before undertaking any wound closure surgical procedure, the wound bed must be clean and clear of infection. Risk factors such as malnutrition, shear force, missing sensibility, moist wound situation and incontinence need to be managed prior to surgery. Any source of infection must be cleared and if the patient requires it, a nutritional support programme should be undertaken.

Negative pressure wound therapy (NPWT) has played an increasingly significant role in wound management and a number of uses for this method have been reported, ranging from acute and chronic wounds, to closure of open sternal and abdominal wounds, and assistance with skin grafts. In terms of wound bed preparation the efficacy of NPWT has been well documented<sup>[1]</sup>. NPWT is a physically acting treatment which is designed to create a moist, sterile wound environment under sub-atmospheric pressure. This helps promote wound granulation, epithelisation and contraction of the wound<sup>[1,8]</sup>.

Due to a number of factors, including less frequent dressing changes, reduced nursing time, improved healing rates, and decreased lengths of hospital stay, cost savings have been reported when using NPWT<sup>[1,9,10]</sup>. In terms of serious adverse events during NPWT, these have been rarely reported<sup>[11]</sup>. In comparison to traditional wet-to-moist dressings, NPWT has shown benefits in the reduction of wound volume<sup>[12]</sup>.

To summarise, NPWT helps increase wound blood flow, increases granulation tissue formation and stimulates wound healing pathways through shear stress mechanisms.

A modification of NPWT added instillation of topical wound irrigation solutions to traditional NPWT. This combined therapy, termed NPWT with instillation (NPWTi), has been shown to be effective in the treatment of a variety of complex wounds and reduces bioburden and biofilms present in wounds, which helps the healing process<sup>[13]</sup>.

Multiple microorganisms, in particular *Staphylococcus aureus* and *Streptococcus spp.* are frequently found to colonise PUs<sup>[14]</sup>. Morbidity and mortality are significantly increased if an infection is caused by antibiotic resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) or extended-spectrum  $\beta$ -lactamase (ESBL)<sup>[15-19]</sup>.

Octenidine is a broad spectrum antiseptic agent which has been demonstrated to be effective in eradicating many microbes, typically found in wounds<sup>[20,21]</sup>. Octenidine has the ability to reduce or prevent the microorganism-induced formation of biofilms in chronic wounds, which is of particular importance as these microorganisms can promote the incidence and the persistence of infections<sup>[22]</sup>. An additional benefit is that octenidine based rinsing solutions have a rapid onset of action and have good tissue tolerability<sup>[23]</sup>.

When NPWT is combined with instillation, the negative pressure is not maintained during the instillation of the rinsing solution and at this time, the system is prone to leakage. Therefore the instillation needs to be kept to a minimum, using a fast acting wound rinsing solution.

The aim of this study was firstly to assess octenidine based wound irrigation solution in ex vivo exudate samples and to compare octenidine with other rinsing solutions. Furthermore, we examined the impact of using NPWTi together with octenilin® wound irrigation solution on 13 patients with category 4 PUs (sacral,

gluteal/ischial or trochanteric, respectively). Whereas the first 3 patients were assessed in 2014, another 10 patients were treated between 2015 and 2017 in a multicentric approach.

## METHODS

### Sampling of wound exudates

To simulate realistic wound conditions, wound exudates from patients with leg ulcers, treated with conventional NPWT, were obtained. This occurred when the foam dressings in the wounds were replaced. At this point they were transferred into sterile containers, then soaked with 5 mL of a protease inhibitor solution (Complete Protease Inhibitor Cocktail Tablets, Roche, Germany). To collect wound exudates, the dressings were cut into appropriate pieces using sterile scissors and then squeezed through a sterile press. The wound exudates were collected and captured in 50 mL centrifuge tubes and stored at -20 °C until processing continued or at 6 °C when processed on the same day as the exudates were collected.

### Microbiological activity test methods

Comparative data was obtained by also testing Serasept® (containing polyhexamethylene biguanide 0.04%; Serag-Wiessner GmbH & Co. KG, Germany) and Prontosan® (containing polyhexamethylene biguanide 0.1%; Braun Melsungen AG, Germany) rinsing solutions. A negative control was provided using saline solution.

Quantitative suspension tests were performed according to the dilution-neutralisation method described in DIN prEN 13727:2009. The tests conformed to the conditions for low organic load (0.3 g/L of bovine serum albumin) and for high organic load (0.3 g/L of bovine serum albumin and 3.0 mol/L of ovine erythrocytes). This method was fine tuned depending on the volume of the extracted wound exudates. One part of load solution was mixed with one part of bacterial suspension. After 2 min, 8 parts of the negative control (0.9% saline solution) or one of the following rinsing solutions - octenilin® Wound Irrigation Solution (containing octenidine dihydrochloride 0.05%), Serasept® 2 or Prontosan® were added and the test mixture was completely blended using a vortex mixer. At the predetermined exposure times - 0.5 and 2 min - the solution was stirred again and 1 part was added to 9 parts of neutralisation solution. After the neutralisation time was complete, a serial dilution up to 10<sup>-2</sup> was prepared and the appropriate amount of solution was placed on agar plates.

### Bacterial count from exudates

The wound exudates were diluted in a sterile dilution series with tryptone sodium chloride (Tryptone-NaCl) and plated on Casein Soy Peptone Agar (CSA) according to the dilution levels. All visible colony forming units (CFU) were counted, regardless of their species. Additionally, the exudate samples were spiked with the test organism *Staphylococcus aureus* ATCC 33592 (MRSA strain) to further increase the microbiological load. Storage and cultivation of the test organism was conducted in accordance with legal regulations (prDIN EN 12353:2011).

The agar plate count and the analysis were conducted in accordance with the legal regulation DIN prEN 13727:2009. The logarithmic germ reduction factor (lg RF) was calculated by applying the following formula:

$$\lg \text{RF} = \lg N_0 - \lg N_t$$

lg RF     reduction of live cell count after exposure time t, given as decadic logarithm

lg N<sub>0</sub>     live cell count per ml in sample solution at the beginning of exposure time t

lg N<sub>t</sub>     live cell count per ml in sample solution at the end of exposure time t

According to the requirements given in DIN prEN 13727:2009, antiseptic agents must reduce the live cell count by five orders of magnitude. This reduction is considered to be a sufficient antibacterial effect.

### Patients

Initially 3 patients with category 4 gluteal PUs were treated with NPWTi in combination with octenilin®



**Figure 1.** Sacral pressure ulcer grad IV (EPUAP) after initial debridement and NPWTi. EPUAP: the European Pressure Ulcer Advisory Panel; NPWTi: NPWT with instillation

wound irrigation solution for wound bed preparation. Gluteal/ischial PUs are at higher risk of infection. In the following period 10 additional patients with various PU localizations were admitted to following hospitals: St. Josef Hospital Vienna, Austria (2 sacral, 1 ischial/gluteal PU), St. Markus Hospital Frankfurt, Germany (2 sacral, 1 ischial/gluteal PU), Innsbruck Medical University, Austria (1 sacral, 1 trochanteric PU), Hospital St. Gallen, Switzerland (1 sacral, 1 trochanteric PU).

### Wound conditioning using NPWT

All patients underwent a surgical debridement of necrotic tissue as the first stage of treatment. This was undertaken to remove fluid, exudates and infectious material. NPWT (V.A.C.ulta™) was applied to the wound. A foam dressing (V.A.C. Granu-Foam™, Kinetic Concepts Inc., San Antonio, TX, USA) was cut into a shape which perfectly fitted the wound cavity. A transparent film was then used to seal the wound and a track pad connected to an adjustable vacuum pump, was applied.

Continuous suction was used to maintain negative pressure at 125 mmHg. Every 12 h, wound rinsing was performed for three minutes using octenilin® wound irrigation solution. To ensure that the ideal quantity of irrigation solution was applied, it was instilled until the foam dressing was completely soaked (in presented cases volumes ranged between 42 mL and 110 mL, depending on the size of defect.)

The treatment continued for 6 days, after which the wound bed was fully prepared for surgery and free from visible signs of infection.

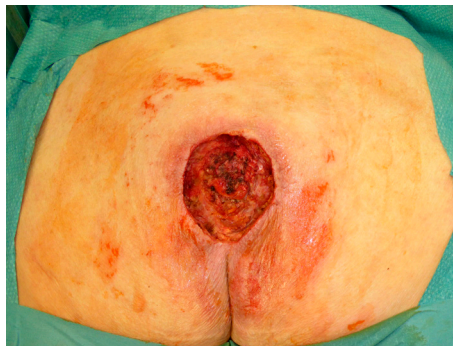
### Flap coverage surgery

Following successful preparation with NPWT and octenilin instillation, wound closure was indicated in all 13 patients. According to the reconstructive ladder, wounds may be covered in ascending order of complexity<sup>[24]</sup>. Flaps in particular - which, unlike skin grafts, have their own blood supply - have shown good results in treatment of complex defects<sup>[7]</sup>. A major challenge in flap coverage is adequate flap selection which involves considering several factors including the site of the pressure sore, flap design and the location of the flap relative to the site of coverage<sup>[7]</sup>. For covering large pressure sores in the gluteal/ischial region the posterior thigh flap is often used due to its large reservoir of skin, fascia and muscle<sup>[25]</sup>.

Local flap coverage was conducted in the first 3 patients, which all suffered from gluteal PU, by using the posterior thigh flap. For the additional 10 patients following local flaps were used: 3 fasciocutaneous VY-flaps [Figures 1 and 2] to cover 2 sacral [Figures 3 and 4] and 1 ischial PUs; 3 fasciocutaneous rotational flaps were chosen to cover sacral PUs; 2 myocutaneous posterior thigh flaps covered ischial/gluteal lesions [Figures 5 and 6] and 2 tensor fascia lata mycutaneous flaps were considered relating to trochanteric PUs.



**Figure 2.** Sacral pressure ulcer after wound closure with bilateral V-Y advancement flap



**Figure 3.** Sacral pressure ulcer grade IV (EPUAP) before debridement. EPUAP: the European Pressure Ulcer Advisory Panel



**Figure 4.** Sacral pressure ulcer after wound closure with gluteal rotational flap



**Figure 5.** Ischial pressure ulcer before debridement





**Figure 6.** Ischial pressure ulcer after wound closure with posterior thigh flap

## RESULTS

### Wound coverage and healing

During the 6 days of NPWT and instillation, visual signs of local inflammation were monitored at each dressing change. It was observed that inflammation decreased over the course of NPWTi treatment. Granulation tissue formation was observed in all thirteen cases.

Six days post-debridement, the wounds were clean with no visual signs of inflammation. The V.A.C. system was removed and wounds were rinsed with the antiseptic agent octenisept®.

The combination of NPWT and octenidine in all 13 patients showed that octenidine is well tolerated and no toxic tissue reactions were reported. These results are consistent with the biocompatibility index (BI) evaluated for octenidine, in which the antimicrobial activity and the cellular cytotoxicity of antiseptic agents are assessed. Octenidine demonstrated excellent results on this index, reflected by a BI greater than 1 and therefore superior to a number of antiseptic agents<sup>[23]</sup>.

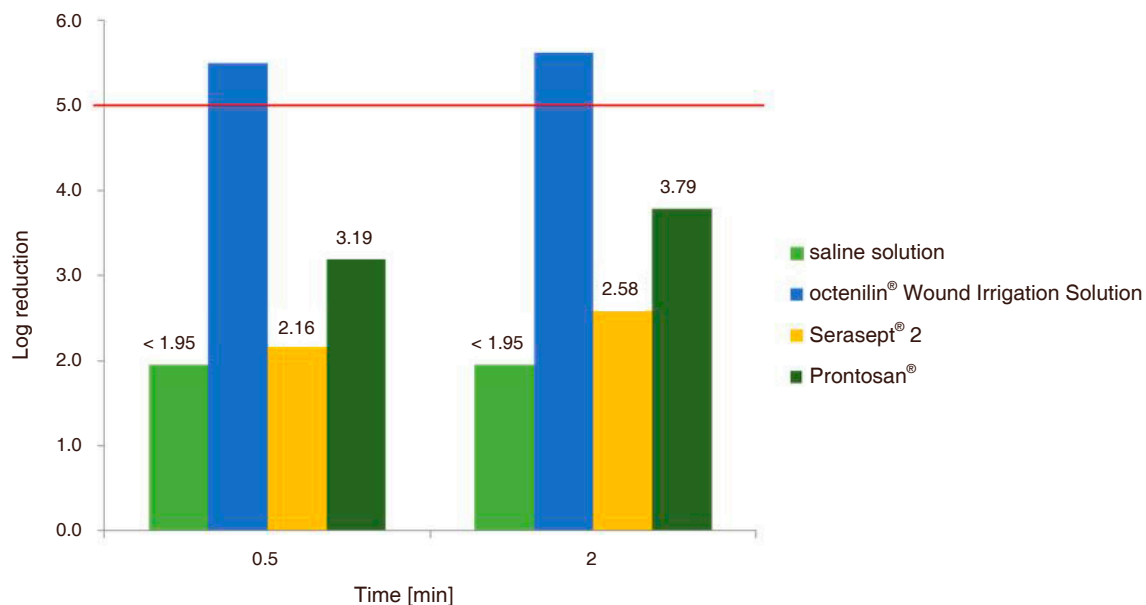
Following NPWTi treatment, the wound beds of all patients were clean and clear of infection. A suction drain was positioned under the flap to prevent postoperative fluid accumulation. Patients were cared for on air-fluidised beds to reduce pressure on the wound site.

No signs of inflammation or wound dehiscence around the wound site were observed on day 10 postoperatively. Every day, wound cleansing was conducted using octenisept®. Three weeks after surgery sutures were removed.

Thirty days post-debridement, normal wound healing without any signs of irritation or infection was observed. In 6 of 13 patients superficial wound healing disorders were reported, maximum until the 25th day after surgery. After 90 days the wounds showed complete healing. No further follow-up visits were required.

### In vitro tests results

Coagulase negative *staphylococci*, *Pseudomonas spp.*, *Proteus mirabilis*, *Acinetobacter spp.* and *E. coli* were



**Figure 7.** Reduction of live cell count given as decadic logarithm following 0.5, or 2 min of wound exudate exposure to saline solution (negative control), octenilin® wound irrigation solution, Serasept® 2, or Prontosan®

found to be the main flora identified on the wound exudates. There were four independent experiments for each rinsing solution. The results examined below represent the mean value for each one.

A sufficient bactericidal effect was achieved both after 0.5 and 2 min of exposure to octenilin® wound irrigation solution on the spiked MRSA strain and the accompanying flora of the vacuum exudates. Although, it also induced a lg RF > 5 after 0.5 min contact time the accompanying flora was not fully eradicated in two exudate samples. However, the polyhexanide (PHMB) based wound rinsing solutions (PHMB 0.04% or 0.1%) were not effective in bacteria eradication [Figure 7]. Saline solution which was used as the negative control induced a lg RF < 1.95 at all time points.

## DISCUSSION

The principal aim of studying the 13 patients was to examine optimal conditions for wound bed preparation following surgical debridement. All studied patients were admitted with category 4 PUs and their wounds were colonised with either *Streptococcus* or *Staphylococcus* species prior to NPWTi using octenilin® wound irrigation solution.

After debridement and a 6-day treatment period, the wounds were free from observed infection and granulation tissue was seen. Microbial load reduction was demonstrated in previously performed *in vitro* tests simulating clinical conditions, when wound exudates were loaded with MRSA. After 30-s exposure to octenilin® wound irrigation solution, a sufficient bactericidal effect was demonstrated. This testing formed the basis for the shortened instillation phase in NPWTi.

The novel concept of combining NPWT with an antiseptic wound rinsing solution was seen to be beneficial in wound bed preparation, prior to flap surgery in the patients studied. All studied patients demonstrated complete healing 90 days after initial wound debridement.

Of particular interest is the short instillation phase of just three minutes, when NPWT is combined with

octenilin® wound irrigation solution instillation. During the instillation of the rinsing solution the negative pressure is not maintained and the system is prone to leakage, so this phase should be as short as possible.

Conventional NPWT or the use of antiseptic soaked dressings are typically the treatments of choice for preparing the wound bed prior to grafting or flap coverage. In the novel approach described in this paper, both methods were combined successfully. A short treatment period was required using this approach, meaning that less than a week was needed for the combined NPWT/instillation phase. After only 6 days, there were no signs of wound infection and granulation was taking place in the studied patients.

Given that chronic PUs can be difficult to treat and are often accompanied by bacterial infections, future studies examining NPWT combined with instillation should be considered. It would be particularly interesting to undertake a comparative study examining different wound rinsing solutions. This could be useful in providing data on which to base optimum care.

Although NPWT is recognised as a useful treatment option for chronic wound management<sup>[1]</sup>, it is possible that in combination with octenilin® wound irrigation solution instillation, NPWT may also be considered as part of the management of other chronic complex wounds. In the “Negative-pressure wound therapy with instillation: international consensus guidelines”<sup>[26]</sup> an instillation time of 10-20 min using non-octenidine based rinsing solutions is regarded as appropriate. At the time of publication, octenidine based solutions were not available in the US. Perhaps it is now time to revisit these guidelines and give consideration to the much shorter instillation times observed in this study.

As seen in this study, the instillation of an antiseptic rinsing solution with proven *in vitro* antibacterial efficacy provides an interesting approach for effective wound healing. This method was found to be successful in all 13 patients studied, in terms of preparing the wound bed prior to surgical intervention.

After 2 min of exposure to octenilin® wound irrigation solution a sufficient bactericidal effect to eradicate MRSA and the accompanying flora of the wound exudates was shown during *in vitro* testing. In comparison the microbial load was not sufficiently reduced within the required contact time when the same wound exudates were exposed to different PHMB based rinsing solutions. Therefore it is worth considering that the short duration of antiseptic wound rinsing during NPWT, may be insufficient if PHMB rinsing solutions are used. This requires further investigation. Our findings are similar to those in a study conducted by Ludolph *et al.*<sup>[27]</sup>, where a total of 111 patients were treated with negative pressure therapy combined with instillation. They also found a positive effect concerning reduction of the bacterial load in contaminated wounds.

It is generally acknowledged that the high treatment costs of managing chronic wounds place a considerable burden on healthcare resources. Given the successful wound healing and absence of observed infection in all 13 patients, the combination of NPWT with octenidine wound rinsing could indicate a novel protocol for chronic wound management.

In conclusion, in this small study, 13 patients with category 4 PUs were managed with NPWT and instillation of octenilin® wound irrigation solution, following surgical debridement. The results demonstrated that this combination was effective in preparing the wound bed before the wound was surgically closed. No signs of infection were observed, good tissue compatibility with octenidine-based solutions was noted and complete healing was seen after 90 days. None of the observed patients required subsequent follow up appointments.

A broad-spectrum antimicrobial efficacy was demonstrated *in vitro* for octenilin® wound irrigation solution, with only a short contact time required and with good tissue compatibility. Further investigations are now required to examine in more depth the possibilities offered by NPWTi and octenilin® wound irrigation

solution instillation in the management of PUs.

## DECLARATIONS

### Authors' contributions

Writing and drafting of the manuscript, treatment of patients at St. Josef Hospital Vienna, Austria, sampling of exudates, microbiology: Matiassek J

Treatment of patients at St. Markus Hospital Frankfurt, Germany and at Innsbruck Medical University, Austria, critically revising the manuscript: Djedovic G

Treatment of patients at St. Markus Hospital Frankfurt, manuscript revision, artwork: Kiehlmann M

Treatment of patients at Hospital St. Gallen, Switzerland, critically revising the manuscript: Verstappen R

Study design, treatment of patients at St. Markus Hospital Frankfurt, Germany, critically revising the manuscript: Rieger UM

### Availability of data and materials

Patient records are available in respective hospital data bases.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

The study involved standard treatment regimens. All procedures were performed with full informed consent of patients. The study was performed in accordance with the Declaration of Helsinki.

### Consent for publication

Not applicable.

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Review

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# Prefabricated flaps and neoangiogenesis initiated via venous grafts in arteriovenous loops

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## Abstract

New developments in regenerative medicine are bound to revolutionize the way we approach loss of function and form in human organisms. Especially in the field of reconstructive plastic surgery new biotechnologies find their way from bench to bed. Biofabrication is an evolving field that aims to combine natural biologic processes with bioartificial constructs with the scope of reconstituting tissue without having to rely on autotransplantation. In this brief review we present the concepts of intrinsic vs. extrinsic neovascularization and we discuss the use of neovascularization in three dimensional matrices. In a clinical context matrix flaps for application in reconstructive surgery can be fabricated this way.

**Keywords:** Plastic surgery, flap prefabrication, tissue engineering, arteriovenous loop, venous graft, neoangiogenesis

## INTRODUCTION

Due to a steadily increasing life span not only in developed countries tissue wear-out or tissue loss becomes a growing problem to preserve sufficient quality of life. This holds especially true for elderly patients<sup>[1]</sup>. The interdisciplinary field of Tissue Engineering (TE) and Regenerative Medicine (RM) is one area where the hope for cure of these problems is seen. Within this specialty of life sciences “Biofabrication” recently has been added as an evolving research field that aims to optimize spatial cell and growth factor delivery into laboratory grown constructs to mimic the natural consistency of tissue like structures. According to Groll *et al.*<sup>[2]</sup>, from a research strategy perspective, Biofabrication within TE and RM aims at exploiting automated processes, for



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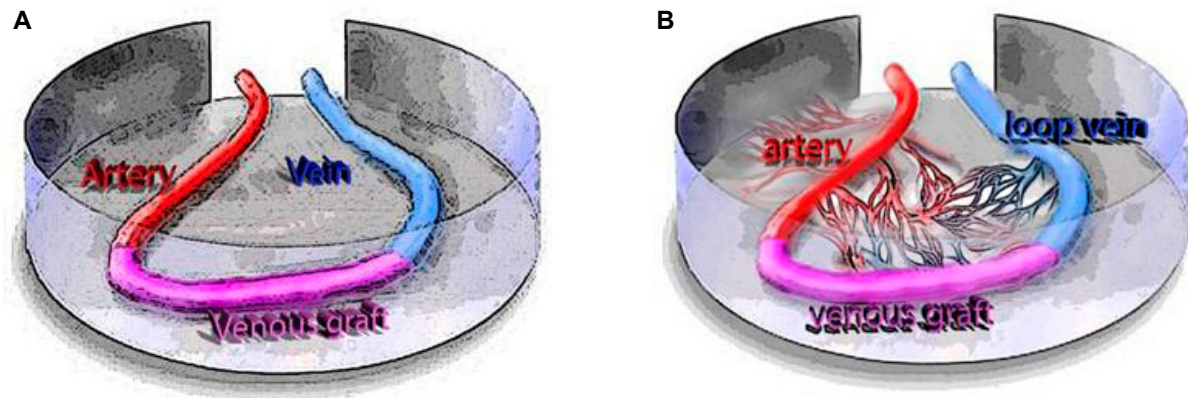
**Figure 1.** Prefabricated flap with skin grafted undersurface of radial arm forearm free flap to reconstruct the lower lip after extensive cancer resection

the most part Additive Manufacturing techniques, to generate cell-biomaterial constructs that, through their internal and external spatial arrangement may mature into functional tissue equivalents. Accordingly, these strategies typically target the development of scaffolds or composite constructs which exhibit tissue mimetic hierarchical features<sup>[3]</sup>. When living single cells, bioactive molecules, biomaterials, or cell-aggregates small enough to be printed are used for fabrication, the mentioned constructs can be achieved by bioprinting as defined by Guillemot *et al.*<sup>[4]</sup> earlier. While these new techniques offer reasonable advantages in TE and RM utilizing a subsequent maturation process after 3D cell printing it may help to yield structural biologically functional constructs, the clinical translation into relevant patient applications is still lacking<sup>[5]</sup>. TE constructs still suffer from a lack of vascularity at the time of transplantation into the human recipient.

Similar to our clinical routine with the prefabrication of individualized customized flaps [Figure 1] for transfer our group has repeatedly investigated the prevascularization of TE scaffolds utilizing an arteriovenous loop to further a clinical translation of laboratory grown tissue substitutes. We have therefore studied the effects of prevascularization in TE constructs using an arterio-venous loop (AV-loop) to 3D vascularize given matrices of relevant size before they are transplanted into the recipient in small and large animal models<sup>[6-8]</sup> and have successfully transferred this technique into clinical application<sup>[9]</sup>.

Nevertheless, efforts have been undertaken to unravel the complex mechanism and receptor network that are involved in neoangiogenesis. To better understand why and how neovascularization effects occur we investigated experimental AV-loop models several times<sup>[10-12]</sup> [Figure 2]. One insight from these experiments was that the interposition of a vein graft into the loop optimally leads to vascularization of the constructs, while this is not working equally well in the case of flaps with an arteriovenous bundle only<sup>[13,14]</sup>. To further enhance neovascularization it has also been demonstrated that a combination of intrinsic and extrinsic vascularization even yields faster neovascularization<sup>[15]</sup>. Polykandriotis *et al.*<sup>[13]</sup> have shown that early arterialization and angiogenesis in the AV-loop in a fibrin matrix with an interpositional venous graft (IVG) segment, which was placed into a closed chamber and embedded into a fibrin gel in an animal model, revealed direct luminal neovascular sprouting, evident between day 10 and day 14 from the vein and the IVG but not from the arterial segment.

Investigating the special role of the venous graft itself within the experimental setting of an AV-loop to vascularize TE constructs seems valuable. From clinical observations in prefabricating flaps or transplanting free flaps with arterial or venous extensions or utilizing AV-loops to connect the flaps<sup>[16]</sup> it seems obvious



**Figure 2.** A: The AV-loop in the isolation chamber. V-femoral vein, A-femoral artery, G-venous graft, C-isolation chamber. After exposure of the femoral neurovascular bundle at the medial thigh of the rat, a femoral venous graft is harvested from the contralateral side and interposed between the femoral vessels by anastomoses. The isolation chamber is placed in the medial thigh of the rat and 300  $\mu$ L of the fibrin matrix are applied at the bottom of the chamber. The arteriovenous fistula is laid onto the clot with the artery and vein exiting through an opening at the proximal pole and are covered with the rest of the fibrin clot. The lid is closed and the chamber with the matrix inside is fixed onto the adductor fascia at the medial thigh; B: after an interval of approximately 6 weeks, neovascular sprouts emerge from the AV-loop and form new fibrovascular tissue

that the interpositional vein graft itself may play a crucial role in neovascularization.

### OWN EXPERIENCE OF THE AUTHORS

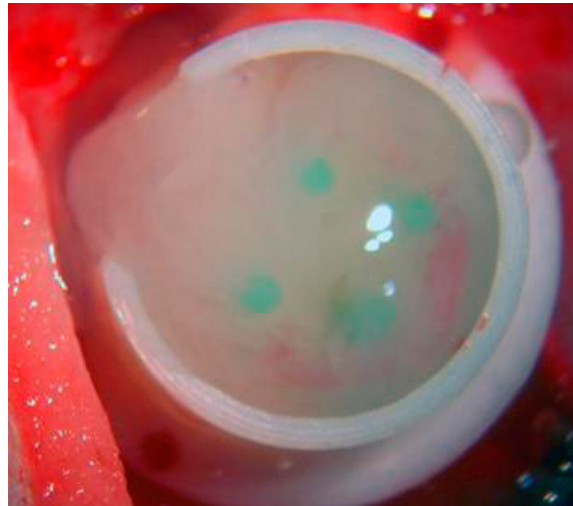
We have reviewed numerous of our own studies utilizing an AV-loop in small and large animals to 3D vascularize scaffolds or to study principles of neoangiogenesis for tissue generation or in the context of cancer research<sup>[3,7,10,11,17-22]</sup>. The process of establishing an arteriovenous loop in a rat model is described in detail by Weigand *et al.*<sup>[23]</sup>. To analyse the phenomenon of neovasclogenesis from such an AV-loop, as previously described in earlier studies<sup>[13,14,24-26]</sup> AV-loops were created in inbred male Lewis rats weighing approximately 250 g (Charles River, Sulzfeld, Germany) in various study designs. The loops were embedded into a custom-made cylindrical Teflon isolation chamber, which was fixed in the medial thigh of the rat by means of polypropylene 5-0 and in most of the studies 300  $\mu$ L of the fibrin matrix were placed at the bottom of the chamber. The arteriovenous fistula was then laid onto this clot with the artery and vein exiting through an opening at the proximal pole and was then covered with the rest of the fibrin clot.

We also performed numerous studies with bone matrices or scaffolds in the small and in the large animal model.

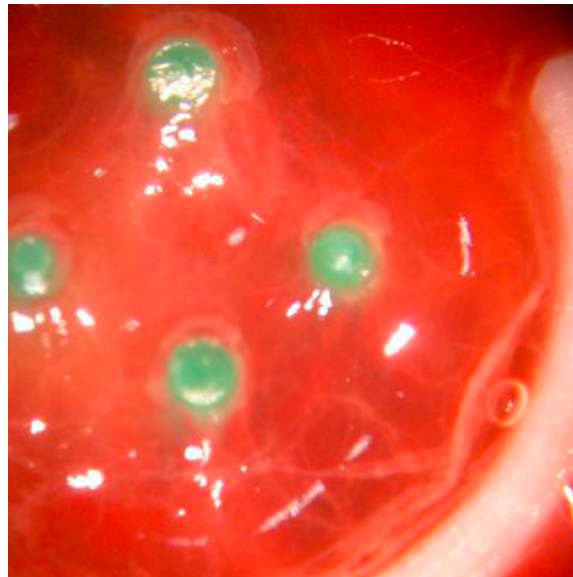
Our primary series utilized the TISSUCOL-Kit 2,0 Immuno (Baxter GmbH, Unterschleißheim, Deutschland) according to the manufacturers recommendations. When using fibrin alone a fibrin clot of 600  $\mu$ L with end concentrations of 33.7 mg/mL Fibrinogen and 25 IU/mL Thrombin was used as previously described<sup>[13,23,27]</sup> [Figures 3 and 4].

To investigate the neoangiogenesis and to study the cycle of sprouting and vasculogenesis in this context, 3D computed tomography was performed in order not to sacrifice the experimental animals. Corrosion casts were another method to visualize vasculogenesis. For this end at different time intervals from implantation to explantation, AV-loops were perfused with a low viscosity resin and were processed for scanning electron microscopy of the vessel wall. Controls were performed with immunohistochemistry and by means of computer tomography which allowed linear *in vivo* investigations.

Visualization of angiogenesis phenomena over various time points was attained with the help of the



**Figure 3.** Fibrin matrix within experimental chamber including an arteriovenous loop: at the time of implantation the gel matrix is covering the AV-loop, which is fixed with 4 pins to prevent dislocation of the loop

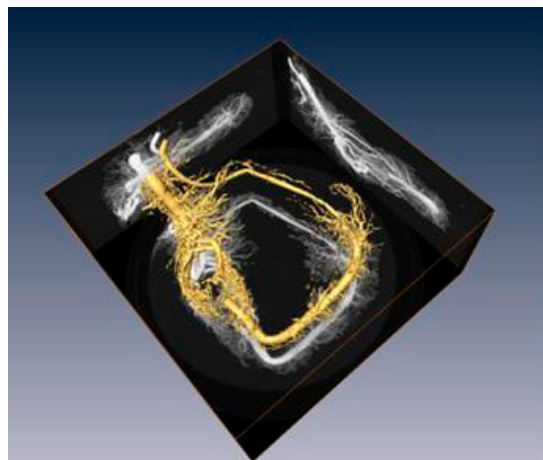


**Figure 4.** Fibrin matrix within experimental chamber including an arteriovenous loop: at day 12 the matrix is showing red colour as a sign of vascularization

corrosion cast technique [Figure 5]. For this purpose the animals aorta and inferior vena cava were exposed through a median incision from the xiphoid process to the pubic symphysis. The aorta was then cannulated through a 24-gauge catheter and the inf. vena cava was severed. After cannulation of the aorta the vascular system of the rat was rinsed with approximately 200 mL of heparinized Ringer solution (100 IU/mL) under a hydrostatic pressure between 80 and 100 mmHg and until fluid escaping from the severed inf. vena cava was clear. Perfusion of the caudal vascular system with 20 mL of a methylmethacrylate resin in a mixture of 4:1 prepolymerized oligomere to methylmethacrylate monomer (Aldrich Chemie, Germany) and benzoyl peroxide as a catalyst (Mercor, Ladd Research Industries, Burlington, VT) was then performed to gain vascular replicas, which could be investigated with a scanning electron microscopy (SEM). In addition to better detect the phenomena of luminal sprouting from the central vascular axis, microdissection under a microscope was undertaken as a modification of a method described previously<sup>[28]</sup>.



**Figure 5.** Example of corrosion cast showing enhanced neovascularization with vessel sprouting and formation of capillary bed from an experiment with a duration of 6 weeks: vasculogenesis is more pronounced from the venous side than from the arterial side



**Figure 6.** Micro-computed tomography of AV-loop in chamber with visibly enhanced neovascularization including vessel sprouting and formation of a capillary bed from the venous side rather than from the arterial side from an experiment with a duration of 2 weeks

Micro computed tomography (CT) was performed with a FORBILD High Resolution Micro-CT (Erlangen, Germany)<sup>[13]</sup> [Figure 6]. We have previously shown another possibility to visualize the vessels fully in 3D by calculating an isosurface for all voxels above a given threshold<sup>[13]</sup>.

### THE ANGIOGENIC CASCADE IN THE AV LOOP MODEL

In a first line of experiments we verified that vascularization of a confined porous matrix was feasible. For this purpose we combined the AV-loop model, with a porous bone matrix and encased the system in an isolation chamber. Explantation times were set to 2, 4 and 8 weeks<sup>[29]</sup>.

Within 8 weeks post implantation, the entire matrix was usually infiltrated with a fibrovascular tissue. Essentially, the matrix was vascularized. We evaluated the results by means of histomorphometry, immunohistochemistry, corrosion casting, micro-magnetic resonance angiography (MRA) as well as micro-



computed tomography. We noticed an undisturbed perfusion of the extremities during the whole period with a general patency rate of 83.3% of the AV-loops as previously shown<sup>[13]</sup>. Pushing on, we found out that the AV loop was able to vascularize a fibrin matrix. However, neovascularization seemed to emerge mainly from the venous part and the interpositional graft of the AV-loop and less from the arterial segment<sup>[13]</sup>.

In another line of experiments, after addition of vasoactive growth factors (VEGF and FGF) at the time of implantation we could observe that the angiogenic events were significantly accelerated in the group with the growth factors, in terms of onset of sprouting as well as progression into the phase of remodelling<sup>[24]</sup>.

With micro-CT it was possible to visualize the patency of the vascular axis which could be confirmed both as was macroscopically seen at the time of explantation. When we compared the findings to long term observations after 6 weeks, the results at two weeks demonstrated initial arteriovenous shunting through the graft. This indicates that the neoformation of the capillary network within the constructs in the chamber forms an organoid like structure with an artery and a draining vein.

In the same time, the prevascularized matrices were secondarily loaded with a plethora of different types of stem cells, including osteoblasts and liver stem cells. It was a natural evolution that the AV loop was evaluated in the big animal model. Beier *et al.*<sup>[30]</sup> performed the AV-loop operations on sheep with great success.

Currently the AV-loop is utilized in selected cases in the clinical setting<sup>[9,11,16,31]</sup>.

## IMPORTANCE OF THE AV LOOP MODEL FOR RECONSTRUCTIVE MEDICINE

In general, phenomena of neovascularization and neoangiogenesis play a crucial role in Plastic Surgery and have led to the prefabrication and preformation of customized flaps<sup>[32]</sup> that are created in situ in the patient<sup>[33,34]</sup>. Flap prefabrication is a clinically applied method to generate custom made transplants with the help of arterIALIZING tissue either with arteriovenous bundles or arteriovenous loops<sup>[35]</sup>. It has been described for various tissues, including skin, fasciae, muscle, periosteum and/or bone<sup>[36-39]</sup>. In the clinical scenario both arterial and venous supercharging have been postulated to potentially improve the survival area of prefabricated flaps and to extend the possibilities of creating custom made tissue flaps<sup>[40-42]</sup>.

The combination of prefabrication and tissue engineering has been investigated intensely<sup>[39,43,44]</sup>. From this clinically proven method we introduced the technique of prevascularizing scaffolds and constructs in the context of Tissue Engineering with the help of an arteriovenous loop incorporated into a given matrix<sup>[3,23]</sup>. In small and large animal models we observed that the arteriovenous loop triggers a vivid and rapid angiogenetic response<sup>[7,11,17-19]</sup>. In our experiments male inbred Lewis rats were used. In personal communications with other groups we were intrigued to hear that on Wistar rats the phenomenon of limb ischaemia was common. Our data shed light on the early phase of angiogenesis between day 2 and day 4, as we could not find vessel sprouting. On the other side between the 10th day up to day 14 a vivid angiogenetic response was seen that led to a rapid induction of a dense neocapillary microvascular network. In our AV-loop model we had expected an early sprouting from capillaries and venules as has been described generally in the context of angiogenesis as soon as 27 h after the angiogenetic trigger<sup>[45]</sup>. The influence of the fibrin matrix that we used might be causative for this observation.

Tissue engineering (TE) has been a promising research field for more than two decades by now. Nevertheless despite recent advances the translation of TE into daily clinical practice has not yet been achieved. One major obstacle is the step of transplanting a generated tissue construct into a recipient site, where it is dependant from the ingrowth of small vessels into the scaffold. Since this process of revascularization takes several days any cell within a matrix rely on nourishing by diffusion only. Intrinsic prevascularization

will allow cells within a matrix to survive the critical time frame until vascularization has taken place and nourishing substances can be delivered from the recipient into the bioartificial construct<sup>[10]</sup>.

Other studies have used Matrigel as a matrix for the AV-loop and showed enhanced neovascularization<sup>[46]</sup>. However, for potential clinical applications, matrigel, extracted from the Engelbreth-Holm-Swarm mouse sarcoma, is not a matrix of choice in patients. In contrast, fibrin as a matrix is a commercially available product that has been in clinical use for decades. It possesses several advantages as a potential matrix, some of which have to do with the interplay between controlled fibrinolysis and onward angiogenesis<sup>[47]</sup>. We have shown that the kinetics of neoangiogenesis and neovascularization can be enhanced by addition of soluble growth factors which boost neovascular growth<sup>[48,49]</sup>. Fibrin is one possible carrier and has been repeatedly demonstrated to be a suitable carrier for cultured cells, such as in cultured human keratinocyte transplantation<sup>[50,51]</sup> and muscle TE.

The formation of new blood vessels is a fundamental process in tissue regeneration and in organ development. Angiogenesis is most frequently associated with inflammation, along with hypoxic conditions and cell infiltration, although it remains elusive how molecular and cellular mechanisms underlying inflammatory reactions in detail regulate angiogenetic processes. Hypoxia-inducible factors (HIFs), HIF1 alpha and HIF2 have been investigated as potential indicators of neoangiogenesis in various contexts<sup>[52-55]</sup>.

The influence of mesenchymal stem cells might also play a critical role in neovascularization<sup>[56,57]</sup>. It has been hypothesized that angiogenesis and vasculogenesis can be studied in the context of TE with regard to similar processes that occur in tumorigenesis and that TE models could help to further clarify these biological events<sup>[58]</sup>. Phenomena of intimal hyperplasia and thickening of the vessel wall during neoangiogenesis have been well described<sup>[59-61]</sup>. It has also been noted that myointimal thickening leads to a continuous decrease in the luminal diameter<sup>[60]</sup>, which is an explanation for the decrease in the luminal vessel diameters that we observed following day 7 in our experiments. It is not clear why the interpositional vein graft shows the highest increase in angiogenesis and if there is a critical length of such an AV axis that would limit the clinical applicability. From clinical data in using long bypass grafts for free flap transplantation we suggest that the length of an interpositional vein in such circumstances graft is limited<sup>[16]</sup>. If bioartificial vessels, which would be desirable in terms of minimizing the donor site morbidity, will become clinically available and will offer the same capacity of sprouting and neoangiogenesis remains yet open.

## CONCLUSION

Although the AV-loop model is rather complex and time consuming, it offers the unique advantage of studying neoangiogenesis and vasculogenesis in a controlled environment, to observe the mechanisms of vessel arborisation and remodelling, and to investigate changes in the perfusion pattern in correlation to the specific segments of the AV-loop.

## DECLARATIONS

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### Authors' contributions

Prepared this manuscript: Polykandriotis E

One of the first to establish the AV Loop Model: Polykandriotis E, Arkudas A, Horch RE

Edited the manuscript and provided valuable illustrations material, developed and established the AV Model: Arkudas A

Currently working with the AV Loop Model, contributed with her own insight for the future of the AV Loop: Weigand A

Edited parts of the manuscript: Weigand A, Cai A

Rewrote a substantial part of the manuscript: Horch RE

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#### **Conflicts of interest**

The authors declare that there are no conflicts of interest.

#### **Ethical approval and consent to participate**

Not applicable.

#### **Consent for publication**

Not applicable.

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Case Report

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# Defect reconstruction of the trochanter major after necrotizing fasciitis and multiple operations using an arteriovenous loop and latissimus dorsi free flap

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## Abstract

Necrotizing fasciitis (NF) is a severe soft tissue infection which has to be treated with a radical debridement as the key element. In the further course often large tissue defects occur, so that a long-term stable defect reconstruction plays a crucial role after any successful debridement. The reconstruction can include split skin grafting or local and free flaps. Here we present a case of a 41-year-old male patient with a NF in the trochanter major region after spondylodesis and spinal cord stimulation (SCS) device implantation. After multiple operations including local and free flaps we performed a defect reconstruction using an arteriovenous (AV) loop and subsequent free latissimus dorsi transplantation leading to no further operations. This complex reconstruction can be considered as the final stage of any reconstruction latter.

**Keywords:** Necrotizing fasciitis, arteriovenous loop, free latissimus dorsi flap transplantation

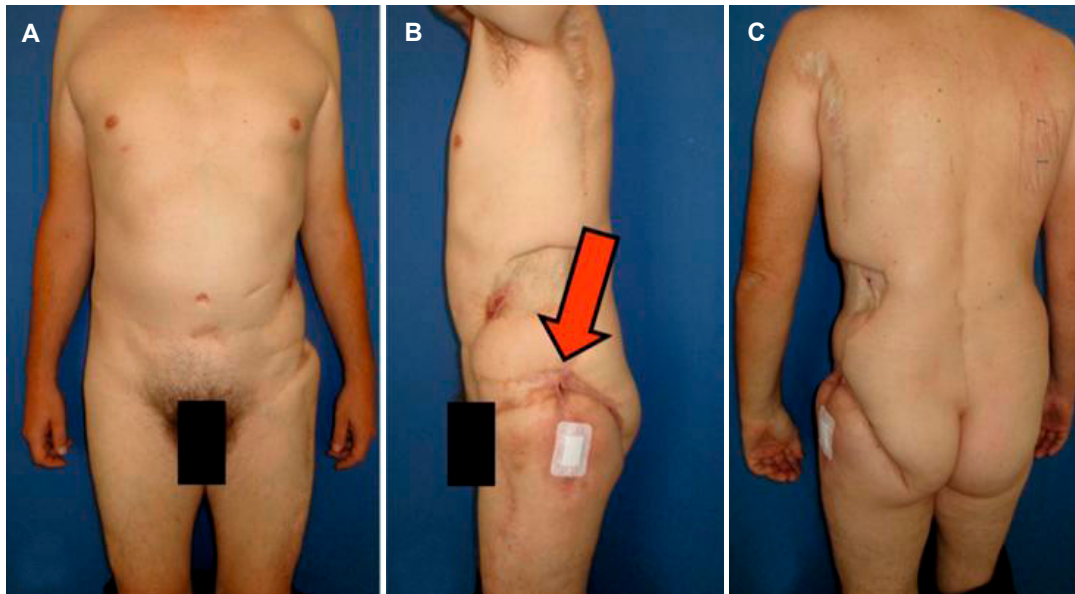
## INTRODUCTION

Necrotizing fasciitis (NF) is a rare and severe infection caused by different kinds of bacteria<sup>[1,2]</sup>. The first and most important therapy is a radical debridement of all infected tissue leading to large soft tissue defects. Mostly, these tissue defects can be reconstructed using split skin grafts, but in areas of joints or when other structures like bone, vessels or nerves are exposed, defect coverage using local or free flaps is required. In the



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**Figure 1.** Forty-one-year-old male patient with an unstable scar and fistula in the trochanter major region (arrow)

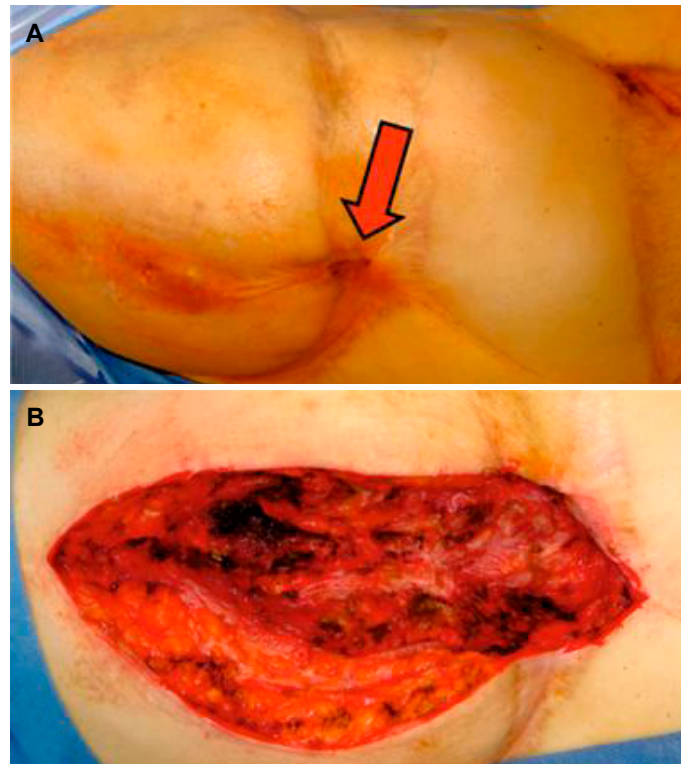
groin and hip region local random pattern flaps such as rotational flaps can be used. Also pedicled flaps such as the anterior lateral thigh (ALT) flap or vertical rectus abdominis myocutaneous (VRAM) flap can achieve stable healing of these defects<sup>[3-5]</sup>. When local flaps are not available due to previous operations or did not lead to the required result, free flaps are the last therapeutical option. Free flaps are raised at a distant body part also known as donor site and are microsurgically anastomosed to recipient vessels at the defect area<sup>[6]</sup>. Typical free flaps are the latissimus dorsi flap, the parascapular flap or perforator flaps such as the deep inferior epigastric perforator (DIEP) or the ALT flap. When local recipient vessels are missing, e.g., in cases of trauma or infection, an arteriovenous (AV) loop from a main vascular axis can be used to enable local microsurgical anastomoses for free flap transfer<sup>[7,8]</sup>.

Here we present a patient with NF and multiple operations including local and free flaps who was referred to our hospital with ongoing fistulas in the trochanter major region. After radical debridement defect coverage was achieved using an arteriovenous loop with subsequent free latissimus dorsi flap transplantation.

## CASE REPORT

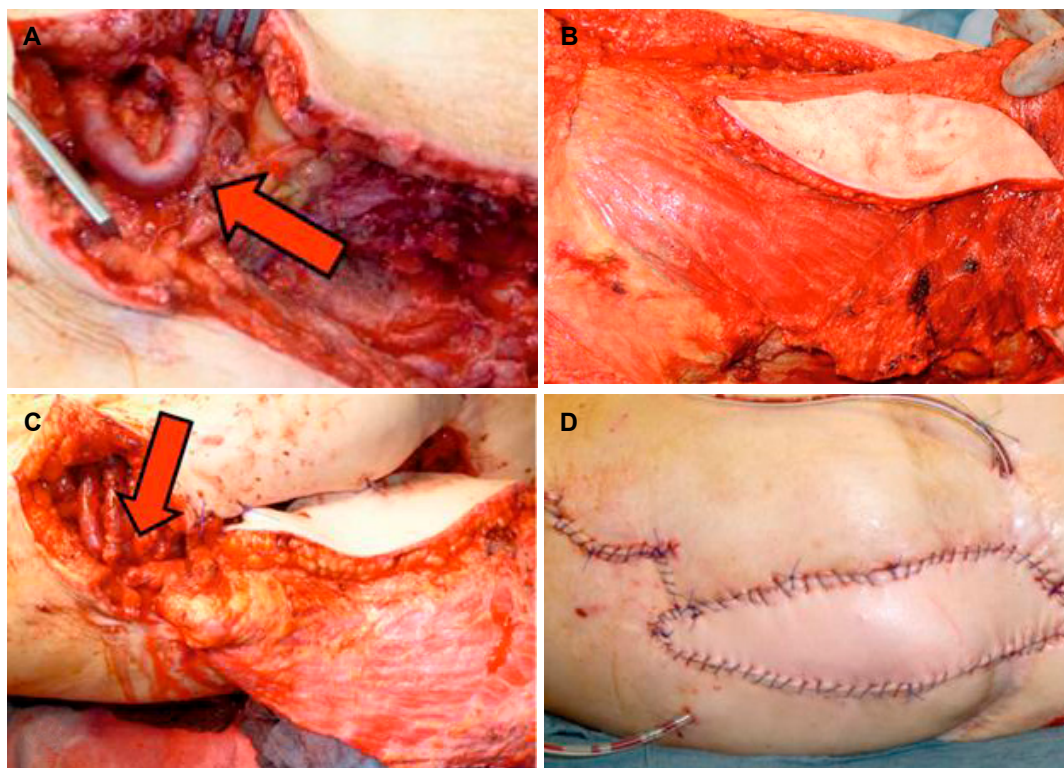
A 41-year-old male patient suffered from back pain since he was 16 years old. He received multiple treatments including a spondylodesis of L4 and L5 using an anterior approach. In the further course the patient developed a wound dehiscence of the abdominal incision which was treated conservatively. Also the spondylodesis was extended to S1. Due to persistent back pain a spinal cord stimulation (SCS) device was implanted leading to a NF of the left flank. Therefore the SCS device was explanted and in the further course a split skin graft transplantation of the left flank was performed. Also a rotational flap was made in the left groin. Due to an unstable scar in the left iliac crest region defect coverage was attempted using a groin flap. Afterwards again a NF occurred in the left hip region resulting in multiple fistulas after several debridements. In the further course a pedicled DIEP flap was attempted and a free parascapular flap anastomosed to the circumflexa iliaca profunda vessels and a pedicled ALT flap were performed in order to achieve a stable healing of this region.

Unfortunately, the patient still suffered from an ongoing fistula and an unstable scar in the left trochanter



**Figure 2.** Before (A) and after (B) radical debridement of the scar tissue in the trochanter major region

major region and was therefore referred to our hospital [Figure 1]. An magnetic resonance imaging (MRI) examination of the left thigh revealed a fistulating process in subcutaneous region of the left upper thigh extending down to the gluteus maximus muscle. Also, bacteria culture of wound exudates showed a staphylococcus aureus contamination. We performed several debridements of the scar tissue and the fistula down to the trochanter major and intermittent negative pressure wound therapy (NPWT) [Figure 2]. Histological examination revealed a chronic granulating and ulcerating soft tissue infection without proof of an osteomyelitis. In a two-step procedure, defect reconstruction was achieved using a free latissimus dorsi flap [Figure 3]. Due to missing recipient vessels in the defect area, AV loop was created from the left femoral vessels using a saphenous vein graft in the first step. Postoperatively patency of the AV loop was checked using Doppler ultrasound. After four days a free myocutaneous latissimus dorsi flap was microsurgically anastomosed to the AV loop. Therefore the AV loop was cut into two legs, and the arterial anastomosis of the subclavian artery and the arterial AV loop leg was performed under microscope magnification using 8-0 suture material. The venous anastomosis of the subclavian vein and the venous AV loop leg was performed using a 4.0 mm coupler device. The latissimus dorsi muscle was used to seal the tissue defect down to the trochanter major whereas the skin island was inserted to close the skin defect without the requirement of a split skin graft. Postoperatively flap perfusion was checked using capillary refill of the skin island and Doppler ultrasound. The flap was adequately perfused at all times and no revision war necessary. Mobilization of the patient was performed using a dangling regime. Cefuroxim was administered intravenously during the hospital stay and afterwards in oral form for a total of six weeks postoperatively. Due to a postoperative anemia the patient received two red cell concentrates in the further course. The patient was discharged from the clinic 13 days after free flap transplantation. In the further course a wound healing disorder occurred in the ventral part of the skin island. MRI examination of the pelvic showed no recurrent fistula, whereas a subcutaneous infection could be observed leading to no further operative intervention.



**Figure 3.** An arteriovenous loop (A, arrow) was created in the left upper thigh using a greater saphenous graft. Afterwards, a latissimus dorsi flap was raised (B) and microscopically anastomosed to the AV loop legs (C, arrow). Result at the end of the operation with a well perfused latissimus dorsi skin island without signs of arterial or venous congestion (D). AV: arteriovenous

## DISCUSSION

NF can be caused by small skin lesions and is predominantly spread along the deep fascia. There are different kinds of bacteria known to be responsible for these massive infections such as beta-hemolytic group A streptococci, anaerobes or clostridium and fungal species<sup>[9]</sup>. In the presented case the staphylococcus aureus was proven to be causally responsible for the ongoing fistula and subacute infections. The bacterium was first documented in the abdominal wound dehiscence after the first spondylodesis operation. After implantation of the SCS device an abdominal NF had occurred as a device-related infection<sup>[10]</sup>. Due to the bacterial biofilm on the SCS device, one important part of healing such infections is the explantation of any alloplastic material. The radical debridement is the key element of any successful NF treatment. Even when the patients are treated correctly, the mortality rate amounts up to 15%-46%<sup>[9]</sup>. Without adequate treatment the mortality rate raises up to nearly 100%. Afterwards a split skin grafting was performed in the groin/hip region. Due to its unstable reconstruction a local flap was performed. Basically, there are two different types of flaps regarding their vascularization: flaps perfused by a random pattern vascular pathway, also known as the extrinsic vascularization, and flaps, which rely on a vascular axis, so called intrinsically perfused flaps<sup>[11,12]</sup>. Furthermore, intrinsically perfused flaps can be transferred as pedicled flaps into the defect or can be transplanted using microsurgical techniques as free flaps to distant parts of the body<sup>[3,13]</sup>. Based on the reconstruction latter, in this case a rotational random pattern flap was performed first to reconstruct the lateral defect in the groin/hip area. Afterwards local pedicled flaps were used to achieve a stable wound healing. Therefore a pedicled groin flap and the attempt of a DIEP flap were performed. As a next step, a free parascapular flap was microscopically anastomosed to the circumflexa iliaca profunda vessels in order to reconstruct the defect in the trochanter major region. Due to its ongoing fistulas also a pedicled ALT flap was transferred to this region. At this stage the patient was referred to our hospital. There were no local flaps



available, neither random pattern nor pedicled flaps. For free flap transplantation, also no recipient vessels such as the circumflexa femoris lateralis vessels (previously used for the ALT flap), the circumflexa iliaca profunda vessels (used for the free parascapular flap), the circumflexa iliaca superficialis vessels (used for the pedicled groin flap) or the deep inferior epigastric vessels (used for the DIEP attempt) were available. Furthermore, the femoral vessels were too distant to the defect. Therefore AV loop was created from the femoral vessels using a great saphenous vein graft<sup>[14,15]</sup>. These kinds of AV loops have a relatively high thrombosis rate compared to short subclavian loops for example<sup>[16]</sup>. Therefore we recommend a two-step procedure with first implantation of the AV loop and in a second procedure free flap transplantation. Using this protocol, flap loss due to an AV loop thromboses can be minimized. Patency was checked preoperatively using a Doppler ultrasound. For defect reconstruction we used a myocutaneous latissimus dorsi flap. This flap possesses a long vascular pedicle with adequate vessel diameter for microsurgical anastomoses to the great saphenous vein of the AV loop legs and it is known for its low flow resistance and therefore low complication rate when combined with an AV loop. Also, the latissimus dorsi flap provides enough muscle tissue for sealing the defect down to the trochanter major. Using the skin island a defect reconstruction without split skin grafting was possible.

Gawaziuk *et al.*<sup>[17]</sup> also previously reported on a case series of free flap transfer after NF and was able to show no flap failures and a minimal complication rate. Beier *et al.*<sup>[18]</sup> were also able to demonstrate a thoracic reconstruction using a bilateral free pre-expanded tensor fascia latae (TFL) flap in an 8-year-old child. Also Barbosa *et al.*<sup>[19]</sup> showed a chest wall reconstruction using a free latissimus dorsi flap after NF. The special feature of the presented case are the multiple previously performed operations including local pedicled and random pattern flaps as well as a free flap, making any local flap impossible and further free flaps significantly more difficult. Therefore we had to perform a combined approach using AV loop and subsequent free latissimus dorsi transfer.

Tissue defects after NF often require an adequate defect reconstruction. Mostly this can be performed using split skin grafts or in regions with exposed structures such as bone or vessels, local or free flaps can achieve long-term stable results. Here we present a case of a NF in the trochanter major region after spondylodesis and SCS device implantation and multiple preoperations including local and free flaps. Therefore we performed a complex microsurgical reconstruction using AV loop and free latissimus dorsi transfer. This can be considered as the final stage of any reconstruction latter due to its high complexity.

## DECLARATIONS

### Authors' contributions

Manuscript preparation: Arkudas A, Regus S, Meyer A, Lang W, Schmitz M, Horch RE

Operative procedure: Meyer A, Lang W, Schmitz M

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Not applicable.



## Consent for publication

Written informed consent for publication was obtained by the patient.

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Review

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# Tissue conditioning - strategies to improve perfusion and reduce ischemia - reperfusion injury

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## Abstract

Ischemia as well as ischemia-reperfusion injury (IRI) can cause serious tissue damage and therefore is a feared complication in reconstructive surgery. This is the reason why researchers around the world invest their efforts to improve tissue viability after ischemic events. Tissue conditioning offers a broad scope of different techniques which can be applied pre-, peri- or postoperatively to adapt the affected tissue to the subsequent stress during and after ischemia to prevent or minimize IRI. The different ways of tissue conditioning in flap surgery include surgical delay, ischemic conditioning, remote ischemic conditioning as well as thermic preconditioning and other techniques, using growth factors, pharmaceutical agents, extracorporeal shock waves as well as stem cells. Therefore, we want to shed some light on the effects of ischemia and ischemia-reperfusion injury and further illustrate the different strategies of tissue conditioning with special concern to flap surgery but also regarding wound healing in general.

**Keywords:** Tissue conditioning, ischemia, ischemia-reperfusion injury, reconstructive surgery, flap surgery, wound healing

## INTRODUCTION

Cell damage caused by ischemia affects almost all clinical disciplines, seen in daily clinical routine for example as heart attacks, strokes, in organ transplantations as well as in reconstructive surgical procedures such as flap surgery<sup>[1]</sup>. Ischemia as well as ischemia-reperfusion injury (IRI) represent a formidable challenge



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in the transplantation of solid organs, in vascularized tissue allotransplantations (VCA) such as hand or face transplantations and in free flaps. In VCA for example, cold ischemia time is 6 h on average<sup>[2,3]</sup>. The importance of ischemia reperfusion-injury in tissue transplantation is clearly illustrated by its impact on early graft function as well as long-term outcomes<sup>[4]</sup>.

Insufficient tissue perfusion plays an important role in chronic wounds as well. Tissue hypoxia is responsible for a lack of energy metabolism, cell proliferation, angiogenesis, cytokine release as well as enzyme activity and therefore leading to an impairment of the tissue repair process<sup>[5-7]</sup>. Common causes for tissue hypoxia in chronic wounds are vascular alterations, oedema and fibrosis resulting in reduced oxygen partial pressure ( $pO_2$ )<sup>[7]</sup>. An interesting discovery is that  $pO_2$  in chronic wounds is 5-20 mmHg compared to 30-50 mmHg in control tissue<sup>[8]</sup>. In plastic surgery, tissue perfusion is of special concern due to the field of reconstructive surgery, where temporary tissue ischemia in free flaps as well as reduced perfusion in pedicled flaps has to be accepted to be able to treat tissue defects. In skilled and experienced hands, total flap loss is reported to occur in 1%-7% of cases, depending on recipient site and cause of the tissue defect<sup>[9-12]</sup>. But the rate of partial flap necrosis is much higher, with rates of 7%-20% in free flaps and even 20%-33% in pedicled flaps<sup>[13-16]</sup>. Partial flap necrosis often requires further operations, thus putting a significant burden on the affected patient as well as the healthcare system.

All those examples illustrate the significance of tissue blood supply and the need for methods to improve it. Or, as Gillies<sup>[17]</sup> once put it, “plastic surgery is the constant battle between beauty and blood supply”.

In this unsystematic review, we want to shed some light on the effects of ischemia and IRI on the affected tissue and illustrate different strategies of tissue conditioning focusing on its use in flap surgery.

### **Pathomechanisms of ischemia and IRI**

The persistence of insufficient tissue perfusion or total ischemia results in a loss of oxygen supply and therefore causes a change of cell metabolism as an adjustment to the lack of the aerobic pathway in the respiratory chain. This leads to an accumulation of metabolites as well as radicals and causes cell death<sup>[18,19]</sup>. Ironically, restauration of perfusion causes additional tissue damage due to inflammatory mechanisms caused by the release of oxygen compounds. Those lead to an activation of neutrophils and a consecutive adhesion between granulocytes and endothelial cells causing segmental vessel occlusion in postcapillary venules, transendothelial leukocyte migration and the release of tissue-damaging enzymes. This pathomechanism is referred to as the IRI<sup>[20-25]</sup>. With regard to flap surgery, flap survival is mainly depending on the integrity of the vascular pedicle and its “macrovascular” perfusion<sup>[26]</sup>. IRI on the other hand affects the microcirculation of the entire flap due to the inflammatory process and the increase in oxygen free radicals in the early stages of reperfusion<sup>[27]</sup>. Therefore, partial flap necrosis is often caused by an insufficient microcirculation mainly in the distal parts of the flap.

Total flap necrosis on the other hand is most often caused by thrombosis of the pedicle. Timely revision of the anastomosis is paramount to reestablish blood flow to the flap. However, such events can lead to an increase IRI which in turn can lead to intravascular hemoconcentration, endothelial swelling, interstitial edema formation as well as inflammatory processes due to the reperfusion injury. In its highest degree, IRI can lead to a no-reflow phenomenon which also leads to complete flap loss<sup>[28-30]</sup>.

### **Tissue conditioning**

There are different means of pre- or peri- and postoperative techniques to adapt the tissue to the subsequent stress during and after ischemia to prevent or minimize IRI [Table 1].

**Table 1. Different ways of tissue conditioning**

<b>Tissue conditioning</b>
Surgical delay
Ischemic preconditioning
Remote ischemic preconditioning
Thermic preconditioning
Growth factors
Extracorporeal shock waves
Stem cells
Pharmaceutical preconditioning

### *Surgical delay*

Surgical delay is the predecessor of modern preconditioning techniques. By raising the flap itself without severing its pedicle, the vessels along the axis of the flap reorganize and increase in size, leading to a better perfusion of the distal flap due to a dilation of linking and choke vessels, causing a connection of adjacent vascular territories which could be demonstrated in animal models as well as in humans<sup>[31,32]</sup>. Direct linking vessels have a large caliber and connect adjacent vascular territories by connecting perforators themselves, while indirect linking vessels, also known as choke vessels, connect vascular territories via recurrent flow through the subdermal plexus<sup>[33,34]</sup>. The mechanisms behind this are still not fully understood but there are many animal studies that could show neovascularisation, vasodilation and reorganization of vessels due to surgical delay<sup>[35-37]</sup>. Although surgical delay proved to increase flap perfusion and therefore increased the survival of flaps in the clinical setting<sup>[38,39]</sup>, there are also major disadvantages to this strategy, especially the need for additional surgery and its risks for the affected patients as well as increased health care costs due to longer hospital stays. Especially in TRAM flaps surgical delay was used but due to the improvement of microsurgical methods free flaps as the DIEP flap have become a safer and more often applied alternative with less donor side morbidity<sup>[40-42]</sup>.

### *Ischemic preconditioning*

Ischemic preconditioning was introduced by Mounsey *et al.*<sup>[43]</sup> for conditioning of the myocardium, but has since been applied to different fields of surgery including flap surgery. Murry *et al.*<sup>[44]</sup> and Jennings *et al.*<sup>[45]</sup> found that brief, intermittent cycles of ischemia have a protective effect on the myocardium resulting in a delay or even protection of lethal injury to the myocardial cells due to metabolic changes in the affected cells in a dog model. Various animal studies showed, that ischemic preconditioning leads to an increase in capillary perfusion, the vascular response to changes in perfusion pressure, a decrease in leukocyte-mediated reperfusion injury, an increase of critical ischemia time tolerated by the affected tissue, a decrease of vasospasms as well as a decrease in the capillary no-reflow phenomenon<sup>[46-49]</sup>. All of these mechanisms lead to a significant decrease in flap necrosis in skin flaps as well as in muscle flaps<sup>[48]</sup>. Because of these positive effects, the ideal application of ischemic preconditioning was examined as well. It was found that three cycles of ischemic preconditioning of 10 min each are superior to the application of only one or two cycles. They also found that a cycle of 10 min of ischemia is superior to 5 min of ischemia<sup>[50]</sup>. It could also be shown that there is no difference in the positive effect of ischemic preconditioning on reducing muscle flap necrosis whether it is applied 24 h or immediately before flap elevation<sup>[51]</sup>. Interestingly, ischemic preconditioning has immediate as well as late protective effects: the immediate effect is an improvement of the blood flow hemodynamics and an attenuation of the leukocyte-mediated reperfusion injury whereas after 24 h of reperfusion the improvement of the hemodynamics has subsided while the protective effect against reperfusion injury was still present<sup>[46]</sup>. Although there are those numerous positive effects of ischemic preconditioning it hasn't found its way into clinical routine use. The main reason for this might be the additional time needed for preparing the pedicle and applying ischemia prior to flap elevation as well as the spreading of new techniques like indocyanine



**Figure 1.** Remote ischemic conditioning: Examining the changes in tissue perfusion on the right hand of the test person after inducing ischemia on the left arm with a tourniquet

green (ICG) angiography, dynamic infrared thermography (DIRT), and photospectrometry which facilitate flap design<sup>[28,52,53]</sup>. One exception where ischemic preconditioning is routinely applied is the pedicled groin flap. It still poses as a viable option when free or local flaps cannot be used to reconstruct tissue defects<sup>[54]</sup>.

#### *Remote ischemic conditioning*

The idea of remote ischemic preconditioning was introduced by Przyklenk *et al.*<sup>[55]</sup> in 1993 with their findings in a dog model that brief cycles of ischemia in a remote vascular bed are also capable of protecting myocardial cells from damage caused by the occlusion of coronary arteries. Plastic surgeons applied this idea to their line of work. Today three forms of remote ischemic conditioning exist: pre-, per-, and post-conditioning. In animal models it could be demonstrated that the induction of ischemia and reperfusion in a body part distant from the flap prior to its elevation could reduce the occurrence of flap necrosis in adipocutaneous flaps as well as in muscle flaps. They also found that ischemia and reperfusion could be induced non-invasively by the application of a tourniquet on a body area distant from the flap prior to flap elevation<sup>[56,57]</sup>. After those first promising results many experimental studies focused on the ideal type of application regarding remote ischemic conditioning. They found that inflating the tourniquet on the upper extremity had better effects on cutaneous microcirculation than on the lower extremity and that three circles of 10 min ischemia each were superior to shorter cycles or more frequent applications<sup>[58,59]</sup> [Figure 1]. Those findings indicate that remote ischemic preconditioning has to be a systemic phenomenon but the mechanisms behind “classic” and remote ischemic conditioning are not yet fully understood. Various factors such as the release of nitric oxide, heat-shock proteins, adenosine, ATP-sensitive K<sup>+</sup> channels, cyclooxygenase as well as bradykinin through sensory nerve stimulation seem to be involved<sup>[60-66]</sup>. The protective effect of remote ischemic preconditioning against ischemia reperfusion-injury can be divided into two different timeframes. The acute effects last about four hours after the initial application of the preconditioning stimulus whereas the late effects occur after 24 h and last for at least another 24 h<sup>[67]</sup>. Furthermore the clinical application of remote ischemic conditioning is rather convenient as it is non-invasive and time-effective. The first study to examine remote ischemic conditioning in the clinical setting regarding flap surgery has shown promising results including an improvement of microcirculation in pedicled and free flaps<sup>[68]</sup>. Although there are many promising results regarding remote ischemic preconditioning there are also certain drawbacks. Some recent studies in the field of cardiac surgery revealed that the positive effects of remote ischemic preconditioning in laboratory studies may not be applied successfully in the clinical setting meaning there are no significant effects on the clinical outcome<sup>[69]</sup>.

#### *Thermic preconditioning*

Other research groups have focused on the protective effects of hypo- and hyperthermia concerning



ischemic events and reperfusion-injury. By heating tissue to a temperature of 42 °C heat shock proteins (HSPs) are upregulated. HSP-70, HSP-72 and HSP-32 are reported to induce mechanisms which protect musculocutaneous, fasciocutaneous and skin flaps from ischemic injury if the hyperthermic preconditioning was conducted 6 to 24 h before flap elevation in animal studies<sup>[70-72]</sup>.

Hypothermia has protective effects caused by the downregulation of cellular metabolism as well as the induction of HSPs. Cooling the donor area 24 h before raising of the flap has shown to increase the expression of HSP-32 as well as significantly increase capillary perfusion and reduce skin flap necrosis in an experimental setting<sup>[73]</sup>.

#### *Other ways of tissue conditioning*

Pretreatment with growth factors which induce neovascularization has been investigated by some research groups. Until now, the application of vascular endothelial growth factor (VEGF) is the most widely investigated growth factor. The intravascular and subcutaneous application of VEGF proved to induce angiogenesis and increase flap survival in a rat model<sup>[74,75]</sup>. There has also been a gene therapeutic approach which showed a reduce of ischemic tissue in random skin flap models in rats by transfection with VEGF plasmids<sup>[76]</sup>. Other studies investigated the effects of human basic fibroblast growth factor (bFGF). Pretreatment with subcutaneous application of bEGF at the future donor site as well as the pretreatment of the recipient site of the flap via gene transfection showed an increase in vascularity and tissue perfusion in skin flap models in rats<sup>[77,78]</sup>.

Other research groups have focused on the effects of extracorporeal shock wave application (ESWA) on angiogenesis and tissue perfusion. Through ESWA, an increase in blood flow and angiogenesis as well as an improvement in tissue metabolism could be achieved in a mouse model<sup>[79-81]</sup>. In a rat model it could even be found that preoperative ESWA has a similar effect as surgical delay regarding microvessel density and perfusion, being non-invasive and easily applicable<sup>[82]</sup>. ESWA even decreases inflammatory reactions and therefore has a protective effect against reperfusion-injury<sup>[83]</sup>.

A further approach is the use of stem cells in tissue conditioning. In an experimental setting with Lewis rats it could be demonstrated that the venous application of adipose derived stem cells during reperfusion after an ischemic event could reduce necrosis in skin flaps and local application of adipose derived stem cells to the wound bed before suturing the flap could increase tissue perfusion and skin flap survival<sup>[84,85]</sup>.

Another means for tissue preconditioning is a pharmaceutical approach. Possible drugs should counteract the pathophysiological processes responsible for ischemia or ischemia reperfusion-injury. Of interest are drugs which improve microcirculation as heparin, drugs which cause vasodilation like beta-mimetics, selective calcium channel blockers and nitric oxide donors or drugs with anti-inflammatory effects like prostaglandin-analogues or cyclooxygenase inhibitors as could be shown in different animal models<sup>[86-91]</sup>.

#### *Tissue conditioning and wound healing*

Many of the above mentioned approaches in tissue conditioning are not only promising in plastic surgery but also seem to be an option for the improvement of wound healing, especially in wounds which are difficult to treat due to their size or the patients comorbidities and the resulting physiological changes in the tissue. For example there are many clinical studies investigating the positive effects of platelet rich plasma (PRP) on wounds, as it contains a large amount of cytokines, growth factors and chemokines<sup>[92,93]</sup>. Another, yet mainly experimental approach is the use of hypoxia to induce angiogenesis and improve wound healing. Therapeutic aspects using hypoxia include preconditioning cells in vitro or inducing hypoxia-mediated pathways in vivo by gene therapy or pharmaceutical agents, which eventually leads to an increase in pro-angiogenic growth

factors and other angiogenic mediators in the wound bed<sup>[94]</sup>. Remote ischemic conditioning for example has also proven to be of use in diabetic patients. There are clinical studies that could show a significantly improved healing of diabetic foot ulcers due to remote ischemic conditioning<sup>[95,96]</sup>. And the effects of extracorporeal shock waves have been investigated in the clinical setting in burn patients as well. Researchers could show better results in terms of wound healing because of its positive effects on angiogenesis<sup>[79,80,97]</sup>.

## CONCLUSION

Despite all the progress made in plastic and especially flap surgery, total or partial flap loss caused by ischemia or ischemia reperfusion-injury is still feared and has common complications. As temporary ischemia is inevitable in free flaps and the tissue of pedicled flaps is initially exposed to changes in perfusion as well, strategies to improve tissue viability are of vital importance. Many of the above mentioned, promising ways of tissue conditioning have yet only been tested under laboratory conditions or in animal models so further studies including clinical trials are needed. Those findings could not only offer great benefits in plastic surgery but in other fields of medicine as well, including the treatment of extensive or chronic wounds as well as transplant surgery. To lean on the words of Gillies<sup>[17]</sup>, tissue conditioning harbors the possibility to be an important weapon in the battle between beauty and blood supply.

## DECLARATIONS

### Authors' contributions

Designed and wrote the article, performed literature research and produced the figures: Krauss S  
Assisted in designing the article, offered ideas concerning content of the article, corrected the article and proofread the final version: Kolbensschlag J  
Read, corrected the article and discussed the content: Rothenberger J, Mayer J, Sogorski A, Held M, Wahler T, Daigeler A

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All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

Consent for publication was obtained.

### Copyright

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Original Article

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# Applying skin graft sheets transversely to manage burn patients

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## Abstract

**Aim:** The aim of this study is to determine whether the split-thickness grafts should be applied to the treatment of burn patients, parallel to the relaxed skin tension lines as described by Kraissl, which would help scarring and reduce the development of abnormal scars.

**Methods:** A descriptive longitudinal case series study was conducted at the Burn Unit of Health Services Simón Bolívar North Subnetwork E.S.E. of the Secretariat of Health in Bogotá, Colombia, from 1 Jan 2016 to 31 Dec 2017. A total of 138 burn patients exhibiting deep partial- or full-thickness burns involving different body regions, except for the face, were included. Burns required split-thickness skin grafts for definite wound coverage, and these were applied transversely following relaxed skin tension lines. Results were assessed according to the Vancouver Scar Scale (VSS) during a 12-month follow-up. Within this period, function was assessed by the rehabilitation unit, after which physical and functional activities were determined and splinting was implemented, as per rehabilitation protocols, to control and improve functional and physical outcomes.

**Results:** Based on the VSS, most patients (134) had a mean score of 5 (range: 3-7), resulting in clinically acceptable scars with no functional limitations.

**Conclusion:** Applying split-thickness skin grafts to cover deep partial- or full-thickness burns along relaxed skin tension lines, such as Kraissl's lines, seems to reduce wound tension force, which constitutes one of the most predominant factors contributing to the development of abnormal scars and functional sequelae.

**Keywords:** Split-thickness grafts, burns, relaxed skin tension lines, hypertrophic scar, keloid, contracture



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## INTRODUCTION

Burns are considered a public health problem worldwide due to their associated high mortality rates as well as their great morbidity incidence and functional impairment<sup>[1-3]</sup>. Severe scars and late contractures occurring after the placement of split-thickness autografts during treatment persist as some of the most relevant and frustrating sequelae in patients with deep burns<sup>[4,5]</sup>. Not only do they result in deformities and functional impairments, but they may also affect the patient's esthetic appearance, which is distinguishable in burn patients<sup>[6,7]</sup>. These sequelae usually cause prolonged disability, job abandonment, and high costs to the health system<sup>[8,9]</sup>.

Generally, multiple reconstructive interventions are required, including Z-plasties, contracture release, skin grafts, flaps, tissue expanders, skin substitutes, and a great variety of auxiliary treatments, in the attempt to improve and preclude recurrence<sup>[10-13]</sup>. Furthermore, lengthened rehabilitation interventions are required in addition to multiple complementary elements, such as Lycra garments, silicone gel sheets, thermoplastic masks, prolonged immobilization, orthosis, moisturizing lotions, lubricants, corticosteroid injections, and even radiotherapy. Varying results obtained are poor and disheartening in some cases<sup>[14-16]</sup>.

In the literature, it is widely reported that the use of full-thickness skin grafts exhibit better texture and color, and they significantly reduce the occurrence of contractures and scarring sequelae. However, the availability of donor sites that will enable the use of such grafts is limited, and thus, the application of split-thickness skin grafts becomes necessary<sup>[17,18]</sup>. Skin substitutes of human or animal origin or synthetic substitutes may be an alternative for reconstructing the dermis, reducing the incidence of retraction from the use of split-thickness skin grafts. These substitutes allow to compensate for the lack of donor sites of full-thickness skin grafts, bringing satisfactory results. Nonetheless, the limited availability of these dermal matrices and their elevated costs for most burn units in developing countries have hindered their use<sup>[19,20]</sup>.

Traction and tension forces on scars also play an important role during the formation of optimal scars. These forces are associated with the orientation of collagen fibers in the lower dermis and are essential for correcting hypertrophic scars, particularly when Z-plasties are performed to redirect scars into the relaxed skin tension lines, i.e., Langer's lines<sup>[21,22]</sup>. Nevertheless, Langer<sup>[21]</sup> studied these relaxed skin tension lines in cadavers, whereas Kraissl's lines were defined in living individuals under no traumatic procedures<sup>[23]</sup>. In this way, Kraissl's lines are found to be more dynamic and to correlate with wrinkle lines during muscle contraction, making them more accurate than Langer's lines. These lines are disposed transversely, run perpendicular to muscle action, and they are vital in normal scarring<sup>[23,24]</sup>. In the light of the foregoing, we have suggested that placing split-thickness skin grafts transversely, following Kraissl's lines, on exposed areas resulting from burns may improve the esthetic and definitive functional outcomes in burn patients. This study aimed at describing patient evolution with split-thickness skin grafts applied by following Kraissl's lines during a 12-month period. To evaluate the functional and esthetic outcomes of scars in patients who underwent split-thickness skin grafting transversely based on Kraissl's lines to cover deep burns.

## METHODS

A descriptive longitudinal case series study was conducted at the Burn Unit of Health Services (HSU) Simón Bolívar North Subnetwork E.S.E. of the Secretariat of Health in Bogotá, Colombia, from 1 Jan 2016 to 31 Dec 2017. The study was approved by the Institutional Ethics Committee, and was based on the ethical principles contained in the declaration of Helsinki.

The study included 138 patients with a mean age of 24.5 years (range: 7-74 years). Of this group, most subjects were men ( $n = 96$ , 70%), with a mean age of 24.5 years (range: 7-74 years). These injuries required definitive coverage, involved any part of the body, with the exception of the face, and were classified as superficial

(affecting only the epidermis), partial-thickness (until papillary dermis layer) or full-thickness (complete dermis and underlying tissue).

Patients were asked to sign an informed consent form to participate in the study and have their photos taken. Patients showing additional comorbidities that could affect scarring, including malnutrition, high blood pressure, diabetes mellitus, and coagulation disorders, were excluded. Patients having severe mental disorders or exposed areas not suitable for graft coverage, including hypertrophic granulation tissues, edematous or pale tissues, or the presence of discharge, were also excluded.

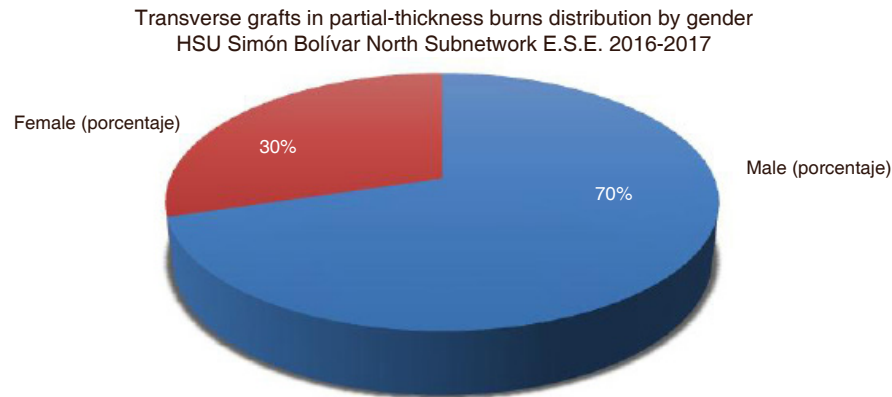
### Procedures

Once the informed consent form was signed, the procedure was performed in operating rooms after the administration of general anesthesia, patients were washed with water and chlorhexidine soap. Granulation tissue curettage was executed for full removal, and wet compresses diluted in 500 cc of 0.9% saline were applied, along with the use of a 1-mg adrenaline ampoule, to achieve hemostasis. In case bleeding was not controlled, hemostasis was ensured by electrocautery. Subsequently, from the available donor sites, such as the lower limbs, back or scalp, a split-thickness skin graft (between 0.25 mm and 0.30 mm) was harvested using an electric dermatome. Following this, bupivacaine 0.25% with epinephrine at a dose of 2 mg/kg was administered to manage postoperative pain at donor site. Upon verifying hemostasis at receptor site, the graft was placed transversely in sheets, without expansion or meshing. Incisions for drainage were made, while ensuring that no exposed spaces were left in between each sheet. Suture immobilization remained at the discretion of the surgeon, but it was usually done on pediatric patients and at flexion creases sites. Next, the graft receptor site was covered with nitrofurazone-impregnated gauzes and cotton padding bandages as secondary dressing. Flexion areas were applied plaster splint intraoperatively. The first cleaning and dressing session took place at postoperative day 5, and from then on, every third day until hospital discharge. Postoperative monitoring varied in frequency, based on the surgeon's judgment, until postoperative month 12. The same two surgeons performed the monitoring.

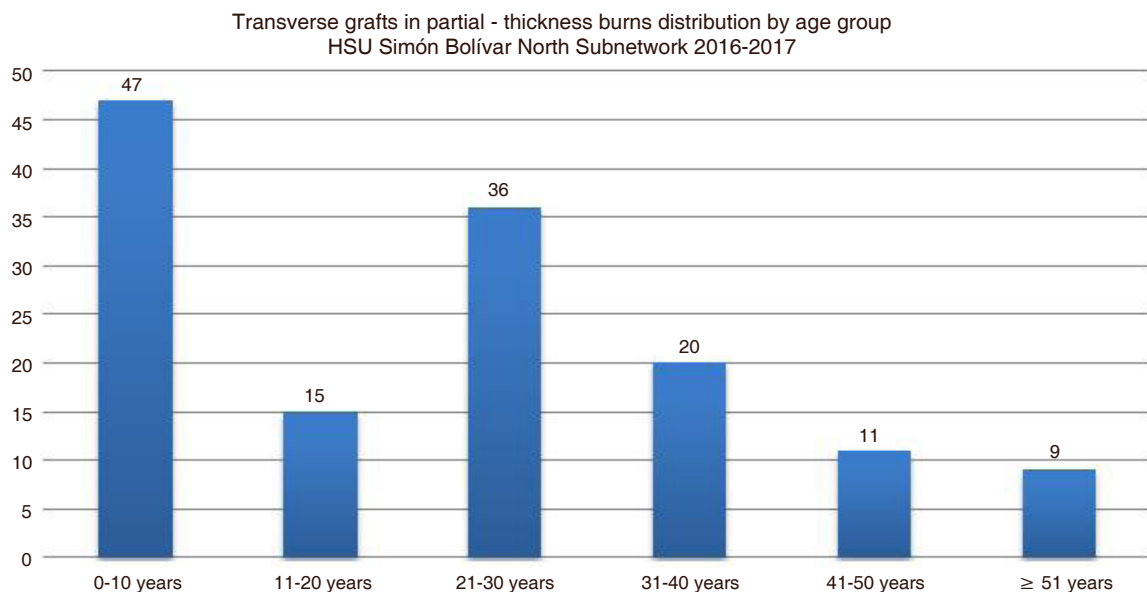
On admission, all patients were evaluated and managed through physical and occupational therapies. Based on the reported findings, the rehabilitation team planned activities aimed at lowering edema, reducing pain, improving ROM, controlling positioning, and recovering sensitivity and strength, to promote the functionality of affected areas and independence of physical and instrumental ADL. Rehabilitation treatment was suspended immediately after surgery and was resumed at day 5 upon verification by the surgeon that there was proper graft integration. Once the physical and occupational therapies were resumed, they were continued during hospital admission and 3 months postoperatively (outpatient), through physical conditioning, digital pressure on the scar, orthotic management, Lycra garments, silicone, moisturizers, and lubricants. The scars had no medication infiltrated.

### Scarring evaluation

The Vancouver Scar Scale (VSS) was used as follows: pigmentation and vascularity was examined visually, pliability was assessed by palpation and digital pressure, and height/thickness was measured with a millimeter ruler<sup>[25]</sup>. Overall scores were categorized in three groups according to the following characteristics: (1) mild scar (score 0-3): characterized by a flat scar having a similar appearance to normal skin. It is supple and elastic, and has a few elements of pigmentation or vascularization; (2) moderate scar (score 4-7): characterized by a fairly thick and wide scar or a slightly wide and raised scar. Pink to red pigmentation changes may be observed, but there is yielding. Some areas may be fragile and less resistant; and (3) severe scar (score 8-13): characterized by clear signs of hypertrophy or keloid. The scar has a red to purple pigmentation, and it is unstable, raised, bulky, firm and indurated. Contractures and retractions may be present. Results were evaluated by a team of experts consisting of two surgeons, who performed the procedures, and a burn specialist.



**Figure 1.** Distribution by gender of the 138 patients whose burns were treated with transverse split-thickness skin grafts. HSU: Unit of Health Services



**Figure 2.** Distribution by age group. HSU: Unit of Health Services

### Statistical analysis

The socio-demographic variables age and sex were registered. Other clinical characteristics were registered as well, including total burned body surface area using the Lund and Browder chart<sup>[26]</sup>, burn depth, compromised body area, eschar removal prior to applying definitive autografts, number of days since admission until definitive coverage, grafted anatomical area, donor sites, graft thickness, and complications. Scars were assessed at month 1 and at month 12 based on the VSS. For qualitative variables, frequencies and percentages were used, whereas for quantitative variables, mean, median and range were preferred. Microsoft Excel® was used.

### RESULTS

A total of 138 patients showing deep burns were admitted. They required definitive coverage with split-thickness skin grafts, which were placed transversely. Of this group, most subjects were men [Figure 1], with a mean age of 24.5 years (range: 7-74 years) [Figure 2]. Among injury mechanisms, the most common etiologic factor was flame with 40% ( $n = 55$ ), followed by electricity 13.7% ( $n = 19$ ), scald 12.3% ( $n = 17$ ), chemical agents 13% ( $n = 18$ ), and other 21% ( $n = 29$ ) [Table 1].



**Table 1. Socio-demographic variables and clinical characteristics of burns**

Variables	Frequency	Percentage
Male	96	70
Female	42	30
Injury mechanism		
Flame	55	40
Electricity	19	13.7
Scald	17	12.3
Deep partial-thickness burn	52	37.7
Full-thickness burn	28	20.3
Mixed burn (deep partial- and full-thickness)	29	21
	Median	Range
Age	24.5	7-74
Burned body surface area	24.34	2-66

The mean extension of total compromised body surface area was 24.34% (range: 2%-66%). Concerning burn depth, 52 (37.7%) patients exhibited partial-thickness burns, 28 (20.3%) patients showed full-thickness burns, and 29 (21%) patients had mixed burns, i.e., both deep partial- and full-thickness burns. The most common compromised anatomical areas were the upper limbs accounting for 77.4% ( $n = 89$ ), face 46% ( $n = 53$ ), trunk 40% ( $n = 46$ ), lower limbs 39.1% ( $n = 45$ ), and neck 21% ( $n = 29$ ). Mean hospital stay consisted of 16 days (range: 8-100 days).

Among the 138 patients, 106 (76.8%) patients underwent a single early eschar removal procedure by tangential excision, 19 (13.7%) patients required 2 escharectomies, 6 (4.3%) patients 3 escharectomies, and 7 (5.0%) patients 4 escharectomies. Patients having full-thickness burns underwent more escharectomies. In 26 (18.8%) patients, the escharectomy area was covered temporarily with skin allografts prior to carrying out the definitive coverage with split-thickness skin autografts, as to promote the formation of granulation tissue suitable for grafts.

In all, 46 (33.3%) patients required several grafting sessions, involving 2-5 additional procedures. These subjects exhibited burns > 20% of extension, full-thickness burns, and limited donor sites. Ten (7.2%) of the 138 patients developed infection, resulting in full or partial graft failure. Reported cultures included *Acinetobacter baumannii* ( $n = 4$ , 2.9%), *Pseudomonas aeruginosa* ( $n = 4$ , 2.9%), and *Klebsiella pneumoniae* ( $n = 2$ , 1.4%). No case of mortality was reported. Initial scars were assessed at first postoperative month, and definitive outcomes were determined at month 12 based on the VSS.

Of the 138 patients, 130 (94.2%) showed mild scars (score  $\leq 3$  in VSS). These were flat and had a similar appearance to normal skin; they were supple and elastic, and had a few elements of pigmentation (hypopigmentation and hyperpigmentation) or vascularization (pink) [Figures 3-6]. Four (2.9%) patients showed moderate scars (score 4-7) having a < 5 mm thickness and width, and a < 2 mm height. There were some changes in pigmentation and vascularization (pink to slight red); nonetheless, there was yielding and no evidence of rigidity or functional limitations, although some developed fragile areas with low resistance. Four (2.9%) patients showed severe scars (score  $\geq 8$ ) having clear signs of hypertrophy or keloid at 12-month follow-up. There was some degree of contracture and functional limitations, particularly in flexion creases sites. These 4 (2.9%) patients developed infection in the grafted areas, and they required surgical correction through contracture release and the application of new grafts [Table 2].

In terms of rehabilitation, upon admission, all patients had developed some degree of edema in their upper and lower limbs. They also reported pain as per visual analog scale (VAS) at rest, which increased during muscle activity. Functional joint limitation was directly associated with skin involvement of finger and wrist



**Figure 3.** A 16-year-old female patient with a full-thickness flame burn to the left upper limb. A: Exposed area suitable for grafts; B: coverage with split-thickness skin grafts placed transversely; C: appearance by postoperative day 45; D: appearance after 6 months, with no functional limitations



**Figure 4.** A 24-year-old male patient with a full-thickness chemical burn (sulfuric acid) to the left upper limb, involving creases. A: Initial appearance, with an adhered and hard eschar; B: formation of a uniform and non-hypertrophic granulation tissue. It was red and had no discharge following two escharectomies. It was covered temporarily with skin allografts; C: placement of split-thickness skin grafts transversely soon after surgery; D: appearance at postoperative month 1

joints, pain degree, and presence and severity of edema, resulting in functional limitation of the involved joint. Sensitivity exhibited mixed impairment, with areas of hyperesthesia associated with superficial burns and areas of hypoesthesia associated with deep burns, as well as non-painful areas corresponding to full-thickness burns. Patients showed decrease in strength, range of motion (ROM) impairment and activities of daily living (ADLs) limitations. This resulted in weakened or non-functional upper and lower limbs, making patients highly dependent.

At week 4 postoperatively, patients having a VSS score below 7 showed resolution of edema, a decrease to 0 for pain at rest and during activity (VAS), and gradual improvement of sensitivity during the following 6 months, as deep sensitivity was regained. There was an increase in strength, as well as greater gains in ROM and complete resumption of instrumental and non-instrumental ADLs. The 4 patients who developed infection and exhibited graft loss in affected areas showed scarring disorders, with signs of hypertrophic scars and keloids, cutaneous and subcutaneous contractures, and fascia contracture. None of them presented ligament



**Table 2. Classification of results based on the Vancouver Scar Scale**

Variable	Number of patients	Percentage
Mild scar (Vancouver score < 3)	130	94.2%
Moderate scar (Vancouver score 4-7)	4	2.89%
Severe scar (Vancouver score ≥ 8)	4	2.89%



**Figure 5.** A: Thirty-two-year-old female patient with a deep partial-thickness flame burn to both lower limbs, who underwent eschar removal by tangential excision; B: placement of split-thickness skin grafts transversely; C: results at postoperative year 1. No evidence of contracture, and both texture and color are adequate



**Figure 6.** A: Twenty-eight-year-old male patient with a full-thickness flame burn of 18% total body surface area to back and gluteal region; B: appearance following 3 escharectomies performed by electric dermatome, and temporary coverage with skin allografts; C: intraoperative appearance after placing split-thickness skin grafts transversely; D: results at postoperative month 12

or muscle contractures, or functional limitations of involved joints; however, they reported persistence of pain at rest and during activity, decreased joint ROM, decrease in strength, and ADLs limitations, which improved at week 6 following surgical contracture release by placing new grafts and restarting rehabilitation.

## DISCUSSION

In the researched literature, we did not find studies evaluating the evolution of split-thickness skin graft sheets in burn patients while taking into account their placement orientation. Conversely, abnormal scarring and

joint contractures following deep burns have been widely reported. In a multicenter study involving 1865 patients, Goverman *et al.*<sup>[27]</sup> described as risk factors and predictors of contracture development male sex, Hispanic ethnicity, medical problems, neuropathy, total body surface area (TBSA) affected by partial-thickness burns, TBSA grafted with split-thickness grafts, and prolonged hospital stay. According to their findings, the most common postburn morbidity was joint contracture, which occurred despite aggressive therapeutic interventions at both occupational and physical levels (positioning and splinting), affecting quality of life and ADLs. Their surgical management required skin grafts, as well as local and distant flaps. The most frequently contracted joint was the shoulder with 23.0%, followed by the elbow (19.9%), the ankle (13.6%), and the knee (13.4%). Schneider *et al.*<sup>[4]</sup> reported among 985 patients a joint contracture prevalence of 39% ( $n = 381$ ), with the shoulder, the elbow, and the knee being the most frequently contracted joints. In total, 39% of all cases developed at least one joint contracture. In 2003, Kowalske *et al.*<sup>[28]</sup> in a study involving 1478 patients with major burns reported a joint contracture prevalence of 43% ( $n = 641$ ). Furthermore, in 2016 Oosterwijk *et al.*<sup>[29]</sup> presented a systematic review according to which the prevalence of postburn contractures is different among studies, ranging from 38% to 54%, and contractures were most likely to develop in deep and extensive burns, as well as in the neck and upper limbs.

In this study, we found that the transverse placement of grafts may lead to clear changes in terms of functionality and esthetics. The study sample revealed a very low incidence of contractures, adhesions, hypertrophic scars, and keloids (4/138, 2.9%), particularly in limbs, which according to the literature constitute the most commonly affected areas by scarring sequelae. We consider that the transverse placement of grafts benefits scarring by reducing both tension of muscle contraction in grafted areas and resting skin tension, as the muscle action generated by Kraissl's lines correspond to the relaxed skin tension lines, which follow wrinkles and skin movement during muscle contraction, mainly in the neck, trunk, and limbs. In this way, such lines should be considered during the planning and placement of grafts. Unlike Goverman *et al.*<sup>[27]</sup>, we believe that a multidisciplinary treatment with rehabilitation upon patient admission greatly influences prevention control of functional and scarring disorders. These observations are preliminary, and therefore, not conclusive, as they require further studies allowing comparisons with a control group.

Nevertheless, surgeons usually determine how to place split-thickness skin grafts on exposed areas, relying on the orientation that will allow the operator to cover the greatest exposed tissue area with the obtained graft. In this sense, the orientation of those forces resulting in the underlying muscle tissue contraction of the area to be grafted are not taken into consideration. Generally, the skin is under constant tension, which varies depending on the area. This static tension follows predictable patterns, and it is defined by Kraissl's lines. The movement of joints and muscles causes dynamic tension, and so placing grafts perpendicular to Kraissl's lines creates more tension, resulting in wider and hypertrophic scars that may even progress to severe contractures and functional impairments, especially in the limbs and neck.

Infection processes in burn patients continue to be a great public health problem associated primarily with an increase in mortality and morbidity, hospital stay, procedures, and costs. In our study, the occurrence of infection caused full or partial graft failure, thereby increasing the number of surgical procedures and prolonging hospital stay, as exposed areas required new grafts. Four of these patients obtained a score of  $\geq 8$  in the VSS, attributable to a more active inflammatory process, increased fibrosis, prompted formation of hypertrophic scars, and some degree of contracture with functional limitations of the limbs. This sample includes patients of all ages, ranging from 1 to 80 years, having extensions of 3-66. Nevertheless, results did not vary based on age or extension.

Although not part of this study's objectives, we noted that placing grafts transversely enables their rationalization, since they are applied from both edges at the exact size of the defect, preventing the loss

of small skin fragments. Conversely, placing grafts without considering their orientation usually involves the cutting of skin segments that protrude from the wound, which results in the loss of multiple small skin fragments.

Based on the results obtained in this study, we believe that tension forces acting on the grafted areas are essential in scarring. Orientation seems to be a relevant factor for such forces to exert more or less tension on the scar. Orienting grafts transversely, following Kraissl's lines, lowers tension of these scarring forces, which translates into more esthetic and functional characteristics. Further studies are required engaging a larger population sample and having multicenter and controlled designs that will allow to determine and measure the static and dynamic forces involved in the scarring of skin grafts.

In conclusion, burns are a type of trauma resulting in great morbidity rates. They compromise large portions of the skin in each patient and require a multidisciplinary and multimodal management to improve functionality and scar appearance. Abnormal scars are caused by several factors that affect scarring. One of the primary factors involves the tension exerted on the wound. Considering these relaxed skin tension lines, when applying split-thickness skin graft sheets transversely, reduces tension and minimizes the risk of developing abnormal scars, thereby achieving better esthetic results.

## DECLARATIONS

### Authors' contributions

Concept and design: Madiedo R

Data acquisition: Gaviria-Castellanos JL

Data analysis, manuscript preparation: Gaviria-Castellanos JL, Zapata-Ospina A

Critical revision and completion of manuscript: Madiedo R, Gaviria-Castellanos JL

### Availability of data and materials

Data were strictly obtained from medical records, in accordance with the privacy policy and code of ethics of our institute.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

This study was approved by the Hospital and all authors gave their consent to participate. Ethical approval number UI-19-15.

### Consent for publication

Not applicable.

### Copyright

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Original Article

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# Low level laser as an adjunct therapy for second degree superficial burns

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## Abstract

**Aim:** Second degree superficial burns are painful and heal over a period of two to three weeks time. Multimodality treatment approach is effective in reducing time of healing, pain, rate of complications and overall cost of treatment. Aim of this study is to observe effect of low level laser therapy (LLLT) as an adjunct to conventional therapy for second degree superficial burn.

**Methods:** This article presents a case series of twenty patients in which LLLT was used as an adjunct therapy for target burn areas.

**Results:** Average time taken for complete healing of areas with second degree superficial burns was 11.75 (SD 2.86) days. One patient was healed on day 6; ten patients were healed on day 10, six patients on day 13, and three on day 17.

**Conclusion:** We could not found significant evidence of positive effect of LLLT over rate of wound healing. However its effects are promising and further large multicentric trials are needed to establish its role and standardize its dose parameters.

**Keywords:** Low level laser therapy, second degree superficial burn, photobiomodulation, rate of healing

## INTRODUCTION

Approximately 6-7 million new burn incidents are occurring in India every year<sup>[1]</sup>. Burn patients are a major



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**Figure 1.** Low level laser therapy being given to the target burn wound (a 40-year-old female patient with 20% total burn area, 10% target area, post burn day 3, deep burn wounds are excised and grafted)

burden over society and effective and rapid treatment of burn wounds is important part of patient care as well as proper healthcare resource utilization. Majority of burn patients have areas of variable burn thickness and thus require multimodality treatment approach.

The healing of second degree superficial burn takes place by epithelialization from epidermal appendages present in dermis. Conventionally these burn wounds are managed by regular dressings. These wounds take around two to three weeks time for complete healing<sup>[2]</sup>. It may take longer in case of wound infection, sepsis or hypoproteinemia. Various treatment modalities are proposed, including collagen dressings, autologous platelet rich plasma therapy, insulin therapy and low level laser therapy (LLLT) to increase rate of healing and decrease complications in these cases<sup>[3]</sup>. Evidence for beneficial effects of these modalities is not sufficient.

Low level laser (LLL) is also known as cold laser as it does not produce heating effect. LLLT affects wound healing on the basis of photobiomodulation effect. LLLT is claimed to have analgesic, anti-inflammatory effects and stimulates wound healing and remodelling<sup>[4]</sup>. An animal study has demonstrated effects of LLL over second degree burn wounds at cellular level<sup>[5]</sup>. However there is no human study for its effects on acute burn wounds. LLLT can be used as an adjunct to the conventional treatment of second degree superficial burn. This article presents our experience of the same.

## METHODS

Twenty acute burn patients admitted into our tertiary burn care center from January 2017 to May 2018 were included in the study. The study is purely descriptive in nature. Both retrospective and prospective data were collected. The patients included in the study were in the age range 18 to 45 years, having less than 40% of total body surface area burnt. The extent and depth of the burn were assessed clinically using Lund and Browder chart and condition of wound respectively. All patients were having variable thickness burns with areas of first degree, second degree superficial and second degree deep burns. For deep dermal burns tangential excision and grafting was performed, while areas with first degree and second degree superficial burns were managed with collagen dressings twice weekly. LLLT was used as an adjunct therapy in all patients. Patients with diabetes mellitus, collagen vascular diseases or any other disease which limits wound healing and patients on medications containing steroids were excluded. Written informed consent was taken from all the patients.

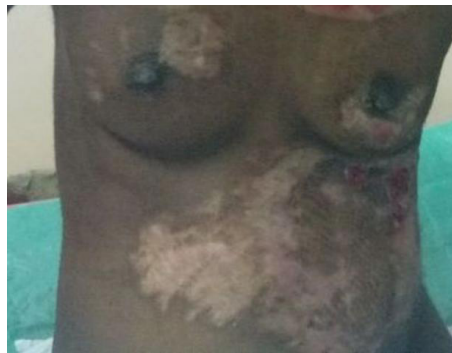
Areas of second degree superficial burns were considered as target area. All wounds were provided LLLT (along with the conventional treatment) in the operation theatre twice weekly with minimum interval of 3 days [Figure 1]. We used Gallium Arsenide (GaAs) diode red laser of wavelength 650 nm, frequency 10 kHz and



**Figure 2.** Same patient as Figure 1 (post burn day 10); wounds are healed, healing time 10 days



**Figure 3.** Low level laser therapy being given to the target burn wound (a 32-year-old female patient with 25% total burn area, 15% target area, post burn day 6, deep burn wounds are excised and grafted)



**Figure 4.** Same patient as Figure 3 (post burn day 17); wounds are healed, healing time 17 days

output power 100 mW. It was a continuous beam laser with an energy density of 4 J/cm<sup>2</sup>. Machine delivers laser in scanning mode (non contact delivery) with 60 cm distance between laser source and wound. Each wound was given laser therapy for duration of 125 second every time<sup>[6]</sup>. Therapy was repeated until the wound epithelialized completely.

Wound area measured with the help of digital planimetry and wound swab was taken for microbiology culture at each therapy session. Wound was considered infected if the swab culture has shown growth of any pathologic organism. Healing time was calculated as the period between day 0 and the day when wound area was 0 cm<sup>2</sup>

**Table 1. Results**

Serial No.	Age	Sex	TBSA burn (%)	% area with second degree superficial burn	Days taken for complete healing of target area	Area of unhealed wound in target area (cm <sup>2</sup> )						Wound culture came positive during treatment
						Day 0	Day 3	Day 6	Day 10	Day 13	Day 17	
1	26	F	20%	10%	10	1550	1470	500	0	0	0	No
2	35	M	15%	5%	10	900	840	81	0	0	0	No
3	28	M	20%	5%	6	730	630	0	0	0	0	No
4	40	F	16%	10%	13	1740	1650	780	320	0	0	No
5	29	M	20%	15%	10	2500	2480	480	0	0	0	Yes
6	25	F	40%	20%	17	3140	3020	1970	940	230	0	No
7	42	M	35%	15%	10	2430	2200	390	0	0	0	No
8	23	F	30%	20%	10	3280	3130	900	0	0	0	No
9	33	M	30%	15%	13	2250	2170	1300	460	0	0	Yes
10	42	M	15%	10%	13	1600	1600	680	120	0	0	No
11	28	F	35%	20%	13	3070	2900	1910	820	0	0	No
12	26	F	20%	10%	10	1790	1680	580	0	0	0	Yes
13	30	M	40%	25%	17	3970	3870	2340	1090	160	0	Yes
14	35	F	25%	15%	10	2100	2100	690	0	0	0	No
15	26	M	36%	10%	10	1560	1500	380	0	0	0	No
16	19	F	20%	15%	10	2380	2190	690	0	0	0	No
17	28	F	30%	15%	13	2430	2300	1400	480	0	0	No
18	40	F	20%	10%	13	1480	1400	740	185	0	0	Yes
19	24	F	18%	10%	10	1740	1650	560	0	0	0	No
20	32	F	25%	15%	17	2290	2200	1740	890	356	0	No

TBSA: total body surface area

[Figure 2]. Findings were recorded and assessment done when wound healed completely [Figures 3 and 4]. Clinical history and examination were done at the time of each dressing to look for any adverse effect related to laser therapy. Any pigment changes, itching, erythema or burning of normal skin were considered as adverse effects related to laser therapy.

## RESULTS

A total of twenty patients are included in the study with the mean age 30.55 years (19-42 years). Eight male and twelve female patients are included. The average time taken for complete healing of areas with second degree superficial burns was 11.75 (SD 2.86) days. Observations are presented in Table 1. Mean area treated was 2146 (SD 804) cm<sup>2</sup> which corresponds to 13.5 (SD 5.2) BSA% second degree superficial burns. The patient with the smallest target area was healed on day 6; ten patients were healed on day 10, six patients on day 13, and three on day 17. Mean sessions of LLLT given for one patient were 3.55 (SD 0.83).

## DISCUSSION

Posten *et al.*<sup>[7]</sup> introduced LLLT to improve wound healing. Standard parameters for LLLT are not defined and various studies used different parameters. The range of parameters used is power output 1-100 mW and wavelength 300-10,600 nm (red and infrared light). It can be continuous or pulsed. It is given in dose of 0.01-100 J/cm<sup>2</sup>. The duration of therapy varies between 10 to 3000 s<sup>[7]</sup>. The commonly used lasers for LLLT are helium-neon (HeNe), GaAs, indium gallium aluminum phosphorous (InGaAlP), and gallium aluminum arsenide (GaAlAs)<sup>[7]</sup>.

The cytochromes in the mitochondria absorb the laser radiation and convert it into ATP's which is used for stimulation of cell proliferation and synthesis of proteins resulting in photobiological activation of the cell<sup>[8]</sup>. Target cells of LLL are myofibroblasts. In animal studies LLLT has been shown to increase myofibroblast



proliferation thus the rate of collagen production and wound contraction are increased. However evidence for its beneficial effects in human wounds is lacking. By decreasing the healing time of open wounds, LLLT may reduce the risk of infection and other complications. LLLT also has positive effect over post burn hypertrophic scars<sup>[6]</sup>.

LLLT has a photobiomodulation effect over tissue; it has photochemical and photomechanical components and no photothermal effect<sup>[8]</sup>. A variety of mechanisms of action are proposed:

- (1) photonic energy is converted to chemical energy within the cell and ATP generated;
- (2) enzymes in the mitochondria may be activated or deactivated;
- (3) DNA replication increases;
- (4) increased DNA leads to increased neurotransmission;
- (5) a cascade of metabolic effects result in various physiological changes, which result in improved tissue repair, faster resolution of the inflammatory response, and reduction in pain<sup>[4,8]</sup>.

The role of LLLT for promoting wound healing has long been studied, still there is insufficient literature to design a standard treatment protocol<sup>[9-11]</sup>. Using LLL as an adjunct to conventional treatment of second degree superficial burns is expected to decrease the time of healing, rate of infection, pain and overall cost of treatment. In our experience we have found acceptable healing of wounds in target areas in all twenty patients. But the observations are not sufficient to conclude that wound healing rates were higher compared to conventional treatment alone. Wound swab culture came positive in five wounds. No effect over infection could be concluded with the observations.

In the diabetic foot LLLT has been shown to have effect on all stages of wound healing by increasing fibroblasts and keratinocyte proliferation, collagen synthesis, neoangiogenesis, improve microcirculation, stimulate granulation tissue formation, cell growth and wound contraction, anti-edema and anti-inflammatory action<sup>[12]</sup>.

Van Breugel and Bar<sup>[13]</sup> has found that the laser can either stimulate or inhibit human fibroblasts *in vitro*, depending on exposure time and power density used. Therefore the configuration of LLL used for treatment is important. We have observed effects of LLLT with 100 mW power output and 125 second exposure time, delivering energy density of 4 J/cm<sup>2</sup>. Twice weekly therapy regime was followed. This is as per the settings used by Gaida *et al.*<sup>[6]</sup>.

Effect of LLLT also depends on the physiological state of the tissue at the time of therapy. This explains the variability of the results reported in the literature. Karu<sup>[14]</sup> stated that light stimulates cell proliferation if the cells are growing poorly at the time of irradiation. Thus, if a cell is fully functional, there is nothing for laser irradiation to stimulate, and therefore no therapeutic benefit will be observed<sup>[14]</sup>.

LLLT is a safe and cost effective treatment modality<sup>[15]</sup>. We have not found any laser related adverse effect in any patient. Hawkins *et al.*<sup>[8]</sup> state that in the clinical situation, LLLT is an accepted, efficient, noninvasive, and painless method of treating edema, inflammation, and pain.

Statistical analysis could not be performed because of less number of cases. No objective evidence of pain relief was recorded. Collagen dressing used along with LLLT is identified as a confounding factor. This study was a pilot study and despite its shortcomings it has promising results and provides a basis for larger studies.

In conclusion, LLLT can be used as an adjunct to the conventional treatment of second degree superficial

burn. We could not find significant evidence of its positive effect over rate of wound healing. However its effects are promising and further large multicentric trials are needed to establish its role and standardize its dose parameters.

## DECLARATIONS

### Authors' contributions

Concept and design: Gupta S, Chittoria RK

Data acquisition and analysis, manuscript preparation: Gupta S, Aggarwal A

Critical revision and finalizing of the manuscript: Chittoria RK, Elankumar S, Reddy KS, Chavan V, Aggarwal A, Reddy CL

### Availability of data and materials

The data were strictly obtained from medical records according to the privacy policy and ethics code of our institute.

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### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Due consent was taken from the patients to participate in the study and separately for the photography. Ethical approval was done according to the hospital and department policy.

### Consent for publication

Not applicable.

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Editorial

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# Wound healing and plastic surgery - an introduction to a special issue

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## INTRODUCTION

“If I have seen further it is by standing on the shoulders of Giants.” (Isaac Newton 1675) John of Salisbury attributed in 1159 the recognition to Bernard of Chartres who expressed that “we see more and farther than our predecessors, not because we have keener vision or greater height, but because we are lifted up and borne aloft on their gigantic stature.” For reconstructive surgery - despite the brilliant innovations in recent times - this especially seems to hold true. Plastic surgery can proudly look back into an astonishing past and also into an even more fascinating future. Truly standing on the shoulder of giants constantly new ideas, techniques and materials have enriched our daily practice for the cure of our patients.

In addition whatever we do is somehow related to wound healing. Thus, the plastic surgeon is permanently confronted with all aspects of proper and disturbed wound healing on a daily basis.

In this issue a broad spectrum of topics related to wound healing shows the diversity of our specialty and highly renowned authors contribute on their experience with special problems of wound healing from different angles.

## SPECTRUM AND DEVELOPMENT OF PLASTIC SURGERY

Plastic surgery is a specialty that dates back to ancient times as far as the descriptions of reconstructions of amputated noses with a frontal forehead flap mentioned in the Sushruta Samhita as early as 1500 B.C. The demand for nasal reconstructions (rhinoplasties) can be explained by the fact that amputation of the nose



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was a traditional punishment for various delicts. In western countries this technique remained unknown for long<sup>[1]</sup>. In Renaissance - probably due to the popularity of duelling with rapier - in the fifteenth, sixteenth and seventeenth centuries it was the Italian Branca family, who lived in 1400 in Catania, who were known to reconstruct amputated noses. They performed rhinoplasties utilizing random pattern skin flaps from the arm that were then transferred to the nose in several stages. A markstone in this regard was the book of the Italian surgeon Gaspare Tagliacozzi (1546-1599) “De curtorum chirurgia per insitionem libri duo” (Venice, 1597), who described the exact technique of this procedure along with various illustrations. However the method was more or less forgotten during the seventeenth century. It was rediscovered and revived by the German surgeon Karl Ferdinand von Graefe in 1800, and hence was widely adopted<sup>[2]</sup>. Along with the evolution of very specialized surgical methods the development of surgical tools also helped to enhance plastic surgery techniques.

The initial breakthrough that sparked the rapid development of plastic surgery was a publication in the Gentleman’s Magazine in October 1794 following its publication in the Indian Madras Gazette one year earlier, where a physician attached to the East India company named B.L. reported the steps of a nose reconstruction with the Indian forehead flap in detail along with a drawing of the technique. The methods were then taken up by a number of pioneering surgeons, such as Graefe and Dieffenbach for instance<sup>[2]</sup>. This eventually led to the application of various grafts, such as skin grafts and further popularization of advancement or rotational flaps.

Nevertheless for long random pattern flaps then remained the mainstay of plastic surgical reconstruction and the tedious and oftentimes uncomfortable course for the patients allowed the restoration of various acquired or inherited defects. Only when the principle of vascularized pedicled flaps, especially the (re-) invention of the latissimus dorsi myocutaneous flap by Olivari became available another giant step was achieved that has been applied ever since for many indications<sup>[3]</sup>.

Because an ideal flap that would provide adequate shape, width, and length of well-vascularized tissues and would not come along with a donor site defect does not exist, the search for better solutions to help our patients has always driven further developments. More or less in the past decade, the so-called perforator flaps which rely on a vascular supply by a defined vascular pedicle rather than a vessel carrying muscle or fascia have tremendously helped to solve many coverage problems without sacrificing a muscle any longer. The advent of microsurgery allowed the transplantation of different types of tissue or various composite tissue flaps to be transposed to any remote recipient area, connecting the nourishing flap vessels to a vascular supply at the recipient site. Prefabrication and prelamination techniques<sup>[4,5]</sup> have made possible that a customized replacement tissue is generated in the patient himself to fit into the desired defect<sup>[6,7]</sup>. Utilizing methods derived from tissue engineering with the help of arteriovenous loops have been shown to even reconstitute bone defects in the long term frame of up to 7 years<sup>[8]</sup>.

### **Wound healing and plastic surgery**

Various highly acclaimed researchers and clinicians have contributed to the principles of wound healing and plastic surgery to bring a special issue together. Contributions include aspects of advanced free flap surgery using autologous extension grafts and bypasses for free flaps. Microsurgical free flaps together with bypass grafts or arteriovenous loops are discussed for extremely difficult-to-treat wounds as a last resort in specialized centers<sup>[9]</sup>.

Despite the advances of microsurgery in high-volume centers it remains to be discussed in which special situations certain pedicled flaps are indicated [Figure 1]. Although the era of microsurgery has broadened our spectrum tremendously, it is not the one and only solution for every indication. Therefore one article





**Figure 1.** A: Sixty years old patient with typical diabetic foot ulcer, not responding to conservative therapy; B: complete healing of diabetic foot ulcer after surgical debridement, negative pressure wound therapy and transpositional flap from the sole of the foot with skin graft to the donor site

reflecting on pedicled flaps in the seldom event when free flaps may not be the first choice for various reasons<sup>[10,11]</sup>.

Techniques optimize results by remote ischemic tissue conditioning to reduce ischemia-reperfusion injury<sup>[12]</sup>.

Osteomyelitis as a typical problem wound is discussed by thoracic surgeons, as well as the worth of interdisciplinary approaches to cure extended sternoclavicular joint infections in cirrhotic patients<sup>[13]</sup>.

The value of negative pressure wound therapy with instillation (NPWTi) in pressure ulcers is described and the use of instillational therapy of infected wounds is discussed by a multi-institutional group of experts<sup>[14]</sup>. A very recent aspect of burn surgery is the advent of enzymatic debridement as an additional tool for wound healing and experts reflect on the state of the art in enzymatic debridement in burn patients<sup>[15,16]</sup>.

The specific problems of wound healing in postbariatric body contouring surgery are pointed out in a review that reflects the specific wound healing problems in this type of surgery<sup>[17]</sup>.

The recent knowledge about the role of adipose derived stem cells in cutaneous wound repair is highlighted with highly interesting results<sup>[18,19]</sup>. Wound healing mediated through the prefabrication of flaps and aspects of neoangiogenesis that is initiated *via* venous grafts in arteriovenous loops are one more outstanding contribution to the interaction of wound healing and plastic surgery<sup>[20-22]</sup>.

Given the various facettes of papers on wound healing and plastic surgery compiled in this special issue the compilation of original papers and reviews certainly is a unique demonstration of the enormously broad spectrum of current superb clinical and research knowledge in plastic surgery and wound healing. It covers important aspects of what is currently on the cutting edge in our specialty.

## CONCLUSION

Because an ideal flap for all defects does not exist, each patient and defect must be evaluated separately to determine the best surgical approach. It turns out that today plastic surgical reconstruction is no more only

tailored to the size or type of defect, but is rather tailored to the patient's individual needs. In addition the patient himself and his individual requirements need to be considered, especially when it comes to complex and stepwise reconstructions, such as prefabrication of customized flaps. Plastic surgeons can now choose from a variety of reconstructive modalities with a broad armamentarium of techniques. In all aspects we must not forget that the basic principles of wound healing play an essential role during every aspect of plastic and aesthetic surgery.

## DECLARATIONS

### Authors' contributions

The author contributed solely to the article.

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

The author declared that there are no conflicts of interest.

### Ethical approval and consent to participate

All our patients sign a consent form at the time of admission that they are informed that any photos may be used for scientific purposes and publication.

### Consent for publication

Not applicable.

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Review

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# Periocular rejuvenation with neurotoxin and dermal filler

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## Abstract

The periocular area is one of the first regions of the body to show signs of aging, which include static and dynamic rhytids as well as subcutaneous volume loss. The complex anatomy and dynamic underlying muscles of facial expression make this region particularly difficult to treat. Botulinum toxins and fillers, especially when used in combination, offer an excellent approach to minimally invasive rejuvenation of this area. This article aims to present a basic overview and clinical primer for the use of these injectables along with advice on avoiding and managing common complications.

**Keywords:** Botox, botulinum toxin, fillers, hyaluronic acid, rejuvenation, periorbital, aesthetics

## FEATURES OF AND FACTORS AFFECTING PERIOULAR AGING

Typical features of facial aging include changes in skin pigmentation, increased skin laxity, rhytid formation, and volume loss<sup>[1,2]</sup>. The periorbital region is particularly vulnerable to the effects of aging based on intrinsic properties of these tissues. For one, eyelid skin is among the thinnest in the body, at around 0.3-0.5 mm<sup>[3]</sup>. It lacks underlying subcutaneous fat to mitigate the contour defects and fat prolapse attendant with age. The delicate nature of this tissue also readily transmits underlying pigments, including blood products, muscle, and vessels. There is less collagen and elastin than surrounding skin, rendering periorbital skin less resilient and prone to early rhytid formation. In addition, eyelid and periocular skin is dynamic and subject to constant tension from the surrounding muscles of facial expression including the orbicularis oculi, corrugators, and procerus, which likely accelerate rhytid development.



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Both the intrinsic factors mentioned above and various extrinsic and environmental factors contribute to accelerated signs of aging in this region. Sun damage is an important contributor, leading to the development of deep rhytids, hyperpigmentation, and a leathery appearance<sup>[2]</sup>. This is exacerbated by the fact that the skin of the eyelids is rarely sufficiently protected even when sunscreen is applied. UV exposure has been shown to lead to the development of reactive oxygen species, which stimulates a milieu that both accelerates collagen breakdown and down-regulates collagen synthesis. Smoking is another important modifiable factor that contributes to premature and accelerated skin aging through a similar free-radical mediated mechanism<sup>[4,5]</sup>.

Techniques for rejuvenation of this area include surgery (i.e., blepharoplasty, brow lift), injectables (botulinum toxin, dermal filler), laser resurfacing and photorejuvenation, and topical therapy. In this article we will focus specifically on the techniques and indications for use of toxins and fillers in the periocular region with the aim to provide the reader with a primer for their use based on our own clinical experience.

## NON-SURGICAL REJUVENATION OF THE PERIOULAR AREA: TOXINS

### Overview

Of the 7 known serotypes of botulinum toxin, A and B are currently available for clinical use. These compounds, produced by the bacterium *Clostridium botulinum*, effect a flaccid paralysis by preventing presynaptic acetylcholine release<sup>[6]</sup>. There are 3 commercially available varieties of botulinum toxin A currently available in the United States: Botox®, Xeomin® and Dysport®, which vary in their molecular weight, concentration, and chemical composition [Table 1].

### Preparation and administration

Each preparation comes as a powder requiring reconstitution. Although the FDA recommends preservative free saline, many injectors favor preserved saline as it may be stored longer and the favorable pH leads to a less painful injection, which has been concluded based both on personal experience as well as scientific studies<sup>[7]</sup>. Both Botox® and Xeomin® are portioned into 50 or 100 unit vials, while Dysport® is packaged in 300 unit increments. Dilution is at the discretion of the practitioner, however we prefer 1 mL saline per 100 unit vial of Botox® or Xeomin®, and 3 mL per vial of Dysport®, thus leading to a concentration of 5 units per 0.1 mL of reconstituted Botox® and Xeomin® and 12 units per 0.1 mL of Dysport®, standardizing administration techniques.

The dispersion area of each injected aliquot is roughly 1 cm<sup>2</sup>. We have found that the Becton Dickinson Ultra Fine II diabetic syringe (0.3 mL syringe with 31 g needle) works particularly well for toxin injection, as there is no hub and thus no wasted product and the needle is very small. Results begin to emerge 1-3 days post-injection, and mature for about 7-14 days afterward. Typically repeat injection is required every 3-4 months. Contraindications to toxin injection include pregnancy, breastfeeding, injection site infection, allergy or hypersensitivity to any component in the formulation, or neuromuscular junction disorders such as myasthenia gravis, amyotrophic lateral sclerosis, or myopathies.

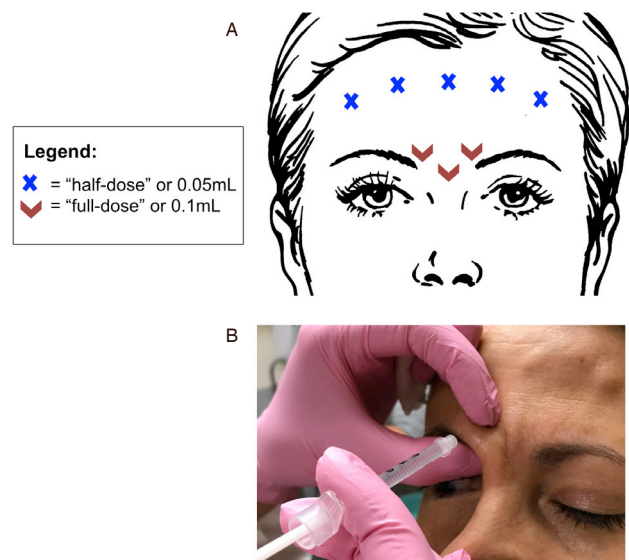
### Techniques and tips by location

“11” lines or frown lines [Figure 1] - glabellar toxin injection targets the medial depressors of the brow (procerus, corrugator supercilii, depressor supercilii, and medial orbicularis) to address rhytids in this region. Treatment of this muscle group also results in a net lift of the medial brow at rest. We aim to inject at the depth of the targeted muscle beneath the subcutaneous layer. There are several potential complications attendant on injection in this area. The first is accidental injection of the frontalis instead of the glabellar muscles, which may lead to brow ptosis rather than elevation (the frontalis being the only medial brow elevator). Eyelid ptosis may also occur if the levator palpebrae superioris is affected. It has been hypothesized that toxin may travel down the anatomical pathway forged by the supratrochlear neurovascular bundle, thus



**Table 1. Properties of commercially available botulinum toxin products**

	<b>Botox® onabotulinumtoxinA</b>	<b>Dysport® abobotulinumtoxinA</b>	<b>Xeomin® incobotulinumtoxinA</b>
Molecular weight	900 kD	≥ 300 kD	150 kD
Preparation	Vacuum dried NaCl + albumin	Lyophilized lactose + albumin	Lyophilized albumin + sucrose
pH	Neutral	Neutral	Neutral
Vial size	50 and 100 units	300 units	50 and 100 units
Storage temperature	2-8 °C	2-8 °C	Room Temperature
Other		Contraindicated if cow milk protein allergy	Retention of particles under lid requires tilting after reconstitution to capture all product

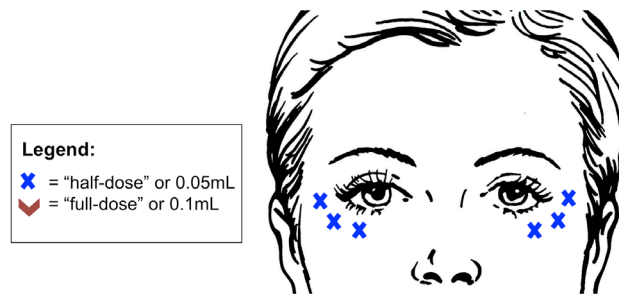


**Figure 1.** A: Botulinum toxin injection for forehead wrinkles and frown lines. Glabellar injections may be performed without treatment of the frontalis, but frontalis injections must always be accompanied with glabellar treatment to avoid brow ptosis. Volumes referenced are independent of neurotoxin variety and assume dilution as specified in the body of the text (i.e., 1 mL saline per 100 unit vial of Botox® or Xeomin® and 3 mL per vial of Dysport®); B: demonstration of injection technique whereby pinching and elevating the tissue protects the underlying neurovascular bundle. While these figures offer a guide, dosing may vary between patients according to their musculature and anatomy

we pinch and elevate the skin during the two lateral injections in this area to occlude this potential pathway and protect the orbit [Figure 1B]. If blepharoptosis should occur, apraclonidine 0.5% eye drops may be used up to three times daily to raise the eyelid approximately 2 mm via stimulation of the sympathetically innervated Müller’s muscle until the effects of the toxin wear off.

Forehead wrinkles [Figure 1] - the frontalis is the major elevator of the brow and is responsible for creating the horizontal rhytids of the forehead. We typically inject roughly  $\frac{2}{3}$  of the way up the forehead (always staying at or above the midline) to limit the risk of inducing brow ptosis. Injections in this area should always be accompanied by glabellar injections, otherwise the unopposed action of the brow depressors will drop the brow and lead to an unattractive, angry appearing facial expression. It is also important to carry injections far enough laterally so that the lateral edges of the frontalis are also treated, otherwise preserved action in this area will elevate the lateral brow, leading to peaking (colloquially referred to as “Spocking”, named for the post-procedure similarity in appearance to the fictional captain). Finally, in patients with significant brow or eyelid ptosis or dermatochalasis who depend on their frontalis for brow elevation, it is wise to avoid injections in this area altogether.

Crow’s feet or laugh lines [Figure 2] - injection of the lateral orbicularis oculi muscle may be used to address fine lines lateral and inferior to the eye. It is important to inject on a superficial plane, just below the skin,



**Figure 2.** Botulinum toxin injection for crow's feet. It is important not to extend medial to the mid-pupillary line to avoid lower lid ectropion. Lateral injection should be placed approximately 1 cm lateral to the lateral canthus. Volumes referenced are independent of neurotoxin variety and assume dilution as specified in the body of the text (i.e., 1 mL saline per 100 unit vial of Botox® or Xeomin® and 3 mL per vial of Dysport®). While these figures offer a guide, dosing may vary between patients according to their musculature and anatomy

to avoid bruising and avoid untargeted muscles. A small welt should be visible after injection similar to a tuberculin skin test. Potential concerns with injections of this area include bruising, as mentioned above, as well as iatrogenic lower lid ectropion if injections are positioned medial to the mid-pupillary line. Injections in this area may also exacerbate symptoms of dry eye in patients with a known history. Finally, if injected too deeply or too inferiorly, muscles of the mid-face may be affected, which may cause an asymmetrical smile.

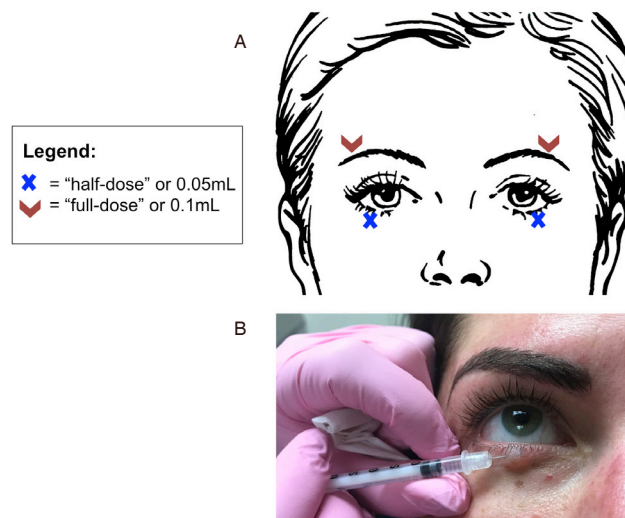
The shape of the brow may also be subtly modified with toxin injection. Lateral injection of the orbicularis may give 1-2 mm of lift to the lateral brow [Figure 3]. This may be combined with filler to further shape and fill out this region. The appearance of larger eyes may also be achieved by injection of the pretarsal orbicularis, which widens the palpebral fissure by weakening the pretarsal muscle [Figure 3]. This injection should also target a superficial plane. Again, one must use caution in patients with a history of dry eye, as this may exacerbate their symptoms.

## NON-SURGICAL REJUVENATION OF THE PERIOCCULAR AREA: FILLERS

### Overview

Facial aging is also characterized by soft tissue volume loss of the periorbital area. Although neurotoxins in isolation may be sufficient to ameliorate dynamic rhytids in younger patients, it is insufficient to address static changes caused by volume loss in the dermis and underlying soft tissue. Thus, botulinum toxin in combination with dermal fillers is an excellent option for non-invasive rejuvenation in patients with deep, static rhytids. The use of fillers in combination with neurotoxins has the added benefit of approximately doubling the half-life of the filler<sup>[8]</sup>.

Dermal fillers are used to restore facial fullness and volume. Common materials include hyaluronic acid, calcium hydroxylapatite, poly-L-lactic acid, polymethylmethacrylate, and autologous fat<sup>[9]</sup>. For periorbital rejuvenation, we almost exclusively use hyaluronic acid products. Hyaluronic acid is a naturally occurring polysaccharide found in the connective tissue of all living species and so is very well tolerated. It is hydrophilic, and this ability to bind water molecules enables its natural contribution to skin turgor and dermal volume. With aging, natural levels of dermal hyaluronans diminish<sup>[8]</sup>. In terms of cosmetic injectables, of particular value is the ability to dissolve this material with hyaluronidase in the event of the rare but very real potential complication of vascular occlusion. This may also be useful if there is need for revision in the case of suboptimal cosmetic outcome, such as irregular surface contour or Tyndall effect, especially important in the delicate and unforgiving periorcular region. Given these factors, hyaluronic acid is our filler of choice in this area. There are a variety of types of hyaluronic acid fillers commercially available [Table 2]. The three major brands in the United States are the Restylane® family, Juvederm® family



**Figure 3.** A: Botulinum toxin injection for lateral brow lift and pretarsal orbicularis injection to widen the palpebral fissure. Volumes referenced are independent of neurotoxin variety and assume dilution as specified in the body of the text (i.e., 1 mL saline per 100 unit vial of Botox® or Xeomin® and 3 mL per vial of Dysport); B: proper technique and position for the pretarsal orbicularis injection. While these figures offer a guide, dosing may vary between patients according to their musculature and anatomy

of products, and Belotero®, each of which offer multiple formulations that vary in concentration, particle size, and cross-linking. In general, products with a higher concentration of hyaluronic acid and higher degree of crosslinking are thought to have a higher viscosity and stiffness ( $G'$ ) and greater duration of effect<sup>[10]</sup>.

### Preparation and administration

Most dermal fillers come preloaded in a 1 cm<sup>3</sup> syringe and include the appropriate needle size. Most are made with powder lidocaine to minimize discomfort, but the addition of topical anesthetic for 15-20 min prior to injection is beneficial for the patient.

### Injection techniques

There are four basic techniques commonly used when injecting dermal filler. Choice of technique depends on the location of injection and the complaint being addressed. The first, threading, is the linear application of a continuous line of filler, typically (although not exclusively) injected in a retrograde fashion. Two additional methods build upon this fundamental technique. The crosshatching technique employs continuous lines applied in an overlapping horizontal and vertical pattern to build volume. Fanning is another technique utilizing multiple continuous lines of filler, this time in a fan shaped projection, where multiple lines emanate from a single point of entry as the needle is advanced repeatedly in a radial fashion without withdrawing from the skin. Finally, the serial puncture method involves the delivery of multiple discreet aliquots of product, each with a separate injection<sup>[11]</sup>. Threading may be the best choice for discrete linear rhytids, such as those in the frontalis or glabellar area. Addressing deeper deformities such as the tear trough may be best approached with a serial puncture technique. Larger areas of treatment such as the temple or forehead may require fanning or cross-hatching to build volume, depending on the patient.

### Techniques and tips by location

Tear trough [Figure 4] - this prominence of the lid/cheek junction (also known as the nasojugal or palpebral-malar groove), has historically been very difficult to address with satisfactory results. The development of this deformity is commonly thought to involve both volume loss at the level of the cheek/lid junction as well as increasing prominence of the overlying fat pad<sup>[12]</sup>. The goal of filler injections in this region is to smooth this transition. This area is the most unforgiving area to inject, so care and conservative measures must be

**Table 2. Summary of hyaluronic acid dermal fillers currently commercially available in the United States. All except for Belotero Balance contain lidocaine**

Product*	Site	HA concentration (mg/mL)	Duration (approximate months)
Belotero Balance	Superficial - mid-dermis	22.5	6
Restylane-L	Superficial - mid-dermis	20	6
Restylane Silk	Superficial - sub-mucosal	20	6
Restylane Lyft	Medium - deep	20	9
Restylane Refyne	Medium - deep	20	12
Restylane Defyne	Medium - deep	20	12
Juvederm Ultra XC	Superficial - medium	24	12
Juvederm Volbella	Superficial - medium	15	12-18
Juvederm Vollure	Medium - deep	17.5	12-18
Juvederm Voluma XC	Medium - deep	20	12-18
Juvederm Ultra Plus XC	Medium - deep	24	18

HA: hyaluronic acid

**Figure 4.** Volume restoration with dermal fillers. Common periocular treatment areas include the temple (A) and tear trough (B)

taken. The authors' choice of filler for this area is a hyaluronic acid with low water affinity, as chronic fluid collection can be a problem leading to the need for surgical excision. We most commonly use Restylane®, but have also used Restylane Refyne®, Belotero®, Juvederm Volbella®, and Juvederm Vollure® in this area. In terms of technique, we introduce the needle bevel down and advance to the periosteum of the inferior orbital rim in order to achieve a sub-orbicularis plane. Deep injection avoids visible product and irregular contour. Product is delivered just above the periosteum in multiple small boluses working from medial to lateral. Prior to injection, it is important to palpate the orbital rim to avoid advancing past this barrier and into the orbit. If midface filler is to be applied, this should be performed prior to tear trough injections, as midface volume often decreases the appearance of the tear trough. It is better to under correct than overcorrect in this delicate area; typically injections are 0.3-0.4 mL per session, per side<sup>[8]</sup>.

Superior sulcus - hollowing of the superior sulcus is one of the earliest signs of aging in the periorbital region<sup>[13]</sup>. Injection should target the underside of the superior orbital rim, again advancing to bone and aiming for a sub-orbicularis plane. Subcutaneous injection is also possible, although more superficial injections are at a higher risk of poor cosmetic outcome. The supraorbital notch should be palpated prior to injection to avoid compromising the eponymous nerve; likewise it is important to avoid injecting into the eyelid, staying above the superior sulcus at all times. Take care not to advance the needle far into the orbit, as the risk of damage to important structures and retrobulbar hematoma will increase.

Temple - volume loss in the temples leads to prominence of the bony orbital rim and lateral brow ptosis<sup>[14]</sup>. A more robust product with a high G', such as Juvederm Voluma®, Restylane Lyft®, or Radiesse® (a calcium hydroxylapatite product), is preferable in this area. When introducing filler in this region, care must be taken to avoid both the blood vessels and branches of the facial nerve coursing through this area. Recall that the path of the facial nerve as it courses through the superficial temporal fascia may be roughly estimated by drawing a line from 0.5 cm inferior to the tragus to 1.5 cm superior to the lateral brow<sup>[15]</sup>. Injection should be initiated in the area of greatest volume loss and typically at least 1 cm lateral to the lateral orbital rim. A deep plane under the fascia of the temporal muscle on the periosteum is generally safe and also provides a nice cosmetic result. Injection volume varies from less than 1 to over 2 mL per side depending on the degree of correction required.

Filler may also be used to address static rhytids in combination with toxin injection, as well as to restore volume and arch to the lateral brow, crow's feet and glabella.

### **Potential complications**

Complications of dermal filler injections include Tyndall effect (a bluish hue to the skin resulting from superficial filler injection), irregular surface contour, hypersensitivity reaction and/or granulomatous inflammation, and the development of festoons or chronic fluid collections. The most serious potential side effects include vascular occlusion leading to tissue necrosis or worse, blindness from retrobulbar hemorrhage or central retinal artery occlusion. In general, proper injection technique and depth minimize the risk of poor cosmetic outcomes such as the Tyndall effect or contour irregularities. As mentioned above, the choice of filler with low water affinity is important to avoiding the development of chronic fluid collections. Vascular occlusions are discussed in more depth below.

### **Vascular occlusion and ocular ischemia: the most devastating potential complications of dermal filler injection**

Intra-arterial injection of filler may result in vascular occlusion with either anterograde or retrograde embolus of product. Local embolus can lead to soft tissue necrosis or a distant embolus can lead to permanent blindness. If the force of intra-arterial injection is greater than mean arterial blood pressure, retrograde flow can potentially introduce filler into the ophthalmic or central retinal artery, or long and short posterior ciliary arteries, leading to visual loss. More proximal flow may introduce filler into the middle cerebral artery resulting in cerebral infarction. If tissue necrosis should occur, there are several important steps to take to restore perfusion. First, warm compresses can be used to promote local vasodilation (this low risk treatment is theoretically helpful, although there is no data to support its efficacy and there is some worry that vasodilation can encourage an embolus to flow further distally). Topical nitroglycerin may also be used to promote vasodilation, with the same theoretical advantages and disadvantages. Again, there is no evidence proving its effectiveness<sup>[16]</sup>. Second, the area should be flooded with injected hyaluronidase; this is the only proven treatment for this complication. Generally, subcutaneous injection is thought to be sufficient, but intra-arterial administration may also be considered if possible and time allows. Practically, reintroduction of the needle into the occluded artery may not be possible, and prior studies have shown that extravascular hyaluronidase is effective on the intravascular material<sup>[17]</sup>.

It is important to have a large volume of hyaluronidase easily accessible for prompt treatment; we recommend at least 10 (unexpired) vials. There are a variety of hyaluronidase formulations available, which may be of human recombinant or animal derived origin. Characteristics such as storage parameters, preservatives, units per vial, and reconstitution requirements vary. Although different types of filler may respond to hyaluronidase differently, there is no evidence to suggest that a specific hyaluronidase formulation is more effective<sup>[18]</sup>. Although there are rare reports of allergic reactions to hyaluronidase, skin



testing is not performed in this acute setting, but may be considered if administered for a non-emergent cause (i.e., cosmetic revision of prior injection)<sup>[19]</sup>. Multiple round of injections of hyaluronidase flooding the ischemic site may be necessary, and the patient should remain in-office until reperfusion is achieved. In the event of occlusion of the ophthalmic circulation, treatment is more complicated, and no treatment has been proven effective. Potential options include a retrobulbar hyaluronidase injection, which comes with a fair amount of risk and must be administered by a trained provider, intra-arterial hyaluronidase injection, and attempts to increase the perfusion pressure of the retina and optic nerve by lowering intraocular pressure<sup>[16]</sup>. Prompt referral to an ophthalmologist should be made. For a more complete discussion of the management of various types of filler complications including vascular occlusion, the authors refer you to the review article by Hwang<sup>[16]</sup>. Given the gravity of these complications, prevention is paramount and conservative injection techniques with background knowledge are essential.

Tips for prevention:

1. Needle positioning: the authors recommend the needle be introduced in a direction perpendicular to arterial vessels OR parallel to vessels with needle pointed in the direction of distal flow;
2. Use a small needle, but not too small so as to avoid arteriolar cannulation;
3. Withdraw slightly after introducing the needle;
4. Inject slowly with low flow, low pressure technique so as to avoid introducing filler at a pressure greater than mean arterial pressure;
5. Severe pain is NOT normal; stop if this occurs;
6. Prior to glabellar and superior sulcus injections, digital pressure is applied to the supratrochlear and supraorbital neurovascular bundles, which theoretically occludes the vessels, raises intra-arterial pressure, and reduces the risk of retrograde flow should intra-arterial cannulation occur.

## CONCLUSION

The anatomy and dynamics of the periorbital region make this area particularly vulnerable to aging and particularly complex to treat. Botulinum toxins and fillers, especially when used in combination, offer an excellent approach to minimally invasive rejuvenation of this area. It is important to consider their use within the context of a comprehensive approach to rejuvenation of this area. Additional techniques including laser resurfacing and photorejuvenation may be used as indicated for each individual patient and a combination approach is often required for optimal results. As with any procedure, a thorough understanding of the underlying anatomy and sound injection technique are important to achieve optimal results and avoid complications.

## DECLARATIONS

### Authors' contributions

Conceptualization, writing, and editing of this manuscript: Lee WW, Levitt AE

### Availability of data and materials

None.

### Financial support and sponsorship

None.

### Conflicts of interest

Lee WW acts as a consultant for Allergan, Merz, Galderma, Ophthalmology Web, and Mallinckrodt. Levitt AE has no conflicts of interest to declare.

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

All photographs were obtained and used with consent.

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Case report

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# Pedicated omentum for coverage of extra-abdominal vascular bypass graft in the groin

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## Abstract

The omentum is a well-established pedicled flap for coverage of intra-abdominal and thoracic pathology, and as a free-flap for a multitude of applications. Its use as a pedicled flap for extra-abdominal applications other than those on the chest is less well described. Here we present a case where a pedicled omental flap was utilized to provide circumferential and buried coverage of an in-line ilio-femoral bypass graft well below the level of the inguinal ligament. The reach of the omentum was more than adequate, and the delicate nature of the flap provided excellent circumferential coverage of a cryo-vein bypass graft.

**Keywords:** Omentum, pedicled omentum, reconstruction, groin reconstruction

## INTRODUCTION

Salvage of infected vascular bypass grafts continues to present one of the most complex reconstructive algorithms for both vascular, and plastic surgeons. Graft infection necessitates graft explantation and extra-anatomic bypass, most often with additional synthetic material. These multiply comorbid patients suffer long periods of convalescence in the ICU with attendant bed-rest, ventilator dependency and sepsis.

The omentum is a well established source of intra-abdominal coverage for gastrointestinal (GI), urologic, and vascular anastomotic coverage<sup>[1-3]</sup>. As a pedicled flap it is often used to cover extra-abdominal pathology on the thorax, and as a free flap it may be used in any location<sup>[4-8]</sup>. However, its use as a pedicled flap for extra-abdominal reconstruction has hitherto been largely limited to chest wall reconstruction. Here we present



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a case where a pedicled omental flap reached well below the inguinal ligament to provide circumferential coverage of a vascular bypass graft.

## CASE REPORT

A 46 year-old male with past medical history significant for obesity, type-two diabetes, and ventricular bigeminy presented to outside emergency care with recurrent chest pain consistent with acute coronary syndrome. Cardiac biomarkers were negative, however the recurrent nature and severity of symptoms generated enough concern that the patient was taken for cardiac catheterization, whereupon no significant stenosis was discovered. The patient was diagnosed with likely upper GI pain and discharged to home.

In subsequent follow-up a common femoral pseudoaneurysm was diagnosed as a complication of cardiac catheterization and the patient was taken for open repair by the vascular surgery service. At the time of pseudoaneurysm repair a large arteriotomy was discovered that required circumferential common femoral artery excision and interposition poly tetra fluoro ethylene (PTFE) graft repair. Two days later the patient was taken back to the operating room with a floridly infected PTFE graft and underwent graft excision and cryo-vein reconstruction. At this time plastic surgery was consulted and we performed a pedicled rectus femoris muscle flap for soft-tissue coverage.

Further complications ensued: six months later the patient was noted to have a large retroperitoneal hematoma as a result of graft rupture. This was rapidly treated with retroperitoneal washout by the vascular surgery service. A covered stent was placed across the new vascular defect that covered the take-off of the ipsilateral deep inferior epigastric artery, which would prove to complicate reconstructive options going forward.

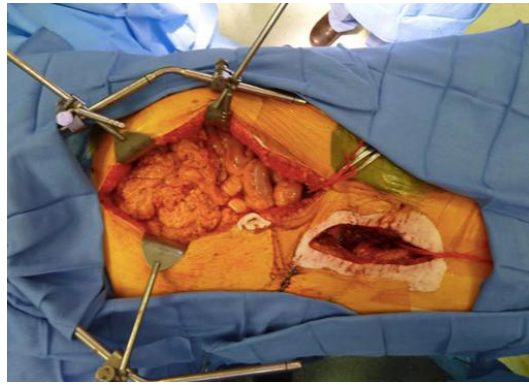
The wound again underwent serial debridement and antibiotic bead therapy under the care of the vascular service with plastic surgical consultation. During this time plans for definitive reconstruction of both the vascular pathology as well as soft tissue coverage were made. Vascular surgery planned to perform open excision of the covered ilio-femoral stent and replace this with a new cryovein conduit.

Following vascular reconstruction, plastic surgery was presented with two wounds. The first a chronic, and serially debrided groin wound with indwelling vascular bypass graft. The second, a midline laparotomy [Figure 1].

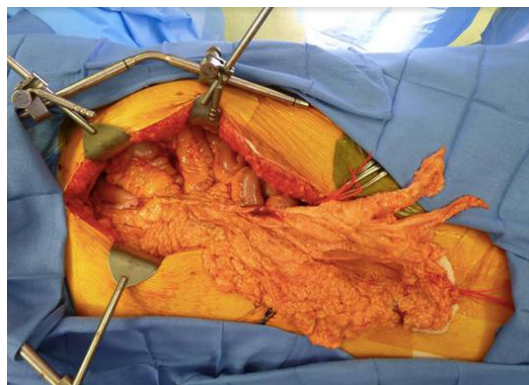
Lengthy discussion was held regarding the method of soft tissue coverage. Because the take-off of the deep inferior epigastric artery was stented across, an ipsilateral pedicled rectus abdominus muscle was not available. The patient had already undergone pedicled rectus femoris transposition, and the plastic surgery service was concerned that additional muscular flaps from the same leg would result in prohibitive disability, especially as the patient previously had an ipsilateral femoral and iliac vein deep vein thrombosis (DVT). Additionally, most of the pedicles for local flap options were “in the zone of injury” of multiple operative debridements and a lengthy period of local infection and inflammation.

Free tissue transfer was also discussed, including free latissimus dorsi and free contralateral antero-lateral thigh (ALT), however, the patient’s clinical condition after prolonged ICU care was seen as potentially prohibitive of these measures.

The plastic surgery service elected to perform pedicled omental flap coverage. Plastic surgery was able to mobilize the patient’s omentum based on the right gastroepiploic artery by dividing the left gastroepiploic artery and serially dividing the arcades to the greater curve of the stomach to within 8 cm of the pylorus. The omentum was unfurled by dividing the entirety of its attachment to the transverse colon and by separating the inner and outer lamellae. Following this dissection, the omentum easily reached below the base of the groin incision to the middle third of the thigh [Figure 2]. The anatomic course of the ilio-femoral



**Figure 1.** A midline laparotomy is seen, in addition to a serially debrided groin wound which contains the bulk of the cryovein bypass graft



**Figure 2.** The omentum has been dissected free of its attachments to the lateral stomach and left gastroepiploic artery. To demonstrate length the omentum has been brought above the inguinal ligament and is seen reaching well below the groin wound to the junction of the middle and upper thirds of the thigh

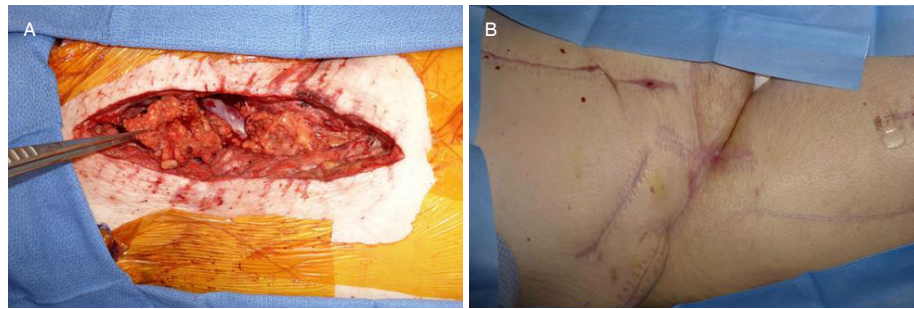
bypass under the inguinal ligament was digitally dilated to allow for the passage of the cryo-vein bypass graft in addition to the omental flap, which was wrapped circumferentially around the graft over its entire length. Following this, both wounds were closed primarily, over closed suction drains.

Post-operatively the patient was kept on bed-rest, and a graduated ambulation protocol was subsequently initiated. The patient was eventually discharged to a local skilled nursing facility. There was evidence of minor superficial wound breakdown at the inguinal crease, which was also the point of maximal tension in our closure. The wound opened over 2 cm in length and 1 cm in depth. This was managed with wet to dry dressings and subsequently resolved [Figure 3]. Six months after reconstruction the patient is ambulatory and there are no indications of recurrent graft infection or vascular compromise. Pre, and post-operative CT images detail the presence of impressive phlegmon with air-fluid levels and subsequent resolution with a functional graft circumferentially wrapped in an omental sheath [Figure 4]. Since surgery the patient has suffered significant GI pathology in the form of nausea, poor oral intake, esophagitis, and duodenal ulcer, though the relation of his GI complaints either to his initial presentation, or to the omental flap is unclear.

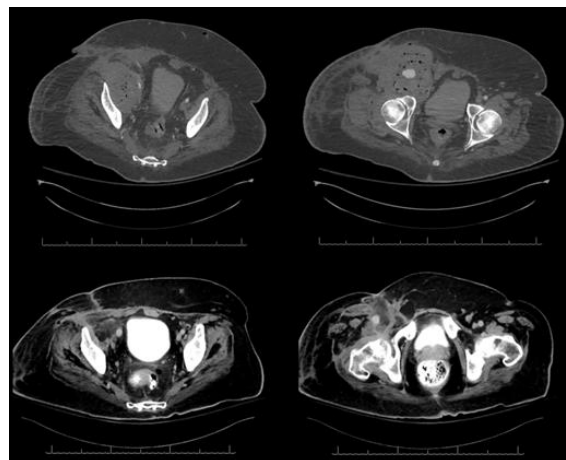
## DISCUSSION

Soft tissue coverage of exposed or infected vascular grafts in the groin presents a difficult challenge for vascular and plastic surgeons alike. In these cases, even when simple soft tissue coverage is available, more robust vascularized tissue is often preferable. A number of established local muscle flaps exist for coverage of femoral bypass grafts including the sartorius, rectus femoris, and gracilis. However, in the multiply re-





**Figure 3.** A: bleeding and viable tunneled omentum providing circumferential coverage of in-line cryo-vein reconstruction; B: six-month follow-up with healed surgical wounds



**Figure 4.** Pre-operative (upper) and post-operative (lower) CT images. Pre-operatively an impressive phlegmon with diffuse gaseous infiltration and mass-effect. Post-operatively the inflammation has resolved, and the graft is seen circumferentially enclosed in an omental sheath

operative groin these options may have already been exhausted the rectus abdominus may also be used, but in our patient the deep inferior epigastric artery (DIEA) had been stented across at the time of secondary pseudoaneurysm repair and was therefore not an option.

In our patient there were little to no options for pedicled reconstruction. In considering free flap reconstruction we evaluated the free ALT and latissimus dorsi, however we preferred to avoid protracted operative time in this multiply comorbid and multiply re-operative patient who had undergone a long ICU course including iliac and femoral vein DVT in the affected extremity.

Omental flaps are well described for chest wall reconstruction based on the right gastroepiploic artery<sup>[7]</sup>. The omentum functions as a physical and immunologic barrier in the abdomen in its native position, and for this reason it is a favorite of general and urologic surgeons for covering anastomoses<sup>[3,5]</sup>.

As a pedicled flap for extra-abdominal and extra-thoracic wound coverage, the omentum is less well documented. In our case the omentum provided an excellent source of circumferential coverage for an inline vascular graft under the inguinal ligament and was delicate enough not to compress a cryo-vein conduit. Additionally, the remaining transposed omentum filled much of the dead space in the large groin wound.

Regarding the reach of the pedicled omental flap, there is little documentation. The size and length of the omentum differs between people widely. Slender people tend to have less robust omentum, however, it is not

always the case that a protuberant abdomen contains a large omental drape, as in many cases mesenteric fat makes up a good proportion of intra-abdominal adiposity in the obese population.

The importance of disinserting the deep lamella of the omentum from the transverse colon cannot be overstated for achieving sufficient length for extra-anatomic applications. Furthermore, by unfurling the internal and external lamellae the length of the apparent omentum may theoretically be doubled.

Though GI complications are known to result from omental flaps, in our patient it is not clear if GI symptoms are a complication of the intervention, or if they are reflective of his inciting pathology. For, the chest pain that he initially underwent negative coronary angiography for was ultimately attributed to recurrent upper GI symptomatology<sup>[5]</sup>. The possibility that these GI complaints are a complication of omental flap is worthy of consideration, and if other pedicled flaps are available in a patient such as this, avoiding these complications should be of prime consideration.

In conclusion, we propose that the pedicled omental flap be considered as a viable option for extra-abdominal vascular coverage option in the groin when either, the abdomen is already open for proximal vascular reconstruction, or when local muscular flap options have been exhausted, or in any case where circumferential graft coverage is required in a confined space.

## DECLARATIONS

### Authors' contributions

Authorship and editing of the manuscript, participation in the procedure discussed: Moores NG, Pannucci CJ

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

IRB approval was not required for this case report.

### Consent for publication

Consent was obtained from the patient for publication of images and details of the clinical case discussed.

### Copyright

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Original Article

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# One-stage mastopexy and augmentation mammoplasty in layers: outcome analysis of first 50 consecutive cases

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## Abstract

**Aim:** The single-stage procedure is a challenging procedure for Plastic Surgeons. The single-stage layered mastopexy with augmentation is a new technique that is aiming to add safety, preserving breast function and to restore normal parameters of breast.

**Methods:** A retrospective chart review of 50 consecutive cases of layered mastopexy with augmentation mammoplasties was performed. All patients had their implants placed in muscle splitting pocket. Incisions for mastopexy were selected on the basis of nipple areolar complex to inframammary crease. Mastopexy is performed using a medially based pedicle, leaving a sufficient tissue covering the implant. Patients were divided into three groups. Group "A" who had periareolar mastopexy, Group "B" had vertical scar mastopexy and Group "C" patients had mastopexy with Wise pattern markings.

**Results:** Group A comprised 11 patients. The mean age was  $28.82 \pm 7.01$  years, mean preoperative and postoperative nipple areolar complex (NAC) to IMC measurement was recorded in 10 patients with the mean of  $7.15 \pm 1.98$  cm and  $8.35 \pm 1.18$  cm respectively. Mean size of the implant used was  $379.55 \pm 77.18$  cm<sup>3</sup>. Group B comprised 29 patients. Mean age was  $35.17 \pm 12.37$  years and the mean preoperative and postoperative NAC to IMC crease was  $8.53 \pm 1.48$  cm and  $9.72 \pm 1.51$  cm respectively. The mean implant size used was  $289.48 \pm 109$  cm<sup>3</sup>. Group C had 10 patients. Mean age was  $39.60 \pm 12.15$  years and the mean preoperative and postoperative NAC to IMC crease of  $10.11 \pm 1.24$  cm and  $8.75 \pm 0.98$  cm respectively. The mean implant size used was  $287.00 \pm 55.08$  cm<sup>3</sup>.

**Conclusion:** The procedure allows better arterial supply, wider area for venous and lymphatic drainage, better sensory innervation to NAC and maximises lactation potential of the breast.



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**Keywords:** Mastopexy, augmentation mammoplasty, augmentation with mastopexy, muscle split technique, one-stage mastopexy with augmentation

## INTRODUCTION

Historically breasts are considered a sign of femininity, fertility and beauty. From the time of puberty, attainment of body silhouette with feminine curve is considered an accomplished milestone. A lack of or loss of such proportions may potentially affect the self esteem in some individuals whether the condition is primary or secondary, following pregnancies, breast feeding, ageing or loss of weight. Augmentation and mastopexy is one commonly performed procedure to restore the body silhouette, feminine curves and attractive body proportions. The procedure can be performed in stages as mastopexy first to be followed by implant placement later or one stage mastopexy with augmentation. One-stage or simultaneous mastopexy with augmentation has an advantage of being cost-effective along with single hospitalisation and single recovery. Even though the procedure was first performed by Gonzalez-Ulloa<sup>[1]</sup> and Regnault<sup>[2]</sup>, one still has to go through a challenging learning curve before starts achieving consistently predictable results. The results of one-stage augmentation mastopexy are frequently compared with mastopexy or breast augmentation when performed alone<sup>[3-8]</sup>. Outcome of these studies have concluded that in suitably selected patients, one-stage augmentation mastopexy procedure is relatively safe. However the analysis was primarily carried out to compare the complications of each constituent components without considering the influence of the technique used for implant placement or markings selection for breast or skin excision and their impact on the physiological, anatomical or aesthetic outcome.

Implant pocket for mammoplasty and skin tightening for mastopexy are two distinctively separate procedures regardless of the stages selected, each influencing the other as well as having an impact on overall results<sup>[9]</sup>. Various implant pockets, from initial subglandular pocket to the most recent Muscle Split Biplane technique, highlight the importance and advantages attached to each<sup>[10-14]</sup>. Scar selection for mastopexy can be a surgeon's choice. However, it is not without its impact on the outcome leading to revision surgeries<sup>[5,15,16]</sup>. There is a lack of information where a technique has been defined for the preservation of the function of breast, the safety of the procedure along with the restoration of normal breast morphometry leading to a predictable aesthetic outcome. The following is the author's experience of having performed 50 one-stage augmentation mammoplasties in two years.

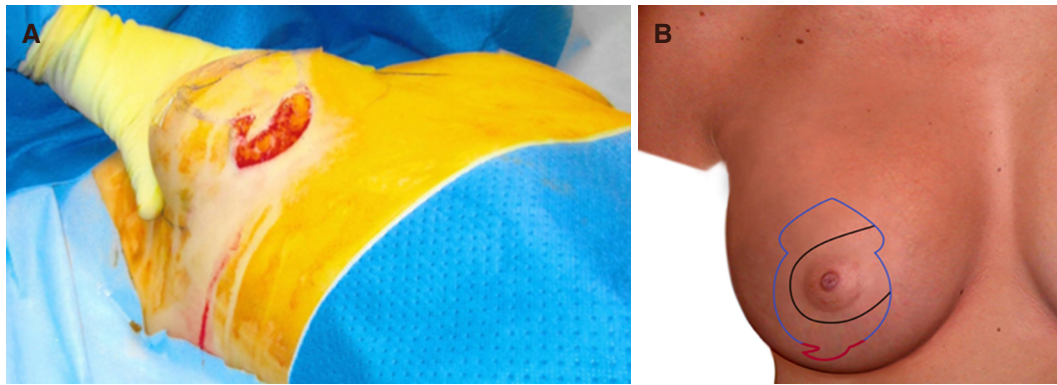
## METHODS

A retrospective analysis of 50 cases of consecutive layered mastopexy with augmentation mammoplasties, over a 2-year period, was carried out. All patients had Regnault Grade II or III ptosis where Grade II ptosis is when nipple areolar complex (NAC) 2-3 cm below infra mammary crease (IMC) and grade III ptosis is when NAC is > 3 cm below IMC. All implants were placed in muscle splitting pocket first and access for the pocket was closed prior to the commencement of mastopexy. Incisions for mastopexy were selected on the basis of pre-existing NAC to IMC. In all cases, mastopexy is performed using a medially based pedicle, leaving a good layer of breast parenchymal tissue covering the implant, below and above the pedicle and where skin excision is performed. Patients were divided into three groups on the basis of existing NAC to IMC measurements.

Group "A" comprised patients who had periareolar mastopexy, Group "B" had patients with vertical single scar markings and Group "C" comprised patients who had their mastopexy carried out using Wise pattern markings.

All patients provided written informed consents. The study was performed with guiding principles set forth in the Declaration of Helsinki.





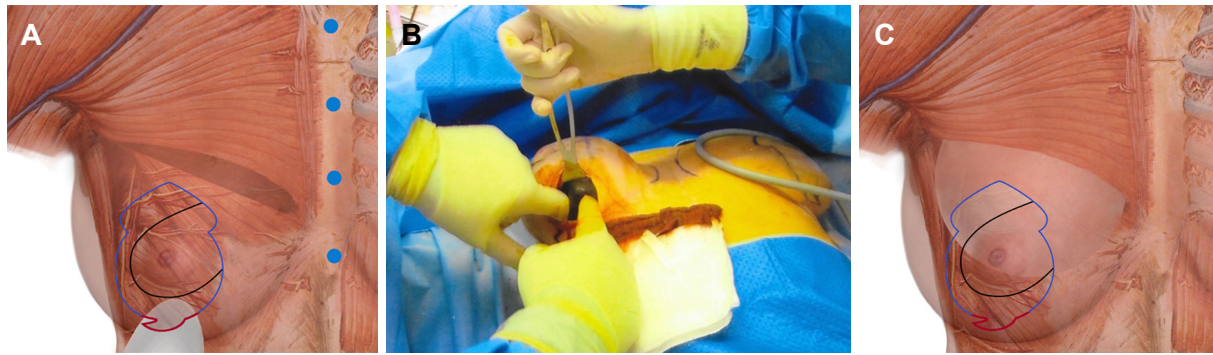
**Figure 1.** Intraoperative picture and illustration of patient showing incision at the lower end of vertical scar single staged mastopexy with augmentation (A, B)

### Markings and technique

After taking careful history and examination, patient's breast measurements are taken. Markings for mastopexy are selected on the basis of NAC and IMC measurements. Selection of size of the implants is made for each patient according to the selected markings and patient's requirements where possible. Limitation of increase in breast cup size is explained to the patient. When vertical or Wise pattern scar is selected, no more than two cup sizes are promised. Patients presenting with breast asymmetry and chosen for vertical or Wise pattern scars, have more tissue excised from larger breast with similar size breast implants placed on both sides. Patients presenting with breast asymmetry and selected for periareolar scars, are managed with different size implants.

All patients are marked in standing position with medially based flap and 4.2 cm NAC. IMC is taken as a reference for neo-NAC repositioning. Patients with NAC to IMC measurements of less than 5 cm and with a lack of skin envelope are selected for Benelli periareolar markings. Patients with measurements between 5 cm to 8 cm are selected for vertical scar and patients with NAC to IMC measurement of more than 8 cm are best suited for Wise pattern scar. Patients with pseudoptosis and wishing for an increment of at least three breast cup sizes are considered for periareolar mastopexy with implants, even if they present with more than 5 cm NAC to IMC distance.

Single-staged mastopexy with augmentation is performed as a day case under full general anaesthetic with full muscle relaxation. A single intravenous dose of Cephalosporin is given followed later by an oral course of antibiotics for five days. No drains are used for this procedure. Existing IMC is marked along with new position of the nipple, usually 1.5 cm higher than IMC. In vertical and Wise pattern scars mastopexy, Keyhole for neo NAC is marked with upper margin of the neo-NAC, 2.5 cm higher than the marked neo-nipple position. Medial and lateral margins of the neo-NAC are marked at 3.5 cm from the centre of the keyhole. From this point two lines, 2.5-3 cm long each, are dropped, gently curving down centrally to leave 5-6 cm as the neck of the keyhole. From the neck of keyhole, 5-7 cm long gently curvilinear lines are dropped down and generally 6-8 cm apart at its widest. In vertical scar markings, the lines are extended inferiorly toward the central line drawn between the mid-clavicular points to a mid-point on IMC, generally 8.5-9 cm from body midline. These vertical markings end 2 cm higher than the existing inframammary crease and a cat's tail extension is drawn laterally for the prevention of dog-ear. In Wise pattern markings, 5-7 cm long medial and lateral markings are extended to the medial and lateral extent of the marked IMC crease. This transverse wedge or ellipse of skin helps to raise the existing IMC, control and reduce postoperative NAC and IMC measurements and limits available skin envelop to prevent future bottoming out. Implant pocket is accessed through an incision made at the lower end of the Cat's tail marking or middle of the transverse crease, which is about 5 cm wide [Figure 1A and B]. After initial subglandular pocket in lower and outer



**Figure 2.** Picture showing showing implant in muscle split pocket (A); illustrations showing level of muscle split at the junction of middle and lower third sternum and implant in muscle splitting pocket (B, C)

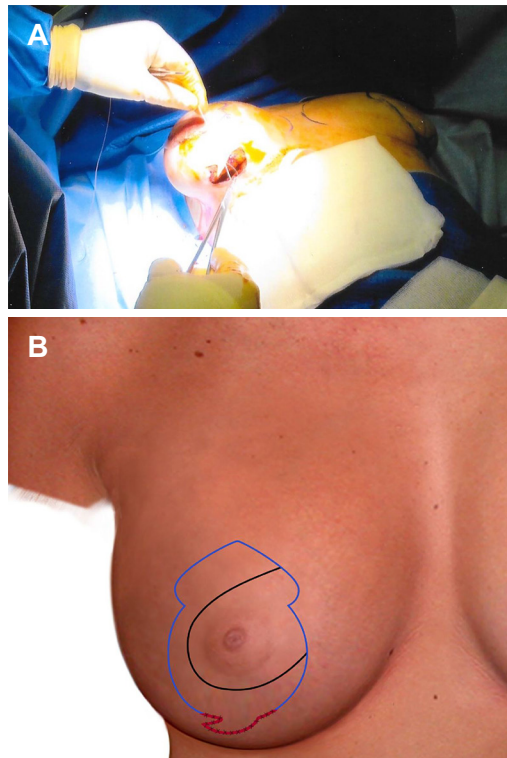
quadrant, a muscle split biplane pocket is created. The pectoralis is split from the junction of middle and lower third of sternal attachment and continues up and laterally to the anterior axillary fold along a line just below Neo-NAC. Round cohesive gel silicone implants are placed in muscle split biplane pocket through the lower end of the vertical scar or Wise pattern markings [Figure 2A-C]. Patients with periareolar markings have their implants placed through a separate access in IMC. Once implant placement is completed, haemostasis is checked and access is closed [Figure 3A and B].

Using Lane's forceps, skin markings are checked for tension free closure with implant already in place. Adjustments are made where required for a safe and tension free closure. Marked medially based flap is de-epithelialized, leaving 4.2 cm wide NAC as a routine in all three types of markings [Figure 4A]. Skin and subcutaneous tissue excision is performed, in moderation, superior and lateral to the de-epithelialised flap to create an adequate space for flap mobilisation and resetting [Figure 4B]. In vertical and Wise pattern markings, skin excision is continued below the medially based flap and according to the skin markings. Between the medial and lateral vertical markings, the tissue excision is little more generous to prevent lower pole redundancy but leaving enough tissue layer and without implant being visible through intermediate layer [Figure 5A]. In Wise pattern markings, tissue is excised from lateral and medial extensions, into the respective pole of the breast, in a similar way. A good layer of breast parenchymal tissue is left for implant coverage [Figure 5B]. Haemostasis is performed, three layer closure is done using absorbable sutures [Figures 6 and 7]. Flap is checked for tension free closure and nipple circulation, if any tightness is observed, piecemeal tissue is removed between flap and new-NAC margins. In case of skin envelope tightening, nipple circulation compromise or venous congestion, I do not hesitate exchanging for smaller size implants.

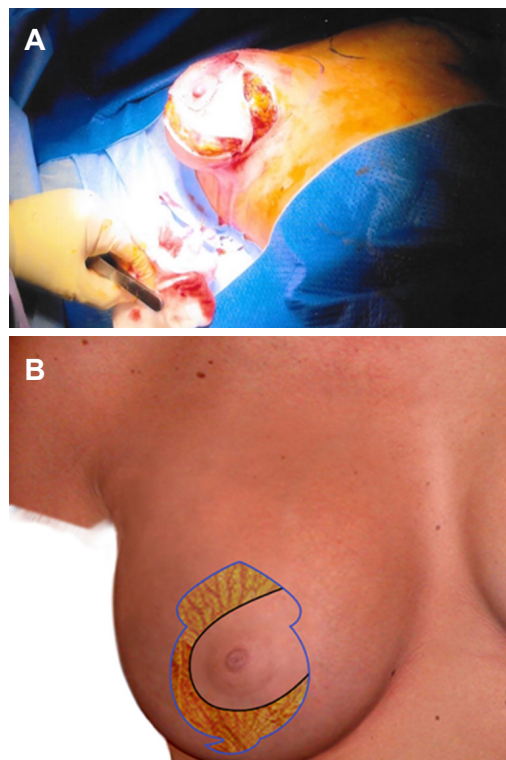
After closure, steri-strips and light adhesive dressings are applied. A decent size hole is left in the dressing covering NAC for its circulation monitoring. A compression brassiere is placed and patients are transferred to the ward for postoperative monitoring. Nipple circulation is checked hourly before the patients are discharged. Patients are advised to take a picture of the nipples and send it to author if they notice any change in colour for an early and timely intervention.

### Statistical analysis

The data were analysed using the Statistical Package for the Social Sciences (SPSS), version 19.0. The results are presented in the text as frequency, percentage for qualitative/categorical variables and mean, Standard deviation for quantitative/continuous variables. The Chi-square/exact test is used to compare the categorical variables and ANOVA test for quantitative/continuous variables. In all statistical analysis, only *P*-values < 0.05 are considered significant.

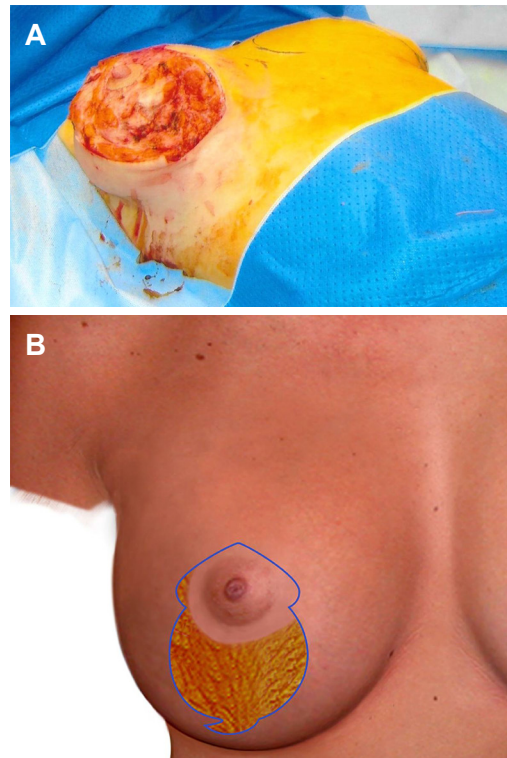


**Figure 3.** Intraoperative picture and illustration showing deep fascial layer of implant pocket access being closed (A, B)

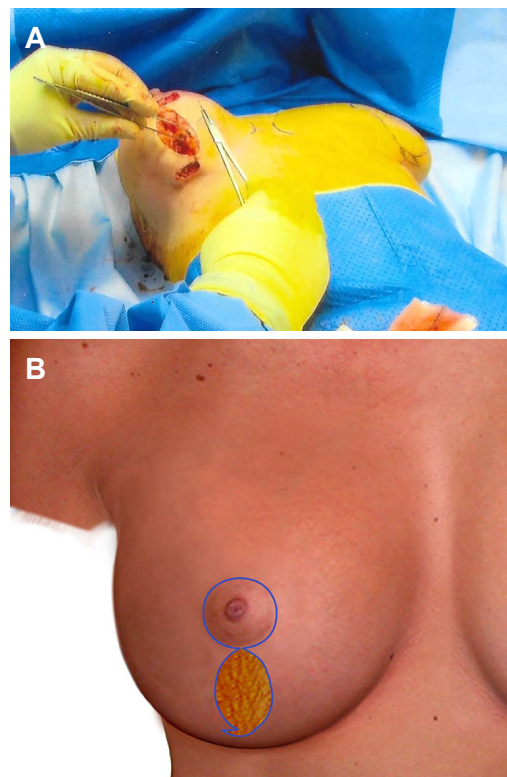


**Figure 4.** Superomedial de-epithelialised pedicle with incised vertical scar margins (A, B)

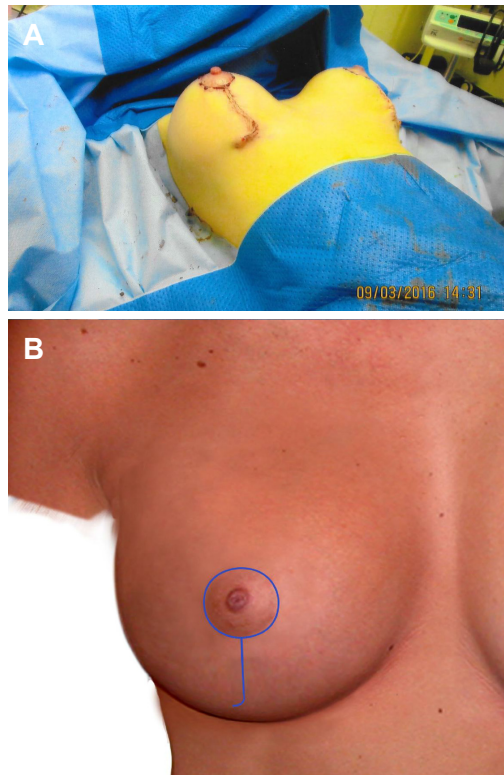




**Figure 5.** Tissue excision superior, lateral and inferior to the pedicle leaving enough tissue cover for the implant cover (A, B)



**Figure 6.** Intraoperative picture and illustration showing mobilised nipple areolar complex into its new position and commencement of layered closure of medial and lateral pillars (A, B)



**Figure 7.** Intraoperative picture and illustration showing completion of procedure (A, B)

## RESULTS

### Group A

The group comprised 11 patients. The mean age of the patients was  $28.82 \pm 7.01$  years (range 20-44), mean preoperative and postoperative NAC to IMC measurement, recorded in 10 patients, was  $7.15 \pm 1.98$  cm (range 4.5-11) and  $8.35 \pm 1.18$  cm (range 7.0-10.0) respectively. Mean preoperative Sternal Notch (SN) to NAC, marked SN to NAC and postoperative SN to NAC measurements were  $22.45 \pm 2.06$  cm (range 19.5-26.0),  $20.95 \pm 1.01$  cm (range 19.5-22.5) and  $22.33 \pm 0.60$  cm (range 22-24) respectively. Tissue excised was minimal and not measured. Mean size of the implant used was  $379.55 \pm 77.18$  cm<sup>3</sup> [Table 1 and Figure 8A-F].

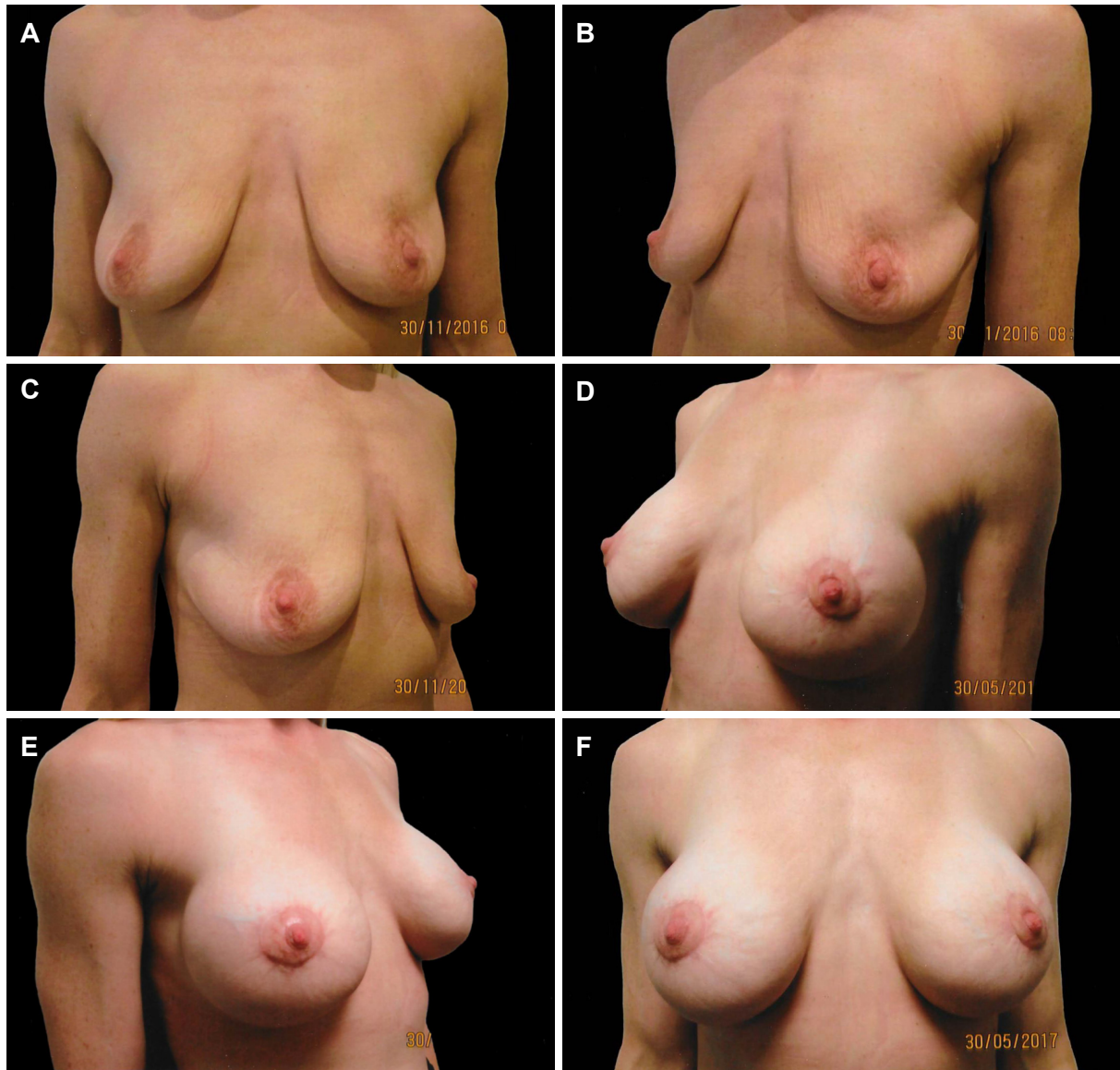
### Group B

The group comprised 29 patients. The mean age of group was  $35.17 \pm 12.37$  years (range 20-66) and the mean preoperative and postoperative NAC to IMC crease of  $8.53 \pm 1.48$  cm (range 5.0-13) and  $9.72 \pm 1.51$  cm (range 6.5-12) respectively. Mean preoperative Sternal Notch (SN) to NAC, marked SN to NAC and postoperative SN to NAC measurements were  $24.69 \pm 2.01$  cm (range 21.5-30),  $21.00 \pm 1.25$  cm (range 18.5-23.5) and  $20.76 \pm 1.40$  cm (range 19-24) respectively. Mean weight of the tissue excised was  $46.67 \pm 17.39$  g (range 17-78) and  $56.00 \pm 23.84$  g (range 28-106) on the right and left side respectively. The mean implant size used was  $289.48 \pm 109$  cm<sup>3</sup> [Table 1 and Figure 9A-F].

### Group C

The group comprised 10 patients. The mean age of group was  $39.60 \pm 12.15$  years (range 23-64) and the mean preoperative and postoperative NAC to IMC crease of  $10.11 \pm 1.24$  cm (range 9-13) and  $8.75 \pm 0.98$  cm (range 7-10) respectively. Mean preoperative Sternal Notch (SN) to NAC, marked SN to NAC and postoperative SN to NAC measurements were  $27.27 \pm 2.70$  (range 23.0-32.0),  $23.30 \pm 3.22$  (range 19.5-31.0) and  $21.92 \pm 2.33$  cm (range 19-25) respectively. Mean weight of the tissue excised was  $138.50 \pm 63.44$  g (range 77-227) and  $124.50$





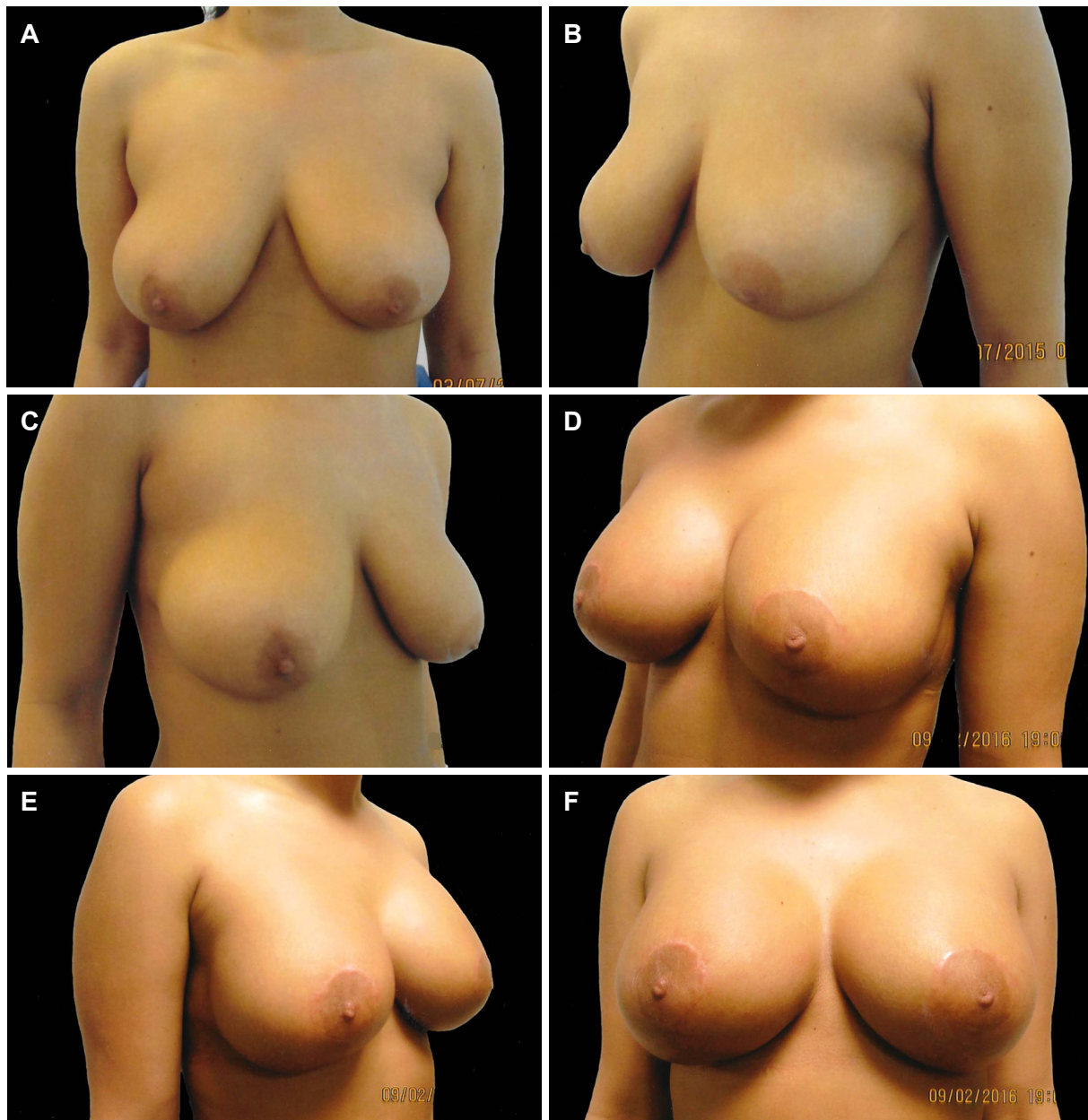
**Figure 8.** Preoperative pictures of a 36-year female following weight loss, presenting with pseudo-ptosis with empty skin envelope (A-C); six months postoperative pictures showing periareolar layered mastopexy using 345 cm<sup>3</sup> high profile round textured cohesive gel silicone implants (D-F)

$\pm 15.28$  g (range 124.50) on the right and left side respectively. The mean implant size used was  $287.00 \pm 55.08$  cm<sup>3</sup> [Table 1 and Figure 10A-F].

In the series, there was no haematoma, wound breakdown or nipple loss. There was one implant related complication in which patient developed a Grade III to IV Capsular contracture without pain or loss of shape. There were two revisions performed/planned related to mastopexy. One patient developed bottoming out following a vertical scar mastopexy where preoperative NAC to IMC measurements on the right larger breast was 9 cm. The other was a patient who presented with a breast hypertrophy and severe ptosis, lost the shape of the breast postoperatively following further weight loss. She is waiting for her scars to settle down before a skin envelope readjustment is performed.

## DISCUSSION

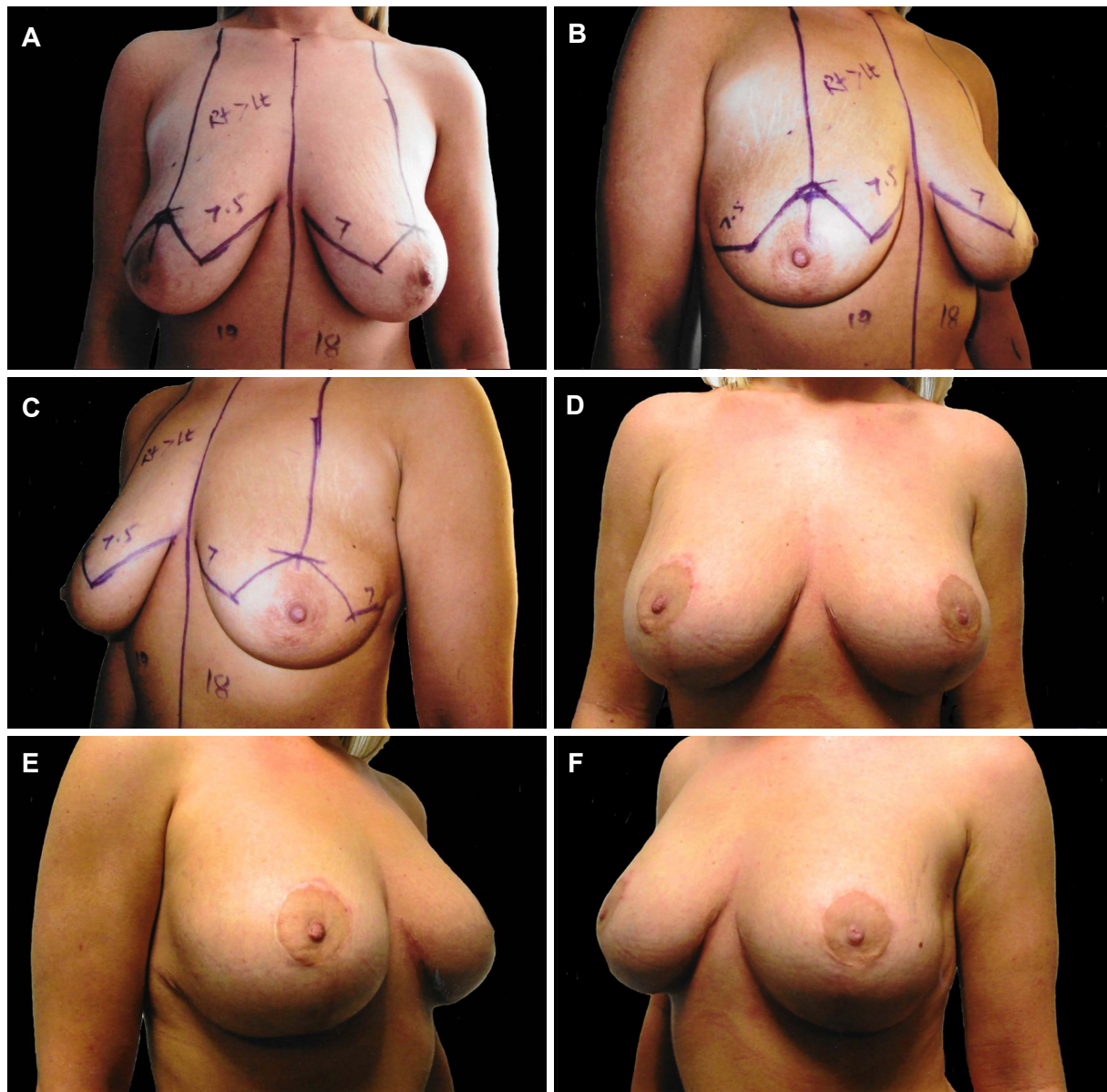
One-stage mastopexy and augmentation mammoplasty remains a challenging procedure for all Plastic Surgeons especially for those who are at the beginning of their career. Since the introduction of the



**Figure 9.** Preoperative pictures of a 19-year-old nulliparous female who presented with asymmetry and Grade C ptosis of breast (A-C); post-operative pictures taken eight months following surgery with 240 cm<sup>3</sup> extra high profile, round textured cohesive gel silicone implants (D-F)

procedure<sup>[1,2]</sup>, single stage mastopexy with augmentation's overall safety, outcome and complications are compared when the augmentation mammoplasty or mastopexy is performed alone<sup>[3-8]</sup>. Intrinsically single-stage mastopexy with augmentation is a combination of two procedures<sup>[9]</sup>, the augmentation, in which an implant is placed in any pocket<sup>[9-14]</sup> and the mastopexy, where markings can be selected on the basis of surgeon's experience<sup>[5-7,16]</sup>. The challenging aspect of the surgery is the combination of the two procedures where mastopexy is performed to reduce and tighten the breast skin envelope and breast implant is placed to expand skin envelope and enhance breast cup size, both being diagonally opposite<sup>[17]</sup>. As opposed to patients requiring breast implants for augmentation or requesting mastopexy for ptosis correction, the cohort of patient requiring single-stage mastopexy with augmentation is a totally different clinical subgroup. In later cohort of patients, mastopexy alone will leave them with too small and disproportionate





**Figure 10.** Preoperative pictures of a 22-year-old patient who presented with Grade B ptosis following pregnancy (A-C); postoperative pictures taken five months following her surgery using 230 low profile textured round cohesive gel silicone implants (D-F)

breasts and augmentation alone will result in a larger breast with displeasing ptosis. A patient requiring augmentation mammoplasty alone generally has a hypoplastic breast with parameters in normal but reduced proportion, in these cases an implant alone will enhance breast proportionally without disturbing overall interrelationship of individual normal breast parameters. On the other hand, a patient requiring mastopexy with augmentation presents with a relatively larger breast accompanied with ptosis along with deranged inter-relationship of its constituent morphological parameters. An ideal breast surgery in this cohort needs to restore the normal parameters, enhance breast size in moderation and reduce skin envelope without compromising safety or physiological function. Ideally, incision and marking selection for single-stage mastopexy with augmentation is paramount to achieve such desired goals and symmetry<sup>[18]</sup>. These parameters are achieved in current series where relative proportions of operated breasts were brought into harmony again. With statistically different preoperative NAC to IMC and STN to NAC measurements in all three types of markings used [Tables 1-3], markings based on preoperative NAC-IMC measurements,

**Table 1. Showing age of the patients, implant size used and tissue removed in relevant groups**

	Type of procedure	Number	Range	Mean	Std deviation	P value
Age in years	PA	11	20-44	28.82	7.01	0.101
	VSCT	29	20-66	35.17	12.37	
	WP	10	23-64	39.60	12.15	
Implant size (cm <sup>3</sup> )	PA	11	275-560	379.55	77.18	0.026
	VSCT	29	240-800	289.48	109.00	
	WP	10	225-420	287.00	55.08	
Tissue excised right side (g)	VSCT	12	17-78	46.67	17.39	0.001
	WP	4	77-227	138.50	63.44	
Tissue excised left side (g)	VSCT	12	28-106	56.0	23.84	0.001
	WP	4	105-142	124.50	15.28	

PA: periareolar; VSCT: vertical scar Cat's tail; WP: Wise pattern

**Table 2. Preoperative and postoperative nipple areolar complex and inframammary crease measurements in three groups**

	Type of Procedure	Number	Range	Mean	Std deviation	P value
NAC-IMC Preoperative	PA	10	4.5-11.0	7.15	1.98	0.001
	VSCT	29	5.0-13.0	8.53	1.48	
	WP	9	9.0-13.0	10.11	1.24	
NAC-IMC Postoperative	PA	7	7.0-10.0	8.35	1.18	0.056
	VSCT	23	6.5-12.0	9.72	1.51	
	WP	6	7.0-10.0	8.75	0.98	

PA: periareolar; VSCT: vertical scar Cat's tail; WP: Wise pattern

**Table 3. Pre and postoperative Suprasternal notch to nipple areolar complex measurements in three groups**

	Type of procedure	Number	Range	Mean	Std deviation	P value
Preoperative STN-NAC	PA	11	19.5-26	22.45	2.06	0.001
	VSCT	29	21.5-30.0	24.69	2.01	
	WP	10	23.0-32.0	27.27	2.70	
Marked STN-NAC	PA	10	19.5-22.5	20.95	1.01	0.003
	VSCT	29	18.5-23.5	21.00	1.25	
	WP	10	19.5-31.0	23.30	3.22	
Postoperative STN-NAC	PA	6	22-24	22.23	0.60	0.063
	VSCT	19	19-24	20.76	1.40	
	WP	6	19-25	21.92	2.33	

STN; suprasternal notch; NAC: nipple areolar complex; PA: periareolar; VSCT: vertical scar Cat's tail; WP: Wise pattern

allowed the postoperative measurement and dimensions in all three subsets to be similar and comparable without any statistical significance [Tables 1-3]. In restoring and achieving such proportions, parameters and desired aesthetic results are achieved when the two components of single stage procedure were performed independently to each other in the same setting. Augmentation mammoplasty is performed first independent of the mastopexy and once accomplished, the access is closed and then operation proceeds to mastopexy at the same time as the second half of the procedure. The independence of each procedure, performed separately at the same time, helps to maintain the integrity of each and without disturbing the other and allowing the surgeon to have a control on each of the procedure's components. When the procedure is performed in layers, as described in the technique section, the process allows maximising safety of the procedure and aims to retain the physiological functions of the breasts at the same time. Medially based NAC flap has an enhanced blood supply due to its broader link to surrounding tissues as it is not entirely based on length and breadth ratios, similarly venous and lymphatic drainage is assisted due to pedicle's wider connections. Retention of the sensory potential of the NAC is more predictable and in childbearing age females, lactation potential of the breast for future pregnancies is sufficiently preserved.

**Table 4. Profile of the cohesive gel silicone implants used in periareolar, vertical scar cat's tail and Wise pattern markings**

Implant profile	Type of procedure			P value
	PA	VSCT	WP	
High profile	5 (45.5%)	6 (20.7%)	1 (10.0%)	0.017
Moderate profile	1 (9.1%)	19 (65.5%)	7 (70.0%)	
Extra high profile	5 (45.5%)	4 (13.8%)	2 (20.2%)	

PA: periareolar; VSCT: vertical scar Cat's tail; WP: Wise pattern

In the series Moderate profile implants were most commonly used in VSCT and WP scars mastopexy as compared to extra high implants used in PA mastopexy with implants [Table 4].

Another safety feature of having an intervening layer of robust tissue, between closure lines and implant, is the potential advantage of implant not being exposed should there be any skin envelope breakdown. This wound breakdown is not uncommon following Wise pattern markings at the junction of vertical and horizontal closure. Wound breakdown with resultant exposure or extrusion of implant necessitates implant removal with a time lapse to allow healing to consolidate before further insertion of the prosthesis is considered possible. The intermediate layer can enable the wound to be treated conservatively obviating the explantation of the device with its concomitant morbidity and patient's disappointment and distress. Even though there is a lack of techniques described to preserve function and add safety to the procedure, a recently published Balcony Technique, has described the preservation and use of lower half of subcutaneous layer of breast tissue as an intermediate layer of balcony sandwiching implant between itself and pectoralis muscle<sup>[19]</sup>. This preserved layer of tissue acts, as a safety net in Wise pattern closure where T-junction wound breakdown is not uncommon. However, lower half of balcony tissue layer requires its dissection separately and once achieved, is discontinuous with the upper half of the breast. The balcony technique is novel on its own but layered mastopexy provides continuity of the intermediate tissue layer without additional dissection that enhances arterial supply to the pedicle with wider area for venous and lymphatic drainage and is associated with least cutaneous sensation and lactation potential discontinuity and disruption. Other breast conserving single stage mastopexy with augmentation procedures have been described. The least invasive being simple deepithelialisation with a temporary overinflated expander and once the mastopexy is completed, the expander would be replaced with suitable smaller size implants in the same setting<sup>[20]</sup>.

Owsley has described breast conserving single stage augmentation mastopexy. The technique involves circumferential skin undermining between proposed new NAC level and existing inframammary crease. Pocket for implant is approached by incising lower edge of the breast and inflatable devices placed and skin only excision performed as Wise pattern<sup>[21]</sup>. Similarly minimal tissue excision in Wise pattern inferior pedicle flap or periareolar markings with submuscular implants is described<sup>[22]</sup>. However almost all of these techniques have limitations in that they are suitable for hypoplastic or small ptotic breasts. Preservation of tissue in lower pole of the breast may result in redundancy and secondary ptosis of lower pole. Layered single stage augmentation mastopexy addresses this issue, with excision of tissue in the lower central pole allowing breast tissue to mould and drape over the implant for natural and aesthetic rejuvenation. The Layered single stage augmentation mastopexy technique also allows the procedure to be performed in less than ideal patients who present with hypertrophy with ptosis without much risk to the safety of the nipple. However, the outcome of these procedures where larger reductions are performed for mastopexy, is less than ideal in aesthetic terms. The aim and priority of an ideal procedure has to be safety of the procedure as well as good aesthetic outcome with longer lasting results. I prefer to operate on this particular group of patients as a staged procedure where reduction and mastopexy should be performed first and augmentation mammoplasty should follow later.

The weakness of the study is that there was no objective and scientific assessment of enhanced arterial supply, better venous and lymphatic drainage performed. There were no tests carried out for claimed sensation



or lactation potential nor were either of these modalities compared to a control group. A larger sample with longer follow up along with quantitative and qualitative assessment of these modalities will be the way forward to establish and quantify increased blood supply, better venous return, improved lymphatic drainage, quality and degree of sensation and lactation potential.

In conclusion, early results of single-stage augmentation with mastopexy have shown that the design of this technique carries a greater potential of conserving physiological function with added safety to nipple circulation, sensation and venous drainage. Selection of incision for skin removal based on preoperative NAC to IMC measurements increases the potential to bring harmony in breast parameters.

## DECLARATIONS

### Authors' contributions

The author contributed solely to the article.

### Availability of data and materials

None.

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None.

### Conflicts of interest

The author declared that there are no conflicts of interest.

### Ethical approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individuals participants included in the study.

### Consent for publication

Not applicable.

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Technical Note

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# Innovative cervical splint: overcoming an obstacle

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## Abstract

Cervical splints are used to maintain the neck position in burn patients with involvement of neck, which provides pain relief and prevent hypertrophic scarring and contracture. Due to the technical difficulty, cervical splinting often deferred in patients with tracheostomy. To overcome the difficulty the authors have described a simple modification of hard cervical collar, which provided adequate immobilization and adequate space for tracheostomy care. Innovative modification of hard cervical collar proposed in this case report can be a solution to overcome the difficulty posed by tracheostomy in patients sustained with neck burns.

**Keywords:** Modified cervical splint, neck burns, tracheostomy, cervical collar

## INTRODUCTION

Partial and full-thickness burns in neck region are reported in 35% of total burn patients<sup>[1]</sup>. Neck burns are associated with inhalational injuries and airway edema; and it is necessary to secure the airway early in these cases either by endotracheal intubation or tracheostomy. The majority of these patients present with airway edema, tracheostomy is preferred over endotracheal intubation in view of difficult airway.

Serghiou *et al.*<sup>[2]</sup> has quoted that “The position of comfort is the position of deformity”. Hence physical rehabilitation of patients who have sustained burn injury is an important part of management and requires multimodality treatment which involves splinting of affected part. In patients of neck burns, neck needs to be maintained in 15 degree extension<sup>[2]</sup>. Tracheostomy tube acts as an obstacle for applying neck splint<sup>[3]</sup>. We present a simple modification of hard cervical collar to be used in tracheostomized patients.

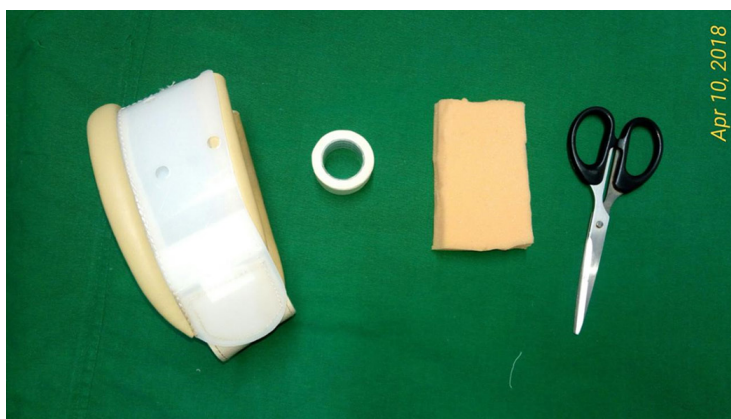


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**Figure 1.** The modified neck splint



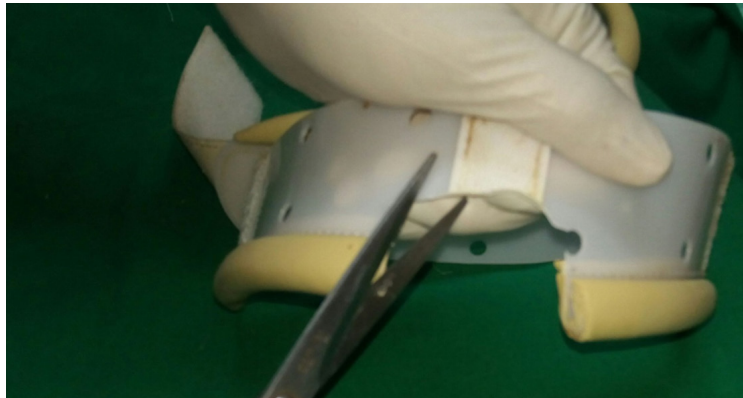
**Figure 2.** Materials required

## METHOD AND MATERIALS

We present a case of a 23-year-old female presented to casualty with history of accidental flame thermal burn involving face, neck, chest and upper limbs constituting 25% of total body surface area with inhalational injury. Patient had stridor suggesting airway compromise, on attempted endotracheal intubation, severe upper airway edema was noted with non visualization of vocal chords so the patient was tracheostomized and was resuscitated as per Parkland formula. Hard cervical collar commonly applied to immobilize neck couldn't be fitted with tracheostomy tube *in situ*. To overcome this problem modification of hard cervical collar was designed [Figure 1].

We used medium size hard cervical collar (cost: INR300; USD5; Dynamic Techno Medicals Pvt. Ltd.) made up of poly vinyl chloride (PVC) [Figure 2]. The lower part of cervical collar was cut with stout scissors in a shape of inverted “U” in its central part. While cutting the collar all the sharp projections were removed to make margins rounded. A clean piece of foam was cut into the half doughnut shape and fixed on the margins with the help of micropore tape [Figure 3]. After this modification collar was fit into the neck, providing pressure and positioning to the neck and simultaneously allowing rotational mobility for physiotherapy. Base of modified collar was stable from lateral sides [Figure 4]. Design map for modified neck splint is shown in Figure 5.

Modified cervical splint served the purpose of providing immobilization and alleviating pain during acute phase. Patient was well compliant to continuous application of modified cervical splint. Nursing caregivers



**Figure 3.** Preparing the modified neck splint



**Figure 4.** Patient wearing modified neck collar

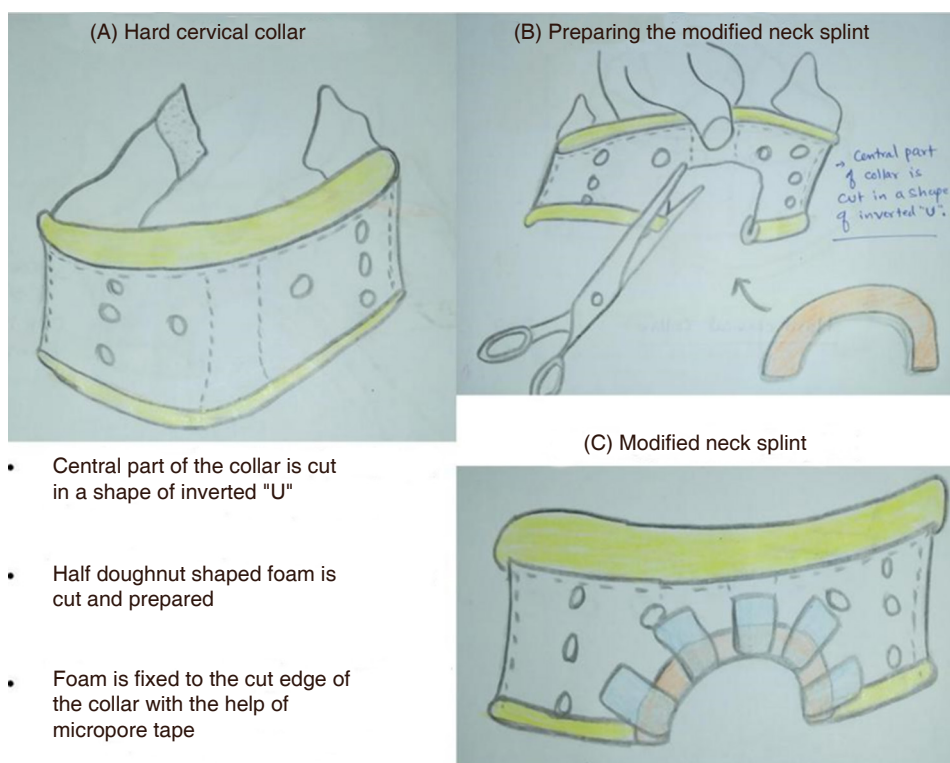
were able to provide tracheostomy care easily with the modified cervical splint *in situ*. During recovery phase wounds were managed with regular hydrojet debridement, low level laser therapy, autologous platelet rich plasma therapy, insulin therapy and regulated oxygenation and negative pressure wound therapy. Once the wound bed became healthy autologous split skin graft was applied [Figure 6]. Patient responded well to the treatment and neck wounds are healing well. Graft take is adequate and there is no restriction in range of motion of neck [Figure 7]. Once the edema settled, planned weaning from the tracheostomy and decanulation has been done during recovery phase. Modified neck splint was applied after tracheostomy removal also. At present the patient is following same neck splint and having no complaint of discomfort.

## DISCUSSION

Cronin was the first to report that post-burn contractures could be prevented with the application of a splint for prolonged pressure<sup>[4]</sup>. Commonly used splinting devices for neck are: (1) customized (patient specific; fabricated with fiberglass or thermoplastic material); and (2) prefabricated (with PVC or silicone or aliplast).

Traditionally, splinting with conforming thermoplastic collars have been utilized for anterior neck burns. However, the cost of thermoplastic material is high. Patient compliance with prefabricated neck collars is good. Prefabricated neck collars are easier to apply, readily available and cost effective. Prefabricated cervical splint can be hard or soft neck collars. Hard collar is made up of PVC while softer materials are aliplast or silicone lined elastic wraps. Prefabricated neck collars are available in different sizes (small, medium or





**Figure 5.** Design map for modified neck splint. A: Hard cervical collar; B: preparing the modified neck splint; C: modified neck splint

large). Hard cervical collars are better for burn patients as compared to soft cervical collar because of ease of application over bulky dressing and ease of cleaning the collar stained with soakage from the wounds<sup>[5-8]</sup>.

In some burn patients it is necessary to secure the airway early (at the time of presentation). Indications of early tracheal intubation mainly include<sup>[9]</sup>: (1) overt signs and symptoms of airway obstruction; (2) extensive burns to the head and neck; (3) inability to protect airway from aspiration; (4) significant toxicity from carbon monoxide or cyanide; (5) respiratory failure; (6) extensive burns (> 40% of total body surface area); and (7) hemodynamic instability. In selected patients tracheostomy is preferred over translaryngeal route for tracheal intubation. Indications of tracheostomy in burn patients mainly include<sup>[9]</sup>: (1) need for prolonged mechanical ventilation; (2) burns that will require multiple anesthesia for surgical procedures; and (3) extensive laryngeal oedema making translaryngeal intubation difficult. Tracheostomy tube should be removed once the need for prolonged or repeated intubation is over.

Putting cervical splint in patients with tracheostomy is difficult and often deferred. This has a negative effect on outcome and increases the need for neck reconstruction in future<sup>[3]</sup>. Modified prefabricated neck collars are designed for tracheostomized patients but they are costlier and not readily available in market. Philadelphia collar is having socket for tracheostomy but it is designed for cervical trauma and not for burns patients. Philadelphia collar does not give freedom of lateral rotational movement of neck.

Our modification of hard cervical collar is very simple and easy to adapt at any burn care centre. It is low cost, light weight, well supported, provides appropriate position and pressure, allows for physiotherapy and comfortable. We observed good compliance and pain relief in the patient to which modified neck splint was applied. It was possible to provide routine tracheostomy care comfortably with the patient wearing the modified neck splint. We look forward to use this modified neck splint in other neck burn patients with tracheostomy from the first day.



**Figure 6.** Burn wounds of the patient during treatment course; poly vinyl chloride tracheostomy tube is replaced with metallic tube



**Figure 7.** Small remaining wounds; tracheostomy tube is removed

## CONCLUSION

Cervical splinting in neck burn patients with tracheostomy is necessary but difficult. The innovative modification of hard cervical collar proposed in our case report can be a solution to overcome this difficulty.

## DECLARATIONS

### Authors' contributions

Concept and design: Gupta S, Chittoria RK

Data acquisition and analysis, manuscript preparation: Gupta S, Aggarwal A

Critical revision and finalizing of the manuscript: Chittoria RK, Subbarao E, Reddy KS, Chavan V, Aggarwal A, Reddy CL

### Availability of data and materials

The data were strictly obtained from medical records according to the privacy policy and ethics code of our institute.

### Financial support and sponsorship

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### Conflicts of interest

All authors declared that there are no conflicts of interest.

**Ethical approval and consent to participate**

Due consent was taken from the patient to participate in the study and separately for the photography. Ethical approval was done according to the hospital and department policy.

**Consent for publication**

Written informed consent for publication was obtained.

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Original Article

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# Autologous platelet rich plasma - an adjunct to early tangential excision and grafting in burns

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## Abstract

**Aim:** To affirm that autologous platelet rich plasma is a useful adjunct to early tangential excision and skin grafting to enhance wound epithelization rates and improve scar quality.

**Methods:** The study was conducted in JIPMER Tertiary Burn Care Center from November 2017 to February 2018. The study was purely descriptive in nature and no statistical analysis was performed. A total of 12 patients were included with burn wounds involving 10% to 25% total body surface area.

**Results:** There was 100% epithelization noted at the end of 2 weeks for all the 12 participants. Skin graft take was faster with mean 85.4% take for all the 12 patients within 5 days.

**Conclusion:** Since it is an autologous component, platelet rich plasma is extremely safe and free of antigenic components. It is relatively simple to prepare, less time taking, cost effective and highly efficacious in improving wound healing and improving the efficacy of the traditional techniques like tangential excision and skin grafting in burn patients.

**Keywords:** Autologous platelet rich plasma, burns, tangential excision, split skin grafting

## INTRODUCTION

Every year in India total 6-7 million people are afflicted with burns<sup>[1]</sup>. Delayed wound healing, sepsis, and



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secondary complications are routine sequelae of burns. Management of deep dermal burns or full thickness burns has been well described in the literature.

Burn wounds are commonly classified as first degree, second degree and third-degree burns, based on the depth of burn injury. Second degree is further classified into second degree superficial and second degree deep. Second degree deep and third-degree burns are generally benefitted by surgical excision, including tangential excision, while second-degree superficial burns are treated conventionally by dressings and intensive care.

The term “tangential excision” implies excision of superficial necrotic tissue by taking repeated slices parallel to the skin surface using a skin graft knife. The role of early tangential excision in deep dermal burns was given as early as 1968 by Janzekovic<sup>[2]</sup>. Hunt *et al.*<sup>[3]</sup> in 1972 published a series of 50 cases being treated by the same technique. Gradually the technique became popular and has now become the standard of care for burn wound management.

In the last century, there has been a lot of research and understanding in the pathophysiology of burn healing, which has led to multitudes of technological innovations in the types of dressings and the approaches to treatment. But in under-resourced health systems like ours, having a huge load of burn patients, there may be limited availability and their cost may be prohibitive for the newer technological innovations and dressings, stimulating the search of cheaper, yet effective adjuncts to the treatment of burn wounds.

One of such innovations is the addition of autologous platelet rich plasma (APRP) to the standard tangential excision and grafting technique.

APRP has been shown to aid wound healing in various aspects of science<sup>[4]</sup>. Platelets have been shown to express around 30 growth factors which besides being chemotactic, also induce proliferation of various cells like fibroblasts, endothelial cells and other precursor cells, which regulate the wound healing<sup>[5]</sup>.

The main growth factors released are platelet derived growth factor (PDGF), transforming growth factor beta 1 (TGF  $\beta$ -1), platelet activating factor and epidermal growth factor (EGF)<sup>[6]</sup>.

Moreover, platelets help in hemostasis by forming a platelet plug and express proteases, which help in rapid degradation of the extra cellular matric and basement membrane.

Skin grafting in burns is a challenge for the surgeon due to a depleted physical condition of the patient, deranged biochemical parameters and systemic sepsis. Also, the rates of graft infection are much higher.

Due to the above factors and ease of preparation, APRP can be used as an adjunct to operative procedure and also as a very handy office procedure to boost the healing.

This study is an attempt to throw light on the role of APRP in wound bed preparation and injection of APRP to the wound bed post tangential excision to boost graft take.

## METHODS

The study was conducted in JIPMER Tertiary Burn Care Center, Pondicherry, India from November 2017 to February 2018.

The study was purely descriptive in nature and no statistical analysis was performed.

A total of 12 patients were included with burn wounds involving 10% to 25% total body surface area (TBSA). The age of the patients varied from 22 to 46 years.





**Figure 1.** Autologous platelet rich plasma being injected immediately following grafting in patient 4 (Patient S. No. 4)

Tangential excision and autologous split skin grafting was performed for deep dermal burns on day 3 following burns. The cause of the deep burn was thermal in all the cases.

The skin grafts were harvested using a Humby's knife by an experienced surgeon.

Patients with comorbid conditions like diabetes, collagen vascular diseases or any other disease which limits wound healing were excluded. Patients under mechanical ventilation were not taken up for surgery, and hence excluded.

Patients were informed about the study and included after providing signed informed consent.

APRP preparation was done in the operation theatre while debridement/dressing change of the patient using standard and validated technique was described.

Four point five mL of whole blood was taken from a vein in the periphery and 0.5 mL of 3.2% sodium citrate was added to it (blood: anticoagulant at 9:1). The centrifugation tube was placed in centrifugation apparatus. The solution was then subjected to centrifugation at 3000 rpm for 10 min. Three portions were seen in the tube post centrifugation: upper portion containing plasma and platelets, middle portion containing white blood cells with some platelets (buffy coat) and lower portion containing red blood cells. Out of these, middle and lower portions are discarded, the upper portion was transferred and taken in a new tube for re-centrifugation at 4000 rpm for 10 min. Following which two portions were seen: upper 2/3rd portion containing platelet poor plasma and lower 1/3rd portion which contained platelet rich plasma. Lower 1/3rd portion was used for APRP therapy.

Multiple subcutaneous injections of 2-3 mL of APRP were given in the selected burn wound following excision of the deep dermal burns using syringe fitted with 26G needle. APRP injection was done on periphery of the residual raw area, and also on the donor areas of the skin grafts. APRP injection was done on excision and subsequently on every dressing change (day 5, day 7, day 10, day 14 post grafting) [Figure 1].



**Figure 2.** Residual raw area following tangential excision (Patient S. No. 1)



**Figure 3.** Raw area grafted (day 0) (Patient S. No. 1)

Area epithelized was measured using digital planimetry.

Incidence of wound infection was examined separately.

It must be noted that APRP injection was used for second degree superficial wounds as well in addition to the wound bed for deep burns.

## RESULTS

Twelve patients from our center were included with second degree burn wounds involving 10% to 25% TBSA. The age of the patients varied from 22 to 46 years, with a mean age of 32.5 years. Five of them were male, and rest seven, female. The mean graft uptake was 85.4% at day 5 and 100% wound epithelization was achieved for all patients by day 14. The results are tabulated in [Table 1](#).



**Figure 4.** Graft on 1st dressing on day 5 (Patient S. No. 1)



**Figure 5.** Autologous platelet rich plasma being injected into the residual raw area on day 5 following debridement of dead graft (Patient S. No. 1)

## DISCUSSION

Skin grafts survival occurs via serum imbibition, direct vessel to vessel re-anastomosis (inosculation), and neovascularization. Neovascularization is defined by ingrowth of new vessels from the recipient site into the graft.

APRP as contains a high concentration of alpha granules, is an easy and a very cost-effective approach to obtaining high concentrations of these growth factors. These alpha granules of platelets are known to contain growth factors such as PDGF, vascular endothelial growth factor, TGF, EGF, which promote angiogenesis, cell proliferation, maturation, and matrix formation as described above<sup>[7]</sup>.

The application of APRP results in prompt tissue regeneration and a reduced risk of infection, pain, and loss of blood. El-Sharkawy *et al.*<sup>[8]</sup> in their study have suggested that platelet rich plasma also suppresses cytokine release, thus limiting inflammation, and promoting tissue regeneration. Pallua *et al.*<sup>[9]</sup> have reported



**Figure 6.** Fully epithelialized wound at day 14 (Patient S. No. 1)

**Table 1. Demographic details of the patients and graft uptake on the specified post operative day**

S. No.	Age	Gender	TBSA burn (%)	Area excised and grafted (%)	APRP used (mL)	Graft take at day 5 (%)	Wound epithelialized at day 7 (%)	Graft take at day 7 (%)	Wound epithelialized at day 10 (%)	Wound epithelialized at day 14 (%)
1	26	F	12%	6%	2	75%	70%	70%	90%	100%
2	35	M	15%	15%	3	90%	75%	90%	95%	100%
3	28	M	20%	15%	4	100%	84%	95%	95%	100%
4	40	F	16%	10%	4	85%	74%	80%	90%	100%
5	29	M	20%	10%	3	95%	85%	90%	100%	100%
6	22	M	18%	15%	3	70%	65%	70%	85%	100%
7	46	F	20%	8%	2	80%	55%	75%	80%	100%
8	42	F	16%	7%	3	90%	65%	85%	75%	100%
9	38	F	18%	12%	2	85%	70%	80%	90%	100%
10	26	M	12%	5%	4	95%	70%	75%	100%	100%
11	22	F	17%	6%	3	85%	60%	85%	70%	100%
12	36	F	15%	4%	2	75%	55%	90%	85%	100%

TBSA: total body surface area; APRP: autologous platelet rich plasma; F: female; M: male

that application of platelet-rich plasma for burn patients accelerates re-epithelization. In another study by Choi *et al.*<sup>[10]</sup>, the subcutaneous injection of platelet rich plasma in a rabbit skin flap was shown to promote vasculogenesis and increase flap survival.

The study shows good graft take, no infections, a smooth post operative course and a faster rate of epithelization. These findings can be attributed to the addition of application of APRP to the wound bed. The serial follow up images of a patient (S. No. 1) are shown after tangential excision [Figure 2], placing the split skin graft [Figure 3], graft inspection on day 5 [Figure 4], APRP being injected after debridement of the necrosed graft [Figure 5] and after the wound was fully healed [Figure 6].

It should be noted, it is prudent to take APRP as the sole factor responsible for a good post operative outcome following tangential excision and grafting. The importance of time tested burn strategies like nutrition, effective nursing and maintenance of strict asepsis are of paramount importance. APRP is just an adjunct which can be effective in improving the results.

Being a pilot study, this shows a lot of promise and further large multicenter trial is needed to substantiate the same.



## DECLARATIONS

### Authors' contributions

Study design and conception: Chittoria RK

Data collection and research: Aggarwal A

Data interpretation and review: Dutta S, Reddy S, Chavan V, Gupta S, Reddy L

### Availability of data and materials

All data supporting the article is available with the medical records department of the institute. Can be reproduced as and when needed.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Due informed consent was obtained from all patients before including them into the study including photographic consent. Ethical clearance was obtained from the institute in which the study was done.

### Consent for publication

Full informed consent for publication has been obtained from the individuals included in the study.

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Manuscript Type	Definition	Abstract	Keywords	Main Text Structure
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#### 2.4.7 Abbreviations

Abbreviations should be defined upon first appearance in the abstract, main text, and in figure or table captions and used consistently thereafter. Non-standard abbreviations are not allowed unless they appear at least three times in the text. Commonly-used abbreviations, such as DNA, RNA, ATP, *etc.*, can be used directly without definition. Abbreviations in titles and keywords should be avoided, except for the ones which are widely used.

#### 2.4.8 Italics

General italic words like *vs.*, *et al.*, *etc.*, *in vivo*, *in vitro*; *t* test, *F* test, *U* test; related coefficient as *r*, sample number as *n*, and probability as *P*; names of genes; names of bacteria and biology species in Latin.

#### 2.4.9 Units

SI Units should be used. Imperial, US customary and other units should be converted to SI units whenever possible. There is a space between the number and the unit (i.e., 23 mL). Hour, minute, second should be written as h, min, s.

#### 2.4.10 Numbers

Numbers appearing at the beginning of sentences should be expressed in English. When there are two or more numbers in a paragraph, they should be expressed as Arabic numerals; when there is only one number in a paragraph, number < 10 should be expressed in English and number > 10 should be expressed as Arabic numerals. 12345678 should be written as 12,345,678.

#### 2.4.11 Equations

Equations should be editable and not appear in a picture format. Authors are advised to use either the Microsoft Equation Editor or the MathType for display and inline equations.

### 2.5 Submission Link

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