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An approach to the prevention and treatment of neuropathic pain at the radial forearm phalloplasty donor site

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How to cite this article: Ferrin PC, Hathaway B, Wilson J, Peters BR. An approach to the prevention and treatment of neuropathic pain at the radial forearm phalloplasty donor site. *Plast Aesthet Res* 2024;11:60. https://dx.doi.org/10.20517/2347-9264.2024. 79

Received: 31 May 2024 First Decision: 25 Nov 2024 Revised: 10 Dec 2024 Accepted: 13 Dec 2024 Published: 23 Dec 2024

Academic Editor: Harvey Chim Copy Editor: Ting-Ting Hu Production Editor: Ting-Ting Hu

Abstract

This article presents a comprehensive strategy for both the prevention and treatment of neuropathic pain at the radial forearm (RF) donor site. This strategy is presented within the framework of RF phalloplasty, based on the senior author's practice and the premise that of all RF reconstructions, phalloplasty holds the greatest potential for postoperative neuropathic pain due to flap size and the inherent division of multiple antebrachial cutaneous nerves to provide for flap sensation. This proposed protocol offers a thorough care pathway that integrates techniques in peripheral nerve surgery with perioperative clinical strategies to prevent and treat neuropathic pain. Specific technical recommendations for the prevention and treatment of postoperative neuromas, compression neuropathies, and hyperalgesia of each peripheral nerve involved in RF phalloplasty flap harvest are proposed. These strategies can be adapted and applied to RF flaps utilized in other reconstructive areas.

Keywords: Radial forearm free flap, nerve pain, neuroma, phalloplasty, nerve allograft capping, targeted muscle innervation, regenerative peripheral nerve interfaces



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INTRODUCTION

While the radial forearm (RF) provides excellent outcomes in many reconstructive domains, the RF has the potential for significant donor site morbidity, including neuropathic pain. This is perhaps most apparent during radial forearm phalloplasty (RFP), where the construction of a sensate phallus of adequate size mandates a much larger flap than traditionally described for other reconstructive indications and additionally involves the harvest of multiple antebrachial nerves for flap innervation^[1,2]. The prevalence of moderate to severe nerve pain after RFP has been reported as high as 16%, which can negatively impact quality of life^[3]. Sensation is a top priority for many individuals seeking phalloplasty, and as efforts are made to continue to improve sensory outcomes, a parallel effort should be made to minimize the potential for neuropathic pain at the donor site.

Several articles have been published that discuss techniques employed to address many areas of RF donor site morbidity, including soft tissue coverage, contour, scarring, strength, range of motion, and edema^[4-10]. Although strategies for minimizing nerve pain after traditional RF flaps have been described^[11], a comprehensive strategy for minimizing neuropathic pain specifically in the setting of RFP has not been proposed.

There are numerous potential sources of neuropathic pain following RFP. Neurotemetic injuries occur to the lateral (LABC), medial (MABC), and posterior antebrachial cutaneous (PABC) nerves to provide flap sensation^[12]. The large flap size also results in exposure of the superficial radial nerve (SRN) and potentially the palmar cutaneous branch of the median nerve over a long distance, creating the possibility of injury. The high degree of dissection and postoperative edema can exacerbate any subclinical nerve compression in the forearm or hand including at the carpal tunnel, Guyon's Canal, and Wartenberg's point. Finally, the extent of forearm denervation predisposes to neuropathic pain and hyperalgesia due to collateral sprouting from adjacent sensory nerves attempting to fill in the resulting sensory deficits. Here, we outline our comprehensive approach to the prevention and treatment of neuropathic pain based on experience as peripheral nerve specialists performing a high volume of RFP. While phalloplasty provides an ideal framework to discuss and present these strategies, they can be considered for RF flaps used for any reconstructive purpose.

PREOPERATIVE SCREENING

Preoperatively, patients should undergo thorough upper-extremity neurological evaluation to identify sites of pre-existing nerve compression, which can be treated with decompression during the RF flap harvest. Screening protocols should specifically test for the presence of carpal tunnel syndrome (CTS), pronator syndrome, and Wartenberg's syndrome [Figure 1]. In our practice, we screen for these nerve compression syndromes using physical exam maneuvers and further diagnostic testing when indicated. We prefer to surgically address CTS, pronator syndrome, and Wartenberg's syndrome at the time of RF flap harvest to save patients an additional operation as well as to prevent potential exacerbation postoperatively as these compression neuropathies are often worsened following flap harvest due to significant anticipated postoperative swelling. Ulnar nerve compression at the wrist should also be screened for preoperatively; however, it is our preference to avoid concurrent operation on the radial artery and ulnar neurovascular bundle due to increased potential risk arising from simultaneous manipulation of both arterial sources to the hand. Ulnar nerve compression syndromes are preferably managed prior to or after RFP to minimize additional risk.

INTRAOPERATIVE STRATEGIES Antebrachial cutaneous nerves The RFP flap template includes the territory of the LABC, PABC, and anterior branch of MABC. Though sensory nerve coaptation choice varies among surgeons, the large flap size guarantees iatrogenic transection of these three nerves [Figure 2]^[12]. The posterior branch of the MABC should be spared to maintain sensation in the remaining ulnar forearm skin. Recognizing the pain risk associated with performing three sensory nerve transections, we have implemented neuroma prevention measures into our RFP care pathway.

Targeted muscle reinnervation (TMR), regenerative peripheral nerve interface (RPNI), and acellular nerve allograft (ANA) capping are all techniques that can be utilized for primary neuroma prevention. For example, in sensate ALT flaps, we perform primary RPNI of the lateral femoral cutaneous and femoral perforating nerves to prevent neuroma formation^[13]. However, primary RPNI is less practical in the forearm due to a relative lack of expendable donor muscle. TMR is likewise impractical due to the limited length of the transected nerve ends to reach expendable motor targets. We have instead found success in performing proximal crush injury and bipolar cap to all antebrachial cutaneous nerves that undergo transection. Creating a crush several centimeters proximal to where the nerve is transected induces axonometric injury^[14] and moves the front of axonal regeneration away from the transected nerve end. The nerve stump is then capped using bipolar cautery and buried proximally and deep under the muscle. We have performed this technique on 91 consecutive RFP patients since August 2020 and no patients have required secondary antebrachial cutaneous neuroma excision.

SRN

The SRN is extensively exposed during RFP flap elevation and is particularly susceptible to postoperative neuropathic pain^[15]. The volar branch innervating the thumb runs close to the radial artery septum and can be mistaken for the LABC, rendering it prone to inadvertent transection [Figure 1B]. To avoid injury, the SRN should be approached from the radial side and identified at Warternberg's interval between the extensor carpi radialis longus and brachioradialis, and then dissected in a proximal-to-distal direction, ensuring all branches are preserved. The SRN is additionally susceptible to compression at Wartenberg's interval, which can be difficult to treat if compression develops in patients who have undergone prior RFP. Therefore, prevention is our preferred strategy, and we now consent all RFP patients for decompression of Wartenberg's interval with brachioradialis tenotomy and reinsertion radially into the extensor fascia with mobilization of the SRN so that it lies in a straight course along the forearm musculature [Figure 3]. This technique preserves the brachioradialis function and provides the SRN with a compression-free path along the entire length of the forearm. Furthermore, there is no discernible morbidity from brachioradialis reinsertion. Since implementing this technique, none of the 40 patients have required revision forearm surgery for SRN pain (though one patient underwent fat grafting for aesthetic purposes, which also improved their mild intermittent SRN pain).

Alongside these preemptive surgical interventions, we implement a regimen of postoperative gabapentin therapy and standardized hand therapy, which includes additional edema management and a course of graded motor imagery (GMI).

TREATMENT OF ESTABLISHED NERVE PAIN

When neuropathic pain does manifest postoperatively, meticulous examination is essential to accurately detect and treat all pain source(s). It is possible to have multiple simultaneous neuropathies, some of which involve overlapping sensory territories (i.e., LABC and SRN). We employ a comprehensive physical exam and the Mackinnon pain questionnaire^[16] to accurately gauge the pain profile for all RFP patients 6 months postoperatively. When concern for nerve compression or neuroma exists, we aim to optimize conservative

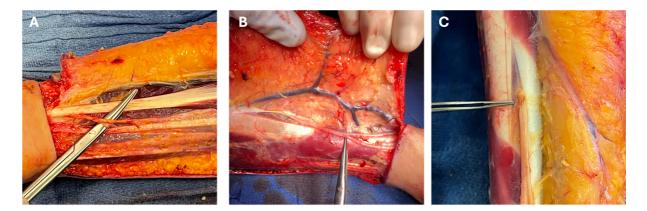


Figure 1. Sites of potential nerve pain following RFP. The palmar cutaneous branch of the median nerve (A) and the volar branch of the superficial radial nerve (B) are at high risk of inadvertent injury. The superficial radial nerve is also prone to compression at Wartenberg's point (C). RFP: Radial forearm phalloplasty.

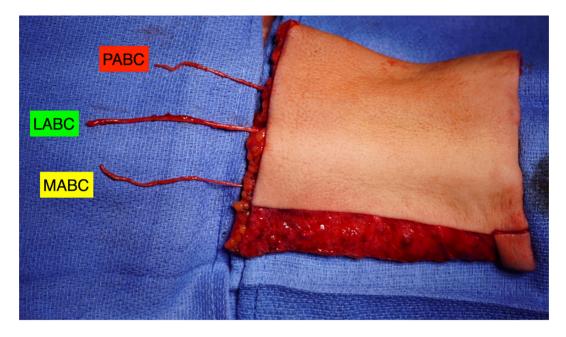


Figure 2. Sensate radial forearm free flap used for shaft-only radial forearm phalloplasty. In our practice, we perform triple neurotization of the phallus using the LABC, PABC, and the anterior branch of the MABC to maximize phallic shaft sensation. This technique necessarily creates iatrogenic injuries to these three sensory nerves, and therefore, neuroma prevention techniques are utilized. The posterior branch of the MABC is left *in situ* to provide sensation to the ulnar skin bridge. LABC: Lateral antebrachial cutaneous nerve; PABC: posterior antebrachial cutaneous nerve; MABC: medial antebrachial cutaneous nerve.

measures including hand therapy, desensitization, GMI, and neuropathic medication (e.g., pregabalin) to minimize background hyperalgesia, an important initial step even when surgical intervention is ultimately necessary. Figure 4 depicts our preferred post-RFP nerve pain management algorithm.

Antebrachial cutaneous neuroma

In the case of antebrachial cutaneous neuromas, nerve continuity cannot be restored due to a lack of distal nerve targets. The remaining proximal nerve length is typically insufficient for TMR and RPNI is impractical given the lack of muscle available for grafting in the upper extremity. Therefore, we perform ANA capping for the management of LABC, MABC, and/or PABC neuromas.

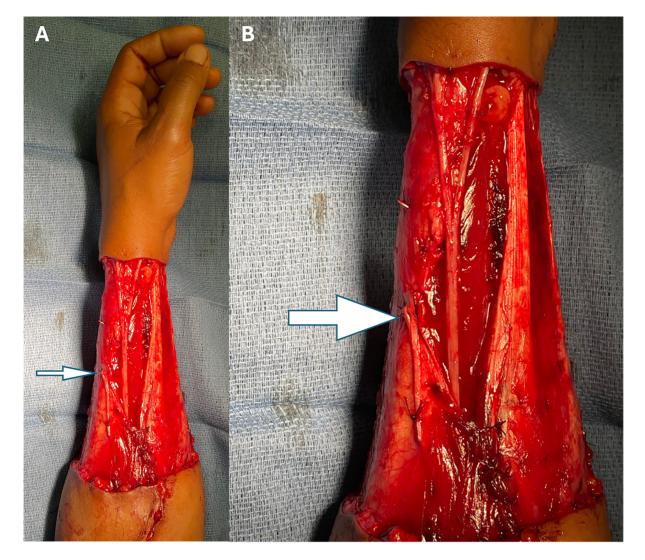


Figure 3. Intraoperative decompression of the SRN at Wartenberg's interval at the time of radial forearm phalloplasty. (A) A brachioradialis tenotomy is performed and the SRN is neurolyzed free from underneath the brachioradialis to lie in a straight course over the forearm musculature; (B) The brachioradialis tendon is then re-inserted into the extensor fascia on the radial side of the SRN. The arrow indicates the new location of the brachioradialis insertion. SRN: Superficial radial nerve.

In our experience, the LABC is the most common antebrachial nerve to develop a symptomatic neuroma, likely due to its location in the antecubital fossa and its higher axon count compared to the MABC and PABC^[17]. During RFP flap harvest, the LABC is transected just lateral to the biceps tendon, distal to where it changes course and travels in a deep plane in the upper arm between the biceps and brachialis muscle [Figure 5]. There is little remaining proximal nerve available in the surgical field at the level of the antecubital fossa for definitive neuroma excision and management of the proximal nerve stump. For this reason, we approach the LABC in the upper arm at the level of the musculocutaneous nerve branches. This allows for abundant nerve length and access to skeletal muscle and expendable motor nerve targets. We have found proximal crush injury with ANA capping to be particularly valuable in this scenario, as this technique does not cause denervation of any major upper extremity muscle to provide a target for TMR and avoids muscle harvest needed for RPNI. Figure 6 demonstrates our technique for LABC neurectomy with proximal crush injury and ANA capping in the proximal arm. At this level, the branches of the musculocutaneous nerve are reliable, with the biceps motor branch superior, the LABC in the middle, and

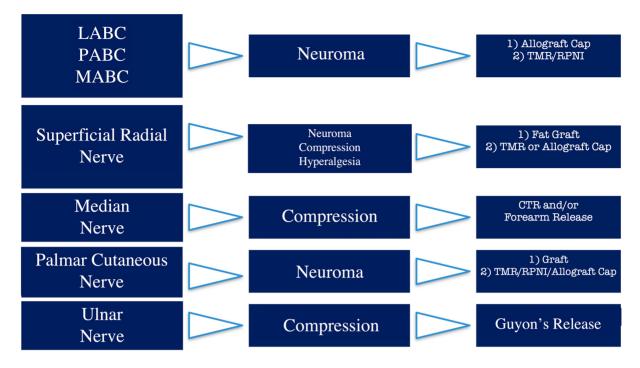


Figure 4. Our preferred post-radial forearm phalloplasty nerve pain management algorithm, by offending peripheral nerve. LABC: Lateral antebrachial cutaneous nerve; PABC: posterior antebrachial cutaneous nerve; MABC: medial antebrachial cutaneous nerve; TMR: targeted muscle reinnervation; RPNI: regenerative peripheral nerve interface; CTR: carpal tunnel release.

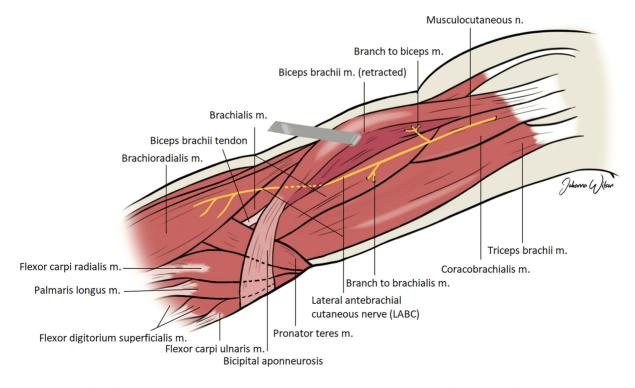


Figure 5. Branches of the musculocutaneous nerve in the proximal arm as it terminates into the lateral antebrachial cutaneous nerve.

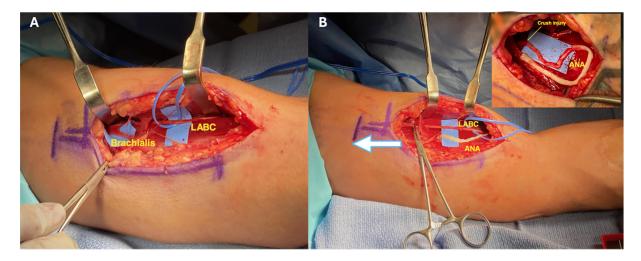


Figure 6. Our preferred technique to address neuroma of the lateral antebrachial cutaneous nerve. (A) The LABC lies between the motor branches of the biceps and the brachialis. In this image, the biceps branch is not visualized but is coming off proximal to the surgical field. The brachialis motor branch can be seen coursing inferiorly to innervate the brachialis. The LABC can be seen continuing distal to this point to emerge lateral to the biceps tendon; (B) A hemostat can be seen proximal on the LABC, distal to the origin of the brachialis motor branch. A crush injury is created at this level. The LABC is then transected as distal as possible. An ANA is sutured to the transected LABC with 9-0 nylon and fibrin glue. The nerve is transposed proximal and deep between the biceps and brachialis, away from the incision and surgical field. The top right image represents a closer look at the proximal crush injury. LABC: Lateral antebrachial cutaneous nerve; ANA: acellular nerve allograft.

the brachialis motor branches inferior. A mosquito is used to create a crush injury to the proximal LABC just distal to the takeoff of the brachialis branches. The LABC is transected as distally as possible, and a 2-3 mm × 50 mm ANA (Axogen Corporation, Alachua, FL) is coapted to the distal end of the LABC. The distal end of the allograft is directed deep and proximal in the muscular interval between the biceps and brachialis, far from the surgical field to avoid stimulation. We have performed this technique on 3 patients with established LABC neuromas following RFP. Table 1 provides a summary of pertinent baseline data and pain scores. All 3 patients reported complete resolution of LABC neuroma pain postoperatively with no evidence of recurrence during long-term follow-up or pain at the surgical site in the upper arm with a mean follow-up time of 2.5 years.

For neuromas of the MABC or PABC, we similarly perform neurectomy with proximal crush injury and ANA capping. The MABC and PABC have more nerve length within the prior operative field, enabling easier access to the neuromas through the existing forearm surgical site. Alternative surgical neuroma management options for the MABC and PABC include simple burial in muscle or RPNI. However, we aim to avoid the need for additional muscle grafts as allograft caps have not failed in our hands when used for the indications described.

Postoperative nerve compression

Post-RFP pain can also arise from other nerves exposed during RF flap harvest. In scenarios involving postoperative nerve compression such as CTS, pronator syndrome, or ulnar nerve compression at Guyon's canal, the treatment is surgical decompression if symptoms persist after a trial of conservative measures.

SRN pain

Figure 7 depicts our management algorithm for post-RFP SRN pain. For intact SRNs manifesting neuropathic pain, it is important to attempt to maintain nerve continuity if possible. An initial course of conservative therapy with pregabalin, GMI, and desensitization is trialed. If this fails, fat grafting can be

	Patient 1	Patient 2	Patient 3
Age	29	39	48
Symptoms	throbbing, aching, shooting, stabbing, hypersensitivity	numbness, stinging, pulling	Throbbing, aching, stabbing, tingling, shooting, numbing, stinging, pulling
Preoperative pain severity (0-10)	6/10	5/10	7/10
Postoperative pain severity (0-10)	0/10	0/10	0/10

LABC: Lateral antebrachial cutaneous nerve; ANA: acellular nerve allograft.

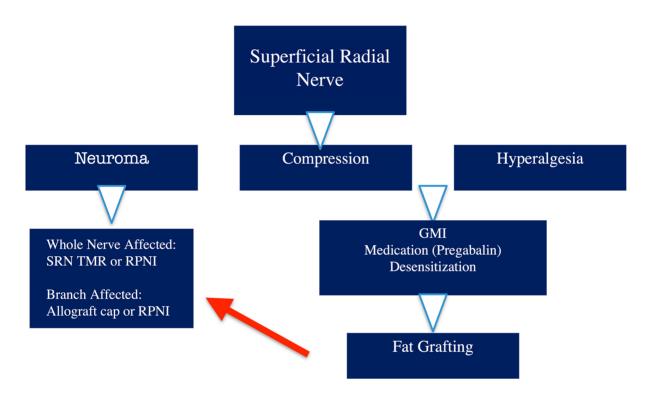


Figure 7. Management algorithm for post-radial forearm phalloplasty pain in the distribution of the superficial radial nerve. SRN: Superficial radial nerve; TMR: targeted muscle reinnervation; RPNI: regenerative peripheral nerve interface; GMI: graded motor imagery.

attempted to increase soft tissue coverage over the nerve, minimize irritation, and decrease neuropathic pain signaling^[18-20]. If conservative therapy and fat grafting fail but the SRN remains intact, a trial of SRN neurolysis and decompression of Wartenberg's interval can be considered. However, given the degree of scarring within the skin-grafted wound bed, the success of this operation is not always reliable and risks SRN injury. If the pain is severe, we instead typically recommend TMR, though patient selection is paramount as low-grade SRN pain can be worsened by SRN transection.

If there is evidence of an SRN neuroma, excision and restoration of nerve continuity should be attempted through nerve grafting if possible. If restoration of continuity cannot be established, TMR can be considered if the entire nerve is injured. We recommend allograft capping or RPNI if only a branch is affected (e.g., isolated neuroma of the volar branch). Several recent publications have described potential TMR targets for the SRN for cases where continuity cannot be restored or neuroma-in-continuity exists, including motor branches to the supinator, extensor carpi radialis brevis, and posterior interosseous nerve^[7,8,21-24]. When TMR

is necessary, we prefer to use the supinator motor branches as the motor target because the supinator is expendable and near the proximal SRN, provides a protected coaptation away from surface stimulation, and is a favorable size match for the SRN^[8].

CONCLUSION

The management of neuropathic pain at the RF donor site is multifaceted. We present an algorithmic approach that spans preoperative risk assessment, intraoperative nerve preservation, and neuroma prevention strategies, and multimodal postoperative pain management strategies that can include secondary nerve surgery. This comprehensive protocol addresses each of these elements to reduce the incidence of neuropathic pain and enhance the quality of life for patients undergoing RFP. Future studies that include patient-reported outcome measures are warranted to validate the protocol outlined here and quantify the impact of each of its components.

DECLARATIONS

Acknowledgments

The authors would like to acknowledge Essie Ghafoor, MD, and Samantha Burch, MD, for assistance with data collection and drafting of the section of the manuscript about LABC neuroma management.

Authors' contributions

Study concepts: Peters BR Study design: Ferrin PC, Hathaway B, Peters BR Data acquisition: Ferrin PC, Hathaway B, Wilson J Manuscript writing: Ferrin PC, Hathaway B, Wilson J, Peters BR Manuscript editing: Ferrin PC, Hathaway B, Wilson J, Peters BR

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

This study was approved by Oregon Health and Science University's Institutional Review Board (STUDY00026060). All patients gave written and verbal consent to participate in this study.

Consent for publication

All photographs were collected by the authors and the subjects gave their consent for publication.

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