

Review

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# The role of endoscopic endonasal surgery in the management of sinonasal malignant tumors with skull base involvement

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## Abstract

Sinonasal malignant tumors (SNMTs) represent a rare and heterogeneous group of tumors. SNMTs often present late which can lead to complex, patient-specific treatment decisions. Over the last two decades, endoscopic endonasal surgery (EES) has become a more frequently utilized surgical approach to removing these tumors. Increasingly, studies have compared the outcomes of this approach to traditional open approaches for different SNMTs. Differences in histology and extent of invasion impact the utility of EES. Negative margins are critical for improving survival; however, skull base involvement can add anatomical challenges for achieving negative margins during EES. This paper reviews the literature on outcomes of EES for SNMTs with skull base involvement and presents evidence supporting the utility of EES for select patients. EES is a safe and effective treatment in patients with less invasive SNMTs or less aggressive histology and can provide patients with fewer complications and morbidity than traditional open approaches. As such, it plays a key role in surgical management, providing either sole access or a critical avenue for SNMT removal. EES plays a key role in the multimodal oncological approach to the treatment of different SNMT histologies.

**Keywords:** Endoscopic endonasal surgery, sinonasal malignancies, sinonasal tumors, skull base invasion, skull base involvement



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## INTRODUCTION

Skull base surgery began with the development of open approaches including transfacial approaches and craniotomies to reach tumors in this anatomically-challenging area. These approaches continue to be used and have a defined role in skull base surgery; however, the introduction of endoscopic skull base surgery has provided skull base surgeons with greater access while reducing the invasiveness of procedures compared to many open approaches. Now, with the advances in instrumentation, visualization, and surgical techniques, endoscopic endonasal surgery (EES) is at the forefront of treatment for anterior midline skull base lesions. This includes sinonasal malignant tumors (SNMT), which traditionally required open approaches and are now amenable to purely EES, with the potential of providing less morbidity while maintaining comparable oncologic outcomes<sup>[1]</sup>. As instrumentation and surgeon technical experience continue to progress, endoscopic endonasal techniques continue to expand providing a growing body of literature on EES for various SNMTs<sup>[2]</sup>. In many cases, EES provides the most direct approach to these tumors with maximal visualization.

SNMTs represent a rare and heterogeneous disease group that presents with unique treatment challenges based on disease characteristics and anatomical limitations<sup>[3]</sup>. A retrospective analysis of the United States National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registry examined patients diagnosed with SNMTs between 1973 and 2011 and found an incidence of 0.83 per 100,000 people with squamous cell carcinoma (SCC) as the most common histology (41.9%)<sup>[4]</sup>. Given the origin of SNMTs and involvement of the sinonasal corridor, otolaryngologists naturally resected the majority of the sinonasal portion of the tumor endonasally and increasingly endoscopically. However, neurosurgeons' comfort with transcranial approaches precluded initial extension of these approaches to the intracranial space. As a result, SNMTs were traditionally approached via open techniques, alone or combined with endonasal exposure and/or debulking. Despite this, a paradigm shift from en bloc tumor resection to piecemeal resection after studies found that piecemeal resection provided equivalent outcomes has pushed EES to the forefront<sup>[5]</sup>. Nevertheless, SNMTs that extend into the skull base can be more challenging for resection through EES. The role of EES in the multimodal treatment of SNMTs also varies depending on the biological behavior of the tumor. This article reviews the current state of EES in surgical resection of SNMTs, describes the advancements and outcomes of EES in SNMTs with skull base involvement, and provides pathology-specific outcomes.

## ANATOMICAL APPROACH AND CONSIDERATIONS PRIOR TO ENDOSCOPIC ENDONASAL SURGERY FOR SINONASAL MALIGNANT TUMORS

The nasal cavity and sinuses serve as surgical corridors for endoscopic endonasal approaches involving the skull base. Advantages of EES include improved visualization and decreased morbidity compared to traditional approaches<sup>[6]</sup>. However, a strong understanding of the endoscopic anatomy is paramount to performing safe EES.

The ventral skull base lies inferior to the frontal lobes with the midline of the ventral skull base consisting of the nasal cavity, ethmoid cells, and sphenoid sinus. The anterior two-thirds of the midline ventral skull base are formed by the ethmoid bone. Critical structures in this area include the cribriform plate, fovea ethmoidalis, and crista galli. The lateral lamella of the cribriform plate is a thin bony structure that connects with the fovea ethmoidalis. The cribriform plate also contains the olfactory nerves and this space is an important risk factor for skull base invasion from extracranial sinonasal tumors<sup>[7]</sup>. Between the cribriform plates, the crista galli joins the plates and serves as the attachment of skull base to the falx cerebri. During EES, the anterior and inferior limits of the crista galli can serve as landmarks for the posterior table of the frontal sinus. The ethmoid bone continues posterior to the cribriform plate portion and, at the midline, a

bony lamina descends to form the perpendicular plate that articulates with the vomer and represents the bony portion of the septum.

The anterior and posterior ethmoid arteries (AEA and PEA) are critical to identify during EES of SNMTs. The AEA crosses the roof of the ethmoid bone after it travels across the superior-medial orbital wall at the level of the posterior globe and approaches the cribriform plate in a posterior-to-anterior fashion from lateral to medial [Figure 1].

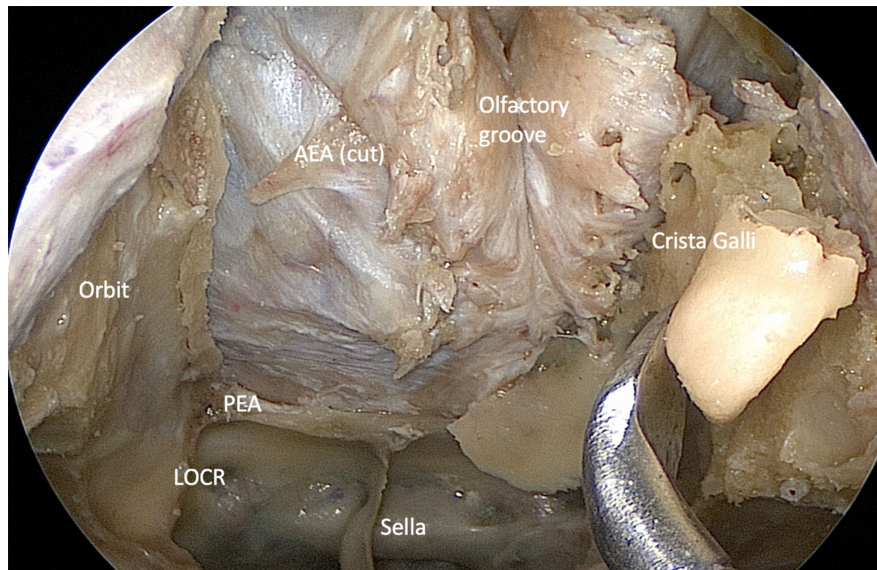
Meanwhile, the PEA runs with the superior rectus and superior oblique muscle before exiting the orbit through the posterior ethmoid canal and course horizontally across the cribriform plate in a more anterior-to-posterior direction. A surgical landmark for the location of the PEA is the basal lamella, which lies anterior to the attachment of the posterior ethmoid canal to the skull base.

Considerations prior to EES include a history of endonasal surgery, sinonasal inflammation or disease, prior radiation, and the extent of neurological deficits<sup>[5]</sup>. As previously discussed, for EES of SNMTs, additional considerations include the histology and biological behavior of the SNMT, stage of disease, and anatomical boundaries and limitations. The majority of SNMTs are epithelial tumors with SCC and adenocarcinoma as the two most common histologies<sup>[8]</sup>. SCC is also the most common histological type of SNMT in the maxillary sinus while adenocarcinoma is the most common histology for SNMTs originating in the ethmoid sinus<sup>[9]</sup>. Other epithelial SNMTs include olfactory neuroblastoma (ONB), adenoid cystic carcinoma (ACC), sinonasal undifferentiated carcinoma (SNUC), and sinonasal mucosal melanoma (SNMM)<sup>[10-12]</sup>. Different tumors of the sinonasal cavity can also be classified by how aggressive the tumor is; low Hyams grade ONB is typically less aggressive while SNUC and SNMM can be very aggressive with worse prognosis<sup>[10]</sup>. Thus, the decision to proceed with EES must depend on many factors and be compared to other treatment options including open surgery and systemic treatment to ensure optimal outcomes for the patient. Induction chemotherapy (IC) is increasingly being used for high-grade tumors such as SNUCs prior to definitive therapy. The timing and overall role of surgery in SNMT treatment is a complex and evolving topic, beyond the scope of this paper.

## **SURGICAL TECHNIQUE AND LIMITATIONS**

Understanding the degree of exposure needed for gross total resection with negative margins and the anatomical limitations of EES is critical for appropriate treatment selection and optimal patient outcomes. EES provides several surgical technique advantages compared to traditional, open approaches including limited brain retraction and manipulation, earlier tumor devascularization, and wide access to the skull base including dura and optic nerves<sup>[13]</sup>.

When performing EES for SNMTs, typically, the intranasal portion of the tumor is first debulked to provide visualization of the margins and assess the extent of the tumor<sup>[7]</sup>. Along with this, the opening of surrounding sinuses is completed to provide the additional exposure necessary to determine tumor margins, visualize the skull base, and identify critical bony landmarks including the carotid canals, optic nerves, and lamina papyracea (LP)<sup>[14]</sup>. When there is skull base involvement, often these landmarks are included in the margins of resection, expanding the exposure from the posterior border of the frontal sinus to the tuberculum sellae and between the medial wall of both orbits. When viable and not involved in tumor, a nasoseptal flap is commonly raised from the contralateral side to the SNMT at the beginning of the case and stored in either the maxillary sinus or nasopharynx until needed. In addition, a reverse rotational flap can be raised to reconstruct the nasoseptal flap donor site if free of tumor<sup>[15]</sup>. Nasal septal margins should be checked to ensure that the reconstructive flap does not harbor residual microscopic tumor.



**Figure 1.** Endoscopic endonasal view of anterior skull base anatomy. AEA: Anterior ethmoid artery; LOCR: lateral optic carotid recess; PEA: posterior ethmoidal artery.

Bilateral ethmoidectomies expose the ethmoid skull base and orbit. When resecting the posterior ethmoids, additional resection of the superior turbinate exposes the sphenoid-ethmoidal recess and ostium of the sphenoid sinus. Identification of AEA and PEA is critical during ethmoidectomies to prevent arterial bleeding and risk of retrobulbar hematoma. The sphenoid sinus can also be dissected for tumor removal and increased exposure of the skull base and planum. Anteriorly, the frontal sinus can be opened using a Draf IIa, Draf IIb (unilateral) or Draf III (bilateral) procedure<sup>[16]</sup>. If deeper margins are needed near the olfactory cleft and anterior skull base, the fovea ethmoidalis and cribriform plate can be carefully dissected off of the dura. Posteriorly, the planum sphenoidale can be removed to the medial extension of the anterior clinoids and optic nerves. After adequate removal of these bony landmarks, the cranial dura can be exposed and can be resected depending on the extent of skull base involvement and histology<sup>[14]</sup>. Lateral extension beyond the boundary of the LP can be achieved by removal of the LP and retraction of the periorbita to allow resection of the orbital roof and/or overlying dura as far laterally as the midorbit.

When adequate tumor resection with margins and hemostasis are completed, the optimal reconstruction process for bone and dura defects at the ventral skull base is a multi-layered technique. This technique includes an intradural collagen graft between the brain and dura, followed by an onlay fascial graft in contact with the surrounding dura and bone with an epidural or supraorbital tuck, and followed by a vascularized flap<sup>[17]</sup>. If a nasoseptal flap was not involved with tumor and raised, it is rotated over the fascial graft. If a nasoseptal flap is not available (typically due to previous surgery or tumor invasion), alternative reconstruction options include a tunneled extracranial pericranial flap (preferred) or a lateral nasal wall flap depending on viable tissue and extent of the defect<sup>[18,19]</sup>. Utilization of vascularized tissue is especially important when adjuvant radiotherapy (RT) is anticipated.

Limitations of EES are based on both anatomical limitations and surgeon expertise<sup>[20]</sup>. A review of anterior midline meningiomas treated with EES found that common sites of residual tumor included the anterior clinoid process (ACP), the superolateral compartment of the optic canal, superolateral to the optic nerve, the lateral to the mid-point of the orbital roof, or the anterior border of the falx<sup>[13]</sup>. Similarly, an anatomical study found limitations in accessing the intracanalicular portion of the optic nerve, the most superior aspect

of the orbit, and the dura mater at the lateral portions of the anterior skull base<sup>[21]</sup>. When deciding on surgical treatment, understanding these anatomical limitations can help surgeons weigh the utility of EES and the ability to achieve a negative-margin resection. Although these limitations exist, EES is constantly evolving with improvements in both surgical skill and surgical technology and equipment that can further expand the degree of exposure and resection available through this approach.

## OUTCOMES OF ENDOSCOPIC ENDONASAL SURGERY FOR SINONASAL MALIGNANT TUMORS WITH SKULL BASE INVOLVEMENT

Comparative studies have supported EES for resection of SNMTs, demonstrating EES can have better postoperative quality of life while maintaining similar oncological outcomes when compared to open approaches<sup>[22]</sup>. Rawal *et al.* demonstrated that EES achieved optimal survival outcomes after reporting a 5-year overall survival (OS) rate of 72.3% which was comparable to or better than previous reports of open craniofacial surgery<sup>[23]</sup>. Moreover, the absence of facial incisions and osteotomies, less postoperative pain, shorter hospitalization stays, and reduced perioperative mortality represent major advantages of EES<sup>[24]</sup>.

When comparing EES to conventional open surgical approaches, multiple studies have reported similar oncologic outcomes with improved morbidity and complications with EES. An early study by Snyderman *et al.* suggested that the oncological outcomes for SNMTs with skull base involvement treated with EES were comparable to outcomes from open approaches<sup>[25]</sup>. In a series of 120 patients, Hanna *et al.* found that disease recurrence and survival did not differ significantly between an exclusive EES and a mixed cranioendoscopic approach. The group reported an overall 11% complication rate, with a 3% rate of postoperative cerebrospinal fluid leakage that was not statistically different between groups<sup>[26]</sup>. A more recent study by Schur *et al.* compared anatomically matched cohorts of patients with stage T4 sinonasal malignancies with skull base involvement and found a lower risk of complications after EES than after open surgical approaches<sup>[27]</sup>. Additionally, no significant differences in OS and progression-free survival were found, although patients treated with EES trended towards lower rates of disease progression and higher OS.

## LONG-TERM OUTCOMES OF EES

Long-term survival is significantly different depending on tumor histology. For example, ONB has an excellent survival rate, with studies measuring 5-year OS ranging from 82.3%-92.9%<sup>[28-30]</sup>. Anscheutz *et al.* also report long-term OS rates of 87.5% for ACC and 65.3% for SCC<sup>[31]</sup>. The most frequent sites for SNMT recurrence are at either local or regional sites<sup>[31]</sup>. In addition, there is also limited data comparing long-term complications for endoscopic and open resections. However, Hagemann *et al.* did report in a long-term study that endoscopic resection was associated with improved OS and disease-specific survival<sup>[32]</sup>.

Reports on long-term complications for SNMTs are limited as these outcomes vary greatly based on tumor stage and histology. A study by Levin *et al.* reports an overall complication rate of 53%<sup>[33]</sup>. Shah *et al.* discussed complications of EES for SNMTs with skull base involvement<sup>[34]</sup>. Arnold *et al.* found that many of the patients who required reoperation (21%) were for postoperative sinusitis (18%). Importantly, studies have found that EES leads to lower long-term complication rates than open approaches<sup>[35-37]</sup>.

## ENDOSCOPIC ENDONASAL SURGERY FOR SELECTED PATHOLOGIES

Although histological confirmation is not always available prior to treatment, differences in SNMT histology may impact outcomes and selection of surgical approaches. Diagnosis and staging of SNMTs is imperative for treatment selection in patients and biopsy is typically indicated prior to any skull base

resection. SNMT pathologies with available literature selected for further discussion regarding the utility of EES include ONB, adenocarcinomas, ACC, SCC, SNUC, and SNMM. Findings are summarized in [Table 1](#).

### Olfactory neuroblastoma

Surgical resection with negative margins and adjuvant radiation therapy is the gold standard for most cases. However, IC may be considered for locally advanced or recurrent disease<sup>[38-41]</sup>. In these cases, patients with good response to IC may be treated with chemoradiation therapy<sup>[42]</sup>. In addition, pediatric ONB is often extensive and invasive and responds well to IC, making this the typical treatment pathway in children<sup>[43]</sup>. EES plays an accepted role in the resection of this tumor, showing encouraging outcomes. In a meta-analysis by Devaiah *et al.* comparing endoscopic with open surgery, endoscopic surgery was associated with better 10-year survival (90% vs. 65%)<sup>[44]</sup>. A retrospective review of 139 patients diagnosed with ONB at MD Anderson Cancer Center was performed between 1991 and 2016, with 72 (69.4%) patients having been treated with EES<sup>[28]</sup>. Endoscopic approaches, either pure endoscopic or endoscopic assisted, were found to be suitable for surgical resection of appropriately selected patients with ONB. In addition, Gallia *et al.* reported on an 11-year experience of 20 patients with ONB treated with purely endonasal endoscopic techniques and found 5-year overall, disease-specific, and recurrence-free survival rates were 92.9%, 100%, and 92.9%, respectively<sup>[29]</sup>. In cases where patients have extensive skull base involvement including dural invasion or orbital invasion, an endoscopic approach can be combined with open approaches if necessary to achieve gross total resection<sup>[45]</sup>. This is purely determined by anatomy and not simply the presence of invasion. Invasion of dura or periorbita lateral to the mid orbit may require an open approach; however, dural and intracranial involvement is not an absolute limitation for EES<sup>[46]</sup>. Rarely, the frontal sinus cannot be fully cleared and requires a bicoronal incision and frontal sinus cranialization.

#### ONB case presentation

A 68-year-old woman presented with nasal congestion, anosmia, and intermittent headaches. Magnetic resonance imaging (MRI) showed a sinonasal mass with bony invasion of medial orbit and fovea ethmoidalis invasion, and bilateral dural and olfactory bulb involvement [[Figure 2](#)]. A gross total resection with negative margins was performed using EES with bilateral resection of dura and olfactory tracts.

### Adenocarcinoma

Adenocarcinomas typically arise within the ethmoid sinuses. Resection remains the primary treatment modality and endoscopic surgical excision has been shown to have comparable oncological results to open approaches while providing less morbidity<sup>[47,48]</sup>. In a multicenter study of 159 patients, Vergez *et al.* found that EES and transfacial approaches had comparable early oncological outcome and morbidity, but hospitalization was significantly reduced in patients treated with EES<sup>[49]</sup>. In a meta-analysis of 39 articles pooling 1,826 patients, EES was associated with lower rates of major and minor complications (16.6%) when compared to open approaches (43.8%)<sup>[47]</sup>. Of note, postoperative RT was utilized in the majority of cases in this metanalysis. In a dual-institutional case-control study, EES was shown to be an effective single treatment modality for primary early-stage low-grade adenocarcinoma resected with negative margins<sup>[50]</sup>. In adenocarcinomas, comparative studies have found EES to be as effective as open approaches although select patients with extensive invasion of the skull base beyond the anatomic limits of endonasal resection (mid orbit, frontal sinus) may benefit from a combined approach.

### SCC

In 2010, the European position paper on endoscopic management of tumors of the nose, paranasal sinuses, and skull base found that only 23 patients underwent purely EES among 150 patients with sinonasal SCC<sup>[51]</sup>. This is possibly related to the aggressive nature of SCC, which has a tendency to have both local invasion and perineural invasion, but also may reflect the lack of widespread acceptance of EES to the skull base at

**Table 1. Summarization of surgical indications based on tumor histology**

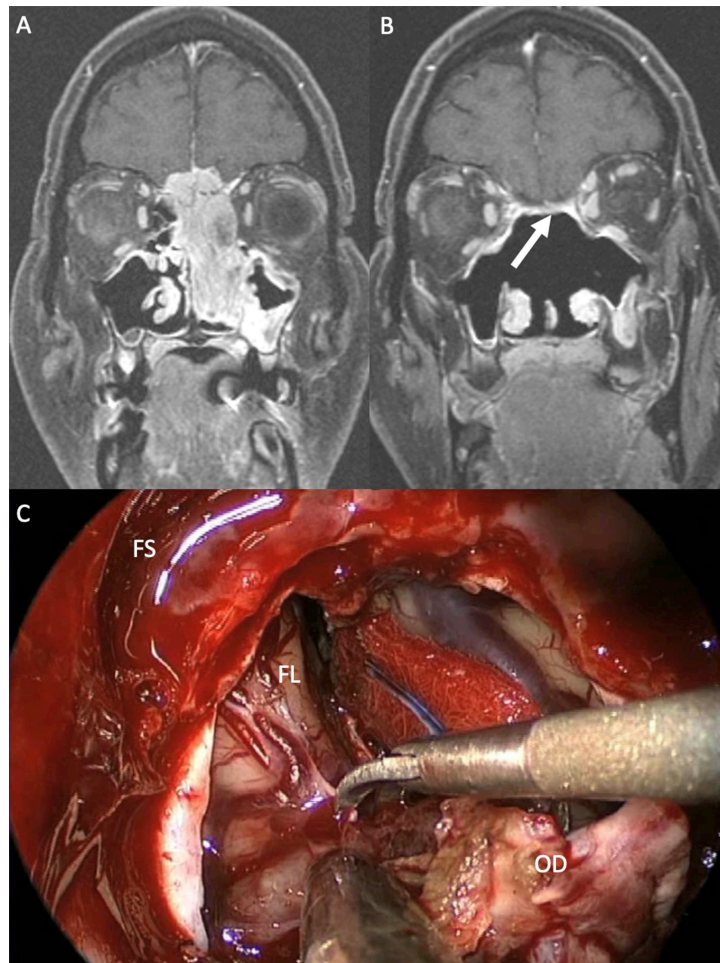
Histology	When is surgery indicated?
Olfactory neuroblastoma	<ul style="list-style-type: none"> <li>• Surgical resection with negative margins and adjuvant radiation therapy is the gold standard for most cases</li> <li>• EES was associated with better 10-year survival (90% vs. 65%) compared to open surgery<sup>[44]</sup></li> <li>• Cases with invasion of dura or periorbita lateral to the mid orbit may require an open approach</li> </ul>
Adenocarcinoma	<ul style="list-style-type: none"> <li>• Surgical resection is primary treatment modality</li> <li>• EES provides comparable oncological results to open approaches with less morbidity<sup>[49]</sup></li> <li>• Postoperative radiotherapy is utilized in the majority of cases</li> </ul>
Squamous cell carcinoma	<ul style="list-style-type: none"> <li>• Surgical resection and adjuvant therapy is the standard of care</li> <li>• Induction chemotherapy may be considered for locally advanced tumors with orbital invasion or unresectable tumors</li> <li>• EES remains an excellent option when amenable to a negative margin resection endonasally</li> </ul>
Adenoid cystic carcinoma	<ul style="list-style-type: none"> <li>• Surgery with adjuvant radiotherapy is the mainstay treatment with the goal of negative margins</li> </ul>
Sinonasal undifferentiated carcinoma	<ul style="list-style-type: none"> <li>• Induction chemotherapy encouraged</li> <li>• Response to induction chemotherapy directs the modality of additional treatment</li> <li>• In responders (partial or complete), chemoradiation therapy should be strongly considered with salvage surgery used after treatment</li> <li>• In non-responders and those with progression of disease, surgical therapy is favored</li> </ul>
Sinonasal mucosal melanoma	<ul style="list-style-type: none"> <li>• EES can be just as effective as open surgery; however, due to poor patient prognosis, adjuvant radiotherapy or immunotherapy is often necessary</li> </ul>

EES: Endoscopic endonasal surgery.

that time. However, due to the advances in EES, more recent studies have shown that endoscopic surgery may offer a safe and less invasive option for select SCC patients compared to open approaches<sup>[36]</sup>. Homma *et al.* provided a review of EES for SCC and found similar oncologic outcomes and the ability to achieve complete resection between EES and open approaches in select patients with SCC<sup>[52]</sup>. Importantly, a retrospective analysis of 15 consecutive SCC patients who underwent EES without an open approach found that patients with negative surgical margins had better disease-specific survival rates than those with positive surgical margins, proving once again that margin status is most important, regardless of technique<sup>[37]</sup>. The standard of care for sinonasal SCC remains surgical resection and adjuvant therapy and EES remains an excellent option for SCC when amenable to a negative margin resection endonasally. In addition, recent studies exploring the addition of IC have found that sinonasal SCC responds favorably to chemotherapy and is associated with improved outcomes and organ preservation<sup>[53]</sup>. These developments may further favor EES approaches to resect shrunken, less invasive tumors after IC.

## ACC

ACC, which is a slow-growing malignant tumor derived from salivary glands and accounts for roughly 5% of sinonasal cancers<sup>[54,55]</sup>, is known to have a propensity for perineural invasion, leading to significant skull base and intradural extension in later stages<sup>[56]</sup>. Therefore, patients with ACC have a high rate of locoregional recurrence and poor long-term survival<sup>[57]</sup>. Advanced ACC is commonly treated with surgery and adjuvant radiation; however, surgery remains the mainstay treatment with the goal of negative margins<sup>[57]</sup>. Volpi *et al.* report on 34 ACC patients treated with EES<sup>[55]</sup>. They found that since ACCs commonly present with perineural spreading, intraoperative frozen sections on the resection margins are also critical. Similar oncological outcomes were found between EES and open craniofacial surgery. Initial treatment of ACC with surgery is focused on negative margins, but the challenge is in long-term care with a dramatic drop in survival from five to ten years, likely due to recurrence. In these cases, adjuvant RT can be used to delay recurrences and improve oncologic outcomes. A retrospective case series of 30 patients found that EES with adjuvant RT for low-grade sinonasal ACC offers 5-year survival similar to that reported by other studies, which include radical, open skull base surgery<sup>[56]</sup>. Gadkaree *et al.* examined ACC with skull base involvement using a National Database<sup>[58]</sup>. The 5-year OS for patients with ACC and without skull base invasion was 67% while for those with skull base involvement, it was 40%. They also found that radiation



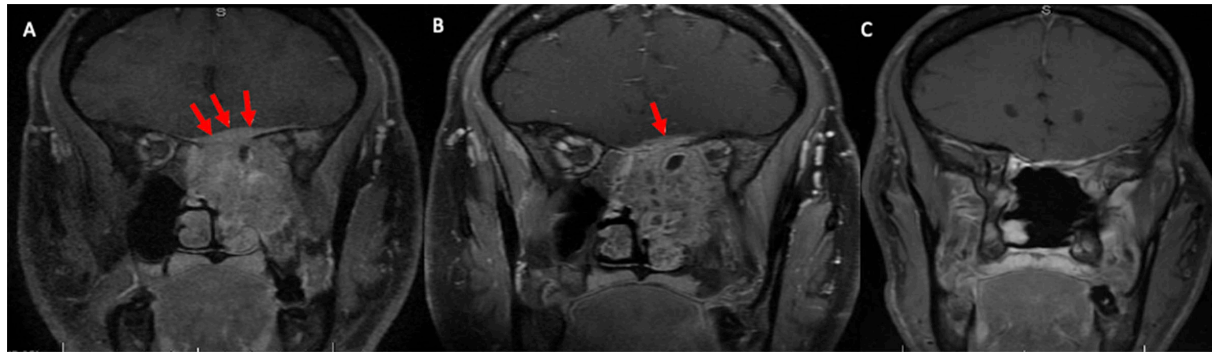
**Figure 2.** A 68-year-old woman with ONB with skull base involvement in [Figure 2A-C](#). (A) Preoperative MRI of ONB; (B) Postoperative MRI showing complete resection with enhancing extracranial pericranial flap (arrow); (C) Intraoperative endoscopic endonasal view of dural dissection of ONB using EES techniques. FS: Frontal sinus; FL: frontal lobe; OD: olfactory dura; ONB: olfactory neuroblastoma; MRI: magnetic resonance imaging; EES: endoscopic endonasal surgery.

was used as the primary form of therapy for 73% of ACC invading into skull base. Given the low likelihood of a cure in the recurrent setting, EES may play an even more important role in limiting the morbidity of treatment and improving local control.

### SNUC

SNUC represents an aggressive sinonasal cancer. Recent treatment paradigms have advocated for the consideration of IC given the tendency for SNUC to have aggressive invasion and poor outcomes<sup>[38,59,60]</sup>. In SNUC, response to IC may direct the modality of additional treatment. In responders (partial or complete), chemoradiation therapy should be strongly considered with salvage surgery used after treatment. In non-responders and those with progression of disease, surgical therapy is favored, though prognosis is likely poor given the disease behavior. In these cases, EES has been reported with similar oncologic outcomes as open surgery while providing less morbidity<sup>[61]</sup>. In short, SNUC is an aggressive malignancy that often presents late in the disease; thus, treatment is commonly IC followed by systemic treatment with chemoradiotherapy. In select patients who do not respond to chemotherapy or have unclear residual disease, EES may be an alternative to open approaches, which are reserved for anatomically inaccessible regions.





**Figure 3.** 49-year-old man with SNUC, pre/post IC (A and B) and post EES MRI images (C). (A) Pre-IC MRI of SNUC, 3 arrows point to dural involvement; (B) Post-IC MRI, 1 arrow points to the continued dural involvement; (C) Post-IC and EES with orbital exenteration MRI. SNUC: Sinonasal undifferentiated carcinoma; IC: induction chemotherapy; EES: endoscopic endonasal surgery; MRI: magnetic resonance imaging.

### *SNUC case presentation*

A 49-year-old man presented with nasal congestion, recurrent epistaxis, decreased left visual acuity, and persistent headaches. MRI showed a left sinonasal and maxillary sinus mass with dural and left orbit involvement. The patient was managed with IC with Etoposide and Cisplatin. A repeat MRI was done after two rounds to measure tumor response to the treatment. Unfortunately, the patient did not respond [Figure 3] and treatment with EES and adjuvant RT was recommended. EES was completed with orbital exenteration and gross total resection with negative margins. Reconstruction consisted of a rotational temporalis muscle flap into the orbit and temporalis fascia duraplasty with vascularized extracranial pericranial flap anterior skull base reconstruction.

### **SNMM**

In combination with the aggressive biologic behavior of this neoplasm, SNMM diagnosis results in a particularly poor patient prognosis with frequent recurrence and a 5-year OS rate of 25% to 40%. In a carefully selected 21-patient study, EES offered comparable survival and even improved local control when compared to open surgery in the treatment of SNMM<sup>[3,62,63]</sup>. A single-institution study of 31 patients surgically managed for SNMM found that 67% of patients were managed with EES and that 57% of stage IVB tumors were successfully managed endoscopically<sup>[64]</sup>. Another single-institution study with 33 patients diagnosed with SNMM who underwent surgery was retrospectively analyzed with 15 patients treated using EES and 18 patients with open resection<sup>[65]</sup>. It was found that disease-free and OS rates did not differ significantly between both groups. In SNMM, EES can be just as effective as open surgery; however, due to poor patient prognosis, adjuvant RT or immunotherapy is often necessary<sup>[66-68]</sup>.

### **Limitations**

Although these studies support the safety and effectiveness of EES, López *et al.* discuss how the strength of many studies may be limited by biases including the patient selection process for EES<sup>[69]</sup>. This review of the literature supports the use of EES in SNMTs with skull base involvement. However, EES is not without its risks and complications, and in cases where a tumor extends beyond the bounds of EES, teams should be prepared to convert to an open approach. Moreover, specific outcomes after EES can vary greatly, and synthesizing outcome research on SNMTs can be challenging due to the rarity of diseases, the variability in tumor size and localization, and the differences in pathology.

## CONCLUSION

The treatment of SNMTs is complex and should be patient-specific. Decision-making for patients with SNMTs should include a multidisciplinary team of neurosurgeons, otolaryngologists, neuroradiologists, radiation and medical oncologists, and histopathologists. Additionally, discussions around treatment should include factors such as SNMT histology, size, location, stage, and extent of involvement of the skull base. Surgical treatment continues to focus on the goal of achieving negative margins. With the continued advancement of endoscopic endonasal approaches, EES has become more commonly included in the skull base surgeon's armamentarium when caring for patients with SNMTs. Studies have found that EES can provide similar oncologic outcomes in many SNMTs compared to open approaches while improving postoperative quality of life and decreasing morbidity. At experienced EES centers, open approaches can be reserved for tumor extending beyond the anatomic reach of the approach (lateral to mid orbit or optic, anterior to the posterior table of frontal sinus). In conclusion, the EES is an effective option and plays a strong role in treating SNMTs with skull base involvement with a goal of margin-negative resection.

## DECLARATIONS

### Authors' contributions

Made substantial contributions to conception and design of the study and performed data analysis and interpretation: Tang A, Adida S, Choby G, Gardner PA

Performed data acquisition and provided administrative, technical, and material support: Tang A, Choby G, Gardner PA

Draft preparation: Tang A, Adida S

Supervision and revisions: Gardner PA, Choby G

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

Not applicable.

### Ethical approval and consent to participate

Data and imaging were de-identified, so institutional review board approval from the University of Pittsburgh was not required.

### Consent for publication

Not applicable.

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