Original Article

# Outcomes following Microvascular Free Tissue Transfer in Reconstructing Skull Base Defects

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## Abstract

**Objective** Successful resection of complex tumors involving the skull base (SB) depends on the ability to reconstruct the resulting defects. The objective of this study was to assess the outcomes of patients undergoing reconstruction after resection of SB tumors with free flaps.

**Methods** From 1995 to 2010 a retrospective review of cases was undertaken. Demographics, histology, surgical management, complications, locoregional control, and survival were analyzed.

**Results** We performed 62 flaps in 57 patients. There was a preponderance of sinonasal malignancies (45%), and most lesions involved the anterior SB (81%). A total of 94% of patients underwent radiotherapy. Reconstruction was undertaken mainly with anterolateral thigh (37%) or radial forearm (34%) flaps. Complications occurred in 17% of patients, and the flap's success rate was 94%.

**Conclusion** Free flaps are versatile and highly reliable for reconstructing defects resulting from resections of the SB. They should be considered for SB reconstruction of large three-dimensional defects as well as defects involving an irradiated field. Successful reconstruction of the SB can be performed using a small number of highly dependable flaps.

**Keywords**
- skull base
- head and neck reconstruction
- skull base defects
- free flaps
- microvascular free tissue transfer

## Introduction

The indications for endonasal endoscopic approaches to diseases of the skull base (SB) have expanded considerably during the last decades. However, in some complex situations open procedures are preferable or even mandatory. In these cases, surgical resection frequently results in the creation of complex defects that expose sterile dural and intracranial compartments to the upper aerodigestive tract and the external environment. Immediate and dependable methods of reconstruction are therefore required to avoid herniation of vital neural structures and ascending intracranial infections.[1]

Local flaps, like a pericranial or galeal-pericranial flap, are effective to separate the nasal cavity from the intracranial space and remain the workhorse for patients treated with limited resection. Regional musculocutaneous flaps are an option in some SB defects, but adequate reach at distant SB sites could be difficult at times. Both options are usually insufficient in more extensive procedures and may be unavailable because of previous radiation or scarring from

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previous operations. Free-tissue transfer has emerged for the past 30 years as a highly reliable method for repairing large difficult wounds in the SB and has been used with increasing frequency to achieve this objective. Moreover, because the overall complication rate with local flaps and with free flaps is approximately similar (39% versus 33%), and significantly smaller than with regional flaps (75%), the use of local and free flaps according to the requirement of an individual case probably will give the best results.[2,3]

Free-tissue transfer facilitates the surgical treatment of extensive primary SB tumors and the retreatment of recurrent tumors. A variety of microvascular free flaps has been described for SB reconstruction. Although free flap SB reconstruction is already well described, most available studies have a limited number of patients. We reviewed our experience with microvascular reconstruction of the SB following the resection of malignant disease, with particular reference to postoperative complications, the reconstructive outcome, locoregional disease control, and disease-specific survival.

## Methods

With approval from the Hospital Universitario Central de Asturias (Spain) institutional review board, the surgical medical charts of the Otorhinolaryngology Department from 1995 to 2010 were reviewed to collect data regarding the clinical data of patients diagnosed and treated for SB tumor resection. The methodology was a retrospective medical chart review. Written informed consent was obtained from each patient.

A total of 300 cases of SB resection were performed at our institution, of which 57 (19%) were reconstructed using microvascular reconstruction. This subgroup of patients was included in this study. Inclusion into the patient group required resection of a portion of the SB and exposure of the intracranial compartments to skin or the upper aerodigestive tract. Patients with cutaneous malignancies requiring only skin coverage, those who underwent endoscopic surgery, and those with small and medium defects were not included.

A SB defect refers to exposed intracranial contents to the skin, paranasal sinuses, nasopharynx, oropharynx, or oral cavity, after resection of a portion of the SB. These defects resulted from resections of primary or recurrent neoplasms or from secondary problems after SB surgery: chronic cerebrospinal fluid (CSF) leak and wound breakdown with dead space and bone exposure (osteoradionecrosis). For the purposes of classification, defects are classified according to the proposed scheme by Irish et al[4] based on anatomical boundaries and on expected tumor spread. Briefly, region I involves defects from tumors arising from the orbits and sinuses, those extending into the anterior cranial fossae, and those originating in the clivus or extending as far posteriorly as the foramen magnum. Region II defects result from tumors originating from the lateral SB, primarily the infratemporal and pterygopalatine fossae, which may extend into the middle cranial fossa. Region III defects are almost all associated with tumors arising from the ear, parotid, or temporal bone, and they may extend into the middle or posterior cranial fossae. These defects resulted from resections of primary or recurrent SB neoplasms. Patients with cutaneous malignancies requiring only skin coverage were not included.

Preoperatively, all patients were evaluated with high-resolution contrast-enhanced computed tomography (CT) imaging, and gadolinium-enhanced magnetic resonance imaging (MRI). CT scans showed the erosion of the SB, and MRI scans were useful to demonstrate the intracranial and/or intraorbital extension. All patients involved in this study were followed for a minimum of 1 year. All calculations were performed using SPSS v.15.0 for Windows.

## Results

A total of 57 patients underwent a total of 62 SB microvascular reconstructions during the study period. Three patients developed a tumor recurrence within a previous free flap and were treated with surgical salvage and a second free flap. Moreover, after initial flap failure, two patients underwent a second free flap. ►**Table 1** shows the patient and disease characteristics. All patients received prophylaxis with subcutaneous low molecular weight heparin. The average follow-up period after SB reconstruction was 4 years (range: 1 to 12 years). All procedures were undertaken by a two-team approach involving SB otolaryngologist and plastic surgeons.

A diverse range of pathologies, with a preponderance of sinonasal malignancies (45%), was encountered (►**Table 1**). Most of the lesions were located in the anterior SB (zone I). Most lesions were confined to a single zone, but in a few cases (16%), lesions traversed the boundary between the anterior and lateral zones.

Tumors were resected via an open extracranial approach. The most common procedures were the total maxillectomy or facial disassembly approaches. Dural tissue was resected in 25 procedures (44%). Primary dural repair was possible in 18 patients, and 7 patients had a watertight fascia lata patch repair with continuous suturing and fibrin glue. ►**Table 2** provides further information about oncologic surgery and tumor location.

Reconstruction was undertaken using mainly the anterolateral thigh (ALT) flap (37%), followed by the radial forearm (RF) free flap (34%) depending on the volume of tissue required. ►**Table 3** provides further details about the reconstructive surgery undertaken. Some RF free flap donor sites (seven cases) were closed either with skin grafts or by means of an ulnar flap as previously described.[5]

Most flaps were anastomosed to the facial vessels, although a range of other recipient vessels were also used (►**Table 3**). The mean skin paddle width was 7 cm (range: 5 to 8 cm), and skin paddle length was 9.3 cm (range: 5 to 12 cm). The mean pedicle length was 13 cm (range: 9 to 18 cm).

The flap's success rate was 94% (58 of 62). Overall, there were four flap failures, with complete necrosis in spite of a prompt reexploration and revision. All flap failures occurred within 48 hours after surgery. A RF flap (melanoma) failed after a venous thrombosis, and it was replaced with a temporal muscle flap. One patient with a mucosal melanoma underwent a reconstruction using an ALT and, after failure of her first free flap, it was replaced with a second RF free flap

**Table 1** Patient and disease characteristics

| Variable | No. of patients ($n = 57$) |
|---|---|
| Age (mean age and range) | 60 ± 15 y (21–84 y) |
| Sex (%) | |
| Male | 38 (67) |
| Female | 19 (33) |
| Tobacco (%) | |
| Yes | 43 (76) |
| No | 14 (24) |
| Alcohol (%) | |
| Yes | 23 (40) |
| No | 34 (60) |
| Presentation (%) | |
| Recurrence | 50 (87) |
| Primary | 7 (13) |
| Tumor stage (TNM 6th ed.) pT4 | 57 (100) |
| Histopathology (%) | |
| Squamous cell carcinoma | 19 (31) |
| Adenoid cystic carcinoma | 9 (14) |
| Basal cell carcinoma | 7 (11) |
| Sinonasal adenocarcinoma | 7 (11) |
| Sarcoma | 7 (11) |
| Malignant melanoma | 4 (7) |
| Undifferentiated carcinoma | 4 (7) |
| Olfactory neuroblastoma | 2 (3) |
| Carcinoma expleomorphic adenoma | 1 (2) |
| Mucoepidermoid carcinoma | 1 (2) |
| Malignant Triton tumor | 1 (2) |
| Prior surgery (%) | |
| Yes | 43 (76) |
| No | 14 (24) |
| Radiotherapy (%) | |
| Preoperative | 39 (68) |
| Postoperative | 15 (26) |
| Not done | 3 (5) |

**Table 2** Ablation surgery, defect location, and residual disease

| Surgical procedure | No. of oncologic procedures ($n = 60$) |
|---|---|
| Extended maxillectomy (%) | 27 (45) |
| Included orbital exenteration | 10 (16) |
| Facial disassembly approach (%)[a] | 12 (20) |
| Included orbital exenteration | 3 (5) |
| Infratemporal fossa C approach (%) | 8 (13) |
| Craniofacial resection (%) | 6 (10) |
| Included orbital exenteration | 3 (5) |
| Isolated orbital exenteration (%) | 5 (9) |
| Petrosectomy (%) | 2 (3) |
| Dural resection (%) | 25 (42) |
| Neck dissection (%) | |
| Unilateral functional neck dissection | 7 (12) |
| Unilateral radical neck dissection | 4 (7) |
| Bilateral functional neck dissection | 2 (3) |
| Radical and functional neck dissection | 1 (2) |
| Defect location | No. of patients ($n = 57$) |
| Zone 1 (%) | 38 (67) |
| Zone 2 (%) | 3 (5) |
| Zone 3 (%) | 6 (11) |
| Zone 1 and 2 (%) | 8 (14) |
| Zone 2 and 3 (%) | 2 (3) |
| Residual disease (%) | No. of surgeries ($n = 60$) |
| Free margins | 51 (85) |
| Affected margins | 9 (15) |

[a]Facial disassembly approach included anterior and lateral facial translocation and orbital or fronto-zygomatic-orbital approaches.

that also failed. The surgical reexploration in both cases showed a correct arterial and venous microanastomosis, so we thought the failure of both flaps was secondary to a “no reflow phenomenon.” A fourth case of free flap loss (parascapular flap in a patient with undifferentiated carcinoma) was managed successfully with a secondary RF flap. It is noteworthy that three of the four flap necroses occurred in patients undergoing excision of a melanoma ($p < 0.001$).

►**Table 4** lists the postoperative complications. They occurred in 10 patients (17%) with local bleed predominating. All CSF leak drainage resolved spontaneously without further surgical intervention. There was no significant difference between the overall rates of complications occurring at each SB region. Previous radiotherapy, dural excision, surgical ablative surgery type, and the type and the surface area of the free flap used were not associated with the occurrence of complications. Two perioperative deaths occurred. One patient died on postoperative day 10 after pneumonia complicated with a respiratory distress syndrome, and the other patient died on postoperative day 14 after myocardial infarction.

At the end of the follow-up period, 16 patients (28%) were alive without evidence of disease, 32 patients (56%) died due to the disease (6 patients died after local recurrence, 13 died due to recurrent locoregional disease, and 13 patients died due to metastatic disease) and 9 patients (15%) died due to unrelated causes. The 5-year locoregional disease control rate for patients undergoing curative resection was 43%. Several factors, including tumor histology and involvement of margins, were found on univariate log-rank analysis to be significantly associated with locoregional control ($p < 0.05$). No association was found between the type of flap used for reconstruction and the likelihood of locoregional recurrence. The only significant independent predictor of locoregional disease control on Cox regression analysis was involvement of the resection margins (hazard ratio: 1.72; 95% confidence interval, 1.06 to 2.78; $p = 0.027$). The 5-year disease-specific survival rate was 36% (►**Fig. 1A**). Univariate log-rank analysis

**Table 3** Reconstructive surgical details

| Flap type | | No. of flaps ($n = 62$) |
|---|---|---|
| ALT (%)<br>Chimera[a] | | 23 (37)<br>8 (35% ALT) |
| Radial forearm (%) | | 21 (34) |
| Parascapular flap (%) | | 12 (19) |
| Scapular-parascapular flap (%) | | 5 (8) |
| Transverse rectus abdominis myocutaneous (%) | | 1 (2) |
| Recipient vessels | Artery ($n = 62$) | Vein ($n = 90$)[b] |
| Facial (%) | 37 (59) | 46 (51) |
| Superior thyroid (%) | 15 (24) | 9 (10) |
| Superficial temporal (%) | 5 (8) | 5 (5) |
| Lingual (%) | 2 (3) | – |
| External carotid (%) | 1 (2) | – |
| Posterior auricular (%) | 1 (2) | – |
| Occipital (%) | 1 (2) | – |
| External jugular vein (end to lateral) (%) | – | 8 (9) |
| Internal jugular vein (end to lateral) (%) | – | 7 (8) |
| Thyrolinguofacial trunk (%) | – | 15 (17) |

Abbreviations: ALT, anterolateral thigh.
[a]Multiple components of different tissue types with spatial independence, each on its own branch.
[b]We performed 90 venous anastomoses; 29 flaps (47%) had two veins. No vein grafts were required.

identified involvement of resection margins ($p = 0.001$) (►**Fig. 1B**) as potential significant prognostic factor (►**Table 5**).

## Discussion

Reconstructions that minimize the risks for complications have become vital to the success of any extirpative procedure, and they are a critical part of most SB surgeries.[6–8] Anticipating the appropriate SB deficit is essential to successful reconstruction. There is no universally accepted defect classification for SB surgery.[4,9–11] We have adapted the Irish system[4] because it seems the most practical of them and is used by many authors. Yano et al[12] recently proposed a new classification that can help select flaps used for subsequent reconstructive procedures.

**Table 4** Complications after skull base reconstruction using free flaps

| Postoperative complications | No. of patients ($n = 57$) |
|---|---|
| No. of patients affected (%) | 10 (17) |
| Local bleed (%) | 6 (10) |
| Cerebrospinal fluid leak (%) | 3 (5) |
| Meningitis (%) | 1 (2) |
| Minor wound breakdown (recipient site) (%) | 2 (4) |
| Perioperative deaths (%) | 2 (3) |
| Flap-related complications | No. of flaps ($n = 62$) |
| Flap loss (%) | 4 (6) |
| Donor-site wound infection (%) | 1 (2) |

Although SB reconstruction needs to be individually tailored for each patient, some considerations must be taken into account such as defect size, need for bone restoration, involvement of an irradiated field, presence of infection, intracranial pressure, history of previous surgery, patient age and comorbidities, and surgeon experience.[13] In any case, dural integrity must be reestablished with a primary closure or with a patch, and it is of paramount importance to the success of reconstruction. Once the dura has been repaired properly, the next goal is to provide a vascularized layer over this dural repair. Reconstruction of bone has several limitations. It should be noted that most of patients have received or will receive radiation, and osteitis, osteonecrosis, or implant extrusion rates are high in these circumstances. As a rule, nonvascularized bone graft or implants should be covered by vascularized tissue. In our experience, it is advisable to use free flaps and avoid implants as far as possible in patients receiving radiotherapy.

In our institution free-tissue transfer is used in ~20% of SB resections, a rate similar to that reported in the literature (18%).[14] According to other authors, this approach is reserved for the reconstruction of extensive and complex three-dimensional defects in cases of revision surgery and

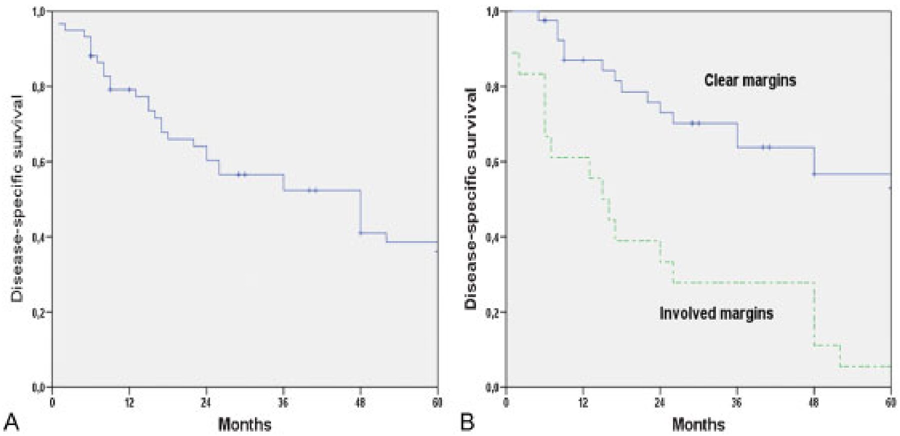


**Fig. 1** (A) Disease-specific survival for patients with skull base malignancy treated with en bloc resection and microvascular reconstruction. (B) Disease-specific survival as a function of the radical surgical resection (Kaplan-Meier analysis).

in previously irradiated fields.[1,9,15,16] Microvascular free-tissue transfer in such cases introduces, in a single stage, large quantities of well-vascularized tissue directly where it is needed with adequate filling of the defects. This technique improves healing, decreases hospitalization, and decreases complications.[17] The reconstruction of the SB with free flaps represents a formidable challenge because of the anatomy of this region and because of the life-threatening consequences of the reconstructive failure. Furthermore, the postoperative management of a neurosurgical patient, geared toward preventing cerebral edema through avoidance of vasodilatation, negative fluid balance, and hypocapnia, is at great variance with the optimal postoperative conditions for the management of a free flap. These considerations make microvascular SB reconstruction a particularly challenging undertaking.[18]

This study shows that microvascular SB surgery can be satisfactorily undertaken using different free flaps. However, although it is important for the reconstructive surgeon to have a broad armamentarium of options to deal with special problems, increased experience has shown that most reconstructive problems affecting the head and neck and SB regions can be effectively addressed using a few highly reliable free flaps. RF and ALT flaps have been the most used flaps in our series, similar to other authors.[11] RF flap, in SB reconstruction, is only indicated in relatively small tissue defect without available local tissue (i.e., orbit) and defects that do not require dead space obliteration. RF flap sacrifices a main artery of the hand, and it has a range of potential donor-site complications, including forearm aesthetics, loss of wrist range of motion, poor healing, and tendon exposure, despite the strategies outlined to avoid them.[16] RF has been largely replaced by the ALT in our current practice.[19] ALT flaps in SB reconstruction provide versatility in flap design and availability of adequate tissues to fill dead space, and it offers vascularized fascia to augment dural repairs. It also provides a long pedicle and allows simultaneous flap harvest with low donor-site morbidity.[19]

Overall, the rectus abdominis muscle remains, in other teams, as the workhorse for the microvascular reconstruction



**Table 5** Survival analysis of clinical and histologic parameters[a]

| | Locoregional control | | Disease-specific survival |
|---|---|---|---|
| | Log rank (*p* value) | Hazard ratio (95% CI) (*p* value) | Log rank (*p* value) |
| Tumor histology | 34.912 (0.0001) | 0.960 (0.881–1.046) (0.351) | 32.282 (0.330) |
| Prior surgery | 1.943 (0.163) | | 0.178 (0.673) |
| Prior radiotherapy | 0.192 (0.661) | | 1.366 (0.242) |
| Defect location | 2.340 (0.673) | | 5.103 (0.277) |
| Surgical procedure | 3.926 (0.560) | | 9.223 (0.100) |
| Residual disease | 3.709 (0.040) | 1.72 (1.06–2.78) (0.027) | 19.505 (0.0001) |
| Postradiotherapy | 0.001 (0.973) | | 0.037 (0.848) |
| Type of flap | 0.898 (0.925) | | 13.745 (0.800) |
| Complications | 0.054 (0.815) | | 7.448 (0.231) |

Abbreviations: CI, confidence interval.
[a]Univariate analysis by Mantel-Cox log-rank test; multivariate analysis by Cox regression.

of SB.[20] This flap provides long vascular pedicles, large skin paddles, and the possibility to form a dural sheath. Like the ALT flap, simultaneous harvest of the flap while tumor resection can be performed. The success rate of this flap is >90% (similar to ALT). However, it has more disadvantages than other flaps (e.g., ALT flap). These include an abdominal scar and hernia formation and its bulkiness (most of the tissue bulk is vascularized fat that does not atrophy over time).[19,21] Although the subscapular system free flaps provide long vascular pedicle with large-caliber vessels and a large amount of available composite tissue, they would be not practical in SB surgery because the patient needs to be turned intraoperatively, which prolongs the operative time in an already lengthy procedure. However, it may be extremely useful in selected cases with special reconstructive needs or due to contraindication of other free flaps, with minimal donor-site morbidity.

The choice of recipient vessels is one of the most critical steps in ensuring a successful outcome in microvascular surgery of the head and neck. Preparation of donor and recipient vessels must be adequate prior to flap transfer. For anterior defects, facial vessels are the most useful donor vessels, but they may be thickened and the flow may be compromised after radiation therapy. If facial vessels are not suitable, the vascular pedicle of the flap can be anastomosed to superficial temporal vessels.

The overall incidence of complications in the present series was 17%, which compared well with the 16 to 64% incidence of complications reported in the literature.[14,22,23] The use of free flaps has significantly reduced postoperative complications, especially nervous complications, after SB resection.[11,14] However, a multi-institutional study[14] analyzing the effect of vascularized versus nonvascularized tissue showed no reduction in overall complications when vascularized tissue was used. This may be explained by the fact that reconstructive technique depends on the size and complexity of the surgical defect. Therefore, free flap reconstruction is most likely to be used when the soft tissue defect is very large. The most frequent complications are primarily acute and related to the wound, as we have seen in our series. Early complications following SB reconstruction include partial or total flap loss, hematoma, meningitis, and CSF leak. The use of free flaps has decreased the incidence of CSF leaks from 25 to 6.5% because of the better vascularity.[14] Reconstructive failure occurred in five procedures. Three flaps failure occurred in patients diagnosed with metastatic melanoma. The immunologic abnormalities that underlie these tumors could be related to the increased frequency of vascular thrombosis and flap failure.

Nevertheless, Moncrieff et al[24] showed free flap viability in 15 of 16 flaps for reconstruction of large melanoma defects, including nine cases involving the SB. No independent risk factors for the occurrence of complications could be identified in this study. In particular, larger reconstructions were not associated with a higher incidence of local or donor-site complications. This observation appear to suggest that there may be room for performing more extensive ablative surgery to achieve complete oncologic tumor clearance, on the basis that the resulting defects can be satisfactorily reconstructed without an increase in the incidence of postoperative complications. Like other authors, we did not found a correlation between the rate of complications and prior treatment with radiation therapy.[25] However, our finding has to be interpreted with some caution because association between complication rates and prior chemotherapy, radiotherapy, or surgery was found in other studies.[11,14] Unlike our series, medical comorbidity seems to be an important significant predictor for postoperative complications.[11] Finally, with regard to postoperative mortality, our rate is similar to that published in other series (>5%).[11,14]

We obtained relatively low local control and survival rates despite free flap surgery. The 5-year locoregional disease control rate in the present series was 43%, and the 5-year disease-specific survival rate was 36%. These low rates are a reflection of the selection of patients rather than surgery. Most of our patients had locally advanced and/or histologically aggressive tumors and had been treated previously. The only independent factor associated with locoregional failure and with disease-specific survival was no clear resection margins. Despite these data, it should be observed that only a few patients die from the surgery or complications, and a significant percentage are alive at least a few years after the salvage with a reasonable quality of life. A SB lesion can be associated with significant local symptoms, a markedly diminished quality of life, and a potentially avoidable and unpleasant death, so in some cases even a palliative surgery must take it into account. Extensive or recurrent SB tumor in a previously irradiated or operated field has a poor prognosis with a median survival of ~6 months with best supportive care. SB reconstruction offers the opportunity of achieving negative margins and therefore better outcomes.

In summary, nonendoscopic SB reconstruction has evolved greatly in the last few decades with the advent of microvascular free-tissue transfer. Free-tissue transfer is the mainstay for reconstruction of large three-dimensional defects as well as defects involving an irradiated field. Free flaps provide reliable and well-vascularized tissue for effective SB reconstruction. The extent of reconstruction does not influence the incidence of postoperative complications, and more extensive ablative surgery can be undertaken in selected cases with the knowledge that the resulting defect can be satisfactorily reconstructed.

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