Research Paper

Interdisciplinary management of skull base surgery

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ABSTRACT

Skull base surgery remains one of the challenging areas in the field of cranio-maxillofacial surgery, otolaryngology and neurosurgery. Subsequent reconstruction of bone and soft tissue are an essential component to restore function and appearance after ablative surgery.

Establishment of interdisciplinary tumor boards with presentation of the individual patient cases have become standard. Multiplanar reconstruction using MRI or CT imaging techniques combined with virtual 3D planning allow precise planning of the procedures. Intraoperative navigation helps for complete resection of malignant findings with safety margins; surgical approaches provide a good overview of the surgical site. Reconstruction using local flaps have a low complication rate with equally reliable results in reconstruction of small tissue defects. Free flap surgery makes reconstruction of large tissue defects possible. Alloplastic materials are alternatively used for reconstruction of bone defects.

Based on selected patients, treatment algorithms and standard surgical procedures in extracerebral skull base surgery will be illustrated. Current techniques and new approaches will be discussed with emphasize on hard and soft tissue reconstruction.

1. Introduction

Pathologies and space occupying lesions of the skull base can be situated intra- or extracranially. Current definitions divide the intracerebral parts of the skull base into an anterior, middle or posterior cranial fossa. However, newer classifications increasingly include extracranial aspects of the skull base.^{1,2} Microsurgical approaches, in particular for the removal of aneurysms, have been described since the 1970s and revolutionized intracranial skull base surgery.^{3,4} The application of endoscopic surgery techniques, originally developed for paranasal sinus surgery, enables far less invasive procedures at the anterior skull base region and within the clivus.⁵

Extracranial skull base pathologies are located in the pterygoid fossa, the infratemporal fossa, or the paranasal sinuses. Cranial nerve foramina represent an entry to the intracerebral area; perineural invasion often limits resectability of extracranial malignant tumors.^{6,7}

The extracranial part of the skull base has been regarded as the limit for many surgeons for a long time. In the last decades, innovative techniques such as high resolution CT or MRI imaging, less invasive surgical approaches and operative techniques, intraoperative navigation

and methods for reconstruction of soft tissue or bone, have made operations in this area predictable and routine.^{8–10}

Based on ten selected patient cases suffering from different malignant findings in the extracranial skull base, typical interdisciplinary diagnostic and treatment algorithms are described and innovative techniques are presented. A short overview of the history and characteristics of the techniques presented is given, and limitations and problems are identified. An outlook on trends for the future, especially in the field of tissue regeneration, is given.

2. Presentation of cases

2.1. Patient selection and patient case discussion in the tumor board for skull base pathologies

In the period from January 31st, 2015 until June 30th, 2021 3532 patient cases have been evaluated at the interdisciplinary tumor board for skull base pathologies at the University Medical Center Freiburg, on average 11.1 patients per meeting with an increasing trend (Fig. 1). For every individual patient, a personalized treatment protocol has been set

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up.

Out of these patients, 10 patients with pathologies infiltrating the skull base have randomly been selected. Five patients had extraoral tumors (2x parotid gland tumors, 1x Tenosynovial Giant Cell Tumor of the mandibular joint, 1x squamous cell carcinoma of the ear, 1x metastasis of breast cancer in the frontal bone), five patients suffered from malignant tumors located intraorally and in the maxillary sinus (1x osteosarcoma, 1x rhabdomyosarcoma, 1x squamous cell carcinoma, 1x adenoid cystic carcinoma, 1x tonsil cancer) (Table 1).

2.2. Preoperative image acquisition and intraoperative navigation

High-resolution CT imaging with slice thickness <1 mm and multi-axial reconstruction was performed in all patients. In eight out of ten cases, preoperative MRI examinations to investigate the tumor extension in greater detail were carried out (Fig. 2).

The acquired image datasets were subsequently presented for discussion and treatment planning in the tumor board for skull base pathologies. In addition to that, this data was needed to perform preoperative planning for intraoperative navigation (virtual surgical planning) in seven out of ten patients (Brainlab AG, München, Germany) (Fig. 3).

2.3. Surgical approach and operative treatment

In three of the patients with intraoral pathologies, a Weber-Fergusson approach was used for resection. In one of these cases, the orbit and the eye were infiltrated by the tumor, so that a unilateral enucleation was required. The patient with an extensive tonsil cancer, which was infiltrating also the base of the tongue, had preoperatively been classified as inoperable at another institution. He was treated using a transoral approach with a temporary mandibular split.

A lateral approach was used in all patients for resection of the extraoral pathologies (Fig. 4a). The facial nerve was protected in the cases showing no preoperative nerve palsy. Intraoperatively, the tumor bed was marked with a radiopaque liquid for future determination of the target volume for radiotherapy (Fig. 5). In the patient case with metastasis from breast cancer in the frontal bone, a modification with a curved coronal incision was used as the approach (Fig. 4b). In an interdisciplinary operation with neurosurgeons and cranio-maxillofacial surgeons, simultaneous resection of the bone and the infiltrated dura, as well as reconstruction of the resected structures was all done as one surgical procedure. Six months previously, the patient had already had removal of a metastasis in the left mandible and had undergone a partial

mandibulectomy.

2.4. Defect reconstruction

Three patients with space occupying lesions of the oral cavity were primarily reconstructed using a vascularized (scapula-)/latissimus dorsi free flap and a radial forearm flap respectively. One patient with an osteosarcoma received prosthetic rehabilitation and in one patient the wound could be closed directly.

In two patients undergoing surgery with a lateral approach, parts of the ascending ramus of the mandible had to be removed. Primarily reconstruction was done using a scapula-/latissimus dorsi free flap and the coronoid process of the ipsilateral side respectively (Fig. 6). The transplanted bones served as joint replacements. In the patient with metastasis of breast cancer, dura reconstruction was performed using a collagen patch and the orbital roof and the frontal bone were reconstructed with patient-specific titanium meshes. Reconstruction of the mandible was done in the operation using a free fibula flap (Fig. 7).

2.5. Additional therapy

All patients were postoperatively presented at our interdisciplinary tumor board. In 8 patients, adjuvant radiotherapy was recommended. Two patients with sarcomas had preoperatively already been included into perioperative chemotherapy regimens, one of them into the EURAMOS-1 study.¹¹ The patient with metastatic breast cancer additionally received postoperative immunotherapy.

3. Discussion

Current skull base surgery techniques have been standardized on a high-quality level due to decisive preconditions such as:

3.1. Interdisciplinary tumor boards

Interdisciplinary tumor boards are defined as multidisciplinary team meetings in which different specialists work closely together share all patient data and plan interdisciplinary treatments in cancer care.¹² They improve diagnosis and staging accuracy and contribute to better clinical and process outcomes.¹³ Retrospective analysis showed that presentation of patient cases increases adherence to national guidelines with a ratio of 98%–83%.¹⁴

Fig. 1. Overview over the total number (A) and average number of patients per session discussed at the interdisciplinary tumor board for skull base pathologies.

Table 1

Overview of the 10 patients with malignancies infiltrating the skull base and their therapy.

Patient	Age	Diagnosis	PreOP CT-Scan	PreOP MRI	Navigation	Surgical approach	Reconstruction	Additional therapy
1	66y	Adenocarcinoma (parotid gland)	+	+	+	Lateral	Scapula/Latissimus dorsi free flap	Adjuvant radiotherapy
2	19y	Mucoepidermoid carcinoma (parotid gland)	+	+	+	Lateral	Primary closure	Adjuvant radiotherapy
3	52y	Metastasis breast cancer (frontal bone)	+	+	+	Lateral (with Extension to coronal)	Alloplastic (Mesh)	Adjuvant immunotherapy
4	80y	Squamous cell carcinoma of skin (ear)	+	–	+	Lateral (Resection Ear)	Latissimus dorsi free flap	Adjuvant radiotherapy
5	34y	Tenosynovial Giant Cell Tumor (temporo-mandibular joint)	+	–	+	Lateral	Autologous (joint replacement with coronoid process)	Adjuvant radiotherapy (Protons)
6	67y	Adenoid Cystic Carcinoma (maxillary sinus)	+	+	–	Weber-Fergusson	Scapula/Latissimus dorsi free flap	Intraoperative radiotherapy
7	63y	Tonsil cancer infiltrating the tongue base	+	+	+	Intraoral with mandible split	Radial forearm flap	Adjuvant radiotherapy
8	60y	Squamous cell carcinoma (maxillary sinus)	+	+	+	Weber-Fergusson	NONE, prosthetic rehabilitation	Adjuvant radiotherapy
9	22y	Osteosarcoma (maxilla)	+	+	–	Intraoral	NONE, prosthetic rehabilitation	Perioperative chemotherapy (EURAMOS study)
10	55y	Rhabdomyosarcoma (maxilla)	+	+	–	Weber-Fergusson	Scapula/Latissimus dorsi free flap	Perioperative chemotherapy
Σ		Intraoral: N = 5 Extraoral: N = 5	N = 10	N = 8	N = 7	Intraoral: N = 2 Lateral: N = 5 W-F: N = 3	Alloplastic: N = 1 Free Flap: N = 5 Primary: N = 1 Prosthesis: N = 2 Others: N = 1	Chemotherapy: N = 2 Immunotherapy: N = 1 Radiotherapy: N = 7

Fig. 2. Axial slices of the patient with an adenocarcinoma in the parotid gland using CT (A) and MRI image (B; T2 weight) reveals a better representation of the malignancy in the MRI image with less artifacts caused by dental restorations [*malignancy].

3.2. Imaging techniques

Today's standard techniques for imaging of pathologies at the skull base are CT and MRI imaging, illustrating pathologies with voxel sizes smaller 1 mm.¹⁵ Ultrahigh-resolution CT also achieves slice thickness of about 250 μ m or less and are capable of imaging the smallest bone structures (U-HRCT).¹⁶ Acquired images are stored as DICOM stack and can be shared among different disciplines involved or external partners.

MRI imaging should be chosen as preferred technique for illustration of soft tissue malignancies.¹⁵ Diffusion-Weighted Imaging (DWI), Dynamic Contrast Enhancement technique (DCE), Ultrashort Time to Echo (UTE) or other sequences have dramatically improved image quality of bony structures over the last few years. However, image quality of CT scans are currently not achieved in routine clinical imaging.¹⁷ “Black Bone”, a further MRI imaging technique, offers the possibility to reconstruct bone surfaces for creating surface meshes that can be used

for 3D printing. This technique has the potential to reduce radiation exposure for bone imaging, especially in young patients.^{18,19} For detection of perineural invasion, contrast-enhanced MRI imaging is recommended with a sensitivity up to 95% in detecting perineural spread. Due to better soft tissue contrast and less artefact caused from any dental hardware, it is even superior to CT imaging techniques in the head and neck area when bone structures are not of importance^{20,21} (Fig. 2). The accuracy is sufficient for successful virtual implant planning.^{22,23}

3.3. Intraoperative navigation and intraoperative marking of the resection margins

Since the first attempts of extremely simple guiding devices, preoperative planning and intraoperative navigation became almost indispensable (Fig. 3).²⁴ Navigation today increases efficiency and reduces

Fig. 3. Virtual planning for intraoperative navigation in two patients (A: Patient with tumor in the temporomandibular joint; B: Patient with tonsil cancer infiltrating the tongue base) [green: tumor mass; red: carotid artery; blue: jugular vein].

invasiveness and operation time in scheduled cases.^{8,25–27} To date, more than 20 different navigation systems have been developed, with an average accuracy rate of <0.5 mm. Translation into a worldwide routine clinical practice has not happened yet due to high acquisition costs for navigation devices. High resolution MRI and CT imaging devices with voxel sizes smaller 1 mm, further indispensable requirements for intraoperative navigation, are unfortunately not available everywhere.²⁸ Intraoperative marking of the resection margins using a radio-opaque fluid helps for better planning of adjuvant radiotherapy (Fig. 5).²⁹

3.4. Surgical approaches

Since the first descriptions of transfacial skull base approaches in the 19th century, with large visible scars in the facial area, adaptations using lateral extraoral or intraoral transantral approaches dramatically minimized invasiveness.^{7,30–32}

For resection of malignant skull base tumors, extension of such limited approaches is still needed to provide a good outcome of the surgical site. The lateral approach, with a preauricular skin incision, can be extended to the neck allowing simultaneous access to cervical structures (Fig. 4a).³³ This approach has proven effective for resection of malignant pathologies in the infratemporal fossa with overall three- and five-year survival rates for patients of 82% and 66% respectively.^{34,35} Modifications with extension to the hairy scalp allow comparable outcomes of the surgical site with the consequence of smaller visible scars.³⁶

Transfacial approaches are used for resection of anterior skull base pathologies and pathologies within the paranasal sinus. The Weber Fergusson's approach is a classical standard and has had many improvements over the many years since it was first described.³⁷ Today, extensions and combinations with intracranial approaches, allow

Fig. 5. Postoperative CT scan showing the resection margins marked intraoperatively with a radio-opaque liquid [blue].

Fig. 4. (A + B): Intraoperative images of the patients with tumor in the parotid gland (A) and metastasis in the frontal bone (B) using a lateral preauricular approach ± extension to coronal [*main trunk of the facial nerve; + metastasis from breast cancer in the frontal bone].

Fig. 6. 3D reconstruction of postoperative CT scans of the two patients with mandibular reconstruction using autologous bone grafts (A: reconstruction using a vascularized scapula flap; B: reconstruction using the coronoid process of the mandible).

simultaneous resections of malignancies in the intracranial anterior fossa compartments (Craniofacial approach CFA).³⁸ Lateral rhinotomy approaches provide exposure to the deep retromolar spaces with simultaneous protection of the infraorbital nerve although length of incision and thus length of resulting scar is minimized.³⁹ In the anterior skull base, these craniofacial approaches have been confirmed as gold standard with an overall survival rate up to 72% and a disease-specific survival rate up to 78% after 5 years.⁴⁰

Endoscopic endonasal approaches have emerged as modern treatment options. Although en bloc resections of malignancies are not possible in all situations, several studies demonstrated equivalent or better results of endoscopic approaches when compared to open approaches.^{41–46}

3.5. Defect reconstruction

Today's standard procedures for defect reconstruction remain autologous tissue transfers. Smaller external soft tissue defects are reconstructed using local skin, fascia, muscle, fat, or localized fat-dermis flaps. They show an overall low complication rate and are suitable for coverage of cerebrospinal fluid (CSF) leakages.¹⁰ The nasoseptal flap, as one of the latest invented flaps, has its particular indication in reconstruction of anterior skull base defects during endoscopic transnasal surgery and enables a reduction of incidence of CSF leakage from 20 to 30% to <5%.^{47–49}

Larger soft tissue defects are reconstructed using vascularized free

Fig. 7. (A): Intraoperative image showing the reconstruction of the orbital roof [*], the dura mater [#] and the frontal/ temporal bone [+] of the patient with metastatic breast cancer. (B): postoperative panoramic X-Ray showing the mandible reconstructed with a free fibula flap.

flaps allowing tailoring the amount and quality of tissue according to the size and complexity of the defect. The most commonly used flaps are rectus abdominis, latissimus dorsi or anterolateral thigh (ALT) flaps because of their large skin paddles.^{50,51} An alternative, easy to harvest flap, is the radial forearm flap with its long thin pedicle that allows great flexibility in flap configuration, pedicle positioning and vascular anastomosis in the neck. Indications for this flap recently have also been described in endoscopic assisted surgery.⁵²

Technical advances, increased experience and robust training programs have improved the success rates of free flap reconstructions up to 97%.⁵³ One of the most dreaded complications remains thrombosis of the arterial or venous branch resulting in flap loss. Different anticoagulation regimes for modification of the secondary hemostasis have been developed and are currently under investigation; further optimization of the protocols already established has been done.^{54,55} Latest findings could even demonstrate the primary hemostasis being responsible for flap loss, especially in severely injured patients.

Simultaneous reconstruction of bone and soft tissue with autologous bone grafts is indicated for skull base defects including aspects of the mandible or the maxilla. Flaps used are from the iliac crest, fibula, or scapula, with the tip of the scapula resembling the shape of the mandibular body more accurately than bone from the iliac crest or fibula.⁵⁶ Recent advances in surgical technique allow the replacement of the mandibular joint using scapula or fibula free flaps without the need of a temporomandibular joint prosthesis (Fig. 6).^{57,58} Function and aesthetics have improved since using pre-operative virtual surgical planning in combination with patient-specific implants and cutting/resection guides manufactured using computer-aided design and manufacturing technology [CAD/CAM technology].⁵⁹ Furthermore ischemic and operating times are reduced while minimizing the complication rate.⁶⁰

Reconstruction of the cranial bones including aspects of the skull base is performed using alloplastic materials such as titanium, PEEK or PMMA.^{61–63} CAD/CAM technology with virtual surgical planning allows an anatomical fitting of the fabricated scaffolds without significant gaps between bone and scaffold.⁶⁴ In experimental settings resorbable polymer materials such as resorbable plates have successfully been used for endoscopic skull base repair.^{65,66} Hydroxyapatite and other bone substitutes have also been used for skull base reconstruction.^{67,68} However, their osteogenic and osteoconductive potential alone is quite low. When using alloplastic resorbable material, a complete histologic regeneration, in particular of critical size defects, is not possible yet. Optimization of scaffold designs using pore sizes >100 µm improved the osteogenic potential and the combination with growth factors or cells (e. g. MSCs) might be a further promising approach to improve the osteogenic potential of resorbable scaffolds.^{69,70} When their osteogenic potential has been improved and a reported increased risk of late infection has been minimized, resorbable materials will certainly replace non-resorbable alloplastic materials and autologous bone transfer in the future.^{71,72}

4. Conclusion

Extracerebral skull base surgery has been a challenging anatomical area and even laid down limits for many surgeons for a long time. Technical progress made operation procedures and outcomes in the last decades predictable and resulted in an implementation of skull base surgeries into a routine schedule. Data acquired from high resolution CT or MRI can be shared among all disciplines involved or even with external partners. Virtual surgical planning and intraoperative navigation allow a precise preoperative definition of safety margins. Improved surgical approaches minimize the lengths of scars visible, give a good outcome of the surgical site and allow the preservation of the facial nerve in certain patient cases. Defect reconstruction can be performed using (non-) vascularized grafts and alloplastic materials. Reconstruction of bones from the skull and the skull base using resorbable materials is under investigation and will soon replace usage of non-resorbable alloplastic materials and autologous bone.

Authors' contributions

RR contributed to the literature review, initiated the work, and wrote the manuscript. RR, MM, VP, BJ and SR were clinicians involved in the assessment and management of the patient cases. SR was the clinical supervisor of all cases. He was additionally responsible for editing and patient selection. All authors corrected and approved the final form of the manuscript.

Declaration of patient consent

Written informed consent was given by the patients for publication of all enclosed images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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