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Unique considerations in pediatric skull base surgery ☆

Irit Duek, MD, Dan M. Fliss, MD

From the Department of Otolaryngology Head and Neck Surgery and Maxillofacial Surgery, Tel Aviv Sourasky Medical Center, Sackler School of Medicine, Tel-Aviv University, Tel Aviv, Israel

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Pediatric skull base and craniofacial surgery presents a unique challenge since the potential benefits of therapy must be balanced against the cumulative impact of multimodality treatment on craniofacial growth, donor-site morbidity, and the potential for serious psychosocial issues. Skull base reconstruction using locoregional flaps or free flaps may be safely performed in pediatrics. Although the general principles of skull base reconstruction are applicable to nearly all patients, the unique demands of skull base surgery in pediatrics merit special attention. Multidisciplinary care in experienced centers is of utmost importance.

Introduction

Cancer is a leading cause of death in children in the western world second only to accidental death. In the United States, approximately 0.35% of the general pediatric population below the age of 20 is diagnosed with cancer.[1] Head and neck malignancy comprises approximately 12% of all pediatric cases with the most common pathologies being lymphoma (27%), primitive neuroectodermal tumor (23%), and soft tissue sarcomas (12%).[2] Pediatric skull base tumors are rare and heterogenous subset of head and neck tumors. Malignant tumors comprise approximately half of the cases, of which about half are soft tissue sarcomas.[3] The age distribution exhibits a bimodal pattern peaking at ages 3.5 and 17.5 years, with different pathologies afflicting each age group.[4] While skull base and craniofacial surgical resection and reconstruction are integral components in the management of many pediatric neoplasms, they pose a particular challenge in this age group. The potential benefits of therapy must be balanced against the cumulative impact on future craniofacial skeletal growth and soft tissue changes, along with donor site morbidity following harvesting tissue from a growing skeleton, and the potentially significant psychosocial impact.[5] Unique anatomical considerations in children include smaller craniofacial complex, cranial fossa, and paranasal sinuses, stage of tooth eruption, absence of anatomic landmarks such as the superior orbital fissure and mastoid pneumatization, and the fragility of neurovascular elements. Moreover, the brain itself

Abbreviations: ASB, anterior skull base; CAD/CAM, computer-aided design and computer-aided design and manufacturing; CSF, cerebrospinal fluid; CT, computed tomography; 3D, three-dimensional; DCR, dacryorhinocystostomy; EEA, endoscopic endonasal approaches; MRI, magnetic resonance imaging; NFO, nasofronto-orbital; RFFF, radial forearm free flap; VRAM, vertical rectus abdominis myocutaneous.

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Address reprint requests and correspondence: Dan M. Fliss, MD, Department of Otolaryngology Head and Neck Surgery and Maxillofacial Surgery, Tel Aviv Sourasky Medical Center, Sackler School of Medicine, Tel Aviv University, 6 Weizman Street, 6423906, Tel Aviv, Israel.
E-mail address: danf@tlvmc.gov.il

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is denser and less amendable to physical manipulation. Major concerns of skull base procedures in children are the potential impact of osteotomies on the subsequent development of the face and paranasal sinuses, and the challenges of performing microsurgery in children whose blood vessel diameters are small, anatomical landmarks are inconsistent, and growth of anastomosed vessels is anticipated. Since children are more likely to suffer from sarcomas and from tumors involving the middle cranial fossa compared to adults, surgical defects are often large and cause significant functional, aesthetic, and psychological issues. Members of a multidisciplinary team consisting of specialists in neurosurgery, head and neck surgery, plastic and reconstructive surgery, maxillofacial surgeons and prosthodontics, pediatric critical care, and pediatric oncology should work in conjunction with child life specialists. Technical developments in the fields of head and neck surgery and neurosurgery in the last few decades, allowed a growth in skull base reconstructive options. As a result of improvements in microvascular technique, endoscopic equipment, image guidance, and biomaterials, the choices in reconstructive technique have expanded, allowing for more radical tumor extirpations, with major impact on the long-term survival of patients with skull base tumors. Although the general principles of various surgical approaches of skull base reconstruction following tumor ablation are feasible, applicable and well-established, the variety of approaches that have been developed over the years have been applied mainly to adult patients while unique issues remain to be established in the pediatric patients.[6] Several retrospective studies have been conducted to shed light on the special considerations related to this age group, but the sample sizes were small, and data are limited.[7] Because of the relative rarity and heterogeneity of skull base neoplasms, protocol-driven research has proven difficult. However, enough experience has accumulated to allow a new focus on the unique demands of skull base surgery in children. In this article, we aim to review the unique considerations of skull base surgery in the pediatric population.

Anatomic considerations

The human skull grows rapidly during the first 4 years of life. The maximal growth rate at birth slopes down to a minimum in prepuberty and returns to a smaller second spike at puberty. The growth of the skull base is slower than that of the calvaria with the anterior, middle, and posterior fossae each developing at different rates. The anterior fossa undergoes ossification starting at birth, when it is still cartilaginous, until the third year of life when it attains almost adult structure. During the second year of life, the mastoid starts to project inferiorly from the squamous and petrous parts of the temporal bone and undergoes pneumatization up until adolescence with the middle fossa reaching its final size approximately at the age of 10. The posterior fossa is the last to attain mature form. It is comprised mainly by the occipital bone with a lesser contribution of the sphenoid anteriorly and the temporal bone laterally. There are 4 synchondroses which begin to fuse during the second year of life but do not fuse completely until the age of 4 at the posterior junction (exooccipital and squamous segment) and 8 at the anterior junction (basioccipital and exooccipital). At the age of 10 the posterior fossa nearly achieves adult proportions. The spheno-occipital synchondrosis, which is the main axis of skull base growth, fuses at the ages 12-15 years and ossifies only at early adulthood.

Several differences exist between adults and children with regard to skull base morphology. The size of the cranial base and maxillofacial complex in children is smaller, the cranial bone is thinner, and the floor of the frontal and middle cranial fossa may be flatter.[6] Neurovascular elements in children are thinner and more fragile than in adults.[3] Another difference is the inconsistency of specific anatomical landmarks in children compared with the fully developed cranium of adults. In children younger than 3 years, the mastoid tip may not be fully developed, so the facial nerve is more superficial and inferior than in adults. The mastoid air cells are not fully pneumatized in very young children, because the mastoid and middle fossa reaches adult size after the age of 10 making the identification of the labyrinth more difficult.[8] The pterion is located more anteriorly in children, and the supraorbital fissure or foramen, which serves as a landmark for orbital and orbitozygomatic approaches, may be absent before the age of 8 years.[6] Another important anatomical discrepancy is the developmental stage of the paranasal sinuses: the frontal sinus starts to develop from the age of 6 years and reaches its full size at the end of puberty.[8] In pediatric craniofacial surgery it is essential to avoid disruption of the permanent dentition within the maxillary complex, because permanent tooth eruption does not take place before the age of 10 years. In terms of general skull base location, the pediatric skull base defects have higher proportion of pure middle area lesions (42%) and a lower rate of posterior lesions (8%) compared to adults.[9]

Reconstruction considerations

The selection of the proper reconstruction technique is dictated primarily by the size of the defect, prior radiation to the area and the need for bone reconstruction.[10] Additional variables which influence the reconstructive approach are the etiology of the defect, the anatomical location, prior surgeries, age, and co-morbidities.[11] Our experience and surgical approach in treating children with skull base lesions was previously published[3] as was our general approach to anterior skull base (ASB) reconstruction.[12] The goals of skull base reconstruction in children are similar to those in adults.[13] Although several

methods for skull base reconstruction have been proposed for adults,[9,13,14] there is no special attention given to the pediatric population in the current literature.

When tumors arising in the skull base invade both soft and bony tissues, tumor resection may create extensive skull base defects and produce a free conduit between the paranasal sinuses and the intracranial space. Following tumor extirpation, skull base cranial base defects require precise and durable reconstruction to (1) support the brain, the orbit, neural and vascular structures; (2) form a watertight dural seal, (3) reestablish separation between the contaminated extracranial oral and sinonasal cavities and the sterile subdural compartment and intracranial contents, (4) prevent airflow into the intracranial space, (5) provide lining for the nasal cavity (6) reestablish the nasal and oropharyngeal cavities and maintain a functional sinonasal system, (7) obliteration of dead space created by the ablative surgery, and (8) provide 3-dimensional (3D) restoration for optimal function, contour, cosmetic outcome, and quality of life.[5] Failure to create adequate reconstruction harbors significant complications, among them cerebrospinal fluid (CSF) leak, meningitis, brain herniation, and tension pneumocephalus.[15] Children with skull base defects pose a special multidisciplinary challenge which requires adaptation of the surgical technique in order to minimize developmental complications and emotional toll.

The areas of skull base defects were first divided by Irish et al.[9] to anterior (44%), lateral (9%), and posterior (32%), types I, II, and III respectively, or a combination of the above (14%). The localization of pediatric cases is not markedly different with most cases afflicting the anterior area (33%) or the anterior and middle areas (17%) but with a much higher proportion of pure middle area lesions (42%) and a lower rate of posterior lesions (8%).[16] Yano et al.[14] proposed a revised classification stating that free flap reconstruction is preferred in areas I and II (cribriform plate and infratemporal fossa, respectively) if there is either a horizontal extension, skin or orbit involvement, a defect combining multiple areas, patients who received preoperative radiotherapy or in local recurrences. Defects limited to area III usually do not call for special reconstructive measures involving flaps. Schmalbach et al.[10] proposed a grading system for defects size which is partially relative to anatomical structures and therefore may be especially relevant to children. Class I defects, which are the largest, involve more than half of the ASB with orbitomaxillary involvement. Class II is the same with no orbitomaxillary involvement. Class III is a paramedian defect of less than 4cm and Class IV is a small defect of 1.5cm or less. Furthermore, bony reconstruction of the orbital rim is indicated if the defects are larger than 30% of the rim.

The choice of local pedicled flaps vs free flaps in children is still a matter of debate. For large defects, we advocate soft-tissue reconstruction as the primary technique, reserving bony flaps for definitive procedures in survivors who have reached skeletal maturity. Free soft tissue transfer in microvascular technique is the mainstay for reconstruction of large, 3D defects, involving more than one anatomical region of the skull base, as well as defects involving an irradiated field. Some authors reserve pedicled flaps only to very limited defects stressing that a better outcome precedes the added complexity to the procedure and prefer free flaps due to their versatility and reliability.[11,13] However, to reduce total operative time, intraoperative blood loss, postoperative hospitalization time, and donor-site morbidity, locoregional flaps are better be considered the flap of first choice for skull base reconstruction in children and adolescents, as long as the flap is large enough to cover the defect.[17] Our "workhorse" for dural reconstruction is the double-layer fascia lata. Advances in endoscopic surgery, image guidance, alloplastic grafts, and biomaterials have increased the armamentarium for reconstruction of small and mid-sized defects.

The developing skeleton

Small bony defects can be reconstructed with a variety of nonvascularized techniques. 3D titanium mesh can be used for small defects of the calvarium following removal of the frontal sinus outer table. Autologous bone, such as a split calvarial bone graft or a posterior frontal sinus wall graft, are used for reconstruction when the tumor involves the nasal bone, nasal septum, or an adjacent fronto-orbital segment, and are considered popular grafts in adults owing to ease of harvest, naturally rounded contour, accessibility within the surgical field, malleability for sizing and shaping, and regeneration of the donor site to a perfect surface.[12,18] However, there is a minimum patient age for the performance of a split cranium graft.[18] Harvesting split cranium graft can be a challenge in children younger than 3 years old because of the thinness and the underdeveloped diploic space of the skull. Another popular source of autologous bone involves split rib grafts. No minimum patient age is associated with the harvesting of rib; however, the procedure requires a second operative site and a longer operating time. The stiff angular grid formation of parallel ribs also makes rib bone unsuitable for use in most cranial defects. Bone yield from iliac crest and rib harvest is limited because of the patient's size and are difficult to contour aesthetically. If nonvascularized bone grafts are utilized in an irradiated field, vascularized tissue should be wrapped around the bone.[10,12] Regardless of the source of autologous bone, grafts can be complicated by infection, exposure, fragmentation, growth restriction, and lifelong risks secondary to lack of incorporation, vascular ingrowth, and remodeling. Grafts may undergo partial absorption and leave an unpleasing and unsound surface that requires secondary revision. Infections with or without resorption of the native bone often complicate the repair.[19] For all of these reasons, the usage of autologous

bone grafts has never become standard practice despite its theoretical advantages.[19] Whereas nonvascularized bone grafts successfully reconstruct small bony defects, titanium mesh is well-suited for reconstructing larger areas requiring structural support.[10,12] Desirable properties include lack of donor site morbidity, malleability, biologic inertness, and MRI compatibility.[10,12] The porosity of titanium mesh necessitates additional tissue such as a pericranial flap or radial forearm free flap to achieve a watertight seal.[10,12] Commercially available alloplastic biomaterials and prefashioned implants for craniofacial reconstruction exist for addressing small- and medium-sized calvarial defects and serve as an alternative to autologous nonvascularized bone grafts.[10] *Porous high-density polyethylene* (Medpor; Porex Surgical, Inc. Newnan, GA) has been described as an ideal alloplastic material for cranioplasty. It produces no foreign body reaction, becomes well incorporated through fibrovascular bony ingrowth at its margins, and can be custom made from computed tomography (CT) imaging to precisely fill the patient's cranial defect.[19] Adequate soft tissue is a requirement before alloplastic implant cranioplasty. If soft tissue coverage is inadequate, tissue expansion of the scalp and scalp regeneration with acellular dermal matrix are useful tools to optimize overlying soft tissue before cranioplasty, to prevent complications of implant extrusion and wound breakdown, and to improve outcomes.[19] While porous polyethylene has been extensively and successfully used in adult craniofacial reconstruction, its use has been less well documented in the pediatric population.[20] Lin et al.[19] reported that custom made porous polyethylene implant cranioplasty can be used safely and successfully for pediatric large-scale calvarial defects, even in the setting of a previously infected, multiply operated wound bed. The potential advantages are immediate one-stage reconstruction, avoidance of donor-site complications, and excellent contour matching. However, the risks include restriction of normal calvarial growth, long-term compromise of overlying soft tissues, and possible increased incidence of infection. Furthermore, alloplastic agents should not be used in an irradiated field owing to the high rate of extrusion.[12] A major concern important to bear in mind with the use of alloplastic materials in the pediatric population is the inability of the implant to grow and retain the appropriate contour with the growing skull, necessitating replacement of the implants with the skull and maxillofacial bones complete maturation, reserving definitive reconstruction with vascularized bone until skeletal maturity is completed.

Endoscopic skull base surgery

Endoscopic expanded endonasal approaches (EEA) to the ASB spare the morbidity of an open craniofacial resection and offer excellent visualization. Studies have shown that EEA to sellar lesions can be safely and successfully performed in young patients.[21] However, it is less clear whether the smaller facial structures of pediatric patients can accommodate reconstruction of surgical skull base defects with vascularized tissue flaps. Effective and consistent reconstruction following EEA requires complete separation of the cranial cavity from the sinonasal tract, obliteration of dead space, preservation of neurovascular, and ocular function, and reconstruction of tissue barriers.[22] The most popular flap described for reconstruction in the setting of endoscopic ASB, trans-sellar, and transclival resection or CSF leak in adults is the neurovascular pedicled nasoseptal flap (NSF), a flap of nasal septum mucoperiosteum and mucoperichondrium based on the posterior septal branch of the sphenopalatine artery,[22,23] avoiding separate external incision. A significant decrease in the incidence of postoperative CSF leaks following EEA surgery has been reported with the adoption of the NSF.[24] Although the use of NSF has been studied and proven adequate in adults,[25] little is known about its use in pediatric patients. Shah et al.[22] used CT measurements to evaluate NSF size among pediatric patients. Their findings suggested that children younger than 6-7 had inadequate NSF length for reconstruction of sellar defects; the investigators also noted that NSF width did not appear to be a limiting factor in reconstruction. As opposed to Shah et al., Ghosh et al.[25] reported that NSF provide sufficient and reliable coverage option in reconstruction of suprasellar defects in pediatric patients. They demonstrated that septal lengths in children less than 10 years of age were adequate to cover the defects created by the suprasellar resections. When compared with older patients, younger patients tend to have greater NSF length relative to the length of sellar defects. They concluded that preoperative radiographic assessment of NSF feasibility is critical to ensure adequate flap coverage for suprasellar defects. Purcell et al.[26] attempted to use a standardized measurement method to characterize the relationship between potential nasoseptal length and sellar defect length in children. This radiographic feasibility study suggested that NSF length is not a limitation in reconstruction of pediatric sellar defects. Due to pneumatization, the volume of the sphenoid sinus expands with age,[26] and this study found that older patients were more likely to have longer sellar defect lengths. Incomplete pneumatization remains an obstacle to performing endoscopic approaches to sellar lesions in very young children. There are case reports of successful endoscopic transsphenoidal procedures with NSF reconstruction in children under the age of 2 years.[26] With the use of image-guided navigation, it is becoming more feasible to perform EEA in the setting of incomplete pneumatization, but this remains an area for future investigation. Smaller defects involving the fovea ethmoidalis, planum sphenoidale, or sella can also be sealed endoscopically using the middle turbinate flap.[27] This pedicled flap is based on the middle turbinate branch of the sphenopalatine artery and is much smaller. Regardless of flap selection, endoscopic visualization of the entire defect is imperative to achieving a successful seal.

Free tissue transfer

Free tissue transfer has been demonstrated to be the preferable technique in the reconstruction of large ASB defects in several reviews, as it restores function, and maintains esthetics, compared with regional or pedicled flaps[7]; provides adequate tissue bulk with a rich, reliable blood supply, allowing for improved healing, decreased hospitalization, and decreased complications including CSF leak and meningitis.[10] Reconstruction with free tissue transfer can minimize late sequelae of chemotherapy and radiation treatment for malignant tumors, such as facial hypoplasia, asymmetry, and postoperative retraction deformity.[7] Free tissue transfer promises flexibility in flap content and design and provides the opportunity to introduce a large quantity of well-vascularized tissue to the reconstructed area in a single-stage operation. However, there are several concerns unique to pediatric patients. Pediatric microsurgery is challenging due to the small size of vascular structures, and the increased risk of donor site long-term functional deficits. In addition to the inevitable compromise at the site of resection, esthetic defects at the donor site can have a major psychological impact on a child.

The choice in free tissue donor site is dictated by defect size, location, need for bony restoration, and pedicle length.[10] Commonly used donor sites, such as the fibula, iliac, and scapula possesses epiphyseal growth centers that are central to skeletal growth and development, and soft tissue architecture must be considered as well. A fibula free flap may continue to grow with the adjacent mandible or maxilla, but the growth of adjacent recipient tissues may be altered. Harvest of a fibula free flap before skeletal maturity may result in tibial overgrowth or a valgus deformity. Although it did not reach to the statistical difference, Yano et al.[17] reported that using free flaps in pediatrics tended to have higher postoperative complication rate than using locoregional flaps compared with that of adult, thus advocated locoregional flaps as the flaps of first choice for skull base reconstruction if they are large enough to cover the defect. It is speculated that free flaps in pediatrics are possibly affected by preoperative chemoradiotherapy or negligible injury to the elevated flaps due to technical error during surgical procedure because a vascular pedicle and perforator of free flaps in pediatrics is rather small and narrow compared with the adult. Thus, the choice of local pedicled flaps vs free flaps in children is still a matter of debate. Some authors reserve pedicled flaps to very limited defects and prefer free flaps due to their versatility and reliability.[11] Others found locroregional flaps preferable in children as they reduce operative time, postoperative hospitalization time and donor site morbidity, and reserve free flaps only for large, complex defects.[17] Locoregional flaps, such as pericranial flaps and temporalis muscle flaps, have sufficient vascularity, area, and thickness to cover skull base defects, even in children and adolescents. These flaps also significantly reduce reconstructive time and postoperative hospital stay. Such flaps are also favorable from the standpoint of donor-site morbidity. Several previous reports[11,17] have suggested that osteotomy and sacrifice of the pericranium have limited effects on postoperative craniofacial development. In a previous study, we reported that wide resection of skull base tumors decreases postoperative quality of life.[28] It can be speculated that decreasing donor-site morbidity in patients undergoing skull base reconstruction favorably affects postoperative quality of life, especially in growing children. Local flaps remain the mainstay for smaller defects.

Discussion

Successful skull base surgery in the pediatric population requires a thorough understanding of the complex process of craniofacial development and of skull base anatomical considerations regarding the differences between children and adults. Although the general principles of skull base reconstruction are applicable to nearly all patients, the unique demands of skull base surgery in children and adolescents merit special attention, since the potential benefits of therapy must be balanced against the cumulative impact of multimodality treatment on craniofacial growth, donor-site morbidity, and the potential for serious psychosocial issues. Multidisciplinary care in centers experienced in the management of these complex tumors is of utmost importance. Given the psychological issues that children and adolescents with skull base malignancies face, experts in child psychology or psychiatry should be involved in these patients' care. Our experience in treating children with skull base tumors has helped us understand the considerable anatomical differences between children and adults, including the small size and fragility of neurovascular elements, the inconsistency of anatomical landmarks, and the need to avoid disruption of permanent dentition.[3,4,29] Pediatric skull base tumors which require reconstruction after extirpation seem to arise irrespective of gender, are benign in half of cases, and are of various histological types.[3,5,11,17,30] Because the pathological types of skull base tumors in children and adolescents vary, it can be difficult to predict the extent of a defect after extirpation and to plan a complicated reconstructive procedure, while considering the potential for subsequent growth. Although skull base surgery has not clearly demonstrated an adverse effect on the remaining craniofacial skeleton development in nonirradiated children,[30] nonoperative modalities such as radiation therapy are associated with significant negative consequences, such as retardation of facial bone and soft-tissue growth, short stature, visual or auditory dysfunction, dental abnormalities, and various endocrinopathies. With nearly half of pediatric patients with skull base tumors demonstrating some adverse effect of radiation, some groups have advocated more aggressive surgical resections to achieve a gross total resection in an

attempt to avoid or delay radiation therapy.[11] In general, pediatric skull base reconstruction follows the principles of adult skull base reconstruction, thus flap selection should be decided with the defect size, surgical stress, and donor-site morbidity. With the evolution of surgical extirpative approaches, refinements in the practice of free tissue transfer and the development of new anesthetic and monitoring techniques, procedures once perceived to be too radical for the pediatric patient have become both safer and more reliable.[30]

Conclusions

Pediatric skull base and craniofacial surgery presents a unique challenge since the potential benefits of therapy must be balanced against the cumulative impact of multimodality treatment on craniofacial growth, donor-site morbidity, and the potential for serious psychosocial issues. Skull base surgery and reconstruction using locoregional flaps or free flaps is practical and appropriate, and may be safely performed in children and adolescents. Because of the potentially synergistic effects of multimodality treatment for skull base malignancies on craniofacial growth and development, we advocate soft-tissue reconstruction as the primary technique, reserving bony flaps for definitive procedures in survivors who have reached skeletal maturity. Free soft tissue transfer in microvascular technique is the mainstay for reconstruction of large, 3D defects, involving more than one anatomical region of the skull base, as well as defects involving an irradiated field. However, to reduce total operative time, intraoperative blood loss, postoperative hospital stay, and donor-site morbidity, locoregional flaps are better be considered the flap of first choice for skull base reconstruction in children and adolescents, as long as the flap is large enough to cover the defect.

Conflict of interest

The authors reported no proprietary or commercial interest in any product mentioned or concept discussed in this article.

References

1. Schwartz I, Hughes C, Brigger MT: Pediatric head and neck malignancies: Incidence and Trends, 1973-2010. Otolaryngol. Head Neck Surg. 152:1127–1132, 2015.
2. Albright JT, Topham AK, Reilly JS: Pediatric head and neck malignancies: US incidence and trends over 2 decades. Arch Otolaryngol Head Neck Surg. 128:655–665, 2002.
3. Gil Z, Constantini S, Spektor S, et al: Skull base approaches in the pediatric population. Head Neck 27:682–689, 2005.
4. Gil Z, et al: Outcome of craniofacial surgery in children and adolescents with malignant tumors involving the skull base: An international collaborative study. Head Neck 31:308–317, 2009.
5. Moore BA, DeMonte F, Robb GL, et al: Reconstruction of ablative skull base defects in the pediatric population. Plast Reconstr Surg 120:719–727, 2007.
6. Brockmeyer D, Gruber DP, Haller J, et al: Pediatric skull base surgery: experience and outcomes in 55 pateints. Pediatr Neurosurg 38:9–15, 2003.
7. Weizman N, Gil Z, Wasserzug O, et al: Surgical ablation and free flap reconstruction in children with malignant head and neck tumors. Skull Base 21:165–170, 2011.
8. Gruber DP, Brockmeyer D: Pediatric skull base surgery. Embryology and developmental anatomy. Pediatr Neurosurg 38:2–8, 2003.
9. Irish JC, Gullane PJ, Gentili F, et al: Tumors of the skull base: Outcome and survival analysis of 77 cases. Head Neck 16:3–10, 1994.
10. Schmalbach CE, Webb DE, Weitzel EK: Anterior skull base reconstruction: A review of current techniques. Curr Opin Otolaryngol Head Neck Surg. 18:238–243, 2010.
11. DeMonte F, Moore BA, Chang DW: Skull base reconstruction in the pediatric patient. Skull Base 17:39–51, 2007.
12. Gil Z, Abergel A, Leider-Trejo L, et al: A comprehensive algorithm for anterior skull base reconstruction after oncological resections. Skull Base 17:25–37, 2007.
13. Pusic AL, Chen CM, Patel S, et al: Microvascular reconstruction of the skull base: A clinical approach to surgical defect classification and flap selection. Skull Base 17:5–16, 2007.
14. Yano T, et al: A new concept for classifying skull base defects for reconstructive surgery. J Neurol Surg B Skull Base. 125–131, 2012.
15. Boyle JO, Shah KC, Shah JP: Craniofacial resection for malignant neoplasms of the skull base: An overview. J Surg Oncol. 69:275–284, 1998.
16. Hanbali F, Tabrizi P, Lang FF, et al: Tumors of the skull base in children and adolescents. J Neurosurg 169–178, 2004.
17. Yano T, Tanaka K, Kishimoto S, et al: Review of skull base reconstruction using locoregional flaps and free flaps in children and adolescents. Skull Base 21:359–364, 2011.
18. Pang D, Tse HH, Zwienenberg-Lee M, et al: The combined use of hydroxyapatite and bioresorbable plates to repair cranial defects in children. J Neurosurg 102(1 Suppl):36–43, 2005.
19. Lin AY, Kinsella CR Jr, Rottgers SA, et al: Custom porous polyethylene implants for large-scale pediatric skull reconstruction: Early outcomes. J Craniofac Surg. 23:67–70, 2012.
20. Brevi BC, Magri AS, Toma L, Sesenna E: Cranioplasty for repair of a large bone defect with autologous and homologous bone in children. J Pediatr Surg. 45:E17–E20, 2010.
21. Kassam A, Thomas AJ, Snyderman C, et al: Fully endoscopic expanded endonasal approach treating skull base lesions in pediatric patients. J Neurosurg Pediatr 106:75–86, 2007.
22. Shah RN, Surowitz JB, Patel MR, et al: Endoscopic pedicled nasoseptal flap reconstruction for pediatric skull base defects. Laryngoscope 119:1067–1075, 2009.
23. Hadad G, Bassagasteguy L, Carrau RL, et al: A novel reconstructive technique after endoscopic expanded endonasal approaches: Vascular pedicle nasoseptal flap. Laryngoscope 116:1882–1886, 2006.
24. Kassam AB, Thomas A, Carrau RL, et al: Endoscopic reconstruction of the cranial base using a pedicled nasoseptal flap. Neurosurgery 63:ONS44–ONS52, 2008 discussion ONS-53.
25. Ghosh A, Hatten K, Learned KO, et al: Pediatric nasoseptal flap reconstruction for suprasellar approaches. Laryngoscope 125:2451–2456, 2015.
26. Purcell PL, Shinn JR, Otto RK, et al: Nasoseptal flap reconstruction of pediatric sellar defects: A radiographic feasibility study and case series. Otolaryngol Head Neck Surg 152:746–751, 2015.
27. Prevedello DM, Barges-Coll J, Fernandez-Miranda JC, et al: Middle turbinate flap for skull base reconstruction: Cadaveric feasibility study. Laryngoscope 119:2094–2098, 2009.
28. Gil Z, Abergel A, Spektor S, et al: Quality of life following surgery for anterior skull base tumors. Arch Otolaryngol Head Neck Surg 129:1303–1309, 2003.

29. Shlomi B, Chaushu S, Gil Z, et al: Effects of the subcranial approach on facial growth and development. Otolaryngol Head Neck Surg. 136:27–32, 2007.

30. Carty MJ, Ferraro N, Upton J: Reconstruction of pediatric cranial base defects: A review of a single microsurgeon's 30-year experience. J Craniofac Surg. 20(Suppl 1):639–645, 2009.