OPEN

PRS GLOBAL OPEN

ORIGINAL ARTICLE
Craniofacial/Pediatric

Current Concepts in Cranial Reconstruction: Review of Alloplastic Materials

Darin T. Johnston, DDS*
Steven J. Lohmeier, DMD*
Hannah C. Langdell, MD*
Bryan J. Pyfer, MD, MBA*
Jordan Komisarow, MD†
David B. Powers, MD, DMD, FACS*
Detlev Erdmann, MD, PhD, MHSc*

Background: Cranioplasty for acquired cranial defects can be complex and challenging. Benefits include improved cosmesis, protection of intracranial structures, and restoration of neurocognitive function. These defects can be reconstructed with preserved craniectomy bone flaps, split autografts, or alloplastic materials. When alloplastic cranioplasty is planned, the material should be carefully selected. There is confusion on which material should be used in certain scenarios, particularly in composite defects.
Methods: The PubMed database was used to conduct a nonsystematic review of literature related to these materials and the following factors: time required in preoperative planning and fabrication, intraoperative time, feasibility of intraoperative modification, fixation method (direct or indirect), implant cost, overall complication rate, and surgical revision rates.
Results: Surgical revision rates for alloplastic materials range from 10% to 23%. Retention of titanium mesh at 4 years is 85% in composite reconstruction with free fasciocutaneous and free myocutaneous flaps. In composite reconstruction with locoregional and free muscle flaps, the retention of titanium mesh at 4 years is 47%. The retention of nontitanium and nonpreserved autogenous reconstruction is 72% and 82%, respectively.
Conclusions: Alloplastic materials should be considered for reconstruction of large (>100 cm^2) cranial defects, especially for adult patients younger than 30 years, and all patients with bone flaps that are fragmented or have been cryopreserved for an extended period. Preformed titanium mesh provides a favorable primary reconstructive option when a staged reconstruction is not possible or indicated but should be avoided in composite defects reconstructed with locoregional scalp and free muscle flaps. *(Plast Reconstr Surg Glob Open 2022;10:e4466; doi: 10.1097/GOX.0000000000004466; Published online 19 August 2022.)*

INTRODUCTION

True to the word's derivation from the Greek *plastos*, or to mold or graft, cranioplasty is the secondary repair of cranial defects caused by surgery or injury. A far cry from the ancient practice of placing precious metals or shells over the defects of trepanned skulls,[1] modern-day cranioplasty allows for a customized approach that considers the size and location of the defect, the quality of the overlying soft tissues, and the timing since original injury. These factors are especially important to consider when reconstructing medium (25–100 cm^2) and large (>100 cm^2) cranial defects, which can be more technically challenging.

These sizable defects often result from decompressive craniectomy performed most frequently following traumatic brain injury. Other reasons for craniectomy include aneurysm, arteriovenous malformations, malignant cerebral edema secondary to ischemic stroke, cerebral abscess, and tumors.[2,3]

Cranioplasty protects intracranial structures and improves cosmesis. It is also indicated when, during rehabilitation following craniectomy, there is stagnation of improvement, acute decline in motor or cognitive function, or sunken skin flap overlying the acquired skull defect.[3]

This phenomenon known as sinking skin flap syndrome or syndrome of trephined is a retroactive diagnosis rendered when a patient has reversal of postcraniectomy symptoms (described below) following cranioplasty.[4–7] The mean onset of sinking skin flap syndrome is approximately 5 months.[7,8] A detailed description of the four theorized mechanisms of this syndrome—atmospheric pressure, craniocaudal

*From the *Division of Plastic, Maxillofacial and Oral Surgery, Duke University Hospital, Durham, N.C.; and †Department of Neurosurgery, Duke University Hospital, Durham, N.C.*

Received for publication December 11, 2021; accepted June 3, 2022.

DOI: 10.1097/GOX.0000000000004466

Disclosure: *The authors have no financial interest to declare in relation to the content of this article.*

cerebrospinal-fluid (CSF) flow, decreased cerebral blood flow, and decreased cerebral metabolism—has been illustrated by Ashayeri et al.[3] The constellation of findings and symptoms includes motor weakness; cognitive and language deficits; altered consciousness; psychosomatic disturbances; seizures; cranial nerve deficits; recent CSF shunts or drains; symptoms that improve in horizontal positions and worsen in head elevated positions; paradoxical herniation; mass effect causing ventricular effacement; and scalp contraction manifested by a visibly sunken skin flap.[3,7] Interestingly, the sunken skin flap was found to be the most sensitive positive predictor at 86%, and to have the most specific ventricular effacement at 95%.[7]

Parallel to these indications for cranioplasty is an ongoing discussion regarding timing, surgical technique, and cranioplasty material. This last element is of particular interest as it tends to have the lowest level of consensus in the current literature.

Cranioplasty with autologous bone can be accomplished with either split grafts harvested at the time of reconstruction or replacement of the preserved craniectomy bone. Cabbad et al[9] recently reported a series of 153 cranioplasties accomplished with fresh split grafts. The outcomes reported, spanning four decades, are remarkable with zero complications. Similar outcomes were reported by Fearon et al.[10] This technique includes additional risks and morbidities at the selected donor site, most commonly the calvaria.

Preserved autologous bone is a commonly used cranioplasty material due to its availability without an additional harvest site, low associated cost, lack of required preoperative planning, and biocompatibility.[11–14] Some degree of resorption following this form of autologous cranioplasty is to be expected in as many as 90% of patients.[15] Clinically significant resorption (type II) is full-thickness bony erosion that results in contour defects, hardware loosening, infection, loss of intracranial protection, and reoperation in up to 20% of preserved autologous cranioplasties.[16] Type II resorption may be clinically detectable as soon as 6 months following cranioplasty. Factors that increase the rate and severity of resorption include patients under 30 years of age,[15–17] fragmentation either from injury or prior craniotomies,[17] and duration of cryopreservation.[17] Alloplastic cranioplasty may be utilized if autologous options are unavailable, contraindicated, or otherwise not desired by the patient.

Alloplastic implants eliminate the resorption risk but carry an overall complication rate that is not insignificant, reported at 20.64% in a recent systematic review.[18] Although the topic is debated, there is currently no consensus on which material is preferable for reconstruction of medium and large cranial defects in the adult population. This work is not a systematic review or report on experimental data. Written photographic consent was obtained from each patient with identifying photographs. The purpose of this article is to describe four alloplastic materials used at our institution—preformed titanium mesh, 3-D printed custom titanium, polyetheretherketone (PEEK), and polymethylmethacrylate (PMMA)—and discuss the indications, advantages, and most prevalent complications of each.

Takeaways

Question: Which alloplastic material should be used for cranioplasty?

Findings: Preformed titanium mesh is available when staged reconstruction is not possible; however, implant extrusion is more common in patients with composite defects reconstructed with regional scalp and free muscle flaps. Custom titanium, polyetheretherketone (PEEK), and polymethylmethacrylate (PMMA) require preoperative virtual surgical planning. These later materials should be considered for large defects in the setting of previous or simultaneous locoregional and free tissue transfer.

Meaning: Selection of a cranioplasty material should be driven by specific patient factors and material characteristics.

ALLOPLASTIC MATERIALS

With advancing technology, reconstructive surgeons can conveniently and accurately design custom-made alloplastic implants, making these materials an appealing option for primary cranial reconstruction. Patient factors that may affect material selection and associated techniques include ongoing need for tumor surveillance, resilience of overlying soft tissue, and whether postoperative cerebral edema is anticipated.

Preformed Titanium Mesh

Advantages

Titanium is a biocompatible metal that is noninflammatory and has been shown to have a low rate of infection (10.7%)[18] and overall complication (21.42%).[18–21] Preformed titanium mesh is not patient-specific (Table 1). However, it is available in various contours and sizes based on anatomic averages and is particularly useful for immediate reconstruction of large cranial defects. It is placed on the margin of bone surrounding the defect. Onlay implants do not occupy the space where bone was previously removed and are, therefore, more forgiving in situations when postoperative cerebral edema may be of concern. The implant is secured with screws directly to bone reducing the potential risk for hardware loosening and failure. When properly contoured, the low-profile transition at the bone-implant interface is generally imperceptible to the patient and cosmetically favorable. The mesh design easily accommodates dural tacking sutures when indicated to reduce the extradural dead space and robust vascularity from soft tissue ingrowth.

Disadvantages

Extrusion of titanium mesh can occur (Fig. 1), particularly in patients with composite defects involving skull and scalp reconstructed with locoregional scalp and free muscle flaps. Kwiecien et al[23] showed in their cohort of 83 patients with composite defects, the long-term retention rate for titanium mesh was 62% at year 2 and 47% at year 4. For nontitanium and autologous reconstructions, the retention rates remained stable through 4 years

Table 1. Alloplastic Materials for Cranioplasty

	Preformed Ti Mesh	3-D Printed Custom Ti Implant	PEEK	PMMA
Preoperative planning and fabrication	None	2–3 wk	2–3 wk	2–3 wk
Intraoperative time	Increased	Reduced	Reduced	Reduced
Intraoperative modifications	Minor	Difficult	Minor	Minor
Fixation method	Direct	Direct	Direct or indirect	Indirect
Relative cost	Low	High	High	Low
Overall complication rate*	22.7%–23%[20,22]	21%[17]	21%–22%[17,22]	19%–21.1%[17,20]
Surgical revision rates	10%–23%[20,22]	12%[17]	13%–18.5%[17,22]	7%–17%[17,20]

*Infection, implant fracture/dislodgement/exposure.

of follow-up at 72% and 82%, respectively.[23] It should be noted that in composite defects reconstructed with free fasciocutaneous and free myocutaneous flaps, the retention rates of titanium mesh reach 85%.[23] Some operating room time is required to shape and contour the mesh, which increases the overall cost. Additionally, titanium is hyperdense on radiographyand causes significant artifact, which limits tumor surveillance. However, large cranial defects are infrequently the result of tumor extirpation.[2,3]

Case Example

A 30-year-old woman presented with a subarachnoid hemorrhage after an all-terrain vehicle accident requiring an emergent right decompressive hemicraniectomy. She underwent reconstruction 5 months after her index operation. A preformed titanium mesh implant was used for reconstruction of the defect measuring 250 cm^2 (Fig. 2). Her postoperative course has been uncomplicated.

3D-Printed Custom Titanium Implant

Advantages

The main advantage of 3D-printed custom titanium implants is the predictable fit. A preoperative high-resolution computed tomography (CT) scan (<1 mm cuts) is used to design and fabricate a patient-specific titanium implant. These implants provide a smooth transition at the implant to bone interface. Custom titanium implants are ideal for larger defects due to their rigidity and stability. Similar to the preformed titanium mesh, the custom implant is thin and placed as an onlay implant, which overlaps the margin of the native bone and is secured with monocortical screws. As a result of the thin profile and onlay design, it accommodates some degree of cerebral edema, as it sits above and not within the bony defect. Some designs include perforations in the implant to allow for some tissue ingrowth as well as dural tacking sutures to reduce the extradural dead space. Their smooth surface reduces friction at the tissue-implant interface and consequently reduces the risk of dehiscence.

Disadvantages

The main limitation of 3D-printed titanium implants is their high cost, although a recent randomized controlled trial noted that they are not associated with increased overall health care costs.[12] In addition, design and fabrication requires high-resolution CT (<1 mm cuts), virtual planning, and a time interval (12–15 business days), which allows for implant fabrication. These implants are used in delayed reconstructions and are, therefore, unsuitable for situations in which immediate or early reconstruction is indicated.

Case

A 45-year-old man presented for evaluation of an infected autologous bone cranioplasty and draining sinus tract 8 years after decompressive hemicraniectomy for hemorrhagic stroke with a subsequent autologous cranioplasty (Fig. 3). Given the contaminated nature of his previously operated site, treatment for this patient was staged. First, the infected bone was removed, and due to a brain abscess, a partial left hemispherectomy was performed. He then underwent a high-resolution CT scan for surgical planning. After completion of 8 weeks of IV antibiotics, he

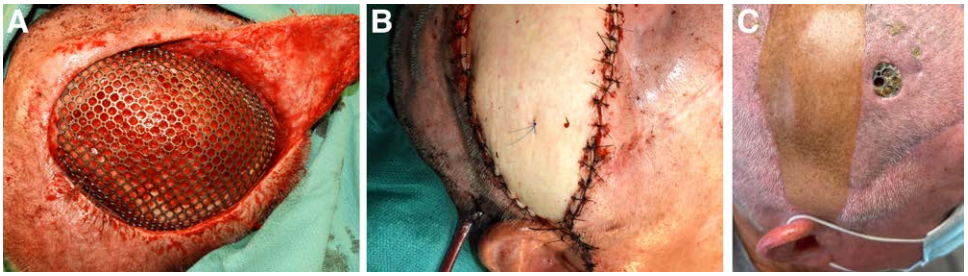

Fig. 1. Extrusion of titanium mesh. Patient underwent craniotomy for intracranial hemorrhage complicated by subsequent removal of exposed and infected bone flap and unstable soft tissue healing. The composite defect was eventually treated with a titanium mesh cranioplasty and scalp advancement flap following single-scalp tissue expander (A). There were partial flap necrosis and exposed hardware within 2 months. Coverage with a 5 × 10 cm myocutaneous free flap (anterolateral thigh) was then provided (B). Examination 2 years later shows mesh extrusion only through the prior advancement flap (C).

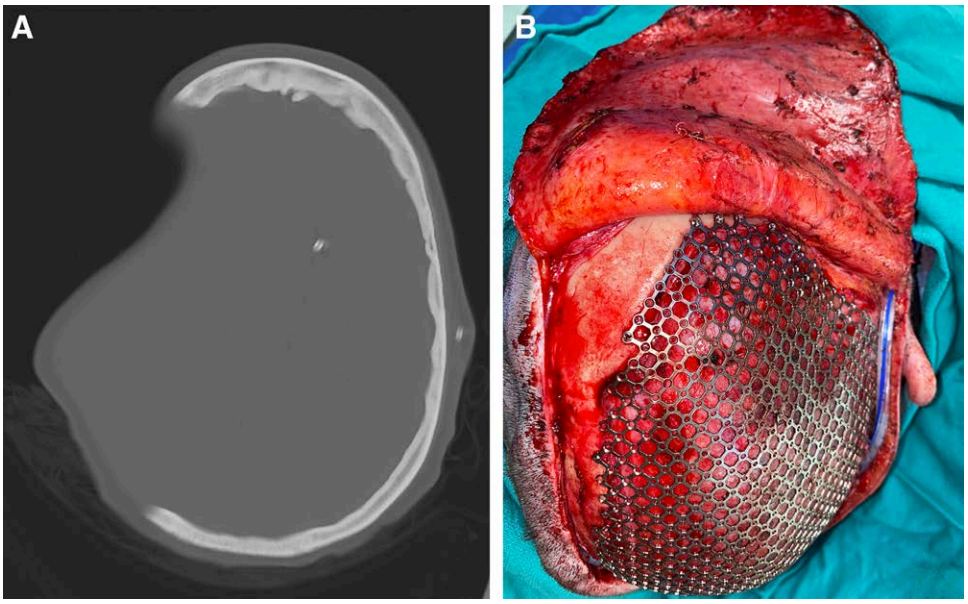

Fig. 2. Preformed titanium mesh. Patient presented 5 months following decompressive hemicraniectomy. Preoperative axial CT (A) and intraoperative adaptation and fixation of mesh (B).

was definitively reconstructed with a custom 3D-printed titanium implant.

Polyetheretherketone (PEEK) Implant

Advantages

PEEK is a synthetic material that can be custom-designed and 3D-printed based on a preoperative high-resolution CT scan (<1 mm cuts). PEEK offers the advantage that it is radiolucent and hypodense and does not cause radiographic artifact on CT or magnetic resonance imaging. This may be helpful in cases where postoperative tumor surveillance is warranted. In addition, PEEK can be trimmed or modified as needed to refine the contour and fit of the implant in real time.

PEEK has been shown to have a lower postoperative infection rate of 7.3% compared with 10.2% in titanium.[18] Similarly, in a recent multicenter retrospective study, PEEK was reported to have a significantly lower overall complication rate compared with titanium, 17.3% and 31.8%, respectively.[24] It can be secured directly to the bone with titanium screws to minimize risk of hardware loosening and implant failure. Additionally, some surgeons prefer PEEK for its handling properties, which resemble bone.

Disadvantages

PEEK shares the same disadvantages related to high cost and presurgical planning as custom titanium implants. Furthermore, PEEK is an inlay implant and does not accommodate postcranioplasty cerebral edema.

Case

An 18-year-old man underwent a right decompressive hemicraniectomy for emergent treatment of intracranial hemorrhage after a motor vehicle collision. Autologous cranioplasty was initially performed. By 3 years postreconstruction, his bone graft had undergone significant resorption (Fig. 4). The bone graft was subsequently removed, and the large cranial defect was simultaneously reconstructed with a patient-specific PEEK implant, designed based on his preoperative CT.

Polymethylmethacrylate (PMMA)

Advantages

PMMA is a biocompatible acrylic material. Benefits include its strength, radiolucency, and relatively low cost.[20,25] It is custom fabricated in advance by an anaplastologist based on a stereolithic model from a high-resolution CT scan. The prefabricated PMMA is porous and permits fibrovascular ingrowth, whereas intraoperatively cured methyl methacrylate is not porous.[26] PMMA was shown to have an overall complication rate of 19.26% and a postoperative infection rate of 10.47%.[18] PMMA implants can be modified using a handpiece and bur intraoperatively.

Disadvantages

The greatest limitation of solid PMMA is its brittleness, which risks fracture when securing it with plates and screws. PMMA is also an inlay implant that requires additional miniplates and screws for fixation, which may increase the risk for hardware loosening and implant failure.

Case

A 38-year-old woman underwent a left decompressive hemicraniectomy for elevated intracranial pressure after a stroke at an outside hospital. She presented 4 months later for a reconstructive evaluation (Fig. 5). Primary cranioplasty was performed using a custom-fabricated PMMA implant.

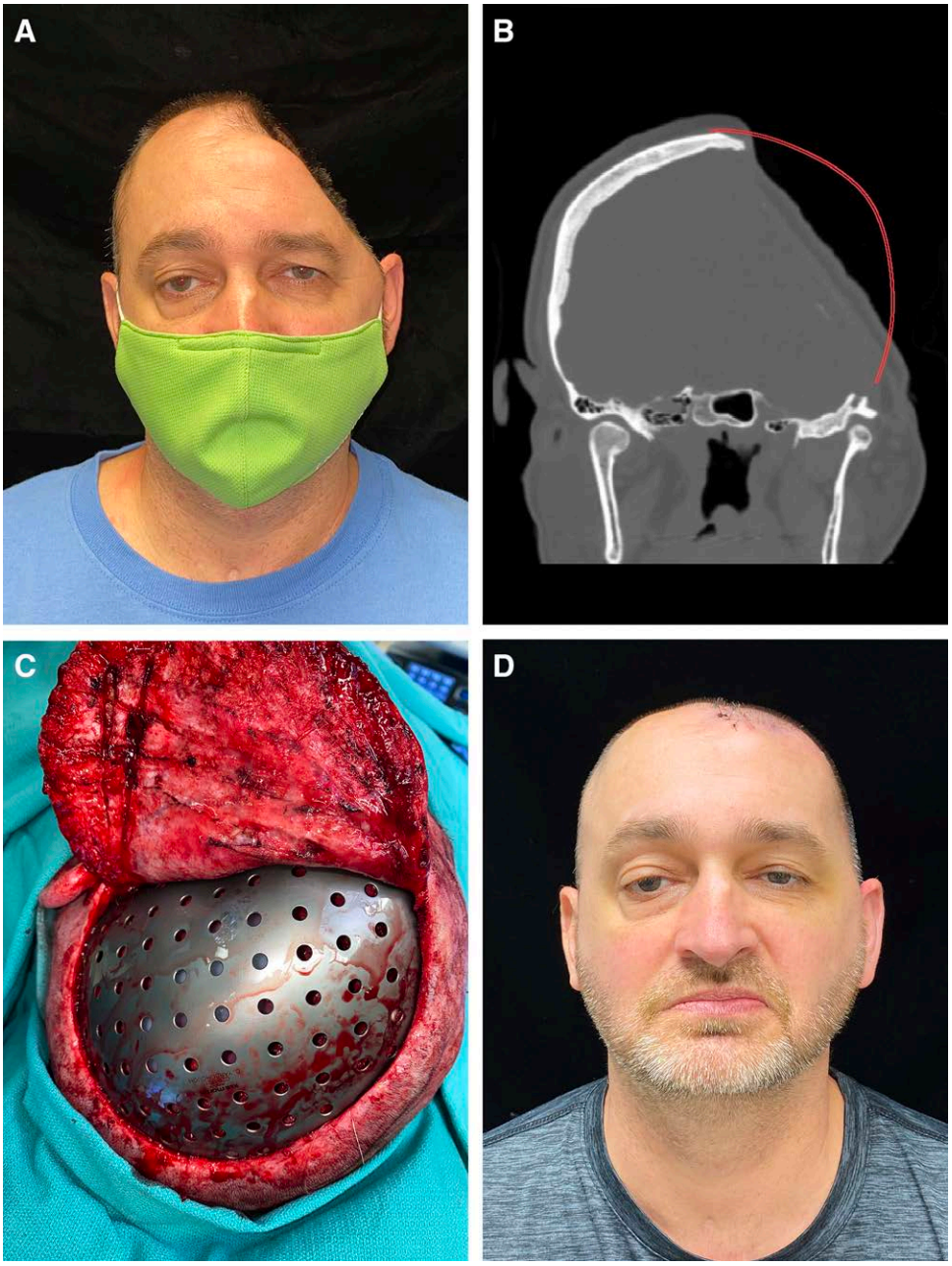

Fig. 3. 3-D printed custom titanium implant. Patient presented 8 years following decompressive hemicraniectomy. Preoperative appearance (A), virtual surgical planning to mirror unaffected side (B), inset of implant (C), and 2-week follow-up (D).

DISCUSSION

Cranioplasty protects intracranial structures, improves cognitive function, and restores cosmesis. Preserved autogenous bone is frequently used and does not require the additional morbidities associated with fresh split autogenous bone cranioplasty. The benefits of preserved autogenous bone cranioplasty may be negated, however, after a complication such as clinically significant bone resorption, which can lead to continuity defects, hardware loosening, infection, and loss of intracranial protection. Factors that increase the rate and severity of resorption include patient age less than 30 years,[15–17] bone fragmentation to prior osteotomies or trauma,[17] and increased duration of cryopreservation.[17]

Although not immune to complication, alloplastic implants eliminate the resorption risk and have gained important clinical utility in recent years. The process of selecting the appropriate implant should assimilate patient-specific factors, including the chronicity of the defect, postoperative management of the adjacent epidural space, indications for oncologic surveillance, urgency of implant placement, local tissue factors, and medical comorbidities. Utilizing a nonideal material or employing incomplete techniques may increase the risk

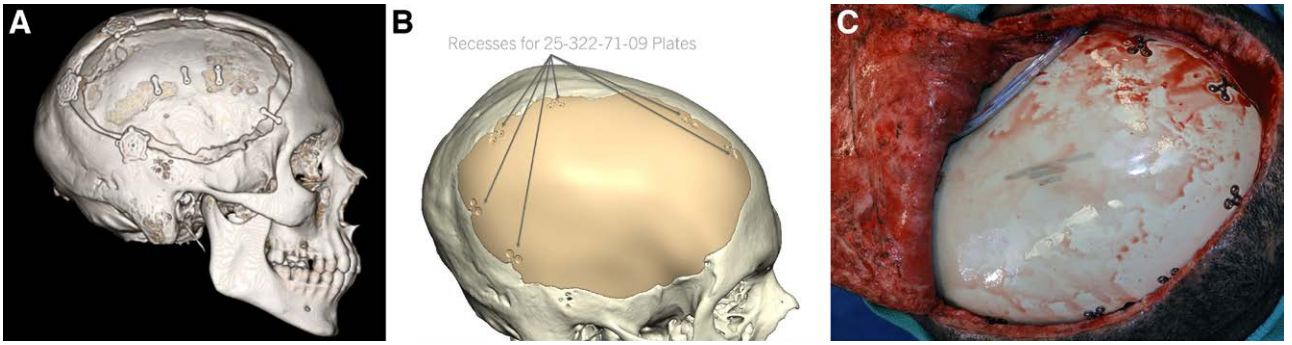

Fig. 4. PEEK implant. Patient presented 3 years following decompressive craniectomy and subsequent autologous cranioplasty. 3-D reconstruction demonstrating type II resorption of prior bone flap cranioplasty (A), virtual surgical plan showing integrated recesses to create a smooth contour following fixation with stock miniplates and screws (B), and inset of implant with patient name obscured (C).

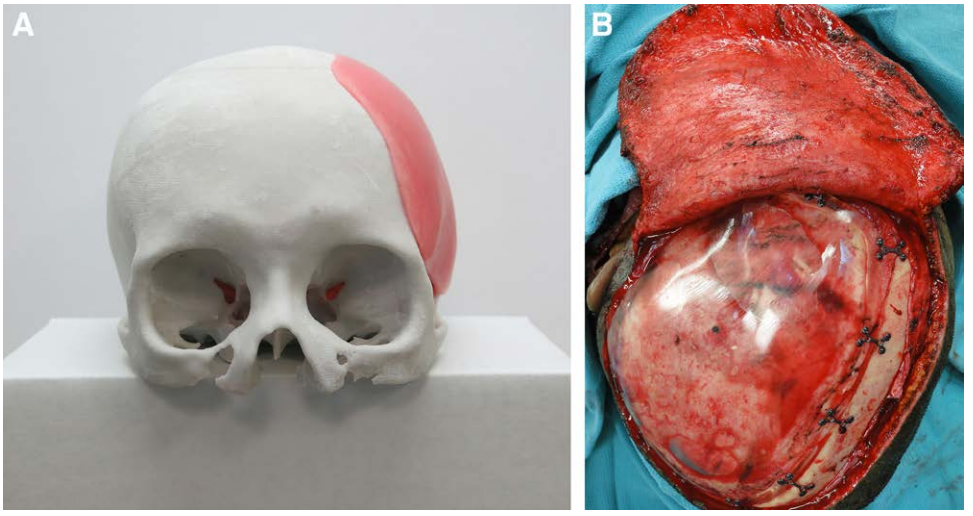

Fig. 5. PMMA implant. Patient presented 4 months following decompressive hemicraniectomy. Wax-up by anaplastologist (A), and inset and fixation of implant (B).

for infection, implant failure, and complicated cranioplasty revision. It is thus imperative for the reconstructive surgeon to integrate knowledge of each material's inherent and contextual strengths and weakness into surgical planning.

Alloplastic materials collectively carry an overall complication rate that is not insignificant, reported at 20.64% in a recent systematic review.[18] Although the topic is debated, there is currently no general consensus on a single material to replace the autologous bone graft as a gold standard for cranial reconstruction. Instead, a multifactorial decision-making approach should be used by a knowledgeable surgical team.[27]

It is worth noting an additional material that has been described in the literature but has yet to be widely implemented for large defects. Porous polyethylene (MEDPOR, Stryker, Kalamazoo, Mich.) has been used for small craniofacial implants, and a few reports have been published for reconstruction of cranial defects.[22] Outcomes have not been studied long term. Like PMMA, it is lightweight, porous, and amenable to fibrovascular ingrowth, which may provide protection from infection, a distinct advantage compared with PEEK.[28] There is little to no osseous ingrowth.[8] It can be custom designed and fabricated. However, it is weak and flexible, making it less likely to provide the structural integrity required for large defects. Our experience demonstrates that it breaks or tears easily when placing fixation screws.

In combination with alloplastic implants, several adjuncts and technique modifications have been useful to improve surgical outcomes. Biologic barriers including collagen matrices like DuraGen (Integra, Plainsboro, N.J.) or autologous fascia lata (FL) grafts are commonly used in dural repair sites. Additionally, FL or Alloderm (Allergan Corp., Dublin, Ireland) may be placed over the implant in cases where the skin-galeal flap is thin. The use of FL grafts for dural repair has been previously reported but has not been prospectively studied.[29] Alloderm (Allergan Corp., Dublin, Ireland) may be used to help maintain the plane of dissection in staged cases in which repeat operation for a custom implant is necessary, or to serve as a barrier between the implant and a thin overlying skin flap, which has also been previously reported in the literature.[30]

Subgaleal closed-suction drains may be useful to prevent postoperative fluid collection, which has been reported at 3.62%, of which 19.67% returned for

reoperation.[18] Subgaleal closed-suction drains have fallen out of favor in the neurosurgical community due to concern for either direct trauma to the sagittal sinus or pressure-induced rupture of its weak lateral wall where it is penetrated by arachnoid granulations.[31] Although there is a paucity of prospective data on the use of subgaleal drains, they have been reported to prevent postoperative seroma formation and facial edema, and shorten hospital length of stay.[32] Typically drains are kept in place until they are low output (<20–30 ml) for at least 2 consecutive days.

Maximizing outcomes in cranioplasty requires an understanding of the best available materials, including autogenous bone. Appropriate implant selection must combine patient-specific factors with a material's strengths and weaknesses. The addition of the adjuncts and technique modifications noted may also contribute to the success of an alloplastic implant.

CONCLUSIONS

Cranioplasty for large defects provides many benefits to patients but presents significant reconstructive challenges. Material selection is a key component of successful reconstruction. Factors to consider include the material's mechanical properties, cost and time to design and fabricate the implant, method of fixation, and intraoperative adjustability. A staged reconstruction may be required depending on the position of the implant relative to surrounding tissue (onlay versus inlay). An additional factor to consider is the material's porosity, which may allow for perivascular ingrowth, resistance to peri-implant infection, and implant incorporation.

Although preserved autologous bone is still commonly used, it has been shown to be associated with high resorption and reoperation rates. Split autologous calvarial and rib grafts may be used; however, the additional donor site and other morbidities should be considered. We recommend alloplastic materials be considered for reconstruction of large cranial defects, especially for adult patients younger than 30 years, and all patients with bone flaps that are fragmented or have been cryopreserved for an extended period. Preformed titanium mesh provides a favorable primary reconstructive option when a staged reconstruction is not possible or indicated but should be avoided in composite defects involving skull and scalp reconstructed with locoregional scalp and free muscle flaps. For cases amenable to preoperative CT-based planning and implant fabrication, custom titanium, PEEK, and PMMA implants are predictable reconstructive options.

Detlev Erdmann, MD, PhD, MHSc
Division of Plastic, Maxillofacial and Oral Surgery
Duke University Medical Center
DUMC Box 3181
Durham, NC 27710
E-mail: detlev.erdmann@duke.edu

REFERENCES

1. Sanan A, Haines SJ. Repairing holes in the head: a history of cranioplasty. *Neurosurgery*. 1997;40:588–603.
2. Rosenthal G, Ng I, Moscovici S, et al. Polyetheretherketone implants for the repair of large cranial defects: a 3-center experience. *Neurosurgery*. 2014;75:523–529.
3. Ashayeri K, M Jackson E, Huang J, et al. Syndrome of the trephined: a systematic review. *Neurosurgery*. 2016;79:525–534.
4. Abdou A, Liu J, Carroll M, et al. Motor and neurocognitive recovery in the syndrome of the trephined: a case report. *Ann Phys Rehabil Med*. 2015;58:183–185.
5. Jeyaraj P. Importance of early cranioplasty in reversing the "syndrome of the trephine/motor trephine syndrome/sinking skin flap syndrome". *J Maxillofac Oral Surg*. 2015;14:666–673.
6. Annan M, De Toffol B, Hommet C, et al. Sinking skin flap syndrome (or Syndrome of the trephined): a review. *Br J Neurosurg*. 2015;29:314–318.
7. Sedney CL, Dillen W, Julien T. Clinical spectrum and radiographic features of the syndrome of the trephined. *J Neurosci Rural Pract*. 2015;6:438–441.
8. Gosain AK, Chim H, Arneja JS. Application-specific selection of biomaterials for pediatric craniofacial reconstruction: developing a rational approach to guide clinical use. *Plast Reconstr Surg*. 2009;123:319–330.
9. Cabbad NC, Stalder MW, Arroyave A, et al. Autogenous bone cranioplasty: review of a 42-year experience by a single surgeon. *Plast Reconstr Surg*. 2019;143:1713–1723.
10. Fearon JA, Griner D, Ditthakasem K, et al. Autogenous bone reconstruction of large secondary skull defects. *Plast Reconstr Surg*. 2017;139:427–438.
11. Goldstein JA, Paliga JT, Bartlett SP. Cranioplasty: indications and advances. *Curr Opin Otolaryngol Head Neck Surg*. 2013;21:400–409.
12. Honeybul S, Ho KM. Cranioplasty: morbidity and failure. *Br J Neurosurg*. 2016;30:523–528.
13. Kim SH, Kang DS, Cheong JH, et al. Comparison of complications following cranioplasty using a sterilized autologous bone flap or polymethyl methacrylate. *Korean J Neurotrauma*. 2017;13:15–23.
14. Ko K, Segan S. In situ hinge craniectomy. *Neurosurgery*. 2007;60(4 suppl 2):255–258.
15. Korhonen TK, Salokorpi N, Niinimäki J, et al. Quantitative and qualitative analysis of bone flap resorption in patients undergoing cranioplasty after decompressive craniectomy. *J Neurosurg*. 2018;130:312–321.
16. Malcolm JG, Mahmooth Z, Rindler RS, et al. Autologous cranioplasty is associated with increased reoperation rate: a systematic review and meta-analysis. *World Neurosurg*. 2018;116:60–68.
17. Brommeland T, Rydning PN, Pripp AH, et al. Cranioplasty complications and risk factors associated with bone flap resorption. *Scand J Trauma Resusc Emerg Med*. 2015;23:75.
18. Morselli C, Zaed I, Tropeano MP, et al. Comparison between the different types of heterologous materials used in cranioplasty: a systematic review of the literature. *J Neurosurg Sci*. 2019;63:723–736.
19. Shah AM, Jung H, Skirboll S. Materials used in cranioplasty: a history and analysis. *Neurosurg Focus*. 2014;36:E19.
20. Matsuno A, Tanaka H, Iwamuro H, et al. Analyses of the factors influencing bone graft infection after delayed cranioplasty. *Acta Neurochir (Wien)*. 2006;148:535–540.
21. Williams LR, Fan KF, Bentley RP. Custom-made titanium cranioplasty: early and late complications of 151 cranioplasties and review of the literature. *Int J Oral Maxillofac Surg*. 2015;44:599–608.
22. Berli JU, Thomaier L, Zhong S, et al. Immediate single-stage cranioplasty following calvarial resection for benign and malignant skull neoplasms using customized craniofacial implants. *J Craniofac Surg*. 2015;26:1456–1462.
23. Kwiecien GJ, Rueda S, Couto RA, et al. Long-term outcomes of cranioplasty: titanium mesh is not a long-term solution in high-risk patients. *Ann Plast Surg*. 2018;81:416–422.

24. Zhang Q, Yuan Y, Li X, et al. A large multicenter retrospective research on embedded cranioplasty and covered cranioplasty. *World Neurosurg*. 2018;112:e645–e651.
25. Iaccarino C, Kolias A, Adelson PD, et al. Consensus statement from the international consensus meeting on post-traumatic cranioplasty. *Acta Neurochir (Wien)*. 2021;163:423–440.
26. Eppley BL. Biomechanical testing of alloplastic PMMA cranioplasty materials. *J Craniofac Surg*. 2005;16:140–143.
27. Servadei F, Iaccarino C. The therapeutic cranioplasty still needs an ideal material and surgical timing. *World Neurosurg*. 2015;83:133–135.
28. Chim H, Gosain AK. Biomaterials in craniofacial surgery: experimental studies and clinical application. *J Craniofac Surg*. 2009;20:29–33.
29. Gupta H, Natarajan S, Vaidya S, et al. Traumatic eye ball luxation: a stepwise approach to globe salvage. *Saudi J Ophthalmol*. 2017;31:260–265.
30. Singh M, Ricci JA, Dunn IF, et al. Alloderm covering over titanium cranioplasty may minimize contour deformities in the frontal bone position. *J Craniofac Surg*. 2016;27:1292–1294.
31. Mohindra S, Mukherjee KK, Chhabra R, et al. Subgaleal suction drain leading to fatal sagittal sinus haemorrhage. *Br J Neurosurg*. 2005;19:352–354.
32. Tong JW, Emelin JK, Wong R, et al. Subgaleal drain placement improves surgical outcomes after primary cranioplasty in craniosynostosis patients. *J Craniofac Surg*. 2015;26:1963–1966.