Evolution of cranioplasty techniques in neurosurgery: historical review, pediatric considerations, and current trends

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Cranial bone repair is one of the oldest neurosurgical practices. Reconstructing the natural contours of the skull has challenged the ingenuity of surgeons from antiquity to the present day. Given the continuous improvement of neurosurgical and emergency care over the past century, more patients survive such head injuries, thus necessitating more than ever before a simple, safe, and durable means of correcting skull defects. In response, numerous techniques and materials have been devised as the art of cranioplasty has progressed. Although the goals of cranioplasty remain the same, the evolution of techniques and diversity of materials used serves as testimony to the complexity of this task. This paper highlights the evolution of these materials and techniques, with a particular focus on the implications for managing pediatric calvarial repair and emerging trends within the field.

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The practice of cranial reconstruction dates at least as far back as 3000 BC, where archeological evidence suggests the repair of head trephination with the use of precious metals, shells, and gourds by the ancient Incans in what is now Peru (Fig. 1). The procedures were probably performed on living subjects rather than postmortem; cases of recovered archaeological finds have yielded crania healed tightly around foreign bodies.100,104 Similar historical evidence has been found from ancient Celtic, Persian, Turkish, and South American civilizations.3,32,34,97,106

Few subsequent advances were made in the practice of cranioplasty until Galen (130–200 AD) and Avicenna (980–1037 AD) started using moistened linen over wounds and performed regular dressing changes to promote wound granulation, a practice that was followed for centuries.52,104

In 1505 AD, the Ottoman surgeon Ibrahim bin Abdullah published the first known written case of cranioplasty in his book, Wonders of Surgeons (Alâîm-i Cerrâhin), a case that was treated using goat- and canine-derived xenografts.1,10 The practice of repairing cranial lesions with metal plates was introduced soon thereafter to Europe by the writings of Fallopius and Petronius in the late 16th century, but it was not until almost a century later, in 1668, that the Dutch surgeon Job Janszoon van Meekeren reported the first successful bone graft cranioplasty. Van Meekeren, although he was not the surgeon who should have received credit, documented the use of a canine xenograft to correct the calvarial defect caused in a Russian nobleman by the blow of a sword. The nobleman, Butterlijn, was restored to full health, but the work was poorly received by Butterlijn’s contemporaries. At the risk of excommunication by the
Russian church for “marrying God’s image,” he begged his surgeon to remove the implant. The surgeon was unable to remove the firmly implanted canine bone, however, and Butterlijn was forced to flee the country.

Such early attempts, however rudimentary, ushered in a new age of innovation in the field, as surgeons realized the need to understand the unique properties of the cranium just as much as those of the brain itself. From the earliest use of gourds and metals until the present day, materials used for cranioplasties have been a reflection of the interplay of durability, biocompatibility, and availability. We offer a brief historical account and review of current literature on such materials.

**Autografts**

Given the ultimate goal of cranioplasty to reproduce the structure and function of absent calvaria to the greatest degree possible, the merits of autologous bone are obvious, including marked strength and elasticity, biocompatibility, general availability, and resistance to infection. Given the low cost of conservation, lower rates of infection compared with many other types of prostheses, and assured biocompatibility, the autologous cranial flap remains the gold standard in calvarial repair.4

In 1821, von Walther performed the first human autologous bone graft shortly following documented animal experiments by Merrem in 1810.90,130 The importance of the periosteum in bone regeneration was established soon thereafter by the work of Ollier in 1859.19 The Scottish physician William MacEwen established himself as the founder of the modern practice of bone grafting following his work in 1878, in which he successfully reimplanted calvarial bone fragments. In 1889, Seydel transplanted a tibial autograft with periosteum intact for the successful repair of a parietal defect, which was followed by the successful transplantations of autologous calvarial bone grafts by Muller (1890), temporalis muscle and fascia by Beck (1906), whole ribs by Dobrotworski (1911), scapula by Röpke (1912), ilium by Mauclaire (1914), and split ribs by Brown (1917).9,27,40,78,103 The technique was further advanced by the work of Longacre and DeStefano in 1957, who pioneered the use of autologous split rib grafts to repair large cranial defects, as is practiced today.69,70 Tessier subsequently ushered in the era of pediatric craniofacial reconstruction through the use of autologous techniques in 1967.116

Today, split calvarial grafts demonstrate relatively low-risk profiles with minimal donor-site morbidity in adult and pediatric populations alike.9,44,58,124 However, this approach is of limited utility in children under the age of 4 years, given the limited calvarial thickness and availability of donor bone. Full-thickness and split rib grafts have also shown satisfactory results in children, even in the setting of large cranial defects, but the pain caused by a multilevel rib resection is considerable.60,80,91,114 Additionally, there have been limited reported cases on the tendency of children to suffer aseptic resorption of sterilized bone flaps, which is hypothesized to be attributable to an array of possible causes, from inherent hyperactive cellular responses to the degree of calvarial thickness in this subpopulation.41,45,51

Disillusionment with autologous bone cranioplasty continues to exist given the propensity for resorption (reported rates are as high at 50% across all age groups),5,41,113 inadequate contouring, debate over optimal means of bone flap preservation,5,50,83,95 and potential for donor-site morbidity; these in sum continue to limit the use of this biomaterial for a broader spectrum of patients.15,120

**Allografts**

Sicard, Dambrin, and Roger introduced the use of cadaveric skull in cranioplasty during the latter half of the 1910s.19 In 1915, Morestin introduced the use of cadaveric cartilage, which became the cranioplasty technique of choice during World War I, but soon thereafter the technique fell out of favor, given the lack of significant tissue calcification and strength.77,81 Additionally, the advent of cadaveric cranial grafts was initially fraught with complications secondary to infection, which limited their practicality and efficacy.104 More recent reports have suggested moderate success in the use of cadaveric bone grafts in cranioplasty, but the use of allografts in contemporary...
cranial reconstruction remains relatively rare compared with the use of autografts and synthetic materials.\textsuperscript{61,122}

**Alloplasts**

Over the history of cranioplasty, surgeons have struggled to find the ideal alloplastic material that confers the advantages of native bone, including durability, biocompatibility, and availability, with a low risk of infection. Even today, no such material possesses all of these properties.\textsuperscript{78} Several options, including metals, acrylics, ceramics, and plastics, have been used with varying degrees of success.

**Metals**

Multiple metals have been the subjects of trials in the quest for the perfect medium since aluminum and gold were popularized by Booth and Gersten, respectively, in the 1890s. Over the past century, metals in which trials have been conducted for use in human subjects have included vitallium alloys by Geib (1941); tantalum by Pudenz and Odom (1942); stainless steel mesh by Boldrey (1944); stainless steel by Scott, Wycis, and Murtagh (1956); and titanium by Simpson (1965).\textsuperscript{94,118} Vitallium, an alloy of cobalt, molybdenum, and chromium, demonstrated decreased bone necrosis and metal corrosion in comparison with pure metals; however, its lack of malleability made intraoperative shaping difficult. By the late 1940s it was no longer used in the repair of cranial defects. Tantalum was used for a brief period during World War II but due to price, limited supply, and complications from high thermal conduction, its use was discontinued shortly thereafter.

Many of the aforementioned metals have fallen out of favor due to the introduction of stronger, more conformable, and osteocompatible materials. Other limitations as well, such as the potential for epileptogenesis, plate dislodgement and subsequent scalp erosion and perforation, and the creation of a potential dead space into which brain can herniate or hematoma can form, have led to diminished interest in the use of metals for cranioplasty.\textsuperscript{105,111} However, titanium has stood the test of time. From its initial use for skull reconstruction given shorter operating times than traditional autograft methods, without associated postoperative pain and donor site disfigurement.

This material continues to be the most widely used choice for adult cranioplasty procedures given its intraoperative malleability and generally favorable long-term outcomes across a wide variety of indications.\textsuperscript{73} However, given its lack of osteointegration and its brittle nature despite attempts at reinforcement with metallic wire mesh and other materials,\textsuperscript{36,47,53,105} MMA also quickly gained favor as an agent for skull reconstruction given shorter operating times than traditional autograft methods, without associated postoperative pain and donor site disfigurement.\textsuperscript{105,111}

Overall complication rates from the use of MMA vary greatly depending on published series, ranging from 5% to 40%. Infection rates of 5% to 20% are particularly elevated in the setting of frontal cranioplasty given sinus communication, risk for infection, and possible fistulization.\textsuperscript{2,15,26,52,73,76,93} Complication rates quoted within the pediatric population reach as high as 23%, as reported by Blum et al. in their 15-year retrospective review of 75 patients, with those patients with large defects, involvement of the frontal sinus, and any history of prior infection at the greatest risk.\textsuperscript{12} Other rare but notable side effects of the material include delayed-type hypersensitivity reactions, which are seen in approximately 1% of patients.\textsuperscript{37}

**Acrylics**

Initially manufactured as an industrial material in the 1930s (Plexiglas), methyl methacrylate (MMA) was repurposed for use in human calvarial repair by Zander in 1940, and was popularized by the published work of Gurdjian et al. soon thereafter.\textsuperscript{43,111,130} As an inexpensive, readily available, and biocompatible polymeric alternative to ceramics and metals, MMA quickly gained favor as an agent for skull reconstruction given shorter operating times than traditional autograft methods, without associated postoperative pain and donor site disfigurement.

**Ceramics**

Materials such as hydroxyapatite and coralline carbonated calcium phosphate cement (CCPC) have gained in-
creasing traction as materials for calvarial reconstruction over the past few decades, given their ease of application and ability to conform to most defect shapes (Fig. 2). Initially limited by its poor tensile strength and impact resistance, more recent formulations of hydroxyapatite coupled with agents such as calcium sulfate hemihydrate (plaster of Paris) and titanium mesh have enabled the isothermic application of the material, which closely mimics the behavior of native bone, with a high degree of biocompatibility, tensile strength, and osteointegration, given its macro-porosity as an organic agent.25,29,30,49,57,98 Additionally, as a synthetic equivalent of the naturally occurring mineral found in bones and teeth, there is virtually no foreign body reaction noted on implantation.

Recent studies indicate that bioceramics are comparable to autologous bone flaps following decompressive craniectomies and subsequent repair, given the advent of computer-assisted design to create custom-fitted materials. Cost, however, remains a large barrier to increased utilization of such materials.6,64,84,112 Other limitations include the increased propensity to fracture due to transfer of CSF pulsations through the dura mater, elevated complication rates in the setting of trauma, and use of hydroxyapatite in areas of potential communication with the sinuses.74,109,129

**Plastics**

Celluloid was one of the first alloplasts for which trials were conducted in the late 1800s by Fränkel, but it was ultimately discarded due to biodegradative processes in tissues comprising its functionality.40 However, the newer plastic polymers, including porous polyethylene and polyetheretherketone (PEEK), have proven advantageous in a number of modern settings as nondegradable and durable agents for calvarial repair. As prefabricated agents that can be used for small and large defects alike, one particular advantage of porous polyethylene is its framework that allows for theoretical bony ingrowth and vascularization, although more recent literature has called such osteoconductive properties into question.68,115,126 Alternatively, although PEEK implants lack osteoconductive properties, as an inert and easily removable material they prove useful in settings where repeated intracranial access may be necessary.

**Considerations in Pediatric Cranioplasty**

Pediatric cranial defects can be acquired (i.e., trauma, infection, neoplasm) or congenital (i.e., parietal foramina, cleidocranial dysplasia, cutis aplasia, craniosynostosis). While many acquired pediatric cranial deformities in very young children may close spontaneously, especially in instances in which dura and pericranium remain intact, larger defects and those secondary to congenital anomalies typically require surgical intervention (Figs. 3 and 4). The osteogenic potential of the cranium is inversely proportional to age and decreases rapidly after 1 year of age. Whereas reconstructive strategies for cranial defects in older children and adults include autologous bone grafts, bone substitutes, and synthetic materials, there are considerations in pediatric cranioplasty limiting the range of available reconstructive options. In addition, the risk for bone resorption with an autologous implant remains high in the pediatric population. Methods to decrease the rate of absorption have included the need to secure the thin flap with additional fixation as well as to augment the gaps with synthetic bone or mesh at the time of the cranioplasty. The autologous flap can often loosen over time due to the prominent brain pulsations in children, which is thought to exacerbate the resorption.41

Growth of the pediatric cranium, with accompanying bony contour changes, places limitations on useable bone substitutes. Similarly, emerging data suggest time as a predictive factor of long-term outcomes, such as for autologous cranioplasty in the setting of pediatric decompressive craniectomy.72 Commonly used bone substitutes in adult cranioplasty do not have the capacity for growth and are thus problematic for applications in pediatric cranioplasty. Many studies have therefore found that autologous skull bone grafts are superior to materials such as acrylic or metals for cranioplasty in children.31,80

![FIG. 2. Representative intraoperative images of current cranioplasty materials. A: Right parietal split calvarial bone graft with titanium plate and mesh used for the repair of a right frontal forehead defect after tumor resection, radiation, and bone flap removal in a 38-year-old patient. Dura was reconstructed with bovine pericardium. B: Hydroxyapatite cement and resorbable plate repair of 2 defects on the upper forehead in a 9-year-old child following metopic repair during the 1st year of life. C: Custom-made PEEK implant used for cranioplasty in a 30-year-old woman with a defect of right frontal and temporoparietal areas.](image)
flaps have also demonstrated success in pediatric cranioplasty. A study in 2002 suggested that osteogaleal flaps are an ideal choice for reconstruction in pediatric defects due to their membranous origin, ease of harvest, reliable vascularity, and applicability to any part of the calvaria.

Although hydroxyapatite and demineralized bone matrix have been used to reconstruct cranial defects in children, such materials are hindered by higher rates of infection (especially adjacent to the frontal sinus), questionable long-term stability, and limited potential for osteointegration in comparison with autologous bone. A study in 1998 used coralline hydroxyapatite granules mixed with Avitene and autologous blood for the reconstruction of pediatric cranial bone defects, with great success. Pang et al. improved the stability of hydroxyapatite by using bi-resorbable perforated plates to dampen CSF pulsations. Other studies have used polylactic acid absorbable plates and carbonated apatite bone cement to similar effect.

The development of such reconstructive strategies by using bone substitutes that avoid rigid fixation and promote graft transformation into viable tissue is a critical step toward improving cranioplasty outcomes in pediatric populations. Biomaterials containing osteoinductive factors such as bone morphogenetic protein (BMP) represent a promising area of research, but their use in clinical settings, particularly for pediatric cranioplastics, needs to be further explored.

Although autologous bone is the standard material used for cranioplasty in adults, its supply is limited in children. A recent study examining the architecture of the pediatric cranium recommended that split cranial bone grafting be performed only after 3 years of age, and in situ cranial bone grafting only after 9 years of age. Before 3 years of age, the diploic space is not reliably present and the skull is thin. Extracranial sources of bone such as the rib and iliac crest are limited in volume, associated with higher resorptive rates than cranial bone, and prone to complications including pneumothorax, chest wall deformity, reduced sensation of the lateral femoral cutaneous nerve, and gait disturbances. Finally, autologous cranial grafts suffer from donor-site morbidity and limited contouring plasticity. A push to use synthetic materials such as porous polyethylene and MMA due to the aforementioned concerns with autologous bone grafts has been met with limited success due to the inability of these materials to osteointegrate and their tendency to destabilize during growth.

Recently, autologous cranial particulate bone grafts mixed with autologous blood have been shown to effectively heal cranial defects in children, with minimal morbidity. Particulate grafts consist of small pieces of bone harvested with a low-speed bit brace and offer a means to use autologous pediatric cranial bone without the shortcomings associated with split cranial bone grafting. Advantages include increased malleability and a larger available volume of bone, in part due to additional regions of harvestable cranium (i.e., mastoid and occiput), which are not amenable to the split calvarial technique. Harvesting particulate bone is both safer and easier than a split cranial graft because a craniotomy is not required. Finally, particulate grafts can be harvested in infants before the formation of the diploic space, a major limitation of the split calvarial technique. However, due to a lack of structural integrity until healing nears completion, particulate grafts cannot be used in cranial sites without underlying bony or dural support.

Scalp reconstruction is closely tied with successful pediatric and adult cranioplasty, because significant scalp contraction can occur with bony skull defects. Primary scalp closure is only possible for small cranial defects (3–4 cm) after wide undermining of the subgaleal plane. In patients undergoing cranioplasty for large cranial defects related to tumor resection or head trauma, primary scalp closure is often not possible. Skin grafting and local rotational flaps may be used in these reconstructions. Free flaps are being increasingly used for reconstruction after large complex cranioplasties. These include latisimus dorsi myocutaneous flap, rectus abdominus flap, radial forearm flap, and omentum flap, among others.

Preoperative subgaleal scalp expansion is another technique that avoids morbidity associated with free tissue transfer, and has been successfully used with large skull reconstructions. Choice of a scalp coverage technique is determined by the anatomy (size, depth, and axial blood supply) and physiology (radiation, infection) of the defect in addition to patient factors such as comorbidities, oncological issues, and cosmetic concerns.

Current Practice and Future Trends

Despite the history of cranioplasty spanning thousands of years, modern cranioplasty has only been in practice since the second half of the last century. As religion, warfare, and primitive medical practices fueled innovation in
the field centuries ago, many of the advances made in the modern day recapitulation of cranial structure and function can be attributed to decompressive craniectomies secondary to acute ischemic stroke and traumatic injury. As enhanced technological capabilities on the battlefield coupled with advances in the operating room have enabled more soldiers to survive traumatic brain injury secondary to blast injuries, the number of craniectomy defects has jumped exponentially over the past few decades, catalyzing the development of new cranioplasty tools and techniques within the realm of regenerative medicine.

Growth Factors

The histological premise behind bone replacement, where transplanted bone cells die but leave a scaffolding on which living bone can form, was first described by Barth (1893). As our understanding of the basic molecular biology and physiology of bone graft healing improves, from the importance of revascularization and osteoinduction to osteoconduction and osteogenesis, the use of novel calvarial reconstruction agents along with recombinant human bone growth factors has become increasingly prevalent. Extensive research exists on the use of recombinant factors such as transforming growth factor β, insulin-like growth factor–I, and BMP-2 in augmenting calvarial closure in animal and human models. In 1965, Urist first documented the osteoinductive capacity of demineralized bone matrix, and subsequent research led to the popularization of BMP-2 and related factors. The field of tissue engineering also bears equally great ramifications, because exogenous production of natural materials could revolutionize therapy, particularly for patients lacking adequate donor sites, those plagued with chronic osteomyelitis, and many others.

Stem Cell–Based Therapies

Despite continued advances, an optimal method for the reconstruction of large calvarial defects remains elusive. Recent advances in laboratory research have shifted the focus of cranioplasty from osteoconduction, relying on the entrance of surrounding osteoprogenitor cells to ensure successful bone grafting, to a more osteoinductive framework, whereby undifferentiated mesenchymal cells can be transformed into osteoprogenitor cells in situ. Stem cell–based therapies hold enormous promise in this regard, with studies in mouse models demonstrating successful repair of critical-sized cranial defects by using human induced pluripotent stem cells (iPSCs), bone marrow-derived stem cells (BMSCs), and adipose-derived stem cells (ASCs). Early clinical trials have yielded similarly promising results. A recent study of 4 patients with large calvarial defects of differing origins showed that beta-tricalcium phosphate scaffolds seeded with ASCs resulted in successful outcomes with no clinically relevant postoperative complications.

Emerging as the frontrunner for stem cell–based repair of cranial defects, ASCs possess several advantages over BMSCs, including rapid in vitro expansion, ease of har-
vest, and higher in vivo abundance. Cranioplastic applications using BMSCs require a 6- to 8-week period of in vitro expansion, which introduces the possibility for malignant transformation and acquisition of foreign antigens. Higher cell numbers achievable through ASC harvests and increased proliferation rates in vitro minimize these concerns. Although the promise of iPSCs for healing cranial defects has been repeatedly demonstrated in mice, safety concerns including teratoma formation and insertional mutagenesis persist. These concerns must be addressed and minimized prior to the use of iPSCs in clinical trials.

Conclusions
Large skull defects have presented clinical challenges since the earliest records of medicine. Recent advances in cranioplasty through use of autologous and alloplastic materials have enabled the repair of increasingly complicated cranial defects. However, cranioplasty is no simpler today than it was centuries ago, with a great deal of care required regarding sterility, flap sculpting and fixation, drain usage, and clinical outcomes, regardless of reconstructive material used. Reported complication rates today range from 16% to 40%, with a general reoperation rate of 25%. Additionally, the optimal materials and approaches remain largely unclear, and the demands on an ideal substitute for decranialized bone are many. Such a biocompatible material should possess a number of features, including ease of sterilization, low thermal conductivity, radiolucency, and biomechanical reliability, all in a cost-effective manner.

In the operating room, surgical preferences for implant materials have traditionally been dictated by several factors, including personal experiences, institutional preferences, and available resources. Given many conflicting reports on the appropriate materials to use in particular conditions and the relative degree of complications across modalities, the evidence base remains slim pending further well-powered cohort studies and randomized clinical trials. However, in addition to highlighting the evolution of materials and techniques involved in the progression of cranioplasty over thousands of years, this review aims to underscore that the choice of ideal material should be made on a case-by-case basis. Whereas the main considerations of material selection in adults are related to cosmetics and biocompatibility, in pediatric populations, continuing skull growth is a consideration to be made that will greatly impact operative success. Therefore, before deciding on a particular reconstructive option, surgeons should take great care to evaluate individual patients and associated factors that may dictate operative success (i.e., surgical site, clinical history) before proceeding. A multidisciplinary team of specialists allows for combined expertise to maximize the cosmetic and structural result for patients. A free flap may also be needed on occasion to fill a soft-tissue void, or for a staged approach to expand the scalp to provide skin coverage so the wound will heal with the new implant in place. If such a comprehensive approach is adopted, given the wide array of materials that exist in the modern operating room and the expansive literature particular to these materials across a number of indications, satisfactory outcomes for patient and physician alike can be achieved.

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