Translucent Customized Cranial Implants Made of Clear Polymethylmethacrylate

An Early Outcome Analysis of 55 Consecutive Cranioplasty Cases

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Background: Large skull reconstruction, with the use of customized cranial implants, restores cerebral protection, physiologic homeostasis, and one's preoperative appearance. Cranial implants may be composed of either bone or a myriad of alloplastic biomaterials. Recently, patient-specific cranial implants have been fabricated using clear polymethylmethacrylate (PMMA), a visually transparent and sonolucent variant of standard opaque PMMA. Given the new enhanced diagnostic and therapeutic applications of clear PMMA, we present here a study evaluating all outcomes and complications in a consecutive patient series.

Methods: A single-surgeon, retrospective, 3-year study was conducted on all consecutive patients undergoing large cranioplasty with clear PMMA implants (2016–2019). Patients who received clear PMMA implants with embedded neurotechnologies were excluded due to confounding variables. All outcomes were analyzed in detail and compared with previous studies utilizing similar alloplastic implant materials.

Results: Fifty-five patients underwent cranioplasty with customized clear PMMA implants. Twenty-one (38%) were performed using a single-stage cranioplasty method (ie, craniectomy and cranioplasty performed during the same operation utilizing a prefabricated, oversized design and labor-intense, manual modification), whereas the remaining 34 (62%) underwent a standard, 2-stage reconstruction (craniectomy with a delayed surgery for cranioplasty and minimal-to-no implant modification necessary). The mean cranial defect size was 101.8 cm^2. The mean follow-up time was 9 months (range, 1.5–39). Major complications requiring additional surgery occurred in 7 patients (13%) consisting of 2 (4%) cerebrospinal fluid leaks, 2 (4%) epidural hematomas, and 3 (4%) infections. In addition, 3 patients developed self-limiting or nonoperative complications including 2 (4%) with new onset seizures and 1 (2%) with delayed scalp healing.

Conclusions: This is the first reported consecutive case series of cranioplasty reconstruction using customized clear PMMA implants, demonstrating excellent results with regard to ease of use, safety, and complication rates well below published rates when compared with other alloplastic materials. Clear PMMA also provides additional benefits, such as visual transparency and sonolucency, which is material specific and unavailable with autologous bone. Although these early results are promising, further studies with multicenter investigations are well justified to evaluate long-term outcomes.

Key Words: cranioplasty, alloplastic, implant, PMMA, methylmethacrylate, cranial, clear

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Large skull defects after craniectomy typically follow cerebrovascular insults, tumors, and/or craniocerebral trauma. Each of these neurosurgical patient types present with varying amounts of functional and aesthetic disturbances. Furthermore, secondary reconstruction with cranioplasty remains challenging to both neurosurgeons and plastic surgeons and is associated with a high complication rate. During recent years, a paradigm shift has been made toward using a higher percentage of synthetic implants—made of sterile alloplastic materials—versus the old dogma of using stored autologous bone flaps.

Interestingly, cranioplasty by way of stored autologous bone flaps was historically the criterion standard because of its availability, cost, and misconception of having an improved complication risk profile versus alloplastic implants.[1–3] Moreover, craniofacial surgery principles provided by Paul Tessier dictated that bone should always replace bone. However, more recently, numerous long-term studies and meta-analyses have confirmed several drawbacks and limitations surrounding stored autologous bone flaps, when compared with prefabricated sterile implants. Evidence-based medicine now shows that pediatric cranioplasty, with autologous bone flaps and split-thickness calvarial grafts, is not equivalent to that of adult cranial defects after neurosurgical craniectomy and delayed reconstruction. High-level, statistical evidence now confirms that large, stored bone flaps are associated with higher rates of aseptic resorption, infectious osteomyelitis, and increased odds for reoperation when compared with customized cranial implants (CCIs).[4,5]

There are several distinct benefits specific to CCIs including zero donor-site morbidity, the ability to correct skull and co-existing soft tissue deformities with dual-purpose cranial/craniofacial implants, and a newfound ability to integrate functional neurotechnologies within the actual implant itself.[6–8] As time passes, more and more studies suggest that CCIs exhibit an improved outcome profile for large reconstruction and that the long-term cost differential is now in favor of implants, especially when all the long-term risk factors for resorption, infection, and persistent temporal hollowing are considered.[9,10]

Currently, the most common materials used for CCI fabrication are polymethylmethacrylate (PMMA) and polyether-ether-ketone (PEEK).[11,12] Polyether-ether-ketone is an aromatic polymer with ether and ketone chains. Advantages of this material include strength, stiffness, durability over time, thermal nonconductivity, and rapid manufacturing process.[13] However, given that the material has been commercially available for only 2 decades, there is less long-term, evidence-based data for time-tested safety versus other biomaterials, such as PMMA, which in contrast was first used in the 1960s.[14]

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Polymethylmethacrylate shares the same advantages as PEEK in terms of strength but has a more textured surface, which increases implant stability via soft tissue adherence. In addition, the chemical composition of PMMA is different and thereby prevents an inflammatory capsule from forming, which in turn decreases risk for peri-implant seroma formation. However, the primary disadvantage of solid PMMA implants is the time for fabrication and sterilization, which can be up to 3 weeks. Although the fabrication and manufacturing processes are different, both PMMA and PEEK can be custom crafted in a patient-specific manner using computer-assisted design/manufacturing technology and dual-purpose design, based on standard, preoperative computed tomography (CT).[15–17]

In 2015, our group published a series of 20 consecutive patients who underwent cranioplasty with solid opaque PMMA implants.[14] In this study, there were no complications related to infection, hematoma, seroma, or cerebrospinal fluid (CSF) leak, although 2 patients (9%) required reoperation because of persistent temporal hollowing. These findings led our group to develop a novel implant design for dual-purpose craniofacial implants to correct temporal deformity with strategic bulking, which used placing the implant over an undisturbed, atrophic temporalis muscle (vs the longstanding method of dissecting the muscle away from the craniectomy site and placing the implant directly on the dura/brain) and incorporating a predesigned "anatomical window" to avoid muscle impingement.[18]

Recently, CCIs fabricated with translucent/clear PMMA became approved by the Food and Drug Administration and readily available within the United States, with the inherent benefits of visible transparency, sonolucent transmission via transcranioplasty ultrasound (TCU), and the potential to integrate embedded neurotechnology (ClearFit; Longeviti Neurosolutions, Hunt Valley, MD).[19,20] This transparency provides unprecedented visualization for real-time assessment of pertinent details, such as dural/brain pulsation visualization, assurance of hemostasis, and potential for CSF leak detection. In addition to being transparent to visible light, our team has previously shown that these translucent properties also allow for unimpeded wireless electrocorticography signal transmission when embedding a 2-way, responsive neurological system deep within the implant using a predesigned cavity (NeuroPace, Calif).[7]

Furthermore, clear PMMA implants permit unaltered transmission of acoustic waves enabling postoperative diagnostic sonography, recently termed TCU.[16,19,20] As such, clear PMMA's sonolucent properties have the potential for future validation regarding ultrasound-based diagnostic and therapeutic application, such as detecting brain tumor recurrence, monitoring cerebral blood flow, measuring ventricular size for hydrocephalus, ablating deep brain lesions, and more. Based on preliminary investigation, TCU has been successfully performed (after scalp closure) for real-time, clinic assessment of epidural bleeding, midline shift, ventriculomegaly, and cerebral bypass graft monitoring.[19–22]

The aim of the current study was to evaluate preliminary outcomes using the newly introduced clear PMMA implant for secondary reconstruction in the setting of large cranial defects. This outcome study encompasses all transparent PMMA implant cranioplasties performed by the senior author with additional comparison to other similar alloplastic materials.

METHODS

An institutional review board–approved retrospective study was conducted examining all clear PMMA cranioplasties implanted by the senior author for a 3-year period (November 2017–November 2019). All patients who received complex cranial implants with embedded neurotechnology, such as hydrocephalus shunts or responsive neurostimulators, were excluded from this study. This was done in an effort to evaluate the implant itself, without the additive confounding variables conferred by the neurotechnology devices themselves and the concomitant neurosurgical intervention required for placement. Furthermore, embedding these neurotechnologies adds considerably more complexity to the implant design and surgical technique and is thus beyond the scope of this report. We previously described our experience thus far with these embedded neurotechnologies as 3 "first-in-human" reports.[6–8]

The specific criteria used to determine which patients are candidates for reconstruction with clear PMMA implants was previously described.[14,23] Basically, no patient with any of the following findings underwent reconstruction with clear PMMA: (1) open scalp wounds, (2) evidence of deep intracranial infection, (3) a genetic disorder known to affect wound healing (eg, Ehlers-Danlos syndrome), (4) cranial defects smaller than 25 cm^2, and/or (5) history of previous failed alloplastic cranioplasty. All cranioplasties were performed in collaboration with a neurosurgeon using a multidisciplinary approach.[24] All custom-designed clear implants were made preoperatively according to a standard protocol CT scan, with further intraoperative customization performed (as needed) by the senior surgeon on an as-needed basis.

Fifty-six consecutive clear PMMA implants were placed during this 3-year study period. Of these, one patient had a limited 22-day follow-up period. Despite all efforts, this patient was lost to follow up and was therefore excluded from this report. Of the remaining 55 patients, 21 (38%) were categorized as "single-stage cranioplasty," meaning that the craniectomy was performed during the same operation as placing the custom implant, thereby requiring intraoperative implant border modification with handheld drill.[25] All single-stage cranioplasties were indicated for oncological resection of tumors involving the skull, with or without co-existing meningeal/brain involvement. Note that only tumor cases are in the single-stage group, because if the patient was undergoing surgery for other neurosurgical indications (eg, aneurysms or functional procedures), the cranial bone flap is simply replaced with no need for alloplastic reconstruction.

To allow for single-stage reconstruction, the surgery was preceded by a virtual planning phase during which preoperative CT scans were analyzed and a patient-specific implant then intentionally fabricated to extend beyond the anticipated skull defect with horizontal excess, while maintaining the patient-specific curvature, thickness, and 3-dimensional (3D) shape. Horizontal oversizing accounted for possible additional tumor growth before resection (during time interval between preoperative imaging and actual date of surgery), and/or possible intraoperative findings necessitating a larger than anticipated craniectomy related to local invasion. This protocol ensured that neither the oncologic resection nor defect repair would be limited by a predetermined implant size and thus is why prefabricated cutting guides are not recommended based on experience.[26] In addition, if there was dural resection due to tumor involvement, dural reconstruction was performed with either autologous rectus fascia, pericranial graft, or synthetic material.[27] Regardless of the material choice, all efforts were made to ensure a watertight dural closure.

After complete tumor extirpation, intraoperative modification of the oversized implants was performed on a sterile back table. To precisely match the final cranial bone defect, we leveraged the transparent property of the PMMA implant to streamline the modification process, as opposed to the standard, labor-intense process experienced previously with opaque cranial implants.[28] By aligning the implant directly over the cranial bone defect and margin boundary (easily visualized through the implant), one can trace the necessary line of customization with a sterile marking pen directly onto the implant. The implants were modified with a craniotome and high-speed burr and the process was repeated until a precise fit was achieved.[25] Of note, for these oncological patients with possible need for postoperative irradiation for local tumor control, these additional efforts seemed well justified, given the highly complicated issues often seen with standard titanium mesh implants placed underneath irradiated scalps including extrusion, scalp imprinting, and magnetic resonance imaging scattering.[24,27,28]

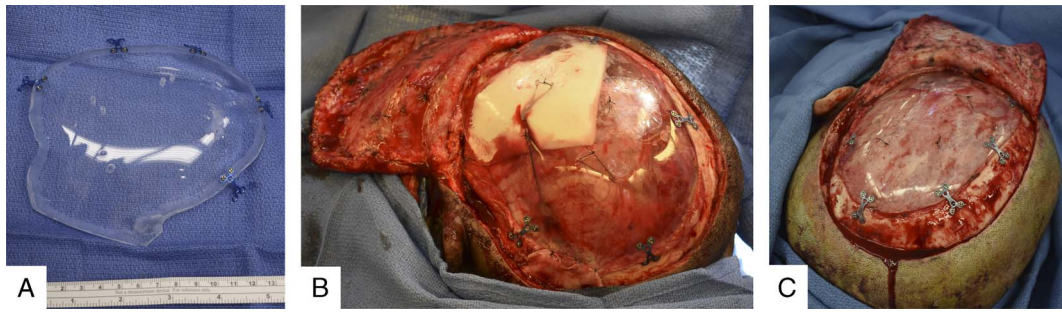

FIGURE 1. Representative images from intraoperative clear PMMA placement. A, Clear PMMA implant after low-profile titanium plates are secured on the back table. Also note the 2 drill holes which are placed to secure the pericranial-dural tack up sutures. B, Clear PMMA implant secured over pericranial-onlay flap. Note the resorbable gel foam placed to fill the vacant space between the implant and the flap. C, Another representative example of the implant after it is placed, this time with no gel foam needed due to absent venous oozing and/or dead space. Note that the implant is custom designed to simply fit within the bony defect, with minimal or no overlap between implant/and bone.

In contrast, "2-stage cranioplasty" was performed for patients presenting after craniectomy and needing delayed reconstruction. It is important to note that for 2-stage procedures, the patient either presented with a craniectomy defect, or with bone flap resorption/osteomyelitis requiring resection and staged reconstruction. For these patients, the index indication for the initial neurosurgical procedure was widely variable, including tumors, hydrocephalus, aneurysms, trauma, or functional neurosurgery. In total, there were 34 (62%) 2-stage cranioplasties performed in this series. Note that some patients underwent additional surgery in the period between craniectomy and cranioplasty for indications, such as removal of resorbed bone flaps and scalp reconstruction. Thus, the "2-stage" designation simply refers to craniectomy and cranioplasty being performed during 2 separate operations, most often several months apart.

All 2-stage cranioplasties were performed using a pericranial-onlay technique as previously described.[24] In this technique, the implant is placed within a vascularized tissue pocket between the galea aponeurosis and the pericranium, thereby avoiding the epidural space. Briefly, a new scalp incision was used, if and when safely possible, to prevent the incision from directly overlying the implant. The scalp was raised in a subpericranial manner until the edge of the bony defect was reached, at which time the dissection was transitioned to a subgaleal plane. This left the vascularized pericranium directly adherent to the underlying dura, such that there was no dural disruption, which has been postulated to reduce risk of seizure, stroke, durotomy, and excessive bleeding.[23,24] Notably, no epidural dissection was performed around the free edges of the bony defect, again to prevent dural exposure or disruption. After dissection, if there were any galeal defects or areas of thin scar on the raised scalp flap, autologous fascia graft augmentation was performed.[29] The translucent PMMA implant was then placed within the cranial defect (with minimal to no overlap between implant and bone) and secured with low-profile titanium plates and screws (Figs. 1A–C). Pericranial tack-up sutures were placed and secured via small drill holes made in the implant. If there was concern for risk of bleeding from the pericranial flap and/or dead space between the implant and the flap (due to sunken flap, encephalomalacia, etcetera), resorbable hemostatic gel foam was placed under the implant (Fig. 1B). For cranioplasties extending into the temporal fossa, an area of additional strategic bulking of the implant was designed via an imaginary boundary line drawn between the zygomatic-frontal suture and the temporal process of the zygoma, to be placed above the temporalis muscle using a computer-assisted design/modeling, "temporal window" process.[18,30] Specifically, no rigid fixation plates are placed over the nonhairbearing forehead or over the temporalis muscle, which is left in continuity with the pericranial-onlay flap (Fig. 1B). Closed suction drains were used in all cases, and the scalp was closed in multiple layers.

Abstracted variables from patient charts included demographics, medical and surgical history, radiation history, body mass index (BMI), indication for craniectomy, skull defect size, and length of follow-up. Complications were defined as "major" if they required any additional surgery or "minor" if they were self-limited and managed

TABLE 1. Study Participant Demographics

Total	N = 55
Age, average (range), y	46 (16–81)
Sex, n (%)	
Male	27 (49)
Female	28 (51)
Comorbidities, n (%)	
Smoking	23 (42)
Diabetes	7 (13)
BMI (average)	28
Preoperative hydrocephalus shunt, n (%)	4 (7)
Preoperative radiation, n (%)	5 (9)
Postoperative radiation, n (%)	3 (6)
Prior cranial surgeries (average)	1.2
ASA (average)	2.7

ASA, American Society of Anesthesiologists.

TABLE 2. Cranial Defect Etiology

Indication	No. Patients, n (%)
Tumor	26 (48)
Trauma	10 (18)
Subdural hemorrhage	4 (7)
Intracerebral hemorrhage	5 (9)
Ischemic stroke	5 (9)
Aneurysm	4 (7)
Autoimmune vasculitis	1 (2)
Location	
Frontal	5 (9)
Parietotemporal	19 (35)
Hemicranial	26 (47)
Occipital	5 (9)

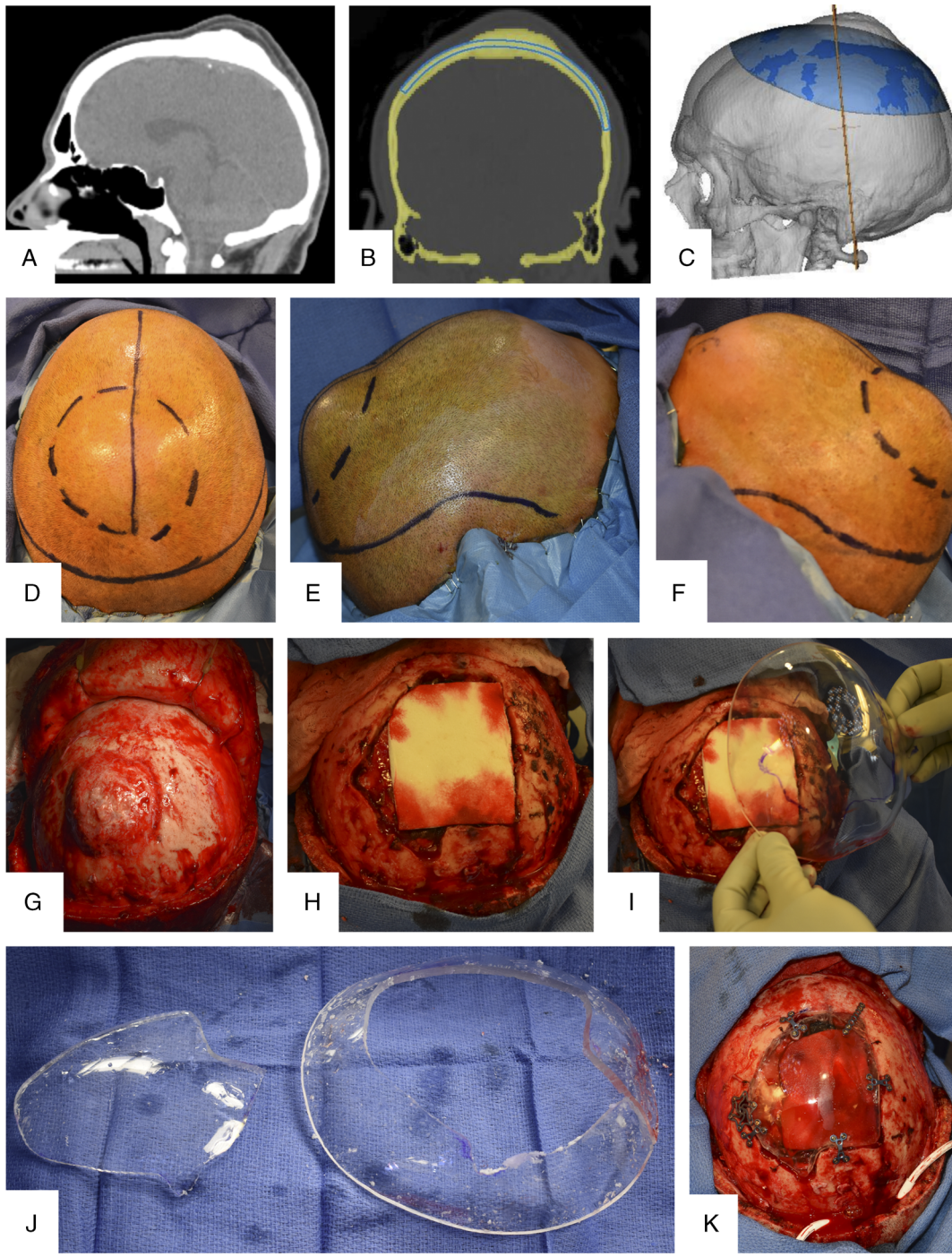

FIGURE 2. Single-stage cranioplasty for intraosseous meningioma resection. A, Lateral view of preoperative CT scan demonstrating large tumor with osseous involvement. B, virtual surgical planning image based on CT scan, coronal view. The bone is outlined in yellow, and the proposed customized implant is outlined in blue. Note that the blue implant model is purposely designed with a patient specific shape but horizontally extends well beyond the tumor size seen on preoperative imaging. C, Lateral view of 3D image used for 3D printing of the implant. The vertical line corresponds to the coronal cut-in (B). D–F, On table preoperative photographs showing horizontal (D) and lateral views (E, F) of the patient's head, with the face oriented to the top of the image in all photos. The dashed line outlines the palpable and visible tumor, and the sagittal midline is also marked. The incision for the bicoronal approach is also marked. G, Intraoperative photo showing tumor after bicoronal flap is dissected and elevated. H, Resultant defect after tumor resection, dural repair, and hemostatic collagen matrix is placed. I, The clear implant being placed over the defect, and a surgical marking pen used to outline the precise template. J, The surgeon uses a drill to intraoperatively cut the implant to the precise defect dimensions on the sterile back table. K, The implant is placed within the defect (note there is no overlap between implant and bone) and secured in place with titanium plates and screws. Surgical drains are placed, hemostasis assured, and meticulous multilayered scalp closure performed.

nonoperatively.[31] Of note, a repeat operation for recurrence of the index indication for surgery (eg, tumor recurrence) was not considered a cranioplasty-related complication.

RESULTS

Fifty-five patients underwent cranioplasty with customized clear PMMA implants for the 3-year period with adequate follow-up. Table 1 summarizes patient demographics. The male-female ratio was 27:28. The mean age at the time of surgery was 46 years (range, 16–81 years; SD, 16.1). The mean follow-up time was 9 months (range, 1.5–39 months; SD, 8 months). With regard to relevant medical comorbidities that may impact wound healing, 42% (n = 23) had a positive history of tobacco smoking, and 13% (n = 7) had a diabetic history. Four patients (7%) had cranial hydrocephalus shunts placed before cranioplasty, and 5 patients (9%) had a history of preoperative cranial radiation. The mean American Society of Anesthesiologists Classification was 2.7, and the average BMI was 28.

Cranial defect etiology included oncologic resection (n = 26, 48%), decompressive craniectomy for trauma-induced hemorrhage (n = 10, 18%), subdural hemorrhage (n = 4, 7%), intracerebral hemorrhage (n = 5, 9%), ischemic stroke (n = 5, 9%), aneurysm (n = 4, 7%), and autoimmune vasculitis (n = 1, 2%; Table 2). The average defect size was 101.8 cm^2, ranging up to 240.3 cm^2. The most common location of the cranial defect was in the tempo-parietal (ie, pterional) region, which was noted in 19 patients (35%). The defect locations for the remaining patients were hemicranial (n = 26, 47%), frontal (n = 5, 9%), and occipital (n = 5, 9%).

Notably, 21 cases (38%) were performed as single-stage cranioplasty. The indication for all single-stage cranioplasties was tumors with osseous involvement necessitating bone excision, from either metastases, brain, meninges, and/or skull origin. A representative case is shown in Figures 2 and 3, demonstrating a 31-year-old man who underwent resection for intraosseous meningioma with immediate "single-stage" reconstruction using a customized, clear PMMA implant via intraoperative modification.

The remaining 34 cases (62%) were performed as 2-stage cranioplasties. Figures 4 and 5 demonstrate a representative patient who underwent a 2-stage cranioplasty. This 30-year-old man presented 10 years after initial injury. He had sustained a traumatic brain injury for which he underwent decompressive craniectomy, with subsequent replacement of his stored autologous bone flap. On presentation, he was found to have significant bone resorption; thus, the bone flap was surgically removed. Given the possibility of bony resorption secondary to osteomyelitis, cranioplasty was performed as staged operation to allow for 6-week, culture-guided antimicrobial treatment before implant placement. The patient recovered well after cranioplasty with no complications.

In this series, 7 patients (13%) developed a major complication requiring reoperation. Among these, 4% (n = 2) were durotomy with subsequent CSF leakage, 4% (n = 2) were epidural bleeding, and 4% (n = 3) was infection. Only one of these (a CSF leak) occurred in a single-stage cranioplasty, whereas the rest were in the 2-stage cohort. The infection necessitated removal of the implant and eventual replacement with titanium mesh. Two patients (4%) experienced new onset, postoperative seizures requiring antiepileptic medications. Another patient had a small area of delayed wound healing that resolved with local wound care. Data on postoperative complications is summarized in Table 3. Importantly, there were no occurrences of chronic pain,

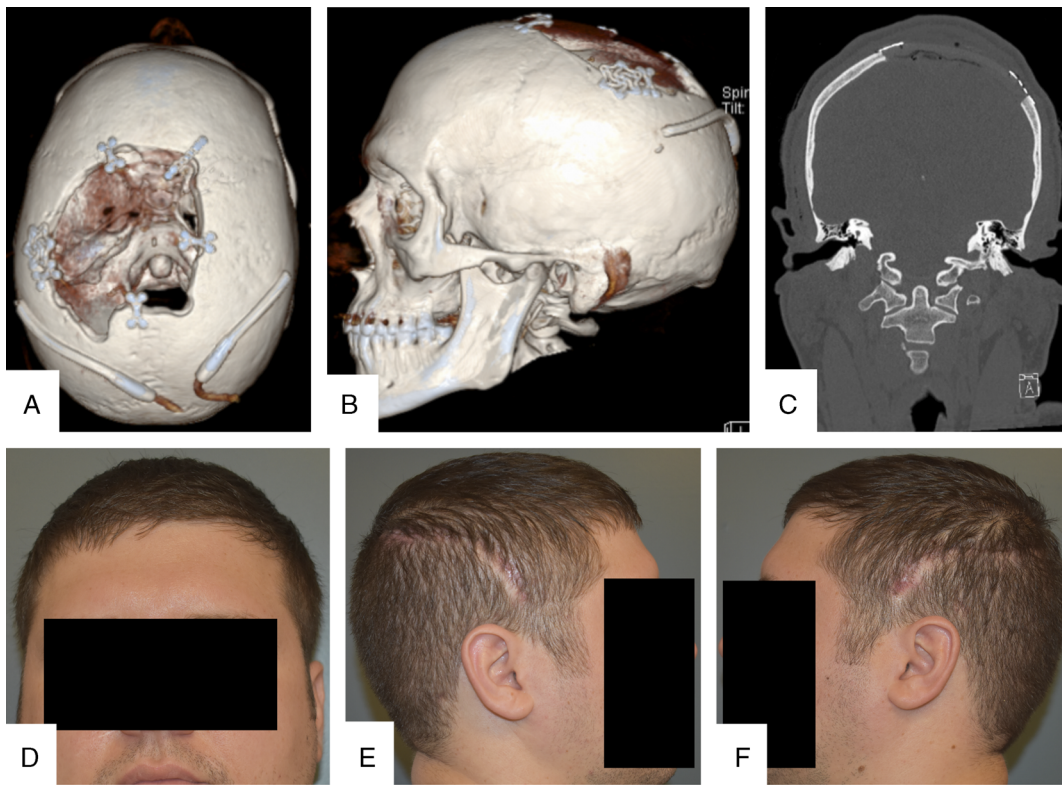

FIGURE 3. Postoperative images of the single-stage cranioplasty case demonstrated in Figure 1. A and B, Horizontal and lateral views of 3D reconstructed CT scan showing cranial implant. Temporary postoperative drains are also seen. C, Coronal view of CT scan showing the implant in the bone defect. Note that the titanium plates securing the implant are visible; however, the implant itself is radiolucent. D–F, Postoperative photographs of patient at 2 months. Note symmetric cranial contour and appropriately healing incisions.

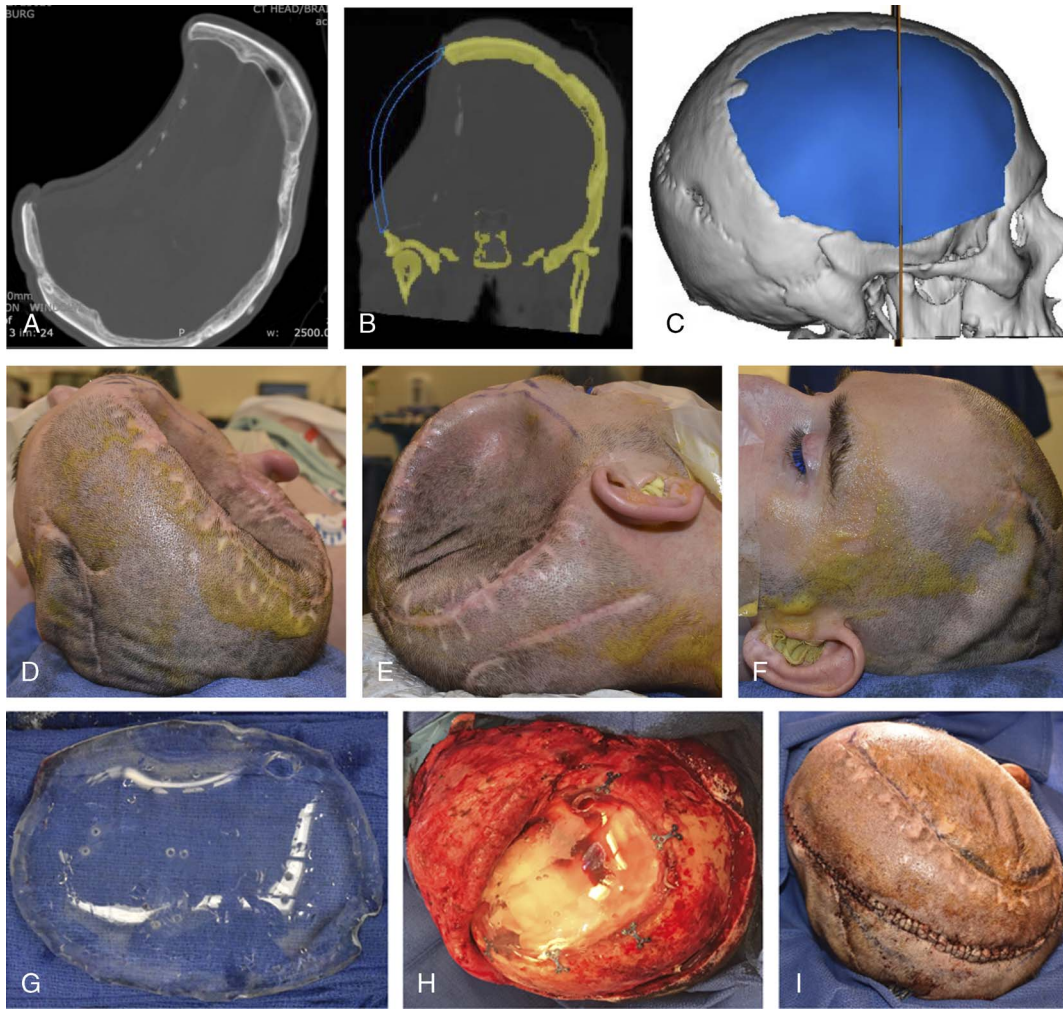

FIGURE 4. Two-stage cranioplasty for hemicranial defect status post traumatic brain injury. A, Horizontal CT scan image showing large right-sided hemicranial defect with severe encephalomalacia and sunken scalp flap. B, Virtual surgical planning image based on CT scan, coronal view. The bone is outlined in yellow, and the customized implant with precise fit is outlined in blue. C, Lateral view of 3D image used for 3D printing of the implant. The vertical line corresponds to the coronal cut-in (B). D–F, On table preoperative photographs showing large-sized, right-sided hemicranial defect with severe sunken scalp flap. There is extensive scarring from multiple prior surgeries, including (1) initial decompressive hemicraniectomy, (2) cranioplasty with replacement of autologous bone flap, and (3) removal of resorbed bone flap. Note also the prominent hydrocephalus shunt device, visible on the left side in images (D) and (F). G, Customized cranial implant on table. H, Intraoperative photograph showing pericranial-onlay flap dissection and implant secured in place with titanium plates and screws. Hemostatic gel foam is visible under the implant. I, On table postoperative photograph showing scalp sutured close. Note the location of the incision, since a new incision is created away from the edges of the bony defect, such that the incision is not directly overlying the implant.

seroma, dislocation/migration of implant, scalp flap necrosis, stroke, or death.

DISCUSSION

Although cranioplasty is one of the most commonly performed procedures in neurosurgical patients, it is associated with an excessively high complication rate. Large cranial defects after craniotomy is always at risk given that craniotomy requires circumferential disruption of the bone's blood supply. Although neurosurgeons have traditionally viewed cranioplasty reconstruction after craniectomy as "cosmetic," more recent studies have confirmed that cranioplasty protects from external atmospheric pressure distortion, potential for traumatic injury, and restores several critical physiologic processes including glymphatic circulation, CSF/cerebral blood flow dynamics, and several cellular mechanisms.[32–34]

Over the last century, numerous materials have been used for skull reconstruction in addition to autologous bone. Polymethylmethacrylate, originally applied as a liquid, was first introduced during World War II by combat surgeons.[35] The material gained favor because of its biocompatibility and co-existing heat/chemical resistant properties. Fast forward to today, we have demonstrated that solid PMMA implants—prefabricated and customized with full translucency—provide a safe and promising option for both preexisting skull defect reconstruction (ie, "basic" cranial implants), and the more complex low-profile intracranial device reconstruction designed to house embedded neurotechnologies, such as hydrocephalus shunt devices,[7] neuromodulatory devices,[6] and wireless intracranial pressure monitors (ie, "smart" cranial implants).[8]

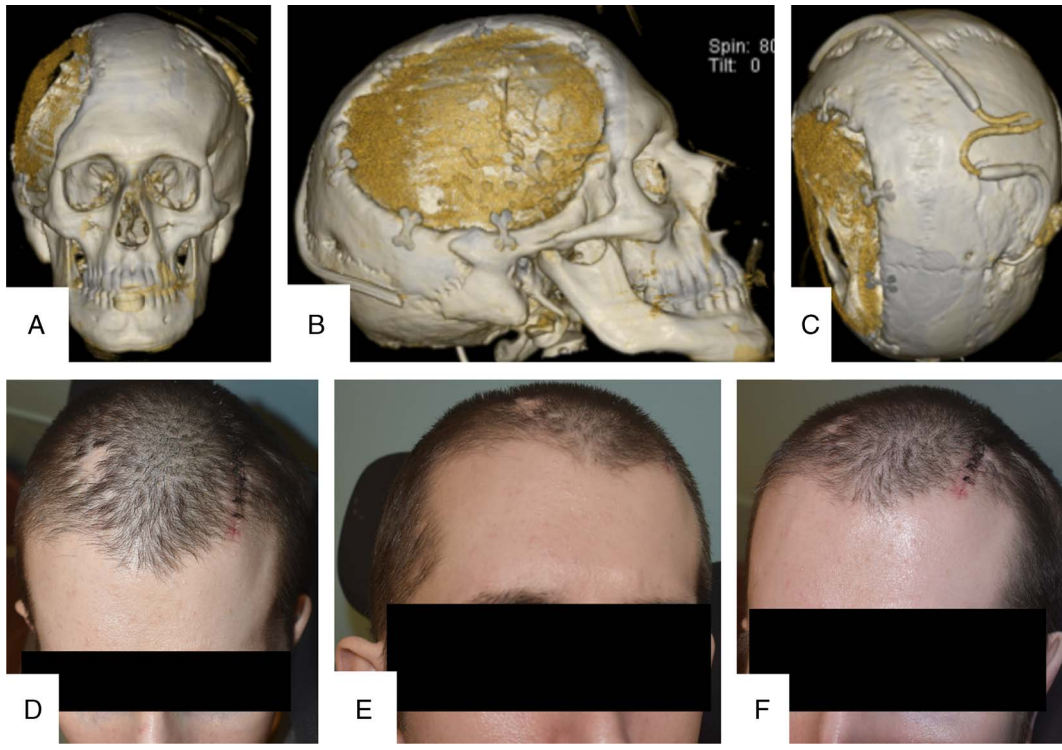

FIGURE 5. Postoperative images of 2-stage cranioplasty case demonstrated in Figure 3. A–C, Coronal, lateral and horizontal views of 3D reconstructed CT scan showing cranial implant. The hydrocephalus shunt and 2 postoperative drains are seen. D–F, Postoperative photographs of patient at 1 month just before suture removal. Note symmetric cranial contour and healing incisions.

Moreover, we have demonstrated clear PMMA to be sonolucent, thereby permitting postoperative diagnostic imaging.[19,20] Although PEEK and opaque PMMA are also sonolucent, they lack the transparent properties of clear PMMA, which remains critical for future integration of functional components.[36] Indeed, given recent findings that ultrasound targeting amyloid aggregates may be used as a therapeutic strategy in Alzheimer disease and that high-frequency, focused ultrasound can effectively treat movement disorders, these sonolucent properties may one day be leveraged for nonsurgical therapeutic acoustic interventions using a multitude of indications.[37]

Here, we present our experience using the clear implant made of solid PMMA, which not only provides the same biomechanical safety and benefits as the opaque model but has the added advantages of visual translucency. To our knowledge, this is the largest cranioplasty outcome study of customized clear PMMA implants to date. During this study, 7 (13%) of our 55 patients experienced a major complication requiring additional surgery. Of these, only one occurred in the single-stage cohort (a CSF leak). It should be noted that for most single-stage cases, the scalp is typically healthy, and the patient may never have undergone a cranial surgery. In contrast, most of the 2-stage cranioplasties are complex patient referrals, with patients often having multiple cranial surgeries (some patients >100 scalp and cranial surgeries), infections, co-existing devices such as hydrocephalus shunts, and/or history of cranial radiation. All efforts are taken to optimize these reconstructions, including staged reconstruction, dural or scalp augmentation with fascia or pericranial grafts, and utilization of a pericranial-onlay technique.

TABLE 3. Complication Rate With Clear-Colored, Solid PMMA Implants

Complications	No. Patients, n (%)
Major	7 (13)
CSF leak	2 (4)
Epidural hematoma	2 (4)
Infection	3 (4)
Minor (nonoperative)	3 (5)
Delayed wound healing	1 (2)
Seizures	2 (4)

Given that this is the first reported series using clear customized PMMA implants, a literature review was performed to contextualize complication rates versus prefabricated, opaque, solid PMMA implants. Literature reported that complication rates for opaque PMMA are highly variable, ranging from 21% to 78% (Table 4).[38–44] Cerebrospinal fluid leaks and bleeding account for the greatest proportion of adverse events. From a high-level view, our complication rates of 4% CSF leaks and 4% bleeding are much less than most other series. Seromas are also quite common in the literature, with a rate of 65% in one reported study.[41] We believe that the avoidance of PEEK material accounts for the absence of seromas in this series, secondary to the inflammatory capsule aspect, based on our team's experience with more than 500 CCIs.[31] In addition, our infection rate of 4%, when using clear PMMA, falls well below published ranges of 6% to 13%.[38,42] In particular, no patients experienced any chronic scalp pain, headache, imprecise fitting of the implant, implant migration or displacement, seroma development, and/or implant exposure.

Notably, seizure incidence after cranioplasty is highly variable, with rates as high as 36%.[36] For example, in a recent meta-analysis, Yao et al[45] showed a pooled incidence of 9% postcranioplasty seizures. Injury before cranioplasty (ie, the index indication for craniectomy), as well as dural disruption when the full-thickness scalp is elevated off the

dura during cranioplasty using a standard approach other than the pericranial-onlay technique, is postulated to cause most postcranioplasty seizures.[36] Indeed, given that there is minimal risk for dural disruption using the pericranial-onlay scalp dissection technique, this most likely contributes to our low incidence of seizures.[24] In addition, because the innovative technique and dual-purpose implant design together allow for the temporalis muscle to remain adherent to the underlying dura, this protects the neovascularization between the temporalis and brain dura from being disrupted—as opposed to dissecting the muscle and attaching it to the outside of the bone flap or implant.[46] Again, because the dual-purpose customized implant is designed to replace both the missing bone and the soft tissue atrophy including temporalis muscle deformity, raising the temporalis off the dura is not necessary for restoring proper symmetry and contour.[18]

Beyond simply comparing opaque to clear-colored PMMA implants, we sought to also evaluate our findings to customized PEEK implants (Table 5). Notably, PEEK implants have a reported complication rate approaching 36%.[48] Therefore, we postulate that the relatively low complication rate observed with our clear PMMA experience is multifactorial, relating to the implant itself (PMMA being less inflammatory), clinical judgment on patient selection, surgical planning by way of a variety of newly developed neuroplastic surgery/scalp reconstruction techniques, and/or surgical method using the pericranial-onlay technique. Of note, for 2-stage cranioplasty patients—with a prior bone flap resorption or infection—the senior surgeon mandates a 3-month minimum time interval between infection clearance and/or complete wound healing.[49] In addition, the pericranial-onlay implantation technique allows the implant to be completely encased within a vascularized tissue pocket, potentially improving antibiotic delivery by having both a vascularized flap both below and above the implant.[24] Furthermore, per the senior author's experience, a capsule frequently develops around PEEK implants, unlike solid PMMA implants, which may explain our reduced incidence of seromas and secondary infections.

A limitation of this study is the difficultly of directly comparing the complication rates of each implant material due to the various patient complexities, such as scalp condition, calvarial defect size, patient population, time intervals from craniectomy to cranioplasty, and inconsistently reported follow-up durations. Furthermore, most of the published data using PEEK and PMMA implants referred to 2-stage cranioplasty, with minimal data available on single-stage cranioplasty. In studies where both single- and 2-stage cranioplasty was performed (Jonkergouw et al[13] and Höhne et al[40]), the authors often did not differentiate the complication profile, except in one study where it was clearly stated that there was no significant difference between complication rates in the single-stage versus the 2-stage population (Alonso-Rodriguez et al).[48] The indications for using PEEK or PMMA in the published literature are similar to that noted in our series. Even with these similar features, the complication rates noted in our series are considerably lower than those in other reported series. In the senior author's experience of more than 500 cranioplasties using autogenous bone, liquid PMMA, porous polyethylene, PEEK, solid PMMA, and titanium mesh, solid opaque PMMA has been shown to have the most acceptable complication risk profile.[31] The complication rates seen with clear PMMA is comparable with what we have observed when using opaque solid PMMA, with the multiple added benefits discussed.

The retrospective nature of this study is another limitation. However, its design strength is that all procedures were performed by the same surgeon, and thus, the surgeon-related variables in other studies do not apply. Secondly, although the sample size is relatively small (n = 55), this will be the largest published series to date. Unquestionably, a larger multicenter study with long-term follow-up is necessary to ultimately define improved outcomes with clear PMMA implants.

TABLE 4. Literature Review of Cranioplasty Complication Rates With Opaque PMMA Implants

Authors	No. Patients	Indication for Cranioplasty (%)	Overall Complication	Implant Removal/ Revision	Infection	Other Complications (%)
Vince et al[38]	65	DC for TBI (43) or stroke (26), ICH (17), tumor/infection/other (14)	24.6%	24.6%	6.4%	Hematoma (12.1) Loosening (6.4)
Bobinski et al[39]	19	DC for TBI (100)	21%	21%	10.5%	Displacement (10.5)
Höhne et al[40]	60	*DC for TBI (32) or stroke (32), tumor (13), hemorrhage (13), revision (7), empyema (3)	33.3%	33.3%	10%	Hemorrhage (10) CSF fistula (5) Imprecise fitting (5) Tissue necrosis (1.6) Neuropathy (1.6)
Maricevich et al[41]	63	DC for TBI or stroke, neoplasia (distribution not included)	77.8%	17.4%	3.2%	Extradural hematoma (7.9) Seroma (65) Dehiscence (4.8) Extrusion (4.8) Prosthesis fracture (1)
Jaberi et al[42]	70	DC for TBI (64) or stroke (1), ruptured aneurysm (16), tumor (7), hematoma (6), epilepsy (4), abscess (2)	40%	14.3%	12.9%	Chronic pain (14.2) Hematoma (10) Implant exposure (1.4) Migration (1.4)
Sharavanan et al[43]	29	DC for TBI (86) or stroke (14)	24.1%	6.8%	17.2%	Hematoma (1) Pain (1)
Oliver et al[44]	1459	No data	19.3%	4.7%	8%	Local complication (165)

*In this article, a fraction of cases was performed as immediate reconstruction (single-stage), while the remaining cases were delayed (2-stage reconstruction). However, it was not stated which indications were for immediate reconstruction versus delayed.

DC, decompressive craniectomy; ICH, intracranial hemorrhage; TBI, traumatic brain injury.

TABLE 5. Literature Review of Cranioplasty Complication Rates With PEEK Implants

Author	No. Patients	Indication for Cranioplasty	Overall Complication	Implant Removal/ Revision	Infection	Other Complications (%)
Zhang et al[47]	75	DC for trauma (83) or cerebrovascular disease (13), infection (1), skull disease (3)	17.3%	1.3%	2.7%	Seizures (4) Hematoma (4) Subgaleal effusion (8) Implant exposure (1.3)
Jonkergouw et al[13]	38	*Stroke (34), trauma (39), tumor (21), infection (5)	28.9%	26.3%	13.2%	Hematoma (10.5) CSF leak (2.6) Wound (2.6)
Alonso-Rodriguez et al[48]	14	†Trauma (7), congenital defects (36), tumor (57)	35.7%	21.4%	14.3%	Seroma (7) CSF leak (7) Implant exposure (7)
Oliver et al[44]	221	Not stated	24%	8.6%	6.8%	Local complication (38)

*In this article, a fraction of cases was performed as immediate reconstruction (single-stage) while the remaining cases were delayed (2-stage reconstruction). However, it was not stated which indications were for immediate reconstruction versus delayed.

†In this article, 1 congenital defect (7%) and 2 tumors (14%) were reconstructed in a single stage, the remaining cases were done in a 2-stage, delayed fashion.

DC, decompressive craniectomy.

Despite these limitations, this study demonstrates safety, efficacy, and satisfactory outcomes with the use of CCIs made of translucent PMMA.

Given these preliminary findings and the numerous advantages of clear PMMA over other alloplastic materials, clear PMMA is an excellent option for cranioplasty reconstruction, especially as the burgeoning field of neuroplastic surgery works to develop "smart" cranial implants accompanying embedded functions analogous to the cellular phone.[30] As clear PMMA is visually translucent, intraoperative implant modification is straightforward as the implant may be easily compared against the underlying, visualized skull defect and traced simply with a marking pen. In addition, it allows for optimal integration of implantable neurotechnologies and removes risk for accidentally injuring the encased components during size modification with drill (Fig. 6).[6–8] Furthermore, in instances of standard cranioplasty use, the visual transparency permits one to assess the underlying brain structures, dural pulsations, absent cerebrospinal leaking, and assure important hemostasis in real time—up until the last minute of scalp closure. Then, once the scalp is inset and closed above, the demonstrated sonolucency of clear PMMA allows for postoperative diagnostic imaging at bedside and the future potential of therapeutic intervention.[19,20]

CONCLUSIONS

Our sentinel experience with clear-colored, customized solid PMMA implants (n = 55) shows a relatively low major complication rate of 13%. Further long-term, multicenter studies assessing cranioplasty with clear PMMA implants will be invaluable for cross-comparison with other alloplastic materials. In addition, such studies will assist the field of neuroplastic surgery's transition from "basic" prosthetics (simply replacing missing skull) to "smart" cranial implants with embedded neurotechnologies for improving brain function and enhanced options for brain disease management. As evidenced by the increasing frequency of "first-in-human" surgeries demonstrating the ability to house technologies within these skull implants, neuroplastic surgery is poised for a radical transformation similar to the shift from "flip" phones to "smart" phones. Given this relatively low complication rate observed, combined with the additional clinical benefits of clear PMMA over alternative implant materials, these findings suggest clear PMMA may be an optimal vessel for emerging "smart" cranial implants and the next generation of implantable neurotechnologies.

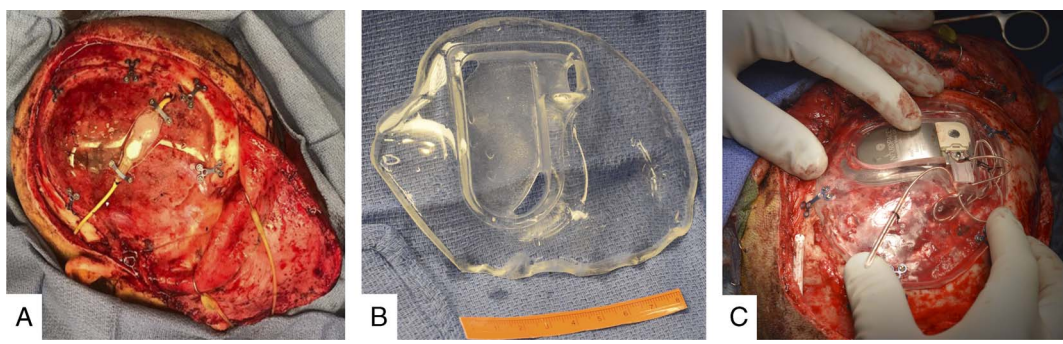

FIGURE 6. Representative examples of embedded neurotechnologies within a clear PMMA implant. A, This intraoperative photograph represents a "first-in-human" experience in the treating a co-existing hemicraniectomy defect and trauma-induced hydrocephalus with a single implant, via an embedded, high-profile shunt within clear implant. B, Photograph of a clear PMMA implant with a device-specific cavity for responsive neuromodulation device insertion. C, Postinsertion photograph with small lid piece attached above the neuromodulation device, which can easily be removed for future battery exchange, thereby preventing the need for repeat craniotomy.

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