Efficacy of immediate replacement of cranial bone graft following drainage of intracranial empyema

Orgest Lajthia, BS,^{1,2} Jerry W. Chao, MD,³ Max Mandelbaum, BS,³ John S. Myseros, MD,¹ Chima Oluigbo, MD,¹ Suresh N. Magge, MD,¹ Christopher S. Zarella, MD,⁴ Albert K. Oh, MD,³ Gary F. Rogers, MD,⁵ and Robert F. Keating, MD¹

¹Department of Neurosurgery, Children's National Medical Center, Washington, DC; ²Department of Neurosurgery, Georgetown University Medical Center, Washington, DC; ³Department of Plastic Surgery, The George Washington University School of Medicine and Health Sciences, Washington, DC; ⁴Department of Plastic Surgery, Randall Children's Hospital, Portland, Oregon; and ⁵Department of Plastic Surgery, Children's National Medical Center, Washington, DC

OBJECTIVE Intracranial empyema is a life-threatening condition associated with a high mortality rate and residual deleterious neurological effects if not diagnosed and managed promptly. The authors present their institutional experience with immediate reimplantation of the craniotomy flap and clarify the success of this method in terms of cranial integrity, risk of recurrent infection, and need for secondary procedures.

METHODS A retrospective analysis of patients admitted for management of intracranial empyema during a 19-year period (1997–2016) identified 33 patients who underwent emergency drainage and decompression with a follow-up duration longer than 6 months, 23 of whom received immediate bone replacement. Medical records were analyzed for demographic information, extent and location of the infection, bone flap size, fixation method, need for further operative intervention, and duration of intravenous antibiotics.

RESULTS The mean patient age at surgery was 8.7 ± 5.7 years and the infections were largely secondary to sinusitis (52.8%), with the most common location being the frontal/temporal region (61.3%). Operative intervention involved removal of a total of 31 bone flaps with a mean surface area of 22.8 ± 26.9 cm². Nearly all (96.8%) of the bone flaps replaced at the time of the initial surgery were viable over the long term. Eighteen patients (78.3%) required a single craniotomy in conjunction with antibiotic therapy to address the infection, whereas the remaining 21.7% required more than 1 surgery. Partial bone flap resorption was noted in only 1 (3.2%) of the 31 successfully replaced bone flaps. This patient eventually had his bone flap removed and received a split-calvaria bone graft. Twenty-one patients (91.3%) received postoperative CT scans to evaluate bone integrity. The mean follow-up duration of the cohort was 43.9 ± 54.0 months.

CONCLUSIONS The results of our investigation suggest that immediate replacement and stabilization of the bone flap after craniectomy for drainage of intracranial empyemas has a low risk of recurrent infection and is a safe and effective way to restore bone integrity in most patients.

<https://thejns.org/doi/abs/10.3171/2018.3.PEDS17509>

KEYWORDS intracranial empyema; immediate replacement; bone flap; bone resorption; craniotomy; intracranial infection

INTRACRANIAL empyema is a life-threatening condition that frequently necessitates emergency drainage and decompression.¹ The infection can exist in the subdural/epidural spaces or both compartments, and often arises from the spread of adjacent infection. Sources of infection include meningitis, paranasal sinus infection, otitis media, periorbital cellulitis, or as a complication of localized trauma.^{1,4} Clinical manifestations may include

fever, headache, meningismus, “Potts” puffy tumor, and signs of focal or general neurological deficits secondary to meningeal inflammation (elevated intracranial pressure [ICP], seizures). The most common infectious agents are *Streptococcus pneumoniae* (16.1%), group B streptococcus (12.9%), *Haemophilus influenzae* type B (12.9%), *Salmonella* spp. (12.9%), *Escherichia coli* (9.7%), and *Pseudomonas aeruginosa* (9.7%).¹⁰ Despite improvements

ABBREVIATIONS EBL = estimated blood loss; ICP = intracranial pressure; LOS = length of stay.

SUBMITTED September 9, 2017. **ACCEPTED** March 14, 2018.

INCLUDE WHEN CITING Published online June 22, 2018; DOI: 10.3171/2018.3.PEDS17509.

in treatment, the mortality rates of patients with subdural collections remain challenging at 4%, and 12%–40% experience residual deleterious neurological effects.^{1,4}

The type and extent of the surgical intervention required is dependent upon the location of the infection (epidural or subdural), the extent of disease (localized or diffuse), the presence of cerebral edema, and the presence or absence of devitalized tissue. Localized epidural collections of purulence, without cerebral edema, may often be successfully managed by a single burr hole and antibiotics, although this modality does not address any concomitant cerebral edema and elevated intracranial pressure.^{8,10} More severe infections, especially those that are multiloculated or involve different areas of the brain (e.g., bilateral disease), require removal of large bone segments to permit adequate cerebral decompression, debridement of devitalized cerebrum, and thorough drainage of all abscesses.^{1,4,8} Due to the frequent re-accumulation of empyemas as well as the frequent delayed presentation of multifocal areas of infection, it is recommended to approach all subdural empyemas via a bicoronal incision in anticipation of future surgical intervention distant from the initial site. Removed bone is typically separated from all of its soft-tissue attachments, thus rendering it avascular, and is irrigated to reduce any bacterial contamination. Standard practices regarding the disposition of the bone include immediate replacement, “banking” the bone flap with subsequent replacement in 3–6 months after resolution of the infection and cerebral edema,² or discarding it.

Advocates of delayed cranial reconstruction argue against immediate replacement because the bone is devascularized and contaminated, thus potentially acting as a nidus for infectious agents, and retention could potentially constrict cerebral swelling (especially if fixated). Many surgeons prefer to defer reconstruction for 3–6 months to allow resolution of the infection and cerebral edema;⁵ the calvarial defect is later addressed by reinsertion of the banked cranial bone flap, other sources of autologous bone (such as split or particulate graft), or some form of alloplastic reconstruction. This approach necessitates a second procedure, some form of cerebral protection between interventions (helmet), and a more challenging dissection through atrophied scalp and scarred tissue planes. In particularly challenging cases (large defects), lengthy surgical times predispose this patient population to further surgical site infections.⁹ When compared to autograft, alloplastic implant reconstruction also bears the added cost of the material (> \$10,000 for a custom implant), a long-term risk of implant infection or rejection, and migration when used in young children.

The merits of a single procedure in this cohort of patients are obvious. Avoiding additional procedures for repair of a calvarial defect mitigates surgical risk to the patient as well as saving resources. Success of an autologous reconstruction rests on the rapid revascularization and gradual osseointegration of the current bone flap, which depends on many variables, including the condition of the surrounding soft-tissue envelope, the presence of bacterial contamination, and the viability (living osteocytes) of the bone flap itself. Despite the intuitive advantages of this approach, outcomes of immediate reinsertion of the bone

TABLE 1. Patient population

Patients	Bone Graft Replacement		Total
	Immediate	Delayed	
Included			
No. of patients	23	10	33
Bone flaps	31	33	64
Excluded			
Burr hole			5
Other (<6-mo follow-up)			8

flap have been poorly described. This investigation represents our institutional experience with the safety and efficacy of immediate reimplantation of the craniotomy flap in patients treated for intracranial empyema and evaluates the success of this method in terms of cranial integrity, risk of recurrent infection, and need for secondary procedures.

Methods

We performed a retrospective review of all patients who underwent craniotomy for management of intracranial empyema at our center during the study period 1997–2016. Inclusion criteria were 1) intracranial empyema requiring removal of a bone segment for drainage with or without cerebral decompression; 2) bone flap irrigated and replaced during the initial procedure; and 3) follow-up duration of more than 6 months. Bone integrity and healing was determined by clinical evaluation by the attending pediatric neurosurgeon and/or by a CT scan. Patient records were culled for demographic information, empyema etiology and location, approximate size of the bone flap, method of osseous fixation, need for further operative intervention, and duration of intravenous antibiotics.

Results

Forty-six patients were identified who were treated for intracranial empyema during the study period (Table 1). Of these, 10 patients underwent cryopreservation of the bone flap for delayed cranioplasty. In these cases, cryopreservation was chosen because brain edema obviated immediate replacement. Five patients received burr holes instead of a craniotomy, and thus were omitted from the study. Eight patients were excluded due to inadequate follow-up, including 1 patient who died in the perioperative period. The single patient who died in this series had been transferred to our institution in critical condition after unsuccessful management at another hospital.

Immediate Replacement

In the remaining 23 patients, a total of 31 bone flaps were studied. The anatomical distribution of empyema was subdural in 18 patients (58.1%), epidural in 6 patients (19.4%), intraparenchymal in 3 patients (9.7%), both epidural and subdural in 2 patients (6.5%), and unspecified in 2 patients (6.5%). The most common location of infection was the frontal/temporal region (61.3%), followed by pa-

TABLE 2. Features of included patients

Feature	Replacement		Total
	Immediate	Delayed	
Demographics			
No. of patients	23	10	33
Males, n (%)	16 (70.0%)	10 (100%)	26 (79.0%)
Females, n (%)	7 (30.0%)	0 (0 %)	7 (21.0%)
Mean age at initial symptoms, yrs (range)	8.7 ± 5.7 (0.1–16.4)	12.8 ± 3.0 (8.6–16.6)	9.9 ± 5.3 (0.1–16.6)
Mean follow-up ± SD, mos (range)	43.9 ± 54.0 (7.9–198.8)	22.0 ± 15.2 (7.4–45.9)	36.9 ± 46.1 (7.4–198.8)
Surgical characteristics (range)			
Mean no. of surgeries ± SD	1.5 ± 0.8 (1.0–3.0)	4.4 ± 0.7 (3.0–5.0)	2.4 ± 1.5 (1.0–5.0)
Mean bone flap surface area ± SD, cm²	22.8 ± 26.9 (2.3–120.0)	51.8 ± 33.3 (6.0–105.0)	33.4 ± 32.1 (2.3–120)
Mean EBL ± SD, ml	163.8 ± 239.0 (5.0–1200.0)	186.7 ± 137.5 (20.0–500.0)	177.0 ± 186.0 (5.0–1200.0)
Mean LOS ± SD, days	19.9 ± 12.3 (7.0–48.0)	15.7 ± 16.7 (1.0–55.0)	17.7 ± 14.7 (1.0–55.0)
No. of patients w/ bone resorption	1	2	3
Bone flap fixation, n (%)			
None	3 (10.3)		
Titanium	20 (69.0)		
Resorbable plates	4 (13.8)		
Suture	2 (6.9)		

rietal (19.4%), posterior/occipital (6.5%), interhemispheric (9.7%), and hemispheric (3.2%). The mean perioperative characteristics for this group, shown in Table 2, were the following: age at craniotomy, 8.7 ± 5.7 years; size of the removed bone flap, 22.8 ± 26.9 cm²; estimated blood loss (EBL), 163.8 ml; hospital length of stay (LOS), 19.9 days; antibiotic therapy, 5.4 weeks; and follow-up, 43.9 months (range 7.9–198.8 months).

Twenty-four bone flaps were rigidly fixed (82.8%; 20 using titanium hardware, 4 using resorbable hardware) in clinical situations in which elevated ICP was not considered problematic. Nonrigid fixation was used in 5 cases (2 using Vicryl suture, and 3 without any fixation; Table 2). For patients with concerns about potential intracranial hypertension, the returned bone flap was anchored on one side with nonabsorbable sutures to allow the flap position to accommodate elevated pressure. The only difficulty in this technique was the common problem of the bone flap sinking in when the elevated ICP had resolved. This was addressed by placing 2 small titanium plates fixed to the leading edge of the bone flap (opposite from the “hinge” sutures) that would not impede any outward deflection of the flap under pressure, but in turn would prevent the edge of the bone flap falling below the surface of the remaining calvaria. The empyemas were largely secondary to sinusitis (19 patients, 52.8%); other causes were periorbital cellulitis (6 patients, 16.7%), meningitis (4 patients, 11.1%), cerebritis (1 patient, 2.8%), and unknown (6 patients, 16.7%; Tables 3 and 4). The empyema layer and source are also graphically depicted in Fig. 1, while Fig. 2 shows a subdural collection along the left frontal/temporal convexity, the most common location of infection in our cohort.

A total of 96.8% (30/31) of the bone flaps were successfully replaced. Eighteen patients (78.3%) required a single craniotomy in conjunction with antibiotic therapy to treat

the empyema. Five patients (21.7%) required additional craniotomy for irrigation and debridement procedures (mean 1.5 ± 0.8, range 1–3) with eventual clearance of in-

TABLE 3. Empyema characteristics

Characteristic	Bone Graft Replacement		Total (%)
	Immediate	Delayed	
Empyema source*			
Sinusitis	19	9	28 (45.9)
Periorbital cellulitis	6	2	8 (13.1)
Meningitis	4	0	4 (6.6)
Dental infection	0	0	0
Cerebritis	1	2	3 (4.9)
Otitis media	0	0	0
Unknown	6	12	18 (29.5)
Empyema layer†			
Epidural	6	2	8 (12.5)
Subdural	18	23	41 (64.1)
Epidural & subdural	2	6	8 (12.5)
Intraparenchymal	3	0	3 (4.7)
Unspecified	2	2	4 (6.3)
Empyema location			
Frontal/temporal	19		
Parietal	6		
Posterior/occipital	2		
Interhemispheric	3		
Hemispheric	1		

* p value = 0.623.

† p value = 0.940.

TABLE 4. A comparison of empyema layer versus source

Empyema Layer	Empyema Source						
	Sinusitis	Periorbital Cellulitis	Meningitis	Dental Infection	Cerebritis	Otitis Media	Unknown
Epidural	7	2					2
Subdural	19	6	3		2		10
Epidural & subdural	2				1		3
Intraparenchymal			1				2
Unspecified					1		2

fection. During subsequent irrigations, the bone flap was removed and immediately reattached using new hardware but with the same bone. Only 1 patient ultimately lost the bone flap secondary to persistent infection and empyema re-accumulation. While none of the patients developed clinical evidence of osteomyelitis (e.g., chronic nonhealing wounds, drainage, or erythema), partial resorption of the bone flap was noted in 1 patient (3.2%) who ultimately required cranioplasty using autogenous split calvaria without sequelae.

Delayed Replacement Group

We included our cohort with delayed replacement bone flaps, which, in essence, served as the control group. The delayed bone flap replacement group contained a total subset of 10 patients who had their bone stored in a freezer. Six of these 10 patients with cryopreserved bone underwent replacement between 4 and 14 months after the initial surgery for empyema drainage. Five of the 6 patients (83.3%) with cryopreserved bone flaps developed an infection after the stored bone was replaced, despite negative cultures at the time of replacement. Furthermore, 3 of the patients in this same cohort underwent another surgery to remove the infected bone, 1 received burr holes in the grafted calvarial bone flap, and 1 patient responded to antibiotic therapy without necessitating bone removal. The most common pathogen responsible for the infection, both on presentation and after replacement of the frozen bone

flap, was found to be *Streptococcus intermedius*. Bone resorption occurred in a single patient.

Four patients in the delayed bone flap replacement group did not utilize cryopreserved bone: 3 of these patients had their bone flap discarded at the time of initial surgery due to infection, and a fourth had the bone stored in the freezer, which was not used due to concerns regarding processing. All 4 patients received cranioplasty with autologous split-thickness bone graft taking place between 6 and 15 months after the initial surgery. Two subjects experienced minimal bone resorption and 1 patient had a second cranioplasty using a hydroxyapatite analog.

The anatomical distribution of empyema was subdural in 23 patients (69.7%), epidural in 2 patients (6.1%), both epidural and subdural in 6 patients (18.2%), and unspecified in 2 patients (6.1%). The mean perioperative characteristics for this group were age at initial craniotomy, 12.8 ± 3.0 years; size of the removed bone flap, 51.8 ± 33.3 cm²; EBL, 186.7 ml; hospital LOS, 15.7 days; and follow-up, 22.0 months (range 7.4–45.9 months). In the group of patients with cryopreserved bone flaps, a total of 33 bone flaps were studied; 54.5% (18/33) of the bone flaps were successfully replaced and patients had an average of 4.4 surgeries.

All patients recovered well and were discharged from the hospital, on average, 15.7 days from the date of admission. Comparison of follow-up periods between patients with immediate replacement and those with delayed replacement at greater than 6-month minimum follow-up yielded a p value of 0.096.

FIG. 1. Graph of empyema layer versus empyema etiology. Figure is available in color online only.

Discussion

Although treatment of intracranial empyema is reasonably well established, the approach to cranial reconstruction following decompressive craniectomy for this condition is variable among surgeons and centers. One of the most widely practiced techniques is storage of the removed bone flap in a deep freeze at -35°C or cryopreservation at -84°C .⁵ In cases of gross infection, the bone is washed in hydrogen peroxide or other disinfectant prior to storage.⁵ This approach incurs a cost for storage and a secondary procedure. In addition, there is evidence to suggest that cryopreserving bone flaps destroys the osteocytes, and delaying reconstruction with this material results in higher rates of resorption (up to 50%), infection, and overall complications.^{2,3,7} In an effort to avoid this issue, some surgeons bank the bone flap in the abdominal subcutaneous tissues; this approach maintains the disadvantages of delayed cranioplasty, does not sterilize the bone graft, and may not be feasible in young children with reduced abdominal subcutaneous fat.⁵

For many neurosurgeons, the concept of placing a devascularized and contaminated segment of cranial bone back into the compromised soft-tissue bed from which it was taken would be considered controversial; intuition would imply that the devascularized bone and the hardware used to fixate it would harbor bacteria and make resolution of the existing infection more difficult. Moreover, the physiologically challenged condition of the soft tissue in the acute stages of the infection strengthens the prospect that the reinserted bone flap would fail to revascularize and heal. This has been addressed by sterilizing the bone (autoclaving, pasteurizing, or irradiating the graft¹¹) prior to reimplantation. Regardless of the method used, the process of sterilization effectively kills all living cells, including those that orchestrate bone healing and viability, and the osseous segment acts only as scaffolding for bone ingrowth from the periphery.^{5,6,11} The long-term outcomes of these reconstructive efforts remain unknown.

The results of the current investigation demonstrate that concerns related to immediate reinsertion of the bone flap may be unfounded and that efforts to decontaminate the bone are unnecessary. The vast majority of our patients who had immediate reinsertion and fixation of the craniotomy flap had full resolution of their intracranial infection with a very low rate (2.8%) of bone resorption requiring secondary cranioplasty. These favorable results, coupled with the aforementioned disadvantages of delayed reconstruction, suggest that immediate reinsertion of the bone flap should be considered in all patients treated for intracranial empyema. For individuals with increased intracranial pressure, one can leave the bone flap partially free-floating by attaching one edge of the flap with sutures, which will permit the flap to elevate when under pressure but settle back in place when the infection has resolved.

There are several limitations to this study. At the outset, this study focuses on the outcomes of only one treatment alternative for intracranial empyema, i.e., immediate reimplantation of the bone flap. There were many patients treated at our institution who underwent delayed autologous reconstruction using cryopreservation, and the retrospective nature of this study makes it impossible to

FIG. 2. Axial CT image showing subdural collection along the left aspect of the falx and the left frontal/temporal convexity.

determine the basis for the surgeon's selection process of one treatment over another. Nevertheless, it was not the purpose of the present study to compare treatments, but to evaluate the outcome of the much less common method of treatment discussed herein. A prospective trial comparing immediate versus delayed bone flap replacement would provide a stronger level of evidence comparing the two approaches. Second, this is a relatively uncommon diagnosis and, consequently, our sample is relatively small. Lastly, some patients ($n = 21$, 91.3%) did not undergo a CT scan to document bone integrity but were followed clinically long-term and noted to have no clinical evidence for significant calvarial resorption or migration. To minimize exposure to ionizing radiation, patients were assessed only by palpation unless there were clinical signs of nonunion or resorption. While it is possible that this method may overstate the degree of bone healing, there were no indications that any areas of potential lack of bone fusion were clinically relevant.

Conclusions

Immediate replacement and stabilization of the bone flap after craniotomy for drainage of intracranial empyema has a low risk of recurrent infection and provides excellent bone integrity in the vast majority of patients (96.8%), while minimizing the need for subsequent surgery and its associated risks. The safety and efficacy of this method permit its application in the patient with intracranial empyema. Factors as to why bone replaced immediately appears to do better than delayed bone replacement remain unclear at this time, but they are expected to become better understood over time with additional investigation.

References

1. Bockova J, Rigamonti D: Intracranial empyema. **Pediatr Infect Dis J** **19**:735–737, 2000
2. Bowers CA, Riva-Cambrin J, Hertzler DA II, Walker ML: Risk factors and rates of bone flap resorption in pediatric patients after decompressive craniectomy for traumatic brain injury. **J Neurosurg Pediatr** **11**:526–532, 2013
3. Chang V, Hartzfeld P, Langlois M, Mahmood A, Seyfried D: Outcomes of cranial repair after craniectomy. **J Neurosurg** **112**:1120–1124, 2010
4. Hendaus MA: Subdural empyema in children. **Glob J Health Sci** **5**:54–59, 2013
5. Josan VA, Sgouros S, Walsh AR, Dover MS, Nishikawa H, Hockley AD: Cranioplasty in children. **Childs Nerv Syst** **21**:200–204, 2005
6. Menon S, Banu K, Veena R, Srihari V, Sham ME, Vinay M: The recycling of autoclaved autografts in mandibular reconstruction: case report and review of literature. **J Maxillofac Oral Surg** **14** (Suppl 1):308–312, 2015
7. Rocque BG, Amancherla K, Lew SM, Lam S: Outcomes of cranioplasty following decompressive craniectomy in the pediatric population. **J Neurosurg Pediatr** **12**:120–125, 2013
8. Smith HP, Hendrick EB: Subdural empyema and epidural abscess in children. **J Neurosurg** **58**:392–397, 1983
9. Sundseth J, Sundseth A, Berg-Johnsen J, Sorteberg W, Lindgaard KF: Cranioplasty with autologous cryopreserved bone after decompressive craniectomy: complications and risk factors for developing surgical site infection. **Acta Neurochir (Wien)** **156**:805–811, 2014
10. Wu TJ, Chiu NC, Huang FY: Subdural empyema in children—20-year experience in a medical center. **J Microbiol Immunol Infect** **41**:62–67, 2008
11. Yasin NF, Ajit Singh V, Saad M, Omar E: Which is the best method of sterilization for recycled bone autograft in limb salvage surgery: a radiological, biomechanical and histopathological study in rabbit. **BMC Cancer** **15**:289, 2015

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Keating, Lajthia, Chao, Rogers. Acquisition of data: Lajthia, Chao, Mandelbaum. Analysis and interpretation of data: Keating, Lajthia, Chao, Rogers. Drafting the article: Keating, Lajthia, Chao, Rogers. Critically revising the article: Keating, Lajthia, Chao, Myseros, Oluigbo, Magge, Zarella, Oh, Rogers. Reviewed submitted version of manuscript: Keating, Lajthia. Approved the final version of the manuscript on behalf of all authors: Keating. Statistical analysis: Lajthia, Chao. Administrative/technical/material support: Lajthia. Study supervision: Keating, Lajthia, Chao, Rogers.

Correspondence

Robert Keating: Children's National Medical Center, Washington, DC. rkeating@childrensnational.org.