



Utilization of carbonated calcium phosphate cement for contouring cranioplasty in patients with syndromic craniosynostosis

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Abstract

Purpose Carbonated calcium phosphate (CCP) cement is an alloplastic material which has been increasingly utilized for cranioplasty reconstruction; however, there is a paucity of data investigating its use in patients with syndromic craniosynostosis. The purpose of this study was to characterize our institutional experience with CCP cement for secondary contouring cranioplasty in these patients to establish safety and aesthetic efficacy.

Methods Patients with syndromic craniosynostosis undergoing cranioplasty with CCP cement from 2009 to 2022 were retrospectively reviewed for prior medical and surgical history, cranioplasty size, cement usage, and postoperative complications. Aesthetic ratings of the forehead region were quantified using the Whitaker scoring system at three timepoints: preoperative (T1), < 6 months postoperative (T2), and > 1 year postoperative (T3).

Results Twenty-one patients were included. Age at surgery was 16.2 ± 2.8 years, forehead cranioplasty area was 135 ± 112 cm², and mass of cement was 17.2 ± 7.8 g. Patients were followed for 3.0 ± 3.1 years. Whitaker scores decreased from 1.9 ± 0.4 at T1 to 1.4 ± 0.5 at T2 ($p = 0.005$). Whitaker scores at T2 and T3 were not significantly different ($p = 0.720$). Two infectious complications (9.5%) were noted, one at 4.5 months postoperatively and the other at 23 months, both requiring operative removal of CCP cement.

Conclusion Our results suggest that aesthetic forehead ratings improve after CCP contouring cranioplasty and that the improvement is sustained in medium-term follow-up. Complications were uncommon, suggesting that CCP is relatively safe though longer-term follow-up is needed before reaching definitive conclusions.

Keywords Cranioplasty · Craniosynostosis · Calcium phosphate · Complications · Aesthetics

Introduction

Patients with syndromic craniosynostosis undergo multiple surgical interventions to expand intracranial volume and improve skull dysmorphism [1–3]. While the type and timing of interventions remain a matter of debate, these patients are at increased risk of re-operation when compared to patients with single-suture, nonsyndromic craniosynostosis [4, 5]. As such, these patients are at particular risk for

persistent bone defects and frontal contour irregularities as they progress to skeletal maturity which may precipitate the request for onlay, contouring cranioplasty.

Choice of reconstructive material utilized in secondary cranioplasty is hotly debated, and this study is not designed to answer which technique is optimal, but rather to describe our experience with carbonated calcium phosphate (CCP) bone cement. Autologous grafts, such as rib [6], iliac [7], and calvarium [8], have the benefits of being host-derived, with calvarial grafts providing a particularly natural contour. However, potential drawbacks of these grafts include donor site morbidity and resorption [9–12]. In recent decades, alloplastic reconstructive materials such as CCP cement and polyetheretherketone (PEEK) have been used as substitutes to autogenous grafts [13, 14]. CCP demonstrates structural similarity to bone matrix and, to an extent, is replaced via ingrowth of native bone [15, 16]. While aesthetic outcomes of CCP cranioplasty are favorable, the risk of CCP infection

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ranges from 10 to 50% based on defect size and proximity to sinus cavities [13, 16–20]. This wide range of infection rates is also attributable to heterogenous study populations. At our institution, CCP is used for a variety of cranial defects, most commonly partial thickness contour irregularities, including those caused by cranial vault reconstruction for craniosynostosis, trauma, and neurosurgical interventions, and our previously reported complication rate is 13.2% [19].

The ongoing need for secondary craniosynostosis surgery and the wide range of complications observed after cranioplasty call for focused examinations in specific subpopulations to further delineate indications and contraindications for the use of CCP cement. Patients with syndromic craniosynostosis are of specific interest as they often have a greater number of prior reconstructive surgeries, the potential need for greater volumes of CCP, and intrinsically abnormal bone homeostasis due to *FGFR2* or *TWIST* gene mutations [21–23]. Indeed, existing literature has suggested that patients with syndromic craniosynostosis have a higher incidence of persistent postoperative defects following reconstruction with demineralized bone matrix than nonsyndromic patients [24]. The purpose of this study is to investigate the aesthetic outcomes and risk profile associated with CCP cement cranioplasty in patients with syndromic craniosynostosis.

Methods

Patient selection and study variables

Following approval from the Institutional Review Board, patients with a diagnosis of syndromic craniosynostosis treated with secondary frontal cranioplasty utilizing CCP cement from 2009 to 2022 at our institution were identified. Only patients with reconstructions of the forehead and frontotemporal region were included. Both partial and full thickness cranial defects were included. For all patients, the methodology of cement application has been previously described [19, 25, 26]. Information obtained for each patient included demographics, syndromic diagnosis, prior surgical history including age at initial fronto-orbital advancement (FOA), age at secondary contouring cranioplasty, operative duration, defect area and location (frontal, temporal, parietal), mass of cement used, length of postoperative hospital stay, complications, and most recent clinical follow-up. Defect area was determined by intraoperative measurements of total cranioplasty construct area, and mass of cement used was acquired from operative reports. Clinical photographs were obtained preoperatively (T1), at less than 6 months postoperatively (T2) and at > 1 year postoperatively (T3, Fig. 1). Forehead contour in each photograph was scored I–IV utilizing the Whitaker classification system [5, 27]. Scores were averaged across two craniofacial surgeons, and

photographs were not scored if patient hair significantly obscured the forehead contour. All postoperative complications were noted. For each complication, the elapsed time from the initial operation was recorded as well as the outcome of the complication (operative or nonoperative). Complications were classified as infectious, cement exposure/extrusion, or contour abnormalities.

Data analysis

Data analysis was conducted in JASP (Version 0.16.3; JASP Team, 2020). Demographic variables and operative data were assessed with descriptive statistics. Whitaker scores were assessed between T1, T2, and T3 with paired-sample *t*-tests. Patients demonstrating improved postoperative Whitaker scores were compared to patients without improved scores with unpaired *t*-tests to identify factors associated postoperative aesthetic improvement. CCP cement use, defect size, and rate of complications in patients with syndromic craniosynostosis undergoing contouring cranioplasty in the present cohort was compared to the complication rate observed in age-matched patients with nonsyndromic craniosynostosis using previously published institutional data [19].

Results

Twenty-one patients with a diagnosis of syndromic craniosynostosis underwent secondary cranioplasty with CCP by two craniofacial surgeons during the study period. Apert syndrome was the most common diagnosis treated, followed by Pfeiffer, Saethre-Chotzen, Muenke, and Crouzon syndromes. The patient cohort was 81% white and 52% female. Seventy-six percent of patients had bicoronal craniosynostosis, 19% were unicoronal, and 5% were sagittal (Table 1).

Operative characteristics

Age at surgery was 16.2 ± 2.8 years. Average defect area was 135 ± 112 cm² and average cranioplasty construct utilized 17.2 ± 7.8 g of CCP cement. In addition to CCP cement, 13 patients' reconstructions also utilized titanium mesh and 9 utilized cranial bone grafting. Operative duration was 179 ± 66 min. Postoperative length of stay was 1.9 ± 0.8 days and postoperative follow-up was 3.0 ± 3.1 years (Table 1).

Aesthetic outcomes

T1 photographs ($n = 19$) were taken 3.4 ± 2.4 months preoperatively, T2 photographs ($n = 17$) were 4.6 ± 3.5 months postoperatively, and T3 photographs ($n = 13$) were 19.9 ± 10.0 months postoperatively. Ninety-one percent of Whitaker ratings either agreed or fell within one level of

Fig. 1 (Left) Preoperative photographs of a patient with Crouzon syndrome who underwent prior FOA with noticeable frontal bone irregularities and temporal narrowing. (Middle) Same patient 6 months after contouring cranioplasty with 20 g of CCP cement demonstrating improved forehead contour. (Right) Same patient at postoperative year 4 demonstrating stable forehead contour



disagreement. Average Whitaker score at T1 was 1.9 ± 0.4 . Scores decreased at T2 to 1.4 ± 0.5 ($p = 0.005$). Average Whitaker score at T3 was 1.3 ± 0.3 , which was not

significantly different from T2 ($p = 0.720$, Fig. 2). Comparing patients with improved postoperative Whitaker scores to patients without improved scores, those with improved scores had, on average, smaller cranioplasty defect areas than patients without improved scores ($89 \pm 50 \text{ cm}^2$ vs $168 \pm 90 \text{ cm}^2$, $p = 0.046$). There were no differences between patients with and without postoperative aesthetic improvements in terms of number of preceding vault surgeries, age at initial fronto-orbital advancement, or age at secondary cranioplasty (Table 2).

Table 1 Diagnostic and surgical characteristics of the patient cohort

Patient characteristics	n (%)
Diagnosis	
Apert	6 (29)
Pfeiffer	4 (19)
Crouzon	3 (14)
Saethre-Chotzen	4 (19)
Muenke	4 (19)
Sex	
Male	10 (48)
Female	11 (52)
Age at surgery (years)	16.2 ± 2.8
Operative time (minutes)	179 ± 66
Defect area (cm²)	135 ± 112
Additional reconstructive materials	
Titanium mesh	9 (43)
Autologous bone	5 (24)
Titanium mesh + bone	4 (19)
Postoperative length of stay (days)	1.9 ± 0.8
Postoperative follow-up (years)	3.0 ± 3.1

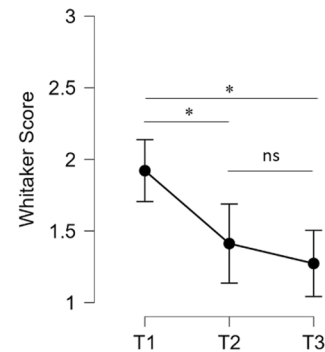


Fig. 2 Whitaker classification scores across T1, T2, and T3. Scores were averaged across two craniofacial surgeons. * $p < 0.05$, ns = not significant

Complications

There were two complications in the patient cohort (9.5%). Both were infectious in nature and necessitated operative removal of CCP cement. Both complications occurred in patients who, in addition to CCP cement, had titanium mesh implanted to cover a full thickness calvarial defect. One complication occurred 4.5 months postoperatively and the other complication occurred 23 months postoperatively. The amount of cement used in these cases were 30 g and 40 g, respectively. These were the two largest masses in the cohort, but we are underpowered to make definitive conclusions regarding the relationship between volume used and complications. There were no complications of cement fragmentation in patients included in this study.

The complication rate of secondary cranioplasty in patients with syndromic craniosynostosis was compared to patients with nonsyndromic craniosynostosis previously published from our institution [19]. In that cohort, patients underwent cranioplasty at 15.0 ± 1.8 years of age. Five out of 65 patients (7.7%) had postoperative infections necessitating CCP cement removal, which was not significantly different than the rate of reoperation noted in the present study ($p = 0.790$). The cranioplasty construct area in the nonsyndromic patients was 105 ± 76 cm² which was not significantly lower than the 135 ± 112 cm² seen in syndromic patients ($p = 0.273$). Similarly, CCP cement mass was not different between syndromic and nonsyndromic patients (17.2 ± 7.8 g vs 14.8 ± 7.7 g, $p = 0.242$). Ten patients in the present study have had follow-up for more than 3 years postoperatively and 5 have had follow-up for 5 or more years (range 3.0–7.8 years) None has undergone additional contouring cranioplasty or developed an indication for cement removal.

Discussion

There are many options for, and no consensus as to, the optimal reconstructive material for secondary cranioplasty. Alloplastic materials, such as CCP cement, have several advantages yet literature suggests cautious patient selection is necessary to avoid adverse outcomes, namely infection

and fragmentation leading to extrusion. The present study was carried out to assess the use of CCP cement in a specific population with a high risk of needing secondary surgery, patients with syndromic craniosynostosis. Additionally, this study aimed to add precision to the risk profile associated with CCP given the ambiguity surrounding the risk profiles of alloplasts in the literature. The results of this study provide evidence that CCP cement reconstruction improves forehead contour with reasonable risk of infection or the need for re-contouring.

The patients in the present study experienced postoperative improvement in forehead contour as quantified using the Whitaker classification system [5]. Improvement in cranial contour with this alloplastic material is generally well accepted [19, 24, 28, 29]. The immediate postoperative improvement in this patient cohort was sustained at an average of over 18 months postoperatively, indicating that at least in medium-term follow-up, the aesthetic improvement is durable. Additionally, none of the 10 patients with 3 years or more follow-up underwent additional contouring, providing additional evidence of patient satisfaction.

The rate of infectious complications in the present study was 9.5%, similar to the complication rate observed in patients with nonsyndromic craniosynostosis. This is not necessarily intuitive as syndromic patients generally have a more complex surgical history, which has previously been implicated as a risk for cement infection [19, 20]. Both infections in this cohort occurred within 2 years and none of the patients followed for 3 or more years developed late postoperative infections. This finding, when considering that the cranioplasty construct area was an average of 135 cm², seems initially at odds with prior research which has suggested that defects over 25 cm² have increased risk of infection [17, 20, 30]. However, the difference in mass of cement used likely accounts for this finding, as high complication rates have been seen with average CCP cement construction up to 80 g [20]. A separate study reported that mean cement use in cases with infectious complications was 43 g, 20 g greater than cases without infectious complications [26]. Here, the average amount of CCP cement used was 17.2 g. Thin layering likely lowers the infectious risk, as it is known that neovascularization is limited to the periphery of the cement construct [31, 32]. Further, the two patients with infectious complications in this cohort had the

Table 2 Comparison between patients experiencing postoperative improvement in forehead contour versus those who did not, as assessed by the Whitaker classification system. Significance ($\alpha < 0.05$) bolded

	Patients with improved scores	Patients without improved scores	<i>p</i>
Number of preceding vault surgeries	2.5 ± 1.3	1.8 ± 0.4	0.228
Age at initial FOA (days)	430 ± 319	394 ± 39	0.879
Age at cranioplasty (years)	16.2 ± 2.9	15.9 ± 3.7	0.235
Defect area (cm ²)	89 ± 50	168 ± 90	0.046

largest construct masses at 30 g and 40 g, providing additional evidence that lack of neovascularization in the center of a thick cranioplasty may increase risk of chronic infection. Conversely, no complications were seen when 20 g or less was used.

There are several technical considerations for CCP cement cranioplasty in patients with syndromic craniosynostosis that may serve to mitigate risk while allowing for aesthetic improvement. First is a contraindication for the application of CCP cement to regions communicating with the frontal or ethmoid sinuses or nasal cavity, as previously described [18, 26]. By extension, hardware overlying sinuses is not removed during cranioplasty. Additionally, alloplastic material is rarely placed near the coronal incision during reconstruction, as exposure to skin flora may seed the CCP cement construct. Second, it is critical that CCP bone cement be placed on dry bone. We spend a great deal of time and energy ensuring the surface of the bone is *absolutely dry* without any small amount of blood. Third, the volume of the overall cranioplasty construct should ideally be kept low, smoothing contour but not providing for large frontal protrusion, in line with prior evidence [19, 26]. In cases of severe dysmorphology and frontotemporal retrusion, staging cranial bone grafting and/or repeat FOA followed by CCP cement cranioplasty may be necessary to avoid the higher risk of large-volume cement cranioplasty. Fourth, as seen in this study, patients with syndromic craniosynostosis may present for secondary cranioplasty with full thickness defects from prior craniotomies. Utilization of titanium mesh to absorb dural pulsations has been suggested to lower the risk of cement fracture [33, 34]. Finally, thin application of cement, on the order of 5 mm or less, is standard at our institution, as the existing histologic evidence does not suggest that this alloplastic material is replaced by native bone to any great extent, even with long-term follow-up [29, 35]. Still, there is limited revascularization and replacement of CCP cement particularly at the periphery of the implant [36], suggesting that optimizing the surface areas to volume ratio with a thin onlay would be more resistant to chronic infection than thick onlays. It is our impression that application of these guiding principles allows for the safe utilization of this reconstructive material, even in patients with complex surgical histories and contour irregularities over a large surface area.

There are limitations to the present study. First, this study is retrospective and cannot assign causality to the findings. Unaccounted for factors may have influenced both the aesthetic ratings and development of complications. Second, surgeon estimates of cement mass used may be unreliable as they are recorded intraoperatively by the surgeon from pre-weighted packaging. Similarly, defect dimensions are estimated from long- and short-sided measurements of the contouring surface and may be inaccurate as they do not

account for curvature. Additionally, the Whitaker classification system, used to assess pre- and postoperative forehead contour, has been shown to have high inter-rater variability [27]. Finally, due to the small number of complications, it was not possible to statistically assess factors associated with postoperative CCP cement infection. Still, by narrowly defining a population for investigation, this study has been able to demonstrate aesthetic efficacy and safety of secondary cranioplasty with carbonated calcium phosphate cement in patients with syndromic craniosynostosis and provide additional evidence for the proper usage of this reconstructive material.

Conclusions

Our results suggest that aesthetic forehead ratings improve after CCP contouring cranioplasty, and that the improvement is sustained, at least in the medium-term. Infection and extrusion were uncommon, suggesting that CCP is relatively safe though longer-term follow-up is needed before reaching definitive conclusions regarding safety and efficacy.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00381-023-05920-5>.

Author contribution All the authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Connor S Wagner, Matthew E Pontell, Sameer Shakir, Emily Zhang, and Emily Xu. The first draft of the manuscript was written by Connor S Wagner and all the authors commented on previous versions of the manuscript. All the authors read and approved the final manuscript.

Availability of data and material The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate This study was approved by the Institutional Review Board at the Children's Hospital of Philadelphia.

Consent for publication The authors affirm that human research participants provided informed consent for publication of the images in Fig. 1.

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

References

1. Fearon JA (2014) Evidence-based medicine: craniosynostosis. *Plast Reconstr Surg* 133:1261–1275
2. Fearon JA, Podner C (2013) Apert syndrome: evaluation of a treatment algorithm. *Plast Reconstr Surg* 131:132–142

3. Taylor JA, Bartlett SP (2017) What's new in syndromic craniosynostosis surgery? *Plast Reconstr Surg* 140:82e–93e
4. McCarthy JG, Glasberg SB, Cutting CB, Epstein FJ, Grayson BH, Ruff G, Thorne CH, Wisoff J, Zide BM (1995) Twenty-year experience with early surgery for craniosynostosis: I. Isolated craniofacial synostosis—results and unsolved problems. *Plast Reconstr Surg* 96:272–283
5. Whitaker LA, Bartlett SP, Schut L, Bruce D (1987) Craniosynostosis: an analysis of the timing, treatment, and complications in 164 consecutive patients. *Plast Reconstr Surg* 80:195–212
6. Laurie SW, Kaban LB, Mulliken JB, Murray JE (1984) Donor-site morbidity after harvesting rib and iliac bone. *Plast Reconstr Surg* 73:933–938
7. Fowler B, Dall B, Rowe D (1995) Complications associated with harvesting autogenous iliac bone graft. *Am J Orthop (Belle Mead NJ)* 24:895–903
8. Kline Jr RM, Wolfe SA (1995) Complications associated with the harvesting of cranial bone grafts. *Plastic Reconstruct Surg* 95:5–13; discussion 14
9. Goldberg VM (1992) Natural history of autografts and allografts. *Bone Impl Graft* 9–12
10. Lee SH, Yoo CJ, Lee U, Park CW, Lee SG, Kim WK (2014) Resorption of autogenous bone graft in cranioplasty: resorption and reintegration failure. *Korean Journal of Neurotrauma* 10:10
11. Posnick JC, Goldstein JA, Armstrong D, Rutka JT (1993) Reconstruction of skull defects in children and adolescents by the use of fixed cranial bone grafts: long-term results. *Neurosurgery* 32:785–791
12. Prolo DJ, Oklund SA (1991) The use of bone grafts and alloplastic materials in cranioplasty. *Clin Ortho Rel Res* 270–278
13. Burstein FD, Cohen SR, Hudgins R, Boydston W, Simms C (1999) The use of hydroxyapatite cement in secondary craniofacial reconstruction. *Plast Reconstr Surg* 104:1270–1275
14. Punchak M, Chung LK, Lagman C, Bui TT, Lazareff J, Rezzadeh K, Jarrahy R, Yang I (2017) Outcomes following polyetheretherketone (PEEK) cranioplasty: systematic review and meta-analysis. *J Clin Neurosci* 41:30–35
15. Costantino PD, Chaplin JM, Wolpoe ME, Catalano PJ, Sen C, Bederson JB, Govindaraj S (2000) Applications of fast-setting hydroxyapatite cement: cranioplasty. *Otolaryngol Head Neck Surg* 123:409–412
16. Ducic Y (2002) Titanium mesh and hydroxyapatite cement cranioplasty: a report of 20 cases. *J Oral Maxillofac Surg* 60:272–276
17. Greenberg BM, Schneider SJ (2005) Alloplastic reconstruction of large cranio-orbital defects: a comparative evaluation. *Ann Plast Surg* 55:43–51
18. Matic D, Phillips JH (2002) A contraindication for the use of hydroxyapatite cement in the pediatric population. *Plast Reconstr Surg* 110:1–5
19. Shakir S, Kalmar CL, Yang R, Taylor JA, Bartlett SP (2021) Indications and limitations of carbonated calcium phosphate cement for secondary contouring cranioplasty: a long-term institutional experience. *J Craniofac Surg* 32:2788–2793
20. Zins JE, Moreira-Gonzalez A, Papay FA (2007) Use of calcium-based bone cements in the repair of large, full-thickness cranial defects: a caution. *Plast Reconstr Surg* 120:1332–1342
21. Holmes G, Rothschild G, Roy UB, Deng C-X, Mansukhani A, Basilico C (2009) Early onset of craniosynostosis in an Apert mouse model reveals critical features of this pathology. *Dev Biol* 328:273–284
22. Marie P, Coffin J, Hurley M (2005) FGF and FGFR signaling in chondrodysplasias and craniosynostosis. *J Cell Biochem* 96:888–896
23. Marie PJ, Kaabeche K, Guenou H (2008) Roles of FGFR2 and twist in human craniosynostosis: insights from genetic mutations in cranial osteoblasts. *Craniofacial Sutures* 12:144–159
24. Plum AW, Tatum SA (2015) A comparison between autograft alone, bone cement, and demineralized bone matrix in cranioplasty. *Laryngoscope* 125:1322–1327
25. Baker SB, Weinzweig J, Kirschner RE, Bartlett SP (2002) Applications of a new carbonated calcium phosphate bone cement: early experience in pediatric and adult craniofacial reconstruction. *Plast Reconstr Surg* 109:1789–1796
26. Gilardino MS, Cabiling DS, Bartlett SP (2009) Long-term follow-up experience with carbonated calcium phosphate cement (Norian) for cranioplasty in children and adults. *Plast Reconstr Surg* 123:983–994
27. Wes AM, Naran S, Sun J, Mazzaferro D, Xu W, Nguyen P, Whitaker LA, Bartlett SP, Taylor JA (2017) The Whitaker classification of craniosynostosis outcomes: an assessment of interrater reliability. *Plast Reconstr Surg* 140:579e–586e
28. Kodera T, Tada H, Akazawa A, Hashimoto N, Arishima H, Yamada S, Arai H, Higashino Y, Kitai R, Takeuchi H (2018) Evaluation of the use of calcium phosphate cement for aesthetic neurosurgical cranial reconstruction. *World Neurosurg* 110:e296–e304
29. Kumar NG, Sudeep S, Balwan R (2015) Cranioplasty of hemispherical defects using calcium phosphate cements along with titanium mesh: our experience. *J Maxillofac Oral Surg* 14:920–924
30. Durham SR, McComb JG, Levy ML (2003) Correction of large (> 25 cm²) cranial defects with “reinforced” hydroxyapatite cement: technique and complications. *Neurosurgery* 52:842–845
31. Gosain AK, Riordan PA, Song L, Amarante MT, Kalantarian B, Nagy PG, Wilson CR, Toth JM, McIntyre BL (2004) A 1-year study of osteoinduction in hydroxyapatite-derived biomaterials in an adult sheep model: part II. Bioengineering implants to optimize bone replacement in reconstruction of cranial defects. *Plast Reconstr Surg* 114:1155–1163
32. Zins JE, Moreira-Gonzalez A, Parikh A, Arslan E, Bauer T, Siemionow M (2008) Biomechanical and histologic evaluation of the Norian craniofacial repair system and Norian Craniofacial Repair System Fast Set Putty in the long-term reconstruction of full-thickness skull defects in a sheep model. *Plast Reconstr Surg* 121:271e–282e
33. Elshahat A, Shermak MA, Inoue N, Chao EY, Manson P (2004) The use of Novabone and Norian in cranioplasty: a comparative study. *J Craniofac Surg* 15:483–489
34. Eppley BL, Hollier L, Stal S (2003) Hydroxyapatite cranioplasty: 2. Clinical experience with a new quick-setting material. *J Craniofac Surg* 14:209–214
35. Smartt JM Jr, Karmacharya J, Gannon FH, Ong G, Jackson O, Bartlett SP, Poser RD, Kirschner RE (2005) Repair of the immature and mature craniofacial skeleton with a carbonated calcium phosphate cement: assessment of biocompatibility, osteoconductivity, and remodeling capacity. *Plast Reconstr Surg* 115:1642–1650
36. Gosain AK, Song L, Riordan P, Amarante MT, Nagy PG, Wilson CR, Toth JM, Ricci JL (2002) A 1-year study of osteoinduction in hydroxyapatite-derived biomaterials in an adult sheep model: part I. *Plast Reconstr Surg* 109:619–630

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