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Clinical Application of Three-Dimensional Printing of Polycaprolactone/Beta-Tricalcium Phosphate Implants for Cranial Reconstruction

Hojin Park, MD, PhD, Jong Woo Choi, MD, PhD, and Woo Shik Jeong, MD

Abstract: Polycaprolactone (PCL) implants are a biodegradable polymeric material with appropriate mechanical strength and durability for use in cranioplasty. They can be manufactured as patient- customized implants using a three-dimensional (3D) printer. Herein, the authors aimed to share our experience in cranioplasty of patients with deformed and asymmetric skulls using PCL/beta- tricalcium phosphate (ß-TCP) implants.

Seven patients underwent cranioplasty using patient-specific PCL/ß-TCP implants. Cranial computed tomography images were converted to a 3D model and mirrored to design a patient-specific implant. Based on the 3D simulation, an implant was 3D printed using PCL/ß-TCP. A 6-month follow-up was conducted with periodic visits and computed tomography scans. Symmetry after surgery and complications were evaluated.

Postoperatively, the soft tissue volumes increased to 15.8 ± 17.2 cm^3 and 14.9 ± 15.7 cm^3 at 2 weeks and 6 months of follow-up, respectively. The volume change from 2 weeks to 6 months was —4.4 ± 2.5%. Six patients achieved complete symmetry after cranioplasty, whereas 1 patient noticed partial symmetry. The symmetry remained unchanged at 6 months of follow-up. Upon palpation to assess smoothness, 6 patients exhibited a smooth edge interface, whereas 1 patient had a slightly irregular edge.

Based on these findings, 3D-printed PCL/ß-TCP implants are an excellent material for cranioplasty, and a favorable cosmetic outcome can be achieved. Specifically, these novel PCL/ß-TCP implants have good biocompatibility and mechanical strength without any postoperative foreign body reaction.

Key Words: Bioabsorbable implants, biocompatible materials, deformational plagiocephaly, three-dimensional printing

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As a surgical procedure of long-standing history, cranioplasty is commonly performed to correct congenital or acquired cranial deformities; it provides cerebral protection and aesthetic improvement. Various surgical techniques and numerous materials for cranioplasty have been introduced in the literature. Among the diverse cranial reconstruction methods reported, onlay or inlay bone grafting techniques are necessary for various purposes, such as congenital or post-traumatic skull depression or original cranial shape restoration, and both autologous and alloplastic materials can be used. However, there is still no consensus regarding the appropriate materials for cranioplasty.[1] The requirements for an ideal material include good biocompatibility, imaging compatibility, ability to provide cerebral protection and skull contour, osteogenic potential, and fewer donor site problems.[2–4]

Autologous bone grafts have been widely adopted in cranioplasty owing to their biocompatibility and osteogenic potential. However, they have some disadvantages, such as resorption, infection, and donor site morbidity.[5] Their use is also often accompanied by difficulties in achieving aesthetically symmetric contours. Several alloplastic materials have been developed as an alternative to overcome the disadvantages of autologous bone grafts. Alloplastic materials offer several advantages over autologous bone grafts, including no donor site morbidity, easier fixation, and easier molding according to the defects. Polymethylmethacrylate (PMMA), polyetheretherketone (PEEK), and porous polyethylene are the most commonly used materials.[6]

Polycaprolactone (PCL) and beta-tricalcium phosphate (ß-TCP) are biocompatible and biodegradable synthetic materials used in the scaffold and show good osteoconductivity.[7,8] Polycaprolactone/ß- TCP scaffolds can offer appropriate mechanical strength and durability in cranioplasty. Moreover, with recent advances in computer- assisted design and three-dimensional (3D) technologies, PCL/ß- TCP allows the production of patient-specific, prefabricated implants, since it is easy to manipulate and manufacture.[9] In this study, we aimed to share our experience in cranioplasty of patients with deformed and asymmetric skulls using patient-specific PCL/ß-TCP implants.

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MATERIALS AND METHODS

Patients who underwent cranioplasty using a 3D-printed PCL implant between January 2000 and January 2010 were included in the study. This study was approved by the relevant institutional review board (approval number: 2019-1201) and informed consent was obtained from the patients. The inclusion criteria were as follows: (1) cranial bone flap loss following craniectomy/craniot- omy, (2) asymmetric cranium due to an acquired or congenital deformity, and (3) no open scalp wounds. The exclusion criteria were as follows: (1) open scalp wounds, (2) evidence of infection, (3) genetic disorder affecting wound healing, (4) immature cranial bone (age: < 18 years), (5) history of scalp reconstruction, and (6) immunosuppressant medication.

The preoperative segmented computed tomography (CT) data were converted into 3D solid models using a software to design the PCL implants. The 3D reconstruction of the normal cranium side was then mirrored or flipped to create a normal smooth-shaped skull. The implants were designed by subtracting the reconstructed 3D cranial model from the preoperative 3D cranial model. The United States food and drug administration-approved PCL (Evonik Industries, Essen, Germany) and ß-TCP (Foster corporation, Putnam, Windham, CT) were used to fabricate the 3D-printed implants (TnR PSI Plus; T&R Biofab, Republic of Korea). The 3D printing system (fused deposition modeling system) had motion, temperature, and pneumatic controllers. The biomaterials were melted, assembled, and extruded by pneumatic pressure. The applied temperature was adjustable at 120 °C. The pore size and porosity of the implants were 500 μm and 50%, respectively. The PCL/ß- TCP implant was irradiated with gamma ray at 25 kGy for sterilization.

Cranioplasties were performed by a single craniofacial surgeon (J.W.C). Previous scalp incisions were used, and the area of skull deformity was completely exposed in the subperiosteal plane. The PCL/ß-TCP implants were placed on the deformity to fit the underlying skull contour. They were fixed by placing titanium screws directly through the implant edge to the bone. Thereafter, a hydroxyapatite paste (HydroSet; Stryker, Kalamazoo, MI) was applied to the implant surface (Fig. 1).

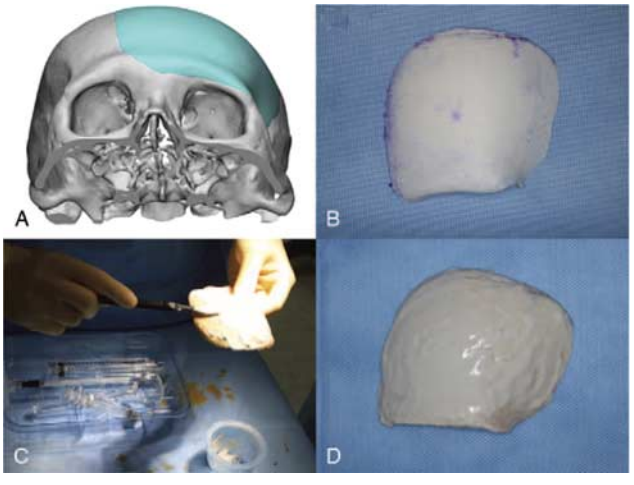

FIGURE 1. Surgical procedure of patient-specific PCL/ß-TCP implant-based cranioplasty. (A) Preoperative simulation of the implant design. (B) Three-dimensionally printed PCL/ß-TCP implant. (C, D) The hydroxyapatite paste was applied to the implant surface. PCL, polycaprolactone; ß-TCP, beta-tricalcium phosphate.

The demographics, including sex and age, surgical complications, radiation history, and diagnosis were evaluated in all patients. Computed tomography images obtained at initial presentation, 2 weeks after surgery, and 6 months of follow-up were compared to analyze the soft tissue volume changes. The soft tissue volume changes were measured using CT and the Mimics software, version 21.0 (Materialise NV, Leuven, Belgium); 3D volumetric rendering was created using this software. Subsequently, the increases in the volumes after surgery were evaluated. In addition, cranial symmetry and smoothness on the implant edges were evaluated qualitatively at 2 weeks and 6 months after surgery.

RESULTS

This study included 7 consecutive patients who underwent 3D- printed PCL/ß-TCP implant-based cranioplasty. Their age ranged from 20 to 62 years (mean age: 34.3 ± 15.4 years). The patients required cranioplasty for craniosynostosis, positional plagioce- phaly, meningioma, asymmetric forehead, fibrodysplasia, and autologous bone resorption after deformity after trauma (Supplementary Digital Content, Table 1, http://links.lww.com/SCS/D911). The defects were located in the frontal (n = 5), fronto- orbital (n = 1), and occipital (n = 1) areas. The mean follow-up period was 8.7 ± 4.5months (range: 6-17 months). One patient experienced seroma at 3 months after insertion, which resolved after seroma aspiration and oral antibiotic medication. During the follow-up period, the remaining 6 patients did not experience postoperative complications, including inflammation, infection, wound problem, and seroma. There were also no clinical signs of foreign body reaction or implant rejection, demonstrating high biocompatibility and tolerability of the 3D-printed PCL/ß- TCP implants.

Implant fracture, mobilization, or dislocation was not observed on the CT images at 2 weeks and 6 months after surgery. This indicated that the PCL/ß-TCPv implants had sufficient mechanical profile for use in cranioplasty. Postoperatively, the soft tissue volumes increased to 15.8 ± 17.2 cm^3 and 14.9 ± 15.7 cm^3 at 2 weeks and 6 months of follow-up (Supplementary Digital Content, Table 2, http://links.lww.com/SCS/D911), respectively. The volume change from 2 weeks to 6 months was — 4.4 ± 2.5%. This change was primarily caused by soft tissue swelling, which demonstrated that the implant volume was well maintained until 6 months after surgery.

Regarding aesthetic results, 6 patients achieved complete symmetry after cranioplasty, whereas 1 patient had partial symmetry (Supplementary Digital Content, Table 3, http://links.lww.com/SCS/D911). The symmetry remained unchanged at 6 months of follow-up. Upon palpation to assess smoothness, 6 patients exhibited a smooth edge interface, whereas 1 patient exhibited a slightly irregular edge. The PCL/ß-TCP implant thickness was undesirably more in the patient with an irregular edge, leading to a diminished aesthetic outcome.

Case 1

A 20-year-old male patient presented with bilateral forehead retrusion. He had a history of fronto-orbital cranial vault remodeling for bilateral craniosynostosis. However, some degree of frontal bone retrusion remained, for which the patient wanted to undergo further correction. Insertion of a 3D-printed PCL/ß-TCP implant was planned. Before surgery, CT images were obtained and imported into a 3D modeling software. The implant shape was designed so that the cranial axial section became an oval shape considering occipital bone contour. Care was taken not to create a stepping where the implant met the temporal bone. The PCL/ß-TCP implant was printed using a

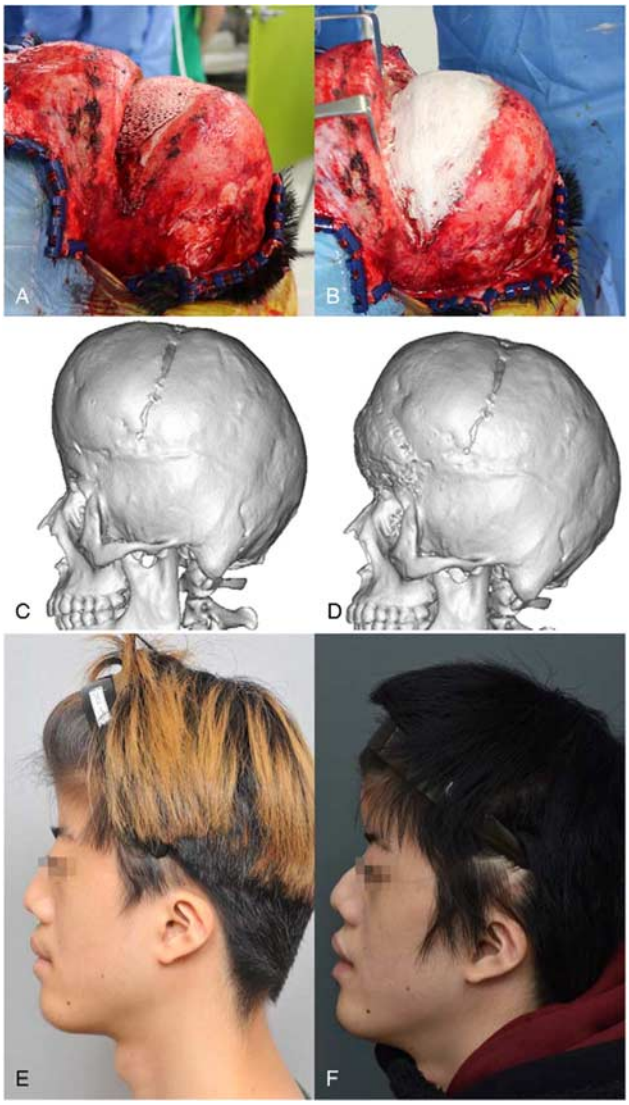

FIGURE 2. A 20-year-old male patient with cranioplasty for bilateral forehead retrusion. (A) Intraoperative placement of PCL/ß-TCP implant. (B) The PCL/ß-TCP implant after hydroxyapatite pasting. (C) Preoperative CT and (D) postoperative 6months follow-up CT demonstrate frontal contour improvement. (E) Preoperative image showing bilateral frontal retrusion. (F) Postoperative image showing an improved frontal shape with a smooth contour. CT, computed tomography; PCL, polycaprolactone; ß-TCP, betatricalcium phosphate.

3D printer according to the simulated design. An incision was created on the previous bicoronal incisional scar, and subperiosteal dissection was performed until the supraorbital rim was reached. A hydroxyapatite paste was applied to the implant surface, and the implant was then placed in the subperiosteal pocket. Proper placement of the implant was confirmed by assessing its fit to the bone contour. At 2 weeks after surgery, the soft tissue volume increased to 20.7 cm^3, which was maintained until the 6-month follow-up. At the 6-month follow-up, his forehead contour improved well, and the edge of the implant could not be discerned (Fig. 2).

Case 2

A 40-year-old male patient presented with forehead asymmetry. He had a history of frontal bone fracture, and some

FIGURE 3. A 40-year-old male patient with forehead asymmetry. (A) The implant was designed to cover the supraorbital and frontal regions. (B) The PCL/ß-TCP implant was placed on the left-side frontal bone. (C) Preoperative image showing left forehead deformity. (D) At 6 months of follow-up, the forehead contour appears to be improved with a smooth implant-bone interface. CT, computed tomography; PCL, polycaprolactone; ß-TCP, betatricalcium phosphate.

degree of forehead asymmetry remained. Cranioplasty was planned using a 3D printed PCL/ß-TCP implant to improve the forehead contour. The implant was designed to cover the left supraorbital and frontal area. The incision was made on the previous bicoronal incisional scar, and the implant was placed under the periosteum, and subperiosteal dissection was performed until the supraorbital rim was reached. At 2 weeks after surgery, the soft tissue volume increased to 7.5 cm^3, maintained until the 6-month follow-up. Six months after the surgery, the forehead and supraorbital contour were improved and became symmetric to the contralateral side (Fig. 3).

Case 3

A 62-year-old male patient presented with occipital bone asymmetry. Since the left side of the occipital bone was depressed, the patient complained that he could not align his head straight when lying down to sleep. Preoperative CT images were obtained, and 3D modeling was conducted as in case 1. The implant was designed to cover the left occipital region and to be symmetric with the right side. A vertical incision on occipital area was created, and subperiosteal dissection was performed to make space for implant insertion. A hydroxyapatite paste was applied to the PCL/ß-TCP implant surface and placed in the pocket. The soft tissue volume increased to 53.3 cm^3 at 2 weeks after surgery and slightly decreased to 48.7 cm^3 at 6 months of follow-up, as swelling diminished. At the 6-month follow-up, his occipital contour was symmetric, and the edge of the implant was not remarkable upon palpation (Fig. 4).

DISCUSSION

The ideal materials for cranioplasty require many characteristics, such as viability that allows growth, resistance against in-

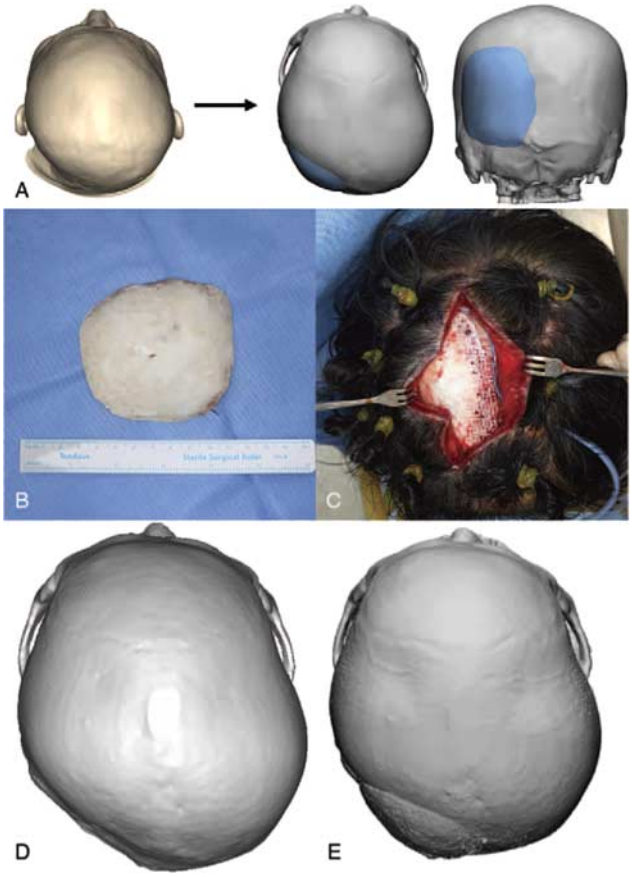

FIGURE 4. A 62-year-old male patient with asymmetry in the occipital area. (A) Preoperative simulation of implant design. (B)Three-dimensionally printed PCL/ ß-TCP implant. (C) Intraoperative placement of PCL/ß-TCP implant on the occipital bone. (D) On the preoperative CT image, the left occipital area appears depressed. (E) On postoperative CT image of implant placement in the left occipital area, the soft tissue contour appears symmetric. CT, computed tomography; PCL, polycaprolactone; ß-TCP, beta-tricalcium phosphate.

fection, and ready availability.[10] They should also be biocompatible, biologically inert, osteoconductive, and osteoinductive.[11,12] As materials are degraded, toxic decompositions or inflammatory triggering factors should not be released, and eventually, the material should be replaced by normal bone.[13,14] Moreover, the materials for cranioplasty need rigidity for mechanical strength and, at the same time, should be easy to manipulate in a patient-specific design.[2] Unfortunately, the currently available materials do not satisfy all the ideal characteristics.

The materials currently used in cranioplasty include bone ceramic (ie, hydroxyapatite), bone cement (ie, PMMA), and polymeric materials (ie, PEEK and porous polyethylene).[15,16] Although hydroxyapatite is easy to mold and allows osteoconduction, it has low mechanical strength postoperatively for 12 months.[10] Polymethylmethacrylate is a moldable acrylic resin with good rigidity and biocompatibility but cannot allow cell infiltration and interaction with the surrounding tissues.[13,17] Polyetheretherketone has a similar stiffness to the cortical bone and good biocompatibility but does not exhibit osteoconductivity. Polyetheretherketone and PMMA are associated with inflammation and implant rejection and can lead to wound healing problems.[18]

Meanwhile, PCL, a hydrophobic, semicrystalline polymer, is a biodegradable polymeric material with appropriate mechanical strength and durability.[9] It undergoes slow degradation over 2 to 4 years and yields less foreign body reaction as compared to other biodegradable materials, including polydioxanone, poly-D-lactide, and poly-L-lac- tide.[20] Its degradation rate can be controlled physically and chemically to suit a specific anatomic site.[21] Moreover, the mechanical properties are controllable by varying mix ratios of PCL and ß-TCP.[7] Since PCL has good biocompatibility, osteoconductivity, and mechanical strength, it can be an alternative material for cranioplasty. Although there have been no clinical reports on PCL/ß-TCP use in cranioplasty, its advantages have been described in several animal studies. Le et al[22] demonstrated high rates of bone ingrowth in a rat calvarial defect, which was reconstructed using a PCL/ß-TCP implant. Schantz et al[23] reported osteogenesis after PCL implant insertion and mesenchymal progenitor cell seeding in a rabbit calvarial defect model. In a clinical study where the orbital floor was reconstructed using a PCL implant, the implant exhibited good mechanical strength and biocompatibility.[24]

The use of patient-specific implants is undoubtedly advantageous in cranioplasty. This technology allows alloplastic implants to be tailored to the cranial defect and permits better fitting. Through 3D modeling and 3D printing technology, better results in restoration of the contour can be achieved, and the operation time can be shortened.[25,26] The process of designing and fabricating implants for cranioplasty has greatly evolved in the past few decades. In the early stages of cranioplasty using alloplastic materials, intraoperative molding has been conducted by pouring liquid PMMA or hydroxyapatite paste into the defect. This early-stage method required a long operation time and was associated with high risks of infection. Thereafter, the recent advances in 3D biomodelling and computer-aided design/computer-aided manufacturing have led to the production of customized implants for cranioplasty to overcome the previous limitations of intraoperative molding.

Several materials, including PMMA, PEEK, hydroxyapatite, porous polyethylene, and titanium, have been reported to be manufactured with a patient-specific design.[27,28] Turgut et al[26] reported the surgical outcomes in patients who underwent computer-aided design/computer-aided manufacturing-based PMMA implant reconstruction of craniofacial defects. They demonstrated that prefabricated PMMA implants could be used safely and achieve better results in restoring cranial contour. Staffa et al[29] conducted cranial reconstruction using patient-specific hydroxyapatite ceramic implants and demonstrated a satisfactory outcome with a good cosmetic appearance at the 2-year follow-up. However, all these studies produced their implants by casting materials in the 3D-printed mold.

Thus, 3D-printed PCL/ß-TCP implants could overcome the previously noted limitations of traditional implants for cranioplasty. They can be fabricated to fit the defect site perfectly, leading to a more satisfactory outcome. These advantages have prompted 3D- printed implants to be investigated as patient-specific implants in cranioplasty. These 3D-printed PCL/ß-TCP implants are different from previous customized implants in that a 3D printer directly produces them. Because PCL has a low melting point (59–64°C), it facilitates 3D printing. Fused deposition modeling is a 3D printing technology where melt extrusion of a powder is used to print implants according to a designed pattern. It has been developed as a promising method for PCL scaffold microstructuring.[9,30]

The composition of PCL implants can be adjusted to have appropriate strength and resorption rate according to the implantation site. Their mechanical strength, osteo-

conductivity, and degradation rate are controlled by adjusting the porosity and mixture ratio of PCL/ß-TCP. The osteoconductive property of PCL can be further enhanced by adding ß-TCP. When PCL is combined with hydroxyapatite, hydroxyapatite decreases the hydrophobic property and subsequently enhances the osteoconductivity of PCL, facilitating osteogenic differentiation.[31] Therefore, the addition of hydroxyapatite and ß-TCP to PCL implants can increase osteoconduction and osteogenic differentiation instead of enhancing the mechanical strength of the scaffold.

In this study, complications, including allergic reaction, infection, and rejection, were not observed during the 6-month followup; this indicates that the implants had comprehensive biocompatibility. Additionally, the cranial symmetry achieved immediately after surgery was well maintained without implant dislocation or fracture until 6 months of follow-up. Thus, the mechanical properties of the PCL/ß-TCP implants were sufficient for these implants to be used in cranioplasty. The cosmetic results, including the symmetry and smoothness, were satisfactory in most patients during the follow-up period, which is a strong advantage of 3D-printed implants. Favorable safety and aesthetic results were achieved using the 3D-printed PCL/ß-TCP implants.

The efficacy and safety of 3D-printed PCL implants have been described in various fields in the literature. Jung et al[32] reported a microtia case successfully reconstructed using a 3D-printed PCL implant. They found that a 3D-printed PCL implant could overcome the earlier limitations of auricular reconstruction (ie, donor site morbidity and cartilage warping), and combining chondrogenic cell culture with a 3D-printed implant could provide an alternative for ear reconstruction. Park et al[20] suggested that a PCL implant for rhinoplasty is safe and effective for maintaining the nasal volume without a foreign body reaction.

This study has a few limitations. There was only 1 case where an implant was used in the cranial defect area, whereas an onlay graft was mostly used to correct cranial asymmetry. Because cranioplasty can also be performed for cranial defects, additional research on osteointegration between the implant and surrounding bone is required. Moreover, this study included only a small number of cases, and there was no control group for comparison of the outcomes. Therefore, the efficacy and safety of the implants might have been underestimated or overestimated. A large-scale outcome study based on a comparison between PCL/ß-TCP and other materials is warranted in the future. Nevertheless, to the best of our knowledge, this study is the first to report the efficacy and safety of 3D-printed PCL/ß- TCP implants in cranioplasty. Given its patient-specific property, sufficient mechanical profile, ease of use, well-documented clinical safety, and good biocompatibility, PCL/ß-TCP is an optimal alternative for conventional alloplastic materials in cranioplasty.

CONCLUSIONS

To summarize, 3D-printed PCL/ß-TCP implants are an excellent material for cranioplasty, and a favorable cosmetic outcome can be achieved. Specifically, these novel PCL/ß-TCP implants have good biocompatibility and mechanical strength without any postoperative foreign body reaction. Polycaprolactone/ß-TCP implants can then be a good alternative to conventional alloplastic materials in cranioplasty and might enable patient-specific reconstruction with enhanced aesthetic outcomes.

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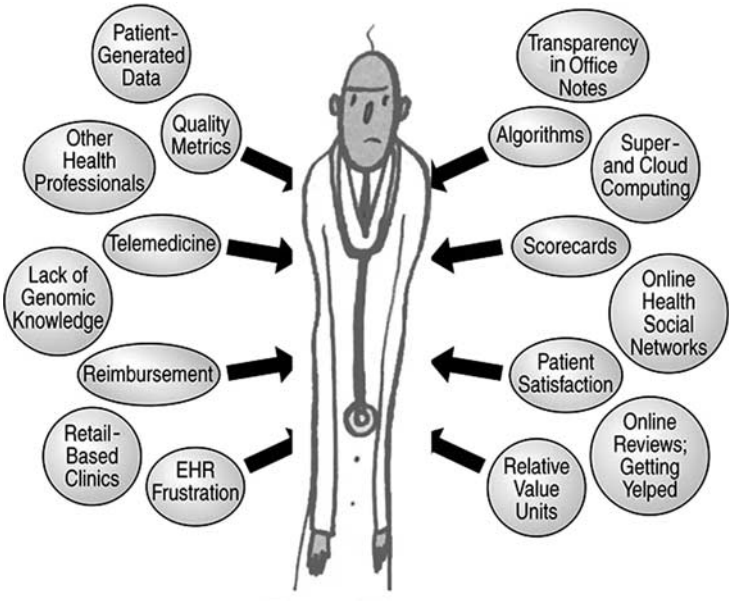

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