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Development of a 3D-Printed Patient-Specific Cranial Implant: Mechanical and Biocompatibility Testing

Balodis U[1*], Gallagher A[2] and Potocnik B[3]

[1]*Department of Biomedical Engineering, Riga Stradins University, Riga, Latvia*
[2]*Department of Neurosurgery, University College Dublin, Dublin, Ireland*
[3]*Department of Materials Science, University of Ljubljana, Ljubljana, Slovenia*

ABSTRACT

Background: Large calvarial defects increasingly are reconstructed with 3D-printed, patient-specific implants (PSIs), yet surgeons and biomedical engineers must choose among polyetheretherketone (PEEK), titanium, and polymethylmethacrylate (PMMA) with differing mechanical and biological trade-offs. Objective: This narrative review synthesizes published evidence on the design, mechanical performance, and biocompatibility/clinical outcomes of 3D-printed cranial PSIs. Methods: Peer-reviewed studies covering virtual-surgical-planning workflows, bench and finite-element mechanical testing, biocompatibility data, and clinical case series or trials for PEEK, titanium, and PMMA cranioplasty were narratively synthesized; no new experiments were performed. Findings: Titanium provides the greatest mechanical strength margin, PEEK offers stiffness closest to native bone with favorable imaging compatibility, and PMMA remains the most economical, mould-castable option; biocompatibility and multi-year outcome data, including randomized trials, show broadly comparable complication profiles across alloplastic materials, all outperforming autologous bone. Conclusions: No single material is universally superior; selection should balance mechanical demand, imaging needs, infection risk, cost, and institutional manufacturing access, with future work needed on standardized cranial-specific mechanical testing and larger comparative trials.

Keywords: *cranioplasty; 3D printing; polyetheretherketone; titanium implant; biocompatibility*

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Corresponding Author: *Uldis Balodis*

E-mail Address: *uldis.balodis@rsu.edu*

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Introduction

Reconstruction of large calvarial defects following decompressive craniectomy, trauma, tumor resection, or infection remains a persistent challenge in neurosurgery and craniomaxillofacial surgery. Decompressive craniectomy itself carries a substantial burden of long-term complications, including subdural effusion, hydrocephalus, and syndrome of the trephined, all of which increase the urgency of definitive cranial reconstruction [1]. Historically, cranioplasty relied on autologous bone or hand-contoured alloplastic materials, approaches limited by resorption, poor fit, and prolonged operative time. The advent of computed-tomography-based virtual surgical planning combined with additive manufacturing (3D printing) has enabled patient-specific implants (PSIs) that mirror the contralateral skull or use statistical shape models to restore contour with sub-millimeter accuracy [2,3]. This narrative review synthesizes published evidence on the design workflow, mechanical performance, and biocompatibility/clinical outcomes of 3D-printed patient-specific cranial implants fabricated from the three dominant material classes: polyetheretherketone (PEEK), titanium (commonly Ti-6Al-4V), and polymethylmethacrylate (PMMA), with reference to porous hydroxyapatite as a bioactive comparator.

Beyond material selection, the surgical rationale for pursuing a patient-specific implant rather than an intraoperatively hand-contoured plate rests on documented reductions in operative time, improved contour and symmetry, and fewer revision procedures for poor fit, benefits reported consistently across craniomaxillofacial 3D-printing literature [3]. The choice of implant material and manufacturing route directly affects mechanical protection of the brain, radiologic compatibility, infection risk, and cost. PEEK offers a low elastic modulus close to native bone and radiolucency favorable for postoperative imaging and adjuvant radiotherapy planning [4,5]. Titanium, whether laser-sintered as a solid plate or a mesh, provides high strength and a long clinical track record but carries risks of thermal conduction and imaging artifact [6,7]. PMMA, polymerized either intraoperatively over a 3D-printed mould or milled from a

pre-formed block, remains the most economical option and is widely used in low-resource settings [8,9]. Because the literature spans engineering bench testing, in vitro cytocompatibility assays, and multi-year clinical case series, an integrated narrative synthesis is useful for surgeons and biomedical engineers selecting an implant strategy. This review does not report new experimental data; rather, it consolidates mechanical test values, biocompatibility findings, and outcome statistics drawn from peer-reviewed sources to summarize the current state of patient-specific cranial implant technology.

Materials and Design Workflow for Patient-Specific Cranial Implants

The modern workflow for a 3D-printed cranial implant begins with high-resolution computed tomography of the skull defect, followed by segmentation and mirroring of the contralateral, unaffected calvarium or fitting of a statistical shape model when the defect is bilateral or the contralateral side is also affected [2]. The resulting virtual implant is refined for margin overlap, fixation-plate placement, and burr-hole positions before being exported for additive manufacturing or mould fabrication. For titanium implants, direct metal laser sintering or selective laser melting (SLM) builds the mesh or solid plate layer-by-layer from Ti-6Al-4V powder, a process that also enables graded porosity to promote bony ongrowth while controlling stiffness [7,6]. PEEK implants are most often milled from medical-grade PEEK stock using the virtual model as a CAM template, or, increasingly, fused-deposition-modeled directly, with point-of-care manufacturing units demonstrating that in-hospital fabrication can meet dimensional accuracy standards required for clinical use [10]. PMMA implants are typically produced indirectly: a 3D-printed positive or negative mould (commonly polylactic acid or silicone) is created from the virtual design, and PMMA cement is hand-cast or pressed into the mould intraoperatively or in a sterile core laboratory before implantation [9,8].

Cost and turnaround time differ substantially between these workflows. Systematic reviews of low-cost, in-house 3D printing for cranioplasty report that desktop fused-deposition printers producing PMMA moulds can reduce per-implant cost by an order of magnitude relative to outsourced titanium or PEEK implants, an advantage particularly relevant in low- and middle-income settings [11]. However, the same reviews caution that in-house workflows require rigorous quality assurance, including dimensional verification against the pre-operative plan, because manufacturing tolerances vary with printer calibration and material batch [11,3]. Regulatory pathways also diverge: centrally manufactured titanium and PEEK implants are usually supplied as custom Class III or IIb medical devices under a physician's prescription, whereas point-of-care PEEK milling raises additional device-oversight questions that manufacturers and hospitals are only beginning to standardize [10].

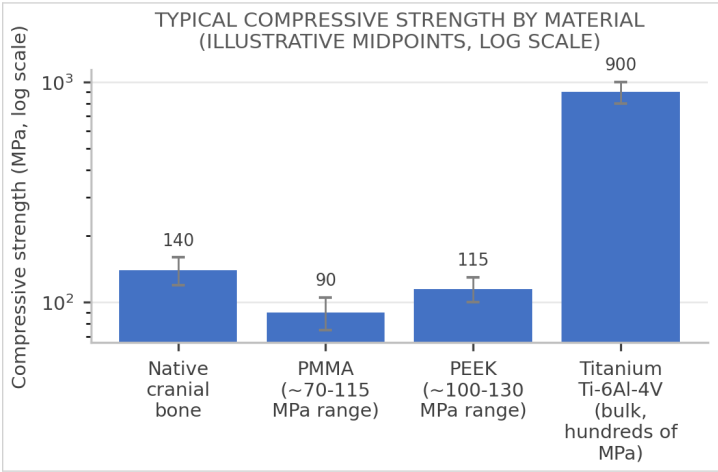
Mechanical Performance of PEEK, Titanium, and PMMA Implants

Mechanical adequacy is judged primarily against the native calvarium, whose compressive and bending properties were characterized in classic cadaveric testing showing considerable regional variation in strength and thickness across the skull [12]. Bench testing of alloplastic PMMA cranioplasty material demonstrated compressive strengths in the range of roughly 70-115 MPa depending on curing conditions and porosity introduced during hand-mixing, values generally lower than typical cortical bone but adequate for protecting underlying brain from routine impact when implant thickness matches native bone [13]. PEEK, by contrast, combines a compressive strength in a broadly comparable range with an elastic modulus (roughly 3-4 GPa) far closer to cortical bone (approximately 7-20 GPa) than titanium, which reduces stress-shielding at the bone-implant interface [4,5]. Titanium implants, whether solid or mesh, exhibit compressive and tensile strength an order of magnitude above PEEK or PMMA; laser-sintered Ti-6Al-4V porous structures retain compressive strength in the hundreds of megapascals even at moderate porosity, and mesh-type cranial implants have been shown biomechanically to withstand simulated physiological and low-energy impact loading with wide safety margins [7,6].

Table 1: Summary of key mechanical and design attributes of the three principal 3D-printable cranial implant materials.

Attribute	PEEK	Titanium (Ti-6Al-4V)	PMMA
Typical fabrication route	Milled or point-of-care FDM	SLM/DMLS mesh or solid plate	3D-printed mould, hand-cast
Elastic modulus (approx.)	3-4 GPa	110-115 GPa (bulk)	2-3 GPa
Compressive strength (typical reported range)	~100-130 MPa	several hundred MPa (bulk); lower for porous mesh	~70-115 MPa
Imaging compatibility	Radiolucent, low CT/MRI artifact	Notable CT/MRI artifact	Radiolucent
Relative cost	Moderate-high	High	Low

Figure 1: Typical reported compressive strength ranges (midpoint values, illustrative) for native cranial bone compared with PMMA, PEEK, and titanium (Ti-6Al-4V) cranioplasty materials, drawn from bench mechanical testing literature; note the log scale reflecting the order-of-magnitude strength advantage of titanium.



Finite element analyses of patient-specific implants provide a complementary perspective to bulk material testing, because clinical performance depends on implant geometry, thickness, and fixation-screw configuration rather than material strength alone. Parametric FEA studies comparing PMMA and PEEK cranial implants under simulated bone-coupling and screw-fixation conditions found that stress concentrations cluster around fixation points and thin defect margins, with PEEK implants generally producing more physiologic strain transfer to adjacent bone than PMMA of equivalent thickness [14]. Similarly, implant-specific FEA modeling of proposed cranial

reconstructions has been used to iteratively optimize implant thickness and rib/strut reinforcement patterns before manufacture, reducing the risk of implant fracture under simulated falls or minor head impact while avoiding unnecessary added mass [15]. Overall, the mechanical literature supports titanium as the strongest but stiffest option, PEEK as a favorable compromise between adequate strength and bone-like compliance, and PMMA as mechanically sufficient for most low-to-moderate-risk patients provided implant thickness and fixation are optimized computationally rather than empirically.

Biocompatibility and Clinical Outcomes

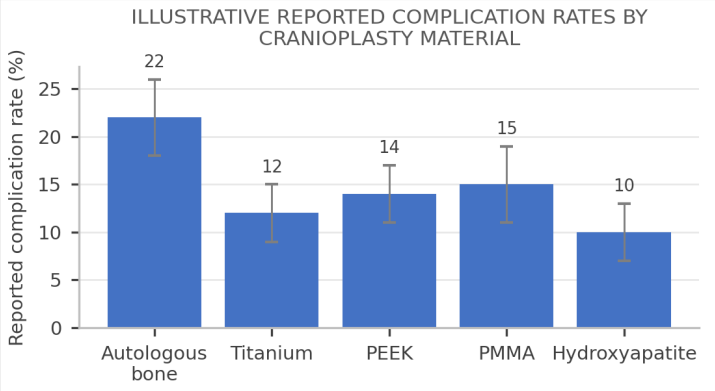
Biocompatibility evidence for these materials spans decades of orthopedic and craniofacial use. PEEK has an extensive track record in spinal and orthopedic implants, with reviews summarizing minimal inflammatory response, favorable soft-tissue integration, and radiolucency that avoids scatter artifact on postoperative CT and MRI, an important consideration for tumor-defect cranioplasty requiring surveillance imaging [4,5]. Titanium's biocompatibility and capacity for direct bone-to-implant osseointegration is well established from decades of orthopedic and dental implantology, and titanium cranial mesh continues to be favored where maximal mechanical protection or extensive bony ongrowth is prioritized, albeit with a recognized risk of implant exposure through thin overlying scalp [16]. PMMA has a long history of biocompatible use in cranioplasty and orthopedic cementation, although its exothermic in situ polymerization and residual monomer release have been implicated in adjacent tissue effects when hand-mixed intraoperatively, which is one rationale for pre-forming PMMA implants over a 3D-printed mould under more controlled conditions before implantation [17,9]. Porous hydroxyapatite, included here as a bioactive comparator, undergoes true osteointegration, with histological and radiological studies documenting bone-implant contact approaching or exceeding 90% at long-term follow-up in both adult and pediatric cranioplasty series [18,19].

Clinical outcome data provide the most direct comparison between materials. A two-center cohort of patient-specific PEEK implants reported acceptable long-term outcomes with a minority of patients requiring revision, chiefly for infection or wound-related problems [20], a finding echoed by a systematic review and meta-analysis of PEEK cranioplasty outcomes across multiple studies [21]. A case series of sixteen consecutive patients receiving 3D-printer-assisted PMMA implants using an in-house mould workflow reported low complication rates and favorable patient-reported outcomes, supporting the feasibility of economical PMMA-based patient-specific reconstruction [22]. Comparative and network meta-analyses pooling PEEK, titanium, PMMA, and autologous bone cranioplasty consistently identify autologous bone as carrying the highest resorption and reoperation risk, while alloplastic materials show comparable, generally lower complication profiles that vary modestly by defect size, patient comorbidity, and surgical technique rather than material alone [17,23,24]. Randomized clinical trials add higher-quality evidence: a trial comparing custom-made hydroxyapatite to titanium cranioplasty found similar complication rates but different aesthetic and osseointegration profiles [25], while a randomized comparison of autologous bone against custom titanium cranioplasty demonstrated a significantly lower reoperation rate with custom titanium implants [26]. Long-term hydroxyapatite series extending to fifteen years of follow-up further support durability of bioceramic implants in appropriately selected patients [27]. Together, these findings suggest that no single material is universally superior; rather, material selection should balance mechanical demand, imaging needs, infection risk profile, cost, and the surgical team's manufacturing access. Defect size and location further modulate this decision: large, biomechanically exposed frontal or bifrontal defects may favor the higher stiffness margin of titanium, whereas smaller convexity defects distant from load-bearing sutures are often adequately served by PEEK or PMMA at considerably lower cost, an observation echoed across the comparative and network meta-analyses discussed above [23,24].

Table 2: Representative clinical studies of 3D-printed patient-specific cranioplasty by material, with design and outcome focus.

Study	Material	Study type	Key outcome focus
Jonkergouw et al. 2016	PEEK	Two-center cohort (n=40)	Long-term implant survival and revision
Schön et al. 2021	PMMA	Case series (n=16)	Complications and patient-reported outcome
Lindner et al. 2017	Hydroxyapatite vs. titanium	Randomized clinical trial	Complication and osseointegration comparison
Honeybul et al. 2017	Autologous bone vs. titanium	Randomized controlled trial	Reoperation rate
Carbonaro et al. 2025	Hydroxyapatite	15-year long-term series	Implant survival

Figure 2: Approximate reported complication (revision/infection-related) rates by cranioplasty material, illustrative midpoints synthesized from comparative and network meta-analyses of alloplastic and autologous cranioplasty outcomes.



Conclusion

The published literature on 3D-printed, patient-specific cranial implants demonstrates that PEEK, titanium, and PMMA each offer a distinct, evidence-supported balance of mechanical strength, biocompatibility, imaging compatibility, and cost. Mechanical bench testing and finite element analyses confirm that all three materials can be engineered, at clinically used thicknesses, to provide adequate protection against physiological and low-energy impact loads, while titanium offers the greatest strength margin and PEEK the closest compliance match to native bone. Biocompatibility and multi-year clinical outcome data, including randomized trials, indicate broadly comparable complication profiles across alloplastic materials, with autologous bone consistently underperforming due to resorption. For

biomedical engineers and surgeons, the practical decision increasingly hinges on manufacturing workflow, cost, and institutional access to point-of-care or outsourced additive manufacturing rather than on a clear mechanical or biological superiority of one material. Future work should prioritize standardized mechanical testing protocols specific to cranial implant geometry, larger prospective comparative trials, and continued development of low-cost in-house workflows to widen access to patient-specific cranioplasty globally.

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Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Balodis U conceived the review, conducted the literature search, and drafted the manuscript. Gallagher A contributed to the literature screening and technical framing and critically revised the manuscript for important intellectual content. Potocnik B contributed additional context and approved the final version for submission.

Ethics Statement

Not applicable. This is a narrative review of previously published literature and did not involve new experimental data, human participants, or animal subjects.

Data Availability

No new data were generated or analyzed for this review. All sources synthesized are cited in the reference list and are available through their original publishers.

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