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Clinical implementation of an EU MDR-compliant point-of-care manufacturing framework for patient-specific 3D-printed PEEK implants in craniomaxillofacial reconstruction

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Abstract

Background Point-of-care (POC) three-dimensional (3D) printing of medical devices presents a paradigm shift in personalized medicine, yet clinical implementation of polyetheretherketone (PEEK) implants remains limited by regulatory, technical, and quality assurance challenges. Traditional external manufacturing timelines of 2–6 weeks constrain immediate reconstruction capabilities, particularly in trauma and oncologic cases requiring rapid intervention. Structured frameworks enabling MDR-compliant hospital-based production of implantable devices remain limited in the literature.

Methods We implemented a comprehensive European Union Medical Device Regulation (EU MDR) 2017/745 Article 5(5)-compliant POC manufacturing framework incorporating an electronic quality management system aligned with ISO 13,485, a manufacturing execution system enabling end-to-end device traceability, risk management, process validation, biocompatibility evaluation, and integrated post-market surveillance. Medical-grade PEEK was processed using validated high-temperature specialised material extrusion 3D printers.

Results Representative clinical applications of the EU MDR-compliant point-of-care manufacturing framework are illustrated in two anatomical contexts: (1) a POC 3D-printed PEEK cranial implant and (2) a POC 3D-printed PEEK facial implant. Manufacturing turnaround from image acquisition to sterile delivery was operationally achievable within 3–5 days. The patient-matched implants demonstrated accurate anatomical fit without intraoperative modification, with no major device-related complications observed. The framework has supported the production of over 40 + POC 3D-printed PEEK implants at the index institution and has since been adopted at multiple European centres, demonstrating transferability beyond the index case series.

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Conclusions This work describes a validated EU MDR Article 5(5)-compliant framework for hospital-based production of patient-matched 3D-printed PEEK implants, demonstrated across cranial and facial reconstruction. Early clinical results support safety and feasibility, with end-to-end manufacturing achievable within a week, enabling flexible surgical planning. The framework provides a replicable pathway for regulated POC implant production, with multi-centre adoption and long-term outcome surveillance as critical next steps.

Keywords 3D printing, Point-of-care manufacturing, PEEK, Craniomaxillofacial reconstruction, Medical device regulation, Additive manufacturing

Background

Point-of-care (POC) additive manufacturing (AM) is a paradigm shift in medical 3D printing, enabling healthcare facilities to produce personalised medical devices directly at the treatment site. This approach integrates design and manufacturing within healthcare institutions, enabling iterative design refinement through direct surgeon-engineer collaboration, optimization of complex patient-specific geometries, and on-demand manufacturing for urgent clinical scenarios. Despite its promise, POC implementation remains constrained by regulatory complexities, reimbursement issues, quality assurance requirements, and technical barriers [1, 2]. Increasing regulatory scrutiny has rendered informal production models progressively untenable, reinforcing the need for structured, validated manufacturing frameworks for hospital-based device production.

Craniomaxillofacial (CMF) reconstruction is among the most demanding surgical fields, requiring precise restoration of complex anatomical structures with both functional and aesthetic outcomes [3, 4]. Conventional reconstruction strategies rely on multiple staged surgical procedures, autologous grafts with associated donor site morbidity, or stock implants that fail to replicate patient-specific anatomy adequately [5]. Translating new manufacturing technologies into tangible clinical benefits remains a central challenge.

Polyetheretherketone (PEEK) has emerged as a preferred biomaterial for CMF reconstruction, offering bone-like mechanical properties (elastic modulus 3–4 GPa), excellent biocompatibility, and radiolucency for artifact-free imaging and reduced infection risk compared to metallic implants [6, 7]. Traditional production of personalized PEEK implants typically relies on external manufacturing workflows inherent to commercial patient-specific implant production models, which involve multi-step design, manufacturing, and logistical processes [8]. These pathways are commonly associated with lead times extending over multiple weeks, depending on device complexity, production scheduling, and administrative factors. In addition to manufacturing lead times, administrative processes such as insurance authorization and reimbursement approval may substantially influence clinical timelines within European healthcare systems. High-temperature 3D printing has enabled PEEK processing at temperatures above 400 °C, creating opportunities for POC implementation under regulatory frameworks such as the European Union Medical Device Regulation (EU MDR) 2017/745 [9, 10]. Yet, clinical translation requires navigating regulatory complexity through validated digital manufacturing workflows and quality management systems.

The unique requirements of CMF reconstruction, including thin-section geometry, complex surface curvatures, and strict aesthetic demands, present challenges that make this a particularly suitable context for evaluating POC manufacturing workflows [11, 12]. Patient-specific PEEK implants produced by commercial vendors are clinically established; however, comprehensive EU MDR-compliant frameworks for hospital-based 3D printing of PEEK implants remain limited in the literature. This clinical implementation builds upon prior investigations of POC manufactured PEEK implants, which provided foundational technical evidence regarding dimensional accuracy and sterilization-related considerations and informed the validation principles adopted for regulated clinical deployment [1, 8]. Recent reports have demonstrated the technical feasibility of POC 3D-printed PEEK implants for cranioplasty [13]. However, detailed descriptions of regulatory-compliant quality management, process validation, and EU MDR implementation frameworks remain limited, which represent the primary focus of the present work.

Here, we present a clinical implementation report describing an EU MDR-compliant POC manufacturing framework enabling hospital-based production of patient-matched PEEK implants for CMF reconstruction. The framework is illustrated through two representative applications: (1) a patient-matched 3D-printed PEEK cranial implant and (2) a patient-matched 3D-printed PEEK facial implant. This work focuses on the regulatory, quality management, and manufacturing workflows required for EU MDR Article 5(5)-compliant production of POC implants. The clinical examples are provided to demonstrate the practical application of the framework across distinct anatomical indications. The described workflow integrates regulatory compliance, validated manufacturing protocols, and clinical implementation considerations, providing a practical pathway for translating POC AM into routine clinical practice and supporting broader

adoption of hospital-based personalized 3D-printed medical device production.

Methods

EU MDR-compliant POC regulatory framework

The POC manufacturing process was developed in accordance with the EU MDR 2017/745, Article 5(5), which permits health institutions to manufacture devices for internal use under defined conditions. Although International Organization for Standardization (ISO) 13,485 certification is not mandatory, the quality management system (QMS) framework was developed in alignment with ISO 13,485 principles to ensure regulatory adherence across the device lifecycle. Formal ISO 13,485 certification was not pursued, as it is not required for health institution manufacturing under EU MDR Article 5(5).

The QMS (POC APP AG, Basel, Switzerland) incorporated risk management according to ISO 14,971, design and development controls, clinical evaluation, process validation, biocompatibility evaluation according to ISO 10993-1 [14], post-market surveillance (PMS), production monitoring, and material handling procedures. The QMS was electronically integrated with a Manufacturing Execution System (MES) to enable complete traceability from raw material to sterilized implant, ensuring compliance with MDR Annex I General Safety and Performance Requirements (GSPR). The MES utilized in this framework (POC APP Online, POC APP AG, Basel, Switzerland) is a proprietary software platform configured to support device traceability, documentation control, and production workflow management within the eQMS environment.

Risk management covers the full device lifecycle, including application risks related to clinical use, design risks related to complex anatomical and technical conformity, and production risks identified and mitigated throughout the manufacturing process, from image acquisition to delivery in the operating room. Critical process parameters were determined, validated, and continuously monitored to maintain reproducibility and quality, including biocompatibility. Systematic quality control included dimensional verification, surface inspection, and biocompatibility testing of representative samples processed through the complete workflow in accordance with ISO 10993-1. Steam sterilization was performed at 134–137 °C for 18 min with a subsequent drying cycle of 30–40 min, following ISO 17665-1 standards [15]. Sterilization validation performed under predefined worst-case conditions confirmed retention of relevant mechanical properties and dimensional stability, consistent with prior technical investigations. PMS activity was integrated into the framework, including structured surgeon feedback questionnaires, adverse event monitoring and reporting, and integration of clinical findings into ongoing risk management processes to support continuous improvement.

POC manufacturing and clinical implementation

Digital Workflow and Design Process: High-resolution computed tomography (CT) scans were acquired (Siemens SOMATOM scanner, Siemens Healthcare GmbH, Erlangen, Germany) with the following parameters: gantry tilt 0°, slice thickness 0.5 mm, matrix of 512 × 512 pixels with pixel size of 0.48 mm, and high-resolution bone reconstruction algorithm. These acquisition settings correspond to the standard clinical CMF imaging protocol used at our institution. CT datasets exported in Digital Imaging and Communications in Medicine (DICOM) format were processed using MIMICS Innovation Suite (v.25.0 for cranial case, v.26.0 for facial case; Materialise NV, Leuven, Belgium). Semi-automatic segmentation based on bone-specific Hounsfield unit (HU) thresholds enabled precise anatomical delineation. The 3D volumetric reconstructions underwent artifact correction and mesh smoothing to generate high-fidelity patient-specific anatomical models. Patient-matched implant designs were generated using a validated, indication-specific design framework for CMF reconstruction. The framework incorporates established CMF reconstruction principles, including contralateral mirroring, anatomical proportional analysis, predefined thickness distributions for functional performance, standardized fixation placement, and feathered edge transitions. Patient imaging data were used to adapt the validated design envelope to individual anatomy while maintaining all predefined design and performance constraints. Computer-aided design (CAD) software (Geomagic Freeform Plus v2022.0.34, Hexagon AB, Stockholm, Sweden) integrated with medical imaging platforms enabled iterative surgeon-engineer design review through haptic feedback, 3D visualization, and virtual fit testing against patient anatomy. Design adaptations were confined to parameters within the validated framework. Final designs underwent technical validation, including manufacturability assessment, AM support structure optimization, and file preparation with validated slicing parameters. Approved designs were converted and saved as standard tessellation language (STL) files for manufacturing.

Manufacturing process: Implants were fabricated from implantable medical-grade PEEK biomaterial (Vestakeep i4 G, Evonik Industries AG, Essen, Germany) using high-temperature material extrusion systems (EXT 220 MED, 3D Systems, Rock Hill, South Carolina, USA) operating within a validated manufacturing envelope defined to support the intended CMF applications. Material handling adhered to strict validated protocols, with storage at below 50% relative humidity and pre-drying at 100 °C for a minimum of 12 h to

eliminate residual moisture that could compromise print quality and mechanical properties. Incoming material inspection verified critical properties, including molecular weight, crystallinity, and moisture content. Validated printing parameters optimized for CMF applications included: nozzle temperatures exceeding 400 °C for optimal layer fusion, build chamber temperatures of 200–250 °C to minimize warping and thermal stress, and application-specific layer heights (0.3 mm for cranial implants requiring structural integrity, 0.28 mm for facial implants requiring enhanced surface finish). All implants were fabricated using predefined and validated printing parameters that were integrated into the design envelope governing both geometric and functional performance. These parameters included a 100% infill rectilinear pattern to ensure a fully solid internal structure. Support structures were oriented according to predefined rules to minimize contact with critical patient-facing surfaces while adequately supporting overhanging geometries within the validated design space. Build orientation was selected using standardized and verified orientation strategies developed for high-temperature PEEK processing, including minimization of support structure interaction with patient-facing surfaces, reduction of thermally induced distortion and residual stress, and preservation of dimensional accuracy in anatomically critical regions. Orientation selection was constrained to configurations demonstrated during validation to ensure stable thermal behavior during fabrication while facilitating controlled support removal and post-processing. Real-time process monitoring systems (LASAL Class 2, Sigmatek GmbH & Co KG, Lamprechtshausen, Austria) continuously tracked critical parameters during printing, including temperature stability and consistent layer adhesion. Fixation hole locations were predefined within the CAD design and manufactured as printed pilot indentations, with final hole preparation performed during post-processing. Following printing completion, specialized post-processing protocols included support structure removal using precision tools appropriate for PEEK's mechanical properties, followed by surface inspection. Steam sterilization was performed at 134 °C using standard hospital autoclave protocols (Getinge series, Getinge AB, Gothenburg, Sweden), validated to ensure sterility without compromising PEEK mechanical properties or dimensional stability. Sterilized implants were packaged in double-barrier sterile packaging and delivered to the surgical suite in coordination with scheduled procedures.

Clinical implementation: Patients were selected for POC PEEK implant applications based on clinical indication and anatomical complexity. Initial cases were strategically selected to demonstrate the manufacturing framework's versatility across cranial reconstruction and facial augmentation surgical procedures involving defect geometries unsuitable for stock implants. All patients provided comprehensive informed consent for the use of POC-manufactured, personalized implants. Intraoperatively, anatomical fit was verified, and fixation was achieved using titanium plates and non-locking screws. Postoperative management followed standard institutional protocols for reconstructive surgery. As part of an EU MDR-compliant PMS, structured surgeon feedback was collected through standardized questionnaires assessing POC manufacturing workflow acceptance, intraoperative implant handling characteristics, anatomical fit quality, and any major complications or adverse events encountered. Clinical follow-up relied on patient-initiated contact for problem reporting, supplemented by clinical and radiographic assessment when patients presented for care. All adverse events and clinical observations were documented and incorporated into the ongoing risk management process per MDR requirements.

Results

Two representative applications are presented to illustrate the clinical implementation of the EU MDR-compliant POC manufacturing framework. The cases, performed in August 2023 (cranial) and March 2025 (facial), demonstrate the application of the workflow across distinct CMF indications. Both applications demonstrated the successful translation of the AM framework into clinical practice.

Application 1: POC 3D-printed PEEK personalized cranial implant

Patient presentation

A 46-year-old male patient presented with a 14.9 cm × 12.1 cm full-thickness cranial defect 18 months following decompressive craniectomy with autologous bone reimplantation for traumatic brain injury. Neurological examination revealed a Glasgow Coma Scale (GCS) of 15 with a stable neurological status and no focal deficits. Clinical evaluation demonstrated progressive resorption of the reimplanted autologous bone flap with fragmented bone loosely attached to the cranial bone, dura, and residual titanium fixation plates. CT imaging demonstrated 30–40% bone flap resorption with irregular defect margins unsuitable for standard prefabricated implants. The defect required protective reconstruction for optimal functional outcomes and cosmetic restoration. Patient reported social limitations and anxiety related to visible deformity.

Design and manufacturing outcomes

High-resolution CT imaging captured detailed cranial anatomy and complex 3D defect characteristics spanning frontal, parietal, and temporal regions. Virtual

surgical planning utilized contralateral mirroring with manual refinement for symmetric reconstruction. Patient-matched design incorporated 3.5 mm thickness distribution optimized for protective functionality while minimizing implant weight. The implant measured 163.5 mm × 127 mm × 45.7 mm, with a surface area of 39,118.9 mm^2 and a volume of 71,140.2 mm^3, weighing 89.05 g (127.33 g total material, including support structures). Four titanium fixation plates with four 2.0 mm diameter screw holes each (16 total fixation points) were incorporated, with 8 mm length screws selected based on bone thickness at fixation sites. The fixation strategy was planned to optimize load distribution across the defect periphery while avoiding critical neurovascular structures. Build orientation was optimized to minimize support structure contact with patient-facing surfaces, facilitating smooth tissue integration. Manufacturing was completed within 24 h from design finalization, with actual print time of 5 h 10 min, followed by post-processing and quality control. Quality control confirmed defect-free implants with anatomical fit verified on physical models and approved by the surgeon. Following approval, implants underwent steam sterilization and were delivered sterile (Fig. 1A-F).

Clinical outcomes

Surgical placement via standard craniotomy approach included careful release of dural adhesions and removal of resorbed bone fragments and existing titanium plates. The implant demonstrated excellent anatomical fit with complete defect coverage requiring no intraoperative modifications (Fig. 1G). Operating time was 75 min with immediate restoration of cranial protection. The patient was extubated in the operating room and had an uncomplicated recovery. Postoperative edema resolved within 14 days, with pain well-controlled on standard analgesic protocol. Postoperative CT imaging demonstrated stable implant integration with cranial contour matching the virtual surgical plan. CT imaging confirmed secure fixation with intact bone-implant interface, no evidence of implant migration or subsidence, and no bone resorption at fixation points. Soft tissue integration remained stable, without palpable implant edges (Fig. 1H). Clinical follow-up at six months revealed no patient complaints, with the patient reporting a return to normal activities and satisfaction with functional and cosmetic restoration. No implant-related complications, infections, seroma formation, or adverse events were observed.

Application 2: POC 3D-printed PEEK personalized facial (Onlay) implant

Patient presentation

A 19-year-old male patient presented for chin enhancement six months after bimaxillary orthognathic surgery for correction of a Class II dentofacial deformity. Clinical assessment revealed 8–10 mm pogonion retrusion relative to aesthetic ideals, with residual horizontal chin deficiency despite successful orthognathic correction.

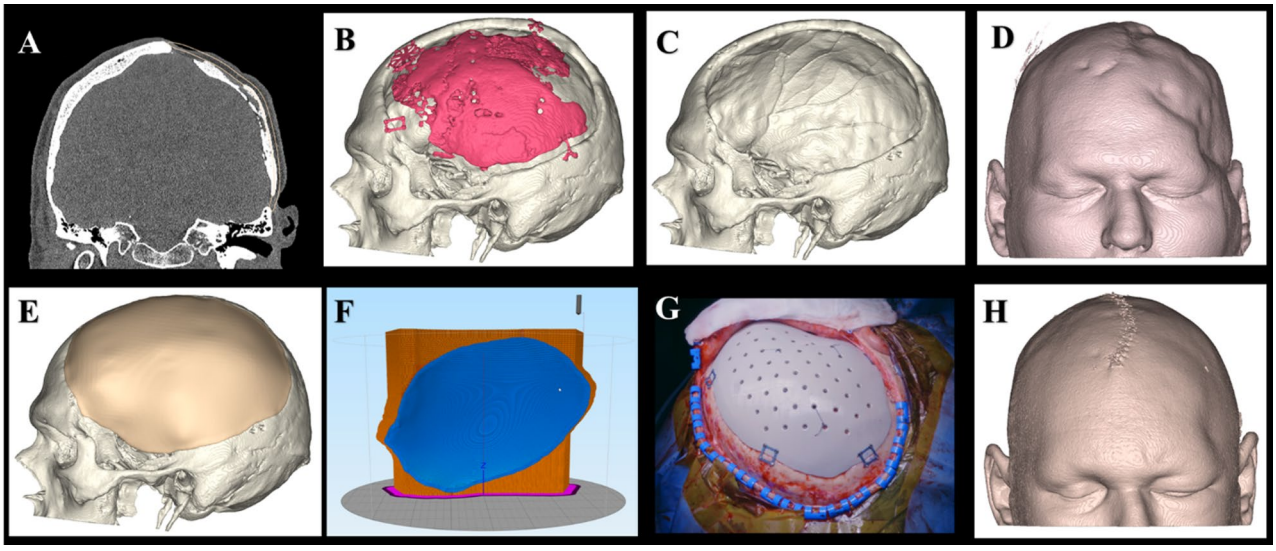

Fig. 1 Point-of-Care (POC) 3D-Printed Polyetheretherketone (PEEK) Cranial Implant for functional reconstruction. **A**: High-resolution computed tomography (CT) scan (axial view) demonstrating the cranial defect. **B**: Three-dimensional (3D) reconstruction delineating resorbed, compromised bone (pink) with pre-existing titanium fixation plates. **C**: Simulated virtual resection illustrating the intended extent of bone removal. **D**: Soft tissue profile depicting the underlying cranial defect. **E**: Virtual surgical planning with cranial implant design showing precise anatomical conformity and smooth transition zones with surrounding bone. **F**: Material extrusion additive manufacturing (AM) setup depicting print orientation and support structure configuration tailored for PEEK cranial implant. **G**: Intraoperative view of the POC-manufactured PEEK cranial implant demonstrating accurate fit. **H**: An immediate postoperative CT scan showed restored cranial contour and soft tissue profile following reconstruction

Preoperative CT imaging demonstrated a stable maxillomandibular relationship with a Class I occlusal relationship. Soft tissue evaluation demonstrated adequate chin pad thickness and absence of scar tissue. Complex anatomical requirements following orthognathic surgery necessitated patient-specific implant design to achieve optimal aesthetic integration with the newly positioned skeletal framework. Medical history was unremarkable, and there were no contraindications to implant placement.

Design and manufacturing outcomes

Patient-matched implant design was based on facial aesthetic analysis and symmetry evaluation. Preoperative assessment revealed 8–10 mm pogonion retrusion relative to aesthetic ideals. Iterative surgeon-engineer design collaboration resulted in four design versions to optimize aesthetic projection and soft tissue integration, achieving thickness variations from 0.6 to 0.8 mm at peripheral edges to 7.0 mm at maximum projection. The final implant measured 42.9 mm × 18.4 mm × 18 mm with a volume of 2814.4 mm^3 and weighed 3.71 g (17.5 g total material, including support structures and purging). Four 2.0 mm diameter cortical screw fixation points were incorporated for 12–14 mm length screws. Following final design approval, manufacturing was completed within 4 h from design finalization, with actual print time of 1 h, followed by post-processing and quality control. Quality control confirmed defect-free implants with anatomical fit verified on physical models and approved by the surgeon. Following approval, implants underwent steam sterilization and were delivered sterile (Fig. 2A-F).

Clinical outcomes

Surgical placement via intraoral approach demonstrated excellent anatomical fit requiring no intraoperative modifications (Fig. 2G-H). Operating time was 30 min with an uneventful patient recovery. Postoperative assessment revealed a stable implant position, with chin advancement closely matching the virtual surgical plan. Clinical examination demonstrated smooth soft tissue adaptation to implant contours with optimal facial symmetry restoration. Functional assessment demonstrated intact mental nerve function bilaterally with no paresthesia of the chin or lower lip. Occlusal stability was maintained without functional limitations. Soft tissue edema subsided within two weeks. Patient reported high satisfaction with aesthetic outcome. No complications, infections, or adverse events were observed.

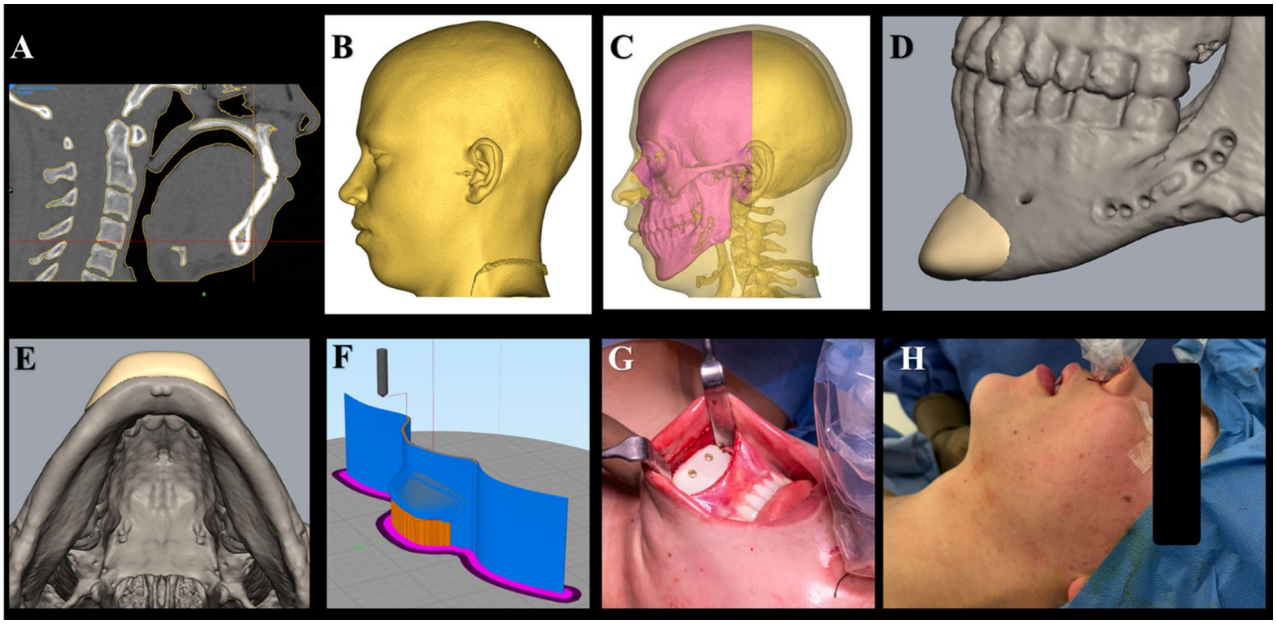

Fig. 2 Point-of-Care (POC) 3D-Printed Polyetheretherketone (PEEK) Facial (Onlay) Implant for Aesthetic Reconstruction. **A**: High-resolution computed tomography (CT) scan (sagittal view) demonstrating facial bone anatomy and regions requiring volumetric augmentation. **B**: Three-dimensional (3D) reconstruction of craniofacial anatomy indicating the retruded (target) chin area for contour enhancement. **C**: 3D reconstruction of the craniofacial anatomy, indicating the bony and soft tissue components. **D**: Virtual surgical planning illustrating the patient's baseline morphology and the planned implant (yellow overlay) to achieve improved facial symmetry and contour. **E**: Inferior view of the patient-matched PEEK facial (onlay) implant design showing precise anatomical adaptation and smooth surface transitions optimized for soft tissue integration. F: Material extrusion additive manufacturing (AM) setup depicting print orientation and support structure configuration tailored for thin-section PEEK fabrication in aesthetic applications. **G**: Intraoperative view of the POC-manufactured PEEK facial (onlay) implant demonstrating accurate fit and seamless integration with native anatomy. **H**: Immediate postoperative profile showing restored facial contour and symmetry following 3D-printed PEEK facial (onlay) implant placement

Table 1 Phase-by-phase manufacturing time and cost for the point-of-care (POC) 3D-printed PEEK implants

Manufacturing phase	Cranial implant	Facial implant
A. Phase-by-phase manufacturing time		
Image acquisition to segmentation (with case manager release)	30–60 min	30–45 min
Segmentation to design finalisation (with case manager/surgeon release)	3–6 h	3–5 h
Printer preparation and preheat	2.5 h	2.5 h
Printing process	~5–6 h	1 h
Printer cool-down	1.5 h	1.5 h
Post-processing and clinical fit verification (with case manager/surgeon release)	60–90 min	30–60 min
Full sterilization cycle	~2.5–3 h	~2.5–3 h
Pre-operative holding period (implant available a minimum of one day before surgery)	≥ 24 h	≥ 24 h
Total lead times: End-to-end from DICOM to sterile delivery)	3–5 days	3–5 days
B. Cost		
Total POC manufacturing cost (CHF)	CHF 5,500	CHF 3,500

Phase durations reflect operational experience from the presented cases. Actual durations may vary depending on anatomical complexity, case volume, and personnel availability, particularly for release steps requiring case manager or surgeon input. The end-to-end duration of 3–5 days reflects real-world operational scheduling, including inter-phase handovers and the minimum pre-operative holding period, rather than continuous uninterrupted production time

Detailed phase-by-phase manufacturing time and cost for the two representative applications are summarized in Table 1. Manufacturing was planned in coordination with the surgical date, with case initiation triggered on DICOM notification. End-to-end turnaround from DICOM acquisition to sterile delivery was achieved within 3–5 days for both cases under routine institutional scheduling conditions.

Post-market surveillance responses

Structured surgeon feedback collected through MDR-compliant PMS questionnaires from September 2023 to October 2024 indicated general satisfaction with the POC manufacturing workflow, including reduced lead times, improved implant quality, and more efficient design collaboration. Surgeons provided positive assessments of manufacturing turnaround times and intraoperative implant handling characteristics. Follow-up relied primarily on patient-initiated contact, without complications reported during the surveillance period. No significant complications requiring implant removal or revision were reported by surgeons across their collective experience with POC 3D-printed PEEK implants during this period.

Discussion

This study reports the clinical implementation of EU MDR-compliant 3D-printed PEEK patient-matched implants for CMF reconstruction, establishing a regulatory-compliant implementation model for hospital-based medical device manufacturing. The early clinical cases in August 2023 (cranial) and March 2025 (facial) demonstrated successful translation of the framework into clinical practice, with both implants achieving an anatomical fit without intraoperative modification. Early clinical experience with the cranial case extending beyond one year, combined with structured surgeon feedback from subsequent cases, revealed no major device-related complications requiring intervention.

Under MDR 2017/745, the custom-made device pathway (Article 2(3), Annex XIII) and Article 5(5) are distinct frameworks that address different manufacturing contexts. The custom-made pathway applies to medical devices manufactured for a single identified patient on the basis of a written prescription that defines specific design characteristics, whereas Article 5(5) governs non-industrial, institutional manufacturing of devices intended to address the specific needs of a target patient group within the same health institution, under a unified QMS and validated design and manufacturing envelope. Article 5(5) was selected for the present framework as it reflects a program-level implementation approach, based on predefined and validated design and manufacturing processes with structured clinical involvement, without requiring individual clinician prescription-defined design specifications for each patient.

The successful EU MDR Article 5(5) compliance represents a significant milestone, demonstrating that healthcare institutions can assume medical device manufacturing responsibilities while maintaining stringent quality standards. Previous POC initiatives often operated in regulatory uncertainty; this framework establishes a compliant pathway for routine clinical application [16–18]. Process validation was performed at the manufacturing framework level using predefined worst-case design configurations and process parameters rather than per-implant testing. Assessments of biocompatibility, mechanical integrity, and dimensional stability conducted within this validated design envelope supported the safe clinical deployment of patient-matched devices [19]. Partnership with specialized regulatory expertise proved essential for QMS, medical device development, and process validation, suggesting a scalable model where centralized regulatory and quality knowledge supports distributed manufacturing across healthcare systems.

Supporting this quality infrastructure, digital infrastructure represents a critical component of regulated POC manufacturing systems. Integration of the eQMS with a MES enabled structured device traceability,

documentation control, and lifecycle management across the manufacturing workflow. Such digital systems support data integrity, version control, and process transparency, which are essential considerations in medical device production. Comprehensive software validation and cybersecurity controls form part of the broader digital manufacturing environment and are not discussed here, as the present work focuses on clinical framework implementation rather than software architecture.

A quality management framework alone is insufficient for MDR-compliant production as consistent and safe device manufacturing requires comprehensive evidence of safety and performance integrated into daily clinical operations throughout the device lifecycle. The integration of eQMS and MES with pre-established device-level technical evidence within the present framework distinguishes this approach from existing solutions for hospital-based POC 3D printing, which address individual components of the compliance infrastructure in isolation. Recent developments include Materialise Mimics Flow (Materialise NV, Leuven, Belgium), a cloud-based case management and collaboration platform [20]; QasE3D, an eQMS with MDR documentation system for custom-made device manufacturers providing checklists, forms, and templates for hospital POC 3D print labs [21]; Qualified AM (Qualified AM GmbH, Wielenbach, Germany), an AM process qualification and certification service applying industrial standards, which supports medical applications but does not address the MDR Article 5(5) requirements or device-level evidence for medical devices [22]; and 3Diamond, a product lifecycle management (PLM) platform providing case documentation and traceability adapted from a clinical trial electronic data capture system [23]. While each solution addresses a specific layer of the compliance or digital workflow infrastructure, none provides an integrated system covering all POC medical device types, such as anatomical models, surgical guides, and implants, with the complete regulatory infrastructure required under MDR Annex I for medical devices, whether produced under the custom-made device pathway (Article 2(3), Annex XIII) or Article 5(5).

Beyond regulatory compliance, the present framework additionally incorporates an integrated PMS module covering adverse event capture, analysis, and risk management feedback, case management, material stock tracking linked to MDR batch traceability requirements, and a cost documentation module designed to support institutional cost tracking and to provide structured data that may facilitate future reimbursement applications. Furthermore, active regulatory support, including preparation of competent authority submissions, was provided throughout implementation. A structured comparison of available solutions is provided in Tables 2 and 3.

Beyond regulatory compliance, risk management and structured clinical feedback were integral components of the EU MDR-compliant manufacturing framework implemented. Hazard identification, mitigation strategies, and lifecycle monitoring activities were maintained within the QMS and technical documentation environment consistent with regulatory requirements. Structured surgical feedback mechanisms supported iterative refinement of design and workflow parameters during early clinical use, reflecting continuous improvement principles inherent to regulated medical device manufacturing. No device-related adverse events were observed within the reported clinical applications.

Clinical performance and safety profiles of outsourced patient-specific PEEK implants have been extensively documented in the literature, primarily focusing on surgical outcomes and complication rates. In contrast, the present work addresses a distinct translational dimension, which is the establishment of a regulatory-compliant manufacturing and quality management framework enabling hospital-based production. The validation principles adopted for POC manufacturing were informed by established knowledge of PEEK biomaterial behavior and prior technical investigations, while additional system-level verification was necessary to ensure reproducibility and compliance within a clinical manufacturing environment.

The manufacturing turnaround achieved in both cases (3–5 days end-to-end from DICOM acquisition to sterile delivery) compares favourably with reported outsourcing lead times of 2–6 weeks for commercial patient-specific PEEK implants [24, 25], which usually include external design, manufacturing, and logistical delays outside institutional control. Importantly, in POC manufacturing, the surgical date dictates the production schedule, unlike outsourced procurement, where surgical timing must accommodate external lead times. Published literature reports commercially outsourced PEEK cranial implant costs ranging from approximately $5,600 to $20,522 across international healthcare systems [26], reflecting variation in manufacturing models, healthcare system structures, and geography. Within the present institutional context, outsourced procurement costs for comparable patient-specific cranial and facial PEEK implants were estimated at CHF 8,000–10,000 and CHF 4,000–5,000, respectively, based on institutional procurement experience. Against these benchmarks, POC manufacturing costs represented estimated savings of 25–45% and 11–30% for cranial and facial implants, respectively. These figures include direct production costs, staff time for design and engineering, and an allocated proportion of operational, equipment, and compliance overhead, but exclude staff training and initial capital investment for the printer and software. A formal cost-effectiveness

Table 2 Characterization of available solutions for point-of-care (POC) 3D printing of medical devices: solution type, primary sector, regulatory pathway, and device coverage

Dimension	Present Study (POC APP)	Materialise Mimics Flow	QasE3D	Qualified AM	3Diamond
Solution category and regulatory scope					
Nature of the solution	Integrated eQMS and MES with case management, stock traceability, PMS, regulatory submission support and cost documentation	Cloud-based case management and workflow platform	MDR compliance documentation system comprising checklists, forms, and templates	Industrial AM process qualification and certification service operating across multiple regulated sectors, including medical	PLM software for case documentation and traceability
Primary sector	Medical	Medical	Medical	Industrial AM (aerospace, automotive, rail, semiconductor, energy, construction, food, space, and medical)	Medical
MDR 2017/745, Article 5(5) explicitly addressed	Yes (present implementation)	No	Partial (addressed through consulting service; MDR management system primarily structured for custom-made device pathway)	No (Industrial AM standards; MDR Article 5(5) not addressed)	Partial (documentation support)
MDR 2017/745, Article 2(3) explicitly addressed	Yes (solution supports both pathways)	No	Yes (MDR management system designed for custom-made devices)	No (Industrial AM standards; MDR Article 2(3) not addressed)	No (case documentation platform; MDR Article 2(3) compliance requirements not addressed)
Dedicated software system provided	Yes (integrated eQMS and MES)	Yes (cloud case management platform)	No (Wiki and document-based system (Confluence); general collaboration platform)	Yes (QamX qualification management platform)	Yes (Clade-IS, a clinical trial EDC platform adapted for 3D printing)
Medical device types covered	Anatomical models, surgical guides, and implants	Anatomical models and surgical guides (workflow management; compliance documentation not included)	Anatomical models, surgical guides, and implants	Anatomical models demonstrated (aortic arch replica, UKM); implant qualification not published)	Anatomical models (primarily)

MDR: Medical Device Regulation 2017/745; QMS: quality management system; MES: manufacturing execution system; PMS: Post-market surveillance; POC: Point-of-Care; EDC: Electronic data capture; AM: additive manufacturing; PLM: product lifecycle management. MDR Article 5(5): health institution exemption for in-house manufacture of medical devices. MDR Article 2(3): custom-made devices manufactured to a clinician's written prescription for a named patient. These are distinct regulatory pathways with different compliance obligations. UKM: Universitätsklinikum Münster, Germany. 3Diamond was developed on the Clade-IS electronic data capture platform originally designed for clinical trial data management [23]. Solution characterisations are based on publicly available information from provider websites at the time of writing [20–22] and do not imply any deficiency in the quality or suitability of comparator solutions for their stated purposes.

analysis comparing POC and outsourced production within a single healthcare system is a priority for future investigation.

While time reduction is often emphasized as a primary advantage of POC manufacturing, its clinical value extends beyond urgency alone. Hospital-based production enables closer integration between surgical planning and device fabrication, facilitates iterative surgeon-driven design refinement, and reduces dependency on external manufacturing cycles. Such flexibility may be particularly valuable in elective, revision, or anatomically complex reconstructions, where scheduling control and workflow predictability contribute meaningfully to clinical decision-making. For trauma cases, this enables immediate protective coverage and for elective procedures, while for planned procedures it eliminates surgical delays and optimizes timing relative to healing phases.

POC manufacturing has demonstrated clinical value in CMF reconstruction, including complex skull-base defects following neurosurgical tumor resections, where personalized implants improved surgical workflow and outcomes [27]. The 3D-printed PEEK framework illustrated in this study extends these POC capabilities with enhanced design flexibility for diverse anatomical applications. The digital workflow, with surgeon-engineer collaboration through physical model verification, proved effective, supporting the observed clinical design accuracy [28]. Following fabrication and post-processing, implants underwent surgeon-guided clinical fit verification using patient-specific anatomical models prior to

Table 3 Comparison of available solutions for point-of-care (POC) 3D printing of medical devices: quality system, technical evidence, ongoing compliance, and clinical workflow capabilities

Dimension	Present Study (POC APP)	Materialise Mimics Flow	QasE3D	Qualified AM	3Diamond
A. Quality and manufacturing system					
MDR compliance documentation system and QMS procedures provided with guided implementation support	Yes (integrated operational system; documentation included)	No	Yes (18-chapter MDR documentation system with guided implementation and annual update)	No	No
Integrated production and quality management system provided	Yes	No	No	No (ISO 13485 readiness achieved through program; no integrated medical device production QMS provided)	No
Pre-established qualified, and validated production processes provided	Yes	No	No	Partial (institution executes process qualification with guidance)	No
Equipment, materials and software qualification provided	Yes	No	No	Partial (equipment qualification conducted during program)	No
Personnel training provided	Yes	No	Yes	Yes (during program)	No
B. Device-level technical evidence (MDR Annex I GSPR)					
Complete GSPR evidence file with backing technical data	Yes	No	No	No	No
Biocompatibility evaluation (ISO 10993) linked to AM process parameters	Yes	No	Partial (template provided; institution must generate evidence)	No	No
Mechanical performance characterisation of printed medical device	Yes	No	Partial (template provided; institution must generate evidence)	No	No
Dimensional accuracy verification per process and medical device configuration	Yes	No	No	Partial (process quality compliance demonstrated for anatomical model under ISO/ASTM 52920)	Partial (case-level dimensional check documented)
Sterilisation validation per medical device geometry, material and process	Yes	No	Partial (documentation structure provided; institution must conduct and document validation)	Partial (sterilisation validation conducted for anatomical model as part of ISO/ASTM 52920 process qualification)	No
Clinical evaluation evidence (MDR Annex XIV)	Yes	No	Partial (template provided; institution must generate evidence)	No	No
C. Ongoing compliance and post-market support					
Integrated PMS - adverse event capture, analysis, risk management feedback	Yes	No	No	No	No
Regulatory update maintenance (MDR evolution)	Yes	No	Partial (annual update session)	No	No
Regulatory authority submission preparation and competent authority inspection support	Yes	No	No	No	No
Expert QA and regulatory affairs support	Yes	No	Partial (consulting available)	Partial (during program)	No
D. Clinical workflow, stock management, and cost documentation					
Integrated case management covering ordering, design review, and release workflow)	Yes	Yes	No	No	Partial
Material stock tracking linked to device traceability and MDR batch records	Yes	No	No	No	Partial

Table 3 (continued)

Dimension	Present Study (POC APP)	Materialise Mimics Flow	QasE3D	Qualified AM	3Diamond
Cost documentation module supporting institutional cost tracking and future reimbursement applications	Yes	No	No	No	No
E. Practical implementation summary					
Institution able to commence compliant device production upon implementation	Yes (anatomical models, surgical guides, and implants)	No (full compliance infrastructure must be built independently)	No (institution must independently generate all device-level safety and performance evidence before compliant production can commence)	No (institution must independently generate device-level safety and performance evidence before compliant production can commence; process quality addressed for anatomical models only)	No (case documentation platform; compliance infrastructure not included)
Additional work required from institution after implementation[a]	+ Minimal	Not applicable as standalone compliance solution; +++ High if used as primary compliance approach	++ Moderate	++ Moderate	++ Moderate

Yes: evidence or capability established and available within the solution. **Partial**: addressed in part or with significant limitations; institution retains responsibility for completing evidence. **No**: not within the scope of the solution

Assessments based on publicly available information from each solution provider at time of writing and do not imply any deficiency in the quality or suitability of comparator solutions for their stated purposes. GSPR: General Safety and Performance Requirements (MDR Annex I); ISO 10993: biological evaluation of medical devices; MDR Annex XIV: clinical evaluation requirements; PMS: post-market surveillance. Regulatory authority submission preparation and competent authority inspection support reflect services provided for MDR Article 5(5) notification to Swissmedic and competent authority inspection by the Federal Office for Safety in Health Care (BASG), Austria.

[a]Implementation burden reflects the combined investment of time, cost, and in-house expertise required from the institution to achieve MDR-compliant production of medical devices. +: the institution receives a working system and follows defined processes; no additional evidence generation required. ++: the institution must independently generate device-level safety and performance evidence, execute qualification programmes, or establish compliance infrastructure; substantial time, cost, and expertise required. +++: the institution must build all compliance infrastructure from scratch, including QMS, process validation, technical evidence, and regulatory submissions. Estimates are based on publicly described implementation models; exact costs were not publicly available for all solutions at the time of writing.

sterilization. This step functioned as an additional clinical quality gate, confirming anatomical conformity and handling characteristics before procedural release.

Despite the observed workflow effectiveness, translating POC manufacturing into regulated clinical environments presents key systematic barriers such as aligning clinical decision-making timelines with manufacturing process constraints, establishing stable and reproducible process windows for high-performance biomaterials, integrating digital workflow, traceability, and documentation infrastructures, and managing competency dependencies across clinical and engineering domains. Unlike conventional medical device procurement models, hospital-based manufacturing requires continuous coordination between regulatory governance, quality management, and procedural logistics. Addressing these challenges necessitates structured workflow design, predefined process controls, and interdisciplinary collaboration rather than reliance on ad hoc technical optimization. The transition from pilot project to sustainable POC production is fundamentally a governance and organisational challenge, requiring defined responsibilities, structured oversight, and long-term institutional commitment.

Within this governance framework, the role of clinical biomedical engineering expertise is critical to the reliability of POC manufacturing workflows. Design and fabrication of personalized implants require competencies extending beyond general engineering or AM skills, including medical image segmentation, anatomical modeling, design for additive manufacturing (DfAM), biomaterial behavior, and regulatory-quality system considerations. Equally, surgeons engaged in POC programmes benefit from familiarity with 3D printing capabilities and design constraints, enabling more effective participation in design review and iterative refinement, while engineers require sufficient anatomical literacy to translate clinical intent accurately into manufacturable device geometries. This bidirectional competency development strengthens the surgeon-engineer collaboration that underpins safe and effective POC implant production. Accordingly, specialized domain-specific training and interdisciplinary collaboration are essential prerequisites for safe clinical implementation. Standardized

workflows, validated process parameters, and structured training frameworks may help mitigate variability associated with operator experience and reduce the learning curve inherent to hospital-based manufacturing environments.

Material selection is a central determinant of variability in POC manufacturing. Outsourced patient-specific PEEK implants are typically produced using subtractive manufacturing or industrial polymer processing techniques within specialized facilities. These approaches benefit from highly controlled production environments but require centralized infrastructure and extended logistical pathways. In contrast, high-temperature material extrusion processing above 400 °C, while technically demanding, is consistent with established thermal processing principles for medical-grade PEEK when supported by stable chamber control and predefined parameter sets and enables direct digital manufacturing within hospital-based environments using clinically compatible workflows. Although extrusion-based 3D printing imposes distinct thermal and process stability requirements, it offers sufficient geometric flexibility and material performance for patient-specific implant fabrication when implemented within validated process windows. The appropriateness of this manufacturing approach, therefore, relates not to replacing industrial methods but to compatibility with decentralised clinical production models.

PEEK's thermoplastic properties enable 3D printing of medical devices using hospital-compatible high-performance equipment, unlike titanium implants, which require advanced fabrication infrastructure [29]. Compared to polymethyl methacrylate (PMMA), PEEK provides superior mechanical strength, biocompatibility, and sterilization stability [30, 31]. The material's established regulatory status facilitated MDR compliance [32]. Systematic reviews of PEEK implants in cranioplasty and CMF reconstruction have demonstrated favorable complication profiles and mechanical suitability [33, 34]. PEEK's radiolucency enabled artifact-free postoperative imaging assessment without beam-hardening artifacts, facilitating clear visualization of the bone-implant interface. The elastic modulus of PEEK (3–4 GPa) is closer to bone than titanium (110 GPa), potentially reducing stress-shielding concerns. PEEK's non-metallic composition eliminates the risks of metal sensitivity relevant to young patients requiring long-term implantation [35–40]. However, PEEK's bioinert nature limits direct osseointegration compared to bioactive materials, relying primarily on mechanical fixation [41, 42].

High-temperature PEEK processing introduces distinct manufacturing constraints. The demanding thermal requirements (> 400 °C nozzle, 200–250 °C chamber) necessitated specialized equipment and environmental controls. PEEK's crystalline structure required precise parameter optimization to achieve adequate layer fusion while minimizing warping in thin-section geometries [43–46]. Application-specific optimization proved essential, such as for cranial implants, which required 0.3 mm layer heights balancing structural integrity with printing time, while facial implants utilized 0.28 mm layers for enhanced surface finish. Support structure strategy critically impacted implant quality, requiring careful build orientation to minimize contact with critical fit surfaces while maintaining geometric fidelity [47].

Single-institution implementation limits generalizability, and economic analysis was not performed. However, the two applications presented are representative of a larger ongoing clinical program. Since the framework's implementation, approximately 35 cranial and six facial POC 3D-printed PEEK implants have been produced at the present institution under the described MDR-compliant framework. The transferability of the framework has been further supported by its successful implementation at an Austrian institution, where a competent authority inspection by the Austrian Agency for Health and Food Safety (AGES) under MDR Article 5(5) was completed without findings. This expanding multi-centre programme provides the case volume and foundation for a dedicated cost-effectiveness and outcomes study planned as the next step. Multi-centre validation and comprehensive long-term follow-up protocols represent further priorities. Patient-reported outcome measures using validated instruments would complement clinical assessments [48, 49]. Technical development should explore additional anatomical sites and emerging PEEK formulations, such as bioactive composites incorporating hydroxyapatite, which could enhance bone integration, carbon fiber-reinforced variants, which offer increased strength, and drug-eluting formulations, which could address infection risks [50–53]. The integration of advanced imaging modalities and artificial intelligence for automated segmentation and design automation represents promising avenues for enhancing digital workflows [54, 55]. Institutionally, establishing governance models that position POC manufacturing as a core clinical service with dedicated infrastructure and long-term planning will be essential for sustainable programme development.

Conclusions

The described MDR-compliant framework demonstrates that hospital-based medical device manufacturing is achievable within a structured regulatory and quality system environment. Early clinical observations indicate practical feasibility and satisfactory procedural performance in the presented applications. This implementation model supports the active participation of

healthcare institutions in the production of personalised medical devices. PEEK's combination of favorable material properties and processability makes it well-suited for POC manufacturing, although systematic long-term surveillance remains essential for comprehensive clinical outcome characterization. This work provides a foundation for broader clinical adoption of regulated POC manufacturing models.

Abbreviations

3D	Three–dimensional
AM	Additive Manufacturing
CAD	Computer Aided Design
CMF	Craniomaxillofacial Surgery
CT	Computed Tomography
DfAM	Design for Additive Manufacturing
DICOM	Digital Imaging and Communications in Medicine
EDC	Electronic Data Capture
EU MDR	European Union Medical Device Regulation
GCS	Glasgow Coma Scale
GSPR	General Safety and Performance Requirements
HU	Hounsfield unit
ISO	International Organization for Standardization
MES	Manufacturing Execution System
PEEK	Polyetheretherketone
PLM	Product Lifecycle Management
PMMA	Polymethylmethacrylate
PMS	Post–Market Surveillance
POC	Point–of–Care
QMS	Quality Management System
STL	Standard Tessellation Language

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Author contributions
Conceptualisation: N.S.; methodology: N.S.; validation: N.S., J.Z.O., D.S.; formal analysis: N.S., J.Z.O.; investigation: N.S., J.Z.O.; resources: N.S., J.Z.O., R.G., F.M.T.; data curation: N.S., J.Z.O.; writing-original draft: N.S.; writing-review and editing: N.S., J.Z.O., D.S., S.A., L.B.S., M.R., R.G., F.M.T.; visualisation: N.S., J.Z.O.; supervision: N.S.; project administration: N.S. All authors have read and agreed to the published version of the manuscript.

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Data availability
The datasets utilised and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted per the Declaration of Helsinki and institutional ethical guidelines. POC manufacturing of patient-specific implants was performed under EU MDR 2017/745 Article 5(5) with notification to Swissmedic (Swiss Agency for Therapeutic Products): CH-202306-0005 and CH-202503-004. Written informed consent was obtained from all patients for surgical intervention with POC-manufactured implants and for publication of clinical data and photographs for academic purposes.

Competing interests
N.S., D.S., and F.M.T. are cofounders and minority shareholders of POC APP AG (Basel, Switzerland). N.S. and D.S. serve as Chief Medical Officer and Chief Technology Officer of POC APP AG, respectively. J.Z.O. is a part-time employee of POC APP AG. The regulatory compliance framework, including the quality management system (QMS) and manufacturing execution system (MES) implemented in this study, was developed and is maintained by POC APP AG. The remaining authors declare no competing interests.

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