



Medical Additive Manufacturing in Surgery: Translating Innovation to the Point of Care

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Abstract

Alongside computed tomography, additive manufacturing (also known as three-dimensional or 3D printing) is a significant MedTech innovation that allows the fabrication of anatomical biomodels, surgical guides, medical/dental devices, and customized implants. Available since the mid-1980s, 3D printing is growing increasingly important in medicine by significantly transforming today's personalized medicine era. 3D printing of biological tissues will provide a future for many patients, eventually leading to the printing of human organs. Unlike subtractive manufacturing (where the material is removed and 3D objects are formed by cutting, drilling, computer numerical control milling, and machining), the critical driver for the exponential growth of 3D printing in medicine has been the ability to create complex geometric shapes with a high degree of functionality. 3D printing also offers the advantage of developing highly customized solutions for patients that cannot be achieved by any other manufacturing technology.

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1 Introduction

In the last few years, three-dimensional or 3D printing (also called additive manufacturing or AM as well as rapid prototyping) has experienced a rapid boom in industry—especially in medicine and surgery. However, the technology itself is not new. Stereolithography or SLA, a key technology for 3D printing, was invented more than three decades ago by Charles W. “Chuck” Hull in the United States (Brooks, 2016). The breakthrough in medical and surgical technology was then led by the availability of affordable and user-friendly 3D printers, software solutions, and the continuous improvement of radiological (slice) imaging to produce virtual and highly realistic anatomical models (Hatz et al., 2020). Before, rapid prototyping was complicated, high-priced, and largely unattractive for the average user. Now, inexpensive, user-friendly, and compact 3D printers make it easy to get started with the basics of AM—even in medicine (Hatz et al., 2020; Wegmüller et al., 2021).

Pioneer clinics in high-medical technology enabled a close link between this technology and clinical processes, advancing early translation. For example, they produced stereolithographic models for oral and maxillofacial surgery applications (see Fig. 1). The essential added value of a technological innovation such as 3D printing to the entire treatment chain became apparent alongside the immediate benefits to patients. For the first time, complex human anatomy could become “comprehensible” to clinicians by making complex surgical procedures safer, simpler, and shorter through 3D models and patient-specific or customized implants.

2 Applications in Medicine

Due to the success of medical 3D printing, more and more physicians and engineers in medical fields grew aware of the advantages of its use in the healthcare sector. New treatment methods were developed, enabling therapy options that were hardly conceivable just a few years ago (Honigmann et al., 2017; Honigmann et al., 2018; Meyer et al., 2019; Msallem et al., 2017; Soleman et al., 2015a; Wegmüller et al., 2021).

In modern dentistry and craniomaxillofacial surgery, 3D printing has now become an integral part of the digital medical treatment process. It is commonly utilized in the production of surgical sawing or drilling templates and guides (Soleman et al., 2015a; Sommacal et al., 2018), dental or anatomical bone models (Hatz et al., 2020), active drinking (feeding) plates and dental appliances for pretreatment of cleft lip and palate patients (Beiglboeck et al., 2019; Wegmüller et al., 2021), orthodontic aligners (transparent splints for the computer-planned movement of teeth), and temporary restorations. It is also used for complex prosthetic solutions, including patient-specific implants made of titanium, ceramics, or high-performance polymers making up a “human replacement part” (Han et al., 2019; Honigmann et al., 2017, 2021; Msallem et al., 2017; Schön et al., 2021; Thieringer et al., 2016, 2017).



Fig. 1 Stereolithographic model for surgical planning (Zeilhofer, University of Basel)

At present, many 3D printing materials are biocompatible. Some are also certified for medical applications and can therefore be used in contact with the human body or even as a substitute for human tissue (bioprinting) (Cao et al., 2020; Dey & Ozbolat, 2020; Honigmann et al., 2018; Zhang et al., 2021; Zhao et al., 2021). These innovative fabrication processes are currently being explored in several interdisciplinary projects led by research groups at the Department of Biomedical Engineering and the Department of Biomedicine at the University of Basel, Switzerland (Figs. 2 and 3).

2.1 Benefits of Medical 3D Printing

3D printing in medicine and surgery offers engineers, developers, and doctors the advantage of segmenting, designing, and constructing anatomical 3D models on a computer. After a brief wait, they can hold these models in their hands—literally “grasping” the anatomy. Whether directly or indirectly 3D printed, these anatomical

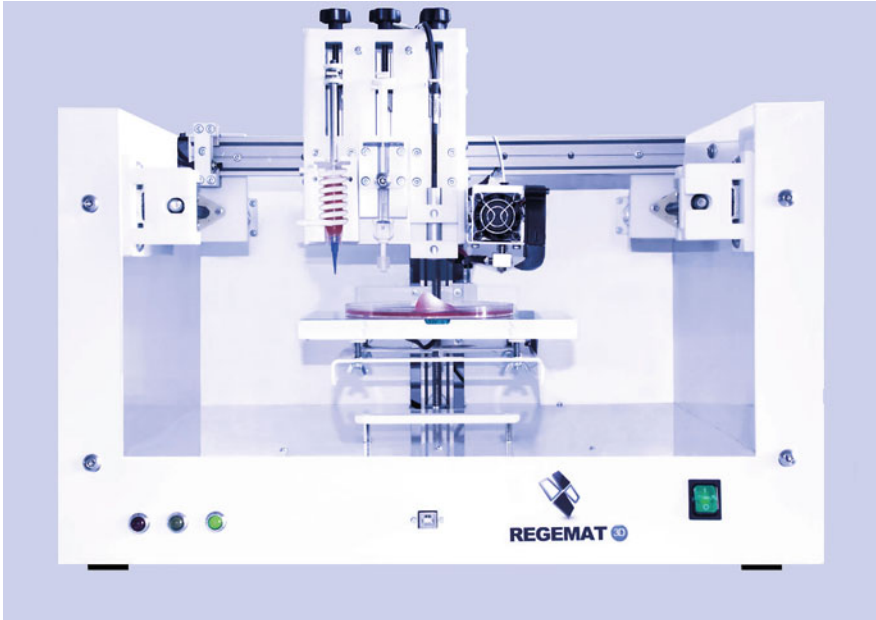


Fig. 2 Bioprinter for bio-ink/gel matrix (Regemat 3D, Granada, Spain)

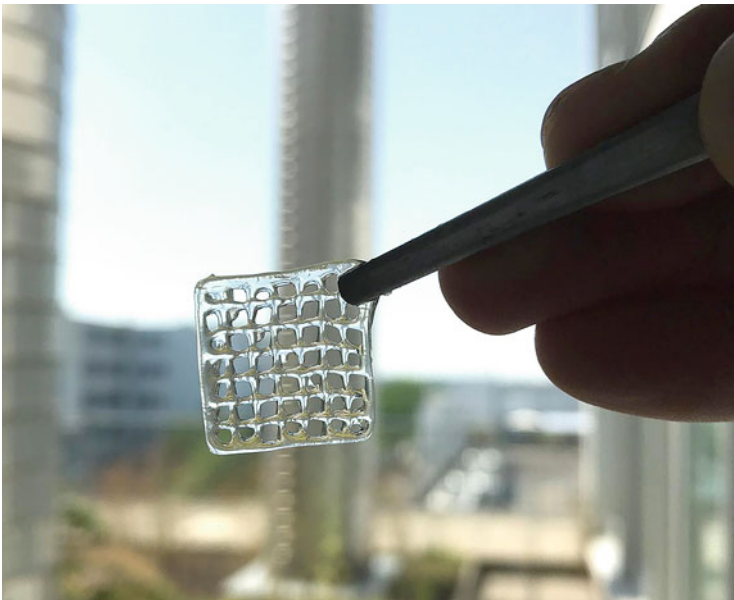


Fig. 3 3D bioprinted bio-ink/gel matrix (Swiss MAM Research Group, Thieringer, DBE)

models and implants allow surgeons to provide highly accurate, patient-specific care that offers numerous benefits at various points in medical and surgical treatment processes (Han et al., 2019; Hatz et al., 2020; Honigmann et al., 2017; Meyer et al., 2019; Sommacal et al., 2018; Wegmüller et al., 2021).

2.2 Popular 3D Printing Technologies in Medicine

In general, the 3D printing processes most widely used in the medical field all apply the raw material (e.g., plastics/polymers, polymer resins, metals, ceramics, and other materials that include biological substances such as body cells) in a layer-by-layer manner—i.e., additively—to a print bed. The material is then cured by either physical or chemical processes. With some 3D printers, these layers are only a few micrometres thin. The printed results are produced to a high resolution, accurately representing the original computer-aided design (CAD) file in all of its geometric dimensions and specifications (Hatz et al., 2020). In addition, 3D printing based on layer-by-layer manufacturing offers almost unlimited freedom in the production of 3D objects. This is a great benefit especially to the production of complex anatomical models or even biomechanically optimized structures with lightweight designs, such as osteosynthesis plates or implants. Layer-by-layer manufacturing enables these products to withstand high loads with low material input (Honigmann et al., 2017, 2018; Thieringer et al., 2016) (Figs. 4 and 5).

2.3 Research Activities in Medical 3D Printing

The research group “Medical Additive Manufacturing” (www.swiss-mam.ch) was founded in 2013 within the Department of Clinical Morphology and Biomedical Engineering. At present, it is firmly integrated into the Department of Biomedical Engineering (DBE) at the University of Basel. There, we deal with all aspects of 3D printing in medicine and surgery. The focus areas of the research projects are:

- Materials and innovative printing processes, including the use of high-performance polymers (such as PEEK) in the manufacture of biocompatible patient-specific implants and various printing processes in medical applications.
- Clinical processes or the integration of medical 3D printing at the point of care.
- Implants or the fabrication of patient-individual, 3D-printed, human “spare parts” from various materials (e.g., PEEK, ceramics, titanium, etc.) and “smart” implants (e.g., with sensor technology in the reconstruction of orbital defects).
- Imaging and planning methods (virtual surgical planning) for the digitalization of the surgical treatment process.
- Software development and surface imaging processes (optical scanning processes in medical use).
- As a new field of research, bioprinting, such as the production of biological, resorbable scaffolds or the combined 3D printing of carrier structures and



Fig. 4 3D-printed skull implant made of polyetheretherketone (PEEK) (Swiss MAM Research Group, Thieringer, DBE)

biological tissues/cells (e.g., cartilage or bone) as essential steps in the field of regenerative surgery.

Other areas of research include the influence of 3D planning and printing processes on the quality of treatment, as well as

- economic aspects, the optimization of patient treatment by integrating three-dimensional, “tangible” anatomical models into the clinical treatment chain, and the integration and evaluation of digital and,
- virtual reality (VR) and augmented reality (AR) methods along with 3D-printed models in:
- medical teaching, further education, and training focused on surgical disciplines/hand surgery and craniomaxillofacial surgery.



Fig. 5 3D-printed polyetheretherketone (PEEK) shell for guided bone regeneration (Swiss MAM Research Group, Thieringer, DBE)

3 Point-of-Care Manufacturing

As a complement to the research group mentioned above, the 3D Print Lab was established in 2016 at University Hospital Basel by the Department of Craniomaxillofacial Surgery and the Radiology Department to install “medical 3D printing and 3D visualization” technology. The point-of-care-established 3D Print Lab is centrally located and easily accessible to all of the medical and surgical specialties at the university hospital. The 3D Print Lab is an essential and valuable addition to the research group at DBE, enabling translational research close to the clinic. Given its spatial proximity to the treatment centre at the hospital and the rapid acceptance by numerous medical disciplines that resulted, it was possible to establish an innovative 3D research and service lab unique in form in Switzerland and Europe. Numerous clinical and scientific collaborations with national and international partners were quickly initiated to advance research into the field of medical 3D printing from a variety of perspectives in order to optimize patient treatment—especially in terms of oral and craniomaxillofacial surgery. The 3D Print Lab is now listed as an exemplar project for medical innovation and successful translation by government representatives, the board of directors, and hospital management at

both the University Hospital and the University of Basel. Additionally, the 3D Print Lab is frequently presented to national and international visitors.

3.1 Prerequisites for Technology Integration

A critical aspect for the clinical translation of these research activities is close collaboration with physicians (particularly surgeons and radiologists), biomedical engineers, and other healthcare stakeholders. This was realized at University Hospital Basel through the provision of a service platform to achieve local acceptance at the point of care. For instance, standard operating procedures were established to meet legal and regulatory requirements. The manufacturing processes for medical models, surgical cutting guides, and implants were all integrated into the existing digital structures of the hospital. The ordering process for 3D models is carried out via the electronic patient file, just as for an X-ray or computed tomography (CT) scan. Additional requirements involve end-to-end, fully digital tracking of the manufacturing and treatment process through a validated digital platform. The platform also serves as a quality management system that ensures a consistently high quality in the products. Finally, these systems enable traceability from models, guides, and implants to medically certified raw materials for the 3D printing workflow and relevant processes.

4 Relevant Studies and Publications for Point-of-Care 3D Printing in Basel

4.1 A Desktop 3D Printer Vs. a Professional Device

Can an entry-level 3D printer create high-quality anatomical models? Assessing the accuracy of mandibular models printed by a desktop 3D printer and a professional device (Hatz et al., 2020).

This study addresses a very clinical question: Can a low-cost, consumer-oriented, Fused Filament Fabrication (FFF) 3D printer produce anatomical mandibular models with a level of precision equal to that of a professional, expensive, industry-oriented, Selective Laser Sintering (SLS) 3D printer? We selected mandibular models as anatomical reference models because they are commonly used in our clinical practice as maxillofacial surgeons to preform (prebend) standard titanium implants (e.g., reconstructive titanium plates) preoperatively—a realistic clinical setup. After comparing the optically scanned 3D-printed exemplary models with the original standard tessellation language (STL) data set, a statistical evaluation of the measurement results revealed that both manufacturing methods showed high accuracy with clinical acceptability. In particular, comparison of the FFF models (the low-cost method) with the original STL files showed a mean difference of -0.055 ± 0.227 mm and a median difference of -0.022 (-0.153 to 0.065) mm. As a

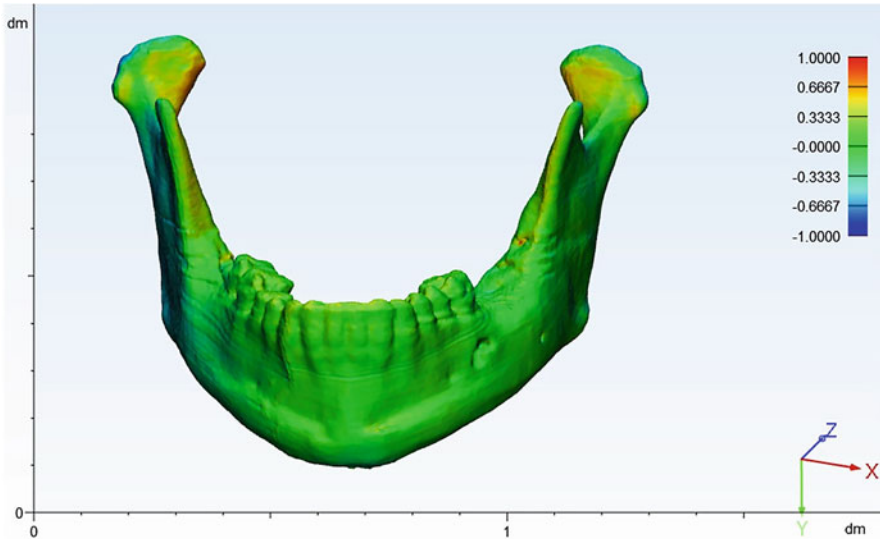


Fig. 6 Part comparison (heat map) analysis of an FFF-printed, low-budget mandibular model (Swiss MAM Research Group, Thieringer, DBE)

result, we demonstrated that mandibular models printed in-house with low-cost FFF 3D printers are serious alternatives to professionally (outsourced and expensive) fabricated 3D models (Fig. 6).

4.2 Evaluation of 3D Printers for Guided Implant Surgery (Wegmüller et al., 2021)

The study addressed a similar question through close cooperation with colleagues from the University Dental Clinics of the University of Basel (Filippi and Kühl). This time, we compared a professional printing process for dental implant surgical guides (digital light processing) to a cost-effective FFF process (see above).

To do so, we produced eight different surgical drill guides using 3D printers. After removal of the support structures, we optically recorded the guides with a surface scanner. Here, too, the STL data from the surgical guides were virtually superimposed in the analysis software to determine deviations; the corresponding measured values were then statistically evaluated. Although the results were promising, the findings contrasted with the previously mentioned study as the manufacturing accuracy of the FFF-printed surgical guides proved unable to meet the requirements of dental implantology (Sommacal et al., 2018). But given the rapid pace of technological advances, especially in FFF printing processes, we can now assume that this technology will be used more and more frequently when

fabricating dental implant surgical guides in the future (for primarily economic and ecological reasons).

Another study by the authors addressed an equally essential and pertinent issue related to the effects of steam sterilization on 3D-printed biocompatible resin materials for surgical guides (Sharma et al., 2020b). Thanks to the continuous development of 3D printing technology, clinicians can now choose between various 3D printers and materials with certified biocompatibility properties. Additionally, 3D printer manufacturers are developing printers and making systems open to the third-party materials of other manufacturers. Third-party biocompatible resin materials are less expensive than proprietary (manufacturer-standard/proprietary) resin materials. This freedom to select from various low-cost biocompatible resin materials appeals to clinicians. Considering these aspects, this study aimed to evaluate the effects of autoclaves on the dimensional accuracy of test bodies manufactured in-house using Class IIa biocompatible resin materials (proprietary and third party) with SLA and PolyJet 3D printers. We observed that the greatest accuracy was produced from proprietary resin materials. However, the dimensional change of third-party resin materials was within close range of proprietary materials, which means they can serve as an economical alternative. The off-site production and shipping of 3D-printed surgical guides can be time-consuming and costly. In contrast, the in-house fabrication of surgical guides can be completed quickly and at a much lower cost.

4.3 An Interactive, Fully Digital Design Workflow for a Custom, 3D-Printed, Facial Protection Orthosis (Face Mask) (Sharma et al., 2020c)

In this paper, we integrated the existing tools of medical image processing software, CAD, 3D digitization, and AM to provide a “no-touch”, practitioner–/patient-friendly solution for a professional football player who had suffered a cheekbone injury during practice and needed a patient-specific, face-protective orthosis or face mask. The player’s 3D face scan and radiological data sets were digitally sent to the authors from our colleague at the University Clinic of Oral and Maxillofacial Surgery in Innsbruck, Austria (Netzer). Design and virtual planning considered which anatomical structures required protection and which rigid anatomical structures could provide support and stability for the face mask. Based on functional and clinical aspects at the fractured site, a virtually designed face mask was fabricated in-house using a carbon-reinforced polylactic acid composite material with an FFF 3D printer. The face mask was tailor-made and fit the player perfectly. The inside of the mask was cushioned by a softer fabric with a high absorption capacity. An elasticated band was used to secure the mask around the player’s head.

The lightweight face mask required no alterations. It had a comfortable fit and shortened the convalescence period for the player. Here, we illustrate the potential for the proposed workflow in similar facial fracture situations—thereby providing



Fig. 7 FFF-printed, carbon-reinforced, polylactide (PLA), custom face mask (Swiss MAM Research Group, Thieringer, DBE)

greater ease of fabrication and cost-effectiveness through an in-house production facility (Fig. 7).

4.4 Computer-Assisted Virtual Planning and Surgical Template Fabrication for Fronto-Orbital Advancement (Soleman et al., 2015b)

In this paper, we described a new digital treatment workflow in the field of craniofacial surgery through an interdisciplinary research project (maxillofacial surgery and paediatric neurosurgery). The subject of this fully digital, virtual planning procedure, which has been established in our clinic for several years now, is based on a CT data set (digital imaging and communications in medicine or DICOM) of paediatric patients. We used 3D-printed incision and deformation templates for the correction of craniosynostoses and other cranial malformations. After segmentation of the radiological image data, we performed virtual surgical planning on the computer by considering all surgical steps for symmetrization/correction of the deformed paediatric skull. Following the 3D printing of biocompatible and sterilizable plastic moulds in our lab, the virtual computer planning data was

transferred to the child intraoperatively. As a final step, the new shape of the “orbital bandeau” and the remaining cranial bone segments were positioned in the 3D-printed moulds and joined together with resorbable osteosynthesis plates (SonicWeld Rx[®] system), precisely as planned preoperatively. We demonstrated a high predictive and repeatability accuracy for the procedures described above. The application of this procedure, which is now established in our clinics, is simple and very cost-effective due to the in-house planning and production of the guides.

4.5 Craniofacial Reconstruction through a Cost-Efficient, Hybrid Process that Uses 3D Printing and Intraoperative Fabrication (Msallem et al., 2017)

This paper evaluated and described a novel, cost-effective process for the in-house fabrication of patient-specific plastic/polymethyl methacrylate (PMMA) implants for the reconstruction of cranial defects. For the reconstruction of complex cranial defects, patient-specific custom implants (either milled PEEK or 3D-printed titanium) have proven successful. Still, they must be purchased from external companies at high cost and sometimes with a considerable time lag. This can be problematic, especially for clinics in countries with financially weak healthcare systems. On the other hand, PMMA is a bone cement that has been tried and tested for decades. Yet the use of this cement to produce cranial roof implants has decisive disadvantages—not only in the direct adaptation of the material to the patient but also in handling the toxic components of PMMA and curing the material at high temperatures. As proof of concept, we developed a simple manufacturing process based on virtual 3D implant planning, in-house 3D printing, and the fabrication of sterilizable silicone moulds for use in the operating room to produce patient-specific “hybrid” implants. This work has been a cornerstone of successful, intensive cooperation between craniomaxillofacial surgery and neurosurgery departments. More than 30 skullcap reconstruction surgeries (cranioplasty) have now been performed (Schön et al., 2021) and are currently being evaluated in further studies. The easy-to-implement procedure can also be used in clinics with limited financial resources, enabling the production of accurate, precisely fitted (Chamo et al., 2020), 3D print-based, patient-specific “hybrid” implants made of PMMA (Fig. 8).

4.6 “Hybrid” Patient-Specific Implants in Orbital Floor Fractures (Sigron et al., 2020, 2021)

This paper evaluated and described another application for 3D printing involving the in-house fabrication of patient-specific “hybrid” implants to reconstruct orbital floor fractures. To repair orbital floor fractures, titanium meshes are generally bent and adjusted during surgery. These adjustments are based on the size and shape of the fractured orbital floor. Due to the complex 3D anatomy of the orbit

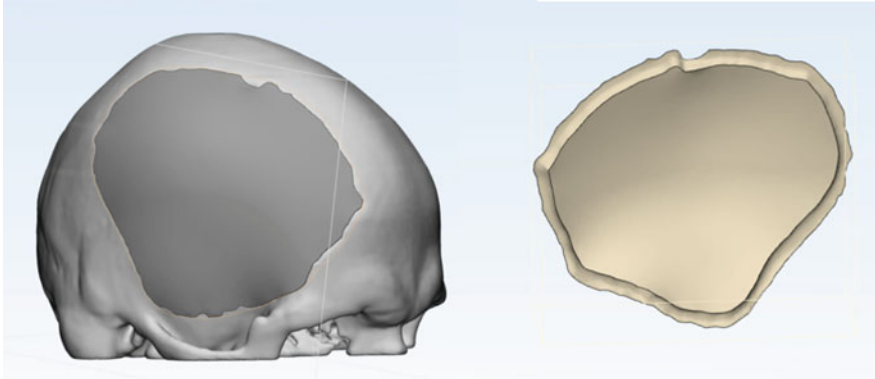


Fig. 8 Design process for a patient-specific skull implant (Swiss MAM Research Group, Thieringer, DBE)

itself, along with limited surgical access, orbital reconstructions continue to be a significant challenge. This leads to increased surgical time and, on occasion, inaccurate results caused by the freehand, manual adaptation of the meshes. In such clinical scenarios, 3D-printed anatomical models can be an asset. So we compared the efficacy of the intraoperative bending of titanium meshes (the conventional approach) with a preformed, patient-specific, “hybrid” titanium mesh implant based on an in-house, 3D-printed, anatomical model. We observed that use of the 3D-printed orbital anatomical model to prebend the plate preoperatively resulted in a considerable reduction to the operation time (by an average of 42.5 mins in our cases). Compared to the conventional approach, the model also provided a more accurate reconstruction of the orbital floor with a better functional outcome.

4.7 A 3D-Printed, Patient-Specific Scaphoid Replacement: A Cadaveric Study (Honigmann et al., 2017)

A close collaboration between our research group and other clinical and research partners, this interdisciplinary study goes a step further in the direction of 3D-printed, patient-specific implants. Within the framework of this research project described in the paper, a novel scaphoid prosthesis was developed based on anatomical data. The prosthesis was then implanted and evaluated at the Institute of Anatomy at the University of Basel within the framework of a cadaver study (static CT motion and dynamic motion analysis/cinematography). An interesting aspect was the innovative design of this implant, which included a curved channel for the passage of the tendon of the *M. flexor carpi radialis* as well as the evaluation of different manufacturing processes based on material-scientific biomechanical and clinical aspects. For this study, sample scaphoid prostheses were 3D printed from titanium, PEEK, and ceramic and compared. In addition, reference scaphoid

implants were manufactured from PEEK blocks. We showed that the 3D printing manufacturing processes allowing the creation of a curved channel for fixing the implant were superior to subtractive manufacturing processes (milling) or injection moulding.

4.8 Patient-Specific Surgical Implants Made of 3D-Printed PEEK: Material, Technology, and Scope of Surgical Application (Honigmann et al., 2018)

Polyetheretherketone (PEEK) is a high-performance polymer used in industry, aerospace, motor racing, and medicine. Unlike metals, PEEK is non-conductive, shows hardly any/no artefacts in radiological imaging examinations, and exhibits excellent tissue compatibility without the classic stress-shielding effect commonly observed in titanium implants. Classical subtractive manufacturing methods for individual implants include the expensive milling process (milling with loss of material). This process cannot produce complex geometric shapes (e.g., hollow bodies, a honeycomb structure, lightweight construction) or the injection moulding of PEEK, which is problematic for individual implants. Until a few years ago, there were no (or only very costly) processes for manufacturing patient-specific implants additively. Our research group recognized the potential application of 3D printing to custom PEEK implants several years ago and has conducted extensive research in this area. Through exclusive cooperation with an industrial partner, we were able to test and evaluate the first industrial 3D PEEK printers within the scope of several studies. In the present paper, aspects of the digital workflow (from the patient's DICOM data set to the material extrusion-based FFF 3D printing of patient-specific PEEK implants in the clinical-medical context) were highlighted and critically evaluated. In another study, we demonstrated the potential for smoother integration and faster implant production (within 2 hours) for the above-mentioned complexly shaped, patented, PEEK, patient-specific scaphoid prosthesis (Honigmann et al., 2021).

Building upon these positive initial findings, we evaluated the performance of in-house, 3D-printed, PEEK cranial implants. We then assessed their clinical applicability in reconstructive surgery applications. We observed that the custom, 3D-printed, cranial implants had high dimensional accuracy, repeatability, and clinically acceptable morphologic similarity in terms of fit and contour continuity. Biomechanically, the tested cranial implants had a mean (SD) peak load of 798.38 ± 211.45 N. In conclusion, the findings from these studies (Sharma et al., 2020a, 2021) revealed the profound effects of bringing in new dimensions to point-of-care manufacturing. Custom implants can be manufactured close to the operating room and directly sterilized, streamlining the entire production workflow. These advancements will result in a paradigm shift that will propel the point-of-care manufacturing digital workflow of customized implants to unprecedented heights. In a nutshell, the addition of in-house 3D printing has brightened the prospects for PEEK, FFF, 3D printing in craniomaxillofacial, trauma, and orthopaedic surgery.

4.9 An in Vitro Study of Osteoblast Response on Fused-Filament Fabrication 3D-Printed PEEK for Dental and Craniomaxillofacial Implants (Han et al., 2019)

Part of an international collaboration, this paper describes the effects of different surface textures of untreated, polished, and sandblasted PEEK test specimens. The specimens were 3D printed by our research group on human osteosarcoma cell lines (cell adhesion, metabolic activity, and proliferation). A fascinating finding from this study is that untreated PEEK surfaces showed a significant increase in cell metabolic activity and proliferation after 5 days, with a higher cell density than in comparison groups. The study promises exciting prospects for possible surface configurations of 3D-printed implants, for example, for use in orthopaedics, spinal surgery, neurosurgery, and, of course, oral and craniomaxillofacial surgery. Our group is already conducting further studies of surface treatment.

4.10 An in Vitro Mechanical and Biological Properties of 3D-Printed Polymer Composite and β -Tricalcium Phosphate Scaffold on Human Dental Pulp Stem Cells (Cao et al., 2020)

As a part of an international collaboration, another paper in the field of regenerative medicine describes the fabrication of a polymer composite with a bone-forming material. We successfully fabricated 3D composite scaffolds with interconnected porous structures made up of poly(lactic-*co*-glycolic acid) with tricalcium phosphate (3D-PLGA/TCP). We also fabricated native 3D-TCP scaffolds using two relatively different 3D-printing technologies and investigated the mechanical and biological responses of human dental pulp stem cells (hDPSCs). Our findings showed that the native 3D-TCP scaffolds have a higher compressive strength than 3D-PLGA/TCP scaffolds, but the 3D-PLGA/TCP scaffolds were more flexible mechanically. We further showed how the addition of a 3D structure and TCP components to PLGA polymer increased the hDPSCs adhesion and proliferation while also promoting osteogenic differentiation. These findings indicate future potential to repair minor and critical bone defects in oral and maxillofacial surgery. Our group is already conducting additional research in this area.

5 Conclusions

Integration of the additive manufacturing of anatomical patient models, surgical templates, and patient-specific implants into hospital processes offers numerous advantages. These include high-level, interdisciplinary exchange between relevant professional groups, a faster turnaround time for implant manufacturing, support for preoperative and intraoperative planning, improved treatment outcomes, and lower

overall healthcare costs in the medium term. We believe that even medical 3D printing of patient-specific implants could become an integral part of larger hospitals, potentially offering numerous applications (especially as relates to reconstructive surgery).

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