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3D printing in palliative medicine: systematic review

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ABSTRACT

Background Three-dimensional printing (3DP) enables the production of highly customised, cost-efficient devices in a relatively short time, which can be particularly valuable to clinicians treating patients with palliative care intent who are in need of timely and effective solutions in the management of their patients' specific needs, including the relief of distressing symptoms.

Method Four online databases were searched for articles published by December 2020 that described studies using 3DP in palliative care. The fields of application, and the relevant clinical and technological data were extracted and analysed.

Results Thirty studies were reviewed, describing 36 medical devices, including anatomical models, endoluminal stents, navigation guides, obturators, epitheses, endoprostheses and others. Two-thirds of the studies were published after the year 2017. The main reason for using 3DP was the difficulty of producing customised devices with traditional methods. Eleven papers described proof-of-concept studies that did not involve human testing. For those devices that were tested on patients, favourable clinical outcomes were reported in general, and treatment with the use of 3DP was deemed superior to conventional clinical approaches. The most commonly employed 3DP technologies were fused filament fabrication with acrylonitrile butadiene styrene and stereolithography or material jetting with various types of photopolymer resin.

Conclusion Recently, there has been a considerable increase in the application of 3DP to produce medical devices and bespoke solutions in the delivery of treatments with palliative care intent. 3DP was found successful in overcoming difficulties with conventional approaches and in treating medical conditions requiring highly customised solutions.

Key messages

What was already known?

⇒ Specialists in palliative medicine often require short term, rapid solutions to alleviate the patients' distressing symptoms and improve their quality of life. Three-dimensional printing (3DP) is becoming more common to manufacture complex patient-specific devices and is recognised for its ability to provide cost-effective and customisable rapid solutions. Patients in receipt of palliative care can benefit from the advantages of 3DP; but in order to highlight potential opportunities, it is necessary to systematically review its use in this clinical field.

What are the new findings?

⇒ The majority of reports of 3DP use in palliative care were published after the year 2017. The studies showcase a versatile range of potential applications, including for the production of anatomical models, endoluminal stents, navigation guides, obturators, epitheses, endoprostheses and others. The main reasons for using 3DP are the difficulty of producing patient-specific devices with traditional methods, and the lack of commercially available solutions to specific patient needs.

INTRODUCTION

Three-dimensional printing (3DP), also known as additive manufacturing (AM), is becoming increasingly common in modern medicine. Initially, it was limited to manufacturing prototypes, and was synonymous with rapid prototyping (RP),[1] but it is being increasingly used to directly produce finished products and components.[2] Physical objects are built from digital data (ie, computer-aided design models) that can be generated anew using 3D-modelling software, or obtained by 3D-scanning of existing objects in the process of reverse engineering (RE). The final designs are then 3D-printed directly (direct AM), or fabricated with the help of 3D-printed tools/moulds (indirect AM).

Presently, 3DP is gaining increasing recognition in a range of medical practices, including diagnostics, surgical planning

Key messages

What is their significance?

Clinical

⇒ Using 3DP-generated applications as a component of the care provided to patients with palliative care needs can lead to a positive impact on palliative care patient outcomes, particularly when cost, time and the possibility of customisation are critical factors. Guidelines are provided regarding the advantages and disadvantages of specific 3DP technologies and materials, both to inform future clinical practice and identify limitations.

Research

⇒ To the authors' knowledge, this study is the first comprehensive systematic review analysing 3DP as a method of producing medical devices that might be applied to patients receiving palliative care.

and reconstruction, patient education, rehabilitation, tissue engineering and pharmacology.[3] In the production of medical devices and tools, 3DP offers a wide range of advantages over traditional methods, most notably the possibility of cost-effective, small-scale, on-demand, in-house fabrication of geometrically and structurally complex patient-specific products in a relatively short time.[4 5] These advantages can add particular value to the delivery of responsive care to patients with palliative care needs. Namely, the possibility of producing highly customised solutions at low cost allows for individualised management of patients' needs to help them cope with their condition and treatment, and experience optimal quality of life despite the disease. Moreover, reduced lead time enables a quick response to alleviating distressing symptoms and allow a person whose health is deteriorating to spend less time away from their home.

It is of note, that in part due to the relatively recent recognition of palliative medicine as a specialty, even among healthcare professionals a common understanding of the roles of palliative care still needs to be established.[6 7] To facilitate this, the International Association for Hospice and Palliative Care published a new 'Consensus-Based Definition of Palliative Care' in 2019.[8] For clarity, the authors of the present work also acknowledge the following: (1) specialist palliative care is given alongside treatments targeting the underlying disease; (2) when the intention is potentially curative, the intervention does not qualify as truly palliative and (3) interventions provided with palliative intent are typically less invasive and less dangerous procedures, although the same medical approaches can have curative effects in some diseases, and palliative in others (eg, central airway obstruction management with stents,[9] radioactive ^{125}I seed implantation for brachytherapy,[10] bone tumour resection[11] and endoprosthetic reconstruction[12]).

Individual literature reviews exist of 3DP in palliative care, focused on specific types of medical devices, such as central airway stents,[9] oesophageal stents[13] and orthoses.[14] However, to the authors' knowledge, no systematic reviews have been published to date in this field. Thus, the aim of this study is to provide a systematic review of studies reporting the use and the potential uses of 3DP in specialist palliative care, with specific emphasis on the fields of application, technology employed and the advantages of 3DP over conventional methods.

METHODS

Literature search and study selection

A systematic literature search was performed during December 2020 using the following databases: EBSCOhost (including Academic Search Complete, MEDLINE with Full Text, CINAHL Complete), PubMed, Scopus, and Web of Science. Articles of interest included terms related to 3DP in the title (ie, "3D print*","3D-print*", "three-dimensional* print*", "additive* manufactur*", or "rapid* prototyp*"), terms related to palliative care in the abstract (ie, "palliat*", "cancer*", "oncolog*", "tumour*", "tumor*", "malignan*", "terminal* ill*", or "terminal* disease*"), and terms related to palliative care in the full text (ie, "palliat* car*", "palliat*", "end-of-life", "end of life", "quality-of-life", or "quality of life"). If necessary, the search string was adapted to meet the search options of specific databases. An additional search was performed using Scopus to identify studies including any of the terms related to 3DP and the term "palliative" in either the title, abstract or keywords. The study selection was limited to full scientific articles in the English language. All included papers were published prior to the date of the search. Reviews, book chapters and non-scientific papers were excluded from the review, as were studies performed on veterinary patients, involving curative or aesthetic surgical reconstructive procedures, and testing diagnostic technology. Also excluded were studies involving palliative surgical correction of paediatric congenital heart defects, as these are typically managed by cardiologists. Regarding bias, all studies which met the selection criteria were included.

The review protocol was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[15] The search and study selection criteria are presented in figure 1. TK confirmed the outcomes of the search and selection performed by NJM and CG. Any disagreements among the reviewers were resolved by LOS.

Data extraction and synthesis

The following data were extracted from the selected studies: (1) field of application of 3DP in palliative care, type of 3D-printed device, its stage of development and application; (2) technology used for device fabrication including 3DP technology, 3D-printer make, material, imaging technique, software used and (3) testing of the 3D-printed device, including number

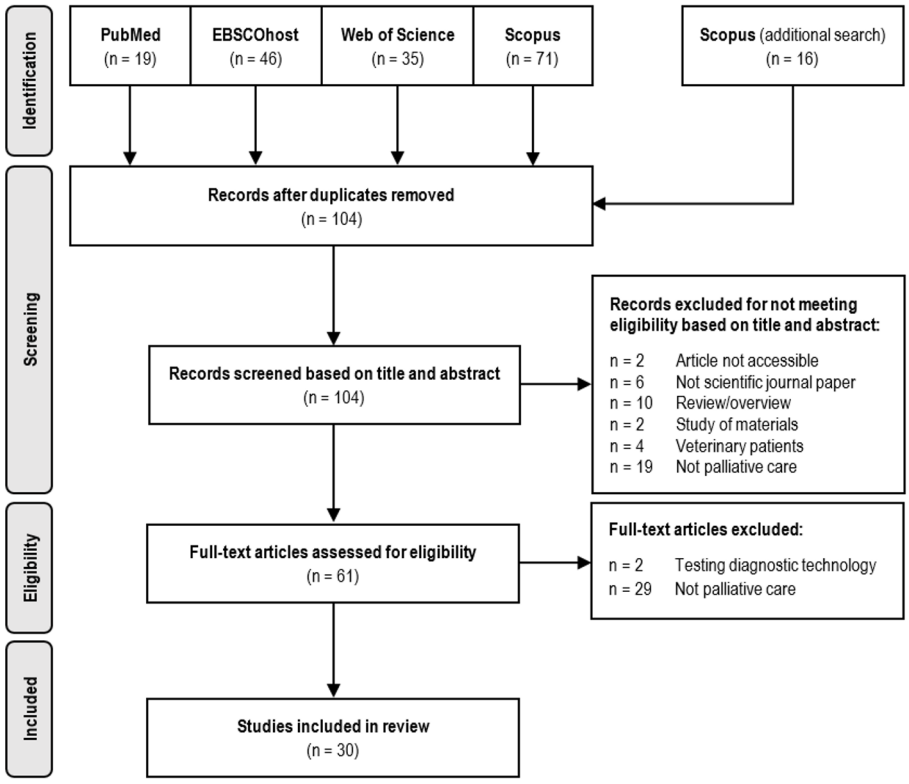

Figure 1 PRISMA flow diagram of literature search and study selection. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

of participants, age and medical status, testing method and outcomes of intervention. 3D-printed device manufacturer, print time and cost were also reviewed.

RESULTS

Thirty relevant papers on the use of 3DP in palliative care were identified and included in the review. The first study was published in 2004, and 20 papers were published in the last 3 years, as shown in figure 2.

Device type and field of application

3DP was applied to different medical sub-specialties within oncology, predominantly gastrointestinal, orthopaedic and radiation oncology. Only three devices were produced for non-oncological applications (figure 3).

In the 30 reviewed studies, 36 different devices were produced (online supplemental table 1). The most common were endoluminal stents (9), however, all were used in proof-of-concept studies. Other most commonly 3D-printed devices were anatomical models (6), brachytherapy navigation guides (5), endoprostheses (including one mould; 4), epithesis casts and moulds (3) and obturator casts (2). In single cases, an injection-moulding chamber, surgical cutting guide, PEG-tube sealing device, respirator mask and positive mould, scaffold for chemotherapeutic delivery, and a

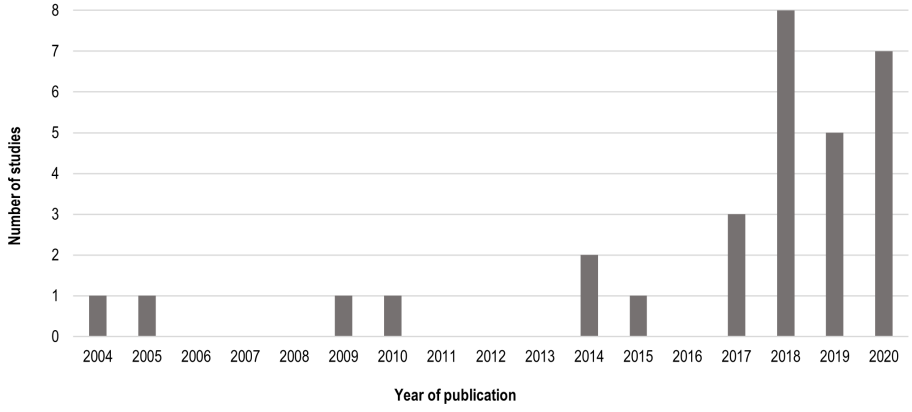

Figure 2 Reviewed studies involving the use of 3DP in palliative care by year of publication. 3DP, three-dimensional printing.

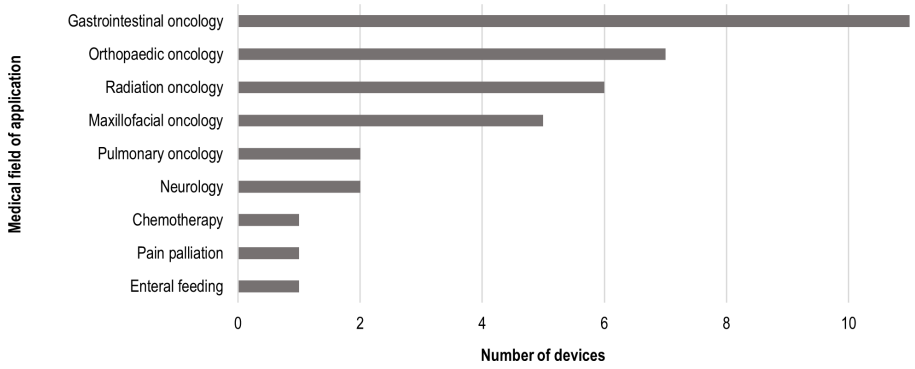

Figure 3 Fields of application of 3DP in palliative care. 3DP, three-dimensional printing.

robot for ultrasound pain palliation were manufactured. Figure 4 summarises the purpose of the devices.

Problems addressed by 3DP

The most common purpose of 3DP was to improve the accuracy and/or efficiency of treatment achievable with traditional methods (13 devices). Seven of the 13 devices were intended to improve the accuracy of drug delivery, 2 were endoluminal stents with improved patency or drug distribution, and 1 was an anatomical model for improved surgical planning. A further three devices were used to address the lack of efficiency in the traditional method (ie, one cutting guide, one endoprosthesis, one obturator mould). In six studies, 3DP was chosen to address the difficulty of device customisation with traditional methods, including endoluminal stents (3), endoprosthesis (1), epithesis (1) and respirator mask (1). In two studies, 3D-printed anatomical models were used to address difficulties of spatial anatomy comprehension from 2D images. Four devices were used to reduce the risks for patients associated with conventional methods, and one anatomical model was used as an alternative to human testing (figure 5).

3DP was used with the intention to reduce the cost and manufacturing time of two epitheses and two endoluminal stents. Time-efficiency was reported in four studies with print durations ranging up to to 36 hours,[16] and two studies highlighted the potential for delivering custom 3D-printed devices to patients within 24 hours.[17 18] Cost-effectiveness of 3DP was emphasised in two cases (US$30 for a head mould to replace a US$200–US$400 CT scan[16] and a US$5 custom-fit BiPAP mask[16]), and one study considered the price disadvantageous (US$500 for materials and printing of an obturator definitive cast).[19]

3DP technology

Thirteen devices were manufactured using Fused Filament Fabrication (FFF),[16 20–30] one of which used a custom built FFF gantry specifically designed for the orbital printing of stents.[26] Six devices were produced using StereoLithograPhy (SLA),[18 22 31–33] five using Material Jetting (MJ),[17 19 34–36] two using Selective Laser Sintering (SLS)[18 33] and in single cases, direct metal laser melting[37] and electron beam melting[33] were employed. One study reported the use of selective laser lithography[12] (the authors of the present review are unfamiliar with this technology). In seven studies, 3DP technology was not specified; however, four of these detailed the type of material used (ie, photopolymer resin, medical resin, and PolyMethyl MethAcrylate (PMMA)).

Ten of the reviewed papers did not detail the material employed. Across the other studies, the most common materials were photopolymer resin (including Flexible Resin, MED610, Tango family and VisiJet C4 Spectrum Core; 8) used with MJ or

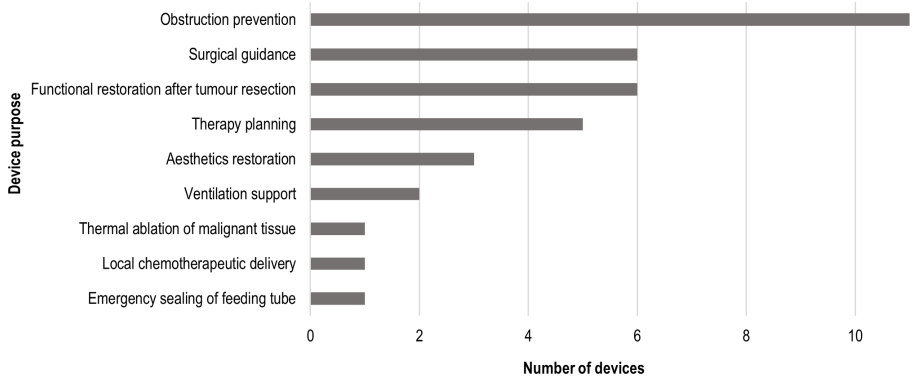

Figure 4 Purpose of the reviewed 3D-printed devices in palliative care. 3D, three dimensional.

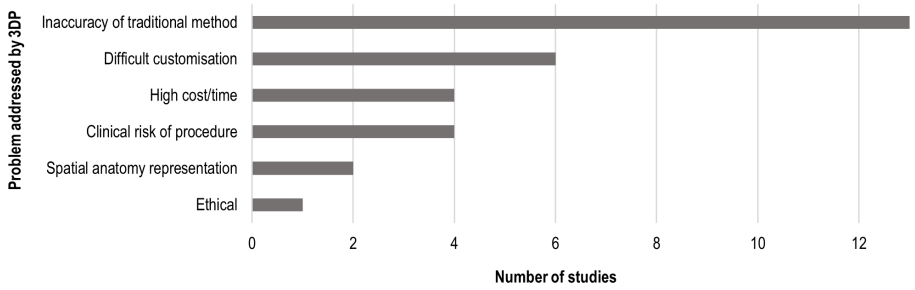

Figure 5 Problems addressed by 3DP in the reviewed studies. 3DP, Three-Dimensional Printing.

SLA, and Acrylonitrile Butadiene Styrene (ABS; 6) used with FFF. Also employed were Polycaprolactone (PCL, including in combination with Paclitaxel—PCL/PTX; 2), PolyLActic acid (PLA, including in combination with thermoplastic polyurethane—PLA/TPU; 2), polymethyl methacrylate (PMMA; 2), PolyVinyl Alcohol (PVA, including in combination with TPU—TPU/PVA; 2), Titanium alloy (2) and Polyurethane (PU; 1).

Patient-specific devices were mainly reverse engineered, which involved surface 3D scanning or CT/MRI, and designing the device based on the digital data of patients' anatomy. Devices that were directly designed included nine endoluminal stents, not tested on patients, a coplanar navigation guide, PEG tube sealing device, scaffold for chemotherapeutic delivery and robotic system for ultrasound palliation of pain. Unlike RE, these devices were designed independently of the specific patients' anatomy. Indirect AM was used to create moulds for obturators, epitheses and respirator masks manufactured from silicone; the other devices were directly 3D printed.

Clinical testing

Eleven papers described proof-of-concept studies that did not involve testing of the devices on human participants. Eight of these were studies of endoluminal stents, one was a phantom model, one a scaffold for chemotherapeutic delivery, and one was a robot for ultrasound pain palliation. In the remaining 19 studies which did include human testing, the number of participants ranged from 1 to 92. The most substantial participant groups were recruited in studies of brachytherapy navigation guides (25–92 participants).[38] The only study that included a control group was of a coplanar navigation guide that was tested on 25 participants.[39] Ten articles were case reports describing the use of 3D-printed devices for clinical care.

The devices were tested using objective methods in 18 studies, 15 of which produced quantitative results and 2 qualitative. Eight studies used qualitative subjective methods. Two studies used a combination of subjective and objective methods, and two did not report any testing of the device.

Outcomes of interventions

All reviewed studies reported generally favourable outcomes. Eleven studies confirmed the feasibility of their concept. Nine of these developed endoluminal stents that showed promising results regarding mechanical[18 29] and drug-eluting properties.[22 25–27] It was also reported that such stents could be delivered to patients within 24 hours[18] or over a weekend at a relatively low cost.[32] In the other proof-of-concept studies, stent abutment was proven to cause prolonged passage of soft and solid diets[35]; a scaffold for chemotherapeutic delivery was shown to significantly reduce the viability of prostate cancer cells[20]; and MRI safety and compatibility were verified for an ultrasound pain palliation robot.[30]

Anatomical models produced positive outcomes in therapy and surgical planning. They demonstrated a high concordance rate with diagnostic accuracy of invasive procedures,[36] and facilitated joint-preserving posterior acetabular resection.[11] In one study, an uncommon anatomical feature was detected that was not recognised in 2D images, but had an important effect on the intraoperative approach.[40] Head models were produced with satisfactory accuracy to make immobilisation masks without the need for additional patient visits, which lowered treatment costs.[16]

All brachytherapy navigation guides were successfully used, with occasional minor side effects related to the treatment itself. One study included a control group and found significantly higher dosimetry values in target tissues when navigation guides were used.[39]

In general, the fit of patient-specific obturators was satisfactory, and few problems were reported in individual cases (eg, leakage while drinking liquid, nasal voice, numbness, dry mouth).[34] Patients' pronunciation, mastication and swallowing were improved, nasal regurgitation was prevented,[19 34] and the overall psychological and social well-being was enhanced.[34]

Epitheses demonstrated the possibility of improving the patients' quality of life and comfort, both semi-functionally and aesthetically.[24] A nasal prosthesis was produced in shorter time and at lower cost compared with traditional techniques.[23] Endoprostheses for palliative orthopaedic reconstruction were successfully implanted, with significant postoperative pain

reduction and improved function of the limb,[28] and with no cases of poor outcome, severe complications, endoprosthesis failure or migration.[12 28 33 37] A PEG tube sealing device enabled recommenced feeding regime without leakage within 24 hours from the clinicians' request.[17] Finally, the vast majority of patient-specific respirator masks were rated higher than generic masks in all aspects of comfort, leakage, preference, recommendation and tolerance.[31]

When referring to the technology employed, the term '3D Printing' was most often used (25), followed by '3DP' (14), 'RP' (12), 'AM' (7) and 'computer-aided manufacturing' (4).

DISCUSSION

The use of 3DP in palliative care

This review identified certain trends in the use of 3DP for the purposes of palliative care. The first study was published in 2004, and two-thirds of the reviewed papers were published after the year 2017. This indicates a considerable increase in the use of 3DP in palliative care in the last few years, which could be directly related to the release/expiration of 3DP patents. Between 2009 and 2014, the original patents for FFF and SLA expired,[41] leading to the expansion of the 3DP market and subsequent decrease of 3DP entry cost. It is likely that the increase in publications presented in this review is directly related to the democratisation of 3DP. The most prominent fields of application that included clinical testing were radiation oncology (brachytherapy navigation guides) and orthopaedic oncology (anatomical models and endoprostheses). These studies also involved the largest numbers of participants. Brachytherapy navigation guides were among the simplest devices manufactured by 3DP in the included studies, making them relatively easy to implement across a larger number of patients. Anatomical models are relatively easy to make, derived from existing medical imaging, with no ethical constraints or need for regulatory approval, being used for training/education purposes with no body contact, implanting, or any procedure directly impacting the patient. 3DP has been used to manufacture anatomical models dating as far back as the early 1990s,[42] recently becoming a more familiar and accessible medical application of this technology. Comparably, there have been enough studies to verify 3DP as a go-to technology for endoprostheses and surgical guides. In a review of 3DP techniques in a medical setting in 2016, surgical guides were listed as the most common devices produced (60.0%), followed by anatomical models for surgical planning (38.7%) and implants (12.7%).[43]

Clinical aspects of 3DP in palliative care

Roughly two-thirds of the reviewed studies reported the outcomes of 3DP-assisted procedures, and one-third were proof-of-concept studies. In general, the clinical outcomes were considered superior to those of conventional approaches. However, only one study (coplanar navigation guide) included a control group that received the treatment without the device.[39] The lack of a control group can impair the validity of the conclusions drawn, as it is uncertain to what extent clinical results can be attributed solely to the use of the 3D-printed device.

In recent years, 3DP has becoming common practice to treat medical conditions that require highly customised solutions (eg, reconstruction after extensive resection in orthopaedic oncology) and/or high-precision treatment (eg, brachytherapy of unresectable visceral tumours). It can also be used to create devices that do not otherwise exist (eg, a PEG tube sealing device[17]) or are difficult to produce with traditional approaches (eg, obturator for patients with trismus[34]).

Technological guidelines for 3DP use in palliative care

The choice of 3DP technology

In the reviewed studies, 3DP was predominantly used to overcome the difficulties of producing customised devices with traditional methods. FFF was the most commonly used 3DP technology (13 of the reviewed devices, including anatomical models and oesophageal stents). Despite the poor surface finish with an apparent staircase effect typical for low-resolution desktop FFF printers,[23] it is favoured for its low cost, versatility and wide range of available thermoplastic filaments, allowing clinicians to match material characteristics of the devices with their function. However, in the studies reviewed, there was little evidence of correlation between the type of medical device produced and the choice of 3DP technology, which suggests that 3DP technology was selected based on availability to the clinician rather than its suitability for the specific device. This suggests that some or many 3D-printed medical devices are produced using suboptimal methods due to the lack of funding, accessibility or familiarity with the technology. Table 1 provides a brief overview of the specifications of 3DP technology to inform future clinical practice.[44–47]

When cost and accessibility are the main concerns, FFF technology is usually opted for, not MJ or SLS. For example, the head mould for radiotherapy immobilisation mask would be too expensive to manufacture using other technologies, and the proof-of-concept studies of stents used FFF possibly due to accessibility for research purposes. For devices in direct contact with the skin or mucosa, such as obturators, smooth surface finish is often important, and thus, SLA, DLP or MJ are favoured. Likewise, the surface finish of epitheses should resemble the texture of skin, which cannot be achieved with FFF, as pointed out in a study of a nasal epithesis.[23] Similar to surface finish, FFF would be rejected for accuracy and resolution in place of MJ, DLP, SLA or SLS, especially when producing highly detailed parts, such as the thread of a Percutaneous

Table 1 Overview of key characteristics of the most common 3DP technologies and materials

	FFF	SLA	DLP	MJ	SLS
Overall cost	Low	Medium	Low	Very high	High
Desktop printers	Yes	Yes	Yes	Yes	Yes
Accuracy	Low	High	High	High	High
Resolution	Low	High	Very high	Very high	Medium
Surface finish	Staircase effect	Smooth	Smooth	Smooth	Grainy
Mechanical properties of printed parts	Satisfactory (anisotropy)	Satisfactory (brittle, affected by moisture and sunlight)	Satisfactory (brittle, affected by moisture and sunlight)	Satisfactory (brittle, affected by moisture and sunlight)	Very good
Complex designs	No	Limited	Limited	Yes	Yes
Multimaterial printing	Yes	No	No	Yes	No
Rigid biocompatible materials—examples	ABS-M30i, PC-ISO, PLA, PMMA, ULTEM™ 1010, ULTEM™ 9085	Accura ClearVue, BioMed Clear, Dental SG Resin, E-Shell 3000, NextDent SG, WaterShed XC 11122	Dental SG Resin, E-Shell 3000	MED610, VeroDent, VisiJet M2R-CL, VisiJet M3 Crystal	CAPA 6501, Duraform PA, EOS PA2200, EOS PEKK, PA 12, PCL
Flexible biocompatible materials—examples	TPU (Tecoflex)	Elastic 50A Resin, E-Guide Soft	E-Guide Soft	MED625FLX, VisiJet M2E-BK70	TPU

ABS, Acrylonitrile Butadiene Styrene; DLP, Digital Light Processing; 3DP, Three-Dimensional Printing; FFF, Fused Filament Fabrication; MJ, Material Jetting; PA, Poly Amide (Nylon); PC, PolyCarbonate; PCL, PolyCaproLactone; PEKK, PolyEtherKetoneKetone; PLA, PolyLactic Acid; PMMA, PolyMethyl MethAcrylate; SLA, StereoLithograPhy; SLS, Selective Laser Sintering; TPU, ThermoPlastic Urethane.

Endoscopic Gastrostomy (PEG) tube sealing device or implants.

The choice of 3DP materials

Half of the reviewed papers did not detail the material employed. Across the other studies, the most common material, ABS, is used largely for moulds for its high strength, toughness and impact resistance, flexibility, durability and temperature resistance which allows for mould reusability.[23 47 48] For other FFF applications, PLA can be favoured over ABS due to its ease of printing, accessibility and price.[16] PCL is used to manufacture endoluminal stents because of its biocompatibility and bioresorbability.[26] Similarly, biocompatibility is the reason for using MED610 for devices that are expected to stay in prolonged contact with the patient's skin.[17] Endoprostheses for palliative purposes can stray from the typical use of titanium alloys,[33 37] as integration between the host bone and endoprosthesis is not expected in patients with bone metastases. In this case, PMMA can be employed as an alternative 3D-printable biocompatible material that is generally available and sufficiently strong to replace non-weight bearing bone, while also being more cost-efficient.[12 49]

Navigation guides for brachytherapy should be safe for skin contact, and are mainly fabricated from photopolymer resins. A common issue with photopolymer resins is the cytotoxicity of the raw material, therefore, a careful balance in its composition is required to preserve printability and ensure safety for use.[50] Among the most versatile biocompatible polymers used with photo-curing techniques are acrylate- and methacrylate-based resins.[47]

Manufacturing approaches

Patient-specific devices are reverse engineered by using digital data of patients' anatomy, as opposed to being directly designed. Indirect AM can be used to create moulds for devices that need to be manufactured from non-printable materials, e.g. silicone, like obturators and epitheses. 3DP materials approved for human use with similar properties to silicone are scarce, and most biocompatible silicone resins are not yet commercially available.[50] Among those currently on the market, 3D-Bioplotter UV Silicone 60A MG (EnvisionTEC) is a transparent medical-grade silicone, approved for 29-day direct skin contact, characterised by medium hardness, no odour, and the possibility of colouring prior to printing.[51] Similarly, TrueSilTM (Spectroplast AG) is biocompatible and available in different hardnesses for different applications (eg, mouthpieces, insoles, earbuds, prosthetics).[52] Elastic Resin (Formlabs) mimics casted silicone well, but it is not biocompatible.[53]

Regulatory aspects of 3DP in medicine

Currently, 3D-printed medical devices must conform to the same regulations as those that are manufactured using traditional methods. The regulations vary across different countries (eg, Regulation (European Union, EU) 2017/745 on Medical Devices Reporting[54] in the EU; Title 21 Code of Federal Regulations[55] in the USA), and have been extensively reviewed in other literature.[56 57] The standard approval process for new medical devices tends to be lengthy, requiring several years of preclinical and clinical testing. As this can present a substantial barrier to urgently treating rare, life-threatening or severely debilitating medical conditions, not uncommon in palliative care, non-standard

regulatory pathways have been established for rapid approval of medical devices in exceptional circumstances. These pathways allow for clinicians and/or manufacturers to apply for exemptions to use non-certified medical devices on humanitarian grounds. The use must be justified through a significant reduction in mortality or morbidity compared with alternative compliant treatments, and applications are assessed on a case-by-case basis.

The vast majority of studies included in the present review did not detail the regulatory frameworks followed. An overview of regulatory aspects applicable is provided the authors' previous systematic review of 3D-printed medical devices used on patients[3]. Especially when bespoke medical devices are 3D-printed to be used without prior testing under the above-mentioned humanitarian exemptions, it is of utmost importance that an appropriate quality management system is in place, which can ensure that appropriate technologies and materials (eg, certified biocompatible materials) are employed in the printing process, and that the postprocessing requirements are met to warrant mechanical, chemical and biological safety of the end product.[58]

3DP and design collaboration

This systematic review highlights how 3DP can potentially be used as part of a design process to address previously unmet clinical needs for which current solutions are either not available or not suitable. The majority of the studies indicated authorships which were interdisciplinary, typically between clinical and design/technical groups. The papers typically focused on the clinical problems and the reporting of the solutions obtained, and therefore, it is not possible to ascertain and synthetise the desgin processes followed across the studies. The current authors anecdotal experience is that clinicians sometimes issue requests to research groups in universities for design assistance with very specific clinical challenges. Arising from these requests, clinical design collaborations are initiated which often form the basis of followon 3DP/innovation research. By way of example, we previously reported on a clincal request to our group for assistance to produce an alternative eye cover for a teen with Rhabdomyoscarcoma.[59] Access to3DP was not part of the initial request but was used by the design group to make the solution. Arising from the engagement, the local palliative care clinical team and the design group thereafter established other research opportunites regarding 3DP in palliative care. Hence, once initial experience is established, then followon design interactions using 3DP are made possible.

Our experience is that some clinicians have experience in 3DP, either through previous clinical innovations or due to access to promoted clinical-based 3DP programmes. In these situations, such clinicians may develop their own concepts for which their key requirement thereafter is access to designers to collaborate in refining the design and print the concepts/devices.

Limitations

There may be other studies not identified by our systematic search due to the terminology issues addressed above, thus, it is possible that some 3D-printed devices intended for palliative care were not included in this review. Moreover, the identified cases of palliative correction of congenital heart defects typically managed by cardiologists were excluded. Nevertheless, the authors expect the key findings of the present work to be a reasonably complete reflection of the current state regarding the use and potential for increased use of 3DP in the provision of care to patients with palliative care needs.

CONCLUSIONS

This systematic review revealed the use of 3DP in palliative care for approximately two decades, with a considerable increase in its use since 2017. Reviewed were 36 devices produced across 30 studies. The device type, field of application, problem addressed, technology used, clinical testing methods and the outcomes of intervention were analysed.

The most common proof-of-concept devices were endoluminal stents, and the most common devices that included clinical testing were anatomical models, brachytherapy navigation guides and endoprostheses. Of the 3DP technologies, FFF was most frequently employed, followed by SLA and MJ. In most of the studies that specified the material used, ABS was chosen, mainly for creating moulds, followed by unspecified photopolymer resins. The majority of devices were designed using RE to correspond to the patient's anatomy. The outcomes of interventions were generally favourable, and the difficulties associated with conventional procedures were successfully overcome. 3DP was found especially valuable in the treatment of medical conditions that require highly customised solutions and/or high-precision procedures, while also ensuring cost-efficiency and time-efficiency. With 3DP, entirely new devices can also be created for rapid response to unique clinical situations.

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Supplemental table Reviewed studies of 3DP in palliative care.

Study **Field of application** Device type and indication	**Problem solved by 3DP**	**Device Production**		**Device testing/use**		
		Imaging technique Software	**3DP technology** 3D printer (manufacturer) Material *Additional procedures (if applicable)*	**Participants** Number, sex, age Medical status	**Methods**	**Outcomes**
[35] Gastrointestinal oncology (gastroduodenal) Anatomical phantom for testing of gastroduodenal stents for treatment of malignant strictures	Ethical unacceptability of investigating the mechanism and significance of stent abutment in the duodenal wall of live patients.	**CT** MeshLab Meshmixer	**MJ** Objet500 Connex3 (Stratasys) Tango family	Retrospective analysis ♂, 62 years Advanced gastric cancer	Measurement of elapsed times at passage of water (300 ml, 4 s), and soft and solid food materials (3 types; 300 ml); partially and fully covered self-expanding metallic stent; 2 locations of distal stent ends; 10 repetitions.	Proof of concept: Stent abutment can cause prolonged passage of soft and solid diets through the stent, impaction of solid diets into stent.
[36] Gastrointestinal oncology (bile duct) Patient-specific anatomical model of tumor and bile duct visualization to aid surgical planning for ERCP biliary stent placement	Difficulty determining target bile duct with traditional imaging techniques in complex HCC.	**CT/MR** Mimics 17.0	**MJ** ProJet 4500 (3D Systems) VisiJet C4 Spectrum Core	Retrospective analysis 6♀, 9♂, 65.4 ± 14.9 years Inoperable hilar cholangiocarcinoma	Target bile duct and Bismuth-Corlette (BC) classification on the basis of 3D models; comparison with those in ERCP.	86.7% concordance rate of target bile duct, 93.3% concordance rate of BC type classification with 3D model compared to ERCP.
[11] Orthopaedic oncology (pelvis) Patient-specific anatomical model of the pelvis for surgical planning to minimize acetabular bone loss and maximally preserve native hip function and stability	Difficulty of safe tumor resection with negative oncological margins, acceptable postoperative function, preservation of critical neurovascular structures and minimal perioperative morbidity, mortality and recurrence within tightly confined, complex anatomical areas.	**CT** N/A	**N/A** N/A N/A Manufactured by Onkos Surgical	♂, 21 years Metastatic osteoblastic osteosarcoma	Clinical follow-up.	Successful joint-preserving posterior acetabular resection of metastatic osteosarcoma with tumor-free margins and preserved hip stability. Improved quality of life, patient returned to athletic and academic pursuits.
[16] Radiation oncology (brain) Patient-specific anatomical model of the head and head-and-neck rest to serve as a volume and position mould for radiotherapy immobilization mask in whole brain radiotherapy	The need for an additional simulation CT-scan in preparation for radiotherapy with traditional methods, which increases the number of patient visits, interventions and waiting times.	**CT** CATIA	Mould: **FFF** BigBuilder Dual-Feed (Builder 3D Printers BV) PLA *Immobilization mask: Thermoplast (Aquaplast RT) moulded onto model head*	Retrospective analysis 9♀, 2♂, 60 ± 11 years (range 47-85) Brain metastases	CT scan of immobilization mask and comparison of volume to patient CT scan in Eclipse. Calculation of simulated radiation dose and comparison.	98.1% similarity between patient head surface geometry and 3D model (model volume 1.6% smaller due to segmentation smoothing), reproduction accuracy for head position within institutional constraints. Minimal differences in dosimetry during whole brain radiotherapy. Lower cost compared to simulation CT-scan, potential for reducing patient visits and waiting times.

[40] Gastrointestinal oncology (pancreas) Patient-specific anatomical model for pylorus-preserving pancreatic head resection and reconstruction planning in locally advanced adenocarcinoma	Difficulty establishing detailed anatomy from 2D CT images, especially in complex and unconventional cases.	**CT-angiography** N/A	**N/A** N/A N/A (multimaterial)	♂, 71 years Locally advanced adenocarcinoma of the papilla vateri; metastatic squamous-cell carcinoma of the lung (4 years stable); previous right hemicolectomy and patch plasty of the celiac trunk and superior mesenteric artery; primary adrenal insufficiency; Bühler anastomosis	/	Successful tumor resection. Bühler anastomosis only detected in 3D reconstruction; perioperative anatomy visualization using 3DP has the potential to increase patient safety.
[29] Gastrointestinal oncology (oesophagus) Self-expanding plastic oesophageal stent to alleviate the symptoms of irresectable oesophageal malignancies	Traditional manufacturing methods do not enable time-efficient production of parts with custom geometry and structure.	/ Multiphysics™	**FFF** Ultimaker 2 (Ultimaker) PLA/TPU composite (0:100, 5:95, 10:90, 15:85)	/	In silico, in vitro and ex vivo evaluation: Finite element analysis, testing of self-expanding properties, compression forces, self-expansion and anti-migration forces (porcine oesophagus), 16-week hydrolytic degradation rate (phosphate buffered saline, simulated gastric fluid), biocompatibility test (human primary oesophageal epithelial cells).	Proof of concept: Significantly higher anti-migration force compared to existing stents, reduced migration distance, adjustable self-expansion force.
[25] Gastrointestinal oncology (oesophagus) Patient-specific oesophageal endoluminal drug-eluting stent for sustained local delivery of 5-FU to achieve short-term reduction of tumor size in patients with oesophageal cancer	Wide morphological and clinical variability of gastrointestinal tumours can affect the performance of non-customisable drug-eluting stents.	/ SolidWorks Cura	**FFF (dual extrusion)** Ultimaker S5 (Ultimaker) PU	/	Material, mechanical and in vitro evaluation: Analysis of 5-FU distribution (photoacoustic Fourier-transform infrared spectroscopy), topography (scanning electron microscopy), mechanical properties (local compressive force, recovery rate), thermal analysis, drug content (high-performance liquid chromatography), in vitro drug release over 110 days, 5-FU stability following stent sterilization (UV, gamma irradiation) and accelerated storage (different temperatures and humidities)	Proof of concept: Confirmed homogeneous dispersion of 5-FU throughout the PU matrix, sustained release profile over 110 days, permeability from stent through oesophageal tissues, negligible degradation during thermal processing, minimal degradation during sterilization, reasonable stability over 3 months of accelerated storage.
[26] Gastrointestinal oncology (oesophagus) Tissue-specific EdECM hydrogel-loaded oesophageal stent to alleviate symptoms of radiation esophagitis	Limited precision and architectural control in hydrogel-loaded stent fabrication using traditional technologies (e.g. braiding, knitting, laser-cutting, segmentation).	/ N/A	**FFF (spindle)** 2RPS (custom) PCL	/	Material, mechanical, in vitro evaluation, and in vivo animal study: Stent surface morphology (SEM) and topography (AFM) analysis, static compression test to evaluate radial forces, cyclic 3-point bending to test flexibility and mechanical stability; rheological assessment of EdECM hydrogel, viability assessment of human oesophageal Het-1A cells in EdECM; radiation esophagitis rat model for evaluation of therapeutic effects.	Proof of concept: Therapeutic effects confirmed on animal model: resolved inflammatory response, facilitated tissue regeneration. Promising clinical approach to local delivering of therapeutic cells/drugs to manage disease.

[22] Gastrointestinal oncology (bile duct) Patient-specific biliary stent with stem cell-collagen-cholangiocyte coating to provide relief from malignant and benign bile-duct obstructions	Progressive loss of biliary stent patency over time due to biofilm and biliary 'sludge' formation.	/ TinkerCAD ImageJ Makerbot	Stent: **FFF** Replicator (Makerbot) PVA (Aquasolve) Collagen injection moulding chamber: **SLA** Form 2 (Formlabs) Flexible Resin *Stem cell collagen injection moulding, stent maturation, cholangiocyte seeding*	/	Material and in vitro evaluation: Stent surface morphology (X-ray), human placental mesenchymal stem cell and cholangiocyte viability assessment (high-resolution Cryo-SEM, phase microscopy, flow cytometry, immunofluorescent imaging)	Proof of concept: Successful incorporation of cholangiocytes to improve stent patency by reducing the entrance and adherence of harmful bacteria.
[27] Gastrointestinal oncology (bile duct) Self-expanding, drug-eluting biliary stent for palliative treatment of biliary obstruction in unresectable hilar malignancies	Limited architectural, dosage precision, drug distribution and release control in drug-loaded stent fabrication using traditional technologies.	/ N/A	**FFF** N/A PCL/PTX	/	Material, mechanical, and in vitro evaluation: Surface morphology (optical microscope, FE-SEM), radial and axial forces, chemical and thermal structure, degradable behaviour and drug release (porcine bile solution, 8 weeks), inhibitory effect on tumor growth (human biliary tract cancer cells, nude mice).	Proof of concept: Confirmed uniform drug distribution and steady release in vitro, no changes in weight and shape over time, inhibitory effect on tumor cell proliferation in small animals.
[32] Pulmonary oncology Stent master for silicone moulds to rapidly produce customised airway stents for treatment of life-threatening tracheobronchial obstructions in patients with respiratory cancer	Long manufacturing times and high costs of conventional manufacturing methods, short durability of silicone moulds.	/ N/A	**SLA** N/A N/A	/	Testing of airway stent customisation protocol: estimation of time required to deliver customised stent to the patient.	Proof of concept: Possibility of providing relief to patients within a day or over the weekend, at a relatively low cost.
[18] Pulmonary oncology Customised tracheobronchial stent to provide relief in respiratory tract obstruction by tumours or other lesions	Need for rapid airway-stent customisation in unusual airway morphology or unresectable, stiffer than normal lesions to suit the airway geometrical and distending strength requirements for effective palliation.	/ N/A	Stent master: **SLA** N/A N/A *Mould and final stent:* *Casting of silicone to create stent mould, vacuum casting of PU-based resin for final stent*	/	Mechanical testing: distending strength, collapsibility; comparison to Dumon stent.	Proof of concept: Distending strength comparable to, collapsibility 17% larger than Dumon stent. The stent could be delivered to the patient in 24 h.
[18] Gastrointestinal oncology (colon) Customised colorectal stent to provide relief in occlusion by colorectal cancer	22-23% mortality rate of surgical procedure to create temporary stoma before resection of the stricture. Existing colonic stents are costly and nonreusable.	/ N/A	Stent master: **SLS** N/A N/A *Mould and final stent:* *Casting of RTV9 silicone to create stent mould, vacuum casting of PU-based resin for final stent*	/	Mechanical testing: distending strength, collapsibility.	Proof of concept: Superior collapsibility ratio to conventional polymer stents, surpassed required collapsibility required for effective irrigation of the bowel. Comparable strength to metal colonic stents (e.g. ChooStent).
[21] Gastrointestinal oncology (oesophagus) Master for vacuum casting of semi-rigid and rigid auxetic oesophageal stents for palliative treatment of oesophageal cancer and prevention of dysphagia	N/A	/ Inventor	Stent master: **FFF** N/A ABS *Stent:* *Vacuum casting of PU resin (PX 212, VC-3300)*	/	Surface characterization (SEM), mechanical characterization (tensile and expansion testing), finite element analysis	Proof of concept: Radial expansion 0.5-5.73 mm, longitudinal extension 0.15-1.83 mm at applied pressures 0.5–2.7 bar from balloon catheter. Possibly good conformation to oesophageal wall due to non-linear anisotropic mechanical response.

[60] Radiation oncology (brachytherapy rectum) Patient-specific non-coplanar navigation guide for RIS implantation in palliative treatment of locally recurrent rectal cancer	Efficiency and accuracy of RIS implantation using traditional approaches relies on operators' experience, and misplacement can lead to unsatisfactory outcomes.	**CT** N/A	**N/A** N/A Photopolymer resin	28♀, 38♂, median 56 years (range 32-79) Recurrent sacral-invasive, lateral-invasive, or localized rectal cancer; post chemotherapy, EBRT, or surgical resection	Post-operative dose evaluation (CT); Clinical evaluation at follow-up (2.5-35.9 months): blood test, tumor markers test, abdominal and chest CT, pelvic MR imaging, tumor response (RECIST guideline version 1.1), pain assessment (Numeric Rating Scale), side-effect evaluation (toxicity criteria of the Radiation Therapy Oncology Group), overall survival time.	Confirmed effectiveness and safety of salvage treatment strategy: 85.1% pain relief, 9.1% severe side effects, median overall survival time 14.7 months, median local control time 12.2 months.
[61] Radiation oncology (brachytherapy head and neck) Non-coplanar navigation guide for RIS implantation in palliative treatment of recurrent malignant head and neck tumours	Limited accuracy of RIS implantation using traditional approaches.	**CT** N/A	**N/A** N/A Photopolymer resin	14♀, 28♂, median 61 years (range 29-79) Recurrent or metastatic head/neck tumor: naso-/hypo-/oropharyngeal, oral, laryngeal, salivary-gland, thyroid, oesophageal, cervical, lung, breast, or colon cancer, soft-tissue sarcoma, lymph-node metastasis of unknown aetiology	Post-operative dose evaluation (CT); Clinical evaluation of side effects at follow-up (4-14 months): skin puncture: bleeding, pain, infection, non-union of puncture point, metastasis due to RIS implantation; radiation (toxicity criteria of the Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer): skin injury, mucosal response, spinal-cord injury, peripheral-nerve injury, xerostomia, blood toxicity; nerve injury (Common Terminology Criteria for Adverse Events v4.0); seed migration.	Successful RIS implantation with good accuracy of positioning. 3 cases of grade 1 acute skin reaction, no cases of grade >3 reactions. No blood toxicity, no spinal cord injury, 1 case of grade 3 nerve response.
[62] Radiation oncology (brachytherapy various) Patient-specific navigation guide for CT-guided RIS implantation in treatment of advanced malignant tumours	Limited accuracy of RIS implantation, and associated unwanted effects using traditional approaches.	**CT** N/A	**N/A** N/A Medical resin	18♀, 24♂, 58.9 ± 14.1 years (range 25-91)	Patients' quality-of-life assessment: EORTC QLQ-C30 (4-point scale: 1 - not at all, 4 - very much): function (physical, role, cognitive, emotional, social), symptoms (fatigue, pain, nausea/vomiting), single measurement items, global quality of life; administered prior to surgery, at 24 h, 1 and 3 months after surgery.	Average EORTCQLQ-C30 score after seed implantation higher at 1-month follow-up compared to 24-hour and 3-month follow-up.
[39] Radiation oncology (brachytherapy pancreas) Coplanar navigation guide for RIS implantation in treatment of pancreatic cancer	Limited accuracy and considerable complexity of RIS implantation using traditional approaches; impossible real-time adjustment of puncture direction with non-coplanar guides.	/ N/A	**N/A** N/A PMMA	Experimental group: 6♀, 6♂, median 65.5 years (range 48-81) Control group: 7♀, 6♂, median 63.8 years (range 47-84) Unresectable pancreatic carcinoma	Between-group comparison of post-operative dose (CT), implementation success rate and complications.	Successful RIS implantation without major complications; 1 self-limiting, clinically insignificant local hematoma due to mesentery vessel injury. Dosimetry values significantly higher in experimental compared to control group.
[38] Radiation oncology (brachytherapy rectum) Patient-specific non-coplanar navigation guide for RIS implantation in palliative treatment of primary or metastatic thoracic tumours	Discrepancy between the postoperative target dose and preoperative plan in freehand RIS implantation.	**CT** N/A	**N/A** N/A Medical curing resin	32♀, 60♂, median 62 years (range 17-88) Primary or metastatic solid, unresectable malignant tumor of the lung, chest wall, or mediastinum	Clinical examination and assessment of toxicity effects (radiation pneumonia, esophagitis, skin reaction, myelitis, cardiotoxicity) at follow-up (median 10.7 months). Overall survival and local control duration and rate at 1 and 3 years.	Toxicity effects: 3 grade ≥2 radiation pneumonia, 2 grade ≥2 radiation esophagitis, 1 oesophageal fistula, 2 tracheal fistulae, 1 chest-wall pain, 3 haemoptysis, 5 grade 2 radiation skin reaction; no defined radiation myelitis or cardiotoxicity. 34 cases of pneumothorax. Overall survival: median 15 months; 59.7% (1 year), 22.2% (3 years). Local control: median 16.4 months; 64.9% (1 year), 32.8% (3 years); significantly better for metastatic than primary cancer.

[19] Maxillofacial oncology Definitive cast for manual fabrication of the mould to produce a patient-specific self-retentive interim obturator for palliative palate reconstruction after partial maxillectomy due to cancer	Inability to fabricate the obturator using impression trays due to limited maximal incisal opening.	**CT** Mimics SpaceClaim	Definitive cast: **MJ** Objet260 Connex 3 (Stratasys) ABS (RGB 515 Digital ABS) *Duplicate definitive cast:* *PolyPour mould, type III dental stone cast* *Obturator:* *Wax positive mould, 3-piece dental stone negative mould, packing of platinum silicone elastomer (A-RTV-40), colouring, trimming, contouring*	♀, 55 years Post unilateral maxillary resection due to T4aN0M0 invasive squamous cell carcinoma with bone and perineural invasion, failed free-flap reconstruction, severe trismus	Visual inspection of fit, patient feedback regarding comfort	Restored functional quality of life: improved speech and mastication, prevented nasal regurgitation. Eliminated need for impression materials.
[34] Maxillofacial oncology Definitive cast for manual fabrication of the mould to produce a patient-specific obturator for palliative palate reconstruction after partial maxillectomy due to cancer	Labour-intensive, time-consuming fabrication of one-piece obturators using traditional techniques because of access limitations due to soft tissue fibrosis and trismus after maxillectomy and radiation.	**CT** Mimics Geomagics Studio 12	Definitive cast: **MJ** ProJet HD 3500 (3D Systems) N/A	4♀, 7♂, 44 ± 16 years (range 25-68) Post partial maxillectomy due to squamous cell, mucoepidermoid or adenoid cystic carcinoma, myofibroblast or fibromyxoid sarcoma	Assessment of obturator retention, marginal fit and occlusion, and excessive tissue displacement. Patient feedback at 1-week follow-up (Obturator Functioning Scale of the Memorial Sloan-Kettering Cancer Center): problems with eating, speech difficulties, dry mouth, poor aesthetics, upper lip paraesthesia, difficulty inserting the obturator, avoidance of routine social interactions); 3-point scale: 1 - not at all/a little, 3 - very much/extremely.	Maximum support, stability and retention; 1 case of leakage drinking liquid, no leakage while swallowing; 2 cases of somewhat nasal voice; 3 cases of clasps noticeable on anterior teeth; 3 cases of extreme numbness; 3 cases of dry mouth. Overall, regained functions of mastication, pronunciation and swallowing, improved psychological and social wellbeing.
[24] Maxillofacial oncology (facial epithesis) Patient-specific working model and mould for facial prosthesis to restore the cosmetic appearance of patients with facial defect after ablative tumor surgery	High cost of customised products, and difficulty producing geometrically complex parts with traditional technologies.	**3D Scanner HD "Ear & Nose Digital Library"** ScanStudio RapidForm	Working model and mould: **FFF** Dimension (Stratasys) ABS P400 *Final epithesis:* *Silicone casting, colouring*	♀, 73 years Recurrent squamous-cell carcinoma, infiltrating facial bone	N/A	Possible improvement of patients' quality of life and comfort, semi-functionally and aesthetically.
[23] Maxillofacial oncology (nasal epithesis) Mould for patient-specific nasal prosthesis to restore the cosmetic appearance of patients with facial defect after ablative tumor surgery	High cost and difficulty producing geometrically complex parts with traditional technologies, especially in the absence of symmetric body part to mirror.	**3D Scanner HD "Ear & Nose Digital Library"** ScanStudio RapidForm	Mould: **FFF** N/A (Stratasys) ABS P400 *Final epithesis:* *Silicone casting, colouring*	♂, 67 years Post ablative surgery of the nose due to recurrent squamous-cell carcinoma, failed plastic reconstruction	Analysis of production cost and time, comparison with traditional techniques.	Reduced time and cost of the procedure compared to traditional techniques.
[12] Orthopaedic oncology (upper extremity) Patient-specific endoprosthesis for palliative upper-extremity reconstruction after bone-metastasis resection	Challenging production, time- and cost-inefficiency of traditional methods for producing patient-specific endoprostheses for reconstruction after extensive bone resection.	**CT** Mimics	**Selective Laser Lithography*** N/A (MTEC) PMMA	16 patients Humeral, ulnar metastases of multiple myeloma, prostate, breast, lung adenocarcinoma, thyroid follicular-cell carcinoma, cholangiocarcinoma, or osteosarcoma	Functional outcome evaluation: MTSS (5-point scale), Mankin score (poor-good); elbow and forearm range of motion assessment; Endoprosthesis failure evaluation: prosthesis fracture, prosthesis-bone interface failure, prosthesis and fixative device failure at follow-up (38-1324 days).	Production of affected-bone replicas within 48 h. Successful reconstruction with good shoulder stability, low rate of complication, and no cases of poor outcome or endoprosthesis failure. 3 of 13 cases of soft tissue failure in first 6 months. Mean MTSS 55%, higher for emotional acceptance and associated pain compared to functional activities, lifting ability, and hand positioning; Mankin score: 64% good, 36% fair.

[37] Orthopaedic oncology (pelvis) Patient-specific pubic bone endoprosthesis for pelvic ring reconstruction after exenteration for anal cancer recurrence	Poor physical well-being and postoperative quality of life after complete pelvic exenteration without pubic symphysis reconstruction when osteosynthesis is not possible.	**CT/MR** Mimics 21.0	**DMLM** Concept Laser M2 cusing (GE Additive) Rematitan (90% titanium, 6% aluminium, 4% vanadium) Designed by TIOS, Ltd. (Moscow, Russia)	♀, 52 years Recurrent anal squamous cell carcinoma with vagina, bladder, and pubic bone invasion, locoregional failure after chemotherapy	SF-36: qualitative assessment of patients' perceptions of their physical functioning, physical and emotional limitations, social functioning, bodily pain, general and mental health.	Successful endoprosthesis implantation 5 weeks after initial pelvic exenteration (R0 resection), without severe complications. Patient started to walk 9 days and resumed normal activities 6 weeks after surgery. No recurrence or implant rejection at 6-month follow-up. SF-36v2: 62% with positive dynamics in physical health status.
[33] Orthopaedic oncology (pelvis) Patient-specific osteotomy guide and hemi-pelvic endoprosthesis for metastatic acetabular carcinoma resection and pelvic reconstruction	High incidence of prosthetic mismatch and loosening in pelvic reconstruction surgery with conventional modular prostheses.	**CT** Mimics 17.0 Magics 18.0	Pelvic model: **SLA** iSLA-450 (Shining 3D) N/A Osteotomy guide: **SLS** Formiga P110 (EOS) N/A Endoprosthesis: **EBM** Arcam A1 (Arcam Corporation) Ti6Al4V	♀, 62 years Destructive metastatic acetabulum carcinoma, right renal clear-cell carcinoma	Clinical assessment preoperatively and at 12-month follow-up: MSTS score: rating (0-5 scale) of pain, function, emotional acceptance, use of external support, walking ability, gait alteration; Harris Hip Score: rating (1-4 scale) of pain, support, walking distance, limp, activities, sitting, stair climbing, public transportation; RoM; SF-36: qualitative assessment of patients' perceptions of their physical functioning, physical and emotional limitations, social functioning, bodily pain, general and mental health.	Accurate tumor resection and pelvic reconstruction without prosthetic loosening or migration, periprosthetic fractures, or infection; walking 1 km with assistance at 6 months, independent at daily activities at 12-month follow-up. Improved MSTS result (from 7 to 16), SF-36 (from 52.7 to 108.2), and Harris score (from 19 to 52).
[28] Orthopaedic oncology (upper limb) Patient-specific mould for bone-substitute endoprosthesis to reconstruct upper-limb long bones after tumor resection	Limited possibilities of traditional methods to produce custom shape, size and complexity of endoprostheses in large limb-segment lesions.	**CT** N/A	Mould: **FFF** Replicator 2 (MakerBot) N/A *Endoprosthesis:* *Casting of bone substitute material (PMMA or Rekost) with allograft chips*	12♀, 10♂, 50.9 ± 7.2 years (range 41-62) Lesion at the humerus, ulna or radius due to enchondroma, osteoblastoclastoma, non-osteogenic fibrosis, solitary bone cysts, osteogenic sarcoma, metastasis of mammary or prostate gland and lung cancer.	Clinical assessment preoperatively and at 12-month follow-up: SF-36: qualitative assessment of patients' perceptions of their physical functioning, physical and emotional limitations, social functioning, bodily pain, general and mental health; MSTS score: rating (0-5 scale) of pain, function, emotional acceptance, use of external support, walking ability, gait alteration; VAS: pain assessment.	Significant postoperative pain reduction and improved function of the upper limb. Benign cases: SF-36: 71.4 ± 6.6, VAS: 2.5 ± 1.5, MSTS: 65.1% ± 8.3%; malignant cases: SF-36: 39.2 ± 4.3, VAS: 4.8 ± 1.4, MSTS: 41.8% ± 5.2%. No statistically significant differences depending on material used. No radiographic evidence of implant migration, 4 cases of marginal osseointegration with Rekost.
[17] Enteral feeding Bespoke sealing device for emergency repair of leaking PEG tubes in patients ineligible for surgical replacement procedure	Disrupted enteral feeding in patient ineligible for surgical PEG-tube replacement, significant risks associated with non-operative methods of replacement, no existing repair kits	/ SolidWorks	**MJ** Connex500 (Stratasys) MED610	♂, 15 years Advanced cystic fibrosis	Application of sealing device, check for leaks at tube flushing.	PEG-tube function restored within 24 h from first contact between medical staff and designers. PEG tube ready for use immediately after application of sealing device, patient recommenced on feeding regime.
[31] Neurology (ALS) Patient-specific interface for a generic mask for noninvasive ventilator support in chronic medical conditions with weakness of respiratory muscles	Generic masks in standard sizes are often uncomfortable, ill-fitting, and leaky, which causes patients to discontinue using them.	**MR** (patient's face) Mimics **Vivid 9i (Konica Minolta)** (modified oronasal mask Veraseal 2) Visualization toolkit library Blender 2.78	Rigid interface, mould for silicone interface: **SLA** Form 2 (Formlabs) Standard clear resin *Silicone interface:* *Casting of Dragonskin10 (Smooth-On)*	♂, age N/A Variant ALS, unique facial contours (high nose bridge, lower-jaw overbite), prescription glasses	1-night trials with 10 modified masks and 2 standard masks; two 7-night trials with favourite mask. Custom questionnaire for patient evaluation of comfort, leakage, preference, recommendation, tolerance (Likert-type 1-5 scale questions), open-ended questions.	Scores for favourite masks over 7-night trials: comfort: 4, 4; leakage: 3, 2; preference: 4, 3; recommendation: 4, 3; tolerance: 4, 3. Compared to standard mask, 8 of 10 custom masks were rated higher in all aspects. Common complaints: masks were unable to accommodate his sleep movement and jaw movement.

[20] Oncology – Chemotherapy (spine) Nanoporous scaffold for local chemotherapeutic delivery in spine metastases of prostate cancer	Severe side effects of high systemic doses of chemotherapeutics; large defects after surgical removal of spine metastases that cannot spontaneously heal and require bone grafting.	/ SketchUp Simplify 3D	**FFF** Creator Pro (Flashforge Corp.) TPU/PVA (PORO-LAY series: Lay FOMM 60, 40; Gel Lay) *Doxorubicin loading on scaffolds*	/	Assessment of doxorubicin release from scaffolds over 7 days (fluorescence detection); tumor-cell metabolic activity and proliferation assessment; scaffold porosity evaluation (SEM).	Proof of concept: 60-75% of doxorubicin loaded onto scaffolds was released over 7 days, significantly reducing metabolic activity and proliferation of prostate cancer cells and spine metastases cells.
[30] Oncology – Pain palliation (bone) Portable MRI-guided robotic system for pain palliation in bone cancer using thermal ablation with focused ultrasound	N/A	/ N/A	**FFF** FDM400 (Stratasys) ABS	/	Evaluation of robot functionality (gel phantoms), and MRI safety and compatibility.	Proof of concept: Verified MRI safety and compatibility, and the capacity for creating discrete and multiple overlapping lesions in a gel phantom.

5-FU – 5-fluorouracil, ABS – Acrylonitrile Butadiene Styrene, AFM – Atomic Force Microscopy, BJ – Binder Jetting, CT – Computed Tomography, DMLM – Direct Metal Laser Melting, EBRT – External Beam Radiotherapy, EdECM – Esophagus-derived decellularized Extracellular Matrix, EORTC QLQ-C30 – European Organization for Research on Treatment of Cancer Quality of Life Questionnaire, ERCP – Endoscopic Retrograde Cholangiopancreatography, FE-SEM – Field Emission-Scanning Electron Microscopy, FFF – Fused Filament Fabrication (also FDM – Fused Deposition Modelling), MJ – Material Jetting, MR – Magnetic Resonance, MSTS – Musculoskeletal Tumor Society, MTSS – Musculoskeletal Tumor Society Score, PCL – Polycaprolactone, PEG – Percutaneous Endoscopic Gastrostomy, PLA – Polylactic acid, PMMA – Polymethyl Methacrylate, PTX – Paclitaxel, PU – Polyurethane, PVA – Polyvinyl Alcohol, RIS – radioactive ^{125}I seed, RoM – Range of Motion, SEM – Scanning Electron Microscopy, SF-36 – 36-Item Short Form Survey, SLA – Stereolithography, SLS – Selective Laser Sintering, TESS – Toronto Extremity Salvage Score, TPU – Thermoplastic Polyurethane. **The authors are unfamiliar with the stated technolog*