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Three-Dimensional Printing in Minimally Invasive Spine Surgery

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Abstract

Purpose of Review To summarize the recent advances in 3D printing technology as it relates to spine surgery and how it can be applied to minimally invasive spine surgery.

Recent Findings Most early literature about 3D printing in spine surgery was focused on reconstructing biomodels based on patient imaging. These biomodels were used to simulate complex pathology preoperatively. The focus has shifted to guides, templates, and implants that can be used during surgery and are specific to patient anatomy. However, there continues to be a lack of long-term outcomes or cost-effectiveness analyses. 3D printing also has the potential to revolutionize tissue engineering applications in the search for the optimal scaffold material and structure to improve bone regeneration without the use of other grafting materials.

Summary 3D printing has many potential applications to minimally invasive spine surgery requiring more data for widespread adoption.

Keywords 3D printing · Additive manufacturing · Minimally invasive surgery · Spine surgery · Biomodels · Templates

Introduction

Three-dimensional printing (3DP), also referred to as additive manufacturing, continues to gain traction in medicine. Additive manufacturing can build three-dimensional structures layer-by-layer from digital images. Spine surgery is the fifth leading surgical field using 3DP as determined by the available evidence-based literature (7.5%) [1]. To date, the field has seen some of the greatest usage of this new technology and continues to drive innovation with several products receiving FDA-approval each year. Minimally invasive spine surgery (MISS) techniques have flourished in an effort to reduce procedure-related morbidity [2]. Both MIS and 3DP are growing disciplines that increase the arsenal of tools at the surgeon's disposal. Synergy between these maturing fields highlights the ability to optimize patient outcomes. 3DP biomodels enhance patient-doctor communication, surgical training, and preoperative planning; surgical guides and templates can increase accuracy of hardware placement; and implants can be tailor-made for patients. However, this technology is still in its infancy with unanswered questions about cost-effectiveness and long-term outcomes [3]. The purpose of this review is to provide insight on the recent uses and current limitations of 3DP within MISS.

Background

There are many types of additive manufacturing, but the most commonly used methods in medicine are powder bed fusion, stereolithography, fused filament fabrication, and liquid-based extrusion (Fig. 1) [4]. Powder bed fusion uses a powerful energy source (i.e., laser for selective laser sintering or electron beam for electron beam melting) to selectively melt a layer of powder. After each successive layer is formed, the powder is refreshed and used for the next layer. The powders consist of metal or polymers like ceramic and minimize waste by only using enough powder to build the model. Commercially available orthopedic products that use metals such as titanium employ this type of 3DP, using this material to build complex geometries. Stereolithography uses a liquid material that is cured by high-energy light which can be used

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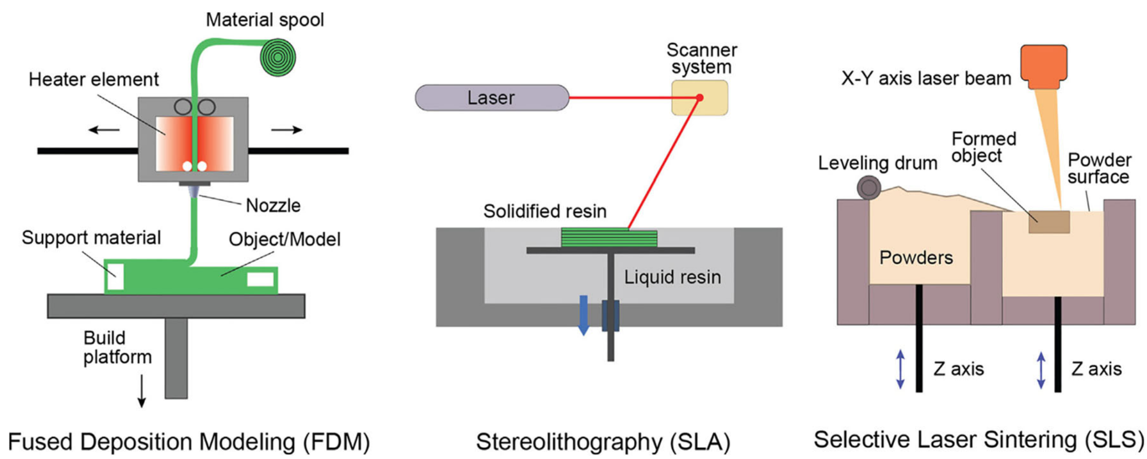

Fig. 1 Schematics of three commonly used 3DP processes for bone engineering. Adapted from Zhang et al. 2019. "3DP scaffold and material selection for bone repair" (Obtained License from Elsevier on 6/17/2019)

to produce biomodels. Fused filament fabrication (also known as fused deposition modeling) melts solid wires of thermoplastic such as poly(lactic acid) (PLA) together, creating the 3D structure. Liquid-based extrusion ejects a liquid from a nozzle that solidifies and constructs the product by through manipulation of the platform. Newer forms of 3DP methods incorporate biological materials and are often referred to as bioprinting [5•].

3DP is still chiefly used by industry for rapid prototyping and is slowly being adopted by surgical fields. Lured by the promise of customizability, speed, reduced waste, and low cost, oromaxillofacial and orthopedic surgery have been two early adopters of this technology. Research into 3DP in spine surgery has grown rapidly after D'Urso et al. first published their results in 1999 [6•]. Early applications focused on biomodels used for preoperative surgery planning and education. However, over the past few years, there has been an increase in the use of 3DP in surgical instrumentation to build patient-specific guides, templates, and implants [7]. To date, there have been few studies about 3DP in MISS, usually restricted to case reports, case series, and reviews [1, 8, 9].

With the advance of this novel technology, there was an increase in the number of clinical trials registered after 2015 [10•]. In response, at the end of 2017, the FDA released regulatory guidelines in regard to these products [11] leading to the approval of several 3DP devices. Orthopedic applications were the most commonly utilized discipline of all clinical trials using 3DP (27%) [10•]. Notably, from an international perspective, China is by far the leader in the number of clinical trials (45%) followed by the USA (14%).

Biomodels

Biomodels were the first adopted application of 3DP in spine surgery [6•], which provide the added benefit of visualizing and touching the structure in a three-dimensional space. Patient-specific 3DP biomodelling involves segmenting patient digital CT or MR images, then converting to a computer-aided design reconstruction, and finally printing the anatomic structure (Fig. 2). Spine biomodels have been shown to have several useful functions that prove useful especially in complex cases.

Education

Biomodels facilitate patient counseling and surgical trainee education. During the surgical counseling session, providing the patient and their family with a biomodel of their own anatomy connects images with their illness and can elaborate on the need for surgery and explains the operation in more detail, reassuring the patient and their family. Use of these models can also demonstrate what the spine will look like after the operation [12•]. One study showed that using 3DP models during patient education sessions can increase patient consent [13] and satisfaction compared to using traditional 2D images [14]. Overall, the purpose of using biomodels should be to forecast the operation in a clearer picture and provide reassurance.

Biomodelling can also help train the next generation of health care providers. Some educators view 3DP as the future of anatomy due to issues with cadavers including cost, availability, and ethics [15, 16]. Junior medical trainees, such as medical students, appear to benefit the most from biomodel training compared to more experienced surgeons [17, 18]. 1:1 scale biomodels help to visualize and rehearse procedures, which have been shown to be beneficial in hardware placement [16, 19] (Fig. 3). In addition to preoperative preparation, young surgeons can use these models to practice technique and obtain a tactile feel for the operation. This is especially important in MISS training where there is a steep learning curve associated with limited exposure around delicate

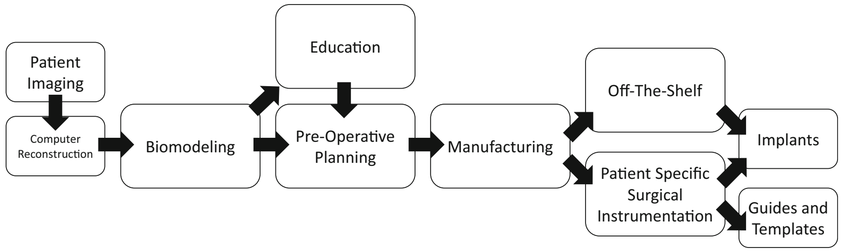

Fig. 2 Current workflow of 3D printing in spine surgery. Patient spine anatomy is simulated using imaging and software to generate a 3D-printed biomodel. This biomodel can then be used both as an educational tool for medical trainees and for patients. Pre-operative planning follows a collaborative approach with engineers and surgeons to simulate and optimize the design and specifics of the 3D-printed materials. Manufacturing using 3D-printing techniques can create more complex off-the-shelf materials (i.e., titanium cages) and/or patient-specific surgical instrumentation such as implants or guides and templates

structures [20]. Other MIS fields have shown the utility 3DP of biomodels including cardiothoracic surgery [21], cranial neurosurgery [22], and otolaryngology [23]. Additionally, surgical simulation with biomodels provides a venue for testing new materials and techniques.

Preoperative Planning

Biomodels can provide insight to complex spine pathologies such as severe scoliosis, rheumatoid cervical spine, spinal tumors, and degenerative spine to create patient-specific anatomic models. A recent survey demonstrated that surgeons believe that having a tangible 3D biomodel is helpful both pre- and intraoperatively [24]. Subjects reported that it was easier to visualize the anatomy in 65% of cases, and these assistive devices changed up to 75% of procedures due to either choice of graft or site. Moreover, these biomodels can help the surgeon plan their hardware and practice the challenging parts of the procedure. Yang et al. highlighted these benefits in a retrospective study of 126 Lenke 1 adolescent idiopathic scoliosis patients [25]. They compared the 3DP biomodel to standard imaging and found biomodels added benefits of decreased operative time, blood loss, and transfusion volume with no difference in complication rate, length of hospital stay, radiological outcomes, or screw misalignment. In a subset of patients with a Cobb angle greater than 50°, they also noticed a significantly decreased rate of pedicle screw misplacement ($p = 0.02$). One proposed reason for this decrease in operative time is that the biomodels can be sterilized and used in the surgical field for quick reference.

A case series by Zhao et al. described a new procedure for the minimally invasive approach to remove the ossification of ligamentum flavum in the thoracic spine [12•]. The surgeons used virtual surgical simulation to optimize the approach angle and retractor depth and created biomodels to identify anatomical variation and rehearse the procedure (Fig. 4). The approach was performed on 13 patients, and the authors concluded that the procedure was safe, effective with minimal complications with faster recovery times, and improved spine stability. In a recent case report, Ling et al. used a similar approach for a 66-year-old man with multilevel ossification of ligamentum flavum that produced similar results [26]. The biomodel was used to preoperatively evaluate the anatomy and plan the osteotomy angle.

Thayaparan et al. reported the use of a biomodel to preoperatively plan for minimally invasive revision lumbar surgery [27•]. The patient was a 72-year-old woman who presented with pseudoarthrosis after 12 months after fixation. The team developed a 1:1 scale biomodel and used the digital reconstruction for preoperative planning, patient counseling, and intraoperative reference. To our knowledge, this was the first use of 3DP in MI spine surgery in the lumbar region demonstrating that it was a safe and viable process at 6-month follow-up. Furthermore, they developed 3DP surgical instrumentation such as patient-specific implant and self-docking nylon tubular retractors specific to the tissue depth and bony anatomy for the MIS approach.

Surgical Instrumentation

Guides and Templates

3DP patient-specific guides and templates can be used to plan pre-operatively which helps to improve accuracy and minimize iatrogenic injury intraoperatively [28]. Together, they decrease the operative time and fluoroscopy exposure for both the patient and surgical team [29–32]. Initially, guides were first cast from biomodels with embedded trajectory pins, but have progressed to in silico modeling and 3DP [33, 34]. 3DP patient-specific guides have proved more accurate and precise than free-hand screw placement. Cadaveric studies have shown that template-assisted screw insertions have high accuracy (> 90%) for cervical pedicle screws in both anterior [35] and posterior [36–38] approaches. This high accuracy translates to patients. Liu et al. showed that in a case series of ten patients with severe scoliosis, the 3DP drill guides improved accuracy from 78.8 to 93.8% [39]. In a retrospective analysis of atlantoaxial vertebral fractures and dislocations, Pu et al. saw high accuracy and faster operative time by using drill

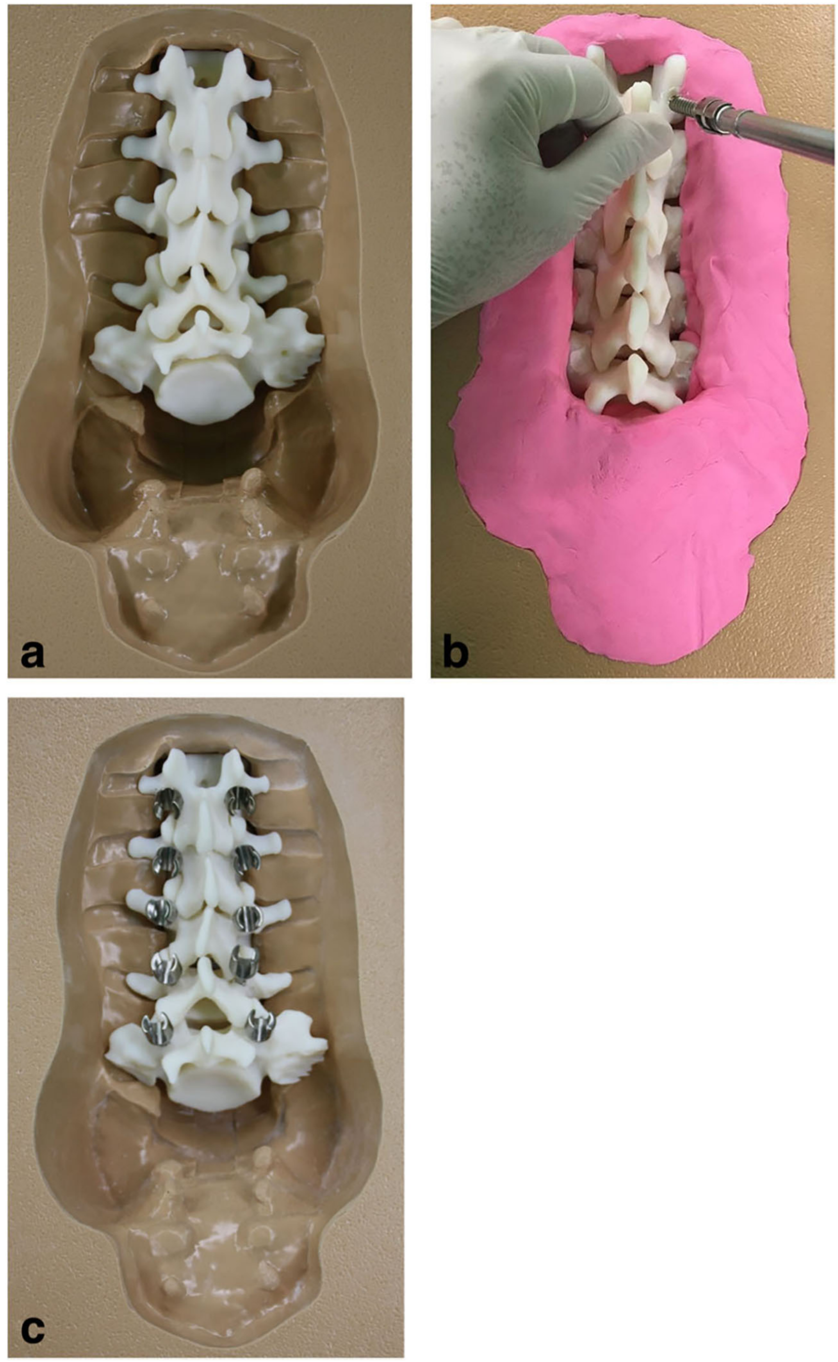

Fig. 3 Example of 3DP spine models used for training. (**a**) 3DP spine models were mounted on a spine holder. (**b**) Clay (pink) was placed surrounding the pedicle to simulate posterior approach. (**c**) Removal of clay allows the trainee to evaluate their pedicle screw placement. Adapted from Park et al. 2018. "Use of a life-size 3DP spine model for pedicle screw instrumentation training"

guides with a long parallel posterior pole (Fig. 5). Similarly, Guo et al. and Cecchinato et al. used 3DP templates for pedicle screw fixation in the upper cervical spine and found similar accuracy and improvement over fluoroscopy [30, 40]. Kaneyama et al. were the first to describe a screw guide template system in the midcervical spine [32]. Their system used a three-step approach with templates: (1) location guide, (2) drill guide, and (3) screw guide. Each of these templates attached to the lamina, making it quick to administer and diminishing the need for intraoperative fluoroscopy. Furthermore, their group recently published on their prospective use of the screw guide template system in the cervical and thoracic spine and demonstrated 98.5% accuracy without cortical violation or injury to adjacent vessels or nerves overall [41•].

In the lumbar spine, Kim et al. described 3DP patient-specific guides for the cortical bone trajectory technique in a 71-year-old woman with L4–5 spondylolisthesis. Biomodels were used to simulate surgery preoperatively, which verified the use of the guides (Fig. 6). Intraoperatively, the guides

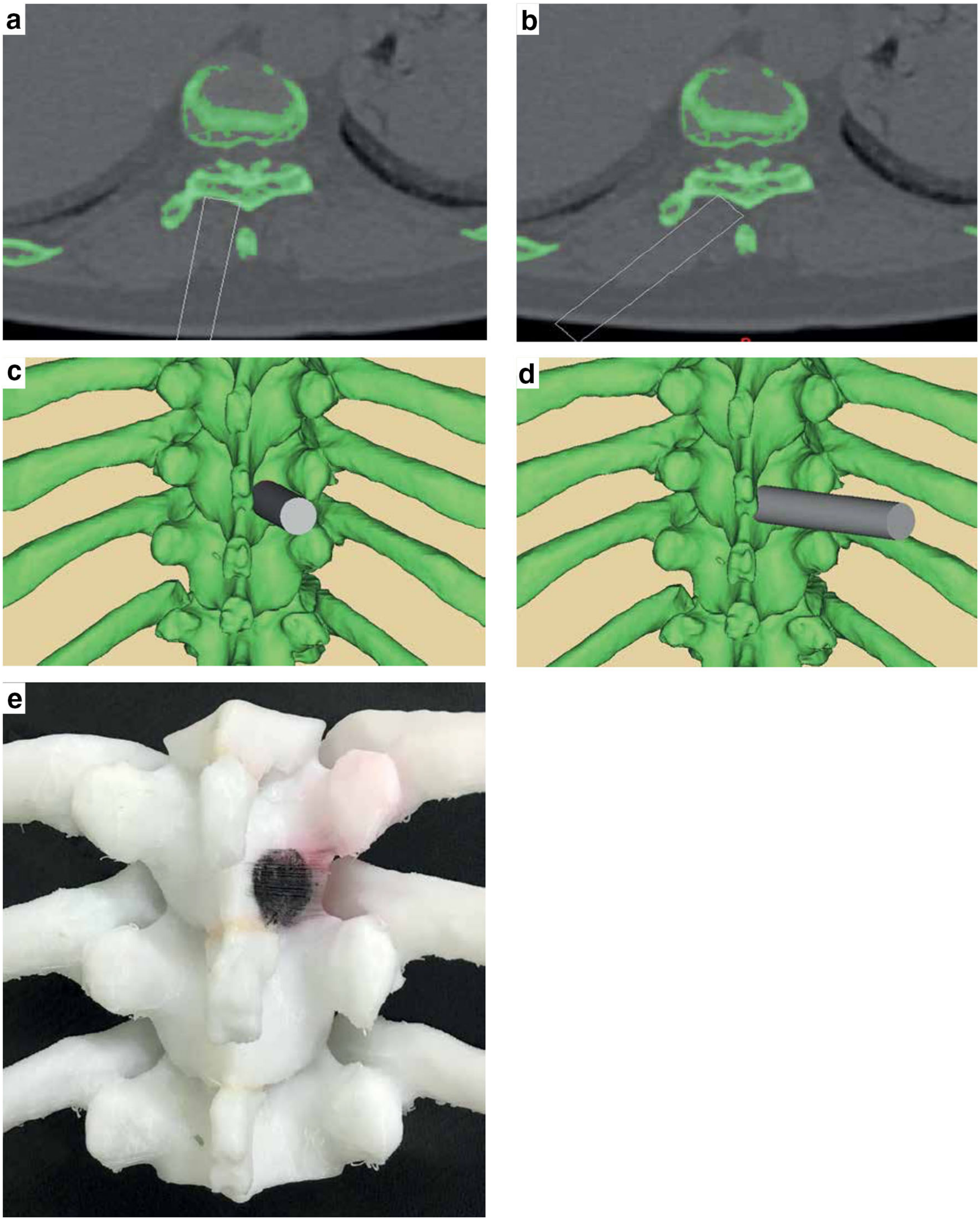

Fig. 4 (**a**-**d**) Virtual surgical simulation with proposed placement of tubular retractors for MIS resection of ossification of the ligamentum flavum. (**e**) A biomodel with the proposed lesion that was used in preparation for surgery. Adapted from Zhao et al. 2017. MIS for resection of ossification of the ligamentum flavum in thoracic spine

facilitated accurate screw placement leading to a reduction of spondylolisthesis at 3 months. These personalized guides are commercially available through Medacta International. Kaneyama et al. stated that their cost was $30 per patient, which included two sets of templates and a biomodel [32]. Additionally, the decreased operative time and need for fluoroscopy or other navigation systems further reduced the cost. This technology can also be useful in developing areas around the world where novel technology such as image navigation is not available. For example, in India, Garg et al. showed that using guides helped patients with complex spinal deformities especially with less experienced surgeons [31].

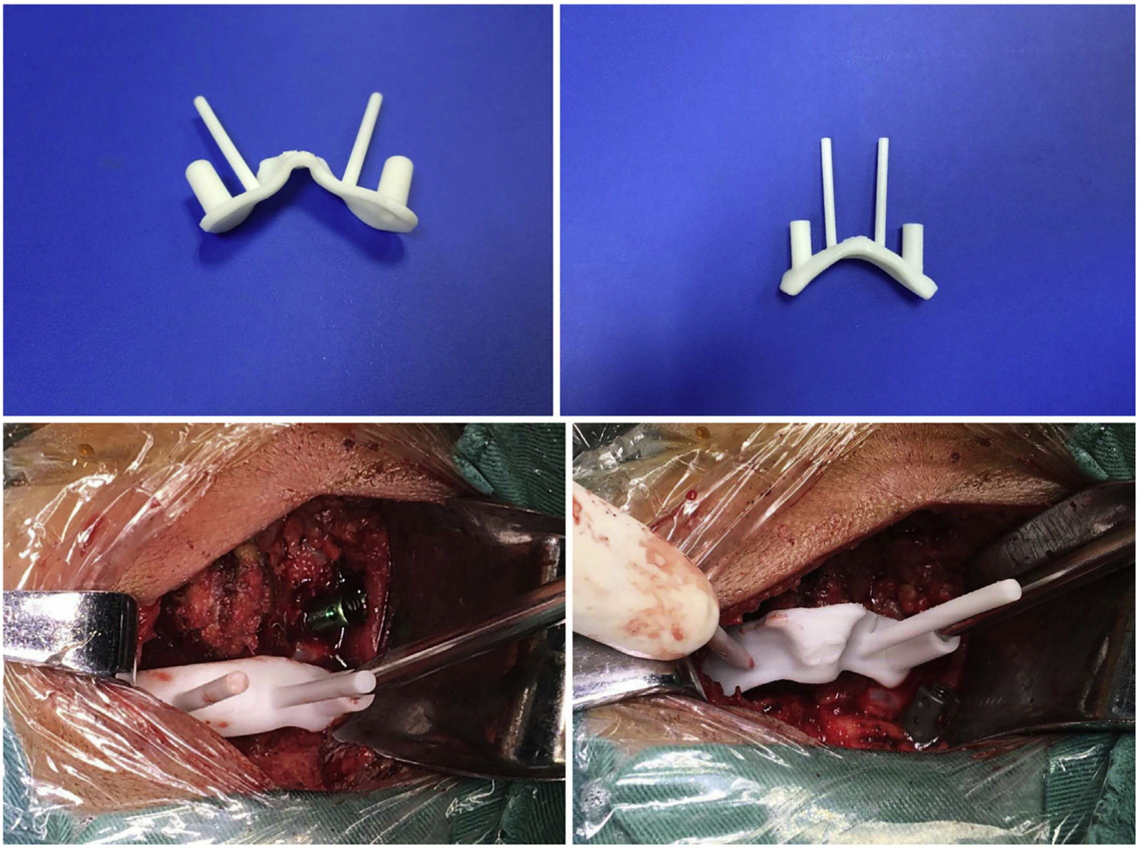

Fig. 5 Example of 3DP drill guide templates showing both the guide and its use intraoperatively. Adapted from Pu et al. 2018 "Design and Application of a Novel Patient-Specific Three-Dimensional Printed Drill Navigational Guiding in Atlantoaxial Pedicle Screw Placement." (Permission granted from Elsevier)

Deriving these guides can be technically challenging and depend on a solid understanding of 3D digital reconstruction and the ability to use software to design the guide under a surgeon's specifications. Feng et al. described a step-by-step approach for making patient-specific reconstructions in silico [42]. Reconstructions and 3DP rarely take soft tissues into account, often leading to full removal of the soft tissues to provide an adequate fit for the guides. Future efforts to retain as much native tissue as possible will require innovative developments on both the surgical and technical sides.

Implants

3DP has opened new doors for MISS implant development, allowing for more complex shapes and patient-specific devices. In the literature, patient-specific 3DP implant categories consist mostly of fusion cages or reconstruction of vertebral bodies. Xu et al. constructed a 3DP titanium self-stabilizing artificial vertebral body for an adolescent with C2 Ewing's sarcoma who had good outcomes and was tumor free at 1-year follow-up [43]. They used CT data to reconstruct C2 to be specific to his anatomy to create a superior fit and allow for retained motion. Li et al. printed a multilevel cervical (C2–C4) self-stabilizing artificial vertebral body to reconstruct the cervical spine after resecting metastatic papillary thyroid carcinoma [44]. They created a columnar titanium construct with bilateral shoulders to fit the inferior articular surface of the atlas. They tested it on a 3DP biomodel prior to implantation and had no implant displacement or subsidence at 1 year. Choy et al. reported reconstruction of T9 in a patient with a primary bone tumor [45]. The implant had angled endplates to restore the sagittal balance and included pedicle screw holes and anterior column attachment to ease the procedure.

For fixation, Phan et al. developed a custom posterior fixation device that attached to the C2 spinous process and lamina with screw holes set at the correct angle for a 65-year-old woman with severe C1–2 degeneration [46]. Lu et al. developed "anatomy-adaptive titanium mesh cages" for single-level anterior cervical corpectomy with simultaneous use of autograft (Fig. 7) [47]. Their case series of 15 patients showed at mean follow-up of 13.4 months that there was no severe subsidence with improved pain on visual acuity score and Japanese Orthopaedic Association score. Within MISS, Siu et al. described the first case of a 74-year-old woman with a history of osteoporotic fractures at L2 and L3 and had subsequent radiculopathy that underwent MIS lateral lumbar

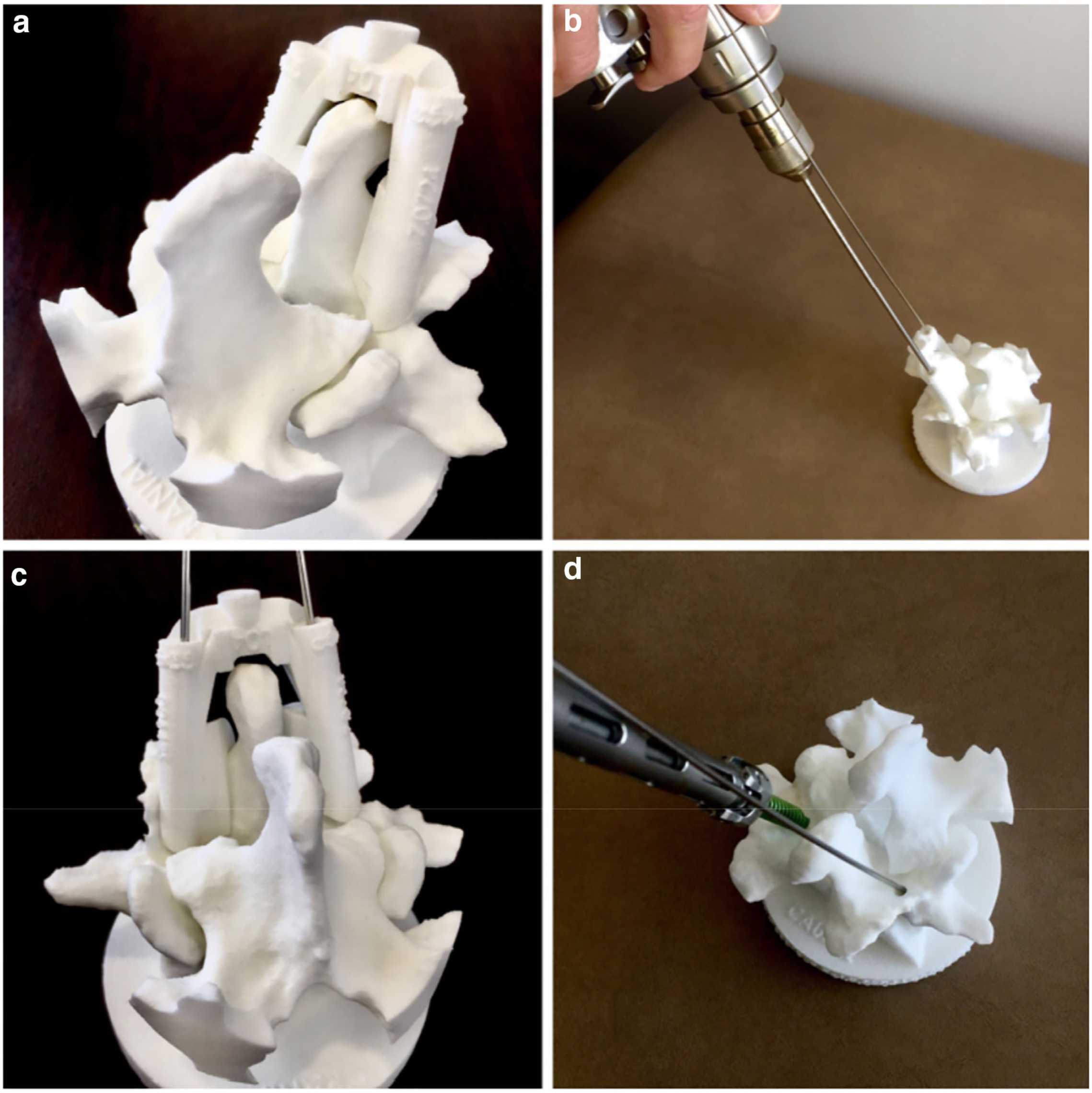

Fig. 6 3DP biomodels and drill guides used for presurgical planning and rehearsal. Sequence of events: (**a**) Placement of drill guide. (**b**) Drilling using the trajectory made from the drill guide. (**c**) Insertion of Kirschner wire. (**d**) Removal of drill guide while keeping Kirschner wire inserted for guided tapping and screw placement. Adapted from Kim et al. 2019 "3D patient-specific guides for intraop navigation for cortical screw trajectory pedicle fixation"

interbody fusion with a 3DP titanium cage [48•]. The previous fractures led to a concave deformity of the endplates negating the use of off-the-shelf implants.

Combining all of these aspects of 3DP, Thayaparan et al. presented a case series of posterior atlantoaxial fixation for three women with osteoarthritis [38•]. They built 3DP biomodels, drill guides, and implants that were practiced on the biomodels prior to use in the patient. Even in this "high-risk" area, they had no intraoperative complications, no readmissions or implant failure at 12-month follow-up, and had acceptable imaging up to 6 months out. They claimed to have more efficient operative time, reduced radiation, and reduced waste for this type of procedure. These techniques have the ability to be translated to MIS.

Preclinical studies demonstrate the advantages of 3DP titanium cages, leading to increased bony ingrowth, decreased subsidence, and better imaging characteristics [49]. 3DP also has more precise control of the size, shape, angle, uniformity, and extent of the pores compared to traditional subtractive manufacturing or titanium plasma spray (TPS) coating. In an ovine study, McGilvray et al. compared polyetheretherketone (PEEK), TPS (PEEK), and 3DP porous titanium interbody cages in lumbar fusions [50]. At 8- and 16-week time points, only the 3DP porous titanium cage had significantly decreased range of motion compared to other groups ($p = 0.02$). In addition, microCT data showed that the 3DP porous titanium cage had a significantly increased bony ingrowth compared to the PEEK cages ($p < 0.01$). The

Fig. 7 Digital renderings and physical production of a new 3DP anatomy-adaptive titanium mesh cage. Adapted from Lu et al. 2017. "Single-level anterior cervical corpectomy and fusion using new 3DP anatomy-adaptive titanium mesh cage for tx of cervical spondylitis myelopathy and ossification of posterior longitudinal ligament: retrospective case series". Granted access from the senior author, Dr. He on 6/23/19

authors postulated that the increased ingrowth and osteogenesis around the osteoconductive implant led to greater implant stability and fusion. MacBarb et al. supported this finding in a separate ovine model showing that both 3DP and TPS had substantial bone ingrowth and ongrowth [49].

Tissue Engineering

There are many aspects of scaffold design that can affect in vivo performance such as the choice of material, geometry, and incorporation of bioactive substances. Porosity of scaffolds has also shown to play an integral role in the ability of bones to embed into the scaffold [49], which has led to integration of 3DP to create geometries unachievable with traditional manufacturing methods. Perhaps most interestingly, 3DP technology can promote bone growth without the need for graft or other exogenous factors like rhBMP-2. Jakus et al. developed a 3DP material known as "hyperelastic bone," which mimics native bone [51]. This product was made from medical-grade polymers and used as a printable "bioink." This removed the need for excessive heat or other chemicals to form the structure. Notably, Jakus et al. showed that the "hyperelastic bone" scaffolds had structural properties similar to bone, but were easier to handle and could customize the stiffness and porosity of the scaffold. Most importantly, though, they showed cell viability as well as prominent osteointegration in vivo. This opens up new doors for customizable, flexible, growth-factor free materials that can be prepared in the operating room and fit for each patient. As seen in these scaffolds, they incorporate biologic materials that can optimize bone formation with incorporation of biologics. The scaffolds could also be given multiple uses. Yang et al. described a 3DP composite scaffold that both promoted bone regeneration and inhibited bacterial biofilm formation in vivo [52]. Furthermore, researchers are looking for alternative ways to implant bone regenerative technologies. For example, printing cells in situ, or directly into tissues during surgery [53] or through minimally invasive injections that can set implants with hydrogels combined with bone mesenchymal stem cells. Although this is in the idea phase, there are ongoing efforts to building extrusion-based printing method that could be utilized in the operating room to fill bone defects in situ [53].

Conclusion

Over the past two decades, 3DP applications in spine surgery has grown rapidly and now has demonstrated efficacy in minimally invasive approaches. As theorized, and now demonstrated by several leaders in the field, there are many practical uses for 3DP within spine surgery. Biomodels provide visual and tactile sensation of the anatomy for preoperative planning, counseling, and education; surgical guides and templates improve accuracy and minimize iatrogenic-induced morbidity; and implants are optimized for a tighter fit and improved bone regeneration capabilities. This is an exciting field that is only limited by our imagination and ability to innovate. Nevertheless, integration of this technology will require further research into long-term outcomes, reducing costs, and establishing best practices. With continued research, we will have a better understanding of the technical aspects and long-term health effects of these devices and our ability to implement them to personalize healthcare.

Author Contributions All of the authors contributed significantly to the development of this manuscript through data analysis, manuscript preparation, or analysis and editing of final manuscript.

Compliance with Ethical Standards

Conflicts of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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