Retracted Article: Application of 3D printing technology in orthopedic medical implant - Spinal surgery as an example

Rong Feng Zhang¹, Peng Yun Wang²*, Ming Yang³, Xuebo Dong¹, Xue Liu¹, Yiguang Sang⁴, An Tong⁵*

¹Department of Orthopaedics, Shandong Hospital of People’s Liberation Army, 89th Hy, Weifang, Shandong Province, Republic of China
²Department of Spine Surgery, Central Hospital, Zibo, Zhangdian, Shandong Province, China
³Traditional Chinese Medicine Hospital, Dongying, Hekou, Shandong Province, China
⁴Qilu Hospital, Shandong University, Shandong, China
⁵Department of Orthopedics, People’s Hospital of Yan’an, Qilipu Street, Yan’an, Baota, Shaanxi Province, China

Abstract: Additive manufacturing has been used in complex spinal surgical planning since the 1990s and is now increasingly utilized to produce surgical guides, templates, and more recently customized implants. Surgeons report beneficial impacts using additively manufactured biomodels as pre-operative planning aids as it generally provides a better representation of the patient’s anatomy than on-screen viewing of computed tomography (CT) or magnetic resonance imaging (MRI). Furthermore, it has proven to be very beneficial in surgical training and in explaining complex deformity and surgical plans to patients/parents. This paper reviews the historical perspective, current use, and future directions in using additive manufacturing in complex spinal surgery cases. This review reflects the authors’ opinion of where the field is moving in light of the current literature. Despite the reported benefits of additive manufacturing for surgical planning in recent years, it remains a high niche market. This review raises the question as to why the use of this technology has not progressed more rapidly despite the reported advantages – decreased operating time, decreased radiation exposure to patients intraoperatively, improved overall surgical outcomes, pre-operative implant selection, as well as being an excellent communication aid for all medical and surgical team members. Increasingly, the greatest benefits of additive manufacturing technology in spinal surgery are custom-designed drill guides, templates for pedicle screw placement, and customized patient-specific implants. In view of these applications, additive manufacturing technology could potentially revolutionize health care in the near future.

Keywords: Additive manufacturing; biomodeling; rapid prototyping; spine deformity; complex spine surgery

*Correspondence to: Peng Yun Wang, Department of Spine Surgery, Central Hospital, Zhangdian, Zibo, Shandong Province, China; wangpengyun1@sina.com; An Tong, Department of Orthopedics, People’s Hospital of Yan’an, Qilipu street, Yan’an, Baota, Shaanxi Province, China; Tongangk@163.com

Received: October 31, 2018; Accepted: April 4, 2019; Published Online: July 1, 2019

Citation: Zhang RF, Wang PY, Yang M, et al., 2019, Application of additive manufacturing technology in orthopedic medical implant – Spinal surgery as an example. Int J Bioprint, 5(2): 168. http://dx.doi.org/10.18063/ijb.v5i2.168

1. Introduction

Spine surgeons engage in complex and innovative surgical procedures to stabilize and improve idiopathic, congenital, degenerative, and injury-related spinal deformaties. Even though surgical treatment strategies and implants have evolved and improved considerably in recent decades, surgical correction of complex deformities remains very challenging. To evaluate the severity of spinal deformities and plan any required surgical procedures, physicians have
traditionally relied on imaging modalities including X-rays, fluoroscopy, CT and MRI. Unfortunately, two-dimensional projections of radiographic images or three-dimensional (3D) scan data will always be limited in their ability to accurately display the complete image of 3D anatomic deformities, detracting from their value during the pre-operative planning process. As presented in the other papers in this article, the use of 3D modeling and rapid prototyping (RP) or additive manufacturing has been increasingly used in complex surgical pre-operative planning, as these techniques can accurately reproduce the anatomic details of highly complex deformities that could be missed or misinterpreted with standard imaging modalities.

The purpose of this article is to explore the existing uses of additive manufacturing in complex spinal surgery and to discuss the future potentials of this technology. The common techniques and requirements for additive manufacturing are addressed elsewhere. Literature search was conducted using PubMed for articles containing the terms “additive manufacturing”, “RP”, “biomodelling”, or “biomodeling”, and in combination with “spine/spinal” and “surgery/surgical planning”. General reviews or discussions of this technology where spinal usage is only briefly mentioned were not included.

2. Method

From the 16 articles that were found, one was excluded from further review as it is not available in English. Publication years ranged between 1999 and 2015, with nearly half of the papers published in the past 5 years, consistent with the rapidly increasing interest in this technology. Three key areas of focus are evident: Complex spinal deformity cases in which models have been printed for surgical planning purposes; the design of patient-specific drill guides; and the very recent advent of printing custom titanium implants.

Interestingly, there is a clear change in focus of the publications from 2009 to 2011 when simple printing for surgical planning was replaced by the printing of surgical tools and finally the implants themselves. Although publications on the use of additive manufacturing for surgical planning have declined in numbers recently, the current usage rates remain unclear. Has the spinal surgical community adopted this as a routine technology, or abandoned it in the past 10 years altogether? To better understand this shift, we conducted a survey of spinal surgeons attending the 2015 Annual Scientific Meeting of the Spine Society of Australia and presented the results here.

3. Historical Usage and Current Trends

The use of additively manufactured models in complex spine deformity surgical planning was first reported in 1999 by a group of researchers from Australia. D’Urso et al. reported the previous use of the technology in craniomaxillofacial surgery and undertook a preliminary prospective study of five complex cases to determine its usefulness in spine deformity surgery. Members of this group continue to be at the forefront in this area, having published a number of other key papers in the field. These papers include a total of 51 cases where spine biomodels have been utilized, with the remaining four papers in this field are from Japan and China, which describe 53 additional cases. All the authors from these published articles agreed that a 3D reconstructed model is required to obtain comprehensive information about the complex spinal deformities that would have been unavailable if conventional imaging modalities were exclusively used. They found that although CT 3D reconstruction could be displayed and viewed from any direction and angle on the computer, these method lack of tactile view which frequently view the biomodel separately and results in some alteration being made to the surgical case, be it an implant, approach, or fixation related.

4. Complex Spinal Deformity Surgical Planning

Literature findings concluded that the use of additively manufactured biomodels offered numerous benefits resulting in better surgical outcomes for the patients for example, Mizutani et al. fifteen cases were evaluated and reported that 3D modeling was beneficial as a pre-operative planning tool in rheumatoid cervical spine surgery. This was attributed to a better assessment of the trajectory and entry points of cervical pedicle screws, as well as allowing for the ability to determine the entire plate-rod contours for occipitocervical junctions, avoiding post-operative dysphagia. Although having a 3D biomodel have advantages such as a detailed representation of anatomy and as a tool for planning surgical procedures, the authors concluded that coupling the 3D model with computer-assisted navigation systems likely provided better surgical results. Izatt et al. aim to quantify the surgeon’s perception on the usefulness of biomodels compared with standard imaging modalities as a pre-operative planning tool and as an intraoperative anatomic reference in 26 spinal tumor and deformity cases. This study entailed a survey completed by the surgeons after each surgical case and found that anatomic details were better or exclusively visible on the biomodel (65% and 11%, respectively) compared with the CT or MRI 3D reconstructions. Therefore, different decisions were made as a direct result of the biomodel regarding the materials used (52%) and implantation sites (74%), thereby reducing the likelihood of surgical revision being required. Importantly, this paper also recorded an estimated 17% decrease in operating time for all 26 patients, with
an 8% reduction in surgery time for tumor patients (mean 46 min per case) and 22% reduction in the deformity cases (mean 68 min per case) which directly reduced the cost of surgery in addition to the other reported benefits. Reasons given for the reduction in surgical time were included: easier, accurate and more efficient implant and screw positioning; less frequent reference to other imaging resources and reduced number of instrumentations due to better anatomic visualization; and detailed pre-operative planning. A recent systematic review paper by Martelli et al.\cite{10} based on 52 papers reported that time was saved due to additive manufacturing. Likewise, Mao et al.\cite{8} also confirmed that 3D biomodels were helpful in improving pre-operative planning and surgical treatment of complex severe spinal deformities compared with either CT or MRI 3D spinal reconstructions. This paper suggested that the biomodels were a superior visual aid when confirming the position of an anatomic landmark, helped the surgeon plan the surgery, facilitated the choice of internal fixation instrumentation, and improved the accuracy, and therefore, the safety of pedicle screw insertion all of which would influence the direct costs of the surgical cases and the risk of revision surgery being required in the future.

Another important factor discussed by both Mao et al.\cite{8} and Izatt et al.\cite{5} was the use of additively manufactured biomodels as a communication tool with both colleagues and patients/parents. Patients (or if they were <18 years old, their parents/guardians) were contacted after the surgery, and all stated that the biomodels improved their anatomic understanding of the condition; the procedure and the risks associated with it, and, therefore, improved their ability to give fully informed consent. Similarly, biomodels enabled better communication and teaching within the surgical team both preoperatively and intraoperatively. Of course, there were also limitations presented in using this technology mainly related to the extra time, labor, and the associated costs of biomodel manufacture. Nevertheless, it was argued that these issues were offset by the cost savings from shorter surgical times, the reduced complication rates, and the likelihood of surgical revision being required in the future.\cite{12,3,3}

Presented below are two case studies performed by the authors of this article where additively manufactured biomodels were used for pre-operative planning.

4.1. Patient A

A 12 year old male, diagnosed with neurofibromatosis type 1 with complex occipitocervical spinal deformities and a large neuroma in close proximity to the upper cervical spine. The patient was demonstrating steadily worsening neurological signs in all limbs and had experienced a number of episodes of intermittent quadriparesthesia indicative of progressive brainstem/spinal cord compression, requiring surgical decompression and stabilization. Preoperatively, the patient had posterior-anterior (PA) and lateral (LAT) cervical and full spine radiographs (Figure 1), brain and full spine MRI (Figure 2), and 3D CT scans (Figure 3). The CT scan was used to create a 3D anatomic biomodel (Figure 4).

After viewing the available imaging data, the initial surgical plan was to perform a posterior instrumented fusion from occiput to T4 with screw fixation into the occiput and thoracic spine only. Due to the small size and deformity of the cervical vertebrae, it was considered that the upper cervical vertebrae were too small to be able to insert any fixation points for the planned posterior construct. After receiving the biomodel, it became evident that the C2 laminae were of sufficient size for small translaminar screws to be used on each side. The surgical instrumentation was changed to include these translaminar screws in addition to the fixation points already planned at the occiput and T3-4 levels.

![Figure 1. Pre-operative lateral and posterior-anterior radiographs of the cervical and upper thoracic spine of 12-year-old male (neurofibromatosis type 1, plexiform neuroma posterior to cervical spine), which did not provide clear anatomic detail of significant upper cervical deformity.](image1)

![Figure 2. Sagittal slices of pre-operative magnetic resonance imaging showing the reduced size of the spinal canal in the upper cervical spine with insufficient posterior element bony detail (patient A).](image2)
The biomodel greatly assisted with the explanation to the child’s parents regarding the surgery planned and the associated risks involved, thereby, helped to obtain informed consent.

The surgeons reported that the addition of fixation to the upper cervical spine had made the instrumented construct more robust and had improved the deformity correction achieved by the procedure in addition to the decompression and stabilization components. With the additional fixation points, the surgeon reported that the risk of requiring a revision procedure in the future was also less likely. Although the pedicle screw placement in the thoracic spine was not optimum, they have held well to date, the patient’s neurological signs have improved and thereafter remained stable, with no loosening or loss of correction now 10 months postoperative. Supine LAT and PA radiographs 1 month after surgery and the most recent LAT view at 10 months post-operative are shown in Figure 5.

4.2. Patient B

A 9 year old female, diagnosed with myelomeningocele spina bifida (neurological deficit below T10) with severe collapsing T10-S1 due to the total absence of posterior elements. The resulting kyphotic deformity was causing seating difficulties and the maintenance of the integrity of the skin over the kyphotic deformity was becoming challenging, with skin breakdown becoming more frequent. It was considered that kyphectomy and posterior instrumented fusion would improve the quality and length of life. Preoperatively, the patient had PA and LAT sitting spine radiographs (Figure 6), thoracolumbar spine CT with 3D reconstruction (Figure 7), and a biomodel was ordered (Figure 8).

The surgical plan was to ideally perform a kyphectomy between two and five levels followed by deformity correction and stabilization with a posterior instrumented fusion from the upper thoracic spine to the pelvis; however, the thoracolumbar anatomy, especially the thoracolumbar junction anatomy, remained unclear. Having no posterior spinal elements to fix...
instrumentation into, alternative fixation points were required. After receiving the biomodel, the anatomy of the lower thoracic and lumbar spine was clear and the decision was made with some confidence to proceed with the kyphectomy of L1-L3 followed by an instrumented fusion from T3-pelvis (Figures 9 and 10).

The biomodel also greatly assisted with the explanation to the child’s parents regarding the planned surgery and the associated risks involved, thereby, helped to obtain informed consent. The patient recovered well, and the parents reported that caring for their child was much easier, as was her comfort when seated in her wheelchair. There was an added benefit of being able to sleep supine for the 1st time in many years. There were no longer any issues with skin integrity or pressure areas over her spine. The fixation has remained stable with no complications.

5. Surgical Tools and Guides

Since 2009, designing and printing guides for pedicle screw placement has emerged as a new area of additive manufacturing for spinal surgical planning, particularly in the cervical spine. The anatomy in this region is quite compact and even more so in pediatric cases, with delicate neural tissue in close proximity making precise screw insertion of great importance.

The earlier papers from Lu et al. utilized additively manufactured drill guides for two kinds of screw placement in the cervical spine. These plastic guides were placed directly in contact with the patient’s exposed bony anatomy in the operating room and used to insert screws along predefined trajectories. The author reported that this technique is highly accurate. Additionally, reduces both the surgery time and radiation exposure. These

Figure 7. Sagittal views from pre-operative computerized tomographic (CT) scan and three-dimensional CT reconstruction (far right) of the thoracic and lumbar spine showing more anatomic detail than radiographs of the deformity, but insufficient detail to decide how many levels to remove and the precise fixation points for the instrumentation (patient B).

Figure 8. Three-dimensional printed biomodel (anterior, posterior, and lateral views) demonstrates the anatomy of the thoracic and lumbosacral spine providing the necessary detail for the kyphectomy and subsequent successful deformity correction and instrumented fusion procedure patient.

Figure 9. Post-operative anterior-posterior (A) and lateral (B) radiographs illustrating the instrumented correction and stabilization achieved surgically for patient B.

Figure 10. Pre-operative (A and B) and post-operative (C) photographs showing cosmetic aspects of the deformity before and after surgical correction assisted by the use of the three-dimensional printed biomodel (patient B).
papers were then followed by a series of cadaveric studies describing the effectiveness of additively manufactured plastic pedicle screw template\cite{13,14}. In summary, the researchers found that by using the screw template the intended insertion location and angle correlate.

As a result, titanium was proposed as an alternative to plastic models for surgical guides; however, it was also found to have disadvantages such as cost and availability. In the study by Takemoto et al.,\cite{15} additive manufactured titanium thoracic pedicle screw templates were assessed specifically looking at the landmarks used as contact points for the template, to ensure reproducibility and stability. This study showed a very high success rate for their templates, with failure defined as perforation of the pedicle wall by the screw, 98.4% of pedicle screws were placed successfully for scoliosis patients and 100% for ligament ossification patients. The issue of cost was also addressed in this study stating that the production cost of 10 templates in a singular patient amounted to $1000 for titanium versus $200 for the plastic polyamide.

The authors pointed out that even though the non-metallic materials have approval from the US Pharmacopeia for use in the human body for 24 h when in contact with drills and surgical tools; the plastic would likely produce debris, which would accumulate in the wound. The long-term effect of this residual material is unknown, and in close proximity to the spinal cord, its safety is clearly questionable. The titanium templates also have the advantage of higher strength and rigidity, being metallic. This ensures greater accuracy and reliability, reduces the chance of warping and flexing, and eliminates the potential of the drill or screw cutting through the material and/or producing debris as is the case for plastic guides.

6. Additively Manufactured Custom Implants

Recent advances and the increased availability of metal-based additive manufacturing technologies such as direct or selective laser sintering (LS) and electron beam melting have allowed for the development of customized spinal implants into current surgical practice.

Off the shelf, vertebral body and intervertebral disc implants are already commonly used, but the ability to 3D print both generic and custom metal implants has a number of potential advantages. For instance, intervertebral discs that can be printed to conform to the patient’s specific vertebral end plate geometry have performed well in cadaveric studies, achieving higher compressive failure loads, and better stiffness characteristics than flat implants produced in the same manner\cite{16}. On the other hand, a high-temperature LS allows fabrication layering of complex structure such as high-performance biomaterial polymer, i.e., polyether ether ketone was applied by Berretta et al. in the manufacturing of cranial implant\cite{17}. Both the mechanical performance, density variation, and dimensional accuracy of the implants were found comparable to the design model and show the highest compressive strength resistance.

Evidently, an additively manufactured porous titanium structures have great potential for use as bone substitute biomaterials. Titanium alloys have been used for decades as a bioactive material\cite{18}, encouraging bony ingrowth onto exposed surfaces. For instance, titanium-tantalum (Ti-Ta) alloy can be fabricated using selective laser melting\cite{19}. Ti-Ta alloys are promising materials for biomedical applications and surgical implants because it has high biocompatibility, corrosion resistance, and good mechanical properties. Besides, electron beam melting allows porous implants made from titanium alloys to be created with control over the shape and pore structure. This technology has the potential to develop both patient-specific custom implants, as well as generic bone substitute implants. Yang et al.\cite{20} examined a self-stabilizing artificial vertebral body created this way in an in vivo sheep model of the cervical spine. This study found that the porous metal implants facilitated bony ingrowth and resulted in very stable fixation in a load-bearing application something that is not currently possible with other additively manufactured scaffold structures.

Worldwide, a number of companies are already making additively manufactured customized surgical tools and templates to aid in spinal procedures, as well as custom spinal implants designed specifically for particular patients. Besides the customized spinal implants, the similar technologies were applied to other recent orthopedic regenerative medicine treatments\cite{21}. A mandible that is coated with hydroxyapatite has been additively manufactured\cite{22}. Furthermore, Mertens et al. constructed a titanium-made midfacial support and a graft fixture through additive manufacturing for patient with midface defect\cite{23}. Customized cranial implants were designed and additively manufactured by Jardini et al. in the surgical reconstruction of a large cranial defect\cite{24}.

7. Surgeon Survey

Spinal surgeons attending the Annual Scientific Meeting of the Spine Society of Australia 2015 held in Canberra, Australia, were asked to complete a short survey on their knowledge and use of RP technology (additive manufacturing) in their surgical practices and experience. 35 surgeons completed the survey, of which 81% (27) were experienced, senior consultants. Although 80% of respondents had heard of using additive manufacturing for surgical planning, only 10 had ever used it. Of these 10, eight reported using it 0–2 times per year and two reported using it 3–5 times per year. Most users (7/10) reported that it improved the surgical outcome, with the
others saying that it made no difference to the surgical outcome. However, additionally, the comment was made that while they felt that the biomodel did enhance surgical planning and the ability to perform the surgical intervention, the outcome to the patient was the same as if they had not used it.

For those who were not using the technology, most reported that this was due to availability issues (44%). However, only 54% said that they would use it should it ever become available in their hospital. Other minority reasons given for not using biomodels were cost (4%, \(n = 1\)) and other reasons (12%, \(n = 3\)), predominantly being that they do not or have not had a suitable case for which to use it to date.

These results, together with discussions with the surgeons while they were completing the survey, highlighted a number of important considerations: That of the suitability of cases for this type of procedure in a particular surgeon’s practice, as well as the usefulness of biomodels for purposes other than developing the actual surgical plan. The surgeons who currently used additive manufacturing for surgical planning all worked with patients who had complex progressive deformities, whereas those who did not use biomodels treated less complex and mainly adult degenerative cases, for which the added expense and time delay to print the model was thought to likely not be of sufficient benefit to their surgical planning and/or surgical procedure.

According to surgeons, the usage of additively manufactured models are often extended, which is beyond the surgical planning phase. Hence, patient or their guardian needs to be aware of this situation when signing the informed consent form. Having a physical model available of a complex spinal deformity made the explanation of the current condition as well as the intended surgical procedure to patients and family much simpler and easier to understand. The description of both the severity and the reasons for the current symptoms caused by the spinal deformity could be explained more clearly as well as exactly what the surgery would entail and the possible complications and consequences that may occur with or without the intended surgical procedure. This sentiment has also been reported in literature discussed above\(^9\). Furthermore, using the additively manufactured models with surgical trainees form an important teaching tool during the surgical planning phase, during the surgical procedure, and as retrospective case studies.

### 7.1. Future Perspectives

As reflected in this review, the use of additive manufacturing as a pre-operative planning tool in spinal surgery is still relatively uncommon, even though the technology has continued to develop over the past three decades. This review raises the question as to why the use of this technology has not progressed more rapidly despite the reported advantages – decreased operating time, decreased radiation exposure to patients intraoperatively, improved overall surgical outcomes, pre-operative implant selection, as well as being an excellent communication aid for all medical and surgical team members. Regardless of the reported clinical success, the lack of usage of 3D RP or printing has been attributed to the availability and cost of the technology, as well as the time delay between the scan of the patient is performed and the biomodel being produced (several days) and then delivered to the requesting surgeon. The other main reason given for not using physical 3D biomodels was that the particular surgeon did not treat the type of spinal deformity patients that would benefit from this technology, who are managed by a small contingent of highly specialized complex deformity surgeons.

The future success of this technology is dependent on how useful surgeons find the biomodels to be for pre-operative planning and consent and/or for intraoperative anatomic reference compared with standard visualization modalities such as CT scans. Do additively manufactured biomodels have the potential to become part of the standard of care, or will it always be used only for the most complex deformity cases by specialist spinal surgeons and how will the success of the technology be measured? Answering these questions will be vital for additive manufacturing to become an essential part of spinal deformity surgery as the technology continues to improve, becomes more affordable and faster to produce. It seems clear that even if biomodels are only used on a limited basis during the surgical procedure for the most complex cases of spinal deformities, there is certainly value in the exercise of virtual planning or 3D computer modeling, a processing step that is generated before final additive manufacturing occurs. The generation of the 3D computer model allows for the on-screen manipulation of the patient’s-specific anatomy generated from their CT scan for the purpose of visualization of the deformity for pre-operative planning and rehearsal of the intended surgery. Therefore, whether or not the final stage of printing goes ahead; utilization of the technology of 3D computer modeling will most likely become a routine part of spinal surgery for the benefit of clinicians and patients alike.

It is worth noting that based on the number of publications found in literature, China has the appearance of leading the medical field in the use of RP technology. Why are some countries such as China more readily accepting RP technology and why are they at the forefront in using it compared with the western world? Perhaps, it is related to the fact that in western countries, private biomedical companies are driving this technology and its use rather than research institutions, which often does not translate into peer-reviewed publications.
In contrast, for the design of surgical tools, templates, and personalized patient implants, additive manufacturing technology has found a new niche which is demonstrating a rapid advance and may be the most promising application in the medical field. We believe that the future of customized patient-specific implants will be the greatest benefit of additive manufacturing technology, potentially revolutionizing health care, and benefitting the largest number of patients. This is especially true as the trend continues toward less invasive and more precise surgical treatment strategies, and as clinicians increasingly relies on advanced technologies for planning and delivering customized and patient-specific medical care.

Further discussion on the techniques, technology, and limitations of additive manufacturing in health care can be found in other articles in this issue.

References

1. Green N, Glatt V, Tetsworth K, et al., 2016, A Practical Guide to Image Processing in the Creation of 3D Models for Orthopaedics. Tech Orthop, 31(3):153-63. DOI 10.1097/BTO.0000000000000181.

2. D’Urso P, Askin G, Earwaker J, 1999, Spinal Biomodeling. Spine (Phila Pa 1976), 24:1247-51. DOI 10.1097/00007632-199906150-00013.

3. D’Urso PS, Williamson OD, Thompson RG, 2005, Biomodeling as an Aid to Spinal Instrumentation. Spine (Phila Pa 1976), 30(12):2841-5. DOI 10.1097/01.brs.0000190886.56895.3d.

4. D’Urso PS, 2006, Biomodelling. In: Gibson I, editor. Advanced Manufacturing Technology for Medical Applications: Reverse Engineering, Software Conversion and Rapid Prototyping. Chichester, United Kingdom: John Wiley and Sons Ltd., p31-57. DOI 10.1002/0470033983.ch3.

5. Izatt MT, Thorpe PLP, Thompson RG, et al., 2007, The use of Physical Biomodelling in Complex Spinal Surgery. Eur Spine J, 16(9):1507-18. DOI 10.1007/s00586-006-0289-3.

6. Yamazaki M, Akazawa T, Okawa A, et al., 2007, Usefulness of Three-dimensional Full-scale Modeling of Surgery for a Giant Cell Tumor of the Cervical Spine. Spinal Cord, 45:250-53. DOI 10.1038/sj.sc.3101959.

7. Mizutani J, Matsubara T, Fukuoka M, et al., 2008, Application of Full-scale Three-dimensional Models in Patients with Rheumatoid Cervical Spine. Eur Spine J, 17(5):644-9. DOI 10.1007/s00586-008-0611-3.

8. Mao K, Wang Y, Xiao S, et al., 2010, Clinical Application of Computer-designed Polystyrene Models in Complex Severe Spinal Deformities: A Pilot Study. Eur Spine J, 19(5):797-802. DOI 10.1007/s00586-010-1359-0.

9. Yang JC, Ma XY, Lin J, et al., 2011, Personalised Modified Osteotomy using Computer-aided Design-rapid Prototyping to Correct Thoracic Deform-ities. Int Orthop, 35(12):1827-32. DOI 10.1007/s00264-010-1155-9.

10. Martelli N, Serrano C, van den Brink H, et al., 2016, Advantages and Disadvantages of 3-dimensional Printing in Surgery: A Systematic Review. Surgery, 159(6):1485-500. DOI 10.1016/j.surg.2015.12.017.

11. Lu S, Xu YQ, Lu WW, et al., 2009, A Novel Patient-specific Navigational Template for Cervical Pedicle Screw Placement. Spine (Phila Pa 1976), 34(26):E959-66. DOI 10.1097/BRS.0b013e3181c09985.

12. Lu S, Xu YQ, Zhang YZ, et al., 2009, A Novel Computer-assisted Drill Guide Template for Placement of C2 Laminar Screws. Eur Spine J, 18(9):1379-85. DOI 10.1007/s00586-009-1051-4.

13. Fu M, Lin L, Kong X, et al., 2013, Construction and Accuracy Assessment of Patient-specific Biocompatible Drill Template for Cervical Anterior Transpedicular Screw (ATPS) Insertion: An in vitro Study. PLoS One, 8(1):e53580. DOI 0.1371/journal.pone.0053580.

14. Hu Y, Yuan Z, Spiker WR, et al., 2013, Deviation Analysis of C2 Translaminar Screw Placement Assisted by a Novel Rapid Prototyping Drill Template: A Cadaveric Study. Eur Spine J, 22(12):2770-6. DOI 10.1007/s00586-013-2993-0.

15. Takemoto M, Fujibayashi S, Ota E, et al., 2016, Additive-Manufactured Patient-specific Titanium Templates for Thoracic Pedicle Screw Place-ment: Novel Design with Reduced Contact Area. Eur Spine J, 25:1698-705. DOI 10.1007/s00586-015-3908-z.

16. de Beer N, Scheffer C, 2012, Reducing Subsidence Risk by using Rapid Manufactured Patient-specific Intervertebral Disc Implants. Spine J, 12(11):1060-6. DOI 10.1016/j.spinee.2012.10.003.

17. Berretta S, Evans KE, Ghita OR, 2018, Additive Manufacture of PEEK Cranial Implants: Manufacturing Considerations Versus Accuracy and Mechanical Performance. Mater Des, 139(1):141-52. DOI 10.1016/j.matdes.2017.10.078.

18. Cook HP, 1969, Titanium in Mandibular Replacement. Br J Oral Surg, 7:108-11. DOI 10.1016/S0007-117X(69)80005-3.

19. Sing S, Yenog WY, Wiria FE, 2018, Selective Laser Melting of Titanium Alloy with 50 wt% Tantalum: Effect of Laser Process Parameters on Part Quality. Int J Refract Met Hard Mater, 77:120-7. DOI 10.1016/j.ijrmhm.2018.08.006.

20. Yang J, Cai H, Lv J, et al., 2014, in vivo Study of a Self-Stabilizing Artificial Vertebral Body Fabricated by Electron Beam Melting. Spine (Phila Pa 1976), 39(8):E486-92. DOI 10.1097/BRS.0000000000002111.
21. Wang X, Xu S, Zhou S, et al., 2016, Topological Design and Additive Manufacturing of Porous Metals for Bone Scaffolds and Orthopaedic Implants: A Review. Biomaterials, 83:127-41. DOI 10.1016/j.biomaterials.2016.01.012.

22. Xillo, 2011, The World’s First 3D Printed Total Jaw Reconstruction. Available from: http://www.xilloc.com/patients/stories/total-mandibular-implant.

23. Mertens C, Lowenheim H, Hoffmann J, 2013, Image Data Based Reconstruction of the Midface Using a Patient-specific Implant in Combination with a Ascularized Osteomyocutaneous Scapular Flap. J Cranio Maxillofac Surg, 41:219-25. DOI 10.1016/j.jcms.2012.09.003.

24. Jardini AL, Larosa MA, Zavaglia CAC, et al., 2014, Customised Titanium Implant Fabricated in Additive Manufacturing for Craniomaxillofacial Surgery. Virtual Phys Prototyp, 9:115-25. DOI 10.1080/17452759.2014.900857.