Introduction

Spondylotic (age-related degenerative changes of the spine) or non-spondylotic lesions that affect the cervical vertebrae can lead to compression of adjacent nervous structures resulting in myelopathic (spinal cord origin) or radiculopathic (spinal nerve origin) symptoms including pain and loss of function (1-4). Non-spondylotic lesions (trauma, tumors, infection and other rarer causes) take up a smaller proportion of myelopathic/radiculopathic causes (1,2), but can result in substantial alteration of the structural anatomy (5-7).

The common mechanism of cervical spondylotic changes include loss of disc height, degeneration of the uncovertebral and facet joints, and disc herniation resulting in spinal nerve encroachment (3). Compression of the nerve root and dorsal root ganglion result in pain (localized neck or may radiate into the upper limbs), which is further...
aggravated by hypoxia and inflammation (8-11). Osteophyte formation can result from the body coping with flattening of the uncovertebral joints. In addition, ossification of the posterior longitudinal ligament, hypertrophy and calcification of the ligamentum flavum and progressive kyphosis of the cervical spine contributes to stenosis of the central canal, thus ultimately compressing the spinal cord (2,4,12-14). Dynamic compression, particularly during cervical flexion and extension movements, can worsen the pathology (13,15). Chronic cord compression results in a cascade of macro- and micro-changes of the cord leading to a variety of neurological problems that can include: localized neck pain and/or radicular pain into the upper limbs; somatosensory dysfunction of the lower limbs; loss of bladder and bowel control (2,13,15,16). If cord compression is significant, symptoms can correlate with magnetic resonance imaging (MRI) findings indicative of cord signal changes (2,13,16).

In the absence of neurological findings, the recommended approach is non-surgical for pain due to spondylosis (13). However, surgical intervention can significantly improve the outcome of patients if neurological symptoms are present and when imaging clearly demonstrates the involvement of neural structures or when other etiologies are involved (e.g., neoplasms and trauma) (2,13,15,17). The end-goal of surgical intervention is to decompress the neural structures and stabilize pathological segments to prevent movements that can result in further damage, which can be achieved via an anterior or a posterior approach (2,13,18,19). Though there are multiple techniques to achieve these goals, anterior cervical decompression and fusion (ACDF) or anterior cervical corpectomy and fusion (ACCF) with/without posterior stabilization has been shown as an effective treatment option for such cervical spine pathologies (20-22).

To date, various ACDF and ACCF implants are available for degenerative changes, but options are more limited for more extreme or distorted anatomies (e.g., traumatic or neoplastic origin). Such extreme pathological anatomy may indicate the design and manufacture of a patient-specific implant (PSI)/custom-made spinal implant.

Since the introduction of three-dimensional printing (3DP) in the 1986 by Hull (23), the manufacturing means have steadily expanded (materials) and improved (precision, reliability) to the point where it is now possible to realize the idea of patient-specific devices. 3DP, also known as Additive Manufacturing or Rapid Prototyping, has been successfully applied in the field of medicine, with orthopedics and neurosurgery being notable early adopters of the technology (24-28). Coupled with advances of medical imaging such as computed tomography (CT) scanning and MRI, accurate (precise and true) 3D models of patient anatomy can be produced. Stereolithographic spinal biomodeling, proposed and adapted by D’Urso et al. in 1999 combined the potential of 3DP with spinal surgery allowing accurate patient-specific spine morphology to be printed in a physical form (29). More recently, 3D printed PSIs have been successfully used to treat patients by Xu et al. in 2016 and Mobbs et al. in 2017 (5,6) (Figure 1). Pre-operative planning, surgical training, intraoperative drill-guides and spinal implants with complex morphology have all been applied with high rates of positive outcomes (24,25,27,28). 3DP applications have been more numerous in the cervical spine, perhaps due to the complex anatomy and the involvement of multiple important structures (vertebral arteries and spinal cord) within a relatively small space, which necessitates higher precision in the engineering of cervical devices (5,30,31).

The principle of Additive Manufacturing (3DP) involves layer-by-layer melting and/or fusing of raw printing material(s) to synthesize a 3D part (32-35). Metal (powder), polymers (solid and liquid), ceramics (powder), bio-gels and living cells are currently used as raw materials for 3DP (34,36,37). Models generated by Computer Aided Design (CAD) and computer aided engineering (CAE) are converted into an .STL (StereooLithography) file for 3DP (34,35,38). In terms of spinal bony anatomy, software is used for CT thresholding, segmentation and boundary representation (b-rep) iso-surface model generation (usually via the marching cubes algorithm, or a derivative thereof) to produce an .STL file of the hard or soft tissue anatomical structures of interest (35,39-42). The .stl file is then oriented relative to the build platform and sliced by the build layer thickness to create 2-dimensional tool paths for the 3D printer to perform the process of additive manufacturing (34,35). Currently, various modalities are used to produce 3D printed objects (32,33,35). Depending on the desired outcomes and materials, different methods of 3DP are utilized in the field of neurosurgery with powder bed fusion (electron beam or laser melting or sintering) the most common approach for spinal implants manufactured from Titanium alloys (33,34).

The purpose of this review is to evaluate the current application of 3DP for cervical spinal implants. This includes a review on the available literature on 3D printed PSIs and current available 3D printed “off-the-shelf” (OTS) implants (3D-OTS). Materials suitable for 3DP of spinal
implants and the future prospect of cervical implants will be
discussed. The review will be concluded with a suggested
guide for performing future studies to evaluate the efficacy
and safety of 3DP for cervical spinal implants.

Methods

A literature search was performed on four online
electronic databases (PubMed, Medline, Web of Science
and EMBASE) on the 1st April 2018. To achieve high
sensitivity, search terms used were of a combination of:
“spine”, “spinal cord”, “cervical”, “neck”, “3-dimensional
printing” and “additive manufacturing”. The reference
lists of potential studies were screened to identify
possible relevant articles. A further search was done
online for information [for example white papers with
scientific data as well as United States Food and Drug
Administration (FDA) 510K approval letters] from spinal
implant companies that had recently adopted 3DP as a
manufacturing method for implants and received FDA
510(k) clearance for these implants.

Selection criteria

Inclusion criteria

(I) All literature that reported the use of 3D printed
implants for the cervical spine was included;
(II) For PSIs, anterior cervical fusion implants either
corpectomy cages or disc implants are included;
(III) The implants have to be placed in humans;
(IV) PSIs for all age groups were included;
(V) Companies with FDA 510(k) clearance for their 3D
printed OTS cervical implants were included;
(VI) All cage materials were included.

Exclusion criteria

(I) PSIs which were not implanted in humans;
(II) Patient-specific devices such as drill guides were not
included;
(III) 3D printed OTS cervical implants without FDA

Figure 1 3D printed PSI with fixation into clivus and C3 vertebra for C1–C2 chordoma. (A) Implant being placed in-situ of a 3D printed
polymer model from CT of the patient; (B) anterior view of both implants with different height; (C) lateral view of both implants (5).
510(k) approval were excluded.

There were no review articles that match our study criteria.

**Results**

Five articles met inclusion criteria (5-7,43). Seventeen patients underwent spinal fusion utilizing 3D printed cervical implants. Three patients with cancer (5-7) and one patient who had spondylotic myelopathy (44) received PSIs. Thirteen other patients with spondylotic myelopathy received pre-planned 3D printed corpectomy implants with 8 different heights (43). A whitepaper from a medical company website [emerging implant technologies (EIT)] (45) reported a patient who underwent two levels ACDF with 3D printed OTS implants. A summary of the articles is provided in Table 1. Table 2 summarizes the FDA 510(k) approval letters for individual cervical implants received by companies that utilizes additive manufacturing (46-50).

**Discussion**

**Current studies for 3D printed cervical implants**

The results of this literature review show the current application of 3DP in manufacturing PSIs for the cervical spine are predominantly due to malignancy (tumor) typically involving the axis (C2 vertebra) (5-7). The axis (C2 vertebra) has a unique anatomy, sitting in the craniocervical junction, allowing the transfer of axial loading from the two lateral masses of the atlas (C1 vertebra) onto the three surfaces (two posterior facets and the anterior vertebral body endplate) of the C3 vertebra (51-53). Malignancies affecting the C2 vertebra are particularly challenging in terms of resection due to their presentation and the unique anatomy of the axis (5-7,53).

The currently available OTS implants for restoration of craniocervical stability post-C2-vertebrectomy requires the use of corpectomy cages, screws and plates (51,52). However, generic OTS cervical corpectomy cages that are suitable for use in vertebrectomy of levels caudal to C2 may not be as suitable for C2 vertebrectomy, with long term efficacy of such construct remains undetermined. Advancements in 3DP provide a potential solution to this scenario. With the use of 3DP, the unique challenges that the anatomy and functionality of the C2 vertebra poses can potentially be addressed prior to the surgical procedure. All three case reports detailed positive biomechanical outcomes with solid fusion and stability (5-7). The reported intra-operative press-fit for patient specific ACDF cage by Spetzger et al. demonstrates the superiority of the PSI in terms of operating room time efficiency (44). However, there is no follow up data for the outcome of this implant, hence the biomechanical results for this implant remain unknown. The small patient cohort (three) discussed above presents as a potential reporting bias due to small sample size. Further studies involving a larger patient cohorts and long term follow up data are required to assess the benefits/ draw backs of 3D printed PSIs.

In a separate study, Zheng et al. compared an integrated artificial axis (IAA), which was additively manufactured to the current available Harms Cage system, in a non-clinical setting. The IAA was manufactured based on a 21-year-old healthy male’s anatomy. The results favored the IAA (53). However, this outcome is limited in terms of external validity as the anatomy of C2 vertebra might vary among individuals. In order to produce a cage suitable for OTS use, population data should be gathered so that normal (and standard shape variation from normal) shape can be defined and used to define the design and size variations of the implants.

The current available 3D printed OTS implants received a class II regulation from the FDA (46-50). This signifies these products must receive a 510(k) letter from the FDA before marketing the implants and the devices are subjected to additional controls. Currently, most of the additively manufactured OTS implants are indicated for ACDFs. The main difference of these devices is the constructs and designs. Since these devices are still new to the market, there is no literature available for short term efficacy and clinical safety of these implants. Laméritable et al. concluded there is complete osseointegration of the EIT Cellular Titanium® implants (45), however based on the histological image provided in their white paper, there is still a significant abundance of soft and fibrous tissue. Hence, studies for short- and long-term outcomes of these implants should be carried out to evaluate the safety and efficacy of them. Radiographs and CT do not provide the resolution to clearly differentiate osseointegration into 3D porous metal implants.

**Materials suitable for 3DP**

Our results demonstrate biomedical grade titanium alloy has been the ‘go-to’ material for 3DP of spinal devices. Titanium by itself or in the form of biomedical grade 5
<table>
<thead>
<tr>
<th>Article</th>
<th>Indication</th>
<th>Implant design</th>
<th>Patient-specific</th>
<th>Material</th>
<th>3DP process</th>
<th>Outcomes/mean outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xu et al. 2016 (Case Report)</td>
<td>C2 spondylectomy for Ewing Sarcoma</td>
<td>Anterior C2 SSAVB</td>
<td>Yes</td>
<td>Titanium alloy</td>
<td>EBM</td>
<td>12 months FU revealed osseointegration into implant, no implant migration/subsidence and 16/17 JOA scale</td>
</tr>
<tr>
<td>Li et al. 2017 (Case Report)</td>
<td>C2–C4 spondylectomy for metastatic papillary thyroid carcinoma</td>
<td>Anterior C2–C4 SSAVB with 32 different heights and widths were printed</td>
<td>Yes</td>
<td>Titanium alloy (Ti₆Al₄V)</td>
<td>Arcam—EBM</td>
<td>16/17 JOA scale at 12 months FU, imaging revealed good cervical sequence and position of implant</td>
</tr>
<tr>
<td>Mobbs et al. 2017 (Case report)</td>
<td>C1–C2 anterior en bloc resection for chordoma</td>
<td>Anterior cage with fixation into clivus and C3 vertebra, 2 cages with 2 different heights were printed</td>
<td>Yes</td>
<td>Medical grade titanium</td>
<td>Commonwealth Scientific and Industrial Research Organization (C.S.I.R.O.)—EBM</td>
<td>Imaging revealed no migration of implant with flexion and extension at 9 months FU</td>
</tr>
<tr>
<td>Spetzger et al. 2016 (Technical Note)</td>
<td>C6/C7 ACDF for spondylotic myelopathy</td>
<td>Anterior cervical intervertebral disc</td>
<td>Yes</td>
<td>Titanium alloy (Ti₆Al₄V)</td>
<td>SLM</td>
<td>Immediate press-fit during implantation</td>
</tr>
<tr>
<td>Lu et al. 2017 (Case Series)</td>
<td>ACCF for spondylotic myelopathy. Four patients at C4; nine patients at C5, Two patients at C6</td>
<td>Anterior cervical corpectomy anatomy-adaptive titanium mesh cage (AA-TMC)</td>
<td>No</td>
<td>Titanium alloy (Ti₆Al₄V)</td>
<td>SLM</td>
<td>Mean JOA scale 14.9±1.39 at mean FU of 13.4±1.4 months. Radiology showed solid fusion and no severe subsidence (&gt;3 mm)</td>
</tr>
<tr>
<td>Lamerigts et al. 2017 [Case Report (whitepaper)]</td>
<td>2 levels ACDF for spondylotic myelopathy</td>
<td>EIT Cellular Titanium® Cervical cage</td>
<td>No</td>
<td>Titanium alloy</td>
<td>SLM</td>
<td>Histological section of retrieved implant showed osseointegration</td>
</tr>
</tbody>
</table>

SSAVB, self-stabilizing artificial vertebral body; AA-TMC, anatomy-adaptive titanium mesh cage; EBM, electron beam melting; SLM, selective laser melting; JOA, Japanese Orthopedic Association scale; FU, follow-up.
Table 2 OTS implants which are additively manufactured that received FDA clearance. DDD implies for patients who present with neck pain of discogenic origin and confirmed radiographically. Prior to surgery, all patients must be skeletally matured and received non-surgical treatment 6 weeks beforehand. All implants consist of a solid and an empty/porous structure to allow packing of bone graft.

<table>
<thead>
<tr>
<th>Implant name</th>
<th>Date approved</th>
<th>Material; method of manufacturing</th>
<th>Indication</th>
<th>Level</th>
<th>Regulatory class</th>
<th>Available design</th>
<th>Use</th>
<th>Non-clinical performance testing summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>EIT Cellular Titanium® Cervical Cage (K170503)</td>
<td>July 11, 2017</td>
<td>Titanium alloy (Ti₆Al₄V); SLM</td>
<td>Single or two contiguous levels T1 disc of cervical DDD</td>
<td>C2/C3–C7/T1 disc</td>
<td>II</td>
<td>Different heights, footprints and lordosis angles</td>
<td>Used with supplementary fixation cleared for the use in cervical spine</td>
<td>Static compression, static compression-shear, dynamic compression, dynamic compression-shear, static torsion, dynamic torsion, expulsion, and subsidence per ASTM F0277-14 and F2267-04</td>
</tr>
<tr>
<td>Stryker Tritanium® C Anterior Cervical Cage (K171496) (47) (Figure 2)</td>
<td>September 6, 2017</td>
<td>Titanium alloy (Ti₆Al₄V); SLM</td>
<td>Single or two contiguous levels T1 disc of cervical DDD</td>
<td>C2/C3–C7/T1 disc</td>
<td>II</td>
<td>Different heights, footprints and lordosis angles</td>
<td>Used with supplementary fixation cleared for the use in cervical spine</td>
<td>Static compression, static compression-shear, dynamic compression, dynamic compression-shear, static torsion, dynamic torsion per ASTM F0277; expulsion per ASTM F04-25-02-02 Draft; subsidence per ASTM F2267; wear debris assessment; and impaction</td>
</tr>
<tr>
<td>Renovis Tesera SC Stand-alone Anterior Cervical Fusion (ACF) System (K153250) (48)</td>
<td>March 16, 2016</td>
<td>Cages are additively manufactured using titanium alloy (Ti₆Al₄V), bone screws manufactured from titanium alloy (Ti₆Al₄V) and cover plate assembly manufactured from titanium alloy (Ti₆Al₄V) and nitinol alloy</td>
<td>Single level cervical DDD</td>
<td>C2/C3–C7/T1 disc</td>
<td>II</td>
<td>The system includes the Tesera Trabecular Titanium (T3) cages, bone screws and anterior cover plate assembly. Different widths, heights, depths, and bone screw sizes</td>
<td>When used with cover plate and screws, the Tesera SC ACF system does not require supplementary fixation. If used without cover plate and screws, the Tesera SC ACF cages require supplementary fixation.</td>
<td>Static compression, static compression-shear, dynamic compression, dynamic compression-shear, static torsion and dynamic torsion per ASTM F0277-14; expulsion testing with and without screws per ASTM F04.25.02.02 Draft; subsidence without screws per ASTM F2267-04; and cover plate assembly corrosion per ASTM F2129-08</td>
</tr>
<tr>
<td>Implant name</td>
<td>Date approved</td>
<td>Material; method of manufacturing</td>
<td>Indication</td>
<td>Level</td>
<td>Regulatory class</td>
<td>Available design</td>
<td>Use</td>
<td>Non-clinical performance testing summary</td>
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<tr>
<td>4Web Cervical Spinal Truss System (CSTS) Interbody Fusion Device (K173159) (49)</td>
<td>January 8, 2018</td>
<td>Titanium alloy (TiAl6V4)</td>
<td>Single or two contiguous levels T1 disc</td>
<td>C2/C3–C7/ T1 disc</td>
<td>II</td>
<td>Different sizes</td>
<td>Must be used with supplementary fixation</td>
<td>Static compression, static compression-shear, dynamic compression, dynamic compression-shear, torsion and dynamic torsion per ASTM F0277; subsidence per ASTM F2267-04; MR image artifact per ASTM F2119; MR induced displacement force per ATSM F2052; MR induced torque per ASTM F2213; MR induced heating per ASTM F2182; and expulsion testing</td>
</tr>
<tr>
<td>K2M Cascadia Interbody System (K160125) (50)</td>
<td>April 22, 2016</td>
<td>Titanium alloy (ASTM standards F3001 and F136); SLM</td>
<td>Single or two contiguous levels T1 disc</td>
<td>C2/C3–C7/ T1 disc</td>
<td>II</td>
<td>Different sizes and heights</td>
<td>Used with supplementary fixation cleared for the use in cervical spine; the hyperlordotic Cascadia cervical implants (≥10°) are required to be used with an anterior cervical plate</td>
<td>Static compression, static compression-shear, dynamic compression, dynamic compression-shear, torsion and dynamic torsion per ASTM F0277; subsidence per ASTM F2267; and expulsion testing</td>
</tr>
<tr>
<td>K2M CAPRI Cervical Corpectomy Cage System (K171704)</td>
<td>August 31, 2017</td>
<td>No summary letter was provided by FDA. Hence no data could be elicited</td>
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</table>

SLM, selective laser melting; DDD, degenerative disc disease.
alloy (Ti₆Al₄V) (not bonded chemically but physically) is an inert metal when oxidized in the TiO₂ form that provides excellent biocompatibility and is resistant to corrosion (54). Although pure titanium is inert once oxidized, titanium alloy (Ti₆Al₄V) has been shown both mechanically and histologically to bond directly with bone under static condition after being implanted for some time (55). The high porosity and interconnectivity of 3D printed titanium lattices potentially serves as a good platform for bone and tissue on and in-growth (54,56). The use of Ti₆Al₄V in 3DP via advanced powder manufacturing routes to create implants for both in vivo and in vitro testing has shown the biocompatibility and osseointegration potential of Ti₆Al₄V (56,57). Radiological fusion as observed clinically from recent use of Ti₆Al₄V in 3DP for spinal implants further confirms the suitability and compatibility of Ti₆Al₄V (58). However, there are a few drawbacks in the use of titanium for spinal implants. The high elastic modulus and stiffness of titanium (110 GPa) compared to cortical (3–30 GPa) and cancellous bone (0.02–2 GPa) serves as a high potential for subsidence (59–61). Titanium itself is a metal which has high radiodensity, making fusion assessment difficult in static radiographic imaging (CT and planar X-ray). Although it is electromagnetically inert, titanium can still cause imaging artefact/flaring in MRIs again making the images difficult to interpret around the implant (62).

Currently other materials such as PolyEther-Ether-Ketone (PEEK) and silicon nitride (Si₃N₄) have been used to manufacture OTS cervical implants but have not yet been used for 3DP of spinal implants. A major benefit for PEEK is its radioluency and biocompatibility (63,64) making it a common material for spinal implants. Having an elastic modulus similar or less than cortical bone is often proposed to reduce the risk of subsidence (65), although recent mechanical testing using the ASTM subsidence test by Suh et al. has shown that this may not be the case (61). However, there is a potential for suboptimal osseointegration for PEEK implants as reported by Phan et al., demonstrating a “PEEK-Halo” effect seen on CT (65). Currently, various techniques are being trialed to improve osseointegration on PEEK implants including coating the surfaces of the implants with a plasma sprayed coating of titanium forming a Ti/PEEK combined cage (66,67). Early clinical data suggest good radiological fusion of such devices (68,69) whilst the risk of delamination of the plasma sprayed coating exists either on implantation or in life service. Incorporating a thin layer of titanium into the PEEK itself is another technique used to provide a titanium interface for biological on growth (70). NanoMetalene (NM) describes the commercial application of this process on spinal interbody implants where a sub-micron layer of commercially pure titanium is molecularly bonded to a PEEK implant using a proprietary, high-energy, low-temperature process that differs from other coating applications and maximizes implant surface area with titanium nanotopography (70).

On the other hand, the inert chemistry of Si₃N₄ serves as a potential candidate for spinal implants (71). Several studies have demonstrated superiority in bacteriostatic behavior of Si₃N₄ compared to PEEK and titanium implants (72–74). Additionally, Si₃N₄ was shown to promote bone growth and fusion (72,75), but there is currently limited literature discussing the outcomes of Si₃N₄ spinal implants.

Both PEEK and Si₃N₄ serve as a potential candidate for 3D printed spinal implants. 3DP of ceramics has advanced to allow the manufacturing of cellular structure which serves as a potential surface for bone in-growth (76,77). With future advances in 3DP technology, materials could potentially be combined to form an implant which serves all three purposes of promoting osseointegration, minimizing subsidence potential, whilst maintaining sterility.

**Subsidence and osseointegration**

Subsidence is a common phenomenon with the use of spinal implants. Since its inception, 3DP allows the fabrication of varying surfaces and structures. This benefit of 3DP as a manufacturing method allows complex structures to be printed such as lattices. This allows medical devices to feature ‘in growth’ topologies and pores that are specifically designed to encourage osseointegration and greater bone bonding strength to the device (59,78). For instance, 3DP

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**Figure 2** An example of 3D printed OTS cervical spinal implant: Stryker Spine ‘Tritanium® C Anterior Cervical Cage (47).
of titanium allows the manufacture of open cellular Ti₆Al₄V lattices with different densities to achieve different elastic moduli, again with the aim of matching the stiffness of spinal bone (79,80). Solid titanium has a very high elastic modulus compared to cortical bone; 110 GPa compared to 3–30 GPa respectively. This differential in stiffness between device material and bone can instigate local bone remodeling leading to ‘stress shielding’. More extreme inflammatory responses and remodeling caused by bone damage (fracture and/or micro fracture) increase the risk of subsidence, bone atrophy and implant failure (54,59,81,82). Device stiffness alone is not responsible for subsidence as although having an elastic modulus lower than cortical bone, subsidence was observed in the use of standalone PEEK cages for ACDFs (83). Some authors argued that subsidence is an inevitable radiological finding but beneficial for fusion in terms of osseointegration (84). Utilizing 3DP, there is the potential of achieving a “sweet spot” to promote osseointegration and reduce the chances of subsidence by altering the porosity of an implant to achieve a lower elastic modulus (78,79). However, this can potentially result in implant failure as highly porous, less stiff implants will be more prone to fatigue failure. Another important factor for the adaptation of PSIs is to increase the contact area between implant and the endplates as reported by Spetzger et al. and Mobbs et al. (44,85). The aim of this is to achieve even load distribution along the implant surface thereby reducing the chance of subsidence (86).

Pros and cons of PSIs

The main benefit for PSIs compared to OTS implants (3DP or traditionally manufactured) are that PSIs are designed based on the patient’s anatomy, surgical and biomechanical requirements. The specificity of PSIs reduces the need of excessive removal of surrounding structures, thereby preserving the anatomy of the patient during implantation. This may lead to shortening of operative time, preservation of anatomy which requires lesser dissection, direct press-fit of implant and improved stability of construct (85). In the cervical spine, the main goal of PSIs is to achieve stability and restoring functionality especially for unique anatomies such as the axis (5-7). The rationale of utilizing PSIs as opposed to OTS implants allows complex anatomical morphology to be accommodated and unique features such as pre-planned screw trajectories to be added, thus improving intra-operative accuracy for screw placement (58) which may have some advantages in specific cases.

However, drawbacks remain with PSIs as they require meticulous planning and design before the implant can be manufactured (44,87,88). The process leads to the increase in requirements for specialized personnel such as biomedical engineers with a good knowledge of CAD, anatomy and surgical procedures. The printing itself requires high-end 3D printers to achieve suitable precision and specialized materials which are not yet widely available, the need for post-processing of the printed implants as well as final cleaning and packaging. The possibility of lack of fit at the time of surgical procedure also remains. Hence, the availability, time and cost remain a drawback for the wide use of PSIs. Long-term studies are also unavailable at the moment to evaluate the efficacy and safety of both 3D printed patient-specific and OTS implants.

Future prospect

With the advancement of technology, 3DP as a manufacturing method will likely become increasingly available and cheaper. This will promote the use of PSIs in the future. The time taken and cost of 3DP PSIs will also reflect advancement in speed of imaging segmentation and device design. New materials that are biocompatible, radiolucent and promote bone on/in-growth will likely replace the current materials such as Ti₆Al₄V and PEEK. Stem cells from patients may be incorporated into 3D printed implants to promote healing (89) and osseointegration. 3DP PSIs may also be widely available in hospitals to allow immediate printing of PSIs when required. Coupled with advancements of preoperative imaging and segmentation, robotics and intra-operative image-based navigation, surgical outcomes for patients receiving 3D printed implants and organs will become faster, more cost effective, safer and less invasive.

Future studies

3DP is still in the early phase in terms of cervical spinal implants. The current sparsity of available literature limits evaluation regarding the safety and efficacy of this technology. With cost and availability being the major hindrance, studies with higher of level of evidence such as randomized controlled trials cannot yet be carried out. However, there is a sparsity of reports currently available in the literature, necessitating short and long-term outcome studies for both 3D printed patient-specific and OTS implants to be carried out. The studies ideally
should include quantitative and qualitative data to assess the outcomes of these implants, for example: pre- and post-operation clinical scores [Japanese Orthopedic Association (JOA) score, Neck Disability Index (NDI) and Visual Analog Scale (VAS) for arm and neck]; (Cobb’s) angles; degree of distraction; rate of subsidence; implant migration and post-operative complications. Other biocompatible materials that may reduce subsidence and promote osseointegration and healing can also be trialed utilizing additive manufacturing. This can include combining different materials to achieve a superior outcome than standalone materials.

**Conclusions**

Although 3DP is still in the early stages of development for cervical reconstructive surgery, there is no doubt of the versatility of this technology for personalization of implants and management of complex anatomical deformities. The current sparsity of available literature limits the evaluation regarding the safety and efficacy of this technology, especially with regards to OTS implants where there is currently no documented clinical benefit as compared with OTS implants produced via subtractive manufacturing techniques.

Cost and speed of access to personalized implants remains a major hindrance to their wide spread adoption, with no studies including higher levels of evidence (such as randomized controlled trials) available. Due to the shortcomings in the literature, we urge that appropriate short and long-term outcome studies for both additively manufactured PSIs and OTS implants to be performed, with quantitative and qualitative data to assess the outcomes. Further works on biocompatible materials utilizing additive manufacturing require investigation, especially as Titanium artefact in postoperative imaging remains an issue to radiographically assess the fusion status.

**Acknowledgements**

None.

**Footnote**

**Conflicts of Interest:** The authors have no conflicts of interest to declare.

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69. Mobbs RJ, Phan K, Assem Y, et al. Combination Ti/ PEEK ALIF cage for anterior lumbar interbody fusion:


