

**DOI : 10.1097/BRS.0000000000002229**

**Multi-level 3D printing implant for reconstructing cervical spine with metastatic papillary thyroid carcinoma**

Xiucan Li, MM<sup>1,\*</sup>, Yiguo Wang, MD<sup>1,2,\*</sup>, Yongfei Zhao, MD<sup>1</sup>, Jianheng Liu, MD<sup>1</sup>, Songhua Xiao, MD<sup>1</sup>, Keya Mao, MD<sup>1,¶</sup>

<sup>1</sup> Department of Orthopaedics, Chinese PLA General Hospital, 28 Fuxing Road, Beijing, China 100853

<sup>2</sup> Medical School of Nankai University, 94 Weibin Road, Tianjin, China 300071

\* These authors contributed equally to this study.

¶ Corresponding author; email: maokeya@sina.com

Acknowledgement: August 22, 2016

1st Revise: December 4, 2016

2nd Revise: January 13, 2017

Accept: February 23, 2017

The manuscript submitted does not contain information about medical device(s)/drug(s).

No funds were received in support of this work.

No relevant financial activities outside the submitted work.

**Study Design.** A unique case report.

**Objective.** A three-dimensional (3D) printing technology is proposed for reconstructing multi-level cervical spine (C2–C4) after resection of metastatic papillary thyroid carcinoma in a middle-age female patient.

**Summary of Background Data.** Papillary thyroid carcinoma is a malignant neoplasm with a relatively favorable prognosis. A metastatic lesion in multi-level cervical spine (C2–C4) destroys neurological functions and causes local instability. Radical excision of the metastasis and reconstruction of the cervical vertebrae sequence conforms with therapeutic principles, while the special-shaped multi-level upper-cervical spine requires personalized implants. 3D printing is an additive manufacturing technology that produces personalized products by accurately layering material under digital model control via a computer. Reporting of this recent technology for reconstructing multi-level cervical spine (C2–C4) is rare in the literature.

**Methods.** Anterior–posterior surgery was performed in one stage. Radical resection of the metastatic lesion (C2–C4) and thyroid gland, along with insertion of a personalized implant manufactured by 3D printing technology, were performed to rebuild the cervical spine sequences. The porous implant was printed in Ti6AL4V with perfect physicochemical properties and biological performance, such as biocompatibility and osteogenic activity. Finally, lateral mass screw fixation was performed via a posterior approach.

**Results.** Patient neurological function gradually improved after the surgery. The patient received 11/17 on the Japanese Orthopedic Association scale and ambulated with a personalized skull–neck–thorax orthosis on postoperative day 11. She received radioiodine I<sup>131</sup> therapy. The plane X-rays and computed tomography revealed no implant displacement or subsidence at the 12-month follow-up mark.

**Conclusion.** The presented case substantiates the use of 3D printing technology, which enables the personalization of products to solve unconventional problems in spinal surgery.

**Key Words:** three-dimensional (3D) printing; multi-levels; reconstruction; porous metal; personalized implant; cervical spine; metastasis; papillary thyroid carcinoma; spondylectomy

**Level of Evidence:**5

Papillary thyroid carcinoma (PTC) is a malignant neoplasm with a relatively favorable prognosis among all subtypes. Despite infrequent distant metastases, bone and lung are vulnerable to involvement.<sup>1</sup> Three-dimensional (3D) printing, an additive manufacturing technology, is the process of manufacturing products by accurately layering material under digital model control via a computer. Reported herein is the case of metastatic papillary thyroid carcinoma in the cervical spine (C2–C4) of a middle-age female patient who underwent a spondylectomy of C2 to C4, which were reconstructed with 3D-printed cervical vertebrae.

## **CASE REPORT**

A 53-year-old female patient complained of neck and upper-extremity pain, dysphagia, and thumb and index finger paresthesia of the right hand. Her muscle strength had degraded to grade IV on the Oxford scale in both lower limbs. Moreover, she demonstrated hyperactive biceps, patellar tendon reflexes, and a positive Hoffman sign.

Imaging examination via X-ray, computed tomography (CT), and magnetic resonance imaging (MRI) on the patient's cervical spine showed a very large lytic lesion involving C2–C4 vertebrae (Figure 1). A Spinal Instability Neoplastic Score (SINS)<sup>2</sup> of 14 was given. Ultrasound-guided percutaneous biopsies of lumps in her thyroid gland confirmed the diagnosis of papillary thyroid carcinoma. According to a literature review,<sup>1</sup> our department speculated that the space-occupying lesion on the cervical spine was thyroid-oriented.

The patient's neurological function was rated 8/17 on the Japanese Orthopedic Association (JOA) scale. Extensive or edge resection could enable long-term local control of a Tomita scoring system<sup>3</sup> rating of three. Continuous deterioration of neurological function and a favorable postoperative long-term prognosis prompted her to opt for the surgery.

## **METHODS**

### **Design of personalized self-stabilizing artificial vertebral body (SSAVB)<sup>4</sup>**

In this case, the main structure of the SSAVB was columnar with bilateral shoulders fitting the atlas

inferior articular surface to ensure sufficient supporting strength and better stability (Figure 2). The design of the internal fixation method stemmed from the cervical zero-profile screw system.<sup>5</sup> The SSAVB computer-assisted design (CAD) model was placed on the 3D cervical spine model to test the fitness and refine the screw incline roads to guarantee security. Internal porous structure for the bone trabecular bionics design balanced the bone growth and biomechanical property with the optimal size and shape of the pores<sup>6</sup>. The titanium powder and 3D printing machine adopted for this study were Ti6AL4V<sup>7</sup> and Arcam, respectively.

Using the standard measure of lytic lesions (C2–C4), a total of 32 implants with different heights and widths were printed in case the tumor was more extensive or more bone had to be removed. The average compressive, tensile, and flexural strengths were 18.766 kN, 10.811 kN, and 4.136 kN, respectively.

### **Personalized surgical plan**

Radical resection of the thyroid gland had to first be conducted. The mass resection on C2, C3, C4 vertebrae and the implant insertion were to be next performed via the anterior approach. Lateral mass screw fixation (C1, C2, C4, C5, C6) was to be performed via the posterior approach (Figure 3).

## **RESULTS**

The thyroid gland and 21 bilaterally cleaned lymph nodes were resected. A pile of grey–red tissue (4 cm × 2.5 cm × 1.5 cm) was excised from the cervical vertebrae (C2–C4) metastatic lesion.

Once the surgery was complete, the patient was transferred to the intensive care unit and remained ventilator-dependent. The superior laryngeal nerve and recurrent laryngeal nerve invaded by the carcinoma were inevitably injured during the surgery. Post-operative unilateral vocal cord paralysis and weakness of laryngeal muscles contributed to the difficulty of expectoration since POD#2. Vancomycin was applied to control potential pulmonary infection, which may have been caused by the sputum stagnation. Since POD#3, a levothyroxine sodium tablet was administered at suppressive doses. The patient was weaned from mechanical ventilation and returned to the orthopedic ward on POD#5. She scored 11/17 on the JOA scale and walked unassisted with a personalized skull–neck–thorax orthosis on POD#11.

The pathological result (Figure 4) confirmed the diagnosis of metastasis papillary thyroid carcinoma in the cervical vertebrae (C2–C4) on POD14#. Neurological function quickly improved and the JOA score reached 14/17 at the same time. A multi-disciplinary consultation concluded that she could be discharged and receive follow-up radioiodine I<sup>131</sup> therapy<sup>8</sup> three months later.

The patient was weaned from the skull–neck–thorax orthosis at the 12-month follow-up point. The plane X-ray and CT revealed a good cervical vertebrae sequence and position of the 3D printing implant (Figures 5 and 6). The patient reported 16/17 on the JOA scale and independently engaged in daily activities.

## DISCUSSION

Favorable prognosis of thyroid carcinoma subtypes contributed to the initial decision for surgery and the final success despite the Stage IV tumor node metastasis (TNM) classification.<sup>9</sup> Radical excision of the cervical vertebrae metastasis and reconstruction of the cervical vertebrae sequence conformed with therapeutic principles to realize local control and stability.<sup>10</sup>

A conventional regular titanium mesh cage (TMC) could not match the remaining osseous structures of axis and atlas with irregular shapes without an adequate anchor to the vertebrae. Several factors also contributed to the TMC subsidence risk:<sup>11–12</sup> limited contact area, multi-level corpectomy leading to a longer implant, osteoporosis, and carcinoma-destroyed C4 vertebra.

3D printing has the advantages of enabling production of personalized implants with excellent physicochemical properties and biological performances, such as biocompatibility, osteogenic activity, and bone ingrowth effect.<sup>13</sup> Personalized implants have an interconnected, highly uniform pore network. The larger pore size and porosity increase the bone-inducing ability<sup>14</sup> and reduce the mechanical properties. With CAD, the size and porosity can be controlled to balance the properties of the compressive strength and Young's modulus, thereby decreasing the stress-shielding effect or long-term subsidence risk.

The presented case thus substantiates the use of 3D printing, an additive manufacturing technology, to enable the personalization of products for solving unconventional spinal surgery problems. Personalized medicine may advance from this research. Because this study was merely a case study,

however, it was limited. Specifically, the high-density shadow from the margin of the preoperatively printed implant frame can disturb observation of original bone growth. This aspect can be improved in a future study.

ACCEPTED

## References

1. Muresan MM, Olivier P, Leclere J, et al. Bone metastases from differentiated thyroid carcinoma. *Endocr Relat Cancer* 2008;15:37-49.
2. Fourney DR, Frangou EM, Ryken TC, et al. Spinal Instability Neoplastic Score: An Analysis of Reliability and Validity From the Spine Oncology Study Group. *Journal of Clinical Oncology* 2011;29:3072-7.
3. Tomita K, Kawahara N, Kobayashi T, et al. Surgical strategy for spinal metastases. *Spine* 2001;26:298-306.
4. Yang J, Cai H, Lv J, et al. In vivo study of a self-stabilizing artificial vertebral body fabricated by electron beam melting. *Spine (Phila Pa 1976)* 2014;39:E486-92.
5. Li Y, Hao D, He B, et al. The Efficiency of Zero-profile Implant in Anterior Cervical Discectomy Fusion A Prospective Controlled Long-term Follow-up Study. *Journal of Spinal Disorders & Techniques* 2015;28:398-403.
6. Li JP, Habibovic P, van den Doel M, et al. Bone ingrowth in porous titanium implants produced by 3D fiber deposition. *Biomaterials* 2007;28:2810-20.
7. Li JP, Li SH, Van Blitterswijk CA, et al. A novel porous Ti6Al4V: characterization and cell attachment. *J Biomed Mater Res A* 2005;73:223-33.
8. Durante C, Haddy N, Baudin E, et al. Long-term outcome of 444 patients with distant metastases from papillary and follicular thyroid carcinoma: benefits and limits of radioiodine therapy. *J Clin Endocrinol Metab* 2006;91:2892-9.
9. Sugitani I, Kasai N, Fujimoto Y, et al. A novel classification system for patients with PTC: addition of the new variables of large (3 cm or greater) nodal metastases and reclassification during the follow-up period. *Surgery* 2004;135:139-48.
10. Jiang L, Ouyang H, Liu X, et al. Surgical treatment of 21 patients with spinal metastases of differentiated thyroid cancer. *Chinese Medical Journal* 2014;127:4092-6.
11. Chen Y, Chen DY, Guo YF, et al. Subsidence of Titanium Mesh Cage A Study Based on 300 Cases. *Journal of Spinal Disorders & Techniques* 2008;21:489-92.
12. Lim TH, Kwon H, Jeon CH, et al. Effect of endplate conditions and bone mineral density on the compressive strength of the graft-endplate interface in anterior cervical spine fusion. *Spine* 2001;26:951-6.
13. Xu N, Wei F, Liu X, et al. Reconstruction of the Upper Cervical Spine Using a Personalized 3D-Printed Vertebral Body in an Adolescent With Ewing Sarcoma. *Spine* 2016;41:E50-E4.
14. Shah FA, Snis A, Matic A, et al. 3D printed Ti6Al4V implant surface promotes bone maturation and retains a higher density of less aged osteocytes at the boneimplant interface. *Acta Biomater* 2016;30:357-67.

Figure 1. Radiograph, CT, and MRI showing a very large lytic lesion involving the vertebrae (C2–C4) with obvious compression on the spinal cord and esophagus.

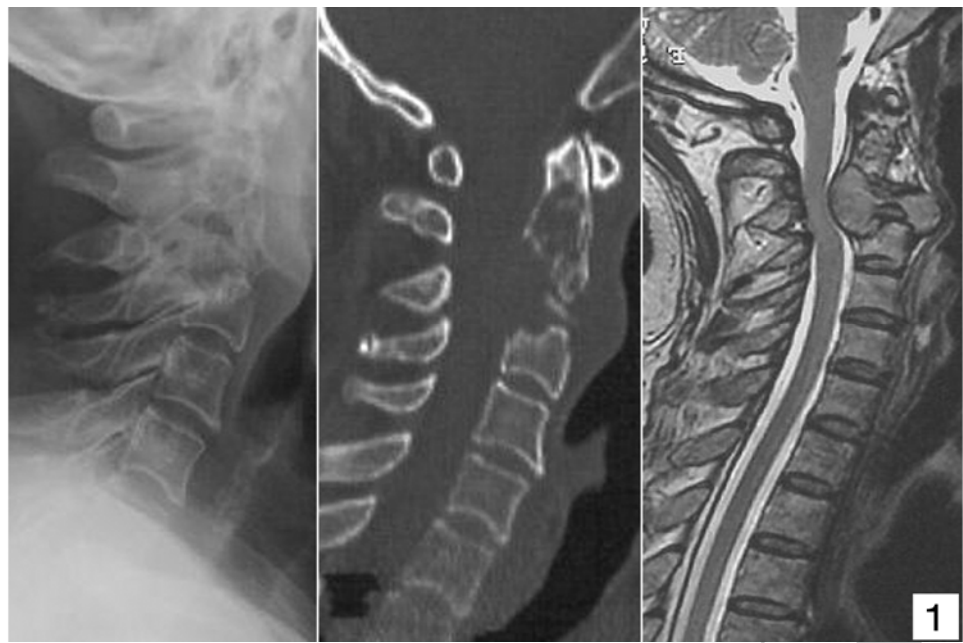




Figure 2. Model showing the columnar main structure of the SSAVB bearing the load. Bilateral shoulders fit the inferior articular atlas surface to ensure sufficient supporting strength and better stability.

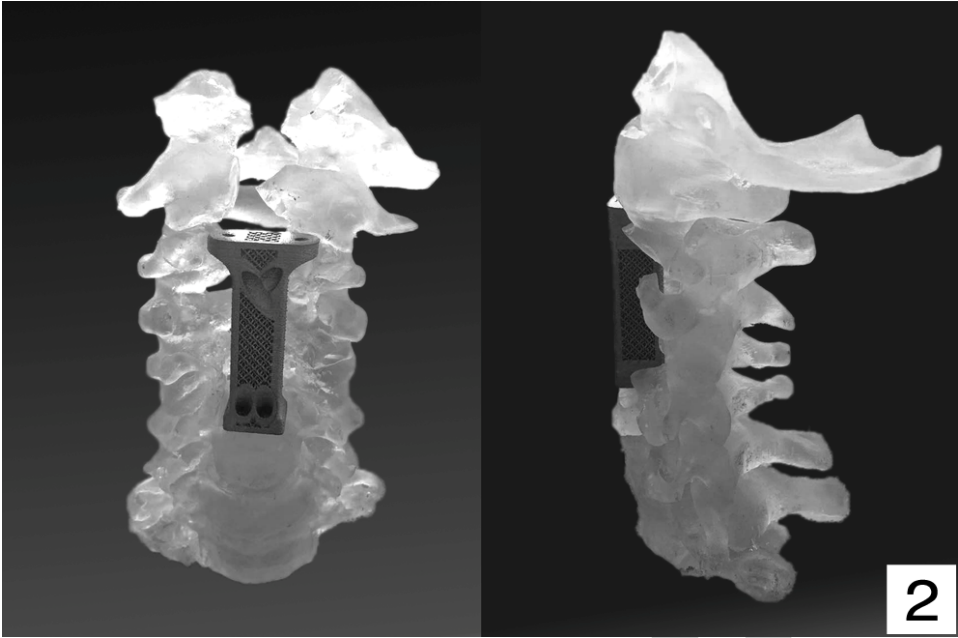


Figure 3. Postoperative lateral radiograph showing C2, C3, and the upper part of the C4 vertebrae, which were replaced by a 3D printing implant via an anterior approach. Lateral mass screw fixation (C1, C2, C4, C5, C6) was performed via the posterior approach.

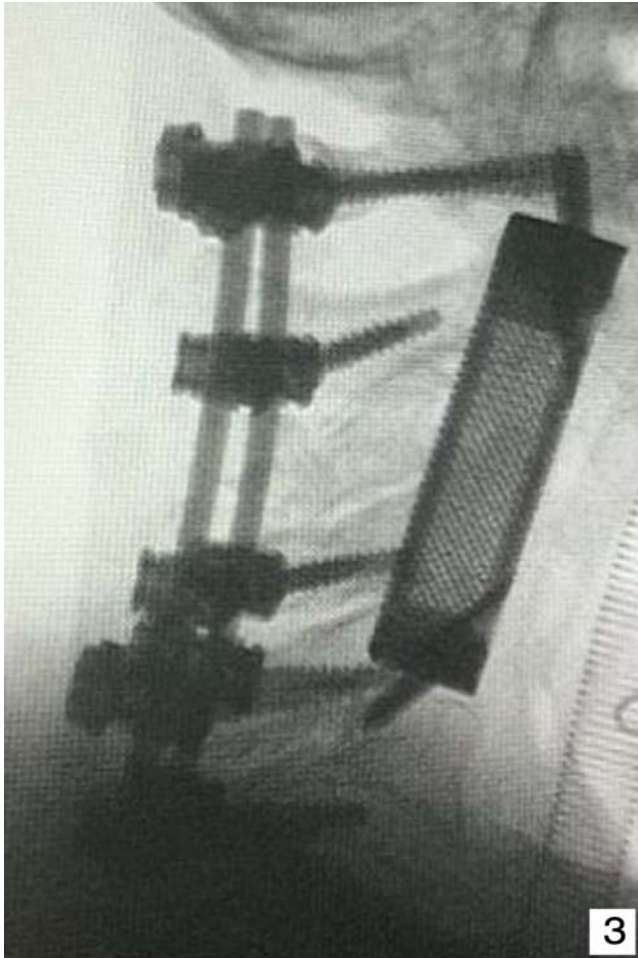


Figure 4. Photomicrographs obtained from cervical vertebrae (C2–C4) and lymph node specimens. Hematoxylin and eosin stained sections of metastatic papillary thyroid carcinoma (original magnification  $\times 100$ ).

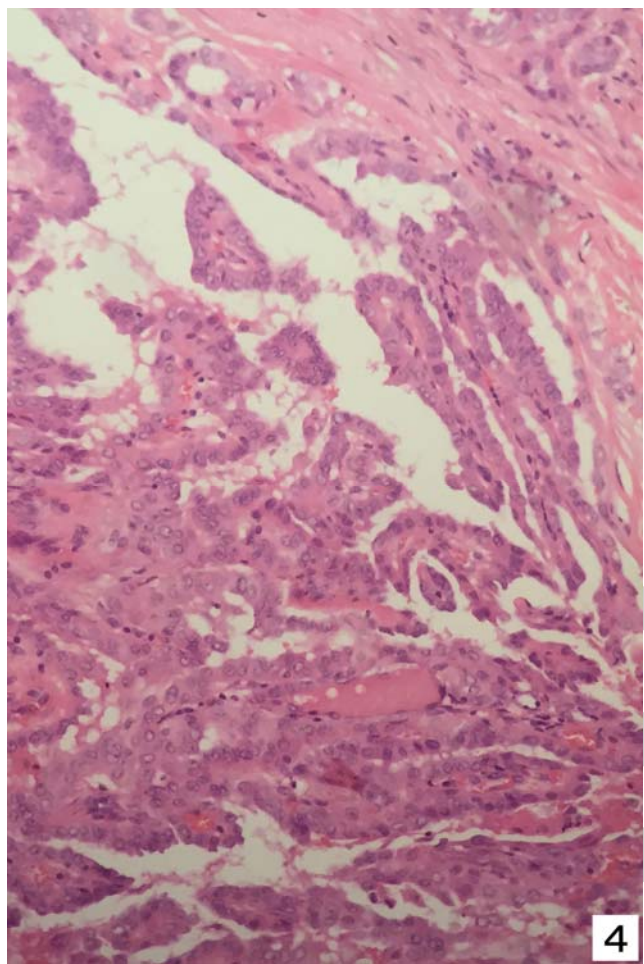


Figure 5. Lateral radiograph and 3D CT show a good cervical vertebrae sequence and position of the 3D printing implant at the 12-month follow-up mark.

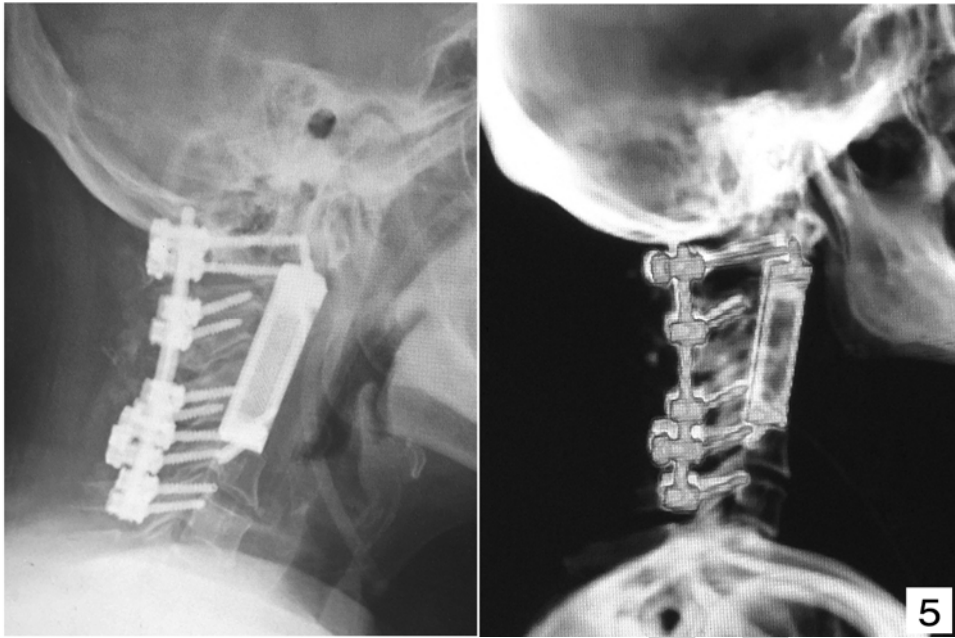


Figure 6. Sagittal and coronal reconstruction of CT images showing high-density shadow of the 3D printing implant well fitted with C1 and C5.

