CLINICAL CASE STUDY

3D-Printed Patient-Customized Artificial Vertebral Body for Spinal Reconstruction after Total *En Bloc* Spondylectomy of Complex Multi-Level Spinal Tumors

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Abstract: Three dimensional (3D)-printing technology facilitates complex spine surgery with unique advantages in artificial vertebral body design and manufacturing. In this study, we aimed to demonstrate how a 3D-printed spinal implant is utilized in the management of multi-level spinal tumors and integrates with comprehensive oncologic treatment. Eight spinal or paraspinal tumor patients requiring spinal reconstruction after total *en bloc* spondylectomy were selected as candidates for 3D-printed titanium artificial vertebral body implants. All patients underwent surgery on three or more vertebral segments or complex spinal junction segments. The clinical, oncological, and surgical characteristics of patients were collected. Of the eight candidates, seven suffered from pain and/or limb disorder. Six underwent successful 3D-printed spinal implantation, while two failed due to implant mismatching and were converted to conventional reconstruction. Of the six patients undergoing 3D-printed spinal implant surgery: (i) Five had recurrent tumors; (ii) three underwent neoadjuvant therapy; (iii) the median surgery time was 414 min; (iv) the median blood loss was 2150 ml; (v) the median blood transfusion was 2000 ml; (vi) the median length of hospital stay was 9 days; (vii) four patients received adjuvant therapy after surgery; and (viii) all patients experienced no pain, moved freely, and had no local recurrence at a median of 11.5 months post-operative follow-up. Spinal reconstruction with a 3D-printed titanium artificial vertebral body allows for total *en bloc* resection of complex multi-level spinal tumors. Combined with neoadjuvant and adjuvant therapy, these patients had excellent postoperative outcomes, long-term normal spinal function, and associated low local recurrence probability.

Keywords: 3D printing; Artificial vertebral body; Spinal tumor; Total *en bloc* spondylectomy; Adjuvant therapy; Multi-disciplinary team

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1. Introduction

Three-dimensional (3D) printing, also known as additive manufacturing, has unique advantages in orthopedic implant design and manufacturing[1,2]. 3D-printed orthopedic implants are customized based on patient-specific preoperative imaging data. One of the applications of this technology involves restoration of bone defects after resection, which provides maximum bone contact surface for reconstruction. In addition, 3D-printed orthopedic implants can mimic cortical and cancellous bone by integration of solid and porous elements, thus promoting bone fusion and long-term stability[3,4].

The spine is a complex skeletal anatomic structure involved in weight bearing, shock absorption, and motion. Tumors involving the spine, whether primary or metastatic, may cause severe back pain, limb numbness, weakness and/or paralysis[5]. Total *en bloc* resection of spinal tumors is the most direct and effective way to relieve symptoms, recover function, and prevent tumor progression[6]. Unlike benign spine lesions, malignant spinal tumors are often difficult to manage surgically because they are invasive, ill-defined, multi-level, and easily recur. In recent years, 3D-printed patient-customized artificial vertebral body implants have been created and are thought as a solution to spinal difficult-to-treat conditions[7-9]. We aimed to demonstrate how 3D-printed spinal implants are applied in surgery for complex spinal tumors, namely, recurrent or multi-level spinal tumors. We also aimed to assess how this implant surgery, when combined with neoadjuvant and adjuvant tumor therapy, impacts tumor local control, and recurrence.

2. Methods

2.1. Patient inclusion and data collection

This study enrolled spinal or paraspinal tumor patients requiring spinal reconstruction after tumor resection from the Department of Musculoskeletal Surgery, Fudan University Shanghai Cancer Center (FUSCC) between November 1, 2018, and November 1, 2021. Candidates for using 3D-printed artificial vertebral body reconstruction were selected based on the following criteria: (i) Spinal reconstruction following total *en bloc* spondylectomy (TES) on three or more vertebral levels; (ii) spinal reconstruction following spinal tumor resection in complex sites, such as cervical, cervicothoracic, or thoracolumbar junction levels. Patients who cannot tolerate general anesthesia and surgery were excluded. Ultimately, eight candidates for using 3D-printed artificial vertebral body were included in the study. All patients signed informed consent. This study was approved by the Review Board of FUSCC (2101230-1), Shanghai, China. All participants had written consent prior to participation.

Patient's age, sex, body mass index, initial symptoms and signs, tumor characteristics, and surgical history were collected. Patient's Karnofsky performance score was performed[10]. Spinal tumor characteristics, including histopathology, vertebral levels, Weinstein-Boriani-Biagini classification, and onset type, were obtained. X-ray, computed tomography (CT), magnetic resonance imaging, and/or positron emission tomography (PET)-CT were scanned. All candidates for using 3D-printed artificial vertebral body reconstruction were assessed and determined by two senior spinal surgeons.

2.2. 3D-printed titanium vertebral body design and manufacturing

The workflow to manufacture a 3D-printed artificial vertebral body is presented in **Figure 1**. First, patient's CT scan data were extracted with DICOM format. CT scan range included at least one vertebra above and below the tumor-affected vertebra was performed. CT scanning layer thickness was <1.5 mm. Second, Mimics 23.0 software was used for 3D imaging reconstruction. Tumors, vertebrae, and blood vessels were visually displayed. Third, Creo 2.0 software was used to design artificial vertebral body in consideration of surgeon's implant pathway and internal fixation method. The artificial vertebral body's upper and lower interfaces were designed to be porous. Porous structures increase the surface area in contact between the artificial and the human autogenous vertebra, which can promote bone ingrowth and fusion. Porous structure parameters were as follows: (i) porosity: 70 ± 10%; (ii) aperture: 600 – 800 micron; and (iii) beam diameter: 0.3 ± 0.1 mm.

Fourth, Magics 24.0 software was used to process design. Fifth, computer-assisted digital control was used to produce 3D-printed vertebral body by sintering titanium alloy powder layer by layer using EOSM280 selective laser melting (SLM) equipment. The material composition of our 3D-printed artificial vertebral body was Ti_6Al_4V, of which Al, V, and Ti account for 5.5 – 6.75%, 3.5 – 4.5%, and the rest, respectively. The printing mode of metal printing was powder printing. Each powder printing height was only 0.03 mm, so that the final printing accuracy can reach 0.1 mm. In general, there is no significant information loss from CT scan to the printing process. Finally, vacuum heat treatment was performed to obtain an ideal mechanical

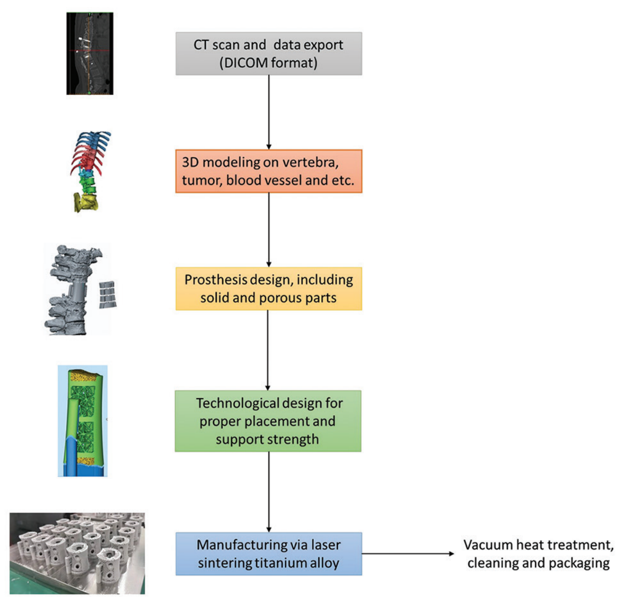

Figure 1. Workflow to design and manufacture a 3D-printed patient-specific titanium artificial vertebral body.

integrity. The 3D-printed artificial vertebral body was cleaned and packaged according to standard factory protocol.

2.3. Surgery, follow-up, and statistical analysis

The American Society of Anesthesiologists grade was used for all patients[11]. TES and personalized spinal reconstruction were performed on eight patients. Surgical approach, duration, intraoperative blood loss, transfusion volume, and length of stay were recorded. Patients were followed up after hospital discharge; the follow-up deadline was January 20, 2022. Data were presented by median with range. All statistical analyses were descriptive and conducted by SPSS 26.0.

3. Results

3.1. Patient's characteristics

Patient's median age was 34 (22 – 53) years old. Six patients had prior related surgical history. The detailed characteristics are presented in **Table 1**.

3.2. Successful implantation

(1) Case 1

A 22-year-old female was found to have a large posterior mediastinal mass on clinical examination. CT revealed an aggressive appearing 16.3 × 15.9 × 11.3 cm posterior mediastinal mass, hypermetabolic on PET-CT (**Figure 2A**). Needle biopsy confirmed malignant peripheral nerve sheath tumor. She underwent mediastinal tumor resection through thoracotomy at an outside facility a month later. The tumor, however, quickly recurred at the T4-7 level, enlarging rapidly just 2 months later (**Figure 2B**). She was referred to FUSCC and underwent neoadjuvant chemotherapy and targeted therapy (oral anlotinib and liposomal doxorubicin injection) based on our multidisciplinary team (MDT) discussion. After three cycles of neoadjuvant therapy, the tumor significantly decreased in size and achieved partial response (PR). The decision was then made to plan for *en bloc* resection of T4 ~ 7 (**Figure 2C**) by designing a 3D-printed artificial vertebral body to reconstruct her spine (**Figure 2D**).

The 3D-printed artificial vertebral body was manufactured (**Figure 2E**). Surgery was successfully performed, as planned (**Figure 2F**). A video visually showing the implantation process is presented in **Video 1**. Post-operative CT demonstrated an excellent fit and stability of the implant (**Figure 2G**). The patient was recommended to undergo adjuvant radiotherapy (**Figure 2H**). At the 9-month post-operative follow-up visit, the patient was doing well, moving freely, without any pain or evidence of local recurrence; radiographic bone ingrowth was evident, with good biological fusion between the porous interface of the

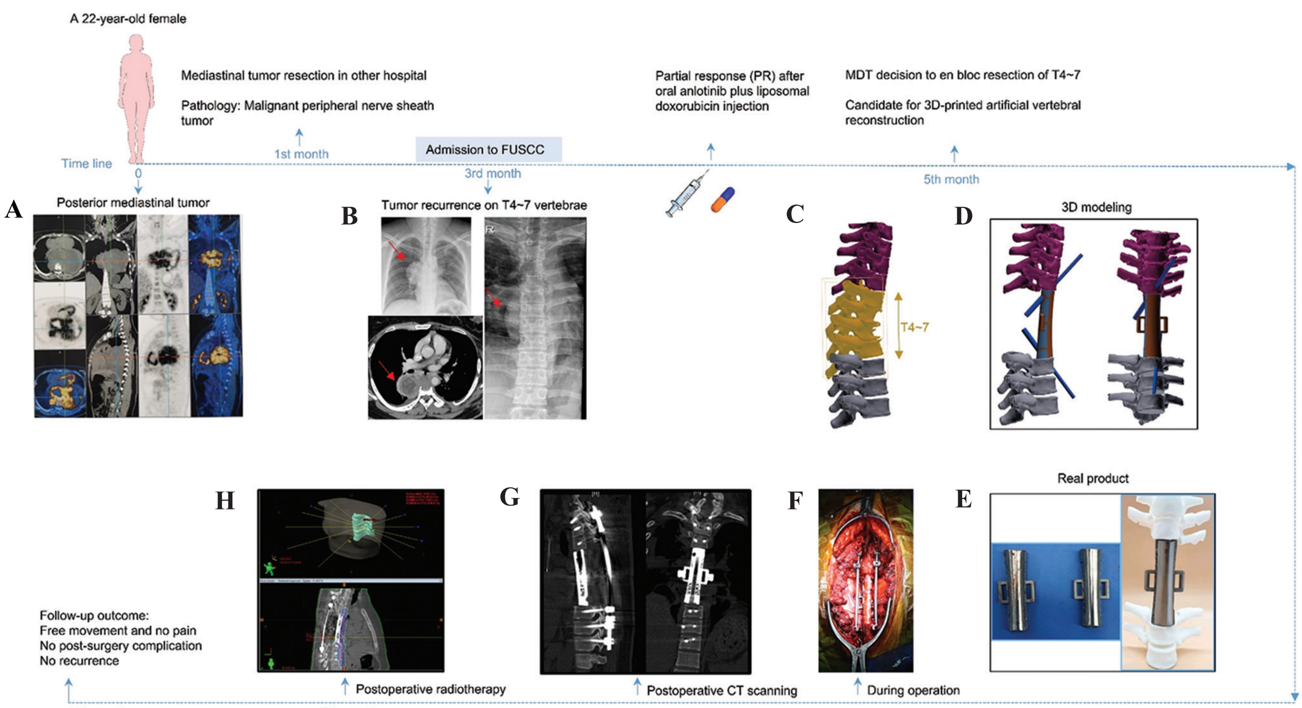

Figure 2. Case 1. (A) Pre-operative CT and PET-CT showing a large malignant posterior mediastinal mass; (B) X-ray and CT showing tumor recurrence on T4~7 vertebrae; (C) 3D imaging visually showing T4~7 level to be resected; (D) 3D imaging showing customized 3D-printed artificial vertebral body and screw rod internal fixation design; (E) Final 3D-printed titanium alloy vertebral body; (F) surgery performed; (G) post-operative CT showing excellent implant fit, stability, and alignment; (H) adjuvant radiotherapy.

Table 1. Patients' demographic and clinical characteristics.

Case number	Age (years)	Sex	BMI (Kg/m^2)	Symptoms and Signs	Diagnosis	Location	WBB classification		Onset type	Surgical history	Neoadjuvant therapy in FUSCC	Preoperative KPS
							Zones	Layers				
1	22	Female	30.5	None	Malignant peripheral nerve sheath tumor	T4~7	5~9	A~C	Recurrent	Posterior mediastinal tumor resection 5 months ago	Chemotherapy and targeted therapy	100
2	28	Female	22.7	Left chest-back pain and numbness	Neurobalstoma	T4~6	4~6	A~C	Recurrent	Posterior mediastinal tumor resection 2 years ago; Left sixth rib recurrent tumor resection 1 year ago	Chemotherapy and radiotherapy	80
3	28	Male	18.7	Paralysis and myophagism of both lower extremities	Aggressive angioma	T6~8	4~10	A~D	Primary	None	None	30
4	53	Female	26.4	Chest-back pain	Metastatic squamous cell carcinoma	T8~10	3~9	A~D	Recurrent	T9 laminectomy 5 years ago; T9 vertebrectomy 4 years ago	None	80
5	31	Female	22.3	Neck and shoulder pain; Paralysis of the right upper limb	Epithelioid heman gioendothelioma	C5~7 and T1	4~10	A~D, F	Recurrent	Anterior cervical decompression and internal fixation 5 months ago	None	70
6	37	Female	26.0	Chest-back pain; Numbness of both lower extremities	Ewing sarcoma	T2~4	1~6	A~C	Recurrent	T3 intraspinal tumor resection 7 months ago	Chemotherapy and radiotherapy	50

(Contd...)

Table 1. *(Continued)*

Case number	Age (years)	Sex	BMI (Kg/m^2)	Symptoms and Signs	Diagnosis	Location	WBB classification		Onset type	Surgical history	Neoadjuvant therapy in FUSCC	Preoperative KPS
							Zones	Layers				
7	51	Male	24.2	Neck pain and limitation of motion; Numbness of both upper extremities	Osteosarcoma	C1~2	5~9	A~D, F	Primary	None	None	60
8	42	Male	24.4	Lower back pain and limitation of motion	Secondary Kyphosis	T12~L2	/	/	Failure of internal fixation	Total *en bloc* spondylectomy for giant cell tumor of bone of L1 4 years ago	None	20

BMI: Body mass index; WBB: Weinstein-Boriani-Biagini; FUSCC: Fudan University Shanghai Cancer Center; KPS: Karnofsky performance score

3D-printed prosthesis and the autogenous vertebral endplate (**Figure 3**).

(2) Case 2

A 28-year-old female was referred to FUSCC due to the left chest-back pain and numbness. She had previously undergone posterior mediastinal tumor resection 2 years prior. Post-operative pathology indicated neuroblastoma. The tumor, however, quickly recurred on the left sixth rib. She, therefore, underwent a left sixth rib resection 1 year later at the same facility. Unfortunately, the tumor quickly recurred again at T5 and metastasized to T4 and T6 6 months ago (**Figure 4A**). She underwent neoadjuvant chemotherapy (COVP regimen) and radiotherapy for 5 months in FUSCC. After tumor PR, we planned to *en bloc* resect T4 ~ 6 and design a 3D-printed artificial vertebral body to reconstruct her spine (**Figure 4B**). A final titanium alloy implant of the 3D-printed artificial vertebral body was manufactured (**Figure 4C**). Post-operative X-ray demonstrated excellent fit, stability, and alignment (**Figure 4D**). During a 15 month-follow-up period after surgery, the patient had an excellent outcome, moving all her limbs freely, without pain or local recurrence.

(3) Case 3

A 28-year-old male was admitted to FUSCC due to paralysis and myophagism of both lower extremities for 3 months. He had a comorbidity of ankylosing spondylitis. CT-based 3D imaging visually displayed a T6 ~ 8 reticular tumor; X-ray showed increased thoracic kyphosis (Cobb = 67.1°) (**Figure 5A**). We planned to *en bloc* resect T6 ~ 8, adjust T1 ~ 5 alignment and design a 3D-printed artificial vertebral body to reconstruct his spine (**Figure 5B**). Surgery was successfully performed. Post-operative pathology indicated aggressive angioma. Post-operative X-ray demonstrated improved thoracic curvature (Cobb = 45.8°) and stable artificial vertebral body implant (**Figure 5C**). During a 14-month-follow-up period after surgery, the patient was doing well, moving all limbs with recovered strength and without any pain or local recurrence.

(4) Case 4

A 53-year-old female was referred to FUSCC due to chest-back pain. She had a previous surgery of gingival squamous cell carcinoma 10 years ago. She underwent T9 laminectomy 5 years ago and T9 vertebrectomy 4 years ago for spinal metastasis in another hospital. She was found to have local recurrence at the T8 ~ 10 level 2 months ago (**Figure 6A**). We planned to *en bloc* resect T8 ~ 10, with reconstruction using a customized 3D-printed artificial vertebral body (**Figure 6B**). Surgery was successfully

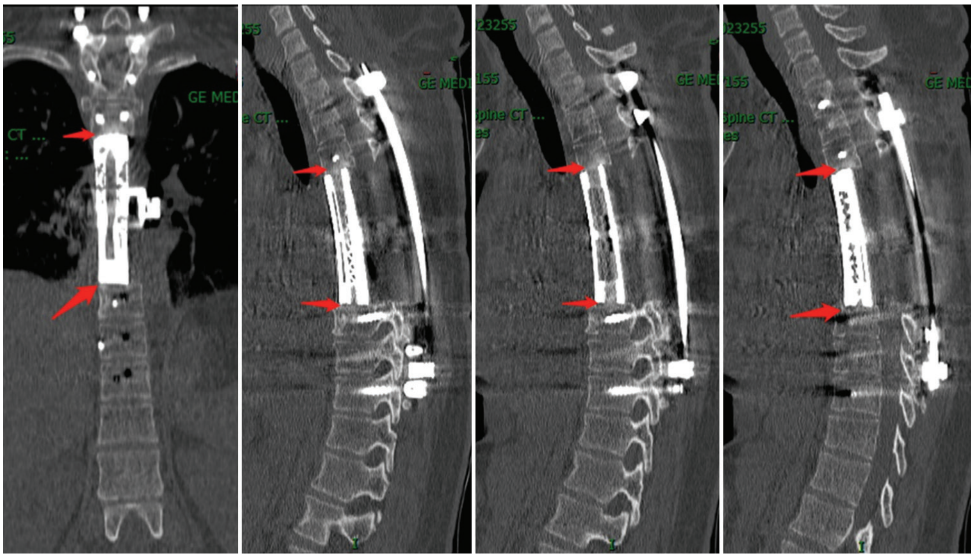

Figure 3. Case 1. CT imaging at the post-operative nine-month follow-up visit. Coronal and sagittal CT images show evident bone ingrowth and good biological fusion between the porous interface of the 3D-printed prosthesis and the autogenous vertebral endplate (red arrow).

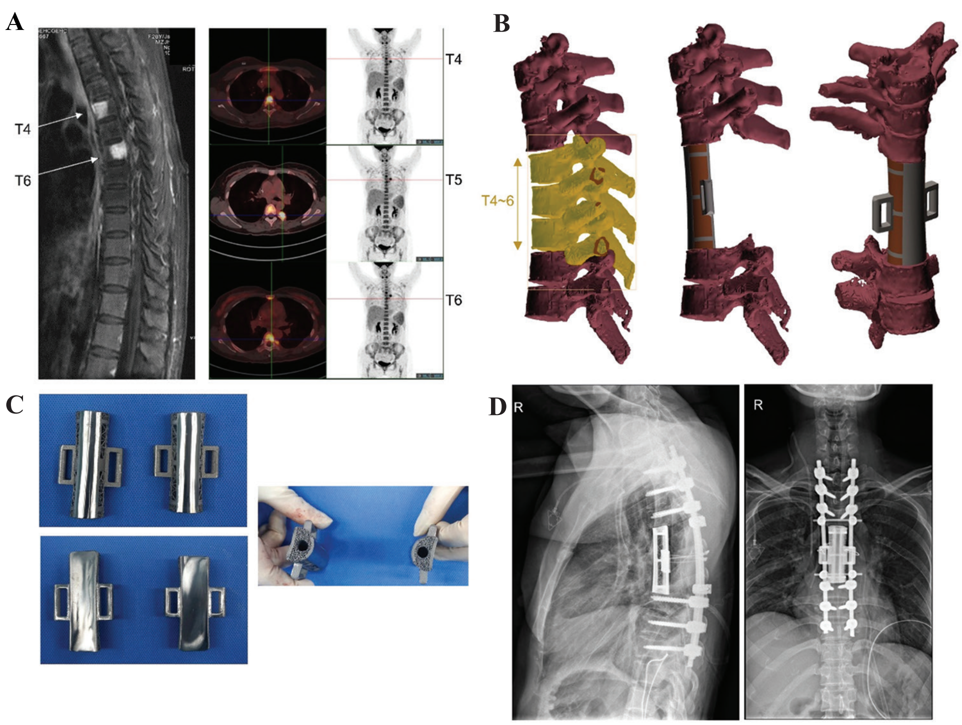

Figure 4. Case 2. (A) Pre-operative MRI and PET-CT showing recurrent tumors on T4, T5, and T6; (B) 3D imaging visually showing T4~6, planned for resection and replacement with patient-specific 3D-printed artificial vertebral body; (C) final titanium alloy implant, including solid and porous parts; (D) post-operative X-ray showing excellent implant fit, stability, and alignment.

performed. Postoperative X-ray and 3D-imaging demonstrated an excellent position and stability of the titanium vertebral body implant (**Figure 6C**). During 3-month-follow-up after the surgery, the patient moved freely and had no pain and no local recurrence. She was recommended to receive adjuvant chemotherapy.

(5) Case 5

A 31-year-old female presented with neck and shoulder pain, and paralysis of the right upper limb. She was found to have a C6 tumor and underwent anterior cervical decompression and internal fixation in another hospital

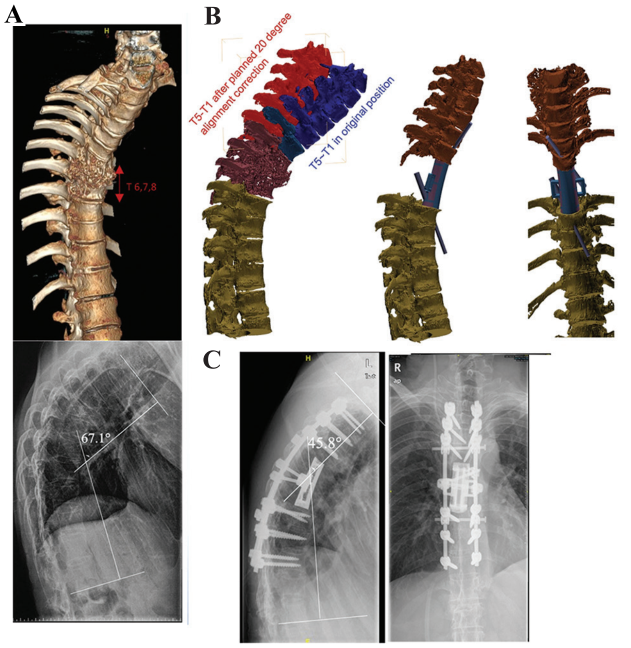

Figure 5. Case 3. (A) Pre-operative 3D imaging visually showing T6~8 reticular tumor and X-ray showing spinal kyphotic abnormality; (B) 3D imaging visually showing T6~8 level to be resected and T1~5 with corrective adjustment in alignment, and patient-specific 3D-printed artificial vertebral body design; (C) post-operative X-ray showing well positioned implant.

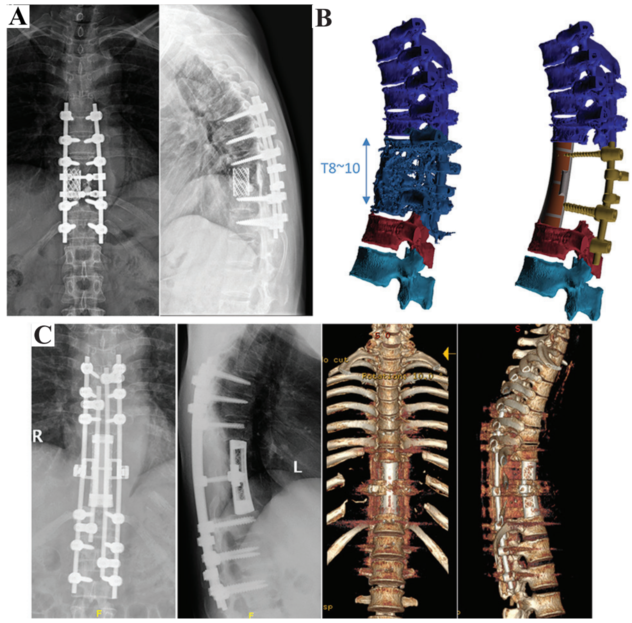

Figure 6. Case 4. (A) Pre-operative X-ray showing T9 post-surgery imaging and soft tissue mass shadow beside T8~10; (B) 3D imaging visually showing T8~10, planned for resection and replacement with patient-customized 3D-printed artificial vertebral body; (C) post-operative X-ray and 3D reconstruction imaging visually showing excellent implant position and stability.

5 months ago (**Figure 7A**). PET-CT demonstrated hypermetabolic lesions in C5-7 and T1 vertebral bodies. Needle biopsy on a swollen cervical lymph node indicated atypical epithelioid hemangioendothelioma. She was referred to FUSCC and underwent partial resection of the cervical and thoracic tumor and internal fixation via a posterior approach (**Figure 7B**). After 2 weeks, we planned to *en bloc* resect C5-7 and T1 through an anterior approach, perform intraoperative radiation, and reconstruct the resulting defect using a 3D-printed artificial vertebral body (**Figure 7C**). Surgery was successfully performed as planned. Post-operative X-ray demonstrated excellent position and stability of the titanium vertebral body implant (**Figure 7D**). During a 10-month-follow-up after the surgery, the patient moved her neck and upper limbs freely, with pain well controlled with oral pain medications as needed. She was recommended to receive adjuvant radiotherapy 1 year later.

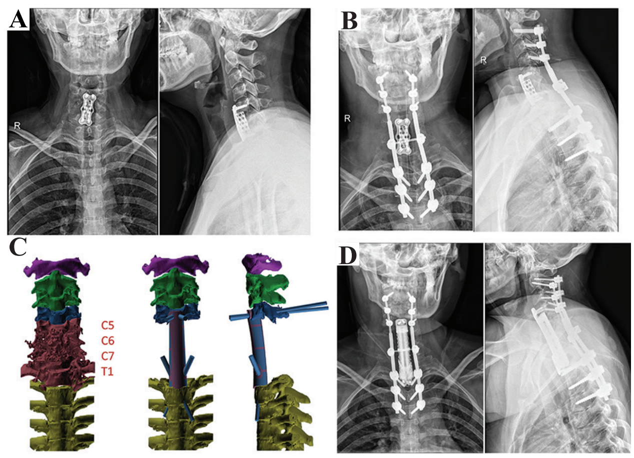

Figure 7. Case 5. (A) Pre-operative X-ray showing C6 cervical decompression and internal fixation; (B) pre-operative X-ray showing cervical and thoracic tumor partial resection and internal fixation; (C) 3D imaging showing C5~7 and T1, planned for resection and replacement with patient-specific 3D-printed artificial vertebral body; (D) post-operative X-ray showing excellent implant position and stability.

(6) Case 6 (Post-surgery infection)

A 37-year-old female presented with chest, back pain and numbness of both lower extremities. She was found to have a T3 intraspinal tumor and underwent surgery in another hospital 7 months ago. Post-operative pathology indicated Ewing sarcoma. Although she underwent adjuvant chemotherapy and radiotherapy, the tumor recurred at the T2 ~ 4 level (**Figure 8A**). We planned to *en bloc* resect T2 ~ 4 and design a 3D-printed artificial vertebral body to reconstruct her spine (**Figure 8B**). Surgery was successfully performed as planned (**Figure 8C**). Post-operative imaging demonstrated a well-positioned titanium vertebral body implant (**Figure 8D**). A video visually demonstrating the implantation process is presented in **Video 2**.

On the 4th day after surgery, the patient developed a fever up to 38.8°C. Wound drainage significantly increased, which was thought to be a result of either cerebrospinal fluid leakage or infection. Bacterial culture of the fluid showed the presence of Gram-positive coccus. Based on susceptibilities, vancomycin was given and was able to quickly control the infection. The infection had not yet caused any adverse effects on the artificial vertebral body implant, therefore the decision was made to retain the hardware. She experienced a lengthy hospital stay (22 days). During the 13-month-follow-up after the surgery, the patient moved freely and had no pain and or local recurrence.

3.3. Unsuccessful implantation

(1) Case 7

A 51-year-old male visited FUSCC for neck pain, limitation of motion, and numbness of both upper extremities. Pre-operative X-ray and CT showed a C1 and C2 tumor resulting in pathological fracture and dislocation (**Figure 9A**). The tumor was located in C1 ~ 2 (**Figure 9B**). We planned to *en bloc* resect C2, partially resect and correct alignment of C1, and design a customized 3D-printed artificial vertebral body to reconstruct his spine (Plan A) (**Figure 9C**). Final titanium alloy implants were manufactured (**Figure 9D**). An alternative preoperative traditional spinal reconstruction plan was prepared, including bone cement formation, internal fixation, and autogenous iliac bone grafting for occipitocervical fusion (Plan B).

An anterior cervical approach was used to resect C2 along with the tumor, the C1 anterior arch and the C2-3 intervertebral disc. However, after placing the 3D-printed artificial vertebra into the resulting bone defect, we found that the prosthesis was smaller than the body's actual bone defect, resulting in a lack of fixation. We then converted to a conventional spinal reconstruction (Plan B). Post-operative pathology results confirmed osteosarcoma. Post-operative X-ray showed excellent reconstruction, according to Plan B (**Figure 9E**). At the 37th month after surgery, the patient's neck moved freely but with pain. He was diagnosed with osteosarcoma local recurrence and was recommended to receive chemo-radiotherapy.

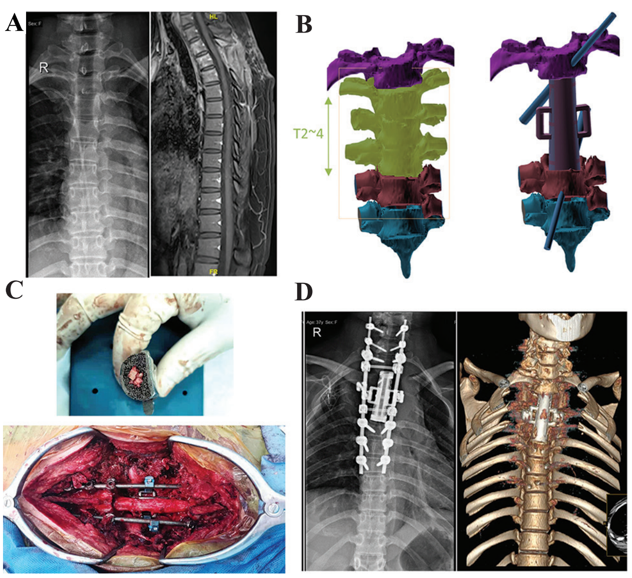

Figure 8. Case 6. (A) Pre-operative X-ray and MRI showing tumor recurrence at the T2~4 levels; (B) 3D imaging visually showing T2~4, planned for resection and replacement with patient-specific 3D-printed artificial vertebral body; (C) surgical clinical photo demonstrating the autogenous bone granule used within the porous part of the prosthesis to promote bone fusion; (D) post-operative imaging showing well positioned implant.

(2) Case 8

A 42-year-old male underwent L1 tumor resection in another hospital 4 years ago. He was admitted to FUSCC for lower back pain and activity limitation. X-ray revealed failed hardware, with a fractured rod and L1 artificial vertebral body subsidence (**Figure 10A**). We planned to design a 3D-printed vertebral body to reconstruct his spine. CT-derived 3D imaging visually displayed the lesion (**Figure 10B**). Individualized 3D-printed artificial vertebral body and screw rod internal fixation system were designed and modeled (**Figure 10C**). During the operation, T12 and L2 bone graft beds were polished. However, the 3D-printed prosthesis could not be completely implanted because of mismatch between the 3D-printed prosthesis and the bone defect height. An alternative solution that allows for extendable artificial vertebra with incorporation of autogenous rib and allogeneic bone was performed on the patient (**Figure 10D**). During the 4-month-follow-up after the surgery, the patient moved freely and had no pain.

3.4. Surgical characteristics

Of the eight patients, six succeeded in 3D-printed spinal implantation, two failed and converted to conventional reconstruction. For patients with 3D-printed spinal implants: (i) the median surgery time was 414 min; (ii) the median blood loss was 2,150 ml; (iii) the median blood transfusion was 2000 ml; (iv) the median length of hospital stay was 9 days; (v) four underwent adjuvant therapy after the surgery; and (vi) they experienced no pain, moved freely, and had no local tumor recurrence during a median 11.5 months-post-operative follow-up. All patients had stable reconstructions without failure and kept in good performance status at the end of follow-up. More details on the clinical characteristics of the patients are presented in **Table 2**.

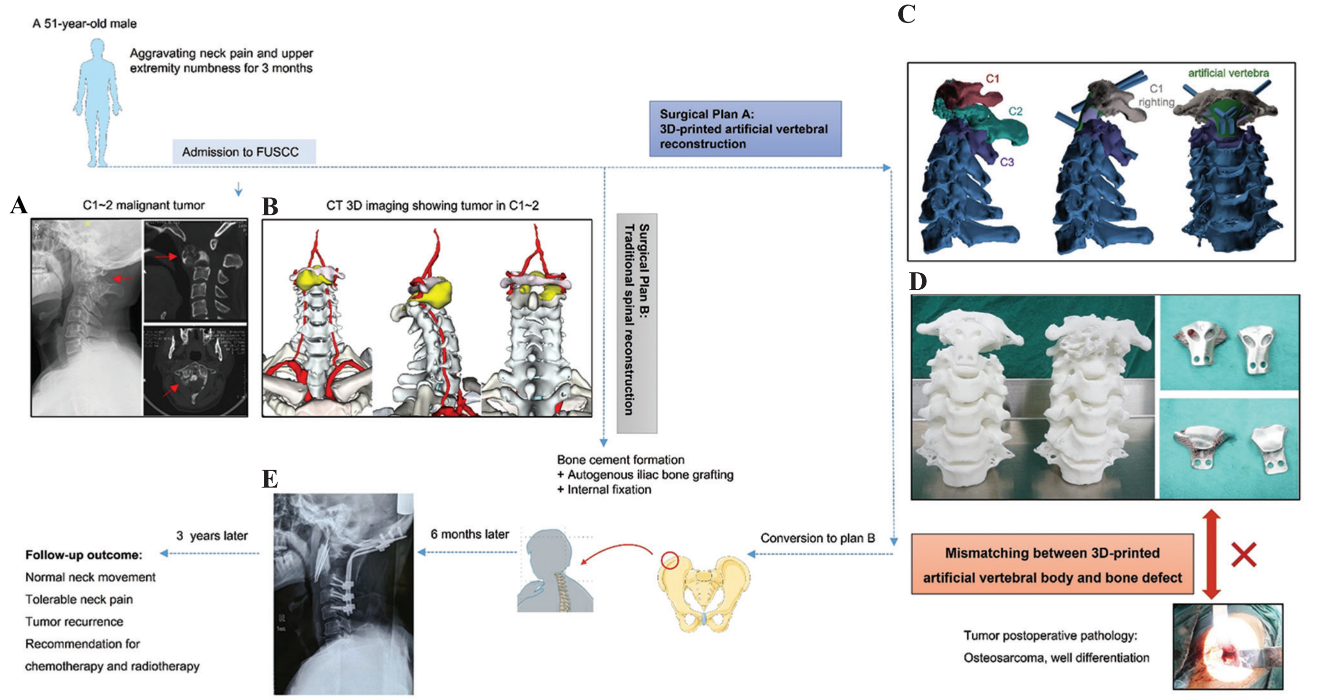

Figure 9. Case 7. (A) Pre-operative X-ray and CT showing C1 and C2 tumor with pathological fracture and dislocation; (B) 3D imaging visually showing tumor in C1~2; (C) 3D imaging visually showing vertebrae planned to be resected and replaced with 3D-printed artificial vertebral body; (D) final titanium alloy implants; (E) post-operative X-ray showing reconstruction according to plan B, without the use of the 3D printed implant due to mismatching.

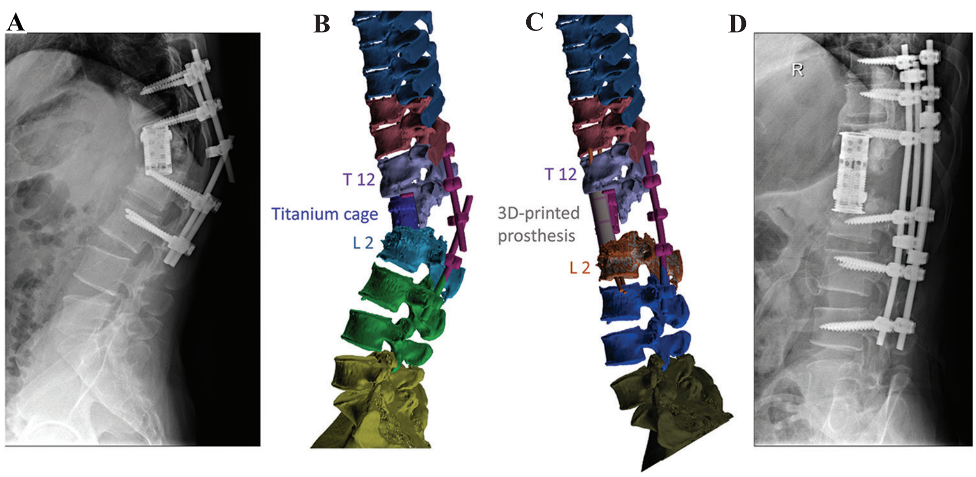

Figure 10. Case 8. (A) Pre-operative X-ray showing fractured internal fixation rod and L1 artificial vertebral body subsidence; (B) 3D imaging visually showing the lesion; (C) 3D-printed artificial vertebral body and internal fixation system design; (D) post-operative X-ray showing spinal reconstruction using extendable artificial vertebra.

4. Discussion

A recent systematic review demonstrated that 3D printing technology in orthopedics improves operative time, blood loss, fluoroscopy times, bone union time, pain, accuracy, function, and without an increase in operative complications[12]. Besides being used for preoperative planning, surgery simulation, intraoperative navigation, patient education, and doctor-patient communication, 3D-printing technology has shown emerging and promising application in personalized spinal implant and reconstructive surgery[13,14]. Given the novelty of 3D-printed spinal implants, it is essential to conduct more prospective studies to explore its specific application scope, experience, outcomes, and potential problems[15,16].

In this study, we utilized 3D-printed spinal implants for reconstruction surgery of complex spinal tumors. Most

Table 2. Surgery characteristics and follow-up outcomes.

Case number	ASA grade	Resected vertebral numbers	Surgical approach	Time of operation (mins)	Blood loss (mL)	Blood transfusion (mL)	3D-printed prosthesis implant	Post-surgery complication	Length of hospital stay (days)	Adjuvant treatment after surgery	Follow-up time (months)	Follow-up outcome		
												Symptoms and signs	Patient satisfaction	KPS
1	II	4	Anterior and posterior approach	666	2000	1800	Success	No	9	Radiotherapy	9	Free movement; No pain; No recurrence	Yes	100
2	III	3	Posterior approach	405	2300	2000	Success	No	8	None	15	Free movement; No pain; No recurrence	Yes	100
3	II	3	Posterior approach	385	6500	4500	Success	No	9	None	14	Free movement; Muscle force recovered; No pain; No recurrence	Yes	100
4	II	3	Posterior approach	424	1600	1500	Success	No	7	Chemotherapy	3	Free movement; No pain; No recurrence	Yes	100
5	II	4	Anterior and posterior approach	326	2000	2000	Success	No	9	Radiotherapy	10	Free movement; No Pain; No recurrence	Yes	90
6	II	3	Posterior approach	518	2300	2200	Success	Cerebrospinal fluid Leakage/ infection	22	Chemotherapy	13	Free movement; No pain; No recurrence	Yes	100

(Contd...)

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												Symptoms and signs	Patient satisfaction	KPS
7	III	2	Anterior and posterior approach	450	1500	1400	Failure	No	12	None	37	Free movement; Pain; Recurrence	Yes	90
8	II	3	Anterior and posterior approach	467	1200	1500	Failure	No	6	None	4	Free movement; No pain; No recurrence	Yes	100

Abbreviations: American Society of Anesthesiologists; KPS: Karnofsky performance score

of the enrolled patients had multi-level or recurrent spinal tumors and presented with pain and limb dysfunction. Our results demonstrated that the use of a 3D-printed spinal implant following TES is an effective reconstruction method, with all included patients demonstrating long-term symptoms relief, with complete resolution of pain and restoration of spine motion. 3D-printed spinal implant following TES was safe and reliable, without long-term surgical complications, for example, 3D-printed prosthesis subsidence and internal fixation rod loosening.

At present, 3D printing techniques mainly include SLM, electron beam melting (EBM), stereo lithography appearance, laser engineered net shaping, digital light processing, fused deposition modeling, and ultraviolet molding[17,18]. Of them, SLM and EBM are the most commonly used methods for orthopedic implant manufacturing[19]. Although SLM has low forming efficiency and large residual stress as well as requires secondary heat treatment, it has high forming accuracy, in particular, in the formation of precision parts and complex structures[20]. Therefore, in our study, we used SLM technique.

Materials used in 3D-printing mainly include titanium alloy, porous tantalum metal, and polyether ether ketone[21-23]. In our study, we used the titanium alloy, Ti_6Al_4V, as it offers many useful advantages. Ti_6Al_4V can achieve precise pore size, pore size ratio, and exhibits excellent mechanical properties thanks to its elastic modulus and biomechanical compatibility.

The advantages of using titanium alloy, Ti_6Al_4V include:

(i) High porosity of porous interface. The increased porosity is conducive to improving the adsorption capacity of osteoblasts and promoting the ingrowth of osteocytes. The material and design promote biological fusion and improves stability of the prosthesis after implantation (**Figure 3**).

(ii) High strength and hardness. It can provide strong fixation for bone defects after orthopedic resection.

(iii) Low elastic modulus. The modulus of elasticity of titanium most closely approximates cortical bone, resulting in superior biomechanical compatibility.

The disadvantages of using titanium alloy, Ti6Al4V include:

(i) Unsatisfactory wear resistance. The implanted prosthesis may wear and collapse over time.

(ii) This alloy contains vanadium, which is toxic to the human body to some extent. An alternative material would be beneficial to reduce the potential vanadium toxicity.

In our study, the implantation with a 3D-printed prosthesis failed in two patients due to mismatching. Although the 3D-printed artificial vertebral body is manufactured under an accurate computer-assisted digital model[24], there are inevitably clinical factors which preclude it from matching with the bone defect. First, tumors cause an extensive and significant anatomic abnormality of the spine, therefore even after tumor resection, the spine structure can be very difficult to correct to our estimated anatomic position. Secondly, it takes time to manufacture a 3D-printed prosthesis after the imaging data acquisition. Some highly aggressive spinal tumors may rapidly grow and invade the spine during the waiting time. 3D-printed spinal implant reconstruction offers many advantages but also comes with uncertainties due to its novel nature. Our experience with these cases demonstrates the importance of having a good backup plan, including having modular prostheses with multiple options and sizes to be used with conventional spinal reconstruction techniques.

Although utilizing 3D-printing implants may improve spinal reconstructive surgery[25], we must keep in mind that surgery is a local therapy, which must be supported with suitable systematic therapy such as chemo-radiotherapy and targeted medications. Our study demonstrated that neoadjuvant and adjuvant therapies combined with 3D-printed spinal implant surgery provides satisfactory control for recurrent spinal tumors. Zhuang *et al*.[26] indicated that 3D-printed spinal implant surgery combined with robotic radiotherapy could be a new treatment paradigm for spinal tumors. In our study, a patient (Case 5) underwent intraoperative radiation. More trials combining neoadjuvant and adjuvant tumor therapies with 3D-printed spinal implant surgery are being explored in our institution.

Compared to conventional spinal construction, our 3D-printed spinal implant has the following custom-made features: (i) Accurate vertebral height with multiple alternative options. According to the CT reconstruction result, 3D-printed artificial vertebral bodies with three different heights were designed and produced: The standard height, the standard height +3 mm and −3 mm. Those 3D-printed spinal prostheses with different heights can maximally meet the surgeon's selection to achieve a precise implant during the operation. Anterior-to-posterior and left-to-right diameters were also precisely customized; (ii) The physiological curvature of the spine can be reconstructed with the 3D-printed spinal prosthesis, as shown in Case 3 in our study; (iii) an optimal contact area can be customized between the 3D-printed and autologous vertebral bodies. The contact area ranged from 60 to 80% with deviations outside of this range lead to complications. If it is too large, the prosthesis will be difficult to insert due to the increased tight fit. If it is too small, the prosthesis will be too lax, leading to increased risk of collapse; (iv) the contact interface can be designed with porous structure, which is conducive to bone ingrowth and fusion (**Figure 3**); and (v) The 3D-printed spinal prosthesis side near the spinal dura is designed to be smooth, while the other side is rough. In addition, if there is a spinal pathological fracture or malformation, it remains difficult to precisely reconstruct the height and curvature of the spine via CT scan parameters. Therefore, two-stage operations are sometimes needed, with 3D-printed spinal implant surgery to be performed in the second operation (Case 5).

5. Conclusion

It is clear that 3D-printed spinal implants will continue to advance spinal surgery to a new level in the next decade[27]. Our present study demonstrated that when combined with tumor comprehensive treatment, 3D-printed spinal implant surgery provides patients with excellent long-term spinal function and low risk of local tumor recurrence. Future directions may show further promise with modifications of the surface of the 3D-printed spinal implants to allow for enhanced osteogenic effects and anti-tumor activity[28,29].

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Conflict of Interest

All authors declared that they have no competing interests.

Author Contributions

X.H. collected and analyzed the data and drafted the manuscript. S.K. critically revised the manuscript. M.C. and W.C. participated in the surgery. W.H. and W.Y. participated in the surgery, designed the study, and revised the manuscript. All authors read and approved the final manuscript.

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