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Three-dimensional printing guide template assisted percutaneous vertebroplasty

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TITLE:

Three-Dimensional Printing Guide Template Assisted Percutaneous Vertebroplasty (PVP)

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KEYWORDS:

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SUMMARY:

Herein, we present a three-dimensional printing guide template for percutaneous vertebraplasty. A patient with a T11 vertebral compression fracture was selected as a case study.

ABSTRACT:

Percutaneous vertebroplasty (PVP) is considered an effective treatment for the back pain caused by osteoporotic vertebral compression fracture. The accuracy of PVP mainly depends on the surgeons' experience and multiple fluoroscopes during a traditional procedure. Puncture related complications were reported all over the world. To make the surgical procedure more precise and decrease the rate of puncture-related complications, our team applied a three-dimensional printing guide template to PVP to modify the traditional procedure. This protocol introduces how to model target vertebrae DICOM imaging data into three-dimensions in the software, how to simulate operation in this 3-D model, and how to use all of the surgical data to reconstruct a patient specific template for application. Using this template, surgeons can identify suitable puncture points accurately to improve the accuracy of the operation. The whole protocol includes: 1) diagnosis of the osteoporotic vertebral compression fracture; 2) acquisition of CT imaging of the target vertebra; 3) simulation of the operation in the software; 4) design and fabrication of the 3-D printing guide template; and 5) application of the template into an

operation procedure.

INTRODUCTION:

As the most common type fracture among all kinds of osteoporotic fractures, osteoporotic vertebral compression fracture (OVCF) is a highly concerning clinical problem nowadays. As current guidelines recommend, percutaneous vertebroplasty is one of the most effective minimally invasive methods to clinically treat osteoporotic vertebral compression fractures[1].

Traditionally, surgeons perform percutaneous vertebroplasty guided by a C-arm fluoroscope to treat a vertebral compression fracture to restore the compressed vertebral body and relieve early-stage pain[2]. Even experienced surgeons err in confirming suitable puncturing points by simply relying on their personal experience. This operation could cause some puncture-related complications (e.g., cement leakage into surrounding tissues, nerve root injury, intra-spinal hematoma, etc.[3-5]); moreover, almost 50% of patients have local complications from traditional PVP with 95% of complications coming from cement leakage into surrounding tissue or embolization of paravertebral veins[6]. With the emergence of precision surgery, a 3-D printing guide template has been used in many spinal surgery operations[7] because it can enhance the procedural accuracy, decreasing the difficulties and minimizing the operational risks. Here, we apply a 3-D printing guide template into the PVP to make the surgical procedure more precise and to decrease the rate of puncture-related complications. Compared with the traditional method, operations assisted by the 3D printing guide template have 1) increased surgical puncture accuracy, 2) minimized the radiation exposure during the operation, 3) shortened the surgical procedure time, and 4) decreased the probability of puncture-related complications.

PROTOCOL:

The present study was approved by the ethics committee of Beijing Friendship Hospital Capital Medical University.

1. Diagnosis of the osteoporotic vertebral compression fracture (OVCF) by X-ray fluoroscopy, magnetic resonance image (MRI), bone scintigraphy, and symptoms

1.1 Identify patients who have OVCF by older patients with back pain, tenderness in the spinous process, paraspinal muscles at back, etc.

1.2 Use posterioanterior X-ray fluoroscopy to check if patient has vertebral compression fracture.

1.3 Use an MRI to diagnosis whether a patient has a newly onset vertebral compression fracture, and determine the target compressed vertebrae. For patients who cannot undergo the MRI, use bone scintigraphy.

1.4 Order PVP treatment for the patient who has an acute vertebral compression fracture and record the Visual Analogue Scale (VAS) score and Oawestry Disability Index (ODI)[8].

NOTE: There are a few criteria for inclusion: 1) vertebra fractured patient whether having history of a low-energy trauma or not; 2) no history or evidence of metabolic bone disease or cancer; 3) VAS score ≥ 7; 4) diagnosis as vertebral fracture by X-ray, MRI or bone scintigraphy.

2. Preoperative localization of target vertebra

2.1 Before the operation, conduct prone computer tomography on the patient with three radiopaque markers placed in the midline of patient's back skin at the compressed vertebral level. While pressing the most painful part, confirm the target area by x-ray fluoroscopy and a physical examination on the patient's back.

2.2 Before the prone computer tomography scan, put a gradienter on the patient's back just inferior to the fixed markers. Record the patient's body position and then remove it. Have the patient stay in the same position during surgery.

2.3 Save the CT images (1 mm scanning layer thickness, 1 mm layer spacing, and either 90 slices (conventional scanning) or 400 slices (thin slice scanning) in a DICOM format. Put a cotton pad on the patient's back to ensure that the markers remain until the operation.

3. Simulating the percutaneous vertebroplasty procedure in the computer software

3.1 Export the CT images in DICOM format into medical imaging processing software (e.g., MIMICS) and select the target slices to reconstruct the compressed vertebra.

3.2 Select **Threshold Segmentation** to adjust the threshold range for the target vertebra from **125-3071H** and create a mask. Press **Duplicate Mask** to make two masks: Mask A and Mask B.

3.3 Click **Mask Edit** to erase the target vertebra in Mask A. Then click **Boolean Operations** to form a new Mask C by using Mask B to minus Mask A. Press **Calculate 3D from Mask** to reconstruct the target vertebra.

3.4 Simulate PVP via a bilateral transpedicular approach in the software. First, define the **Medcad cylinder** in the software as the puncture needle model. Define the cylinders as the same length and radius as the puncture needle (a length of 12.5 mm and a radius of 3.5 mm).

3.5 Simulate the entry point, the entry angle (head inclination angle and abduction angle orientation), and the puncture needle depth for a real PVP with the 3-D views of the target vertebra.

3.6 Adjust the puncture needles to its ideal position by using the **Move and Rotate** function. Keep needle trajectories consistent with these principles: 1) the puncture needles can extrapolate through the pedicle, preferably in its superior half; 2) the ideal location of the tips is at the point within the anterior one third of the vertebral body on the lateral view.

4. Three-dimensional printing guide template

4.1 Save all of the 3D template data and send it in an MCS format to a three-dimensional printing company.

4.2 Convert MCS format data into a STL format and design the template using software. Reconstruct the base, which must cling to patient's back skin, reconstruct the trajectory canal according to all of the parameters, including skin entry points, entry angles and the depth of the two needles' trajectory, print two same templates out for the operation.

NOTE: The guide template is made from polylactic acid, which can be sterilized and by low temperature steam disinfection.

5. Applying the three-dimensional printing guide template to assist the real PVP operation

5.1 Make the patient lie prone on the operation table as for the CT scanning in accordance with the gradienter record. Measure the distance of the three radiopaque markers and draw the outline of the three markers to match the template with the target location.

5.2 Match a skin template along with the skin outline. Insert and press two swabs through the needle's trajectories on the template to mark the insertion points on the skin. Then remove the template and draw the points as point A and B.

5.3 Remove the template and disinfect the skin. Drape the area and put the tips of two puncture needles at the insertion points (point A and B). Then, use the anteroposterior view of C-arm fluoroscopy to confirm whether the puncture points determined by template are feasible.

5.4 Give the patient local anesthesia by injecting a 5 mL mixture of 1% lidocaine and 1% ropavicaine at each puncture point. Fix another sterilized template on the patient's back by sterilized film.

5.5 Tap the two needles into the target vertebra slightly via insertions through the guiding cylinders of the template. Verify with the C-arm fluoroscope that the trajectories are long enough for insertion. Make sure that the punctuation is within the pedicles and then tap the needles to advance further until the end of the trajectory.

5.6 When the whole needles are completely inserted into the guiding cylinders, verify with the C-arm fluoroscope that the needle tips have reached their ideal location.

5.7 Inject bone cement into the vertebral body through the needles. Inject 2 mL of bone cement via each trajectory for a total of 4 mL of bone cement to the vertebra.

5.8 Finally, use fluoroscopy to check the distribution of the bone cement within the vertebral body by anteroposterior and lateral views. Stitch the insertions.

REPRESENTATIVE RESULTS:

Acquisition of CT images and digital modeling were performed in the hospital, while 3-D printing was performed in a 3-D printing company. Thirty minutes were needed to reconstruct the 3-D model from the CT images for the 3-D printing, and the 3-D printing company needed about 6 hours to print 2 guide templates out and send to the hospital.

The pre-operation images of the target vertebra of the patient were shown in **Figure 1** and **Figure 2**: X-ray (A1: Posterioanterior view; A2: Lateral view); magnetic resonance image (A3: TIWI view; A4: T2WI view; A5: FS view). **Figure 3** illustrates the acquisition of CT images, marks the target vertebrae, and records the patient's body position. From the coronal plane (**Figure 4A**), the transverse plane (**Figure 4B**) and the sagittal plane (**Figure 4C**), the CT vertebra image was reconstructed into a 3-D model (**Figure 4D**). The simulation of the PVP operation procedure in the image processing software is shown in **Figure 5**. **Figure 6** presents the length of guiding cylinders of the template, and **Figure 7** shows the procedures to fabricate the guide template. **Figure 8** shows the formation of the base (**Figure 8A**), the formation of the guiding cylinder (**Figure 8B**), the production process (**Figure 8C**), and the final template (**Figure 8D**). **Figure 9** shows typical operation steps.

FIGURE AND TABLE LEGENDS:

Figure 1. X-ray of the OVCF patient. Shows the pre-operation X-ray images of the target vertebra of the patient. (A1: Posterioanterior view; A2: Lateral view)

Figure 2. MRI of the OVCF patient. Shows the pre-operation MRI images of the target vertebra of the patient. (A3: TIWI view; A4: T2WI view; A5: FS view).

Figure 3. Preoperative localization of target vertebra. Illustrates the acquisition of CT images, marking of the target vertebrae, and recording of the patient's body position.

Figure 4. Reconstruction of vertebra in MIMICS. Presents the reconstructed vertebra model from the CT vertebra image from (**A**) the coronal plane, (**B**) the transverse plane, (**C**) the sagittal plane and (**D**) the 3-D model.

Figure 5. Simulation of PVP operation procedure in the MIMICS. Shows the simulation of PVP operation procedure in the MIMICS.

Figure 6. Date of guiding cylinders of the template. Presents the length of guiding cylinders of the template.

Figure 7. The procedures of fabricate the guide template. Illustrates the steps to fabricate the

template, including reconstructing the base and the trajectory canal.

Figure 8. The model of guiding template. Shows (**A**) the formation of the base, (**B**) the formation of the guiding cylinder, (C) the producing process and (**D**) the real template entity.

Figure 9. Typical operation steps. (**A**) Use the gradienter to ensure that the patient is in the same position when the CT was performed; (**B**) Match one template with skin to determine the puncture points; (**C**) Final puncture points; (**D**) Use the puncture needles to double check the puncture points; (**E**) Fix the other sterilized template and insert the needles; (**F**) Tap the needles to the end of the trajectories; (**G**) Inject bone cement bilaterally via the needles; (**H**) Final fluoroscope of the distribution of bone cement within the vertebral body.

DISCUSSION:

Percutaneous vertebroplasty (PVP) is considered one of the best methods to treat osteoporotic vertebral compression fracture[9] due to some distinct advantages: it is minimally invasive; there is less bleeding, and recovery is rapid. Traditional PVP is primarily guided by a C-arm fluoroscope that requires repeated fluoroscopy to determine safe and ideal puncture points, puncture angles and orientations, which increases the intraoperative radiation dosage and the operation time[10]. Moreover, the success rate of the operation relies mainly on the experience of the surgeons. However, there are still 1.2%-15.7% error rates and 0-7.42% reoperation rates, even for operations assisted by an image-guided navigation system[11].

A 3D guide template has some advantages for assisting in thoracic and cervical pedicle screw insertion operations[12-14]. Our team combines a 3-D printing guide template with PVP. The results of our randomized, nonblinded, controlled clinical study show that the template provides many advantages before and during the operations: increased puncture precision; minimized surgical time and radiation exposure; and decreased puncture-related complications. For medical residents with less opportunity to perform the operation on patients, the template could shorten the learning curve of the operation and help them find the puncture points easier.

Moreover, our clinical task research focuses on applying a 3-D guide template into one segment OVCF patients. In the future, we will apply the guide template into complicated OVCF patients with severe osteoporosis, severe kyphosis, scoliosis or multi-segment fractured vertebra. These complicated OVCF operations require multiple fluoroscope scans and have long operational times, even for experienced surgeons. Applying the 3-D guide template for these cases offers a more precise and safer puncture approach, reduces operation time, and reduces radiation exposure.

However, there are some limitations of the three-dimensional printing guide template assisted percutaneous vertebroplasty. Time is required to grasp the use of the medical imaging software. During the template design, any single mistake made by surgeons unfamiliar with the software may lead to an unsuccessful surgery. Hence, this method requires that at least one surgeon in the team is familiar with the software usage as well as the operation procedures. Preoperative design of the template and template printing increase patient costs and the surgeon’s workload.

Sometimes, the template becomes slightly deformed after the sterilization, which impacts the perfect attachment of the template to the patient's back skin and the puncture accuracy. Therefore, our team is seeking alternative materials for template fabrication that would not deform after sterilization.

Collectively, 3D printing guide template assisted percutaneous vertebroplasty could help surgeons comprehensively visualize the fractured vertebra and develop an individualized surgical plan for the patient. It contributes to puncture accuracy during the procedure and decreases puncture-related complications. It minimizes the surgical time and radiation exposure while shortening the PVP learning process for young surgeons.

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DISCLOSURES:

The authors have no conflict of interest regarding any drugs, materials, or devices described in this study.

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Figure

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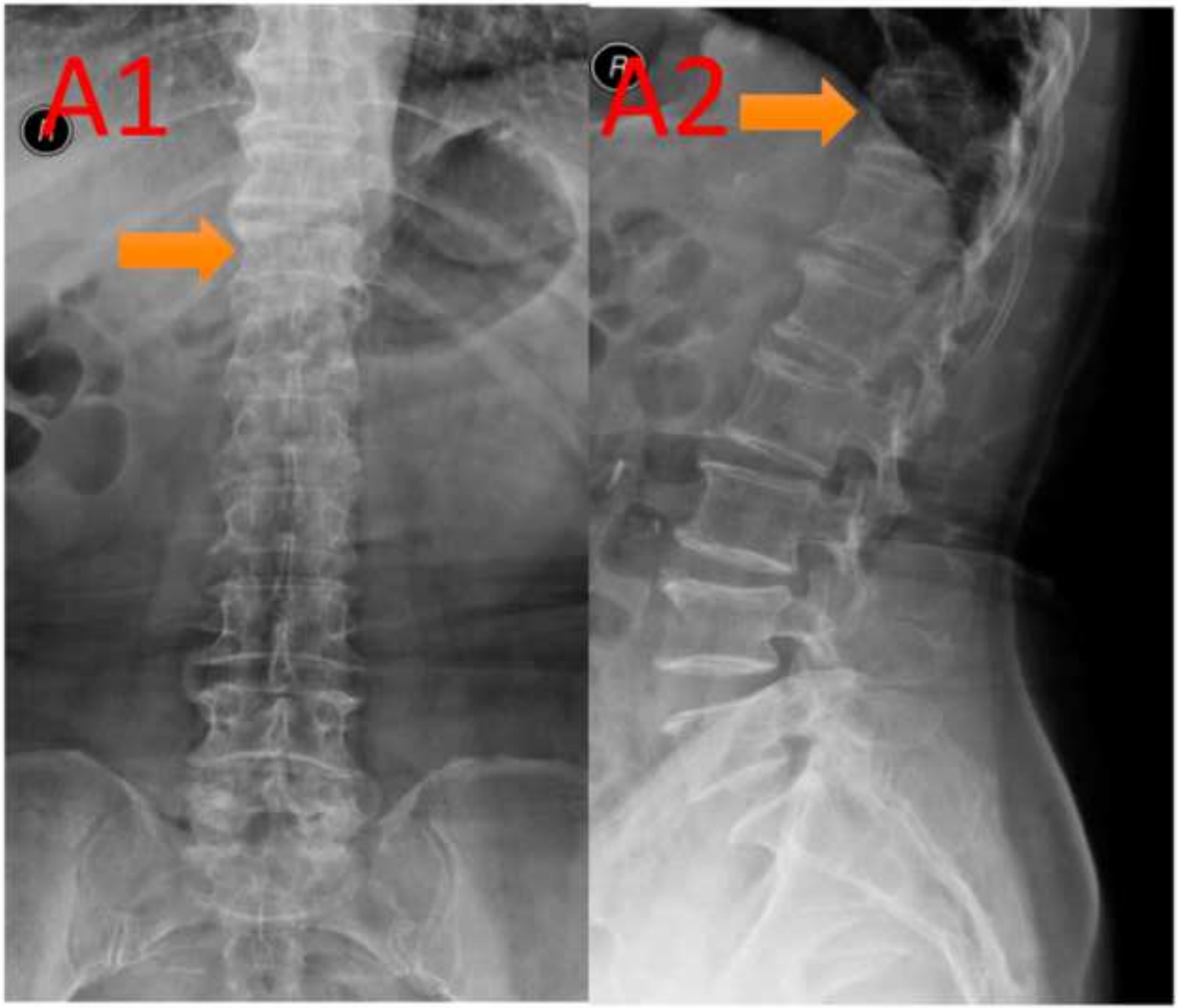

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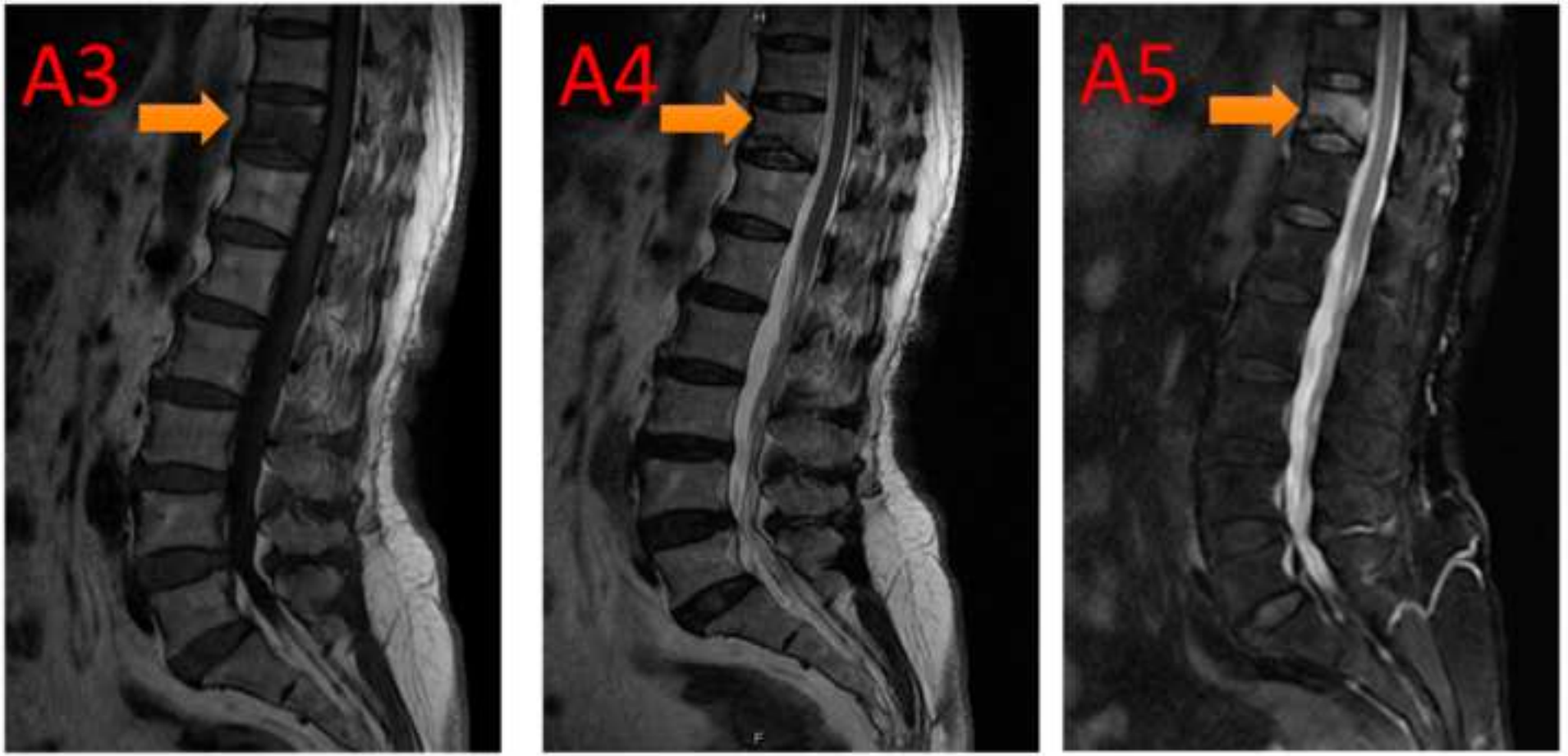

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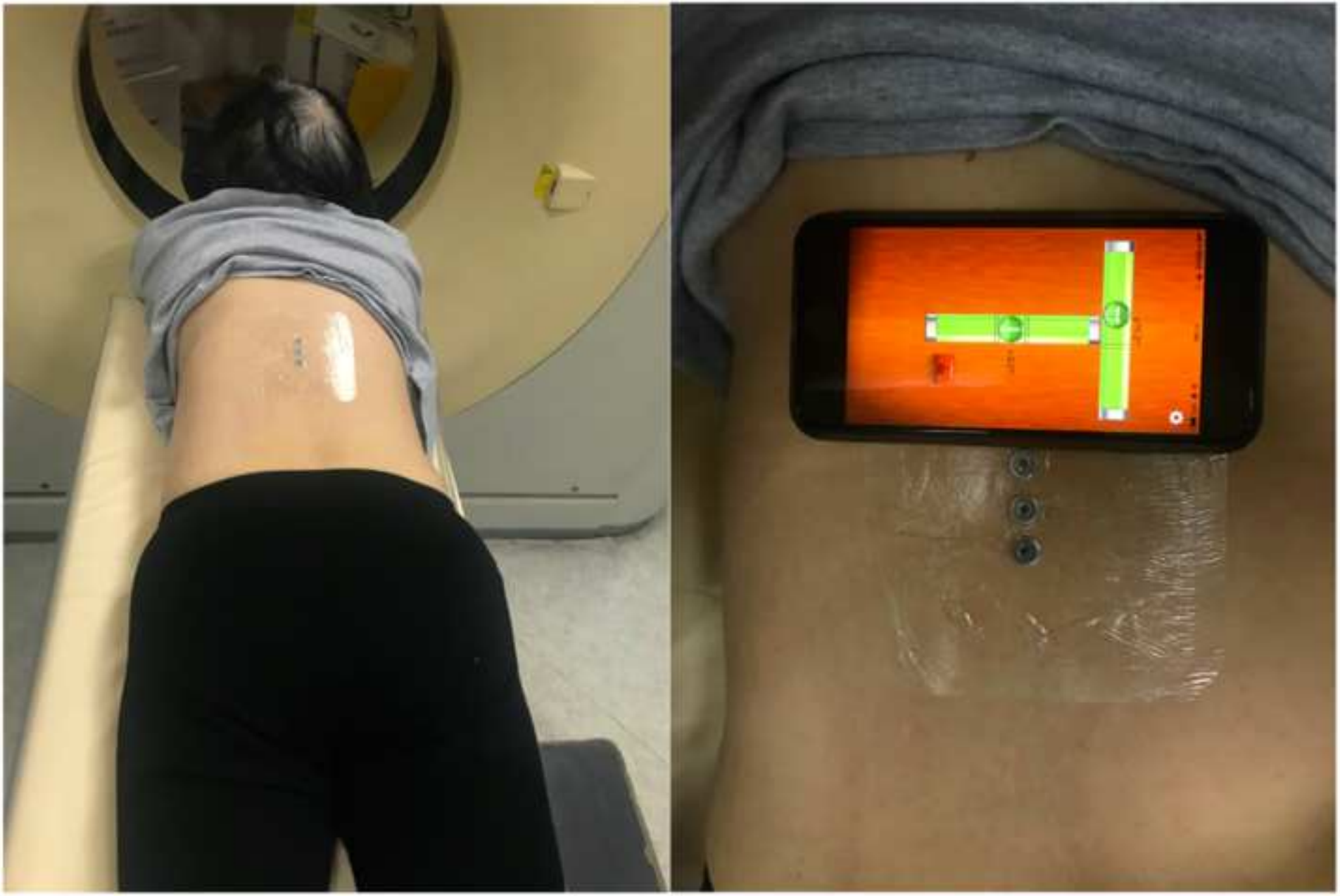

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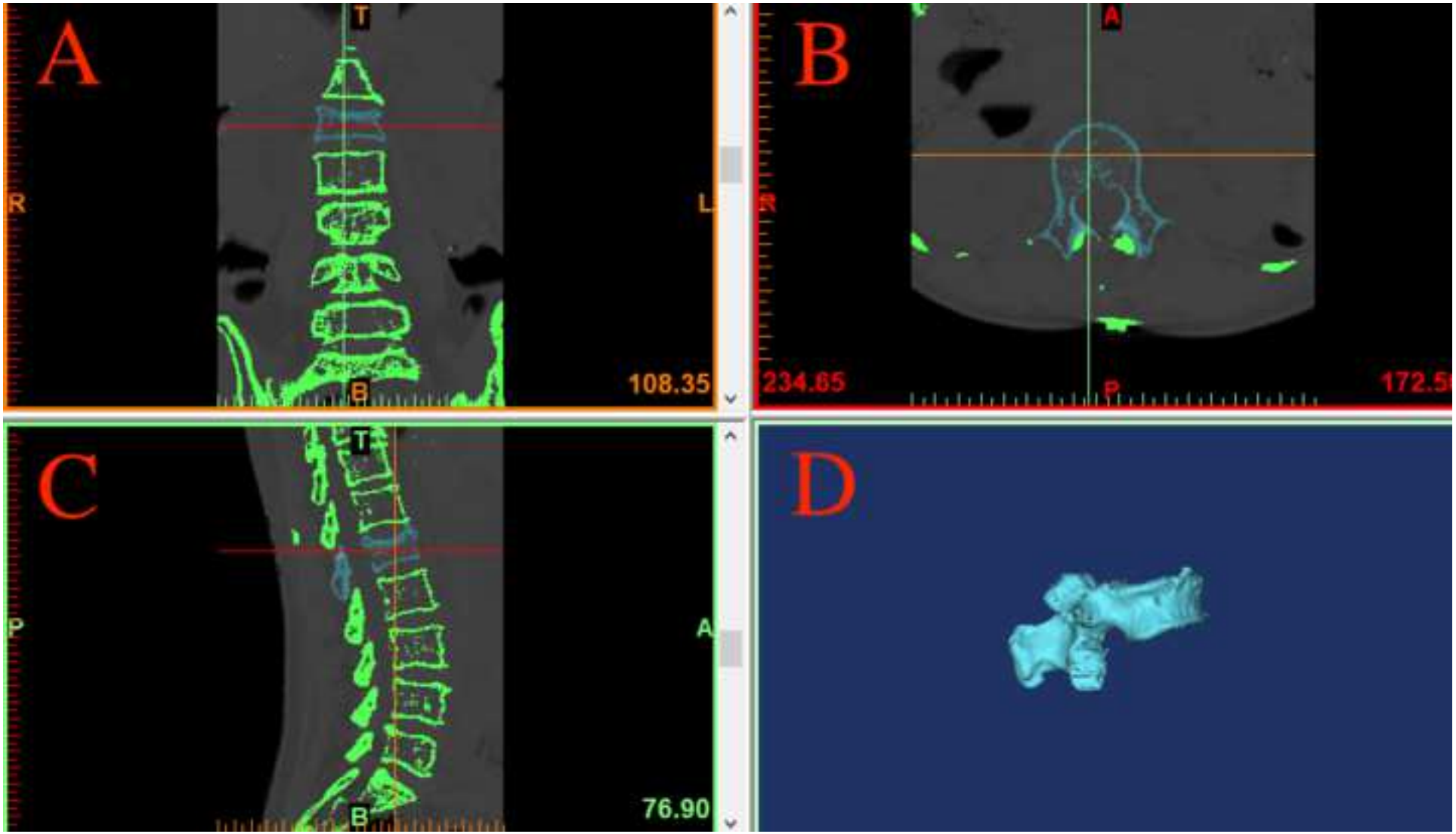

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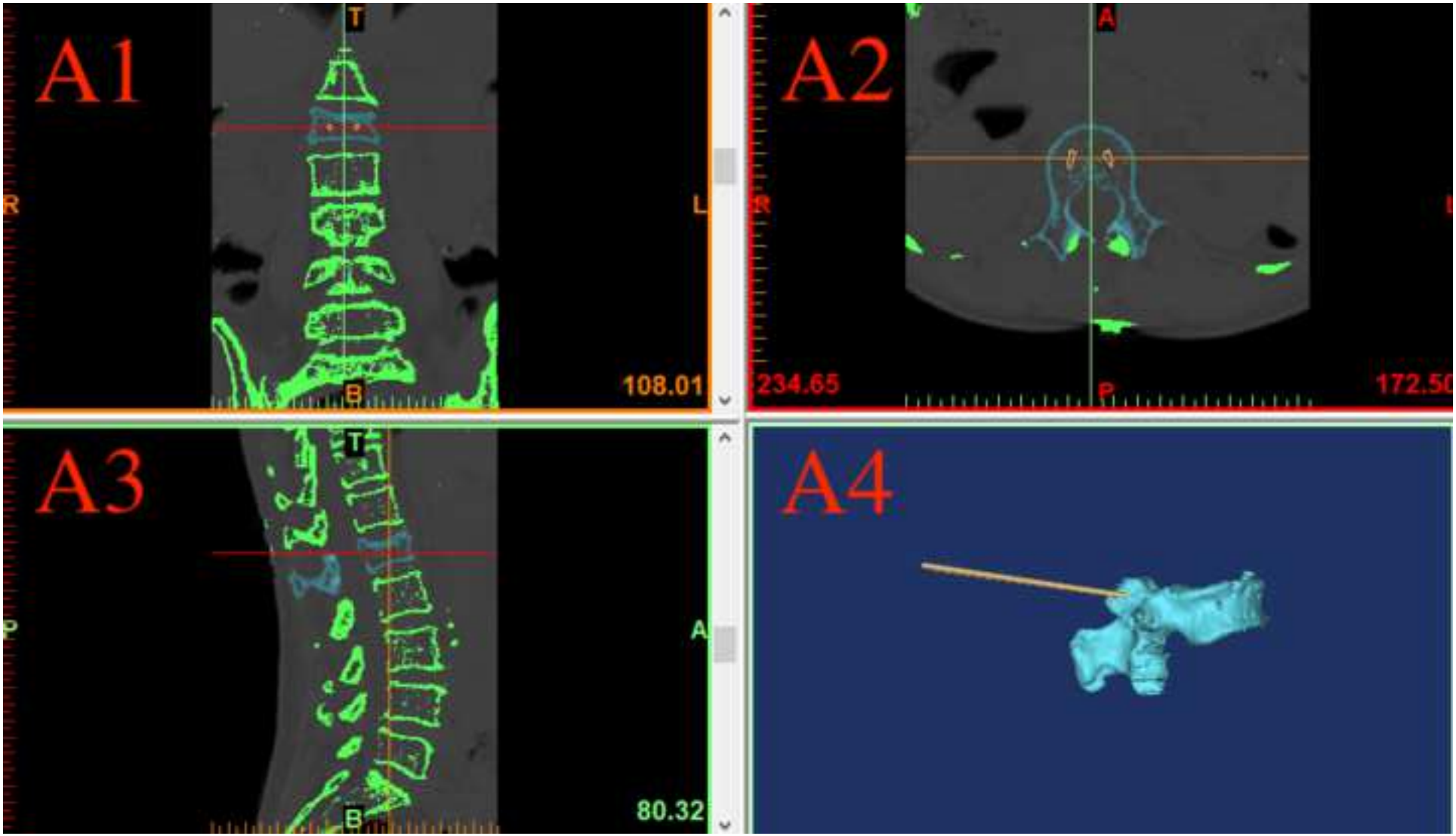

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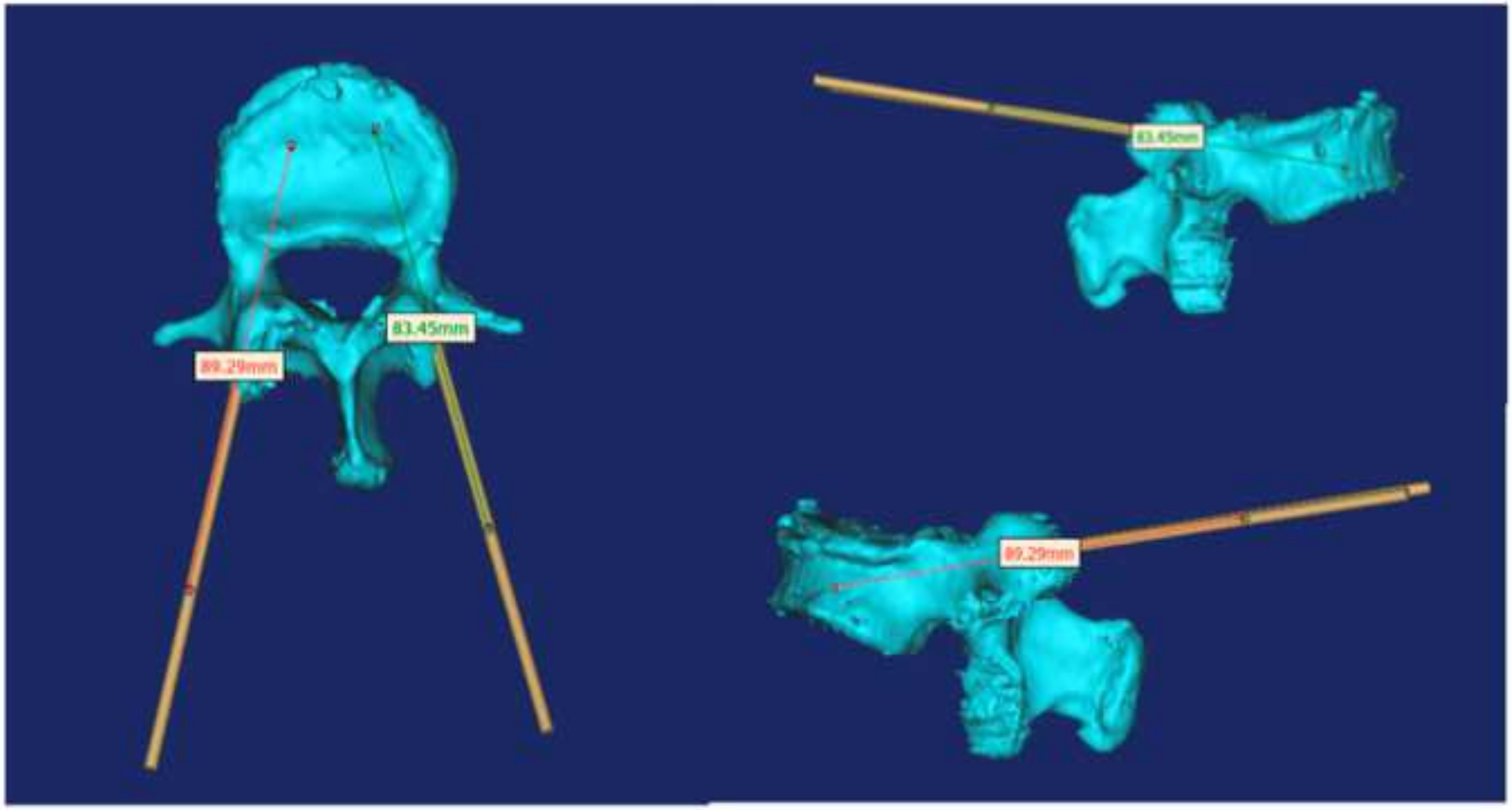

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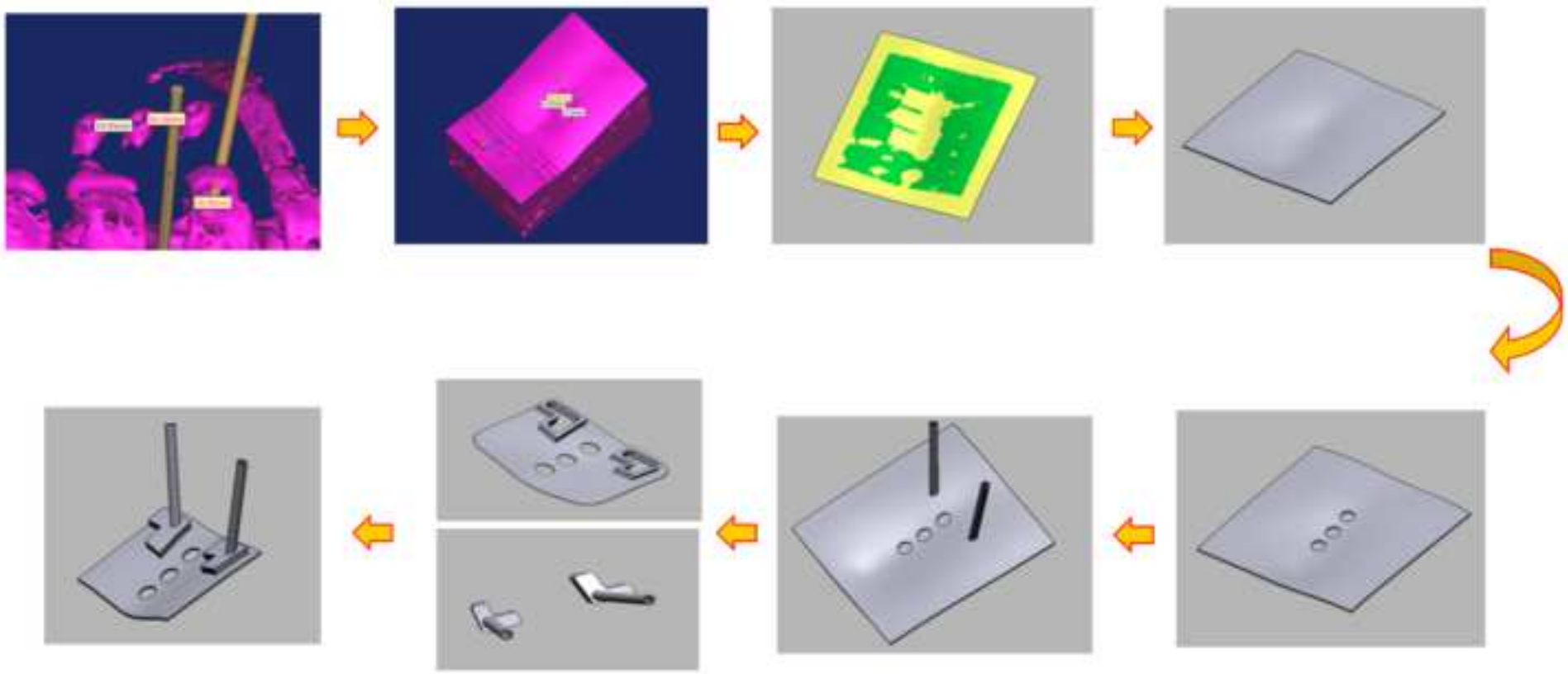

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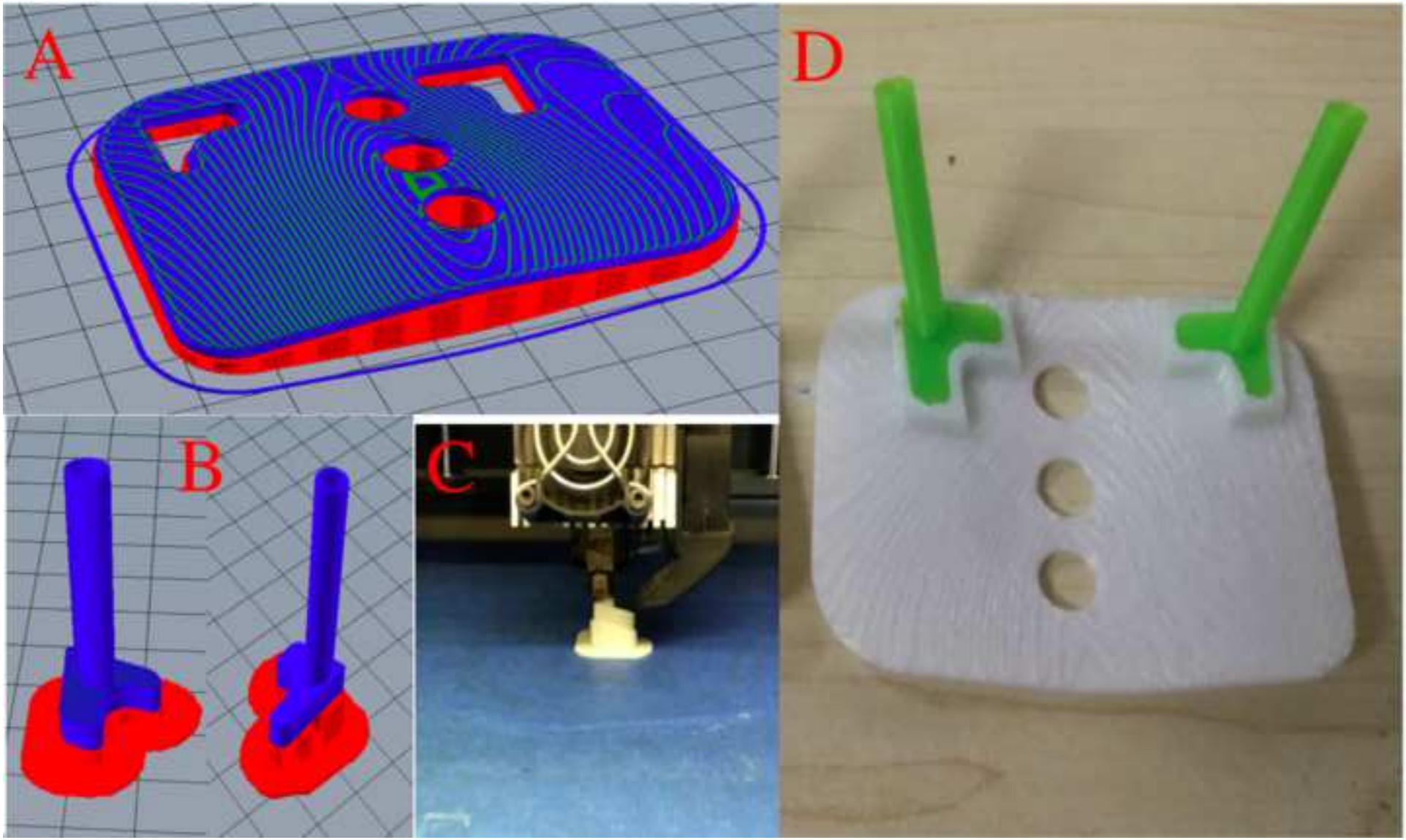

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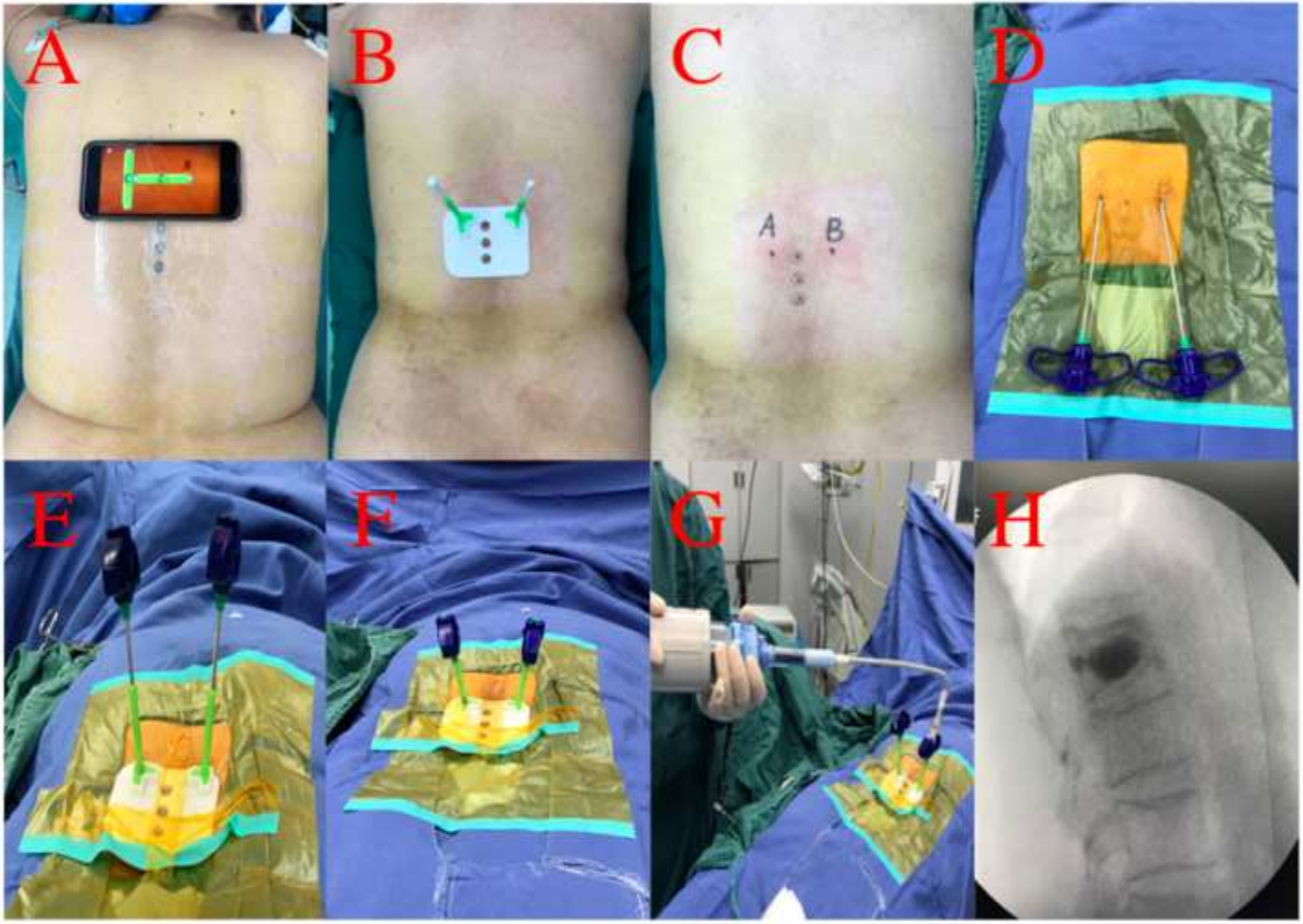

Name of Material/ Equipment
X-ray machine
Magnetic resonance image machine
computer tomography
HORI 3D printing machine
Geomagic Design X
Materialise Interactive Medical Image Control Syste
VertePort needle
Spineplex
Percutaneous Cement Delivery System
Spirit Level Plus

Company

Company Philips

Company GE

Company GE

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3D Systems Company

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software

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CORRESPONDING AUTHOR

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Title:	Three-dimensional printing guide template assisted percutaneous vertebroplasty
Signature:	Qi Fei
Date:	2019. 3. 17

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首都医科大学附属
北京友谊医院
Beijing Friendship Hospital, Capital Medical University

7-7-2019

Dear Editor:

On behalf of my co-authors, we appreciate editor and reviewers very much for the constructive comments and suggestions on our manuscript entitled “Three-dimensional printing guide template assisted percutaneous vertebroplasty”. We have read comments from you and reviewers carefully and made corresponding changes. We have tried our best to revise our manuscript according to the comments as followed.

We would like to express our great appreciation to you and reviewers for comments on our paper. Look forward to hearing from you soon.

Sincerely,

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Response to editor: Thank you very much for giving us constructive comments.

1) Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version.
   There are many missing articles (a, an, the, etc.) that make some of the text awkward. Furthermore, some phrase usage is incorrect especially with the numbered lists.

Answer: We have made according changes in revised manuscript.

2) Please remove the embedded figure(s) from the manuscript. All figures should be uploaded separately to your Editorial Manager account. Each figure must be accompanied by a title and a description after the Representative Results of the manuscript text.

Answer: We have made according changes in revised manuscript.

3) Please ensure that the references appear as the following: [Lastname, F.I., LastName, F.I., LastName, F.I. Article Title. Source. Volume (Issue), FirstPage – LastPage (YEAR).] For more than 6 authors, list only the first author then et al.

Answer: We have made according changes in revised manuscript.

4) Please revise the table of the essential supplies, reagents, and equipment. The table should include the name, company, and catalog number of all relevant materials in separate columns in an xls/xlsx file. Please sort the Materials Table alphabetically by the name of the material.

Answer: We have made according changes in revised manuscript.

5) Please rephrase the title to be more clear. It is a bit wordy.

Answer: We have made according changes in revised manuscript.

6) Please include a Summary that clearly describes the protocol and its applications in complete sentences between 10-50 words: “Here, we present a protocol to …”

Answer: We have made according changes in revised manuscript.

7) For in-text formatting, corresponding reference numbers should appear as numbered superscripts after the appropriate statement(s).

Answer: We have made according changes in revised manuscript.

8) Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique (e.g., "Do this," "Ensure that," etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as "could be," "should be," and "would be" throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a "Note." However, notes should be concise and used sparingly. Please include all safety procedures and use of hoods, etc.

Answer: We have made according changes in revised manuscript.

9) The Protocol should contain only action items that direct the reader to do something. Please move the discussion about the protocol to the Discussion.

Answer: We have made according changes in revised manuscript.

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Answer: We have made according changes in revised manuscript.

11) Please add more details to your protocol steps. Please ensure you answer the "how" question, i.e., how is the step performed? Alternatively, add references to published material specifying how to perform the protocol action.

Answer: We have made according changes in revised manuscript.

12) 1.3: Please provide citations for the VAS and the ODI.

Answer: We have made according changes in revised manuscript.

13) 2.1: Place where on the back skin? In what pattern?

Answer: We have made according changes in revised manuscript.

14) 2.2: Where should the gradienter be placed?

Answer: The gradienter is on patient`s back just inferior to the fixed markers, to record patient`s body position.

15) Please do not use contractions (won't).

Answer: We have made according changes in revised manuscript.

16) How many CT images are taken? Please provide all imaging parameters.

Answer: CT images (scanning layer thickness 1 mm, layer spacing 1 mm, and totally around 400 slices if done is thin slice scanning or 90 slices if done in conventional scanning.)

17) 5: There are many details missing from the surgery. We need these details if any of these steps are to be filmed. Please specify all experimental parameters and instruments used.

Answer: We have made according changes in revised manuscript.

18) How much is injected?

Answer：We injected 2ML bone cement via each trajectory and totally 4ML bone cement were injected to one vertebrae.

19) How much of what anesthesia is used?

Answer: We inject the mixture of 1% lidocaine and 1% ropavicaine 5ml at the each puncture points to do local anesthesia.

20) Please highlight 2.75 pages or less of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol. Remember that non-highlighted Protocol steps will remain in the manuscript, and therefore will still be available to the reader.

Answer: We have made according changes in revised manuscript.

21) Please ensure that the highlighted steps form a cohesive narrative with a logical flow from one highlighted step to the next. Please highlight complete sentences (not parts of sentences). Please ensure that the highlighted part of the step includes at least one action that is written in imperative tense.

Answer: We have made according changes in revised manuscript.

22) Please include at least one paragraph of text to explain the Representative Results in the context of the technique you have described, e.g., how do these results show the technique, suggestions about how to analyze the outcome, etc. The paragraph text should refer to all of the figures. Data from both successful and sub-optimal experiments can be included.

Answer: We have made according changes in revised manuscript.

23) Please discuss all figures in the Representative Results. However for figures showing the experimental set-up, please reference them in the Protocol.

Answer: We have made according changes in revised manuscript.

24) Please ensure that all panels of the figures are labeled and please be consistent with the labeling. Please ensure that the panel labeling is large and high contrast with the image. Some of the red panel labels are too small and hard to see.

Answer: We have made according changes in revised manuscript.

25) Can the STL file for the 3D printer be provided?

Answer：we can upload the MCS file for you, the STL file is converted by the company from the MCS file. However when we try to upload this file, the website shows that this file is over 60 MBs，so it cannot be uploaded. If you want it, maybe we can e-mail it to you.

Thank you again for your constructive comments and suggestions.

Response to Reviewer 1: Thank you very much for giving us constructive comments.

1） In the introduction, the authors are listing several issues associated with the "traditional" surgical procedure. These issues should be clearly documented, including their incidence and associated clinical implication

Answer： We have mentioned the incidence and associated clinical implication of complications of traditional PVP in the introduction part.

2） There is not information on the logistics aspects of the full process: how long does it take to obtain the 3D printed guides, and what is the risk for the skin markers to move during this period

Answer： We need about half an hour to reconstruct the 3-D model from the CT images for the 3-D printing, the 3-D printing company need about 6 hours to print 2 guide templates out and send them to our hospital; if the skin markers move during this period, it will reduce the accuracy of the localization of the operation and require more fluoroscope times to determine the suitable puncture points, even make the template failed to apply in the operation. However, this situation never happened in our 15 operations. We recommend draw the outline of the skin markers after patients lied down in prone position, then remove the skin markers, which could minimize this kind of concern.

3） The most important concern I have relates to the lack of clinical data. While the authors state in their abstract that they have seen "some significant advantages", this should be clearly reported in the manuscript. More specifically, the authors should demonstrate that this new process bring value in terms of puncture accuracy, puncture-related complications, shorten clinical procedure, minimize radiation .... How many patients were operated according to this protocol. What are the outcomes of these surgeries. What are the potential issues encounter while implementing the protocol.

Answer： Up to now, we recruited 30 patients suffering one-level OVCF and treated in our hospital, we randomly divided them into group A (underwent “three-dimensional printing individual guide template assisted Percutaneous Vertebroplasty”) and group B (underwent traditional PVP). Fluoroscopy shot times for skin puncture points (1.71±0.83 in the group A vs 5.31±1.96 in the group B, $P<0.01$), total radiation doses (4.67±2.97)mGy in the group A vs （8.22±5.24）mGy in the group B, $P<0.05$], total fluoroscopy times (16.07±2.67 in the group A vs 26.31±3.12 in the group B, $P<0.01$) and operation time [(20.07±3.65)min in the group A vs (26.19±3.12)min in the group B, $P<0.01$] were presented statistically different in the two groups. The incidence of cement leakage occurred in the group A (2/15, 13.3%) was less than that occurred in the group B (6/15, 40.0%). Our results turn out that, compared with the traditional PVP, “three-dimensional printing individual guide template assisted Percutaneous Vertebroplasty” has some advantages: less fluoroscopy shot times during operation, less total fluoroscopy dose and

shorter operation time; less incidence of cement leakage. But in this article, we are not intended to discuss about those data, we just want to introduce a new surgical method for PVP.
Thank you again for your comments and look forward to your further suggestions.

Response to Reviewer 2: Thank you very much for giving us constructive comments.

1) Introduction, page 3/4, line 40 ff and M+M page 4/5, line 76-94: The manuscript should be rather focused on the technique - the diagnosis of osteoporotic fracture and in indications for vertebroplasty are not concerned by the data reported and need not to be discussed/explained in the M+M section.

Answer： We have already deleted the diagnosis of osteoporotic fracture and the indications for vertebroplasty in our revised manuscript.

2) Is this a cadaver-study? How many cadavers were used, how many vertebrae/trajectories? How were the cadavers obtained (do you have consent from the corresponding ethical committee)?

Answer： This is a randomized, nonblinded, controlled clinical study, not a cadaver-study. Our project is still underway, up to now we have recruited 15 one-level OVCF patients undergoing PVP assisted by 3-D guide template (Group A) and 15 one-level OVCF patients treated by traditional PVP (Group B), there are totally 30 patients and 30 vertebrae in our research.

3） What kind of markers were used (it seems that the patient has to carry them a rather long time - during the printing procedure etc.)

Answer： The markers are tiny radiopaque spacers made of stainless steel. The patients may need to carried them 1-2 days from they underwent the CT scan to the beginning of the operation. Usually the first day we take the patient to undergo the CT scan, reconstruct the 3-D model in MIMICS software and send it to the 3-D printing company to print the templates, the morning of second day, we do the operation for patient.

4） What kind of CT was used? Please specify the CT-settings.

Answer： The CT machine is a 64-slice spiral CT manufactured by the General Electric Medical Group (GE, USA), tube voltage 120 KV, tube current 200 mA, scanning layer thickness 1 mm, layer spacing 1 mm.

5） It is necessary to describe the applied software (what does it do, is it commercial software or a self-programmed protocol…) before describing which keypads should be selected.
What kind of printing process (company, material …) was applied? Are the implants sterile, or can they be sterilized (by which means)?

Answer： The software is a commercial software, which is called Materialise Interactive Medical Image Control System (MIMICS) v17, it is used to modeling target vertebrae DICOM imaging into 3-D data to form the STL file. The 3-D company is Beijing Huashengputian technology co., ltd., a 3-D printing company in Beijing, China. The company use Design X software to modeling

the template. The guide template is made of polylactic acid, it can be sterilized under low temperature steam disinfection.

6） How long did it take to obtain the printed models? Is the patient thought to keep the markers all these times on the back?

Answer： We need about half an hour to reconstruct the 3-D model from the CT images, the 3-D printing company needs about 6 hours to print 2 guide templates out and send them to our hospital. The patients do need to keep the markers on the back until the procedures begin. As the markers are tiny radiopaque spacers made of stainless steel, they will not feel discomfort seriously, which will hardly affect the quality of life of patients.

7） How much and what kind of cement was infused?

Answer： We injected 2ML bone cement via each trajectory and totally 4ML bone cement were injected to one vertebra. The kind of cement is polimethylomethylacrylate cement (PMMA).

8） What were the results? - How frequent did the authors observe cement leakage or other problems.

Answer： We observe the cement leakage or other problems during the whole operation procedure, and one day after the operation. The incidence of cement leakage occurred in the group A (2/15, 13.3%) was less than that occurred in the group B (6/15, 40.0%).

9） The discussion has than to be focused on the data provided - the misplacement and leakage values in literature should be compared to those found in the pilot-study, as yet it is not clear that the proposed technique does improve those rates.

Answer： Up to now, we recruited 30 patients suffering one-level OVCF and treated in our hospital, we randomly divided them into group A (underwent “three-dimensional printing individual guide template assisted Percutaneous Vertebroplasty”) and group B (underwent traditional PVP). Fluoroscopy shot times for skin puncture points (1.71±0.83 in the group A vs 5.31±1.96 in the group B, $P<0.01$), total radiation doses (4.67±2.97)mGy in the group A vs （8.22±5.24）mGy in the group B, $P<0.05$], total fluoroscopy times (16.07±2.67 in the group A vs 26.31±3.12 in the group B, $P<0.01$) and operation time [(20.07±3.65)min in the group A vs (26.19±3.12)min in the group B, $P<0.01$] were presented statistically different in the two groups. The incidence of cement leakage occurred in the group A (2/15, 13.3%) was less than that occurred in the group B (6/15, 40.0%). Our results turn out that, compared with the traditional PVP, “three-dimensional printing individual guide template assisted Percutaneous Vertebroplasty” has some advantages: less fluoroscopy shot times during operation, less total fluoroscopy dose and shorter operation time; less incidence of cement leakage. But in this article, we are not intend to discuss about those data, we just want to introduce a new surgical method for PVP.

Thank you again for your comments and look forward to your further suggestions.

Response to Reviewer 3: Thank you for your thought-provoking questions and giving us constructive comments.

Question: The technique described in this manuscript includes several steps of diagnostics, digital planning, 3D-printing, sterilization and application of a template onto the patient's skin for optimized entry points for percutaneous vertebroplasty. Vertebroplasty is quite a simple and easy to learn surgical method that must be performed under fluoroscopy, because bone cement is injected into the patient. Does the complex planning, fabrication and application of templates, which is time consuming, really justify the use of this patient-specific technique for a simple surgical procedure like vertebroplasty? A one-level vertebroplasty with a bipedicular approach can be done in no more than 15 minutes or even less. What is the time needed for the whole planning, printing, sterilization process of the template? Template-guided techniques are normally designed to apply a template on a bone for firm contact to optimize screw placement accuracy or let's say osteotomy accuracy. In the technique described here, the template is placed on soft tissue, namely the skin of the patient with underlying soft tissue (fat, muscles), which should be critically discussed as this might negatively influences the trajectory of the trocars during surgery. Even more, the template may show signs of deformation after sterilization, which further worsens its accuracy. Another concern is that you still depend on flucoroscopy to visualize the final position of the trocars and the distribution of the bone cement injected. Under these circumstances, given the presurgical effort this technique demands, and the supposed marginal reduction of radiation exposure, it should be critically discussed whether this technique is in any form beneficial in daily practice, which I personally doubt.

Answer： First, we agree with you that applying 3-D guide template into one-level OVCF patient may not save a huge amount of time and reduce radiation exposure massively, however, in our randomized, nonblinded, controlled clinical study, those data do present the statistical difference: up to now, we recruited 30 patients who suffered one segment OVCF and treated in our hospital, we randomly divided them into group A (underwent “three-dimensional printing individual guide template assisted Percutaneous Vertebroplasty”) and group B (underwent traditional PVP). Fluoroscopy shot times for skin puncture points (1.71±0.83 in the group A vs 5.31±1.96 in the group B, $P<0.01$), total radiation doses (4.67±2.97)mGy in the group A vs（8.22±5.24）mGy in the group B, $P<0.05$], total fluoroscopy times (16.07±2.67 in the group A vs 26.31±3.12 in the group B, $P<0.01$) and operation time [(20.07±3.65)min in the group A vs (26.19±3.12)min in the group B, $P<0.01$] were presented statistically different in the two groups. The incidence of cement leakage occurred in the group A (2/15, 13.3%) was less than that occurred in the group B (6/15, 40.0%).

Second, currently, our clinical task research is focus on applying 3-D guide template into one-level OVCF patient, but in the future we will apply the guiding template into complicated OVCF patients with severe osteoporosis, severe kyphosis, scoliosis or multi-segment fractured vertebra. Even the experienced surgeons take many fluoroscope times and consume a pretty long time to deal with those cases throughout the operations. In view of these difficult cases,

“Three-dimensional printing guide template assisted percutaneous vertebroplasty” may offer a safer and more precise puncture approach than traditional procedure, also do better in saving operation time and reducing radiation exposure.

Third, preoperative design in MIMICS provides an intuitive and visual puncture approach of percutaneous vertebroplasty, which may help fresh surgeons learn about the anatomy of vertebra and simulate the optimal puncture trajectory, moreover it can also optimize the learning curve of this kind of procedure for young surgeons.

Additionally, you mentioned the template may show signs of deformation after sterilization, we also agree with you that after low temperature steam disinfection, the templates may be slightly deformable, however in all of our cases, this kind of deformation hardly affects the puncture accuracy. We will explore a much more suitable material to print 3-D templates.

Thank you again for your comments and look forward to your further suggestions.

7-16-2019

Dear Editor:

I really appreciate your constructive comments and suggestions on the manuscript entitled "Three-dimensional printing guide template assisted percutaneous vertebroplasty". I have read comments from you carefully and made corresponding changes. We have tried our best to revise our manuscript according to the comments as followed.

I would like to express my great appreciation to you for your comments on our paper. Look forward to hearing from you soon.

Sincerely,

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1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.
   Answer: We have thoroughly proofread the manuscript.

2. Please provide at least 6 keywords or phrases. There are only 4.

Answer: three-dimensional printing technology; three-dimensional printing guide template; percutaneous vertebroplasty; osteoporotic vertebral compression fracture; spinal surgery; precision surgery

3. Please provide a Summary before Abstract to clearly describe the protocol and its applications in complete sentences between 10-50 words: “Here, we present a protocol to …”
   Answer: Herein, we present this protocol to introduce step by step the appliance of three-dimensional printing guide template for the percutaneous vertebraplasty. A patient with T11 vertebral compression fracture was selected as case study.

4. For in-text referencing, please remove the brackets before and after the reference numbers.
   Answer: We have made according changes in revised manuscript.

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   Answer: We have made according changes in revised manuscript.

6. Please revise the text in Protocol to avoid the use of any personal pronouns (e.g., "we", "you", "our" etc.).
   Answer: We have made according changes in revised manuscript.

7. For steps that are done using software, a step-wise description of software usage must be included in the step. Please mention what button is clicked on in the software, or which menu items need to be selected to perform the step.
   Answer: We have made according changes in revised manuscript.

8. Step 1.3: Please write this step in the imperative tense.
   Step 1.4: Please write this step in the imperative tense.
   Step 2.1: Please write this step in the imperative tense.
   Step 2.2: Please write this step in the imperative tense.
   Step 4.2: Please write this step in the imperative tense.
   Step 5.1: Please write this step in the imperative tense.
   Step 5.2: Please write this step in the imperative tense.
   Step 5.3: Please write this step in the imperative tense.
   Step 5.4: Please write this step in the imperative tense.
   Step 5.5: Please write this step in the imperative tense.
   Step 5.6: Please write this step in the imperative tense.
   Step 5.7: Please write this step in the imperative tense.
   Step 5.8: Please write this step in the imperative tense.
   Answer: We have made according changes in revised manuscript and marked in red

color.

9. Please provide the Figure and Table Legends after the protocol in the manuscript.
Answer: We have made according changes in revised manuscript.