**Peer Review File**

Article Information: https://dx.doi.org/10.21037/jss-23-93

**Reviewer A**

**Comment 1: In the discussion section the cost-effectiveness of the CF/PEEK implants should be mentioned.**

**Reply 1:** Thank you for this suggestion. In Australia, there is no difference in cost between an equivalent CF/PEEK and titanium pedicle screw system. This has been clarified in line 96.

**Changes in the text:**

(Page 3, Line 96) …instrumentation relative to titanium. In Australia, there is no cost difference between CF/PEEK and titanium as materials for pedicle fixation systems.

**Comment 2: To my opinion, missing references should be added, like:**

**Reply:** Thank you for this suggestion. There have been several papers since the conception of this study that have added to the literature on CF/PEEK as a material for pedicle screw systems. The suggested references have been included in the following area.

**Changes in the text:**

(Page 3, Line 88) …biocompatible and osseointegrative properties for pedicle fixation(9,10). Preliminary single-arm studies have demonstrated safe usage of CF/PEEK pedicle screws and other instrumentation for primary and metastatic spinal neoplasms, and early detection of recurrence where long term follow up is anticipated (11-13). However, a systematic review by Khan et al(14) concluded that there was insufficient evidence that postoperative imaging quality translated to benefits in oncological outcomes such as local control and survival, making it difficult to justify usage given its high cost and underdeveloped instrumentation relative to titanium.

**Reviewer B**

**Comment 1: Line 31: please add "screw" after "…longitudinal axis of…"**

**Reply:** Thank you for identifying this error. We have added this to the manuscript.

**Changes in the text:**

(Page 1, Line 31) Dose profiles through the screw, tulip and longitudinal axis of the screw were acquired**…**

**Comment 2: Line 81: please spell out CT-HU as it is the first appearance of the abbreviation in the text.**

**Reply:** Thank you for this suggestion. We have included CT-Hounsfield Units as the full spelling of CT-HU in line 82

**Changes in the text:**

(Page 3, Line 82) … dose calculation algorithms based on converting CT-Hounsfield Units (CT-HU) to tissue density, distorting …

**Comment 3: Line 85: please rename "figure 2" as "figure 1" as it is the first figure cited in the text. Please do the same for figure 1 in Methods (line 128).**

**Reply:** Thank you for identifying this. The included "figure 2" is in error. The "figure 1" in line 149 of the Methods section is correctly referencing the first figure included.

**Changes in the text:**

(Page 3, Line 86) … and delivery, and postoperative monitoring for local recurrence. Carbon fibre-…

**Comment 4: Could you please render a picture of or explain about the configuration of experimental construct. Where was the crosslink bar placed, at the end or in the middle of the construct?**

**Reply:** Thank you for this suggestion. On repeat review of the methodology, a crosslink bar was not used in both experimental constructs. This has been removed in lines 205 – 206. Pictures of the experimental constructs have been included for reference as figures 3 and 4 in line 206, along with an explanatory caption starting on line 625. The previous figures 3 and 4 are now renamed 5 and 6.

**Changes in the text:**

(Page 5, Line 204) … quality of planning CT scans. Both models …

(Page 5, Line 205) …pedicles and 2 screws in the right pedicles – connected by 2 longitudinal rods made of the same material as the pedicle screws (figures 3 and 4).

(Page 18, Line 625)

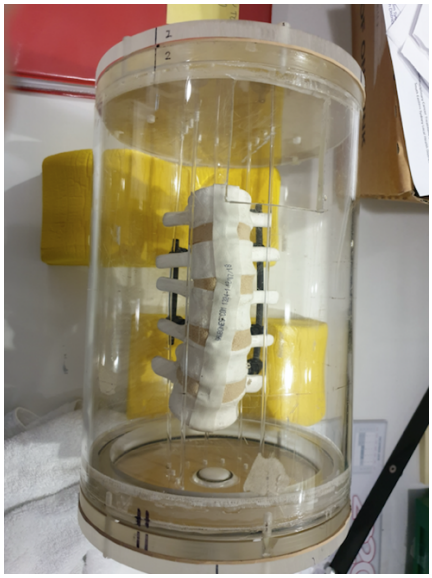

**Figure 3. Experimental construct of lumbar spine model instrumented with titanium pedicle screws.** 4 pedicle screws (CarboClearTM, CarboFix Orthopedics, Herziliya, IL, USA) were inserted into the left pedicles and 2 pedicle screws were inserted into the right pedicles, and connected by 2 longitudinal rods. The model was suspended on plastic rods and immersed in water.

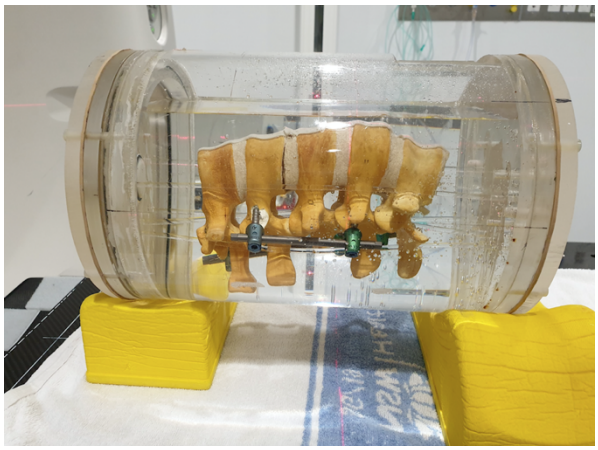

**Figure 4. Experimental construct of lumbar spine model instrumented with CF/PEEK pedicle screws.** A similar configuration to figure 3 is shown with 4 pedicle screws (SmartLoc, A-Spine, New Taipei City, Taiwan) inserted into the left pedicles and 2 pedicle screws inserted into the right pedicles, and connected by 2 longitudinal rods.

**Comment 5: It was noted that 4 patients were selected from a cohort of patients who underwent radiotherapy between December 2009 and May 2020. It is assumed that the patient with CF/PEEK implant (more recent technology) had the procedure done later than the other three scanners' X-ray beam energy over a decade affect the quality if images and the calculation of artefact volume? If so, what measures did the researchers take to mitigate such a measurement bias?**

**Reply:** Thank you for this comment. The time interval over which the review of medical records was performed ranged from December 2009 and May 2020. The patients that met this inclusion criteria had their CT imaging between 2017 – 2020. Over a shorter period of time, the beam energy of the X-ray scanners would not have changed significantly to alter image quality and calculation of artefact volume. The report has been amended in line 242 to clarify the time interval, and another sentence in line 313 has been included that reports the time interval over which eligible CT scans had been performed.

**Changes in the text:**

(Page 6, Line 242) A retrospective review of medical records from December 2009 to May 2020 was performed to identify…

(Page 8, Line 313) …plans available for review on the treatment planning software. The radiotherapy plans were based on CT scans that were performed during the period of 2017 – 2020. There were…

**Comment 6: Please explain how the control patient was selected. Was a random patient selected with CT images who had a spine tumour resected in the same regions?**

**Reply:** Thank you for this comment. The control patient was a patient that had a spinal neoplasm resected in the lumbar region with no pedicle screw fixation, and had a CT scan available for postoperative radiotherapy planning. This additional information has been included in line 246.

**Changes in the text:**

(Page 6, Line 246) … sampling the same regions in a control patient who had undergone surgical resection of a spinal neoplasm with no spinal implants, and had a CT scan for postoperative radiotherapy planning available.

**Reviewer C**

**Comment 1: Line 31: "Dose profiles through the screw, tulip and longitudinal axis of were acquired with […]", please verify the correctness of the sentence.**

**Reply:** Thank you for identifying this error. This has been changed in line 31.

**Changes in the text:** (Page 1, Line 31) Dose profiles through the screw, tulip and longitudinal axis of the screw were acquired**…**

**Comment 2: Line 85: the authors refer to figure 2, further explanations regarding the congruence between the paragraph and the figure contents are advisable.**

**Reply:** Thank you for identifying this error. This has been changed in line 85.

**Changes in the text:** (Page 3, Line 86) … and delivery, and postoperative monitoring for local recurrence. Carbon fibre-…

**Comment 3: Regarding SQUIRE 2.0 checklist, the pages and lines under "Reported on Page Number/Line number" are not in accordance with the manuscript. I suggest a cross-verification of the layout.**

**Reply:** Thank you for identifying this. The line numbers in the submitted manuscript do not correlate with the line numbers in the manuscript you have reviewed. The SQUIRE 2.0 checklist will be resubmitted with line numbers based on the JSS-23-93-CL-peer-review version that was provided for review.

**Changes in the text:** Please see the updated SQUIRE 2.0 checklist.

**Comment 4: The section "1.3 Objective" describes the aim of the work in a general way. It would be useful to anticipate a more detailed description of the objective, by referring to the accomplished dosimetric and artefact image quality analyses, to better guide the reader and make the subsequent sections more seamlessly connected.**

**Reply:** Thank you for this suggestion. Additional sentences have been added to this paragraph to describe the objective in more detail, beginning on line 129.

**Changes in the text:**

(Page 4, Line 129) Radiotherapy planning was investigated by quantifying the extent of imaging artefact on planning CTs in both lumbar spine models and patient scans at various anatomical landmarks. Radiation delivery was assessed by comparing the accuracy of TPS predicted dose to measured radiation doses for both materials.

**Comment 5: Within the manuscript please ensure consistency in using "Hounsfield unit" abbreviating it as either HU or CT-HU. Do the authors intend to convey a distinction between these two abbreviations?**

**Reply:** Thank you for this suggestion. All instances of HU used in the manuscript refer to CT-Hounsfield units. HU has been amended to CT-HU in lines 154, 155, and 423.

**Changes in the text:**

(Page 4, Line 154) … Because the RayStation CT-HU-to-mass density calibration does not extend to titanium's CT-HU value of 6000 CT-HU. This involved …

(Page 11, Line 423) … from normal tissue exceeded 100 CT-HU. While artefact volume reduction …

**Comment 6: Line 126: typo error "were centred".**

**Reply:** Thank you for identifying this error. This has been corrected in line 147.

**Changes in the text:**

(Page 4, Line 147) (SmartLoc, A-Spine, New Taipei City, Taiwan) were centered on the beam central axis…

**Comment 7: Line 131 – 133: The passage "Because the Ray Station […] pre-defined density" is not fully clear and requires major insights.**

**Reply:** Thank you for this comment. This passage attempted to explain a correction that was performed in the treatment planning software when modelling the titanium pedicle screw. Titanium has a natural CT-HU value of > 6000, which is beyond the range where RayStation can correlate CT-HU to mass, the variable that is used to predict radiation dose. The radiotherapist must manually contour the titanium screw and reassign titanium to the correct density preset for the dose plan to generate. This has been clarified in line 153.

**Changes in the text:**

(Page 4, Line 153) … Laboratories, Stockholm, Sweden). Material override was performed for the titanium screws, because the RayStation CT-HU-to-mass density calibration curve does not extend to titanium's CT-HU value of 6000 CT-HU. This involved manually contouring the titanium screws and reassigning them to its density of 4.540 g/cm$^3$. Visible artefact volume was also contoured and reassigned to the density of water (1 g/cm$^3$). The CF/PEEK screws did not require material override.

**Comment 8: A rationale motivation regarding the EBT3 films positioning at 2, 10, and 50 mm has not been indicated. Are these distances related to vertebral anatomical shapes and measures, too?**

**Reply:** Thank you for this comment. The radiochromic films used to measure dose were placed between the Solid Water ® blocks, which are manufactured at thicknesses of 2, 10 and 50 mm. These distances are not related to vertebral anatomical shapes and measures. A sentence in line 174 has been included that explains this.

**Changes in the text:**

(Page 5, Line 174): Solid Water ® slabs, orthogonal to the beam direction. These distances were chosen so that the GafChromic™ films could be placed between Solid Water® blocks, which are manufactured with depths of 2, 10 and 50 mm.

**Comment 9: Line 142-144: the passage needs to be better explained for the sake of clarity. The passage misses of a clear definition of the reference depth and the isocentre. Moreover, observing Figure 2, it is not clear where the screw dose profile must intercept the screw thread. Please provide further details.**

**Reply:** Thank you for this comment. Lines 178 - 180 attempt to describe the process of creating a calibration curve so that optical changes in the radiochromic films could be converted into a received radiation dose. This was achieved by delivering radiation that would be correspond to known doses (up to 200 cGy) received by the radiochromic films at a depth of 1.5 cm. Lines 178 - 180 have been rewritten to clarify this. Regarding figure 2, we realise that the outline of the screw and screw thread is not very clear when the axes for the profiles have been drawn. We have revised figure 2 to include the original picture without modifications, so that the intersection between the dose profile and screw thread is more clear.

**Changes in the text:**

(Page 5, Line 178) A dose calibration curve of optical density change in the radiochromic film to received dose was created for the 6 MV beam by delivering known doses up to 200 cGy to the isocenters of separate EBT3 GafChromic™ films at a fixed depth of 1.5 cm (figure 2).

(Page 17, Line 617)

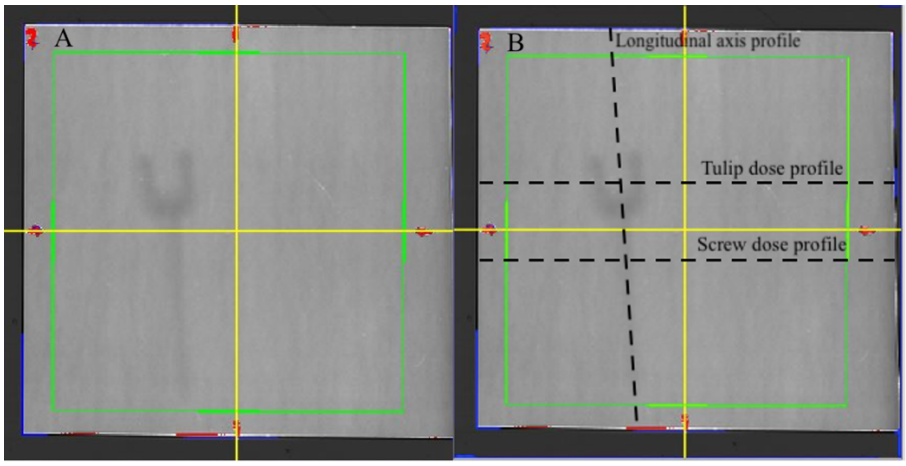


**Figure 2. Digitized EBT3 film of titanium pedicle screw from a 6 MV beam at 10 mm depth.** The isocenter is indicated by the intersection of the yellow lines. The dotted lines in Figure 2B indicate dose profiles through the screw and tulip, as well as the longitudinal axis of the screw.

**Comment 10: Please indicate the material of the tulip. Is it also made in CF/PEEK? The percentage of CarbonFiber is the same of the pedicle screw thread? Eventually, further discussion regarding this aspect should be mentioned in the Discussion section.**

**Reply:** Thank you for this suggestion. The tulips are made of the same material as the screws in both of the arms, and have the same composition of CF/PEEK and titanium. An additional sentence in line 149 has been added to clarify this.

**Changes in the text:**

(Page 4, Line 149) …Water ® below (figure 1). These screws were chosen as the tulips have the same composition as the screws. A radiotherapy plan …

**Comment 11: Please indicate the material of the longitudinal rods and of the cross-link used in the Sawbones phantom. Why an asymmetrical positioning of the screws has been performed on the lumbar models? Why was a cross-link rod also added? An explanation of this rationale should be provided.**

**Reply:** Thank you for this comment. The longitudinal rods were made of the same material as the pedicle screws, so that this investigation would allow comparison of entire pedicle fixation systems. A sentence has been included in line 205 to clarify this.

**Changes in the text:**

(Page 5, Line 205) …pedicles and 2 screws in the right pedicles – connected by 2 longitudinal rods made of the same material as the pedicle screws (figures 3 and 4).

**Comment 12: Few additional information regarding the design of the regions of interest (ROI) for the artefact index is needed:**

**It is not clear whether the ROI was manually assessed or computed by a machine.**

**Reply:** Thank you for this comment. The ROI was manually identified, and a script was used to pull the CT-HU values of each voxel to produce a standard deviation for all the voxels included in that ROI. The paragraph beginning in line 220 has been altered to clarify this.

**Changes to the text:**

(Page 6, Line 220) Scans were transferred onto RayStation, and the presence of artefact was assessed by manually identifying sampling 4 spherical regions of interest (ROI) of radius 0.5 cm at each instrumented vertebral body level – in the vertebral canal, and 0.5 cm posterior, medial and lateral to the protruding tulips of the screw (figure 5). For the vertebral canal ROI, a sphere with 0.5 cm radius that would fit in the vertebral canal was identified. For the ROIs defined relative to the tulips, the transverse and longitudinal axes through the tulip (as indicated by the dotted lines in figure 5) were drawn, and the centre chosen such that the circumference of the ROI would be 0.5 cm away from the extremity of the tulip. The standard deviations of CT-HU values in each ROI were obtained from the software was used to calculate an artefact index (AI) for each region.

**How was the centre of the ROI defined?**

**Reply:** For the vertebral canal ROI, a sphere with 0.5 cm radius that would fit in the vertebral canal was identified. For the ROIs defined relative to the tulips, the transverse and longitudinal axes through the tulip (as indicated by the dotted lines in figure 5) were drawn, and the centre chosen such that the circumference of the ROI would be 0.5 cm away from the extremity of the tulip. The paragraph beginning in line 177 has been altered to clarify this.

**Changes to the text:** please see changes in text in response to comment 12 (i) above.

**Specific mutual distances from the tulip and screw axes have been considered?**

**Reply:** Thank you for this comment. A specific mutual distance could not be reliably identified due to the differences in the angulation between the pedicle screws and the orientation of their tulips in both model and patient scans.

**Has the reproducibility of this methodological pipeline been investigated?**

**Reply:** Thank you for this comment. We hope that the methodology has been sufficiently explained that it is reproducible for future investigators.

**Why do the authors expect small standard deviations within the ROI?**

**Reply:** Thank you for this comment. In regions without artefact, the ROI should lie entirely within a single tissue type (e.g. background tissue), which is relatively homogeneous. This would result in a small standard deviation in the background ROI.

**In figure 3B the left medial to tulip region seems to intersect both soft tissues and the vertebral posterior pedicle, in that case, the AI could not be small even without artefact.**

**Reply:** Thank you for this comment. Figure 5B is a graphical representation of how the ROI was determined. In the collected data from the patient and model CT scans, the ROIs did not overlap bone and soft tissue.

**Comment 13: Table 1 reports a comparison of the mean absolute differences between measured and predicted doses for the titanium (with and without override), why data for CF/PEEK are not also reported?**

**Reply:** Thank you for this comment. Dose differences between measured and predicted doses for CF/PEEK screws are reported in the columns under CF Mean (SD). Material override was not performed for the CF/PEEK screws because the CT-HU value of CF/PEEK is < 4000 CT-HU, which is within the CT-HU-to-mass density calibration curve of RayStation. Hence there was only one difference in means to report.

**Comment 14: The description of Table 2 (lines 234-235) as well as its caption is not totally clear. Please consider improving these parts to better explain the data.**

**Reply:** Thank you for this comment. Relative dose differences were meant as percentage dose differences relative to the measured dose. The results of table 2 show that when dose differences as a percentage of the measured dose were considered, the results for CF/PEEK were non-inferior to titanium. To clarify this, relative dose differences has been replaced with the term "percentage dose differences between measured and predicted doses (relative to the measured dose)" in lines 289 – 290 and the caption for table 2 in line 497.

**Changes in the text:**

(Page 7, Line 289) Percentage dose differences between measured and predicted doses (relative to the measured dose) were…

(Page 16, Line 598) Table 2: Comparison of the percentage dose difference between measured and predicted doses (relative to measured dose) measured in axes through the tulip, screw and longitudinal axis.

**Comment 15: Line 287: it is not fully clear what the "Dose difference" refers to.**

**Reply:** Thank you for this comment. Dose difference in this sentence refers to the observed difference between measured and predicted doses. The term "dose difference" has been altered to "the observed difference between measured and predicted doses" in line 351.

**Changes in the text:**

(Page 9, Line 351) The observed difference between measured and predicted doses can also be explained…

**Comment 16: The discussion shows the limitations of Monte Carlo simulations for calculating dose distribution. A brief comparison with the used TPS could enrich the discussion. For example, what is its computational cost and time performance?**

**Reply:** Thank you for this suggestion. Algorithms such as the collapsed cone algorithm are more efficient in calculating a dose plan compared to the gold-standard Monte Carlo simulations, as the latter includes more variables and particle histories to generate more accurate plans. Simulation times can be further altered by setting a desired level of statistical uncertainty, which is inversely proportional to computational time. However, the magnitude of improvement varies with the complexity of the plan and is difficult to quantify. Further discussion regarding this point has been included in line 384.

**Changes in the text:**

(Page 10, Line 384) The collapsed cone algorithm exponentially reduces computational time by reducing the number of scatter directions that photons are simulated. When used to calculate a radiation plan on the same model, Pereira et al(23) found that a Monte Carlo plan could take more than 2 hours to compute, depending on the set level of statistic uncertainty, compared to less than 4 minutes with a collapsed cone algorithm. Literature investigating …

**Comment 17: Line 365-368: the authors state that thanks to the introduction of the absolute value, the new formula used for AI (line 184) allows the "inclusion of results where the standard deviation of CT-HU in the region of interest was higher than the standard deviation of CT-HU in the control". From a mathematical perspective, in this case, the difference of squares would already be positive without the necessity of the absolute value operation. Please, provide some clarification regarding this statement.**

**Reply:** Thank you for this comment. The formula used to calculate artefact index always subtracts $SD_{background}$ from $SD_{ROI}$ in that order, hence the absolute value was required so that the square root function can still perform functions where results where $SD_{ROI} < SD_{background}$ , can still be included.

**Reviewer D**

**Comment 1: Very nice study BUT 70% of what I read is "Greek" to my cerebral processes.**

**Reply:** Thank you for this comment. We are sorry that some of the terminology is confusing to understand. In the process of addressing the other reviewers' comments we have tried to simplify the intricacies of radiotherapy planning. We would appreciate your input onto what terms should be explained to assist clinical spine specialists in understanding this study.

**Comment 2: Can the authors at least show vivid CTScan images of the artefacts created by CF/PEEK versus Titanium screws in their models.**

**Reply:** Thank you for this comment. An additional figure (described in line 414) has been included in the discussion to demonstrate the difference in artefacts generated on CT.

**Changes in the text:**

(Page 11, Line 414) … and the tissue around the protruding tulips (see figure 7).

(Page 23, Line 651)

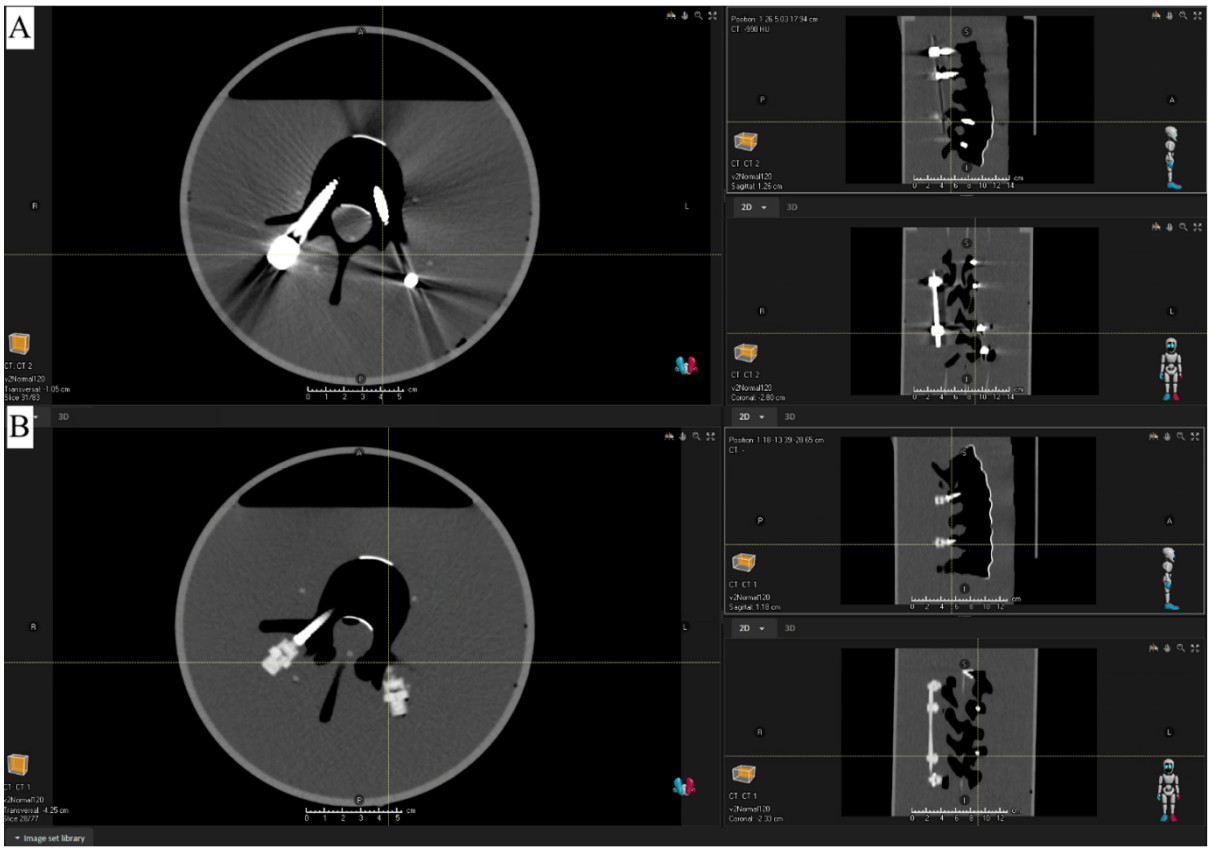


**Figure 7. CT scans of the lumbar spine models instrumented with titanium (Figure 7A) and CF/PEEK (Figure 7B) pedicle fixation systems.** Axial and sagittal views are shown. Significant streaking artefact is generated by the titanium screws, drastically altering the CT-HU values of the surround tissue.

**Comment 3: Wouldn't it be more realistic as well to have applied the screw to human cadavers and take CTScan of the cadavers to simulate real body-anatomical-implantation models to compare artefacts created by the spine implants in contention.**

**Reply:** Thank you for this comment. Compared to other literature, pedicle screw systems had not been investigated while they had been instrumented into a vertebral spine, which mimics how these pedicle screw systems would be implemented in a clinical setting. The use of cadavers to simulate real body a step that mirrors the clinical approach would be an appropriate improvement on this current methodology to translate findings into current clinical practice.

**Comment 4: General readers of this journal are clinical spine specialists with little or no knowledge in the language of medical physics or radiation technology. Can most terms be explained in simpler terms.**

**Reply:** Thank you for this comment. Through the process of addressing the other reviewers' comments, we have further elaborated on some of the concepts in medical physics and radiation technology where the majority of the clinical benefits of CF/PEEK lie. We would appreciate your input on what terms could be further explained to assist the target audience's understanding.