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Peer Review File

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Reviewer A

Comment 1: The authors present a finite element study on lumbosacral bisegmental (L4-S1) or multilevel fusion (L3-S1) without or with different degrees of PMMA cement augmentation of pedicle screws.

With an aging population with mainly degenerative spine diseases this study sheds light on a very important issue.

Spinal instrumentation in an osteoporotic spine should be avoided by all means, but is inevitable in some cases. The complication rate rises with decreasing bone mineral density with regard to implant failure, esp. screw loosening, screw cut-out.

PMMA pedicle screw augmentation is a viable and effective method to decrease the rate of implant failure. However, the risk of cement leakage rises with increasing numbers of augmented pedicle screws, with sometimes dire or even lethal outcome.

Therefore the authors used the finite elements model to simulate biomechanical stability using PMMA augmentation in all implanted PS compared to PMMA augmentation of only the most cranial and caudal PS compared to no cement augmentation.

The authors found only slight increases in loading forces with the B models, where only the uppermost and lowermost PS were augmented.

This technique therefore seems to be almost equally effective in biomechanical stability than augmenting every PS with a reduced risk of possible cement leakage.

Reply 1: Thank you very much for your approval. We appreciate that the major merits of our work have been recognized and recommended publication by you. We will improve our paper according to your good valuable advice.

Comment 2: However, several concerns arise while reading the manuscript:

There were possible mistakes / errors detected in the figures as stated below:

Possible Errors:

1) Labeling of images a to c in figures 3 and 4 has slippe to the right.
2) Why is there labeling a to c in figure 5? it depicts ROM of segments L3-4, L4-5, L5-S1 and not of models a to c.
3) Model labeling in figures 6,7 and 8: Label for model C1 and C2 are missing and need to be added

Reply 2: Thank you for your careful review and kind reminder. We have corrected the mistakes as below.

Labeling of images a to c in figures 3 and 4 has marked in the right place now.

The surgical models were constructed base on the intact lumbosacral model. And according to previous finite element studies, through the validation of the intact lumbosacral model, it can show whether or not the model can simulate the physiological activity of lumbar spine and be used for further analysis (Figure 1) [1,2]. Therefore, figure 5 shows the comparison of the range of motion in different segments between the intact model and the previous reports.

Label for model C1 and C2 has been added in figures 6,7 and 8.

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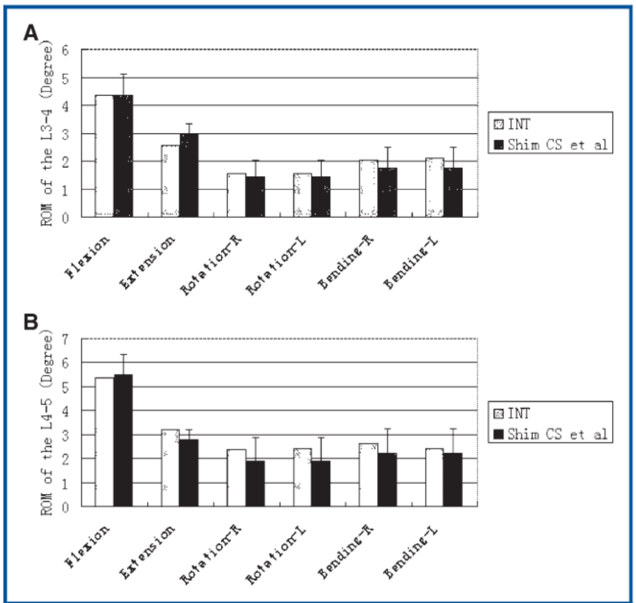

FIGURE 3. *Comparison of range of motion (ROM) between the intact model (INT) and the in vitro study at L3-4 (**A**) and L4-5 (**B**) levels. L, left; R, right.*

Figure 1: Validation of the intact model in previous study showed the comparison of the range of motion in different segment. [1].

Changes in the text: See figure 3, figure 4, figure 6, figure 7, and figure 8.

Comment 3: Furthermore, I strongly advise to proofread the manuscript by a native speaker to improve language, grammar and most importantly understandability of the contents.

Reply 3: Thank you for your good comment. We have revised the manuscript carefully to improve the understandability of the contents. And we also asked for the professional help in revising this manuscript by Editage (Figure 2). The amendments are highlighted in 'track changes' mode in the revised manuscript.

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CERTIFICATE OF ENGLISH EDITING

This document certifies that the paper listed below has been edited to ensure that the language is clear and free of errors. The edit was performed by professional editors at Editage, a division of Cactus Communications.The intent of the author's message was not altered in any way during the editing process. The quality of the edit has been guaranteed, with the assumption that our suggested changes have been accepted and have not been further altered without the knowledge of our editors.

TITLE OF THE PAPER

Selective cement augmentation of cranial and caudal pedicle screws provides comparable stability to augmentation on all segments in the osteoporotic spine: a finite element analysis

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Vikas Narang,
Chief Operating Officer,
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May 30, 2020

Figure 2: Editage certification of this manuscript

Changes in the text: See the revised traces in the manuscript.

Comment 4: For improved visualization I would suggest to omit figure 5 and add 2 more figures with stress distribution images of the B and C models.

Reply 4: Think you for your suggestion, but we cannot fully agree with the comment. Figure 5 comparison of ROM between the intact model and previous published studies. The validation of the intact lumbosacral spine model is a necessary condition for further analysis in finite element study. Therefore, we think it is inappropriate to omit figure 5. Maybe use table instead of picture would be a more reasonable alternative.

In term of add 2 more figure to demonstrate stress distribution on screws. We have added pictures in the manuscript as below.

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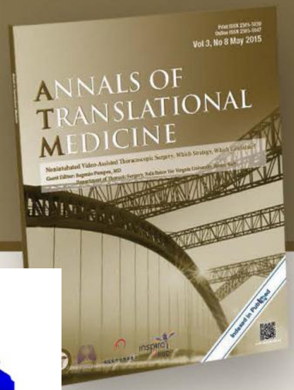

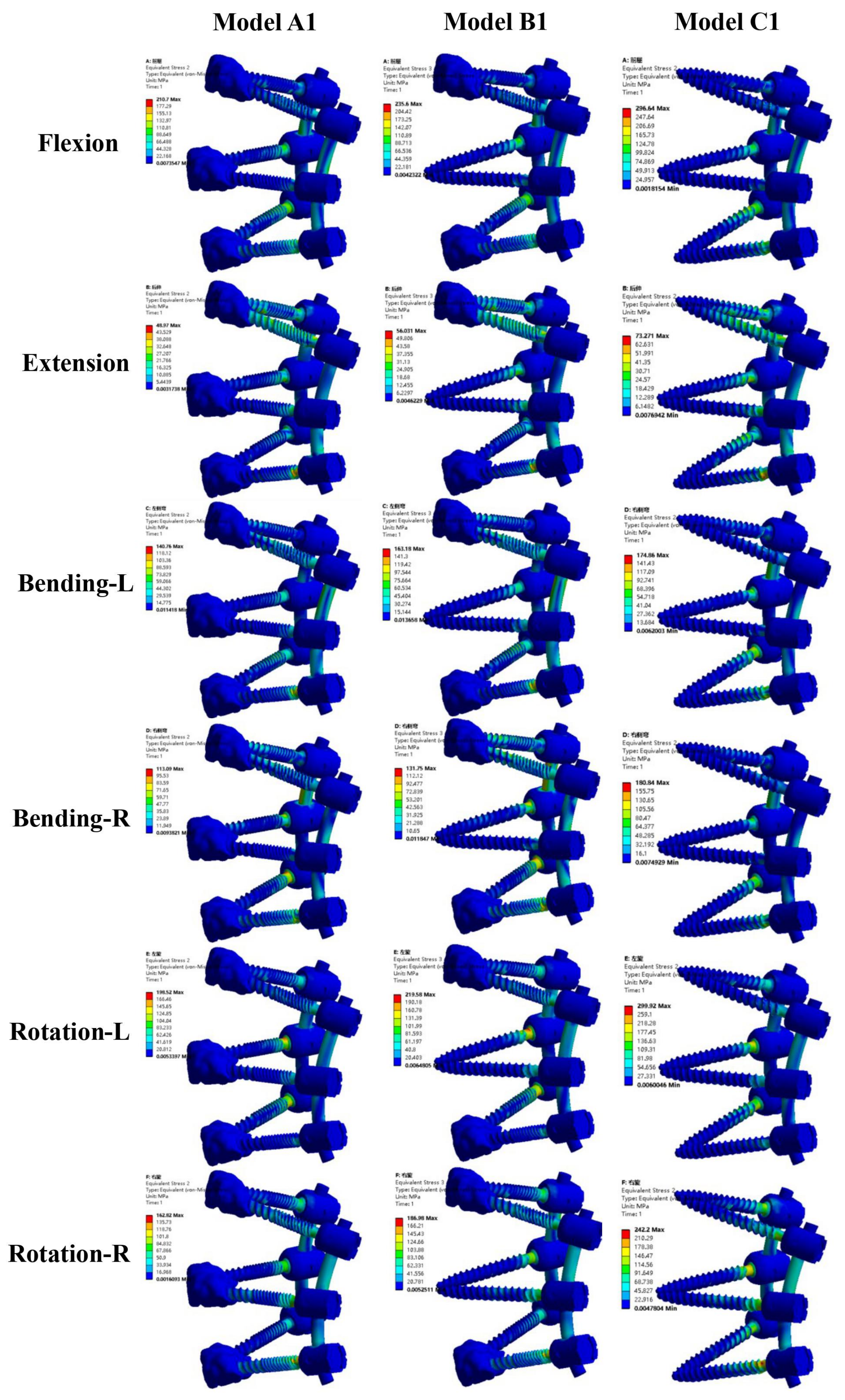

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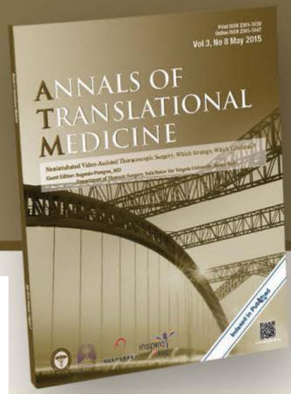

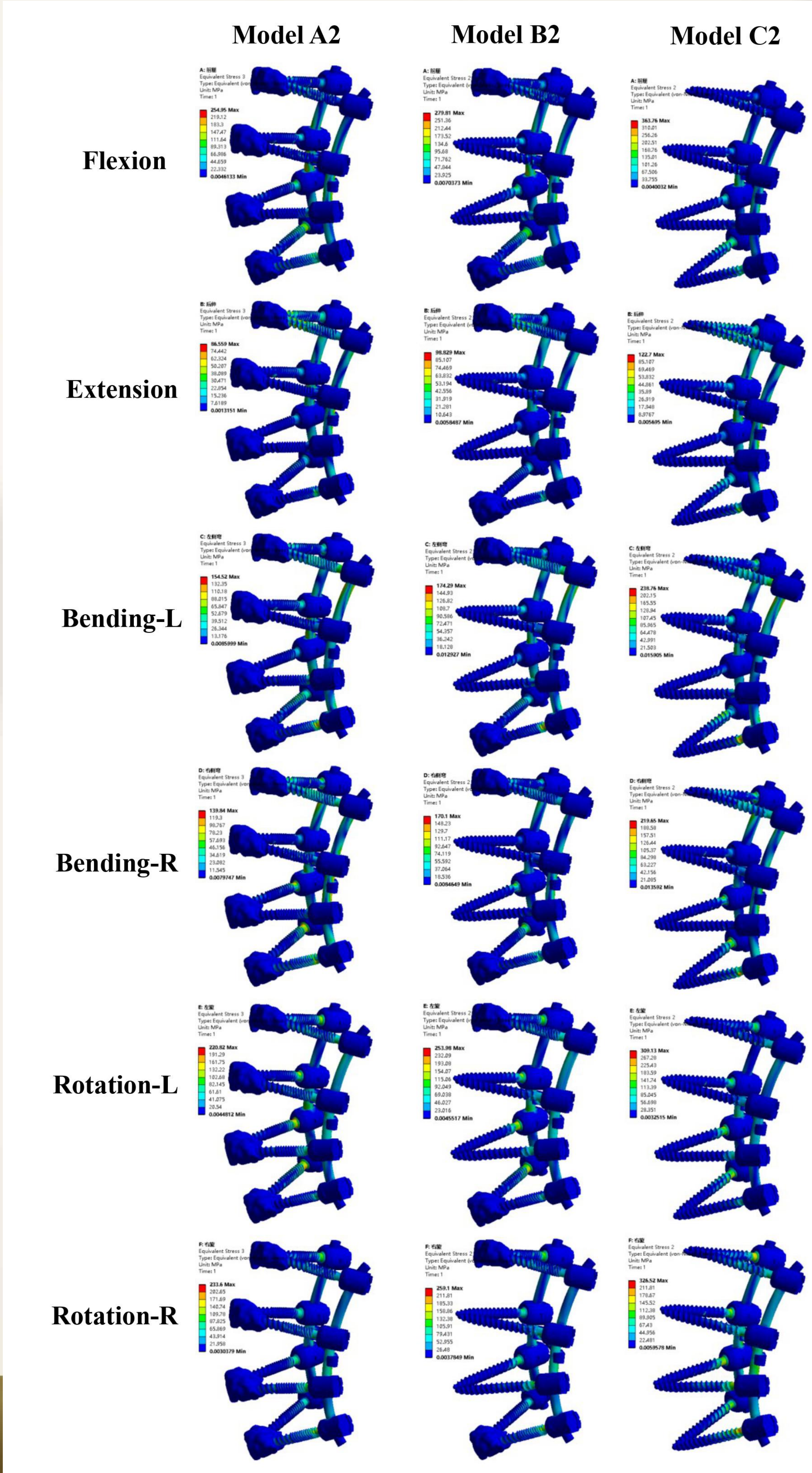

Figure 3: The stress distribution on pedicle screw shows that the stress is mainly distributed at the screw head, the cranial and caudal screws, and rods.

References

[1] Hao X , Hao T , Xuemei G , et al. Biomechanical Comparison of Posterior Lumbar Interbody Fusion and Transforaminal Lumbar Interbody Fusion by Finite Element Analysis[J]. Neurosurgery. 2013;72(1 Suppl Operative):21-6.

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Reviewer B

Comment 1: The authors performed a finite element analysis looking at the use of pedicle screw in degenerative lumbosacral fixation with different patterns of cement augmentation. The authors showed that selective augmentation of the cranial and caudal levels could provide comparable biomechanical stability than augmentation of all instrumentation levels. A good study overall, albeit several issues exist-

1. Quite a few sentences were confusing to read, e.g. "The ROMs of Model B and Model A are similar in each direction, while that of 34 model C and model A is significantly larger", "Epidemiological studies showed that the time of surgery significantly increased from 191 54.6 years in 2004 to 63.7 years in 2015 in Asia", etc. The entire manuscript needs to be revised to flow well.

Reply 1: Special thanks to you for your warm work and good comments. In term of some confusing sentences, we have examined the whole manuscript in detail again to improve the understandability of the contents. e.g. "The ROMs of Model B and Model A are similar in each direction, while that of model C is significantly larger." "Epidemiological studies showed that the average age of patients treated by surgery significantly increased from 54.6 years in 2004 to 63.7 years in 2015 in Asia".

Besides, the manuscript has been edited and proofread by an experienced native speaker to correct the wrong sentences and grammatical errors, including abstract, introduction, methods, results, and discussion section. And the amendments are highlighted in 'track changes' mode in the revised manuscript.

Changes in the text: See the revised traces in the manuscript.

Comment 2: Costs associated with more cement augmentation levels should be included in the discussion in addition to the complications associated with the use of cement augmentation.

Reply 2: Thank you very much for your valuable suggestion. we have made a detailed description about costs associated with more cement augmentation levels in the discussion as below: However, the major disadvantage in this application is related to the cement leakage, which probably leads to radicular compression symptoms, cement embolism, infection, and anaphylactic shock. Additionally, a larger number of cement-augmented segments may also increase the cost of surgery.

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Changes in the text: See page 10, line 14.

Comment 3: What was the bone quality in equivalence of DEXA T-scores used in the model?

Reply 3: Thank for the comment. Relationship between elastic modulus (E) and density (d) is given by: $E = 0.09882\ d^{1.56}$(MPa) [1]. The elastic modulus of osteoporotic cancellous bone is 34 MPa, so the density of cancellous bone is 42.3 g/mm^3. But because of the different units, we cannot convert it to T-scores.

Comment 4: Are crosslinks used in the model? These are generally not used in degenerative spine surgeries and if used may confound the research results.

Reply 4: Thank you for the comment. We agree with you very much that crosslinks are generally not used in degenerative spine surgeries. But according to biomechanical studies and our clinical experience [2-3], the use of cross-links in long-segment fixation (≥3 level) can significantly increase the stability of posterior fixation. Therefore, in this study, a crosslink was only used in multi-segment fusion models, while no crosslink was used in the double segmental fusion model (Figure 1).

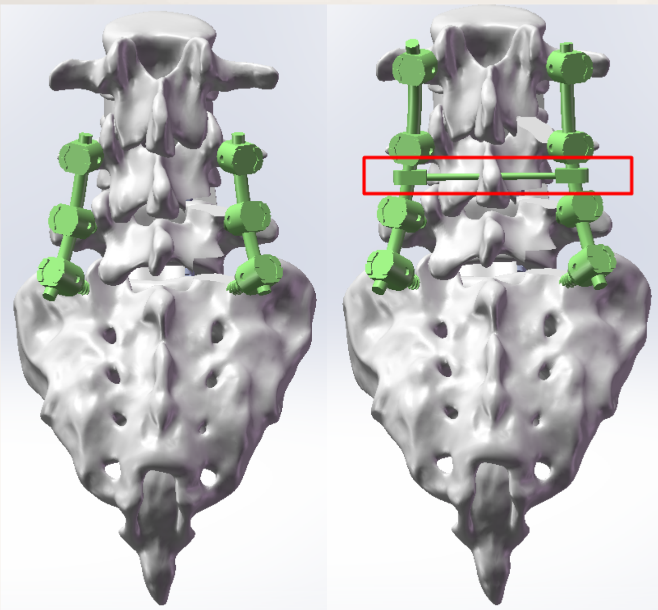

Figure 1: The crosslink was only used in multi-segment fusion models

Comment 5: Was stress analysis performed separately for cage between two augmented levels, one augmented and one non-augmented levels, and two non-augmented levels?

Reply 5: We thank the reviewer for pointing out this issue. In fact, we did compare cage stress at each segment among the three groups separately. The results were same as those of the overall comparison (Table 1 showed the cage stress at different levels in double segmental fixation models). Therefore, to keep the content concise, we only showed the comparison results of all cages among three groups.

Table 1：The separate comparison of cage stress among different models (MPa)

Models	Flexion	Extension	Bending-	Bending-	Rotation-	Rotation-

				L	R	L	R
Model A1	Total	**55.1**	**12.1**	**26.1**	**23.6**	**31**	**34.2**
	cage at L4/5	55.1	12.1	26.1	22.9	21.5	25.8
	cage at L5/S1	48	4.9	21.5	23.6	31	34.2
Model B1	Total	**58.9**	**14.1**	**29.6**	**27.3**	**33.7**	**38.3**
	cage at L4/5	58.9	14.1	29.6	23.3	23.9	31.3
	cage at L5/S1	50.6	6.1	22.3	27.3	33.7	38.3
Model C1	Total	**65.8**	**16.8**	**38.4**	**34.1**	**37.1**	**45.1**
	cage at L4/5	65.8	16.8	38.4	24.1	28.7	36.1
	cage at L5/S1	57.8	7	26.9	34.1	37.1	45.1

Comment 6: Similarly, was stress analysis performed for pedicle screws at different levels in different models?

Reply 6: We agree with you very much that separate comparisons can make the results more accurate. In most cases, the results were same as those of the overall comparison. Besides, compared with screws in middle level, the stress on the cranial and caudal pedicle screws was larger in most loading condition (Table 2).

Table 2：The comparison of pedicle screws stress at different levels in different models (MPa)

Models	Levels	Flexion	Extension	Bending-L	Bending-R	Rotation-L	Rotation-R
Model A1	L4	191.61	48.97	126.89	93.87	116.23	156.56
	L5	152.46	32.71	69.26	88.40	172.42	143.64
	S1	210.70	45.51	140.76	113.09	198.52	162.82
Model B1	L4	186.38	56.03	140.32	117.11	130.38	186.39
	L5	157.34	36.05	84.42	114.85	219.58	155.35
	S1	235.60	50.36	163.18	131.75	202.5	186.98
Model C1	L4	296.64	63.53	168.66	174.86	261.00	232.02
	L5	182.19	45.53	104.60	96.16	238.76	207.61
	S1	255.41	73.27	203.7	125.15	299.92	243.20
Model A2	L3	254.95	86.56	154.52	139.84	186.28	233.6
	L4	167.22	46.04	67.68	76.47	170.18	144.09
	L5	199.57	23.70	78.10	104.95	202.44	181.17
	S1	218.45	44.76	125.22	128.49	220.82	232.75
Model B2	L3	277.29	98.83	165.40	170.10	253.98	224.90

	L4	279.81	48.68	116.25	134.69	161.49	236.57
	L5	166.92	49.53	87.92	113.75	223.99	158.59
	S1	218.61	49.29	163.2	128.55	224.07	259.1
Model C2	L3	363.76	122.7	215.00	219.65	273.29	326.52
	L4	334.20	64.78	128.68	178.18	232.11	278.64
	L5	207.27	51.17	99.09	134.93	219.51	194.44
	S1	234.57	67.20	238.76	219.16	309.13	234.67

Changes in the text: See page 11, table 2

Comment 7: "In all surgical models, the maximum Von mises stress of internal fixation were significantly lower than the yield strength of titanium alloy screw/rod", if this is the case (the maximum stress on pedicle screws without augmentation was lower than the yield strength), how did the use of cement augmentation prevent instrumentation failure (screw pull-out etc.)?

Reply 7: Thank you very much for your kindly comment. The yield strength is the yield limit of metallic materials when yielding phenomena occur, referring to the ability to resist micro-plastic deformation. If the external force exceeds the yield strength of the screw, it is likely to break. Thus, the yield strength is an index to evaluate the risk of screw break rather than screw loosening. The loosening of screws is closely related to the stress on the screw and the bone quality at the bone–screw interface. The results of this study are similar to those of clinical investigations; the breakage of pedicle screws is rare in patients with osteoporosis, while screw loosening is more common due to the weak bone-screw interface.

Comment 8: P-values were not provided in the analysis.

Reply 8: As this study is a finite element analysis, only one volunteer's CT data was used to build the finite element model and only one model was constructed for each surgical method; therefore, the statistical analysis cannot be carried out (independent sample t-test for measurement data comparison generally requires more than 10 samples per group). A descriptive analysis was conducted in the present study, which is also the practice of most finite element literature (Figure 2) [4–6]. Therefore, please excuse the fact that *P*-values were not provided in the analysis.

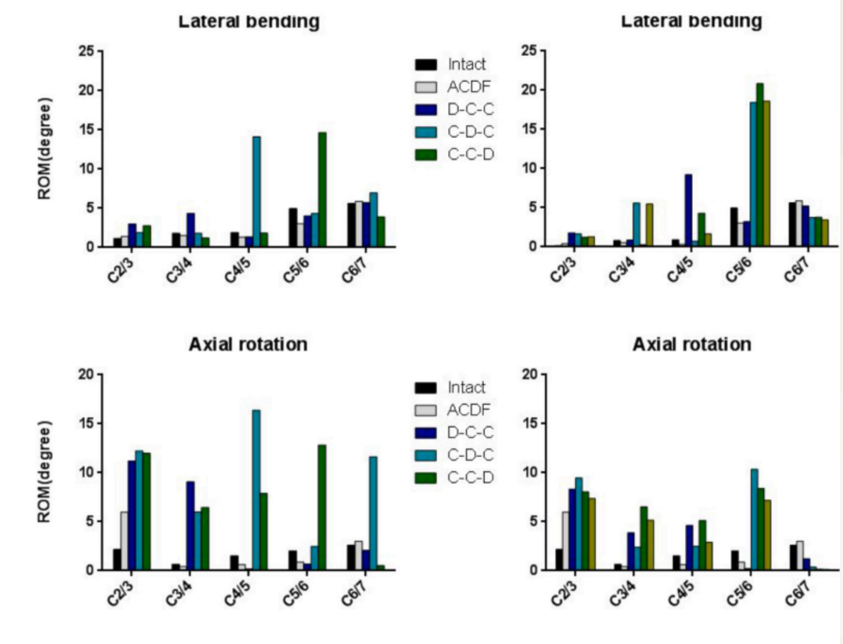

FIGURE 4 | Range of motion and distribution in different cervical constructs.

Figure 2 The comparison in previous finite element study showed that there was no statistical analysis was used [4].

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[6] Kim HJ, Kang KT, Son J, Lee CK, Chang BS, Yeom JS. The influence of facet joint orientation and tropism on the stress at the adjacent segment after lumbar fusion surgery: a biomechanical analysis. Spine J. 2015;15(8):1841-1847.