Peer Review File

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Review Comments (Round 1)

Reviewer A

Overall, this is a well written, nicely organized manuscript. I have a few minor questions and/or comments.

Comment 1: Methods: Where any statistical tests conducted? If so, please include this in the Methods.

Reply 1: We have included the two-tailed t-tests used to assess for clinically-significant differences in the average segmental motion fractions for all cervical spine motion segments (from C2-C3 and C6-C7 levels). The p values are reflected in Table 3.

Changes in text: Methods – Statistical Analysis: " Continuous variables were presented as mean ± standard deviation. Individual two-tailed t-tests were used to assess for clinically-significant differences in the average segmental motion fractions for all cervical spine motion segments, comparing C5-C6 disc arthroplasty versus C6-C7 disc arthroplasty patients. Statistical significance was assessed at p values < 0.05."

Comment 2: Results: From the segmental % contribution numbers presented in Table 3, segmental motion at C5/6 appears comparable with and without a CDR at that level. In contrast, segmental motion at C6/7 appears to be considerably lower with a CDR at this level. Were these differences statistically significant?

Reply 2: The two-tailed t-test analyses performed did not demonstrate statistically-significant differences in the average segmental motion fractions at the C5-C6 and C6-C7 levels with and without cervical disc arthroplasty. The p values are recorded in Table 3.

Changes in the text: Please refer to Table 3 and Results: The differences in average segmental motion fractions at the C5-C6 and C6-C7 index levels did not show statistical significance compared to the same levels without arthroplasty ($p = 0.98$ and 0.25, respectively).

Comment 3: Discussion: Please discuss the differences in segmental motion at C6/7 with and without CDR at that level. Why do you think that motion was comparable at C5/6 for native v. CDR, yet reduced at C6/7? Do you think that the devices were sized properly? Should a 7mm device have been used at C6/7, perhaps?

Reply 3: Based on previous studies, insertion an artificial disc implant that is of a greater height compared to the disc space can result in over-distraction of the disc space, reduction of range

of motion, and increased facet joint pressure. Statistical analyses in this study demonstrated absence of statistical significance in the difference in segmental motion fraction at C6-C7 level with and without cervical disc arthroplasty.

Changes in the text: Results: Based on previous studies, insertion of an appropriately-sized artificial cervical disc prosthesis is essential to avoid over-distraction of the disc space with associated reduction in range of motion and increased facet joint pressure. In this study, all implanted devices were M6-C artificial discs measuring 6mm in size.

Comment 4: Limitations: Please include an acknowledgement that successful retention of motion at ~16 mos post-op is very short and that additional follow-up of 5-10 years, at a minimum, is necessary to evaluate performance of CDRs.

Reply 4: Thank you. We have added this to the Discussion – Limitations.

Changes in the text: Discussion – Limitations: We acknowledge that successful preservation of range and quality of motion at an average of 16.2 months after the surgery constitutes a relatively short period of follow-up. An additional 5 to 10 years of follow-up, at a minimum, is necessary to evaluate the performance of this cervical disc arthroplasty device.

Comment 5: Conclusions: Please remove the sentence about potentially reducing the risk of adjacent segment degeneration. This appears to be beyond the scope of the study.

Reply 5: Thank you. This has been amended in the Conclusions.

Changes in the text: Conclusions: The sentence "This can potentially reduce the risk of adjacent segment degenerative diseases." has been replaced with "Further long-term studies are required to examine if this quality of motion alleviates the risk of adjacent segment degeneration.".

Reviewer B

Comment 1: I am very sorry, but I was unable to find anything in this work interesting enough to deserve publication. Perhaps the very idea of using serial functional radiographs for the evaluation of functional spine after arthroplasty is interesting, but with such a short series one could possibly be tempted to report the method description, and drawing any conclusions is completely unauthorized. Unfortunately, I do not know any possibility of redrafting the work. It just requires rethinking and trying to get much larger, more representative material.

Reply 1: We agree that this study has a small sample size of ten participants. We have acknowledged this in the Discussion – Limitations section and note that this may limit the ability to generalise the findings from our study to the wider population. However, this is the first in vivo study of the kinematics and quality of motion of implanted M6-C prostheses. It serves as a pilot study to assess the feasibility of this novel motion-quality metric. The

methodology possibly allows planning of further studies with a larger sample size comparing different types of cervical disc arthroplasty prostheses in the future.

Reviewer C

Comment 1: This is an interesting study with a lot of potential. It is important to investigate quality of motion rather than (s)ROM and its relation to adjacent segment degeneration. However, the study misses in depth-argumentation and the methodology could be a lot stronger. The study does not provide answers to the hypothesis of the influence of increased stress by fusion on adjacent segments, nor on the decreased risk of adjacent segment degeneration after cervical disc prothesis.

Reply 1: We have amended the introduction to provide clarity on the objectives of this study. We agree that the study does not have sufficient long-term follow-up to assess for the risk of adjacent segment degeneration after cervical disc arthroplasty.

Changes in the text: Introduction – Objectives: This is a unique study investigating the quality of in vivo kinematics of implanted M6-C prostheses using fluoroscopic images. In this study, we aimed to assess: (1) segmental and global range of cervical spine motions from C2 to C7 (2) the relative contribution by individual motion segments to the total cervical spine motion, termed segmental motion fraction (3) its variation through the arc of flexion-extension motion between index and adjacent cranial and caudal segments (if available) (4) centre of rotation.

Comment 2: It would be good to emphasise that this is a pilot study, focusing on the investigation of motion patterns after cervical disc prothesis.

Title - As the authors state in the discussion/conclusion, this is a pilot study. I would suggest that this is described in the title.

Reply 2: We have made the following the changes to emphasise that this is a pilot study.

Changes in the text:

Title: Assessing in vivo flexion-extension quality of motion after cervical disc arthroplasty: A pilot study

Introduction: The present pilot study serves to assess the quality of index segment motion in relation to the whole cervical spine using dynamic fluoroscopic images obtained over the full range of flexion-extension motion following cervical disc arthroplasty using an M6-C artificial disc.

Comment 3: Introduction - The authors clearly describe the rationale behind ACDA and its potential to prevent ASD by maintaining segmental range of motion. However, this study investigates the quality of segmental motion after ACDA. In my opinion, the study does not answer this question.

Reply 3: We acknowledge that the study investigates the quality of in vivo kinematics of implanted M6-C prostheses but does not assess the risk of adjacent segment degeneration after cervical disc arthroplasty. We have amended this in the Introduction and Conclusions.

Changes in the text: Conclusions: The sentence "This can potentially reduce the risk of adjacent segment degenerative diseases." has been replaced with "Further long-term studies are required to examine if this quality of motion alleviates the risk of adjacent segment degeneration.".

Comment 4: The introduction could use more detail concerning the current knowledge on ROM and quality of motion in normal physiology, and after these surgeries. To date, several motion studies are available, including quality of motion analyses. What makes this technique different from the current ones. What does it add to the existing literature?

Reply 4: Range of motion at the index level after a cervical disc arthroplasty has been studied extensively in the past using static radiographic images at the end of flexion-extension range of motions. Segmental contributions to the cervical spine motion (term segmental motion fractions in this study) has also been studied in asymptomatic healthy subjects but there is minimal literature on this topic in patients following cervical disc arthroplasty, especially not following arthroplasty with an M6-C prosthesis. In this study, we aimed to study the segmental motion fractions and the quality of motion following M6-C cervical disc arthroplasty.

Changes in the text: Introduction: Segmental contributions to the global cervical spine motion in healthy adult subjects have been shown to vary during different motion ranges of flexion and extension. The highest average contribution is typically contributed by the mid-cervical spine, with successively reduced contributions from the adjacent levels during flexion-extension motion. A study on the ProDisc-C prosthesis (Synthes Spine, West Chester, PA) has shown maintenance of relative contributions from the index operative level to the total cervical range of motion. This was statistically equivalent from baseline to 24 months of follow-up, in contrast to the comparison group with cervical arthrodesis. However, *in vivo* segmental motion contribution following an M6-C cervical disc arthroplasty has not previously been studied.

Comment 5: Center of rotation is also assessed. It would add more substance to the article if the introduction includes previous knowledge on the center of rotation in healthy individuals as well as in index segments of patients undergoing disc arthroplasty.

It remains unclear what the gap in knowledge is and what led to initiating this research. There is no clear research question/ nor objectives stated.

Reply 5: We have included studies on the centre of rotation in healthy individuals and in patients following cervical disc arthroplasty. We have amended the final paragraph of the Introduction to provide further clarity on the objectives of the study i.e. to study the quality of motion and shift in centre of rotation after cervical disc arthroplasty with an M6-C prosthesis.

Changes in the text: Introduction: The notion of instantaneous centre of rotation was first described by Penning in 1988. A recent study in asymptomatic subjects with a mean age of 46 years old shows that the average superior-inferior instantaneous centre of rotation moves progressively more superior from C2-C3 motion segment to C6-C7 motion segment; and the average anterior-posterior location of the instantaneous centre of rotation path is posterior to the geometric centre of the caudal vertebral body. Various studies using this kinematic quality parameter has been performed to assess the quality of motion after cervical disc arthroplasty, with variable results in preserving the physiological location of pre-operative centre of rotation. Nonetheless, the centre of rotation at the index level after cervical disc arthroplasty with an M6-C prosthesis has not been investigated in the past.

Methods - I have several concerns concerning the methods of this study. Could the authors please elaborate:

Comment 6: When was the data collected?

Reply 6: The data was collected over a period of 2 months in October 2020 to December 2020.

Changes in the text: Results: The data was collected over a period of two months in October to December 2020.

Comment 7: How were patients selected? Were they collected in a consecutive way?

Reply 7: The patients were recruited consecutively from a patient database based on the inclusion and exclusion criteria outlined in Methods – Patient Population. All the patients underwent single-level cervical disc arthroplasty performed by a single surgeon (senior author) at the institution.

Changes in the text: Methods – Patient Population: Subjects older than 18 years of age and had a single-level C5-C6 or C6-C7 M6-C cervical disc arthroplasty performed by the senior author (N Thani) in 2019 and 2020 were recruited consecutively.

Comment 8: Was there a minimum time between the surgery and recordings?

Reply 8: The minimum time between the surgery and the recording of the fluoroscopic images was 3 months.

Changes in the text: Methods – Patient Population: The minimum duration between the arthroplasty surgery and the recording of the fluoroscopic images was 3 months for all the participants.

Comment 9: No power calculation is mentioned in the study. How did the authors decide to include 10 patients? Does this suffice to answer the research question?

Reply 9: Power calculation was not performed in this study. The subjects were recruited from

the senior author's patient database based on inclusion and exclusion criteria described. This is a pilot study to assess the feasibility of this novel motion-quality metric.

Comment 10: How did the authors choose to only include a disc arthroplasty group. No comparable group is available. How does this influence the conclusions to be drawn from the results? Is there quality of motion data available for healthy individuals, ACDF patients or patients with different types of discs protheses. Can we compare the findings of this study?

Reply 10: The M6-C prosthesis is the artificial device that is used for cervical disc arthroplasty at the institution. There was no direct comparison to the pre-operative findings or a comparable group of patients with other artificial cervical disc. The retrospective nature of this study, unfortunately, precluded us from obtaining fluoroscopic images of the cervical spine prior to the cervical disc arthroplasty surgery. The findings from this study were compared to findings from healthy asymptomatic subjects and in vitro cadaveric specimens in the literature. We acknowledged this in the Discussions – Limitations.

Changes in the text: Discussions – Limitations: It would have been interesting to perform the above fluoroscopic imaging prior to the cervical arthroplasty operation for direct comparison with the post-operative findings, or to compare the findings to another artificial cervical disc device.

Comment 11: How are the recordings made? Are patients seated or standing? The position of the patient has been described to influence (s)ROM. How can this influence the current recordings.

Reply 11: The patients were standing for the recordings. The thoracolumbar spine is known to demonstrate changes in configuration during standing and sitting as reported by Tsagkaris et al.(1) However, Kusakabe et al showed that patients with good spinal sagittal alignment do not undergo any changes in cervical alignment during standing and sitting.(2) We have specified in the manuscript that the fluoroscopic images were captured with the subjects in standing position.

Changes in the text: Methods – Radiographic Analysis: In standing position, the subjects were instructed to continuously move their head and neck through the entire range of flexion-extension (from neutral to full flexion, then to full extension, and back to neutral position) at a constant rate over a period of 10 seconds, with 15 frames captured per second.

Comment 12: How are the vertebrae tracked throughout the recordings; how is the software validated? Do you have a reference? Could you elaborate on how the quality of motion is assessed with this method?

The authors state that the reproducibility of these measurements has been validated (p.6). How has the reproducibility of this method been validated? Are ICCs available for the different

analysts?

Reply 12: The vertebral movements were tracked based on anatomical landmarks i.e. the anterior and posterior corners of the superior and inferior endplates of C2 to C7 vertebrae. The translational and angular movements during the flexion-extension motion were normalised to the static neutral image for each subject. The size of the M6-C implant was used for calibration purposes. The accuracy and reproducibility of Quantitative Motion Analysis (QMA, Medical Metrics Inc., Houston, TX) has been validated by multiple studies in the past including in the cervical spine. These studies include Reitman et al, Sears et al, Ghiselli et al, and Taylor et al.(3-6) The radiographic analysis of the fluoroscopic images was independently performed by Medical Metrics Incs, an external certified imaging core lab well-known for its experience in multi-centre clinical trials and research studies. The intraclass Correlation Coefficients (ICCs) > 0.85 of agreement amongst QMA observers has previously been validated.

Changes in the text: Methods – Radiographic Analysis: Data analysis was performed using custom digitised software (Quantitative Motion Analysis, Medical Metrics Inc., Houston, TX). Anatomical identifications based on bony landmarks were digitised using the software for radiographic analysis. The image study encompassed the anterior and posterior corners of the superior and inferior endplates from C2 to C7 vertebrae. This validated radiographic motion analysis software uses advanced pattern recognition algorithms to generate accurate measurements of intervertebral rotation, translation and change in disc height measurement error of no more than 0.5 degrees and 0.5 mm. The reproducibility of the measurements has also been validated in various studies including in the cervical spine. The fluoroscopic images were subsampled (every 10^{th} frame were tracked) to obtain 15 frames for motion analysis. The frame numbers were assigned such that Frame 1 corresponds to full extension, Frame 8 corresponds to neutral, and Frame 15 corresponds to full flexion. The intervertebral flexion-extension angle in each frame of the dynamic fluoroscopy was normalised to the static neutral image for each subject. The size of the M6-C implants was used for calibration purposes. For distance-based analysis, we reported the data normalised to the superior enplate of the caudal vertebra.

Comment 13: If I understand correctly, motion is assessed from maximum extension to maximum flexion. It has been described that motion patterns differ for extension and flexion. Why did the authors decide to analyse flexion only?

Reply 13: In this study, the quality of motion was assessed from maximum extension to maximum flexion as demonstrated in the Methods and Results, not just flexion.

Changes in the test: Methods – Radiographic Analysis: The frame numbers were assigned such that Frame 1 corresponds to full extension, Frame 8 corresponds to neutral, and Frame 15 corresponds to full flexion.

Comment 14: Are a final 15 frames per recording analysed for all patients? How was this

number chosen? The authors state that 15 frames per second are recorded during 10 seconds. How are the frames to be analysed selected from these 150 frames?

Reply 14: 150 frames were recorded per patient. Frame 1 corresponds to full extension, Frame 8 corresponds to neutral, and Frame 15 corresponds to full flexion. Every 10^{th} frame (out of 150 frame per subject) were tracked to obtain 15 frames for motion analysis.

Changes in the text: Methods – Radiographic Analysis: The fluoroscopic images were subsampled (every 10^{th} frame were tracked) to obtain 15 frames for motion analysis.

Comment 15: Segmental motion fractions were determined, was this based on a rotational component only? Or was translation also taken into account?

Reply 15: The segmental motion fractions were determined based on angular (rotational) motions alone, while the changes in the centre of rotation were derived from both angular and translational components of the flexion-extension arc of motion, consistent with methods described in the literature.(7)

Changes in the text: Methods – Data Analysis: The fluoroscopic images were analysed to calculate segmental motion fractions as the ratios of angular motion contributions made by individual segments to the motion of the C2-C7 spine at each of the intermediate image collected over the flexion-extension arc of motion.

In this study, the centre of rotation was determined by the amount of translation for each degree of angular motion using the Cartesian coordinate system as the point about which the superior vertebra rotates relative to the inferior vertebra.

Comment 16: Relative contributions from index levels – adjacent levels are compared; although the index levels are the adjacent levels in the other recordings?

Reply 16: In this study, we quantified the segmental motion fraction for each motion segment and compared its variation throughout the arc of flexion-extension between index and adjacent segments. The index levels were defined as C5-C6 and C6-C7 arthroplasty levels. The comparisons were only made for the index levels and adjacent levels – C4-C5 and C6-C7 for C5-C6 arthroplasty; C5-C6 alone as the adjacent level for C6-C7 arthroplasty.

Comment 17: Please elaborate on the importance of the footprint of the prothesis

Reply 17: This has been described in Results, along with the footprint sizes for devices placed in this study.

Changes in the text: Results: Footprint mismatch has been known to cause subsidence, heterotopic ossification, and device failure due uneven load distribution. An implant with the largest footprint was chosen for individual patients to provide maximal coverage of the endplates. In four subjects, a large footprint implant was chosen. A large, long footprint prosthesis was inserted for six patients.

Comment 18: “We hypothesised that the range and quality of cervical spine motions after cervical disc arthroplasty using the M6-C disc prosthesis closely resembles normal physiological movements.” How are the normal physiological movements are determined?

Reply 18: This was demonstrated in Figure 4: Segmental motion versus global range of motion showing harmonious movement of the index C5-C6 and C6-C7 arthroplasty levels in relation to the neighbouring segments. The findings on segmental motion fractions and shift in the centre of rotation at the index level were also comparable to healthy asymptomatic subjects in the literature.

Results

Comment 19: P.8 “Three subjects had C5C6 cervical disc replacement and seven had C6-C7 cervical arthroplasty”. Please be consistent in terminology throughout the article. (disc replacement/arthroplasty).

Reply 19: Cervical disc replacement has been amended to cervical disc arthroplasty throughout the manuscript.

Comment 20: P.9 results are presented in degrees and percentages, this is confusing, please use one outcome measure and if they both represent percentages, please clarify. E.g. 18.9 ± 2.1% □ 18.9% ± 2.1%

Reply 20: The findings presented in the second paragraph of Results are all presented in percentages. They are also reflected in Table 3: Average and peak segmental motion fractions. In order to avoid confusion, the sentence “Overall, the C2-C7 cervical spine had a flexion-extension range of 66.7 ± 7.7 degrees.” has been removed from the body of the text.

Changes in the text: Results: The sentence “Overall, the C2-C7 cervical spine had a flexion-extension range of 66.7 ± 7.7 degrees.” has been removed to avoid confusion.

Comment 21: Results are presented for those with C5-C6 and C6-C7 arthroplasty. They are also described for index/adjacent segments. How are these grouped in figure 3 and 4(C5-C6 is the index segment in 1 case, and the adjacent segment in another)? Can we differentiate which one is an index vs adjacent segment?

Reply 21: Figure 3 (Centre of Rotation) and Figure 4 (Segmental motion vs global range of motion) combine data on changes in centre of rotation and segmental motions for both C5-C6 and C6-C7 arthroplasty groups, demonstrated harmonious movements among the cervical spine motion segments.

Discussion

Comment 22: The current study analyses a patient population. Other segments may also be degenerated, how can this influence the findings? Is there more data available concerning the degree of degeneration in the segments (e.g. Kellgren Score)?

Reply 22: Thank you for the suggestion. We have described Kellgren grading of the motion segments adjacent to the index levels.

Changes in the text: Results: The motion segments adjacent to the index level (C4-C5 and C6-C7 levels for C5-C6 arthroplasty; C5-C6 level for C6-C7 arthroplasty) showed either Kellgren grade 1 (minimal) or 2 (mild) spondylosis in all subjects in this study.

Comment 23: The study represents a typical population undergoing disc arthroplasty. However, we know that sROM declines with age. Did you find a difference in quality of motion in your younger patients in comparison to elderly?

Reply 23: Cervical disc arthroplasty surgery is generally performed for young patients with minimal spondylotic changes and osteophytic formation to maximise the potential of the operation, which is for motion preservation at the index level. The subjects in this study had an average age of 43.8 years old. Due to this patient selection, this study is not powered to investigate the difference in quality of motion in younger patients compared to the elderly patients. However, we are aware of a recent publication comparing cervical disc arthroplasty surgery in patients at the two extreme ends of the age distribution (above 65 and below 40 years old) which demonstrated reduction in mean range of motion post-operatively for the elderly group.(8)

Comment 24: The discussion focusses specifically on the design of the M6-C prothesis and the influence of quality of motion. However, since other designs of protheses are not investigated, can we actually know whether these findings are dependent on the specific design? Or just the fact that a prothesis is used and maintains motion.

Reply 24: We agree that comparison with another artificial device, particularly a non-constrained prosthetic disc, will shed some light on the difference in the prosthesis design and associated kinematics. The methodology described allows planning of further studies with a larger sample size comparing different types of cervical disc arthroplasty prostheses in the future.

Changes in the text: Discussion – Limitations: it would have been interesting to perform the above fluoroscopic imaging prior to the cervical arthroplasty operation for direct comparison with the post-operative findings, or to compare the findings to another artificial cervical disc device.

Comment 25: Line 275 “an abnormal motion path can alter the adjacent segmental loading”. What is defined as an abnormal motion path? Can we conclude this from this study? What is

defined as a ‘normal’ motion path?

Reply 25: An abnormal motion path in the cervical spine is akin to gear-shift movements, with intermittent locking of the prosthesis over a portion of the arc of motion. Our study demonstrated smooth, harmonious movements of the index levels in relation to the global cervical spine motion, with minimal variations in peak segmental motion fractions. Our study also demonstrated physiological shift in centre of rotation as demonstrated in Figure 3.

Comment 26: Line 294 “individual variables such as patient efforts and body habitus can alter the range of cervical spine motion”. Do you have more baseline characteristics; e.g. BMI? NDI?

Reply 26: We acknowledge that these baseline characteristics were not collected in addition to the patients’ age and gender. It will be difficult to draw conclusive correlations between the patients’ body mass index and the ability to perform full flexion-extension range of neck motions. Improvement in clinical grading systems such as the Neck Disability Index has previously been demonstrated through multiple clinical studies and we did not seek to replicate those findings in this study.

Review Comments (Round 2)

Reviewer B

Thank you for significantly improving the manuscript. There are several things I find important to adjust before accepting the article for publication.

Comment 1: Most importantly, when reading this article, it feels like the authors are trying to ‘sell’ the M6-C prothesis. I think this should be nuanced throughout the article and especially in the conclusion. As I interpret this article, I think the conclusion should be that this is an interesting method to investigate protheses, which is technically feasible, but however needs a larger group to be able to draw conclusions. Especially because this is a pilot study, solid conclusions cannot be drawn.

Reply 1: Thank you for the comment. “M6-C cervical disc” has been largely replaced by “cervical disc prosthesis” in the manuscript to place less emphasis on this particular device and the product name. The conclusion has been modified accordingly.

Changes in the text: Conclusions – This pilot study demonstrated the feasibility of investigating cervical disc prostheses using the novel concept of segmental motion fraction as a motion-quality metric. Further long-term studies with large sample size are required to draw solid conclusions.

Some minor points to address:

Comment 2: "Previous studies of in vivo motion assessment have been limited to measuring the range of motion from static lateral radiographs taken at the extremes of full flexion and extension.(1)"

There are several other methods than sROM to investigate motion; please have a look at these studies & nuance this statement.

https://pubmed.ncbi.nlm.nih.gov/27879563/ & (https://pubmed.ncbi.nlm.nih.gov/23429677/

Reply 2: Thank you for sharing the articles. We have included the study protocol paper by Boselie et al. The team described using the sequence of segmental cervical spine contributions to determine the motion patterns at the index level after cervical disc arthroplasty. The result of this study is yet to be reported. The paper on 'instant centre of rotation' by Anderst et al has previously been cited and discussed in the Introduction and Discussion sections of the manuscript, showing the normal path of instant centre of rotation in asymptomatic subjects.

Changes in the text: Introduction – The limitations of this quantitative motion assessment have been addressed by Boselie et al. The team previously published a study protocol describing the assessment of the dynamic process of cervical spine motion using the sequence of segmental contributions.

Comment 3: "Motion segments with these implanted devices have been demonstrated in a cadaveric study to function in harmony with other segments of the cervical spine as before cervical disc arthroplasty".

Please specify what is meant with "in harmony"? Do you mean a fluid movement?

Reply 3: "In harmony" refers to the smooth sequence of movements across the arc of flexion-extension motion, unlike gear-shift movements with intermittent locking of the prosthesis over the arc of motion.

Changes in the text: Introduction – Motion segments with these implanted devices have been demonstrated in a cadaveric study to function in harmony with other segments of the cervical spine as before cervical disc arthroplasty, with smooth sequence of movements across the arc of motion without gearshift-like intermittent locking of the prosthesis.

Comment 4: "Our results showed physiology motion quality at the index segment and harmony among neighbouring segments following cervical disc arthroplasty using a M6-C device."

Again, please specify what is meant with "in harmony"?

Reply 4: Same as above.

Changes in the text: Conclusions – Our results showed physiologic motion quality at the index segment and harmony among neighbouring segments following cervical disc arthroplasty using a M6-C device, without gearshift-like intermittent locking of the prosthesis during the arc of flexion-extension motion.

Comment 5: You state that the fraction decreases caudally, which is true for the averages. However, 4 out of 9 patients show more movement in C6-8 than in C5-6 [table 2]?

Same accounts for 'harmony' between neighbouring segments, which is only true for group averages?

Reply 5: Thank you for pointing this out. Review of the data showed that three out of these patients had cervical disc arthroplasty performed at the C5/C6 level, which may explain the reversal of segmental motion contributions between C5/C6 and C6/C7 levels. We have noted this in the Discussion section.

Changes in the text: Discussion – Of note, the three patients who had cervical disc arthroplasty at the C5-C6 level had reversal of these segmental motion contributions between the C5-C6 and C6-C7 levels, with an average difference of 1.9 degrees.

Comment 6: Figure 3 suggests that there is a high variation in locations of COR (with large error bars). Did you have a look at individual segments? There are 3 patients with a prothesis on C5-6; these are added in the average group together with the 6 remaining patients without a prothesis on C5-C6. This does not seem fair? Can you get an average location of the operated segments (either C5-C6 or C6-C7?). This gives better insight into the influence of the prothesis. And then compare with the non-operated segments?

Reply 6: Thank you for the suggestion. We have created Figures 2a and 2b (previously labelled Figure 3) for illustration of the shift in centre of rotation in patients who had C5-C6 and C6-C7 disc arthroplasty, respectively. The centre of rotation did not change between operated and non-operative C6-C7 levels but has shifted anteriorly in patients who had C5-C6 arthroplasty, in comparison to the non-operated C5-C6 levels. This may be confounded by the small sample size in this group.

Changes in the text: Results – However, when this is analysed in individual arthroplasty groups, the centre of rotation at C6-C7 level did not change significantly between operated and non-operated cases but has shifted anteriorly at C5-C6 level in the operated cases.

Discussion – Nonetheless, subgroup analysis showed that the centre of rotation at C5-C6 level has shifted anteriorly in the operated cases, compared to the non-operated cases. This may be confounded by the small sample size in this group.