Author's response to reviews

Title: Preoperative assessment and evaluation of instrumentation strategies for the treatment of adolescent idiopathic scoliosis: computer simulation and optimization

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Preoperative assessment and evaluation of instrumentation strategies for the treatment of adolescent idiopathic scoliosis: computer simulation and optimization

Younes Majdouline, Carl-Éric Aubin et al.

The authors wish to thank the reviewers for their in-depth and comprehensive feedback. The manuscript has been reworked significantly to address their comments and concerns. Reviewers’ comments are in italics followed by detailed responses in indented paragraphs. The page numbers in the response correspond to those in the revised version of the manuscript.

Reviewer #1

The authors present a computer simulation study in which the ‘ideal’ surgical correction profile for a single scoliosis patient was identified by 11 different experienced surgeons. The extent to which different surgical strategies achieved the desired correction objectives were then explored by running multiple computer simulations of the correction procedure. The study concludes that different surgeon-specified objectives can result in different optimal surgical strategies. Overall, this is a well performed study which demonstrates the growing ability of computer simulations to assist in surgical decision making.

Major compulsory revisions

1. Clarification of terms in objective function

The objective function is defined as a weighted sum of squares of post-op to pre-op ratios in which each square term tends to zero as that correction objective is ‘optimized’. However in the case of the two sagittal plane angles (thoracic kyphosis and lumbar lordosis), these terms are referenced to arbitrary ‘normal’ values of 35 and 40 degrees respectively. I am concerned that in the case of AIS patients who may already be normokyphotic (i.e. with preop kyphosis in the normal range), the denominator will tend to zero and the term will therefore become infinite. Please address this.

On Pages 6 and 7, more details were provided on the formulation of the objective function and how to avoid small denominators so as to improve numerical stability. For instance:

The objective function \( \Phi \) was computed as the sum of the weighted square of the ratio of these descriptors over their initial values with the introduction of a mobility factor defined as the ratio of the number of unfused vertebrae (\( F \)) over the maximum number of unfused vertebrae in all the strategies (\( F_0 \)). The choice of the square of the ratio was from the consideration of making each descriptor positive and dimensionless, i.e. without an associated physical unit so that the weighted summation of descriptors of different natures can be performed to form the objective function of a minimization problem. In this way, before the spinal instrumentation, the ratios of all descriptors were equal to 1, allowing consistency for different cases and numerical robustness of the solution of the optimization. […..] The ‘normal’ thoracic kyphosis (\( \theta_{Tk}^0 \)) and lumbar lordosis (\( \theta_{LL}^0 \)) were
defined as arbitrary values within the normal ranges with their absolute differences from the patient’s preop values greater than 5° to avoid numerical instability arising from small denominators [14,15]. From the same numerical consideration, initial values which were less than 5° were rounded to 5°.

Also, the F/Fo ‘mobility factor’ ratio (num unfused vertebrae/ max num unfused vert in all strategies) appears problematic because as the number of unfused vertebrae approaches the maximum for all strategies, this term approaches 1 from a value less than 1, therefore this term should not be minimized but rather needs to be maximized. Again, please address.

Thanks for your remarks. Having looked into the implementation codes, what was actually used in the summation was the inverse of the mobility factor which was defined as the ratio of the number of unfused vertebrae (F) over the maximum number of unfused vertebrae in all the strategies (F0). The error in the manuscript has been corrected in the Revised version.

2. Comment on model validation

Although the authors have a strong track record in the development of computer simulations of scoliosis surgery, I still believe it is necessary to include specific comment on model validation in the current study, and particularly on the potential limits of model validation when running large numbers of simulations (702 in this case) across a wide ‘solution space’. Can we have equal confidence in the model predictions across all instrumentation strategies? Or are there some instrumentation combinations where the model’s ability to correct predict post-operative spinal shape has been less thoroughly tested against actual patient data? In other words, what is the confidence in the model validity across the solution space investigated in this study? How well did the model predictions for this patient match the actual surgical outcomes for the strategy used with this patient? At the very least a paragraph on model validation and a statement detailing the author’s level of confidence in the predictions across the parameter space explored in this study should be included in the Discussion.

Firstly, a brief description of our previous model validation work was added on Page 9. Then in the Discussion (Pages 13 and 14), a paragraph was added to discuss the potential limitations of the simulator when simulating a great number of different instrumentation strategies.

Simulations performed in our previous studies showed that the prediction errors for the instrumented spinal segments were not clinically significant. Due to the extremely high heterogeneity among patients and the great variation on the instrumentation strategies among surgeons, the confidence levels in the predictions of particular instrumentation strategies could not be precisely established. However, this study still revealed the inherent variability factors associated with surgical-planning and decision-making in AIS.

3. Additional methodological details

While it is appreciated that the paper refers to previous model development work by the authors for some aspects of the model development, additional methodological details for the single patient simulated in this study are still required. In particular, how was the patient-specific
anatomy generated given that the radiographs in Figure 1 seem to be of quite low contrast (there is almost no visible endplate definition in the sagittal radiograph)?

Details and references on the geometric reconstruction of the patient’s spine were added on Page 8.

For the spine geometry, high resolution numerical preoperative radiographs (> 150 DPI) and reconstruction software Spine3D (developed by our research group) were used. The contrast and brightness of images can be adjusted and optimized during the reconstruction to facilitate the identification of the anatomical landmarks. Figure 1 was intended to show the deformity characteristics of the patient, therefore images with reduced resolution were used to avoid large-size image files.

Also, the authors seem to imply that patient-specific spinal stiffness values were determined for this particular patient – is this the case?

Side bending radiographs were used to calibrate and optimize the mechanical properties of the spine model such that the shapes of the spine from bending simulations agree with the shapes of the spine from the actual bending. Techniques to estimate the patient-specific absolute stiffness of the spine are still not available in the literature.

Thirdly, what was the goodness of fit between the ‘simplified model representing the 12 geometric measurements as a function of the six instrumentation variables’ and the actual outputs of the S3 model? What were the maximum errors between S3 output and simplified model output? Were the errors significant relative to the quantities being optimized?

The independent variable space (the six instrumentation variables) to be searched is a vast space, given the available computational capacity; walking through this space and solving the dependent variables (the 12 geometric parameters) is a complex process (simulation of the complete instrumentation at each point), therefore extremely time-demanding. To reduce the searching time and make the process implementable in a clinical context, only a limited number of points were sampled (702 simulations). Then the search was conducted by solving the dependent variables through linear interpolation of sampled points. Differences between solutions from the interpolations and those from S3 simulations depend on the values of the independent variables. Estimation of the maximum value of these differences and the optimal number of sampling points is a complex mathematic issue, thus out of the scope of this paper. However, the optimal solutions from the interpolation functions were simulated again with S3, and for this particular case, the differences were under 8°. In the Discussion of the revised manuscript, attention was brought to the potential errors due to this optimization technique (at the end of the first paragraph on Page 14).

What loading was applied to the models? Please give a statement in the Methods on how the models were ‘loaded’ when adding the instrumentation.

Details were given (second paragraph on Page 9).

4. Discussion of model limitations
The choice of boundary conditions applied to the spine model has already been discussed by the authors as a limitation. Please also make the point that the analysis performed in this study only considers geometric aspects of the deformity correction, and there is no consideration of predicted biomechanical quantities in the study. For instance, some of the instrumentation configurations simulated might be more prone to implant loosening or inducing junctional kyphosis at the proximal uninstrumented than others under post-operative loads, but these biomechanical factors have not been considered in the identification of ‘optimal’ surgical outcomes in the present study.

Your comments and recommendations were addressed on Page 13, last paragraph in Discussion

**Minor essential revisions**

5. **Inconsistencies between text and Tables**

Results paragraph 2 states that the upper instrumented level varied from T2 to T6, whereas Table 2 shows the range as T2 to T5. Similarly the range of lowest instrumented vertebrae is stated as L1 to L5 in the text and L1 to L4 in Table 2. The PT region Cobb angle range is stated as 26 and 42 degrees in the text, where in Table 3 it is given as 26 to 40 degrees, and similarly for the TL/L Cobb angle range which is given as 13 to 28 degrees in the text and 13 to 27 degrees in the Table. Please correct these inconsistencies.

The inconstancy in the presentation has been addressed.

**Discretionary revisions**

6. Figure 2 seems redundant as it is very difficult to see the differences between instrumentation strategies at the scale of the images given. It may be better to include 2 (larger) images which show the difference in surgical strategy and post-operative spinal shape between two of the surgeons with clear differences between them.

7. Abstract, Methods subheading, sentence 2 is not clear ‘For each surgeon, 702 surgical configurations were simulated and eleven were sorted out which were the most favourable…’ This sounds like 11 configurations were selected for each surgeon, rather than that each of the 11 surgeons selected his particular preferred surgical correction outcome. Please rephrase more accurately.

8. Background last sentence, ‘was examined’.


10. Methods first paragraph, please give the thoracic kyphosis and lumbar lordosis angles for the patient.

11. Methods 4th page, line 9 ‘but its parametric formulation will allow the use of more detailed data…’.

12. Discussion last paragraph, lines 7/8, ‘further studies are required to elucidate their role’.

13. Conclusions line 1 ‘our study’.

Thanks for these constructive comments which have been taken into full consideration when revising the manuscript.
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Reviewer #2

Introducing patient specific models for designing treatment intervention is a novel approach and various groups are working in this area. Although, this is a well written report, I would like the authors to consider the following points.

Background: The manuscript will benefit from a paragraph highlighting the usefulness of patient specific models. Provide a succinct review of your previous work and the origin of the model that you have within this study.

One paragraph has been added (from the end of Page 3 to the beginning of Page 4) to highlight the role of computer modeling and simulations of patient-specific spinal instrumentation. A brief presentation of our previous work on model development could be found in the Methods section.

Methods: I suggest that the authors should consider subheadings within this section which will make the section easy read for clinical practitioners.

As you advised, this section was divided into two subsections: “Corrective objective function” and “Simulation model and optimization technique”

Discussion: Please highlight that this is a “case series” analysis than a “full study”.

Your comment was addressed at the end of the Discussion section.

Line 7: “thus impacting” – please check and rephrase this sentence.

The sentence has been rephrased.

Line 10-12: This is an important finding and I suggest that the authors should further discuss this and relate it to clinical practice

A couple of sentences were added to take advantage of your comments.

Last paragraph: This again is an important point for discussion. The authors should clearly highlight and discuss the limitation. Whilst the authors have attempted to discuss this – the manuscript will benefit from a clearer description with a focus on clinical practitioners.

The paragraph has been reworked to integrate your comments and suggestions.

Conclusion: Line 1. Avoid “ours”. Rephrase to “This study...”

OK.