**Author’s response to reviews**

**Title:** RESULTS OF ULTRASOUND-ASSISTED BRACE CASTING FOR ADOLESCENT IDIOPATHIC SCOLIOSIS

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**Author’s response to reviews:**

The following is the response to the reviewers’ comments. The highlighted texts were added to the revised manuscript.

Reviewer #1: In general, this manuscript has been well prepared and the following suggestions are for further improvements.

Page 5

Paragraph 1 "Background" Line 5

Regarding the long term effects of untreated AIS curves, the authors only addressed the back pain. Pulmonary dysfunction and other complications should be mentioned as well.

The sentence has been changed to “Patients with untreated curves usually have more back pain [2, 5], loss of function, external deformity, poor self-image, and in more severe cases, can impair respiratory capacity later in their life.”

Paragraph 1 "Background" Line 9-15
Prognostic model of brace treatment outcome is an outstanding model to show the combined effect of brace usage in terms of quantity and quality. However the results of that study were all extracted from a single center and the quality of brace design in that unique clinic might be consistent; it would be promising to increase the number of orthotic centers to facilitate the generalization of the results.

We agree with the reviewer’s comments and we added few words to indicate that is a pilot study

“Recent scientific evidence has shown that brace treatment is effective [11-14], and a pilot study from a single centre has shown a predicted success rates of 95%, when brace wear quantity combined with the brace wear quality is over 43% of the prescribed dosage [15].”

Page 6

Paragraph 1 Line 4

"Radiographs are not used during brace design and construction to minimize radiation exposure …" It is suggested to replace verb (taken) with (used) as still the pre-brace X-ray is considered as a reference for orthotist to design the brace accordingly, but as authors mentioned no further X-ray will be taken during the construction procedure.

We made the changed as suggested by the reviewer.

“Radiographs are not taken during brace design and construction to minimize radiation exposure to growing children because of the increased risk of cancer.”

Page 7

Paragraph 1 Line 5&6

Orthotists in this study were aligned with the same scoliosis program to provide similar brace design for this study participants. As authors previously mentioned (Page 5, Paragraph 1 Line 18 "The in-brace correction may be affected by the brace design and spinal flexibility."); how did the investigators control the parameter of “flexibility” in control and experimental groups?

In this study, we did not control the flexibility parameter. For the control group, the 17 patients were consecutive, recruited retrospectively (within 6 months) for those who met the inclusion
criteria. The intervention group was also recruited consecutively for those who met the inclusion criteria and agreed to participate into this study.

Paragraph 2 "Control Group Protocol" Line 6

Providence frame is originally designed to apply the forces to trunk to move the spine toward the midline or beyond the midline. What was the routine practice of orthotists in that clinic?

The orthotists in our clinic aim to get the spine toward the midline, but not beyond the midline.

Paragraph 2 "Control Group Protocol" Line 7

More elaboration on CAD/CAM scanning of the hardened plaster cast after removal can better clarify the application procedure.

After the plaster hardened, the subject stood up again to remove the hardened cast. Reflective markers were then placed around the cast and then scanned by a handheld laser scanner to create a 3D casting image file. The 3D file was then imported into software that was linked to a carving machine. Some minor adjustment was done at this stage to smooth the surface. A 3D body mold was then carved using foam material.

Page 8

Paragraph 1 "Intervention Group Protocol" Line 1

Application of a custom Providence standing frame for the intervention group compared to supine providence frame in the control group raises the question regarding the implementation of two totally different approaches. Neglecting the effect of gravitational forces in brace design of control group might be one of the reasons for different results and necessity of further adjustments as mentioned by authors in the result section.

The custom Providence standing frame provided the pad locations and pressure information to the orthotists while they perform the casting in the supine position. Both the control and intervention groups were casted while they were lying on the supine providence system.

We made the changes in the manuscript to clarify the procedures

The location of each bolster relative to the waist level was recorded. The orthotist then applied a plaster rigid wrap and identical pressure levels to the subject to the best stimulated in-brace
correction configuration on a supine position with the Providence system. The pads’ positions and pressure levels recorded from the standing frame were applied.

Paragraph 1 "Intervention Group Protocol" Line 17

"The procedure of [altering bolster location and pressure] were repeated until the orthotist attained the best simulated in-brace correction configuration." Shall the authors explain on number of arrangement altering and the definition of "best simulated in-brace configuration"? Did they consider the same amount of target threshold of in-brace correction in follow-up clinic (50%) for the simulated US in-brace measurement, as well?

The following sentence was added to the manuscript on Page 8. The target goal was still to try to get at least 50% correction. For this study, the orthotists altered the arrangement of the pads a maximum of 2 times.

We added the words “one time” in the following sentence to clarify.

In the result section, the third lines of the 2nd paragraph, we reported “The orthotist was satisfied with the first attempt with the US information in 8 out of 17 cases. With 9 subjects the location and pressure level of the bolsters were altered one time. Among these 9 revised cases, 7 showed better stimulated in-brace corrections, 1 had no change and 1 got worse.”

Paragraph 1 "Intervention Group Protocol" Line 21-23

What is the justification for selection of these specific pressure levels for air bags (60-75 and 90 mmHg) among wide-range of available quantities?

These pressure levels were recorded on the air bags which were applied by the orthotists based on their experience and subjective feeling. We did not purposely apply specific pressures at the air bags.

Page 9

Paragraph 2 "First Follow-up Clinic" Line 3

The target threshold of in-brace Cobb correction of 50% may not be applicable to some cases with more rigid curves.
We agree that 50% correction is not a practical goal for rigid curves. The statement has been modified to “The treating orthopedic surgeons used the target threshold of in-brace Cobb correction of 50%. They also used their clinical experience to consider whether the in-brace correction was optimal because the target threshold may not be attainable for rigid curves.

Page 10
Paragraph 2 Line 3
Typo for P-value as it is mentioned "0.0.22".
Thank you. We made the changes.

Reviewer #2: This paper presented a method of using 3D ultrasound imaging to increase the effectiveness of brace fitting for patients with scoliosis, which can avoid radiation exposed by the patients during traditional X-ray evaluation. From the results of the study, the assistance of ultrasound during the brace fitting and readjustment does reduce the need of repeated X-ray evaluation and the time needed for brace adjustment, in addition with a better improvement of curve correction. The followings comments can be considered for improving the manuscript:

Background

* The potential of using 3D ultrasound imaging has recently been reported by different groups. It is suggested to include some published papers most relevant to the content of this paper so that readers can have a better understanding about the feasibility of 3D ultrasound imaging, such as followings:


It is a little bit surprised that the above mentioned paper, Li et al (2012) about the brace fitting using 3D ultrasound, has not been included in the background, as this the best reference for the current paper. Proper description about the difference between the present study and Li et al. (2012) may better be given to give reader a clearer view about the motivation of the present study.

We added the following sentences in the last paragraph of the introduction section

Recently, ultrasound (US) imaging, a real-time non-invasive and non-ionizing method, was demonstrated to be successful in measuring proxy Cobb angles, vertebral rotation and flexibility [21-27]. The proxy Cobb angles which use vertebrae lamina positions rather than end plates, measured from ultrasound images have high intra- and inter-reliability as well as correlate well with radiographic measurements [22, 26]. Furthermore, there were studies applying ultrasound to determine the optimum location of the major brace pad [28, 29], but their approach did not provide real-time feedback nor determine the optimum pad pressure. Their ultrasound data were processed between the time the patient had their brace fitting and returned to receive the modified brace. Researchers were also able to use ultrasound to investigate the time lag between application of spinal orthosis and its effect on scoliotic curvature [30].

We added the following references [27] – [30] in the reference section


Methods

* Since the two groups of subject were not recruited during the same period (control group, retrospectively; intervention group, prospectively), there are a number questions readers can ask: what is the time interval between the recruitment of the two groups? are the types of scoliosis matched? what is the range as well as mean (SD) of the Cobb angles of the two groups, any difference? how to make sure the bracing techniques of the clinic and the staff are consistent during the two period of the recruitment time, i.e. whether any techniques, practice, or awareness (such as the use of X-ray) improved? The authors should give more information about these.

Thanks for the comments. We added more information as requested in the manuscript.

Seventeen consecutive AIS subjects (2M, 15F; age 13.2 ± 1.5 years, Cobb 32 ± 9°), with retrospectively collected data who were prescribed a new full time TLSO between January to June 2013 and met the inclusion criteria, served as the control group to match the intervention group recruitment. Another 17 new AIS subjects (2M, 15F; age 13.2 ± 1.4 years, Cobb 35 ± 8°), who were prescribed TLSO were prospectively recruited between January 2014 to April 2015 into the intervention group. There was no significant difference of the Cobb angle between groups.

All subjects are diagnosed with AIS and mentioned in the above paragraph.

On the last sentence of the “Patients” section, we mentioned

Both participating orthotists are aligned with the same paediatric scoliosis program and worked together using the same methodology to design spinal brace for over 10 years. There was no change on the X-ray system and the clinical protocol during the entire recruitment period (Jan 2013 – April 2015).

* Page 6 line 57: should be (2M, 15F; age 13.2 ± 1.4 years) - Fixed

* Page 7 Line 8: Since females have their puberty ages started earlier than males, will generalizing the inclusion age the same amount them affect the results?

We used the Scoliosis Research Society guidelines as the inclusion criteria of this study. We understand that the puberty of females was earlier than males. However, since there are only 2 males in each group and the proportion of males to females is the same in each group, the impact of later maturation in males should not unduly impact the results.
The air bag was attached on the surface to measure the interface pressure applied between the bolster and body. As bolsters were applied in different regions at the trunk, thus the pressure distribution of the air bags attached on them will vary between regions. Is there any related concern of the pressure difference during the placement of the bolster?

There is no concern of the pressure difference between the placement of the bolster as this is the design of the Providence system. The function of the air bag was used to record the interface pressure applied between the bolster and body.

As mentioned in the text, 2nd ultrasound image was overlapped with the in-brace radiograph. It seems that the lamina positions do not always appear in line with the lateral contour of the vertebral body. Is it the reason that causes the approximately 2 degrees discrepancies between the lamina method and the Cobb's method? If so, is it solvable?

According to one of our recent ultrasound study [22], there was no significant measurement accuracy differences between the thoracic and lumbar regions. Unfortunately, the 2 degrees difference was not a systematic error. There is no simple way to solve this discrepancy.

Results

Again, are both groups having the same distribution of the primary curves? As mentioned below in the discussion session, the region of interest of the spine might have correlation with the amount of curve correction improvement.

The curve distribution of the major curve were added to the manuscript under the “Patients” section.

The distribution of the primary curve of the control group were 7 major thoracic, 6 thoracolumbar and 4 lumbar curves. Another 17 new AIS subjects (2M, 15F; age 13.2 ± 1.4 years, Cobb 35 ± 8°), who were prescribed TLSO were prospectively recruited between January 2014 to April 2015 into the intervention group. The distribution of the primary curve of the intervention group were 6 major thoracic, 6 thoracolumbar and 5 lumbar curves.

Page 10 line 23: should be 0.02 to 0.22 - Fixed
Discussion

* In figure 3, lamina seems to be less observable in the lumbar region. Hence readers may want to know whether the difference of the anatomic shape of the thoracic and lumbar vertebrae has an effect of the accuracy on the brace correction. For instance, in Page 11 line 8, 7/17 patients in the intervention group were benefitted after the US-assisted adjustment, are the improved regions happen most likely in a certain region, or the improvements are randomized in different regions of the spine? More detailed discussion is needed.

* In general, the discussion is too superficial, and the authors should discuss their findings in related to available knowledge so that readers can understand better what additional knowledge the paper adds to the literature. Since Li et al (2012) has reported that 3D ultrasound imaging can help bracing, the authors need to enhance the discussion.

* In addition, any potential drawbacks in using the new approach? Any limitations in the current study, which can be improved along this research direction?

The following paragraphs have been added to the discussion section.

Even though Li et al. [28-29] applied the ultrasound method to assist brace fitting by investigating the locations of pressure pads, they did not provide the real-time feedback to the orthotist. They processed the data later to determine the optimum pad location and required patients to have an extra visit to receive the final brace. In this study, the intervention group has 7/17 (42%) that benefitted from having a brace adjustment after the initial setting of the pad placements. Those 7 cases which included 3 thoracic, 2 thoracolumbar and 2 lumbar cases, did not indicate this method was only beneficial for specific types of curves. However, since the number of cases are still limited, no conclusive statement can be made. The advantage with the intervention group was that the adjustment was made prior to brace fabrication rather than after the first follow-up visit. ........ This demonstrates how importantly the pressure pads location affects the effectiveness of the brace treatment. ......More clinical data are required to truly answer the total benefits of using ultrasound to assist brace casting. The limitation of this method is an experienced ultrasound technician is required during the brace casting to acquire and analyze the data. To overcome this, an automatic ultrasound machine which can scan the back automatically is being considered for future improvements. Also, the custom software developed for the ultrasound imaging measurement needs to be enhanced so that 3D information and automatic measurements can be obtained without requiring significant operator experience.