Semi-automatic ultrasound curve angle measurement for adolescent idiopathic scoliosis

Abstract

Purpose

Using X-ray to evaluate adolescent idiopathic scoliosis (AIS) conditions is the clinical gold standard, with potential radiation hazards. 3D ultrasound has demonstrated its validity and reliability of estimating X-ray Cobb angle (XCA) using spinous process angle (SPA), which can be automatically measured. While angle measurement with ultrasound using spine transverse process-related landmarks (UCA) shows better agreed with XCA, its automatic measurement is challenging and not available yet. This research aimed to analyze and measure scoliotic angles through a novel semi-automatic UCA method.

Methods

100 AIS subjects (Age: 15.0 ± 1.9 years, Gender: 19 M & 81 F, Cobb: 25.5 ± 9.6°) underwent both 3D ultrasound and X-ray scanning on the same day. Scoliotic angles with XCA and UCA methods were measured manually; and transverse process-related features were identified/drawn for the semi-automatic UCA method. The semi-automatic method measured the spinal curvature with pairs of thoracic transverse processes and lumbar lumps in respective regions.

Results

The new semi-automatic UCA method showed excellent correlations with manual XCA (R^2=0.815: thoracic angles R^2=0.857, lumbar angles R^2=0.787); and excellent correlations with manual UCA (R^2=0.866: thoracic angles R^2=0.921, lumbar angles R^2=0.780). The Bland-Altman plot also showed a good agreement against manual UCA/XCA. The

MADs of semi-automatic UCA against XCA were less than 5 °, which is clinically insignificant.

Conclusion

The semi-automatic UCA method had demonstrated the possibilities of estimating manual XCA and UCA. Further advancement in image processing to detect the vertebral landmarks in ultrasound images could help building a fully automated measurement method.

Level of evidence: Level III

Key words: Transverse process, 3D ultrasound, AIS, Scoliotic angles, Cobb

1. Introduction

Clinically described as a lateral curvature of the spine, scoliosis is a common spinal deformity that affects 0.5-5.2% of the population [1]. 70% of scoliosis cases occurred during the growth spurt of teenagers, known as adolescent idiopathic scoliosis (AIS) [2]. AIS has high chance to progress rapidly without proper intervention [3]. Except for cosmetic impairment, severe AIS may cause cardiopulmonary disability or restricted physical mobility [4].

X-ray is commonly used in evaluating spine conditions for AIS clinical management [5]. Cobb angle measurement (XCA) on radiographs is the standard protocol to assess the conditions [6]. AIS progression is indicated by the increase of Cobb angle large than 6° between visits. However, studies had shown the caveats of frequent radiation exposure to teenagers using radiography [7-9]. Doody et.al (2000) even revealed that AIS radiography may induce breast cancer [9].

Scolioscan, a three-dimensional ultrasound imaging system, led the trends in radiation-free spine imaging [10]. Scolioscan reconstructs 3D spinal volume through stacking each frame of B-mode ultrasound image with spatial and directional information. In order to compare with conventional anterior-posterior standing radiography, the 3D volume data is then projected to coronal plane. Such imaging technique is known as volume projection imaging (VPI) (**Fig.1(a)**) [11], and had been consistently and steadily improved throughout years [12,13]. In our previous works, Scolioscan had been demonstrated its validity and reliability for coronal spinal curvature measurement compared against X-ray [14-16]. In these previous studies, ultrasound spinous process angle (USSPA), the angle measured based on the shadow of the spinous processes, was used to evaluate the magnitude of the scoliotic curve (**Fig.1(b)**). This compromise came from the invisibility of the vertebra body by the nature of ultrasound imaging. USSPA values were generally slightly underestimated XCA (0.833-0.866) [14], due to the morphological difference between spinous processes and vertebrae bodies [17]. Brink et al. (2017) attempted to identify most tilted transverse processes from coronal spine ultrasound to estimate XCA, and harvested higher correlation against USSPA [15]. Lee et al. (2020) extended to a larger cohort and proved the value of transverse process features in ultrasound measurements [18]. The results of the spinal transverse process features inspired studies and various earlier validation studies using USSPA are presented in **Table.1** [14-16,18]. It could be judged that using transverse features achieved higher correlation with XCA than USSPA [15,18]. Assumption from observation shows that the lines drawn on the bilateral transverse processes on ultrasound images resembled that on the endplates of the vertebrae on radiographs.

Automatic USSPA measurement had been proved its validity and reliability in previous endeavors [12,14]; while an automatic UCA method, which demonstrated better agreement with XCA, is challenging and yet to be developed. Therefore, the objective of this study is to propose a systematic framework to identify spinal transverse processes features at all levels; and to calculate the AIS angles semi-automatically. This work also targets at validating the results of the proposed framework.

2. Materials and Methods

2.1. Subjects and Data Acquisition

This study included 100 AIS subjects (Age: 15.0 ± 1.9 years, Gender: 19 M & 81 F, Cobb: 25.5 ± 9.6°) that intended as trial cases for Scolioscan validation research. Two spine imaging modalities were involved: low-dose X-ray EOS imaging system (EOS Imaging, France) and Scolioscan 3D ultrasound imaging system (Model SCN801, Telefield Medical Imaging Ltd, Hong Kong) with a linear probe (central frequency of 7.5 MHz and 7.5 cm width). Each subject underwent both ultrasound and X-ray scanning on the same day with standing posture. The subjects were asked to stand with arms naturally rested in ultrasound scanning. The average scanning time for ultrasound assessment was 30-40 seconds. The scoliosis angle measurements of various methods were performed after data acquisition [12,18].

2.2. Scoliosis angle measurement methods

In order to validate the proposed semi-automatic method, manual X-ray Cobb and ultrasound transverse angle measurement were included for comparison. The measurements and respective annotations of all methods had been performed by the same spine imaging analyst. For the ease of elaboration, two terms were developed: X-ray Cobb angle (XCA) method, manual angle measurement using Cobb angle on X-ray image; manual ultrasound curve angle (manual UCA) method, manual angle measurement using ultrasound transverse angle on 3D ultrasound volume projection image (VPI) [18]. Semi-automatic UCA method (this method), semi-automatic angle measurement based on drawn transverse features upon 3D ultrasound VPI.

XCA method had been well-accepted as the gold-standard for quantifying the severity of scoliosis in clinical management [6]. Lines were drawn to characterize the most tilted vertebras as the start/end of the curves presented in the X-ray film (**Fig.2(a)**). Manual UCA method (**Fig.2(b)**) had been proven to have better correlation with XCA method than USSPA [15,18]. Since vertebral body could not be observed with ultrasound, alternate landmarks were selected to follow the similar inclination of the tilted end vertebras of scoliotic curves. In the thoracic region, lines were drawn passing the centers of the pairs of the thoracic transverse processes of the upper and lower end-vertebra of the curves (**Fig.3(a, b)**). The upper and lower end-vertebra thoracic transverse processes were manually identified by the nature of spinous process shadow from the coronal ultrasound VPI image. Distinct from coronal X-ray film, the lumps in the lumbar region are the combined shadow of the laminae and the inferior articular processes of the superior vertebrae and the superior articular processes of the inferior vertebrae (**Fig.3(a, c)**). Commonly, six lumbar lumps could be observed in the ultrasound images [18]. Five lumbar vertebrae together with the T12 laminae and the upper part of the sacrum contribute the lumps. The upmost lumbar lump is formed by the T12 laminae and the L1 articular processes; the last lumbar lump (usually 6th) is formed by the L5 laminae and the upper part of the sacrum; the rest N^{th} lump is formed by the L(N-1) laminae and the articular process of the L(N) vertebrae (N=2-5). Lines were drawn passing through the lower boundary of the most titled lumbar lumps to characterize the curve magnitude. The contours on the discussed anatomical features that shown in **Fig.3(a)** were not drawn on the ultrasound image by the manual UCA method: they were shown as the decision-making process of the image analysts on locating the desirable landmarks.

In contrast with the XCA method and manual UCA method which are manual procedures, our proposed method is divided into two stages: 1) Manual spinal transverse process-related features identification and contouring; and 2) Automatic angle measurement based on manual contoured masks. In the first stage, inspired by the manual UCA method, the identification of transverse process-related features was similar to manual contouring (**Fig.4(a), (b)**). Instead of only locating the most tilted transverse processes pairs, semi-automatic UCA method required drawing all transverse process-related features. This step required clinician's involvement in determining the related important spinal transverse-related features. Prior training for the clinician for identifying relevant features from different depths of the ultrasound VPI images was needed. Similarly, pairs of thoracic transverse processes (in green) were drawn for subsequent comparison of the tilting angles of each pair. Lumbar lumps (in red) were drawn for evaluating the thoracolumbar/lumbar angles. In addition, ribs (in blue) were drawn to provide reference of vertebrae levels. Due to the limitations of ultrasound scanning around the cervico-thoracic region, which may affect the upper thoracic region imaging [19]. Ribs are also contoured for vertebrae levels referencing. For example, 12th rib commonly points downwardly in spine ultrasound coronal images; it could be used to navigate through the VPI image. In the second stage, the manual contours were forwarded to the program for automatic filling to create masks for subsequent analysis. The color code for the mask was adhere to the contours: thoracic transverse processes (green), ribs (blue) and lumbar lumps (red) (**Fig.4(c)**). The program ran in parallel for each mask, and the overall schematic diagram is shown in **Fig.5**. After integrating the analysis from different masks, the curve characteristics (number of curves, number of level and start/end level of each curve) could be established; and the transverse process angle could be calculated accordingly.

2.3 Statistical analysis

Statistical analyses were conducted using SPSS 25.0 for Mac (SPSS Inc., Chicago IL, USA). Our proposed semi-automatic UCA method were compared with the manual UCA and XCA methods using linear correlation for thoracic curves, thoracolumbar/lumbar curves and combined curves. Linear regression equations with intersections were studied. Correlation efficient 0.25 to 0.50 indicates a poor correlation; 0.50 to 0.75 indicates moderate/good correlation; and 0.75-1.00 indicates very good/excellent correlation [20]. In order to validate the usefulness of the proposed method, its correlation with manual XCA should be at least comparable to manual UCA. Bland-Altman method was adopted to test the agreement between the semi-automatic UCA and manual UCA/XCA. In order to measure the differences in agreement for the semi-automatic UCA method against others, the mean absolute differences (MAD) were calculated. The MADs of the mentioned three methods were paired for the paired t test. The significance level was 0.05.

3. Results

From the cohort of 100 AIS subjects (Age: 15.0 ± 1.9 years, Gender: 19 M & 81 F, Cobb: 25.5 ± 9.6°), for the average of thoracic angles: XCA, manual UCA, and semi-automatic UCA methods were 25.8 ± 10.9°, 25.6 ± 11.1°, 26.7 ± 11.4°, respectively; for the average of thoracolumbar/lumbar angles: 25.1 ± 8.4°, 23.2 ± 8.2°, 23.3 ± 8.6°; for the average of all angles: 25.5 ± 9.6°, 24.3 ± 9.7°, 24.9 ± 10.1°, respectively.

Very good to excellent correlation between the proposed semi-automatic ultrasound-based transverse process-related features angle measurement method and manual UCA / XCA method. For proposed method with manual UCA, correlation coefficient $R^2=0.866$ ($p<0.05$), with thoracic angles $R^2=0.921$ ($p<0.05$) and lumbar angles $R^2=0.780$ ($p<0.05$), respectively (**Fig.6**); for proposed method with XCA, correlation coefficient $R^2=0.815$ ($p<0.05$), with thoracic angles $R^2=0.857$ ($p<0.05$) and lumbar angles $R^2=0.787$ ($p<0.05$), respectively (**Fig.7**). The results had demonstrated that the performance of semi-automatic method was as good as manual UCA, while at the same time semi-automatic UCA was capable of estimating XCA measurements. We had observed that both manual UCA and this method were slightly larger than XCA, the transformation coefficients were between 0.86-0.93. In addition, the results of our method were very close to the results of manual UCA, with the transformation coefficient of 0.92.

The Bland-Altman plot demonstrated a good agreement between pairs of the semi-automatic method with manual UCA and XCA corrected with the linear regression equations (**Fig.8**). Regarding the MADs for measurement results validation, no clinical difference was found. MADs of the proposed method and manual UCA: 2.9 ± 2.4°, range 0-16.8° (thoracic angles: 2.7 ± 2.1°, range 0-11.4°; lumbar angles: 3.0 ± 2.7°, range 0.1-

16.8°); MADs of the proposed method and XCA: 3.5 ± 2.7°, range 0-18.1° (thoracic angles: 3.6 ± 2.5°, range 0-14.8°; lumbar angles: 3.4 ± 2.9°, range 0-18.1°).

4. Discussion

Using spinal transverse process-related features to estimate scoliosis angles had demonstrated promising results, when compared with XCA: R^2=0.815, with thoracic angles R^2=0.857 and lumbar angles R^2=0.787 (**Fig.7**). MADs were smaller than 5°, which indicates no significant difference between ultrasound and X-ray measurements on the same batch of subjects. These findings further strengthened the pioneer study of manual UCA measurements with main thoracic curve $R^2 \geq 0.892$ and lumbar curve $R^2 \geq 0.872$ [18]. Strong correlations were established between transverse process-related method and XCA. Compared with the USSPA method from the early Scolioscan validation study: R^2=0.760, with thoracic angles R^2=0.780 and lumbar angles R^2=0.721 against XCA [14]; and large-scale Scolioscan research on 952 subjects with thoracic angles R^2=0.762 and lumbar angles R^2=0.548 against XCA [16]; transverse process angle showed better correlation with the XCA. The clinical significance was established that transverse process angle measurements could accompany the conventional Scolioscan USSPA method in AIS management and reduce the use of X-ray. Also, X-ray complement was very meaningful in screening, as normal subjects could avoid unnecessary radiation exposure [21].

The proposed method also showed comparable results with manual UCA. These two methods both involved using transverse process-related features from ultrasound. The identification of these features required expertise. Anatomical abnormalities including deformity of the transverse process could cause difficulties in the interpretation of the anatomy, thus the corresponding features in the ultrasound images as well. This is a limitation for the manual contouring process introduced in this study. Considering the acquired ultrasound images about spine are in 3D, future studies will be focused on whether some types of anatomical abnormalities can be identified in the 3D image data set. The training involved an orientation from an ultrasound expert with knowledge of spine anatomy. The experienced operator first explained the related anatomical landmarks (thoracic transverse process, rib and lumbar lump) of transverse process on ultrasound spine images; a guidance sheet of typical shapes of these features were provided to the "non-experienced" operators. Then a practice set was given to the "non-experienced" operators for practicing contours; and their results would be reviewed by the experienced operator. Moreover, the "non-experienced" operators were guided to contour pertinent features when encountering missing or deformed transverse process. Two assumptions were used for the interpretation. First, we assumed that the transverse processes came in pairs. If one side of the transverse process was deformed or unable to identify, we would consider its respective position and shape with the reference of the other side. Second, if the pairs of transverse process could not be properly shown on the same layer (depth) of the spine VPI image; we would search for the features from adjacent layers and fused the features on the same image. Contours drawn by "unexperienced" operators would be assessed by the expert for "fine-tuning". Once the designated personnel grasp the technique for contouring transverse features, the angle measurement would be processed by the software automatically. With such insights, semi-automatic UCA method saved substantial human efforts in angle measurements, users only needed to circle the relevant features; and the program would compute the results. As discussed, the semi-automatic method also demonstrated very good correlation with XCA (R^2=0.815). Since the prior knowledge for this study was given by the same expert who practiced manual UCA, we could understand that its performance was constrained by the manual UCA. Comparing with manual UCA results, we can observe that very close correlations R^2=0.866, with thoracic angles R^2=0.921 and lumbar angles R^2=0.780 (**Fig.6**). MADs were smaller than 5°, which indicates no significant difference between manual UCA and our method. Therefore, it could be judged that the semi-automatic UCA method was valuable. It reduced human efforts and errors in measurement after manual identification step. At the same time, the semi-automatic results were comparable upon manual ones. Our method further implied that as long as the segmentation of the relevant features could be extracted, the performance of the angle measurements could be guaranteed. For our current practice, we invited an experienced operator to manually contour the transverse process-related features; then the contours together with the raw ultrasound images were passed to two other experienced operators to confirm whether they have been correctly drawn. If the drawn pieces could not be mutually agreed, re-drawing of the contour was conducted until all the three operators agreed the result. Intra-rater/operator or inter-rater/operator reliability test upon contour drawing was not conducted, which was a limitation for this validation study and will be investigated in our future studies. The future direction of the fully-automatic system is to generate segmentation of the transverse features as of manual contouring.

Spine transverse process angles were slightly smaller than XCA, the transformation coefficients were between 0.908-0.969 (**Fig.7**). XCA were slightly underestimated the transverse angles from ultrasound. The consistency indicated that the cause was from anatomy. Transverse process and spinous process are posterior structure where vertebra body that projected on coronal plane is anterior structure. Linking the tips of a pair of transverse process is differently angulated compared with projecting the vertebra body arc [22]; which could be partially explained this phenomenon. In our future studies, large-scale validation research would be conducted to prove the discovery.

Implied from semi-automatic UCA method, major limitations came from the prefix ‘semi-automatic’. The program required manual input in transverse process-related features identification, which relied on the subjective expertise of contouring on ultrasound at Stage 1 of the proposed method. Obviously, manually contouring each pair of transverse process-related features can document all features and standardize the protocol, which could lower the risks of arbitrarily defining the transverse process angle from observation. However, the performance was still affected by manual UCA, when the two methods were practiced by the same person. In our next step of the endeavor of transverse process angle, we would test on intra-operator and inter-operator reliability on the manual contouring part of the semi-automatic UCA method.

Moreover, fully-automated version of the proposed method would be our next milestone. Manual contouring of transverse process-related features still cost human efforts and suffered from human errors. As described in **Section 2** and shown in **Fig.3**, transverse process features are in distinct shapes from thoracic (circular disk) and lumbar regions (lumbar lump). Hence, the classification and contouring of related features could be automated through machine learning. Our group had put forward a bone feature segmentation model for the spine coronal ultrasound VPI images using a hybrid U-net and showed promising possibilities of supervised deep learning in features contouring [23]. The experience could be used in the fully-automated protocol drafts. With the continuous development of series of imaging processing methods and deep learning approaches, the next-generation of automated version of the proposed method can be pervasive on AIS measurements.

5. Conclusions

To conclude, the proposed semi-automatic UCA method had demonstrated very good correlations (R^2=0.815) with conventional XCA method, which could be taken as good reference in scoliosis assessment. The proposed method also had shown comparable results (R^2=0.852) against manual UCA, which indicated the possibilities of reduction of manual efforts in transverse process angle measurements. Reliability test should be conducted to further strengthen the effectiveness of the proposed method. The current method was limited by the quality of the input coronal ultrasound VPI image and the manual contouring process. Thus, future studies would focus on development a fully-automated version of this method with 3D spine profile and supervised deep learning.

List of figure captions and table

Fig.1 **(a)** Illustration of the generation process of ultrasound coronal spine image by Scolioscan volume projection imaging (VPI) technique. 3D spinal volume representation is formed by stacks of 2D B-mode ultrasound images with spatial and directional information. 2D coronal projection plane is cut from a customized skin-bone depth. **(b)** An example of conventional Ultrasound Spinous Process Angle (USSPA) measurement by Scolioscan. Both manual and automatic measurement results were presented. Lines in blue are manual drawn along with the medial spinous process shadow; while the curve in red is automatically interpolated by Scolioscan. (Images were extracted from [13])

Fig.2 **(a)** An example of X-ray Cobb Angle (XCA) method* on coronal X-ray images, lines were drawn crossing the middle of the most tilted vertebra to characterize a scoliotic curve. Two curves were presented, thoracic curve (T6-T11) and thoracolumbar curve (T11-L3).*This is a revised XCA method in order to compare with UCA method directly. Lines were drawn passing through the midpoint of the vertebrae **(b)** an example of Ultrasound Cobb Angle (UCA) on ultrasound coronal VPI image, lines were drawn linking the centers of transverse processes in thoracic region and passing through the lower boundary of lumps in lumbar region to characterize a scoliotic curve. Two curves were presented, thoracic curve (T6-T11) and thoracolumbar curve (T11-L3) Both scans were taken on the same subject on the same day

Fig.3. **(a)** Illustration of semi-automatic transverse process-related features used by the Ultrasound Cobb Angle (UCA) method. The contours are used in UCA calculation. **(b)** An example of the contour showing a pair of thoracic transverse process. **(c)** An example of the contour showing a typical lumbar lump (combined shadow of the laminae of the superior vertebrae and the articular processes of the inferior vertebrae) [18]

Fig.4 Illustration of the process of the proposed semi-automatic UCA method using transverse process-related features. **(a)** Raw ultrasound VPI image; **(b)** spinal transverse process-related features identification (contours were drawn manually): green - thoracic transverse process; blue - rib; red - lumbar lump; **(c)** transverse process-related features mask generation for image processing purpose; **(d)** automatic angle calculation based on the masks

Fig.5 Schematic diagram of the automatic program (the proposed semi-automatic UCA method, Stage 2) for computing angles based on transverse process-related features. The block diagrams are color coded according to the respective color of masks (Thoracic transverse process: green; Lumbar lump: red; Rib: blue. Each mask was processed in parallel until the curve characteristics (number of curves, start/end levels) were understood by the program; then the angles were automatically calculated

Fig.6 Correlation and linear equations between manual calculated Ultrasound Cobb Angle (UCA) (x) and the proposed semi-automatic UCA method (y). **(a)** Thoracic angles; **(b)** thoracolumbar/lumbar angles; **(c)** combined angles of (a)&(b)

Fig.7 Correlation and linear equations between manual measured X-ray Cobb Angle (XCA) (x) and semi-automatic Ultrasound Cobb Angle (UCA) method (y). **(a)** Thoracic angles; **(b)** thoracolumbar/lumbar angles; **(c)** combined angles of (a)&(b)

Fig.8 Bland-Altman plots indicate the differences between the pairs **(a)** manual UCA and the proposed semi-automatic UCA method; **(b)** XCA and the proposed semi-automatic UCA method corrected with the linear regression equations for all angles (combination of thoracic and lumbar angles)

References

[1] Konieczny MR, Senyurt H and Krauspe R (2013), Epidemiology of adolescent idiopathic scoliosis, J Child Orthop, vol.7, May 2013, pp.3-9.

[2] Weiss HR, Goodall D (2008). The treatment of adolescent idiopathic scoliosis (AIS) according to present evidence. A systematic review, *European Journal of Physical and Rehabilitation Medicine*, vol.44(2), Jun 2008, pp.177-193.

[3] Ylikoski M (2005). Growth and progression of adolescent idiopathic scoliosis in girls, *Journal of Pediatric Orthopaedics B,* vol.14(5), Sep 2005, pp.320-324.

[4] Koumbourlis AC (2006). Scoliosis and the respiratory system. *Paediatric Respiratory Reviews*, vol.7(2), Jun 2006, pp.152-160.

[5] Altaf F, Gibson A, Dannawi Z, Noordeen H (2013). Adolescent idiopathic scoliosis. *British Medical Journal*, vol.346, May 2013, pp.30-34.

[6] Morrissy RT, Goldsmith GS, Hall EC, Kehl D, Cowie GH (1990). Measurement of the Cobb angle on radiographs of patients who have scoliosis. Evaluation of intrinsic error. *The Journal of Bone & Joint Surgery,* vol.72, Jul 1990, pp.320-327.

[7] Bolling T, Schuck A, Pape H, Rube C, Meyer FM, Martini C, Timmermann B, Asadpour B, Kortmann RD, Beck JD, Langer T, Paulides M, Konemann S, Willich N((2007). Register for the evaluation of side effects after radiation in childhood and adolescence, first results. *Klinische Padiatrie*, vol.219(3), May 2007, pp.139-145.

[8] Himmetoglu S, Guven MF, Bilsel N, Dincer Y(2015). DNA damage in children with scoliosis following X-ray exposure. *Minerva Pediatrica*, vol.67, Oct 2015, pp.1-2.

[9] Doody MM, Lonstein JE, Stovall M, Hacker DG, Luckyanov N, Land CE (2000). Breast cancer mortality after diagnostic radiography: findings from the U.S. scoliosis cohort study. *Spine*, vol.25(16), Aug 2000, pp.2052-2063.

[10] Zheng YP, CW Cheung. A three-dimensional (3D) ultrasound imaging system for assessing scoliosis. Patent issued: US 8,900,146 B2; China 201080040696.0; Japan 5849048. Pending in Canada, Australia, and EU. Filled in Jul 2009.

[11] Cheung CWJ, Zhou GQ, Law SY, Mak TM, Lai KL, Zheng YP (2015). Ultrasound volume projection imaging for assessment of scoliosis, *IEEE Transactions on Medical Imaging*, vol.34(8), Aug 2015, pp.1760-1768.

[12] Zhou GQ, Jiang WW, Lai KL, Zheng YP (2017), Automatic measurement of spine curvature on 3-D ultrasound volume projection image with phase features, *IEEE Transactions on Medical Imaging*, vol.36(6), Jun 2017, pp.1250-1262.

[13] Jiang WW, Zhou GQ, Lai KL, Hu SY, Gao QY, Wang XY, Zheng YP (2019), A fast 3-D ultrasound projection imaging method for scoliosis assessment, *Mathematical Biosciences and Engineering*, vol.16(3), May 2019, pp. 1067-1081.

[14] Zheng YP, Lee TTY, Lai KKL, Yip BHK, Zhou GQ, Jiang WW, et.al (2016). A reliability and validity study for Scolioscan: a radiation-free scoliosis assessment system using 3D ultrasound imaging, *Scoliosis and Spinal Disorders*, vol.11(1), Sep 2016, pp.1.

[15] Brink RC, Wijdicks SPJ, Tromp IN, Schlosser TPC, Kruyt MC, Beek FJA, Castelein RM (2017), A reliability and validity study for different coronal angles using ultrasound imaging in adolescent idiopathic scoliosis, *Spine*, vol.18(6), Jun 2018, pp.979-985

[16] Wong YS, Lai KKL, Zheng YP, Wong LLN, Ng BKW, Hung ALH, Yip BHK, Chu WCW, Ng AWH, Qiu Y, Cheng JCY, Lam TP (2019). Is radiation-free ultrasound accurate for quantitative

assessment of spinal deformity in idiopathic scoliosis(IS): a detailed analysis with EOS radiography on 952 patients, *Ultrasound in Med. & Biol.,* vol.45(11), Oct 2019, pp.2866-2877.

[17] Herzenberg JE, Waanders NA, Closkey RF, Schultz AB, Hensinger RN (1990). Cobb angle versus spinous process angle in adolescent idiopathic scoliosis. The relationship of the anterior and posterior deformities. *S*pine, vol.15(9), Mar 1990, pp.874-9.

[18] Lee TTY, Lai KKL, Cheung JCY, Castelein RM, Lam TP, Zheng YP (2020). 3D Ultrasound imaging provides reliable angle measurement with accuracy comparable to X-ray on patients with adolescent idiopathic scoliosis. *15th International Society on Scoliosis Orthopaedic Rehabilitation and Treatment Meeting (SOSORT)*, Jun 2020.

[19] Folsch C, Schlogel S, Lakemeier S, Wolf U, Timmesfeld N, Skwara A (2012). Test-retest reliability of 3D ultrasound measurements of the thoracic spine, *PMR*, vol.4, May 2012, pp.335-341.

[20] Dawson B, Trapp RG (2004). Basic and Clinical Biostatistics. 4th ed. New York: Lange Medical Books/McGraw-Hill; 2004.

[21] Lam TP, Wong YS, Yip BHK, Ng BKW, Hung ALH, Chu WCW, Zheng YP, Lai KKL, Lee W, Qiu Y, Cheng JCY (2019). Using ultrasound for screening scoliosis to reduce unnecessary X-ray exposure: a prospective diagnostic accuracy study on 442 schoolchildren from a scoliosis screening program, 2019 IMAST, Apr 2019.

[22] Louis R (2012). Surgery of the Spine: Surgical Anatomy and Operative Approaches. Reprinted (1983) Springer New York: Science & Business Media; 2012.

[23] Huang ZX, Wang LW, Leung FHF, Banerjee S, Yang D, Lee TTY, Lyu J, Ling SH, Zheng YP (2020). Bone feature segmentation in ultrasound spine image with robustness to speckle and regular occlusion noise, *2020 IEEE Intl Conf on SMC*, Oct 2020.