Shear wave elastography of the maternal cervix: A transabdominal technique

Sandra O'Hara MMS, DMU,AMS, AFASA [1,2];Marilyn Zelesco BSc MSc AMS FIR[3];Zhonghua Sun PhD, FSCCT[2]

[1]SKG Radiology, West Perth, Perth, Western Australia, Australia
[2]Department of Medical Radiation Sciences, Curtin University, Perth, Western Australia, Australia
[3]Department of Medical Imaging, Fiona Stanley Hospital, Murdoch, Western Australia, Australia

Corresponding Author:

Zhonghua Sun PhD, FSCCT
Department of Medical Radiation Sciences, Curtin University
Perth, 6845, Australia
Email: Z.Sun@curtin.edu.au
Tel | +61 8 9266 7509
Fax | +61 8 9266 2377

Abstract

Introduction: Reduced cervical length with transvaginal ultrasound is a strong indicator of spontaneous preterm birth in the high risk population. In low risk women the appropriate method to assess this risk is still debatable. Ultrasound elastography has been used to assess cervical strength. This research aimed to assess the accuracy of shear wave speeds obtained deep to echo free fluid filled structures, and the use of two dimensional shear wave on the maternal cervix using a transabdominal ultrasound approach.

Method: Agreement of shear wave speeds obtained through fluid and directly onto an ultrasound phantom was assessed for accuracy. Speed measurements were obtained in the anterior and posterior portions of the internal and external cervical os on 50 gravid participants in the mid trimester of pregnancy.

Results: No difference in shear wave speeds was obtained in the phantom with either direct contact or through the saline water-bath (p<0.05). In 50 participants, measurements were obtainable at the external os anterior and posterior in 49 and 38 participants respectively and in 47 and 42 participants for internal os anterior and posterior. The mean speed at the external os anterior and posterior, was 2.01 ± 0.51m/s and 2.38 ± 0.47m/s respectively, and at the internal os anterior and posterior, 2.49 ± 0.50m/s and 2.58 ± 0.41m/s.

Conclusion: Shear wave speed measurements can be obtained in the maternal cervix using a transabdominal approach with a moderately full maternal bladder, with a larger number of shear wave measurements obtained in the anterior cervix compared to posterior.

Key words

Shear wave, elastography, cervix, preterm birth, ultrasound

Introduction

Ultrasound shear wave elastography (SWE) is a relatively new technique that can produce a quantifiable measurement of stiffness of tissues in-vivo. SWE utilises a modified sound wave to produce shear waves within tissues.[1] Faster shear wave speeds are produced in stiffer tissues, with slower speeds being recorded in softer tissues.[2]

Preterm birth continues to have significant implications for the risk of neonatal mortality and morbidity,[3] with the preterm birth rate being 7.5% in Australia in 2011.[4] A shortened maternal cervix as measured by transvaginal ultrasound has been shown to be a strong indicator of subsequent spontaneous preterm birth (SPTB).[5] Even so, a shortened cervical length has a low sensitivity for SPTB in the low risk population.[6, 7] Elastograhic assessment of cervical strength may have the potential to predict cervical insufficiency with greater accuracy than length alone.[2] It may be possible to identify women who are at increased risk of SPTB due to cervical softening that occurs before a reduction in cervical length with strain elastography, but this method lacks standardization between operators.[8, 9] SWE is advantageous as it provides a quantitative evaluation of the speed of propagation of the shear wave in tissues with less operator dependance.[10, 11]

Research utilising an intracavity transducer and the transvaginal ultrasound approach using SWE has shown that it may be possible to identify a reduction in shear wave speed indicating cervical softening, prior to a reduction in cervical length.[8, 11] It has also been found that some patients will decline the transvaginal approach and that problems with language barriers can also impede consent.[12, 13] The cervix has viscoelastic tissue properties that may alter during pregnancy, [14]and with preterm cervical insufficiency. This research assesses the use of a transabdominal (TA) ultrasound approach with a moderately full maternal bladder to acquire shear wave speeds in the maternal cervix.

The Canon Aplio 500 system utilises a two dimensional shear wave technology (2DSWE). 2DSWE utilises a B-mode image that is overlayed by the elastogram in real time. Ultrasound pulses are modified to a high intensity to produce shear waves in the region of interest. Shear waves cannot be produced in fluid, but it has been shown that it may be possible to obtain accurate shear wave measurements deep to echo free fluid filled structures.[15] This research also assesses if shear wave speeds obtained with direct transducer contact onto an ultrasound phantom are the same as if the transducer is placed on a fluid filled stand-off.

Materials and Methods

Subject recruitment

This study was conducted at branches of SKG Radiology.

A prospective study of women presenting for their routine second trimester fetal morphology ultrasound was performed. All participants were over 18 year of age with varying pregnancy history and ethnicity and body habitus. All participants were required to read an information sheet and give informed consent to be enrolled into the study. Exclusions were women with a multiple gestation or women already receiving vaginal progesterone or with current cervical cerclage placement. Patients unable to give informed consent due to language barriers were also excluded. Ethics approval was granted from the clinical site and Curtin University Human Research Ethics Committee.

This study represents the first 50 cases obtained as part of a larger research design, and presents the use of a new technique utilising 2DSWE to obtain shear wave speed measurements on the maternal cervix using a transabdominal approach.

Study design

All imaging was performed on the Canon Aplio 500 version 6 ultrasound machine (Otawara-shi, Tochigi, Japan), using the 6C1 curvilinear transducer. The elastogram was set to a size of 20 x 20mm with the region of interest (ROI) set to a 5mm sphere for the maternal cervix. The elastogram opacity was set to 0.6. Transducer shear wave frequency was 2.2MHz with a tracking frequency of 0, equating to a 2.2MHz push pulse and 2.2MHz tracking pulse. A 'continuous' mode cine-loop of frames of greater than three seconds of stable elastogram was stored at each region.[16] A frame rate setting of 1, equating to 0.4 frames per second was used. All data was collected by a single operator with over 20 years' experience in the field of sonography. Intra-operator testing was performed on 20 of the participants. Shear wave speed measurements obtained twice in each region and were compared for repeatability by the single operator.

Phantom testing

The Elastography Quality Assurance Phantom (CRIS, Norfolk, VA, USA) with a background speed of 2.94m/s and lesion speed of 1.91/s was used for this experiment. This phantom was used to enable testing of the specified lesion speed with both direct transducer contact and through the saline standoff. The lesion is located at a depth of 3cm and the ROI was set to a 20mm sphere to encompass the lesion. The transducer was supported independently with a transducer clamp and stand as shown in figure 1. Acoustic ultrasound gel was used to facilitate transducer contact. A total of fifteen shear wave speed (SWS) measurements were acquired with the transducer in direct contact with the phantom and a further fifteen through a saline stand-off with a depth of 4.5cm. The saline standoff is intended to mimic the urinary bladder and to this end normal saline was utilised with an osmolality of 300mOsm/kg,[17] similar to that of urine. Other factors remained stable as above.

Figure 1. Image of transducer placement during SWS acquisitions using the Elastography QA Phantom with the saline standoff. Clamp and stand support of the transducer is also demonstrated.

Imaging methodology

The maternal bladder was partially filled to an amount required to provide a B-mode window for visualisation of the cervix posterior to the bladder, and to achieve adequate through transmission of the SWE main pulse to the cervix. The total bladder volume was variable dependant on individual participant anatomical characteristics, with bladder filling adequate to allow the superior to inferior dimension of the bladder to cover the length of the cervical canal as demonstrated in figures 2 and 5. The patient is placed in the supine position with transducer placement inferiorly in the midline just superior to the symphysis pubis. Measurements were acquired in the mid-sagittal plane of the cervix. The cervical canal, internal and external os were identified.[18]Transducer orientation was aligned to the length of the cervical canal and tilted to as close to a perpendicular approach to the canal as technically possible. Increasing transducer pressure has been shown to cause compression of tissues that can cause an increase in SWS, particularly in superficial tissues.[19] In this study transducer pressure was kept to a minimum. The 5mm ROI was positioned adjacent to the endocervical canal and mucosa and central to the outer serosal layer, in the circumferential layer of smooth muscle and collagen thought responsible for cervical dilatation.[20] Shear wave speed measurements were obtained at the internal and external os, anterior and posterior portions as can be seen in Figures 2 A-D. The mean speed was recorded three times in each anatomical location.

Figure 2A-D. Example of elastogram and ROI placement in the anterior and posterior portions of the internal and external os. Shear wave speed obtained at the internal os anterior and posteriorly is 2.17 ± 0.19m/s and 2.16 ± 0.12m/s. Shear wave speed obtained at the external os anteriorly and posteriorly were 1.73 ± 0.07m/s and 1.72 ±0.06m/s respectively.

Shear wave speed accuracy The main pulse used in SWE, and the propagation of the shear waves can both be affected by ultrasound artifacts.[19] The Canon Aplio 500 SWE device gives indications of accuracy of shear wave propagation. The ROI registers many hundreds of SWS values simultaneously and the mean speed and one standard deviation (SD) of the values is recorded. ROI placement into regions of reliable shear wave propagation is aided by the use of the elastogram and propagation maps. The regions of most homogenous colour in the elastogram and the most parallel and equidistant lines on the propagation map are indicative of consistent shear wave propagation and will return the lowest SD.. Regions with in-homogenous or loss of colour fill in the elastogram and erratic lines in the propagation map are indicative of inconsistent shear wave propagation and will indicate a high SD. The high SD is indicative of a large variation in SWS obtained within the ROI, and measurements obtained with a high SD usually exhibit a higher mean speed than those obtained in the same region with a lower SD.

SWS measurements were obtained at the anterior and posterior portions of the internal and external os in all 50 participants. Regions exhibiting anin-homogenous or a non-filled elastogram and erratic propagation lines and an SD of greater than 20% of the mean value were considered to be indicative of inaccurate shear wave propagation Inaccurate measurements were excluded from the data set prior to statistical analysis. The elastogram also gives indications of increased transducer pressure, which can be identified by a red band of colour in the elastogram near field. All imaging was taken with minimal transducer pressure and devoid of the red band.

Safety considerations

It has been recommended that SWE be used with the same safety considerations as Doppler ultrasound.[19] and recommendations have been made for further investigations into the effects of SWE technology on the fetus.[21] Though Doppler technology has become standard practice for fetal examinations, for this study the elastogram was not placed on or closely adjacent to any fetal parts and use of SWE was kept to a minimum.. The moderately full bladder was advantageous in that the fetus was displaced cephalad from the maternal cervix.

Statistical analysis

SPSS version 26.0 (SPSS V26.0, Chicago, USA) was used to analyse data. The mean ± standard deviation (SD) was used to present continuous variables The variables were assessed using a Kolmogorov-Smirnov Test. The data did not differ significantly (p>0.05) from normality. The speed measurements acquired at each region of the cervix and for phantom testing were compared using a paired samples t-test. The null hypothesis used as follows, H_0 : speed measurements from region 1 = speed measurements from region 2, is formulated as the paired differences in speed with a theorized mean of zero, tested at a 5% level of statistical significance($p<0.05$).

Intra-operator agreement was assessed with the null hypothesis, H_0 : mean bias between repeated measurements = 0 using a one sided t-test Testing incorporated a 5% level of statistical significance ($p<0.05$).

Results

Fifty women participated in this study over a 7 month period commencing in November 2016. All participants were between 17 and 28 weeks of gestation. The mean age was 28 years (19-43 years). Varying gestational status was included with a mean gestation of 2 (0-9 gestations) and 1 prior delivery (1-3 deliveries). All SWS measurements obtained exhibiting a non-uniform elastogram and propagation map and an SD of greater than 20% of the mean speed were excluded as previously described. A minimum of 2 reliable measurements was required to formulate the mean speed obtained at each region of the cervix. Results incorporating the number of successful measurements and mean speed for each region of the cervix are shown in Table 1, with Table 2 outlining the results of the paired t-test comparing the mean speed obtained at each region of the cervix.

Intra-operator testing was performed on 20 participants. Differences were not statistically different in all regions. The mean difference at external os anterior and posterior was 0.002 ± 0.03m/s (p=0.789) and 0.010 ± 0.06m/s (p=0.505) respectively. The mean difference at internal os anterior and posterior was 0.003 ± 0.04m/s (p=0.735) and -0.004 ± 0.04m/s (p=0.592) respectively.

Phantom testing

Fifteen SWS measurements were obtained in the phantom lesion with both direct transducer contact (Figure 3) and through the saline standoff (Figure 4), with a saline depth of 4.5cm. The mean speeds obtained in the lesion with direct contact and through the standoff were 1.94 ± 0.04m/s and 1.96m/s ± 0.01m/s respectively. The mean difference between SWS with saline standoff and direct contact being -0.01(SE 0.01); $t(15) = -1.26$ p=0.229. Figure 3. Shear wave speed measurement obtained at the level of interest in the Elastography QA phantom with direct transducer contact. Mean speed of 1.95m/s ± 0.18ms.

Figure 4. Shear wave speed measurement obtained at the level of interest in the Elastography QA phantom with saline standoff at a depth of 4.5cm. Mean speed of 1.95m/s ± 0.23ms.

Discussion

SWE utilises a sound beam modified to a high intensity, forming the main pulses that are sent vertically into the tissues to be interrogated. The main pulses create sideways movement of shear waves away from the main pulse that are tracked by the ultrasound machine in a similar way to Doppler technology.[19] The main pulse can also be focused to the region of interrogation to improve reliability.[15] As opposed to other SWE devices, 2DSWE is able to be utilised deep to echo free fluid filled structures.[15]

Results of the phantom testing showed that it is possible to obtain accurate SWS measurements with 2DSWE when placing the elastogram deep to an echo free fluid filled structure. The comparison of SWS measurements obtained in the ROI with and without the fluid filled stand-off showed no significant difference between SWS obtained. . .T

In this study the cervix is visualised with a moderately full maternal bladder. As with B-mode imaging the bladder was used as an acoustic window to visualize the maternal cervix deep to this and to also allow transmission of the main pulses used in 2DSWE to the cervix. Though shear waves cannot be produced in fluid filled structures,[10] it is possible to produce shear waves in tissues deep to the fluid filled structure if we place the elastogram in this region as shown in figures 1 and 5.

A recommendation for 2DSWE in the liver is that reliable shear wave propagation can be produced at a depth of up to 7cm from the transducer face.[15] As figure 5 demonstrates it appears possible to produce reliable shear wave propagation at a depth greater than 7cm from the transducer face to the cervix through the maternal bladder. The ROI placement in figure 5 can be seen at a depth of 84.6mm from the transducer face. The depth of the maternal bladder is measured at 61.7mm; and the overall depth of tissue to the ROI is measured at close to 22.9mm.

Figure 5. Region of interest (ROI) placed at external os anterior with a depth measurement of 84.6mm to the ROI; bladder height is measured to be 61.7mm and the depth of tissues measured at 22.9mm.

For the 50 participants presented in this study, the greatest number of reliable SWS speed measurements were obtained at the external os anterior at 49, with 47 measurements obtained at the internal os anterior. The least number of reliable measurements were obtained at the external os posterior at 38, with the internal os posterior achieving 42 reliable SWS measurements. A greater depth of the main pulse penetration from the transducer face is required to reach the posterior cervix and produce shear wave propagation. As demonstrated in figures 2 and 5, the external os posteror is at the greatest depth from the transducer face in most patients, and this is the region that produced the least number of reliable SWS values for this study.

It is an observation from the results of these 50 participants that a cervical canal close to horizontal in orientation so that the internal and external os are a similar distance to the transducer face is the most optimal position to obtain reliable shear wave propagation in all regions. When there is an anterior angulation of the internal os, the internal os is markedly closer to the transducer than the external os and the depth to the external os from the transducer face can be problematic. Increasing depth to all regions of the cervix may be a factor in patients with a large body mass index. A consideration for penetration of the main pulse to the posterior portion of the cervix is the acoustic attenuation properties of the cervix. The cervix has an acoustic attenuation of at 1.3 to 2.0 dB $cm^{-1}MHz^{-1}$ which is over twice the acoustic attenuation of the liver.[3] It would thus be an expectation that the distance of penetration of the main pulse is reduced in the cervix compared to what would be expected in the liver. The cervical canal also has opposing layers of mucosa surrounding a central canal, and it has also been shown that tissue interfaces may be problematic in shear wave elastography.[22]

The results of this study have shown a statistically significant difference between shear wave speeds obtained in the anterior compared to the posterior external os, with the posterior external os registering a higher mean speed. Interestingly, our results showed no statistical difference between the anterior and posterior internal os. Hernandez et al[11] reported an increase in SWS in the cervix posteriorly using a transvaginal ultrasound approach as did Carlson et al[22] using a linear array transducer to measure SWS on chemically ripened and unripened specimens of the cervix. This study reported a small difference in SWS obtained between the anterior and posterior cervix, with greater speeds obtained in the posterior portion, with these differences being greater in the ripened specimens.[22] Using a transvaginal ultrasound approach Peralta et al[23] also found increased stiffness in the posterior cervix using SWE and research into the use of strain elastography has shown no difference or reduced stiffness posteriorly in the cervix.[8, 24] As reported by Carlson et al[22] and Peralta et al[23] the results of this research have also shown an increase in shear wave speeds obtained at the internal os compared to the external os, both anteriorly and posteriorly.

The one experienced operator in this study showed good reproducibility of SWS in each region of the cervix, but this study is limited by the data collection being performed by one operator. A recommendation would be that this technique is now disseminated to other operators with varying levels of experience and inter-operator testing be performed to assess the reproducibility of the technique.

Conclusion

Results of this study show that it is possible to measure shear wave speed in the maternal cervix using a transabdominal approach. A larger number of accurate shear wave measurements can be obtained in the anterior cervix compared to the posterior, with higher shear wave speeds obtained at the internal os compared to external os. Further assessment of shear wave speeds obtained in the maternal cervix may be useful for the identification of softening of the cervical tissues and their possible relationship to cervical insufficiency and spontaneous preterm birth. Practical application of this technology could be the use of a non-invasive technique to assess cervical strength in the mid-trimester, with the potential to predict imminent cervical insufficiency and subsequent spontaneous preterm birth with a greater sensitivity than cervical length alone.

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Tables

Table 1. Number of successful measurements and mean speeds obtained in each region of the maternal cervix

	Successful measurements over 50 participant	**Mean speed (m/s)**	**Standard Deviation (SD)**	**Number of accurate measurements out of a possible 150**
External os Anterior	49	2.01	±0.51	144
External os Posterior	38	2.38	±0.47	115
Internal os Anterior	47	2.49	±0.50	139
Internal os Posterior	42	2.58	±0.41	118

Table 2. Results of paired t-test comparing different regions of the maternal cervix

Comparisons	**Number of cases compared**	**Mean difference in speed (m/s) & SD**	**SE of mean**	**t(df)**	**Significance (*p*=0.05)**	**Statistically significant difference**
External os anterior vs posterior	38	-0.46 (±0.45)	0.07	-6.33(37)	.001	Yes
Internal os anterior vs posterior	41	-0.10 (±0.56)	0.09	-1.18(40)	.243	No
Anterior internal os vs external os	44	0.48 (±0.39)	0.06	8.01(43)	.001	Yes
Posterior internal os vs external os	36	0.188 (±0.19)	0.51	2.20(35)	.035	Yes

SD – Standard Deviation

Figures

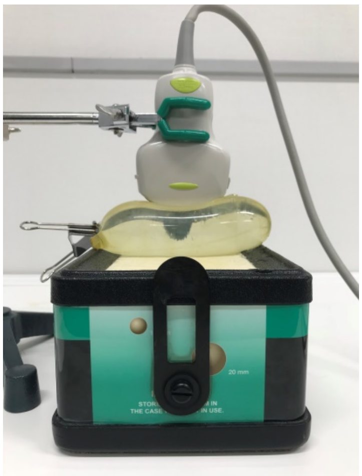

Figure 1.

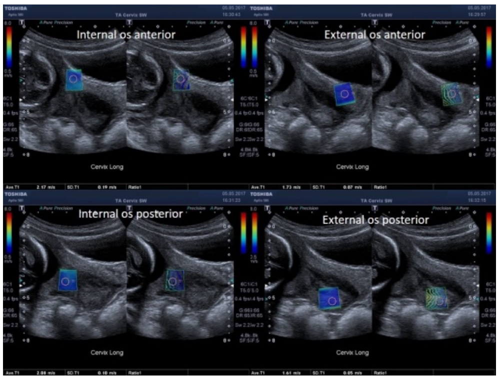

Figure 2.

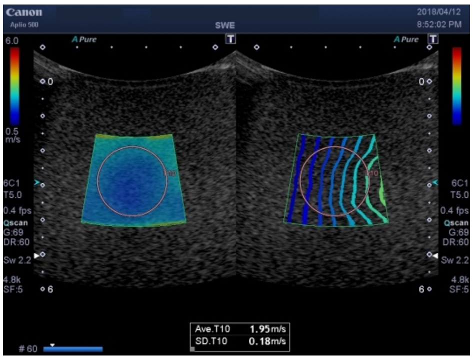

Figure 3.

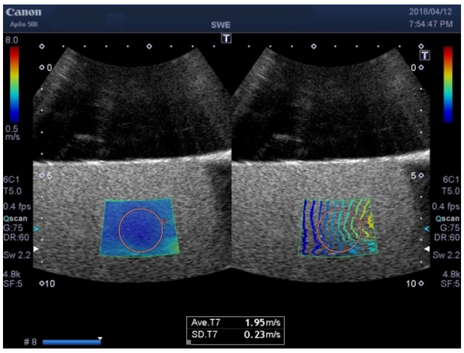

Figure 4.

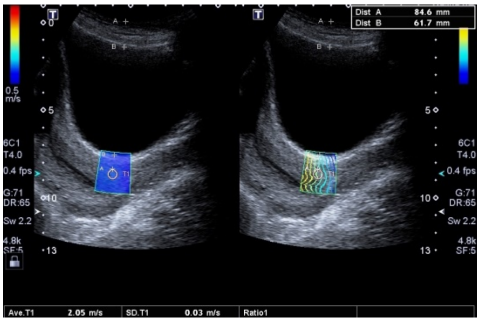

Figure 5.