Shear wave elastography on the uterine cervix: Technical development for the transvaginal approach

Short Title: SWE of the cervix using transvaginal ultrasound

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Abstract

Objectives This research aimed to identify biological and technical confounders in the non-pregnant cervix when applying shear wave elastography with an endovaginal transducer.

Methods Cervical speed measurements were obtained at the internal and external os, anterior and posterior portions of the cervix using a transvaginal approach in 69 non-gravid patients.

Results Reliable measurements were obtained at the external os and internal os, anteriorly and posteriorly, in 63, 55, 55 and 26 patients respectively. The mean speed obtained at the external os, anteriorly and posteriorly, was 2.52 ± 0.49m/s and 2.87 ± 0.63m/s respectively, and at the internal os anteriorly and posteriorly, 3.29 ± 0.79m/s and 4.10 ± 1.11m/s respectively. The difference in speed between all regions was statistically significant (p<0.05).

Conclusion Ultrasound -induced artifacts appear to affect the transmission of the elastographic main pulse, with cervical position contributing to suboptimal shear wave production in the posterior cervix. Reliable shear wave propagation can be achieved in the anterior cervix in most patients.

Keywords Shear wave, elastography, cervix, preterm birth, transvaginal ultrasound

Introduction

Retention of a pregnancy requires the cervix to maintain strength to withstand multiple forces from the uterus, from the weight of the growing fetus and amniotic sac, and also passive pressure from the uterine wall. The cervix softens and shortens throughout pregnancy and finally dilates for the fetus to be delivered vaginally. Premature softening of the cervix is associated with early shortening of cervical length and subsequent spontaneous preterm birth (SPTB).[1] The cervix can be described as soft, firm or medium based on a digital examination, but this method is subjective to the clinician, and creates difficulties due to the expectation that the cervix will soften initially at the proximal portion.[1]

Currently, the length of the cervix assessed with transvaginal ultrasound (TVU) is the feature that is assessed to indicate cervical strength and premature softening.[2] A short cervix has been shown to be a significant risk factor for subsequent SPTB.[3] In women with a high risk of SPTB due to medical history, a shortened cervical length on TVU has a sensitivity of over 50% for subsequent SPTB. However, in low risk women the sensitivity is reduced to 37%,[4,5] and the appropriate method for screening for SPTB in these women is yet to be established. With preterm birth affecting 13 million babies every year and the implications for neonatal mortality and morbity,[6] there is a need for a non-invasive technique to assess cervical strength with greater sensitivity than length alone.

Ultrasound elastography assesses mechanical properties of tissues in the region being examined. The basis for this technique is that soft tissue deforms differently from firm tissue and the elastographic images reflect this difference.[7] Utilizing strain elastography, it has been proposed it may be possible to identify women in the historically low risk who are at an increased risk of SPTB due to softening of the cervical tissues which precedes a reduction in cervical length.[8] A more successful induction of labor has also been observed in patients with a softer internal os.[9]

When applied to the cervix, elastography techniques based on strain imaging have difficulties due to the lack of surrounding reference tissue and the inability to reliably quantify, and hence reproduce, transducer pressure applied to the cervix.[10] Shear wave elastography (SWE) produces an acoustic radiation force impluse (ARFI) excitation to produce shear waves.[11] By quantifying parameters related to the propagation of the shear wave, such as shear wave speed, one can infer an estimate of tissue stiffnes.[6] It is expected that this technique will produce a more objective and reproducible mechanical evaluation of the cervix than strain elastography.[12,13]

There is promise for the use of SWE on the maternal cervix during pregnancy to assess cervical strength. It has been shown that it is feasible to examine the external os anteriorly with TVU SWE and that a reduction in speed in this region is evident in women who deliver preterm.[14] It has also been shown with SWE that the cervix softens as gestational age advances,[15] and in women who have cervical ripening following induction of labor.[16] The cervix has been shown to be softer during pregnancy than the non-gravid state.[1] An increase in stiffness in the cervix has been shown in the region of cervical carcinoma with the use of strain elastography.[17] This study investigates the use of shear wave elastography with an endovaginal ultrasound technique applied to the non-pregnant human uterine cervix. Experimentation and technique development was performed on a low risk non-gravid population. The goal being to identify biological and experimental variables that affect the interpretation of shear wave speed (SWS) estimates in the non-gravid population to contribute to the standardization of the technique for application in the non-gravid population, and in the main part to the pregnant cervix. With the consideration that there may be some differences observed in the technique applied in the obstetric popluation due to extrinsic pressure from fetal parts at the internal os.

Material and Methods

This pilot study was conducted at branches of SKG Radiology in Perth, Western Australia. A convenience sample was utilized from women presenting for a routine gynecological ultrasound. All participants were between 18 and 49 years of age, menstruating regularly with varying pregnancy history and ethnicity. All patients were required to read a patient information form and give informed consent before being enrolled in the study. Ethics approval was granted from the clinical site and the Curtin University Human Research Ethics Committee.

Data collection occurred over a 13 month period commencing in July 2016. Estimation of sample size was performed with consultation from a statistician. The research by Carlson et al [16] identified a statistically significant difference between the stiffness of cervical tissue in ripened and unripened hysterectomy specimens of the cervix utilizing SWE. The difference between the mean values and the standard deviations of the values were utilized to formulate a sample size using the equation for Samples Sizes for Comparative Research Studies by Eng. [18] A level of significance of $p<0.05$ was utilized. This calculation resulted in a minimum of 50 normal (stiff/non-pregnant) cervix needed to formulate a baseline cervical stiffness for non-pregnant patients.

Imaging protocol

All imaging was performed on the Toshiba Aplio 500 versions 6 and 6.5 ultrasound machines (Otawara-shi, Tochigi, Japan). Cervical stiffness measurements were acquired using the 11C3 PVT-781VTE intra-cavity transducer. The machine setting of a shear wave frequency of 4MHz, tracking of 0 was employed. This setting utilizes a 4MHz push pulse and 4MHz tracking pulse. SWS measurements were obtained using continuous mode and the lowest frame rate setting of 1, equating to 0.4 frames per second. The elastogram map was stable for at least 3 seconds before speed measurements were obtained.[19]

Measurements were registered in the mid-sagittal plane of the uterine cervix, midway between the canal and serosa at the internal and external os, anterior and posterior. This plane was used as it allows operators to identify the required anatomical landmarks. Once in contact with the cervix, the transducer was withdrawn to minimize transducer pressure on the cervix whilst not compromising the B-mode image.

Inter-operator testing was performed on 15 participants. The primary SWE operator had over 20 years of experience in the field of sonography with two secondary operators having less than and more than 5 years of experience, respectively. Both secondary operators underwent training in the technique before commencement of data collection. The primary and senior secondary operators are both skilled in liver shear wave elastography and all operators have experience in gynecological and obstetric applications of ultrasound.

Imaging methodology

Elastogram Map Placement

The elastogram map opacity was set to 0.3 to allow for visualization of the cervical anatomy through the elastogram. Similar to other authors,[10,15] initially (the first eight participants) the elastogram map was placed over the entire length of both anterior and posterior portions of the cervix, with placement of all four regions of interest simultaneously to obtain speed measurements (Figure 1). Utilizing a large elastogram box resulted in difficulties in focusing the region of greatest sensitivity of the main pulse to the region of interest (ROI). The recent EFSUMB update on the use of liver ultrasound elastography recommends that the main pulse focus should be placed at the level of the ROI.[20]

To improve shear wave propagation and repeatability, the authors reduced the elastogram box size to an anterior-posterior (AP) dimension of 15mm and the bottom width of the box was set to 20mm. The focus was set to the center of the elastogram box at the level of intended ROI placement. Each part of the cervix was interrogated separately so that the region of greatest sensitivity could be positioned more effectively to the anterior and posterior uterine cervix for both internal and external os (Figure 2).

Shear wave region of interest placement

In the non-gravid state, the uterine cervix measures approximately 25mm in length and 20 to 25mm in total width, equating to an approximately 10mm width of collagenous and smooth muscle tissue around the central canal.[21] Histological evidence shows that the cervical canal is surrounded by a layer of longitudinal smooth muscle fibers adjacent to the canal. Wrapping circumferentially around the longitudinal layer is a layer of smooth muscle and collagenous cells (Figure 3). At the internal os there is a 50-60% concentration of smooth muscle cells in the circumferential layer, reducing to 40% at the mid cervix, and to 10% at the external os,[22] with no appreciable difference in this structure between nulliparous and multiparous specimens.[22] The longitudinal fibers are thought to be responsible for the action of cervical effacement and the circumferential layer to prevent cervical dilatation.[21] It has been hypothesized that the circumferential layer may be acting as a 'sphincter' to retain pregnancy.[21,22] A 5mm ROI (Figure 2) has been utilized for this study to facilitate ROI placement in the circumferential layer of collagen and smooth muscles thought responsible for pregnancy retention.

Shear wave precision

Utilizing Toshiba technology, the precision of the shear wave propagation can be assessed in a number of ways. This elastogram speed map was set to a scale of 0.5 to 8.5cm/s with blue being indicative of softer tissues. Regions of heterogeneous color or loss of color indicate a loss of precise shear wave propagation. A red band of color in the near field and extending into the elastogram map is indicative of increased transducer pressure on the skin or organ and vertical artifacts through the elastogram are indicative of transducer movement. As with B-mode ultrasound imaging, shear waves are also prone to scattering, reflection or refraction and these artifacts further affect the precision of shear wave speeds.[24] Planar wave propagation is an assumption in the estimation of SWS. The validity for this assumption can be tested using the waveform propagation maps provided by the scanner. The wave front propagation map is unique to Canon technology and indicates shear wave arrival time as represented by contour lines. The shear wave arrival time is inversely related to the material stiffness, and thus wider spacing indicates a faster shear wave, and therefore, a stiffer material. The wave front map also indicates precision of shear wave propagation. Regions of highest precision are those where the contour lines are shown to be parallel and equidistant, with a loss of parallel lines being indicative of non-planar shear wave propagation. Due to the curvature of the intra-cavity transducer face, there is some divergence of these parallel lines. This effect would be more apparent in the far field of the elastogram box.

The ROI also gives indications of the precision of the shear wave propagation. Many hundreds of values are obtained from the 5mm ROI and the mean speed and one standard deviation (SD) of these values is displayed. The regions within the elastogram with the most homogenous color and straightest, most parallel and equidistant propagation lines will also correlate with the lowest SD of the mean. Regions of heterogeneous or loss of color and distortion of propagation lines are indicative of non-planar shear wave propagation; these regions also exhibit a higher SD of the mean and a higher mean speed. Figure 4 demonstrates a range SD's obtained: ranging from an SD of 2.1% through to an SD of 38%, with examples of the elastogram and propagation maps and mean speeds obtained.

The aforementioned factors should be considered when ascertaining the precision of the SWS. The authors considered regions of the elastogram with loss of color fill and concordant distorted propagation maps and an elevated SD to have non-planar shear wave propagation. These qualitative factors and an SD of greater than 20% of the mean speed (quantified mathematically) was used as a cut off above which mean SWS was considered artifactually increased and not reliable. Unreliable measurements were excluded during statistical analysis.

Transducer pressure

As mentioned previously the transmission of the main pulse and resultant shear waves can be affected by numerous ultrasound induced artifacts. [24] It is ideal to optimize the b-mode image and obtain an optimal ultrasound window before the application of SWE. [20] Care should be taken to minimize probe pressure on the tissue of interest, whilst maintaining a good b-mode window.[12] A localized pre-stress can result in apparent high SWS values due to non-linear tissue responses.[24]

To assess the magnitude of this effect, we studied if a change in transducer pressure on the cervix alters the resultant shear wave speeds. To this end, ten participants were examined with increased and reduced transducer pressure. All regions of the cervix were interrogated as previously described. The change in distance to the ROI between increased and reduced pressure was as follows: external os anterior 4.3mm (2-10mm), external os posterior 4.2mm (1-9mm), internal os anterior 4.2mm (2-7mm), internal os posterior 4.2mm (1-8mm).

Inter-operator testing

Inter-operator testing was performed on 15 participants. For each participant the first operator obtained shear wave readings at all 4 regions of interrogation. The secondary operator then performed the same set of readings at each of the 4 regions. The mean speed obtained by each operator was tested for concordance.

Statistical analysis

Data analysis was performed using SPSS version 26.0 (SPSS V26.0, Chicago, USA). Descriptive data were presented as mean ± standard deviation (SD). The variables were input to assess normality using a Kolmogorov-Smirnov Test. The data did not differ significantly ($p>0.05$) from normality. A paired samples t-test was used to compare the speed measurements obtained from each region of the cervix. The null hypothesis, H_0 : speed measurements from region 1 = speed measurements from region 2, which is operationalized as the paired differences in speed with a posited mean of zero, was tested against a two-sided alternative, at the 5% level of statistical significance, ($p<0.05$).

Inter-operator agreement compares the speed obtained from each operator using an Intra-class Correlation Coefficient (ICC). A low level of agreement being close to 0 and a high level of agreement 1. ICC estimates and their 95% confidence intervals were calculated based on a mean rating ($k = 3$), absolute agreement, 2-way mixed effects model.[25,26]

Results

Seventy three women were considered eligible for this study. Four did not give consent to having the elastography imaging performed due to the extra time required. Sixty nine participants had a mean age of 34 years (range: 18-49 years), with a mean gestation of 1 delivery (range: 0-8 gestations). All measurements returning a SD of greater than 20% of the mean speed were removed. Participants with two or more reliable measurements obtained in each region of the cervix were included in the statistical data set to facilitate a mean speed obtained over more than one measurement. Of the 69 participants 3 were unsuccessful in obtaining any reliable shear wave measurements in all regions due to the cervix being in the vertical position relative to the transducer face.

The number of reliable measurements obtained in each region for the remaining 66 participants, and the mean cervical speed and standard deviation for each region can be seen in Table 1. Stiffness results for each region were assessed for differences in concordant pairs as shown in Table 2. The number of reliable measurements obtained was assessed dependent on cervical canal position. The number of measurements obtained with differing positions of the uterine cervix, are presented in Table 3, with a diagrammatic representation of the positions presented in Figure 5. SWS values for different age ranges, stage of menstrual cycle medical history and ethnicity are presented in Table 4. The mean speed measurements obtained with normal and reduced probe pressure are shown in Table 5.

Inter-operator testing was performed on 15 participants. The external os anterior and posterior were comparable for 15 participants; the internal os anterior was comparable for 14 participants, with measurements unobtainable in 1 participant for both operators. The internal os posterior was comparable for only 6 participants, with shear wave propagation in the remaining 9 participants unobtainable for both operators. The ICC obtained at the regions of the cervix was as follows - external os anterior 0.83 (CI 0.45 – 0.95), external os posterior 0.69 (CI 0.07-0.90), internal os anterior 0.92 (CI 0.76 – 0.97), internal os posterior 0.90 (CI 0.37-0.98)

Discussion

The cervix creates a challenge in the accurate use of SWE to assess its stiffness. Spatial variations of cervical tissue composition and structure can complicate shear wave propagation. Transducer positioning is limited to the anterior fornix adjacent to the external os with transducer angulation required to interrogate the internal os. As our results show, reliable shear wave production is more likely to be produced anteriorly in the cervix, with a greater number of reliable speeds obtained at the external os than the internal os. The internal os posterior is most likely to produce inaccurate or a loss of shear wave propagation in all anatomical positions, with depth of interrogation appearing to be problematic in some patients.

The research by Peralta et al[15] used SWE to measure elasticity of the external os and mid cervix. This research used 6mm ROIs at the external os, with the mid cervix measurements placed at a close distance from these. In this study of 40 participants mid cervix anterior and posterior measurements were not obtainable in one and two participants, respectively.[15] Our results showed a greater proportion of unsuccessful SWE measurements at the internal os. Depending on cervical position the posterior portion of the internal os in particular can reach a depth greater than 3cm from the transducer face (Figure 6). A recommendation from Canon Medical (Otawara-shi, Tochigi, Japan) is that utilizing the endocavity transducer as described previously; the main push pulses can be expected to produce shear waves to a depth of 3cm using an ultrasound phantom with an acoustic attenuation of 0.5 dB cm^{-1} MHz^{-1}. The cervix has a high acoustic attenuation of over double that of the liver, at 1.3 to 2.0 dB $cm^{-1}MHz^{-1}$.[6] This increased attenuation decreases the penetration depth of the main push pulse, and reduces its ability to generate measurable tissue displacements.[6] The challenges for SWS estimates of the cervix with an endovaginal transducer may relate to its depth-dependent signal-to-noise ratio. In tissues this is relative to the focal depth of the transducer, and thus the regions that are deep and proximal in the cervix can be difficult to access with the main pulse.[6]

Too much transducer pressure can produce a pre-stress load,[24] that can falsely elevate shear wave speeds. As shown in Table 5, increased probe pressure caused an increase in resultant shear wave speeds both anteriorly and posteriorly in the cervix. It was noted that on two participants the increase in pressure resulted in an improvement in shear wave propagation posterior to the cervical canal, but in most participants the pre-stress was transferred to both the anterior and posterior cervical tissues. Of note was that when the increased transducer pressure was applied the SD of the mean speed also increased. Figure 7 is an example of the change in SWE speed obtained with gentle and then increased probe pressure. The transvaginal approach can be problematic as a small amount of transducer pressure is required to make contact with the anterior fornix to acquire a good B-mode window prior to the application of the SWE. The transducer can be withdrawn to release this pressure but a level of contact is still required. We conclude that pre-compression can alter the SWS estimation in the cervix and that non-linear tissue responses or mechanical compression of the collagen layers by the transducer may be possible causes.

As shown in Table 4 there appears to be minimal difference in SWS between nulliparous and parous patients. There were similar speeds obtained for women with vaginal deliveries and c-sections and also similar speeds between ethnicities. It also appears that mostly there is an overall increase in cervical stiffness with age, and that SWE speed at the internal and external os may alter at different stages of the menstrual cycle. The cervix has been shown to alter its width and length throughout the menstrual cycle. The sphincter-like effect of the collagenous and muscular fibers at the internal os has its greatest strength during the luteal phase of ovulation and relaxes up to two days prior to menstruation.[21] Our results showed the greatest speeds at the internal os were obtained during the secretory phase of the endometrium, corresponding to the luteal ovarian phase. Further research could incorporate shear wave speeds obtained during the first few days of menstruation when the internal os should be at its softest. Larger numbers from each group would be needed to draw robust conclusions.

The internal os showed a significant increase in speed compared to external os both anteriorly and posteriorly. The research by Carslon et al[23] also demonstrated this phenomenon with greater differences in shear wave speed between the external and internal os on the unripen cervix specimens versus the specimens that had been chemically ripened.

Research on the use of strain elastography on the maternal cervix for the prediction of preterm birth documented no appreciable difference in cervical stiffness between the anterior and posterior cervix,[27] with the study by Molina et al[10] showed a reduced stiffness in strain values in the posterior cervix. As reported by Hernandez et al[13] and Peralta et al[15], our results also show that the posterior part of the cervix appears to register a higher speed than the anterior part in this cohort, with greater differences registered at the internal than the external os. As can be seen in Figure 2, when obtainable, the arrival time of the shear wave appears to be faster in the posterior cervix with widening of the propagation lines posteriorly compared to anteriorly. There was also a greater divergence from parallel of the propagation lines deep to the endocervical mucosa and canal in the posterior cervix, with less measurements being obtainable in this region. Carlson et al[23] utilized hysterectomy specimens of the cervix to obtain shear wave speeds. The specimen was dissected and a 9MHz linear array transducer was used to take measurements from the canal surface of the specimen. This research found a small difference between anterior and posterior shear wave speeds in the unripen cervix, with average speeds formulated of 3.45±0.97m/s and 3.56±0.92m/s respectively. Larger differences were observed in ripened specimens. Our results show a larger difference in speeds obtained between the anterior and posterior cervix at the internal os with a similar difference as Carlson et al[23] at the external os.

The cervical canal could be considered a shear wave boundary, surrounded by aligned collagen fiber bundles as previously described.[23] The appendix to the EFSUMB Guidelines and Recommendations[12] states that boundaries between tissues may reduce or prevent shear wave penetration across the boundary. Shear wave scattering, reflection and refraction artifacts can also be caused by variations in tissue density which may result in errors in shear wave estimation.[12] Material anisotropy can alter resultant shear wave speed.[12] In patients with an axial position ranging from mild to fully axial, the main pulse may be approaching the collagen fibers at an angle that may cause anisotropy of the muscular collagen layer. Reducing the elastogram box size improved the interrogation of the axial cervix, however in the axial position the internal os is difficult to interrogate in most cases. We hypothesize that this anisotropy may be causing artifactual increases in shear wave speed deep to the cervical canal or a loss of effective shear wave propagation.

The internal os anterior showed a good level of agreement between operators, as did the internal os posterior and external os anterior, though these regions had a broader confidence interval reducing the reliability of the result. The external os posterior showed poor to moderate agreement with a wide confidence interval obtained for the ICC in this region.

We can conclude from this study that the attenuation properties of the cervix and shear wave artifacts are reducing the production of, and precision of, shear wave measurements obtained deep to the cervical canal. It is important to reduce transducer pressure to the anterior fornix to minimize the pre-stress that may cause an increase in shear wave speeds in both the anterior and posterior cervix. The anterior cervix is more likely to produce more precise shear wave values than the posterior cervix, with the anatomical position of the cervix appearing to affect the success of resultant shear wave measurements, with the ideal position being a canal that is horizontal in position.

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Table 1. Summary of shear wave measurements obtained for the uterine cervix

Participants in total-66	Successful measurements obtained (participants)	Mean speed (m/s)	Standard Deviation (SD)	Total number of successful measurements for all participants out of a possible 198
External os Anterior	63	2.52	0.49	184
External os Posterior	55	2.87	0.63	158
Internal os Anterior	55	3.29	0.79	157
Internal os Posterior	26	4.10	1.11	78

Table 2. Summary of statistical differences in stiffness between regions of the cervix for all participants

Comparisons	Number of cases compared	Mean difference in speed (m/s) & SD	SE of mean	Significance (p=0.05)
External os anterior vs posterior	52	-0.44 (0.69)	0.09	$p<0.001$
Internal os anterior vs posterior	22	-1.13 (1.11)	0.24	$p<0.001$
Anterior internal os vs external os	55	0.79 (0.70)	0.09	$p<0.001$
Posterior internal os vs external os	21	1.42 (0.88)	0.19	$p<0.001$

Table 3. Summary of number of reliable interrogations registered in each region of the cervix with varying anatomical position

Cervical Canal Orientation	Total	Number of accurate interrogations in each region External Os Anterior	External Os Posterior	Internal Os Anterior	Internal Os Posterior
Horizontal	21	21	17	20	10
Angled	33	33	30	31	11
Vertical	7	7	5	3	3
Posterior angulation	2	1	2	1	1

Table 4. Summary of mean speed obtained in each region dependent on patient characteristics

		Mean speed in m/s and SD for regions of the uterine cervix			
Participant characteristics	**Number of participants**	**External Os Anterior**	**External Os Posterior**	**Internal Os Anterior**	**Internal Os Posterior**
Age range 18-25	13	2.27 (SD 0.33)	2.61 (SD 0.63)	3.19 (SD 0.77)	3.67 (SD 0.15)
Age range 26-33	16	2.47 (SD 0.42)	2.86 (SD 0.59)	3.02 (SD 0.49)	4.15 (SD 0.98)
Age range 34-41	19	2.49 (SD 0.46)	2.96 (SD 0.61)	3.17 (SD 0.37)	4.10 (SD 1.37)
Age range 42-49	18	2.77 (SD 0.58)	2.95 (SD 0.72)	3.66 (SD 1.11)	4.22 (SD 1.34)
Early Proliferative	15	2.60 (SD 0.52)	3.04 (SD 0.37)	3.29 (SD 1.23)	4.87 (SD 1.37)
Late Proliferative	24	2.39 (SD 0.48)	2.88 (SD 0.72)	3.22 (SD 0.61)	4.03 (SD 1.40)
Early Secretory	23	2.57 (SD 0.47)	2.84 (SD 0.66)	3.31 (SD 0.61)	3.69 (SD 0.49)
Late Secretory	4	2.85 (SD 0.62)	2.46 (SD 0.51)	4.48	4.61
Nulliparous	22	2.39 (SD 0.47)	2.71 (SD 0.52)	3.20 (SD 0.59)	3.90 (SD 0.47)
Primiparous	16	2.63 (SD 0.41)	2.82 (SD 0.56)	3.13 (SD 0.58)	4.26 (SD 0.88)
Multiparous	28	2.56 (SD 0.53)	3.00 (SD 0.73)	3.45 (SD 1.01)	4.13 (SD 1.50)
Vaginal deliveries	27	2.64 (SD 0.477)	2.82 (SD 0.66)	3.56 (SD 0.95)	4.46 (SD 1.24)
C-section	13	2.45	3.03	2.89	3.90

		(SD 0.54)	(SD 0.53)	(SD 0.43)	(SD 1.51)
European	46	2.54 (SD 0.51)	2.94 (SD 0.66)	3.41 (SD 0.82)	4.07 (SD 1.10)
Asian	15	2.51 (SD 0.39)	2.74 (SD 0.59)	3.09 (SD 0.53)	4.47 (SD 0.71)
Middle Eastern, Indian & African	5	2.39 (SD 0.50)	2.92 (SD 0.64)	2.39 (SD 0.87)	4.04 (SD 1.10)

Table 5. Comparison of shear wave speeds obtained with reduced probe pressure and pressure on anterior fornix increased to a level appropriate for B-mode imaging

	External Os Anterior	**External Os Posterior**	**Internal Os Anterior**	**Internal Os Posterior**
Reduced probe pressure	2.42 (SD 0.52)	2.64 (SD 0.57)	3.36 (SD 0.51)	4.62 (SD 1.18)
Increased probe pressure	4.89 (SD 1.79)	5.13 (SD 1.91)	5.23 (SD 2.04)	5.26 (SD 0.65)

Figure Legends

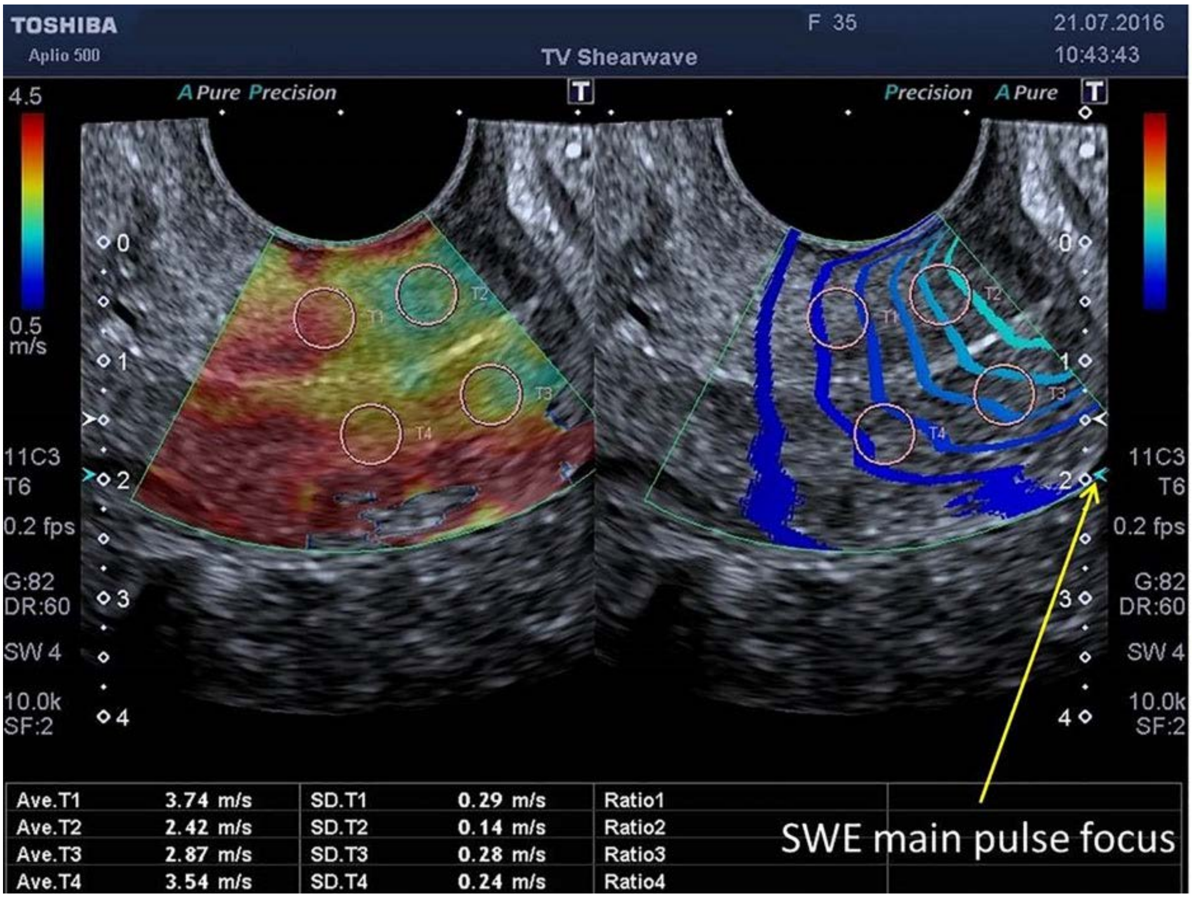

Figure 1. Large elastogram displaying placement of four ROI's in the different regions of the cervix being interrogated and the arrow highlighting the region of greatest sensitivity of the SWE main pulse.

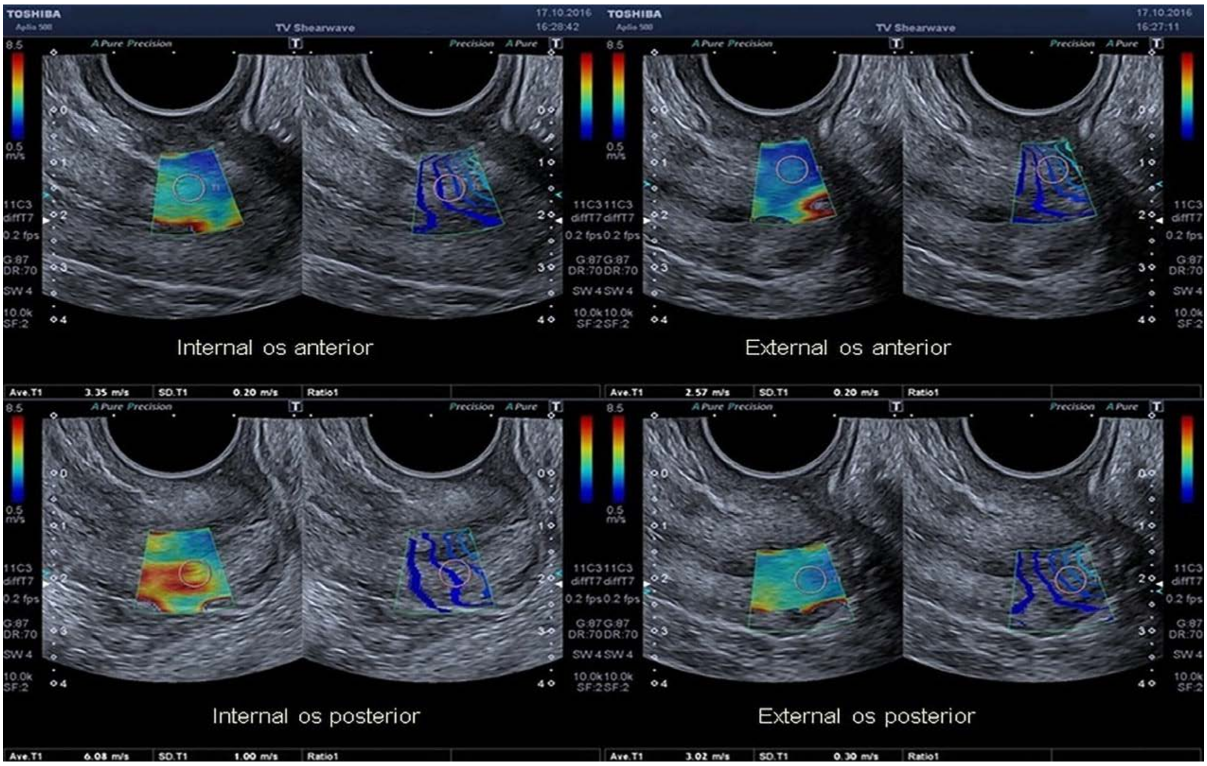

Figure 2. Cervical SWE with reduced elastogram size and a 5mm ROI, showing separate interrogations at each region of the cervix, with mean speeds for the internal os anterior and posterior of 3.35m/s and 6.08m/s, and for the external os anterior and posterior of 2.57m/s and 3.02m/s respectively.

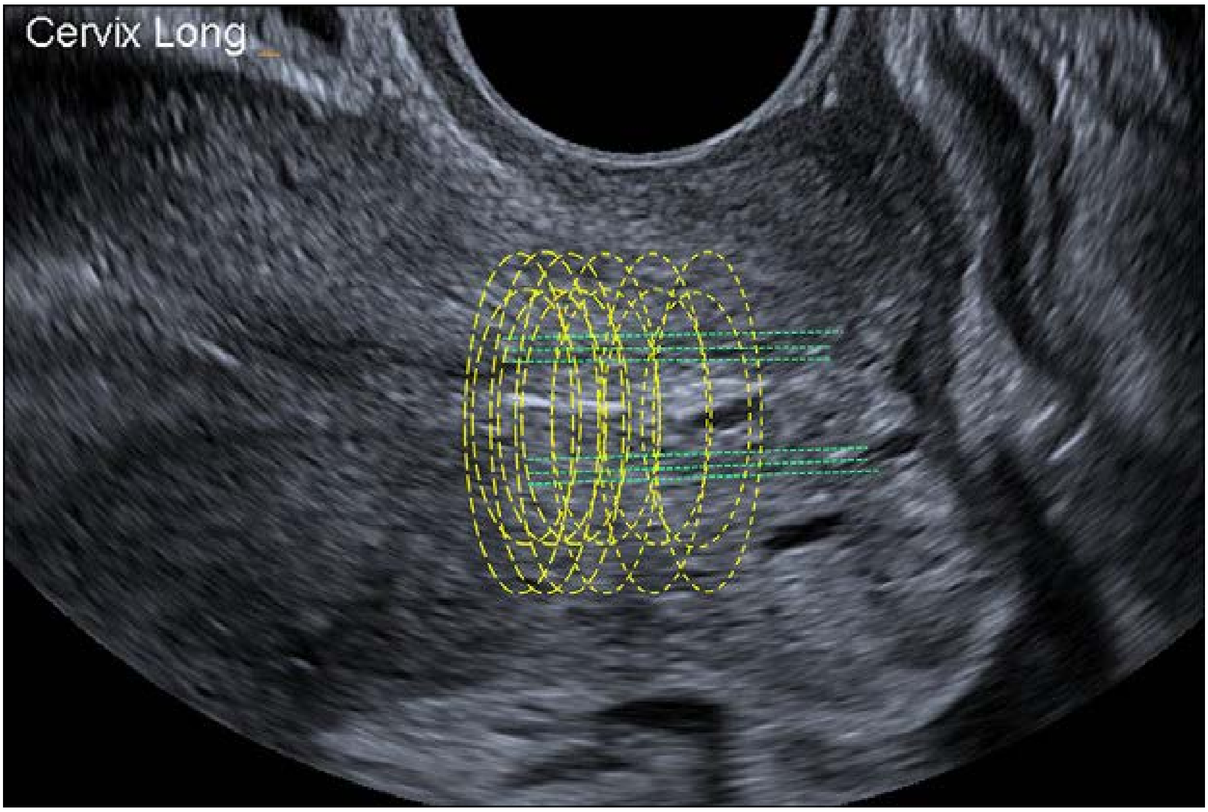

Figure 3. Ultrasound image of the uterine cervix demonstrating the central layer if smooth muscle fibers running parallel to the cervical canal and the circumferential layer of smooth muscle and collagenous fibers where the ROI is placed for SWE sampling.

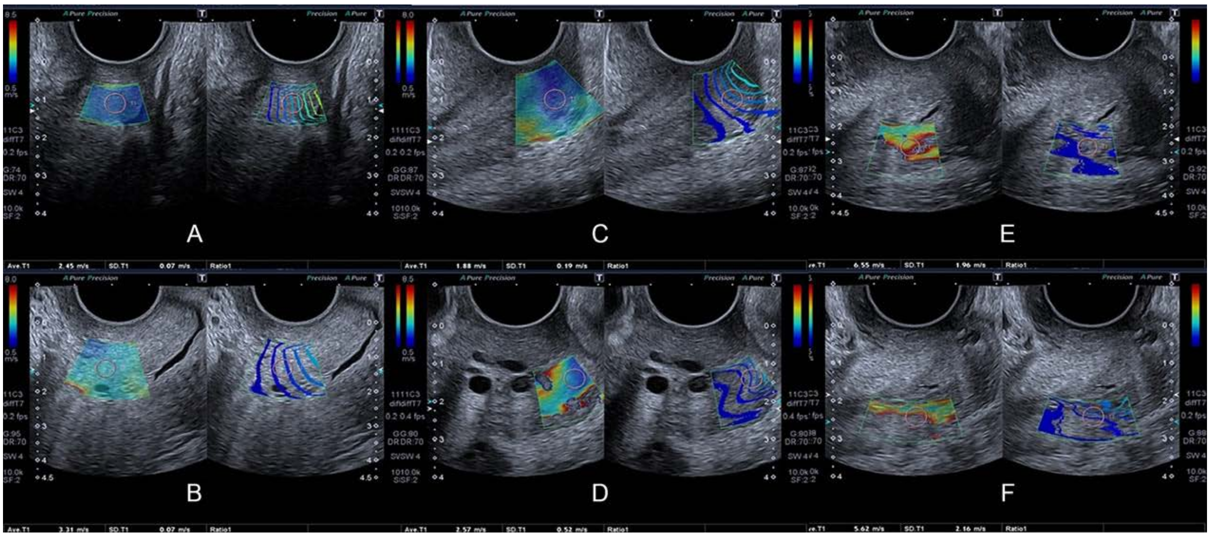

Figure 4. Example of changes in distortion of propagation lines and loss of elastogram color with increasing % of SD of the mean speed:

A- Mean speed 2.45m/s (SD 0.07): 2.8%

B- Mean speed 3.31m/s (SD 0.07): 2.1%

C- Mean speed 1.88m/s (SD 0.19): 10%

D- Mean speed 2.57m/s (SD 0.52): 20%

E- Mean speed 6.55m/s (SD 1.96): 30%

F- Mean speed 5.62m/s (SD 2.16): 38%

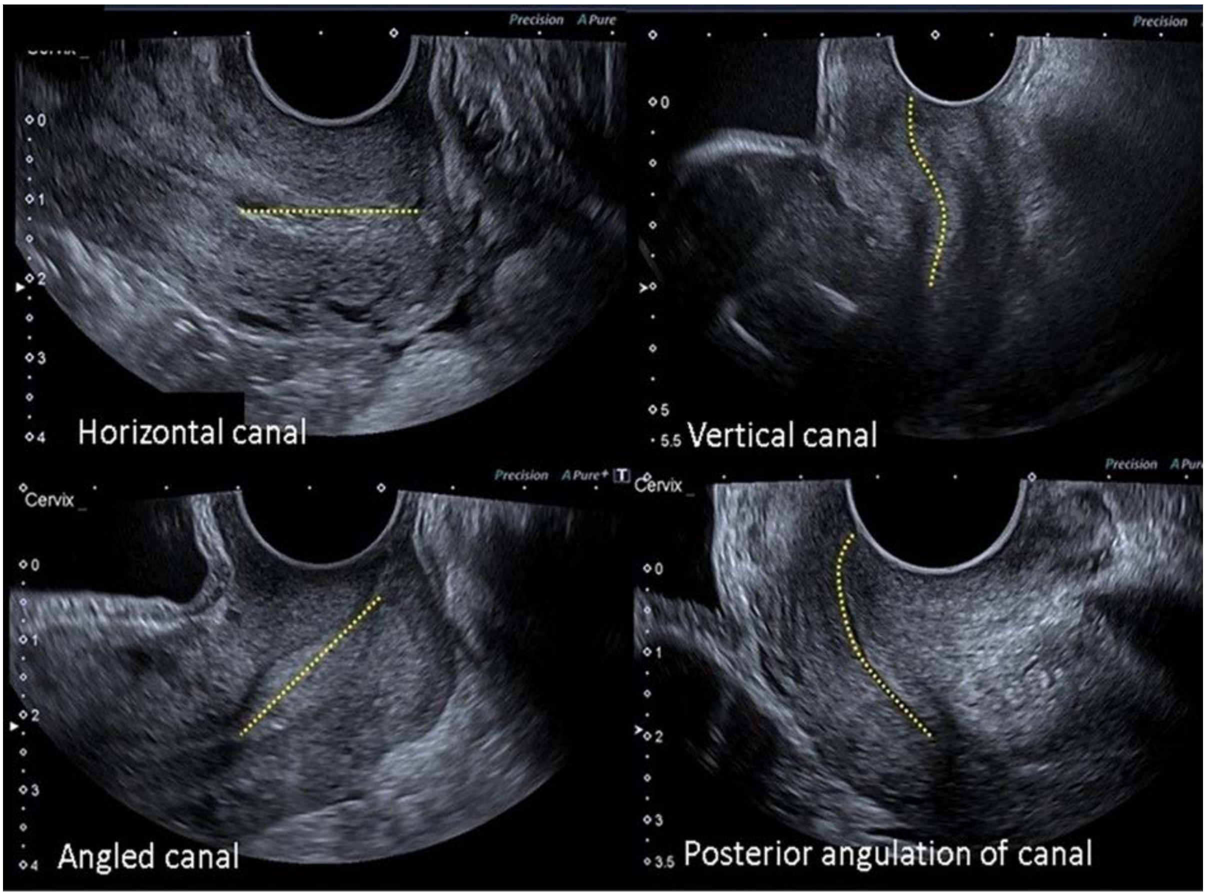

Figure 5. Example of anatomical positions of the uterine cervix that correlate to the results in Table 3. Horizontal Canal – cervical canal is approximately 90° to the transducer face. Angled canal – cervical canal increases the angle with the transducer face with the external os being closer to the transducer, and internal os moving superiorly and a great distance from the transducer face. Vertical canal – cervical canal is vertical to the transducer face. Posterior angled canal – cervical canal is at an angle to the transducer face with external os being close to the transducer and the internal os moving posteriorly and a greater distance from the transducer face.

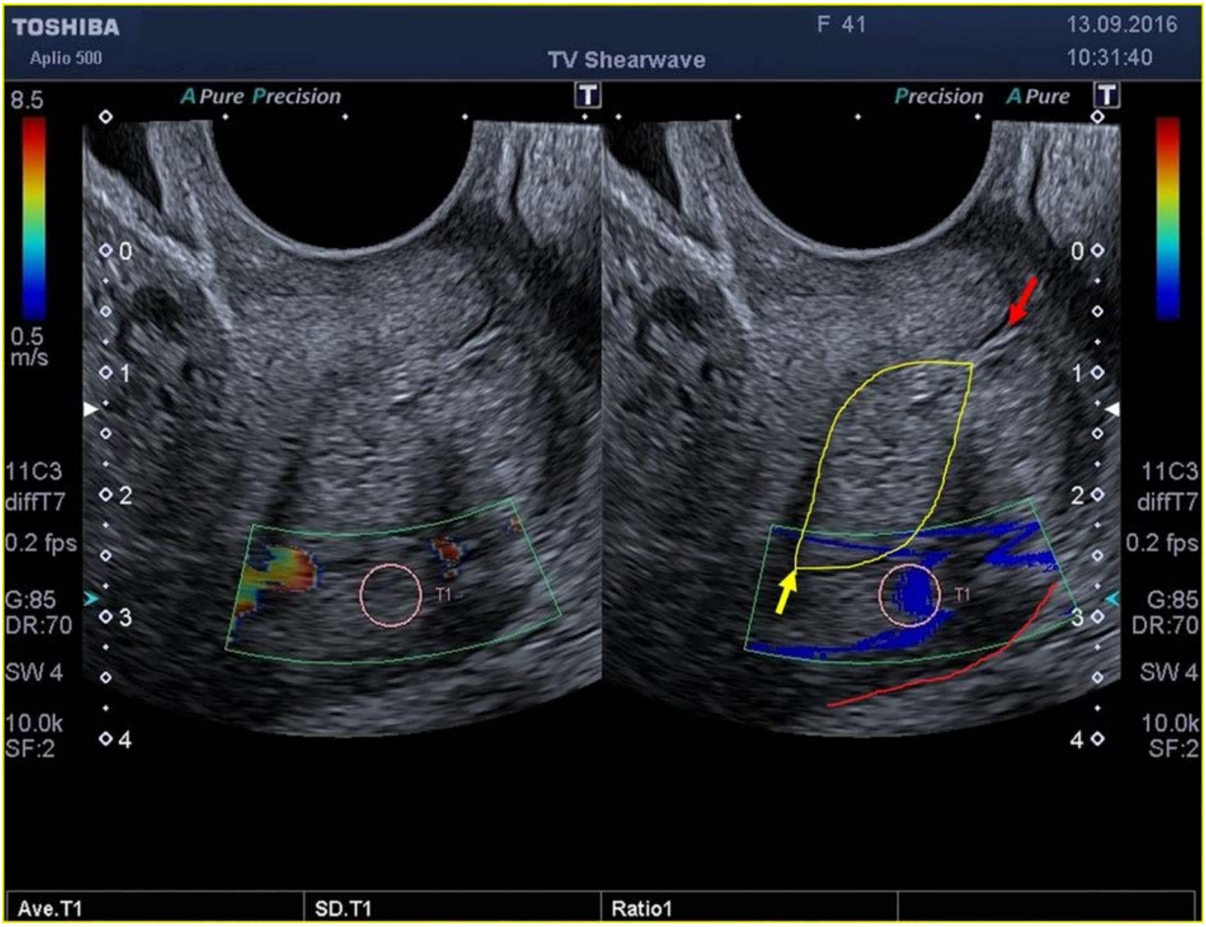

Figure 6. SWE of the internal os posterior with a ROI placed at a depth of 3cm, resulting in a non-registration of SWE measurements. The red arrow is pointing to the external os, yellow to internal os and the endocervical mucosa and posterior margin of the cervix has been outlined in yellow and red respectively.

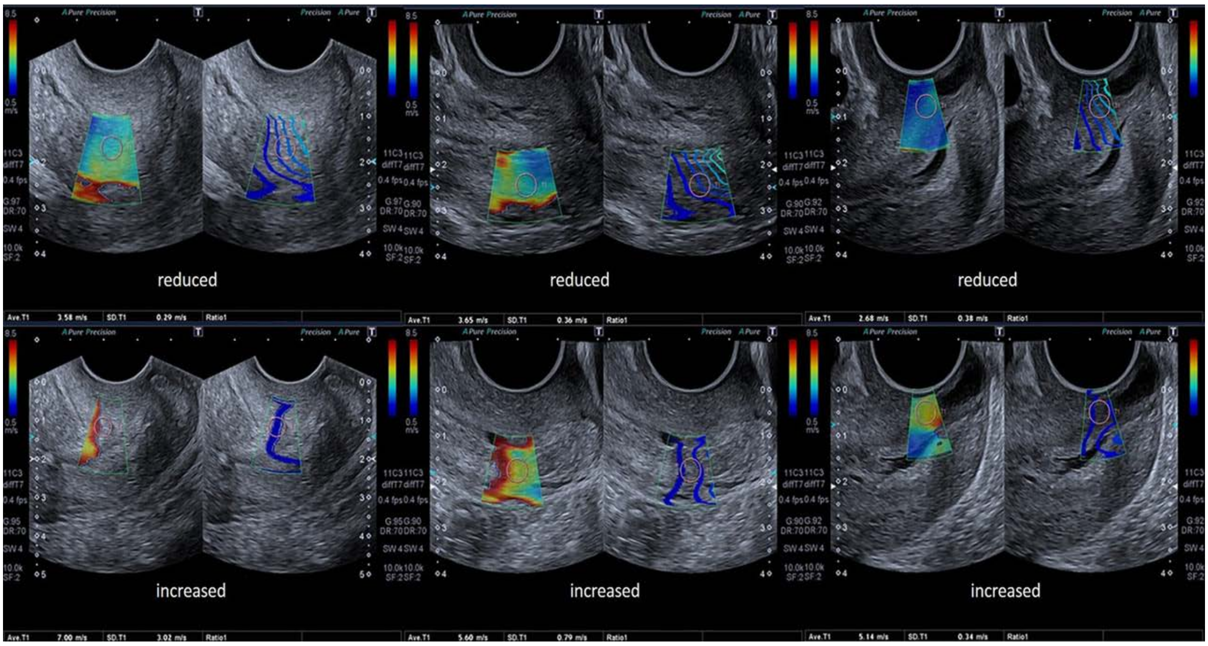

Figure 7. SWE elastography demonstrating changes in shear wave speeds obtained with gentle and increased probe pressure in the internal os anterior and posterior and external os anterior.