Real-Time Tissue Elastography in Gynecology and Obstetrics

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ABSTRACT

Reports on the use of elastography in gynecology and obstetrics remain scarce, and most have used static sonoelastography. In gynecology, most studies are related to the field of oncology. In obstetrics, the primary research object has been to estimate cervical stiffness during pregnancy. The accuracy and reliability of the quantitative evaluation of cervical stiffness using elastography has not yet been established due to the lack of comparative reference materials. More studies are needed to determine the utility of the technique in these fields.

Keywords: Cervical elasticity, Cervical stiffness, Elastography, Obstetrics, Gynecology, Sonoelastography.


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INTRODUCTION

Elastography is a noninvasive technique that estimates the stiffness of body tissues. The index of stiffness is an elastic modulus. There are two basic principles to measure an elastic modulus.

The first is Hooke’s law expressed as the following equation:

\[ P = c e \]

\( P \): stress, \( c \): elastic modulus, \( e \): strain (displacement)

Body tissues have elasticity, which is the property of a material restored to its original shape after distortion. This restoring force is stress, which is proportional to strain. If stress and strain were measured, the elastic modulus could be estimated. Though strain can be measured by ultrasound, stress is difficult to measure; consequently, the elastic modulus itself cannot be estimated. In this case, the strain is used as an index of stiffness instead of the elastic modulus. A strain image, therefore, does not precisely demonstrate the stiffness itself.

The second principle of measuring an elastic modulus is an equation of an elastic wave. When vibration is added to an elastic body, an elastic wave transmits through the body. The speed of the elastic wave depends on the elastic modulus and the density of the tissue. The elastic wave is composed of longitudinal and transverse waves. The elastic modulus is estimated by measuring the speed of the transverse elastic wave.

CLASSIFICATION OF ELASTOGRAPHY

Elastography can be classified as follows:

Classification by the kind of stress: Elastography is classified into static and dynamic elastography. In static elastography, static compression is used as the stress to distort tissue, while dynamic vibration is used in dynamic elastography. Hooke’s law is the basic principle in static elastography, and the elastic wave equation is the basic principle in dynamic elastography.

Classification by the origin of stress: The stress added to the body tissue originates either from intra- or extracorporeal forces. For example, the stress originates from an extracorporeal force when the tissue is compressed by the ultrasound transducer. On the other hand, the stress origin is intracorporeal when heart beats and respiratory movements result in distortions to body tissues. Furthermore, in acoustic radiation force impulse imaging, the radiation force of ultrasound is used to produce elastic waves. In this method, ultrasound is an extracorporeal force, while the elastic wave originates intracorporeal.

Classification by technology used to estimate stiffness: Ultrasound elastography (sonoelastography) and magnetic resonance elastography are both used to perform elastography.

OBSTETRICS AND GYNECOLOGY

Reports on the use of elastography in the field of gynecology and obstetrics are scarce, and almost all have used static sonoelastography. This method is usually based on tissue compression by an ultrasound transducer during ordinary B-mode scanning. In several studies, movements generated only by the patient’s breathing and arterial pulsation were used instead of compression. Then tissue displacement is measured by tracking...
ultrasonographic speckles. The relative displacement is color-coded and superimposed on the corresponding B-mode image. In general, dark purple or blue indicates harder tissue; green or yellow indicates moderately stiff tissue and orange or red indicates soft tissue. When a Region of Interest (ROI) is determined on the B-mode imaging, the degree of strain within that region can be displayed. However, the degree lacks a standard and is not a reliable quantitative value. In the breast, adipose tissue, which is considered to have low interindividual differences regarding stiffness, is used as a standard. Subsequently, the strain ratio between the ROI and the fat region is calculated. In obstetrics, the lack of a standard is currently one of the challenges for the clinical use of elastography.

Gynecology

Elastography has been utilized to assess tumors in various organs. Similarly, most studies using elastography in gynecology are related to the field of oncology.

Malignant Tumors

In a study by Thomas et al., a total of 113 women underwent real-time transvaginal elastography; 13 had cervical cancer, and 11 had cervical intraepithelial neoplasia (CIN). The images were analyzed with a software tool for the colors: red (soft), green (medium) and blue (hard), and the percentages of the three colors of the total area were determined. Significant differences in the blue color spectrum were found between the 13 cervical cancer patients (34 ± 15%) and the normal group (26 ± 13%) but not between the CIN (19 ± 12%) patients and normal women. In addition, the images were evaluated subjectively by two readers on an analog scale from 1 (definitely normal) to 5 (definitely abnormal). The subjective scores differed significantly between the normal group (1.8 ± 0.7) and patients with cervical lesions (3.5 ± 0.9). The authors concluded that the use of both computer-assisted and subjective evaluation of cervical elastography allows for the differentiation of carcinoma from normal findings; however, CIN could not be identified with this modality. Sun et al. also evaluated the clinical value of transvaginal elastography in diagnosing cervical lesions. The authors recruited 110 women with cervical lesions, including 81 women with cervical malignancy. The results showed that the mean strain ratio of malignant lesions was higher than that of the benign lesion (8.19 ± 5.66 vs 2.81 ± 2.24). The best cut-off point of the strain ratio value in differentiating benign and malignant cervical lesions was 4.53, and the specificity and sensitivity for this value were 0.788 and 0.897 respectively. However, the authors acknowledged in the discussion that reference tissues surrounding the cervix are limited. In this study, the depth of invasion into the stroma was measured by elastography and compared with the pathological results. The mean depths of the 56 malignant lesions were 17.8 ± 7.4 mm when measured by elastography and 11.5 ± 8.8 mm by pathological examination. The authors concluded that transvaginal elastography was a useful technique in the differential diagnosis of cervical cancer and in quantifying the infiltration region.

Xie et al. evaluated ultrasound elastography for the discrimination of low- and high-grade serous ovarian carcinoma. There were 64 women with serous ovarian carcinoma; of these women, 39 had high-grade and 25 had low-grade ovarian carcinoma. The section of the ovarian tumor with the largest solid component was selected for analysis. The elastograms were evaluated by a scoring system that referred to a five-point scale from a study of breast lesions and was based on a four-point scale used to grade cervical lymph nodes. The mean elasticity score (±SD) was statistically higher for low-grade lesions (3.40 ± 0.76) than high grade lesions (2.08 ± 0.58). When a score of 4 was used for diagnosis of low-grade carcinoma, elastography had 56.0% sensitivity, 100% specificity, 100% positive predictive value and 78.0% negative predictive value. When a score of 2 was used for the diagnosis of high-grade carcinoma, elastography had 66.7% sensitivity, 84.0% specificity, 86.7% positive predictive value and 61.8% negative predictive value. The authors identified that there was a trend for high-grade lesions to be less stiff than low-grade lesions due to rapidly developing necrosis; conversely, low-grade lesions developed relatively slowly, so that their solid areas were stiffer and less elastic. The authors concluded that real-time qualitative ultrasound elastography was a feasible technique for the discrimination of ovarian low- and high-grade serous ovarian carcinoma.

Krzysztof et al. studied elastography application to assess the indication for dilation and curettage of the uterine cavity in patients with wide endometria. The authors recruited 25 perimenopausal women with endometrial thickness greater than 5 mm; 14 of these women had normal findings, eight had endometrial polyps, one had cancer and two had hypertrophy. The endometrium was described by the elastography index (purple was assigned 0 points, blue 1 point, green –2 points, yellow –3 points and red –1 point). The results revealed significant differences of the index between women with normal endometria confirmed by pathological examination and women with abnormal findings. The elastography index was 0 or 1 point in the group with normal endometria and ranged from 2 to

4 points in the group with endometrial pathology. The authors concluded that elastography was a valuable tool for differentiating endometrial pathologies from normal endometria in perimenopausal women.

Nitta et al\textsuperscript{11} reported a case of uterine sarcoma using elastography. In this case, real-time tissue elastography showed a typical mosaic pattern in the uterine sarcoma lesion (Figs 1A to C). The final pathological diagnoses were undifferentiated endometrial sarcoma. The authors concluded that real-time tissue elastography might be a new diagnostic modality for uterine sarcoma.

**Benign Tumors**

Ami et al\textsuperscript{12} observed 10 patients with uterine fibroids who were referred for infertility and who subsequently underwent conservative surgical treatment. The authors stated that all fibroids were seen easily on the color display in elastography mode, and the extents of the fibroids were easier to define than in conventional B-mode. The distance between the fibroid and the endometrial cavity or uterine serosa could be measured readily in each case. The authors concluded that real-time elastography was a promising tool that could provide detailed mapping and characterization of uterine fibroids.

Tessarolo et al\textsuperscript{13} evaluated 30 women with suspected uterine adenomyosis using standard B-mode and sonoelastography. In 15 cases, the diagnosis was confirmed by histology. The adenomyotic area exhibited more softness (red and green) compared to the surrounding uterine tissue (blue), and the borders of the adenomyotic area corresponded with the borders of the green area. The authors defined this elastographic pattern 'the cockade sign'. The authors concluded that elastography could be considered a useful tool in the diagnosis of adenomyosis. In a study performed by Stoelinga et al\textsuperscript{14} a total of 218 women underwent elastographic imaging. MRI or histological examination was performed in 69 patients. Using elastography, the uterus was well delineated from the surrounding bowel for each case. Fibroids and adenomyosis had different elastographic characteristics and different color patterns. In general, fibroids were darker and adenomyosis was brighter than the adjacent myometrium. The authors concluded that elastography was able to identify discriminating characteristics of the uterus, fibroids and adenomyosis, and elastography-based diagnoses showed substantial agreement with MRI- or histology-based diagnoses.

Figure 2 shows a transvaginal ultrasonographic B-mode and elastographic image in a woman with fibroids and adenomyosis. The fibroid is easily defined as a round-shaped blue lesion on the color display in elastography mode. The adenomyotic area is exhibited as softer area (red and yellow) in the adjacent right side of the fibroid.

Xie et al\textsuperscript{15} used elastography in patients suspected of having abdominal wall large-scar endometriosis. According to the authors, abdominal wall endometriosis is an uncommon extrapelvic form of endometriosis, and most cases are associated with obstetric and gynecological procedures. A diameter of 3 cm or greater is considered an indicator of large-scar endometriosis, and its clinical characteristics differ from small-scar endometriosis. In the study, eight women with large-scar endometriosis underwent transabdominal sonography, strain elastography, MRI, and wide surgical excision. The vertical and horizontal infiltration scales of the postoperative specimens were consistent with strain elastography and were evaluated insufficiently by transabdominal sonography and MRI. The authors concluded that elastography could improve the diagnostic accuracy of large-scar endometriosis.
Obstetrics

In obstetrics, normal tissues, not tumors, are the objects of observation. The primary use of elastography is to estimate cervical stiffness during pregnancy by transvaginal sonoelastography.

Transvaginal Cervical Sonoelastography

Cervical length estimated by transvaginal sonography has been widely used for the management of pregnancy. Cervical length in the second trimester is currently accepted as the best predictor of spontaneous preterm delivery. Furthermore, some studies indicated that ultrasound assessment of the cervix was a more sensitive tool to predict successful induction than the Bishop score. However, cervical length alone is not enough to evaluate all cervical situations. At the time of cervical shortening, various microstructural changes have already occurred. Hydration and elasticity have increased and collagen has become disorganized. Transvaginal sonoelastography has been used to evaluate the elasticity or stiffness of the uterine cervix as a supplement to cervical length assessment in pregnant women.

Reliability of Sonoelastography to assess Cervical Stiffness during Pregnancy

Elastography has been utilized successfully to assess tumors in various organs because tumors generally have been shown to be stiffer than normal adjacent tissues, and the degrees of stiffness of benign and malignant tumors are different. Changes in cervical stiffness, however, are physiological phenomena that occur during pregnancy. In cervical elastography during pregnancy, normal tissues, not tumors, are the objects of observation, and the elastographic color of the cervix has been reported to be heterogeneous, and different parts appear to have different degrees of stiffness. Furthermore, the application of elastography to the cervix lacks natural reference tissue in that anatomical area. For this reason, it has not been possible to make a quantitative comparison of cervical stiffness among women. There have been several studies regarding the reliability of elastography in assessing cervical stiffness during pregnancy.

Hernandez-Andrade et al performed sonoelastography in 262 women between 8 and 40 weeks of gestation. Three cervical projections were selected for evaluation: a mid-sagittal, a cross-sectional at the level of internal os, and another cross-sectional at the level of external os. Continuous oscillatory pressure with the ultrasound probe was manually applied to the cervix by the operator. The intensity of the pressure was controlled by the pressure-level bar displayed on the ultrasound monitor. The results were as follows: (1) cervical tissue strain estimates obtained in the endocervical canal were on average 33% greater than those obtained in the entire cervix, (2) measurements obtained in the cross-sectional plane of the external cervical os and in the sagittal plane were 45% and 13% greater respectively, than those measured in the cross-sectional plane of the internal cervical os, (3) mean strain rates were 14% and 5% greater among parous women with and without a history of preterm delivery respectively, compared to those of nulliparous women, and were on average 13% greater among women with a cervical length of between 25 and 30 mm compared to those with a cervical length > 30 mm, and (4) cervical tissue strain was more strongly associated with cervical length than with gestational age. The authors concluded that semiquantitative elastography could be employed to evaluate changes in cervical stiffness during pregnancy. The authors commented that strain estimation performed in the cross-sectional plane of the internal cervical os might be the most reliable.

Tomasz et al performed cervical sonoelastography in 59 pregnant women between 28 and 39 weeks of gestation. After measuring cervical length in the sagittal plane, the sonoelastography mode was turned on, with the ROI 1 cm in diameter set on the anterior and posterior cervical labia. The results showed a negative correlation between cervical length and the elasticity of the anterior cervical labium. The authors stated that elastography of the uterine cervix might be helpful in assessing the risk of premature labor or cervical insufficiency.

Fruscalzo et al evaluated the reliability of cervical elastography. Cervical sonoelastography was performed by two blinded operators in 10 pregnant women in the late...
first and early second trimester of pregnancy. Two cycles of compression and relaxation of the anterior labium of the cervix were exerted through the vaginal transducer. A circular ROI was placed on the full thickness of the anterior cervical labium in the sagittal plane, and strain values were measured. The interobserver reliability of strain measurements was evaluated using the intraclass correlation coefficient (ICC). The mean strain value (± SD) was 0.33 ± 0.05. The mean of the differences between the measurements was 10.77% ± 4.41%. The interobserver ICC agreement values comparing the different subsets of strain measurements ranged between 0.91 and 0.96. The authors concluded that cervical elastography was feasible and had high interobserver reliability.

Molina et al.\(^3\) carried out cervical elastography twice by a single operator in 112 pregnancies, and these data were used for intraobserver analysis. In 50 of these cases, another operator also performed a single measurement of cervical elastography, which was used to determine interobserver reproducibility. The transvaginal probe was used to produce four to five compression and decompression cycles. Four ROIs, 6 mm in diameter, were selected in the cervix: the external superior labium internal superior labium, external inferior labium and internal inferior labium. The results showed that measurements obtained by the same and by two different observers for different regions in the cervix were reliable and reproducible, except for measurements of the external and superior part of the cervix. The authors concluded that it was possible to provide an objective quantification of elastographic colors in the cervix. However, the external superior parts of the cervix, which were subjected to a greater degree of pressure by the transducer, appeared to be softer than the internal inferior parts, which were further away from the pressure. The authors discussed that there was no evidence of a true variation in the stiffness of different parts of the cervix and, therefore, the measurements obtained by elastography might be merely a reflection of the force applied by the transducer to different part of the cervix. The authors stated that it was too premature to suggest that measurements of the rate-of-change in tissue displacement reflect histological changes, which could provide a measure of cervical ripening.

Figure 3 shows transvaginal sonographic B-mode and elastographic images of the cervix of a pregnant woman. Anterior parts of the cervix, which are subjected to a greater degree of pressure by the transducer, appear to be softer than the posterior parts, which are further away from the pressure. The authors concluded that cervical elastography was feasible and had high interobserver reliability.

Cervical Sonoelastography for Induction of Labor

Induction of labor is needed in several obstetric situations, such as premature rupture of membranes, fetal growth restriction (FGR), pre-eclampsia and prolonged pregnancy. Cervical assessment is important to predict whether the induction would succeed or fail. The traditional and global method for the assessment has been the Bishop score; however, the Bishop score has been shown to have a poor predictive value for the outcome of induction.\(^3\) Some studies have indicated that ultrasound assessment of cervical length was a more sensitive tool to predict the success of induction than the Bishop score.\(^1\) Additionally, sonoelastography has been proposed as a new technique to assess the cervix before induction of labor.

Swiatkowska-Freund et al.\(^3\) assessed the uterine cervix by elastography in 29 patients before the induction of labor. The authors used a numeric scale called the elastographic index (E). A color map from purple to red was produced, and values were assigned according to the following scheme: 0 point for purple (hardest tissue), 1 point for blue, 2 points for green, 3 points for yellow and 4 points for red (softest issue). During the examination,
no additional pressure was applied to the cervix; the operator did not move the probe. Elastographic images of the cervix were achieved as a result of movement generated only by the patient’s breathing and arterial pulsation. The mean EI of the internal os in the group of patients with successful induction of labor was 1.23, while in the group with failed induction of labor it was 0.39 (p = 0.024). No differences were found for the EI of the middle part of the cervical canal or the EI of the external os in relation to the success of induction of labor. The authors pointed out that palpation of the internal os is frequently impossible, and stated that a decrease in the consistency of the tissue around the internal os might be a symptom of approaching delivery. The authors concluded that, in cases of induction of labor, elastography might help to decide whether to use prostaglandins or oxytocin in the induction of labor.

Hwang et al36 studied the value of elastography to predict successful induction of labor in 145 nulliparous women at term. Bishop scores, cervical lengths and cervical elastographic parameters, including cervical areas, mean elastographic indexes, and cervical hard areas were measured. Like the study of Siwatkinska-Freund et al,35 the operator did not move the probe, and elastographic images of the cervix were achieved as a result of movement generated only by the patient’s breathing and arterial pulsation. The elastographic images in this study were made in gray scale and analyzed by an image automatic analyzing program. The areas under the curves for cervical lengths, cervical areas, Bishop scores, mean elastographic indexes and cervical hard areas were 0.63, 0.64, 0.47, 0.68 and 0.70 respectively, for the onset of active labor within 9 hours and 0.70, 0.68, 0.63, 0.71 and 0.76 for delivery within 24 hours. The combination of cervical length and elastographic data was most predictive of successful labor induction. The authors concluded that imaging analysis of cervical elastography was available to predict successful induction of labor.

Muscatello et al37 also studied the value of elastography for successful induction in 53 women. In this study, the acquisition of a sonoelastogram was also performed while maintaining the probe steady and using only the movements of the cervix generated by the pulsation of pelvic great vessels and breathing movement of the subject without applying any pressure with the probe. The authors classified the sonoelastogram into five elastic index categories (EI1-5). In the index, 1 denoted the softest tissue, and the maximum value of 5 denoted the hardest tissue. There were significant differences in the prevalence of spontaneous delivery (EI1-3: 82.75%, and EI4-5: 45.8%) vs cesarean section (EI1-3: 17.25%, and EI4-5: 54.16%) (p = 0.0072). The diagnostic validity of EI1-5 was evaluated with the ROC curve, and the cutoff for the predictive value was EI3 (sensitivity 68.57% and specificity 72.22%). The authors concluded that sonoelastography was an innovative technique that could allow for a more objective preliminary evaluation of the cervix before induction of labor.

Cervical Sonoelastography for Preventing Preterm Labor

The length of the cervix observed by transvaginal ultrasoundography in the second trimester is currently the best predictor of spontaneous preterm delivery. However, treatment for short cervix is still controversial.38 Cerclage for cervixes being less than 25 mm in an unselected population demonstrated no benefit; however, cerclage has been shown to reduce the risk of preterm delivery in individuals with history of preterm delivery.39 Intramuscular progesterone for cervixes <30 mm demonstrated no benefit,40 but vaginal progesterone gel for cervixes 10 to 20 mm reduced preterm delivery.41 On the contrary, most women with short cervixes deliver at term without intervention. This discrepancy could be partly due to the fact that cervical length alone is not enough to evaluate the cervical situations. Recently, sonoelastography has been proposed as a new technique to assess risk relating to cervical insufficiency and imminent premature labor.

Thomas42 highlighted the potential of sonoelastography to provide insight into cervical insufficiency and premature delivery. He suggested from his experience that there were age-related differences in the cervical elasticity of pregnant women. Feltovich et al38 also stated that elastography could be promising if data acquisition were standardized.

Hernandez-Andrade et al43 performed cervical sonoelastography in 189 women between 16 and 24 weeks of gestation. Like the methods reported previously,34 three cervical projections were selected for evaluation: a mid-sagittal, a cross-sectional at the level of internal os and another cross-sectional at the level of external os. Each plane was examined in two ROIs: the endocervical canal and the entire cervix. Continuous oscillatory pressure with the ultrasound probe was manually applied to the cervix by the operator. Out of 189 women, 21 women subsequently experienced spontaneous preterm labor. The results showed that the strain measurements obtained in the cross-sectional view of the internal cervical os were associated with spontaneous preterm labor. Women with strain values in the endocervical canal and the entire cervix in <25th percentile were 80% less likely to have a spontaneous preterm labor than
women with strain values in >25th percentile. Strain values obtained from the external cervical os and, from the sagittal view, were not associated with spontaneous preterm labor.

**Additional Applications of Elastography in Obstetrics**

Other than cervical sonoelastography, there have been few reports of the applications of elastography in obstetrics.

Matsumoto et al. investigated whether abdominal sonoelastography was useful for evaluating uterine muscle contractions in two women with threatened premature labor and 15 women with terminal labor. Elastographic images of abdominal fat and the uterine muscle layer were recorded during uterine contractions and relaxations (Figs 4A and B), and elasticity of the uterine muscle (lower circle) and the fatty tissue (upper circle) was measured. Fatty tissue was used as a natural reference. The color of uterine muscle layer became blue from yellow or green when the muscle contracted. There were differences in the elasticity ratios of muscle to fatty tissue between during contractions and relaxations. The authors concluded that elastography made it possible to evaluate whether uterine muscle contracted or not; however, the degree of the contraction strength could not evaluated.

Static sonoelastography is based on tissue compression followed by computerized analysis of changes in the speckle distance. The compression is caused directly by the hand using the ultrasound transducer in the aforementioned reports. However, there is another new method of ultrasound-based elastography, which uses an acoustic radiation force impulse to cause tissue displacement. This displacement generates a lateral shear wave, and its velocity is correlated with the stiffness of the tissue; faster shear wave speeds and less tissue displacement are associated with stiffer tissue, and slower wave speeds and greater tissue displacement occur in more compliant tissue. Sugitani et al. measured the velocity of a lateral shear wave in the placenta after delivery in 115 patients using ex vivo acoustic radiation force impulse imaging. The authors also examined histological changes in the placenta after the imaging to estimate the safety of the acoustic radiation force impulse. The velocity values in the FGR group were significantly higher than those in the normal group. In addition, no histological changes were noted after the imaging. The authors speculated that measuring the placenta using this technique was safe and did not cause thermal or mechanical damage to the placental tissue. Additionally, the authors concluded that the placentas from the FGR group were significantly firmer than from the cases without FGR.

**CONCLUSION**

Elastography appears to be a promising technique; however, there has been limited research on the use of elastography in gynecology and obstetrics. In gynecology, it seems the advantages of sonoelastography to other imaging modalities, such as CT and MRI have not been clarified. In obstetrics, the reliability of elastography in quantitative evaluations has not been established yet. More studies are needed to determine the utility of the technique in these fields.

![Figs 4A and B: Transabdominal B mode and elastographic images of abdominal fat and uterine wall when the uterine muscle relaxes (A) and contracts (B). The elasticity of uterine muscle (lower circle) and fatty tissue (upper circle) is measured. The color of uterine muscle layer becomes blue (B) from yellow or green (A) when the muscle contracts (Courtesy: Reprinted with permission from Matsumoto Y et al.).](image)
REFERENCES


