Ultrasound Obstet Gynecol 2012; **39**: 685–689
Published online 22 May 2012 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.11067

Quantification of cervical elastography: a reproducibility study

F. S. MOLINA*†, L. F. GÓMEZ*, J. FLORIDO†, M. C. PADILLA*† and K. H. NICOLAIDES‡

**Maternal-Fetal Medicine Unit, Department of Obstetrics and Gynaecology, San Cecilio University Hospital (HUSC), Granada, Spain; †Department of Obstetrics and Gynaecology, University of Granada, Granada, Spain; ‡Harris Birthright Research Centre for Fetal Medicine, King's College Hospital, London, UK*

KEYWORDS: cervical assessment; cervical deformability; elastography; reproducibility; transvaginal ultrasound

ABSTRACT

Objectives *To assess a new method for numerical quantification of cervical elastography during pregnancy and to evaluate the repeatability of the measurements.*

Methods *Cervical elastography was carried out twice by a single operator in 112 singleton pregnancies at a median of 21 (range, 12–40) weeks' gestation. In 50 of the cases a second operator performed another elastography measurement. The intraobserver and interobserver repeatability of measurements in different parts of the cervix were assessed using intraclass correlation coefficients with 95% CI and by Bland–Altman analysis.*

Results *There were no statistically significant differences in the elastography measurements made by the same and by two different observers in each area measured, except in the area that receives the force of the transducer directly. The distribution of elastographic measurements obtained in different regions of the cervix demonstrated that the external and superior parts were significantly softer than the internal and inferior parts.*

Conclusion *It is possible to provide an objective quantification of elastographic colors in the cervix. The measurements obtained by elastography may be a mere reflection of the force being applied by the transducer to different parts of the cervix. It is too premature to suggest that the measurements of rate-of-change in tissue displacement reflect histological changes that could provide a measure of cervical ripening. Copyright © 2012 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Cervical ripening in pregnancy is associated with dispersion of collagen and gradual depolymerization caused by an increase in matrix metalloproteinase (MMP) and a decrease in tissue inhibitors of MMP, resulting in increased osmotic pressure of cervical tissue with subsequent edema and therefore softening[1]. Such cervical softening is essential before myometrial contractions can act to produce shortening and dilation[2]. If these changes begin too early in pregnancy or do not begin at term we face preterm delivery or post-term pregnancy, respectively.

Currently, the ultrasonographic approach for prediction of preterm delivery or assessment of successful induction of labor at term relies on the measurement of cervical length[3–5]. The performance of sonographic screening may be improved by elastography, which provides information on the mechanical properties of tissues. When pressure is applied to the cervix with the vaginal transducer the compressibility is represented with colors, where hard tissue appears purple and soft tissue appears red. Swiatkowska-Freund and Preis[6] performed cervical elastography in 29 patients before induction of labor and reported that the tissue around the internal os in the group of patients with successful induction of labor was softer than in the group with failed induction.

The aims of this study were to provide an objective quantification of elastographic colors in the cervix and to examine the reliability of the measurements.

METHODS

Cervical elastographic measurements were carried out twice by a single operator in 112 singleton pregnancies at a median of 21 (range, 12–40) weeks' gestation, and these data were used for intraobserver analysis. In 50 of these cases a second operator also performed a single measurement of cervical elastography and this was compared with the first measurement made by the previous operator to determine the interobserver

Correspondence to: Dr F. S. Molina, Maternal-Fetal Medicine Unit, Department of Obstetrics and Gynaecology, San Cecilio University Hospital, Avenida Dr. Olóriz, 16. 18012 Granada, Spain (e-mail: fsoniamolina@gmail.com)

Accepted: 23 November 2011

reproducibility. All measurements were performed offline on stored images from videoclip sequences, with the operator blinded to previous measurements. Elastography was performed using a vaginal probe (PVT-681 MV, Toshiba Aplio MX; Toshiba Medical Systems Europe, Zoetermeer, The Netherlands) and analyzed with the software Elasto-Q (Toshiba Medical Systems Europe).

The women were asked to empty their bladder and were placed in the dorsal lithotomy position. The vaginal probe was placed in the anterior fornix of the vagina and a sagittal view of the cervix, with the echogenic endocervical mucosa along the length of the canal, was obtained. The probe was used to produce four to five compression and decompression cycles, each lasting for about 1 second. With each compression the probe was advanced into the cervical tissue by about 1 cm. The waveforms of compression and decompression were displayed automatically, as shown in Figure 1.

We selected four regions of interest in the cervix: external and superior lip (Region A), internal and superior lip (Region B), internal and inferior lip (Region C) and external and inferior lip (Region D), as shown in Figure 2. A circle, 6 mm in diameter, was then placed in each of the four regions and the machine automatically displayed a value for each circle. Essentially, the transducer receives two sets of radiofrequency signals, before and after cervical compression, and from the difference in waveforms the amount of shift in the tissue is estimated. The rate-of-change in tissue displacement as a function of the distance from the transducer is computed for all points in the image. These rate-of-change values are known as strain values and are displayed in different colors to give an elastographic image on a continuous scale ranging from red, yellow, green to blue for softer to harder tissues, respectively. From the four to five compression–decompression cycles we selected the most symmetrical waveform and compared the radiofrequency signals at the peak of the compression and at the trough of the decompression in the same cycle (Figure 1).

Statistical analysis

We used descriptive analysis to examine the population in the study.

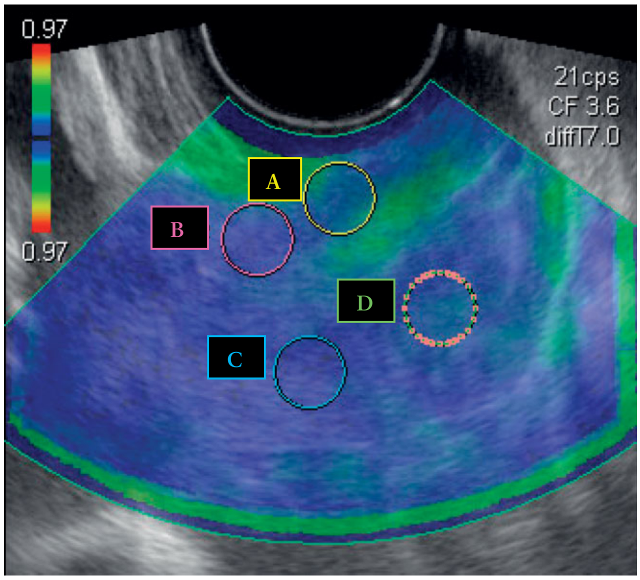

Figure 2 Cervical elastographic image showing regions of interest selected for quantification. Region A: external and superior cervical lip. Region B: internal and superior cervical lip. Region C: internal and inferior cervical lip. Region D: external and inferior cervical lip.

The intraobserver and interobserver repeatability of measurements was assessed using intraclass correlation coefficients (ICCs) with 95% CI[7,8]. The Bland–Altman plot[9] of the average against the differences of the two measurements was performed and the 95% limits of agreement were calculated for each measurement to examine the agreement and bias for a single examiner and between two examiners for each measurement.

The ANOVA test with Bonferroni correction was performed to compare the mean of the elastographic values in the four different regions selected.

Data were analyzed using the statistical software MedCal® Version 9.3.7.0 (MedCalc Software bvba, Mariakerke, Belgium) and SPSS 18.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

Demographic and pregnancy characteristics of the population are summarized in Table 1. No patients had a history of cervical conization or other conditions affecting

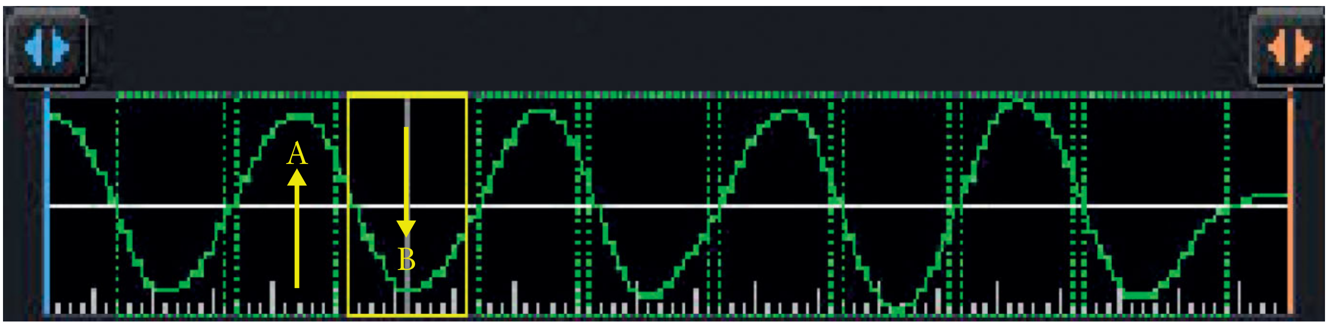

Figure 1 Graphical representation of tissue compression and decompression in the cervix. The peak of the compression (A) and the trough of the decompression (B) in the same cycle are shown.

Table 1 Maternal and pregnancy characteristics of the study population

Characteristic	*Value*
Maternal age (years)	33.0 (18.0–46.6)
Gestational age at measurement (weeks)	26.6 (12–40.1)
Body mass index (kg/m^2)	25.7 (19.6–38.8)
Nulliparous	56 (50)
Cervical length (mm)	36.0 (12.0–55.0)

Data are given as median (range) or *n* (%).

the cervix, and the preterm delivery rate in our population was 9.3%. The median (range) gestational age at delivery was 39.2 (33.0–41.7) weeks.

The intraobserver and interobserver ICCs were statistically significant in each area measured, except for the interobserver ICC for Region A (Table 2).

Bland–Altman plots, demonstrating the degree of concordance between pairs of measurements made by the same observer and by the two different observers, are given in Figure 3 and the data are presented in Table 3. There was no significant bias in any case ($P > 0.05$) because the difference between measurements remained stable as the average increased. The mean and SD of differences appeared to be constant throughout the range of measurements for all comparisons.

The distribution of the elastography measurements demonstrated that the external and superior parts of the cervix were significantly softer than the internal and inferior parts (Figure 4, Table 4). This was calculated using the 112 first measurements performed by Observer 1.

DISCUSSION

The findings of this study demonstrate that it is possible to provide an objective quantification of elastographic colors in the cervix. The rate-of-change in tissue displacement as a consequence of compression–decompression cycles exerted by a vaginal transducer is converted into a measurement that may reflect the stiffness of the cervix. We have shown that the measurements obtained by the same and by two different observers for different regions in the cervix are reliable and reproducible, except for Region A (external and superior part of the cervix) and two different observers.

Table 3 Degree of concordance between pairs of elastographic measurements made by the same observer and by two different observers in selected regions of the cervix

Measurement	*Same observer*	*Two observers*
Region A	0.00 (−0.10 to 0.09)	0.00 (−0.23 to 0.23)
Region B	0.00 (−0.07 to 0.07)	−0.01 (−0.15 to 0.12)
Region C	0.00 (−0.06 to 0.05)	0.00 (−0.05 to 0.07)
Region D	−0.01 (−0.07 to 0.05)	0.01 (−0.09 to 0.11)

Numbers represent mean differences between measurements (or bias) and 95% limits of agreement.

Hard or stiff tissues tend to move as a unit, with all points displaced by about the same amount when they are compressed with the transducer. Consequently, the rate-of-change in displacement vs. depth is either zero or very small. In contrast, soft tissues compress like a sponge, with the tissue closest to the probe displacing much more than the tissue further away, resulting in a large rate-of-change in displacement[10].

Elastography has been successfully utilized to assess tumors in various organs, including the prostate, thyroid gland, liver and breast, because malignant tumors have been shown to be stiffer than benign tumors[11–13]. In contrast to the study of tumors, where the stiffness is compared with that of normal adjacent tissues equidistant from the tip of the transducer, the application of elastography in the study of the healthy cervix in pregnancy is limited by the lack of a reference tissue for comparison. The hypothesis being tested is that the histological changes which accompany cervical ripening would be reflected in a detectable reduction in stiffness compared with that of the unripe cervix. However, previous studies have described that the elastographic color of the cervix is not homogeneous but different parts appear to have different degrees of stiffness[14]. Our study has confirmed this apparent lack of homogeneity in the measurable stiffness of the cervix. The outer and

Table 2 Intraclass correlation coefficients (ICC) of elastographic measurements in different regions of the cervix

Measurements	*ICC*	*95% CI*	*SD of difference*	P
Region A				
Same observer	0.82	0.75 to 0.87	0.05	< 0.001
Two observers	0.16	−0.13 to 0.43	0.12	0.136
Region B				
Same observer	0.92	0.88 to 0.94	0.04	< 0.001
Two observers	0.80	0.60 to 0.86	0.07	< 0.001
Region C				
Same observer	0.82	0.75 to 0.87	0.03	< 0.001
Two observers	0.72	0.55 to 0.84	0.03	< 0.001
Region D				
Same observer	0.90	0.86 to 0.93	0.03	< 0.001
Two observers	0.70	0.51 to 0.82	0.05	< 0.001

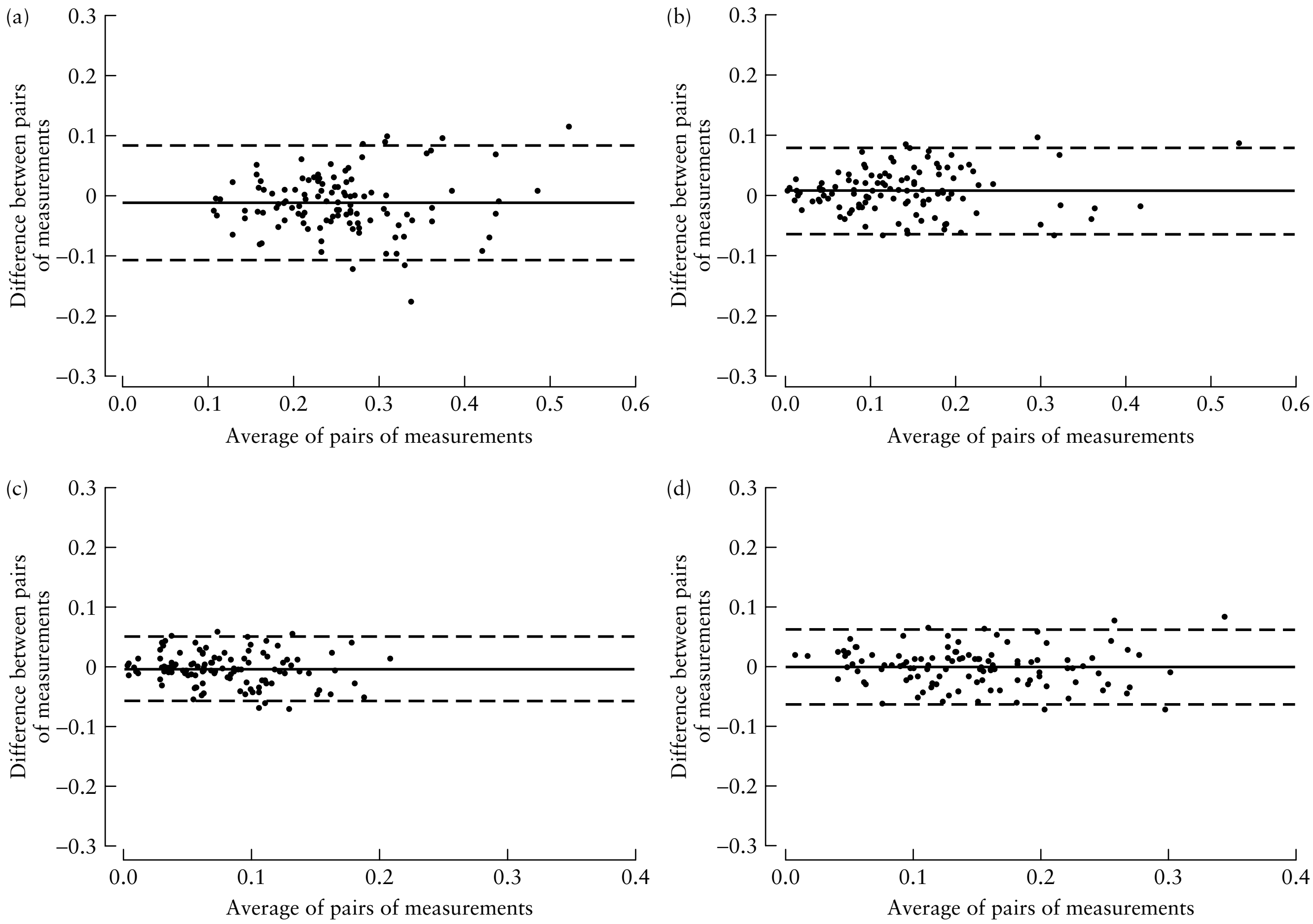

Figure 3 Bland–Altman plots demonstrating degree of concordance between pairs of cervical elastography measurements obtained by the same observer in different regions of interest. (a) Region A: external and superior cervical lip. (b) Region B: internal and superior cervical lip. (c) Region C: internal and inferior cervical lip. (d) Region D: external and inferior cervical lip. Mean difference (———) and 95% limits of agreement (— — —) are shown.

Table 4 Mean differences in cervical elastography measurements between different regions of interest

Cervical regions	*Mean difference*	*Standard error*	*95% CI*		*Significance*
			Lower bound	*Upper bound*	
Region C − Region A	−0.176	0.008	−0.191	−0.160	< 0.001
Region C − Region B	−0.062	0.009	−0.080	−0.044	< 0.001
Region C − Region D	−0.065	0.005	−0.076	−0.055	< 0.001

Region A: external and superior cervical lip. Region B: internal and superior cervical lip. Region C: internal and inferior cervical lip. Region D: external and inferior cervical lip. External and superior cervical areas were softer than were internal and inferior parts.

superior parts of the cervix, which are subjected to a greater degree of pressure by the transducer, appear to be softer than the inner and inferior parts, which are further away from the probe. Unlike the comparison of malignant tumor with benign adjacent tissue of the breast, there is no evidence of a true variation in the stiffness of different parts of the cervix, and therefore the measurements obtained by elastography may be merely a reflection of the force applied by the transducer to different parts of the cervix. This explains why the repeatability of measurements in the area that received the force directly was poor between the two different observers.

The study has therefore highlighted that it is too premature to suggest that the measurements of rate-of-change in tissue displacement reflect histological changes which could provide a measure of cervical ripening. Investigation of the extent to which elastography could provide additional useful information on pregnancy outcome, over and above what is currently achieved by measurement of cervical length, will require standardization of both the force being applied by the transducer and the

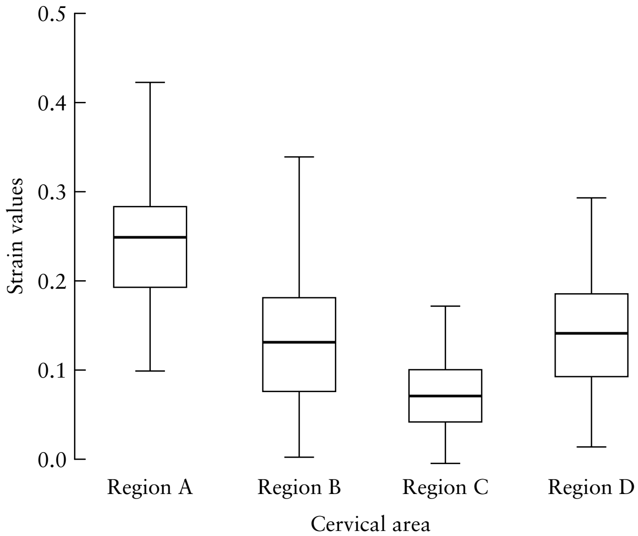

Figure 4 Box-and-whisker plots of elastographic measurements of different regions of the cervix. Region A: external and superior cervical lip. Region B: internal and superior cervical lip. Region C: internal and inferior cervical lip. Region D: external and inferior cervical lip. Median (lines within boxes), interquartile range (IQR, boxes) and values within 1.5 IQR (whiskers) are shown.

distance of the tissue of interest from the tip of the transducer.

REFERENCES

1. Stygar D, Wang H, Vladic YS, Ekman G, Eriksson H, Sahlin L. Increased level of matrix metalloproteinases 2 and 9 in the ripening process of the human cervix. *Biol Reprod* 2002; **67**: 889–894.
2. Lopez Bernal A. Mechanisms of labour – biochemical aspects. *BJOG* 2003; **110** (Suppl 20): 39–45.
3. Celik E, To M, Gajewska K, Smith GC, Nicolaides KH. Cervical length and obstetric history predict spontaneous preterm birth: development and validation of a model to provide individualized risk assessment. *Ultrasound Obstet Gynecol* 2008; **31**: 549–554.
4. Gomez R, Galasso M, Romero R, Mazor M, Sorokin Y, Goncalves L, Treadwell M. Ultrasonographic examination of the uterine cervix is better than cervical digital examination as a predictor of the likelihood of premature delivery in patients with preterm labor and intact membranes. *Am J Obstet Gynecol* 1994; **171**: 956–964.
5. Rao A, Celik E, Poggi S, Poon L, Nicolaides K. Cervical length and maternal factors in expectantly managed prolonged pregnancy: prediction of onset of labor and mode of delivery. *Ultrasound Obstet Gynecol* 2008; **32**: 646–651.
6. Swiatkowska-Freund M, Preis K. Elastography of the uterine cervix: implications for success of induction of labor. *Ultrasound Obstet Gynecol* 2011; **38**: 52–56.
7. Bartko JJ. The intraclass correlation coefficient as a measure of reliability. *Psychol Rep* 1966; **19**: 3–11.
8. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. *Psychol Bull* 1979; **86**: 420–488.
9. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**: 307–310.
10. Ophir J, Alam SK, Garra B, Kallel F, Konofagou E, Krouskop T, Varghese T. Elastography: ultrasonic estimation and imaging of the elastic properties of tissues. *Proc Inst Mech Eng H* 1999; **213**: 203–233.
11. Gong X, Xu Q, Xu Z, Xiong P, Yan W, Chen Y. Real-time elastography for the differentiation of benign and malignant breast lesions: a meta-analysis. *Breast Cancer Res Treat* 2011; **130**: 11–18.
12. Ding J, Cheng H, Ning C, Huang J, Zhang Y. Quantitative measurement for thyroid cancer characterization based on elastography. *J Ultrasound Med* 2011; **30**: 1259–1266.
13. Kapoor A, Kapoor A, Mahajan G, Sidhu BS. Real-time elastography in the detection of prostate cancer in patients with raised PSA level. *Ultrasound Med Biol* 2011; **37**: 1374–1381.
14. Yamaguchi S, Kamei Y, Kozuma S, Taketani Y. Tissue elastography imaging of the uterine cervix during pregnancy. *J Med Ultrasonics* 2007; **39**: 209–210.