In vivo high resolution MR elastography of the uterus and cervix

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Target audience: Physicians interested in the mechanical properties of the uterus and physicists interested in MR elastography development.

Background: Early detection of uterine lesion is limited and differentiation of uterine sarcoma from leiomyoma still remains challenging[1]. MR elastography (MRE)[2] is a unique imaging modality for non-invasively measuring mechanical properties of the abdominal soft tissue[3-5]. Recently, high resolution MR elastography (MRE) based on a nonmagnetic driver, single shot wave field acquisition and multifrequency dual elasto-visco (MDEV) parameter recovery was introduced [3,6] and it can be used to further study details of viscoelastic properties of uterus and cervix.

Purpose: To develop 3D multifrequency MRE (3DMMRE) for the application in uterine tissue and to test the method in healthy volunteers with consideration of individual variations, reproducibility and variations over menstrual cycle of the obtained viscoelastic values.

Methods: 10 healthy volunteers were included in this study (age range 22 to 51 years), one subject was examined several times within two menstrual cycles. All experiments were conducted on a 1.5-T MRI scanner. A spin echo EPI sequence with flow compensated motion encoding gradient (MEG) (TR / TE = 1590 / 55) was used. 7 vibration frequencies (30 to 60 Hz with 5 Hz increment) were induced by a nonmagnetic vibration lever attached as shown in Fig.1. At each frequency, the full wave field was measured in 9 adjacent transverse image slices of 2.5×2.5×2.5 mm^3 resolution with 8 dynamics over a vibration period. The total acquisition time was ca. 9 min. For data processing, the complex MR images were smoothed using a 2D Gaussian filter for noise reduction, then gradient-based unwrapping was performed as described in [3]. First-order in-plane derivatives along the image coordinate axes of the spin phase were calculated. After Fourier transformation we obtained six complex-valued strain images for each frequency invoked by MDEV inversion [3] resulting in two independent mechanical constants, $|G^*|$ and φ, corresponding to the magnitude and phase of the complex shear modulus G^*.

Results: Example wave images in a central image slice of one volunteer are shown in Fig.2. Fig.3 illustrates the MRE magnitude image and elastograms ($|G^*|$ and ϕ maps) of uterine tissue in the same volunteer. It is noticeable that the uterus is well resolved in both maps and the cervical region appears to be softer. Additionally, the endometrium is distinguishable from the outer myometrium in the $|G^*|$-map. Notably, the group-mean shear modulus $|G^*|$ of the uterine corpus ($|G^*| = 2.515 \pm 0.511$ kPa) is significantly higher compared to that of the cervix ($|G^*| = 2.000 \pm 0.432$ kPa, P = 0.012), whereas group-mean ϕ value are not distinguishable between uterine corpus and cervix (uterine corpus: 0.54 ± 0.09, cervix: 0.49 ± 0.10, P = 0.214). Fig. 5 presents the change of $|G^*|$ of the uterine corpus (endometrium and myometrium) over the menstruation cycle indicating that uterine stiffness in the order of 3 kPa after menses is reduced during the proliferative phase towards a level of 2 kPa in the late secretory phase.

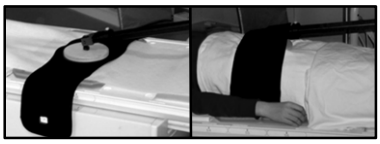

Fig.1: Driver setup with disk transducer

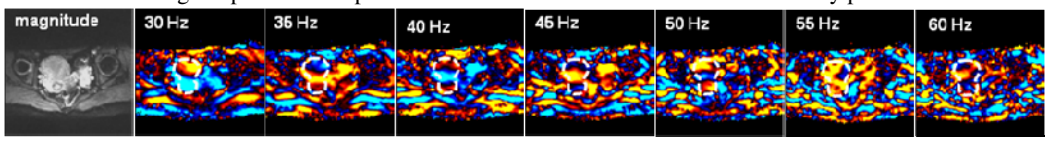

Fig.2: Wave images (real part of one complex-valued wave component) in one central slice at seven drive frequencies.

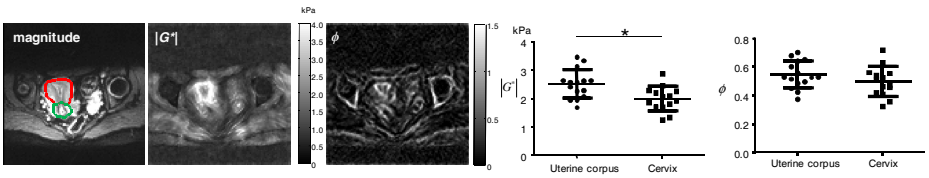

Fig.3: (a) MRE magnitude image and MRE parameter maps of the uterus (uterus body and cervix are outlined by red and green lines, respectively). (b) Mean values of $|G^*|$ and ϕ in uterine corpus and cervix.

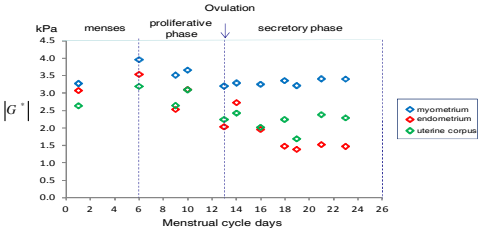

Fig.4: $|G^*|$ of uterine tissue over the menstrual cycle.

Discussion: In the past MRE was applied to uterine leiomyomas, however, without report of uterus viscoelasticity values [7]. Elastography on ex vivo tissue samples reported similar modulus values in cervix and uterine corpus [8]. Our in-vivo results suggest that the uterine corpus is stiffer than the cervix. Differences between the previous ex-vivo study and this in-vivo study may arise from the preparation of excised hysterectomy specimens versus in vivo conditions which is further highlighted by our observation of stiffness changes of uterine tissue during the menstrual cycle. As shown in Fig. 4, this behavior is less obvious in the myometrium while it is pronounced in endometrium. In a first interpretation, the menstrual stiffness variation of the uterine corpus appears to be dominated by anatomic and functional alteration of the endometrium. The endometrium is divided into two layers, functionalis and basalis. In Fig. 4, the highest value measured on the last day of menstruation reflected the stiffness of the basalis which is consisted of branching glands and dense stroma [9,10]. When entering the proliferative phase, under the influence of increased estrogen secretion, functionalis started to reconstruct and its thickness increased until ovulation. Functionalis is softer than basalis due to its composition from glands loosely connected by supportive stroma [9,10] resulting in a reduction of endometrial stiffness (including both basalis and functionalis) by increasing thickness of the functionalis layer. In the secretory phase, the rising progesterone level impedes further proliferation of functionalis tissue, so that thickness and gross stiffness of the endometrium remain unchanged throughout the late secretory phase [11,12].

Conclusion: We present for the first time viscoelastic properties of the in vivo healthy human uterus. Using 3DMMRE high resolution parameter maps of the mechanical properties of the uterine corpus and cervix were generated. Furthermore, we studied uterine tissue stiffness with respect to the menstrual physiology. The observed stiffness alteration correlated well with known anatomical and functional changes in the endometrium during different phases of the menstruation cycle.

Literature: [1] Brocker et al. *Strahlentherapie und Onkologie* 2011;187;611-618. [2] Muthupillai et al. *Science* 1995;269;1854-1857.[3] Hirsch et al. *Magn Reson Med* 2013;doi 10.1002/mrm.24674. [4] Warner L et al. *Investigative Radiology* 2011; ;46: 509-514. [5] Chopra et al. *Magnetic Resonance in Medicine* 2009; 62: 665-671. [6] Guo et al. *PlosOne* 2013;8; e71807.[7] Stewart et al. *Fertility and Sterility* 2011; 95; 281-284. [8] Kiss et al. *Phys Med Biol* 2006; 51; 3683-3695.[9] Chan et al. *Biol Reprod* 2004; 70; 1738-1750.[10] Uduwela et al. *Obstet Gynecol Surv* 2000; 55: 390-400. [11] Hoad et al. *American Journal of Obstetrics and Gynecology* 2005; 192; 648-654. [12] Raine-Fenning et al. *International Journal of Obstetrics and Gynaecology* 2004;111; 944-94