Cyclic changes of the uterus and cervix in young and middle-aged women during the menstrual cycle: an initial 3T MR functional imaging study based on T2 mapping and diffusion tensor imaging (DTI) sequences

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Aims and objectives

Quantitative T2 Mapping imaging was found to provide an effective means of classifying uterus and cervical anatomy and neoplastic disease (1).

Recent technical advances in diffusion weighted imaging (DWI) greatly enhanced the clinical value of magnetic resonance imaging (MRI) of the female pelvis (2,3). DWI can quantitatively measure the apparent diffusion coefficient (ADC) of the water in tissue, reflecting the cell density, cellular oedema, microcirculation, which are increasingly used as a quantitative parameter to distinguish malignant tissue from non-malignant tissues, as recent studies in gynaecological imaging have reported that ADC values that were lower than normal in uterine cervical cancer, endometrial cancer and leiomyosarcoma (3-6). Diffusion tensor imaging (DTI) is an extension of DWI, and it has emerged as a unique non-invasive imaging technique that can be used to determine the directionality of water diffusion in great detail (7). Water diffusion directionality is expressed by an anisotropy index (eg fractional anisotropy, FA), indicating microstructural organization, such as the density and orientation of fibrous tissue, which cannot be extrapolated from conventional MRI techniques (8-11).

Till now, just few studies focused on the normal values of these MRI functional values, especially the changes of the values during the menstrual cycle (12-18).

The aim of our study is to prospectively investigate the cyclic changes of T2, FA and ADC values of the normal uterus and cervix in a larger population divided into different age groups during 4 phases of the menstrual cycle, and the correlation with the basic serum hormone levels in menstrual phase (MP).
Methods and materials

Volunteer Data

This prospective study was approved by our local institution's ethics committee, and written informed consent was obtained from all participants. The inclusion criteria are healthy women of 20-40 years old, with regular menstrual cycle (28 ± 7 days) and biphasic basal body temperature, without history of gynecologic diseases or operation, without taking oral contraceptives or hormone replacement therapy in last 6 months, without MR scanning contraindication. 27 normal volunteers (age range, 22-40 yrs; mean age, 29 yrs) (20-30 yrs, \( n = 15 \); 31-40 yrs, \( n = 12 \)) completed four MR scans in our study.

Preparation and MR Imaging Acquisition

For each volunteer, MR scans were scheduled during four phases of the menstrual cycle respectively (the 2nd or 3rd days of MP, follicular phase (FP), peri-ovulatory phase (OP) and luteal-phase (LP)).

MR imaging of the female pelvis were performed in a 3T MRI scanner (Skyra, Siemens Medical Solution, Erlangen, Germany) with a 18 channels phase array body coil. Prone and feet first scanning mode was used to reduce the motion artifacts from the small intestines. Sagittal and axial turbo spin-echo (TSE) T2 weighted images and axial TSE T1 weighted images were obtained to define the anatomy of pelvic organs and to screen for gynaecological abnormalities. Sagittal T2 Mapping imaging and DTI were obtained parallel to the long axis of the uterine corpus the same imaging plane as sagittal T2WI.

The parameters for T2 Mapping sequence were as follows: repetition time/echo time (TR/TE) 2610/13.8,27.6,41.4,55.2,69.0,82.8 ms; field-of-view (FOV) 200mm; averages 1; slices 25; slice thickness 3mm, distance factor 20%; voxel size 1.0×1.0×3.0mm. The acquisition time was 6 min 17 s. The parameters for DTI were as follows: TR/TE 4500/66 ms; FOV 250mm; b-values 0 and 600 s/mm²; diffusion direction 20; averages 3; slices 26; slice thickness 3mm, distance factor 20%; voxel size 1.6×1.6×3.0mm. For fat suppression, the SPAIR technique was used. The acquisition time was 5 min 06 s.

Imaging Analysis

T2 Mapping and DTI datasets were transferred to a post-processing workstation (WWMP3960#Siemens Medical Solution, Erlangen, Germany) and processed using Viewing and Neuro 4D software. T2, FA and ADC maps were automatically calculated.

Images were blinded evaluated by two radiologists with expertise in female pelvic imaging. Data analysis was based on final consensus readings. Polygonal-shaped
regions of interest (ROIs) were drawn to cover the corresponding three zonal structures of the uterus and cervix (Fig.1-4).

**Fig. 1:** T2 mapping images of a 31-year-old healthy woman on peri-ovulatory phase. Means and standard deviation of T2 values were measured. (a) selected mid-sagittal plane of the uterus showing distinct layers of endometrium, junctional zone and myometrium. (b) regions of interest (ROI) were obtained using polygonal-shaped tool. (1) endometrium, (2) junctional zone, (3) myometrium.

*References:* Radiology, Peking Union Medical College Hospital - Beijing/CN
Fig. 2: T2 mapping images of a 31-year-old healthy woman on peri-ovulatory phase. Means and standard deviation of T2 values were measured. (c) selected mid-sagittal plane of the cervix showing distinct layers of anterior/posterior cervical endometrium, cervical stroma and cervical myometrium. (d) ROIs were obtained using polygonal-shaped tool. (1) cervical endometrium, (2) anterior cervical stroma, (3) anterior cervical myometrium, (4) posterior cervical stroma, (5) posterior cervical myometrium.

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Fig. 3: T2 weighted, FA map and ADC map images of the uterus of a 26-year-old healthy woman on luteal-phase. Means and standard deviation of FA and ADC values were measured. (a) T2-weighted image of the uterus on selected mid-sagittal plane showed the distinct layers of endometrium (red), junctional zone (green) and myometrium (purple). Regions of interest (ROI) were drawn by polygonal-shaped tool. (b) FA values of ROIs were obtained simultaneously on FA map. (c) ADC values of ROIs were obtained simultaneously on ADC map.

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Fig. 4: T2 weighted, FA map and ADC map images of the cervix of a 26-year-old healthy woman on luteal-phase. Means and standard deviation of FA and ADC values were measured. (a) T2-weighted image of the cervix on selected mid-sagittal plane. Regions of interest (ROI) of cervical endometrium (yellow), anterior cervical stroma (sky blue), anterior cervical myometrium (pink), posterior cervical stroma (lime), posterior cervical myometrium (dark blue) were drawn by polygonal-shaped tool. (b) FA values
of ROIs were obtained simultaneously on FA map. (c) ADC values of ROIs were obtained simultaneously on ADC map.

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Serum hormone examination

Serum concentrations of oestradiol (E), progesterone (P), luteinizing hormone (LH), follicle stimulating hormone (FSH) were measured in MP just before MR scanning to evaluate the basic hormone levels.

Statistical Analysis

Statistical analysis was performed using SAS 9.2.3 (SAS Institute Inc., Cary, NC, USA) and SPSS 19.0 (SSPS Inc., Chicago, IL, USA). A p value of 0.05 was chosen to indicate a statistically significant difference. Mixed liner models (considering interaction effect) were used to evaluate the differences of T2, FA and ADC values of three zonal structures of the uterus and cervix between two age groups and among four menstrual phases. One-way ANOVA analysis was used to evaluate the difference of T2, FA and ADC values among the three zonal structures of uterus and cervix. Correlation between serum levels of E, P, LH, FSH and the variation of T2, FA, ADC values during the menstrual cycle was estimated by Pearson correlation analysis.
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Results

T2 Mapping

T2 values of junctional zone and cervical myometrium showed significant differences among the four phases (p<0.05). There were significant differences of T2 values between the extension structures of uterus and cervix (p<0.05).

DTI

When age increased, FA values of the three layers of uterus and cervix declined with no statistical difference (p>0.05). Anisotropy of endometrium declined (Fig.5) while anisotropy of endocervix increased (Fig.6) during the menstrual cycle with statistical differences (p<0.05).

ADC values of endometrium (Fig.7), myometrium, endocervix (Fig.8) showed significant differences during the menstrual cycle (p<0.05).
**Fig. 5:** Boxplots of FA values of the uterus endometrium during the menstrual cycle. FA values of the endometrium during the menstrual cycle showed a decreasing pattern. FA values in LP were significant lower than that of MP (P<0.05) and FP (P<0.05).

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**Fig. 6:** Boxplots of FA values of the endocervix during the menstrual cycle. FA values of the endocervix in LP were significant higher than that of FP (P<0.05).

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Fig. 7: Boxplots of ADC values of the uterus endometrium during the menstrual cycle. ADC values of the endometrium during the menstrual cycle showed an increasing pattern. ADC values in LP were significant lower than that of MP (P<0.05).

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Fig. 8: Boxplots of ADC values of the endocervix during the menstrual cycle. ADC values of the endocervix in LP were significant lower than that of FP (P<0.05).

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**Correlation with hormone levels**

Change rate of FA values of endometrium correlated moderately with P levels (p=0.026, r=0.436). Change of ADC values of cervical myometrium between LP and MP correlated moderately with FSH levels (p=0.019, r=0.465).
Fig. 5: Boxplots of FA values of the uterus endometrium during the menstrual cycle. FA values of the endometrium during the menstrual cycle showed a decreasing pattern. FA values in LP were significant lower than that of MP (P<0.05) and FP (P<0.05).

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**Fig. 6:** Boxplots of FA values of the endocervix during the menstrual cycle. FA values of the endocervix in LP were significantly higher than that of FP (P<0.05).

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Fig. 7: Boxplots of ADC values of the uterus endometrium during the menstrual cycle. ADC values of the endometrium during the menstrual cycle showed an increasing pattern. ADC values in LP were significant lower than that of MP (P<0.05).
Fig. 8: Boxplots of ADC values of the endocervix during the menstrual cycle. ADC values of the endocervix in LP were significant lower than that of FP (P<0.05).

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Conclusion

Dynamic changes of T2 values, FA values and ADC values of uterus and cervix was observed during the menstrual cycle, which showed significant differences between the extension structures. Cyclic change of FA values of endometrium and ADC values of cervical myometrium correlated moderately with basic hormone levels.
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