Clinical Radiology 74 (2019) 81.e19–81.e24

Contents lists available at ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Visualising the boundary sharpness of uterine zonal structures using high-resolution T2-weighted images during the menstrual cycle

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ARTICLE INFORMATION

Article history:
Received 28 April 2018
Accepted 24 September 2018

AIM: To investigate whether there is an optimal time in the menstrual cycle to obtain the best image quality of uterine zonal structures with high-field magnetic resonance imaging (MRI).

MATERIALS AND METHODS: Thirty-eight normal volunteers with regular menstrual cycles underwent pelvic 3 T high-resolution T2-weighted three-dimensional (3D) turbo spin echo (TSE) with variable flip angle MRI examinations during the menstrual phase (MP), follicular phase (FP), peri-ovulatory phase (OP), and luteal phase (LP). Two radiologists blinded evaluated the boundary sharpness of the three zonal structures of the uterine corpus and cervix on mid-sagittal images using a three-point Likert-scale. The signal intensity (SI) on T2-weighted sequences of each zonal structure was measured and the ratio between the SI of adjacent structures was calculated. Paired Wilcoxon's test and repeated measurement analysis of variance were used to investigate the differences among the four phases.

RESULTS: No variation during the menstrual cycle was found in 10.5% (4/38) of volunteers and their boundaries were all well-defined. The OP exhibited the clearest boundaries of the corpus zonal structures. For the endometrium to junctional zone, mean scores of boundary sharpness from high to low were 3 (OP), 2.97 (FP), 2.76 (LP), 2.74 (MP); that for the junctional zone to myometrium were 2.76 (OP), 2.42 (FP), 2.32 (LP), 2.11 (MP); which were consistent with the SI ratio results. The results for the cervix showed no statistical difference during the menstrual cycle ($p>0.05$), and was well-defined throughout.

CONCLUSIONS: The OP is recommended as the best phase to investigate zonal-related uterine corpus diseases due to the best contrast. For cervical diseases, imaging could be performed when necessary at any time point, due to the limited influence of menstrual phases on cervical zone delineation.

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https://doi.org/10.1016/j.crad.2018.09.008
0009-9260/

Introduction

First described by Hricak in 1983, the uterine corpus in women of reproductive age was visualised as three zonal structures on T2-weighted images: endometrium visualised in high signal intensity (SI), outer myometrium visualised in medium SI, and the junctional zone between the endometrial stripe and outer myometrium visualised in low SI.[1–3] Although no obvious histological zonal evidence has been found on optical microscopy, the lower SI of the junctional zone is primarily caused by a lower water content, a threefold increase in nucleus-to-cytoplasm ratio, and a smaller extracellular space, compared with the outer myometrium.[4–6] Similar to the uterine corpus, the uterine cervix on T2-weighted images is also normally depicted as three layers: an inner layer with high SI corresponding to the endocervical mucosa, a middle layer with low SI corresponding to cervical stroma, which mainly consists of conjunction tissue, and an out-layer with intermediate signal intensity corresponding to the myometrium.[7]

It is known that uterine zonal anatomy is partially influenced by female hormones.[8,9] Visualising the sharpness of the boundaries and consecutiveness of the uterine zonal structures at the best time point plays an important role in the evaluation of some uterine diseases, such as endometrial carcinoma and adenomyosis.[2,3,10] One early study based on the images from six healthy women performed using 0.15 T magnetic resonance imaging (MRI) showed that the best contrast between the uterine layers was demonstrated during the first half of the menstrual cycle[11]; however, the signal-to-noise ratio (SNR), spatial resolution, and population size of that result were limited.

Several previous MRI studies reported that the thickness, T2 and T1 measurements, diffusion patterns (e.g., apparent diffusion coefficient [ADC] and fractional anisotropy [FA] values) of certain uterine zonal structures changed dynamically during the menstrual cycle[12–16]; however, to the authors' knowledge, no guidelines until now have pointed out which is the best phase to perform female pelvic MRI examinations. Thus the purpose of this study was to investigate whether there is an optimal time in the menstrual cycle to obtain optimal images of the uterine zonal structures using high-field MRI.

Materials and methods

Ethics statement

The ethical committee of Peking Union Medical College Hospital, PR China approved this prospective study. Information was gathered in compliance with Health Insurance Portability and Accountability Act guidelines. Informed written consent was obtained from all participants.

Study population

The inclusion criteria were healthy women between 20–40 years old, with regular menstrual cycles (28±7 days) and biphasic basal body temperature (BBT); without pregnancy, history of gynaecological diseases or surgery, oral contraceptive administration or hormone replacement therapy (HRT) in the last 6 months, and without contraindications to MRI. Women who had congenital uterine anomalies, multiple uterine leiomyoma or leiomyoma >1 cm, and adenomyosis detected at the first MRI examination and abnormal serum hormone levels were excluded. Fifty-six volunteers who met the inclusion criteria were enrolled. A total of 18 were excluded: six subjects had uterine anomalies, two subjects had uterine leiomyomas >1 cm, two subjects had adenomyosis, three had abnormal serum hormone levels, one subject was MRI intolerant, and four subjects failed to complete the four MRI examinations. Thirty-eight volunteers (age range, 20–40 years; mean age, 29±5 years; 20–30 years, n=22; 31–40 years, n=16) completed the four MRI scans (Fig 1).

MRI acquisition

Four pelvic MRI examinations were scheduled during the menstrual cycle, including the second or third day of the menstrual phase (MP), follicular phase (FP), peri-ovulatory phase (OP), and luteal-phase (LP). The date of ovulation was estimated as 14 days before the anticipated first day of the next menstrual cycle or based on elevated basal body temperature. MRI examinations during the FP and LP were performed approximately in the middle of the phases.

A moderately full bladder was required. To reduce the air in the rectum and sigmoid, 10 ml of glycerine enema (Beijing Maidihai Medical Business, Beijing, China) was administrated into the rectum 1 hour before the MRI examination. MRI of the pelvis was performed using a Magnetom Skyra 3 T MRI system (Siemens Healthcare, Erlangen, Germany) with an 18-channel phased-array body coil and a 32-channel phased-array spine coil. Prone and feet-first scanning was used to reduce motion artefacts from the

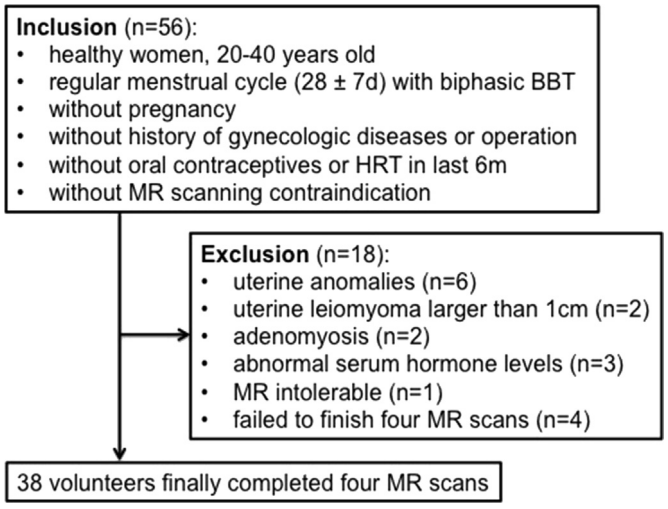

Figure 1 Flowchart of study population with inclusion and exclusion criteria. (BBT, basal body temperature; HRT, hormone replacement therapy).

small intestines. Three-dimensional (3D) high-resolution T2-weighted images were acquired using a 3D turbo spin echo (TSE) with variable flip angle sequence with the following parameters: TR/TE = 1,500 ms/137 ms, field of view (FOV) = 300×240 mm^2, sections per slab = 88, section thickness = 0.9 mm, voxel size = 0.9×0.9×0.9 mm^3, matrix size = 320×256, base resolution = 320, total acquisition time = 7 minutes 59 seconds.

MRI image analysis

The images in DICOM (digital imaging and communications in medicine) format were anonymised and the MRI menstrual phase information was removed. All 3D high-resolution T2-weighted images were transferred to a multi-modality post-processing workstation (*syngo*.via, Siemens Healthcare, Erlangen, Germany) and processed using 3D processing software to reconstruct and display the mid-sagittal images of the uterus.

Qualitative analysis

Two board-certified radiologists with 4 and 6 years of experience in genitourinary MRI reviewed the randomised images of each volunteer. The readers independently evaluated the boundary sharpness of the three zonal structures of uterine corpus and cervix on mid-sagittal images based on a three-point Likert-scale (3, well-defined; 2, obscure; 1, ill-defined; Fig 2).

Quantitative analysis

Region of interest (ROI) analysis was performed by a third radiologist with 3 years of experience in genitourinary MRI. The T2-weighted SI was measured by drawing polygonal-shaped ROIs to cover each zonal structure of the uterine corpus and cervix on the mid-sagittal image plane, respectively. The ratio of the SI on T2-weighted sequences between adjacent zonal structures was calculated.

Statistical analysis

Statistical analysis was performed using SPSS 20.0 (IBM, Armonk, NY, USA). The ranking scores were presented as mean with minimum and maximum values. Wilcoxon's test was utilised to compare the differences between the two age groups. Paired Wilcoxon's tests were used to evaluate the differences among the four phases during the menstrual cycle. The SI ratio was presented as the mean ± standard deviation (SD). The Kolmogorov–Smirnov test was used to confirm normality of the data distribution. For normally distributed data, an unpaired *t*-test was used for comparisons between the two age groups, and Wilcoxon's test was applied to non-uniform distributed data. Repeated measurement analysis of variance was used to evaluate the differences of SI ratios among the four phases. A *p*-value <0.05 was considered to be statistically significant. Inter-observer agreement was evaluated by Cohen's kappa analysis. Kappa values ≤ 0 were taken to indicate no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.

Results

All pelvic MRI examinations were performed successfully. No image data were excluded due to poor image quality.

Qualitative image analysis

Boundary sharpness of the three uterine zonal structures showed no significant difference between the two age groups (all $p>0.05$). Only 10.5% (4/38) of volunteers, all in the 20–30 years age group, exhibited no variation during the menstrual cycle, and their boundaries were all well-defined (Fig 3). The OP exhibited the highest mean scores of boundary sharpness of the corpus zonal structures during the menstrual cycle. For the endometrium to junctional zone,

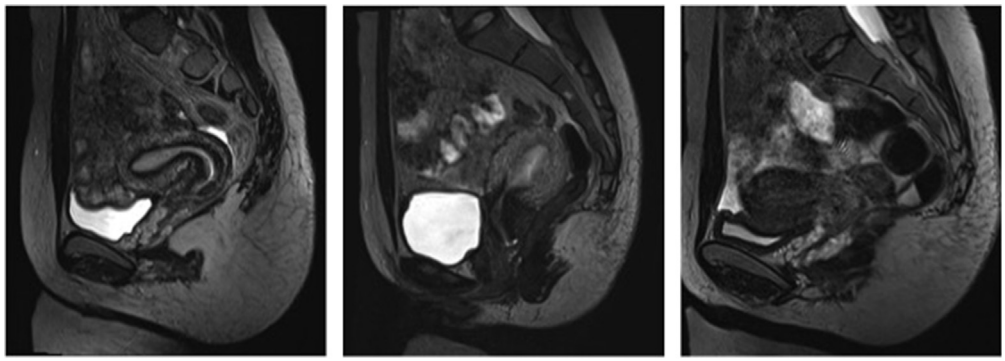

Figure 2 Examples of the three-point Likert-scale scoring system on the evaluation of boundary sharpness of uterine three zonal structures on high-resolution 3D T2-weighted images in mid-sagittal plane. (a) The uterus of a 25-year-old volunteer in the OP. The boundary sharpness of the uterine three zonal structures was well-defined with score of 3. (b) The uterus of a 22-year-old volunteer in the LP. The boundary between the junctional zone and myometrium was obscured with a score of 2. (c) The uterus of a 26-year-old volunteer in the MP. The boundary between junctional zone and myometrium was ill-defined with score of 1.

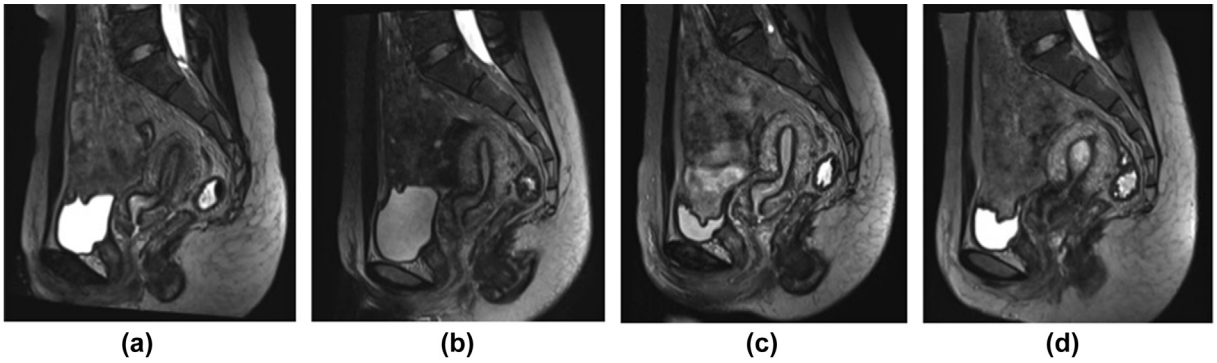

Figure 3 High-resolution 3D T2-weighted images in the mid-sagittal plane of a 28-year-old volunteer during the menstrual cycle including (a) MP; (b) FP; (c) OP; (d) LP. The boundary sharpness of the uterine three zonal structures was well-defined in all four phases.

mean scores of boundary sharpness from high to low were 3 (OP), 2.97 (FP), 2.76 (LP), 2.74 (MP), with significant differences between MP-FP, MP-OP, FP-LP, OP-LP. For the junctional zone to myometrium, mean scores of boundary sharpness from high to low were 2.76 (OP), 2.42 (FP), 2.32 (LP), 2.11 (MP), with significant differences between the MP–FP, MP–OP, FP–OP, OP–LP (Table 1; Fig 4). The boundary sharpness of the cervical zonal structures showed no statistical difference during the menstrual cycle (all $p>0.05$; Table 1) and demonstrated a well-defined boundary. Inter-observer agreement was excellent (all kappa >0.80).

Quantitative image analysis

The SI ratios between the uterine adjacent zonal structures are listed in Table 2. No statistical significant difference was found between the two age groups (all $p>0.05$). The results of the corpus showed the corresponding tendency with that of subjective scoring in qualitative image analysis. The highest SI ratio was found in the OP for both the endometrium–junctional zone and myometrium–junctional zone. There were significant differences in the SI ratio in the endometrium–junctional zone among the four phases (all $p<0.05$; Table 2). The SI ratio between the cervical adjacent zonal structures were not significantly different during the menstrual cycle (all $p>0.05$; Table 2).

Discussion

The present study was the first attempt to prospectively investigate menstrual-related dynamic changes of boundary sharpness of the uterine zonal structures on 3D high-resolution T2-weighted images obtained using a 3 T MRI system during the four phases of the menstrual cycle. 3D high-resolution T2-weighted imaging with an isotropic resolution of 0.9 mm enabled interactive multiplanar reconstruction at free orientations of the normal uterus.[17] According to the results in 38 volunteers, the peri-ovulatory phase represented the clearest boundaries of the corpus zonal structures; however, the phase of the menstrual cycle showed little influence on the depiction of cervical zonal structures.

The OP exhibited the clearest boundary sharpness of the uterine corpus zonal structures, following by the FP, LP, and MP. The results of the subjective scoring assessment showed the same tendency with the quantitative analysis of SI ratio between adjacent zonal structures, which indicated that higher SI ratios produced clearer boundaries. The dynamic changes of boundary sharpness of the uterine corpus zonal structures visualised by 3D high-resolution T2-weighted images were correlated with the physiological variation and water content of the uterine tissue as reflected by the T2 relaxation time, which depends on the hormonal state during the menstrual cycle. The OP has shown unique characteristics in previous studies. As Hoad *et al.* reported, based on the data collected in the FP, OP, and LP, the volume of endometrial and junctional zones reached a maximum in the OP. The regularity index of the junctional zone was smoothest in the OP and less regular in the LP.[9] The SI of the uterus showed the most rapid increase during the proliferative phase.[13] The SI of the endometrium increased significantly between the FP and OP, and decreased

Table 1
Evaluation of the boundary sharpness of the corpus and cervical zonal structures during the menstrual cycle.

	n=38				*p*-values					
	MP	FP	OP	LP	MP-FP	MP-OP	MP-LP	FP-OP	FP-LP	OP-LP
Endometrium–junctional zone	2.74 (1–3)	2.97 (2–3)	3.00 (3–3)	2.76 (1–3)	0.003	0.004	0.808	0.317	0.011	0.007
Junctional zone–myometrium	2.11 (1–3)	2.42 (1–3)	2.76 (2–3)	2.32 (1–3)	0.032	0.000	0.169	0.001	0.453	0.001
Endocervical mucosa–cervical stroma	2.97 (2–3)	2.97 (2–3)	2.95 (2–3)	2.92 (2–3)	1.000	0.564	0.157	0.564	0.157	0.655
Cervical stroma–myometrium	2.87 (2–3)	2.87 (2–3)	2.95 (2–3)	2.82 (2–3)	1.000	0.257	0.414	0.083	0.527	0.059

Data are presented as mean scores (score range).
MP, menstrual phase; FP, follicular phase; OP, peri-ovulatory phase; LP, luteal phase.

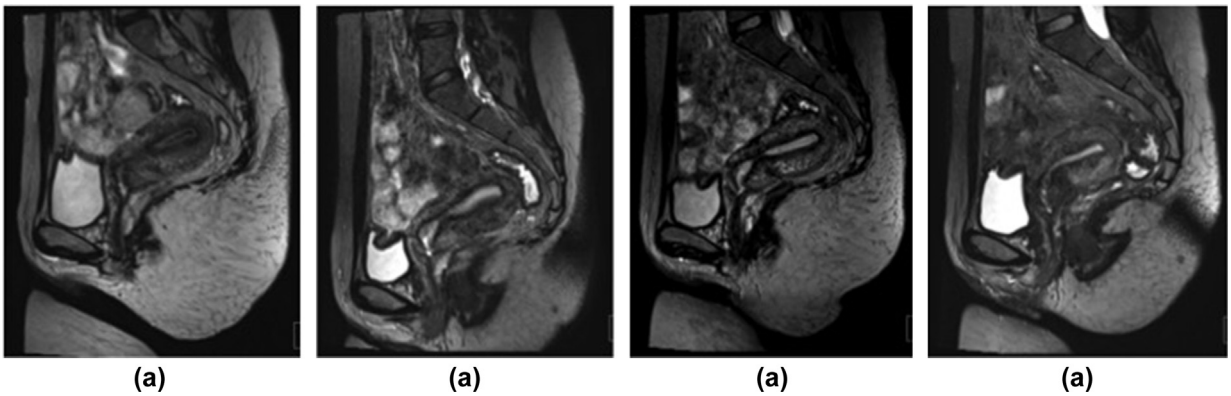

Figure 4 High-resolution 3D T2-weighted images in the mid-sagittal plane of a 34-year-old volunteer during the menstrual cycle including (a) MP; (b) FP; (c) OP; (d) LP. OP exhibited the clearest boundary sharpness of the uterine zonal structures, following by FP, LP, and MP.

Table 2
The T2 SI ratio between corpus and cervical adjacent zonal structures.

	n=38				*p*-values					
	MP	FP	OP	LP	MP-FP	MP-OP	MP-LP	FP-OP	FP-LP	OP-LP
Endometrium– junctional zone	1.72±0.36	2.42±0.53	2.62±0.47	2.11±0.50	0.000	0.000	0.000	0.025	0.000	0.000
Myometrium –junctional zone	1.59±0.35	1.65±0.39	1.70±0.28	1.64±0.27	0.379	0.013	0.247	0.452	0.825	0.147
Endocervical mucosa–anterior cervical stroma	3.03±1.13	2.88±0.83	2.98±0.74	3.02±1.02	0.137	0.178	0.639	0.488	0.109	0.217
Endocervical mucosa–posterior cervical stroma	2.85±1.00	2.60±0.81	2.69±0.74	2.74±0.85	0.152	0.292	0.614	0.506	0.389	0.730
Cervical myometrium–anterior cervical stroma	2.06±0.55	1.94±0.47	1.91±0.54	2.01±0.45	0.087	0.119	0.549	0.496	0.091	0.110
Cervical myometrium–posterior cervical stroma	1.84±0.66	1.79±0.41	1.84±0.44	1.82±0.59	0.167	0.968	0.819	0.305	0.215	0.791

Data are presented as mean ± standard deviation (SD).
MP, menstrual phase; FP, follicular phase; OP, peri-ovulatory phase; LP, luteal phase.

significantly between the OP and LP, which might be due to a change in blood flow or in blood vessels at the boundary between the endometrium and myometrium.[14] The SI of the corpus zonal structures during the OP was different to that during the other phases, which might be responsible for the obvious contrast revealed in the present study.

Additionally, uterine contraction and peristalsis might have influence on the boundary sharpness of the uterine zone. There are three types of uterine peristaltic contractions: cervico-fundal, fundo-cervical, and isthmical peristaltic activity, which change in direction and frequency during the menstrual cycle with lowest activity during menstruation and highest activity at mid-cycle, controlled by the dominant ovarian structure via the secretion of sex steroids systemically and into the utero-ovarian vascular counter-current system.[18–20] The significant differences of uterine peristalsis in different phases, especially the active role in rapid and sustained directed sperm transport and high fundal implantation in the OP, and serving retrograde menstruation for the preservation of body iron content in the MP, may result in zonal boundary sharpness differences during the menstrual cycle. Thus, the OP could be selected as the best phase to investigate zonal-related uterine corpus diseases, especially in the evaluation of inner myometrium invasion of lesions arising from endometrium or uterine cavity, which plays a crucial role in conservative treatment, or in the evaluation of the depth of myometrium invasion of gynaecological malignancies.

In contrast to the uterine corpus, the uterine cervix shows only little variation in its zonal anatomy as depicted by MRI with age, phase of the menstrual cycle, hormone replacement therapy, or use of oral contraceptives.[21] In the present study, the cervical zonal structures were almost well-defined throughout the menstrual cycle. The SI ratio between the adjacent cervical zonal structures was higher than that of the uterine corpus and did not show a statistical difference during the menstrual cycle. So it could be inferred that the phase of menstrual cycle is not a key factor in the interpretation of cervical lesions.

The present study has the following limitations: first, the study population only included 38 healthy volunteers. The significance of the results should be further investigated with a larger population. Second, dynamic imaging depicting uterine contraction and peristalsis was not included in this study. Concerning this limitation, a further study using cine mode MRI is planned to investigate contraction and peristalsis of the normal uterus during the menstrual cycle. Third, for clinical use, particularly with regard to staging uterine malignancies, assessment following contrast medium administration could also be of great clinical value, which would be performed in the future study. Fourth, the present study included non-pregnant healthy women of reproductive age with regular menstrual cycles. Future studies should be carried out in women with uterine abnormalities, representing a more clinically realistic study cohort.

In conclusion, the OP is recommended as the best phase to investigate zonal-related uterine corpus diseases due to provision of the best contrast. For cervical diseases, imaging could be performed when necessary at any time point, due to the limited influence of menstrual phases on cervical zone delineation.

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this article.

Acknowledgement

This research is partially supported by Beijing Natural Science Foundation 7184234.

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