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IMAGING

Uterine tissue development in healthy women during the normal menstrual cycle and investigations with magnetic resonance imaging

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KEY WORDS
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Objective: High-resolution magnetic resonance imaging (MRI) was used to monitor both uterine endometrial and junctional zone morphometry during the normal menstrual cycle.
Study design: Twenty-four healthy, ovulating women were studied during a single menstrual cycle. Three scans were performed to prospectively coincide with the follicular, periovulatory, and luteal phases of the cycle.
Results: MRI data showed a significant increase in endometrial and junctional zone volume, between the follicular and periovulatory phases, with a significant decrease in endometrial volume observed from the periovulatory to luteal phases. The regularity index, which is a novel subjective assessment of junctional zone structure, varied significantly and demonstrated a less regular junctional zone in the luteal phase.
Conclusion: This study has quantified the normal developmental changes of uterine tissue during the menstrual cycle with MRI. Junctional zone data from MRI may play a major role in future studies that investigate menstrual disorders, subfertility, and pathologic changes.

Ultrasound endometrial thickness measurements are used widely to determine endometrial receptivity and to detect potential pathologic conditions in gynecology.[1,2] Such measurements have reasonable negative predictive value, in that malignant change and conception are unlikely with an endometrial bilayer of <5 mm,[3,4] but disease and pregnancy still occur in patients with thin endometria.[5,6] However, morphometry alone has limited value in the prediction of endometrial function and disease. Dynamic changes in endometrial growth could be monitored over the menstrual cycle to address this problem. With the use of currently existing imaging techniques such as transvaginal 3-dimensional ultrasound scanning[7] and magnetic resonance imaging[8]

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(MRI), dynamic changes in thickness and multidimensional information (eg, volume) can be determined.

MRI is now used widely to image pelvic pathologic condition[9] and has been shown to be superior to ultrasound scanning in the staging of some uterine cancers.[10,11] However its role in other areas of gynecology is yet to be realized. MRI is inherently 3-dimensional in nature and, with correct sequences, can define clearly the endometrial, myometrial, and junctional zone regions.[12] It is noninvasive; therefore, serial measurements during the menstrual cycle may be conducted. Several studies have already looked at changes in endometrial and junctional zone thickness in both normal and hormonally modified menstrual cycles.[12-14] These studies examined small groups of women (<10 women in a group) and were not always controlled for the exact date of ovulation.[12,14] The aims of this current study were to use MRI to monitor both endometrial and junctional zone morphometry during the normal menstrual cycle and to examine whether volumetric analysis provides improved information on tissue development compared with thickness measurements. These measurements form part of a wider study to evaluate the roles of quantitative MRI and 3-dimensional ultrasound in gynecology.

Material and methods

Experimental design

This study was a longitudinal, observational study. Subjects were asked to call on the first day of menstruation (day 1) to book their first appointments for ultrasound scans (day 3) and MRI (between days 5 and 7 of the menstrual cycle). Blood samples were taken, and 3-dimensional ultrasound was performed on alternate days from day 3 until ovulation was detected ultrasonographically by the collapse of the dominant follicle and then every 4 days until the next menstrual period. Ovulation was confirmed initially ultrasonographically and subsequently was verified by observation of a surge in plasma concentrations of luteinizing hormone. Depending on the length of their typical menstrual cycle, a second MRI scan was booked to coincide with the periovulatory period (day 13-15 for a 28-day cycle); however, if ultrasound scans showed the dominant follicle to be developing either more quickly or slowly than this, then the scan was rebooked accordingly. A final MRI scan was undertaken at approximately 6 to 8 days after the periovulatory scan. The dates of each scan were then reclassified to $\pm$ days from ovulation, which was defined as day 0. Data were grouped according to the phase of the cycle: follicular phase, 12-5 days before ovulation; periovulatory phase, $\pm$3 days from ovulation; luteal phase, 4-10 days after ovulation.

Volunteer selection

Twenty-four women with regular ovulatory cycles and no history of infertility, miscarriage, or endometriosis formed the study group. These women were of reproductive age and were not using hormonal or intrauterine devices as contraception. This study was approved by the Local Hospital Ethics Committee. All volunteers were interviewed by a clinician (N.J.R.-F.) to determine their eligibility, to explain the study, and to obtain written consent before entering the study.

Data acquisition

A 0.5 T scanner with a Marconi (Surrey Medical Imaging Systems, UK) console was used for the MRI scan. Volunteers were allowed to lie either prone or supine in the scanner with their arms placed by their head to avoid motion artifacts from them. A set of 20 echo planar images (8-mm slice thickness) was used to determine the approximate central slice of the uterus. High-resolution fast spin-echo images were also acquired in the sagittal plane to determine endometrial and junctional zone development. Twelve slices were acquired with the following sequence parameters: slice thickness, 7 mm; interslice separation, 0.5 mm; repetition time, 4000 msec; interecho time, 25 msec; effective echo time, 125 msec; echo train length, 8, in plane resolution 1.17 mm $\times$ 1.17 mm, 256 $\times$ 192 image matrix.

Data analysis

Volume and thickness measurements were carried out by 1 observer (C.L.H.) to reduce variability. Figure 1 shows typical, central sagittal slice images through the uterus at various time points over the menstrual cycle. Endometrial and junctional zone thickness measurements were carried out on the central slice using Analyze software (Biomedical Imaging Resource, Mayo Foundation, Rochester, Minn). Endometrial thickness was measured at the maximum width of the tissue region, perpendicular to the long axis of the uterus.[14,15] In previous MRI studies of endometrial thickness, no indication was given of the variability of an individual's measurements, whereas for this study 5 measurements were averaged for each central slice image. Junctional zone thickness was measured as the average of 5 thickness measurements equally spread around the uterus,[14] perpendicular to the visible endometrial/junctional zone intersection on the central slice image. Volumes of the endometrium and junctional zone were also calculated with the Analyze region of interest program, with which each uterine tissue volume was identified on each slice. Total volumes were then calculated from all the slices. As with the thickness measurements, the average of 5 drawings of the region of interest was calculated for each set of data.