Physiological change of the human uterine myometrium during menstrual cycle: evaluation using BOLD MR imaging

A. Kido[1], T. Koyama[1], M. Kataoka[1], A. Yamamoto[1], S. Umeoka[1], S. Fujii[1], T. Saga[1], K. Togashi[1]

[1]Kyoto University, Kyoto, Kyoto, Japan

Introduction Uterus exhibits impressive hemodynamic change during menstrual cycle phases. During menstrual phase, prostaglandins are at their highest concentration (1). It induces uterine myometrial contractions and lead to decrease local uterine blood flow (2). Uterus also shows morphological changes in myometrial thickness, myometrial signal intensity and junctional zone thickness which can be observed by MR imaging (3). Recently, developments of MR imaging techniques have enabled the non-invasive measurements of uterine blood oxygenation using blood oxygenation level-dependent magnetic resonance imaging (BOLD MRI). This technique applies the fact that the magnetic properties of hemoglobin vary depending on whether it is in the oxygenated or deoxygenated form. This affects the T2* relaxation time of the neighboring water molecules and thus influences the MRI signal on T2*-weighted images. Because the ratio of oxyhemoglobin to deoxyhemoglobin is related to the pO2 of blood, and the pO2 of capillary blood is thought to be in equilibrium with surrounding tissue, changes expressed by BOLD MRI can be considered as changes in tissue pO2 (4-6). This technique has been originally developed for brain functional imaging. Now it has been widely used for several organs, including heart, kidney and muscle in mice (5, 7, 8). Although this technique does not measure blood flow directly, many studies on brain functional MRI suggest a strong correlation between BOLD measurements and blood flow (6). Thus it is assumed that blood flow of various tissues and organs can be estimated by BOLD measurement. This study was aimed to evaluate the hemodynamic changes of the uterus during menstrual cycle phases using BOLD MR imaging.

Materials and Methods **1) Study population**The study was carried out in 12 healthy female volunteers of reproductive age (age range: 21-37 years, mean: 28.6 years). Exclusion criteria included previous gynecologic disease, abnormal findings on MR images, a use of contraceptive medication or methods at the time of this study. Women with poor MR image quality so as not to allow BOLD measurement were also excluded from the analysis.

2) MR scanning protocol MR images were obtained with a 1.5-T magnet unit (Symphony, Siemens) using a phased-array coil. A multiple gradient recalled echo(mGRE) sequence (TR=1000msec, TE=23,28,33,38,43,100,150, flip angle=90 deg., band width=2894 (Hz/Pz)) was used to acquire seven T2* weighted images within a single breath hold of less than 20 seconds 64x64 pixels and slice providing oxygen of flow rate 2 liter/min. The field of view was 200mm, matrix size was thickness was 5mm. The T2* was used as a semiquantitative measure of relative tissue oxygenation. A decrease in T2* indicates a decrease in tissue pO2. Sagittal FSE T2-weighted image (WI)(TR = 5470 msec, TE = 122 msec) and spin echo T1-WI (TR = 592 msec, TE = 15 msec) were obtained at each scanning session with the constant FOV of 19.5 x 26 cm, slice thickness of 5 mm, and matrix of 512 x 384.

MR images were obtained at three phases of the menstrual cycle (menstrual, periovulatory, and luteal phases) for each person.

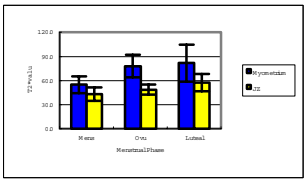
3) Image Analysis and Statistical analysisT2* map was obtained using a satellite console of the MR unit. Two different Regions of interest (ROI) were placed over the myometrium, excluding the area affected by susceptibility artifact from the intestinal air on T2* map. The area suffering severe artifact was evaluated on the image obtained with TE=150, in which the severity of artifact was most sensitively expressed. Statistical analyses were performed to evaluate the difference in T2* value.

Results Leiomyoma was diagnosed on static MR studies for one person and then excluded from the analysis. One person was excluded from the analysis due to severe susceptibility artifact caused by intestinal air on MR imaging. A total of 30 studies (10subject, three phases) were analyzed. The mean T2* values in the outer myometrium were 54.7, 77.8 and 81.7 in menstrual, ovulatory and luteal phase, respectively (Fig1). The differences of T2* values were statistically significant between menstrual and ovulatory phase and between mestrual and luteal phase ($p<0.001$, $p<0.001$). The difference of T2* value between ovulatory and luteal phase was not statistically significant. The mean T2* value in junctional zone was 43.0, 48.6 and 57.3 in menstrual, ovulatory and luteal phase, respectively (Fig1). The T2*value of junctional zone was significantly lower than that of the myometrium in all through the menstrual cycle phases (Fig1).

Discussion The BOLD MRI technique, developed by Ogawa et al. in 1990, has enabled to examine blood oxygenation, and has been mainly applied to functional brain MRI (4, 9). This technique has also been applied to other organs these days. The correlation between T2* value and blood oxygenation had already been shown in several organs such as kidney, heart and muscle using animals (5, 7, 8) In this study, we applied this new technique to the human uterus, which is mostly composed of the smooth muscles.

The result from our study indicates that 1) T2* value of junctional zone was significantly lower than that of outer myometrium at every menstrual phases, 2) T2* value of the outer myometrium in menstrual phase was significantly lower than those in the other menstrual cycle phases. The reason for these decreased T2* value seems resulting from physiologic changes of the uterus. Uterine peristalsis may cause the decreased T2* values of junctional zone. This movement is known to be propagated myometrial contractions within the inner myometrium and shown by TVUS (transvaginal ultrasonography) and MR imaging (10, 11). On the other hand, the myometrium in the menstrual phase also show vigorous contraction to expel menstrual blood and may cause the reduced T2* value of outer myometrium during menstruation. Decreased T2* value in the contracted muscles may be explained by either increased oxygen consumption, or decreased blood flow. In the uterus, these two parameters are closely correlated with each other. The menstruation begins as a result of vascular spasm of the uterine spiral artery, which also leads to decreased myometrial blood volume, and subsequently, decreased oxygen consumption in the myometrium.

In experimental study of skeletal muscles, Jordan BF et al concluded that the maintenance of BOLD signal intensity in moderately exercising skeletal muscle depends mainly on changes in pO2, rather than changes in blood flow or T2 effects. In their study, the blood oxygenation in the muscle was constantly decreased after contraction while blood flow change was variable (8). In the skeletal muscles, muscle oxygenation also decrease according to the strength of muscle contraction (12). Although theory in the striated muscle may not be applied to the uterus that is composed of smooth muscle, it is certain that the contraction of the smooth muscle and decreased blood oxygenation closely relate to the alteration of the T2* value of the myometrium.



In conclusion, on BOLD MRI technique, T2* value of the outer myometrium during the menstrual phase is significantly lower than those in other phases, and that in the junctional zone is lower than that of the outer myometrium. Although this study is preliminary, the decreased T2* value of the myometrium may represent physiologic changes of the uterus, relating to uterine contraction and oxygen consumption in the myometrium.

1, Olive DL. et al. Clin Obstet Gynecol 1991; 34:157-166. 2, Palter SF. In: Berek J, ed. Novak's Gynecology. 2002; 124-174 3, Haynor DR. et al. Radiology 1986; 161:459-462. 4, Ogawa S. et al. Magn Reson Med 1990; 14:68-78 5 Prasad PV. et al.Circulation 1996; 94:3271-3275. 6. Li L. et al. J Magn Reson Imaging 2003; 17:671-675 7, Wendland MF. et al. Magn Reson Med 1993; 29:273-276. 8, Jordan BF. et al. Magn Reson Med 2004; 52:391-396. 9, Ogawa S. et al. Proc Natl Acad Sci U S A 1990; 87:9868-9872 10, de Vries K. et al. Am J Obstet Gynecol 1990; 162:679-682. 11, Nakai A. et al. J Magn Reson Imaging 2003; 18:726-733. 12, Murthy G. et al. J Orthop Res 1997; 15:507-511.