Junctional zone thickness in young nulliparous women according to menstrual cycle and hormonal contraception use

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JUNCTIONAL ZONE THICKNESS IN NULLIPAROUS WOMEN BETWEEN 19 AND 35 YEARS OLD ASSESSED BY MRI, AS A FUNCTION OF MENSTRUAL CYCLE AND HORMONAL CONTRACEPTION. UTERINE JUNCTIONAL ZONE IN NULLIPAROUS WOMEN

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1.1 Abstract

This prospective study aims to determine the optimal menstrual phase and uterine location to detect the thickest junctional zone (JZ) by magnetic resonance imaging (MRI). This study is performed on volunteer healthy nulliparous women, subdivided according to their use of hormonal contraception. Each women was investigated three times during their menstrual cycle.
Eighteen nulliparous non-users and 29 nulliparous users of hormonal contraception (mean age 26.4 and 25.8 years, respectively) underwent a pelvic MRI (1.5T) examination during the follicular, ovulatory and luteal phase. The JZ thickness was measured at six locations in the uterine wall.
A significantly thinner JZ was observed at the anterior and posterior wall of the midcorpus and fundus, in the contraception users compared to the non-users. No differences in JZ thickness were noticed between the menstrual phases and the uterine wall locations. The ratio of JZ versus total myometrial thickness also demonstrated differences between both groups and between the assessed uterine locations.
To conclude, any phase in the menstrual cycle and location within the uterine wall was validated to determine the junctional zone thickness on MRI, although the fundal location is preferred.

KEYWORDS: Junctional Zone; Uterus; MRI; Thickness; Fertility

1.2 Introduction

One of the fundamental functions of the uterus in reproduction is directing sperm transport into the tube ipsilateral to the dominant follicle, which is provided by uterine peristalsis (Kunz et al., 1996, 2000a; Lyons et al., 1991; Wildt et al., 1998). This function is dependent upon the architecture of the myometrial wall, more particularly the junctional zone (JZ), also called archimyometrium or stratum subvasculare. This layer is characterized by predominantly circular arrangement of muscular fibers and bipartition at the level of the mid- and upper corporal region. Its origin is dedicated to the fusion of the paramesonephric ducts during early ontogeny (Fusi et al., 1996; Leyendecker et al., 1998; Leyendecker, 2000; Noe et al., 1999; Werth and Grusdew, 1898; Wetzstein, 1965).
During the reproductive period of women, three distinct layers can be recognized in the uterine wall: the endometrium, the JZ and the outer myometrium. This uterine zonal anatomy was first identified in 1983 by means of magnetic resonance imaging (MRI) (Hricak et al., 1983). On T_2-weighted MR images, the endometrium is presented as a high signal-intensity zone, the JZ as a low signal-

intensity zone and the outer myometrium as a medium signal-intensity zone (Hricak et al., 1983; McCarthy et al., 1986, 1989; Scoutt et al., 1991). The JZ is only clearly defined during the reproductive years, implying that it represents a hormone dependent differentiation process. This is reflected by the cyclic changes in immunoreactive estrogen and progesterone receptor expression in JZ myocytes which mimic those observed in the endometrium, whereas no cyclic changes are detectable in the outer myometrial smooth muscle cells (Hauth et al., 2001, Noe et al., 1999).

Adenomyosis is a gynecological disorder of the myometrium, characterized by a benign invasion of basal endometrial glands and stroma into the JZ and outer myometrium. Also growing evidence exists linking a thickened JZ in adenomyosis, as seen on a pelvic MRI scan, with primary/secondary infertility in young adults (Barrier et al., 2004; de Souza et al., 1995; Devlieger et al., 2003; Garavaglia et al., 2015). Inner myometrium adenomyosis is expressed by an abnormal thickening and disruption of the JZ, which is considered the MR imaging criterion for diagnosing this condition, although myometrial hyperplasia as a normal variant could not be excluded (Reinhold et al., 1998, 1999.; Novellas et al., 2011). The diagnosis of JZ adenomyosis on the basis of MR images remains difficult because of the difficulty in determining a strict cut-off value for the JZ thickness from which adenomyosis is assumed. First of all, it is of importance to define normal limits of the JZ thickness in healthy women.

The purpose of this study was to define the optimal menstrual cycle phase and uterine wall location in order to measure the normal JZ thickness. This optimal menstrual phase and uterine wall location will be defined by the menstrual phase and location where the thickest JZ can be measured. To determine this, this study investigates whether there are cyclic or location dependent changes in JZ thickness, outer myometrial thickness and the ratio of JZ to the total myometrial thickness, by measuring this thickness in 47 healthy nulliparous women (18 non-users and 29 users of hormonal contraception), at six different uterine wall locations, in which each women is investigated three times during a menstrual cycle.

1.3 Material and Methods

The health insurance, study protocol and informed consent were approved by the local hospital ethics committee in order to perform this longitudinal study on volunteers.

1.3.1 Study population

Over a recruitment period of approximately 50 months (21/12/2007 – 12/01/2012), 47 voluntary nulliparous Caucasian women were included in this single center, prospective study divided in two groups: 18 non-users (group 1) and 29 users (group 2) of hormonal contraception. The different types of hormonal contraception were oral contraceptive pills and hormonal vaginal rings. The age of the participants ranged between 19 and 35 years (mean age for group 1 and 2 are respectively 26.4 and 25.8 years). Inclusion criteria comprises Caucasian, nulliparous women between 18-35 years old with no medical history of infertility and no gynecological history (no bleeding disorders, irregular menstrual cycle). The women were hence of unknown fertility status as they were nulliparous. Exclusion criteria were women with a pacemaker, clips or other MRI-incompatible implanted devices, pregnancy, diminished renal function and previous unknown uterine morphologic abnormality found on the first MRI examination. Recruitment was achieved by emailing and writing co-workers in our hospital, students and PhD students at the University of Hasselt (local university), personal contacts and cooperation with external physicians. All volunteers provided a written informed consent and filled out an epidemiological questionnaire.

1.3.2 Blood laboratory tests

Blood samples were collected from each subject prior to each MRI examination to assess human chorionic gonadotrophin (hCG), creatinine, follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol and progesterone levels. The follicular phase was considered around day 6-13 of the menstrual cycle, the ovulatory phase around day 14-16 and the luteal phase around day 17-28. The exact phase of the menstrual cycle was determined based on the hormone levels, for each MRI examination in all participants who did not use hormonal contraception.

1.3.3 Magnetic Resonance Imaging

Three MRI scans were performed during the menstrual cycle in the non-users of hormonal contraception: one in the follicular phase (n = 17), one in the ovulatory phase (n = 17) and one in the luteal phase (n = 16). Fifteen out of 18 women who did not use hormonal contraceptives underwent an MRI examination in the three phases, one only in the follicular phase, one in the follicular and ovulatory phase and one in the ovulatory and luteal phase. This resulted in a total of 50 MRI examinations for the non-users of contraception. The majority of the women in the group of the users of hormonal contraceptives also underwent three MRI scans during their cycle resulting in a total number of 83 MRI investigations for the 29 users of hormonal contraception. Two women underwent only two MRI investigations during their cycle, whereas one woman only underwent one MRI investigation.

All MRI scans were performed on a 1.5T MR imaging system (Siemens Magnetom Symphony Tim (4G-Dot upgraded), Siemens, Erlangen, Germany; Software Syngo MR B15). The study women were positioned on the table of the scanner in head first - supine position and an eight channel receive only body array was placed on the pelvis of the women. An intravenous catheter was inserted in the elbow crease. The MRI examination started with a localizer sequence followed by T_2-weighted turbo spin echo (T_2 TSE) sequences acquired in three different planes: transversal, coronal and sagittal. After manual injection of the abdominal-specific antispasmodic Hyoscine Butylbromide (buscopan, 1 ml, 20 mg/ml, Boehringer Ingelheim, Germany), diluted in sodium chloride (10 ml, 0.09%, Baxter, Lessines, Belgium), sagittal T_2 TSE images with and without fat suppression were acquired (table 1). The antispasmodic agent was used to reduce bowel movement artefacts and uterine peristalsis. All images were sent to a dedicated workstation.

Table 1: Overview of the performed MRI-scan parameters.

Parameters/Sequence	Localizer	T_2 TSE	T_2 TSE	T_2 TSE	T_2 TSE: buscopan	T_2 TSE: buscopan
Orientation	Sagittal	Transversal	Coronal	Sagittal	Sagittal	Sagittal
Repetition time (msec)	20	5100	5000	5000	5610	4060
Time to echo (msec)	5	88	89	89	89	93
Field of view (mm)	400	370	320	340	360	360
Slice thickness (mm)	10	5	5	5	4	4
Flip angle (degree)	40	180	180	180	180	180
Voxel size (mm x mm x mm)	3.1 x 1.6 x 10	1.1 x 0.8 x 5	0.8 x 0.6 x 5	0.9 x 0.7 x 5	0.9 x 0.7 x 4	0.9 x 0.7 x 4
Acquisition time (min.sec)	0.14	1.03	2.52	2.02	2.22	3.12
Fat suppression	No	No	No	No	Yes	No

T2 TSE: T2-weighted turbo spin echo sequences; T2 TSE: T2-weighted turbo spin echo sequences after manual buscopan injection.

1.3.4 MR image analysis

All measurements were performed on a specialized workstation (MMWP, Syngo MMWP VE36A) by two independent observers, an experienced radiologist and an intern in radiology with 3 years of pelvic MRI experience, using the measuring cursor included in the workstation's software. Both observers were blinded for the hormonal contraception status of the women and examinations were evaluated consecutively. The T_2 TSE images obtained in the three anatomical planes before buscopan injection were used to localize the uterus in the pelvis and to ensure that the uterus was within normal limits (no congenital or acquired uterine abnormalities; assessed by a radiologist). The corpus and cervix sizes latero-lateral (transverse) (LL) were measured on the coronal image (figure 1C). The T_2 TSE sagittal images after buscopan injection with and without fat suppression were compared and used to measure the following parameters: corpus and cervix length, antero-posterior

(AP) uterus size (figure 1A), JZ and outer myometrium thickness at six different locations in the uterine wall. The six locations at which the JZ and myometrium thickness were measured are the uterine anterior and posterior wall at the level of the isthmus, the middle (midcorpus) and the fundus (figure 1B). According to this method, both the uterine anterior and posterior wall were divided into three parts equally in length. Subsequently, the JZ and outer myometrial thickness were measured at a central point in each part.

The ratio of the JZ thickness to total myometrial thickness was measured by dividing the thickness of the JZ and the corresponding thickness of the total myometrium at the same location (JZ thickness/ (JZ thickness + outer myometrial thickness)).

Fig. 1
Uterine measurement parameters.
A and B. On the T_2-weighted turbo spin echo (T_2 TSE) sagittal MR image after buscopan injection without fat suppression, the junctional zone (JZ) thickness and the thickness of the outer myometrium (OM) [A] were measured at the level of the isthmus (I), the midcorpus (M) and the fundus (F) of the uterine anterior and posterior wall [B]. On this image, the antero-posterior (AP) size of the corpus was also determined.
C. The latero-lateral (LL) size of the corpus was measured on the coronal T2-weighted MR image obtained before buscopan injection.

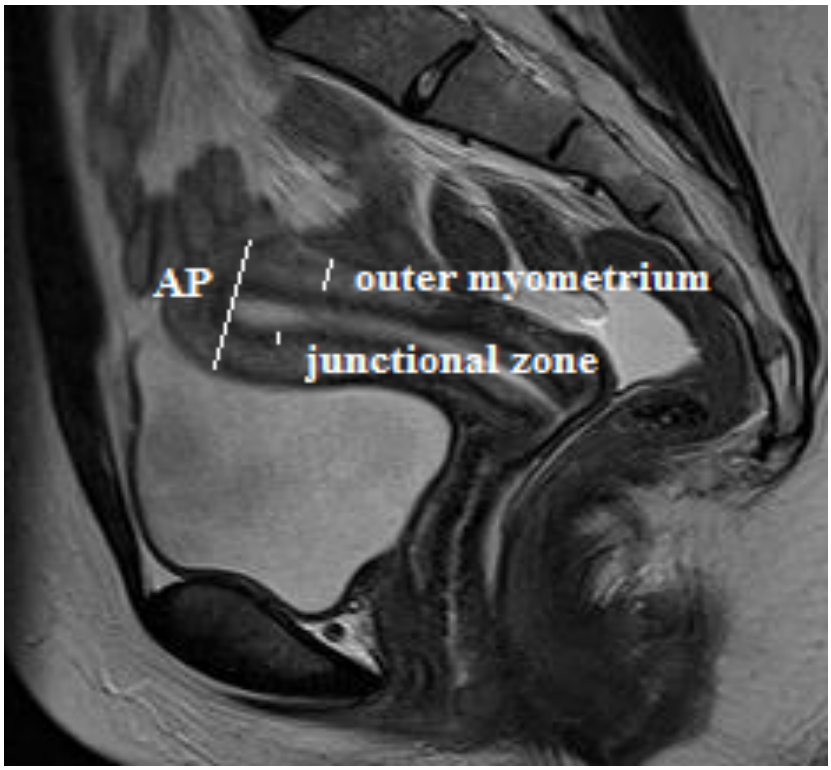

Fig. 1A

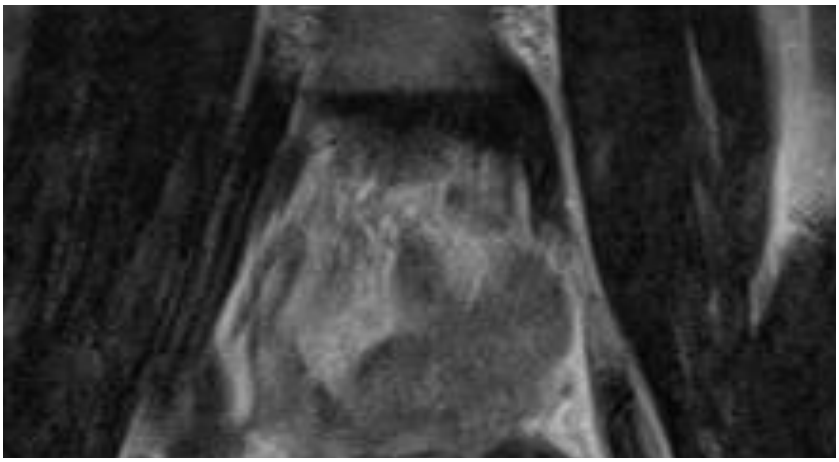

Fig. 1B

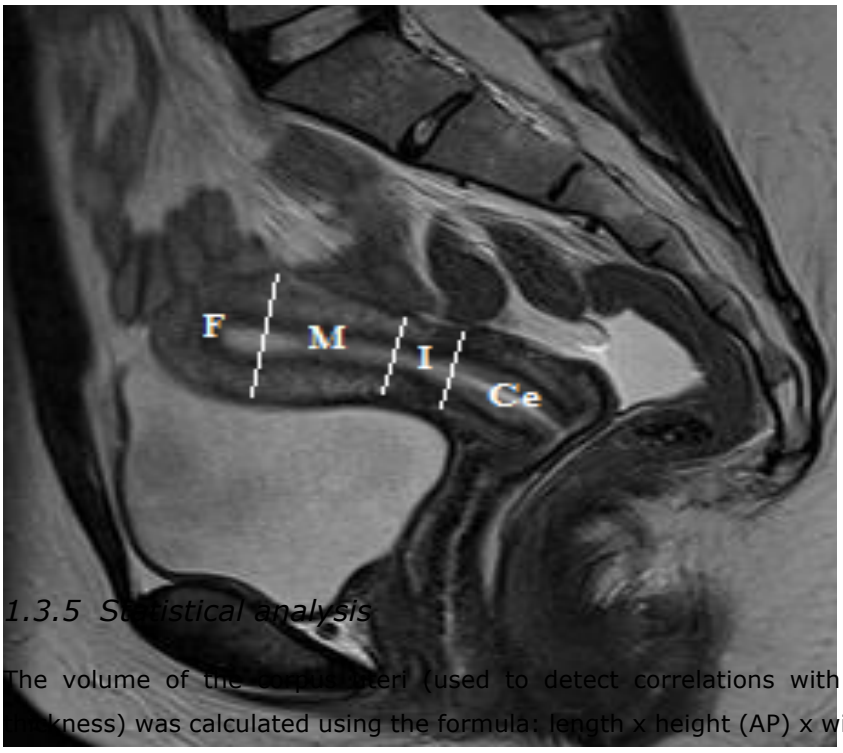

Fig. 1C

1.3.5 Statistical analysis

The volume of the corpus uteri (used to detect correlations with the JZ or outer myometrial thickness) was calculated using the formula: length x height (AP) x width (LL) x 0.523 (Goldstein et al., 1988).

All statistical analyses were performed by means of the computer program SAS version 9.4. A 5% level of significance is used. No correction for multiple testing was applied.

Inter-observer statistics was performed for the consistency in measurements by means of the informal Bland-Altman test (Bland JM and Altman, 1986; Altman DG, 1991).

Linear mixed models were used in order to investigate the effect of hormonal contraception, the effect of menstrual phase (for woman not using hormonal contraception) and the effect of the location in the uterine wall on the JZ thickness, on the outer myometrial thickness, and on the ratio of JZ versus total myometrial thickness. The statistical model includes two main fixed effects and their interaction. The first fixed effect combines the use of hormonal contraception and the menstrual phase. This fixed effects has four levels, i.e. phase 1 for non-users, phase 2 for non-users, phase 3

for non-users, and users of hormonal contraception. This effect allows the comparison of (1) users and non-users (per menstrual phase for the non-users or averaged over the three menstrual phases for the non-users) and (2) the different menstrual phases for the non-users of hormonal contraception. The second fixed effect is the location in the uterine wall. The association between measurements of the same woman (e.g. JZ thickness measured in the three menstrual phases) is incorporated by means of a random intercept at woman level. A parsimonious model is obtained by backward elimination of the fixed effects terms not statistically significant at a 5% level of significance. In order to normalize the data, statistical analyses were performed on the natural log transformed outcome data.

2.3 Results

The T_2 TSE sagittal MR images after buscopan injection without fat suppression provided the best delineation of the JZ compared to the images with fat suppression. Therefore, we used the MRI images without fat suppression to perform the thickness measurements at the different locations of the uterine wall.
The informal Bland-Altman test showed no significant differences between the measurements of the two investigators, as the kappa value equaled 0.87. The data of the JZ thickness, outer myometrium thickness and ratio of JZ to total myometrium thickness (mean, minimum and maximum) at the six different locations in the uterus are presented in figure 2, 3 and 4 respectively.
No statistical correlations were found between JZ thickness and other parameters such as uterus volume, height and weight of the women, age at menarche and smoker status.

The mean JZ thickness of the non-users of contraception, averaged over all locations, was 3.2 mm during the follicular phase, 3.0 mm during the ovulatory phase and 3.1 mm during the luteal phase. The users of contraception had a mean JZ thickness of 2.7 mm.

According to the linear mixed model analysis comparing the non-users and users of hormonal contraception, the effect of menstrual phase on the JZ thickness in the non-users was dependent upon the uterine wall location and vice versa. The JZ thickness in the users of hormonal contraception was significantly thinner compared to the JZ of the non-users at both the anterior and posterior wall of the midcorpus during each menstrual phase ($p = 0.0123$, $p = 0.0458$ and $p = 0.0356$, for respectively the follicular, ovulatory and luteal phase in the anterior wall of the midcorpus; and $p = 0.0108$, $p = 0.0089$ and $p = 0.0280$, for respectively the follicular, ovulatory and luteal phase in the posterior wall of the midcorpus). The JZ thickness was also thinner in the users at the fundus in the anterior wall during the follicular and luteal phase ($p = 0.0105$ and $p = 0.0261$, respectively) and at the fundus in the posterior wall during the follicular phase ($p = 0.0377$). Furthermore, a trend towards a thinner JZ was noticed in the users of contraception compared to the non-users of hormonal contraception at the anterior wall of the fundus during the ovulatory phase ($p = 0.0613$) and at the posterior fundus wall during the ovulatory and luteal phase ($p = 0.0597$ and $p = 0.0823$, respectively).

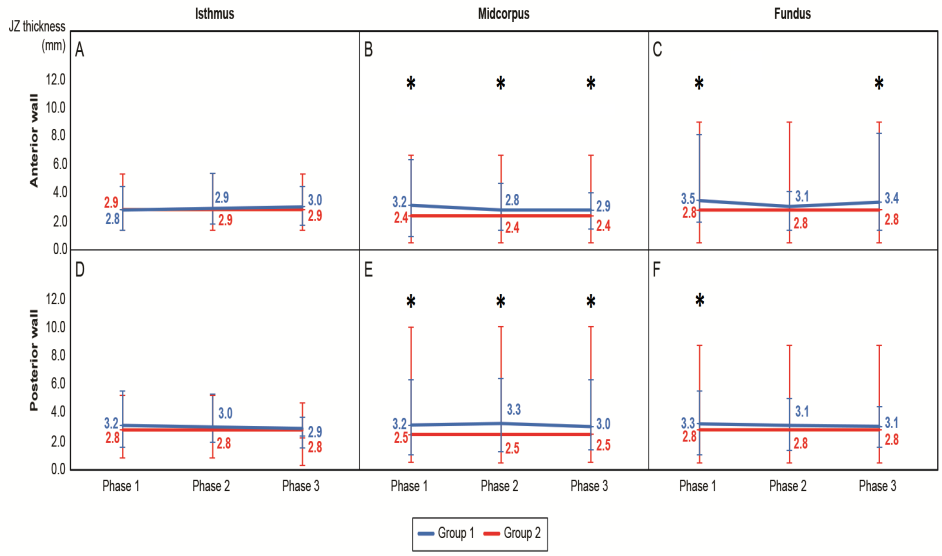

Fig. 2:
Junctional Zone (JZ) thickness of healthy nulliparous non-users and users of hormonal contraception. The minimum, maximum and mean JZ thickness measurements are represented at 6 locations in the uterine wall, in the follicular phase (phase 1), ovulatory phase (phase 2) and luteal phase (phase 3) of non-users (group 1) and users (group 2) of hormonal contraception. * : $p < 0.05$ between the non-users and users of hormonal contraception, NS: $p < 0.1$ between the non-users and users of hormonal contraception.

In non-users, no differences were observed by comparing the JZ thickness during the different menstrual phases. In this group, the JZ thickness was also not significantly different between the anterior and posterior wall, nor between the isthmus, midcorpus and fundus.
In the non-users of contraception, the thickest mean JZ (3.5 mm) was measured in the anterior uterine wall at the level of the fundus during the follicular phase.

The mean outer myometrial thickness, averaged over all measured uterine locations, was 8.1 mm, 8.0 mm and 8.5 mm respectively during the follicular, ovulatory and luteal phase in the non-users of hormonal contraception, whereas this thickness in the users of hormonal contraception equaled 8.4 mm. The thickness of the outer myometrium was not significantly different between both groups, nor between the menstrual phases in the non-users of hormonal contraception. However, the outer myometrial thickness differed depending on the location in the uterine wall. In the non-users of hormonal contraception, a significantly thicker outer myometrium was observed at the anterior and posterior wall of the midcorpus and fundus compared to the anterior and posterior wall of the isthmus ($p < 0.0001$, for all comparisons).

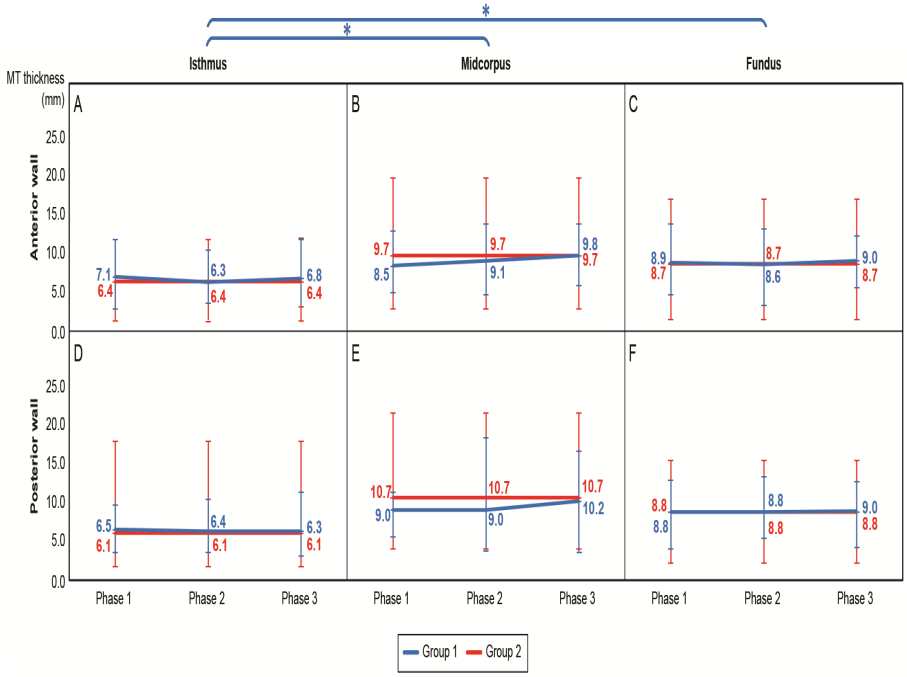

Fig. 3: **Myometrial (MT) thickness of healthy nulliparous non-users and users of hormonal contraception.** The minimum, maximum and mean MT thickness measurements are represented at 6 locations in the uterine wall, in the follicular phase (phase 1), ovulatory phase (phase 2) and luteal phase (phase 3) of non-users (group 1) and users (group 2) of hormonal contraception. * (blue): $p < 0.05$ between the locations in the uterine wall (both anterior and posterior wall) for the non-users of hormonal contraception.

The mean ratio of JZ versus total myometrial thickness averaged over all measured sites in the uterus was 29% during the follicular and ovulatory phase and 28% during the luteal phase of the non-users of contraception, whereas this mean ratio numbered 26% in the contraception using group. Similarly as with the JZ thickness, by comparing both groups, the effect of the menstrual phase of the non-users of hormonal contraception on the ratio varies according to the location in the uterine wall and vice versa. The ratio of JZ to total myometrial thickness was significantly lower in the users of hormonal contraception compared to the non-users of hormonal contraception at the anterior midcorpus during the follicular phase ($p = 0.0136$) and at the posterior midcorpus during the follicular ($p = 0.0052$), ovulatory ($p = 0.0032$) and luteal phase ($p = 0.0322$). A trend towards a lower ratio was observed in the users of hormonal contraception in comparison to the non-users at the anterior midcorpus during the ovulatory ($p = 0.0568$) and luteal ($p = 0.0996$) phase, at the anterior fundus during the follicular ($p = 0.0517$) and ovulatory ($p = 0.0900$) phase and at the posterior fundus during the follicular phase ($p = 0.0856$).

This ratio was not significantly affected by the menstrual phase in the non-users of hormonal contraception.

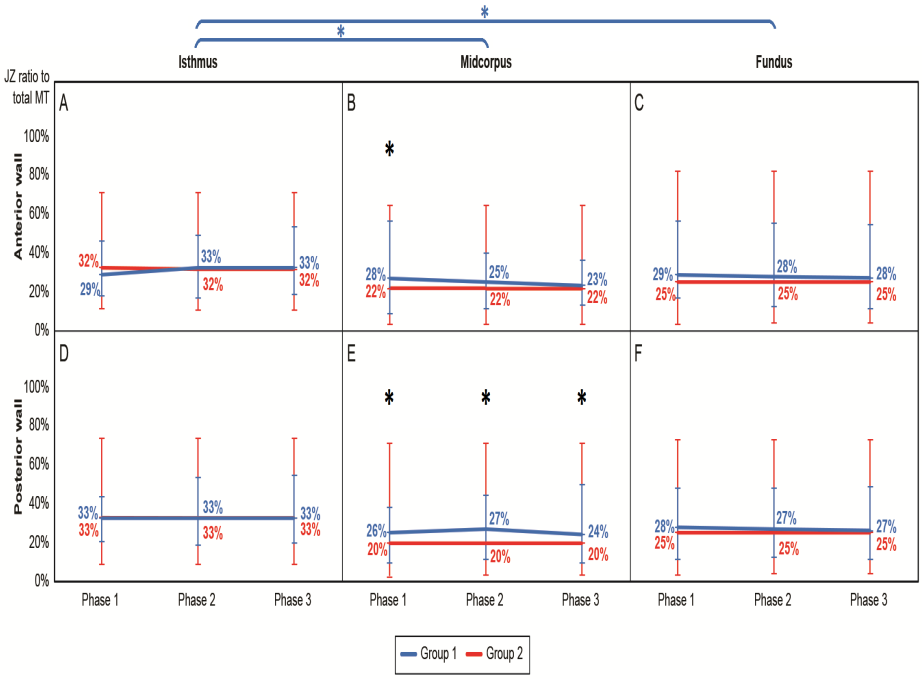

Fig. 4: **The ratio of junctional zone thickness versus total myometrial thickness of healthy nulliparous non-users and users of hormonal contraception.** The minimum, maximum and mean ratios are represented at 6 locations in the uterine wall, in the follicular phase (phase 1), ovulatory phase (phase 2) and luteal phase (phase 3) of non-users (group 1) and users (group 2) of hormonal contraception. * (black): $p < 0.05$ between the non-users and users of hormonal contraception, NS: $p < 0.1$ between the non-users and users of hormonal contraception, * (blue): $p < 0.05$ between the locations in the uterine wall (both anterior and postior wall) for the non-users of hormonal contraception.

Furthermore, the ratio of JZ versus total myometrial thickness was dependent upon the site in the uterine wall where the thicknesses were measured. This ratio in the non-users of contraception at the anterior and posterior wall of the isthmus was significantly higher compared to the anterior and posterior wall of the midcorpus ($p = 0.0004$ and $p = 0.0011$, respectively for the anterior isthmus and $p < 0.0001$ and $p < 0.0001$ for the posterior isthmus) and the anterior and posterior wall of the fundus ($p = 0.0454$ and $p = 0.0210$, respectively for the anterior isthmus and $p = 0.0051$ and $p = 0.0021$, respectively for the posterior isthmus).

1.4 Discussion

In order to be able to diagnose JZ adenomyosis or to assess JZ thickness in infertility workup, one must know the normal values of the JZ thickness. As mentioned above, it is clear that age, the use of hormonal contraceptives, the exact location of the measurement in the uterine wall and the medical history of the women are all features which need to be considered in evaluating the thickness of the JZ (Devlieger et al., 2003; Garavaglia et al., 2015; Hauth et al., 2007; Noe et al., 1999). This study was designed and performed in order to determine the best menstrual phase and uterine wall location to measure the thickest JZ on MRI examinations. We prospectively investigated the JZ thickness, outer myometrial thickness and the ratio of JZ versus total myometrial thickness in 47 healthy nulliparous women between the age of 19 and 35 years on T_2 images acquired on a 1.5T MRI (a total of 133 MRI examinations). These women were subdivided based on the hormonal contraception status. To our knowledge, this study is the first in literature to perform MRI

examinations during three menstrual phases in the same woman in a group of women between the age of 19 and 35 years.

1.4.1 Normal JZ thickness and ratio as a function of the menstrual cycle and uterine location

Our results revealed in non-users that the menstrual phase nor the uterine wall location affected the JZ thickness significantly. However, the outer myometrial thickness and the ratio of JZ versus total myometrial thickness were dependent on the location in the uterine wall, and not on the menstrual phase. This thickness and ratio were significantly lower at the midcorpus and fundus in both the anterior and posterior wall. The thickest mean JZ was measured at the anterior fundal wall during the follicular phase. The mean thickness in this phase and location equaled 3.5 mm, with a ratio of 29% to the total myometrial thickness. During the evaluation of the MR images, we noticed empirically that the JZ thickness measurements at the anterior wall of the fundus and midcorpus has the benefit of minimal bowel movement artefacts. Another advantage of the fundal site is its direct relation to fertility, namely the integral part in embryo implantation.

Our findings concerning the JZ thicknesses are consistent with previous studies which assume the normal JZ to be 5-8 mm in thickness (Hauth et al., 2007; Kunz et al., 2000a; Novellas et al., 2011). The group of Hauth et al. (2007) evaluated the normal thickness of different uterine wall layers (endometrium, JZ and outer myometrium) in 100 women (47 women with and 53 women without adenomyosis and/or myomas with age between 20 and 80 years) as a function of age and menstrual cycle phase. They noticed an increase in JZ thickness until the age of 41-50 years, followed by a decrease in thickness. The mean JZ thickness in a similar group as this study of 16 healthy women without adenomyosis and myomas between the age of 20 and 30 years was 5 mm and a mean thickness of the myometrium was 10 mm. They did also not observe a significant difference in the JZ thickness between the women who were in the follicular and those who were in the luteal phase. Different to our study was that they used MR images with 8 mm slice thickness (4 mm was used in our study) and they did not compare the JZ thickness within the menstrual cycle of each women.

The JZ thickness and the ratio in the non-users of hormonal contraception did not differ significantly between the three menstrual phases. This is consistent with previous studies, where also no significant changes in JZ thickness between the follicular phase and luteal phase have been reported (Hauth et al, 2007; McCarthy et al, 1986).

1.4.2 Normal JZ thickness and ratio as a function of the use hormonal contraception

The users of contraception revealed a statistically significant thinner JZ than the non-users at both the anterior and posterior wall of the midcorpus and fundus. Furthermore, in the non-users, the ratio of JZ to total myometrial thickness was significantly higher at the anterior and posterior wall of the midcorpus and fundus compared to the anterior and posterior wall of the isthmus. The use of

hormonal contraception significantly lowered this ratio at the midcorpus in both the anterior and posterior wall and at the fundus in the anterior wall. The significant lower ratio in the hormonal contraception users can be explained by the significantly thinner JZ measured at these locations in those women.

Our findings are in line with previous results including those by McCarthy et al. (1986) and Kido et al. (2005). McCarthy et al. also indicated that the JZ thickness was significantly smaller in the pill-using group (9 subjects) than in the non-pill-using group (12 subjects) ($p < 0.005$). Kido et al. reported a significantly thinner JZ in the posterior uterine wall in women who use oral contraceptives (23 women) in comparison to women who did not use oral contraceptives (15 women) at mid-cycle (day 11-15 in the non-users of oral contraceptives and day 11-13 in the users of oral contraceptives). He and his colleagues also observed a markedly suppressed uterine peristalsis in oral contraceptives users which could contribute to the prevention of conception by disturbing the upward sperm transport. This finding of a thinner JZ in the users of hormonal contraception suggests that the thickness of the JZ at the midcorpus and fundus can be involved in the prevention of conception.
Our findings concerning the JZ ratio to total myometrial thickness were in concordance with the findings of Kido et al. (2005), who also found a significantly lower ratio of JZ thickness versus myometrium thickness in the oral contraceptive users than in the non-users of oral contraceptives in both the anterior and posterior uterine wall.

1.4.3 The normal limits of JZ thickness in healthy women

In literature, disagreement exists in defining a clear threshold for the maximum JZ thickness in order to declare it within normal limits. Previous research revealed that JZ adenomyosis can be diagnosed by MRI when a JZ thickness of 12 mm or higher is measured, whereas a JZ thickness of lower than 8 mm excludes adenomyosis (Kang et al., 1996; Kissler et al., 2008; Novellas et al., 2011, Reinhold et al. 1996). When the measured thickness is within 8-12 mm, the diagnosis of adenomyosis requires specific secondary criteria such as relative thickening of the JZ in a localized area, poor definition of the borders of the JZ or high signal intensity foci (Reinhold et al., 1998, 1999). However, according to Bazot et al., the threshold of 12 mm carries a sensitivity of only 63% (2001). Kunz et al. (2005) investigated the impact of adenomyosis associated with endometriosis on fertility and determined a maximal diameter of 10 mm in a healthy control group (age between 21-46 years) as a cut-off value beyond which adenomyosis was assumed. He and his colleagues showed a statistically significant difference in the posterior wall JZ thickness between healthy women and women with known endometriosis (as there is evidence of high association between adenomyosis and endometriosis).
Our study, performed in 47 young healthy women between 19 and 35 years old, measured a maximum JZ thickness of 10.1 mm in a total of 133 MRI examinations across different menstrual phases and contraception and non-contraception users.

Reinhold et al. (1996) and Bazot et al. (2001) introduced the JZ to total myometrial thickness ratio, measured at the same place in the uterine wall. This ratio gives additional information about the JZ thickness, more specifically about the relationship between JZ and the total myometrial zone. The ratio of these two parameters can also be considered in the diagnosis of adenomyosis, as a ratio

higher than 40% is one of the specific MRI criteria for diagnosing the condition. Reinhold et al. found a significant difference in this ratio between patients with adenomyosis (69%) and a control group (44%) (Reinhold et al, 1996). Bazot et al. concluded that a ratio higher than 40% allows a diagnosis of adenomyosis with a sensitivity of 65% and a specificity of 92% (Bazot et al, 2001). The results obtained for the ratio in this study also fit this criteria. A maximum ratio of 33% was observed, which is clearly below the defined threshold of 40%.

The limitation of our study is the low number of participating nulliparous non-users of hormonal contraception. Despites the low number of subjects, these findings are useful to contribute to uniform future measurements of the JZ thickness.

1.5 Conclusion

To conclude, the present MRI study in nulliparous women demonstrated that JZ thickness is statistically significant affected by the use of hormonal contraception, not by the uterine wall location or the menstrual phase. A statistically significant thinner JZ was observed in users of contraception in comparison to non-users at the anterior and posterior uterine wall at the level of the fundus and midcorpus. However, in contrast to the junctional zone thickness, the outer myometrial thickness varied according to the location in the uterine wall. A thicker outer myometrium was noticed at the level of the fundus and midcorpus. These differences observed in thickness of the JZ and the outer myometrium were reflected in the ratio of JZ versus total myometrial thickness, as it demonstrated differences between both groups and between uterine wall locations. We do recommend to perform the measurements of JZ thickness at the level of the midcorpus and fundus.

1.6 References

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