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ARTICLE

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

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Abstract This prospective study aims to determine the optimal menstrual phase and uterine location to detect the thickest junctional zone by magnetic resonance imaging (MRI). Healthy nulliparous women were 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 junctional zone thickness was measured at six locations in the uterine wall. A significantly thinner junctional zone was observed at the anterior and posterior wall of the midcorpus ($P = 0.01$ and $P = 0.004$ respectively) and fundus ($P = 0.009$ and $P = 0.023$ respectively), in the contraception users compared with the non-users. No differences in junctional zone thickness were noticed between the menstrual phases and the uterine wall locations. The ratio of junctional zone versus total myometrial thickness was also different 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: fertility, junctional zone, MRI, thickness, uterus

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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, 2000b; Lyons et al., 1991; Wildt et al., 1998). This function is dependent on the architecture of the myometrial wall, more particularly the junctional zone, also called archimyometrium or stratum subvasculare. This layer is characterized by predominantly circular arrangement of muscle fibres 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., 2006; Leyendecker, 2000; Leyendecker et al., 1998; Noe et al., 1999; Werth and Grusdew, 1989; Wetzstein, 1965).

During a woman's reproductive period, three distinct layers can be recognized in the uterine wall: the endometrium, the junctional zone and the outer myometrium. This uterine zonal anatomy was first identified in 1983 by means of magnetic resonance imaging (MRI) (Hricak, 1994). On T_2-weighted magnetic resonance images, the endometrium is presented as a high signal-intensity zone, the junctional zone as a low signal-intensity zone and the outer myometrium as a medium signal-intensity zone (Hricak, 1994; McCarthy et al., 1986, 1989; Scoutt et al., 1991). The junctional zone 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 oestrogen and progesterone receptor expression in junctional zone myocytes, which mimic those observed in the endometrium, whereas no cyclic changes are detectable in the outer myometrial smooth muscle cells (Hauth et al., 2007; Noe et al., 1999).

Adenomyosis is a gynaecological disorder of the myometrium, characterized by a benign invasion of basal endometrial glands and stroma surrounded by the hypertrophic and hyperplasic myometrium into the junctional zone and outer myometrium. It is most likely found in the fourth and fifth decade and after childbearing. With most women now delaying childbearing, however, adenomyosis has come to be diagnosed more frequently in fertility clinics (Kishi et al., 2014; Vercellini et al., 2014). Growing evidence links a thickened junctional zone in adenomyosis, as seen on a pelvic MRI scan, to primary and secondary infertility in young adults (Barrier et al., 2004; de Souza et al., 1995; Devlieger et al., 2003; Garavaglia et al., 2015).

A possible beneficial effect of adenomyomectomy on patients who experience IVF failures, especially at ages younger than 39 years, is suggested by Kishi et al. (2014). Around 60% of women aged younger than 39 years succeeded in postoperative IVF treatments. They also considered a posterior wall involvement of adenomyosis negatively affected the process of embryo implantation. The dominant implantation site for human embryos has until recently never been evaluated. Previous research has only focused on sites of human embryo implantation dominantly around the fundus area (Kishi et al., 2014).

Benaglia et al. (2014), however, suggest that patients can be reassured that asymptomatic adenomyosis does not impair the rate of success of IVF. Together with other investigators, they suggest that the possible harmful effects of adenomyosis may not be limited to the implantation of the embryo, and also claim a role for abnormal utero-tubal sperm transport. Inner myometrium adenomyosis is expressed by abnormal thickening and disruption of the junctional zone, which is considered the magnetic resonance imaging criterion for diagnosing this condition, although myometrial hyperplasia as a normal variant could not be excluded (Novellas et al., 2011; Reinhold et al., 1998, 1999). The diagnosis of junctional zone adenomyosis on the basis of magnetic resonance images remains difficult because of the difficulty in determining a strict cut-off value for junctional zone thickness from which adenomyosis is assumed. First, it is of importance to define normal limits of the junctional zone thickness in healthy women.

The purpose of this study was to define optimal menstrual cycle phase and uterine wall location so that normal junctional zone thickness could be measured. This optimal menstrual phase and uterine wall location is defined by the menstrual phase and location where the thickest can be measured. To determine this, we investigated whether changes in junctional zone thickness, outer myometrial thickness and the ratio of junctional zone to the total myometrial thickness were cyclic or dependent on location, 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 was investigated three times during a menstrual cycle.

Materials and methods

Health insurance, study protocol and informed consent for this longitudinal study of volunteers were approved by the Ethical Committee of Ziekenhuis Oost-Limburg (registration number 056) (07/061) on 20 November 2007.

Study population

In this single-centre, prospective study, 47 voluntary nulliparous white women were recruited between 21 December 2007 and 12 January 2012. The women were divided into 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 participants were aged between 19 and 35 years (mean age for group 1 and 2 are 26.4 and 25.8 years, respectively). Inclusion criteria were white, nulliparous women aged between 18 and 35 years old with no medical history of infertility and no gynaecological history (no bleeding disorders or 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 to coworkers in our hospital, students and PhD students at the University of Hasselt (local university), personal contacts and cooperation with external physicians. All volunteers provided

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