

The Effect of High-Intensity Focused Ultrasound for the Treatment of Uterine Fibroids

Review

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Abstract – High-intensity focused ultrasound (HIFU) is increasingly used for the treatment of uterine leiomyomata. However, the efficacy of HIFU therapy targeting the blood vessels of uterine leiomyomata remains to be studied in detail. This study aims to evaluate the efficacy of fibroid devascularization by ultrasound-guided HIFU (USgHIFU) and the effect of treatment on ovarian reserve and endometrial damage.

Keywords – High-Focus Ultrasound Guided, Uterine Leiomyoma, Devascularization.

I. Introduction

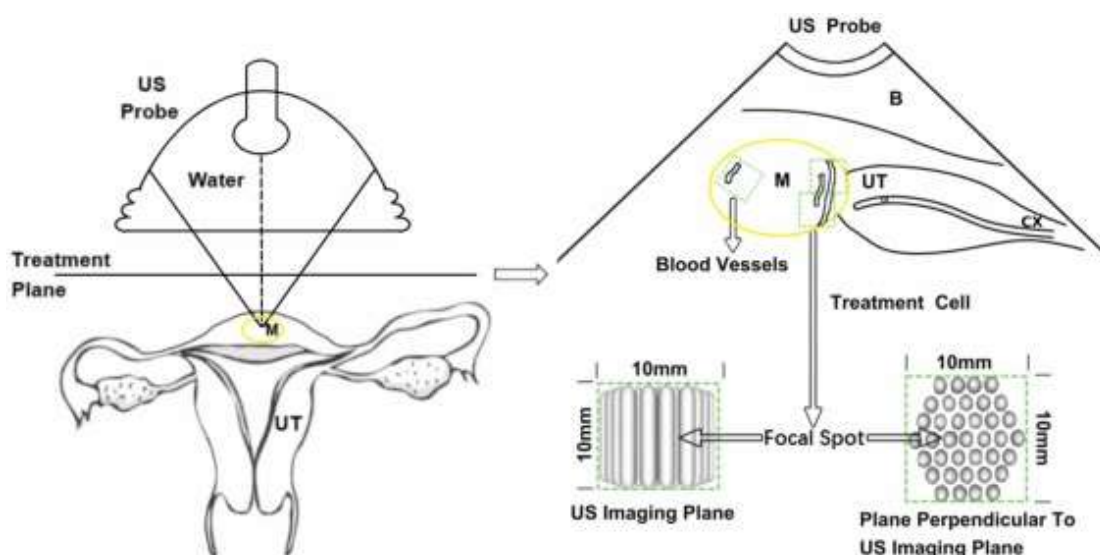
Uterine fibroids are the most common gynecological disease among women of childbearing age and affect up to 70% of women worldwide [1]. Although benign, approximately 30% of uterine fibroids can cause serious symptoms, such as menorrhagia, pelvic pain, frequent urination, miscarriage, or infertility [2, 3]. Evidence shows that women with uterine fibroids are at increased risk of emotional distress, depression, and anxiety, which can affect their health and quality of life [4]. The most common treatment options for symptomatic uterine fibroids include medical management (hormonal drugs and progesterone receptor modulators), surgical procedures to remove uterine fibroids (myomectomy and hysterectomy), and non-surgical treatments (uterine artery embolization and high-frequency focused ultrasound [HIFU] [5]. Obviously, before starting a non-surgical treatment, it is necessary to make a differential diagnosis with uterine sarcoma, an aggressive, rare and poor-prognosis uterine neoplasm. The gold standard surgery for uterine sarcoma typically includes hysterectomy and bilateral salpingo-oophorectomy, and fertility preservation procedures are only suitable for well-selected patients with a strong desire to preserve their fertility [6]. The American College of Obstetricians and Gynecologists recommends that, with the most minimally invasive approach treatment for uterine fibroids [7]. HIFU is a non-invasive treatment procedure performed under diagnostic ultrasound or MRI guidance that uses multiple high-energy ultrasound waves to stimulate focal thermocoagulation and eliminate vascular fibroids. This method has been used for many years in the last decades and has achieved good clinical results in the treatment of uterine fibroids [8,9,10]. Furthermore, studies have shown that HIFU treatment is associated with shorter hospital stays, fewer side effects and fewer complications compared to traditional surgery [11, 12]. However, data on whether HIFU affects healthy women in terms of quality of life or causes short- or long-term ovarian dysfunction are still limited. Anti-Müllerian hormone (AMH), a hormone produced by small, developing primary antral follicles, does not affect changes in the menstrual cycle. Compared with follicle-stimulating hormone (FSH) or inhibin B, AMH is considered a good indicator of ovarian reserve [13,14,15]. Therefore, this study was conducted to evaluate the changes in ovarian function and quality of life of women after USgHIFU treatment for uterine fibroids.

1. Pre-procedure preparation and evaluation

Colon preparation is done with nutritional supplements 3 days before the scheduled procedure. The skin under the abdomen is scraped in the tract and damaged to prevent burns. HIFU treatment was performed using a system (SUA-I, Shanghai Zhonghui Medical Equipment) and an ultrasound imaging device as a guide. Preimplantation evaluations included conventional ultrasound, non-contrast T1 and T2 images, and contrast-enhanced T1 images. MRI images were obtained in the axial and sagittal planes with a 5 mm slice and a 1 mm spacing with a 1.5 T MRI scanner. The volume of fibroids on T1-weighted contrast images is calculated according to the ellipsoid calculation method: $V = 0.523 \times D1 \times D2 \times D3$, where V is the volume of fibroids and D1, D2 and D3 are the diameters of fibroids in the longitudinal, anteroposterior and axial plane, respectively [16]. Preoperative information, including the patient's age, height, weight, location, type, size, and blood supply of the fibroid, were recorded.

2. Ultrasound examination

A transabdominal ultrasound was performed to determine four imaging planes for Adler's level, uterine diameter, and fibroid diameter. Two of them are used to measure the three upper dimensions of the fibroid (longitudinal and anteroposterior diameter in the sagittal plane, transverse diameter in the transverse plane).



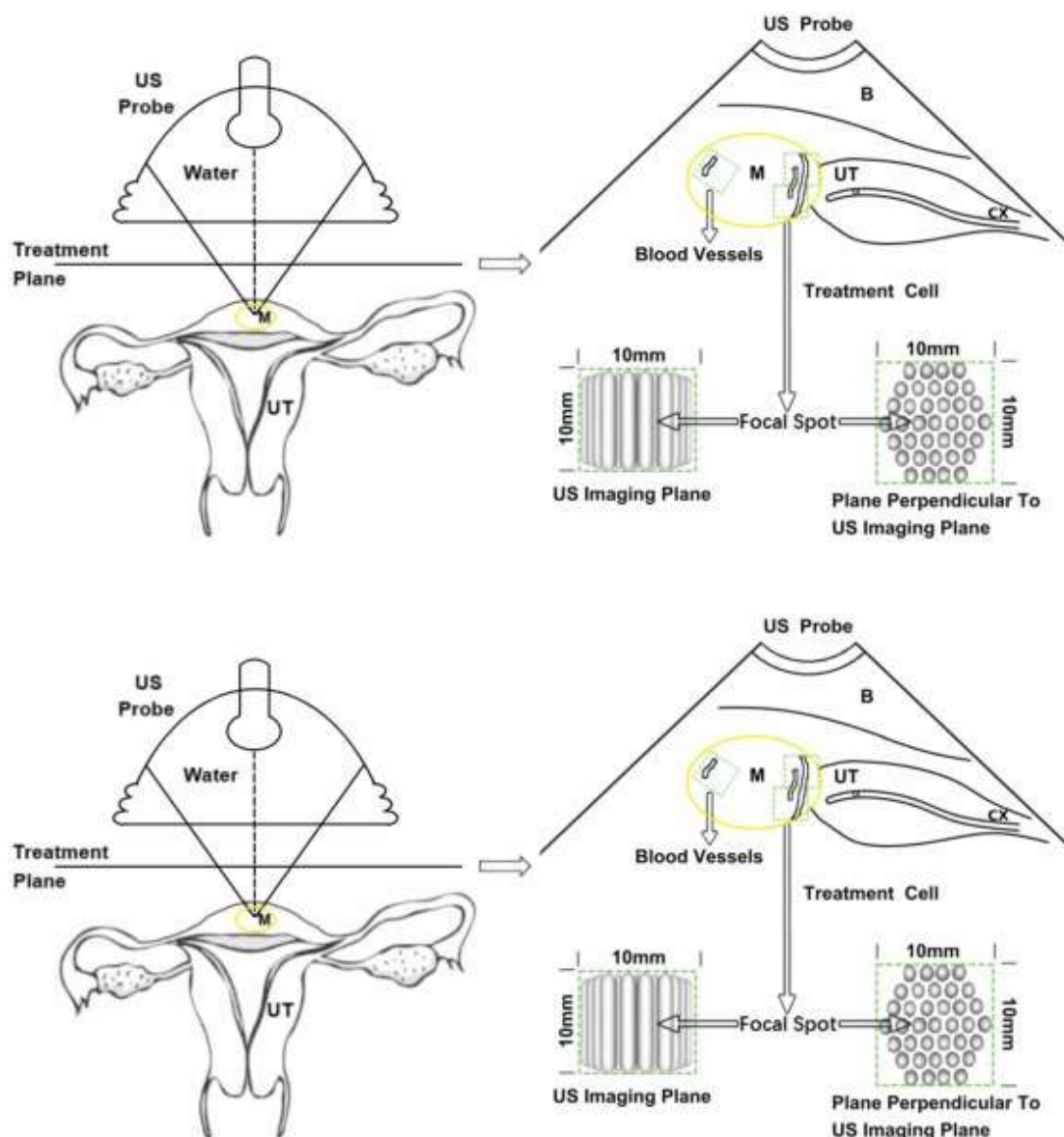


Figure 1 The procedure of fibroid devascularization. The main branch and its relative position of the fibroid are shown. The focal spots distributed in the treatment cell (1 cm × 1 cm × 1 cm) are projected in two orthogonal planes. The yellow ellipsoid denotes the fibroid envelope and the green box denotes the treatment cell. B, bladder; CX, cervix; M, myoma; US, ultrasound; UT, uterine.

3. MRI Evaluation

Pelvic MRI scans using T1-weighted (T1W), T2-weighted (T2W), and evaluation-enhanced T1W (CE-T1W) sequences were performed before and at 1, and 6 months after treatment. MRI sequences were scanned in the sagittal and axial planes. Fibroid diameters and non-perfused volume (NPV) were measured using T2W and CE-T1W photographs, respectively. NPV is the ratio of NPV to VF. The FV shrinkage rate (FVSR), (OVSR) was calculated as (FV 1 post-treatment/FV pre-treatment).

4. Ovarian reserve and endometrial damage

10 ml blood samples were obtained for anti-Müllerian hormone (AMH) testing before and 6 months after HIFU treatment. The change in AMH level after treatment can be measured to assess the effect of fibroid devascularization on ovarian reserve. Contrast-enhanced MRI is performed as a standard medical protocol for assessing the integrity of the endometrial lining. Failure to assess the endometrium in any direction or to any extent on MRI was considered endometrial damage. Endometrial deterioration was graded as 0 (generally involved endometrium), 1 (pin factor, full-thickness discontinuity of involved endometrium), 2 (between grades 1 and 3), or 3 (full-thickness discontinuity of involved endometrium > 1 cm in length) (18,19). Follow-up To evaluate efficacy and protection, NPVR and FVSR were calculated at 1 and 6 months based on MRI images. Pain scale, uterine fibroid symptoms, and first-class life questionnaire (u.s.QOL) were used (20). Negative outcomes and headaches were recorded. Regarding long-term effects, investigations were conducted with US QOL and Symptom Severity Score (SSS), fertility outcomes, and presence of re-intervention treatments. Patients were required to undergo ultrasound evaluation of treated uterine fibroids 1, 2, and 3 years after treatment. The u.s.QOL questionnaire is a tested questionnaire designed to assess the effect of uterine fibroid signs on women's health-related quality of life [20, 21]. It assesses the physical, social and emotional effects in patients with uterine fibroids, including symptoms such as pelvic pain, bleeding and urinary problems, as well as the effect on daily activities, emotional well-being and sexuality. The USQOL questionnaire consists of 31 questions that patients must complete before and 1 and 6 months after USgHIFU treatment. Each item is assigned a raw score of 1 ~ 5 points, representing moderate to high signs and symptoms, and the final score is obtained by adding the raw scores of the related items [22].

As women age, the quantity and quality of primordial follicles decreases and the ovarian reserve decreases. AMH is a member of the beta-reducing protein family. It is produced in the granulosa cells of ovarian follicles and its expression increases as the follicles develop from the number one stage to the small antral stage [26]. AMH levels are not affected by the menstrual cycle and more accurately reflect ovarian reserve than follicle-stimulating hormone levels and antral follicle content. It is an excellent indicator of the number of small antral follicles present in the ovaries, which is directly related to ovarian reserve [23, 24]. A current meta-analysis of 6 studies and 353 participants found no impact on ovarian reserve, as measured by AMH and FSH levels at 365 days after the procedure [25]. The limited number of available studies makes it difficult to draw firm conclusions on ovarian reserve with uterine artery embolization [26]. During HIFU treatment, high-depth ultrasound waves are directed to the ideal site of the fibroid, causing the fibroid vasculature to be ablated. This may be an advantage of HIFU over uterine artery embolization since it no longer interferes with ovarian perfusion aided by blockage of the uterine arteries. It is known that AMH levels decline with age. The results found that there were no changes in AMH levels regardless of age (less than 40 years, 40 to 45 years, or 45 years or older). Larger fibroids may require a higher overall treatment energy and longer treatment times, and ovarian function after HIFU may be related to the location of the fibroids. However, studies found that HIFU treatment had no effect on AMH levels regardless of the location, type, or duration of treatment of the fibroid, type or timing of the remedy.

The current studies have several implications for medical practice and future studies. First, confirmed that USgHIFU is safe and effective in improving quality of life. Second, confirmed that USgHIFU treatment did not have a generalized effect on ovarian reserve. This is particularly reassuring for patients receiving counselling, especially young women concerned about future pregnancies. At some point, based on current results, future research may focus on directly assessing whether USgHIFU treatment has a negative effect on maternal and neonatal outcomes. Compared to previous studies on comparable topics [27], the strength of current studies lies in the sequential magnitude of AMH at various time points after USgHIFU, providing a more nuanced understanding of AMH changes. Although this prospective study could also effectively demonstrate the efficacy and safety of USgHIFU in the treatment of uterine fibroids, several obstacles to this research exist. The main difficulty of these studies is the small sample size. In addition, the follow-up duration was only six months. Large, multicenter, randomized, controlled trials with other biomarkers of ovarian reserve, such as serum follicle-stimulating hormone and estradiol, are planned for the future. Importantly, USgHIFU does not affect ovarian function; therefore, further studies are needed to fully understand the impact of USgHIFU treatment on pregnancy outcomes. Ultimately, evaluating ultrasound with different fibroid treatment modalities, including uterine artery embolization, may provide more information on the effect of ovarian reserve.

II. Conclusion

Ultrasound is an effective and non-invasive system for the treatment of uterine fibroids. For patients with uterine fibroids, ultrasound-induced devascularization HIFU is a safe and effective treatment option. It has little effect on ovarian function and endometrial damage is reversible, which may be of interest to patients planning pregnancy. It has been shown to improve quality of life and has no harmful effects on ovarian reserve in the short or long term.

Conflict of Interest

All authors declare no conflicts of interest.

Author Contribution

Authors have equally participated and shared every item of the work.

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