European Journal of Obstetrics & Gynecology and Reproductive Biology 146 (2009) 92–95

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Decreasing margins to the uterine serosa as a method for increasing the volume of fibroids ablated with magnetic resonance-guided focused ultrasound surgery

Yutaka Morita [a,*], Sawako Takeuchi [a], Hiromi Hikida [a], Hirofumi Ohashi [a], Naoki Ito [b]

[a] Department of Obstetrics and Gynecology, Itabashi Chuo Medical Center, 2-12-7 Azusawa, Itabashi City, Tokyo, 174-0051, Japan
[b] Department of Radiology, Itabashi Chuo Medical Center, 2-12-7 Azusawa, Itabashi City, Tokyo, 174-0051, Japan

ARTICLE INFO

Article history:
Received 13 January 2009
Received in revised form 18 March 2009
Accepted 1 May 2009

Keywords:
Uterine fibroids
MRgFUS
Serosa
Sonication

ABSTRACT

Objective: To demonstrate the safety of magnetic resonance-guided focused ultrasound surgery (MRgFUS) treatments regardless of the distance between the treatment region and the uterine serosa.
Study design: 83 pre-menopausal women with symptomatic uterine fibroids were treated with MRgFUS in 88 treatments. Treatment data was analyzed, measuring the distance between the treatment spots (sonications) and the serosa. Patients were followed up for 1 year and adverse events were collected.
Results: 79% and 37% of the sonications were less than 15 mm and 10 mm from the serosa, respectively. Treatment was always confined to the fibroid capsule. There were no unexpected or serious adverse events.
Conclusion: Reducing the margin between the fibroid treatment area and the uterine serosa, when possible, enables MRgFUS treatment of greater fibroid volume, while maintaining a high safety profile. Special attention should be paid when the uterus lies adjacent to other sensitive organs to avoid unintentional heating of these organs, using the planning and real-time MR images.

1. Introduction

Uterine fibroids are common benign neoplasms found in women of childbearing age and are symptomatic in 25% of women [1,2]. Symptoms include pelvic pain, excessive and/or irregular menstrual bleeding, pain during intercourse, feelings of pelvic fullness, urinary frequency and infertility [3,4].

Magnetic resonance-guided focused ultrasound surgery (MRgFUS) is a relatively new non-invasive approach for treating symptomatic uterine fibroids. The procedure is performed on an outpatient basis under conscious sedation, and patients typically return to a normal daily routine within 1 to 2 days post-procedure. This treatment modality has been shown to reduce symptoms and improve patient quality of life [5–11], and is associated with a low rate of complications. [5,7].

Several studies have shown that high treatment volumes (expressed as the non-perfused volume of the fibroid after treatment) correlate with long-term symptoms relief and fibroid volume reduction [9,11]. Due to safety concerns, early clinical studies implemented several safety measures to reduce the likelihood of adverse events, especially those related to unintentional heating outside the fibroid capsule. These included margins between the planned treatment area and the surrounding structures: of 15 mm from the endometrium, 5 mm from the fibroid capsule, and 15 mm from the uterine serosa. With experience and the growing confidence in the MRgFUS treatment, the margins from the fibroid capsule and from the endometrium were deemed unnecessary [11]. The margin limitation from the serosa, however, was still maintained. Since the external layer of a fibroid can account for up to half of its volume, maintaining a 15 mm margin from the serosa can substantially reduce the treated fibroid volume, thus reducing the clinical improvement. For example, an untreated 15 mm margin in a fibroid measuring 100 mm in diameter leaves more than 40% of the entire fibroid volume untreated. Thus treating as close to the serosa as possible should lead to greater treatment volumes and better results, assuming that safety can be maintained.

We previously reported on our initial experience, at Itabashi Chuo Medical Center in Tokyo, where MRgFUS was added to our uterine fibroid treatment armamentarium [8]. Given the relatively high treatment volumes, we hypothesized that some of the success was due to decreasing the margin to the serosa. In this study, we retrospectively examined the distance between the location of treatment sonications and the uterine serosa.

2. Matherials and methods

2.1. Patient enrolment

A total of 83 pre-menopausal patients with symptomatic uterine fibroids were treated with MRgFUS at our institution

* Corresponding author. Tel.: +81 3 3967 1181x9108; fax: +81 3 3967 0572.
E-mail address: moririn@yf6.so-net.ne.jp (Y. Morita).

0301-2115/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ejogrb.2009.05.004

between January 2005 and March 2006. Patients were followed for 12 months post-procedure in order to assess outcomes. All patients were diagnosed with uterine fibroids by clinical examination and ultrasound imaging, and all were seeking treatment for their fibroids. Exclusion criteria included the presence of other pelvic or systemic disease, presence of scar or excessive bowel in the potential beam path, and an inability to communicate with the operator during MRgFUS treatment. Additional screening criteria were as previously described for this indication [7]. Having understood the limitations of the early studies, our local institutional review board approved MRgFUS for the treatment of uterine fibroids in this patient population, without specifying the safety margins from the various organs – leaving it to the discretion of the treating physician. All patients provided written informed consent prior to undergoing the procedure.

2.2. Treatment procedure

All treatments were performed using the ExAblate 2000 System (InSightec, Haifa, Israel). The system is integrated with a 1.5-T MRI scanner (GE Medical Systems, Milwaukee, WI) and provides real-time thermometry during treatment [3,5]. Each patient was positioned prone on the treatment table with her abdomen resting on a gel pad located directly above the transducer. Prior to treatment, hair was shaved from the umbilicus to the pubis to ensure acoustic coupling. Conscious sedation (diazepam 5 mg PO, pentazocaine 15 mg IV and hydroxyzine hydrochloride 25 mg IV) was administered before treatment in order to relieve anxiety, minimize discomfort and reduce movement. With this light sedation, patients retain the ability to communicate with the operator during the procedure. In the event of pain or discomfort, patients are able to immediately halt the treatment by pushing a stop button.

Prior to treatment, T2 weighted MR images were acquired in order to identify and measure the target lesion(s) and to evaluate the pelvic anatomy around the targeted area(s). The treating physician planned the treatment by drawing contours around the targeted fibroids (those most likely to cause symptoms). The system then automatically calculated the energy, location, and number of sonications needed to cover the drawn area(s) and generated a treatment plan.

During the treatment, a series of sonications were delivered until the pre-defined treatment volume was ablated. Before each sonication the treating physician examined the spot location and the beam path, to avoid passing through sensitive tissues. When needed, the operator optimized the spot location or angle of the sonication. During each sonication, real-time temperature maps and magnitude (anatomical) images were carefully examined to identify any patient or organ movement. In such cases, the operator immediately stopped the sonication and evaluated the extent of the movement. At the end of the treatment upon completion of all sonications, T1 weighted contrast-enhanced images were acquired in order to determine the non-enhanced volume of the treated area.

2.3. Data analysis and statistics

Treatment data and images were analyzed to calculate the distance between the edge of the sonication overlay and the uterine serosa. The sonication spot overlay was extracted from the treatment data, and its size and location corresponded to the predicted volume of the thermal ablation (the size automatically changed when the sonication parameters were changed). This analysis was conducted using Matlab software (Mathworks, Massachusetts, USA). The algorithm determines the shortest distance between the serosal lining (retrospectively drawn on the planning images) and the sonication edge. Fig. 1 shows an example of the measurement method. A statistical analysis of the results was conducted using Excel software (Microsoft, Redmond, WA) and was used to calculate mean values and standard deviation.

2.4. Adverse events

Adverse events were collected during the treatment and in the follow up periods of 1 month, 6 months and 12 months. Post-treatment MR images were reviewed for unexpected findings outside the uterus.

3. Results

3.1. Demographics

A total of 88 treatments were performed on 83 patients (five patients required two treatments in order to treat the total planned volume). All patients were pre-menopausal, mean age 43 ± 5 years [range 24–51 years], mean body mass index 21 ± 3 [range 17–35] and had a mean total number of fibroids 1.6 ± 1 [range 1–5]. Average pre-treatment total fibroid volume for the 83 patients was 321 ± 171 cc [range 18–720 cc]. The mean diameter of the treated fibroids was 7.7 ± 1.9 cm [range 3.3–11.5 cm].

3.2. Treatment results and margin analysis

The average number of sonications in the 88 treatments was 94 ± 33 [range 32–172]. A total of 8,231 sonications were examined. The distribution of the minimal distance of the sonications and the serosa is shown in Fig. 2. 79% of the sonications were less than 15 mm from the serosa and 37% of the sonications were less than 10 mm from the serosa. The median spot distance to the serosa was 11 mm, and the range was from 0 to 24 mm.

3.3. Adverse events

There were no unexpected or serious adverse events and the safety profile was better than those reported elsewhere [9,12,13]. Five patients reported adverse events during the 1 year follow-up period. Four patients had post-treatment skin redness, which resolved in three patients within 3 days and in one patient within 1 week, using dimethyl isopropyl azulene ointment (10 g). One patient had transitory sciatic neuralgia resulting from disc herniation at L4-L5 and L5-S1. This resulted from an underlying disease condition and was determined to be unrelated to MRgFUS. No evidence of unexpected damage outside the uterus was seen in the post-treatment MR images.

4. Comments

In earlier studies of MRgFUS for the treatment of uterine fibroids, a minimal margin of 15 mm between the sonication spot to the serosa was maintained in order to avoid unintentional heating of the serosa or organs immediately adjacent to the uterus. Recent studies demonstrated a correlation between post-treatment non-perfused volume and long-term fibroid shrinkage, relief of symptoms, and need for alternative treatments [9]. Thus, by treating close to the serosa and expanding the treatment volume, better clinical results can be expected.

On average, 79% of the sonications in this analysis were less than 15 mm from the serosa and 37% of the sonications were less than 10 mm from the serosa. In spite of the fact that a high percentage of sonications were close to the serosa, no safety issues were reported, and no cases of ablation or damage outside the