Uterine leiomyomas (fibroids) are the most common benign neoplasm in women of childbearing age. Magnetic resonance-guided focused ultrasound ablation (MRgFUS) has been used worldwide to treat symptomatic uterine fibroids over the past few years. This paper describes our experiences with three patients that were treated with MRgFUS for uterine fibroids and their follow-up status after 3 months.

Three patients with uterine fibroids underwent MRgFUS on February, 2009. Before the treatment and at 3 months post-treatment, we used the Uterine Fibroid Symptoms and Quality of Life Questionnaire (UFS-QOL) to determine symptom severity scores (SSS). We also evaluate the change in fibroid volume after 3 months using T1-weighted contrast enhanced MRI images.

No serious or unexpected adverse events arose during the study. All patients were followed up for 3 months. The fibroid volume reduction after 3 months was 30.8% in average, and SSS reduction after 3 months was 30.6%.

Our results demonstrate that MRgFUS can safely and effectively ablate uterine fibroids to produce a significant decrease in mean fibroid volume and improvement in SSS for up to 3 months post-treatment.

Uterine leiomyomas (fibroids) are the most common benign neoplasm in women of childbearing age. Fibroids have been identified clinically in at least 25% of women [1], and pathologic analysis suggests that the prevalence of fibroids may be as high as 77% [2]. Symptoms include heavy and prolonged menstrual flow, pelvic pain and pressure, pain in the legs and back, pain during sexual intercourse, frequent urination, constipation, abnormally enlarged abdomen, and infertility [3-5]. The common treatment is hysterectomy or myomectomy. However, both procedures are associated with general anesthesia, hospitalization and lengthy recovery time [6].

Many alternatives to hysterectomy and myomectomy for uterine myomas are currently available, such as laparoscopic myomectomy, hysteroscopic resection of myoma, and uterine artery embolization (UAE) [7]. In addition, there are imaging guided ablation methods that destroy the structure of myomas and spare normal tissue including laser ablation, cryoablation, radiofrequency ablation, and magnetic resonance-guided focused ultrasound ablation (MRgFUS) [8, 9].

MRgFUS has been used worldwide to treat symptomatic uterine fibroids over the past few years [10, 11]. It was approved by the U.S. Food and Drug Administration (FDA) for the treatment of uterine fibroids [12]. It is the least-invasive method for the...
treatment of uterine myomas, because the procedure does not require any incision, any puncture of the uterus, anesthesia, or radiation exposure [13]. The energy from multiple elements of the phased array transducer passes through the anterior abdominal wall and causes protein denaturation, cell death and coagulative necrosis only at the focal volume where the ultrasound waves converge [14]. Reports from the US, Europe and Japan have confirmed the safety and the effectiveness of the procedure, which is unique in the sense that only the targeted areas are affected, leaving the surrounding tissue unharmed [15, 16].

In this study, we used the Uterine Fibroid Symptoms and Quality of Life Questionnaire (UFS-QOL) [17] to determine a symptom severity score (SSS). The UFS-QOL has been utilized as the chief outcome measure after treatment with this technique and the key measure of treatment response leading to approval of this technology. This paper describes our experiences with three patients that were treated with MRgFUS for uterine fibroids and their follow-up status after 3 months.

**MATERIALS AND METHODS**

ExAblate 2000 is a non-invasive treatment for uterine fibroids approved by the U.S. Food and Drug Administration (FDA) in October 2004. The technology uses highly focused ultrasound to ablate, or destroy, fibroid tumors. The device works with an MR scanner to enable the physician to determine the level of heating and to monitor the progress of treatment during and after the procedure. The ExAblate 2000 (InSightec, Haifa, Israel) was installed in our department on January, 2009. In February, three patients with uterine fibroids underwent treatment of uterine fibroids with this therapy. We excluded women with contraindication to MRI or inability to lie prone on the treatment table for 3 hours. For safety reasons, women who had anatomical obstacles that could interfere with ultrasound beam path between the transducer and the targeted fibroids, such as scars or unavoidable bowels, were also excluded. The ethics committee approved the MRgFUS method for the treatment of uterine fibroids and signed informed consent was obtained from all three patients.

To identify and measure the target lesions and to evaluate the surrounding pelvic anatomy during treatment, the patient underwent an initial MRI scan using a 1.5-T MRI scanner (GE Medical Systems, Milwaukee, WI) with T1 weighted, T2 weighted and enhanced T1 weighted (axial, coronal and sagittal) sequences. In this pre treatment MR-scan, the exclusion criteria were fibroids that are larger than 10 cm or smaller than 3 cm; fibroids number is more than four, or fibroids located on the subserosal layer of uterus. We calculated the volume of each fibroid. The area of the fibroid slices were measured by slice with GE workstation AW4.4, then multiply the area with its thickness and sum all at last. In addition, the subjects were asked to complete the UFS-QOL before treatment. The UFS-QOL was developed by Spies et al., in 2002, to assess the symptom severity

<table>
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<tr>
<th>Table 1. Symptom severity score (SSS) questionnaire¹</th>
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<tr>
<td>During the previous 3 months, how distressed were you by…</td>
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<tr>
<td>Patient 1</td>
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<tr>
<td>baseline</td>
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<tr>
<td>1. heavy bleeding during your menstrual period</td>
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<td>2. passing blood clots during your menstrual period</td>
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<td>3. fluctuation in the duration of your menstrual period compared to your previous cycle</td>
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<td>4. fluctuation in the length of your monthly cycle compared to your previous cycles</td>
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<td>5. feeling tightness or pressure in your pelvic area</td>
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<td>6. frequent urination during the daytime hours</td>
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<td>7. frequent nighttime urination</td>
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<td>8. feeling fatigues</td>
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¹symptom severity score: 1=not at all, 2=a little bit, 3=somewhat, 4=a great deal, 5=a very great deal.
scores. The symptom severity scores use eight questions assessed on a 5-point scale (Table 1). Raw scores are transformed by using formulas and a 100-point scale:

\[
\text{Transformed score} = \frac{\text{actual raw score} - 8 \text{ (lowest possible raw score)}}{32 \text{ (possible raw score range)}} \times 100
\]

The ExAblate 2000 (InSightec, Haifa, Israel) was integrated with a 1.5-T MRI scanner. During the treatment, the treating radiologist evaluated the images and marked the treatment boundaries using the ExAblate system software, which in-turn produced a plan consisting of several focal energy deliveries (called sonications). Ultrasound energy sensitive regions such as bone, bowel and nerves were also marked to ensure safety (Fig. 1). During the treatment, patients felt nothing except warm at the treatment area. Two patients felt sour at the waist because of the prone position for 3 hours. We don’t suggest anesthesia for patients so that they might get hurt when the temperature arises at the wrong position. At the end of the MR-guided focused US ablation treatment, T1-weighted contrast enhanced images (axial, coronal, sagittal) were acquired to evaluate the results.

We evaluated the therapeutic effect by the changes in nonperfused areas using the following formulas:

\[
\text{Nonperfused volume (NPV) ratio} = \frac{\text{nonperfused volume}}{\text{fibroids volume}} \times 100.
\]

The overall treatment duration lasted for 3 to 4 hours. Afterwards, the patients were sent to a recovery room with accompanying person and may be discharged within an hour.

We followed-up the status of patients until May 2009. The same SSS questionnaire was used.

**Figure 1.** T2-weighted sagittal scan for pre-procedure planning. The sensitive regions such as bone, bowel and nerves (arrows) were marked to ensure safety of MRgFUS ablation.

**Figure 2.** Patient 1: pre-treatment T2-weighted sagittal image demonstrated a large uterine fibroid (arrow) measuring about 9.5 cm in diameter.
to calculate the scores to evaluate the improvement of symptom. In addition, T1-weighted contrast enhanced images were acquired to evaluate the status of the uterine fibroids.

**RESULTS**

The mean age of the three patients was 38.3 years (range 37 to 40 years). No serious or unexpected adverse events arose during the study. All patients were followed up for 3 months, and no procedure-related complications were recorded throughout this period.

The NPV ratio, measured change in fibroid volume and symptom severity scores before and after treatment for 3 months are shown in Table 2. The average fibroid volume reduction after 3 months was 30.8%, and symptom severity scores reduction after 3 months was 30.6%, compatible with symptomatic relief after MRgFUS treatment (Fig. 2-10). In addition, the raw SSS at baseline and 3 months for each patient were listed in table 1.
Figure 5. Patient 2: pre-treatment T2-weighted sagittal image demonstrated a large uterine fibroid (arrow) measuring about 6.5 cm in diameter.

Figure 6. Patient 2: post-treatment enhanced T1-weight image demonstrated the NPV ratio is 49.99%. The low signal intensity area (arrow) indicated the post-treatment necrotic area.

Figure 7. Patient 2: follow-up enhanced T1-weight image at 3 month showed that the diameter of fibroid decreased to 5.2 cm and the NPV ratio is 36.14%.

Figure 8. Patient 3: pre-treatment T2-weighted sagittal image demonstrated a large uterine fibroid (arrow) measuring about 10.3 cm in diameter.
DISCUSSION

Uterine fibroids represent a significant women’s health problem with symptoms ranging from abdominal distension to bleeding. Treatment options vary from hysterectomy and uterine artery embolization (UAE) to less invasive methods. The use of MRgFUS for the treatment of uterine fibroids may help patients avoid major surgery and organ loss. The principle behind MRgFUS is the application of heat to a local tissue causing fibroid ablation. Since the resulting cell necrosis is due to coagulation rather than an ischemic process, the painful infarction syndrome recognized after UAE is avoided [18].

Our study demonstrated that the MRgFUS is effective in improving symptom severity after 3 months of treatment. The mean reduction in symptom severity scores in our patients after 3 months was 30.6%. In Harding’s study [19], 102 women were assessed after MRgFUS using UFS-QOL at baseline, at 3 months post treatment and at 6 months post treatment. The average score reduction at 3 and 6 months was 39.7% and 44.9%, respectively, which is similar to our findings. In Yoon’s study [6], they evaluated the short-term efficacy of MRgFUS on uterine fibroids in 29 Korean women. The average symptom severity score before the treatment was 54.1 ± 23.8. The symptom severity scores decreased 43.3% at 3 months after the treatment and were maintained at 6 months. In Smart’s study [20], women received a 3 months course of GnRH agonist treatment followed by MRgFUS treatment. The SSS was compared at enrollment, at 3, 6, and 12 months post treatment. There was a 50% reduction in mean SSS at 6 months and 48% at 12 months post treatment. 83% of women achieving at least a 10-point reduction in SSS. In our study, in response to the questionnaire at 3 months after MRgFUS, all patients reported significant improvement in their symptoms, similar to the results of earlier studies.

In this study, the mean fibroid volume was also reduced from 319.1 to 224.0 c.c (30.8% reduction).
These results demonstrate that MRgFUS is an effective method for selective ablation of tissue within the uterus. In Ren's study [21], they analyzed the fibroid volume reduction after MRgFUS in 119 patients. They found that the mean reductions in tumor size, as a percentage of initial tumor volume at 1, 3, 6, and 12 months after MRgFUS treatment, were 21.2%, 29.6%, 44.8% and 48.7%, respectively. In Morita's study [22], they described their early results regarding efficacy and safety of MRgFUS among a population of Japanese women. They found that the average reduction in fibroid volume, as determined by MR imaging at 6 months after treatment, was 33%, which is very similar to our findings.

In MRgFUS therapy, ultrasound beam is focused on diseased tissue, and due to the significant energy deposition at the focus, temperature within the tissue rises to between 65° and 85°C, destroying the diseased tissue by coagulation necrosis [14]. This is the reason why the fibroid volume decreased significantly in our study after 3 months. We think that the reduction in fibroid volume is closely associated with the improvement of symptom severity scores and we conclude that the MRgFUS is effective in fibroid volume reduction and symptom relief.

In 2009, O'Sullivan et al [23] compared the cost-effectiveness of MRgFUS and UAE of uterine fibroids in the United States from several prospective studies by using the Markov model. Their results showed that screening costs of these two methods are both 826 American dollars. However, the procedure-related costs of UAE and MRgFUS are 11341 and 6768 American dollars respectively. For the treatment safety, the probability of major complications is 0.5% for UAE and 0% for MRgFUS. The probability of procedure-related death is 0.15% for UAE and 0% for MRgFUS. In Taiwan, MRgFUS is a non-insurance covered procedure with the cost about 150,000 NT dollars. UAE is relatively inexpensive with the cost about 20,000 NT dollars. However, our patients felt no-pain during the MRgFUS treatment. Pain following UAE is common and partly explained by myometrial ischemia [24].

This is the first use of MRgFUS for treatment of uterine fibroids in Taiwan. Our results demonstrate that MRgFUS can safely and effectively ablate uterine fibroids sufficiently to produce a decrease in mean fibroid volume and significant improvement in symptom severity scores for up to 3 months posttherapy. Further studies are necessary to assess the long term safety and efficacy of MRgFUS in a larger population.

References

以磁振導航超音波手術治療子宮肌瘤：臺灣之初期經驗

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子宮肌瘤是婦女常見之良性腫瘤，以往大部分的治療方法是使用手術治療。磁振導航超音波手術是過去幾年來用來治療子宮肌瘤之新方法，主要是以高能聚焦超音波將能量聚焦於病變組織，使組織造成凝固性壞死。本文報告三位罹患子宮肌瘤之婦女，在接受磁振導航超音波手術治療3個月後，其肌瘤體積變化及症狀嚴重度之改善情形。

本研究募集三位罹患子宮肌瘤之婦女，平均年齡為38.3歲。在治療前以磁振造影來評估子宮肌瘤之體積，並以Uterine Fibroid Symptoms and Quality and Life Questionnaire（UFS-QOL）問卷來計算其症狀嚴重度分數。在治療3個月後，同樣再測量一次肌瘤之體積，並再做一次問卷以計算症狀嚴重度分數，以評估磁振導航超音波手術對於子宮肌瘤之治療效果。

結果顯示，三位病患在接受治療後，皆無嚴重副作用之發生。在進行治療3個月後，三位病患之平均肌瘤體積下降30.8%，而平均症狀嚴重度分數則下降30.6%。

以磁振導航超音波手術來治療子宮肌瘤是一安全且有效之治療方法。本研究也建議一個較長期且較多病例數之研究是必要的。