·非血管介入 Non-vascular intervention·

磁共振引导高强度聚焦超声完全消融子宫肌瘤:可行性、安全性和远期疗效

许永华, 陈文直

【摘要】 **目的** 评估 MRI 引导高强度聚焦超声(MRgHIFU)完全消融子宫肌瘤的可行性、安全性和远期疗效。**方法** 对 43 例(平均年龄 41.4 岁)共 51 个子宫肌瘤,平均大小为(7.1 ± 1.4)cm,均进行一次 MRI 引导高强度聚焦超声消融术。治疗后即刻 MRI 增强测量靶肌瘤的体积及其无灌注区的体积,子宫肌瘤无灌注区的完全覆盖靶肌瘤为完全消融。对完全消融的子宫肌瘤在治疗后 3 个月、6 个月、1 年、2 年和 3 年通过 MRI 进行随访复查肌瘤的体积变化;在术前、3、6 个月采用 UFS-QOL 症状评分方法对患者症状评分,并随访 3 年观察其症状的变化。同时对这些肌瘤的特征、治疗后不良事件、聚焦超声能量及治疗效率等进行了分析。**结果** 经 MRgHIFU 治疗后肌瘤平均消融率为 84.3% ± 15.7%(范围 33.8% ~ 100%),肌瘤部分消融(消融率 < 90%)、几乎完全消融(消融率为 90% ~ 99%)和完全消融的病例分别为 23 例、10 例和 10 例,平均治疗时间为(2.2 ± 0.8)h(范围 1.0 ~ 4.3 h),治疗后均未发生并发症。10 例 13 个完全消融的肌瘤术前 MRI 均为 T2 低信号表现而其血供类型不同;超声治疗的能效因子(EEF)为:(3.6 ± 2.1)J/mm^3(0.7 ~ 6.8 J/mm^3)。治疗后 3、6 个月症状严重程度评分(SSS)分别为从术前的 33.9 ± 7.1 下降至 16.6 ± 9.0 和 8.1 ± 3.4(P < 0.01),1 年或 2 年后 10 例患者的症状完全消失。治疗后 3、6 个月和 3 年肌瘤体积分别缩小 39.5% ± 10.2%、59.1% ± 9.0%和 93.3% ± 3.1%(P < 0.01)。治疗后 3 年随访肌瘤均未出现复发。**结论** MRI 引导高强度聚焦超声完全消融子宫肌瘤是可行的、安全的和有效的,MRI T2WI 低信号肌瘤可在治疗后取得完全消融。

【关键词】 磁共振; 高强度聚焦超声; 子宫肌瘤; 消融

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Complete ablation of uterine fibroids by MR-guided high intensity focused ultrasound: feasibility, safety and long-term outcome

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【**Abstract**】 **Objective** To assess feasibility, safety and long-term outcome of the complete ablation of uterine fibroids by using MR-guided high intensity focused ultrasound (MRgHIFU). **Methods** Fifty one symptomatic fibroids [Mean size (7.1 ± 1.4) cm] in 43 subjects (Mean age 41.4 years) were treated with MRgHIFU and the characteristics of fibroids, sonication energy, treatment efficiency and severe adverse events were analyzed. The complete ablation of fibroids is defined as non-perfusion area covering all volume of the treated fibroid in contrast enhanced MR imaging. The symptom outcomes of patients were

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assessed with symptom severity scores, and the volume reduction and recurrence of the fibroids were followed up at 3 month, 6 month, one year and two year through 3 years after the procedure. **Results** All of MRgHIFU treatments showed technical successes in one session and mean treatment time was 2.2 ± 0.8 hours (Range: 1.0 – 4.3 hours). The mean non-perfused volume(NPV) ratio was 84.3 ± 15.7% (Range, 33.8% – 100%) immediately after the treatment, and the partial ablation (NPV ratio < 90%), almost complete ablation (NPV ratio of 90 – 99%) and complete ablation (NPV ratio of 100%) of fibroids occurred in 23, 10 and 10 patients, respectively. The 13 completely ablated fibroids in 10 patients had hypointense signal on pretreatment T2 weighted imaging but their blood supply patterns were different. The mean energy-efficiency factor (EEF) was 3.6 ± 2.1 J/mm^3 (Range, 0.7 – 6.8 J/mm^3). The patients whose fibroids were completely ablated had significant decrease in transformed symptom severity scores from a baseline of 33.9 ± 7.1 to 16.6 ± 9.0 and 8.1 ± 3.4 after 3 months and 6 months, respectively ($P < 0.01$) and were free from the fibroid-associated symptoms after one or two years. The mean volume reduction in treated fibroids was 39.5 ± 10.2%, 59.1 ± 9.0% and 93.3 ± 3.1% at 3 months, 6 months and 3 years follow-up, respectively ($P < 0.01$). **Conclusion** Complete ablation of fibroid by using MRgHIFU is feasible, safe and effective. The completely ablated fibroids might more likely be hypointense on pretreatment T2 weighted imaging.(J Intervent Radiol, 2014, 23: 959-968)

【**Key words**】 Magnetic resonance imaging; High intensity focused ultrasound; Uterine fibroid; Ablation

1 INTRODUCTION

Uterine fibroids are estimated to be clinically significant in over 25% of the reproductiv-age women in the United States, however, 77% of hysterectomy specimens performed in patients with or without clinical history of myomatous uteri had fibroids[1]. The fibroids can become quite large and are frequently associated with infertility, menorrhagia and spontaneous abortion. Since the hormonal milieu has a key impact on the development and growth of uterine fibroids, development of new fibroids will be seen in 42 – 55% of patients undergoing a myomectomy for complete removal of the tumors[2]. It is not reasonable for the patients to experience one more surgery procedure. High intensity focused ultrasound (HIFU), a non-invasive interventional procedure, had been clinically applied for treatment of solid tumors; and magnetic resonance-guided focused ultrasound for treatment of uterine fibroids was approved by the Food and Drug Administration (FDA) in the United States[3]. Many patients, who underwent magnetic resonance-guided high intensity focused ultrasound (MRgHIFU) treatment, had their uterine myoma shrunk and the symptomatic relief was sustained for more than two years[3-4]. However, up to 16% – 20% of the patients would require an additional treatment for treated fibroids because of partial volume ablation[4]. Therefore, complete ablation of fibroid is probably the optimal choice for HIFU to potentially achieve similar outcome as myomectomy. This study is to investigate the feasibility, safety and long-term outcome of complete ablation treatment of uterine fibroids by using MRgHIFU.

2 MATERIALS AND METHODS

2.1 Patients

This was a prospective study and approved by the institutional review board and written informed consent for the MR-guided HIFU procedure was obtained from all patients.

Inclusion criteria for MRgHIFU treating uterine fibroids were: ① Pre- or perimenopausal woman between 18 and 55 years old; ② Symptomatic uterine fibroid greater than or equal to 3 cm and less than 12 cm, and not more than 2 fibroids in MR imaging; ③ Not pregnant currently and no plan for future pregnancy; ④ No contraindications to MR imaging or MR contrast agents; ⑤ No evidence of calcification or substantial degeneration in the uterine fibroids found with plain radiography or MR imaging.

From July 2008 to May 2010, 43 patients (mean

age 41.4 years; age range, 24 – 50 years) with 51 symptomatic uterine fibroids [mean size: (7.1 ± 1.4)cm; size range, 3.7 – 10.7 cm] were recruited according to the inclusion criteria. The choice to choose MR guided HIFU instead of surgery was based on patient preference.

2.2 Pretreatment Imaging

All patients underwent MR imaging by using a standardized protocol including T1WI, T2WI with and without fat saturation, pre- and post-contrast T1-weighted fast low-angle shot (Flash) MR images at axial, coronal and sagittal planes on a 1.5 T MR imager (Avanto; Siemens Healthcare, Germany). The patients received an intravenous injection of Gd-DTPA-BNA contrast (Omniscan,0.1 mmols/kg of body weight, GE Healthcare). Parameters for T1-weighted FLASH MR images were: TR/TE 18/4.8, flip angle 75°, matrix 250 × 106, FOV 300 mm, slice thickness 5 mm. MR images were analyzed to determine the number, location, size, T2-weighted signal intensity and contrast enhancement patterns of all fibroids. T2-weighted signal intensity of myoma was classified as hyperintense or hypointense as compared with skeletal muscle signal intensity[5].

2.3 MR-guided HIFU System

Uterine fibroid ablations were performed by using the clinical extracorporeal MR-guided HIFU system (JM 2.5C; Chongqing Haifu (HIFU) Tech Co. Ltd., Chongqing, China) fully integrated into a 1.5 T MR imager (Avanto; Siemens Healthcare, Germany) which provides real-time temperature mapping system for treatment control. Therapeutic ultrasound energy was produced by a transducer with 18 cm diameter, a focal length of 15 cm, and operating at a frequency of 1.0 MHz. The table, which the patient was placed in the prone position on, contained a diameter transducer array in a water tank. The dimensions of physical focus are 8 mm along the beam axis and 5 mm in the transverse direction. The system worked as in the previous report[6].

2.4 Patient preparation for the procedure

A careful bowel preparation was performed for 2 – 3 days, including liquid food, no milk, fasting for 12 hours before MRgHIFU treatment, and an enema in the early morning on the day of treatment. Degassed water balloons of different size were prepared to compress and push away the bowel from the acoustic pathway if it lies between the transducer and targeted fibroid during procedure[6].

2.5 MR-guided HIFU procedure

All MR-guided HIFU procedures were performed by one interventional radiologist (Y. XU) with 10 years of experience in image-guided tumor ablation. The patients received intravenously fentanyl, 50 – 400 ug, and midazolam hydrochloride, 1 – 4 mg, for conscious sedation. The patients were monitored to track respiration rate, heart rate, blood pressure, and oxygen saturation level. The sedation nurse accompanied patients in the same room and patient held up a balloon to stop sonication if she could not endure discomfort during the procedure.

Before the treatment, coronal, sagittal, and transverse T2-weighted turbo spin echo (TSE) images (TR/TE: 4 800/120 ms; slice thickness = 5.0 mm, Matrix 256 × 100, FOV 36 × 36 cm) were obtained for treatment planning. The treatment area was outlined and "seeds" were drawn by an interventional radiologist and a MRI technologist (Fig. 1). To test the accuracy of targeting, a series of 50 w/cm^2 focused ultrasound sonications were performed while the treatment effects were monitored by sagittal plane images (5 slices). The physical focus was to be adjusted to match biological focus shown at Proton Resonance Frequency-shifted (PRF-shifted) temperature mapping imaging. After confirming the accuracy, treatment was performed by increasing the power to achieve 60℃ and above at the targeted tissue (Fig. 2). The duration of each sonication was 2 seconds, followed by 2 or 3 seconds of a cooling period, while PRF-shifted MR imaging was performed to monitor temperature to elevate in real time; and if sonication power was raised up to 400 w but not reach to 60℃, the therapeutic run would be repeated until 60 – 65℃, however, if focus temperature was more than 70℃, the sonication power would be decreased according to the real-time monitoring temperature. Depending on the volume of the targeted myoma and target treatment zone, a

variable number of sonications were performed to cover all area of fibroid except if the patient felt extremely severe or intolerant pain to endure and nerve num or pain spreading to lower legs. All of patients received only one treatment session.

2.6 Posttreatment Imaging and Follow-up

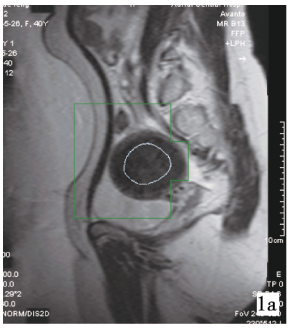

Fig. 1 Setting up HIFU therapeutic area of the targeted fibroid at each slice(1a), then the system will automatically generate the treatment plan (1b).

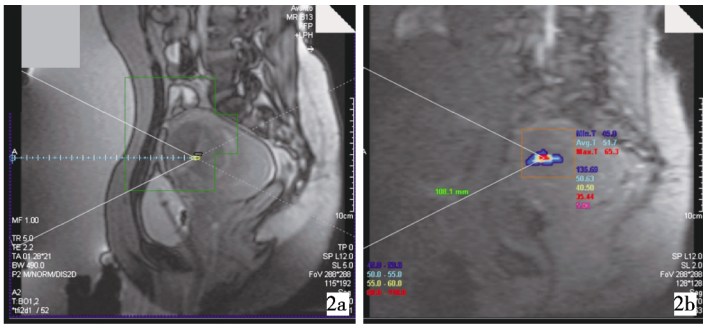

Fig. 2 Sagittal T2 weighted imaging showed the targeted acoustic focus in the fibroid based on the treatment plan (2a) and real time Proton Resonance Frequency - shifted temperature mapping showed the temperature elevating to 65.3℃ (maximum) at the target region of same slice position (2b), red color representing ≥ 60℃, yellow color representing 55 – 60℃.

Immediately following treatment, axial, sagittal and coronal T1 - weighted FLASH images were acquired for assessment before and after administration of contrast agent, and the fractional of ablation was defined as non-perfused volume divided by the fibroid volume. Fibroid and ablation volumes were calculated using the prolate ellipsoid volume formula. All patients were followed up after three months, six months, one year, two years through three years and the MR imaging protocol and parameters were same as those of pretreatment.

Patients' symptoms associated with fibroids were prospectively collected and quantitatively analyzed with UFS-QOL symptom severity scores (SSS)[7-8]. Eight questionnaires especially for myoma were administered and the responses were rated on a scale from 1 to 5 (1, none; 2, mild; 3, moderate; 4, severe; 5, very severe). Raw scores were converted to a score on a 100 scale by using the following formula: transformed score = (raw score – 8)/32 × 100; lower scores indicated better relief of symptoms on the symptom severity scale. The questionnaires were given before treatment and at 3 month, 6 month follow-up. Other symptom changes were obtained after one year through three years following MRgHIFU procedure.

2.7 Data analysis and statistics

All data were presented as mean ± SD. Statistical analyses of the data were performed by ANOVA and Student's t test. A p value of < 0.05 was used to define statistical significance.

3 RESULTS

3.1 Baseline Characteristic and Immediate Treatment Outcomes

All of MRgHIFU treatments showed technical successes in one session and mean treatment time was 2.2 ± 0.8 hours (Range: 1.0 – 4.3 hours). The mean non-perfused volume (NPV) ratio was 84.3% ± 15.7% (Range, 33.8%– 100%) immediately after the treatment.

Complete ablation was achieved in 13 (25.5%, 13/51) fibroids of 10 (23.3%, 10/43) patients based on immediate contrast-enhanced MR images after sonication treatment. The mean size of the 13 fibroids was (6.1 ± 1.7)cm (Range, 3.7 – 9.3 cm) and their average non-perfusion volume (NPV) value per case was 157.8 ± 70.2 cm^3 (Range, 77.7 – 272.1 cm^3) or 100% of the fibroid volume (Table 1). Average age of these patients was(40.6± 6.6)yr. The mean transformed scores of symptom at baseline were (33.9 ± 7.1) (Range, 25 – 52) before MRgHIFU surgery. All of the thirteen fibroids were hypointense on pretreatment T2WI Image. Their blood supply patterns were

hypervascular in two cases, moderate - vascular in three cases and hypovascular in five cases (Table 1).

Table 1 Complete ablation of fibroid(s) MRg HIFU

Case No.	1	2	3	4	5	6	7	8	9	10
Age(year)	39	50	48	45	37	28	35	38	41	45
Main Symptoms	Dysmenorrhea back pain, Urinary symptoms	Menorrhagia	Menorrhagia, Urinary symptoms	Menorrhagia	Menorrhagia, Astriction, low back pain	Menorrhagia	Menorrhagia	Dysmenorrhea	Astriction, Dysmenorrhea	Menorrhagia, Anemia
Fibroids										
Number	1	1	2	1	1	1	2	1	1	2
Size/cm	5.6	8.5	7.3/3.7	8.4	6.3	9.3	5.9/3.9	7.3	6.2	6.2/4.5
Location	I	I	I/S	I	I	I	I	S	S	S/S
Vascularity	hyper-	moderate	hypo-	moderate	hyper-	hypo-	hypo-	hypo-	moderate	hypo-
Volume/cm^3	85.6	267.8	134.3[b]	189.7	102.4	272.1	124.9[b]	191.6	77.7	131.9[b]
Sonication										
Mean Power/W	325	371	356	296	377	308	354	178	297	240
Energy/J	540 283	1 022 532	494 443	337 052	693 679	378 276	575 424	138 861	381 162	268 369
Time/min	27.8	46	23.1	18.9	30.6	20.4	27	12.9	21.4	18.6
EEF/(J/nm^3)	6.3	3.8	3.7	1.8	6.8	1.4	4.6	0.7	4.9	2.0
Treatment										
Time/min	240	250	170	155	180	170	170	110	140	160
speed/(cm^3/h)	21.4	63.8	50.0	73.0	34.1	97.2	44.6	106.4	33.8	48.9
Symptom severity score[a](SSS)										
Baseline	30	36	32	34	52	30	32	25	32	36
After 3 months	0	9	20	25	32	11	14	16	23	16
After 6 months	7	5	16	9	7	9	5	7	5	11
Reduction rate of fibroid(s) volume										
After 3 months	N/A	32%	26%	60%	43%	34%	41%	32%	48%	40%
After 6 months	66%	59%	57%	79%	52%	59%	53%	47%	56%	63%
3 year	90%	92%	95%	98%	95%	92%	91%	88%	93%	95%

I = Intramural; S = subserosal; [a]Transformed to 0 - 100 point scale; [b]volume sum of two fibroids

The partial ablation (NPV ratio < 90%) and almost complete ablation (NPV ratio of 90% - 99%) of fibroids occurred in 23, 10 patients, respectively.

3.2 Treatment parameters for completely ablating fibroids

Mean treatment time was(174.5 ± 42.2) minutes (range, 110 - 250 minutes), the mean sonication time was (24.7 ± 9.1) minutes (range, 12.9 - 46.0 minutes) and (8.4 ± 1.5)minutes/hour. The treatment speed based on the immediate NPV results and treatment time (from first sonication to last sonication) was(57.3 ± 27.8)cm^3/h (Range, 21.4 - 106.4 cm^3/h). Average power of sonication was 310.2 ± 62.5 W, the average treatment energy was(483 008 ± 248 232)J (Range, 138 862 - 1 022 532 J). Mean energy-efficiency factor (EEF) was(3.6 ± 2.1)J/mm^3 (Range, 0.7 - 6.8 J/mm^3).

3.3 Tolerance of patients and complications

No patient felt any extreme or intolerable pain during the MRgHIFU. One patient with fibroid nearby sacrum had mild sacrococygeal (lower back) pain sustaining to the second day following the treatment. Three patients complained of mild pain in lower abdomen for 1 - 3 hours after the procedure. No abdominal skin burn or nerve injury occurred in the ten patients.

3.4 Completely ablated Fibroid Volume and Symptom Changes after MRgHIFU

The mean volume reduction was 39.5% ± 10.2% (Range 26% - 60%) and 59.1% ± 9.0% (Range 47% - 79%) at 3 months and 6 months, respectively ($P < 0.01$). Of the ten patients, non-perfused ablation region was close to completely disappeared or replaced by the granulation tissue after 2 - 3 year follow-up (Fig. 3, Fig. 4), and the sizes of treated fibroids finally shrank to 2 - 3 cm or less and their mean volume reduction was 93.3 ± 3.1%(Range 88 - 98%)($P < 0.01$) at 3 year after MRgHIFU.

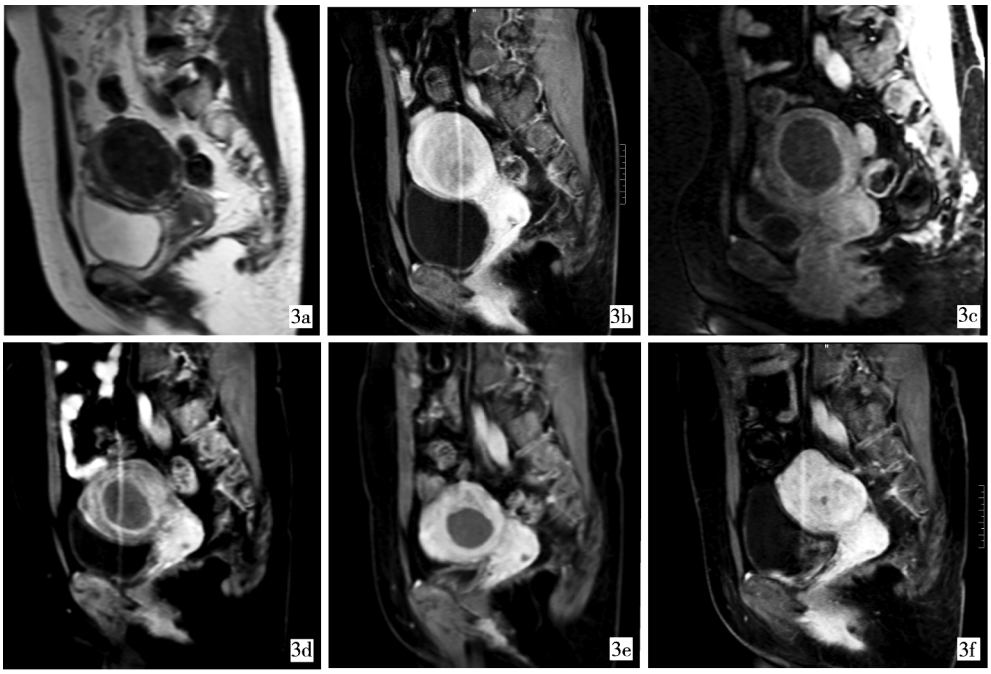

Fig. 3 (case 4). Pretreatment sagittal T2WI showing the hypointensity fbroid selected for treatment (3a); Pretreatment CE (contrast enhanced) T1WI showing vascularization of the fibroid (3b). Immediate posttreatment CET1WI showing complete ablation of the tumor(3c); CE T1WI acquired 3, 6 months after treatment showing reduction of ablative fibroid volume at 60% and 79%, respectively (3d、3e); CE T1WI acquired 2 year posttreatment showing ablated necrosis was almost absorbed(3f).

Mean transformed symptom severity scores fell from the baseline to 16.6 ± 9.0 (Range, 0 – 32) and 8.1 ± 3.4 (Range 5 – 16) at three months and six months, respectively ($P < 0.01$). There is no reintervention for all of 10 patients. Nine patients were free of symptoms after one year and one patient after two years, which sustained to the three year follow-up point.

4 DISCUSSION

Uterine fibroid is a common pelvic benign tumor that causes bleeding, press introduced pain and inferterity or miscarrage in reproductive women, requiring hysterectomy and myomarectomy. Many women choose more conservative treatments in order to potentially be able to bear children and avoid surgical incisions. Recently, MRgHIFU has become a non - invasive therapeutic option for patients with symptomic uterine fibroids. The complete ablation of all fibroid volume by using HIFU would probably be a desired alterative to myomarecotmy without surgical complications. So far, there have been very few reports on using MRgHIFU or MRgFUS to achieve complete ablation of fibroids. Meng et al. had reported that complete ablation of fibroids was achieved successfully by using Ultrasound guided HIFU (USgHIFU)[9]. Their work showed that it was safe and feasible to completely ablate fibroids without severe complication, and the successful rate was around 50% , which was assessed by using contrast - enhanced ultrasound (CEUS). However, CEUS might overestimate the NPV rate of fibroid because the ablation depth and total extent of the treated fibroids are hard to discern as a result of acoustic shadowing. In our study, the treated fibroids showing complete ablation by CEUS still had residual tumor tissue at the rear regions in contrast enhanced MR imaging. The definition of complete ablation of fibroids is that the fraction of ablation, non-perfused volume divided by the fibroid volume immediately after HIFU treatment, is 100% without any residual viable tissue in MR imaging. Our results in this study showed that 13 fibroids (13/51, 25.5%) in 10 patients (10/43, 23.3%) had been completely ablated, which was assessed by CE-MRI and followed up for three years. To our best knowledge, this is the first time that

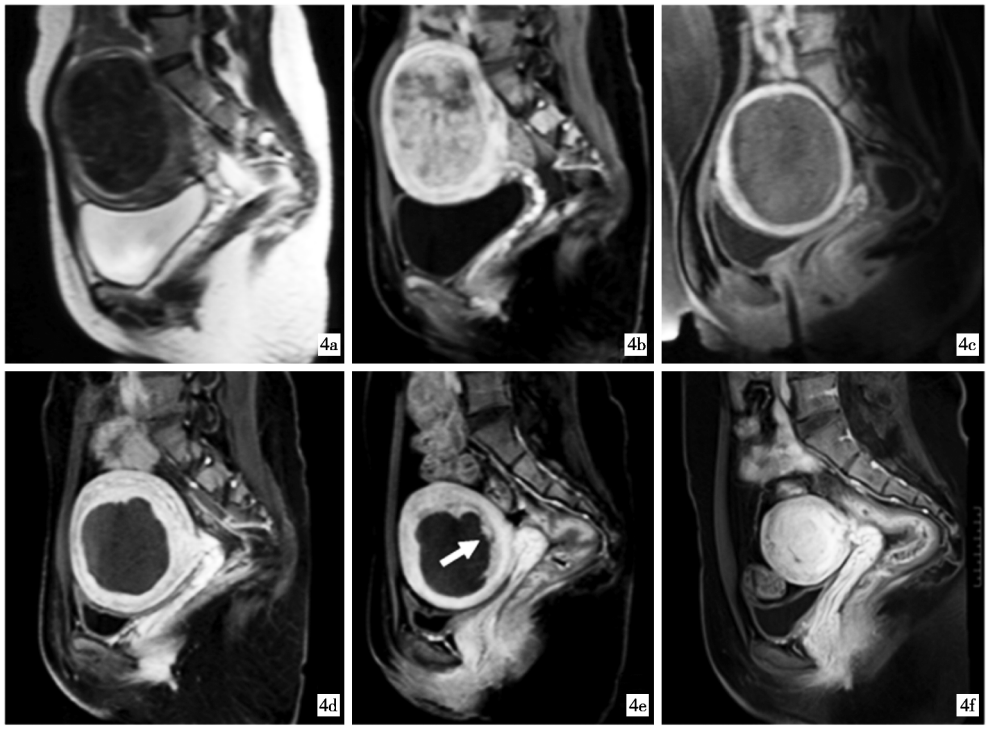

Fig. 4 (case 6). Uterine fibroid in a 28-year-old woman was hypointense signal on pretreatment T2WI (4a). Sagittal CE T1WI showed inhomogeneous enhancement before MRgHIFU treatment (4b). Sagittal CE T1WI showed 100% NPV of fibroid volume immediately after sonication treatment (4c), volume shrinkage of fibroid (59% of baseline) with sustained non-perfused area at 6-month follow-up (4d). The fibroid continued to shrink at 78% of the baseline volume with proliferation of the granulation tissue in the rear periphery (arrow) after 1 year (4e), and NPV was completely disappeared and replaced the granulation tissue at 3 year follow-up (4f).

results from a long-term follow-up were obtained for evaluation of the efficacy and safety in the patients with completely ablated fibroids. The prior studies showed that the efficacy for both volume reduction and symptom relief would be improved with an increase in NPV rate[10-11]. Maximizing the ablated volume of fibroid was to achieve sufficient volume reduction as to prevent the symptoms and recurrence of this disease in the long term, thus, complete ablation of fibroid would probably be a radical cure equivalent to myomarectomy. Many researchers, however, claimed that partial ablation of fibroid could make tumor volume shrink and it is not necessary to completely ablate fibroids in order to provide the symptom relief[12-13]. We found that if only a small portion of non-ablated fibroid was left, the treated fibroid could be recurrent and the associated symptoms would occur again in the subjects. In our study, there were other ten patients who had more than 90% NPV rate (Range: 90.7% – 98.9%) of fibroid (s) by using MRgHIFU ablation. Four of them had recurrence because of rapid growth of residual viable tissue in fibroid (s), and the patients suffered from same symptoms as before and even more severe with follow-up (Fig. 5). These cases would be referred to the gynecologists for other therapeutic modalities, resulting in failure of MRgHIFU for treatment of the benign myoma. Like majority of interventional or minimally invasive treatments such as uterine arterial embolization, radiofrequency etc, partial ablation MRgHIFU will still be considered as a palliative modality for the symptom relief. Therefore, the complete ablation of the targeted solid tumors would be pursued as the ideal choice of the non-invasive procedure.

The results of initial clinical trials of MRgFUS showed only limited (10% – 20%) treated volume of the treated fibroids due to the safety requirement of US FDA[14]. Besides, many factors, such as hypervascular blood perfusion of fibroids, characteristics of

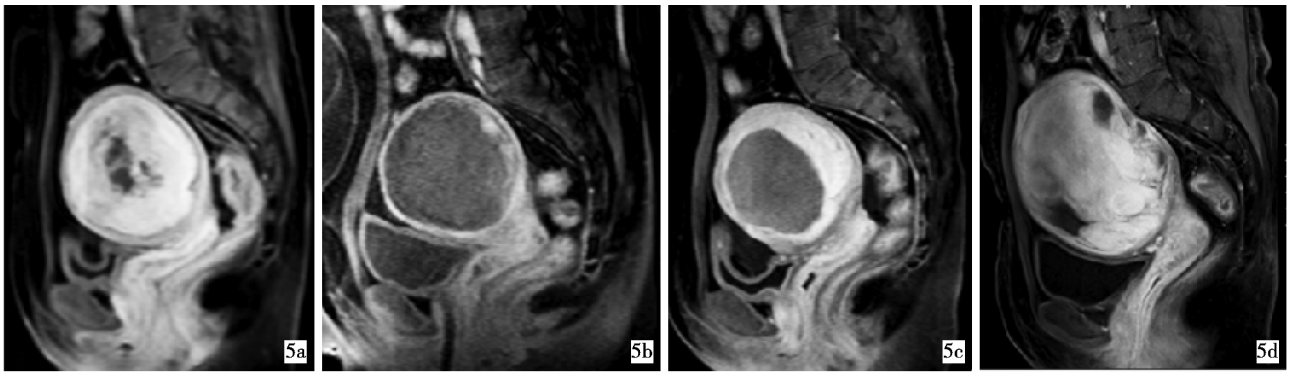

Fig. 5 Sagittal CE-T1WI pretreatment showing inhomogeneous contrast enhanced uterine fibroid (5a), almost all NPV but a small portion of residual tissue immediately after MRgHIFU (5b), significant shrinkage of fibroid NPV volume and regrowth of the residual tissue after 6 months (5c) and the fibroid recurrence after 3 years with larger volume than before the treatment (5d).

tumor tissue and low time efficiency of procedure etc., influence the therapeutic outcomes of focused ultrasound.

Hypervascular blood perfusion of tumors during thermal therapy would prevent the temperature from elevating due to the heat-sink effect. In this study, however, there were two patients (20%) with hypervascularity fibroid(s) and three (30%) with moderate-vascularity fibroid(s) that were completely ablated. These fibroids were considered as the suitable candidates for HIFU therapy because of their hypointense signal on pretreatment T2WI. There was no complete ablation in hyperintense fibroids on pretreatment T2WI even if some T2 hyperintense fibroids showed hypovascular blood perfusion during dynamitic contrast-enhanced MR imaging in our study (Fig. 6). The vascularity in fibroid had been thought to mainly represent high T2 signal intensity previously [12-13]. Our result was not in line with their findings because all of thirteen fibroids had hypointense signal on pretreatment T2WI but their blood supply patterns were different. These findings indicated that the property of fibroid texture (celluarity density, fluid-rich tissues or degeneration etc.), the determinant of tumor signal intensity on T2WI, was more important than its blood supply perfusion pattern for patients to be selected in successful MRgHIFU treatment. This is because the untreated visible tissue between adjacent ablation focuses will be eliminated by heating diffusion in the tissue based on the characteristics of fibroids[15].

The time efficiency seemed not optimistic for

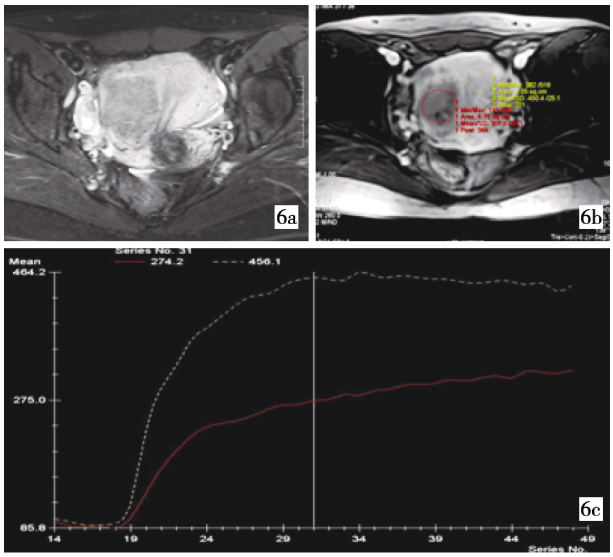

Fig. 6 (6a) Axial T2WI showing hyperintense fibroid, (6b) Dynamic CE T1WI showing hypovascularity with lower perfusion in fibroid (red line) than myomanium (yellow line) (6c).

MRgHIFU ablation of fibroid to become a popular clinical therapeutic option, because the whole procedure lasted 3 – 4 hours or more and the ablation fraction was around 50% of fibroid volume in a recent volumetric ablation study [10]. In our study, the mean treatment time for complete ablation of whole fibroid was (174.5 ± 42.2) minutes [(2.9 ± 0.7 h)] and the treatment speed of (57.3 ± 27.8) cm^3/h was very close to their result. Targeted vessel ablation strategy could achieve more non-perfusion volume than predicted thermal dose volume, and the treatment time was shorten to 132 and 213 minutes for partial ablation volume (195 ml and 282 ml) of treated fibroids in two cases (16). The authors explained that segmental branches of the uterine arteries were

ablated, which was similar to the infarction effect caused by uterine arterial embolization. It was the preliminary data only in two cases, moreover, the size of the targeting vessel could not be mentioned and the detecting method during the procedure was still not resolved. Kim et al. suggested a one layer strategy to be employed for HIFU to ablate large fibroid in order to decrease the treatment time and increase ablation efficiency[17]. They reported that average NPV of (301.3 ± 119.1) ml could be achieved in large fibroids within (166.2 ± 38.9) minutes of treatment. The use of cavitation effect to enhance sonication ablation volume in tumors was also investigated and would be available in future therapy [18]. Many efforts still need be devoted to increase the efficiency of MRgHIFU ablation, although the shortest treatment time was less than two hours in this study.

Sonication dosage issue of MRgHIFU still needs to be addressed for treatment safety and efficacy[15-19]. In this study, mean EEF was (3.6 ± 2.1)J/mm^3 (Range, 0.7 – 6.8 J/mm^3) in the 13 fibroids of ten patients. Although the non-perfused area could extend to regions in the myoma that were definitely not heated with treatment volume increase[15], the difference is almost ten times between the smallest and largest EEFs. Because the whole thermal procedure was monitored with the real time MR temperature mapping and all volume of fibroid was completely ablated, there was no overtreatment and undertreatment during the procedure. The blood perfusion in the tumor would take the thermal energy away from the treated area, and the tissue components and characteristics are different even with the same kind of tumor, so it is difficult to estimate the precise thermal dose for a complete ablation.

For treatment safety and efficiency, it would be ideal that the lowest acoustic energy would be utilized to maximize ablation. The average treatment sonication energy was 483 008 J and its range was 138 862 – 1 022 532 J for these ten patients without severe complications and skin injury. The maximal sonication energy was almost eight times as much as the minimal and over two times more than the average sonication energy for complete ablation of fibroid. Only one patient had mild sacrococygeal pain for two days, which indicated possible sacral vertebrae burn, and she occasionally felt mild back pain until 2 years after procedure. Other three patients had lower abdomen mild pain for 1 – 3 day(s). The results showed that MRgHIFU for complete ablation of fibroid was safe and had minor adverse events in comparison of previous survey for fibroid treatment by ultrasound guided HIFU, which had 10.2% complications including never injury, hematuria, skin burn, severe abdomen pain and vertebra burn[20]. New guidelines of the Food and Drug Administration for MRgHIFU were that the maximum treatment volume was 150 cm^3 and limited to 50% of the total fibroid volume[21]. In this study, average ablation volume was 157.8 cm^3 and maximum 272.1 cm^3 for complete ablation of fibroids. Other studies had successfully achieved NPV of (301.3 ± 119.1) ml (64.2% ± 19.9% of treated fibroid volume) in large fibroid without severe complication[17]. Therefore, we suggested that these guidelines should be relaxed in order to achieve better efficacy. When complete ablation of the treated volume was not confirmed and relatively low or moderate sonication was delivered, a certain amount of acoustic energy could be added to eradicate the possibly alive tumor tissue.

The objective of complete ablation of targeted fibroids is to make tumors shrink without regrowth in order to avoid additional therapies. Smith reported that 17 of 79 women (21.5%) underwent an additional procedure at about average one and half year after uterine fibroid embolization[7]. In this study, the 13 completely ablated fibroids had around 60% volume reduction after 6 months, and continued to shrink to 2 – 3 cm or less and average reduction rate of treated fibroids was 93.3% ± 3.1% at 3 year follow-up without rebounding. Meanwhile, with the reduction of the ablated tumor (s), patients' symptoms improved significantly and all of them completely recovered at 1 – 2 year after treatment. Since the ablated volume correlates linearly with relief of clinical symptoms[21-22], it will be expected that complete ablation of fibroids by using non-invasive MRgHIFU will be an

alternative to myomectomy.

The limitations of this study were that only small number of completely ablated uterine fibroids by MRgHIFU was evaluated. Ten patients with over 90% partial ablation fibroids and two patients with two myomas of one complete ablation and other partial ablation were excluded for the evaluation because the residual viable tissue might have an impact on the efficacies. Moreover, almost one third of patients with incompletely ablated fibroid (s) could not been followed up since they had other therapeutic modalities after one or two years. Further investigation is needed for understanding mechanism and factors influencing the long term outcomes. In conclusion, the complete ablation of fibroid by using MRgHIFU is feasible, safe and effective, and the completely ablated fibroids might more likely be hypointense on pretreatment T2WI.

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