Leiomyoma Shrinkage After MRI-Guided Focused Ultrasound Treatment: Report of 80 Patients

Suzanne D. LeBlang[1]
Katherine Hoctor
Fred L. Steinberg

OBJECTIVE. The purpose of this study was to assess the degree of leiomyoma ablation and shrinkage after MRI-guided focused ultrasound treatment performed according to U.S. Food and Drug Administration protocols for commercial trials.

MATERIALS AND METHODS. A total of 147 symptomatic leiomyomas in 80 women (average age, 46 years; range, 34–55 years) were managed with MRI-guided focused ultrasound. The average volume of treated fibroids was 175 ± 201 (SD) cm^3. Before treatment, T2-weighted MR images in three planes were obtained to measure leiomyoma volume. Immediately after treatment, T1-weighted contrast-enhanced fat-suppressed MR images in three planes were used to measure nonperfused volume ratio. Similar images obtained 6 months after treatment were used to determine leiomyoma shrinkage. Qualitative and quantitative relations between fibroid volume, nonperfused volume ratio at treatment, and 6-month shrinkage were measured.

RESULTS. The average nonperfused volume ratio was 55% ± 25% immediately after treatment. Six months after treatment, the average volume of treated fibroids had decreased to 112 ± 141 cm^3 ($n = 81$) ($p < 0.0001$) with an average volume reduction of 31% ± 28%. A linear regression model showed highly significant correlation between posttreatment nonperfused volume ratio and shrinkage at 6 months ($p < 0.0001$).

CONCLUSION. MRI-guided focused ultrasound therapy for leiomyoma can result in nonperfused volume ratio and shrinkage that exceed those in previous clinical trials because the treatment guidelines have been relaxed to allow a greater amount of tissue ablation. The results suggest that a larger nonperfused volume ratio can be achieved, resulting in greater shrinkage and improved relief of symptoms.

Uterine leiomyoma (fibroid) is the most common nonmalignant tumor in women of childbearing age, affecting more than 20% of women younger than 50 years [1–3]. Although many women with uterine fibroids may have no symptoms and be unaware of the disease, approximately 25% have symptoms such as pelvic pain, prolonged or excessive menstrual bleeding, urinary symptoms, and infertility [4–6]. Symptomatic uterine fibroids have typically been managed with surgical approaches such as hysterectomy and myomectomy. Less-invasive approaches include hysteroscopic or laparoscopic myomectomy and uterine artery embolization (UAE) [7–11]. Most of these procedures, however, have a recovery period of one to several weeks, often necessitate general anesthesia, and are associated with risks of bleeding and infection. UAE, a percutaneous procedure, requires only conscious sedation and can decrease the risk of bleeding and infection, but postprocedure pain has been reported in 92% of patients (555 patients in one study), leading to an average recovery time of 13.1 days [12]. Patients who are reluctant to undergo such procedures may choose to forgo treatment entirely and endure the symptoms.

MRI-guided focused ultrasound is a noninvasive therapy for symptomatic uterine fibroids [4, 13–15] approved by the U.S. Food and Drug Administration (FDA) in 2004. This outpatient procedure is performed with conscious sedation, and patients usually return to a normal routine in 24–48 hours. In the technique, focused ultrasound waves are used to generate sufficient heat at the focal point to thermally ablate targeted tissue while damage to normal, near-field tissue is avoided [16, 17]. Symptomatic improvement is the result of resorption and shrinkage of

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[1]All authors: Department of Radiology, University Imaging-Guided Therapy Center, 3848 FAU Blvd., Ste. 200, Boca Raton, FL 33431. Address correspondence to S. D. LeBlang (sleblang@universitymri.com).

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the necrotic fibroid and defunctionalization of the intrinsic tissue, as in UAE.

Previous studies [18, 19] have shown that nonperfused volume ratio (volume of fibroid tissue without blood flow after treatment) is predictive of long-term reduction in tumor volume and relief of symptoms for at least 24 months. It has been found [18, 19] that a higher nonperfused volume ratio (posttreatment nonperfused volume ratio divided by pretreatment fibroid volume) correlates with marked reduction in symptom severity and a significant decrease in the number of patients undergoing other fibroid treatments 12 and 24 months after MRI-guided focused ultrasound treatment. Assessment of nonperfused volume ratio immediately after MRI-guided focused ultrasound treatment allows physicians to predict long-term symptomatic relief.

To our knowledge, the published results on MRI-guided focused ultrasound in the management of uterine fibroids were based on findings in clinical studies used to support FDA approval of the technique. These clinical studies [18, 20, 21] were conducted with varying protocols, some of which had greater limitation on ablation treatment (e.g., ablation time, volume of fibroids treated) than the protocol used in our study and therefore resulted in a relatively low nonperfused volume ratio of less than 40%. The protocol used in our study allowed greater treatment volumes (50% of total fibroid volume compared with 33%) and longer treatment duration (180 minutes compared with 120 minutes) than previous protocols. The purpose of this retrospective study was to assess the degree of leiomyoma ablation and shrinkage after MRI-guided focused ultrasound treatment performed according to protocols that allow greater treatment volumes. The finding of greater fibroid shrinkage as a result of greater treatment volume (> 50% nonperfused volume ratio) would lead to improved symptomatic relief among patients with a reduction in fibroid volume.

Materials and Methods

Patients

Eighty patients (average age, 46 years; range, 34–55 years) were treated consecutively for symptomatic uterine fibroids from October 2004 through February 2007. The 80 patients had 204 fibroids, of which 147 were treatable with MRI-guided focused ultrasound according to the FDA guidelines for commercial trials [22]. The patients were treated for the fibroids that correlated with the symptoms. Reasons for not treating 57 fibroids were FDA limitation of treatment time (180 minutes), distance between the serosa and the fibroid (at least 15 mm required), proximity of fibroids to sensitive structures (e.g., bowel) that could not be mitigated by patient or transducer positioning. Table 1 shows the size distribution of the 147 treated fibroids. The average fibroid volume was 175 ± 201 (SD) cm^3, and 56% of the fibroids had a volume less than 100 cm^3.

Eighteen of the 80 patients (22.5%) underwent two treatments, one (1.3%) underwent three treatments, and one (1.3%) needed four treatments because of large fibroid volume. Treatment volume was determined by a summation of sequential axial slices with software included in the MRI system (Signa 1.5T, GE Healthcare). Five patients with particularly large fibroids (> 650 cm^3) underwent pretreatment with three injections of gonadotropin-releasing hormone agonist (leuprolide acetate for depot suspension, Lupron Depot, TAP Pharmaceutical Products) before undergoing MRI-guided focused ultrasound treatment. Researchers [23, 24] have found that pretreatment of large (> 10 cm in diameter) fibroids with gonadotropin-releasing hormone increases the effectiveness of treatment because it shrinks fibroids, decreases the volume of tissue to ablate, and increases the heat sensitivity of the tissue owing to a reduction in vascularity. Informed consent was obtained before treatment, and HIPAA compliance was used to ensure that patient identification was not compromised.

Inclusion criteria for the treatment required that patients be at least 18 years old and premenopausal and have fibroid-related symptoms, no desire for future fertility, and no other major medical disease, such as those that would necessitate concurrent acute care with medication, chemotherapy, or surgery. Exclusion criteria included positive pregnancy test result (a urine test was administered immediately before the procedure), uterine size larger than 24 weeks' gestation (based on MRI screening images obtained within 4 weeks of treatment), hematocrit less than 25%, and contraindication to MRI. Patients underwent prescreening MRI to determine that the fibroids could be safely and efficaciously managed with the MRI-guided focused ultrasound system.

TABLE 1: Size Distribution of Treated Fibroids (*n* = 147)

Fibroid Volume (cm^3)		
Range	Mean	No. of Fibroids
0–50	21.7	55
50–100	73.7	28
100–150	129.6	13
150–200	172.0	9
200–300	250.3	4
300–400	351.1	17
400–500	440.9	5
500–600	550.5	7
> 600	682.5	9

Treatment Device

All treatments were conducted with the same MRI-guided focused ultrasound system (ExAblate 2000, InSightec). The system consisted of a phased-array transducer (0.95–1.3 MHz), computer-controlled positioning system, radiofrequency amplifier system, and user interface [17]. These components operate in conjunction with a 1.5-T MRI unit.

MRI-Guided Focused Ultrasound Treatment

The treatment protocols have been described previously [25]. Patients arrived at the outpatient clinic 30 minutes before the MRI-guided focused ultrasound procedure for preparation that included introduction of an IV line and a Foley catheter. The patient was instructed to consume no food or drink after midnight and to shave the area between the umbilicus and pubic bone. Conscious sedation (fentanyl, midazolam) was administered as needed during the treatment.

Patients were placed in a prone position on the treatment table, and T2-weighted MR images of the pelvic region were obtained in three planes for calculation of the pretreatment volume of the fibroids. A region of treatment indicating the volume of fibroid to be ablated was drawn inside the fibroid. Sensitive structures adjacent to the fibroid (e.g., skin, bowel, sacral nerve) were identified so that the ultrasound beam would be prohibited from passing through these structures. A test sonication with a small dose of energy was administered to ensure the system was properly calibrated before definitive treatment.

Treatment was initiated with high-energy (average, 2,000–4,000 J) bursts of ultrasound waves, each lasting 15–25 seconds (each burst is a sonication), to ablate the predefined fibroid volume. During each sonication, gradient-echo thermal images (TR/TE, 27/13; flip angle, 30°; bandwidth, 5.67 kHz; matrix size, 256 × 128; field of view, 280 × 280 mm; slice thickness, 3–5 mm; number of signals acquired, 1) were acquired every 3.4 seconds during the sonication. A reference image was obtained for each sonication before energy delivery, and images were acquired every 3.4 seconds during energy delivery to ensure that the heat was accurately deposited into the targeted volume with temperatures sufficient for thermal necrosis (65–85°C).

At the end of the ultrasound procedure, the patient was given an injection of 17 mL gadolinium contrast material, and contrast-enhanced T1-weighted fat-suppressed MR images were obtained to measure the nonperfused volume ratio of each fibroid. The nonperfused volume ratio of a fibroid was defined as the nonperfused tissue volume measured with a sum of slices method on the contrast-enhanced T1-weighted images after treatment divided by the fibroid volume measured on the T2-weighted images before treatment on the day of treatment. Any adverse events during and immediately after the procedure, such as skin burns, bowel injury, and sciatica, were recorded.

Patients returned for follow-up evaluation 6 ± 1 months (median, 6.7 months) after the MRI-guided focused ultrasound procedure. During the follow-up visit, another set of T2-weighted and contrast-enhanced images were obtained. To determine fibroid shrinkage, the fibroid volume at the 6-month follow-up visit was measured, and the result was divided by the fibroid volume on the day of treatment.

Data and Statistical Analyses

All data, including treatment and posttreatment results and surveys of treated patients, were collected in accordance with guidelines approved by the institutional review board. A paired Student's *t* test was used for statistical comparisons of baseline and 6-month mean fibroid volumes. The analysis of variance single factor test was used to evaluate shrinkage. Linear regression was used to measure the relation between 6-month fibroid shrinkage and treatment-day nonperfused volume ratio. A value of $p < 0.05$ was considered to indicate a significant difference.

Results

Table 2 shows the nonperfused volume ratios of the treated fibroids immediately after treatment. The average nonperfused volume ratio was 55% ± 25% (n = 147). Factors that limited complete fibroid ablation included obstacles to passage of the ultrasound beam (scars, bowel), nonresponsive vascular fibroids, and deep (> 12 cm) location of part of the fibroid.

Six months after treatment, the average treated fibroid volume had decreased to 112 ± 141 cm^3 (n = 81) with average fibroid shrinkage of 31% ± 28% (n = 81), a significant reduction compared with the baseline volume of these fibroids ($p < 0.0001$). Figure 1 describes the fibroid shrinkage at 6 months for three ranges of nonperfused volume ratios. The mean 6-month shrinkage of treated fibroids that had a nonperfused volume ratio less than 50% was 17%, whereas fibroids that had a nonperfused volume ratio of 50–75% had shrinkage of 33% and fibroids with nonperfused volume ratio of 75–100% had an average shrinkage of 51%; the difference in shrinkage among groups was significant ($p < 0.001$). Table 3 summarizes mean fibroid volume ratio, nonperfused volume, and shrinkage in response to MRI-guided focused ultrasound treatment.

TABLE 2: Nonperfused Volume Ratio of Fibroids Immediately After Treatment (n = 147)

Nonperfused Volume Ratio (%)		
Range	Mean	No. of Fibroids
0–25	14.8	26
25–50	40.2	31
50–75	61.5	55
75–100	87.5	35

Note—For fibroids treated more than once, the final nonperfused volume ratio was calculated.

The linear regression curve in Figure 2 shows significant correlation between posttreatment nonperfused volume ratio and fibroid shrinkage at 6 months ($p < 0.0001$), greater shrinkage occurring in patients with higher nonperfused volume ratios. Figure 3 shows the relation between initial pretreatment fibroid volume and posttreatment nonperfused volume ratio and 6-month shrinkage. For all groups of fibroids (independent of size) it was possible to achieve a nonperfused volume ratio of at least 50%. Larger nonperfused volume ratios (> 60%), however, were achieved in treatment of smaller fibroid volumes.

Examples of the various nonperfused volume ratios on treatment day and the corresponding 6-month follow-up images are shown in Figures 4 and 5. The patient in Figure 4 had an 87% nonperfused volume ratio with 50% shrinkage; her condition was clinically improved with no need for further definitive treatment. In Figure 5, the patient had only a 14% nonperfused volume ratio because the fibroid, which was hyperintense on T2-weighted images, was not responsive to thermal ablation and exhibited no shrinkage 6 months after treatment. The patient underwent hysterectomy after MRI-guided focused ultrasound treatment, and pathologic examination revealed a benign fibroid.

There were two instances of first-degree skin burns and one instance of mild sciatica, all of which resolved without sequelae within 6 weeks. One instance of endometritis was reported 6 weeks after the procedure, and the patient needed hysterectomy. It is uncertain whether the endometritis was a result of the MRI-guided focused ultrasound procedure or of a complicated inadequately managed yeast infection the patient reported 6 weeks after the procedure. There were no serious adverse events within 1 week of treatment that required surgery or hospitalization. All patients returned home after recovery from conscious sedation, typically within 1 hour after completion of the treatment.

Discussion

This study is the first, to our knowledge, evaluation of the results of management of uterine fibroids with MRI-guided focused ultrasound performed with the less restrictive FDA commercial treatment guidelines implemented in October 2004. In previous studies, the patients were treated according to the more stringent guidelines used in clinical trials. This series of patients is also, to

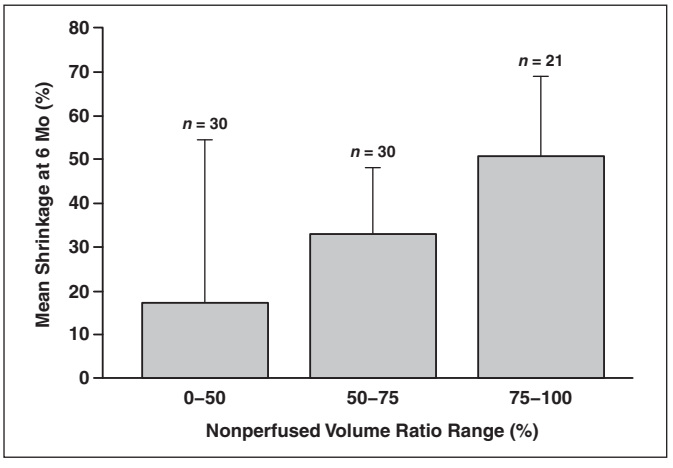

Fig. 1—Graph shows mean fibroid shrinkage 6 months after MRI-guided focused ultrasound for three ranges of nonperfused volume ratios. Greater shrinkage was found for fibroid treatments resulting in greater nonperfused volume ratios. n = number of fibroids.

TABLE 3: Response to MRI-Guided Focused Ultrasound Treatment

Variable	Mean	Range	*n*	*p*
Fibroid volume before treatment (cm^3)	175	2–764	147	
Nonperfused volume ratio immediately after treatment (%)	55	0–100	147	
Fibroid volume 6 mo after treatment (cm^3)	112	1–736	81	< 0.0001
Shrinkage 6 mo after treatment (%)	31	0–100	81	< 0.0001

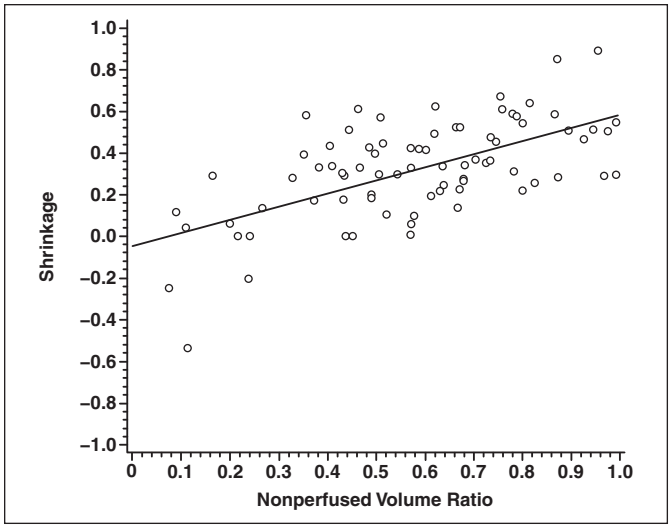

Fig. 2—Graph shows relation between nonperfused volume ratio immediately after MRI-guided focused ultrasound treatment and leiomyoma shrinkage 6 months after treatment. Shrinkage is calculated as percentage change in volume of treated leiomyomas from treatment day to 6 months after treatment. Line represents results of regression analysis ($p < 0.0001$).

our knowledge, the first to be treated according to the commercial guidelines in a private practice setting. Consistent with previous reports [18], this study confirmed a highly significant correlation between posttreatment nonperfused volume ratio and reduction in fibroid volume 6 months after treatment. Greater shrinkage was found in patients with higher nonperfused volume ratios. These results suggest that all practitioners using MRI-guided focused ultrasound should strive to achieve the largest nonperfused volume ratio that results in maximum reduction in fibroid size. In this study, we aimed for a nonperfused volume ratio of 50% for each treatment on the basis of previously reported results [18] indicating that with a 50% nonperfused volume ratio, fewer than 10% of patients needed an alternative treatment 1 year after treatment. Our results show that more than one half of the patients (61%) had a nonperfused volume ratio greater than 50%. In previous clinical trials, a similar percentage (≈ 60%) of patients had a posttreatment nonperfused volume ratio less than 30% [18].

In 80 patients treated, the average shrinkage of fibroids 6 months after treatment was slightly greater than 30%, which compares favorably with results of previous clinical studies, in which maximal shrinkage at 6 months was approximately 20% [18]. Our finding is likely due to the use of relaxed treatment guidelines, which allow more complete ablation, improved practitioner experience, and improved patient selection. The greater nonperfused volume ratio correlates with greater shrinkage and has been found to correlate with decreased symptoms [18]. As a result of a learning curve effect and permissible dose escalation, practitioners can achieve results with MRI-guided focused ultrasound that exceed those previously reported.

The shrinkage we found is less than the 42% at 3 months reported for UAE [26]. It should be noted, however, that the ideal UAE achieves 100% nonperfused volume ratio. For MRI-guided focused ultrasound, approximately 50–60% nonperfused volume ratio is required to achieve technical treatment success similar to that of UAE in terms of the need for alternative treatment [18]. Because shrinkage is correlated with nonperfused volume ratio, fibroids with a nonperfused volume ratio greater than 75% in our study had approximately 51% shrinkage 6 months after treatment, whereas fibroids with a nonperfused volume of 50–75% had 32% shrinkage at 6 months. As such, it can be inferred that patients undergoing MRI-guided focused ultrasound treatment with a high nonperfused volume ratio of 50–100% can have fibroid shrinkage similar to that of UAE while undergoing a less invasive procedure.

A relation was found between fibroid volume and posttreatment nonperfused volume and 6-month shrinkage. For all groups of fibroids (independent of size) it was possible to achieve a nonperfused volume ratio of at least 50%, yet larger nonperfused volume ratios (> 60%) were achieved in the management of smaller fibroid volumes. These larger nonperfused volume ratios also resulted in greater 6-month fibroid shrinkage.

In addition to the FDA inclusion and exclusion criteria for MRI-guided focused ultrasound treatment, appropriate patient selection is critical, and only patients with fibroids that can potentially reach greater than 50% nonperfused volume ratio should be treated. On the basis of our experience and the reported patient selection criteria described by others [27], we recommend candidates for the procedure have fewer than five fibroids measuring 2–10 cm in diameter that are hypointense on T2-weighted MR images and become enhanced after IV contrast administration. Fibroids that are isointense

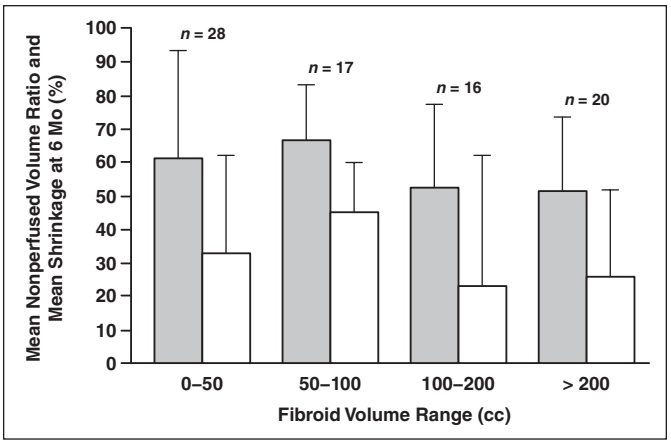

Fig. 3—Graph shows mean nonperfused volume ratio (*gray*) and mean shrinkage 6 months after treatment (*white*) for different sizes of fibroids. For all groups of fibroids (independent of size) it was possible to achieve nonperfused volume ratio of at least 50%, yet larger nonperfused volume ratios (> 60%) were achieved in management of smaller fibroid volumes. *n* = number of fibroids.

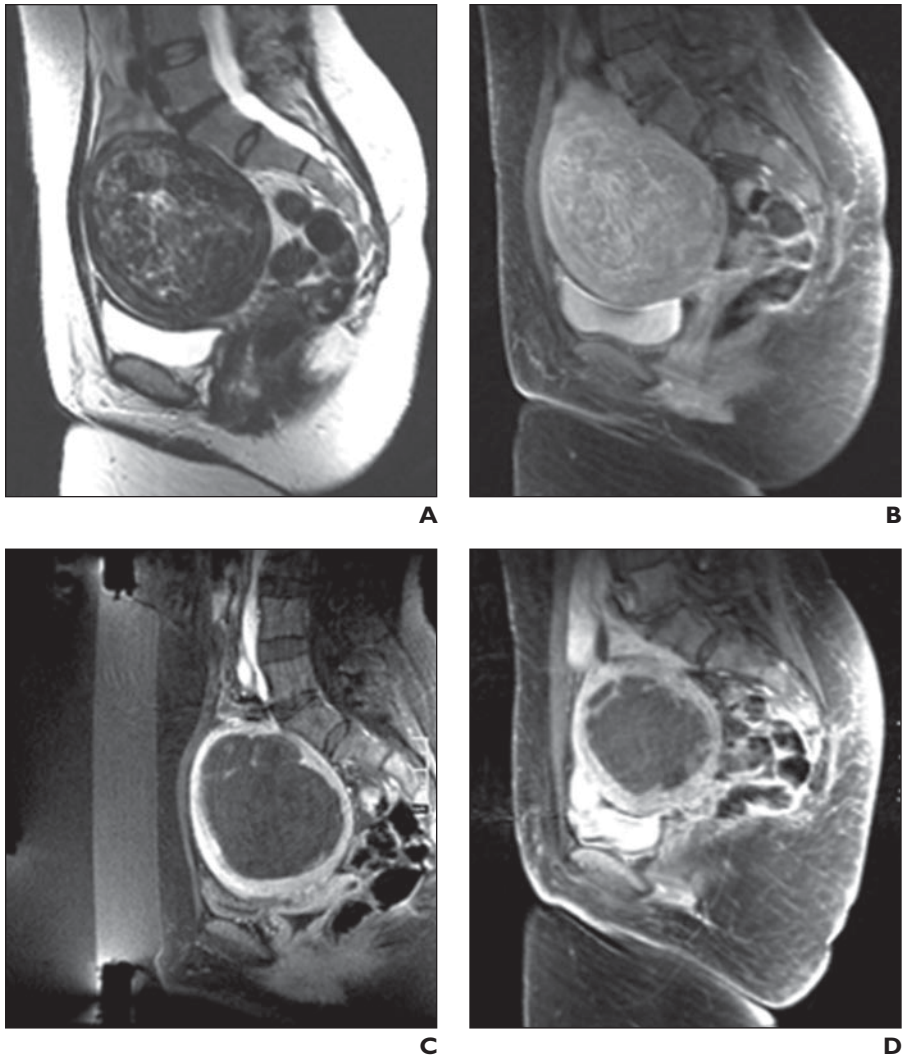

Fig. 4—53-year-old woman with 348-cm^3 fibroid.
A, Sagittal T2-weighted MR image obtained before treatment shows predominant hypointensity with striated hyperintense regions.
B, Sagittal contrast-enhanced fat-suppressed MR image before treatment shows homogeneous enhancement.
C, Sagittal contrast-enhanced fat-suppressed MR image after treatment shows 94% nonperfused volume ratio.
D, Contrast-enhanced fat-suppressed sagittal MR image obtained at 6-month follow-up examination shows 47% shrinkage with residual necrotic cavity that resulted in further shrinkage on later images.

to uterine muscle respond slightly less well, and T2-hyperintense fibroids and those larger than 10 cm should be pretreated with leuprolide acetate to enhance the sensitivity to thermal ablation and decrease fibroid volume to optimize the nonperfused volume ratio.

A limitation of this retrospective analysis was that shrinkage was not correlated with an objective measure of improvement in patient symptoms. Other studies, however, have established a significant correlation between nonperfused volume ratio and symptomatic improvement and the need for additional fibroid treatment [18, 24]. The need for additional treatments after MRI-guided focused ultrasound ablation by itself is an important indicator of the efficacy of the procedure. Eight of the 80 patients in this study needed hysterectomy within 1 year of treatment. Six of them were, in retrospect, not ideal candidates for the procedure and had a nonperfused volume ratio less than 15%. Two of the six patients had too many fibroids (> 10), one patient was found to have adenomyoma rather than a fibroid, and three patients had highly vascular fibroids that were hyperintense on T2-weighted images. The other two patients had nonperfused volume ratios greater than 50%, but one needed surgery for bladder prolapse and underwent concurrent hysterectomy, and the other chose hysterectomy because of insufficient symptom relief. Therefore, among the 49 patients who had a nonperfused volume ratio greater than 50%, which is considered technical success, only one needed hysterectomy because of incomplete symptom relief.

Further studies should be performed to investigate whether there is a correlation between fibroid location, initial symptoms (menorrhagia, dysmenorrhea, pelvic pressure, urinary frequency and urgency), and outcome. Although clinical symptoms were not studied because pretreatment symptom scores were not collected, our results are useful for validating that, as in UAE, fibroids do shrink after MRI-guided focused ultrasound and that the greater the nonperfused volume ratio, the greater is the shrinkage. For patients with symptoms that may be alleviated by a reduction in fibroid volume, MRI-guided focused ultrasound ablation is a viable and noninvasive outpatient procedure, if the patient is a suitable candidate.

The procedure-related complications included two minor skin burns that resolved with topical cream. One of these patients had a cesarean section scar and moved during treatment, intermittently placing the scar in and out of the beam path; the other patient had a burn in the shape of the adhesive that was used to secure a vitamin E pill over an unusually high inguinal hernia scar. One patient with a posterior fibroid had mild temporary sciatica. One patient with a submucosal intramural 10-cm fibroid had endometritis 6 weeks after the procedure that ultimately necessitated hysterectomy. It is unclear whether incomplete management of a yeast infection immediately before the onset of endometritis led to the endometritis or whether the endometritis was a procedure-related complication. There have been no published reports of this complication of MRI-guided focused ultrasound treatment.

Additional questions that arise from our work relate to other factors that influence thermal ablation and shrinkage of uterine fibroids after contrast-enhanced treatment. These factors include initial fibroid vascularity, hormone levels, and the metabolic rate of tissue growth within the fibroid. Further studies addressing these questions will provide important insight into optimizing shrinkage outcomes for patients with uterine fibroids.

This retrospective analysis showed that 6 months after treatment, more than 30% fibroid shrinkage can be achieved with MRI-

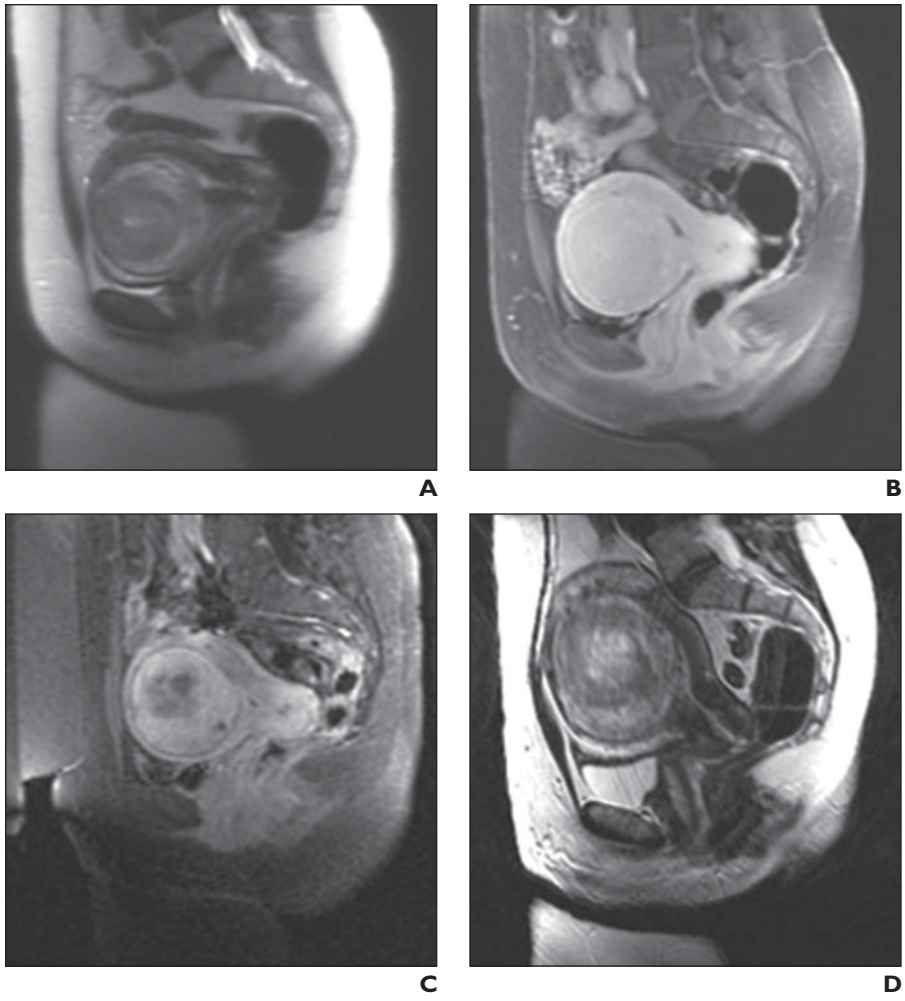

Fig. 5—Woman with 130-cm^3 fibroid.
A, Sagittal T2-weighted MR image obtained before treatment shows hyperintense signal in periphery of fibroid.
B, Sagittal contrast-enhanced fat-suppressed MR image before treatment shows homogeneous enhancement.
C, Sagittal contrast-enhanced fat-suppressed MR image obtained after MRI-guided focused ultrasound treatment shows minimal 7% nonperfused volume ratio.
D, Sagittal T2-weighted MR image obtained at 6-month follow-up examination shows no shrinkage.

guided focused ultrasound ablation treatment performed according to current guidelines. This study also showed statistically significant correlation between nonperfused volume ratio and fibroid shrinkage. The results suggest that greater fibroid volume reduction after treatment can be achieved with a greater nonperfused volume ratio. MRI-guided focused ultrasound should be considered a safe and viable treatment option for symptomatic uterine fibroids in suitable patients who want fibroid shrinkage.

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References

1. FDA Office of Women's Health. Fibroids. U.S. Food and Drug Administration Website. http://www.fda.gov/downloads/ForConsumers/ByAudience/ForWomen/ucm121872.pdf. Accessed September 28, 2009
2. Walker CL, Stewart EA. Uterine fibroids: the elephant in the room. *Science* 2005; 308:1589–1592
3. Parker WH. Uterine myomas: management. *Fertil Steril* 2007; 88:255–271
4. Fennessy FM, Tempany CM. MRI-guided focused ultrasound surgery of uterine leiomyomas. *Acad Radiol* 2005; 12:1158–1166
5. Parker WH. Etiology, symptomatology, and diagnosis of uterine myomas. *Fertil Steril* 2007; 87:725–736
6. Somigliana E, Vercellini P, Daguati R, Pasin R, De Giorgi O, Crosignani PG. Fibroids and female reproduction: a critical analysis of the evidence. *Hum Reprod Update* 2007; 13:465–476
7. Edwards RD, Moss JG, Lumsden MA, et al. Uterine-artery embolization versus surgery for symptomatic uterine fibroids. *N Engl J Med* 2007; 356: 360–370
8. Stewart EA. Uterine fibroids. *Lancet* 2001; 357: 293–298
9. Pinto I, Chimeno P, Romo A, et al. Uterine fibroids: uterine artery embolization versus abdominal hysterectomy for treatment—a prospective, randomized, and controlled clinical trial. *Radiology* 2003; 226:425–431
10. Broder MS, Goodwin S, Chen G, et al. Comparison of long-term outcomes of myomectomy and uterine artery embolization. *Obstet Gynecol* 2002; 100:864–868
11. Lumsden MA. Embolization versus myomectomy versus hysterectomy: which is best when? *Hum Reprod* 2002; 17:253–259
12. Pron G, Mocarski E, Bennett J, et al. Tolerance, hospital stay, and recovery after uterine artery embolization for fibroids: the Ontario Uterine Fibroid Embolization Trial. *J Vasc Interv Radiol* 2003; 14:1243–1250
13. Hindley J, Gedroyc WM, Regan L. MRI guidance of focused ultrasound therapy of uterine fibroids: early results. *AJR* 2004; 183:1713–1719
14. Stewart EA. Magnetic resonance imaging-guided focused ultrasound: no panacea, but nevertheless a safe step forward. *Fertil Steril* 2006; 85:49
15. Stewart EA, Rabinovici J, Tempany CM. Clinical outcomes of focused ultrasound surgery for the treatment of uterine fibroids. *Fertil Steril* 2006; 85:22–29
16. Chapman A, Ter Haar G. Thermal ablation of uterine fibroids using MR-guided focused ultrasound: a truly non-invasive treatment modality. *Eur Radiol* 2007; 17:2505–2511
17. Fennessy FM, Tempany CM. A review of magnetic resonance imaging-guided focused ultrasound surgery of uterine fibroids. *Top Magn Reson Imaging* 2006; 17:173–179
18. Stewart EA, Gostout B, Rabinovici J, Kim HS, Regan L, Tempany CM. Sustained relief of leiomyoma symptoms by using focused ultrasound surgery. *Obstet Gynecol* 2007; 110:279–287
19. Stewart EA, Gedroyc WM, Tempany CM, et al. Focused ultrasound treatment of uterine fibroid tumors: safety and feasibility of a noninvasive thermoablative technique. *Am J Obstet Gynecol* 2003; 189:48–54
20. Funaki K, Fukunishi H, Funaki T, Sawada K, Kaji Y, Maruo T. Magnetic resonance-guided focused ultrasound surgery for uterine fibroids: relationship between the therapeutic effects and signal intensity of preexisting T2-weighted magnetic resonance images. *Am J Obstet Gynecol* 2007; 196:184e1–184e6

21. Morita Y, Ito N, Hikida H, Takeuchi S, Nakamura K, Ohashi H. Non-invasive magnetic resonance imaging-guided focused ultrasound treatment for uterine fibroids: early experience. *Eur J Obstet Gynecol Reprod Biol* 2008; 139:199–203
22. Fennessy FM, Tempany CM, McDannold NJ, et al. Uterine leiomyomas: MR imaging-guided focused ultrasound surgery—results of different treatment protocols. *Radiology* 2007; 243:885–893
23. Smart OC, Hindley JT, Regan L, Gedroyc WM. Magnetic resonance guided focused ultrasound surgery of uterine fibroids: the tissue effects of GnRH agonist pre-treatment. *Eur J Radiol* 2006; 59:163–167
24. Smart OC, Hindley JT, Regan L, Gedroyc WG. Gonadotrophin-releasing hormone and magnetic-resonance-guided ultrasound surgery for uterine leiomyomata. *Obstet Gynecol* 2006; 108:49–54
25. McDannold N, Tempany CM, Fennessy FM, et al. Uterine leiomyomas: MR imaging-based thermometry and thermal dosimetry during focused ultrasound thermal ablation. *Radiology* 2006; 240:263–272
26. Pron G, Bennett J, Common A, Wall J, Asch M, Sniderman K. The Ontario Uterine Fibroid Embolization Trial. Part 2. Uterine fibroid reduction and symptom relief after uterine artery embolization for fibroids. *Fertil Steril* 2003; 79:120–127
27. Yoon SW, Lee C, Cha SH, et al. Patient selection guidelines in MR-guided focused ultrasound surgery of uterine fibroids: a pictorial guide to relevant findings in screening pelvic MRI. *Eur Radiol* 2008; 18:2997–3006