Technical Developments

MR Imaging–guided Focused Ultrasound Surgery of Uterine Leiomyomas: A Feasibility Study

The feasibility and safety of magnetic resonance (MR) imaging–guided focused ultrasound surgery for uterine leiomyomas is reported. Sequential sonications were delivered to nine targets. Temperature-sensitive phase-difference MR imaging monitored the location of the focus and measured tissue temperature elevations, ensuring therapeutic dose. MR images and hysterectomy specimens were evaluated. Six leiomyomas received full therapeutic doses, and 98.5% of the sonications were visualized. MR imaging-guided focused ultrasound causes thermocoagulation and necrosis in uterine leiomyomas and is feasible and safe, without serious consequences.

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Focused ultrasound surgery is an attractive method of noninvasive thermal ablation. The ultrasound beam penetrates through soft tissues and can be focused to target sites causing localized high temperatures (55°C–90°C) for a few seconds. As a result, well-defined areas of protein denaturation, irreversible cell damage, and coagulative necrosis are produced, while overlaying and surrounding tissues are spared.

Lynn et al investigated the potential surgical application of focused ultrasound over 5 decades ago (1). Since then, therapeutic ultrasound has been tested extensively for noninvasive surgery in both animals and humans (2–4). During the past 2 decades, clinical trials of focused ultrasound for noninvasive surgery of the prostate and other sites have been conducted with use of diagnostic ultrasonography (US) for localization and targeting (5). Although the use of a focused ultrasound beam for the ablation of malignant tumors has been shown to be promising, its widespread acceptance has been limited because of the lack of precise target definition and the difficulty in controlling the focal spot position and beam dosimetry without a temperature-sensitive imaging method.

Magnetic resonance (MR) imaging can satisfy these requirements of focused ultrasound therapy (7–11). It has excellent anatomic resolution for targeting, high sensitivity for localizing tumors, and temperature sensitivity for online treatment monitoring. Several MR imaging parameters are temperature sensitive, and the one based on the proton resonant frequency allows relatively small temperature elevations to be detected prior to any irreversible tissue damage (12). Thus, the location of the focus can be detected at relatively low powers, and the accuracy of targeting can be verified. In addition, by using calibrated temperature-sensitive MR imaging sequences, focal temperature elevations and effective thermal doses may be estimated (13,14). Such thermal quantification allows online feedback to verify that the treatment is safe, by ensuring that the focal heating is confined to the target volume and is below the level for boiling, and effective, by verifying that the temperature history is sufficient to ensure thermal coagulation.

The technical feasibility of performing focused ultrasound surgery with MR imaging to guide and monitor the therapy has been established in animal experiments (14–16). Clinical feasibility has been demonstrated with benign and malignant tumors of the breast (17–19). Adequacy of
Leiomyomas are very common, causing a range of clinical symptoms from severe bleeding to minor discomfort (24). Treatment options include hysterectomy, myomectomy, uterine artery embolization, and hormonal therapy. Thermal ablation of uterine leiomyomas with percutaneous interstitial laser therapy or cryoablation has been investigated as a potential minimally invasive treatment (25–27). Focused ultrasound, which delivers thermal energy without the need to insert a probe, has the potential to become a fully noninvasive choice for selected patients. The purpose of this study was to test the feasibility and safety of MR imaging-guided focused ultrasound surgery for treatment of benign leiomyomas of the uterus.

1 Materials and Methods

This was a prospective phase I/II study approved by our institutional review board, and all patients gave informed consent after the nature of the focused ultrasound procedure was explained to them.

Patients

The eligibility criteria for enrollment were as follows: adult women (age greater than 18 years), premenopausal status with a uterine size of less than 20 weeks, and no dominant leiomyoma larger than 10 cm in diameter. All had symptomatic leiomyomas requiring treatment and were scheduled for elective hysterectomy for treatment of them. We enrolled nine women (age range, 39–51 years; mean age, 43.4 years) with symptomatic leiomyomas who agreed to undergo MR imaging-guided focused ultrasound surgery prior to the surgical excision of their leiomyomatous uterus. The hysterectomy was to be performed 3–30 days after the focused ultrasound procedure. They all agreed to undergo pre- and posttreatment MR imaging. Pregnant women and women with standard MR imaging contraindications were excluded from the study.

Pretreatment Image Planning

All women underwent pretreatment MR imaging with a standardized protocol including T2-weighted imaging and T1-weighted imaging before and after administration of gadopentetate dimeglumine (dose, 0.1 mmol per kilogram of body weight) (Magnevist; Berlex Laboratories, Wayne, NJ). MR images helped define the leiomyomas for size, volume, location, and presence of enhancement after administration of gadopentetate dimeglumine. They were also used to plan the beam path and to ensure that each targeted leiomyoma was in an accessible location. Because the focused ultrasound beam is delivered through the anterior abdominal wall with the patient lying prone, it was important to evaluate the images for possible obstacles to treatment, such as bowel loops between the leiomyoma and the anterior abdominal wall. These images were used to determine which leiomyoma could be treated safely. If there were multiple leiomyomas in safe locations, the larger one was selected. The goal of this treatment was to safely induce thermocoagulation that could be demonstrated at pathologic examination.

All MR imaging examinations were performed with a 1.5-T standard whole-body system (Signa; GE Medical Systems, Milwaukee, Wis), with the patient lying prone. Standard T2-weighted fast spin-echo (SE) images were obtained in three planes through the uterus by using either a body coil or an external multicoil array. Initial localization T2-weighted images with large field of view were acquired to localize the transducer, uterus, and leiomyomas (Fig 1). Typical parameters used for the T2-weighted fast SE sequence were as follows: 4–5,000/90–120, field of view of 160–250 mm, matrix size of 256 × 192, three data acquisitions, section thickness of 4 mm, with 1-mm gap, and bandwidth of 16 kHz. Then T1-weighted SE MR imaging (600/20, field of view of 160–250 mm, matrix size of 256 × 128, four data acquisitions, section thickness of 4 mm, with 1-mm gap) was performed. For contrast material–enhanced images, multiphase fat-suppressed T1-weighted spoiled gradient-recalled-echo MR imaging started soon after intravenous injection of gadopentetate dimeglumine. Pre- and posttreatment follow-up MR images were obtained according to the same protocol.

Equipment

Sonications were performed with a clinical MR imaging–compatible focused ultrasound system (ExAblate 2000; InSightec-TxSonics, Haifa, Israel) that is based on experience with an earlier clinical system and included improvements in transducer design, real-time MR thermometry feedback, and volumetric planning (28,29). A focused piezoelectric transducer array with 120-mm diameter and operating frequency between 1.0 and 1.5 MHz generated the ultrasound field. The array was located in the MR imaging table in a water tank. It could electronically control the location of the focal spot and the volume of the coagulated tissue volume. Lateral motion of the transducer was achieved with a mechanical positioning device (28,29). A thin plastic membrane window covered the water tank and allowed the ultrasound beam to propagate into the patient’s pelvis.
Treatment

The patients were evaluated and an informed consent was obtained for the use of anesthesia, especially for intravenous conscious sedation. Prior to treatment, a history and physical examination was performed, and informed consent was obtained according to hospital guidelines. Prior to coming to the hospital, the patients were asked to shave the hair from the anterior abdominal wall down to the pubic crest. On the morning of the procedure, the patients came to the radiology department after fasting, with a companion to escort them home. The patient was instructed to empty her bladder, and an intravenous catheter was placed for administration of sedatives. The goal of sedation was to reduce pain and prevent any motion. This was achieved by using either oral antianxietyotics, such as diazepam, or intravenous conscious sedation with intravenous fentanyl citrate and midazolam hydrochloride. The patients who received conscious sedation were monitored during the procedure by a nurse, who regularly measured heart rate, blood pressure, and oxygen saturation level.

The decision to use intravenous conscious sedation was based on the patient’s comfort while lying prone during the initial MR imaging examination and on whether she experienced joint pain, such as shoulder or neck pain. During the procedure, the patient was asked to report any symptoms, especially pain or heat. These were reported to the nurse in the room and to the radiologist at the treatment console outside the room. Similarly, at the end of the procedure, the patient was asked to rate her overall discomfort and any pain on a four-point scale (0 = no pain, 1 = mild pain, 2 = moderate pain, and 3 = severe pain). These data were collected and recorded by the study research assistant.

We measured and recorded the length of each procedure in two ways: overall time in the MR imaging room and sonication and actual treatment times.

The patient was positioned in the magnet lying prone on the focused ultrasound device (Fig 1). The anterior abdominal wall was placed over the water tank, which contained the transducer and a custom-made receive-only pelvic coil (USA Instruments, Aurora, Ohio) mounted on top. The coil consisted of two parts: a fixed surface-coil base and a flexible coil that was wrapped around the patient.

In most cases, the acoustic coupling between the patient and the water in the positioner was achieved by placing a thin (2–4-cm-thick) gel pad (Parker Laboratories, Fairfield, NJ) on top of the positioner under the pelvis. The gel was flexible and contoured around the pelvic wall under its weight. A layer of degassed water was poured on top of the gel. In some cases, a degassed water pillow was placed on top of the gel. This pillow was necessary for the thinnest patients when the fibroid was inferiorly located and the gel pad was insufficient to contour to the pelvic wall.

Pretreatment MR imaging was performed with T2-weighted fast SE imaging in three orthogonal planes. Then the radiologist (C.M.C.T.) outlined the volume to be treated within the leiomyoma, on the basis of a selected section from the coronal T2-weighted images, by using the system software. The same radiologist and two physicists (K.H., N.M.) performed the treatment of all patients in this study. The volume was then visualized in two imaging planes, usually coronal and sagittal. The software in the system allowed display of the ultrasound beam overlaid on all tissues through which it would pass (Figs 1, 2). This allowed evaluation of all tissues or structures in the beam path. Care was taken to avoid any possible contact with bowel loops. If necessary, the beam could be repositioned or even tilted to optimize the path (Fig 2).

After an appropriate volume was selected, the sonication plan was developed in the computer. In this initial plan, equally spaced overlapping focal volumes were placed such that the entire target was covered. Positioning of the focal sonications was selected such that the induced tissue coagulation would induce complete coverage in the selected volume. The volume to be treated can be calculated by measuring the volume of the sonication cylinder on the basis of the size of the focal spot (range, 4.3–6.0 mm) and the spot length (range, 18.0–28.0 mm). Locations of the planned sonications were modified interactively during the treatment by the operator to obtain complete MR thermometry-derived thermal dose and complete coverage of the target volume. In each treatment, all the sonications were at the same depth (ie, only one plane was sonicated). The locations of the planned sonications were also monitored interactively and were changed if any motion occurred during the examination.

Before the therapy-level sonications, low-energy test pulses were aimed within the target volume. The power was then increased until the location of the focus was visible on the temperature-sensitive images. These sonications were below the level for thermal tissue damage and were used to align the coordinates of the focused ultrasound system with the MR coordinates. When the test pulse was located in the planned position, the complete target volume was then sonicated with a series of higher power pulses such that adequate temperature and thermal dose was reached. The pulse duration was generally 16 seconds, and the interval between pulses was generally 3 minutes. These times were used to allow cooling of the tissues between each thermal treatment. During each treatment, we re-

Figure 2. Patients 3 and 4. Transverse (left, patient 3) and sagittal (right, patient 4) T2-weighted fast SE MR images (2,500/98) with the patient in position for ultrasound surgery of uterine fibroids. In these cases, the transducer was angled during the treatment. The arrow on the right indicates the bowel loop that was avoided by angling the transducer.
corded the number of sonications delivered, the number that were visible on MR temperature maps, and the number that were analyzable, as well as the power used and the changes in temperature.

**Temperature Monitoring with MR Imaging**

Temperature elevations during the 16-second sonications were monitored across the focal plane by obtaining temperature-sensitive MR images before, during, and after each sonication. Phase imaging was used to estimate the temperature-dependent proton resonant-frequency shift and was performed with a fast spoiled gradient-recalled-echo sequence (30). The following imaging parameters were used: 39.9/19.7; flip angle, 30°; bandwidth, 3.57 kHz; matrix, 256 × 128; field of view, 28 cm; and section thickness, 3–5 mm. Five to 10 images were obtained in a series, with a total acquisition time of 26–52 seconds. The first image was triggered 5 seconds prior to the start of the sonication. The MR imager was programmed to reconstruct the magnitude and both the real and imaginary images for each of these time points. The real and imaginary parts were used to calculate the phase difference between the two time points (30).

The temperature dependence of the proton resonant frequency has been shown to be linear above the coagulation threshold (29,31,32). To judge the adequacy of treatment, the MR imaging–derived temperature information was analyzed and the temperature-time history for each image voxel was calculated. The peak temperature and thermal dose derived from the MR images was used as a guide to ensure that adequate powers were delivered to coagulate the target tissue. The power level was set after the initial localization pulse by increasing the power and repeating the sonications in the central area of the tumor. The power was kept constant at each sonication level unless MR thermometry indicated that the temperatures were too low or that the thermal dose coverage was insufficient. In the latter case, the power was increased for all the remaining sonications.

**Posttreatment Follow-up**

After the treatment, the patient was discharged and returned within 72 hours for a follow-up clinic visit and MR imaging. At the follow-up clinic visit, any complications were noted, as well as postoperative complications after the hysterectomy. These were evaluated by the obstetrician/gynecologist (E.A.S.). MR imaging was performed in the same way as was initial pretreatment MR, again with gadopentate dimeglumine, to allow direct image comparison.

**Posttreatment Image Analysis**

The volumes of the treated leiomyomas were calculated by assuming the volume \( v \) of a prolate ellipsoid with the equation \( v = \frac{4}{3} \pi \times a \times b \times c \), where \( a \), \( b \), and \( c \) are the diameter in three orthogonal directions as measured on T2-weighted images.

All the images were compared simultaneously by the same radiologist (C.M.C.T.) for the size of the leiomyoma and especially for any changes in contrast enhancement within the leiomyoma. All new regions of nonenhancement were measured carefully, and size and volume were calculated. The volume of the nonenhancing area was calculated in two ways: first, with the standard measurement shown previously, and second, with a three-dimensional computed volume (Fig 3). The latter was performed with three-dimensional software (3D Slicer [33, available at www.slicer.org]), with which the radiologist manually contoured all the nonenhancing areas on all relevant sections, and the total volume was calculated by summing all the voxels included. The same radiologist calculated all MR-based volumes. Sagittal spoiled gradient-recalled-echo images acquired immediately after injection of the contrast agent were used for this calculation. The patient then underwent hysterectomy as planned.

**Pathologic Analysis**

After removal of the uterus, the radiologist (C.M.C.T.) and pathologist (B.J.Q.) met, reviewed the MR images together and, if necessary, examined the specimens to ensure identification of the treated leiomyoma. The specimens were examined to identify the target leiomyoma, the approximate path of the ultrasound energy, and other landmark features. Initial gross inspections focused on comparing the serosa in the ultrasound beam with untreated serosa. After thorough external gross examination, specimens were cut at 0.5-cm intervals in planes perpendicular to an axis defined by the uterine cavity. All cut surfaces were examined grossly for necrosis, hemorrhage, and edema, and any other unusual pathologic findings. All targeted tumors were grossly identified, and then the following gross and histologic parameters were noted: the extent of necrosis, hemorrhage, calcification, hyalinization, or inflammation and the histologic leiomyoma subtype. Representative samples of serosa, myometrium, and endometrium in the treated path, as well as remote from the treated volume, were also evaluated for histologic abnormalities.

**Results**

Eight of the nine patients underwent surgery. The mean age of our patients was 43.4 years; all had symptomatic leiomyomas and were planning to undergo hysterectomy. An overview of the nine patients and the leiomyomas is given in
Radiology

bowel loops were interposed between the could not be treated because multiple were no serious consequences. Patient 3 temperature at the focal point increased resulted in local heating after the peak scar. The scar tissue caused increased los- pain was located in a prior abdominal wall. In patient 5, the initial treatment was stopped when she experienced no surgery: No adverse event
First-degree skin burn

Six of the nine patients received full focused ultrasound therapy with the entire planned thermal dose delivered (Table 2). In the remaining three patients, the treatment plan could not be executed fully. In patient 1, the treatment was stopped when she experienced pain in the anterior abdominal wall. The pain was located in a prior abdominal scar. The scar tissue caused increased local ultrasound beam absorption, which resulted in local heating after the peak temperature at the focal point increased by 10.8°C, with resulting pain. There were no serious consequences. Patient 3 could not be treated because multiple bowel loops were interposed between the target in the uterus and the anterior abdominal wall. In patient 5, the initial low-power sonifications (radio-frequency power range, 55–150 W) could not be visualized on the temperature maps; therefore, the procedure was stopped. The most likely reason for this failure was that the US coupling was lost below the US gel pad after numerous repositionings.

Six patients (patients 2, 4, 6–9) underwent complete treatments, with all sonifications successfully monitored and delivered as planned (Figs 2, 4, 5). On the day of the treatment, therapy planning on the basis of T2-weighted MR images was feasible in all cases. An example is shown in Figure 5, with the planning target volume outlined in a plane perpendicular to the ultrasound beam. Posttreatment images in sagittal and transverse planes clearly show the well-defined nonenhancing area of treatment in the center of the leiomyoma (Fig 5). The number of sonifications in all cases ranged from six to 31 (mean, 20.6 sonifications). The number planned and delivered is related to the volume of tissue to be treated. In the six cases, 130 sonifications were delivered to the tissue, and 98.5% of the sonifications or hot spots were visualized. In these patients, 100% of the visualized sonifications were analyzable for temperature, which meant that the image quality was adequate to obtain the temperature history.
and to estimate the peak temperature increase and the thermal dose (Table 2). In these cases, the measurements of temperature increase over time were analyzed for the hottest voxel at the focal spot. An example of the average peak temperature increase as a function of time for one of these treatments (patient 8) is given in Figure 6. The temperature increase in these six cases ranged from a minimum of 6.3°C to a maximum of 55.4°C, with an overall mean (maximum) increase of 29.5°C. The mean temperature increases ranged from 9.2°C to 35.7°C. In the six patients who received the full therapeutic dose, MR thermometry depicted the temperature changes, with a mean range of 15.3°C–35.7°C.

Details for the length of the procedure are as follows: The room times ranged from 3 hours 19 minutes to 4 hours 55 minutes. The overall treatment times ranged from 1 hour to 2 hours 32 minutes. We also calculated the sonication time, defined as the time from the first to the last sonication, which ranged from 32 to 135 minutes. In five patients, the actual treatment plan was redrawn during the procedure as a result of target motion secondary to bladder filling. This caused a procedure delay ranging from 20 to 66 minutes.

Of the nine patients treated, seven received intravenous conscious sedation with both midazolam hydrochloride and fentanyl, and two received oral diazepam. In patient 1, the treatment was stopped because she experienced pain in her skin scar. In the group who received conscious sedation, the average score for pain was 1.7 and for overall discomfort was 1.5. The two patients who were treated with diazepam both rated pain and overall discomfort as 2. All patients went home after a short observation time, and none reported any clinically important symptoms at the 72-hour posttreatment visit.

Patients 2 and 8 experienced minor skin burns, with blisters in the anterior abdominal wall that corresponded to the treatment beam. In one of these patients, there was a vertical midline scar in the lower pelvis. After hysterectomy, three patients had fevers (34). The fever was from an unknown cause in patient 2, was secondary to vaginal cuff cellulitis in patient 4, and was a result of a urinoma in patient 6. This latter patient had an ipsilateral endometrioma and adhesions that were also removed at surgery. At this time, as a precaution, the study protocol was amended to include administration of antibiotics.

Figure 4. Patient 8. Treatment planning, monitoring, progression, and posttreatment follow-up. A, Coronal T2-weighted fast SE MR image (4,000/90) was used for treatment planning. Sonication locations and sizes (green lines) were determined with the system planning software from this prescription (and the tissue depth) and were displayed on top of the treatment plan. During treatment, the accumulated thermal dose (yellow area) was displayed on top of treatment planning images. Dose threshold of 240 equivalent minutes at 43°C is displayed. B, Sagittal T2-weighted MR image (2,500/98) shows treatment plan and area that achieved threshold thermal dose. C, D, Temperature-sensitive phase-difference fast spoiled gradient-recalled-echo MR images (39.9/19.7) were acquired at peak temperature increase during two sonications. C (coronal view) was acquired perpendicular to the direction of the ultrasound beam, while D (sagittal view) was acquired parallel to the direction of the beam. C and D were used to estimate the thermal dose (blue line) for each sonication. E, F, Images depict result of treatment. E, Sagittal contrast-enhanced gradient-recalled-echo MR image (245/1.8) was acquired 2 days after ultrasound surgery. Nonenhancing area (arrow) is seen clearly in F, which is a gross pathologic cut specimen that shows the central area of hemorrhagic necrosis.
of antibiotics before the focused ultrasound procedure. On the basis of the contrast-enhanced T1-weighted images, six (67%) of the total of nine lesions, or six (100%) of the six fully treated lesions, showed discrete areas of decreased contrast material uptake, which implied successful treatment. Decreased contrast material uptake implied tissue devascularization and necrosis (Figs 3, 5). In five of these patients, we were able to obtain pathologic confirmation of the presence of necrosis in the corresponding locations. Pathologic analysis showed gross evidence of necrosis and hemorrhage in these five patients (Figs 3, 5). The sixth patient did not undergo hysterectomy before the end of the study.

We compared the pathologic volumes of necrosis and hemorrhage with the planned treatment volumes and the non-enhancing tissue volumes depicted on MR images (Table 3). In four cases, both MR-based volumes and pathologic volumes were greater than the planned treatment volumes. In case 6, the pathologic volume was larger than all the other volumes. In case 4, the pathologic and MR-based volumes were less than the treatment volumes. This case was also the one in which the lowest mean temperature increase was recorded (15.3 °C), and it was one of the cases in which a very small volume of tissue was targeted for treatment (4.9 cm$^3$). It should also be noted that the pathologic findings showed three small (≤1 cm) and separate areas of necrosis, as were seen on the contrast-enhanced MR images. Both the treatment volumes and MR-based treated tissue volumes were calculated in two ways, which resulted in different volumes in all cases. The range of differences was quite wide in cases 2, 4, and 6 but was less in cases 7–9.

**Discussion**

MR imaging-guided focused ultrasound therapy is a completely noninvasive local thermal ablation method (11). The feasibility for the treatment of benign fibroadenomas of the breast has already been demonstrated (17). In this article, we describe the first clinical trial of MR imaging–guided and –monitored focused ultrasound surgery for uterine leiomyomas.

Results of our study show that noninvasive treatment of uterine leiomyomas with MR imaging-guided focused ultrasound surgery is both feasible and safe, without marked adverse effects. The results also demonstrate the advantages of combining a noninvasive focused ultrasound technique with MR imaging in a clinical setting. Furthermore, we show that MR imaging is suitable for both focused ultrasound treatment planning.

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**Figure 5. Patient 9.** A, Planning coronal T2-weighted fast SE (4,000/90) MR image shows the treatment plan. Inset shows sagittal view. B, Gross specimen shows central necrosis after focused ultrasound treatment. Inset photomicrograph shows microscopic view of treated area, with microscopic hemorrhagic necrosis in the right corner. (Hematoxylin-eosin stain.) C, D, Contrast-enhanced MR images show central area (arrow) of nonenhancement. C, Sagittal gradient-recalled-echo MR image (195/1.8) was acquired 2 days after treatment. D, Transverse SE MR image (600/14) was acquired 2 days after treatment.

**Figure 6. Patient 8.** Line graph depicts temperature measured at the focus for 23 sonications in one treatment. The focal temperature increase was sufficient to cause thermal damage in each case. The variation from location to location was significant. Error bars = SD, dotted line = baseline body temperature (37°C).
and delineation of focused ultrasound beam–induced tissue changes in uterine leiomyomas.

MR imaging is ideal for localization and targeting. The most important feature of MR imaging with respect to focused ultrasound therapy, however, is its ability to localize focal sonications or hot spots and to measure temperature and dose during treatment. This ability of MR imaging allows monitoring of both the efficacy and safety of focused ultrasound. The proton resonant-frequency shift is temperature dependent in leiomyomatous tissue. The temperature history during the sonications could be obtained in 100% of the sonications (Table 2) by using the triggered series of phase images to monitor the temperature elevation. All the treatment focal spots were visible and analyzable for temperature in the serial phase-difference images in all cases, which confirmed that the correct target was sonicated and treated in every instance. In patient 5, the initial sonications were not visualized; thus the treatment was not performed. We speculate that this was a result of poor coupling.

The temperature change was calculated by subtracting that in the phase before the sonications from that in the phase during the sonications to obtain the temperature elevation. Any patient or tissue motion can be easily detected by monitoring the difference in signal in voxels outside the sonicated volume; therefore, the operator can avoid using motion-distorted temperature values. Focused ultrasound therapy could benefit from thermal mapping sequences that would be less motion sensitive, although even the tested sequences worked adequately for treatment-monitoring purposes. The magnitude images were particularly helpful in the monitoring of the volume of the bladder and any resulting uterine motion. It should be noted that in this phase I/II trial, we did not place a Foley catheter in the bladder. The lack of a Foley catheter accounts for a procedure delay in the five patients who required repeat drawing of the treatment plan as a result of uterine shift. It is hoped that this delay can be avoided by placing a Foley catheter prior to the procedure.

Treatment was completely successful in six of the nine lesions. Success was judged on the ability to visualize the sonications and the temperature history. It was also based on the contrast-enhanced T1-weighted images showing focal areas of partial or complete lack of contrast material uptake, implying devascularization and tissue necrosis. This nonenhancement is similar to that found in various histologic studies of focused ultrasound effects in animals in vivo (35–37,40). These contrast changes were present after the treatment. In five of these six patients, findings at pathologic examination confirmed the presence of necrosis. The sixth patient, for whom the surgery was rescheduled several times, did not undergo hysterectomy before the end of the study period. In four patients, the MR imaging–calculated nonenhancing volumes and the pathologic volumes were larger than the treatment volumes. One likely explanation is that the focused ultrasound beam caused coagulation of a blood vessel, which resulted in downstream necrosis (38). Two sets of volume measurements were obtained (three-axes calculated volumes and three-dimensional computed volumes) from both the prescribed volumes and the posttreatment MR-based ablated volumes or nonenhancing tissue volumes. We obtained the three-dimensional volumes because we believe, on the basis of prior work (41), that this approach is the most accurate way to calculate the volume of an imaging finding. In the present study, the three-dimensional measurements were generally closer to the pathologic volumes than were the three-axes measurements. This is not surprising because the three-dimensional method involves delineation of each nonenhancing area, regardless of shape and size, on all relevant MR images. The three-axes measurements may result in overestimation of the volume because they are more general and are made with the assumption that the lesion is the shape of a prolate ellipse.

Therapy in patient 1 resulted in tissue hypercellularity but not necrosis, as described previously, as a result of insufficient power that resulted in below-threshold temperatures after the treatment was stopped because of the patient’s pain in her scar. Thermal dose maps derived from MR thermometry verified the subthreshold exposures. No nonenhancing tissue was seen on the posttreatment MR images. Findings in this case and in the other six cases demonstrate the way posttherapy MR imaging can be used to ensure that the desired end result has been achieved, which will provide a surrogate marker of treatment effect. The ultimate measure of focused ultrasound effect will be the change, if any, in the patient’s symptoms.

The use of continuous-wave ultrasound phased-array technology reduced the treatment time significantly compared with that with the previous single-element transducer (39,40). This has made the treatment of clinically important large leiomyoma possible. The treatment time for these relatively small volumes of tissue was relatively short, which was acceptable, with eight patients tolerating the entire procedure well and only one patient terminating prematurely as a result of pain. We hope to reduce the procedure time further by avoiding repeat planning during treatment.

The present study is limited because it was a feasibility study with a small number of patients. We were not able to correlate the treatment effect with any change in symptoms. The study is also limited because we did not treat large volumes of tissue in each leiomyoma. Our goal was to treat enough tissue to allow direct MR and pathologic visualization. Thus, the treatment volumes varied from patient to patient, depending on

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Note.—Standard measurement of three axes = d1 × d2 × d3 × 0.525.
the leiomyoma size and the access route. Further study is warranted, especially after these promising preliminary results. Future studies will require treatment of more patients, larger volumes, and careful evaluation for safety and outcomes. In the next prospective trial, we will use focused ultrasound therapy as the primary treatment, and we will follow the patient’s symptoms as a measure of treatment effect. One important lesson we will learn during this upcoming trial will be the way to select the symptomatic leiomyoma(s) to target for treatment.

The other important question not addressed in the present study is the way results with focused ultrasound therapy will compare with those with other available therapies, such as uterine artery embolization (42). We believe that patients with mild to moderate symptoms from their leiomyomas will be more likely to seek focused ultrasound therapy, which is relatively painless, less invasive, and more localized.

In summary, in the present study, we successfully performed clinical MR imaging-guided focused ultrasound surgery for uterine leiomyomas. The surgery can noninvasively cause thermocoagulation that results in necrosis of uterine leiomyomas. MR Imaging provided excellent guidance for treatment planning and direct monitoring of treatment delivery and thermal changes in the sonicated tissue. On the basis of the small number of patients studied to date, the focused ultrasound surgery used in this trial with women with symptomatic uterine leiomyomas appears to be feasible and safe, without serious consequences. MR imaging-guided focused ultrasound surgery can be recommended for further testing as an alternative to currently available therapies, such as surgery or uterine artery embolization, for treatment of uterine leiomyomas.

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References