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Uterine Leiomyomas: MR Imaging– based Thermometry and Thermal Dosimetry during Focused Ultrasound Thermal Ablation¹

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Abstract

Purpose—To retrospectively evaluate magnetic resonance (MR) imaging–based thermometry and thermal dosimetry during focused ultrasound treatments of uterine leiomyomas (ie, fibroids).

Materials and Methods—All patients gave written informed consent for the focused ultrasound treatments and the current HIPAA-compliant retrospective study, both of which were institutional review board approved. Thermometry performed during the treatments of 64 fibroids in 50 women (mean age, 46.6 years $\pm$ 4.5 [standard deviation]) was used to create thermal dose maps. The areas that reached dose values of 240 and 18 equivalent minutes at 43°C were compared with the nonperfused regions measured on contrast material–enhanced MR images by using the Bland-Altman method. Volume changes in treated fibroids after 6 months were compared with volume changes in nontreated fibroids and with MR-based thermal dose estimates.

Results—While the thermal dose estimates were shown to have a clear relationship with resulting nonperfused regions, the nonperfused areas were, on average, larger than the dose estimates (means of 1.9 ± 0.7 and 1.2 ± 0.4 times as large for areas that reached 240- and 18-minute threshold dose values, respectively). Good correlation was observed for smaller treatment volumes at the lower dose threshold (mean ratio, 1.0 ± 0.3), but for larger treatment volumes, the nonperfused region extended to locations within the fibroid that clearly were not heated. Variations in peak temperature increase were as large as a factor of two, both between patients and within individual treatments. On average, the fibroid volume reduction at 6 months increased as the ablated volume estimated by using the thermal dose increased.

Conclusion—Study results showed good correlation between thermal dose estimates and resulting nonperfused areas for smaller ablated volumes. For larger treatment volumes, nonperfused areas could extend within the fibroid to unheated areas.

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See Materials and Methods for pertinent disclosures.

Abbreviation

V_{TD} = percentage of fibroid volume that reached thermal dose of at least 18 minutes at 43°C

Quantitative magnetic resonance (MR) imaging–based temperature mapping based on the temperature dependence of the water proton-resonance frequency shift (1) has been extensively tested in animals as a method of monitoring thermal ablation therapies such as focused ultrasound. The temperature dependence of the water proton-resonance frequency shift is approximately -0.01 ppm per degree Celsius (2). This thermometry method is unique among the current temperature imaging methods in that it does not appear to depend on the (nonfat) tissue type (3) or change owing to thermally induced tissue effects (4). Standard MR imaging sequences can be used to acquire the temperature maps (1). The main limitations of this method are its sensitivity to motion and its lack of sensitivity in fat tissue (5). Quantitative temperature monitoring has been shown in animals to be useful at all stages of thermal ablation therapies, from visualization of subthreshold heating (for targeting) (6) to prediction of threshold values for thermal damage (for safety monitoring) (7) and prediction of the extent of tissue that will receive a lethal thermal dose (for therapy guidance) (8).

Advances in Knowledge

- The results of quantitative MR imaging–based thermal imaging and thermal dosimetry indicated a large variation in the temperature distribution per sonication, both between patients and within single treatments.
- The acoustic parameters were compensated online on the basis of the imaging findings so that thermal necrosis could consistently be achieved without boiling.
- Although thermal dose predictions strongly correlated with nonperfused tissue areas, good agreement was seen for only the smaller treatment volumes and at a thermal dose threshold of 18 minutes at 43°C.
- For the larger treatment volumes, the nonperfused regions were largely underpredicted with use of the dose estimates.

While the results of several studies have demonstrated the feasibility of using this thermometry method in humans during thermal therapies (9–15), no large group of patients has been available for the evaluation of this method and the testing of its capability in the prediction of the extent of the ablated area. Since 2001, women with uterine leiomyomas, or fibroids, have been treated in a prospective multicenter clinical trial with MR imaging–guided focused ultrasound surgery. Although there have been initial reports of some discussion of temperature monitoring, these accounts have been dedicated primarily to relaying the feasibility, safety, and effectiveness of MR-guided focused ultrasound for treatment of uterine fibroids (14,16,17). These treatments provide a first-time opportunity to evaluate the use of proton-resonance frequency shift–based temperature imaging and thermal dosimetry in a large number of patients. Thus, the purpose of this study was to retrospectively evaluate MR imaging–based thermometry and thermal dosimetry during focused ultrasound for treatment of uterine leiomyomas (ie, fibroids).

Materials and Methods

Patients

All patients gave written informed consent for the MR-guided focused ultrasound treatments and our Health Insurance Portability and Accountability Act–compliant retrospective study, both of which were institutional review board approved. Authors who were not consultants to

InSightec (Haifa, Israel), the manufacturer of the ultrasound ablation system (ExAblate 2000) used in this study, had control over the inclusion of any data that might have posed a conflict of interest for those authors who have been consultants to InSightec (C.M.T., E.A.S., F.A.J., K.H.).

Data on the consecutive treatments performed in 50 women (mean age, 46.6 years $\pm$ 4.5 [standard deviation]; range, 37–58 years) with 64 fibroids were analyzed. Twenty-four women were patients at our institution who had also been part of a recently completed multicenter nonrandomized clinical trial (17), which also was Health Insurance Portability and Accountability Act compliant and institutional review board approved. The remaining patients were the first 26 individuals who were treated at our institution as part of a subsequent trial involving the use of identical enrollment criteria and treatment protocols. Inclusion criteria were as follows: pre-menopausal women older than 18 years, symptomatic fibroids that would otherwise be treated with other conventional therapy, no plans for future pregnancies (a negative pregnancy test result was required on the day of MR-guided focused ultrasound), raw symptom severity score higher than 21 at completion of the uterine fibroid symptoms—quality of life questionnaire (18), and fibroid diameter greater than 2–3 cm but not greater than 10 cm. The volume of fibroid targeted depended on the location of the fibroid with respect to the serosal and mucosal borders of the uterus and our ability to stay within the safety margins specified by the Food and Drug Administration.

Exclusion criteria were as follows: contraindications to MR imaging, fibroid diameter greater than 10 cm, uterus size larger than the uterus size at week 24 of pregnancy, other pelvic or uncontrolled systemic disease, excessive abdominal scarring, change in oral contraceptive within 3 months before MR-guided focused ultrasound, change in nonsteroidal preparations within 3 months before MR-guided focused ultrasound, patient inability to communicate with researchers during MR-guided focused ultrasound, and MR imaging screening findings of adenomyosis alone, no identifiable fibroids, inaccessible fibroids (because scar tissue, bone, bowel, or bladder was completely blocking the path of the ultrasound beam), or fully necrotic or degenerating fibroids.

MR-guided Focused Ultrasound Treatments

The goal of the treatments was the ablation of a subvolume of the fibroid (within protocol limits, description to follow) to reduce the tumor volume and provide symptom relief. Additional technical and clinical details of these treatments are published elsewhere (14,16, 17). All patients were treated on an outpatient basis. They had fasted since the midnight before the treatment and shaved the anterior abdominal area. On arrival, they gave informed consent for intravenous conscious sedation. Then, intravenous and urinary catheters were inserted. The urinary catheter ensured that the bladder did not fill and move the fibroid during treatment. Conscious sedation—induced with oral antianxiolytics, including diazepam, intravenous fentanyl citrate, and/or midazolam hydrochloride titrated to the patient's symptoms—enabled the patient to remain awake and responsive. She could pause or halt the treatment by pressing a button if she experienced severe pain or heating during any sonication. The patient lay prone on the treatment table; acoustic coupling to her bare skin was achieved by using degassed deionized water and a gel pad. The treatments were performed by six authors (N.M., C.M.T., F.M.F., M.J.S., F.J.R., K.H.).

For treatment planning, T2-weighted MR images were acquired (Table 1) and transferred to a user interface, where the radiologist (C.M.T., F.M.F., M.J.S., F.J.R.) then prescribed the desired treatment volume. When more than one fibroid was present, the criteria for selecting which one(s) to treat were based on (a) the gynecologist's and the radiologist's best estimate of which fibroid(s) was most likely responsible for the patient's symptoms and (b) the fibroid(s) determined to be accessible with the treatment device (ie, it was not blocked by scars, bone,

bowel, or bladder). The ultrasound beam path for each sonication was examined to ensure that the treatment was safe with respect to scars, bladder, bowel, and bone. In addition, the skin was outlined on the treatment-planning images (by N.M. or K.H.) by using ExAblate 2000 software. The depth from the skin of the sonication targets was used by this software to estimate the acoustic parameters to use at the start of the treatment. After treatment planning, low-power (initially below the thermal threshold for tissue damage) sonications were performed to ensure accurate targeting of the focal coordinate in three dimensions.

The parameters for the treatment sonications—specifically, target location, acoustic power, sonication frequency, and focal volume—were initially determined by the ultrasound ablation system (ExAblate 2000) on the basis of acoustic and thermal model findings and were modified online on the basis of temperature mapping results. In addition, feedback from the patient was used to change these parameters if the sonications caused discomfort. This discomfort was typically a heat sensation in the skin or pain in the buttocks, in the lower back, or radiating down the legs, presumably from heating in the sacral plexus. There were no serious adverse events related to the use of the ultrasound ablation device. Four patients reported having transient leg or back pain during treatment, and two had unrelated postoperative complications: Bell palsy more than 60 days after treatment and hemorrhagic ovarian cyst with pain 3 weeks after treatment.

All of the sonication targets were prescribed at one depth in a single plane. Individual sonication locations and/or the entire plan was then modified according to the following criteria, which were defined on the basis of consultation with the Food and Drug Administration: The target volume was limited to 100 cm³ per fibroid (150 cm³ per treatment), and the treatment time was limited to 3 hours. A 1.5-cm margin of nontargeted tissue had to be maintained at both the serosal and mucosal borders of the uterus. In some treatments, sonications were performed in overlapping locations; in others, they were performed in a sparse pattern with spaces of a few millimeters between the treated sites (19). Sparse-pattern targets were typically chosen for treatments in which we desired to maximize the extent of fibroid tissue that could be targeted within the described time frame, such as treatments of large or multiple fibroids.

Phase-difference fast spoiled gradient-echo MR imaging was used to construct the temperature images (1). For construction of phase maps, the MR imaging unit (GE Signa) was programmed to save complex data instead of only the typical magnitude image data (20) (Table 1). The proton-resonance frequency shift was estimated by dividing the value for the phase changes by 2π times the time that the phase developed (ie, the echo time of the imaging sequence). A time-based series of temperature images acquired in a single imaging plane was used to calculate maps of the thermal dose, a measurement originally developed during hyperthermia research that is a conversion of an arbitrary temperature trajectory to a temperature trajectory expressed in an equivalent number of minutes of constant heating at 43°C. Herein, this dose value is reported in minutes (21). A complex phase subtraction scheme (20) and pair-wise image subtraction (22) were used to avoid phase wrapping.

Immediately following treatment, coronal T1-weighted fast spoiled gradient-echo MR images were acquired before and after injection of an MR imaging contrast agent (Table 1). After contrast agent administration, transverse T1-weighted spin-echo MR images were acquired. Approximately 6 months (mean, 183 days $\pm$ 13 [standard deviation]) after treatment, this imaging protocol was repeated.

Treatment Devices

The ExAblate 2000 system was used to perform focused ultrasound ablation. This system consists of a phased-array transducer (208 elements, frequency of 0.96–1.14 MHz), a computer-controlled positioning system, a multichannel radiofrequency amplifier system, and

a user interface. All of these components are integrated with a standard 1.5-T clinical MR imaging unit (GE Signa). The lateral position and angle of the transducer were mechanically controlled, and the focusing depth and size of the focal zone were controlled by the phased array with beam steering. Imaging was performed with a custom pelvic coil (USA Instruments, Aurora, Ohio). The system automatically prescribed and started the temperature-sensitive imaging sequence.

Data Measurement

The peak temperature achieved with every sonication was recorded. To estimate the noise and stability of the thermometry, we also recorded the apparent temperature change in four regions of interest (3×3 voxels) in unheated areas close to the heated zone. For each treatment, maps of the total accumulated thermal dose produced by all of the sonications were generated in a coronal plane at the center of the targeted volume. When transverse or sagittal imaging was performed, the dose in the coronal plane was estimated from the mean temperature in a 3-mm-wide strip centered at the correct depth; cylindrical symmetry was assumed. Total areas that reached dose thresholds of at least 240 and 18 minutes were calculated. These thresholds were previously found in animals to be the value above which tissue damage always occurs (240 minutes) and the estimated value associated with a 50% probability for necrosis (18 minutes) (22,23). In addition, we approximated the total volume that reached these thresholds by multiplying the calculated area by the length of a dose contour at sagittal or transverse MR imaging for a typical sonication (typically about 3 cm).

The nonperfused regions seen on contrast material-enhanced MR images were manually segmented in the central coronal plane closest to the coronal plane used for the thermal dosimetry analysis. No grading scheme was used. Fibroid volumes were measured on T2-weighted images immediately before and 6 months after treatment by using three perpendicular length measurements and assumed an elliptical shape. Sixteen patients had at least one additional nontreated fibroid; one of the largest of these fibroids was measured in each of these patients. All data measurements and analyses were performed by one author (N.M.) by using software developed in house for Matlab (Mathworks, Natick, Mass). A radiologist (M.J.S.) checked the fibroid volume measurements for accuracy.

Data Analyses

The percentages of all sonications that reached 55°C, a therapeutic temperature, and 94°C, the temperature 2 standard deviations of noise away from boiling, were calculated (with a body temperature of 37°C assumed). All patients and sonications were included in this analysis, the aim of which was to examine how well the temperature was controlled. To investigate the variation in peak temperature increase across treatments, five patients with similar sonication parameters (ie, same treatment frequency, duration, and phased-array pattern, and at the same treatment depth within 7 mm) were identified. The temperature increase was scaled on the basis of the acoustic power so that the measurements could be compared. This scaling was justified because the ultrasound propagation was linear with the tightly focused transducer, power levels, and treatment durations that were used (24).

The areas in the central coronal plane that reached thermal doses of at least 240 and 18 minutes were compared with the areas that contained nonperfused regions. Four fibroids were excluded because they had preexisting nonperfused regions at MR imaging screening (two from prior MR-guided focused ultrasound treatments). The percentage fibroid volume change after 6 months was compared with the percentage of the fibroid volume that reached a thermal dose of at least 18 minutes (V_{TD}). For this comparison, the V_{TD} values were divided into three groups: values of greater than or equal to 0 but less than 20%, values of greater than or equal to 20% but less than 40%, and values of greater than or equal to 40% but less than 60%. The

percentage fibroid volume change after 6 months was also compared with the percentage nontreated fibroid volume change. One additional patient with a treated fibroid was excluded from this analysis because she received hormonal therapy after undergoing MR-guided focused ultrasound. One nontreated fibroid was excluded because it was found to be entirely nonperfused at MR imaging screening.

Statistical Analyses

The Bland-Altman method (25) was used to compare the areas that reached thermal dose thresholds of 18 and 240 minutes with the corresponding nonperfused areas. In addition, linear regression analysis was performed and correlation coefficients were calculated. Bias between measurements was tested by using a paired two-tailed Student *t* test. Unpaired two-tailed Student *t* tests were used to compare percentage fibroid volume changes among different percentages of treated fibroid. Paired two-tailed Student *t* tests were used to perform the comparisons described in Table 2. For absolute volume measurements (ie, not measurements of percentage change), log-normalized data were used owing to nonnormal distributions; in such cases, data were reported as nontransformed units. Data normality was verified by using the Kolmogorov-Smirnov test. Artifacts, such as those caused by patient motion, and noise at temperature imaging were quantified per fibroid by measuring the absolute value and the standard deviation, respectively, in the unheated regions of interest in the temperature maps.

Results

Temperature Analysis

In every treatment, the temperature distribution during sonication—even that during low-power subthreshold sonications—was clearly visible at thermometry (Fig 1). Substantial variation in the peak temperature increase was observed, both between patients and within single treatments (Fig 2). In the extreme cases, the peak value varied by more than a factor of two. For most sonications, the spatial temperature distribution was shaped as expected, but the magnitude of the heating varied. However, during some sonications, the shape of the temperature distribution was different from that expected owing to events that could be clearly determined from temperature imaging (Fig 3).

Due to these variations and feedback from the patients and to achieve sufficient heating, the acoustic parameters often were modified from those prescribed by the treatment planning software. The mean peak temperature achieved during the 3077 sonications delivered during 64 treatments was $67.9^{\circ}\text{C} \pm 10.5$ (standard deviation). During 2762 (89.8%) sonications, a peak temperature greater than or equal to 55°C was achieved. A temperature of 94°C (the value 2 standard deviations of noise away from boiling) or higher was achieved during only 25 (0.8%) sonications.

Nonheated regions of interest in the temperature maps had a mean standard deviation of $2.9^{\circ}\text{C} \pm 1.0$ (range, 1.4° – 8.5°C). When the ultrasound was being applied, the mean standard deviation was $3.0^{\circ}\text{C} \pm 1.1$; when the ultrasound was not being applied, the mean standard deviation was $2.8^{\circ}\text{C} \pm 1.0$. The absolute apparent temperature change measured in the unheated regions of interest in the temperature maps was $1.2^{\circ}\text{C} \pm 0.4$ (mean $\pm$ standard deviation) and ranged from 0.6°C to 2.4°C .

Thermal Dosimetry Analysis

Nonperfused regions were detected in 63 of the 64 treatments and were wholly contained within the targeted fibroids. In only the one unsuccessful case did the thermal dose not reach 240 minutes. The sonications produced either contiguous or spotty distributions of thermal dose at the two thresholds tested (18 and 240 minutes) (Fig 4). However, in most treatments,

contiguous nonperfused areas were observed, with some larger treatments extending to areas clearly not heated at all. In other, smaller volume treatments, the outline of the nonperfused area matched the outer boundary of the spotty thermal dose distribution.

These observations were evident when all of the thermal dose and nonperfused area measurements were compared (Fig 5). While there was good correlation ($R = 0.88$ and $R = 0.89$ for thresholds of 240 and 18 minutes, respectively) between the two measurements overall, in some—mostly larger volume—treatments, the nonperfused area was larger and deviated from a linear relationship. The area of nonperfused regions was larger on average than the dose prediction. For the 240-minute threshold, the mean nonperfused area-to-thermal dose area ratio was 1.9 ± 0.7 (range, 0.8–3.7; limits of agreement, 0.5–3.2). For the 18-minute threshold, this mean ratio was 1.2 ± 0.4 (range, 0.4–2.5; limits of agreement, 0.4–2.0). For smaller treatment volumes, there was good agreement between the two measurements for areas that reached the 18-minute threshold. For example, for areas 10 cm^2 or smaller, the mean nonperfused area-to-thermal dose area ratio was 1.0 ± 0.3 . For this subset of areas, the difference between measurements was not significant ($P = .46$).

Fibroid Volume Analysis

At 6 months, the mean volume of the treated fibroids had decreased (Table 2). The volume reduction depended on the MR imaging–based thermal dose volume estimate (Fig 6), although considerable variation was observed: The only significant difference among the V_{TD} groups tested was that observed at comparison of the V_{TD} greater than or equal to 0% but less than 20% treatment group ($n = 33$) and the V_{TD} greater than or equal to 40% but less than 60% treatment group ($n = 8$) ($P < .05$). Large variations in volume reduction were also observed among the nontreated fibroids. The difference in percentage fibroid volume change after 6 months between the treated and nontreated fibroids was significant ($P < .05$) for all V_{TD} groups tested. This difference was also significant ($P < .05$) when comparing the volume changes of all of the pairs of treated and nontreated fibroids within the individual patients by using a paired Student t test.

Discussion

Other than the overall underprediction of the nonperfused area based on thermal dose estimates for the larger treatment volumes and the lower dose threshold needed for agreement of these values for smaller treatment volumes, the study results were in general agreement with those of the large body of animal studies of thermal ablation methods that have shown good correlation between MR imaging–based thermometry or dosimetry values and the resulting thermally induced tissue effects (8,21,22,26–31). A conservative dose threshold of 240 minutes, while correlating strongly, led to substantial underprediction of the size of the resulting nonperfused area. These results agree with those of previous studies of MR-guided focused ultrasound treatment of uterine fibroids, in which it was found that the prescribed treatment volume was an underprediction of both the resulting nonperfused volume and the volume of tissue necrosis seen at pathologic analysis (14,16,17). However, in animals, there typically is good agreement between areas that reach a 240-minute dose threshold and the resulting thermally ablated areas, and differences between 240-minute dose estimate and lower dose estimate results typically are small. There are several possible explanations for the difference between our results and those of previous animal studies, none of which have been validated yet. In our opinion, the most likely explanation from a physiologic standpoint is that vascular occlusion caused the underpredictions.

By this, we mean that occlusion of a vessel caused the downstream necrosis of nontreated tissue. Such enhancement of a nonperfused region was clearly evident in the larger treatment volumes—since regions that were not directly heated became nonperfused—and possibly was

the cause of the underpredictions overall. As to why this effect was observed in our study and not in animal experiments, it could be that vascular occlusion is more likely to occur inside a tumor, where the pattern of the vasculature can differ strongly from that in normal tissue.

It could be, alternatively, that there is a more pronounced effect when the treatment volume is large. In animal experiments, smaller tissue volumes—either entire volumes in normal tissue, such as muscle, or volumes in implanted tumors with surrounding rims of normal tissue—typically are ablated. In the current study, the entire treatment region and resulting nonperfused area were always contained within the fibroid. If occlusion was the explanation for the enlarged nonperfused areas, then it may be useful as a future treatment strategy when it is further understood in this setting.

A second explanation could be that the temperature measurements at the edge of each focal zone were underestimated owing to the large imaging field of view required. At the edge of the focal zone, temperature gradients were sharp, so the temperature may have been more underestimated there owing to averaging effects and more so in this investigation than in the animal studies, in which smaller fields of view were possible.

Another explanation could be that the ultrasound focus was more diffuse in our study; this could explain the difference between the 240- and 18-minute dose areas. The treatments were deep and passed through multiple tissue structures and interfaces, which can diffuse the beam (32). Also, a small degree of tissue motion (on the order of 1 mm) occurred during sonication and caused the heated region to broaden over time. In comparison, the animal examinations were performed in anesthetized animals, without deep penetration through multiple tissue layers.

It is also possible that thermal buildup occurred over the course of the treatments and was not detected at MR thermometry. It is well known that low-level residual heat can accumulate after sonications when they are performed at multiple neighboring locations—mainly those in the beam path in front of the focal zone—and result in a treatment volume larger than that prescribed (33). Because proton-resonance frequency shift–based MR thermometry can depict temperature changes only, such buildup possibly occurred without our knowledge, despite the fact that the delay between sonications (~2 minutes) was considered conservative (ie, adequate for cooling). Finally, it could be that the temperature sensitivity of the proton-resonance frequency shift is different in fibroids or that the thermal threshold for fibroid damage in humans is lower than that for normal animal tissue damage.

A limitation of this study was the inherent uncertainty in the mapping of the temperature rise and the thermal dose. This uncertainty stems from noise, uncertainty in the temperature sensitivity of the proton-resonance frequency, volume-averaging effects, small motion artifacts, and our estimation of coronal thermal dose distributions from transverse and sagittal imaging. There was additional uncertainty regarding the ablated volume estimates, because we approximated the length of the ablated areas. Moreover, although the growth rate of fibroids is expected to be relatively small, a nonzero value probably confounded our attempts to compare the fibroid volume changes with the dosimetry estimates. Such growth might partly explain the large variation we observed.

In conclusion, the results of quantitative MR imaging–based thermal imaging and thermal dosimetry indicated a large variation in the temperature distribution, both between patients and within single treatments. The acoustic parameters were compensated online on the basis of the imaging findings so that thermal necrosis could be achieved without boiling. Although thermal dose predictions strongly correlated with nonperfused tissue areas, good agreement was seen for only the smaller treatment volumes and at the 18-minute dose threshold. For the larger treatment volumes, the nonperfused regions were largely underpredicted with use of the dose

estimates. We suspect that vascular occlusion caused the increased size of these nonperfused regions, although other factors could have been involved. MR imaging–based dosimetry volume estimates and fibroid volume reductions at 6 months were related, but substantial variations were seen.

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Figure 1.

Temperature-sensitive phase-difference fast spoiled gradient-echo (40/20 [repetition time msec/echo time msec], 30° flip angle) MR images acquired during sonications to ensure correct targeting of focal coordinate. *A* and *C* were acquired before focal coordinate was corrected; *B* and *D* were acquired after correction. *A, B*, First, sonications were performed with temperature imaging in the coronal plane, or perpendicular to direction of the ultrasound beam. *C, D*, Next, sonications were performed with imaging orientation sagittal or transverse, parallel to the ultrasound beam direction. Target locations are indicated by a circle in *A* and *B* and by a rectangle in *C* and *D*.

Figure 2.

Left: Graph illustrates mean temperature increase as a function of time for all sonications performed during five separate treatments. Right: Graph illustrates mean temperature increase as a function of time for the individual sonications performed during a single treatment. For each sonication, the measured temperature increase was detected in a 3×3 -voxel region centered on the hottest voxel. Each temperature profile was scaled on the basis of the acoustic power levels used so that they could be compared with one another. Inset in left graph illustrates the mean peak temperature increase values achieved ($\pm$ standard deviation). Actual acoustic power levels were 117–195 W (mean, 172.3 W $\pm$ 24.7) for patient 1, 116–160 W (mean, 146.5 W $\pm$ 20.1) for patient 2, 130–145 W (mean, 140.0 W $\pm$ 7.3) for patient 3, 110 W for patient 4, and 100–160 W (mean, 131.3 W $\pm$ 20.3) for patient 5.

Figure 3.

Normal and atypical heating distributions observed on temperature-sensitive phase-difference fast spoiled gradient-echo (40/20,30° flip angle) MR images. *A*, Normal heating distribution. *B*, Temperature distribution when boiling or cavitation occurred. *C*, Temperature distribution when the ultrasound beam was focused on a blood vessel or fluid-filled region (gap near center of region of heating). *D*, Temperature distribution when sonication of a calcified fibroid (patient treated in a later study) was performed. In all examples, imaging was performed parallel to the direction of the ultrasound beam.

Figure 4.

Three typical examples of (left) areas that reached thermal dose values of at least 240 and 18 minutes and (right) corresponding posttreatment contrast-enhanced T1-weighted fast spoiled gradient-echo MR images (200/1.8, 80° flip angle). The thermal dose was estimated from temperature-sensitive image findings. Imaging was performed perpendicular to the direction of the ultrasound beam (coronal). On the dose images (left), areas that reached a thermal dose of at least 240 minutes are red and areas that reached a thermal dose of at least 18 minutes are white.

Figure 5.

Top: Scatterplots illustrate comparison between the areas in the central coronal plane of the treatments that reached thermal dose values of 240 (left) and 18 (right) minutes and the corresponding nonperfused areas at contrast-enhanced MR imaging performed immediately after the treatments. Linear regression of the data yielded correlation coefficients of 0.88 and 0.89 for the 240- and 18-minute dose thresholds, respectively. The line indicates unity. Bottom: Corresponding Bland-Altman plots of the ratio of the two area measurements (thermal dose and MR perfusion) as a function of the average of the two measurements. Shaded areas indicate limits of agreement (mean ratio $\pm$ 1.96 standard deviations). Solid lines indicate ratio of 1.

Figure 6.

Graph illustrates fibroid volume reduction 6 months after treatment as a function of the estimated percentage of the fibroid volume that was treated (ie, V_{TD}). The treated volume was estimated from the MR imaging–based thermal dose estimates; the 18-minute threshold was used for these estimates. The mean volume change ($\pm$ standard deviation) for 15 fibroids in the patient group that were not treated with focused ultrasound also is shown.

Table 1

MR Imaging Parameters

Sequence*	Repetition Time (msec)	Echo Time (msec)	Flip Angle (degrees)	Echo Train Length [†]	Field of View (cm)	Matrix Size	Section Thickness (mm)	Bandwidth (kHz)	Imaging Plane (s)
T2-weighted fast SE	3000–6950	99–104	90	12–16	20–28	256 × 224	5–6	31	Sagittal, transverse, coronal
T1-weighted fast SPGR	150–325	1.5–1.8	80	NA	20–30	256 × 160	5–6	31–42	Coronal
T1-weighted SE	500–850	8–14	90	NA	20–30	256 × 224	5–6	16–31	Transverse
Phase-difference fast SPGR	40	20	30	NA	28	256 × 128	3	3, 6	Sagittal, transverse, coronal [‡]

* All MR imaging examinations were performed at 1.5 T with a GE Signa MR unit (GE Medical Systems, Milwaukee, Wis). T2-weighted fast spin-echo (SE) imaging was performed for treatment planning, and phase-difference fast spoiled gradient-echo (SPGR) imaging was performed for temperature analysis. T1-weighted examinations were performed with gadopentetate dimeglumine (Magnevist, 0.1 mmol per kilogram of body weight; Berlex Laboratories, Wayne NJ) enhancement.

[†] NA = not applicable.

[‡] During sonication, temperature analysis imaging was performed in a single plane, which was selected by the operator (N.M. or K.H.) and could be varied between sonications.

Table 2

Patient Information

Datum	Value
Total no. of patients	50
Patient age (y) [*]	46.6 ± 4.5 (37–58)
No. of treated fibroids	64 [†]
No. of nontreated fibroids	16 [‡]
Body mass index [*]	25.9 ± 5.7 (18.6–43.9)
No. of fibroids treated per patient [§]	
One	37
Two	12
Three	1
Fibroid location ^{//}	
Submucosal	7
Intramural	55
Subserosal	2
Volume of treated fibroids (cm ³) [#]	
Before ultrasound	151.1 (22.5–1067.8)
6 mo after ultrasound	132.8 (13.4–1087.5)
Volume of nontreated fibroids (cm ³) [#]	
Before ultrasound	33.5 (12.7–162.0)
6 mo after ultrasound	36.9 (13.1–188.8)

^{*} Mean value ± standard deviation. Numbers in parentheses are the range.

[†] Four treatments were excluded from dosimetry analysis because of nonperfused areas observed at MR imaging screening. An additional patient was excluded from fibroid volume analysis because she received hormonal treatment after MR-guided focused ultrasound. All treated fibroids were assessed at temperature analysis.

[‡] Sixteen patients had at least one additional fibroid that was not treated. Volume changes were measured in 15 of these fibroids, one of which was excluded because it was entirely nonperfused at MR imaging screening.

[§] Based on the total of 50 patients.

^{//} Based on a total of 64 treated fibroids.

[#] Mean volumes before and 6 months after MR-guided focused ultrasound. Numbers in parentheses are ranges. Seventeen of 59 treated fibroids and 11 of 15 nontreated fibroids increased in size after 6 months. The difference between the treated fibroid volumes measured before and those measured 6 months after focused ultrasound was significant ($P < .05$). The difference between the nontreated fibroid volumes measured before and those measured 6 months after focused ultrasound was nonsignificant ($P = .15$).