Published in final edited form as:

J Magn Reson Imaging. 2009 March ; 29(3): 649–656. doi:10.1002/jmri.21677.

Proton, Diffusion-weighted Imaging, and Sodium (^{23}Na) MRI of Uterine Leiomyomata after MR-guided High Intensity Focused Ultrasound: A Preliminary Study

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Abstract

Purpose—To determine the feasibility of using combined proton (^1H), diffusion-weighted imaging (DWI), and sodium (^{23}Na) magnetic resonance imaging (MRI) to monitor the treatment of uterine leiomyomata (fibroids).

Materials and Methods—Eight patients with uterine leiomyomata were enrolled and treated using MRI-guided high intensity frequency ultrasound surgery (MRg-HIFUS). MRI scans collected at baseline and post-treatment consisted of T_2 -, T_1 -, and ^1H DWI, as well as post-treatment ^{23}Na MRI. The ^{23}Na and ^1H MRI were co-registered using a replacement phantom method. Regions of interest in treated and untreated uterine leiomyoma tissue were drawn on ^1H MRI and DWI, wherein the tissue apparent diffusion coefficient of water (ADC) and absolute sodium concentrations were measured.

Results—Regions of treated uterine tissue were clearly identified on both DWI and ^{23}Na images. The sodium concentrations in normal myometrium tissue were 35.8 ± 2.1 mmol (mM), in fundus; 43.4 ± 3.8 mM in bladder; and 65.3 ± 0.8 mM with ADC in normal myometrium of $2.2 \pm 0.3 \times 10^{-3} \text{mm}^2/\text{sec}$. Sodium concentration in untreated leiomyomata were 28 ± 5 mM, and were significantly elevated (41.6 ± 7.6 mM $p < 0.05$) after treatment. Apparent diffusion coefficient values in the treated leiomyomata ($1.30 \pm 0.38 \times 10^{-3} \text{mm}^2/\text{sec}$) were decreased compared to areas of untreated leiomyomata ($1.75 \pm 0.36 \times 10^{-3} \text{mm}^2/\text{sec}$; $p = 0.04$).

Conclusion—Multiparametric imaging permits identification of uterine leiomyomata, revealing altered ^{23}Na MRI and DWI levels following non-invasive treatment which provides a mechanism to explore the molecular and metabolic pathways after treatment.

Keywords

magnetic resonance; Diffusion Weighted Imaging (DWI); MRg-HIFUS; high-intensity focused ultrasound; sodium (^{23}Na) MRI; ADC mapping; Uterine leiomyoma

Introduction

Uterine leiomyomata, more commonly referred to as uterine fibroids, are benign, solid masses that arise from the smooth muscle (myometrium) of the uterus. Leiomyomata are more prevalent during the reproductive years, occurring in 20-50% of women with symptoms of menorrhagia or hypermenorrhea (1,2). These tumors can be asymptomatic or present with pelvic pain, and may be associated with dysmenorrhea or pressure, and/or loss of reproductive function. Intervention strategies focus on reducing major symptoms and improving the patient's quality of life (1,2). Hysterectomy is a surgical option that can completely alleviate symptoms. Indeed, uterine leiomyomata are the underlying cause of more than 30% of the 300,000-600,000 hysterectomies performed in the United States per year (2,3). The cumulative risk of a hysterectomy due to leiomyomata for all women between the ages of 25 and 45 is seven percent. While hysterectomy is effective, it is nevertheless a major surgical procedure with life-changing complications that include loss of hormonal and reproductive functions. Therefore, alternative methods for treating uterine leiomyomata are critically needed. (4)

Alternative treatments for benign uterine tumors include less invasive surgical options and/or hormonal manipulation, such as laparoscopic myomectomy, gonadotropin-releasing hormone analogues (GnRHa), radio-frequency ablation (RFA), uterine artery embolization (UAE), and magnetic resonance imaging (MRI)-guided high-intensity frequency ultrasound (MRg-HIFUS) (5-12). After treatment, the radiological challenge is to provide an anatomical and pathophysiological imaging assessment of the treated and surrounding tissue. Current MRI methods of assessment include post-gadolinium T_1 -weighted contrast imaging ($T_1\text{WI}$), wherein successfully treated tissue appears hypointense due to the disruption of tissue blood flow, which limits access of the contrast agent to the treated area (10) and more recently, T_2 -weighted imaging ($T_2\text{WI}$) (12). Funaki, et al, (12) reported that leiomyomata could be classified into treatment categories from the signal intensity values on a $T_2\text{WI}$. However, $T_1\text{WI}$ contrast or $T_2\text{WI}$ MRI provides, at best, only limited pathophysiological information about the endogenous cellular-level environment of the treated tissue and does not provide metabolic or physiologic information of the treated tissue. This limitation can be overcome by using advanced MR methods as described below.

Newer MRI approaches, such as diffusion-weighted imaging (DWI) and sodium (^{23}Na) MRI, can provide radiological pathophysiological information about the molecular-level environments to which they are sensitive. DWI is sensitive to translational motion and changes in the diffusion of endogenous water molecules within the intra- and inter-cellular environments and can reveal disruptions or restrictions to the flow of water within a tissue (13). The apparent diffusion coefficient of water (ADC) is a quantitative biophysical parameter that can be derived from DWI (13). The ADC measures the average rate of

transfer of water molecules across a unit area of a section, which has been shown to change with pathological events, for example, after treatment in uterine leiomyoma (11,14-16). These changes are probably related to subtle changes in the intracellular and interstitial compartments available for diffusion of water protons. Moreover, when using DWI, the T2WI information is captured when the diffusion sensitive gradients are off.

Sodium is very abundant in tissue, second only to water protons and ^{23}Na MRI can interrogate and detect changes of the cellular level sodium concentration within different tissue types after treatment. Specifically, tissue sodium levels can change quite drastically as a result of changes in the ion balance or intra- and extra-cellular volume fractions. Healthy cells maintain large sodium and potassium concentration gradients across the cell membrane via an energy-consuming cation exchange through the $\text{Na}^+/\text{K}^+-\text{ATP-ase}$ reaction and the extracellular space.

Any alteration of the extracellular space or membrane integrity can lead to a failure of the cells to maintain these ion gradients, resulting in a large sodium ion influx from the blood pool, and an increase in tissue intra-cellular sodium and potential expansion of the extracellular space, which will result in increases of the total sodium concentration (17,18).

Therefore, such changes in the total sodium concentration within a tissue can be readily observed with ^{23}Na MRI (19-24). This sensitive indicator of cellular integrity may, therefore, be useful in assessing the therapeutic response to interventions that disrupt cellular structures, such as RFA, UAE, and MRg-HIFUS. Thus, noninvasive DWI and ^{23}Na MRI methods may both have potential value for the molecular assessment of treatment response in uterine leiomyomata.

To date, there have been no published investigations of the combined potential application of sodium MR, DWI, or ADC mapping in the treatment of uterine leiomyomata. Our hypothesis is that ADC mapping and sodium concentrations will demonstrate changes in ablated tissue, and that such changes may serve as useful cellular-level biomarkers of therapeutic response. Therefore, the purpose of this prospective study is to investigate the feasibility of using combined ^{23}Na , DWI, and ADC imaging to noninvasively monitor uterine leiomyoma before and after MRg-HIFUS.

Materials and Methods

Clinical Subjects

Eight patients (age range, 35-55yrs; median age, 44) with symptomatic leiomyomata and one volunteer (age=29) were enrolled into *this prospective study*. Patients were imaged within one week before treatment (baseline) and immediately after treatment. Leiomyomata were identified based on clinical symptoms and characterized at baseline MRI examination several days prior to treatment using T₂-weighted (T2WI), contrast-enhanced T₁-weighted (T1WI) images, and DWI. These leiomyomata were treated with MRg-HIFUS under conscious sedation, during which patients were continuously monitored by a physician (HSK). The IV sedation consisted of *versed* (mean, 3mg; range, 0.5-6) and *fentanyl* (mean, 150 microgram; range, 25-300). Post treatment imaging consisted of T2WI, contrast T1WI,

DWI, and ^{23}Na MRI performed on the same day as treatment. The time taken for a single complete contrast T1WI, T2WI, DWI, and ^{23}Na MRI exam time was approximately 30 min. The efficacy of treatment for (a) ameliorating symptoms, and (b) reducing lesion mass as characterized by MRI, was assessed according to standard clinical criteria (25). Written, informed consent and HIPAA consent were obtained from patients before treatment with this protocol, which was approved by the Institutional Review Board.

Uterine Leiomyoma Treatment Method

Magnetic Resonance Image-guided Focused Ultrasound Surgery (MRg-HIFUS)

—Ultrasound treatment was performed using a modified MRg-HIFUS system (InSightec, Haifa, Israel), coupled with a GE 1.5T MR system (General Electric Medical Systems, Waukesha, WI), and is fully described elsewhere (10). Briefly, the patient was placed on the MRg-HIFUS table with the 120mm diameter ultrasound piezoelectric transducer array operating in the frequency range of 1-1.5MHz in a water tank. The transducer can move along two axes with a mechanical positioning device and tilt up to 18° . To improve acoustic coupling, a thin (2-4 cm thick) gel membrane (Parker Laboratories, Fairfield, NJ) with degassed water was placed between the patient and the transducer. A series of coronal, sagittal, and transverse T2WI fast spin echo (FSE) scans (pulse repetition time [TR]/echo time [TE] = 5000/100ms; echo train length = 12, slice thickness = 4.0mm, 256×100 , field of view = $36 \times 36\text{cm}$) were acquired for calibration and treatment planning.

Calibration was performed to ensure that the patient was properly positioned with the MRg-HIFUS system aligned with the MRI coordinate system. To accomplish this, the transducer and the skin line were outlined by the clinician (HSK), and the expected path of the ultrasound beam was visualized (HSK, MAJ) to avoid injury to sensitive adjacent structures, such as bowels or nerve bundles. The treatment area was outlined within the targeted leiomyoma on an image by a board-certified body radiologist (HSK), as shown in Figure 1. Then, a series of low-power ultrasound sonications were performed interactively and viewed by the radiologist in at least two different planes using real-time MRI to accurately calibrate the unit to MRI coordinate space. For treatment, sonication power was increased to achieve a temperature between $60\text{--}70^\circ\text{C}$. Each ultrasound sonication lasted for approximately 30s, followed by a 60-90s cooling period, during which temperature was monitored by phase-sensitive (PS) MRI (26). Total MRg-HIFUS treatment time ranged from 1-3 hrs and was limited to one treatment by FDA regulations.

Proton (^1H) MRI—During and after treatment, scans were performed in the prone position on a 1.5 T MR scanner, using a dedicated phased array pelvic coil (USA Instruments, Aurora, OH). T_1 fast spoiled gradient refocused echo (FSPGR) phase-sensitive scans (T_1 -PS; TR/TE = 26/13ms, flip angle = 30° , 256×128 points FOV = $28 \times 28\text{cm}$ slice thickness (ST) = 5mm) were acquired after each sonication by MR-gFUS. After treatment, SE-echo planar DWI (TR/TE = 5000/90ms, 128×128 , FOV = $28 \times 28\text{cm}$, ST = 6mm, $b = 500\text{--}1000\text{ s/mm}^2$ on all three axes) and T_1 FSPGR (TR/TE = 185/1.5ms, 256×100 , FOV = 28×28 , ST = 6mm) pre- and four post gadolinium scans were acquired for verification of ablated tissue. Gd-DTPA (0.01 mg/kg, OmniscanTM, Amersham Health Inc., Princeton, NJ, USA) was injected into the antecubital vein, 45 seconds after the start of the scan (pre-

contrast) using an MR-compatible power injector (Medrad, Pittsburgh, PA). The Gd-DTPA bolus was followed by a 20 cm³ saline flush.

Diffusion Weighted Imaging and Data Analysis—MRI analysis was performed using a SUN T2000 server (Sun Microsystems Inc., Mountain View, CA.) and processed using user developed analysis software (27,28). Leiomyomata were identified on ¹H MRI by a board-certified body radiologist (IK). Trace ADC maps were constructed on a pixel-by-pixel basis for quantitative analysis from the DWI according to the equation:

$$ADC = \sum_{i=1}^n \frac{\ln(S_i/S_0)}{b_i} \quad [1]$$

where b_i = the diffusion gradient values, S_0 = 1st image signal intensity ($b=0$), and S_i = i th image signal intensity.

Regions of interest (ROI) were drawn within the leiomyoma on the post-treatment contrast T_1 images as well as on the DWI. Signal intensity levels of non-treated tissues were sampled at least 1-2 cm from hypointense regions on T_1 images, to reduce possible contamination from surrounding treated tissue. ROI image data were obtained from baseline, post-, and untreated uterine tissues. Ratios of the ADC (ADCr) values were calculated by dividing regions of treated tissue by non-treated tissue for each time point and contrast to noise ratios were determined.

Quantitative ²³Na Sodium MRI—For quantitative ²³Na MRI, subjects were repositioned prone after the MRg-HIFUS for the placement of the ²³Na transmit/receive surface coil (25×25cm). Scouts were performed to position the patient in the same orientation of the MRg-HIFUS using anatomical landmarks. The ²³Na surface coil excites a nonuniform B1 field over the volume of interest. Therefore, adiabatic excitation pulses were used to provide a homogeneous excitation flip angle (23). Three tubes filled with 2% aqueous agarose gel and 100 ml NaCl served as fiducial markers and as a calibration reference for determining coil-loading factors. The body coil was used to record ¹H images, which were co-registered with the sodium images in Matlab (Mathworks, Natick, MA) software developed in-house. With this software, intensity level contours are copied between co-registered images to guide the placement of regions of interest (ROI) on the ²³Na images to determine total sodium concentration (TSC) and signal to noise ratio (SNR) and contrast to noise (CNR). A projection imaging sequence was used with a TR of 100ms (> 3 times T_1), an ultrashort TE of 0.2 ms and 400 μs adiabatic excitation pulses. The resolution is 6mm isotropic (0.2 ml voxel volume) with a 22 cm FOV interpolated to 128×128 points by 64 slices (3.4 mm slice and 1.7×1.7mm in-slice resolution). These parameters obviated the need for correcting signals for T_1 and T_2 relaxation when calculating absolute TSC. The TSC in uterine tissue was determined as previously described in breast, brain, and cardiac tissues (21-24). Briefly, separately recorded scans of a polypropylene bag containing 10 liters of 150 mmol/l NaCl solution in water doped with 2g/l CuSO₄ were used as a concentration reference. The method was previously validated for quantitative TSC measurements (23). The noise level in each 3D ²³Na MRI data set was measured in a slice devoid of signal, by averaging the

absolute pixel intensity values over an ROI of 1-2 thousand pixels. All other intensity measures were corrected for noise by subtracting the mean noise value, $\hat{I}_{noise}$, found in this ROI. The standard deviation (SD) of the noise in this ROI, SD_{noise} , was used to calculate the observed SNR for the uterine tissue as:

$$SNR_{tissue} = \frac{\hat{I}_{tissue} - \hat{I}_{noise}}{SD_{noise}} \quad [2]$$

Where $\hat{I}_{tissue}$ is the mean absolute pixel intensity in the tissue ROI.

Total sodium concentration in an ROI was calculated from the ratio of $\hat{I}_{tissue}$ to the mean intensity, $\hat{I}_{conc-ref}$, in the same location in the concentration reference. TSC is corrected for differences in coil-loading between the patient (scan 1) and the concentration reference (scan 2), using the ratio of the noise-corrected signals from the tubes embedded in the coil, $\hat{I}_{ring}$, measured from scans 1 and 2:

$$TSC_{tissue} = C_{conc-ref} \cdot \left[\frac{\hat{I}_{tissue} - \hat{I}_{noise1}}{\hat{I}_{ring} - \hat{I}_{noise1}} \right]_{scan1} \cdot \left[\frac{\hat{I}_{ring} - \hat{I}_{noise2}}{\hat{I}_{conc-ref} - \hat{I}_{noise2}} \right]_{scan2} \quad [3]$$

Statistical Analysis—Paired t-tests were used to determine the statistical significance of any differences between the pre-treated, untreated, and treated ADC and TSC data.

Quantitative values are presented as mean $\pm$ SD. Statistical significance was assigned at $p < 0.05$.

Results

1H , Diffusion, and ^{23}Na MRI Observations

At baseline MRI, leiomyoma in normal and untreated patients appeared isointense within the uterus on proton, DWI, and ^{23}Na images. On a number of ^{23}Na images, an increase in signal intensity within the myometrium tissue surrounding the uterus, was observed in both normal subjects and patients with leiomyoma (Figures 2-3). After MRg-HIFUS treatment, all patients exhibited increased DWI and ^{23}Na signal intensity differences within the leiomyoma, as compared to the surrounding normal and untreated tissue with an increase of signal to noise ratio (11.9 ± 1.5) and contrast to noise ratio of (17.2 ± 6.5) between the tissue types. Figure 4a demonstrates typical results from a 44y/o female pretreatment. There was marked heterogeneous contrast enhancement on the T_1 image, but no increased signal intensity on the DWI ($b=1000$) (Fig. 4a) as compared to surrounding uterine tissue. After treatment, the contrast- T_1 –weighted image demonstrated a marked decrease of contrast uptake within the treated region compared to the untreated region (Fig. 4b). In addition, both DWI and ^{23}Na MRI (Fig. 4c) showed increased signal intensity that corresponds to the region on the contrast- T_1 MRI. A corresponding decrease in signal within the ADC map suggested cytotoxic edema, which was consistent with an observed increase in signal intensity on T2WI that is typically associated with vasogenic edema. Similar results are shown in Figure 5. Thus, Figures 4 and 5 demonstrate the ability of the DWI, ADC

mapping, and ^{23}Na MRI to demarcate non-perfused areas of treatment that coincide with the contrast- T_1 weighted image.

Baseline Leiomyoma and Normal Uterine Tissue ADC and Sodium Concentration values

The mean ^{23}Na concentration values in normal myometrium were $35.8 \pm 2.1\text{mM}$, in fundus; $43.4 \pm 3.8\text{mM}$ in bladder; and $65.3 \pm 0.8\text{mM}$ in the control. Fatty tissue had a sodium concentration of $22 \pm 11\text{mM}$. Apparent diffusion coefficient values in myometrium were $2.2 \pm 0.3 \times 10^{-3}\text{mm}^2/\text{sec}$; and in bladder, $3.5 \pm 0.50 \times 10^{-3}\text{mm}^2/\text{sec}$. The mean baseline ADC values in untreated leiomyomata were $1.75 \pm 0.36 \times 10^{-3}\text{mm}^2/\text{sec}$ and the ^{23}Na sodium concentration was $28 \pm 5\text{mM}$.

Post-treatment ADC and Sodium Values

The mean treated leiomyoma ADC values ($1.30 \pm 0.38 \times 10^{-3}\text{mm}^2/\text{sec}$) were significantly ($p=0.04$) reduced compared to baseline leiomyoma ($1.75 \pm 0.36 \times 10^{-3}\text{mm}^2/\text{sec}$) and untreated uterine tissue ADC values ($2.2 \pm 0.30 \times 10^{-3}\text{mm}^2/\text{sec}$). Mean sodium concentration values were significantly increased by 50% ($p<0.05$) in the treated tissue to $41.6 \pm 7.6\text{mM}$ (Figure 7).

Discussion

We have demonstrated that the use of ^1H and ^{23}Na MRI combined in a single exam is feasible for identifying and monitoring treatment of uterine leiomyomata. In particular, DWI and ADC mapping, coupled with ^{23}Na concentrations, may provide useful radiological-physiological biomarkers (the ADC and total sodium concentration) for uterine leiomyomata response to therapy and provide a basis to investigate malignant tumors. Indeed, there was increased signal intensity in both DWI and sodium images within the area of treated tissue, which coincided with the hypointense areas on the T_1 post-contrast image indicative of successful treatment. Regions of signal hyperintensity on the DWI and sodium images were not evident within the leiomyoma tissue on baseline exams before treatment. In addition, the ADC value within the treated region was decreased on average, and the sodium concentration was elevated compared to untreated tissue. These data are consistent with restricted tissue perfusion, protein denaturation produced during ablation, and/or cellular disruption of the cell membrane following therapy, and previous reports of the ADC value (14,29).

The ADC and sodium changes within the uterine tissue after treatment reflect complex changes in the water environment, including disruption of sodium-potassium pump function within cells, decreased vascularization, and/or cytotoxic edema. Disruption of the cell membrane by thermal ablation alters the cellular integrity and perfusion of the tissue, inevitably impacting energy metabolism, which, in turn, affects the water (ADC) and sodium ion exchange across the cell membrane. This manifests as increased TSC and decreased ADC. With the development of cytotoxic edema, interstitial space is also increased due to a change in cellular organization and/or increased vascular volume, which leads to an influx of extracellular sodium from the plasma and a net increase in the observed average TSC (30). Altered Na^+/H^+ exchange kinetics and the acidic extracellular

microenvironment can also lead to an increase in intracellular Na^+ concentration (31,32). Indeed, increased intracellular sodium concentration (33,34), increased Na^+/H^+ transporter (35), and Na^+/K^+ -ATP-ase activity (36) have all been linked to cell changes that lead to abnormal growth of tissue.

Similarly, the ADC value is a biophysical marker of the perfusion and inversely correlated with the cellularity of the tissue of interest. The ADC is believed to measure cytotoxic edema due to cell swelling (37), and diffusion path tortuosity (38), and is very sensitive to acute changes in tissue water (39,40). For example, a decrease in the ADC suggests a loss of movement of water/blood flow within the tissue. These observed differences in the ADC and sodium concentration may find value in the evaluation and management of uterine disease after treatment and such changes can be monitored in real time with DWI and sodium imaging. Thus, combining DWI and sodium imaging will extend tissue characterization beyond standard anatomical imaging.

Our data demonstrated there is an initial decrease in the ADC after treatment, which may be associated with cell loss and/or apoptosis, and the development of cytotoxic edema with concurrent increases in TSC. The exact mechanisms involved in the changes in ADC and sodium concentration in treated uterine tissue is unknown at present, but these changes may provide a measure by which to gauge the efficacy of treatment.

There are a number of potential advantages in using advanced MRI to monitor minimally invasive and noninvasive treatment of uterine tissue after treatment with MRg-HIFUS, which include: (a) the ability to provide accurate and sensitive soft-tissue anatomical information in the pelvic area, free from diffraction and scattering artifacts from bone that can arise with other imaging modalities; (b) the ability to evaluate multiple treated lesions simultaneously after treatment; (c) the ability to map and quantify ADC and sodium within the normal and treated tissue to provide novel insights into cellular level changes responsive to treatment, and to define lesion areas for further treatment and/or follow-up. In particular, the use of advanced radiological imaging to probe the molecular environments for changes after treatment may provide tools for targeted therapeutics and to evaluate physiological changes beyond normal anatomical imaging parameters; finally, (d) may provide an alternative to MRI contrast injection for enhancing lesion conspicuity post-treatment, given emerging concerns over systemic reactions to contrast agents.

There are, however, some technical limitations to the use of DWI and sodium imaging of the uterus. First, DWI is more sensitive to motion artifacts than most standard MRI pulse sequences. In the present study, motion artifacts were reduced by performing the exam with patients lying prone, and by scanning patients under conscious sedation. This allowed the study to be completed in a reasonably short period of time with less breathing and abdominal motion, but may be a limitation for the use of DWI. Second, although the use of ^{23}Na MRI is now finding some applications in the brain, breast, and heart (21,22,24), the multinuclear hardware and ultra-short TE pulse sequences used here are not widely available as of yet. Third, and more specific to the present study, any assessment of the clinical value of ADC and sodium MRI in the treatment of leiomyomata will require additional studies in a larger patient population, with subsequent follow-up and histological evaluation to discern

the sensitivity and specificity of this approach and mechanisms underlying the changes; however, larger studies are planned. Note that in this study, ADC mapping and ^{23}Na MRI results were not used to alter treatment, but rather, to demonstrate the feasibility of identifying and monitoring treated tissue.

In conclusion, we have demonstrated that ADC mapping and sodium MRI are feasible for identifying treated uterine leiomyomata after treatment, and may provide a basis to investigate a wide range of pathology within the uterus and cervix. That both TSC and ADC measurements reflect cellular level properties that show significant changes upon MRg-HIFUS, offers hope that such measures will prove useful for assessing and managing therapy, even though the time course of such changes is yet to be determined.

Acknowledgments

We thank the reviewers for their efforts and gratefully acknowledge partial financial and equipment support from InSightec, Haifa, Israel, We thank Diane Reyes, BS, for clinical support and Dr. Donald Peck, Dr. Hamid Sohanian Zadeh, and Lucie Bower, Henry Ford Hospital, Detroit, MI for the Eigentool image analysis software used for image processing.

This work was supported in part by NIH 1R01CA100184 and P50CA103175

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Figure 1.

Representative example of an MR-guided high intensity focused ultrasound surgery (MRg-HIFUS) treatment plan. a) The treatment plan outlined using green cylinders on the targeted leiomyoma. b) Axial T₂ (TR/TE=5000,100ms) MR images with the cylinders and fans (near and far zones) show the treatment area of the high-intensity focused ultrasound beam. The blue fan area shows each individual treatment area and the underlying structures that may be affected, and demonstrates the ability to “tilt” the ultrasound unit to obtain adequate coverage. c) Sagittal T₂ MR image at the same location.

Figure 2.

Representative T₂-weighted (top) and ^{23}Na (bottom) MR images from a normal participant.

a) Normal uterine tissues (fundus) were isointense on baseline T2WI (TR/TE=3000/98ms) and the bladder was hyperintense. b) Different regions of the uterus can be identified on the sodium images, where the myometrium is hyperintense, as are the bladder and the ovaries.

Figure 3.

Representative T₁-weighted and ²³Na MR images from a baseline study. a) Uterine leiomyomata were isointense to hypointense on baseline T1WI (TR/TE=185/1.5ms) (left). b) Different regions of the uterus can be identified on the ²³Na images, where the leiomyoma appears isointense, whereas, the myometrium is hyperintense, as is the bladder.

Figure 4.

Representative post-contrast T₁-weighted, diffusion-weighted, ²³Na, and T₂-weighted images of a leiomyoma. a) On pre-treatment MR images, there is contrast enhancement on the T₁-weighted image (TR/TE=185/1.5ms) in the leiomyoma. On DWI (b=1000), the leiomyoma is isointense at this time point. The T₂-weighted image (TR/TE=5000/90ms) shows small regions of hyperintensity with the leiomyoma. b) After MRg-HIFUS treatment, the T₁ shows decreased contrast uptake within the treated region and decreased signal intensity on the ADC map. The T₂-weighted images demonstrate increased signal intensity, indicative of vasogenic edema. c) The ²³Na images show marked increase in total sodium concentration. Taken together, both the proton (T₁, DWI, T₂) and ²³Na images demonstrate the potential of multiparametric and multinuclear imaging to characterize leiomyoma treatment.

Figure 5.

Representative post-contrast T_1 -weighted, diffusion-weighted, ^{23}Na , and T_2 -weighted images from a patient undergoing MRg-FUS. a) On pre-treatment MR images, there is contrast enhancement on the T_1 -weighted image ($\text{TR}/\text{TE}=185/1.5\text{ms}$) within the leiomyoma and little or no signal changes on the DWI (isointense) and the ADC map. In addition, the T_2 -weighted images ($\text{TR}/\text{TE}=5000/90\text{ms}$) do not show any regions of hyperintensity with the leiomyoma. b) As expected, after treatment, the post-contrast T_1 shows a focal area of hypointensity that corresponds to decreased contrast uptake within the treated region. This focal region of treated tissue is also well demarcated on the T_2 -weighted image DWI ($b=1000$) and on the ADC map. c) Similarly, increased signal intensity on the ^{23}Na images in the same focal region within the treated area is observed. However, there is a bright focus on the ^{23}Na images corresponding to a fluid/cystic follicle at the 2:00 position outside the treatment area and is not related to the treatment.

Figure 6.

Bar graphs of the apparent diffusion coefficient of water (ADC) derived from the diffusion weighted imaging in untreated and treated uterine leiomyoma tissue. There was a significant decrease ($p < 0.05$) in the ADC within the tissue after treatment.

Figure 7.

Bar graphs of sodium concentration in millimolar (mM) in uterine fatty, leiomyoma tissue and in treated uterine leiomyoma tissue. After treatment, there was a significant increase ($p < 0.05$) in sodium concentration within the treated tissue compared to untreated tissue.