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Simultaneous MR Thermometry and Acoustic Radiation Force Imaging Using Interleaved Acquisition

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Abstract

Purpose—A novel and practical method for simultaneously performing MR acoustic radiation force imaging (ARFI) and proton resonance frequency (PRF)-shift thermometry has been developed and tested. This could be an important tool for evaluating the success of MR-guided focused ultrasound procedures for which MR-thermometry measures temperature and thermal dose and MR-ARFI detects changes in tissue mechanical properties.

Methods—MR imaging was performed using a gradient recalled echo segmented echo-planar imaging pulse sequence with bipolar motion encoding gradients (MEG). Images with ultrasound pulses (ON) and without ultrasound pulses (OFF) during the MEG were interleaved at the repetition time (TR) level. ARFI displacements were calculated by complex subtraction of ON–OFF images, and PRF temperature maps were calculated by baseline subtraction. Evaluations in tissue-mimicking phantoms and ex vivo porcine brain tissue were performed. Constrained reconstruction improved the temporal resolution of dynamic measurements.

Results—Simultaneous maps of displacement and temperature were acquired in 2D and 3D while keeping tissue heating <1°C. Accuracy of the temperature maps was comparable to the standard PRF sequence. Using constrained reconstruction and subsampled k-space ($R=4.33$), 3D simultaneous temperature and displacement maps can be acquired every 4.7 s.

Conclusion—This new sequence acquires simultaneous temperature and displacement maps with minimal tissue heating, and can be applied dynamically for monitoring tissue mechanical properties during ablation procedures.

Keywords

MRI; acoustic radiation force; ARFI; MR thermometry; PRF; focused ultrasound; constrained reconstruction

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SUPPORTING INFORMATION

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INTRODUCTION

MR-guided focused ultrasound (MRgFUS) is a noninvasive therapeutic modality that shows great promise for treating diseases such as cancer of the breast, brain, and liver (1–5), as well as movement disorders such as essential tremor (6,7). The ability of MRI to measure temperature change in real time using the proton resonance frequency (PRF) shift method (8,9) enables precise treatment monitoring and thermal dose determination (10) for ablation (11) and hyperthermia (12) applications. By tracking the delivered thermal dose, clinicians can ensure that the targeted volume has been adequately heated to induce cell death and that surrounding tissues are undamaged. In addition, MR thermometry has enabled the use of feedback controllers capable of automatically controlling the delivery of thermal dose during treatment (13–16). For improved monitoring, temporally constrained reconstruction (TCR) methods can reduce the update time between subsequent MR thermometry readings (17–19).

MR acoustic radiation force imaging (MR-ARFI) (20), which measures an effective tissue displacement induced by short (typically 1–20 ms), precisely timed, bursts of focused ultrasound (FUS), has been used to enhance FUS treatments by accurately and safely localizing the focal zone in both 2D and 3D (21,22) without the use of low-power heating sonications. MR-ARFI also has been used for correcting phase aberrations caused by aberrating media such as the skull or ribs (23–28). Multiple acquisition schemes have been proposed for acquiring MR-ARFI measurements, including spin echo sequences, which are inherently insensitive to temperature change; and gradient recalled echo (GRE) pulse sequences, which are sensitive to temperature changes. Although the majority of ARFI techniques have been demonstrated in phantoms and ex vivo tissues, in vivo studies recently have been published (29,30) as well. Depending on the application, MR-ARFI scan time has been reduced using keyhole or parallel imaging techniques when multiple MR radiofrequency (RF) coils are available (31,32).

The correlation between changes in tissue mechanical properties and thermal dose has been investigated using both ultrasound (US) and MR imaging (32–36). For MRI assessment of tissue mechanical properties, this typically has been accomplished using a standalone MR-ARFI sequence, but methods for acquiring simultaneous MR-ARFI and PRF thermometry have been proposed (30,32,37,38). These combined MR-ARFI/PRF sequences are valuable because they can improve the safety of using MR-ARFI for tissue stiffness investigation, focal spot localization, and phase aberration correction by simultaneously measuring temperature rise to ensure no thermal dose is delivered by the ARFI pulses. These simultaneous methods can further provide clinicians with information about how the mechanical properties of the tissue are changing during ablative treatments, in addition to temperature change and thermal dose accumulation.

The primary challenge in all proposed methods for acquiring MR-ARFI simultaneously with PRF thermometry is that both PRF thermometry and MR-ARFI encode their signal into the phase of the acquired image; thus, it is necessary to differentiate between the phase resulting from tissue displacement versus tissue heating. Separation of the phase contributions is possible because the displacement phase depends both on the tissue displacement and the simultaneously applied motion encoding gradients (MEG), whereas the temperature phase

only depends on tissue temperature. One method for separating these two contributors is to alternate the MEG polarity used to encode the tissue displacement (32,37). However, interleaving two gradient polarities can induce eddy current effects, requiring additional corrections. A second method is to maintain the same MEG polarity but alternate between applying the FUS sonication during the first and second lobe of the bipolar gradient (30). One challenge facing this method is that tissue relaxation can take several milliseconds; consequently, any remaining displacement during the second gradient lobe will reduce the phase accrued during the first lobe, resulting in phase measurement errors. This can be mitigated by inserting a delay between the two lobes, or by making the gradient lobes longer than the ultrasound pulse, at the expense of reducing the overall efficiency of the sequence. Neglecting phase imbalance due to eddy currents and the differential phase accrual of the second method, both methods extract the phase contribution due to temperature by adding two successive phase measurements. Assuming the displacement is identical in each measurement, this mathematical operation cancels out the displacement phase, leaving the temperature component, which depends only on the echo time (TE) and the magnitude of the temperature change. A third method is to use a standard, nonalternating MEG with a multi-contrast (multiple echo time) readout (39,40). The temperature-induced phase will evolve linearly for each contrast, whereas the displacement-induced phase will be a fixed offset that does not depend on the TE of each contrast. By performing a linear least-squares fit to the phase evolution for each contrast, the phase from temperature is represented by the slope of the best-fit line, whereas the offset (phase at TE=0 ms) represents the tissue displacement phase. Challenges for this approach include performing a good fit in the presence of eddy currents, stimulated echoes, and motion.

This paper presents a novel pulse sequence for performing simultaneous 2D or 3D MR-ARFI and MR-PRF thermometry by interleaving the acquisition of images with FUS sonications (ON images) and without FUS sonications (OFF images) every repetition time (TR). The sequence is based on a GRE segmented (multi-shot) echoplanar imaging (EPI) sequence and does not require alternating the motion encoding gradients' polarity; changing the timing of the FUS sonication to coincide with one MEG lobe or the other; or using multiple contrasts, as in the previously described methods (30,32,41). This simultaneous thermometry and ARFI (STARFI) sequence has the additional advantage of being well suited to the application of TCR for improving temporal resolution. Simultaneous monitoring of temperature and displacement would provide clinicians with another metric for assessing treatment progress, safety, and success.

METHODS

Pulse Sequence and Separation of Effective Displacement and Temperature

Figure 1a illustrates how the STARFI sequence alternates between acquiring measurements for the OFF and ON images every TR. During ON images, the FUS generator was synchronized with the second MEG lobe via an optical trigger signal emitted from the pulse sequence. Tissue displacement occurring during the MEG interval of the ON image will result in a phase change ϕ_D given by:

$$\Delta\phi_D = \gamma \int_0^\tau G_{MEG}(t) \cdot \Delta D(t) dt, \quad [1]$$

where γ is the gyromagnetic ratio; $G_{MEG}(t)$ is the amplitude of the MEG; τ is the duration of the MEG; and $\Delta D(t)$ is the magnitude of the tissue displacement. Energy deposited from each ultrasound burst will increase the tissue's temperature and cause a phase change $\Delta\phi_T$ given by:

$$\Delta\phi_T = \alpha \gamma B_0 TE \Delta T, \quad [2]$$

where α is the PRF coefficient (assumed to be -0.01 ppm/°C throughout this work); B_0 is the main magnetic field strength; TE is the echo time; and ΔT is the temperature change in °C. Because only the ON images have FUS bursts, and thus tissue displacement, the total phase changes due to displacement and temperature change for the ON and OFF images are given by:

$$\Delta\phi_{OFF} = \Delta\phi_T \quad [3]$$

$$\Delta\phi_{ON} = \Delta\phi_T + \Delta\phi_D. \quad [4]$$

The phase contribution due to temperature, $\Delta\phi_T$, will be assumed to be equal in both the ON and OFF images because they are acquired in an interleaved fashion on the TR level. Thus, the phase due to displacement, $\Delta\phi_D$, can be separated from that of temperature by performing a complex phase subtraction between an interleaved ON:OFF image pair, resulting in:

$$\Delta\phi_D = \Delta\phi_{ON} - \Delta\phi_{OFF} = \text{angle}(e^{i\Delta\phi_{ON}} \cdot e^{-i\Delta\phi_{OFF}}). \quad [5]$$

Because the tissue displacement varies with time during the FUS burst, the area of the motion encoding gradient during the displacement, A_{MEG} , can be used to convert $\Delta\phi_D$ to an effective tissue displacement, ΔD_{eff} , given by:

$$\Delta D_{\text{eff}} = \frac{\Delta\phi_D}{\gamma \cdot A_{MEG}}. \quad [6]$$

Because the radiation force displacement is not constant during the motion encoding gradient, the measurement is an effective average of the displacement during the gradient. Because it is proportional to, but may not be exactly equal to, the actual displacement, we refer to it as an effective displacement.

The temperature change ΔT can be calculated using a complex subtraction between a baseline image acquired before the start of the sonication and any later OFF image during the sonication. So-called referenceless PRF methods (42), with which the baseline phase is estimated from the phase of an unheated area of the ON phase image itself, can also be used. Both methods will result in the phase change solely due to temperature.

A subsampled k-space reconstruction using the TCR algorithm, described fully elsewhere (17,43), was used to obtain temperature and ARFI measurements with higher temporal resolution. In brief, TCR generates a time series of images by iteratively minimizing a cost function consisting of a temporal constraint term and a data fidelity term. In the case of the STARFI sequence, the ON and the OFF images were reconstructed separately using the TCR algorithm, and then the phase difference for effective displacement measurement was obtained by the complex difference of the ON and OFF images.

Experimental Setup

All experiments used a 256-element phased array ultrasound transducer (Imasonic Inc., Voray-sur-l'Ognon, France; $F=1$ MHz, focal spot full width at half maximum (FWHM)= $2\times 2\times 8$ mm). The FUS driving electronics and control software were developed by Image Guided Therapy (Pessac, France). The transducer was coupled to the phantom and ex vivo tissue (see Fig. 1b) using a bath of degassed and deionized water. All MRI scans were performed on a 3T scanner (Siemens Prisma^{Fit}, Siemens AG, Erlangen, Germany) with gradient system capable of producing amplitudes of 80 mT/m and slew rates up to 200 T/m/s. An in-house built, single-channel RF loop coil (11.2 cm diameter) was used for signal detection in all scans. All scans used a spatial resolution of $1.25\times 1.25\times 3.00$ mm, an echo-train length of 7, a flip angle of 20° , and a monopolar (flyback) echo-planar readout. The 3D scans used a field of view (FOV) of $160\times 114\times 36$ mm, whereas the 2D scans used a FOV of 200×140 mm. All other MR and FUS parameters that varied by experiment are summarized in Table 1.

Five different experiments were performed. Experiments 1 and 2 (see Table 1) were performed in a single, custom tissue-mimicking gelatin phantom (44) fabricated in a cylinder 11 cm in diameter and 20 cm tall. Experiments 3 through 5 were performed in an ex vivo porcine brain removed from the skull and placed in a cylindrical holder (diameter=11 cm, height=20 cm).

Experiment 1 evaluated the accuracy and precision of the STARFI PRF measurements. The sequence was run for a total of 34 dynamic measurements (17 interleaved ON:OFF image pairs). Specifically, the STARFI sequence had four measurements (2 interleaved ON:OFF image pairs) acquired with no FUS applied so that two baseline PRF temperature measurements and two baseline ARFI effective displacement measurements could be calculated. Then, 10 images (5 interleaved ON:OFF image pairs) were acquired with FUS applied in alternate TRs so that five PRF temperature maps and five ARFI effective displacements maps could be reconstructed. Lastly, 20 images (10 interleaved ON:OFF image pairs) were acquired without FUS to measure phantom cooling. To provide an independent PRF measurement for comparison, the same FUS power (50 W) and duty cycle

(15/65 ms, or 24%) was then applied while scanning with the higher temporal resolution 3D segmented EPI PRF sequence. These two scans were repeated twice.

Experiment 2 tests the TCR algorithm for the first time in a simultaneously acquired temperature and ARFI dataset. k-space from the STARFI sequence was retrospectively downsampled by a factor of $R=4.33$ using an equally spaced sampling pattern in the k_y -phase encoding direction (45). This resulted in fully sampled k-space frames being “split” into multiple subsampled frames without discarding any data. The subsampled data was reconstructed using the TCR algorithm, achieving an acquisition time of $2 \times 2.34 \text{ s} = 4.7 \text{ s}$ for each pair of ON:OFF images. Full scan parameters can be found in Table 1. The FUS duration in this experiment was longer than the MEG duration to cause intentional tissue heating. The same number of baseline, heating, and cooling measurements as in experiment 1 were acquired, and the STARFI PRF temperature measurements were again compared to those acquired with a standard 3D segmented EPI sequence.

In experiment 3, the linearity of temperature rise and the effective displacement with FUS power were investigated. The FUS power was increased from 10 W to 50 W in increments of 10 W, with the duration held constant at 15 ms. All other MR and FUS parameters can be found in Table 1. At each power level, a total of four dynamic measurements (i.e., 2 interleaved ON:OFF image pairs) were acquired sequentially (with no cooling time between pairs of measurements) so that two temperature maps and two effective displacement maps could be calculated.

Experiment 4 compares PRF temperature measurements from STARFI and a standard segmented EPI sequence in ex vivo porcine brain (see Table 1). The same number of measurements for baseline, sonication, and cooling as in experiment 1 were acquired (a total of 34 measurements to produce 2 baselines, 5 sonications, and 10 cooling). Scans with both pulse sequences were repeated three times.

Finally, experiment 5 demonstrates the STARFI sequence in 2D mode with faster acquisition time. In this experiment (Table 1-experiment 5), 36 different scans were performed in which for each scan the single 3-mm 2D slice was moved 1mm closer to the transducer to cover the same 36mm FOV as the 3D scans. Moving the slice by 1mm for each new scan corresponds to zero-filling the 3D data to 1mm voxel spacing. For each position, a total of 20 images were acquired so that 10 temperature maps and 10 effective displacement maps could be calculated; the first four images were baseline images (i.e., no FUS), and the last 16 images were acquired during FUS sonication.

Data Analysis

To minimize the partial volume effects, all data were zero-filled interpolated by factors of $2 \times 2 \times 4$ in the frequency encoding, phase encoding, and slice encoding dimensions, respectively (46,47). The voxel spacing after zero-filling was $0.625 \times 0.625 \times 0.75 \text{ mm}$ in all scans, except the 2D scans in experiment 5, for which zerofilling was only possible in the frequency and phase encoding dimensions.

In experiments 1, 2, 4, and 5, the PRF temperature maps were calculated using single baseline subtraction (to remove phase wraps), followed by referenceless PRF reconstruction (to correct for field drift (42)). The ARFI effective displacement was calculated by complex subtraction of the interleaved measurements according to Equations [5] and [6]. In experiment 3, because no presonation (baseline) data were acquired, the PRF temperature maps were calculated by first unwrapping the image phase using a Goldstein flood-fill algorithm (48), followed by referenceless MRTI (42). ARFI effective displacement maps were calculated by complex subtraction according to Equations [5] and [6].

To estimate the minimum changes in displacement and temperature that can be detected in the various experiments, the spatial standard deviation (SD) of an unheated region was calculated and summarized in Table 2. For experiments 1, 2, 4, and 5, the spatial SD was computed using the baseline images before the start of the FUS. For experiment 3, which did not contain any baseline images without FUS, the spatial SD was computed over an unheated region away from the focal spot. In experiment 3, the displacement-to-noise ratios were further calculated as maximum focal spot displacement divided by SD of background displacement to compare the five different power levels.

In experiment 4, a one-way analysis of variance (ANOVA), with follow-up multiple comparison of means tests using Bonferroni adjustments with a level of significance $\alpha=0.05$, were performed to investigate if there were any significant increase in displacement for the five repeated displacement measurements.

RESULTS

Figure 2 shows three orthogonal views of the temperature maps from the standard PRF sequence, and the temperature and effective displacement maps from the STARFI sequence acquired in experiment 1. Good spatial agreement (less than 0.8mm difference in the mean center of mass) between the temperature maps from the standard PRF sequence and the STARFI sequence can be observed in Figures 2a and 2b. In Figure 3a, it can further be seen that the temporal evolution between the two sequences agree both when the FUS is applied and during the cooling period. Figure 2c shows the orthogonal views of the effective displacement map, and Figure 3b shows the temporal behavior of the effective displacement for the two scans. The measured effective displacement matched the expected behavior of being near zero when the FUS is off and only rising during the five measurements when FUS was on. In both trials, the phantom became softer as it warmed up, causing measured effective displacement to increase for successive measurements within each scan, as well as for the two repeated scans.

Results from the TCR reconstruction (experiment 2) are shown in Figures 4 and 5, where the STARFI temporal resolution for an ON:OFF image pair was improved by a factor of 4.33, from 20.3 s to 4.7 s. Figure 4a compares TCR-STARFI and standard segmented EPI PRF measurements, and Figure 4b shows the temporal evolution of the effective displacement as temperature increases. In Figure 4c and Supporting Figure S1, the effective displacement's spatial FWHM is seen to decrease as temperature increases. This is a consequence of the decreased shear wave propagation velocity resulting from reduced phantom stiffness at

higher temperature. Figures 5a and 5b show three orthogonal views of the STARFI temperature and effective displacement maps, respectively, at the time of maximum heating/displacement. These data show that longer duration and higher power FUS result in a substantially higher temperature rise compared to experiment 1.

The results from experiment 3 given in Figures 6a and 6b show that the temperature rise and effective displacement in the porcine brain increase linearly with applied FUS power. Supporting Figure S2 shows two orthogonal views of effective displacement maps from the 50 W case overlaid on a magnitude image. Figures 6c and 6d highlight that the in-plane focal spot position agrees well for all FUS power levels (to within the zero-filled voxel spacing of 0.625 mm). The effective displacement is relatively uniform in the through plane direction, as shown in Figure 6e, consistent with the thinness of the excised porcine brain in the ultrasound propagation direction. The spatial SD in a background area away from the focal spot varied between 0.4 to 0.5 μm for the five scans at the different powers. This variation resulted in displacement-to-noise ratios for the five power levels (10–50 W) of 9.7, 26.0, 38.2, 39.5, and 58.7.

The results from experiment 4 (shown in Fig. 7) further demonstrate that, just as in the phantom, there is a good agreement between the PRF temperature measurements from the standard segmented EPI sequence and the STARFI sequence. In this case, there is no clear increase in effective displacement with temperature, but it should be noted that the maximum temperature rise was only approximately 4°C. Thus, thermal dose was insufficient to cause tissue coagulation. The ANOVA test showed that there was no significant displacement difference for the five repeated displacement measurements in Figure 7b. There also was no increase in effective displacement in the three consecutive scans, contrary to the increase in effective displacement observed in the phantom (compare to Fig. 3b).

Finally, the 2D data from experiment 5 in Figure 8 show that the STARFI sequence can also be utilized in 2D mode for fast simultaneous PRF and ARFI displacement measurements. As in Supporting Figure S2, the effective displacement is seen to cover most of the brain in the through-plane z-direction, as can be observed in the orthogonal views in Figure 8a. Figure 8b shows a line plot through the z-direction for all 2D slices, highlighting a general challenge with 2D imaging—if a single 2D slice is acquired and is not localized properly, the effective displacement (and temperature) will be underestimated due to partial volume effects. Figure 8c shows effective displacement and temperature rise for the 10 consecutive ON:OFF image pairs at the center of the focal spot from the 2D slice with most effective displacement and temperature rise. It can be observed that three consecutive displacement maps, each with an effective displacement of approximately 13 μm , can be acquired before the temperature rises above 1°C; and after 10 consecutive measurements, the temperature rise is approximately 2.5°C.

DISCUSSION

This study has described and evaluated a novel segmented-EPI pulse sequence that can simultaneously acquire PRF temperature measurements and MR-ARFI effective tissue displacement measurements. Using a gradient echo, this sequence can acquire measurement

data about four times more rapidly than a corresponding spin echo sequence (49). The PRF temperature measurements from this sequence agree well with PRF measurements from a standard segmented EPI pulse sequence in both phantom and ex vivo porcine brain tissue. In phantom experiments, the effective tissue displacement was observed to increase as a function of temperature due to softening of the phantom gelatin material during warming. In the ex vivo brain tissue, the temperature rise was low and a negligible thermal dose was accumulated; therefore, effective displacement was not seen to change as a function of temperature. However, both temperature and effective displacement increased linearly as a function of increasing FUS power. It was demonstrated that the novel STARFI sequence can be applied in both 2D and 3D mode, with the time to acquire a set of temperature and displacement maps in 2D being approximately 1.5 s and in 3D being approximately 20 s. It was further shown that the 20 s scan time for the 3D case can be reduced to approximately 4.7 s using k-space subsampling and constrained reconstruction. The pulse sequence accurately measured PRF temperature for both low-temperature rise conditions and ablation-like conditions for which the temperature rise is $>20^{\circ}\text{C}$.

Interleaving the ON and OFF images at the TR level, using the same MEG polarity for every TR and always applying the FUS on the second MEG lobe, has some advantages over previously described approaches. By maintaining the same MEG polarity for each TR, identical eddy currents are created in both the ON and the OFF image, and their effects cancel when subtracting the images, resulting in reduced artifacts. Always applying the FUS on the second MEG lobe of the bipolar gradients also means that no delay needs to be inserted between the two MEG lobes to ensure an accurate displacement-phase measurement. Minimizing the amount of “dead time” in the sequence reduces TR and improves the efficiency of the sequence for a given MEG duration.

In all but one experiment, the FUS duty cycle was kept low (FUS duration $\ll$ MEG duration $\ll$ TR) to show that effective displacement maps in both 2D and 3D could be obtained without causing significant tissue heating. It was shown that 2D and 3D temperature and effective displacement maps could be acquired while limiting the temperature rise to 0.5°C for the 2D case and 1°C for the 3D case. For 3D scans, the temperature rise can be further reduced by only applying the FUS to some fraction of the central k_z -slice encodings, thereby reducing the FUS duty cycle, as previously shown (49).

Experiment 2 represents the first application of TCR to a simultaneously acquired temperature and displacement dataset. Using k-space subsampling and TCR, the temporal resolution of the 3D STARFI sequence was increased by a factor of 4.33. The STARFI sequence is well suited for TCR because the ON and OFF images are interleaved at the TR level, which results in smoothly varying phase in both the ON and OFF image.

To demonstrate the ability to simultaneously track large temperature increases and to monitor changes in effective displacement due to temperature increase, the duty cycle was increased so that the FUS duration (40 ms) was much greater than the MEG duration (15 ms), resulting in a temperature rise $>20^{\circ}\text{C}$. To make the sequence even more suited for ablative therapies, higher FUS power and longer FUS durations can be applied after the end of the MEG, as described by Bour et al. (32). It was shown that a 10 ms “dead time” without

FUS before the start of the MEG lobes was enough for the tissue to relax back to its initial state so that accurate displacement maps could be achieved. In Bour et al.'s study, this resulted in a duty cycle of 98.75% (FUS on for 790 out of 800 ms); using the same "dead time" with our TR would result in an approximate duty cycle of 85% (55 out of 65 ms). For ablative therapies, 3D temperature and effective displacement maps can be advantageous for ensuring that the center of the focal spot is monitored and that no off-focal heating is occurring. Furthermore, unlike 2D scans, 3D datasets can be zero-filled interpolated in all three dimensions, reducing partial volume effects even in the slice direction.

TCR, which was used in this study to improve the temporal resolution, is not well suited for real-time applications because it is an iterative method. However, close to real-time availability of the PRF temperature maps has been described (19). The scan time of 4.7 s that was achieved in this study is on the longer end of what would be desirable for clinical use. This can be further reduced by either increasing the k-space subsampling factor (a factor of $R=7$ has been used previously (45)), or by combining TCR with alternative approaches. Alternatives to TCR include utilizing parallel imaging, as described by Bour et al. (32); or utilizing keyhole imaging, as described by Paquin et al. (31). Parallel imaging approaches require multiple RF receive coils, which only are available on a few MRgFUS systems, and result in at least a $\sqrt{R}$ decrease in image SNR. Keyhole approaches can work well if the phase encoding direction is applied along the long axis of the FUS beam. However, for 2D imaging this can result in partial volume effects because the slice encoding direction, which usually is the lowest resolution, is then applied along one of the in-plane dimensions of the FUS beam where the beam is narrow (i.e., imaging a narrow beam dimension with a thick slice). Furthermore, a small offset of the 2D slice from the center of the focal spot can result in underestimating both temperature and displacement. The keyhole approach may be better suited for 3D imaging in which the frequency and phase encoding directions can be applied along the narrow FUS beam direction and the keyhole can be applied along the slice encoding direction. By modeling the phase change due to tissue displacement, (50), fitting and model-based reconstruction methods potentially could also be used to reduce scan time (51,52).

Interleaving the ON and OFF image at the TR level further ensures accurate temperature measurements at the time of the ON image. Interleaving between complete ON and OFF images can result in incorrect displacement measurements due to the difference in temperature between the ON and OFF images. With TR level interleaving, there essentially is no time between the ON and OFF images, and accurate displacement and temperature maps are obtained even in 3D.

The 2D and 3D data in Figures 7 and 8 show that by using a short FUS pulse duration of 6 ms, the temperature rise can be kept very small to ensure that minimal thermal dose is deposited. This will be of particular interest for applications such as tissue stiffness investigation, focal spot localization, and phase aberration correction for which no thermal dose should be deposited by the ARFI sonications. For in vivo cases, the temperature rises likely will be even lower due to blood perfusion acting as a heat sink. Because perfusion does not impact acoustic radiation force, effective tissue displacement still can be detected, even if the temperature rise is very small.

Future in vivo experiments will allow for detailed study of how changes in tissue stiffness correlate to thermal dose. This will provide an additional treatment feedback metric and potentially improve the effectiveness and safety of MRgFUS therapies.

CONCLUSION

This study describes the development and evaluation of a novel method for acquiring MR-ARFI and PRF thermometry simultaneously by interleaving the TRs of images with and without FUS. The sequence was demonstrated in both 2D and 3D modes, and in phantom and ex vivo porcine brain tissue. A temporally constrained reconstruction method was applied to retrospectively increase the time resolution of the acquired images. This new tool could benefit clinical MR-guided focused ultrasound treatments by measuring and correlating changes in tissue mechanical properties with temperature and thermal dose exposure, all with a single, practically implemented, pulse sequence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIG. 1.

Pulse sequence diagram and experimental setup. **(a)** STARFI sequence diagram. The first two TR intervals shown, OFF TR1 and ON TR1, illustrate how data for the OFF and ON images are acquired in interleaved fashion by alternating between TRs without FUS bursts (OFF) and with FUS bursts (ON). **(b)** Experimental setup. STARFI, Simultaneous thermometry and ARFI; RF, radiofrequency excitation; G_{SE} , slice-encoding gradient; G_{PE} , phase-encoding gradient; G_{FE} , frequency-encoding gradient; FUS, focused ultrasound.

FIG. 2.

Comparison of STARFI and standard segmented EPI measurements in phantom. Three orthogonal views at time of maximum temperature and displacement for (a) Standard segmented EPI PRF temperature maps, (b) STARFI PRF temperature maps, and (c) STARFI displacement maps.

FIG. 3.

Temperature and displacement measured in phantom. **(a)** Mean and standard deviation (of two repeated runs) of hottest voxel as a function of time, as measured using standard segmented EPI and STARFI sequences. **(b)** STARFI displacement measurements for two scans. The temperature measurements agree well, and the displacement measurement increases as the phantom warms up. Temp, temperature.

FIG. 4.

TCR applied to STARFI in phantom. **(a)** Temperature rise as a function of time as measured using standard segmented EPI and STARFI after k-space subsampling ($R=4.33$) and TCR reconstruction. **(b)** STARFI displacement as a function of time with STARFI temperature rise (same data shown in **(a)**) plotted as a temporal reference. **(c)** STARFI displacement FWHM as a function of time with STARFI temperature rise (same data shown in **(a)**) plotted as a temporal reference. disp, displacement; TCR, temporally constrained reconstruction; FWHM, full width at half maximum.

FIG. 5. TCR applied to STARFI in phantom. (a) and (b) Three orthogonal views of STARFI temperature and displacement maps at time of maximum heating and displacement, respectively.

FIG. 6.

STARFI temperature and displacement measurements in ex vivo porcine brain. **(a)** Temperature rise for the two consecutive measurements acquired at five FUS powers. At each power, the second measurement is acquired 19.4 s after the first measurement. **(b)** Corresponding displacement measurements. **(c–e)** Line plots through the frequency encoding, phase encoding, and slice encoding directions, respectively, of the displacement for the two consecutive measurements and the five FUS powers. Displacement increases with applied power (10 W=smallest peak displacement, 50 W=largest peak displacement). FE, frequency encoding; PE, phase encoding; SE, slice encoding.

FIG. 7.

Segmented EPI and STARFI in porcine brain. (a) Mean and standard deviation of temperature rise as a function of time for standard segmented EPI PRF and STARFI PRF. (b) Mean and standard deviation of displacement and temperature rise, both for STARFI. Analysis of variance test showed that there was no significant change in displacement with temperature in the brain tissue at this level of heating.

FIG. 8.

2D STARFI displacement and temperature measurements in porcine brain. **(a)** Orthogonal views of displacement maps from 2D imaging. The sagittal and transverse views show reformatted cuts through the stack of 2D slices, with the slice-encoding direction going left-right and up-down, respectively. Slice position increases with increased distance from the transducer. **(b)** Line plot through the stack of 2D slice at the in-plane location of maximum displacement showing falloff in maximum displacement for off-center slice locations. **(c)** Displacement and temperature rise as a function of time for 10 consecutive measurements. Sag, sagittal; Cor, Coronal; Tra, Transverse.

Table 1

Scan Parameters.

Pulse sequence	Experiment 1		Experiment 2		Experiment 3		Experiment 4		Experiment 5	
	STARFI	SegEPI	STARFI	SegEPI	STARFI	STARFI	STARFI	SegEPI	STARFI 2D	STARFI 2D
TR, TE (ms)	65, 44	26, 11	65, 44	26, 11	62, 44	62, 44	65, 44	26, 11	52, 34	52, 34
BW (Hz/px), ESP (ms)	752, 2.5	752, 2.36	752, 2.5	752, 2.36	752, 2.5	752, 2.5	752, 2.5	752, 2.36	744, 2.52	744, 2.52
Tacq (s)	20.3	4.1	4.7 (R=4.33)	4.1	19.4	19.4	20.3	4.1	1.6	1.6
MEG Amp (nT/m)	50	50	35	35	40	40	50	50	60	60
MEG Dur (ms)	15	15	15	15	15	15	10	10	10	10
FUS Pwr (W), Dur (ms)	50, 15	50, 15	65, 40	65, 40	[10, 20, 30, 40, 50], 15	[10, 20, 30, 40, 50], 15	50, 6	50, 6	50, 6	50, 6

For STARFI sequence, the listed Tacq is for a pair of interleaved images (ON:OFF).

SegEPI, segmented echo-planar imaging; BW, readout bandwidth; ESP, echo spacing; Tacq, acquisition time; MEG Amp, motion encoding gradient amplitude; MEG Dur, motion encoding gradient duration; FUS Pwr, focused ultrasound power; FUS Dur, focused ultrasound duration; R, k-space subsampling factor (only used for experiment 2).

Estimated Minimum Detectable Changes in Displacement and Temperature from Spatial SD Measured in Unheated Region.

Table 2

	Spatial SD: STARFI Displacement (µm)	Spatial SD: STARFI Temperature (°C)	Spatial SD: SegEPI Temperature (°C)
Experiment 1	0.54	0.37	0.13
Experiment 2	0.49	0.11	0.10
Experiment 3	0.48, 0.47, 0.42, 0.38, 0.47	0.30, 0.41, 0.28, 0.34, 0.39	
Experiment 4	0.66	0.30	0.14
Experiment 5	0.57	0.18	

For experiments 1, 2, 4 and 5, the spatial SD was computed from the acquired baseline images. For experiment 3, which did not contain baseline images without FUS, the spatial SD was computed over an unheated region away from the focal spot.

SD, standard deviation.