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Improved MR Thermometry for Laser Interstitial Thermotherapy

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Abstract

Objectives: To develop, test and evaluate improved 2D and 3D protocols for proton resonance frequency shift magnetic resonance temperature imaging (MRTI) of laser interstitial thermal therapy (LITT). The objective was to develop improved MRTI protocols in terms of temperature measurement precision and volume coverage compared to the 2D MRTI protocol currently used with a commercially available LITT system.

Methods: Four different 2D protocols and four different 3D protocols were investigated. The 2D protocols used multi-echo readouts to prolong the total MR sampling time and hence the MRTI precision, without prolonging the total acquisition time. The 3D protocols provided volumetric thermometry by acquiring a slab of 12 contiguous slices in the same acquisition time as the 2D protocols. The study only considered readily available pulse sequences (Cartesian 2D and 3D gradient recalled echo and echo planar imaging [EPI]) and methods (partial Fourier and parallel imaging) to ensure wide availability and rapid clinical implementation across vendors and field strengths. In vivo volunteer studies were performed to investigate and compare MRTI precision and image quality. Phantom experiments with LITT heating were performed to investigate and compare MRTI precision and accuracy. Different coil setups were used in the *in vivo* studies to assess precision differences between using local (such as flex and head coils) and non-local (i.e., body coil) receive coils. Studies were performed at both 1.5 T and 3T.

Results: The improved 2D protocols provide up to a factor of two improvement in the MRTI precision in the same acquisition time, compared to the currently used clinical protocol. The 3D echo planar imaging protocols provide comparable precision as the currently used 2D clinical protocol, but over a substantially larger field of view, without increasing the acquisition time. As expected, local receive coils perform substantially better than the body coil, and 3T provides better MRTI accuracy and precision than 1.5 T. 3D data can be zero-filled interpolated in all three dimensions (as opposed to just two dimensions for 2D data), reducing partial volume effects and measuring higher maximum temperature rises.

Conclusions: With the presented protocols substantially improved MRTI precision (for 2D imaging) or greatly improved field of view coverage (for 3D imaging) can be achieved in the same

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

acquisition time as the currently used protocol. Only widely available pulse sequences and acquisition methods were investigated, which should ensure quick translation to the clinic. *Lasers Surg. Med.* 51:286–300, 2019.

Keywords

magnetic resonance temperature imaging; magnetic resonance thermometry; laser interstitial thermal therapy; proton resonance frequency shift

INTRODUCTION

Laser interstitial thermal therapy (LITT) has been used to treat a wide variety of diseases and disorders, such as epilepsy and tumors in the brain, breast, prostate, liver, and bone [1–7]. Ablations using LITT can be used on its own, but also in, for example, conjunction with radiotherapy [8] or after injection of light-activated photosensitizer in photodynamic therapy [9]. LITT is especially well suited for magnetic resonance imaging (MRI) guidance since the thin fiberoptic applicator and the catheter used for cooling fluid do not create large susceptibility artifacts in the MR images. For this reason, most LITT treatments are monitored by MR temperature imaging (MRTI) [10]. The localized heating around the fiber can be monitored with a relatively small field of view (FOV). This limited FOV around the applicator can be traded for faster and/or higher resolution imaging, since FOV and spatial and temporal resolutions inherently conflict in MRTI.

Nearly all studies utilizing MRTI to monitor LITT procedures have used the proton resonance frequency shift (PRFS) method. The shift in the proton resonance is due to temperature-induced changes in intermolecular hydrogen bondings [11–13]. This frequency shift is encoded in sequential MR phase images and can be converted to a relative temperature change. The method has been shown to work well over an absolute temperature range of approximately 20–100 °C [11] and is nearly tissue type agnostic (except for adipose tissues which lack the necessary hydrogen-bonding) [10,14].

Most LITT studies have used a standard single echo (i.e., single contrast), 2D gradient recalled echo (GRE) pulse sequence [15–22] with single slice acquisition times between 4.5 s to approximately 10 s, depending on resolution and field-of-view. To achieve larger coverage in the slice direction, Kickhefel et al. used a multi-slice 2D GRE [23] to acquire three slices with 2.5 mm isotropic inplane resolution updated every 970 ms. 2D multi-slice segmented echo planar imaging (EPI) pulse sequences, where multiple lines of k-space are sampled after each RF excitation pulse, have allowed for between three to five slices to be imaged in between 4 and 6 s [24–27]. Fuentes et al. and Kickhefel et al. [23,26] further described the use of parallel imaging (which utilizes the spatially varying sensitivity from different MR RF receive-coils to reconstruct under-sampled k-space data) to speed up the image acquisition by a factor of approximately 2.

In this study, we investigate possible improvements in measurement precision and coverage to the MRTI protocol currently used during LITT brain treatments with a commercially available LITT system (Visualase, Medtronic, Louisville, Colorado). The current protocol acquires two single-echo (i.e., single contrast) 2D, interleaved and orthogonal slices, aligned

with the fiber optic applicator. The proposed improvements include acquiring multiple echoes to fill up the available repetition time (TR) with sampling time to improve MRTI precision. Volumetric 3D acquisitions using GRE and EPI sequences were further investigated to monitor a larger FOV covering the fiber optic applicator and surrounding tissues more completely than what is done with the two orthogonal slices. To allow immediate clinical adaptation the protocols investigated were based on widely available 2D and 3D GRE and EPI pulse sequences and the acquisition times matched that of the currently used protocol. LITT heating experiments were performed in tissue mimicking gel to evaluate MRTI accuracy and precision. Experiments without LITT were performed in human volunteers to investigate the relative precision that could be achieved *in vivo*. The experiments were performed at 1.5T and at 3T, and the *in vivo* experiments were performed using three different RF coil setups. To our knowledge this is the first study investigating multi-echo and 3D acquisition MRTI for improved precision and increased FOV coverage in LITT.

MATERIALS AND METHODS

General MRTI Considerations

In the PRF method [10,14,28] the temperature-dependent frequency change is proportional to the difference in phase between the current dynamic time frame and an image obtained before the start of the treatment. The proportionality constant α (measured in ppm/°C) is approximately -0.01 ppm/°C for most aqueous tissues [28]. Since the phase difference increases linearly with the echo time (TE), and the image signal to noise ratio (SNR) decreases exponentially as e^{-TE/T_2^*} , the optimal TE for MRTI measurements occurs when $TE = T_2^*$. In practice, the T_2^* is usually fairly long which would result in very long imaging times, so $TE < T_2^*$ is usually employed.

The precision of MRTI measurements, which can be defined in terms of the standard deviation of the temperature measurements, depends on a variety of factors. The standard deviation of the temperature measurements is inversely proportional to the imaging SNR, which can be expressed as [29–32]

$$SNR \propto \Delta x \Delta y \Delta z \sqrt{N_x N_y N_z \Delta t}$$

where x , y , and z are the voxel dimensions, N_x , N_y , and N_z is the matrix size, and t is the sampling time (time between samples). The total sampling time, which is the product of number of readout samples, N_x , and time between samples, t , is proportional to $1/BW$ where BW is the readout bandwidth (in Hz/pixel). It can be seen that a lower BW prolongs the readout time and results in higher SNR and hence better precision MRTI measurements. An alternative way to improve the MRTI precision, while keeping the BW fixed, is to acquire multiple echoes or signal pathways in a single TR, effectively increasing the total time which is spent sampling the data [33–35]. By acquiring multiple echoes, the later echoes might also have longer TEs, and hence be closer to the T_2^* of the tissue and provide even better MRTI precision. For multi-echo imaging each echo will be sampled with a

different TE. Appendix A derives what relative weights should be used when combining the MRTI data from the different echoes to optimize the temperature precision. It is shown that weighting by $TE^2|m|^2$, where $|m|$ is the absolute value of the complex MR image, creates the optimal temperature measurement precision.

Because MRI uses magnetic field gradients to link the resonance frequency with position, any other effects that further change the local resonant frequency will cause spatial shifts and distortions in the resulting image. The magnitude of the image distortions depends directly on the magnitude of the frequency shift relative to the sampling BW. The frequency shifts can be due to off-resonance shifts, such as those induced by difference in tissue resonance frequency (e.g., between aqueous and adipose tissues) and by change in resonance frequency due to, for example, PRF shift with temperature.

For standard GRE sequences, any distortions are determined by the readout BW, which is typically in the range of a few hundred to a few thousand Hz/pixel. For EPI sequences the time between samples in the phase encoding direction is much larger than in the readout direction, resulting in a phase encoding sampling bandwidth that is much lower than the frequency encoding sampling bandwidth. This lower bandwidth results in larger distortions and shifts in the phase encoding direction for EPI pulse sequences. Since both the frequency offset due to chemical shift and susceptibility increase linearly with the main magnetic field strength, for a given BW, the distortions will be half as large at 1.5 T than at 3T. Because the magnitude of distortion that can be tolerated will depend on the application and possibly also on the physician's personal preference we have in this manuscript chosen to list the magnitude of the fat/water shift (in number of pixels) for each method and show representative images of areas that can be considered challenging to image (such as close to tissue-air interfaces).

Protocols

To investigate possible improvements that can be made to the currently used 2D protocol, and highlight trade-offs between 2D and 3D imaging approaches, 8 different MRTI protocols (four 2D and four 3D protocols) were developed and compared. All protocols are based on basic product GRE and EPI pulse sequences (to enable fast and wide clinical adaptation across vendors and field strengths), with the added option of flyback-gradients between the frequency encoding readout gradients in the EPI sequence [36,37] to enable mono-polar readouts. All protocols used an in-plane FOV of $240 \times 240 \text{ mm}^2$ (i.e., in the frequency $\times$ phase encoding directions) and a 256×128 in-plane sampling matrix, for an in-plane resolution of $0.94 \times 1.88 \text{ mm}^2$. All other scan parameters for the different protocols and both field strengths are listed in Table 1.

Following is a brief description of each of the eight protocols.

1. **2D Single Echo GRE (2D GRE), Current protocol** The 2D GRE protocol currently used during clinical treatments acquires two orthogonal slices sequentially in 5.9 seconds. The long TR (23 ms) and moderate readout BW (260 Hz/pixel or readout duration of 3.85 ms) results in substantial non-sampling "dead time" in the sequence.

2. 2D GRE with 3 mono-polar echoes (2D GRE, 3xMono) To minimize the “dead time” compared to 2D GRE this protocol acquires three monopolar echoes (i.e., sampling in the same direction for all echoes). The increased sampling time ($3 \times 3.85 = 11.55$ ms) theoretically increases the temperature measurement precision by $(3)^{1/2} = 1.73$. The actual precision can vary because each of the echoes have a different TE, with the longest TE (18.6ms) closer to the optimal TE = T_2^* .
3. 2D GRE with 4 bi-polar low bandwidth echoes (2D GRE, 4xBi)
To further increase the sampling time this protocol acquires bi-polar echoes increasing the total sampling time to 15.38 ms and doubling the theoretical precision compared to 2D GRE. The bi-polar readouts will result in bi-directional off-resonance effects.
4. 2D GRE with 11 bi-polar high bandwidth echoes (2D GRE, 11xBi)
To reduce ghosting artifacts this protocol employs higher readout bandwidth and more echoes resulting in theoretical precision improvements of approximately $1.8\times - 1.9\times$ compared to 2D GRE.
5. 3D GRE
This protocol acquires a contiguous 3D slab of 12 slices (10 slices + 20% slice oversampling) using bipolar echoes. To achieve the same scan time as the other sequences, slice partial Fourier (6/8) and parallel imaging (GRAPPA with R = 2 and 24 integrated reference lines) were used. Temperature precision was reduced by the short TR and TE as well as the use of partial Fourier and GRAPPA.
6. 3D EPI
This EPI protocol uses a short echo train length (ETL) of five resulting in a phase encode bandwidth of 179 Hz/pixel, resulting in larger off-resonance effects than for 2D GRE. However, this 3D EPI protocol acquires a 3D slab of 12 slices (10 slices + 20% slice oversampling) in the same time as the two orthogonal slices of 2D GRE.
7. 3D EPI, Fatsat
This EPI protocol adds a frequency selective fat saturation pulse to mitigate off-resonance effects from fat-signal. Scan time was held constant by using a longer ETL to compensate for the longer TR. The longer ETL lowers the phase encoding bandwidth.
8. 3D EPI, Flyback
This EPI protocol uses monopolar flyback readout to make the fat-water shift in the readout direction mono-directional. The flyback gradients results in longer echo spacing which in turn results in lower phase encoding BW.

MRI Experiments

To compare the eight different protocols, temperature precision measurements were made in human volunteers and heating comparisons were performed in phantoms. These experiments

were repeated at 1.5 T and 3T, the two most commonly used field strengths, and were also repeated for different RF coil setups.

The 1.5 T MRI system used was an ultra-short, wide (70-cm) bore scanner (Espree, Siemens Medical Solutions, Erlangen, Germany), with a gradient system capable of 33 mT/m maximum amplitude and slew rates up to 170 T/m/s. The 3T MRI system used (Prisma^{Fit}, Siemens Medical Solutions) has a 60-cm bore, and a gradient system capable of up to 80 mT/m maximum amplitude and 200 T/m/s slew rates.

For the *in vivo* studies, the experiments were repeated for three different setups of the manufacturer supplied RF coils (Siemens Medical Solutions) at each field strength: a) the system body coil, b) a flex coil wrapping around the posterior part of the head, and c) a head coil. The body coil is a single channel at 1.5 T and two channels at 3 T. The flex coil was a 6-channel torso array coil at 1.5 T and a 4-channel flex coil at 3 T. The head coil was an 8-channel head coil at 1.5 T and at 3T the posterior part of a 20-channel head coil was combined with the 4-channel flex coil wrapped around the anterior part of the head. For the phantom studies, the flex-coil setups were used.

1. In-vivo human studies for precision: To investigate and compare the *in vivo* MRTI precision, healthy volunteers were scanned with all protocols at both field strengths after informed consent. 20 dynamic images were acquired for each protocol, for a total scan time of approximately 2 minutes per protocol.

All scans were centered on a mid-line sagittal scan plane. The 2D protocols also acquired an interleaved coronal slice whereas the 3D protocols acquired 12 sagittal slices in the 3D volume. An ROI in the posterior part of the brain was used to evaluate the MRTI precision, as this region had relatively high SNR in all coil setups. The MRTI precision was measured as the voxel-wise standard deviation through time of the MRTI measurements with these values then averaged over the 21×21 voxels in the ROI. To compare the performance of the three different coil setups the precision measurements for all eight protocols were averaged for each of the three coil setups. The ratio between the different coil setups were then calculated (i.e., Body/Flex, Body/Head, Flex/Head), and a ratio >1 in, for example, the Flex/Head-ratio means that the head coil performed better than the flex coil in that particular location in the brain.

2. Phantom studies for accuracy and precision: To evaluate and compare the accuracy of the different protocols, LITT heatings were performed using a commercially available LITT system (Visualase, Medtronic, Louisville, CO. 15-W diode laser, operating at a wavelength of 980 nm, 400 μ m fiber core, 10 mm diffusing tip) in a plastic skull (model A20, 3B Scientific, Tucker, GA) filled with tissue mimicking Gellan gum gel (Fisher scientific, Pittsburgh PA. 10 g Gellan gum powder per 1000 ml deionized water). The T_1 relaxation time of the phantoms was estimated to be approximately 1500 ms at 1.5 T and approximately 1900 ms at 3 T. A new phantom was made for the experiments at each field strength.

For all protocols, three repeated heatings were performed at a power of 7W for 1.5 T and 3W for 3T. The laser was kept on for eight dynamic image acquisitions, corresponding to 47–49 seconds depending on the protocol. The flex receive-only RF coil was wrapped around the plastic skull and used for signal detection. A fiber optic temperature sensor (Neoptix, Qualitrol, Québec, Canada) was inserted next to the laser fiber to measure the “true” temperature rise. Care was taken so that the fiber optic temperature probe was close enough to measure a temperature increase of at least 2°C, but far enough away that its measurements were not affected by the emitting laser fiber.

Data Reconstruction

All data was reconstructed in Matlab (R2017a, The MathWorks Inc., Natick, MA). MRTI data was reconstructed assuming a PRF coefficient $\alpha = -0.010$ ppm/°C and single baseline subtraction followed by reference-less reconstruction utilizing a second order polynomial fit to the unheated background phase [10,38]. All multi-echo data was optimally combined for temperature measurement precision by weighting by the square of the temperature-SNR (Appendix A). Multi-coil MR data was optimally combined using a modified Roemer’s equation (i.e., Equation 24 in Roemer et al., with further details given in Parker et al.) using the noise covariance matrix, which was estimated from the readout oversampling region [39,40]. All data was zero-filled interpolated to 0.5-mm in-plane voxel spacing to minimize partial volume effects [41–43]. The 3D data was further zero-filled to 0.5-mm voxel spacing in the slice encoding direction as well, whereas this is not possible for the 2D protocols. For the phantom study, the fiber optic probe temperature measurements were sampled every 1 second. For comparison to MRTI the probe measurements were linearly interpolated to align with the MRTI, which was sampled every 5.9–6.1 seconds (Table 1), depending on protocol.

RESULTS

All figures from the 3T study are included in the main manuscript whereas all figures from the 1.5T study are included as supplementary materials with corresponding figure numbers. In general, the conclusions drawn from the 3T study are well supported by the 1.5T study, but the 3T protocols showed higher MRTI accuracy and precision as expected.

In Vivo Study

Figure 1 shows a mid-line sagittal view of *in vivo* temperature precision and magnitude images for the three different coil setups for the 3 T study. In the temperature precision images, the red square shows the 21×21 voxels where the precision is evaluated. Table 2 summarizes all precision measurements for all 48 scans (8 protocols $\times$ 3 coil setups $\times$ 2 field strengths).

In Figure 2 the ratio between different coils for the average temperature standard deviation of the eight protocols are shown for the 3T data. A ratio >1 means that the coil setup in the denominator had (on average, across protocols) better precision than the coil setup in the numerator. In general, the precision is higher for the local receive coil setups (i.e., the flex and the head coil setups) when compared to the body coil. As expected, the flex coil performs best in the posterior part of the brain, where it is up to eight times better than the

body coil (Fig. 2a). The head coil is uniformly better than the body coil (Fig. 2b). Finally, the head coil performs better than the flex coil in the anterior part of the brain (Fig. 2c).

At 3 T the currently used protocol (2D GRE) and the three 3D EPI protocols demonstrated a precision within one standard deviation of each other for all coil setups. The multi-contrast 2D protocols showed the best precision, generally having approximately 2× the precision of the currently used protocol and the 3D EPI protocols. In general, the protocol with low bandwidth and 4× bi-polar echoes had the best precision, as predicted, by having the longest sampling time (Table 1). For all coil setups, the 3D GRE protocol further had the worst precision— approximately 1.5–2× lower than the currently used protocol.

Figure 3 shows full FOV magnitude images for the 8 protocols from the scans using the head coil at 3 T, to show differences in SNR, image quality, artifacts and distortions. In Figure 4 cropped FOVs zooming in on the skull cap and the base of the brain are shown, as these areas close to tissue-air interfaces can be prone to image artifacts and are susceptible to distortions.

In general, the best image quality with least distortions are seen in the high BW 2D GRE protocol (Fig. 3d and Fig. 4d and l), and the 3D GRE protocol (Fig. 3e and Fig. 4e and m) which also has high readout BW. The lower BW 2D GRE protocols and the EPI based protocols all show more distortions, especially towards tissue-air interfaces as shown in Figure 4.

At 1.5 T the currently used protocol (2D GRE) and two of the 3D EPI protocols (3D EPI and 3D EPI with fatsat) demonstrated a precision within one standard deviation of each other for all coil setups, whereas the 3D EPI protocol using flyback was slightly better for all coil setups. This 3D EPI protocol showed similar precision as 2D GRE with 3xMono and with 11xBi, whereas 2D GRE with 4xBi had the best precision, as predicted by having the longest sampling time (Table 1). The 3D GRE protocol had the worst precision of all protocols as expected.

Phantom Study

Figure 5 shows two orthogonal views through the laser hot spot at the time of maximum heating for all eight protocols for the 3T study. The precision measurements from the *in vivo* study (Fig. 1 and Table 2) are consistent with a qualitative estimate of the background noise visible in this figure; the multi-echo 2D protocols have the best precision, followed by the single echo 2D protocol and the EPI protocols, and the 3D GRE protocol shows the lowest precision. Table 3 summarizes the precision in the red ROIs shown in Figure 5. For the 2D data, Table 3 lists the precision for both the coronal and the sagittal slices, and for the 3D protocols the precision both for zero-filling in two and three dimensions are listed. For the 2D data the precision can be seen to be slightly higher in the sagittal plane than in the coronal plane since the ROIs in the sagittal plane are located closer to the receive coil (which was wrapped around the posterior part of the skull phantom) than the ROIs in the coronal plane. For the 3D data it can be seen that, as expected, the precision is not affected by zero-filled interpolation (since image SNR is not affected by zero-filled interpolation, and SNR is proportional to MRTI precision). All 2D multi-echo protocols outperform the currently used

protocol (2D GRE). At 3T two EPI protocols (3D EPI and 3D EPI with fatsat) are slightly better, whereas one EPI protocol (3D EPI with flyback) is slightly worse. In all cases 3D GRE is substantially worse than all other protocols.

Figure 6 shows a comparison of the measured MRTI to the fiber optic temperature probe measurements for the 3T study. The accuracy in the MRTI measurement, evaluated as the RMSE and the mean error between the MRTI and the fiber optic temperature probe measurements are shown in Table 3. Excluding 3D GRE, the RMSE is between 0.2°C and 0.4°C for 3T and between 0.4°C and 0.7°C for 1.5 T. The mean error is below 0.1°C for 3T and between 0.1°C and 0.4°C for 1.5 T.

Supplementary Figure S7 shows temperature rise versus time curves for the voxel experiencing the greatest temperature rise for all eight protocols, for both the 3T and 1.5 T studies. For the 2D protocols (subfigures a and c) MRTI measurements from the coronal and sagittal slices are plotted in the interleaved order that they are acquired.

The effect of applying zero-filling in two versus three directions is shown in Supplementary Figure S8. Zero-filling in the slice encoding direction creates much smoother looking temperature maps in this direction. Due to decreased partial volume effects the maximum measured temperature rise also increased by 4–8% in the 3T study, and by 8–17% in the 1.5 T study (data not shown).

DISCUSSION

This study has developed, tested, and evaluated a set of 2D and 3D protocols for MRTI in an attempt to improve upon the 2D protocol currently used during clinical treatments with a commercially available LITT system. We investigated four different 2D protocols and four different 3D protocols and showed that improved precision could be achieved in the 2D protocols by adding multi-echo readouts, and that fully volumetric 3D imaging can be achieved with similar precision and accuracy as the currently used 2D protocol (although not with as high precision as for the multi-echo 2D protocols).

The three 2D multi-echo protocols showed that by simply adding multiple echoes to convert “dead-time” to sampling time, large improvements in precision, which are expected theoretically, could be achieved. The protocol with high bandwidth and 11xBi-polar echoes showed that using a higher readout bandwidth, which yields smaller distortions due to off-resonance effects and fat-water shifts, and adding even more echoes still gave significantly improved precision. The improved precision is due to both the prolonged sampling time and to longer TEs for the later echoes. The longer TEs are closer to the optimal TE of $TE = T_2^*$, which in this case was achieved without negatively affecting the acquisition time by increasing the TR.

Multi-echo sequences will produce more data than a single echo sequence, but the echo combination that is optimal for MRTI precision is a simple weighted summation and is not anticipated to create any problems in terms of reconstruction time on modern imaging hardware. If reconstruction time were a problem, the last echo of the multi-echo scan, which

has the longest TE and hence the best precision, could be used by itself for temperature calculation without substantial decrease in precision.

All three suggested segmented EPI protocols overall showed accuracy and precision similar to the currently used 2D GRE protocol. They also measured higher temperatures when zero-filling was performed in all three directions compared to only in-plane, due to reduced partial volume effects. Monitoring a contiguous 3D volume around the LITT fiber should allow for more accurate predictions of treatment effect and volume of necrotized tissue.

The 3D GRE protocol, while producing good magnitude images, suffered from the short TE associated with the short TR required to get scan times comparable to the other protocols. If the constraint on scan time was relaxed, a longer TR and TEs could be used for improved MRTI precision. For example, for the 3 T protocol if the TR and TE were both increased by 5 ms, five to six echoes could be sampled with the latest having a TE similar to the 10 ms TE of the currently used 2D GRE protocol. The scan time for this protocol would be 9.69 s, but the fact that it is 3D (resulting in a SNR improvement of $\sqrt{N_z}$ and multi-echo should result in better precision than the currently used 2D GRE protocol. It is therefore possible that a 3D GRE protocol with a scan time around 8–9 seconds could produce similar precision as the currently used 2D GRE protocol. It should, however, be noted that the 3D GRE protocol used GRAPPA ($R = 2$) and will only be a viable option with adequate RF coils. In the current set of experiments, GRAPPA was used for all 3D GRE scans except for the 1.5 T *in vivo* body coil scan. On the 3T system, the body coil contains two channels, so GRAPPA could be used but it left clearly noticeable ghosting artifacts in the images, as can be seen in Figure 1a.

As can be seen comparing the magnitude images in Figure 3 to those in Supplemental Figures S3, the image quality is better at 3T than at 1.5T, as expected. In general, GRE protocols show the least amount of artifacts, with 2D GRE 11xBi showing the cleanest images. However, this protocol results in slightly lower SNR than the other 2D protocols, as can be seen in the higher background noise level. The EPI images have more blurring artifacts, but show better contrast between white and gray matter, and between brain tissue and CSF. Overall the image quality of the EPI images can be deemed adequate for clinical applications.

The three coil setups used in the *in vivo* part of this study were chosen to cover a wide range of coil options from non-local body coil to local, dedicated flex and head coils. The quantitative comparison between the different coil setups (Fig. 2) demonstrates that both the flex coil and head coil provided up to eight times better MRTI precision than the body coil. The flex coil, which was wrapped around the posterior part of the head, had equivalent precision to the head coil and much better precision compared to the body coil in this area. The flex coil was less precise than the head coil in the anterior part as expected. In general, some form of wrap around/flex coil provides a good trade-off between improved imaging and high SNR while still allowing the surgeon access to the necessary anatomy during LITT treatments. Flex coils also provide flexibility as they can be relatively freely positioned to provide good SNR at the intended target region. Depending on the target, using the posterior part of a head coil together with a flex coil wrapped anteriorly is also a good approach.

In this study temperature accuracy was evaluated by comparing MRTI measurements to fiber optic temperature probe measurements. One challenge with this approach is that the fiber optic temperature probes are affected by the laser light emitted from the LITT system. The probes have to be placed far enough away to give meaningful measurements, but still close enough to measure noticeable temperature rises. Another challenge is for 2D imaging, where it is hard to know that the single 2D slice is really centered exactly on both the laser fiber/catheter and the fiber optic temperature probe. For the 3D protocols, zero-filling can be performed in all directions including the slice direction and a full stack of slices is also available, so it is easier to ensure that temperatures at the actual fiber optic temperature probe position are investigated. For the 1.5 T study, the fiber optic probe measurements gave non-meaningful readings for the last runs for protocols 2D GRE 9xBi and 3D EPI with flyback, as can be seen in Supplemental Figure S6 and in Table 3. For these cases we only included the first two runs in the accuracy measurements listed in Table 3.

One of the main goals of this work was to utilize only widely available pulse sequences with straightforward real-time reconstruction approaches to enable fast and vendor-neutral clinical adaptation. However, a wide range of more advanced pulse sequences and reconstruction methods for MR thermometry have been developed and should be considered in the future as they become more widely available. Non-Cartesian pulse sequences using, e.g., radial and spiral trajectories have been described [35,44–47]. Non-Cartesian acquisitions are inherently less sensitive to motion as the center of k-space is sampled more frequently than in Cartesian approaches. However, reconstruction time can be a challenge as the data is commonly re-sampled onto a Cartesian grid and depending on the acquisition scheme time-consuming off-resonance corrections might be needed. To improve temporal resolution, which can be traded for larger field of view, various dedicated reconstruction methods for sub-sampled k-space data have also been described. These include compressed sensing-like constrained methods, (thermal) model-based approaches, and utilizing Kalman filters [17,48–54]. If multiple RF receive coils are available both parallel imaging and simultaneous multi-slice approaches, where the different coil sensitivity from multiple RF coils are used to unwrap aliasing, further offers potentially faster imaging and/or larger field of views [46,55–57].

CONCLUSIONS

This work has shown that substantially improved MRTI precision, by approximately a factor of 2×, can be achieved by using multi-echo readouts to reduce “dead time” and increase the sampling time. It was further shown that 3D volumetric measurements with the same precision and accuracy as the currently used protocol can be achieved in the same scan time. With 3D MRTI acquisition, zero-filling can be performed in all three dimensions, minimizing partial volume effects. Further, the full 3D volumetric monitoring of the target should also enable more accurate treatment evaluations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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APPENDIX A

This *appendix* derives the optimal weights to combine multi-echo PRF MRTI data to achieve the optimal temperature precision. The variance, σ^2 , of the MRI phase, ϕ , can be written as

$$\sigma^2(\phi) = \frac{1}{|m|^2} \sigma^2(m) \quad (\text{A1})$$

where m is the complex MRI signal

$$m = |m| e^{i\phi}. \quad (\text{A2})$$

The well-known PRF equation gives the phase change, ϕ , between some baseline image and the current image as

$$\Delta\phi = \gamma\alpha B_0 TE \Delta T \quad (\text{A3})$$

where γ is the gyromagnetic ratio, α is the PRF coefficient (assumed to -0.01 ppm/ $^{\circ}\text{C}$), B_0 is the field strength of the main magnetic field, TE is the echo time, and T is the change in temperature giving rise to ϕ . For j different echoes, with echo times $TE_{1\dots j}$, this can be rearranged as

$$\Delta T_j = \frac{\Delta\phi_j}{\gamma\alpha B_0 TE_j} \quad (\text{A4})$$

and the corresponding variance is

$$\sigma^2(\Delta T_j) = \frac{\sigma^2(\Delta\phi_j)}{\gamma^2 \alpha^2 B_0^2 TE_j^2}. \quad (\text{A5})$$

Combining Equations A1 and A5 results in

$$\sigma^2(\Delta T_j) = \frac{\sigma^2(m_j)}{\gamma^2 \alpha^2 B_0^2 TE_j^2 |m_j|^2}. \quad (A6)$$

To get the optimal temperature measurement precision we want to find the optimal weights, w_j , for

$$\overline{\Delta T} = \sum_{j=1}^{Ne} w_j \Delta T_j \quad (A7)$$

where that $\sum_{j=1}^{Ne} w_j = 1$ and Ne is the total number of acquired echoes, such that the variance $\sigma^2(\overline{\Delta T})$ is minimized. Hence, to find the optimal weights we minimize

$$\sigma^2(\overline{\Delta T}) = \sum_{j=1}^{Ne} |w_j|^2 \sigma^2(\Delta T_j) \quad (A8)$$

such that $\sum_{j=1}^{Ne} w_j = 1$. The Lagrangian L can be written as

$$L = \sum_{j=1}^{Ne} |w_j|^2 \sigma^2(\Delta T_j) + \lambda \left(\sum_{j=1}^{Ne} |w_j| - 1 \right) = 0 \quad (A9)$$

where solving $\frac{\partial L}{\partial w_j} = 0$ gives

$$2 \sum_{j=1}^{Ne} |w_j| \sigma^2(\Delta T_j) + \lambda = 0. \quad (A10)$$

Combining Equations A6 and A10, and solving for the weight gives

$$\sum_{j=1}^{Ne} w_j = \frac{-\lambda \gamma^2 \alpha^2 B_0^2 TE_j^2 |m_j|^2}{2 \sigma^2(m_j)} = \left(\frac{-\lambda \gamma^2 \alpha^2 B_0^2}{2 \sigma^2(m_j)} \right) TE_j^2 |m_j|^2 = \lambda' (TE_j |m_j|)^2 \quad (A11)$$

where everything in λ' , including the variance of the signal $\sigma^2(m_j)$, is constant for all echoes since there is no noise correlation between the different echoes (as opposed to, e.g., different coil-images which experience noise-correlation). The optimal weights for the echo combination is hence to weight the individual echoes by $(TE \cdot |m|)^2$.

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Fig. 1.

Temperature precision and magnitude images for 3T *in vivo* experiment. Temperature precision is measured as temporal standard deviation in ROI shown in red box (21×21 voxels over 20 dynamics). Three different coil setups are shown; **a)** Body coil, **b)** Flex coil, and **c)** Posterior head coil + Flex coil.

Fig. 2.

Ratio of mean standard deviation through time for the different RF coils used for the 3T study. To compare the performance of the different coils the mean of the standard deviation through time for all eight protocols using the same coil was calculated, and the ratio of these means between the different coils were then calculated. (a–c) show ratios for Body coil versus Flex coil, Body coil versus Head coil, and Flex coil versus Head coil, respectively. A ratio of, for example, ~8 as can be seen in the posterior part of subfigure a) indicates that the flex coil had ~8 times better precision than the body coil in this region.

Fig. 3.
Magnitude images from 3T volunteer study. Full FOV for the head coil setup, for all eight protocols. Red boxes in **a)** show locations for cropped FOVs in Figure 4.

Fig. 4.

Cropped magnitude images from 3T volunteer study. (a–h) Show the cropped FOV of the scalp for the eight different protocols (Fig. 3), and (i–p) show the cropped FOV for the base of the brain (Fig. 3), all images are using the head coil setup.

Fig. 5.

Two orthogonal views of temperature maps for 3 T phantom experiment. (a–h) show sagittal (top row) and coronal (bottom row) temperature maps for the eight different protocols, respectively. The in-plane FOV is cropped to better show details. Temperature precision is measured as temporal standard deviation in ROI shown in red box (21×21 voxels over 20 dynamics).

Fig. 6.

Accuracy for 3 T phantom experiment. (a–d) show MR thermometry for the three repeated runs (solid lines) compared to fiber optic temperature probe measurements (dashed lines), for the four 2D protocols. (e–h) show corresponding data for the four 3D protocols.

TABLE 1.

Scan Parameters for the Eight Protocols, for Both Field Strengths (1.5 T and 3T)

Protocol	Slices	TR/TE (ms)	BW FE/PE (Hz/px)	Contrasts	Sampling time (ms)	ETL	ES (ms)	PF (SE)	t _{acq} (s)	Fat/Water shift (px)
1.5 T										
1. 2D GRE, Current protocol	3 mm, 1 + 1	23/15	260	1	3.85	na	na	na	5.888	0.8
2. 2D GRE, 3 × mono-polar	3 mm, 1+1	23/...18.62	260	3× Mono	11.54	na	na	na	5.888	0.8
3. 2D GRE, 4 × bi-polar	3 mm, 1+1	23/...18.62	260	4× Bi	15.38	na	na	na	5.888	±0.8
4. 2D GRE, 9 × bi-polar	3 mm, 1+1	23/... 19.94	700	9× Bi	12.86	na	na	na	5.888	±0.3
5. 3D GRE, 2× bi-polar	2.5 mm, 10 + 20%	8.6/...5.58	700	2× Bi	2.86	na	na	6/8	5.882	±0.3
6. 3D EPI	2.5 mm, 10 + 20%	25/14	698/111	1	7.16	5	1.8	6/8	5.85	±0.3/1.9
7. 3D EPI, Fatsat	2.5 mm, 10 + 20%	45/12	698/62	1	12.89	9	1.8	6/8	6.075	±0.3/3.4
8. 3D EPI, Flyback	2.5 mm, 10 + 20%	35/16	698/43	1	10.03	7	3.34	6/8	5.985	0.3/4.9
3 T										
1. 2D GRE, Current protocol	3 mm, 1+1	23/10	260	1	3.85	na	na	na	5.888	1.6
2. 2D GRE, 3 × mono-polar	3 mm, 1+1	23/...18.61	260	3× Mono	11.54	na	na	na	5.888	1.6
3. 2D GRE, 4 × bi-polar	3 mm, 1+1	23/...18.61	260	4× Bi	15.38	na	na	na	5.888	±1.6
4. 2D GRE, 11 × bi-polar	3 mm, 1+1	23/...20.00	810	11×Bi	13.58	na	na	na	5.888	±0.5
5. 3D GRE, 3× bi-polar	3 mm, 10 + 20%	7.75/...4.76	930	3× Bi	3.23	na	na	6/8	5.89	±0.4
6. 3D EPI	3 mm, 10 + 20%	25/17	1302/179	1	3.84	5	1.12	6/8	5.85	±0.3/2.1
7. 3D EPI, Fatsat	3 mm, 10 + 20%	35/12	1302/128	1	5.38	7	1.12	6/8	5.985	±0.3/2.9
8. 3D EPI, Flyback	3 mm, 10 + 20%	25/13	1302/90	1	3.84	5	2.21	6/8	5.85	0.3/4.1

Slices = slice thickness and number of acquired slices (20% = slice over sampling for 3D protocols), TR/TE = repetition time/echo time, BW FE/PE = Bandwidth in frequency encoding/phase encoding direction, Contrasts = Number of acquired echoes, with mono-polar or bipolar readouts, ETL = echo train length, ES = echo spacing, PF = partial Fourier (in slice encoding direction), t_{acq} = acquisition time.

TABLE 2.

Summary of *In Vivo* Temperature Precision

Precision (°C)	Protocol: Coil:	1. 2D GRE	2. 2D GRE 3× mono	3. 2D GRE 4× bi	4. 2D GRE 9/11× bi	5. 3D GRE	6. 3D EPI	7. 3D EPI F atsat	8. 3D EPI Flyback
1.5T	Body coil	4.85 ±1.38	3.00 ±0.65	2.44 ±0.49	2.98 ±0.56	25.69 ±5.95	4.89± 1.41	4.49 ±1.13	3.10±0.81
	Flex coil	0.74 ±0.13	0.53 ±0.09	0.45 ±0.08	0.50 ±0.09	4.89 ±0.93	0.84±0.18	0.64 ±0.12	0.54±0.11
	Head coil	0.84 ±0.15	0.61 ± 0.11	0.54±0.13	0.56±0.11	6.05 ±1.55	0.95 ±0.22	0.71 ± 0.17	0.60±0.13
3T	Body coil	2.35 ±0.47	1.06±0.21	0.99±0.17	1.06 ±0.22	3.33 ±0.59	1.79 ±0.38	2.25 ±0.41	2.10 ± 0.44
	Flex coil	0.43 ±0.08	0.22 ±0.05	0.19±0.04	0.20 ±0.04	0.92± 0.18	0.37 ±0.06	0.54 ±0.13	0.45±0.10
	Posterior Head + Flex coils	0.43 ±0.08	0.21 ±0.04	0.19±0.04	0.21 ±0.04	0.91 ± 0.18	0.39 ±0.08	0.51 ±0.12	0.50±0.10

Temperature precision, in °C, for all eight protocols for the three coil setups, for both field strength of 1.5 T and 3T.

TABLE 3.

Temperature Precision and Accuracy for 1.5T and 3T Phantom Experiments

Precision (°C)	Protocol: Orientation:	1. 2D GRE	2. 2D GRE 3× mono	3. 2D GRE 4× bi	4. 2D GRE 9/11× bi	5. 3D GRE	6. 3D EPI	7. 3D EPI Fatsat	8. 3D EPI Flyback
1.5T	Sagittal with ZFI in 3D	n/a	n/a	n/a	n/a	1.19±0.17	0.29±0.04	0.26±0.04	0.22±0.03
	Sagittal with ZFI in 2D	0.38±0.05	0.25±0.04	0.22±0.04	0.24±0.04	1.19±0.18	0.29±0.04	0.26±0.04	0.22±0.03
	Coronal with ZFI in 2D	0.39±0.05	0.26±0.04	0.23±0.03	0.25±0.03	n/a	n/a	n/a	n/a
3T	Sagittal with ZFI in 3D	n/a	n/a	n/a	n/a	0.41±0.06	0.19±0.02	0.19±0.02	0.26±0.03
	Sagittal with ZFI in 2D	0.20±0.03	0.08±0.01	0.08±0.01	0.08±0.01	0.41±0.06	0.19±0.02	0.19±0.02	0.27±0.03
	Coronal with ZFI in 2D	0.22±0.03	0.10±0.01	0.09±0.01	0.09±0.01	n/a	n/a	n/a	n/a
Accuracy (°C)	Protocol: Measure:	1. 2D GRE	2. 2D GRE 3× mono	3. 2D GRE 4× bi	4. 2D GRE 9/11× bi	5. 3D GRE	6. 3D EPI	7. 3D EPI Fatsat	8. 3D EPI Flyback
1.5T	RMSE between fiber optic probe and MRTI	0.72±0.21	0.47±0.08	0.63±0.32	0.43±0.01 [*]	2.17±0.13	0.51±0.09	0.57±0.16	0.53±0.12 [*]
	Mean difference between fiber optic probe and MRTI	±0.30	±0.12	±0.37	±0.05 [*]	±0.80	±0.24	±0.09	±0.12 [*]
3T	RMSE between fiber optic probe and MRTI	0.33±0.07	0.17±0.07	0.19±0.07	0.17±0.05	0.62±0.04	0.31±0.01	0.32±0.02	0.40±0.02
	Mean difference between fiber optic probe and MRTI	±0.03	±0.06	±0.05	-0.02	±0.09	±0.07	±0.04	±0.10

For 2D protocols the precision for the two orthogonal slices (sagittal and coronal) are shown. For 3D protocols the precision for zero-filling in 2D (only in-plane) and 3D (in all three directions) are shown. For accuracy, the mean and standard deviation of the RMSE between the probe measurements and MR thermometry for all three repeated runs, and the mean of the difference between the probe measurements and the MR thermometry for all three repeated runs, are listed.

* Note: Run three for protocol #4 and #8 for the 1.5T study gave non-meaningful fiber optic probe readings, so these runs are excluded from the analysis.