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Ultrafast 1D MR thermometry using phase or frequency mapping

Chang-Sheng Mei^{1,2}, Robert V. Mulkern^{2,4}, Koichi Oshio², Nan-kuei Chen³, Bruno Madore², Lawrence P. Panych², Kullervo Hynynen^{5,6}, and Nathan McDannold²

¹Department of Physics, Boston College, Chestnut Hill, MA, USA

²Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

³Brain Imaging and Analysis Center, Duke University Medical Center, Durham, NC, USA

⁴Department of Radiology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

⁵Department of Imaging Research, Sunnybrook Research Institute, Toronto, Canada

⁶Department of Medical Biophysics, University of Toronto, Toronto, Canada

Abstract

Object—To develop an ultrafast MRI-based temperature monitoring method for application during rapid ultrasound exposures in moving organs.

Materials and Methods—A slice selective 90° – 180° pair of RF pulses was used to solicit an echo from a column, which was then sampled with a train of gradient echoes. In a gel phantom, phase changes of each echo were compared to standard gradient-echo thermometry, and temperature monitoring was tested during focused ultrasound sonications. SNR performance was evaluated in vivo in a rabbit brain, and feasibility was tested in a human heart.

Results—The correlation between each echo in the acquisition and MRI-based temperature measurements was good ($R=0.98\pm0.03$). A temperature sampling rate of 19 Hz was achieved at 3T in gel phantom. It was possible to acquire the water frequency in the beating heart muscle with 5-Hz sampling during a breath hold.

Conclusion—Ultrafast thermometry via phase or frequency monitoring along single columns was demonstrated. With a temporal resolution around 50 ms, it may be possible to monitor focal heating produced by short ultrasound pulses.

Keywords

echo-planar magnetic resonance imaging; thermometry; proton resonance frequency shift; MR spectroscopy

Introduction

Minimally-invasive thermal ablation using radio frequency, microwave, laser, and focused ultrasound (FUS) are evolving alternatives to surgical resection. FUS is of particular interest due to its noninvasive nature and successful treatments in several clinical applications [1]. MR thermometry is a natural choice for guidance of FUS surgeries, given its ability to visualize, monitor, and evaluate the success of treatments.

MR thermometry is made possible by the fact that several MR parameters exhibit a temperature-dependence. Among these parameters, the measurement of water proton resonance frequency (PRF) may be the best candidate for temperature measurements [2,3]. PRF shifts linearly with temperature in the range of interest for thermal ablation [4]. It can be mapped using spectroscopic imaging to detect the water proton chemical shift between the water peak and a reference peak that remains constant with temperature, such as lipids [5]. Alternatively, one can use the phase change resulting from the temperature-induced PRF shift with a gradient-recalled echo (GRE) imaging sequence [6]. Both approaches are able to quantitatively monitor tissue temperature.

The implementation of MR temperature measurements, however, remains challenging for some applications, such as FUS ablation in the beating heart, where very short, high-power exposures may be required. Temporal resolution must be sufficient to capture rapid changes induced either by temperature or by motion. Many fast imaging methods, including echo-planar [7,8], spiral [9], PRESTO [10,11] and SSFP [12–14] have been proposed to accelerate acquisition in temperature mapping. A sub-second temporal resolution has been achieved, with a temperature sensitivity comparable to classical GRE MR thermometry. Parallel imaging has also been proposed to accelerate the image acquisition process [15,16]. However, improving imaging speed is still very much a need for cardiac FUS ablation [17].

The purpose of the present study is to test a one-dimensional method for rapidly monitoring temperature changes. The ultimate goal is to monitor heating induced by short ultrasound pulses in moving organs, such as the heart. To this end, a line scan echo planar spectroscopic imaging sequence [18] (called ‘LSEPSI’ below) was tested for thermometry via frequency and phase mapping. In previous work, the sequence was demonstrated for temperature monitoring in the breast in volunteers [19]. In that study, 64 adjacent columns were sequentially sampled throughout both breasts to acquire spectra for a 2D chemical shift image from 4096 voxels in a scan time of 6.4 s. Although this is considered fast for 2D spectroscopic imaging, it is not sufficient for imaging the heart, where sub-second imaging may be required. In comparison, in the present work, the 2D spatial coverage was sacrificed to allow ultra-rapid, serial, 1D acquisition. We tested whether data from each echo time in the gradient-echo train could be used individually to detect phase changes, allowing multiple temperature measurements in a single column acquisition. Signal-to-noise ratio (SNR) properties were tested in vivo in a rabbit model, and feasibility in the context of cardiac imaging was tested in a healthy volunteer.

Materials and Methods

Pulse sequence

The LSEPSI sequence shown in Fig. 1 and described in [18–20] was implemented on GE scanners (Milwaukee, WI) (3.0-T for rapid measurement experiments and 1.5-T for others). With this sequence, a selective 90° pulse and a selective 180° pulse were applied to intersecting slices, so that only the line located at the intersection of the two planes generates a spin echo signal. The second half of the spin-echo formed at TE = 10 ms was sampled repeatedly, using an asymmetric (i.e., fly-back) echo-planar readout waveform. The inter-echo spacing in the echo-planar waveform was in the range from 2.1 to 3.7 ms, with different values used for different experiments. Additional image parameters of the LSEPSI sequence included the column sample rate (i.e., TR), field of view (FOV), slice thickness, number of frequency encoding steps per gradient echo, and receiver bandwidth (BW) are listed in Table 1, for the various experiments performed here. The spoiler gradients following the echo-planar readout train were modified from TR to TR, based on a 6 step phase cycling scheme (x, y, z, -x, -y, -z) to eliminate ghosting artifacts from indirect echoes [18].

The first half of the spin-echo was not sampled due to the design of the sequence, where the time between the 90° and 180° pulse was made as short as possible. As a result, there was essentially no time to sample data since the duration between the refocusing pulse and the spin echo was only enough to play the right element of the crusher pairs and the prephasing gradient lobe. In addition, the spin echo itself was not a good time to sample temperature information as all phase changes (including temperature-induced phase changes) were refocused, we effectively could only sample from the spin echo onward, i.e., the second half of the spin echo.

The effective echo time (TE_{eff}) for the i^{th} gradient echo in the echo train is defined as the interval between the moment the spin-echo is formed and the center of the i^{th} gradient echo, where i ranges from 1 to the echo-train length. For example, the TE_{eff} of the very first echo ($i = 1$) is 0, and the TE_{eff} of the i^{th} echo is $(i - 1) \times \text{echo spacing}$. For simplicity, the TE_{eff} of the LSEPSI sequence is represented by “TE” throughout this paper.

Heating experiments

All heating experiments were performed in a homogeneous gel phantom (ATS Laboratories, Bridgeport, CT, see reference [21] for its ultrasound properties). The experimental setup is shown in Fig. 2. The transducer was mounted in an MRI-compatible positioning system and submerged in a tank of degassed, deionized water. The positioner was built into a cradle that fit the scanner bore and was used to control the transducer position. The phantom was placed in the sonication path of the transducer. Ultrasound propagated through the water and focused inside the phantom. A receive-only surface coil (GE Healthcare, Milwaukee, WI) with a diameter of 7.6 cm was positioned around the phantom at the level of the heating focus. The experimental setup was described in detail in reference [22]. The transducer, ultrasound driving system, and positioning system were constructed in-house.

Calibration experiments—A 1.63-MHz focused ultrasound transducer was used (diameter/radius of curvature: 10/8 cm). The transducer was a 16-channel phased array cut into a sector-vortex configuration and operated in “mode 4” to increase the focal volume [23]. In this mode, sixteen foci were produced simultaneously that were arranged around the central axis of the transducer in the focal plane in a ring pattern. Initially, the heating pattern mimicked this focal pattern. Over time, the center of the ring was heated via thermal conduction and a relatively uniform temperature distribution resulted. Using this mode created a wider focal zone (12×12mm) and reduced the effects of voxel averaging. The transducer was driven by a multi-channel amplifier system [24].

To ensure that the LSEPSI sequence correctly measured temperature changes, comparisons were made with a standard thermometry sequence. Dynamic 1D imaging using the LSEPSI sequence was performed over a 40-s period using a TR of 2-s, so that 20 echo trains (each consisting of 32 gradient echoes) were obtained. Heat was generated by a 20-s sonication with an acoustic power of 11 W. After a cooling period that allowed the temperature to return near baseline, another sonication with the same ultrasound parameters was delivered at the same location. A GE product 2D spoiled-GRASS (SPGR) gradient-echo sequence was used to map the temperature changes [6] (FOV: 10×10 cm, TR/TE: 40/20 ms, matrix size: 256×128, flip angle: 30°, slice thickness: 3 mm, BW: ±3.57 kHz, time frames: 10). Both the LSEPSI column and the SPGR plane were placed perpendicular to the direction of the ultrasound beam, and the frequency encoding of both sequences were oriented in the same direction. In addition, the 1D column was prescribed to be enclosed by the 2D plane and to pass the focus. For both sonications, a baseline image was acquired before the ultrasound was turned on. The calibration experiment was repeated at five different locations in the same phantom.

Because data were sampled at different spatial and temporal locations with the LSEPSI and the SPGR sequences, careful consideration was required when performing comparisons. A 5×1 region of interest (ROI) was defined at the center of the 1D column along the frequency encoding direction. As the LSEPSI column was solicited by two orthogonal, oblique slices, this ROI was in the shape of a diamond (see Fig. 1) in the slice and phase encoding directions. All SPGR voxels that mapped onto the diamond-shape ROI were scaled by a distance d , shown in Fig. 1. The phase change of the LSEPSI column in the ROI was then compared to the weighted average of the temperature changes within those mapping SPGR voxels. The ROI (3.9×4.2 mm, where 3.9 mm was the size of the 5 voxels along the frequency encoding direction, and 4.2 mm was the distance of the diamond shape from corner to corner) was at the very center of the focal region; therefore, a partial volume effect was not expected. Temporally, 19 LSEPSI-derived phase changes were interpolated down to 9 phase changes, which coincided with the 9 time points acquired with the SPGR.

Phase changes of all 32 echoes obtained from all 5 sonicated locations were then calibrated as a function of the temperature rises estimated from the SPGR temperature mapping. Least-square fitting was used to derive the temperature sensitivity of the LSEPSI sequence in radians/ $^{\circ}\text{C}$, as well as in ppm/ $^{\circ}\text{C}$ as a function of the LSEPSI echo time.

Rapid measurement experiments—A single-element, spherically-curved, piezoelectric transducer (frequency: 1.5 MHz; diameter/radius of curvature: 10/10 cm) generated the ultrasound fields. The transducer was driven by an amplifier system described in details in reference [25].

The LSEPSI sequence used a column sample rate of 19 Hz (i.e., TR of 53 ms). Data were acquired continuously for 53 s while sonication with 32W acoustic power was delivered for 20 s. Images acquired 13 s before heating were used as baselines. The column was placed parallel to the ultrasound beam and through the focus. A 5×1 ROI in the focus was selected for temperature estimation. Temperature rises were estimated using 7 out of all 8 echoes, those with a TE greater than or equal to 3.3 ms. The temperature noise level was estimated using the standard deviation of the temperature changes over the time frames before FUS heating, in the same ROI.

LSEPSI temperature estimation—Complex data were acquired to produce phase-difference maps. The phase difference between an image Z_t^i acquired from the i^{th} echo at time t and a preheating baseline Z_0^i was calculated by:

$$-\pi \leq \Delta\phi_t^i = \text{phase}(Z_t^i / Z_0^i) = \text{phase}(Z_t^i Z_0^{i*}) \leq \pi$$

where $*$ denotes complex conjugation. Temperature changes from one column acquisition to the next (i.e., from one TR to the next) were estimated by exploiting the temperature dependence of the PRF, which changes at a rate of -0.01 ppm/ $^{\circ}\text{C}$, or -0.64 Hz/ $^{\circ}\text{C}$ at 1.5T, in water [6]. Changes in the PRF were estimated by dividing the phase difference by $2\pi\text{TE}^i$ where TE^i was the i^{th} effective echo time.

Not all echoes were appropriate for temperature estimations, due to $\text{SNR}_{\Delta\phi}$ considerations, which can be estimated as follows:

$$\text{SNR}_{\Delta\phi} = |\Delta\phi(\Delta T)| / \sigma_{\Delta\phi} \quad (1)$$

where $\Delta\phi(\Delta T)$ is an echo's phase difference between the column at the current time and the column of baseline, and $\sigma_{\Delta\phi}$ is the standard deviation of the phase-difference image, which can be approximated as [26]:

$$\sigma_{\Delta\phi} = 1/SNR \quad \text{if } SNR \gg 1 \quad (2)$$

where $SNR = A/\sigma$ is the magnitude signal, and σ is the Gaussian noise in a real or imaginary image. Eq. 1 then becomes:

$$SNR_{\Delta\phi} = |\Delta\phi(\Delta T)| \cdot SNR \quad (3)$$

As TE increases, SNR decreases exponentially with $T2^*$, yet $\Delta\phi$ (ΔT increases linearly with TE. The TE dependence of $SNR_{\Delta\phi}$ can be written as follows:

$$SNR_{\Delta\phi} \propto TE e^{-TE/T2^*} \quad (4)$$

Therefore, poor $SNR_{\Delta\phi}$ is expected in early echoes due to their short TE values and possibly in some later echoes, depending upon the $T2^*$. Optimal $SNR_{\Delta\phi}$ is expected at $TE = T2^*$ [27]. Note that this analysis is true only for $A \gg \sigma$. However, for $3 A/\sigma \geq 3$, a fairly low SNR, it is still considered to be approximately true [26]. Image reconstruction, phase-difference calculations and data analysis were all performed in MATLAB (MathWorks, Natick, MA).

In vivo experiments

Rabbit brain imaging—Our institution's animal committee approved the experiments. Based on Eq. 4, some early and later echoes might not be utilized for temperature measurements. To experimentally evaluate the $SNR_{\Delta\phi}$ performance as a function of TE in vivo, non-heating experiments were performed in the brain of a male New Zealand white rabbit. The rabbit was placed supine in the setup as described above. A 7.5 cm diameter receive-only surface coil (GE Healthcare) was placed below the rabbit head at the level of the imaging column. LSEPSI imaging with TR= 15 s was performed in a location in the thalamus. A total of 128 echoes ranging from 0 ms to 469.4 ms (echo spacing of 3.7 ms) were acquired during each TR period. Two acquisitions of a column, obtained in consecutive TR periods, were used to produce phase-change and temperature-change maps. To test the T1 saturation effect, a dynamic dataset of TR = 206 ms was acquired in the same location with a total of 48 echoes ranging from 0 ms to 173.7 ms. After steady state was reached, two acquisitions were obtained sequentially to produce phase-change and temperature-change maps. See Table 1 for other imaging parameters. Noise (standard deviation) in the phase-change map, as well as in the temperature-change map, for an ROI of 4×1 voxels in size, was plotted as a function of the echo times.

Volunteer imaging—Our institutional review board approved the imaging protocol and the volunteer provided written informed consent. To test whether spectroscopic temperature imaging in the heart was feasible with the proposed method, a 52 year-old male was imaged with a column sample rate of 5 Hz. A 2D chest image was first acquired during a breath hold by sweeping the columns stepwise across an image plane [18] (64 adjacent columns, 32×32 cm FOV, 12.8 s scan time). The column through the heart muscle was selected for frequency mapping. A time series of 1D images were then acquired for a 40.0 s period. The images were acquired using a receive-only surface coil (GE Healthcare) with a diameter of 18.0 cm with a breath hold but without cardiac gating (echo spacing = 2.1 ms, spectral bandwidth = $(2.1 \text{ ms})^{-1} = 476 \text{ Hz}$, other imaging parameters in Table 1). $SNR_{\Delta\phi}$ performance in the ROI

of myocardium was evaluated in a manner similar to the rabbit brain experiments. Two consecutive time frames in the dynamic 1D dataset were taken to analyze the noise levels in the phase-change and temperature-change maps.

Results

Calibration experiments

The temperature calibration results in the gel phantom are shown in Fig. 3. The correlation between the LSEPSI-measured phase changes for different echo times and the temperature as measured with the SPGR sequence are shown in Fig. 3a. Data from the first echo time ($TE = 0$) were excluded since there is no expected phase change. For clarity, in Fig. 3a, data for only nine out of the 31 echoes are shown. Good correlation was found through linear regression ($R = 0.98 \pm 0.03$) for all echoes. Fig. 3b shows the temperature sensitivity (radians/ $^{\circ}\text{C}$) obtained through the linear regression described above, as a function of TE. In other words, the slope of each line in Fig. 3a gives rise to one point in Fig. 3b (31 points for 31 echoes, 9 of which are actually displayed in Fig. 3a). The standard errors estimated from the fits in Fig. 3a are shown in Fig. 3b as the error bars. The solid line represents a linear fit of the temperature sensitivity as a function of TE (slope: $4.2 \times 10^{-3} \pm 1.4 \times 10^{-5}$ radians/ $^{\circ}\text{C}/\text{ms}$, intercept: $3.5 \times 10^{-5} \pm 9.4 \times 10^{-4}$ radians/ $^{\circ}\text{C}$). This result shows that the temperature-induced phase changes scale linearly as expected with the TE setting, and that the sensitivity extrapolates to zero with a zero TE. The temperature sensitivity in ppm/ $^{\circ}\text{C}$ as a function of TE is plotted in Fig. 3c. Most of the values were consistent between -0.0100 and -0.0105 ppm/ $^{\circ}\text{C}$, except the TE values ranging from 3.7 ms to 14.8 ms. This discrepancy is not surprising due to the low expected $SNR_{\Delta\phi}$ (Eq. 4) obtained for a short TE value. The average value was -0.0103 ± 0.0004 ppm/ $^{\circ}\text{C}$, in good agreement with the generally-accepted -0.01 ppm/ $^{\circ}\text{C}$ value for pure water [28]. In Fig. 3d, temperature-change measurements at the focus are compared for our proposed method ('o' markers in the solid line) and for the reference SPGR sequence ('x' markers in the dashed line). Temperature curves from all 5 sonicated locations were averaged. For the LSEPSI results (solid line), data from all echoes were averaged with a weighted combination, where weights were derived based on the expected $SNR_{\Delta\phi}$ in Eq. 4 (T_2^* value of the gel phantom = 111 ms). Good agreement was observed between the LSEPSI and reference sequence.

Rapid measurement experiments

Focal heating along the ultrasound beam was quantified using phase mapping at a column sample rate of 19 Hz (i.e., $TR = 53$ ms). A weighted combination of echoes ≥ 3.3 ms, based on the expected $SNR_{\Delta\phi}$ of each echo, was used to illustrate inter-TR temperature mapping. Fig. 4b shows the time series of the one-dimensional temperature mapping during FUS heating and cooling periods. The vertical dimension represents the along-column spatial dimension and the horizontal dimension represents time. It suffers from high temperature noise due to the high temporal resolution. Fig. 4a shows a time series of magnitude images from 5 to 10s, where signal voids around the center, caused by a small hole in the gel phantom, might account for the horizontal artifacts in Fig. 4b. The maximum heating was observed at 33 s, which is when the transducer was turned off. Fig. 4c shows the temperature rise over time from the ROI at the focus. Seven out of eight echoes were utilized for temperature measurements, which are displayed in different colors in Fig. 4c. In total, 6993 measurements were achieved in 53 s (7 echoes per TR period $\times$ 999 TR periods = 6993 echoes). The noise levels were 2.4 and 1.5 $^{\circ}\text{C}$ for the first two echoes (TE values of 3.3 and 6.5 ms), and 0.8 ± 0.1 $^{\circ}\text{C}$ for the rest of the echoes (TE values of 9.8 ms or greater).

Rabbit brain imaging

Data of TR = 15 s were analyzed in Fig. 5a,b. Fig. 5a plots the noise level in the temperature maps of a non-heated ROI in the rabbit brain, as a function of the TE value. Fig. 5a is used to determine the lowest value of TE that should be utilized for the temperature measurement. For 127 echo times ranging from 3.7 ms to 469.4 ms, the temperature noise level settled down to a level of about 0.5 °C for TE values greater than about 50 ms. Fig. 5b plots the noise level in the phase-change maps and is used to determine the highest value of TE. The phase noise is theoretically a good surrogate for the reciprocal of the SNR, as long as the mean signal in the magnitude images divided by the noise level in the real and imaginary images gives a number larger than 3 [26]. For echo times larger than 200 ms, phase noise rose above 0.3 radians, and SNR dropped below 3. This suggests that TEs larger than 200 ms should be discarded for the temperature measurement. From the analysis of Fig. 5a,b, TEs between 50 and 200 ms could be utilized for thermometry and noise of 0.5 °C is expected.

The same analysis was performed using data of TR = 206 ms in Fig. 5c,d. TEs between 50 ms and 100 ms could be utilized for the temperature measurement and a noise level of 2 °C is expected. Please note that the temperature noises in Fig. 5a,c (for TR=15 s and 206 ms, respectively) decay at about the same rate; both curves reach a steady value around 50 ms. This is reasonable because T2* was the same on both measurements. It is also reasonable that the temperature noise in Fig. 5c for the data with TR = 206 ms is higher than the data with 15 s in Fig. 5d, due to signal saturation. The comparison between datasets with long and short TR suggests that the lower limit of TE is independent of TR, and further suggests temperature noise and the lower limit of TE are determined by SNR.

Volunteer imaging

An axial chest image using 2D LSEPSI imaging is inset in Fig. 6. Each vertical line in the image was obtained sequentially, in an interleaved pattern. The periodic artifact from column to column and the artifact at the bottom of the heart were caused by cardiac motion. One line location over the heart was selected, and imaged 200 times over a 40 s period (i.e., TR = 200 ms), with 32 gradient-echoes acquired during every TR period. Fig. 6 shows a spectrum from one voxel located in the heart muscle in the inset image, where a water spectral peak can be observed. Note that it was possible to measure the PRF in a beating heart muscle, during breath hold.

The noise levels of both phase and temperature maps from two column acquisitions over the ROI of myocardium were analyzed. With a total of 32 echoes in 200 ms TR, the 15th to the 32nd echoes ranging from 30 to 66 ms could be used for measuring temperature, where the temperature noise of $1.4 \pm 0.6^\circ\text{C}$ is expected.

Discussion

It has been shown that ultrafast MR temperature measurement using the LSEPSI sequence is feasible. Each echo in the acquisition can be used as separate temperature measurements via phase mapping, although earlier and later echoes might not be useful for temperature-mapping purposes, due to high temperature noise. Phase changes of each echo in the echo train were calibrated so they could be converted into temperature changes. In one of the phantom experiments, 7 echoes out of the acquired 8 echoes were used with a sample rate of 19 Hz; i.e., 7 measurements were achieved every 53 ms. The signal from each one of these 7 echoes could be converted into a temperature curve with 53 ms resolution, and combining information from all 7 curves gives temperature-change results with uneven temporal resolution (resolution = echo spacing $\approx$ 3 ms during the echo train, with gaps about 30 ms

wide in between echo trains). The acquired cardiac data showed that spectral information could be obtained from the gradient echo train, allowing the PRF to be measured every TR.

In an alternative processing, one might be able to reconstruct all echoes in one step, rather than using different baseline data for each. However, the relationship between temperature change and phase would no longer be linear. For example, if one assumes that the temperature change ΔT over the very short echo train period is linear, the phase change $\Delta\phi$ could then be estimated as a parabolic function of TE according to:

$$\Delta\phi = \alpha \cdot \gamma \cdot B_0 \cdot 2\pi \cdot \int_0^{TE} \Delta T dt, \text{ where } \Delta T = at - b (a, b \text{ are both constants}) \quad (5)$$

where α is the apparent PRF-thermal coefficient (units of ppm/°C), γ is the gyromagnetic ratio for the ^1H nucleus, B_0 is the main magnetic field strength, and TE is the effective echo time. Temporal resolution can then be further improved to the level of echo spacing (a few ms). It is very challenging to validate the parabolic phase change relation in Eq. 5, due to the fact that the phase change over two immediate TEs is small and often overwhelmed by noise. However, heating by several degrees Celsius within a sub-second period could provide measurable phase changes. Lasers, for instance, make such rapid heating possible. For a 5°C increase in 200 ms within a $5 \times 5 \times 5 = 125 \text{ mm}^3$ volume in water gel phantom, we need a power of 5.4 W (specific heat capacity of water = 4.186 joule/gram°C). Modern laser systems for thermal ablation can easily achieve this. For example, the LITT Brain system, developed by Visualase (Houston, Texas), delivers up to 30 W.

The LSEPSI sequence provided a simple way to accelerate MR thermometry imaging as compared to echo-planar imaging (EPI). Modern parallel single-shot EPI sequences could achieve temporal and spatial resolutions comparable to the LSEPSI sequence that was implemented with sampling time of 53ms. However, the coil sensitivity encoding introduces noise enhancement and image artifacts. It also increases significantly the amount of computing time in post processing. In addition, EPI often suffers from distortions, signal voids, and ghosting. Distortion can be a considerable concern in the context of thermal ablation, as lesions must be located and tracked accurately. One can of course mitigate the distortion by shortening the echo-train length, for example by using interleaved EPI, or reducing the number of echoes, but there are always tradeoffs that compromise either temporal or spatial resolutions.

The advantage of an EPI sequence vs. the LSEPSI sequence is its 2D spatial coverage. However, while an EPI sequence provides better spatial coverage, the proposed technique provides better spectral coverage. Please note that the proposed method features a readout waveform very similar to that of an EPI sequence, and is just as efficient in terms of data acquisition rate. The main difference is that EPI has y-gradient blips in order to encode a second spatial frequency dimension in addition to the frequency-encoded dimension, while LSEPSI has no blips and covers one spatial dimension (frequency-encoded) and one spectral dimension. It is a trade-off for the purpose of ultra-fast thermometry. LSEPSI makes it possible to measure temperature via phase changes from TE to TE. It also makes it possible to measure temperature spectroscopically from TR to TR. Neither of these options is possible with a standard EPI. Concerning 2D spatial coverage, the present method could achieve it by sweeping columns through the desired ROI [20], although this comes with a price of reduced temporal resolution. Parallel imaging has also been applied to linescan sequences to increase scan efficiency [29] when more spatial coverage is necessary.

The spatial resolution of the present method is not as good as a regular 2D sequence, which could result in a partial volume effect in MR temperature imaging. However, LSEPSI could achieve a reasonable voxel size for thermal ablation applications. For example, the InSightec ExAblate 4000 TcMRgFUS system has a half-width-full-maximum focal region of about $3.0 \times 3.0 \times 5.8$ mm, as provided by the manufacturer, so a resolution of 3.0 mm could therefore be considered reasonable. Column selection is performed through two intersecting RF-excitation profiles and a slice thickness of 3.0 mm is readily achievable. LSEPSI has been implemented with an even better resolution down to 1.5 mm (data not shown). Therefore, the partial volume effect can be avoided. In the case of a very small focus region, this method might not be applicable. High temporal resolution and high spatial resolution inevitably result in very low SNR, a problem shared by all MR imaging techniques.

In the calibration experiment, temperature changes over heating and cooling periods were compared between the LSEPSI sequence and a SPGR reference sequence (Fig. 3d). Both measurements appeared to agree well, except for the peak temperature at 20 s. We suspect this might have been caused by the lower temporal resolution of the reference SPGR data, which were too low to accurately catch the peak temperature.

A study by Peters and Henkelman [30] showed that temperature-induced changes in electrical conductivity of the imaging object could result in phase-shift offsets in temperature sensitivity vs. TE, i.e., a non-zero intercept. A phase offset as large as -0.33 $^{\circ}$ / $^{\circ}$ C was reported under certain experimental conditions. However, as seen in Fig. 3b, we did not observe this effect (phase offset in our study: 0.002 $^{\circ}$ / $^{\circ}$ C). As suggested in the paper, it was most likely because the heating source in our study was relatively small, as opposed to other calibration experiments [31] where heating occurred in large volumes. It was also possibly because the changes in electrical conductivity in our phantom were small, although this needs further investigation.

The temperature column mapping along time in Fig. 4b does not show high image quality. This is mainly due to the high column sampling rate, which results in T1 saturation, and therefore images feature low SNR and high temperature noise. A possible way to tackle the issue is with FLASE [32], where flip angles larger than 90° are used to reduce T1 saturation for spin-echo sequences.

Accuracy of LSEPSI temperature measurements depends upon the phase-difference SNR, $SNR_{\Delta\phi}$, of the echo setting, which should be predetermined for different tissues before implementation of heating experiments. In the case when $T2^*$ is known, $SNR_{\Delta\phi}$ can be approximated with Eq. 4 and therefore TEs with acceptable noise levels could be derived. Otherwise, a non-heating experiment as done in rabbit brain followed by analysis of noise levels in both $^{\circ}$ C and radians could help determine the appropriate echo setting. For some sampling rates, e.g., 20 Hz in the rapid measurement experiments, almost all echoes could be included in the echo setting and be utilized for temperature measurement. For others, the later echoes in the echo train might be discarded, which results in increased dead time without measurements, and decreased efficiency. This could be overcome by reducing readout bandwidth and performing complex average over these later echoes, and therefore most echoes could be used for temperature measurements.

The method is insensitive to motion outside of the column, potentially allowing for applications in the heart, such as for monitoring during thermal generation of transmural myocardial lesions for the treatment of tachyarrhythmias. Measurements of the water frequency in the heart were encouraging, indicating that a gating or triggering of the sequence could allow for stable measurements to permit temperature measurements via phase changes with adequate accuracy for monitoring thermal ablation.

Conclusion

We have demonstrated an ultrafast method for monitoring frequency or phase changes along selected columns, allowing for inter-TR temperature change estimates. With temporal resolution on the level of 50 ms, it may be possible to monitor the focal heating produced by short (less than one second) ultrasound pulses, such as thermal ablation in the heart.

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Fig. 1.

Diagram of an LSEPSI [18] sequence used to generate 1D temperature maps. 90° and 180° pulses were used to elicit a spin echo from a single column. Multiple gradient echoes were then generated using an echo planar readout. These echoes could be used separately for individual temperature measurements, or after FFT, to produce spectra to directly measure the water PRF. The cross-section of the imaged column has a diamond shape, and the indicated distance d , varying with y , was used as a weighting factor when comparing temperature measurements in ROIs from LSEPSI and SPGR data sets

Fig. 2.

A diagram of the experimental setup. The transducer was immersed in a bath of degassed, deionized water and mounted in a three-axis manual positioning system. The cylindrical phantom was tilted so its rim reached the center of the receiver coil. It was fixed in place on a tray above the tank. A thin, plastic bag filled with degassed water ensured an acoustic beam path into the phantom. A receive-only MRI surface coil (7.6-cm diameter, GE Healthcare) was placed around the phantom at the level of the focus. Both the LSEPSI column and the SPGR plane passed the focus and were placed perpendicular to the direction of the ultrasound beam. In addition, the 2D plane was prescribed to enclose the 1D column

Fig. 3.

a Plot of the phase change measured at the focus using the LSEPSI method as a function of the temperature rise measured using the standard method. Data for nine of the 32 echoes obtained in each TR are shown. Solid lines are linear regressions. **b,c** Plot of the temperature sensitivity of the sequence as a function of the echo time for the 32 echoes obtained with each acquisition of the LSEPSI. **b** sensitivity in radians/°C; **c** sensitivity in ppm/°C. **d** Comparison of the average temperature/time profile using the 1D LSEPSI approach with a standard sequence used for MRI-based thermometry (phase-difference SPGR imaging [6])

Fig. 4.

a A time series of 1D magnitude images in baseline (5 to 10s). Signal voids near the center of the columns might account for the horizontal artifacts in temperature mapping. **b** Images showing 1D temperature measurements during a 20s sonication in a phantom. This "M-mode" MRI shows the temperature evolution as a function of time. **c** Plot of temperature rise vs. time at the focus during the sonication. By using 7 out of 8 acquired echoes in TR of 53 ms, $7 \times 999 = 6993$ temperature measurements could be made over a 53 s period (1000 time frames), with a noise level below 1°C for echoes greater than 9.8 ms. Measurements from different echoes were distinguished by colors

Fig. 5.

a,c Standard deviations in the temperature maps of a non-heated ROI in a rabbit brain as a function of the echo time for TR = 15 and 0.2 s. After about 50 ms, both noise levels settle down to steady values **b,d** Noise levels in the phase-difference images, in radians, for TR = 15 and 0.2 s. The noise represents the reciprocal of the signal-to-noise-ratio (SNR) as long as the SNR remains larger [26]

Fig. 6. Single-line data from the heart muscle of a human subject showing the water spectral peak. The spectrum was generated through a (zero-filled) FFT of 32 echoes acquired during a single TR interval. The same column was acquired repeatedly at a sample rate of 5 Hz (i.e., TR = 200 ms) over a 40 s period. Inset: Breath-hold 2D LSEPSI image of a volunteer showing the heart (18-cm receive-only surface coil, no cardiac gating)

Table 1

LSEPSI sequence parameters used in the experiments.

	TR (ms)	slice thickness (mm)	ETL [*]	echo spacing ^{**} (ms)	FOV (cm)	matrix size	BW (kHz)
Sequence calibration	2000	3	32	3.7	10	128×1	48
Rapid monitoring	53	4	8	3.3	16	128×1	48
Rabbit Brain imaging	15000/206	4	128/48	3.7	10	128×1	48
Volunteer imaging	200	5	32	2.1	32	128×1	64

* echo-train length

** rounded to tenths