Assessment of ultra-high-field Magnetic Resonance

Imaging safety via temperature increase monitoring with Magnetic Resonance Thermometry

Laura Biagi

*Medical Physics and Magnetic Resonance Lab*

*IRCCS Stella Maris*

Pisa, Italy

0000-0003-2159-439X

Massimo Marletta *Diagnostic and Imaging Department Public University Hospital of Pisa*

*(AOUP)*

Pisa, Italy m.marletta@ao-pisa.toscana.it

Francesco Campanella

*National Institute for Insurance against Accidents at Work (INAIL)* Rome, Italy fr.campanella@inail.it

Vito Gagliardi

*Medical Physics and Magnetic Resonance Lab*

*IRCCS Stella Maris*

Pisa, Italy

0000-0003-2840-4499

Giacomo Aringhieri

*Department of Translational Research on New Technologies in Medicine and*

*Surgery University of Pisa* Pisa, Italy

0000-0003-0842-5372

Michela Tosetti

*Medical Physics and Magnetic Resonance Lab*

*IRCCS Stella Maris*

Pisa, Italy

0000-0002-2515-7560

Alessandra Retico

*Pisa Division*

*National Institute for Nuclear Physics*

Pisa, Italy

0000-0001-5135-4472

Gianluigi Tiberi

*Medical Physics and Magnetic Resonance Lab*

*IRCCS Stella Maris*

Pisa, Italy

0000-0001-8787-1295

***Abstract*—Patient safety during Magnetic Resonance Imaging (MRI) examinations is currently guaranteed through the compliance with the limitations on the Specific Absorption Rate (SAR) exposure provided by the current regulations. SAR limits are implemented by scanner vendors in a strictly conservative way to nullify the risk of patient hazard, even at the cost of limiting sometimes the diagnostic power of the exam. Nonetheless, both in the case of ultra-high field applications (i.e. with static magnetic field of 7 T and above) and at clinical field strengths for example in the presence of metallic prosthetic implants, the inhomogeneities in the RF excitation field distribution may cause a local and subject-specific SAR increase. In those cases, local tissue temperatures could reach damaging levels. To directly quantify the local temperature increase caused by the more commonly used RF acquisition sequences in MRI of the human extremities, we have implemented Magnetic Resonance Thermometry (MRT) techniques on a 7 T MRI scanner. We demonstrated that temperature increase maps are easily and fast obtainable with MRT techniques, which are sensitive enough to detect potential hazardous tissue heating.**

***Keywords—Patient Safety, Magnetic Resonance Imaging, Ultra High Field, Specific Absorption Rate, Magnetic Resonance Thermometry***

1. INTRODUCTION

Diagnostic imaging based on Magnetic Resonance (MR) has the invaluable advantage of being multiparametric, which means that different ways to provide tissue excitations lead to a variety of informative high-resolution and high-contrast either structural or functional images of living tissues. At the

National Institute for Insurance against Accidents at Work (INAIL): Research Grant number BRiC-ID39.

same time, MR-based techniques are extremely safe for the patients, as they do not involve the use of ionizing radiation. Nonetheless, the use of exciting radiofrequency (RF) pulses during the execution of a set of MR acquisition sequences causes electromagnetic power deposition in tissues, which can result in tissue heating. Patient safety during MR examinations is currently guaranteed through the compliance with the limitations on the Specific Absorption Rate (SAR) exposure. These limits are imposed by the International Electrotechnical Commission (IEC), as reported in the standard IEC-60601-2- 33 [1]. As an example, the values of maximum local SAR and global SAR in a MR exam of the human knee are fixed to 20 W/kg and between 8 and 10 W/kg, respectively. SAR limits are implemented by scanner vendors in a strictly conservative way to ensure patient safety at any time, even at the cost of limiting sometimes the performances of the scanner and/or the diagnostic power of the exam.

It has to be considered that, both in the case of ultra-high field MR applications (7 T and above) and even at clinical field strengths for example in the presence of metallic prosthetic implants, inhomogeneities in the RF excitation field distribution may cause a local and subject-specific SAR increase, producing possible *hot spots* in tissues. In those cases, local tissue temperatures could increase excessively, reaching damaging levels. To directly quantify the local temperature increase caused by the more commonly used RF acquisition sequences in MR imaging (MRI) of the human extremities, we have implemented Magnetic Resonance Thermometry (MRT) techniques [2] on a 7 T MR scanner.

The main aim of this work has been the investigation of the possibility to apply MRT techniques to monitor any increase in temperature due to RF exposure during MR exams.

This work is organized as follows: first, the MRT techniques are introduced, together with the experimental set up adopted in this 7 T MRI study. In particular, phantom cooling down experiments have been set up to explore the accuracy and sensitivity of MRT techniques at 7 T; then, the RF sequences used in clinical protocol for knee imaging are briefly described, to provide the information about the expected amount of SAR exposure delivered in a typical diagnostic MRI exam of the human knee; finally, the experimental results obtained in the evaluation of the MRT method and its capability to monitor the possible temperature increase due to the application of the RF sequences in a phantom study are discussed.

1. MATERIALS AND METHODS
2. *Magnetic Resonance Thermometry*

To monitor the temperature increase of tissues or tissue- equivalent samples, specific MRI sequences can be implemented. The latter exploit the temperature dependence of the following physical quantities: proton density, relaxation times T1 and T2, diffusion coefficients, resonant frequency of the water protons, etc. (see the recent review by Winter *et al*. [2]). One of the most popular techniques is that based on the temperature dependence of the resonant frequency of the water protons, known as Proton Resonance Frequency (PRF) shift Thermometry, or Magnetic Resonance Thermometry (MRT) [3]. This technique is based on the evidence that the relationship between the shift of the PRF of water and the temperature remains linear over a wide range of temperature variations, and it is sufficiently independent of the type of tissue under investigation [4]. The temperature variation is obtained from the phase difference between the image acquired before *heating* and that acquired either during or after the *heating event*. The difference of the two phase maps is however affected by errors caused by variations in the magnetic field B0, due for example to movement of the tissues, variation of the susceptibility of the tissues and temporal drift of the B0.

To carry out MRT measurements it is possible to acquire two phase maps with a gradient-echo (GRE) sequence, before and after the event that can cause overheating (e.g. hyperthermic treatments, high-SAR sequence going on for tens of minutes). The temperature variation is therefore obtained as follows:

∆T = ΔΦ − ΔΦdri$t

α γ B& TE

where ΔΦ is the measured phase change, ΔΦdrift is the phase change due to system drift, α is the PRF shift coefficient for water (α = -0.01 ppm/o C) [5], γ is the gyromagnetic ratio (γ =

42.58 MHz/T), B0 is the main magnetic field strength, and TE is the echo time. It is thus necessary to implement methods that involve acquiring a reference image, in order to take into account possible phase drifts occurring between the two measurements which are not related to the temperature variation. To accomplish this task it is possible to take advantage of the fact that the chemical shift of fat is largely independent of temperature variations [6].

MRT techniques have proven to be particularly suitable for monitoring the temperature rise induced in thermal ablation and hyperthermia treatments. In general, however, the accuracy of the measurement is not better than about 1o C

at 1.5 T. Whereas this level of accuracy is appropriate for monitoring temperature increase in thermal treatments, it is not suitable to monitoring RF exposure in MRI, where the capability of measuring small temperature variations due to SAR delivering during the MRI clinical examinations is required. In that case a sensitivity of the order of a few tenths of a degree would be necessary. Luckily, the sensitivity of the MRT method is expected to increase with increasing static field [7][8].

To carry out MRT measurements at 1.5 T, Hofstetter *et al*.

[9] implemented an experimental design that allowed to measure temperature increases with MRT referenced technique, which showed accuracy around 0.5 o C in phantom measurements. The proposed methodology is based on the three-point Dixon technique for acquiring phase images of water and fat [10], and uses the reference information of the fat to correct the alterations of the B0 occurred between the different acquisitions made at different time points. Following this approach, the above outlined formula for ΔΤ computation becomes:

∆T = ΔΦW − ΔΦ(

α γ B& TE

where ΔΦW and ΔΦF are the measured phase changes on the water and fat images, respectively. The latter images (both magnitude and phase images) can indeed be separately obtained in the Dixon-based acquisition scheme [10].

1. *Experimental set up at 7 T*

To explore the possibility to measure temperature variations related to SAR delivery at 7 T, we set up an experimental design similar to the one implemented by Hofstetter *et al*. [9]. In particular: first of all, we measured the sensitivity of the method at 7 T; then, we explored the effect of repeatedly running high-SAR MR sequences (the same used in real clinical diagnostic protocols) on phantoms to detect a possible temperature increase with the validated MRT technique.

As already stated, to be able to effectively monitor possible hazardous temperature increase during a MR exam, a sensitivity of the MRT technique of order 0.1-0.2 o C is required. Cooling down experiments were conducted to achieve this goal. Magnitude and phase images were acquired by using a GRE sequence, available at the 7 T MR scanner (GE Healthcare, MR950).

A cylindrical phantom, mimicking the shape of a human lower limb was filled with heavy cream (thus containing both water and fat). The sample was heated up to about 50 o C and its cooling down was monitored with a MR compatible fiber optic temperature probe (Neoptix, Canada) during the MRI acquisitions.

By running GRE acquisition sequences at several time points during the cooling down process it was possible to derive the ΔT measures from the phase images and to compare the so-obtained MRT-based ΔT values with the reference ΔT measures acquired with the optical probe. This first experimental set up (*cooling down experiment*) was designed to validate the sensitivity and accuracy of the MRT method at 7 T.

The second experiment we carried out was devoted to measure through MRT a possible increase of temperature due

to the run of high-SAR MR sequences on the phantom during its cooling down (*cooling down experiment with high-SAR RF sequences*). This experiment was conducted during a cooling down instead of at a fixed temperature due to the experimental difficulties in implementing the necessary thermal insulation of the phantom for the duration of the experiment (hours). In this experimental framework, the possible temperature increase induced by the delivery of high-SAR RF sequences can be derived from the point by point difference between the two cooling-down curves.

1. *RF sequences used in a typical MRI protocol for human knee*

To carry out a realistic estimate of the possible temperature increase induced by SAR delivery during an MR clinical exam, we implemented in our experiments a series of widely used RF sequences, including both those with average and those with high SAR levels. A realistic clinical protocol for knee/lower limb imaging will include the following imaging sequences:

* + 2D multi-echo Spin Echo (SE);
	+ 3D multi-echo Gradient-echo (Susceptibility Weighted Angiography, SWAN);
	+ 3D balanced steady-state gradient echo sequence (FIESTA-C);
	+ 3D zero-TE sequence (SILENT);
	+ 3D Dixon-type pulse sequence (IDEAL).

Some of these sequences, due either to the high flip angle (FA) required or to the large number of RF pulses they deliver per unit time, are more prone to release higher SAR to tissues with respect to other sequences in the pool.

The SE, FIESTA, SILENT and IDEAL are the high- SAR sequence we have considered in the *cooling down experiment with high-SAR RF sequences*.

1. EXPERIMENTAL MEASUREMENTS AND RESULTS

We report in this section the experimental details and the results obtained in the cooling-down experiment and in the same experiment repeated while running high-SAR RF sequences.

1. *Cooling-down experiment*

The phantom used for the cooling-down experiment is a cylindrical bottle with diameter of 11 cm filled with heavy cream (36% fat). The phantom was heated in a microwave oven up to a temperature of about 50 ° C and it was then placed into the RF coil previously developed for knee and lower limb imaging at 7 T [11]. The MR compatible fiber optic temperature probe was positioned inside the phantom through a hole allowing the probe placement at the desired depth within the sample. The phantom temperature during the cooling down was monitored with the optic probe, and the acquisition of the GRE images at consecutive time points needed to derive the ΔT maps began when the phantom reached the temperature of about 45 ° C. Magnitude and phase GRE images were acquired every two minutes, until the temperature of the phantom dropped down to about 31 ° C. The GRE sequence parameters are reported in Table I. It should be noticed that the acquisition of the fat and water

images through a three-point Dixon technique was implemented by running three consecutive GRE sequences at each investigation time point, with the three different echo times (TEs) reported in Table I. The echo times have been chosen so that the signals of the three sequences can be combined to recover the water and fat signals at each voxel [9]. Their numerical values reported in Table I are approximated with respect to the theoretical computation.

TABLE I. ACQUISITION PARAMETERS USED FOR THE GRE SEQUENCE IMPLEMENTED IN THE MRT MEASURE BASED ON THE DIXON METHOD (WATER-FAT SEPARATION)

|  |  |
| --- | --- |
| Repetition Time (TR) | 20 ms |
| Echo Times (TE) | 6.5 ms, 7 ms, 7.6 ms |
| Flip Angle (FA) | 40° |
| Field of View (FOV) | 16x16 cm |
| Slice Thickness | 5 mm |
| Acquisition matrix | 128x128 |

The ΔT maps were obtained by subtracting the phase maps acquired at two adjacent time points, i.e. with a two-minute delay. The quantitative evaluation of the method was carried out by taking the average value and the standard deviation measured within a region of interest (ROI) of 10 pixels of radius chosen at a position near where the probe sensor was placed.

The ΔT measurements derived from the phase images were compared with the acquisitions of the temperature probe in the following way: a starting point for temperature measure was identified at which the absolute temperature value measured by the probe was set as a reference also for the MRT measurements (which allow only ΔT measures). The temperature cooling graph was then obtained by iteratively subtracting the ΔT values measured with the MRT technique to the initial temperature measure. The comparison between the cooling down curve measured with the probe and the MRT curve is shown in Figure 1.



Fig. 1. Comparison between the cooling down curves measured with the probe and MRT curve.

In general, in the temperature range of interest for *in-vivo* imaging (36 ° C - 40 ° C) a good agreement is observed between the cooling curves shown in Figure 1. A quantitative analysis of the discrepancies between the probe and the MRT measures has been conducted.

The average mismatch (|ΔTprobe - ΔTMRT|) between the probe and the MRT measures of ΔT, which represent the method accuracy, is of 0.14 ° C. The method average sensitivity, or precision, computed as the standard deviation of the signal computed in a circular ROI placed close to the position where the thermometric probe is located, is of 0.2 ° C. The sensitivity and the accuracy of the MRT method are thus proven to be adequate for ΔT monitoring during MRI exam sessions.



Figure 2 Temperature maps of the phantom during the cooling down. An axial view of the phantom is visible. The acquisition times are indicated at the top left corner of each map.

A set of the phantom temperature maps obtained during the cooling down experiment is shown in Figure 2. The temperature maps shown in Figure 2 are very uniform, as expected in a sufficiently slow cooling-down process, where a global temperature change of about 15 o C occurs on a time scale of about one hour and a half.

1. *Cooling-down experiment with high-SAR RF sequences*

The same experimental measurements reported in the previous paragraph for the cooling down of a cream phantom have been conducted while repeatedly running high-SAR RF sequences (SE, FIESTA, SILENT and IDEAL).

The data analysis revealed that the temperature rise due to the run of high-SAR sequence was actually very small, despite high-SAR sequences have been repeatedly run. It is possible that the fast cooling down process occurring in the heavy cream dominates over the small temperature increase due to the RF-delivered SAR. In any case it was possible to measure a global temperature rise due to RF of 0.8 ° C.

Further experiments are in progress to explore the detectability through MRT of local hot spots in temperature maps. In particular, the strategies we are putting in place to study in deep this process, include the use of a non-liquid sample where thermal diffusion is reduced with respect to the liquid cream phantom, to obtain non-uniform ΔT maps, as we expect in case of inhomogeneous field distribution, e.g. at ultra-high magnetic field strength. In that case, local hot spots would become visible.

1. CONCLUSIONS AND DISCUSSION

Patient safety in MR examination is guaranteed by operating the MR scanners in compliance to the SAR limits reported in the regulations. SAR limits are set up in a conservative way to ensure to avoid exceeding absolute

temperatures and temperature increases which can be hazardous for humans. A direct monitoring or possible temperature increase during MR exams would be useful to push the diagnostic performance of MR systems, while respecting patient safety. This kind of approach would be the method of choice in situations where inhomogeneities of the RF excitation field may cause local SAR and temperature increase, e.g. at ultra-high magnetic fields, or in the presence of metallic prosthesis in the field of view, even at clinical field strengths.

We described the MRT procedure we set up to measure temperature variations during MRI acquisitions at 7 T field strength. We validated at 7 T the Dixon-based MRT method proposed by Hofstetter *et al*. [9], and we found out that both its accuracy and sensitivity are below 0.2 o C, thus this method could be suitable to monitor SAR-induced small temperature variations. A 0.8 o C temperature increase has been detected in a cooling down experiment where high-SAR RF acquisition sequences where repeatedly applied to overheat the phantom. Further tests are in progress to detect a spatial distribution of the temperature rise. It would require the use of solid phantoms with lower internal thermal conductivity.

The applicability of the MRT-based method for SAR monitoring during a real MRI exam has been also evaluated. The execution of 2D GRE sequences to derive phase maps before and after running the high-SAR imaging sequences to monitor the temperature rise they may cause is feasible and will not prolong the scan time excessively (less than one minute is necessary to map the phase in the area of interest for monitoring). The phase data processing to obtain the temperature variation maps is straightforward once the appropriate script has been completely automatized and it is executable in real time. The measurement of ΔT is not predictive, i.e., it is possible to know how much the high-SAR RF sequence increases the temperature only after its application. However, real-time ΔT monitoring could be very useful to follow temperature variations step-by-step and consequently act directly on protocol and sequences, in order to control the overall heating of the organ during the entire exam.

Among the limitations of the proposed method for monitoring the possible temperature increase during a clinical MRI exam, it should be considered that, while MRT techniques allow to estimate temperature variations, current regulations provide limitations both on the absolute temperature values and on possible temperature increase. Therefore, expectations are not in favor of the possibility of using MRT techniques for safety purposes to monitor the possible temperature increase induced by RF sequences used in clinical diagnostic protocols targeting the musculoskeletal system. Nevertheless, two interesting studies have recently been published focusing on MRT measurements in imaging of the limbs below 3 T: the first is focused on the study of the feasibility of measuring thermoregulation *in vivo* through MRT methods [12]; the second one uses MRT techniques to validate temperature simulations in the lower limbs with the ultimate goal of translating the safety limitations of magnetic resonance scanners from the SAR to guidelines referring to temperature changes directly [13]. A step in the directions highlighted by [12] and [13] has already been taken by our group with the aim of validating subject-specific RF and thermal simulations at 7 T [14]. In particular, whereas electromagnetic simulations devoted to single-subject realistic

SAR prediction have already been conducted [14], the implementation of the heat equation to convert SAR maps into temperature maps and the cross validation with *in-vivo* T acquisitions is part of the planned work to be completed.

ACKNOWLEDGMENT

This research received grant from INAIL (Istituto Nazionale per l’Assicurazione contro gli Infortuni sul Lavoro, National Institute for Insurance against Accidents at Work), scheme BRiC 2016, grant number BRiC-ID39.

REFERENCES

1. I. 60812, “International Standard International Standard,” *61010-1 © Iec2001*, vol. 2006, p. 13, 2006.
2. L. Winter *et al.*, “Magnetic resonance thermometry: Methodology, pitfalls and practical solutions,” *International Journal of Hyperthermia*, vol. 32, no. 1. Taylor and Francis Ltd, pp. 63–75, 02- Jan-2016.
3. V. Rieke and K. B. Pauly, “MR thermometry,” *Journal of Magnetic Resonance Imaging*, vol. 27, no. 2. pp. 376–390, Feb-2008.
4. Y. Ishihara *et al.*, “A precise and fast temperature mapping using water proton chemical shift,” *Magn. Reson. Med.*, vol. 34, no. 6, pp. 814– 823, 1995.
5. J. C. Hindman, “Proton Resonance Shift of Water in the Gas and Liquid States,” *J. Chem. Phys.*, vol. 44, no. 12, pp. 4582–4592, Jun. 1966.
6. J. de Poorter, “Noninvasive MRI thermometry with the proton resonance frequency method: Study of susceptibility effects,” *Magn. Reson. Med.*, vol. 34, no. 3, pp. 359–367, 1995.
7. S. Oh, Y. C. Ryu, G. Carluccio, C. T. Sica, and C. M. Collins, “Measurement of SAR-induced temperature increase in a phantom and in vivo with comparison to numerical simulation,” *Magn. Reson. Med.*, vol. 71, no. 5, pp. 1923–1931, 2014.
8. T. M. Fiedler, M. E. Ladd, and A. K. Bitz, “SAR Simulations & Safety,” *Neuroimage*, vol. 168, pp. 33–58, Mar. 2018.
9. L. W. Hofstetter, D. T. B. Yeo, W. T. Dixon, L. Marinelli, and T. K. Foo, “Referenced MR thermometry using three-echo phase-based fat water separation method,” *Magn. Reson. Imaging*, vol. 49, pp. 86–93, Jun. 2018.
10. J. Ma, “Dixon techniques for water and fat imaging,” *J. Magn. Reson. Imaging*, vol. 28, no. 3, pp. 543–558, 2008.
11. R. Stara *et al.*, “A Degenerate Birdcage with Integrated Tx/Rx Switches and Butler Matrix for the Human Limbs at 7 T,” *Appl. Magn. Reson.*, vol. 48, no. 3, pp. 307–326, 2017.
12. F. F. J. Simonis, E. T. Petersen, J. J. W. Lagendijk, and C. A. T. Van Den Berg, “Feasibility of measuring thermoregulation during RF heating of the human calf muscle using MR based methods,” *Magn. Reson. Med.*, vol. 75, no. 4, pp. 1743–1751, Apr. 2016.
13. F. F. J. Simonis, A. J. E. Raaijmakers, J. J. W. Lagendijk, and C. A. T. van den Berg, “Validating subject-specific RF and thermal simulations in the calf muscle using MR-based temperature measurements,” *Magn. Reson. Med.*, vol. 77, no. 4, pp. 1691–1700, Apr. 2017.
14. V. Gagliardi *et al.*, “Subject-specific knee SAR prediction using a degenerate birdcage at 7T,” *MeMeA 2018 - 2018 IEEE Int. Symp. Med. Meas. Appl. Proc.*, 2018.