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MPI-based spatio-temporal estimation of a temperature profile induced by an IR laser

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Abstract

Separation of signals based on particle type, their environment or temperature has added a useful layer to the foundation of spatial MP imaging. The multi-color approach of signal reconstruction offers a far reaching option for clinical interventions such as controllable and precise application of hyperthermia. In this study a multi-color reconstruction approach was applied to highlight the potential of MPI for temperature monitoring. For this purpose, we heated a solution of SPIO nanoparticles with a high-power laser and reconstructed the corresponding dynamic temperature maps by MPI data acquisition. A good temporal and spatial correlation between the MPI-based temperature maps and fiber optic thermometer measurements was observed.

I. Introduction

To date non-invasive real-time guidance of hyperthermia therapy is exclusively achieved by MRI which is hampered by the availability of appropriate devices and unrecoverable costs [1]. Progress of alternative imaging modalities such as multi-color MPI thermometry are therefore highly sought-after. Multi-color reconstruction makes it possible to report nanoparticles' coupling to their micro-environment, like the surrounding temperature, during MP imaging [2]. Consequently, hyperthermia guided by MPI is an increasingly researched application [3, 4]. Multi-color MPI thermometry could vastly improve clinical hyperthermia application by providing prompt feedback of local temperatures, thereby enabling real time adjustments [5, 6]. Here we report on the temporal progression of localized heating a solution of superparamagnetic iron oxide nanoparticles (SPION) using the multi-color approach to generate 3D temperature maps. Heating was induced with a glass fiber coupled IR laser allowing for high temperatures and precise spatial control.

II. Methods and materials

II.I. Calibration measurements

All MPI measurements were performed using a commercially available preclinical MPI system (MPI 25/20 FF, Bruker BioSpin MRI GmbH) with a cylindrical bore and field-free-point gradient topology. Two system matrices at sample temperatures within the anticipated range of the subsequent laser heating (20 °C and 30 °C) were acquired. A 3D printed sample holder connected to water tubes leading to a heating water bath (STANDARD Series - Heated Immersion Circulators SC100 and SAHARA Series - Heated Bath Circulators S5P; Thermo Fisher Scientific) was constructed enabling stable control of sample tem-

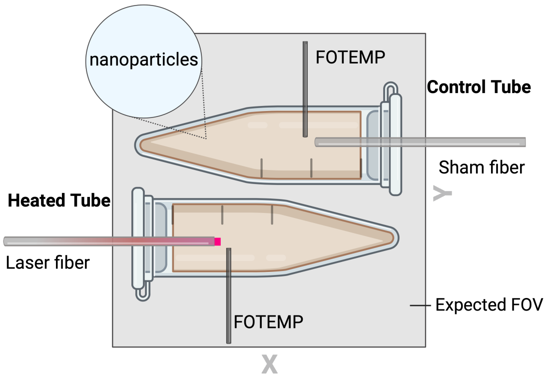
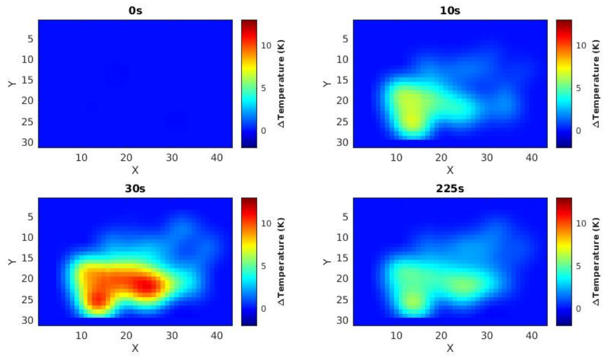


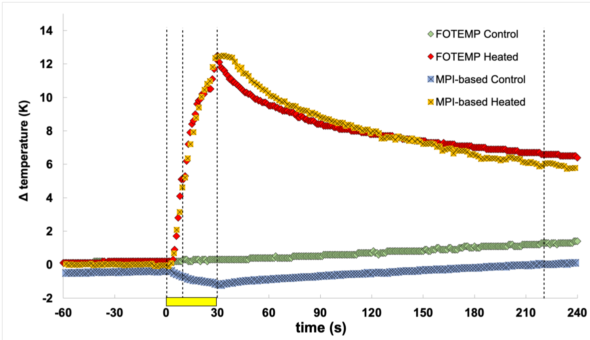
Figure 1: Experimental set up: Two 1.5ml Eppendorf tubes filled with SPION were placed opposing each other on an animal bed inside the expected FOV. One glass fiber (⌀1 mm) tunneled into the 'heated' sample was connected to a high power IR laser. Control was left unconnected in the other tube. A fiber optic thermometer (FOTEMP) was added to both tubes approximately at the site of glass fiber termination.

perature during calibration measurements.

The calibration sample consisted of a cubic temperature-stable PVC tube (Bruker BioSpin MRI GmbH) filled with 15.625 µl SPION (synomag®-D, 70nm plain, micromod, 1 mg(Fe)/ml). MPI calibration measurements were performed using following parameters: Set average: 50; bandwidth: 1.250 MHz; drive field (DF)-Phase: cosine; DF- amplitude 14, 14, 14mT for x, y, z; gradient strength (GD): 1.00T/m; drive field field of view (DFFoV): 56 , 56 , 28 mm; FOV: 57 , 41 , 17 mm; image size: 43, 31, 13; background (BG) measurement increment: 43; number of BG scans: 5. This resulted in a total measurement time of approximately 12h per temperature calibration.



(a) MPI-based temperature maps for different time points.



(b) FOTEMP and MPI reconstructed temperature curves.

Figure 2: Spatio-temporal multi-color reconstruction of MPI data and corresponding FOTEMP measurements during IR laser heating. 2a: Temperature maps for four different time points (0s, 10s, 30s, 225s) of the spatio-temporal reconstruction of laser heating where the voxel numbers are displayed in x and y direction of the FOV. 2b: FOTEMP (red dots) and MPI- based (yellow) temperature curves of the heated sample. Control shown in dark (FOTEMP) and bright blue (MPI). Laser illumination is depicted in yellow below. Exemplary time points shown for MPI-based temperature maps in 2b are depicted with dashed lines.

II.II. Experimental set up and IR laser heating

Two 1.5ml Eppendorf tubes filled with the same SPION used for calibration were placed in the front end of an animal bed (Multimodal Animal Cassette (MMAC) for MPI (Bruker BioSpin MRI GmbH)). Optic glass fibers (⌀ =1mm) were introduced through the lid of each tube and fixed in place with paraffin. Only one glass fiber was connected to an IR laser (ML7710, Modulight), while the other one served as control. A fiber optic thermometer (FOTEMP) was added to both tubes approximately at the site of the IR glass fiber termination. FOTEMP temperature values were acquired with a sampling rate of 1/s. An overview of the experimental set up is shown in Figure 1. IR laser heating ($\lambda = 1470$ nm) was performed using following settings: continuous wave illumination at 2 W for 30 s.

II.III. MPI measurements

Background correction was performed by subtracting empty (without phantom) measurements from data acquired during the experiment. MPI measurements (baseline and experimental) were performed using the same parameters as for calibration measurements described in subsection II.I. IR laser illumination began after baseline MPI data was acquired.

II.IV. Multi-color reconstruction

Multi-color reconstruction was performed based on the method described by Stehning et al. [6]. Whereby every channel is reconstructed by a system matrix acquired with a probe at a given temperature. In this study, MPI measurements were reconstructed with 2 concatenated system matrices, acquired with a water bath tempered

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probe at 20 °C (cold channel) and 30 °C (warm channel). The following parameters were applied to our reconstruction: relative regularization value: 0.005; number of iterations: 15; dynamic block average with number of averaged repetitions of 120 which achieved an effective repetition time of 2.6 s per time point. The reconstructed image intensity of the 2 channels (I_{cold} and I_{warm}) were used to compute a relative intensity difference (ΔI):

$$\Delta I = \frac{I_{warm} - I_{cold}}{I_{warm} + I_{cold}}. \quad (1)$$

For the temperature reconstruction, ΔI and the temperature of each measurement time point was calculated. The lowest calculated ΔI was matched to the lowest FOTEMP- measured temperature, the highest values were likewise matched to the highest measured temperature. The relative temperature (ΔT) rise was visualized by firstly subtracting the baseline ΔI map, acquired at the beginning of the measurement, from the ΔI maps at every time point.

The calculated MPI-based ΔI values were manually rescaled to fit the FOTEMP dynamic range and to achieve a qualitative comparison between both temperature measurements. The resulting ΔT maps are shown in Figure 2a. For visualization purposes, a Gaussian filter (window size=5, standard deviation=2.5) was applied to the ΔT maps. To visualize the dynamic trends of measured FOTEMP and ΔT values, the voxel containing the maximal value of ΔT for each measurement time point was plotted and compared to FOTEMP read-outs (see Figure 2b).

III. Results

To compare FOTEMP and MPI-based temperature progression, the later values were corrected for the device specific delay (approximately 20s). The laser heated SPION sample showed a similarly rapid temperature increase upon laser heating in the FOTEMP measurements and the MPI-based reconstructed temperature values. Furthermore, the temperature values following laser switch off, showed a comparatively faster decay of the FOTEMP values. FOTEMP measurements of the control sample displayed a small but steady temperature increase over the duration of the experiment. The same increase was observed in the reconstructed temperature maps. However, interestingly, immediately after heating started, the spatio-temporal progression (see Figure 2) of the relative temperature differences report a slight decrease in temperature of the MPI-based reconstructed temperature values of the control.

IV. Discussion and Conclusion

FOTEMP values and the MPI-based reconstructed temperature maps are largely in consensus which indicates high accuracy of the multi-color MPI method within the setting described in this study. However, the FOTEMP temperature curve shows a sharper peak and faster temperature decrease right after laser switch off. A possible explanation for these discrepancies could be the placement of the FOTEMP in relation to the laser fiber's working end which could have an impact on the temporal progression of heating as well as on the obtained temperature values. Acquiring further system matrices could extend the possibility of the different temperature range and improve the precision of temperature reconstruction. An unnoticed mismatch between MPI's FOV and the FOTEMP's sensing end and especially the selected voxel to derive the temperature profile might affect temperature results as well. A slight temperature decrease of control sample could be observed for the reconstructed temperature values right after laser heating has started. We associated this observation with an artifact from reconstruction. The heat progression was otherwise followed by spatiotemporal reconstructed temperature maps very well as can be seen in Figure 2b.
In summary, this study showed feasibility and validation of multi-color reconstruction for a highly dynamic temperature profile generated by an IR laser. Calculation of the absolute temperature using the multi-color reconstruction method is in the scope of future publications.

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Author's statement

KS, JCC and JF are employees of Bruker BioSpin MRI GmbH.

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