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Extending a commercial preclinical MPI scanner into an MPI-MFH platform using a hyperthermia insert

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Abstract

Magnetic particle imaging (MPI) and magnetic fluid hyperthermia (MFH) have the potential of being integrated in a single device to allow for seamless switching between imaging and therapeutic modes. In an MPI-MFH platform, the field free region of an MPI scanner can serve not only for imaging diagnostics but, by adding a radio-frequency magnetic field, also for therapeutic use of the magnetic particles by heating. It enables precisely localized heating to a specific target temperature deep in the tissue via MFH. In addition, MPI provides targeted visualization and temperature information of systemically injected magnetic nanoparticles providing direct feedback. In this work, the integration process of a hyperthermia insert which is capable of extending a commercial magnetic particle imaging scanner with the functionality of magnetic fluid hyperthermia is presented. Furthermore, the thermal resolution of the MPI-MFH platform is measured.

I. Introduction

As an emerging imaging technique, MPI has shown great potential in a wide variety of fields in the last two decades since its invention. Recently, efforts have been made to equip MPI systems with MFH capabilities to enable a new therapeutic approach, which combines therapy and diagnostic imaging [1]. Magnetic fluid hyperthermia is very promising for biomedical applications, which reaches from cancer treatment to controlled drug delivery [2]. In MFH, MNPs are heated up by driving them with an alternating high frequency magnetic field. An MPI-MFH platform can help play out the advantages of both sides and overcome the current limitation of MFH as a clinical technique, which is the lack of precise control of the heating area and the tissue temperature. First, localized MFH can be realized with the MPI selection field as the field-free region (FFR) used for spatial encoding in MPI can be used to enable spatial selectivity in MFH. Second, MPI can serve as a guidance of the MFH treatment planning by providing the spatial distribution of the MNPs as the MNP concentration is key for the heating rate, and enabling non-invasively temperature measurement during heating [3].

In our previous work [4], we have implemented a hyperthermia insert, which can be placed in the imaging bore of a preclinical MPI system (MPI 25/20 FF, Bruker BioSpin MRI GmbH), generate the magnetic field for hyperthermia, which is decoupled from the MPI transmit and receive path. To protect the low noise electronics of the MPI receive chain, we have proposed a coil topology to minimize the mutual effect between the two systems using passive cancellation. In this work, the integration of the hyperthermia insert into the MPI scanner and the first results of localized MFH are presented.

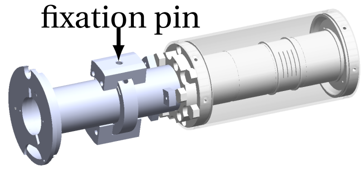

Figure 1: The insert fixation part (left) attached on the cover plate of the hyperthermia insert (right). The fixation pin locks the hyperthermia insert through the hole on the fixation part.

II. Material and Methods

To realize the MPI-MFH platform, an MFH system is implemented based on the hyperthermia insert and integrated into the commercial preclinical MPI 25/20 FF scanner manufactured by Bruker BioSpin MRI GmbH. The MFH system is composed of the hyperthermia insert with an impedance matching network, the radio-frequency (RF) power amplifier and the transmit and receive notch filters. A RF amplifier (AG 1012, T&C Power Conversion, USA) is used to generate and amplify a high frequency signal (around 700 kHz) for the hyperthermia insert. A band pass filter is implemented to remove the noise generated by the amplifier from the MFH signal. According to our previous results, most power on the hyperthermia insert is decoupled from the the MPI receive chain through the cancellation effect of the hyperthermia coil. The remaining signal is handled by three low-pass-filters in the MPI receive chain. A reproducible positioning of the hyperthermia insert is ensured by a dedicated fixation part at the scanner bore. As shown in Figure 1, the insert fixation part is connected to the hyperthermia insert and can be fixed by the pin in the MPI scanner bore. The fixation part ensures the center of the heating coil aligns with the center position of the MPI scanner and prevents rotation of the insert. The inner diameter of the fixation part is 3 mm smaller than the hyperthermia insert to avoid damage of the insert by robot collision. As the total power consumption does not allow for passive cooling, the hyperthermia insert and the impedance matching network are connected to the cooling system of the MPI scanner to ensure stability and high duty cycle. To protect and ensure proper functioning of both MPI and MFH systems, basic inter-system communication needs to be established. The MPI system should have full control of the MFH system and to be able to monitor its status such that measures can be taken in case of a fault condition is detected. An analog control of the RF amplifier, a temperature sensor and a flow sensor are implemented. Therefore, the power level, the coil temperature and the cooling flow of the MFH system can be monitored by the MPI system.

To validate the integrated MPI-MFH system, high power tests are performed on the integrated MPI-MFH platform to measure the residual MFH signal after passive compensation and filtering. MPI data acquisition is conducted while applying high power (600 W) on the hyperthermia insert. The power level of the residue MFH signal are obtained from the signal spectra of the LNA output signal. During the test, the coil temperature is measured by the temperature sensor using the MPI control system.

To test the localized heating with the gradient field, the thermal resolution of the MPI-MFH platform is measured. 27 µL undiluted Synomag-D 70 nm MNP solution with 10 mg mL^{-1} iron concentration in a 3 mm × 3 mm × 3 mm calibration sample tube is moved by the robot along the x,y and z direction in 2 mm, 1 mm, 0.5 mm steps respectively. At each location, the sample is heated with 8.4 mT at 714 kHz for 30 s and the temperature of the sample is recorded using a fiber optic temperature sensor (TS2, Weidmann-optocon, Germany). The FFP is fixed at (0,0,0) for all measurements and the gradient field of x, y, z direction is 1.25 T m^{-1}, 1.25 T m^{-1}, 2.5 T m^{-1}. Same localized MFH is applied on a 27 µL water sample as control, and the temperature increase of the water sample is subtracted from the temperature increase of the particle sample to eliminate the influence of environment heating. The specific absorption rate (SAR) of the sample at at different positions along the spatial axes is calculated based on the temperature increase using the method presented in [1].

III. Results

The installed hyperthermia insert and impedance matching network with the cooling connection are shown in Figure 2. The components of the MFH system are properly integrated into the MPI system. During the high power tests, the power provided by the RF amplifier, the temperature and cooling flow of the hyperthermia insert can be controlled and monitored by the MPI system.

A signal peak at the MFH frequency can be observed on the MPI signal spectrum in all three channels. The amplitude increases with the power applied on the hyperthermia insert. At full power 600 W, the amplitude of the residue MFH signal is −27.8 dBm, −32.6 dBm, −21.6 dBm of x, y, and z channel respectively. In all tests, the temperature of the insert stays below 40 °C. The measured SAR results are plotted as a function of position and fitted to Gaussian functions in Figure 3. The full-

Figure 2: Hyperthermia insert and the impedance matching network integrated in the MPI scanner. Left: the hyperthermia insert installed in the scanner bore seen from the bore opening side of the scanner. Right: the impedance matching network placed beside the robot with the cooling connections.

width-at-half-maximum (FWHM) of the fitted curve is considered as the thermal resolution for the single vial sample. As the heating is depending on the magnetic field sequence at a specific position, the FWHM is stated as a field value. It was calculated by the spatial FWHM (given in the brackets) of Figure 3 divided by the gradient strength of these measurements in the respective directions. The FWHM values are 5.5 mT (4.4 mm), 5.875 mT (4.7 mm), and 5.9 mT (2.4 mm) for x, y and z direction respectively matching nicely the gradient strength in these directions.

IV. Discussion

The high power test shows that the components of the MFH system are installed successfully and can be controlled by the MPI system. The analog control of the RF amplifier can be further improved by implementing a digital control of the amplifier using serial connection, which provides the monitoring of the real-time frequency and power on the hyperthermia insert. The weak residue MFH signal measured by the scanner proofs that by the combination of using passive compensation and filtering, the sensitive low noise amplifiers of the MPI system are protected against over voltage from the fast oscillating magnetic fields. The thermal resolution of the MPI-MFH platform is obtained using the SAR profiles. The z direction has highest resolution because of the highest field gradient. On x direction, the FFP is moved back and forth by the MFH field. However, no broadening of the SAR profile on x direction is observed. We assume that with 8.4 mT, the particles away from the center position is driven by a minor loop, which significantly reduces the area of its hysteresis loop and results in less heat generation. More accurate SAR profiles could be obtained with smaller measurement step, smaller sample volume and more measurement times. The measured SAR profiles are not symmetric to the 0 position, which is potentially due to the inhomogeneity of the MFH field, differing heat transfer conditions and sample concentration changes due to evaporation could also have contributed to the observed variation.

V. Conclusion

In this work, a hyperthermia insert is integrated and works properly in a preclinical MPI system, marking the realization of a MPI-MFH platform. 3D localized MFH is achieved with the platform with a thermal resolution of 4.4 mm, 4.7 mm, 2.4 mm for x, y and z direction with 8.4 mT. The platform can be used for further exploration of localized MFH and unlock various researches in drug delivery, cancer treatment and other medical applications.

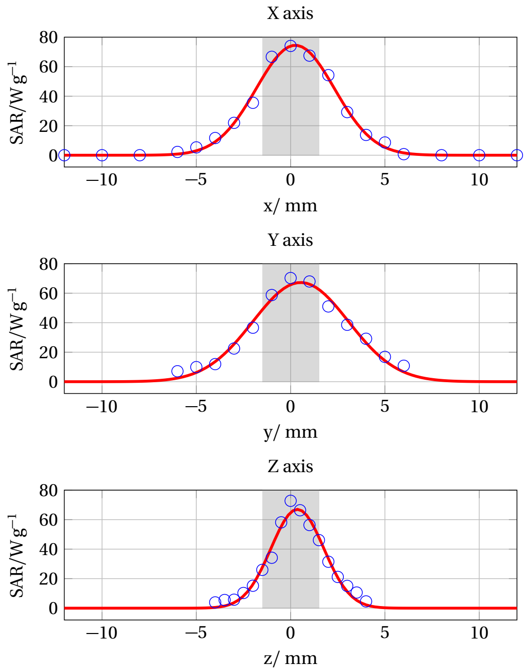

Figure 3: SAR values profile of x, y and z axis. The FFP is fixed at (0, 0, 0). The measured values are marked with blue circles and the red curves are the fitted Gaussian function. The width of the particle sample is marked with gray. Due to the measurement errors, the SAR values at (0,0,0) are slightly different for each axes.

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Author's statement

Conflict of interest: Jochen Franke is an employee of Bruker bioSpin MRI GmbH.

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