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Combined workflow for targeted magnetic fluid hyperthermia: Using MPI to inform treatment plan.

Introduction

Magnetic Fluid Hyperthermia (MFH) for activation of magnetic nanoparticles (MNP) offers considerable potential for numerous applications, especially the clinical treatment of cancers. MFH relies on the delivery of MNPs to tumors followed by the application of alternating magnetic fields (AMF), causing local heating of tissue and killing of tumor cells, either directly or by enhancing the cytotoxic effects of radio/chemotherapy. Current MFH implementations are limited by the accumulation of MNPs away from the lesion of interest, the inability to visualize MNP distribution during treatment, and the limited ability to monitor tissue temperature. These limitations result in poor MNP heating control, reduced therapeutic effect, and increased collateral damage.

Magnetic Particle Imaging (MPI) is an emerging imaging technology that directly quantitates MNP concentration in tissue. The technique has broad applications in diagnostic imaging, especially for cellular imaging of immune cells and immunotherapies and quantitative measurement of perfusion. Fundamentally, MPI directly images the concentration of an MNP tracer through the scanner. MPI images work by producing a strong magnetic field gradient containing the Field Free Region (FFR) where the magnetic field is ~zero. Only the MNPs in the FFR are magnetically unsaturated and can produce a signal. The FFR is moved across the sample to make an image.

To remedy many of the limitations of MFH, we have developed localized MFH, which can exert spatial control of MNP heating. Localized MFH works by applying a strong magnetic field gradient to produce an FFR while using an AMF. This technique then heats only MNPs inside the FFR.

In this white paper, we combine MPI and localized MFH to produce a technique capable of prescribing hyperthermia treatment parameters according to the measured MNP concentration. We demonstrate an MPI prescription that enables precise heating of the kidneys while preventing off-target heating of the liver. This approach allows for precise, pre-computed temperature control and can prevent off-target tissue damage.

Methods

Commercially available Synomag®-D70 nanoparticles (micromod.de, Germany) were loaded in the virtual kidneys and liver of a 3D printed Fillable Mouse Phantom™ (BIOEMTECH, Greece). The liver was loaded with the same concentration as one of the kidneys and half the concentration of the second kidney. The total iron content of each organ was then estimated using MPI (MOMENTUM™, Magnetic Insight, USA). ROIs were drawn manually as all three organs were identifiable by MPI. Iron concentration was compared against empirical data (previously acquired) to estimate the required AMF and gradient to heat both kidneys by +2.5°C despite their differing MNP concentration while preventing heating in the liver. The sample was then moved to the HYPER™ system (Magnetic Insight, USA) to apply the magnetic heating sequences. Changes in temperature in each kidney as well as the liver were monitored using fiber optic sensors.

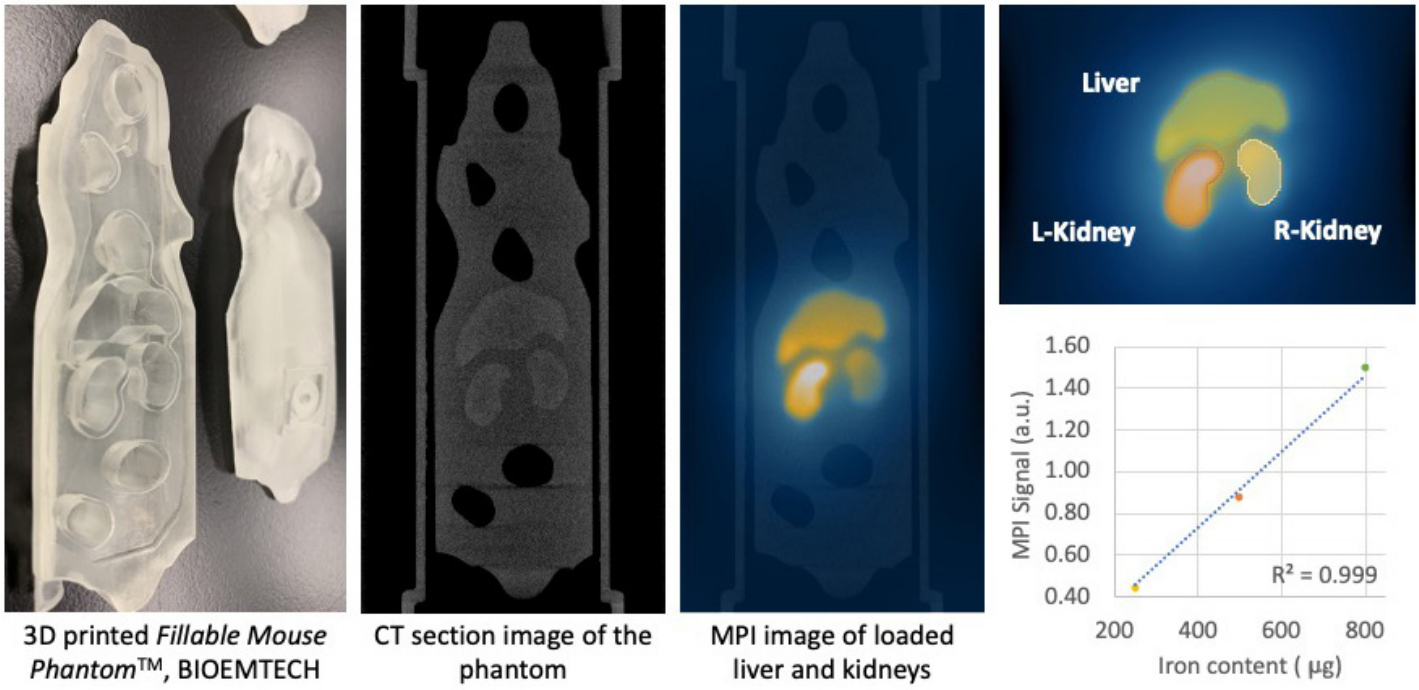
Results

Figure 1 images confirm that the tracer concentration in the right kidney is half that of the left kidney and the same as the liver. The calibration curve also enables the estimation of iron content using image intensity. When performing MFH heating of both kidneys simultaneously, no significant rise in temperature was observed in the liver (ΔT =0-0.5°C), demonstrating localized treatment and prevention of off-target heating. Temperature monitoring confirmed similar temperature rises in both Kidneys (ΔT = 2.5°C), despite the difference in super paramagnetic iron oxide (SPIO) concentration.

Conclusion

Here we presented a novel theranostic workflow using MPI and MFH to image and quantify local concentrations of SPIO in a mouse phantom and prescribe an MFH treatment that normalizes heating across the kidneys, despite varying nanoparticle concentration while minimizing off-target liver heating. This new approach has potential applications in targeted tissue ablation, thermosensitive nano-therapies, and immune stimulation.

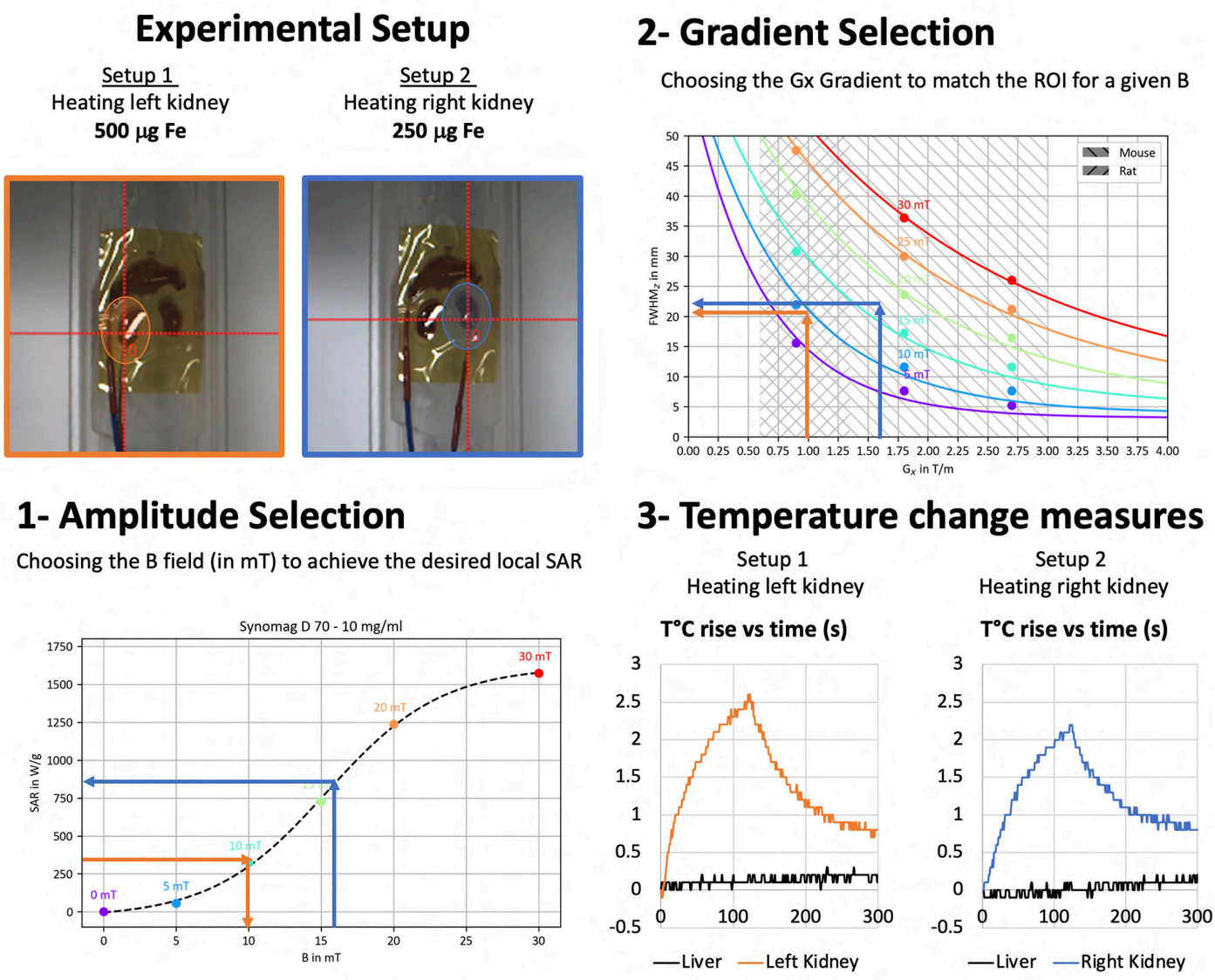
Figure 1:



3D printed *Fillable Mouse Phantom*™, BIOEMTECH | CT section image of the phantom | MPI image of loaded liver and kidneys

(From Left to Right) The empty *Fillable Mouse Phantom*™ from BIOEMTECH is loaded with Synomag-D 70 nm in the liver (10% vol/vol), the left kidney (10% vol/vol) and the right kidney (20% vol/vol). The CT image shows different contrast between loaded and unloaded wells but no observable changes between loading concentrations. The MPI images show the difference in concentration between the two kidneys. The total signal from manually drawn ROIs is plotted against the actual iron content (µg), showing a linear relationship between the MPI signal and the iron content.

Figure 2:



Top Left: Temperature probe positioning measuring the liver and the kidney simultaneously. Note the overlay of the heating region based on the center position. **Bottom Left:** Empirical measurement for SAR (W/g) for Synomag-D 70nm. **Top Right:** ROI size estimation for chosen RF amplitude and gradient. **Bottom Right:** Temperature rise during the experiment (RF ON = 120 s, RF OFF = 180 s).