Real-time tracking of temperature, T1 and T2* during the onset of thermal damage in ex vivo and in vivo rabbit thigh muscle

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INTRODUCTION:

The MR parameters T1 and T2* have proven to be reliable indicators of thermal damage effects during post-treatment evaluation of thermal therapies, but are not currently used to assess the state of the tissue as the treatment is being carried out. In this work we use a hybrid PRF/T1/T2* sequence to measure all three parameters in real time during MR-guided focused ultrasound (MRgFUS) heating of in vivo and ex vivo rabbit thigh muscle. T1 and T2* are analyzed as functions of temperature and thermal dose to investigate whether they can detect the onset of tissue thermal damage.

METHODS:

Hybrid PRF/T1/T2 Sequence*. The 2-D gradient echo sequence acquires multiple echoes per excitation and alternates between two flip angles every other time frame. The variable flip angle approach is used to measure T1, T2* is calculated from the multiple echoes, and PRF temperatures are obtained from the standard phase-based approach[1,2,3]. Sequence parameters were: 1.5 x 1.5 x 3.5 mm resolution, TR = 40 ms, 12 TE's of 2.32, 4.61, … 27.51 ms, monopolar echo readout, 810 Hz/pixel bandwidth, flip angles of 15° and 70°, and 3.8 seconds per scan.

Experimental Data. MRgFUS heating experiments were performed on the thigh muscles of six rabbits. In vivo heating of the left thigh was performed first, the animal was then euthanized and both legs were removed, and then ex vivo heating was performed on the right thigh of the rabbit. In this way, the ex vivo experiments used tissue from the same animal that was very fresh, but did not have blood pressure, a blood supply, or connection to the lymphatic system. For both in vivo and ex vivo heatings, varying levels of ultrasound power and duration were applied to induce a range of thermal damage effects in the tissue, from only very mild heating to clear denaturation and necrosis. A fiber optic temperature probe was used to measure baseline temperature and convert the measured PRF temperature changes into absolute temperatures.

To isolate the effects of tissue changes due to thermal damage, the temperature dependencies of T1 and T2* were calibrated (mT1 and mT2) and removed, leaving $T1_{corr}$ and $T2^*_{corr}$ to be analyzed in terms of temperature and dose:

$$T1_{corr} = T1_{meas} - T1_{baseline} - mT1' \; T_{PRF} \qquad \text{and} \qquad T2^*_{corr} = T2^*_{meas} - T2^*_{baseline} - mT2^{*\prime} \; T_{PRF}$$

RESULTS & CONCLUSIONS:

$T1_{corr}$ results did not show definitive trends with respect to temperature or thermal dose and therefore are not presented in this abstract due to space limitations. Two trends in $T2^*_{corr}$ behavior were observed in both the ex vivo and in vivo heating cases: 1) a sharp rise in the $T2^*_{corr}$ values occurs when the tissue temperature reaches approximately 40°C to 45 °C; 2) The $T2^*_{corr}$ values decrease during cooling for regions of tissue that receive significant thermal dose. Figure 1 shows PRF temperature, thermal dose, and $T2^*_{corr}$ maps at various time points during an MRgFUS heating of in vivo muscle. Figure 2 shows scatter plots of $T2^*_{corr}$ vs temperature for all voxels in the heated region at two different time points during the early stages of heating, showing the jump in $T2^*_{corr}$ for both ex vivo and in vivo heating cases. Figure 3 shows similar plots for $T2^*_{corr}$ vs dose at the peak of heating and after 120 seconds of cooling.

The first result indicates a change in the state of the tissue is occurring before significant thermal dose has been delivered. It does not appear to be related to edema or inflammation mechanisms because it is seen in both the in vivo and ex vivo cases. It may be related to cellular membrane disruption that has been reported to occur at lower temperatures than denaturation and coagulation[4], but this is speculation at this point and investigation into the physical effect is ongoing. The second result is consistent with observations that thermally damaged tissue often presents as having a hyperintense ring surrounding an isointense core on T2-weighted post-treatment images[5,6], however the current approach also allows characterization of the time course of the effect, which is part of ongoing work.

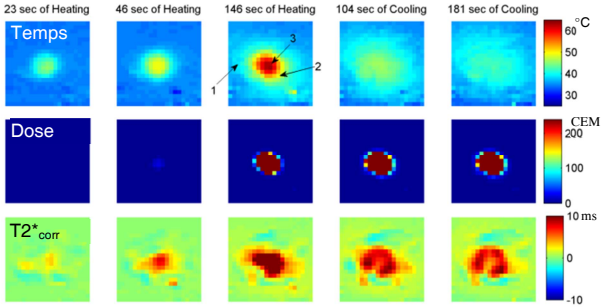

Figure 1: Maps of PRF temperature, thermal dose and $T2^*_{corr}$ during heating and cooling of in vivo muscle. Note the jump in $T2^*_{corr}$ at 46 sec before the thermal dose reaches 240 CEM, and the subsequent drop in $T2^*_{corr}$ for the central region where significant damage was done.

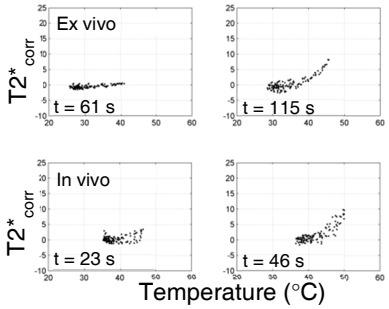

Figure 2: $T2^*_{corr}$ vs temperature scatter plots at two different time points of heating for ex vivo and in vivo heating. Both cases show a jump in $T2^*_{corr}$ between 40°C and 45°C.

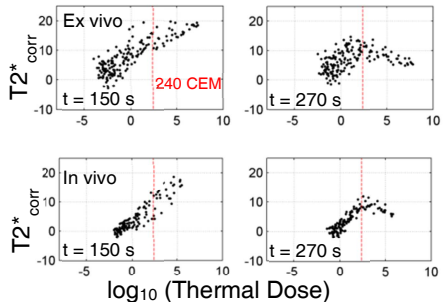

Figure 3: $T2^*_{corr}$ vs thermal dose scatter plots at the time of maximum heating and after 120 seconds of cooling for ex vivo and in vivo cases. Both show a decrease in $T2^*_{corr}$ for regions with significant dose.

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