Investigation into non-thermal changes in R2* during HIFU heating

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INTRODUCTION:

The MR tissue property R2*, as measured by a multi-echo gradient echo sequence (ME-GRE), has been shown to have a temperature dependence, to change irreversibly with thermal damage, and may be valuable for helping to monitor and assess thermal therapies[1,2,3]. During recent experiments, R2* measurements were performed during high intensity focused ultrasound (HIFU) heating of tissue and changes in R2* were seen along with temperature changes, as expected. However, the data indicates that there is another process occurring, independent of the HIFU-induced heating, that affects the R2* values. Although the origin is not clear, the process has a viscoelastic mechanical nature, and appears to have a longer time constant than the rapid physical displacement of tissue measured by acoustic radiation force imaging (ARFI). This effect has not been reported yet to our knowledge. To tease out the nature of this "mechanical" process, HIFU heating experiments were carried out while imaging with an ME-GRE sequence in order to simultaneously measure R2* changes and PRF temperatures and attempt to separate the "mechanical" effects from the thermal effects.

METHODS:

Theory. We assume the behavior of R2* during the application of focused ultrasound depends on two independent processes, one thermal and one "mechanical". The spatiotemporal equation for R2* can then be written as Equation 1, where the function *f* defines the thermal dependence and the function *g* defines the "mechanical" dependence. We make the assumption that the R2* dependence on temperature can be modeled linearly, giving Equation 2, where α must be determined from the data. Since both R2* and PRF temperature information are measured, the "mechanical" contribution can be isolated (Equation 3).

Equations for R2* dependence

1. $R_2^*(\vec{x},t) = f(T(\vec{x},t)) + g(M(\vec{x},t))$
2. $R_2^*(\vec{x},t) = \alpha T(\vec{x},t) + g(M(\vec{x},t))$
3. $g(M(\vec{x},t)) = R_2^*(\vec{x},t) - \alpha T(\vec{x},t)$

Experimental Data. Several HIFU heating runs were performed on an *ex vivo* pork muscle sample using a 256-element phased array transducer (Imasonic, Besancon, France): 3 identical single point heatings at 10.2 acoustic Watts for 30 seconds; single point heatings at 10.2 W for 30 seconds, 16.2 W for 30 seconds, and 27 W for 60 seconds; and a circular trajectory consisting of a 16-pt circle, 6mm radius, 54 W, 50 ms/pt, 90 seconds total heating. Significant cooling time was allowed between each run and the circular trajectory was carried out on a different sample. All imaging was done on a Siemens 3T TIM Trio scanner using an ME-GRE sequence with a flyback gradient to read out each echo in the same direction (2x2x3mm resolution, 3.2 sec/scan, 16 echoes, TR = 45 ms; TE's = 2.32, 4.64, ... 37.12 ms; Flip Angle = 20°; Bandwidth = 800 Hz/pixel). All images were smoothed with a Hanning filter to avoid Gibbs artifact at the longer echo times and zero-filled to 0.5 x 0.5 mm voxel spacing.

RESULTS & CONCLUSIONS:

The R2* change vs PRF temperature curves in Figure 1A demonstrate the repeatable nature of the hysteresis behavior. The two R2* vs temperature curves in Figure 1B are from the center and edge of the 27 W heating, where the edge voxel clearly shows that even while the temperature is almost constant, the R2* value is changing. This would indicate that something besides temperature is affecting the R2* value. Figure 2 shows data from the circular trajectory heating. The R2* vs temperature curve for the voxel in the center of the circle does not show the hysteresis behavior, potentially due to the fact that it did not receive direct ultrasound radiation and all changes are due to thermal effects only. This voxel was used to calibrate α from Eq. 2. Figure 3 shows R2* change vs time plots for three single point heatings at different powers, where the thermal effects have been subtracted out (Eq 3), leaving only the changes in R2* due to the "mechanical" process. Figure 4 shows the PRF temperature map from the hottest time frame of the circular heating and two R2* change maps – one showing the total R2* change and one showing the "mechanical" only change.

Although very preliminary, these results are highly repeatable, and demonstrate that in addition to the thermal dependence, R2* also experiences a "mechanical" effect. More tests, both *ex vivo* and *in vivo*, will need to be performed to elucidate the exact behavior of this effect and its underlying cause. For now we can only speculate that it is a viscoelastic mechanical process caused by the forces of the ultrasound beam. Once understood, this phenomenon could have several applications for monitoring and assessing MR-guided HIFU treatments.

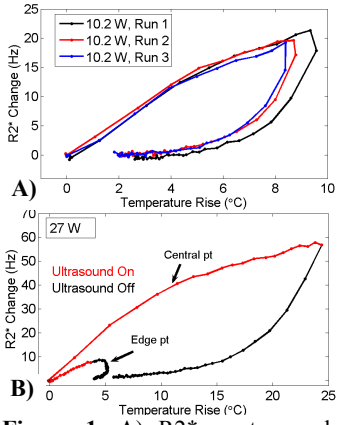

Figure 1. A) R2* vs temp plots showing repeatable hysteresis. B) R2* vs temp plots showing R2* changes even when no temperature changes are occurring (Edge pt).

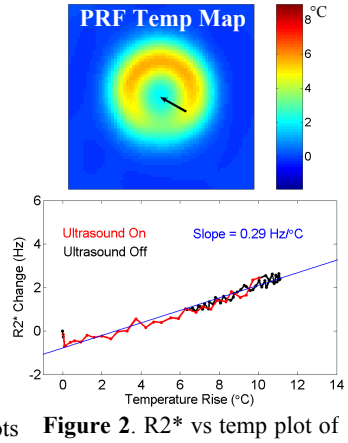

Figure 2. R2* vs temp plot of central voxel that did not receive direct US does not show hysteresis. Slope of this line used for α in Eqs 2 & 3.

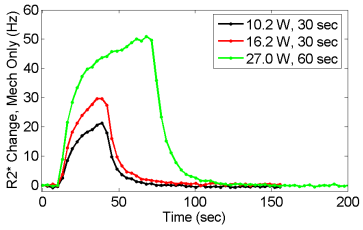

Figure 3. R2* change vs time plots where the thermal dependence has been removed, leaving only the "mechanical" effects. A viscoelastic type of behavior can be seen, especially in the 27W data, where the R2* value rapidly increases right after the US is turned on, slows its rate of change, and then relaxes back when the ultrasound is turned off.

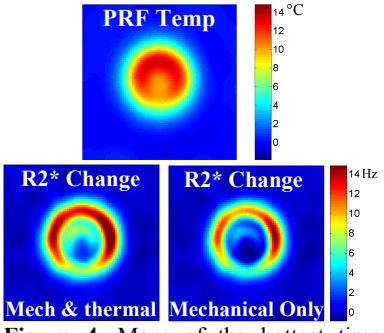

Figure 4. Maps of the hottest time frame from the circular heating – PRF temperature, R2* change, and R2* change with the thermal effects removed. The "mechanical" only R2* map shows the largest change on the edge of the circle where direct US was applied and less change in the middle.

REFERENCES: 1. Graham et al. MRM 39:198-203 (1998). 2. Taylor et al. Med. Phys. 35 (2), 2008. 3.Taylor et al. NMR Biomed. 2011 Early View DOI: 10.1002/nbm.1707

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