MRI Guided High Intensity Focused Ultrasound (HIFU) of Visceral Fat in Overweight Rats

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Target Audience: Basic researchers interested in thermal ablation of fat using MRI-guided high intensity focused ultrasound.

Purpose: MRI-guided high intensity focused ultrasound (MR-HIFU) allows non-invasive ablation of deep tissues with only limited heating of surrounding areas. MR-HIFU uses MRI to precisely target the HIFU beam and to monitor the temperature of the target and nearby regions. A novel application of MR-HIFU is heating fat tissue to reduce the metabolic activity of fat deposits and reverse the development of obesity, diabetes and metabolic syndrome. Visceral fat may play a central role in fatty liver disease because of its proximity to the hepatic portal vein, allowing direct exposure of liver cells to the metabolites and signaling molecules from visceral adipocytes [1, 2]. Animal studies have shown that surgical reduction of visceral fat volume can reduce liver fat accumulation and improve glucose tolerance [3-4]. Unfortunately, accurate monitoring of HIFU-induced temperature changes in fat is not possible with the Proton Resonance Frequency Shift (PRFS) method used for most MR-HIFU procedures [5]. To overcome this limitation, we used T2 mapping to evaluate the effects of HIFU on fat while using PRFS to monitor the temperature of surrounding tissues in real time.

Methods: The relationship between the change in the T2 relaxation time of fat at 1.5T and the change in temperature was assessed by heating the whole body of overweight rats with a water recirculating heating blanket while measuring the T2 of the visceral fat deposits. The temperature of the fat was measured with fiber optic temperature probes placed in the perinephric fat.

MR-HIFU was performed in a second cohort of animals using a 1.5 Tesla whole body scanner (Philips Ingenia^{TM}) equipped with a Philips Sonalleve^{TM} HIFU system. The HIFU transducer is integrated into the MRI table and can be translated and rotated to aim the HIFU beam at specific targets within the body. The 256-element focusing transducer produces a focal spot approximately 2 mm in diameter and 10 mm in length. MR-HIFU was used to heat perinephric visceral fat (70-100 watts of acoustic power applied for 16 seconds) under MRI guidance in overweight male Sprague-Dawley rats (initial body weights of 400-550 g). Real time MRI thermometry (2.5 second temporal resolution) via PRFS was used during the HIFU treatment to monitor temperature in nearby tissues, such as in the kidneys, muscle, skin, etc. Fat tissue does not display a PRFS dependency on temperature, so heating in the fat was assessed by measuring the T2 before and immediately after HIFU ablation. T2 maps were acquired with a multi-echo sequence (scan time of 1 minute and 22 seconds) with 8 echo times ranging from 21 to 266 ms. The change in body weight was measured 10 days after HIFU and compared with untreated animals (no anesthesia or MR-HIFU) and sham animals (anesthetized in MRI scanner, but no MR-HIFU).

Results: Whole body heating experiments showed that the T2 of fat increased by 3.3 ms for every °C of heating (**FIGURE 1**). At 1.5 T, the T2 of fat was 112.0 ± 3.3 ms before HIFU treatment. As expected, no temperature change was detected in the fat with the PRFS-based sequence during the HIFU procedure. Immediately after HIFU treatment, the T2 of the targeted fat increased by 17.7 ms to 129.6 ms ($p=0.001$ vs. pre-HIFU). Ten days after the MR-HIFU procedure, the treated rats lost an average of 7.5 ± 1.2 % of their body weight, while the sham rats lost only 1.9 ± 0.5 % body weight ($p<0.05$, **FIGURE 2**) and the untreated rats gained 1.3 ± 0.3 % ($p<0.05$). These results suggest that HIFU treatment increased the fat temperature by 5.4 °C, reaching a final temperature of 42.4 °C. However, the cooling constant of fat, 250 seconds [6], is similar to the scan time of our T2 mapping sequence, 82 seconds, which could lead to underestimation of the maximum fat temperature during treatment.

Discussion: We have demonstrated that T2 mapping can be used to monitor the heating of fat tissue after the application of focused acoustic energy. Our temperature calibration agrees with previous studies on fat tissue [6]. This approach can be used together with PRFS imaging methods to monitor temperature changes in surrounding tissue to ensure procedure safety. After the MR-HIFU treatment, we estimate that the fat temperature was 42.4 °C. However, using a faster T2 mapping sequence may show that the fat temperature at the end of HIFU treatment is actually higher. Although only a relatively small increase in the fat temperature was measured, MR-HIFU of visceral fat in these overweight animals yielded a clear therapeutic effect, decreasing the body weight by 7.5 %.

References:

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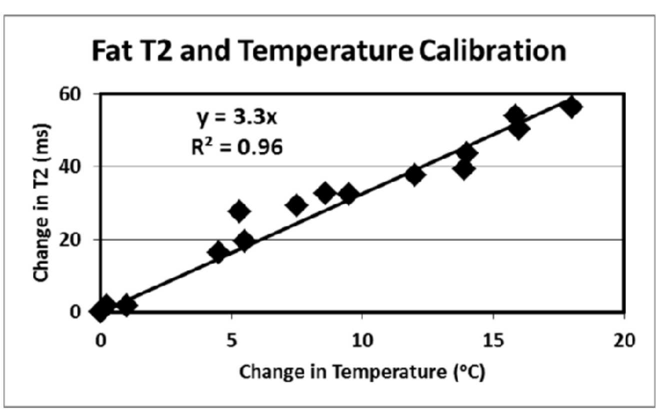

Figure 1: Monitoring the T2 of fat during whole body heating showed a linear relationship corresponding to 3.3 ms per °C, with $r^2 = 0.96$.

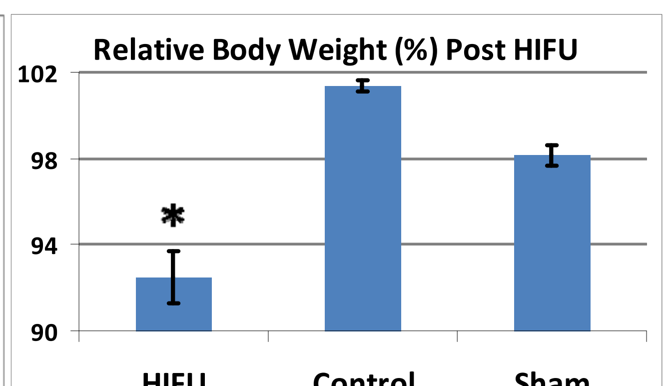

Figure 2: HIFU ablation of visceral fat produced a significant reduction of body weight compared to sham and untreated animals (* $p < 0.05$).