Non-invasive temperature mapping using temperature-responsive water saturation shift referencing (T-WASSR) MRI

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Target audience: MRI researchers interested in developing MR thermometry or oncologists needing a noninvasive imaging method for monitoring cancer thermotherapy.

Purpose: To develop a new non-invasive MRI method for assessing water proton resonance frequency (PRF) shifts in response to changes in temperature[1,2] that can be applied reliably in tissues with high fat content.

Methods: We adapted the previously reported Water Saturation Shift Referencing (WASSR)[3] approach for detecting temperature induced water PRF changes. In principle, the water signal (Ms) upon the application of a weak RF saturation (strength ω_1 and saturation frequency ω) follows Eq [1]: $M_S(\omega)/M_0 = 1/(1+(T_1/T_2)\times(\omega_1/(\omega_0-\omega))^2)$, where ω_0 is the resonance frequency of water protons, M_0 is the water signal without saturation, and T_1 and T_2 are the spin-lattice and spin-spin relaxation times of water, respectively. Sweeping the ω allows one to determine the water PRF (ω_0) using Lorentzian fitting.[4] Consequently, temperature changes can be determined by comparing the water PRF (ω_0) determined for each pixel in the B_0 shift map at two temperatures: $\Delta T = T_{measure} - T_{ref} = (\omega_0(T_{measure}) - \omega_0(T_{ref}))/2\pi\alpha B_0$ (Eq. [2]), where γ is the gyromagnetic ratio of water protons (42.58 x10^6 Hz/Tesla) and α is temperature coefficient (-0.01 ppm/°C)[1].

The capability of measuring temperature was demonstrated on a 2% agarose gel phantom containing a piece of cheese (8.9 % fat) (Fig.1a) in a 10 mL plastic vial. The *in vitro* MRI acquisition was performed on a vertical bore 11.7 Tesla Bruker Avance system equipped with a 15 mm birdcage RF coil. A NMR thermocouple was used to control intra-bore temperatures at 297K, 302K, 310K, and 313K. The T-WASSR images were acquired using a modified RARE sequence (RARE factor =16, TR=1.5 sec, TE=5 ms, matrix size=128x128, slice thickness= 1 mm, NA=1, and total acquisition time= 2 mins). The saturation of water or lipid protons was implemented using a single continuous wave (CW) RF pulse (t_{sat}=500 ms, B_1=0.5 μT), with saturation offsets swept from -0.5 ppm to + 0.5 ppm with respect to the water or fat frequencies at a resolution of 0.1 ppm. At each temperature, a phase map[5] and a single-voxel ^{1}H NMR spectrum[4] were also acquired. The *in vivo* feasibility of the method was also tested on mouse legs receiving hyperthermia using cycling water connected with a water bath.

Results: When applied to fat-containing phantom, the T-WASSR method was able to provide steady temperature mapping of both regions containing water only and regions containing both water and fat. For example, as shown in Fig. 1a, when the nominal temperature of the sample was elevated from 310K (37°C) to 316K (43°C), T-WASSR determined a mean ΔT of 5.7K and 4.6K for the agarose and cheese respectively. These findings were consistent with the ΔT calculated using the water PRF shifts determined by the single-voxel MRS method (5.6 K and 5.0 K respectively, Fig. 1b). A good correlation (r^2>0.996) was shown between ΔT measured by the two methods for both the agarose and the cheese regions over a temperature range from 297K to 316K (Fig. 1b). In contrast, the temperature map produced by a phase mapping method (Fig.1a right) clearly showed an inaccurate measurement for the cheese area when no fat correction was used. Moreover, the T-WASSR method was also capable of determining the chemical shift of lipid protons (Fig. 1c). As shown in Fig. 1d, the water-lipid PRF difference maps were calculated at four temperatures, which correlated well with nominal temperatures (r^2>0.999). These results indicate that it is possible to use the T-WASSR method to directly assess absolute temperature for fat-containing tissues similar to that reported previously[6]. When applied to *in vivo*, the measured temperature maps using T-WASSR were consistent with those of phase mapping (data not shown), indicating the T-WASSR is ready to be used *in vivo*.

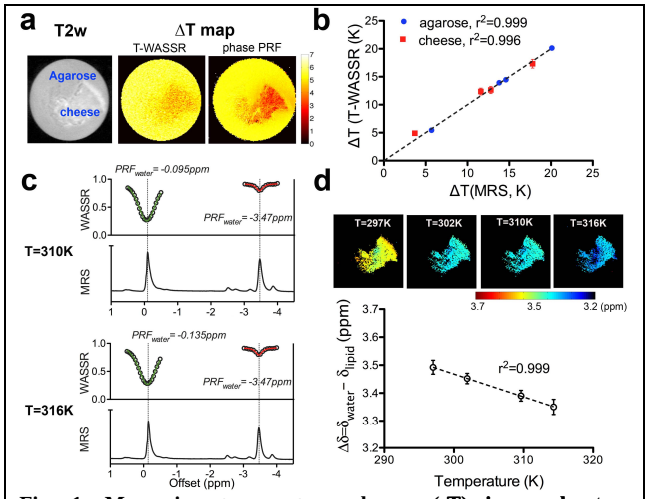

Fig. 1. Measuring temperature change (•T) in a phantom containing both fat and water using T-WASSR. a) T2w image of the phantom and the ΔT maps obtained by T-WASSR (middle) and phase mapping (right) when temperature was changed from 310K to 316K. **b)** Correlation of the measured mean ΔT (agarose ROI (blue) and cheese ROI (red)) obtained by T-WASSR and MRS when temperature was changed from 297K to 316K. **c)** Comparison between ^{1}H NMR spectra measured using a single-voxel localized MRS (PRESS) method and the T-WASSR spectra (both water and fat) of a manually drawn cheese ROI. **d)** Water-lipid chemical shift difference (ω) maps of cheese region (top panel) at each temperature and the mean ω with respect to the NMR thermocouple readings (bottom panel). The error bars are the standard deviation of the calculated ω.

Discussion: We have demonstrated a water direct-saturation-based approach for temperature mapping, adding additional methodology to the arsenal of non-invasive, high-resolution MRI thermometry. Our results demonstrate that the T-WASSR has an improved robustness of high-resolution temperature mapping in fat-containing tissues when compared to phase mapping. Similar to the phase mapping method, the T-WASSR was capable of mapping temperature changes at high spatial resolution. The temporal resolution can be further improved via using other fast imaging sequences.

Conclusion: The T-WASSR approach provides a suitable alternative for non-invasive temperature mapping by MRI, especially for temperature measurements in fat-containing tissues.

Reference (1)Ishihara, Y., *et al. Magn. Reson. Med.* **1995**, *34*, 814-823. (2)De Poorter, J., *et al. Magn. Reson. Med.* **1995**, *33*, 74-81.(3)Kim, M., *et al. Magn. Reson. Med.* **2009**, *61*, 1441-50. (4)Liu, G., *et al. Contrast Media Mol. Imaging* **2010**, *5*, 162-170.(5)Mulkern, R. V., *et al. J. Magn. Reson. Imaging* **1998**, *8*, 493-502.(6)Galiana, G., *et al. Science* **2008**, *322*, 421-4. This research was supported by NIH grants R21EB008769, R21EB015609, R01EB015031, R01EB015032, P41EB015909 , and S10RR028955