Measurement of the temperature dependence of the susceptibility of human breast fat tissue

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Introduction The increasing interest in MRI-guided thermal ablation therapy for breast tumors has heightened the need for reliable MR thermometry (MRT) techniques in tissues containing fat. The currently most widely used MRT technique is proton resonance frequency shift (PRFS)-based MRT, which exploits the temperature dependence of the electron screening constant of water ($d\sigma_{water}/dT$ = -0.01 ppm/°C [1]). In fat tissue, large susceptibility-related temperature errors can be expected [2], because temporal changes in tissue susceptibility (χ) can lead to non-local magnetic field changes. This, in turn, affects the PRF and, hence, the measured temperature of all water protons that experience this magnetic field change, leading to temperature errors. The $d\chi_{fat}/dT$ values reported so far were based on in vitro experiments in porcine fat samples ($d\chi_{fat}/dT$ = 0.00804 ppm/°C [3] and 0.0094 ppm/°C [4]). The only reported human in vivo study on $d\chi_{fat}/dT$ was performed on a 1 T system in a human calf and showed no temperature dependence of the susceptibility of fat [5]. In order to conclusively assess the impact of temperature-induced χ changes on PRFS-based MRT in the breast, accurate and precise susceptibility measurements in human tissue are a prerequisite. We therefore aimed to measure $d\chi/dT$ of fat tissue of the human breast. Experiments were performed on a 14 T NMR spectrometer for increased accuracy and precision.

Materials & Methods *Tissue sample* Fat tissue was collected from the breast of a woman, whose body was donated to medical science, directly post mortem. The tissue sample was transferred into a 5 mm NMR sample tube. *Experimental set-up* The experiments were performed using a double-reference method [6]. This method allows for the measurement of the susceptibility of a sample without being hampered by its chemical shift. The experimental setup consists of a capillary-sphere (cs) tube, filled with a reference solvent, which is placed inside an NMR sample tube. The field experienced by the nuclear spins inside the reference solvent depends on whether they are located in either the capillary or spherical part of the cs-tube. This results in two separate reference solvent peaks in the spectra, originating from the same reference fluid. The difference in the positions $\delta_{ref,capillary}$ and $\delta_{ref,sphere}$ of the two reference solvent peaks in the spectrum is related to the difference in susceptibility between the reference solvent and the sample:

$$\chi_{sample}(T) = \chi_{ref}(T) - \frac{\delta_{capillary} - \delta_{sphere}}{G} \qquad (1)$$

where G is the geometric factor of the set-up, which was determined by a calibration step prior to the experiment. Chloroform ($CHCl_3$) was chosen as a reference solvent for our application, since its peaks lie well outside the fat spectra. The temperature dependence of the susceptibility of deuterated chloroform has been reported [7]. We used $CHCl_3$, because of the increased signal intensity required for the detection of the reference peaks in the fat spectra. The $CHCl_3$-filled cs-tube was transferred into the tissue sample tube. This cs-setup was placed in a 600 MHz NMR spectrometer (Bruker Ultrashield) and high resolution 1D NMR spectra were acquired. The temperature of the sample was altered using the air-blower device incorporated in the spectrometer, from T = 298 K to T = 328 K in steps of 1 K. Sufficient time was allowed between the measurements to ensure a homogeneous temperature distribution inside the NMR sample tube (>20 min). *Data analysis* All spectra were analyzed using MestReC [Mestrelab Research, Spain]. The acquired data were apodized with a 10-Hz exponential filter prior to the Fourier transform. A zeroth and first order manual phase correction was applied per spectrum. The peak positions $\delta_{capillary}$ and δ_{sphere} of the reference solvent were determined by the peak picking algorithm as implemented in MestRec. The sample susceptibility was calculated per spectrum (i.e. per temperature step) using Eq. 1 and plotted against temperature. A linear fit was performed to determine $d\chi_{fat}/dT$.

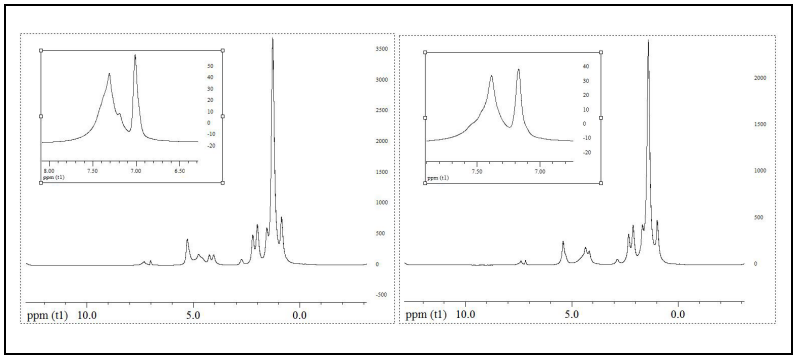

Figure 1. Two 1D spectra of human breast fat tissue, at 298 K (left) and at 328 K (right). On the far left, the two $CHCl_3$ reference peaks are visible. A zoomed version of both spectra at the location of the reference peaks is shown in the inset.

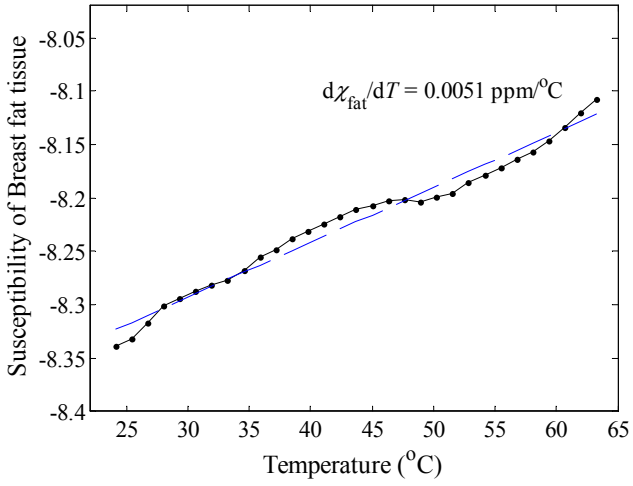

Figure 2. Susceptibility of human breast fat, over temperature. A linear fit through the data is depicted with the blue line.

Results Figure 1 shows two spectra of fat tissue of the human breast, at two different temperatures: T = 298 K (a) and T = 328 K (b). A section of the spectrum zoomed at the location of the $CHCl_3$ reference peaks is also shown in the upper left corner, where $\delta_{capillary}$ and δ_{sphere} are clearly visible. Figure 2 shows the susceptibility of breast fat over temperature. The linear fit through the data is shown (blue line) and gave the following value: $d\chi_{fat}/dT$ = 0.0051 ppm/ºC.

Discussion and conclusion A temperature dependence of the susceptibility of human breast fat of 0.0051 ppm/ºC was found. This is smaller than the reported values for pork-fat. However, its influence is still not negligible in PRFS-based MR temperature measurements in the surroundings of heated fat.

References [1] Hindman JC. J. Chem. Phys. 1966; 44:4582-4592 [2] Sprinkhuizen SM *et al*. Proc. #2532 ISMRM 17 (2009) [3] Stollberger R. *et al.* J Magn Reson Imaging. 1998 Jan-Feb;8(1):188-96 [4] de Poorter J. Magn Reson Med. 1995 Sep;34(3):359-67 [5] Young IR *et al.* MRM 36:366-374,1996 [6] Frei K *et al*. J. Chem. Phys. 37, 1891 (1962) [7] Hoffman RE *et al*. Journal of Magnetic Resonance 2005; 176(1):87-98