Heat Induced Contrast Mechanisms in MRI: in vivo Tissue Characterization by MR Thermal Response

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Purpose: Clinical applications of Magnetic Resonance (MR) imaging in oncology has been rapidly evolving from being a subjective and interpretive diagnostic test based on tissue morphology to a more quantitative technique probing tissue biology [1]. MR imaging provides excellent spatial resolution and anatomical soft tissue contrast, yet there are still limitations in detecting and delineating early-stage cancer lesions when they are curable [2]. This is a major clinical impediment in cancer screening and therapy planning—even in the most common cancer types such as breast and prostate [3]. In hopes of extending ideas for a multiparametric, quantitative MRI data set, we evaluated a unique approach for MR contrast by utilizing the thermal responses of heat-sensitive MR parameters such as longitudinal relaxation time (T_1), transverse relaxation time (T_2), water proton chemical shift (CS), and apparent diffusion coefficient (ADC) [4-7]. We measure these thermally sensitive MR parameters at various temperatures to determine salient characteristics of *in vivo* tissue. We look for the accuracy and repeatability in measuring these parameters, and evaluate if heat-induced contrast mechanisms have the potential to add information to conventional MR imaging contrast types for better identification and characterization of tumors.

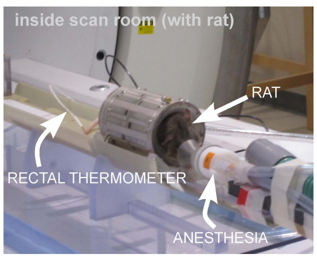
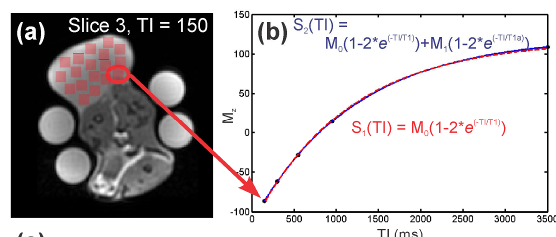


Fig 1 *Shows the general setup used for imaging / heating experiments, shown without oil vials or insulation*

Methods: Our *in vivo* model included Fischer 344 rats injected with a breast adenocarcinoma cell line, Copenhagen rats injected with a rat prostate carcinoma cell line, and Sprague Dawley rats that have developed spontaneous benign mammary tumors. Rats were administered anesthesia and placed into a rat-sized transmit/receive quadrature Litz rat coil (Doty Scientific) as shown in Fig 1. The body temp of the rats were maintained at temps from ~20-40^{o}C. T_1 data sets were acquired using a 2D axial inversion recovery (IR) sequence at the following inversion time (TI) values: 3500, 2000, 950, 550, 350, 150, 50 with all times in ms. Other parameters included flip angle (θ) = 180°/90° set with proper TG, TR = 4500ms, TE = 4ms, freq FoV = 13cm, phase FoV = 6.5cm, matrix 128 x128, NEX = 1, 5 slices, 3-4 mm slice thickness. T_2 data sets were acquired using a 2D axial spin echo (SE) sequence with the following TE values: 300, 150, 100, 125, 50, 25 and 4 ms, θ = 90°/180° (set with proper TG), and same parameters as the IR experiments. ADC data sets were acquired from diffusion weighted images (DWI) using a 2D axial spin echo (SE) sequence with echo-planar imaging (EPI) readout at multiple b-values of 300-1200 s/mm^2, and other parameters the same as the T_2 images.



(c) slice 3, n = 18

1179.3	1239.5	1237.9	1199.2	1184.2	1220.1
1185.6	1212.8	1163.9	1212.7	1204.3	1231.2
1134.3	1186.9	1202.5	1212.5	1201.0	1231.6

Fig 2 *Depiction of data processing algorithm. (a) Axial inversion-recovery image (TI = 150ms) through the center of malignant breast tumor. Average signal intensity in each ROI makes one point in a T1 plot similar to (b). (c) Shows the calculated T1 values for each ROI.*

Fig 2a illustrates the data processing algorithm on a single slice example. Here 18 ROIs of ~38x38 voxels were taken at each inversion time (TI = 150 ms in Fig 2a) and T_1 plots were made for each ROI. This procedure was repeated for a 3-5 slice acquisition giving typically 60-80 T_1 measurements (depending on the number of ROIs) to be used for averaging and standard deviation calculation. A similar approach was used for measuring T_2 and ADC, allowing for the formation of distribution plots for all tumor and muscle tissue types. MR thermometry (MRT) was used during temp transition periods to (i) assess the apparent heating rate in different tissue structures and (ii) ensure that steady-state temps were achieved before relaxation parameter measurement. A 3-echo spoiled gradient echo (SPGR) imaging sequence (TE_1~5ms, TE_2~8ms, TE_3~11ms, TR=75ms, θ=20°, FoV=(13x6.5)cm^2, matrix size=(128x128), 3x7mm slice acquisition) was used to perform MRT measurements. **Results:** For all animal models, we found a statistically significant difference ($p < 0.05$) between quantitative contrast measurements for all tumor/muscle pairs. Percent change of thermal MR parameters Γ ($\Gamma = T_1, T_2$, ADC) was measured as a function of temp ($\%\Delta\Gamma/^oC$). Calculations were made using the equation $\%\Delta\Gamma/{}^oC = \left(\left(\Gamma_{highT} - \Gamma_{lowT}\right)/\Gamma_{lowT}\right)/\Delta^oC \times 100\%$ where Γ_{highT} is the high temp measure of Γ, and Γ_{lowT} is the low temp measure. A Student's t test was performed to determine statistically significant differences ($p < 0.05$) between tumor and muscle for each thermal parameter $\%\Delta\Gamma/^oC$. Results are summarized in Fig 3.

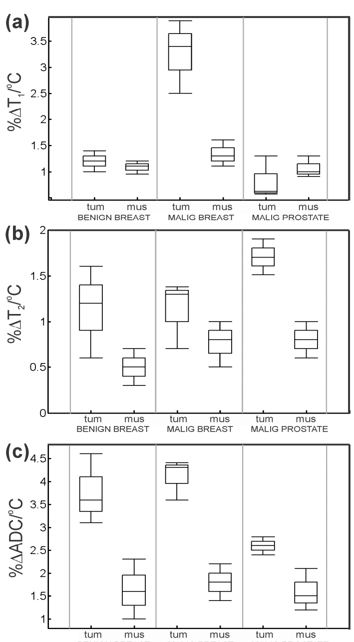


Fig 3 *Box plots of MR thermal contrast change with temperature. Columns represent benign mammary, malignant breast, malignant prostate (and muscle regions that were selected near those respective tumors—labelled "mus"). (a) Shows results for % $\Delta T1/^oC$, (b) % $\Delta T2/^oC$, and (c) % $\Delta ADC/^oC$*

Conclusions: Most notably, we found significant difference in % $\Delta T_1/^oC$ and % $\Delta ADC/^oC$ for the malignant breast adenocarcinoma compared to its surrounding muscle, along with a significant difference in % $\Delta T_2/^oC$ for the prostate carcinoma compared to its surrounding muscle tissue. These findings indicate a link to a new method for improved MR imaging visualization/characterization of tissue with heat-induced contrast types. Specifically, the thermal responses of conventional MR imaging contrast mechanisms in different tissue types may contain new information for improved (i) delineation of tumor/tissue boundaries for diagnostic and therapy purposes, and (ii) characterization of salient characteristics for cancer diagnosis, e.g., malignant versus benign tumors.

References: [1] Gillies et al. JMRI 2002;16:430, [2] Wu et al. Radiology 2009;2:253, [3] Mountford et al. Chem Rev 2004;104:3677, [4] Bloembergen et al. Phys Rev 1948;73:33, [5] Parker DL IEEEBME 1984;31:161-7, [6] Riecke et al. JMRI 2008;27:376-90, [7] Chenevert et al. JMRI 2011;34:983-7