Apparent Diffusion Coefficient Decrease During Thermal Ablation of the Prostate as an Early Indicator For Loss of Tissue Viability.

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Purpose: The safety and efficacy of MR-guided thermal therapies is dependent on the ability to predict tissue response. Most predictions rely on indirect measures such as temperature and estimated thermal dose to infer expected tissue viability [1]. Diffusion weighted MRI (DWI) has demonstrated a 36% reduction in apparent diffusion coefficient (ADC) following HIU induced tissue damage of the prostate [2]. Our aim was to demonstrate that the decrease/plateau seen in ADC during sonication of the prostate was indicative of a transition from viable to non-viable tissue. We monitored treatments on healthy tissue as well as previously damaged tissue to assess whether our proposed marker of tissue viability is reliable and agrees with histology.

Methods: Interleaved ADC and temperature measurements were obtained *in vivo* during a high intensity ultrasound treatment of the canine prostate (baseline temperature 33°C). Heating was performed using a customized transurethral transducer and two protocols high power (8-10 Watts/cm^2, 6.8MHz, 10min) and low power (2-3 Watts//cm^2, 6.8MHz, 3min). Temperature images were obtained using proton resonant frequency (PRF) shift measurements from a GRE sequence (TR=70ms, TE=8ms, FOV=15cm, res=1.17mm). ADC measurements were computed using diffusion images from three orthogonal directions using a diffusion weighted spin echo sequence (b=1000 s/mm^2) with an EPI readout (TR=1250ms, effective TE=80ms). Initially both sides of the prostate were treated using the high power setting (Fig.1, Fig.2, Fig.3). For the second sonication, only the left side was treated using the high power setting (Fig.4). The device was then rotated to aim towards the lower left healthy region of the prostate and two low power sonications were performed (Fig.5). Temperature values were used to calculate predicted ADC. We found the relationship between the temperature data and Ausing a least squares fit between percent increase and change in temperature [3]. To avoid tissue viability sensitivity on ADC only data from ROIs that did not receive sufficient thermal dose were used. Tissue damage visible in H&E digital slices was outlined using image scope software.

Results: For sonications that result in loss of tissue viability, there is good correlation between predicted ADC and measured ADC until sufficient thermal dose is delivered to destroy the tissue. At that point, the deviation indicates loss of viability. To further demonstrate the drop in ADC indicates loss of tissue viability, heating previously ablated tissue with the high power protocol did not result in an additional drop in ADC during sonication. Delivering multiple low temperature sonications resulted in repeatable agreements between both ADC calculations without a drop in ADC.

Discussion: Drops in ADC during thermal heating were only seen during sonications were a transition between viable and non-viable was predicted from thermal dose and later verified by histology.

References: [1] V. Rieke, K. Butts Pauly, J. Magn Res Imag 2008, 27, 376-90[2] J. Chen, *et al.*, Magn Res Med 2008, 59, 1365-72. [3] Le Bihan, et al, Therap Rad. 1989, 171, 853-57.

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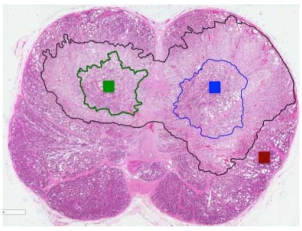

Figure 1: H&E stain image with outlines defining the heat fixed region (inner boundary) and fragmented zones (outer boundary). The green region was treated once. Blue region was treated twice, orange region received minor temperature increases but did not present any tissue damage.

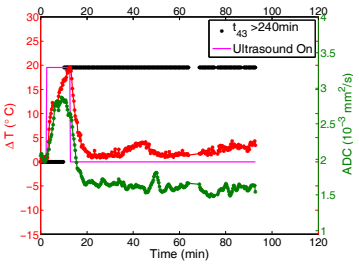

Figure 2: Green ROI Temperature and ADC changes plotted on the same figure for the sonication on the right side of the prostate. Temperature values were later used to compute predicted ADC values.

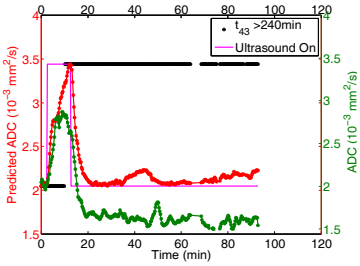

Figure 3: Green ROI Predicted ADC based on temperature (red) compared to measured ADC. The drop in measured ADC compared with predicted ADC corresponds with TEM43 near 240min (black dots step function). As expected, measured ADC does not return to baseline due to destruction of the tissue.

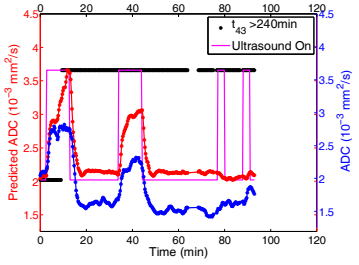

Figure 4: Blue ROI Predicted ADC (red) compared to measured ADC. First sonication induced damage as seen by thermal dose threshold, and ADC measurement drop during and following treatment. Second treatment shows no decrease in measured ADC during sonication because tissue is already destroyed.

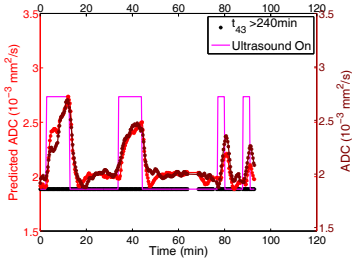

Figure 5: Maroon ROI Predicted ADC (red) compared to measured ADC In the absence of sufficient thermal dose predicted ADC agrees with measured ADC and values return to baseline.