Contrast Kinetics as a Histopathological Surrogate for Improved Assessment in Thermal Therapy

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INTRODUCTION

Thermal ablation has gained considerable interest in recent years as a minimally invasive alternative to surgery. Magnetic resonance imaging (MRI) is particularly successful as a candidate imaging system, due to its sensitivity to changes in temperature and tissue structure upon heating. Thermal lesions are easily visualized on conventional MRI, but the true border of damage is often obscured and the progression of necrosis is not known at the time of therapy (1). Furthermore, it may be impossible to predict the extent of damage from measures of peak temperature, due to changes secondary to acute thermal injury (2). However, an analysis of Gd-DTPA kinetics (GdK) can reveal the true border of damage and give finer differentiation of tissue effects immediately after thermal ablation (2).

In this work, we study the progression of thermal necrosis up to 1 week post-ablation in focused ultrasound (FUS)-induced lesions. The potential of GdK is explored for improved tissue characterization and early indication. Specifically, the uptake of Gd-DTPA is analyzed for the permeability-surface area product (K^{trans}) and EES volume fraction (v_e), and then compared to conventional post-treatment T2-weighted (T2w) MR and to histology.

METHODS

Twenty lesions were induced in the thigh muscle of 5 New Zealand white rabbits using a spherical transducer (1.68 MHz, 10 cm diameter and focal length). The rabbits were sacrificed at three different times post-therapy (40 hours, 3 days, and 1 week), and the lesions were studied on gross and HPS sections. All MRIs were performed on a clinical 1.5-Tesla MRI system (Signa Echo-Speed CV/I, GE). Temperature images were acquired from phase differences of a FSPGR sequence (θ/TE/TR=30°/25/50.6 ms, BW=2.78 kHz, FOV=16 cm, matrix=256x128, 3 mm thick slices, 1 average). Within 20 minutes post-heating and again prior to sacrifice, a 0.1 mmol/kg bolus of Gd-DTPA was injected and the uptake was monitored using T1w FSPGR (θ=20°, BW=15.63 kHz, FOV=16 cm, matrix=256x160, 3 mm thick slices, 1 average). T2w FSE images were acquired throughout the session (TR/TE=2000/75 ms, 8 ETL, FOV=16 cm, matrix=256x192, 3 mm thick slices, 2 averages).

Tofts' model (3) was used to produce maps of K^{trans} and v_e. Images of T2w MRI, K^{trans}, and v_e, were segmented based on a histogram-like analysis of changes in image intensity. Areas enclosed in these segmented regions were compared to regions determined with histopathology assessment

RESULTS

Figure 1 shows a typical lesion for each of the three time points post-ablation. Regions of different tissue changes (colored contours) are compared to MRI, using linear regression (Figure 2). A subset of these colored contours is overlaid on the best MR representation to illustrate key observations. Generally, the coagulated core is best represented by the hypointense center on T2. Regions of greatest inflammatory activity are best represented by hyperintensity on K^{trans}; while the central region of lower K^{trans} is consistent with vascular compromise found in damaged tissue. The total extent of the lesion is best represented on v_e at all times.

A time-course study over 1 week shows that while the total extent of the lesion remains fairly stable (12 ± 3% decrease in area), the once viable outermost region undergoes latent necrosis. In this region, enzyme-releasing neutrophils dominate by 40 hours and are replaced by macrophages by 3 days. At 1 week, fiber regeneration and scarring are evident. A complex evolution is seen centrally also. At 40 hours, severely compromised vasculature extends over a region of structural vacuolation but, by 3 days, has advanced outward and includes dead sarcomeres still beyond the advancing front of inflammatory agents. Recession of edema is also seen by 3 days.

CONCLUSIONS

Images of GdK (K^{trans} and v_e) better differentiate sub-acute and sub-chronic changes in the thermal lesion, changes not visible on conventional MR. The extent of damage is best indicated on v_e, whereas the borders of inflammation are shown on K^{trans}. The full extent of necrosis and latent changes are also better predicted by GdK images compared to standard techniques taken at early times after heating. Together with conventional MRI, GdK may improve evaluation of thermal ablation by providing finer differentiation of necrotic states, inflammation, and repair processes.

REFERENCES

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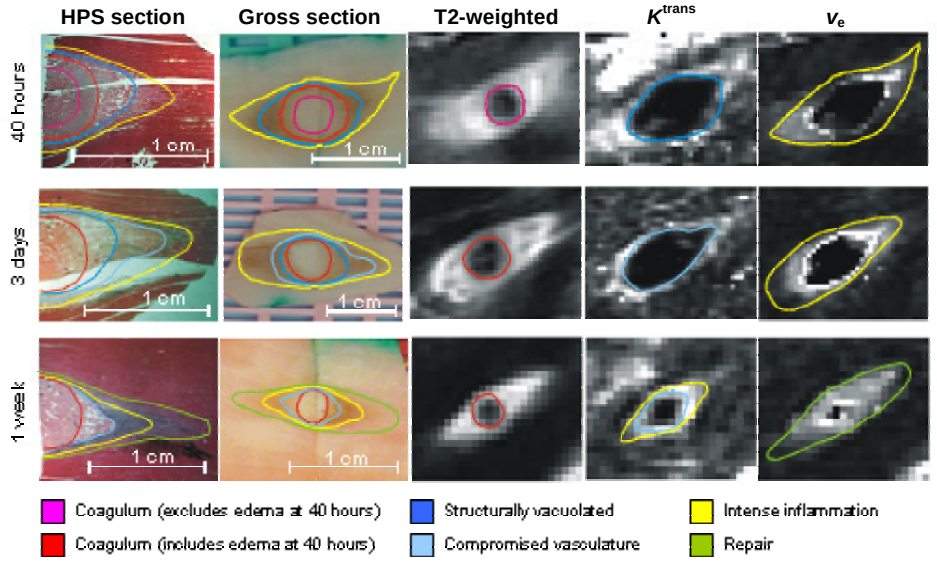

Figure 1. Histopathology regions (colored contours) at different times post-ablation overlaid on conventional T2w MRI and kinetics maps K^{trans} and v_e.

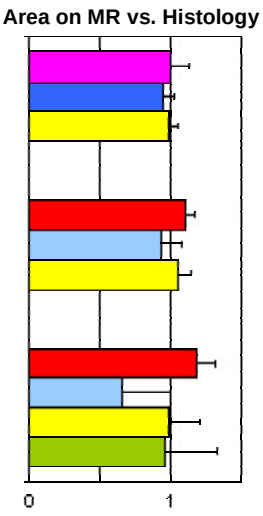

Figure 2. Segmented areas on MRI correlated to histopathology (regression slope ± 95% conf. int.). Vertical axis is the time post-ablation, as in Figure 1.