Characterization of the *in vivo* Histotripsy Lesion Using High Field MRI

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Introduction: Ultrasound based cavitation can non-invasively fractionate tissue (histotripsy) down to sub-organelle granularity. Previous work has shown how *ex vivo* histotripsy lesions exhibit T2 contrast while remaining well confined within the planned treatment zone[1]. However, it is unknown how bio-effects may alter *in vivo* histotripsy lesions. Here, we use T1 and T2 weighted MRI of harvested prostates to characterize the *in vivo* histotripsy lesion into three zones: a liquefied focal zone, a margin of partially disrupted tissue, and a hemorrhage zone of negligible damage.

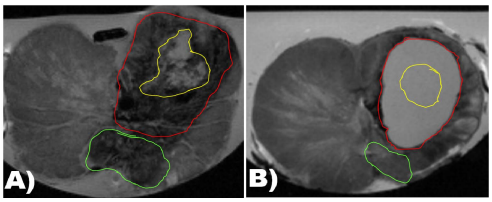

Figure 1: ***Axial slice of a typical histotripsy lesion of acute(A) and chronic (B)* in vivo *canine prostate. The three proposed damage zones are superimposed: Tissue homogenate (yellow), a terminally damaged marginal zone (Red), and the clinically negligible hemorrhage zone (green).***

Methods: Following UCUCA regulations, seven canine prostates were subjected, *in vivo,* to historipsy (750kHz, f number ~0.85). The ultrasound focus was mechanically steered to cover a 12x12mm square. A transrectal probe (GE, ERB 6.5MHz) confirmed the formation of the cavitation cloud within the prostate. Four prostates were harvested immediately after treatment while the other three were harvested two weeks later. After harvest, the prostates were immobilized in a holder, immersed in saline, and then imaged by a 7T small animal scanner (Varian, Inc), acquiring T1 and T2 weighted spin-echo images (TR: 4000-250 ms, TE: 150-13 ms, Nex: 2, Resolution: 1mm isotropic or 0.25x0.25x1mm, FOV : 64x64mm). In all cases, the imaging planes were oriented such that the MR image was in standard histologic orientation. After imaging, the prostates, still immobilized, were fixed in buffered formalin for one week, sectioned, and prepared for histologic processing. The holder prevented the prostates from deforming during handling, improving coregistration between MR and histologic images.

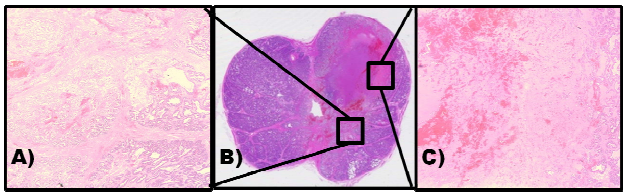

Figure 2: ***Histologic examination of a slice near that imaged in Figure 1.A. The full slide (B) demonstrates the three treatment zones. A sample of the clinically negligible hemorrhage zone (A) and the severely damaged marginal zone (B) are magnified 2x.***

Results/Discussion: Example T1/T2 weighted images for acute and chronic cases of histotripsy are shown in Figure 1 superimposed with the three proposed treatment zones. In the acute case, lesions in MRI exhibit hypo-intense regions surrounding and penetrating a hyper intense central zone. Hypo-intense regions may also extend along the path of the ultrasound beam toward the ventral side of the prostate. Figure 2 displays a histologic examination of a slice near that shown in Figure 1.A. Correlation between the histologic slice and the MR image suggests that the T2 bright areas correspond to liquefied debris at the treatment focus while the T2 dark areas correspond to regions with hemorrhage[2]. In particular, hemorrhagic regions between the treatment focus and healthy tissue possess large pools of homogenate with small islands of semi-intact glandular tissue[3]. However, regions containing hemorrhage that follow the ultrasound beam ventrally maintain nearly all their glandular structure. In MR images of chronic lesions, the hypointense regions have been replaced with either normal appearing tissue or T2 bright fluid. Comparison between acute and chronic cases suggests that much of an acute lesion's surrounding hemorrhagic regions, where a significant portion of the glandular tissue has been destroyed, will disintegrate in time and fill with fluid. The comparison also suggests that hypo-intense regions distal to the acute lesion, where tissue is nominally intact, will resume a normal appearance in MRI. Unfortunately, histology for chronic instances could not be prepared in time for publication. Also, T1 and T2 maps of an acute lesion along with a spin-echo image demonstrating the three treatment zones are shown in Figure 3. Contrast between these three zones rests mainly upon T2 decay as well as location. T2 dark regions correlate to histologic presence of hematoma while T2 bright regions are correlate to tissue homogenate. Meanwhile, change in T1relaxation rates are not highly correlated with the disruption zones.

Conclusion: Comparison between histology and MRI shows that T2 weighted images of acute, *in vivo* histotripsy lesions can be divided into three separate zones. The T2 bright regions correspond to homogenized tissue, the surrounding T2 dark region corresponds to hematoma and heavily damaged tissue, and the beam-like T2 dark region below the focal region corresponds to hemotoma with negligibly damaged tissue. T1 relaxation correlates poorly with these three treatment zones.

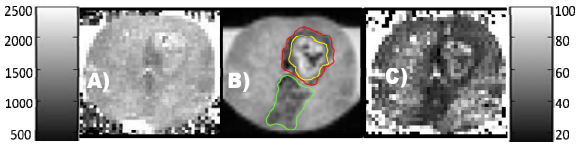

Figure 3*: T1 (A) and T2(C) maps of an acute histotripsy lesion (B) made in in vivo canine prostate. Superimposed are the three proposed damage zones. Differentiation between these zones depends primarily upon T2 contrast and the zone's location.*

References: 1) Hall, ISMRM 2007 Berlin; 1118.
2) Balci, MRM 1999; 17: 207-211
3) Roberts, Hall, J Urol 2006; 175: 734-738