**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-organellar 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.

**Methods:** Following UCUCA regulations, seven canine prostates were subjected, in vivo, to histotripsy (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 0.25x0.25x1 mm, FOV: 64x64xmm). 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 formaldehyde 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.

**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 hypointense regions surrounding and penetrating a hyper intense central zone. The three proposed damage zones are superimposed: Tissue homogenate (yellow), a terminally damaged marginal zone (Red), and the clinically negligible hemorrhage zone (green).

**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 hemotoma 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.

**References:**
2. Balci, MRM 1999; 17: 207-211
3. Roberts, Hall, J Urol 2006; 175: 734-738

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**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).

**Figure 2:** Histologic examination of a slice near that imaged in Figure 1A. 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.

**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.