

# Acute Histopathological Changes in Canine Prostates Treated with High Intensity Ultrasound or Cryosurgery: Correlation with Contrast Enhanced MR Images

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## Introduction

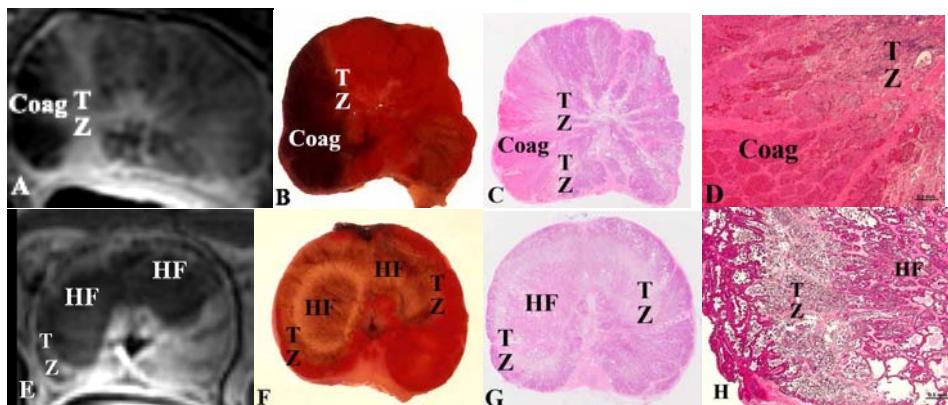
High intensity ultrasound (HIFU) and cryosurgery, both valuable treatments for prostate cancer, represent opposite ends of the minimally invasive temperature based therapies. However, in many respects, both types of thermally-induced lesions appear similar on MR images. For example, both types of thermal lesions lack contrast enhancement after injection of the contrast agent gadolinium (Fig. 1, A and E). Therefore, in order to optimize these MRI monitored treatments, this study was conducted to compare the acute histopathology of HIFU and cryosurgery-induced lesions in the dog prostate model, and to correlate patterns of tissue injury with contrast-enhanced MR imaging.

## Methods

Studies using either transurethral or interstitial ultrasound probes (n=6) or transperineal cryoprobes (n=4) were used to ablate target regions within the prostates of 10 dogs. Following treatment, dogs were euthanized and the prostates were harvested, sliced, and stained with triphenyl tetrazolium chloride (TTC), a vital dye that stains viable tissues red. TTC-stained prostates were then fixed in 10% buffered neutral formalin, processed for routine histopathology and stained with Hematoxylin and Eosin (H&E). Oversized glass slides with complete transverse sections of prostate were scanned at 2400 dpi resolution on a flat bed-scanner for comparison with TTC-stained wet tissues and contrast-enhanced MR images. Histopathology of the lesions was analyzed at high magnification.

## Results

The pathology of the prostatic lesions induced by HIFU vs cryotherapy differs in several respects. Grossly, prostates treated with HIFU develop lesions that are firm, discrete, dry, gray regions, sunken below the gland cut surface. Cryolesions are dark red, moist, soft, slightly mucinous, and do not retract beneath the cut surface. Following TTC staining, cryolesions are difficult to distinguish from the surrounding red-stained viable tissue whereas thermal lesions sharply contrast with untreated gland (Fig. 1, B, and F). Thin zones of pale TTC-stained tissue, referred to as the transition zone (TZ), borders the lesions created by both treatments. These areas correlate to hyperintense lesion borders on contrast-enhanced MR images (Fig. 1, A and E). Microscopically, both HIFU and cryo lesions have relatively distinct zones of injury characterized by severe damage surrounded by the TZ, where damage to glands and interstitial vasculature is less severe or sublethal. The TZ in turn merges irregularly with the normal, untreated glands. Prostatic glands subjected to severe cold temperatures in the center of the cryosurgery -“ice-ball” undergo total coagulation with loss of gland structure, gland remnants filled with eosinophilic coagulated cell debris, nuclear lysis, and extensive interstitial hemorrhage (Fig. 1, D). In contrast, the most intensely heated zones within the HIFU treated regions undergo heat fixation and maintain histologically “normal” appearing glands lined by epithelium that appears to be minimally altered (Fig. 1H). Irreversible cell death and vascular destruction in the coagulated cryolesions and the heat fixed zones in the HIFU lesions appear similarly as hypointense areas in the contrast-enhanced MR images. Areas of variable, sublethal or partial tissue injury to glands and blood vessels result in uptake of gadolinium on contrast enhanced MR images in the TZ of both.



**Figure 1.** Images of canine prostate treated with either cryosurgery (A-D), or HIFU (E-F). The coagulated tissue (Coag) and heat fixed tissue (HF) do not enhance with gadolinium, while the transition zones (TZ) in the prostates treated with both the cryosurgery and HUS are enhanced on MR.

## Conclusions

Contrast-enhanced MR images, TTC staining and detailed histopathological analysis of HIFU and cryosurgery-induced lesions in a canine prostate model can provide a reliable means of predicting cell death in desired target areas. The implication of this work is that areas lacking contrast enhancement are lethally ablated, while the areas with partial or full contrast enhancement require further treatment. Understanding the patterns of acute tissue injury that correspond to *in vivo* MR images should improve clinicians’ ability to accurately predict the success of these minimally invasive cancer therapies.

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## References

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