Image Guided Focal Therapy for Magnetic Resonance Imaging Visible Prostate Cancer: Defining a 3-Dimensional Treatment Margin Based on Magnetic Resonance Imaging Histology Co-Registration Analysis

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Abbreviations and Acronyms

3D = 3-dimensional
GS = Gleason score
HCyl = histological cylinder
Hausdorff Max = Hausdorff maximum principle
HD = Hausdorff distance
MCyl = MRI cylinder
MRI = magnetic resonance imaging
ROI = region of interest
SS = suspicion score
T2WI = T2-weighted imaging

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Purpose: We compared prostate tumor boundaries on magnetic resonance imaging and radical prostatectomy histological assessment using detailed software assisted co-registration to define an optimal treatment margin for achieving complete tumor destruction during image guided focal ablation.

Materials and Methods: Included in study were 33 patients who underwent 3 Tesla magnetic resonance imaging before radical prostatectomy. A radiologist traced lesion borders on magnetic resonance imaging and assigned a suspicion score of 2 to 5. Three-dimensional reconstructions were created from high resolution digitalized slides of radical prostatectomy specimens and co-registered to imaging using advanced software. Tumors were compared between histology and imaging by the Hausdorff distance and stratified by the magnetic resonance imaging suspicion score, Gleason score and lesion diameter. Cylindrical volume estimates of treatment effects were used to define the optimal treatment margin.

Results: Three-dimensional software based registration with magnetic resonance imaging was done in 46 histologically confirmed cancers. Imaging underestimated tumor size with a maximal discrepancy between imaging and histological boundaries for a given tumor of an average $\pm$ SD of 1.99 $\pm$ 3.1 mm, representing 18.5% of the diameter on imaging. Boundary underestimation was larger for lesions with an imaging suspicion score 4 or greater (mean 3.49 $\pm$ 2.1 mm, $p < 0.001$) and a Gleason score of 7 or greater (mean 2.48 $\pm$ 2.8 mm, $p = 0.035$). A simulated cylindrical treatment volume based on the imaging boundary missed an average 14.8% of tumor volume compared to that based on the histological boundary. A simulated treatment volume based on a 9 mm treatment margin achieved complete histological tumor destruction in 100% of patients.

Conclusions: Magnetic resonance imaging underestimates histologically determined tumor boundaries, especially for lesions with a high imaging suspicion score and a high Gleason score. A 9 mm treatment margin around a lesion visible on magnetic resonance imaging would consistently ensure treatment of the entire histological tumor volume during focal ablative therapy.

Key Words: prostatic neoplasms; magnetic resonance imaging; image processing, computer-assisted; pathology; risk

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FOCAL therapy is gaining increasing interest as primary treatment for prostate cancer.[1] This trend is partly driven by growing awareness of the indolent nature and excellent survival rate of most newly diagnosed lesions such that radical prostatectomy and radiation therapy with their associated impact on quality of life may not be warranted.[2] Although active surveillance provides a reasonable alternative in many patients with low risk tumors, this approach has limitations, including the intensity of followup evaluation to which patients are subjected and the associated anxiety of potentially missing the window of opportunity for cure.[3]

While ablative therapy for prostate cancer historically entailed total, subtotal or hemitotal ablation, more recent reports describe truly focal ablation procedures targeting the expected location of dominant tumors.[4,5] This approach is supported by the emergence of newer ablation technologies, including laser based thermotherapy,[4,6] focal cryoablation[7] or photodynamic therapy,[8] which allow for more precise definition of tissue destruction margins. Thus, such procedures require a method to anticipate tumor margins and thereby guide decisions on the boundary of the ablated region to avoid under treatment.

The ability to precisely define focal lesion volume by MRI would have immense value for guiding focal ablative therapy.[9] Past studies compared tumor volumes between MRI and histopathology assessment.[10–13] Using affine transformation and compensation for changes in volume and shape[14] we previously performed such an investigation with a validated, automated 3D co-registration system.[15] We observed consistent underestimation of tumor volume by MRI, indicating that actual tumor boundaries are expected to be located beyond the boundaries predicted by the visualized lesion on MRI. This difference in lesion boundaries has a critical impact in planning and performing focal therapy procedures, given that treatment of only the MRI visualized lesion leaves a portion of tumor untreated due to the larger histological volume. Therefore, a method is needed to define a target volume for focal therapy of an MRI visualized lesion to reliably treat the entire tumor volume. Such a methodology would be important to achieve optimal oncologic control using emerging MRI targeted focal therapeutic procedures.

Thus, in the current study we compared the boundaries of prostate tumors between MRI and histopathology evaluation using co-registration software to define an optimal treatment margin and achieve complete tumor destruction at image guided focal ablation.

MATERIALS AND METHODS

Study Population

This retrospective study was approved by our institutional review board. A waiver of written informed consent was granted. We initially identified 37 patients who underwent MRI at our center before prostatectomy. In these patients a dominant tumor was identified on histopathology assessment and visualized on MRI. This cohort was evaluated in a prior study comparing tumor volumes on MRI and radical prostatectomy pathological assessment.[15] Four of the 37 patients were excluded from analysis because of tumor volume greater than 3 cc on preoperative MRI since patients with a lesion of this size would not be selected for focal therapy. Thus, the final cohort comprised 33 patients with a mean ± SD age of 60.7 ± 5.4 years. Median preoperative PSA was 4.8 ng/ml (range 0.32 to 19.5), including 27 patients with PSA less than 10 ng/ml, 4 with PSA 10 to 15 ng/ml and 2 with PSA greater than 15 ng/ml.

MRI Data Acquisition

MRI was performed using a 3 Tesla whole body system and a pelvic phased array coil. Sequences included multiplanar T2WI and axial diffusion-weighted imaging of the prostate (b-values 50 and 1,000 seconds per mm^2) with apparent diffusion coefficient reconstruction. Dynamic contrast enhanced imaging of the prostate was done with 0.1 mmol/kg gadolinium chelate and 5.5-second temporal resolution.

Histopathology Analysis

A standard Stanford protocol was used for pathological assessment as previously described in detail.[15,16] Photographs were taken of intact slices using a digital camera before further processing. Subsequent histological slides underwent high resolution digitalization at 400× magnification using a Leica SN400 (Leica Microsystems, Wetzlar, Germany). Digital images were combined with Photoshop® to form virtual whole mount images using the photographs of intact slices for guidance. A single uropathologist marked tumor borders and recorded the GS of each lesion. Tumors were stratified into a low grade group (GS 6) and a high grade group (GS 7 or greater).

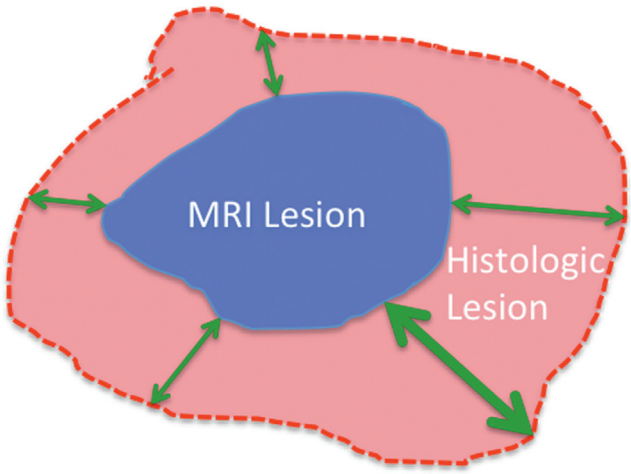

Figure 1. MRI lesion encompassed by histological lesion. Red outline indicates histological boundary. Small 2-headed arrows indicate HD. Large 2-headed arrows indicate Hausdorff Max.