Prostate Cancer Detection: Multi-parametric MRI with Diffusion-Weighted Imaging and Dynamic Contrast Enhanced MRI

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Introduction
Characterization of tumor location and extent in prostate cancer (PCa) is essential for accurately targeting focal therapies, and may also affect patient management decisions during active surveillance. MRI provides the opportunity to image both anatomy and multiple physiologic properties in the same session. The use of multiple MRI modalities to optimize PCa localization is an active area of study [1-4]; however, interpretation of multi-parametric datasets presents a number of challenges, both in terms of decision making for resolving conflicting results between modalities as well as workflow management when review of each image set is required. Generation of a map, developed as a quantitative combination of parameters, would simplify the review process and provide an objective guide for determination of tumor location and boundaries. Our study includes diffusion weighted imaging (DWI), quantitative T2, and dynamic contrast enhanced (DCE) MRI in a radical prostatectomy patient cohort, followed by whole mount pathology. We have explored the optimal combination of parameters for localization of PCa in the peripheral zone (PZ).

Purpose
To develop a multi-parametric model suitable for prospective tumor mapping using whole mount pathology during model development.

Materials and Methods
Twenty-five men with biopsy-confirmed PCa underwent endorectal MRI on a 1.5T GE Excite HD platform prior to prostatectomy. Ethics board approval and informed consent were obtained. T2-weighted fast-spin echo (FSE) images were acquired, followed by diffusion-weighted imaging (TR/TE = 4000/77ms, 128x256 matrix, 10 NEX, FOV = 14cm, b = 0.600ms/mm²), multi-echo FSE imaging (TR = 2000ms, 10 echo times (9.0-90.0ms), 256x128 matrix, 1 NEX, FOV = 20cm), and dynamic contrast-enhanced (DCE) MRI (TR/TE = 4.3/1.9ms, 256x128 matrix, 0.5 NEX, FOV = 20cm, α = 20°, 10s temporal resolution, 50 phases). All MRI datasets were obtained at identical slice locations with 3mm slice thickness and no intersection gap. ADC and T2 maps were generated, and a Tofts model [5] with assumed arterial input function [6] was used to calculate Ktrans and vve maps. The ADC map was resampled to match the resolution of all other images. Hematoxylin and eosin stained whole mount sections were prepared to match in vivo MRI [7]. PZ tumors >3mm were outlined on all slides by a GU pathologist, and the section with the largest cross-sectional area of tumor used in analyses. All tumors were included; thus, multiple slices were used for patients with multi-focal disease (9 in 25 patients). A region of interest (ROI) in normal PZ was delineated by the pathologist. All tumor and normal ROIs were transferred to MRI. The significance between median tumor and normal values for each parameter in each patient was tested using both unpaired and matched-pair (same slice tumor and normal ROI) non-parametric tests. Receiver operating characteristic (ROC) curves were generated for each parameter using all ROI values. Bootstrapping was used to determine mean areas under the ROC curves (AUC), and to compare performance between parameters. Feature vectors (FVs) for logistic regression (LR) modeling were generated, corresponding to the set of parameter values at each spatial location within each ROI (i.e., a subset of (ADCj(µ), T2j(µ), Ktrans(µ), vve(µ))). The model was optimized by adding parameters step-wise based on decreasing AUC testing each parameter addition for significance and accounting for correlated data within patients. The final model was compared against each parameter. Bonferroni-adjusted α’s were used for multiple comparison significance tests.

Results and Discussion
Thirty-eight tumors from the twenty-five patients were reviewed. Median ADC and T2 values in PCa (1.275 x 10⁻³ mm²/s and 88.7ms, respectively) were significantly lower than in benign PZ (1.467 x 10⁻³ mm²/s and 111.6ms, respectively) both overall (P<0.005), and for matched-pair tests (P<0.001). There were no overall differences between tumor and normal values for Ktrans or vve (PCa and normal: 0.298 and 0.253 min⁻¹ for Ktrans (P=0.168), 0.283 and 0.290 for vve (P=0.670)); however, in matched-pair tests, median Ktrans values in PCa were significantly higher than normal PZ (P=0.013), and vve values showed a trend towards being significantly lower (P=0.069). 6460 voxels were extracted from all ROIs (4152 PCa, 2308 benign). ADC had the highest ROC performance (mean AUC: 0.689), and was significantly greater than AUC for both Ktrans (mean: 0.592, P<0.002) or AUC for vve (mean: 0.543, P<0.002), but not AUC for T2 (mean: 0.673, P=0.026). Additions of ADC, T2, and Ktrans to the LR-model were significant, with the probability of a voxel being malignant determined as P=e⁻^(β+αADCj+αT2j+αKtransj+βvvej)/[1+e⁻^(β+αADCj+αT2j+αKtransj+βvvej)], where β=3.176-1378ADC-0.008972T2-0.715Ktrans. The LR model was optimized by adding parameters step-wise based on decreasing AUC testing each parameter addition for significance and accounting for correlated data within patients. The final model was compared against each parameter. Bonferroni-adjusted α’s were used for multiple comparison significance tests.

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Conclusion
We have developed a multi-parametric model incorporating ADC, T2 and Ktrans to create a single quantitative map of tumor probability, which may improve localization of cancer in the peripheral zone of the prostate.

Figure 1. Whole mount section (a), T2-weighted MRI (b), input parameter maps ADC (c), T2 (d), and Ktrans (e), and LR map using final model (f). (map valid for PZ tissue) tumor: black/solid line, normal: blue/dotted line) The lesion is clearly visible in (f), with much of the noise from the input datasets removed. The tumor/normal regions identified were added to the overall training dataset.

Figure 2. ROC curves for all parameters and LR-model. ADC was the top single-parameter; AUC was significantly higher than AUC for Ktrans, and vve, and greater than AUC for both. However, the addition of T2 and Ktrans was significant in the model, and may lead to a method to detect PCa with ADC values comparable to normal PZ.

References