Machine learning for target selection in MR-guided prostate biopsy: A preliminary study

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Introduction – With an estimated 240,890 cases to be diagnosed in 2011, prostate cancer (PCa) remains among the most common male malignancies with an annual death toll of 33,270 men. Prostate tumors are not visible in the transrectal ultrasound (TRUS) B-mode images used for the guidance of routine biopsies. Therefore, TRUS biopsy is not targeted. There is strong evidence that multiparametric MRI (mpMRI) including Diffusion Weighted (DW) and Dynamic Contrast-Enhanced imaging (DCE) in addition to the T2-weighted MRI can improve the accuracy of PCa localization and staging [1]. We have reported transperineal MR-guided prostate biopsy with highly accurate targeting as a solution to improve the accuracy of the biopsy process in detection of prostate cancer [2, 3]. The targets are selected by a team of three radiologists, based on pre-operative mpMRI (Fig. 1). The objective of the work presented here is to assess the feasibility of quantitative analysis of mpMRI aided by a machine learning approach to assist the target selection process. The idea is to train a classifier on the mpMRI data from radical prostatectomy patients with histologically confirmed PCa. The resulting classifier is used retrospectively on the data from patients that have undergone MR-guided prostate biopsy, in the areas selected as targets by the radiologists, to compute a measure of the probability of cancer and compare with the histological analysis of the core biopsy samples.

Materials and Methods – *Data:* All patients were enrolled in a prospective clinical study approved by the institutional review board. All patients underwent mpMRI exams in a GE 3T MR scanner using an endorectal coil and included T1w, T2w, DWI and DCE sequences. The training group (N=13) comprised of the patients that had confirmed PCa and underwent radical prostatectomy. In this group, an expert radiologist contoured areas of the prostate peripheral zone (PZ) that were cancerous as reported in the histopathology report *and* suspicious on T2W (low SI), raw DCE (rapid enhancement and wash out after gadolinium agent administration) and Average Diffusion Coefficient ADC maps (low SI) sequences. The opposite characteristics were considered true of normal prostate PZ. This yielded 16 cancerous and 5 normal regions with a total voxel count of 1499. The second group of patients included all of the cases that have undergone 3T MR-guided biopsy with our current protocol in place as of January 2011, *and* have at least one biopsy target in the PZ. This amounted to five cases with a total of ten PZ biopsies.

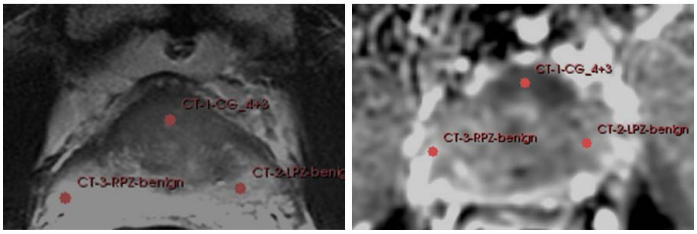

Fig 1. Sample T2 (left) and ADC (right) images for target selection.

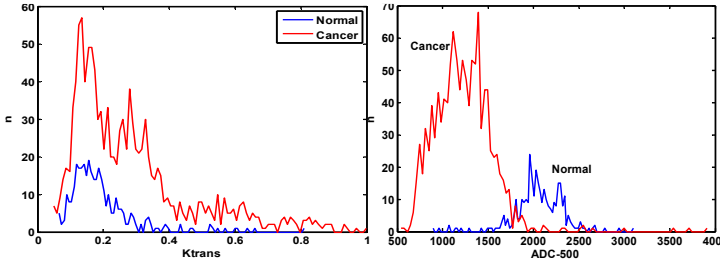

Fig 2. The distribution of K^{trans} and ADC in cancer and normal ROIs.

Classification approach: The values of ADC from DWI b0-500, and K^{trans}, v_e, time to peak (TTP) and area under the curve (AUC) from perfusion imaging were available for each pixel. It was observed that only the values of ADC formed distinctly different distributions in the cancer *vs.* normal regions in the training dataset (Figure 2). We employed two machine learning approaches. First we used our previously reported multi-feature support vector machine (SVM) for mpMRI classification [4] with all possible combinations of the five available parameters. Training and cross-validation was performed on the prostatectomy dataset with a leave-one-patient-out validation scheme. The best outcome was achieved when only ADC was used as the sole feature. Guided by this outcome, we then used a single-feature Bayesian framework using only ADC to build a machine learning solution to predict the outcome of the biopsies. In the Bayesian approach, based on the bell-shaped distributions of the ADC values in the two classes, we assumed Gaussian distributions for the likelihood of ADC values in cancer $P(ADC=a \mid C)$ and normal areas $P(ADC=a \mid N)$. The mean and standard deviations for these distributions were derived from a Gaussian fit to the ADC in each class. The priors for cancer and normal were set to $P(C) = P(N) = 0.5$. Using the Bayes rule, we computed the posterior probability of cancer $P_c = P(C|a) = P(a|C)P(C) / [P(a|C)P(C)+P(a|N)P(N)]$.

Samples	Finding	P_c
P1 – RPZ	Benign	**0.0**
P1 – LPZ	Benign	**0.4**
P1 – LPZ	Benign	0.9
P2 – LPZ	Benign	**0.4**
P2 – LPZ	Benign	**0.0**
P3 – Mid RPZ	3 + 4	**1.0**
P4 – Mid LPZ	Benign	0.9
P5- RPZ (Apex)	3+3	**0.9**
P5- RPZ (Base)	3+3	**0.8**
P5 – LPZ	Benign	**0.1**

Table 1. The biopsy findings and the computed value of P_c.

Results – The leave-one-patient-out cross validation in the prostatectomy dataset yielded an area under the ROC curve of 0.966 using SVM with ADC as the only feature. It was noted that adding the other features to ADC did not improve this results. In a similar cross-validation, the Bayesian classifier resulted in an area under ROC curve of 0.964. Then, using the Bayesian classifier, with the likelihoods estimated on all the 13 training cases, we created maps of P_c values for the patients in the second group. The results are listed in Table 1 and show that in eight of the ten PZ targets, the classification outcome was confirmed by the biopsy finding (P_c close to 1 for cancer and $P_c < 0.5$ for benign findings). All three cancer outcomes are correctly classified. Five of the seven benign outcomes are also correctly identified. This outcome suggests that the classification method, if validated on a larger sample size, has the potential to be used to improve the biopsy yield by testing the regions of the proposed targets, maintaining a high sensitivity and removing some of the false suggested targets.

Conclusions and limitations – In this retrospective feasibility study, we conducted a preliminary evaluation of a classifier in identifying cancer areas in the prostate peripheral zone. Our results show that classification results in the majority of cases agree with the histopathology analysis of the collected sample. The process of ROI selection for training in this work was guided by approximate histology location, the ADC maps and *raw* DCE data. Among the five parameters we considered, only ADC was used directly for visual differentiation in the training stage which likely explains the strong separation in distributions we observed. Our results confirm the value of ADC in PCa characterization and suggest that the supervised classification approach may have assistive value in target selection for biopsy planning. In the future, we will move towards using wholemount histopathology as the gold standard for ROI selection in the training stage. This might also enable us to extend the methodology beyond the peripheral zone. The number of patients in both training and testing stages will increase as we continue our 3T MR guided biopsy program.

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