Aggressiveness Biomarker for Prostate Cancer in ADC-T2W MR Feature Space

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Target audience: The research benefits radiologists, urologists, radiation and medical oncologists.

Purpose: Accurate localization of prostate cancer (PCa) is fundamental for guiding diagnostic and therapeutic interventions and permitting active surveillance to be performed with confidence. In patients undergoing active surveillance[1], current monitoring methods based on prostate-specific antigen (PSA) testing[2] and periodic random transrectal ultrasound (TRUS)-guided biopsy create uncertainty leading to a large number of patients opting for potentially unnecessary radical therapies. By contrast, increasing evidence supports multi-parametric MRI (mp-MRI) as a suitable imaging biomarker for detecting and monitoring PCa patients. mp-MRI[3] is highly insightful and informative with its description of various phenotypes, such as water content (T2), tissue microstructure (diffusion), micro-vascularity and permeability (DCE) in attaining accurate localization of PCa. However, data underutilization and inter- and intra-observer bias impede the method's full potential. Nonetheless, mp-MRI has already improved tumor recognition even though the data may be confounded by benign conditions with malignant appearance, such as prostatitis, hemorrhage, benign prostatic hyperplasia (BPH), atrophy and post–treatment changes[4]. On the other hand, evaluation of a large number of longitudinal images obtained from multiple sections with many imaging sub-modalities (e.g., ADC, T2W) creates a data deluge. This overburden for physicians defeated PCa detection strategies. Herein, a novel approach based on a joint, integrative, direct and objective visualization and analysis of multimodal imaging data is proposed to improve PCa localization, evaluation, staging and surveillance by addressing mp-MRI's challenges.

Methods: The approach is based on the MR feature space (MR-FS) of dimension equal to the number of imaging modalities (e.g., ADC and T2W). The feature vector at a given location is constructed by stacking the signal values from each modality into an array of numbers (see Figure 1). Fundamentally, feature vectors located in the neighborhood of a given FS position represent similar tissue characteristics. Accordingly, the identification of the regions within the FS characterizing malignant tissue types has potential biomarker properties with further predictive value after suitable physician training.
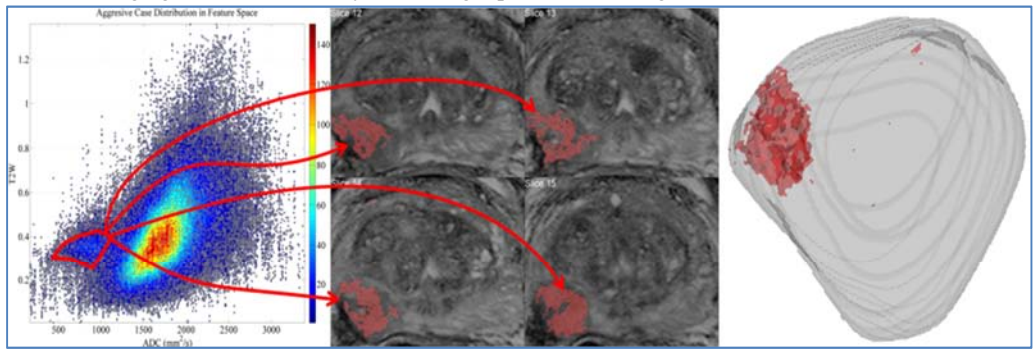

Figure 1 Aggressive bulge demarcated with the red ROI in MR-FS (81yrs old patient) reflects on multiple tumorous pixels demonstrating one-to-many nature of the correspondence. On the right the burden identified by MR-FS in the whole gland is shown in a 3D reconstruction from MRI slices.

In the past, PCa's complexity has thwarted computer algorithms that were successfully designed for and applied to different problems. Herein, by using the in-house developed software, InFS-Explorer©, physician experience and knowledge is incorporated into the detection algorithm. The software acts as a diagnostic support system for the interpreting imager. InFS-Explorer© interactively displays pixels associated with an FS region demarcated by the user and vice versa. In a cohort of 44 consecutive patients (62.07 ± 6.32 yrs), all, with documented prostate cancer but with 15 demonstrating aggressive tumors (Gleason score $\geq$ (4+4)), two radiologists with extensive experience in mp-MRI identified highly suspicious lesions and targeted biopsies into them. The cohort's ADC and T2W data (3T, endorectal coil) was analyzed using InFS-Explorer©.

Results: The analysis revealed a characteristic bulge in the [low ADC]-[mid-low T2W] MR-FS region (see Figure 1 and Figure 2) that identified aggressive PCa. There were 13 true positives and 1 false positive and 2 false negatives and 28 true negatives leading to a sensitivity of 0.87, specificity of 0.96, positive predictive value 0.93 and negative predictive value of 0.93.

Discussion: The demarcation of the bulge in the ADC-T2W FS with InFS-Explorer© could be used to semi-automatically detect aggressive PCa in a manner that integrates well with present workflow, including an easy addition into existing PACS setup. With reduced inter- and intra-observer bias, robust localization of aggressive anatomic regions results in consistent decisions and appropriate actions (e.g., biopsy vs. monitoring).

Conclusion: With the utilization of InFS-Explorer©: 1) Accurate localization of aggressive tumor burden could improve accuracy of biopsies and radiation therapy guidance while decreasing the time needed for interpretation 2) Observing the changes in the MR-FS in a single instance (see Figure 2), in addition to being more time efficient than evaluating a large number of images longitudinally, may reduce inter and intra-observer variability 3) Extraction of relevant information from standard imaging data leads to potential improvements in the accuracy of clinical decisions that will reduce health care costs while providing optimal personalized care.
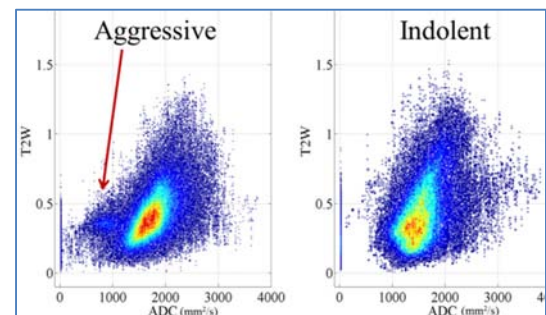
Figure 2 Comparison of ADC-T2W FS of an aggressive case (81 yrs.) with an indolent case (63 yrs.). The bulge is an aggressiveness biomarker

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