Prospective Study using Delta-Radiomics and MRI Biomarkers to Assess Tumor Response of the Dominant Intraprostatic Lesion (DIL) at Multiple Treatment Time Points

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Purpose

An IRB approved prospective clinical trial was developed to test longitudinal multi-parametric MRI (MP-MRI) (DWI, DCE) features used as imaging biomarkers to assess treatment response for prostate radiotherapy.

The study aims to characterize longitudinal changes of MRI imaging features between the dominant intraprostatic lesion (DIL) and normal prostate (NP) over the radiation treatment. The use of MP-MRI provides morphological assessment with T2 imaging and functional assessment with diffusion-weighted imaging (DWI) and dynamic contrast-enhanced imaging (DCE). Multiple time points provided evidences how the DIL responded to radiation dose over the treatment course. Identifying relevant radiomic features to relate to biomarkers over the course of treatment can help provide important information in the prognosis, treatment outcome prediction, and the association with tumor aggressiveness.

Methods

- MRIs were taken at four time points: pretreatment, mid-treatment, end of treatment, and two months post treatment. This study currently has seven patients enrolled. Radiation treatment consisted of 78 Gy prescribed to the entire prostate.
- The extended Tofts model was used for pharmacokinetic modeling. Parametric maps were generated with dynamic contrast enhanced (DCE) data for volume transfer constants K^{trans} and K_{ep}. An experienced radiologist contoured DILs on each MRI modality (T2, ADC, K^{trans} and K_{ep}). Additionally, a NP contour was drawn on the contralateral side to calculate relative response.
- Histogram based intensity features, GLCM, GLRLM, GLSZM, and NGTDM features were generated by the Cancer Imaging Phenomics Toolkit (CaPTK).
- Spearman's Rank correlation coefficient identified relevant trends in 300 features extracted. Relevant features were identified comparing pretreatment to mid-treatment threshold change.
- MR scan parameters: T_2 weighted imaging with a FRFSE (fast recovery fast spin echo) sequence: T_R/T_E = 3500/110 ms, 18 cm FOV, voxel size = 0.42 x 0.42 x 2.5 mm^3; Diffusion Weighted (DW) echo planar imaging and trace diffusion sensitization for 4 *b*-values: 0, 500, 1000, and 1500 s/mm^2, and following parameters: T_R/T_E = 5000/77.7 ms, 1.25 x 1.25 x 5.5 mm^3 voxel size; DCE and T1 mapping (flip angles 2°, 5°, 10°, 15°, 20°, 25°) using a 3D SPGR sequence with T_R/T_E = 3.6 ms/1.3 ms/15°, 22 cm FOV, 0.75×0.75×2mm voxel size & 9 sec temporal resolution.

Results

- Over the four imaging modalities, 62 features were identified that related dose response of the DIL relative to the NP.
- These features either trended monotonically over time (such as the histogram texture energy), or there was an initial change from pretreatment to mid-treatment that subsequently recovered back towards the pretreatment value in the following scans (gray level busyness).
- Strong trends were found in the histogram texture energies, which showed up to a 65% changes between the pretreatment and mid-treatment scans.

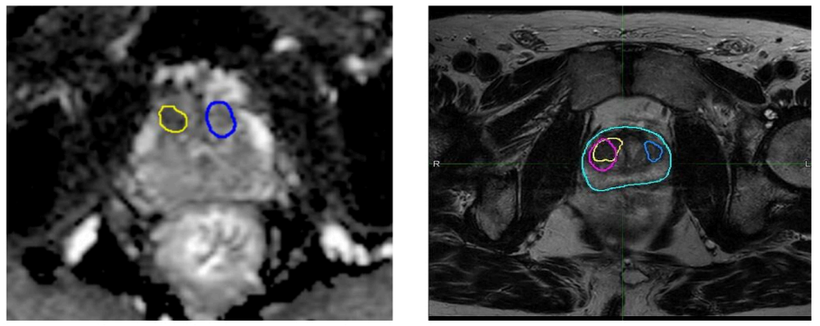

Figure 1: (a) ADC axial image. (b) T2 axial image. The blue contour is the NP, yellow contour is the ADC DIL, and the red contour is the T2 DIL. For ADC images the hypo-intense region indicates the tumor location due to lower water content in the extracellular space of the tumor vs NP. Note the delineation differences between T2 and ADC DIL contours, these changes show the need for multiple parametric imaging modalities in determining the true extent of the intraprostatic tumor.

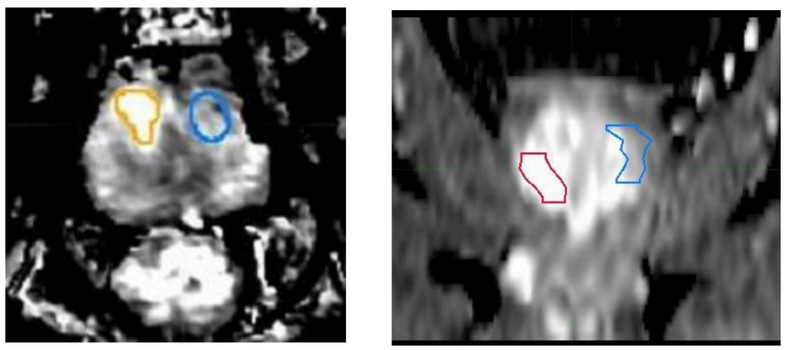

Figure 2 (a) is the axial view of the K_{ep} calculated image. The next image is the coronal view of the K^{trans} MR image. The blue contour is the NP, red contour is the K^{trans} delineated DIL, and the orange contour is the K_{ep} DIL contour. Hyperintense areas on these images correlate to high transfer value in (K^{trans}) and out (K_{ep}) of the region, which indicate higher microvascular permeability (common to tumors).

Results

Scan Modality	T2	ADC	Kep	Ktrans
Number of Features	19	12 (3)	19	12

Table 1: Relevant features identified in each modality. For T2, Kep, and Ktrans scans, features were identified with a 40% threshold, that is the feature changed by at least 40% from the pre to mid treatment scan. ADC features did not show as substantial of a change (see Figure 3), consequently a 20% threshold was used. Three ADC features did meet the 40% threshold. A few of the features identified were kurtosis, energy, skewness, entropy, strength, contrast, zone percentage, short run low gray level emphasis offset_8, long run high gray level emphasis offset_6.

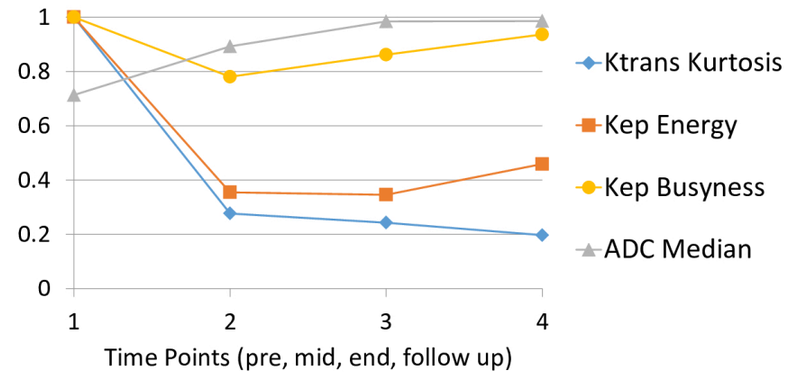

Figure 3: Relative Temporal Response of MP-MRI Features. The graph shows how a few key features change over the course of the radiation treatment. K_{ep} energy and busyness changed 65% and 22% respectively at the first time point after radiation treatment. These metrics subsequently started to recover to pretreatment levels, which is expected following radiation recovery. ADC median values trended up over the course of treatment. This agrees with the expected result of a higher water content (see Figure 3). K^{trans} kurtosis showed a sharp drop initially of 72%. By the follow up scan it had dropped by 80%.

Conclusions

This study identified 62 relevant features that correlate to radiation dose over treatment. This work demonstrated metrics to track DIL changes with radiation dose, and subsequent post treatment stability. The changes of these features over the treatment course have potential to predict DIL recurrence or progression in the prostate.

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