

Radiomics Driven Image Analysis and Coregistration Scheme to Identify DCE MRI Markers for Microvascular Density

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INTRODUCTION

Prostate cancer is the second leading cause of cancer mortality in men. Measures such as gleason scores and microvascular density (MVD) are well established indicators of CaP outcome. However, invasive procedures are necessary to obtain these measurements. Dynamic contrast enhanced (DCE) magnetic resonance imaging (MRI) has emerged as a promising functional modality for CaP assessment. Since it captures dye permeation into the vasculature, we hypothesize that DCE MRI parameters can serve as indicators of CaP outcome by revealing tumor vascularity. Therefore, we seek to identify DCE MRI perfusion parameters that correlate with MVD using sophisticated image analysis and registration methods, in order to establish non-invasive methods of assessing tumor outcome.

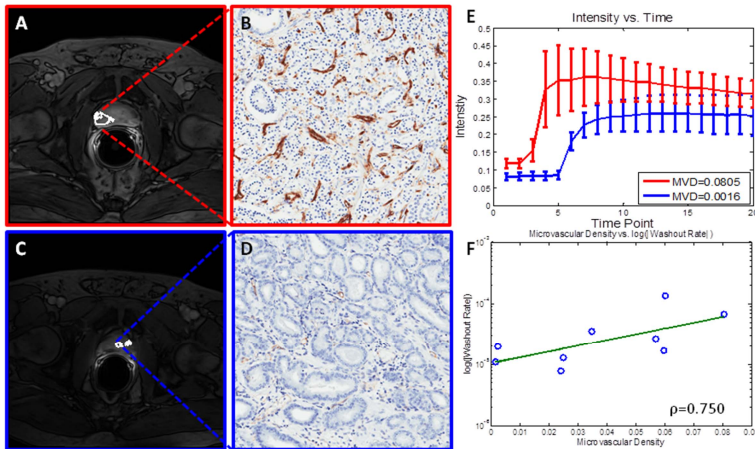


Figure 1. DCE-MRI with tumor annotation (white) and corresponding CD31 stained histology for tumors with (A-B) high and (C-D) low vascular density. (E) Signal Intensity vs. time curve for tumors with high vascular density (red) and low vascular density (blue) (F) Semilog plot of Washout Rate and MVD

METHODS

Six patients with biopsy confirmed CaP of gleason score 7 underwent multiparametric (MP) MRI prior to radical prostatectomy (RP). RP specimens were sectioned into quadrants and stained with vascular marker, CD31. Tumor was annotated by an expert pathologist. The quadrants were stitched into whole mount sections using Histostitcher, an interactive program that combines quadrants into a contiguous slice based on user provided landmarks [1]. Histology to T2-w MR slice correspondences were determined by pathologist and radiologist on the basis of slice location and anatomical landmarks. The stitched sections were registered to corresponding MR slices using thin plate splines (TPS) [2]. In this registration framework, the user selects corresponding points on prostate boundaries on the two modalities. Transformation of the moving image is calculated such that the overlap between corresponding points is maximized while the bending energy is minimized. This histology MRI co-registration method allowed us to localize CaP on MRI based on the annotations provided on histology [2].

Kinetic parameters were extracted from signal intensity vs. time curves within CaP regions using in-house matlab program [3]. On the corresponding histological regions, vascular stain was segmented using hNCut. hNCut an algorithm that combines frequency weighted mean shift and normalized cuts algorithms to segment user defined color swatch [4]. MVD was computed as the fraction of stained area within total CaP area. Spearman's rank correlation test was used to correlate tumor MVD and DCE kinetic parameters obtained from the six patients, each of whom had 1-2 CD31 stained slices. We chose this particular statistical test for correlation as it accounts for general trends in the data without assuming linearity.

RESULTS & DISCUSSION

Figure 1A-E qualitatively show differences in signal intensity vs. time curves for representative cases of tumors with low and high vascular density.

Kinetic Feature	Correlation Coefficient	p-value
Maximum Uptake (MU)	0.452	0.223
Time to peak (TTP)	0.050	0.912
Rate of Uptake	0.633	0.076
Rate of Washout	0.750	0.026
Enhancement	0.717	0.037
Enhancement ratio	0.717	0.037

Table 1. Spearman's correlation coefficient and p values for CaP DCE MRI kinetic features and MVD

Preliminary results shown in Table 1 indicate that rate of washout, enhancement and enhancement ratio are significantly correlated with MVD. Figure 1F shows the semilog correlation plot for washout rate, the kinetic feature with the highest correlation coefficient. Linearity of data points in the semilog space suggests a nonlinear relationship between washout rate and MVD. The nonlinearity may be explained from the fact that washout rate is a function of both vascular density as well as permeability, the latter of which is not accounted for in histological assessment of MVD. These results suggest that rate of washout is a promising imaging marker for tumor outcome.

REFERENCES

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