Prostate cancer detection from contrast enhanced T1 time course without pharmacokinetic modeling

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Introduction – Dynamic contrast enhanced (DCE) magnetic resonance imaging (MRI) has shown great potential in differentiating normal and tumor tissues [1]. With DCE MR imaging, the diagnosis is based on quantitative parameters extracted from the series of T1-weighted images acquired after the injection of a contrast agent. The commonly used parameters are volume transfer constant, K^{trans}, fractional volume of extravascular extracellular space, v_e and the fractional plasma volume, v_p [2]. To calculate these parameters, a pharmacokinetic model is fitted to the T1 time series. Most models make simplistic assumptions about the perfusion process. Moreover, these models require accurate estimation of the arterial input function, which itself is a difficult task. In this work, we propose a data-driven approach to characterizing T1 time course. This method which is free of physiologic modeling is used to classify prostate tissue into cancer and normal, based on dynamic contrast enhanced T1-weighted images. The reference standard is the wholemount histopathologic analysis of extracted prostate specimens. Our approach is to design a learning agent that can detect cancer directly from the T1 time course without modeling the physical phenomenon. The dimensionality of the T1 time course is reduced using Principal Component Analysis (PCA) and the resulting parameters are used with Support Vector Machine (SVM) classification.

Materials and Methods - *Data:* The DCE MRI data used here was obtained with the approval of the UBC Clinical Research Ethics Board. The recruited patients provided written consent for imaging prior to radical prostatectomy. The MRI scans were performed a week before the surgery on a 3 Tesla (T) MRI scanner (Philips Healthcare, The Netherlands) and MRI signals were acquired with a combination of an endorectal coil and a cardiac phased-array coil. Fast spin-echo T2-weighted images were acquired, followed by DCE T1-weighted images, acquired with a 3D T1-weighted spoiled gradient echo-sequence (TR/TE = 3.4/1.06 ms, flip angle = 15^0, FOV = 24 cm, 256×163 matrix). The contrast agent used here was Gd-DTPA (Magnevist, Berlex Canada) and 0.1 mmol/kg of Gd-DTPA was injected with a motorized power injector within 10 s at the rate of 2 mL/s, followed by a 20 mL flush of saline. The time resolution was 10.6 s per 12 slices. After the surgery, the wholemount pathology analysis was acquired by dissecting the radical prostatectomy specimens. Depending on the size of the prostate, 9-13 slides were produced and cancer regions were marked in the pathology slides by an expert anatomic pathologist.

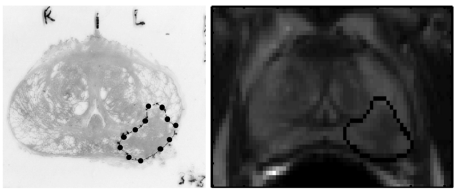

Fig 1. The wholemount histology slides are automatically registered to T2-weighted MRI.

Registration: Each pathology slide was registered with the corresponding MR T2-weighted slice using affine transformation followed by B-spline deformable registration. The T2-weighted MR slices were also registered to their corresponding DCE-slices with affine and B-spline registration. These transformations were then used to map the marked cancer regions from the pathology slides to the corresponding T2-weighted, and then to DCE slices (Fig. 1). As a result, each area marked as a tumor on the histology slides was transferred to a corresponding area in DCE. For the purpose of this abstract we limited our analysis to the peripheral zone.

Features and classification: The registration resulted in 57 cancer regions and 57 normal regions in the data from the 12 wholemount cases available so far in the study. Feature extraction and classification was performed on a pixel level. For each pixel, three pre-injection DCE MR image intensities and 72 post-injection image intensities were obtained. The mean pre-injection intensity was subtracted from each of the post-injection intensities to find the change in image intensity after injection of the contrast agent. This resulted in a 72 dimensional feature vector corresponding to each pixel. The high dimensionality of this feature vector poses computational difficulties in training a classifier. Therefore, we reduced the dimensionality of the feature vector using PCA analysis. The PCA decomposition revealed that the first seven principal components explain 97% of the total variance of the T1 time course in the dataset (Fig. 2). Therefore, each feature vector was replaced by the seven-dimensional vector comprised of only the first seven principal components. Similar to previous work in [3], we used leave-one-patent-out cross validation to determine the set of SVM parameters for classifying each pixel as cancer or normal. Radial Basis Function (RBF) was used as the kernel for SVM [4].

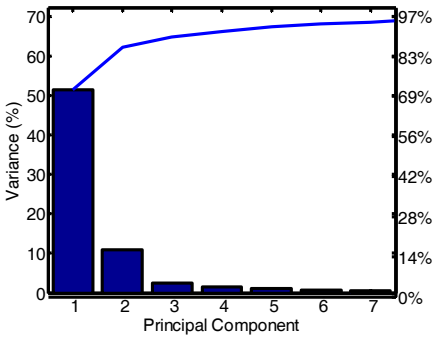

Fig 2. The variance of the time T1 DCE course explained by the principal components of the intensities.

Results – The classification was pixel-by-pixel. The reported results are calculated in leave-one-patient-out cross validation and averaged over 12 cases. The area under the receiver operating characteristics curve (AUC) was 0.87(0.02) with the first seven principal components of the T1 time course (Fig. 3). For comparison, we also used SVM on this data along with the most common the pharmacokinetic parameters- K_{trans}, v_e and v_p. The area under ROC curve with the pharmacokinetic parameters was found to be 0.81(0.07).

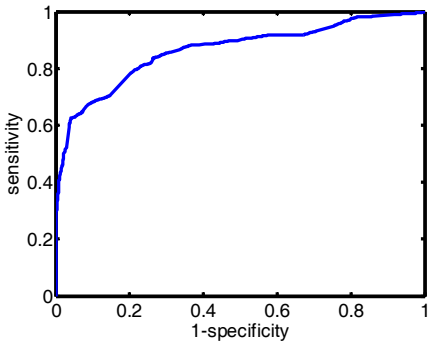

Fig 3. Receiver operating characteristic curve with the PCA of the DCE time course.

Conclusions and limitations – This study shows the potential of model-free analysis of DCE T1 time course for detection of peripheral prostate tissues. In the future we will validate this method on a large dataset (22 patients imaged so far). We will also apply this technique to classify the central zone tumors and evaluate other data-driven methods for feature extraction from the T1 DCE time course.

Acknowledgement: CIHR Operating Grant, NSERC Discovery. **References:**

[1] Barentsz JO, *et al.*, JMRI 1999;10(3):295–304. [2] Tofts PS, et al. *JMRI*, 1999, 10, 223-232; [3] Moradi, M., *et al.*, JMRI 2012; 35(6): 1403-1413. [4] Vapnik VN, *The Nature of Statistical Learning Theory,* Springer-Verlag, 1995.