Diffusion-Weighted MRI Based System for the Early Detection of Prostate Cancer

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Abstract—**Prostate cancer is the second most diagnosed cancer in men. In this paper, we propose a diffusion-weighted MRI based computer-aided detection system for the early detection of prostate cancer. The proposed system calculates seven apparent diffusion coefficients (ADC) for each subject based on the b values at which the scans are acquired. The 3D maps are then represented in a lower dimensional space using a data-driven approach. The reduced maps are fed into seven independent artificial neural networks, each corresponding to the** b **value at which the ADC maps are calculated. The final decision of malignancy is obtained by aggregating the outputs of all learners in a score-fusion scheme. Essentially, this pipeline is expected to reveal discriminative 3D patterns relevant to subject malignancy. Preliminary results show that the proposed system yields an accuracy of 100% in a leave-one-patient-out cross validation scheme, competing well with state of the art methods.**

***Index Terms*—diffusion weighted MRI, computer-aided detection, prostate cancer, artificial neural networks**

I. Introduction

Being the second most common cancer and the third cause of cancer death in the US [1], Prostate Cancer (CaP) has grabbed the attention of the research community to address new approaches of diagnosis and treatment. Obviously, early detection of the tumor is the key for an effective treatment.

Several tests are considered in the daily clinical routine to diagnose a patient with prostate cancer. Usually, a blood test is conducted to check the Prostate-specific antigen (PSA) level. An increased PSA level may be a symptom for prostate cancer. However, this increase is also related to other common health issues such as benign prostatic hyperplasia (BPH) and Prostatitis. Recently, the USPSTF recommended against PSA-based CaP screening to reduce the over-diagnosis and overtreatment associated by this screening tool [2].

After a positive PSA blood test, a Transrectal Ultrasound (TRUS) guided biopsy (GB) is carried on to further confirm the presence of prostate cancer. TRUS is an imaging technique that depends on measuring the echoes of initially sent ultrasound waves. It is used to guide a needle to take small samples of the prostatic tissue [3]. The samples are then analyzed and given a score called the Gleason Score (GS). Due to its 'blind' nature, TRUS-GB often leads to over-diagnosis and hence over-treatment [4], [5]. Also, significant tumors in the prostate may be missed by the biopsy for the same reason. Surprisingly, prostate cancer is still the only solid organ cancer that is diagnosed by randomized sampling biopsies [5]. In addition, the invasive nature of prostate biopsy is a key disadvantage for this diagnosis approach.

In the past few years, the use of magnetic resonance imaging (MRI) was proposed by the CaP research community as the most accurate noninvasive screening tool for prostate cancer diagnosis and staging [6]. Especially in the case of active surveillance, MRI can greatly assist doctors in disease monitoring and treatment management [7]. In this context, four MRI modalities are used for CaP detection. These are: T2 weighted (T2W), Dynamic Contrast Enhanced (DCE), Magnetic Resonance Spectroscopy (MRS) and diffusion-weighted (DW) MRI. The DW is an imaging modality at which the motion of water molecules is reflected in each voxel intensity value.

Recent studies have focused on computerized realization and interpretation of the prostate MRI to: (1) evaluate its effectiveness in localizing the tumor in the prostate and compare its performance to the radiologist's performance, (2) reduce the human error caused by analyzing a large number of volumetric images by the radiologist, (3) reduce the need of frequently taking unnecessary biopsies from patients, which has many side effects and does not usually provide an accurate evaluation of the tumor presence, and (4) reduce the time and effort required to read these images by a radiologist.

This paper proposes a computer-aided detection (CAD) system that can accurately distinguish between malignant and benign subjects using only DW MRI series. The system takes DW-MRIs that are acquired at seven different b values as an input and calculates the ADC-maps of each of them. This is followed by a data-driven approach that takes raw voxel intensity values and represent them in a space of lower dimension, this step is crucial to compensate for the inter- and intra-patient variability. Finally, the reduced features of each b value are used to train an artificial neural network. The output of the seven parallel networks is then fused in a voting

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function to produce the final decision. The remaining of the paper is organized as follows: section 2 discusses the related work, while section 3 describes data acquisition parameters. The proposed system and the methodology are presented in section 4. Section 5 reports and discusses the results. The paper terminates with concluding remarks in Section 6.

II. Literature Review

A recent review of parametric CAD systems shows very few DW-MRI based CAD system [4]. Instead, the common trend is to fuse multi-parametric MRI, including T2W, DCE and MRS in a CAD system to diagnose CaP. Even though multi-parametric fusion may provide extra information for the classification phase, the registration process of each modality usually yields some errors that may reduce the overall accuracy of the system. On the other hand, Litjens *et al.* [8] conducted an experiment that shows that a CAD system that uses features from DWI alone performs as good as another one which uses features from the combination of T2W, DCE and DW MRI. Although seems to have great potential in CaP diagnosis, DW images are not yet appropriately exploited for this application.

In [1], the authors proposed a fully automated CAD system that segments the prostate, calculates the Apparent Diffusion Coefficients (ADC) maps and then classifies the subjects into benign and malignant classes using the Cumulative Distribution Function (CDF) of the ADC-maps as a global feature. A stacked non-negativity constraint auto-encoder (SNCAE) is used in the classification stage. An accuracy of 92.3% on a leave-one-patient-out (LOPO) cross validation is obtained using their system.

In the same context, Firjani *et al.* [9] used an automated approach to segment the prostate. Nevertheless, boundaries of the suspected tumors were first delineated using a level-set based deformable model. Later, a k-nearest neighbor classifier was used to determine the malignancy of the tumor. The mean intensity values of the DW-MRI at b=0 sec/mm2, b=800 sec/mm2 and the ADC mean intensity value were found to be the most discriminant features.

Peng *et al.* [10] extracted several features from T2W and DW images. The aim of their study was to examine and compare the effectiveness of these features in distinguishing CaP tissues from normal tissues. ADC 10th percentile and ADC average which are obtained from DWIs were among the best discriminative features with area under the receiver operating characteristic curve of 0.95 and 0.94, respectively.

In this paper, we highlight two main contributions of our work: (1) A data-driven approach that is independent of the size of the prostate or the number of scans per patient, and (2) A fully automatic CAD system that shows outstanding performance in the detection of CaP at early stages. We also show that our system outperforms that of Reda et al. [1] in terms of accuracy.

III. Data

The DW-MR images of 22 patients (11 benign and 11 malignant cases) have been acquired in the axial plane with a body-coil Signa Horizon GE scanner using the magnetic field strength of 1.5 Tesla; TE of 84.6 ms; TR of 8s; bandwidth of 142.86 kHz; field of view of 34 cm; slice thickness of 3 mm with no inter-slice gap; conventional EPI acquisition sequence; mono-directional diffusion weighting, and range of b-value from 0 to 700 s/mm2.

On average, each patient's prostate was covered by 26 slices with the voxel size of 1.25×1.25×3.00 mm3 obtained in 120s. All cancers are biopsy-proved. We performed a systematic biopsy with 11 cores taken from the whole prostate. In some patients who cannot tolerate the 11 cores, only 6 cores were taken. The prostate area was manually segmented by an experienced radiologist. Tumor diameters and volumes for all the subjects were in the range of 0.92 – 4.3 cm (mean = 2. 3 ±0.91 cm) and 0.66 – 24.0 cm3 (9. 7 9.0 ± 3 cm), respectively.

IV. Methodology

Fig. 1 shows the pipeline of the proposed CAD system. First, DW MRI are acquired at seven different b values which are {100, 200, 300, 400, 500, 600, 700}. Note that the b value depends only on the gradient pulse intensity and duration.

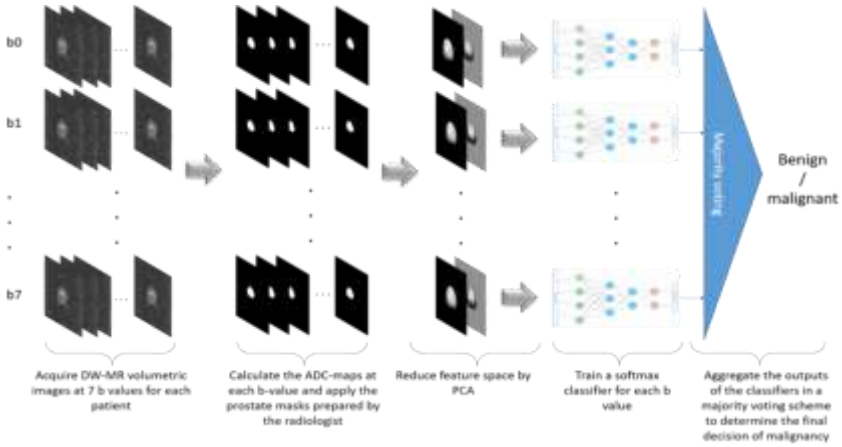

Figure 1. Proposed CAD system overview.

Fig. 2 shows a sample DW-MRIs for the same patient at different b values. Note the difference in the intensity level and the contrast of each b value which is crucial to extract information about the lesions.

Figure 2. Example of DW-MRI obtained at different b values (low to high).

The 3D ADC-map for each b value is calculated as follows:

$$ADC = \frac{\ln(\frac{S(b_1)}{S_0})}{b_1} \quad (1)$$

Where b0= 0 sec/mm^2 and b1∈ {100, 200, 300, 400, 500, 600, 700}, S(b1) and S0 are the measured signals at b1 and b0 respectively [4].

The output of this step yields seven 3D maps per patient, each of different size depending on the number of scans that were acquired to cover the whole prostate. The ADC maps are then reshaped into a vector form, where each vector represents a slice in the volume. Finally, the vectors are concatenated to form a matrix ($X_{r\times c}$, where r is the slice resolution and c is the number of slices) that represents the ADC values of the prostate volume for one patient.

Since the number of slices is different for each case, the lengths of the vectors in the matrix are inconsistent. To address the problem of varying data size, we define an orthogonal linear transformation that reduces the feature space of the current data. An n dimensional feature space for each volume is defined by the coordinate system of weights w where

$$w_{(k)} = arg\ \max\{\frac{w^T \hat{X}_k^T \hat{X}_k^T w}{w^T w}\} \quad (2)$$

Where k=1, 2, …, c and $\hat{X}_k$ is defined as follows:

$$\hat{X}_k = X - \sum_{l=1}^{k-1} X w_{(l)} w_{(l)}^T \quad (3)$$

To ensure a consistent matrix size for all the subjects, we choose k such that

$$1 < k < c \quad (4)$$

Finally, we reflect the original matrix X back into the new reduced coordinates as in the equation below:

$$T_k = X w_k \quad (5)$$

Where T is the representation of X in the lower dimensional space. For illustration, we set k=8, and perform the above calculations. We then reshape each column (component) of matrix T into a matrix of size (r×c). Fig. 3 shows the resulting slices.

Again, the reduced features are reshaped in a vector form and concatenated to form the feature vector. These vectors are considered as the global features at which seven identical neural networks with two hidden layers at each are trained (one for each b value). In our case, we empirically teat and set the hidden layer sizes to be 10 and 5, respectively. Note that the size of the input layer is 256×256×2. Finally, the output score S_i where i=1,2,…7 of all the seven classifiers are fused in the following score fusion scheme:

$$O(X) = \begin{cases} 1 & , \sum_i S_i \geq \frac{n_b}{2} \\ 0 & , \sum_i S_i < \frac{n_b}{2} \end{cases} \quad (6)$$

Where O(.) is the binary output decision of malignancy and n_b is the number of volumetric scans taken at different gradient pulse intensities.

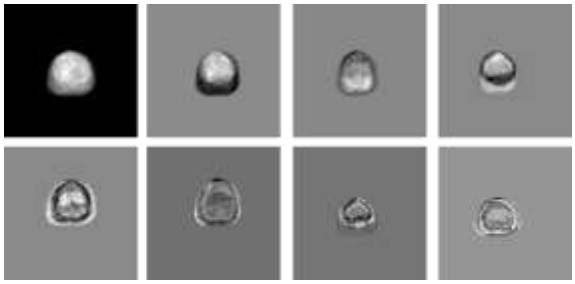

Figure 3. lices of one patient represented in a lower dimensional space. The top slices correspond to k=[1,4] from left to right, while the bottom slices correspond to k=[5,8].

For comparison purposes, the same vectors are used to train and test a support vector machine (SVM) classifier. Results using two different validation schemes are reported in the next section.

V. Results

A. Optimizing the Value of k

The maximum value of k that could be used in our application is equal to the minimum number of slices per patient in our dataset, which is 20. However, k was varied between 2 and 20 in order to determine the optimum number of components that maximizes the overall system accuracy. Figure 4 shows the results of this experiment on 11-folds cross validation scheme. Clearly, the overall accuracy tends to decrease when increasing the value of k (i.e. the number of features) at the input of the classifier. This could be justified by the overfitting caused by increasing the space dimensionality of the input vector.

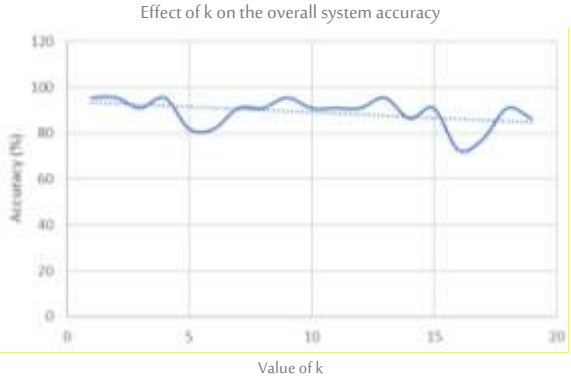

Figure 4. Overall system accuracy versus the number of principle components used at the input layer of the classifiers.

B. Comparing Different CAD Architectures

We compare the performance of our system with the performance of Reda *et al.* [1] which uses CDFs of ADC-maps at seven b values as global features to train an SNCAE. In addition, the system accuracy is compared to the same system when using the conventional SVM instead of the seven parallel artificial neural networks. Results at different cross-validation schemes are tabulated in Table I.

TABLE I. OVERALL ACCURACY OF THE PROPOSED SYSTEM AND TWO OTHER ALTERNATIVE SYSTEMS

Cross validation	CDF +SNCAE [1]	PCA+ SVM	PCA+ ANN (proposed)
LOPO	92.3%	100%	100%
11-folds	-	95%	95%
2-folds	-	50%	86%

VI. DISCUSSION

Results show that performing a data-driven approach on the ADC-maps outperforms the method of finding the CDF of the whole prostate. This can be explained by the fact that transforming the pixel intensities to a more representable coordinates preserves the original data structure much more than the CDFs where the whole prostatic volume is summarized in only 100 points [1]. In other words, our algorithm operates on the ADC values directly rather than extracting engineered features that may not fully represent each subject.

On the other hand, the adapted score fusion scheme of the seven classifiers outperforms the conventional SVM classifier in the 2-folds cross validation scheme. Although both classifiers yield an accuracy of 100% in the LOPO scheme, the learning process looks faster and more robust in our approach as it preserves a reasonably high accuracy even when trained with small number of subjects. In contrast, the accuracy of the SVM falls to 50% in the 2-folds cross validation scheme, which means that it becomes totally random.

VII. CONCLUSION

In this work, we proposed a method for the early detection of prostate cancer using DW-MR images, whereby the patient data is a group of DW-MRI scans obtained at seven different b values. Our original contribution is a novel approach for fusing the DW-MR scans that are acquired at seven different b values. Each b value scan instance is processed slice wise, to extract the ADC-maps which are aggregated then reduced using a dimension reduction scheme. The selected components derived from each b value are eventually fed into a dedicated and trained artificial neural network which acts as a classifier . The classifier outcomes are fused afterwards using a score-fusion scheme. The system achieves promising results in terms of accuracy in distinguishing between benign and malignant cases even with a small training data set. These accuracies of our mono-parametric system are comparable to multi-parametric CAD systems proposed in the literature. In addition, these accuracies indicate that the system could potentially be used in the daily clinical routine as a tool for the early detection of CaP.

VIII. LIMITATIONS AND FUTURE WORK

We acknowledge that our experiments have some limitations in terms of the dataset size and variability. We aim at validating our scheme on a larger dataset in the future.

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REFERENCES

[1] I. Reda, A. Shalaby, M. Elmogy, A. A. Elfotouh, F. Khalifa , M. A. El-Ghar, *et al.*, "A comprehensive non-invasive framework for diagnosing prostate cancer," *Computers in Biology and Medicine*, vol. 81, pp. 148-158, 2017.

[2] U.S. Preventive Services Task Force, "Screening for prostate cancer: U.S. preventive services task force recommendation statement," *Annals of Internal Medicine*, vol. 157, no. 2, pp. 120-134, 2012.

[3] American Cancer Society Inc., *Key Statistics for Prostate Cancer*, USA, 2017.

[4] G. Lemaitre, R. Marti, J. Freixenet, J. Vilanova, P. Walker, and F. Meriaudeau, "Computer-aided detection and diagnosis for prostate cancer based on mono and multi-parametric MRI: A review," *Computers in Biology and Medicine* , vol. 60, pp. 8-31, 2015.

[5] A. Rastinehad, B. Turkbey, S. Salami, O. Yaskiv, A. George, M. Fakhoury, *et al.*, "Improving detection of clinically significant prostate cancer: Magnetic resonance imaging/transrectal ultrasound fusion guided prostate biopsy," *The Journal of Urology*, vol. 191, pp. 1749-1754, 2014.

[6] B. Turkbey and P. Choyke, "Multiparametric MRI and prostate cancer diagnosis and risk stratification," *Current Opinion in Urology*, vol. 22, no. 4, pp. 310-315, 2012.

[7] D. Margolis, *Everything You Need to Know about Prostate MRI*," Los Angeles: Prostate Cancer Research Institute, 2015.

[8] G. Litjens, O. Debats, J. Barentsz, N. Karssemeijer, and H. Huisman, "Computer-aided detection of prostate cancer in MRI," *IEEE TRANSACTIONS ON MEDICAL IMAGING* , vol. 33, no. 5, pp. 1083-1092, 2014.

[9] A. Firjani, A. Elnakib, F. Khalifa, G. Gimel'farb, M. A. El-Ghar, A. Elmaghraby, *et al.*, "A diffusion-weighted imaging based diagnostic system for early detection of prostate cancer," *J. Biomedical Science and Engineering* , vol. 6, pp. 346-356, 2013.

[10] Y. Peng, T. Jiang, T. Antic, M. Giger, S. Eggener, and A. Oto, "A study of T2-weighted MR image texture features and diffusion-weighted MR image features for computer-aided diagnosis of prostate cancer," in *proceedings SPIE Meical Imaging*, Florida, 2013.

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