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A self-tuned graph-based framework for localization and grading prostate cancer lesions: An initial evaluation based on multiparametric magnetic resonance imaging

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ABSTRACT

Multiparametric magnetic resonance imaging (mpMRI) has been established as the state-of-the-art examination for the detection and localization of prostate cancer lesions. Prostate Imaging-Reporting and Data System (PI-RADS) has been established as a scheme to standardize the reporting of mpMRI findings. Although lesion delineation and PI-RADS ratings could be performed manually, human delineation and ratings are subjective and time-consuming. In this article, we developed and validated a self-tuned graph-based model for PI-RADS rating prediction. 34 features were obtained at the pixel level from T2-weighted (T2W), apparent diffusion coefficient (ADC) and dynamic contrast enhanced (DCE) images, from which PI-RADS scores were predicted. Two major innovations were involved in this self-tuned graph-based model. First, graph-based approaches are sensitive to the choice of the edge weight. The proposed model tuned the edge weights automatically based on the structure of the data, thereby obviating empirical edge weight selection. Second, the feature weights were tuned automatically to give heavier weights to features important for PI-RADS rating estimation. The proposed framework was evaluated for its lesion localization performance in mpMRI datasets of 12 patients. In the evaluation, the PI-RADS score distribution map generated by the algorithm and from the observers' ratings were binarized by thresholds of 3 and 4. The sensitivity, specificity and accuracy obtained in these two threshold settings ranged from 65 to 77%, 86 to 93% and 85 to 88% respectively, which are comparable to results obtained in previous studies in which non-clinical T2 maps were available. The proposed algorithm took 10s to estimate the PI-RADS score distribution in an axial image. The efficiency achievable suggests that this technique can be developed into a prostate MR analysis system suitable for clinical use after a thorough validation involving more patients.

1. Introduction

Prostate cancer is the most common non-skin cancer in the United States with an estimated of 220,800 new cases in 2015 [1]. In Hong Kong, prostate cancer was the third most common cancer in men and accounted for 11.3% of all new cancer cases [2]. Fortunately, more than 90% of all prostate cancers are diagnosed at the localized stage and five-year survival rate is almost 100% for men diagnosed with localized cancer [3]. Hence, it is important for men with elevated risk to be periodically screened. The first-line screening tests include Digital Rectal Examination (DRE) and serum Prostate Specific Antigen (PSA) tests. If the DRE or PSA result is suspicious for cancer, transrectal-ultrasound-guided (TRUS-guided) biopsy is performed. Since prostate cancer lesions are difficult to be seen in ultrasound, TRUS-guided biopsy is not a procedure that targets suspicious lesions but a systematic technique that samples prostate regions in which tumours occur most frequently [4]. As a result, TRUS-guided biopsy missed 20 – 35% of detectable lesion in the first biopsy [5–8]. To increase the cancer

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detection yield, repeated biopsies are required, leading to increased anxiety pain and morbidity for patients. Thus, sensitive image-based tools allowing for precise lesion localization are required in the development of targeted sampling strategies.

The widespread use of PSA screening since the early 90's has led to a higher detection rate of localized and less aggressive tumours [9]. The development of focal therapies, such as cryotherapy and high-intensity focused ultrasound, has provided options for localized tumours to be treated with a lower risk of morbidity. Delineation of tumours is required for the administration of these therapies in order to minimize damage to the surrounding healthy tissues and organs. In addition to tumour localization, risk assessment is also important to identify suitable candidates for focal therapies.

Multiparametric MRI (mpMRI) combines anatomic and functional imaging techniques and has been shown to have high sensitivity and specificity in cancer localization [10–12]. Consensus guidelines have been established for the use of mpMRI [13], which recommended the combination of T2-weighted (T2W) images with at least two functional MRI techniques, typically the dynamic contrast enhanced (DCE) and diffusion-weighted (DW) MRI. T2W MR imaging is the most widely used MR sequence for anatomy visualization. It has high tissue contrast and spatial resolution for visualization of zonal anatomy and tumours, which typically appears as homogeneous low-intensity regions in the peripheral and transition zones [13][Fig. 1 (a)]. However, the specificity of T2W imaging is limited since benign abnormalities, such as post-biopsy hemorrhage and prostatitis, may mimic cancer in T2W images [14]. DW imaging measures the Brownian motion of water molecules and can help localize cancer as the mean water path length is shortened by cell membranes of malignant lesions. The apparent diffusion coefficients (ADC) characterizing the amount of diffusion are calculated from multiple DW images, and are typically displayed as a parametric map with lesions appearing hypointense due to reduced water diffusion [Fig. 1(b)] [10,15,16]. The addition of DW imaging to T2W imaging significantly improves the sensitivity and specificity of cancer detection [13,15]. Prostate cancer tissue can also be characterized by DCE-MRI as the increased vascularity of cancer leads to early hyper-enhancement and rapid washout of the gadolinium contrast agent (Fig. 2) [17,18]. High temporal resolution DCE-MRI is typically performed to characterize the rate of uptake and washout of the contrast agent. When used alone, DCE-MRI does not have a high sensitivity in cancer detection [11]. However, the sensitivity of T2W imaging is shown to increase significantly when combined with DCE-MRI [11,19].

Although prior studies have been performed to investigate the use of mpMRI for prostate lesion detection and localization [10,11,15,19–24], most studies involved visual identification of lesions from 6 to 30 coarse regions in the prostate instead of pixel-accurate lesion delineation. The need for manual identification in these studies was time-consuming and added observer variability to the result. Since these studies defined prostate regions differently, there is a large variation in the results obtained across studies; for example, the sensitivity and specificity in lesion detection from T2W images ranged from 54 to 91% and 27–91% respectively [10,11,25]. Turkbey et al. [11] divided the prostate into 30 regions and compared two ways of quantifying sensitivity and specificity. In the first approach, known as the stringent approach, a lesion was deemed to be undetected if it is not detected in the exact region where the lesion was detected in the histological examination, even if it was detected in one of the neighbouring regions in mpMRI. In the second approach, known as the neighbouring approach, a lesion is deemed to be detected if it is detected in a neighbouring region. The sensitivity and specificity for lesion localization obtained in the neighbouring approach were much higher than in the stringent approach (sensitivity: 42% vs. 73%, specificity: 83% vs. 89% in T2W), suggesting that localization accuracy is sensitive to the detection criterion and the region size. To address these issues, pixel-wise binary cancer classification algorithms using mpMRI have been proposed [26–31], but these algorithms were not evaluated on mpMR images acquired according to the clinical consensus guidelines [13,32]. In particular, pixel-by-pixel T2 maps were available as inputs to the algorithms proposed in Refs. [26–31]. Although quantitative T2 maps are superior to T2W imaging in that it is not affected by variabilities in TR and the bias field inhomogeneity due to the use of endorectal coils, repeated T2W acquisitions are required at tens of echo times, thereby substantially lengthening the acquisition time. Considering that the acquisition protocol specified in the consensus guidelines already take 30–45 min, the further lengthening of the acquisition time cannot be afforded in clinical practice. Furthermore, although binary classifiers discussed above can provide information on the location and size of cancer foci, the knowledge of how likely these foci are clinically significant will further optimize diagnosis and treatment planning. It has been demonstrated that ADC is correlated with tumour aggressiveness [20], but this information could not be conveyed by the results generated by binary classifiers described above. The study reported in Ref. [31] is a notable study that estimated the pixel-based malignancy probability using a logistic regression model. Although the model provided a pixel-based malignancy probability in the continuous range from 0 to 1, it was trained using binary classified data [i.e., malignant and benign regions of interest (ROIs)] and the intermediate probabilities were obtained by mathematically model fitting. Without concrete examples of lesions associated with intermediate cancer risk to establish the clinical meaning of the fitted malignancy probabilities and to train the model, it is unclear how the likelihood generated by the model should be interpreted clinically. In addition, it is not possible to validate the malignancy likelihood against expert observations without

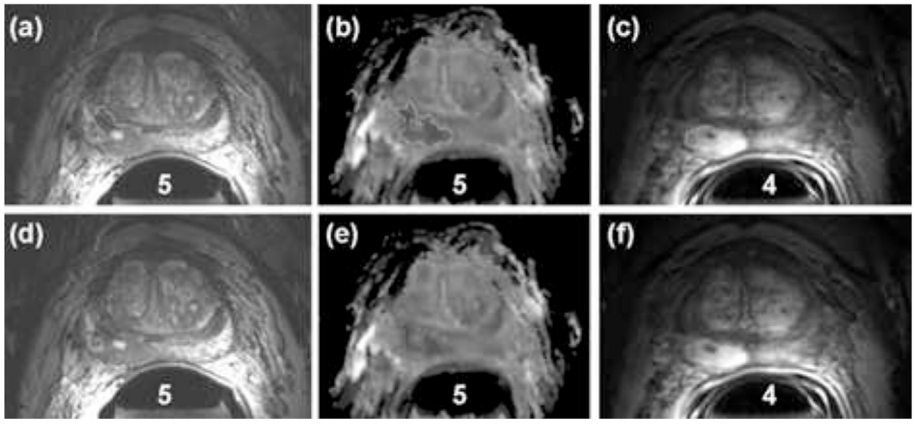

Fig. 1. Outlines of prostate lesions by two radiologists on T2W, ADC and DCE images. Each row shows the contour drawn by a radiologist. 7 DCE images were acquired sequentially (Fig. 2) and the one with the maximum enhancement is shown. The radiologists assigned a PI-RADS score to each lesion shown in the three sequences. The score is shown at the bottom of each image.