Prostate Cancer Detection in Patients with Intermediate Prostate Specific Antigen Level Using Combined Trace Apparent Diffusion Coefficient and Nodular Size: Comparison with Transrectal Core Biopsy

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Introduction

Prostate cancer (PCA) is the leading cancer in males with the first- or second-highest mortality rate in the developed countries. Conventionally, patients with palpable mass in digital rectal examination (DRE) or elevated prostate specific antigen (PSA) are admitted to receive transrectal ultrasound (TRUS)-guided needle biopsy. However, in patients presenting with intermediate level of PSA (4~20ng/ml), the positive rate of TRUS biopsy is relatively low (~17%). Selection of probable candidates among this group of patients for TRUS biopsy can potentially reduce the suffering and cost arising from the procedure. Recently diffusion weighted imaging (DWI) has shown its better sensitivity than conventional T2-weighted images in detecting prostate cancer by quantifying the apparent diffusion coefficient (ADC) (1). The purpose of this study, therefore, is to investigate the efficacy of diffusion MRI to select probable candidates among patients with intermediate PSA level. Specifically, we used two threshold criteria, one using average ADC only and the other using a combined threshold of average ADC and nodular size, to diagnose cancerous nodules and compared the results with the TRUS biopsies. The aim was to determine the most appropriate threshold that can yield the closest agreement with the TRUS biopsies.

Materials and Methods

Twenty four male patients (55-75 years; average, 64 years; median, 63 years) with intermediate PSA levels (mean: 9.7 ng/ml) were recruited in the study. For each patient diffusion tensor MRI (DTI) and subsequent TRUS biopsy were performed within two weeks. MR images were acquired on a 1.5T scanner (GE, Echo Speed, Milwaukee, WI, USA) with an endorectal coil. DTI was acquired using spin-echo echo planar imaging with multiple transaxial slices of the prostate from base to apex, TR/TE=17000/79ms; slice thickness=1mm; in-plane resolution=1mmx1mm; NEX=6; six diffusion-sensitive gradients at $\{\pm1,0,1\}$, $\{0,1,\pm1\}$,$\{\pm1,1,0\}$ with b=500 s mm^{-2}. Core specimens of TRUS biopsy were sampled systemically from 12 segments in the prostate gland, from right lateral, right medial, left medial to left lateral aspects at three levels at base, mid and apex. For image analysis, the peripheral zone was identified and categorized into twelve regions as those in the TRUS biopsy. Average ADC, or trace ADC (tADC), was determined by calculating the mean of the eigenvalues of the diffusion tensor at each pixel. According to our previous work, nodules with tADC values lower than 1.1 μm^2/ms were considered positive (2). The DTI results were compared segment by segment with pathological results obtained from the TRUS biopsies. The volumes the tADC-positive nodules were also calculated. With the TRUS biopsy results as a gold standard, all tADC-positive nodules were analyzed with Receiver Operating Characteristics (ROC) curve analysis. Best cut-points of nodular sizes were determined by the largest product of sensitivity and 1-specificity in the ROC curves. Diagnostic performance of DTI using tADC threshold only and DTI with a combined threshold of tADC and cut-point size were assessed and compared.

Results

Among 24 patients, a total of 288 segments were analyzed. There were 73 segments showing tADC values lower the threshold level of 1.1 μm^2/ms. Figure 1 shows the ROC curve analysis of nodular sizes at basal, middle, and apical levels. Based on the largest area under the curve, the best cut-point nodular sizes were 302 mm^3 at the basal, 84 mm^3 at the middle, and 66 mm^3 at the apical level. As listed in Table 2, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy for DTI using tADC criterion were 96%, 89%, 63%, 99%, and 90%, respectively. For DTI with the combined threshold of tADC and cut-point size, they were 92%, 97%, 88%, 99%, and 97%, respectively.

Discussions and Conclusions

As compared with TRUS biopsy results, DTI with tADC threshold shows a high NPV (99%). This indicates that this criterion can effectively exclude patients who would likely to have negative results in biopsy. On the other hand, the criterion with tADC threshold only shows a poor PPV (64%) and moderate specificity (89%) indicating that substantial amount of segments considered malignant by the tADC threshold are found to be benign in biopsy. The mismatch between tADC and biopsy may arise from two sources. First, the nodules are malignant but their sizes are too small to be hit by the needle biopsy. Second, other benign foci such as chronic inflammation, fibrosis or calcification may also present with low tADC values. By adding the cut-point sizes as another threshold, the combined threshold of tADC and nodular size showed much closer agreement with the biopsy results, with the improved PPV (90%) and specificity (98%). This implies that nodular size threshold can be used to further filter out tADC-positive segments that would likely to have negative results in TRUS biopsy. In conclusion, DTI with the combined threshold of tADC and nodular size have high agreement with TRUS biopsy results. A prospective study using this combined threshold is warranted to validate the value of DTI in pre-biopsy screening of patients with intermediate PSA level.

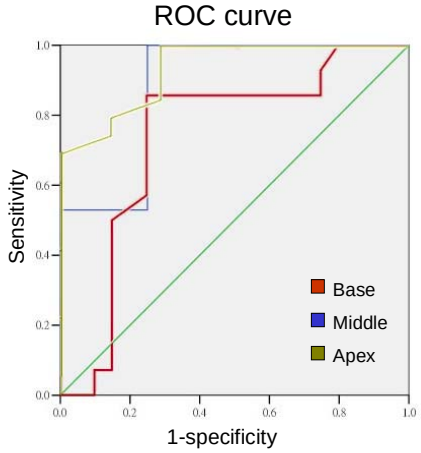

Fig 1. The ROC curves of DTI with thresholds at basal, middle, and apical levels.

	tADC only		Combined tADC and nodular size	
	Positive	Negative	Positive	Negative
Biopsy-True	47	2	45	4
Biopsy-False	26	213	5	234
Sensitivity	96(47/49)		92(45/49)	
Specificity	89(213/239)		98(234/239)	
Positive predictive value	64(47/73)		90(45/50)	
Negative predictive value	99(213/215)		99(234/238)	
Accuracy	90(260/288)		97(279/288)	

Table1 The comparisons between DTI judgments and pathologies. Left column showed the DTI method without thresholds of nodule sizes, and the right column showed the DTI method with thresholds with totally 24 patients separated into 288 segments.

References

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