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Original contribution

Slow component apparent diffusion coefficient for prostate cancer: Comparison and correlation with pharmacokinetic evaluation from dynamic contrast-enhanced MR imaging

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ABSTRACT

Purpose: Dynamic contrast enhancement (DCE)-MRI has high diagnostic performance of prostate cancer. However, it is preferable to avoid the use of MRI contrast media. A study reported that the diagnosability of the wash-in index of DCE-MRI was equivalent to the intravoxel incoherent motion of the diffusion weighted image.

The purpose of this study was to examine the correlation between the slow component apparent diffusion coefficient (ADC) and the wash-out index of the DCE.

Materials and methods: Thirty-eight patients diagnosed with prostate cancer by biopsy were enrolled in this study. The fast and slow component ADCs of the DWI were calculated for 76 points of the tumor and the contralateral normal parts. Furthermore, the wash-in and wash-out indices of the DCE-MRI were calculated. The correlations for each calculated index were compared.

Results: There was a significant difference between the tumor and the contralateral normal parts for both fast ($p = 0.03$) and slow component ($p < 0.01$) ADCs. In addition, the slow component ADC was correlated with the wash-out index ($r = 0.64$).

Conclusion: The slow component ADC was correlated with the wash-out index, and may, therefore, be a suitable substitute for DCE-MRI.

1. Introduction

The morbidity rate associated with prostate cancer was found to be 15% in an age-specific investigation of the world population [1]. Further, prostate cancer was the fourth most common cancer in both sexes combined and the second most common cancer in men in 2012 [1]. The Gleason score procured by cellular biopsy is the most highly-detailed for the diagnosis of prostate cancer, but diagnosis with magnetic resonance imaging (MRI) has increased due to invasiveness and positioning limitations of biopsy.

It has been reported that dynamic contrast-enhanced (DCE)-MRI using contrast media has high diagnosability [2–7]. However, in recent years, it has been reported that the use of gadolinium contrast in MRI may result in serious adverse drug reactions (ADRs) including induction of renal dysfunction, asthmatic attacks, and nephrogenic systemic fibrosis [8–12]. Moreover, even a healthy person may experience an allergic reaction, which could result in anaphylactic shock. Therefore, in the Prostate Imaging – Reporting and Data System, it is noted that DCE-MRI is not an essential examination [13]. Therefore, for both safety and economic considerations, use of contrast media should be refrained from, if possible.

In addition, the improvement of image quality in diffusion weighted imaging (DWI) has provided more diagnostic information [14–16]. A study reported that intravoxel incoherent motion (IVIM) using low b values of diffusion weighted images was a suitable substitute for the perfusion index of DCE-MRI. However, this report indicated that only

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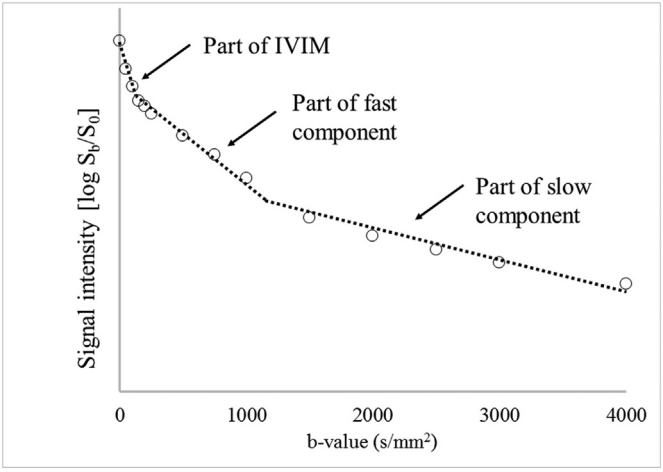

Fig. 1. The triexponential diffusion decay in the restricted diffusion of the human body. Diffusion decay recurs in three exponentials, as incoherent intravoxel movement, fast component, and slow component.

the wash-in, and not the wash-out, index of the DCE-MRI was obtained with IVIM [17].

The diffusion coefficient of the human body attenuates tri-exponentially by restricted diffusion. (Fig. 1) These diffusion coefficients are influenced by the size of the cell structure. Here, a high DWI b value is equivalent to a slightly large cell structure. This diffusion coefficient is shown as a slow component apparent diffusion coefficient (ADC). Therefore, we hypothesized that the wash-out index of the DCE-MRI was obtained using the ADC of the slow component with high b value. Verification of our hypothesis would indicate that the risky contrast enhancement examination would become needless by the measurement of both the IVIM and slow component ADC.

The purpose of this study was to examine the correlation between the wash-out index of DCE-MRI and the slow component ADC of DWI.

2. Materials and methods

2.1. Subjects and scanning parameters

Ethical review board approval was secured for this study, and informed consent was obtained from all patients. Thirty-eight patients (age range 52–87) diagnosed with prostate cancer by biopsy that underwent DWI and DCE-MRI in four institutions were included in this study.

The MRI devices used at each institution were Philips 3.0 T, 1.5 T, (Philips, Best, The Netherlands), Siemens 3 T, 1.5 T (Siemens Healthcare, Erlangen, Germany), Toshiba 3 T (Toshiba medical Systems, Tochigi, Japan) with phased array coils. The b values of the diffusion weighted image were 0, 1000, and 2000 s/mm^2. The acquisition timings of DCE-MRI after contrast administration were 30, 60, 90, 120, and 150 s. Three-dimensional imaging was used for T1 weighted image acquisition with fat suppression.

2.2. Analysis of data

Regions of interest (ROIs) were set in a tumor region and the contralateral normal region on the DW image of patients diagnosed with prostate cancer, and those signal intensities were measured for b values = 0, 1000, and 2000 s/mm^2. (Fig. 2) Similarly, the signal intensity of ROIs was measured in the images at each phase (0, 30, 60, 90, and 120 ms) in DCE-MRI. The ADC values were calculated from b values between 0 and 1000 s/mm^2 (fast component ADC) and b values between 1000 and 2000 s/mm^2 (slow component ADC) of the diffusion weighted images. Furthermore, the value of the divided difference of

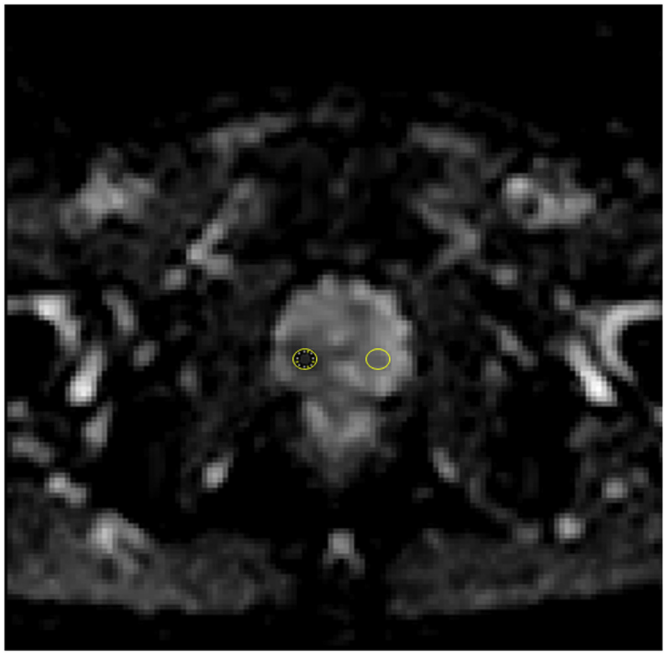

Fig. 2. The apparent diffusion coefficient map image of the prostate. Regions of interest were set in tumor and contralateral normal regions.

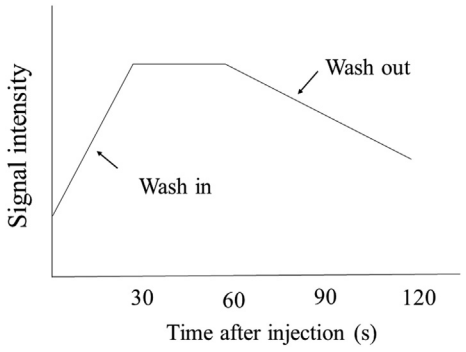

Fig. 3. Schema of time intensity curve of dynamic contrast enhancement. In this study, we defined 0–30 s as wash-in and 60–120 s as wash-out.

the signal intensity of 0 and 30 s by the time lag in DCE-MRI was defined as the wash-in index, and the difference value of the signal intensity between 60 and 120 s by the time lag was defined as the wash-out index. (Fig. 3) The calculation formulas of each index are the following.

$$\text{Fast component ADC} = (\log(SI_{b0} - SI_{b1000}))/1000 \quad (1)$$

$$\text{Slow component ADC} = (\log(SI_{b1000} - SI_{b2000}))/1000 \quad (2)$$

$$\text{Wash} - \text{in index} = ((SI_{30s} - SI_{0s})/SI_{0s})/30 \times 100 \quad (3)$$

$$\text{Wash} - \text{out index} = ((SI_{120s} - SI_{60s})/SI_{60s})/60 \times 100 \quad (4)$$

where, SI_{b1000} = signal intensity of DWI of b value 1000, and SI_{30s} = signal intensity of the DCE image of 30 s after injection.

2.3. Comparison of the wash-in and wash-out indices and the ADCs of prostate cancer

A total of 72 data points, which included 36 tumor and 36 normal regions, were used in this analysis. The StatMate (GraphPad Software Inc., San Diego, CA) software package was used for all statistical analyses.

The wash-in and wash-out indices of DCE-MRI were compared for

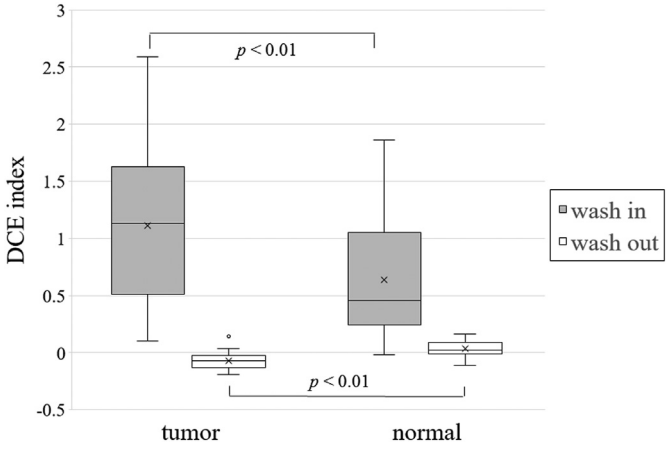

Fig. 4. Box-and-whiskers plot of the comparison between the prostate tumor and the normal part in the wash-in and the wash-out indices. For the wash-in index, the tumor region showed significantly higher values than the normal region ($P < 0.01$). For the wash-out index, the tumor region showed significantly lower values than the normal region ($P < 0.01$).

each tumor region and its contralateral normal region. The presence of significant differences was examined with Mann-Whitney U statistical analysis between the tumor and normal regions for each wash-in and wash-out index. Similarly, comparisons were performed between fast and slow component ADCs.

In addition, the correlations among fast and slow component ADCs and wash-in and wash-out indices were examined.

3. Results

Regarding the wash-in and wash-out indices of DCE-MRI in the tumor regions and the contralateral normal regions of the prostate, the wash-in index showed significantly higher value and the wash-out index showed significantly lower value in tumor regions ($p < 0.01$, Fig. 4). Regarding the ADC, the fast and the slow component ADCs both showed significantly lower values in tumor regions ($p = 0.03$, Fig. 5).

There was no correlation between the wash-in index and the slow component ADC, but there was ($r = 0.549$) between the wash-in index and the fast component ADC (Fig. 6). Moreover, there was a significant correlation ($r = 0.353$) between the wash-out index and the fast component ADC, but a stronger correlation ($r = 0.640$) was found between the wash-out index and the slow component ADC (Fig. 7).

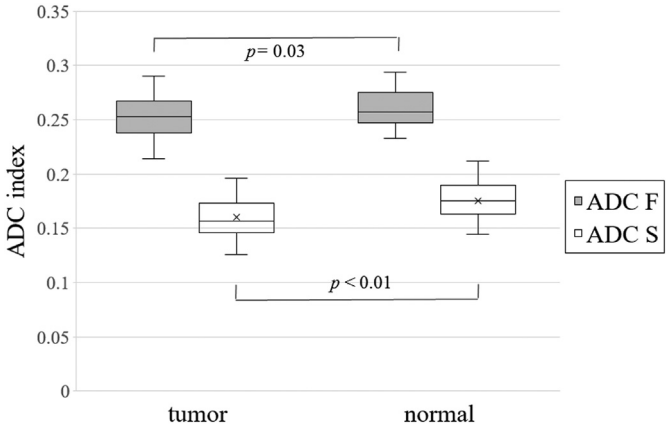

Fig. 5. Box-and-whiskers plot of the comparison between the prostate tumor and the normal part in the fast and the slow component ADCs. Regarding the fast and slow component ADCs, both showed significantly lower values in the tumor regions than in the normal regions ($P = 0.03$ and $P < 0.01$, respectively).

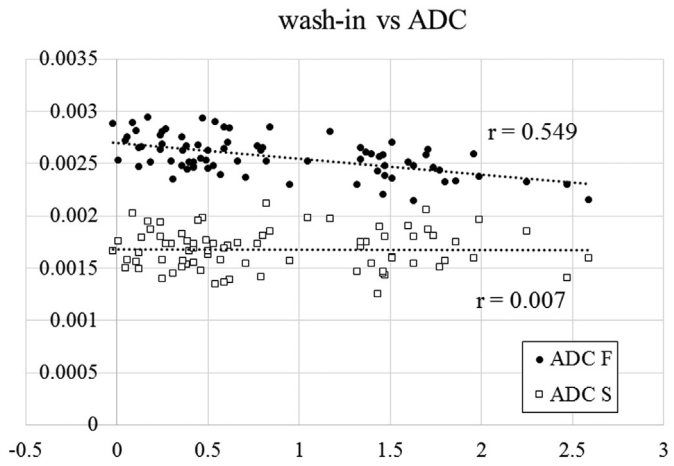

Fig. 6. Correlation between the wash-in index and the ADC. The correlation coefficient between the wash-in index and the fast component ADC was 0.549, while with the slow component ADC, it was 0.007.

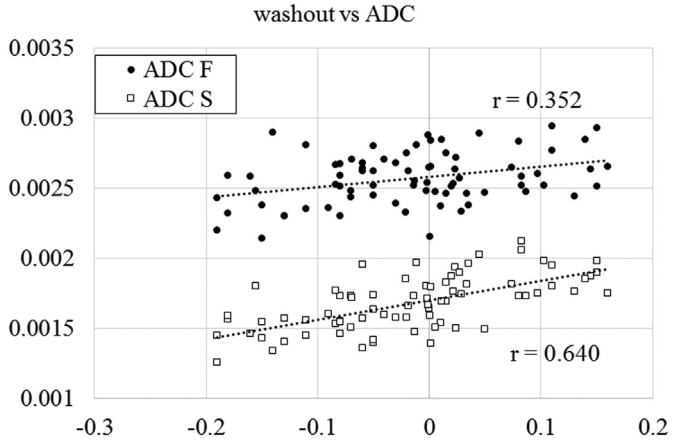

Fig. 7. Correlation between the wash-out index and the ADC. The correlation coefficient between the wash-out index and the fast component ADC was 0.352, while with the slow component ADC, it was 0.640.

4. Discussion

This study was based on the hypothesis that a diffusion weighted image could be used as a suitable substitute for DCE-MRI in prostate cancer. The slow component ADC is thought to be influenced by the restricted diffusion of more major cell structures compared to the fast component ADC. While the mechanism involved in the presence of wash-out on the malignant tumor in DCE-MRI is not clear, it is predicted based on the reasoning that vascular density is high and vessel walls are leaky, that tumor vessels have uneven diameters, and there is no retentivity of the blood of the tumor tissue [3,18–22]. These vasculatures form a relatively major cell structure, and restricted diffusion is thought to be closely associated with the slow component.

We believe that our results supported our hypothesis, as we found a relatively strong correlation between the wash-out index and the slow component ADC, whereas, in a different study, a strong correlation between the wash-in index and IVIM was reported. From these two results, we propose that diagnostic information equally valuable as that from DCE-MRI may be obtained by acquiring b values of 0–500 s/mm^2 for the IVIM part and 1000–2000 s/mm^2 for the slow component DWI part.

As limitation of this study, we calculated wash-in and wash-out with three points of the DCE in simply. However, there is the time when wash-out is mixed with wash-in in tumor ROI. About this timing, it is an

examination problem.

5. Conclusions

With regard to prostate cancer diagnosis, we found that information equivalent to that from DCE-MRI may be obtained with measurement of IVIM and slow component ADC in DWI. This may provide safety and financial benefits for patients.

However, we should note as limitations of this study, the sample size, which may have been insufficient, and the necessity to examine the association with the Gleason score in the future.

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