Objective prostate cancer detection: discriminant analysis combined the apparent diffusion coefficient map with diffusion-weighted MR imaging

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Purpose

Conventional MR imaging has been used to plan treatment and stage prostate cancer confirmed by biopsy [1, 2]. However, the diagnosis rate from biopsy specimens remains at 50% [3] and the risk of complications persists. The performance of MR imaging devices has improved, and targeting biopsies using this modality [4] has become useful. Thus, the importance of localized diagnosis using MR imaging has increased. Many studies have shown that prostate cancer, compared with non-cancerous regions, usually appears as regions of low signal intensity on T2-weighted (T2W) images and appears as regions of high signal intensity on diffusion-weighted (DW) images. Recent reports have described the usefulness of apparent diffusion coefficient (ADC) (×10⁻³ mm²/S) maps based on DW imaging for detecting prostate cancer as the ADC values of prostate cancer regions are significantly lower than those of normal prostate tissues [5-9, 11, 13, 15-17]. However, to distinguish cancer from non-cancer regions based only on ADC maps is difficult, because ADC values considerably overlap. Image interpretation using combined parameters such as T2W images and ADC maps have improved diagnostic power [6,12]. In addition, since subjective evaluation of signal changes in cancer lesions depend on the image display conditions and the experience of image interpreters [6,12], we applied discriminant analysis using the pixel value of DW images, ADC maps and T2W images to provide a more objective assessment.

The present study determines which parameters or combination of parameters is optimal for distinguishing prostate cancer from normal prostate tissue by comparing MR images of a histologically defined specimen and obtaining a discriminant function.
Methods and Materials

This retrospective study was approved by the ethics review board of our institution, and the requirement for informed consent was waived.

Patients

We analyzed data from patients with suspected cancer and high PSA levels who were examined by MRI and underwent preoperative systematic biopsies between May 2008 and November 2011.

Twenty-three patients with prostate cancer confirmed by biopsy underwent radical prostatectomy. Data from eight patients were excluded due to incomplete MR imaging or pathological data. Therefore, data from 15 patients aged a mean of 67 (range, 56-74) years were analyzed in this study. Seven patients from whom a biopsy was obtained a mean of 23 (range, 14-30) days before MR imaging were included. The mean interval between MRI and radical prostatectomy was 73 (range, 37-171) days. None of the patients had a history of pelvic radiation or thermal therapy applied to the prostate or a history of chemotherapy. Table 1 shows the clinical details.
Table 1. Clinical information.

<table>
<thead>
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<tbody>
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<td>Total number of patients</td>
<td>15</td>
</tr>
<tr>
<td>Mean age (range) (y)</td>
<td>67 (56—74)</td>
</tr>
<tr>
<td>PSA</td>
<td>4.47—43.29 ng/ml, mean 12.08 ng/ml</td>
</tr>
<tr>
<td>Number of patients with hemorrhage</td>
<td>7</td>
</tr>
<tr>
<td>Interval from biopsy to MRI</td>
<td>14—30 days, mean 23.8 days</td>
</tr>
<tr>
<td>Gleason score</td>
<td></td>
</tr>
<tr>
<td>3+2</td>
<td>2</td>
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<tr>
<td>PT3b</td>
<td>3</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
</tr>
</tbody>
</table>

**Table 1**

**References:** Department of Radiology, Tottori prefectural central hospital

**Imaging protocol**

Axial fast spin-echo T2W and axial DW images were acquired. All examinations proceeded using a 1.5-T MRI system (Excite HD; GE Healthcare, Little Chalfont, UK) and an 8-channel phased-array surface coil. Imaging parameters for the T2W images were TR/TE, 3,400/85; echo-train length, 20; field of view, 24 cm; slice thickness, 3 mm; gap, 1 mm; no phase wrap; phase-encoding direction, left to right; matrix, 224 × 288. An axial echo-planar DWI pulse sequence (b value = 0 and 1,500 s/mm²) with the same slice locations as the T2 sequence then proceeded using the following parameters: TR/TE, 5,000#8,000/85; field of view, 36 cm; slice thickness, 3.5 mm; gap, 0.5 mm; matrix, 128 × 128. All images were acquired within 2 min and 30 s.

**Histological evaluation of surgical specimen**
All radical prostectomy specimens were fixed in 10% formalin, cut into 10-mm transverse contiguous slices, processed, embedded in paraffin and stained with hematoxylin and eosin. When prostate cancer was histologically diagnosed, location, size and type of cancer were also reported. A histological map of the prostate cancer was then created by circling each section on photocopies of the specimens.

**MR image analysis**

Each prostate was divided into base, mid-gland and apical regions. The base was determined as the region extending from the cranial margin of the prostate to its widest transverse diameter. The mid-gland was defined as the region between the widest transverse diameter and the orifices of the ejaculatory ducts at the verumontanum. The apex was defined as the region inferior to the mid-gland.

Thus, three MRI sections and histological slices were matched using the urethra as a landmark in the longitudinal orientation and the shape of the inner gland (IG) and peripheral zone (PZ) for corresponding cross-sectional orientation. Histological maps and T2W images were retrospectively correlated section by section.

Anatomical ROIs identified on the DW images and ADC maps were compared with those of T2W-fast spin echo (FSE) images. We manually defined ROIs on cancer regions and changed the size of each ROI considering the size of the cancer lesion. Cancer lesions #8 mm in diameter were included in the evaluation because those <8 mm in diameter were undetectable on MR images. Non-cancer ROIs were randomly placed on the PZ and IG. Each ROI comprised a circle with an area of 45-205 mm$^2$. **Figures 1 and 2** show examples of ROI placement.
Fig. 1: Non-cancer regions of interest (ROIs). Purple ROIs are randomly placed on peripheral zone (PZ) and inner gland (IG). Blue ROI (blue circle) is placed on the left obturator internus muscle.

References: Department of Radiology, Tottori prefectural central hospital
**Fig. 2**: Cancer regions of interest (ROIs). A. Cancer regions (red outlines) are shown on fresh slice of macroscopic specimen. B-D. Cancer regions of interests (red circles) are placed on T2-weighted image (B), diffusion-weighted image (C) and ADC map (D).

**References**: Department of Radiology, Tottori prefectural central hospital

Fusion images, ADC maps and the mean pixel value of each ROI were generated using Functool software (GE Healthcare) and ADC values were calculated as:

$$\text{ADC} = \frac{1}{b} \ln\left(\frac{S}{S_0}\right)$$  \hspace{1cm} (1),

where $S_0$ and $S$ are signal intensities on diffusion-weighted images at $b = 0$ and 1,500 sec/mm$^2$, respectively.

Normalized T2 signal intensity (SI)-to-muscle ratios ($n$-T2) and normalized diffusion SI-to- muscle ratios ($n$-Diffusion $b = 1,500$, $n$-Diffusion $b = 0$) were then calculated for all
ROIs. The ROI of the left obturator internus muscle was obtained using a 2-cm\(^2\) circular ROI [19].

The mean ADC values were evaluated by measuring ROIs on ADC maps.

High signal areas on ROIs in T1W images were considered to indicate hemorrhage.

**Statistical analysis**

The mean and standard deviation of the ADC values, n-Diffusion (b = 1,500), n-Diffusion (b = 0) and n-T2 were calculated for cancer and non-cancer regions and then differences in these values were evaluated using Welch's t test. A value of p < 0.01 was considered to indicate statistical significance.

Each of ADC, n-Diffusion (b=1,500), n-Diffusion (b=0) and n-T2 was assessed from the areas under the receiver operating characteristic (ROC) curves (Az) using ROCKIT software version 0.9.1-Beta (CE Metz, University of Chicago, Chicago, IL, USA) [18]. These parameters were also combined and assessed by Az.

The optimal combination of parameters was iteratively determined by plotting values on two-variable scattergrams. The best line to maximize Az was drawn using linear discriminant analysis to separate cancer from non-cancer regions. The y-intercept of the line with this slope was determined to achieve at least 90% sensitivity while varying.

The mean and standard deviation of the ADC values, n-Diffusion (b = 1,500) and n-Diffusion (b = 0) of ROIs with hemorrhage that appears as areas of high signal intensity on T1W images, were calculated for cancer and non-cancer regions. Individual parameters were also statistically compared among all cancer and non-cancer regions with and without hemorrhage.
**Fig. 1:** Non-cancer regions of interest (ROIs). Purple ROIs are randomly placed on peripheral zone (PZ) and inner gland (IG). Blue ROI (blue circle) is placed on the left obturator internus muscle.

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Results

Histopathological assessment detected cancer lesions in 50 (18%) of 277 ROIs with all regions. Seventeen (34%) of 50 ROIs were detected in IG and 33 (66%) of 50 ROIs were detected in PZ.

Table 2 and Figure 3 summarize the ADC values, n-Diffusion (b = 1,500), n-Diffusion (b = 0) and the n-T2 of cancer (n = 50) and non-cancer (n = 227) ROIs.

Table 2. ADC value, n-Diffusion (b = 1,500 and b = 0) and n-T2 of cancer and non-cancer regions.

<table>
<thead>
<tr>
<th></th>
<th>Cancer</th>
<th>Non-cancer</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ± SD</td>
<td>Range</td>
</tr>
<tr>
<td>ADC ($\times 10^{-3}$ mm$^2$/s)</td>
<td>0.42—0.97</td>
<td>0.74±0.13</td>
<td>0.52—1.55</td>
</tr>
<tr>
<td>n-Diffusion (b = 1,500)</td>
<td>1.18—2.5</td>
<td>1.62±0.33</td>
<td>1.02—0.97</td>
</tr>
<tr>
<td>n-Diffusion (b = 0)</td>
<td>2.54—6.23</td>
<td>3.46±0.79</td>
<td>1.71—9.87</td>
</tr>
<tr>
<td>n-T2</td>
<td>2.04—3.56</td>
<td>2.60±0.34</td>
<td>1.78—5.35</td>
</tr>
</tbody>
</table>

*Comparison of cancer and non-cancer regions, ADC, apparent diffusion coefficient ($\times 10^{-3}$ mm$^2$/S); n-Diffusion (b = 1,500), normalized diffusion (b=1,500) of signal intensity (SI) of tissue/SI obturator muscle; n-Diffusion (b = 0): normalized diffusion(b=0) signal intensity (SI) of tissue/SI obturator muscle; n-T2: normalized T2 signal intensity (SI) of tissue/SI obturator muscle.

Table 2

References: Department of Radiology, Tottori prefectural central hospital
Fig. 3: Scatter plots of relationships between ADC values, n-Diffusion (b = 1500), n-Diffusion (b = 0) and n-T2 with cancer and non-cancer regions. All are statistically significant (p

References: Department of Radiology, Tottori prefectural central hospital

All these parameters significantly differed between cancer and non-cancer regions (P < 0.0001).

The diagnostic power of single parameters showing high Az were in the order of n-Diffusion (b = 1,500): Az, 0.87 (95% confidence interval [CI] 0.81, 0.92); ADC: Az, 0.82 (95% CI, 0.77, 0.88); n-T2: Az, 0.73 [95% CI, 0.66, 0.78] and n-Diffusion (b = 0): Az, 0.61 (95% CI, 0.52,0.68).

The combination of ADC and n-Diffusion (b = 1,500) had the highest Az of 0.97 [95% CI, 0.95,0.98] among all single parameters and any combination of parameters (P < 0.0001).

Table 3 and Figure 4 show the results of the ROC curve analysis with sensitivities and specificities for cancer detection.
Table 3. Area under receiver operating characteristics curves (Az) and sensitivity and specificity of parameters studied alone and in combination.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Az [95%CI]</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC</td>
<td>0.82 [0.77, 0.88]</td>
<td>75.0%</td>
<td>76.3%</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>n-Diffusion (b = 1,500)</td>
<td>0.87 [0.81, 0.92]</td>
<td>80.0%</td>
<td>79.1%</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>n-Diffusion (b = 0)</td>
<td>0.61 [0.52, 0.68]</td>
<td>60.0%</td>
<td>56.0%</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>nT2</td>
<td>0.73 [0.66, 0.78]</td>
<td>70.0%</td>
<td>65.0%</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>ADC + n-Diffusion (b = 1,500)</td>
<td>0.97 [0.95, 0.98]</td>
<td>94.0%</td>
<td>91.2%</td>
<td>—</td>
</tr>
</tbody>
</table>

CI, confidence intervals. *Difference between single parameter alone and combination of ADC and n-Diffusion (b=1500). Sensitivity and specificity in cancer detection are significantly higher for combination of ADC and n-Diffusion (b=1500).

Table 3

References: Department of Radiology, Tottori prefectural central hospital

Fig. 4: Receiver operating characteristics (ROC) curves. Area under ROC curve (Az) show diagnostic power of n-Diffusion (b=1,500) (blue line, Az = 0.87), ADC (brown line, Az = 0.82), n-T2 (purple line, Az = 0.73), n-Diffusion(b=0) (green line, Az = 0.61). The
combination of ADC and n-Diffusion (b=1,500) had the highest Az, 0.97 [0.95,0.98], compared to any single parameter (P

References: Department of Radiology, Tottori prefectural central hospital

The line that optimally discriminated cancer from non-cancer regions in two variable scatter diagrams combining ADC with n-Diffusion (b = 1,500), was ADC = 1.23 × n-Diffusion (b = 1,500)#0.00075 (Fig. 5).

Fig. 5: Scatter plots of ADC versus n-Diffusion (b=1,500) in cancer (solid red squares) and non-cancer (open blue squares) regions. Line that best discriminated cancer from non-cancer regions is ADC = 1.23 × n-Diffusion(b = 1,500) #0.00075.

References: Department of Radiology, Tottori prefectural central hospital

All hemorrhagic regions due to systematic prostate biopsies were detected in PZ regions. Only one of 50 cancer and 49 of 227 non-cancer ROIs were accompanied by hemorrhage. The ADC values, n-Diffusion (b = 1,500) and n-Diffusion (b = 0) significantly differed among all cancer and non-cancer regions with and without hemorrhage (Tables 4 and 5).
### Table 4. Comparison between cancer and non-cancer regions with and without hemorrhage.

<table>
<thead>
<tr>
<th></th>
<th>Number of foci</th>
<th>ADC (×10³ mm²/s)</th>
<th>n-Diffusion (b=1,500)</th>
<th>n-Diffusion (b=0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer with hemorrhage</td>
<td>1/50</td>
<td>0.914</td>
<td>1.53</td>
<td>3.85</td>
</tr>
<tr>
<td>Cancer with no hemorrhage</td>
<td>49/50</td>
<td>0.74±0.13</td>
<td>1.62±0.33</td>
<td>3.46±0.79</td>
</tr>
<tr>
<td>Benign PZ with hemorrhage</td>
<td>49/227</td>
<td>1.17±0.25</td>
<td>1.35±0.17</td>
<td>5.09±2.31</td>
</tr>
<tr>
<td>Benign PZ with no hemorrhage</td>
<td>178/227</td>
<td>0.94±0.18</td>
<td>1.21±0.14</td>
<td>3.66±0.89</td>
</tr>
</tbody>
</table>

Data are shown as means ± standard deviation.

### Table 4

**References:** Department of Radiology, Tottori prefectural central hospital

### Table 5. Statistical comparison of individual parameters between tissues with and without hemorrhage.

<table>
<thead>
<tr>
<th>Tissues</th>
<th>ADC</th>
<th>n-Diffusion (b=0)</th>
<th>n-Diffusion (b = 1,500)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td></td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Cancer</td>
<td></td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Benign without hemorrhage</td>
<td></td>
<td>P&lt;0.001</td>
<td>P=0.001</td>
</tr>
</tbody>
</table>

**Table 5**

**References:** Department of Radiology, Tottori prefectural central hospital

**Figures 6, 7, 8 and 9** show representative clinical images.
Fig. 6: MR Images of 74-year-old man with prostate cancer. Prostate-specific antigen, 6.7 ng/mL. Two ROIs (1 and 2) circled in red are placed on histologically diagnosed cancer lesion in IG (Gleason grade 4+3). ROI (3) is placed on histologically diagnosed cancer lesion in IG (Gleason grade 3+2) on each image. A. T2-weighted image shows unclear signal changes in all ROIs. B. Diffusion-weighted MR image (b=1,500) shows faintly high signal change in ROIs (1 and 2) and obvious high signal change in ROI (3) in left lobe. Measured n-diffusion values of the ROIs are shown. C. ADC map shows low signal change in all ROIs (1, 2 and 3). Measured ADC values of the ROIs are shown. D. Values of ROIs (1, 2 and 3) are plotted as red squares (histologically diagnosed cancer regions are shown in red) on same scatter diagram as Fig. 4. Area above line indicates non-cancer and that below line indicates cancer. All red squares are located in cancer area, therefore all ROIs are correctly distinguished as cancer on diagram.

References: Department of Radiology, Tottori prefectural central hospital
Fig. 7: MR Images of 68-year-old man with prostate cancer (Gleason grade, 4 + 3). Prostate-specific antigen, 9.89 ng/mL. ROI circled in blue is placed on nodular lesion (histologically diagnosed as a hyperplastic nodule) in IG of left lobe on each image. A. T2-weighted image shows unclear signal change in ROI. B. Diffusion-weighted MR image (b=1,500) shows obvious high signal change in ROI. Measured n-diffusion value of the ROI is shown. C. ADC map shows low signal change in ROI. Measured ADC value of ROI is shown. D. Value of ROI is plotted as blue square (histologically diagnosed non-cancer region is shown in blue) on same scatter diagram as Fig. 4. Area above line indicates non-cancer and that below indicates cancer area on diagram. Blue square is located in cancer area, therefore ROI is incorrectly distinguished as cancer on diagram.

References: Department of Radiology, Tottori prefectural central hospital
**Fig. 8**: MR Images of 74-year-old man with prostate cancer. Prostate-specific antigen, 6.7 ng/mL. ROIs are circled in red. ROI (1) is placed on histologically diagnosed cancer lesion in peripheral zone of right lobe (Gleason grade 3+2) and ROI (2) is placed on histologically diagnosed cancer lesion in peripheral zone of left lobe (Gleason grade 4+3) on each image. A. T2- weighted MR image shows low signal change in all ROIs (1 and 2). B. Diffusion-weighted MR image (b = 1,500) shows no signal change in ROI (1) in right lobe, but high signal change in ROI (2) in left lobe. Measured n-diffusion values of the ROIs are shown. C. ADC map shows no signal change in ROI (1) in right lobe, but low signal change in ROI (2) in left lobe. Measured ADC values of ROIs are shown. D. Values of ROIs (1 and 2) are plotted as red squares (histologically diagnosed cancer regions are shown in red) on same scatter diagram as Fig. 4. Area above line indicates non-cancer area and that below line indicates cancer area on diagram. Red square (1) is located in non-cancer area and is incorrectly
distinguished as non-cancer and red square (2) is located in cancer area and is correctly distinguished as cancer on the diagram.

**References:** Department of Radiology, Tottori prefectural central hospital

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**Fig. 9:** MR images obtained at three weeks after prostate biopsy of 63-year-old man with prostate cancer. Prostate-specific antigen, 16.6 ng/mL. Two red ROIs (1 and 2) are placed on histologically diagnosed cancer lesion in peripheral zone of right lobe (Gleason grade 4+3) on each image. Two blue ROIs (3 and 4) are placed on histologically diagnosed non-cancer regions with hemorrhage in peripheral zone in the left lobe on each image. A. T2-weighted image shows low signal change in two red ROIs (1 and 2) in right lobe and high signal change in two blue ROIs (3 and 4) in left lobe. B. Diffusion-weighted MR image (b = 1,500) shows high signal change in red ROIs (No. 1 and 2) in right lobe and low signal change in blue ROIs (No. 3 and 4) in left lobe. Measured n-diffusion values of the ROIs are shown. C. ADC map shows low signal change in two red ROIs (No. 1 and 2) in right lobe and high signal change in two blue ROIs (No. 3 and 4) in left lobe. Measured ADC values of the ROIs are shown. D. T1-weighted MR image shows no signal change in two red ROIs (No. 1 and 2) in right lobe and high signal change, reflecting hemorrhage, in two blue ROIs (No. 3 and 4) in left lobe. E. Values of ROIs (1 and 2) are plotted as solid squares (histologically diagnosed cancer regions are shown in red) those of ROIs (3 and 4) are plotted as blue squares (histologically diagnosed non-cancer regions in blue) on the same scatter diagram as Fig. 4. Area above line indicates non-cancer area and that below indicates cancer area on the diagram. Red squares (1 and 2) are located in cancer area and
blue squares (3 and 4) are located in non-cancer area. Therefore all ROIs are correctly distinguished.

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A. T2-weighted MR image shows low signal change in all ROIs (1 and 2).

B. Diffusion-weighted MR image (b = 1,500) shows no signal change in ROI (1) in right lobe, but high signal change in ROI (2) in left lobe. Measured n-diffusion values of the ROIs are shown.

C. ADC map shows no signal change in ROI (1) in right lobe, but low signal change in ROI (2) in left lobe. Measured ADC values of ROIs are shown.

D. Values of ROIs (1 and 2) are plotted as red squares (histologically diagnosed cancer regions are shown in red) on same scatter diagram as Fig. 4. Area above line indicates non-cancer area and that below line indicates cancer area on diagram. Red square (1) is
located in non-cancer area and is incorrectly distinguished as non-cancer and red square
(2) is located in cancer area and is correctly distinguished as cancer on the diagram.

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Fig. 9: MR images obtained at three weeks after prostate biopsy of 63-year-old man with prostate cancer. Prostate-specific antigen, 16.6 ng/mL. Two red ROIs (1 and 2) are placed on histologically diagnosed cancer lesion in peripheral zone of right lobe (Gleason grade 4+3) on each image. Two blue ROIs (3 and 4) are placed on histologically diagnosed non-cancer regions with hemorrhage in peripheral zone in the left lobe on each image. A. T2-weighted image shows low signal change in two red ROIs (1 and 2) in right lobe and high signal change in two blue ROIs (3 and 4) in left lobe. B. Diffusion-weighted MR image (b = 1,500) shows high signal change in red ROIs (No. 1 and 2) in right lobe and low signal change in blue ROIs (No. 3 and 4) in left lobe. Measured n-diffusion values of the ROIs are shown. C. ADC map shows low signal change in two red ROIs (No. 1 and 2) in right lobe and high signal change in two blue ROIs (No. 3 and 4) in left lobe. Measured ADC values of the ROIs are shown. D. T1-weighted MR image shows no signal change in two red ROIs (No. 1 and 2) in right lobe and high signal change, reflecting hemorrhage, in two blue ROIs (No. 3 and 4) in left lobe. E. Values of ROIs (1 and 2) are plotted as solid squares (histologically diagnosed cancer regions are shown in red) those of ROIs (3 and 4) are plotted as blue squares (histologically diagnosed non-cancer regions in blue) on the same scatter diagram as Fig. 4. Area above line indicates non-cancer area and
that below indicates cancer area on the diagram. Red squares (1 and 2) are located in cancer area and blue squares (3 and 4) are located in non-cancer area. Therefore all ROIs are correctly distinguished.

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Conclusion

Discussion

For distinguishing cancer from non-cancer regions, a previous subjective evaluation of ADC maps combined with T2W images has shown areas under ROC curves (Az), sensitivity, specificity and accuracy for cancer detection of 0.9, 88%, 88% and 88%, respectively [12]. Another study evaluated by the same method showed an Az of 0.89 [6]. However, their visual determinations of signal intensity were subjective and depended on image interpretation experience, which seems to affect results.

In our study, the objective evaluated parameters had high Az in the order of n-Diffusion (b = 1,500) (Az = 0.87), ADC values (Az = 0.82), n-T2 (Az = 0.73) and n-Diffusion (b = 0) (Az = 0.61). The Az was relatively higher for n-Diffusion (b = 1,500) and ADC values. The performance of T2W imaging was not as good as ADC values and n-Diffusion (b = 1,500), although cancer lesions are usually detectable as low signal intensity in PZ that has high signal intensity. The presence of benign hypertrophy nodules with low signal intensity in PZ and/or cancer lesions in the inner gland with low signal intensity might affect the T2W images results. As previously reported, the ADC value was significantly lower in cancer than non-cancer regions in the present study, although both regions considerably overlapped. The ADC value was also lower for several non-cancer regions than for normal tissue (Fig. 7). We used an echo planar imaging-based pulse sequence to acquire DW images, which might be affected by susceptibility artifacts due to intestinal gas and bowel peristalsis. Therefore, differentiating cancer from non-cancer regions based only on the ADC value might be difficult.

Riches et al. objectively distinguished cancer lesions from a combination of parameters obtained from metabolite ratios using MR spectroscopy, and vascular parameters using contrast media, that is advanced physiological MR imaging, showed Az, sensitivity, specificity and accuracy for cancer detection of 0.95, 100% and 92%, respectively [20]. Furthermore, Reinsberg et al. found an Az of 0.81 using the same method [21]. In our study using discriminant analysis comprising picture element values of ADC maps combined with DW images, the combination of ADC and n-Diffusion (b = 1,500) had the highest Az (0.97 [95% CI, 0.95,0.98]) of any single parameter and of any combination of parameters (P < 0.0001). The diagnostic power was almost equal or superior to those of advanced MRI [20, 21]. A potential limitation of the ADC map in cancer detection might be its variability as the diffusivity of specific tissues might change according to biological factors, such as the age of the patient, body temperature, and technical factors, or b values, location and area of ROIs [22-27]. Therefore, the ADC threshold values for differentiating cancer from non-cancer regions might vary, and thus to apply a specific ADC threshold for cancer detection would be difficult. Although the detailed mechanism is
unknown, the diagnostic power was improved by combining DW images and ADC maps in this study. Anatomical information about the prostate was required for T2W imaging.

We found that post-biopsy hemorrhage did not influence the ability to distinguishing prostate cancer from normal prostate tissue. With respect to signal changes after biopsy, some studies have shown high signal intensity on T1W images and a slightly low signal intensity on ADC maps compared with normal tissue [29-31]. Therefore, post-biopsy hemorrhage does not affect the detection of cancer lesions [19]. Furthermore, other studies have demonstrated that cancer often does not cause a signal increase on T1W images, because of resistance caused by penetration by hemorrhage [7,28]. Our results corresponded with these findings. Therefore, because the ADC values of hemorrhagic regions are significantly higher than those of the cancer regions, the influence of post-biopsy hemorrhage in distinguishing between the two might be minimal.

Limitations

This was a retrospective study and radiologists drew ROIs knowing that the patients had prostate cancer, which might have introduced potential bias and increased the sensitivity. Cancer lesions <8 mm in diameter, which were not detected on MR images, were not included in the analysis. Susceptibility artifacts might have affected MR images obtained without using parallel imaging. Correlation between MR images and histological findings were inherently limited for some patients due to a long interval between MRI examination and surgery.

Nevertheless, the discriminant function of pixel values of DW images (b = 1,500) combined with ADC map could be a good objective indicator of cancer regions. Cancer might be detected by target biopsies using this method more correctly than systematic biopsies, which could minimize the number of required biopsies.

Conclusion

We discovered an excellent method of maximizing detectability within a short scan duration without the need for contrast media. The combination of ADC and n-Diffusion (b = 1,500) can improve the diagnostic performance of MR imaging and objectively distinguish prostate cancer from normal prostate tissue.
References


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