Effect of intravenous contrast medium administration on prostate diffusion-weighted imaging

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Aims and objectives

With advances in technology and growing reader experience, prostate multiparametric magnetic resonance imaging (mp-MRI) that combines anatomic T2-weighted (T2WI) with functional imaging techniques including diffusion-weighted imaging (DWI) and dynamic contrast-enhanced imaging (DCE) MRI has been widely used, not only staging, but also tumor detection, localization, aggressiveness assessment, risk stratification, active surveillance, image guidance for biopsy and post-treatment follow-up [1].

Of mp-MRI sequences, DWI is a key component [1, 2]. The apparent diffusion coefficient (ADC) and exponential apparent diffusion coefficient (EADC) maps generated from DWI data reflect the diffusion state of water molecules at the cellular level [2, 3]. A prostate cancer with high cellularity causing the diffusion restriction typically manifests as a focal area of low ADC value on the ADC map, or a focal area of high EADC value on the EADC map. However, DWI has inherent limitations, such as image distortion and susceptibility artifacts.

MR contrast medium (CM) include paramagnetic compounds, such as Gadolinium (Gd), Mn$^{2+}$ or Fe$^{3+}$. These paramagnetic agents shorten both T1-relaxation time and T2-relaxation time. Thus, current DWI has been obtained before intravenous CM administration in prostate MRI, to avoid or minimize paramagnetic effects of CM on DWI. To our knowledge, only a previous study has reported the results of effect on ADC values and DW imaging quality before and after CM administration in prostate [4]. However, no published results for EADC values have been reported. The purpose of our study is to prospectively investigate the quantitative and qualitative effect of EADC as well as ADC in the prostate cancer and benign prostate tissues before and after intravenous administration of gadolinium-based CM (GBCM) on DWI at 3T.
Methods and materials

Subjects

- The Institutional Review Board approved this study and written informed consent was obtained from all patients.
- Between December 2013 and February 2014, 109 consecutive men with biopsy-proven prostate cancer who were scheduled to perform prostate MRI for local staging at 3T in our institutions were recruited for obtaining DWI before and after GBCM administration.
- The exclusion criteria were as the followings: no radical prostatectomy (n=53), invisible cancer focus on DWI (n=11) and severe DWI artifacts (n=2).
- Finally, 34 consecutive patients (mean age, 67.6 ± 7.3 years; range, 49-81 years) were enrolled in our study group.

MRI technique

- All patients underwent prostate MRI at 3T (Intera Achieva 3TX, Philips Medical System, Best, The Netherlands) using a phased-array coil.
- The routine MRI protocol was composed of T1-weighted imaging, T2WI, DWI and DCE-MRI.
- DWI was obtained in the transverse plane using the single shot echo planar imaging technique before and after GBCM administration (TR/TE, 5250/68#70 msec; slice thickness, 3 mm; interslice gap, 1 mm; matrix, 124 × 121; FOV, 20 cm; SENSE factor, 2; NSA, 4; b-values, 0, 100 and 1000 s/mm²; and acquisition time, 3 min 35 sec). The phase-encoding gradient moved from left to right to minimize motion artifacts. The equation for calculating the ADC and EADC value was as follows: \( EADC = \frac{S_b}{S_0} = e^{b \times ADC} \), where \( S_b \) and \( S_0 \) were signal intensities of DWI when the diffusion sensitization is present or absent, respectively; \( b \) was the maximal b value of DWI sequence; and \( e \) was the mathematical constant, the base of the natural logarithm [5].

Histopathological and MR image analysis

- All surgical specimens were fixed overnight in 10% buffered formalin. From prostatic base to apex, the transverse sections with an interval of 3 mm were obtained, perpendicular to the prostatic urethra. An experienced genitourinary pathologist blinded to the MRI findings reviewed all slides of the transverse section, and the cancers were thus localized. The tumor volume, location, and Gleason score were also assessed.
- Two genitourinary radiologists analyzed the MR images on the basis of cancer location shown on the histopathologic cancer map and a consensus was reached.
• Typical MR findings of cancer foci in the peripheral zone (PZ) and transition zone (TZ) on T2WI and DWI were defined as the ESUR prostate MR guidelines: prostate imaging-reporting and data system (PI-RADS) score with 4 or 5 [1].

• Based on the radiologic-pathologic correlation, the radiologists measured both ADC and EADC values in the cancers and benign tissues. For measuring each ADC and EADC value of the cancers, an ellipsoid region of interest (ROI) was first drawn within a cancerous area of ADC map, which was subsequently copied onto the EADC map at the same transverse plane. To minimize the mismatch of tumors between the ADC/EADC maps and the histopathologic findings, the tumor areas on the ADC/EADC maps were smaller than those on the histopathologic findings.

• To allow for reasonable differences in registration and deformation between the MR images and histopathologic findings, the histopathological and imaging-detected cancers were considered to be of comparable sizes if the maximal transverse diameter calculated on MRI was within 50% to 150% of that on histopathology [6]. The same process was applied for measuring both ADC and EADC values in the benign tissues outside the cancerous lesions.

• The ADC and EADC values were assessed two times at the same site and an average was recorded.

• Overall imaging quality of the DW images before and after GBCM administration was rated using the following 4-point score: (1), poor (not interpretable with severe artifacts); (2), fair (interpretable with moderate artifacts); (3), good (interpretable with mild artifacts); and (4), excellent (interpretable without artifacts).

• Lesion-to-background contrast ratio of ADC and EADC for estimating tissue contrast: the lesion and background were PZ cancer and benign PZ tissue, respectively [7].

Statistical analysis

• Between precontrast and postcontrast images, comparisons of ADC or EADC values in the cancers and benign tissues were using Student paired t-test.

• For evaluating the reliability and variability of ADC or EADC values between precontrast and postcontrast images, the intraclass correlation coefficient (ICC) and Bland-Altman test were used.

• The Wilcoxon-signed rank test was used to compare the lesion-to-background contrast ratio of ADC or EADC maps and imaging quality, precontrast and postcontrast images.

• A two-sided P-value< 0.05 was considered statistically significant.
Results

Table 1 summarizes the patient characteristics.

Quantitative analysis

Table 2 presents the results of ADC an EADC values precontrast and postcontrast images in the cancers and benign tissues.

Between precontrast and postcontrast images, ADC and EADC values in the cancers and benign TZs were not statistically different, respectively ($P > 0.05$), while those in the benign PZs (ADC, $1.625 \pm 0.271$ and $1.593 \pm 0.264$; EADC, $0.206 \pm 0.053$ and $0.213 \pm 0.053$) were statistically different, respectively ($P = 0.03$ and $0.037$, respectively) (Fig. 1).

For the reliability precontrast and postcontrast images, both ADC and EADC values showed excellent agreement in the cancers, benign PZ and benign TZ (ICC # 0.894) (Table 3).

At Bland-Altman test, the variability of ADC and EADC values precontrast and postcontrast images in the cancers and benign tissues was 3.2% or less.

Qualitative analysis

Lesion-to-background contrast ratios of ADC and EADC were statistically inferior on post-contrast DW images to on pre-contrast DW images ($P = 0.015$ and $0.006$, respectively).

Between precontrast and postcontrast, the overall imaging quality of ADC and EADC maps was fair or more in all patients without decreasing imaging quality ($P > 0.05$).
Fig. 1: Fig. 1. Right peripheral zone cancer. ADC and EADC values were similar in the cancer (arrow) between precontrast and postcontrast images. All DW images on precontrast and postcontrast images shows excellent imaging quality without artifacts. As compared with precontrast ADC and EADC maps, postcontrast ADC and EADC maps reveal decreased lesion-to-background contrast ratio.

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Table 2: ADC and EADC values in cancers and benign tissues between precontrast and postcontrast

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<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Data</th>
</tr>
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<tbody>
<tr>
<td>Mean PSA (ng/mL)</td>
<td>8.59 (2.5-29.3)</td>
</tr>
<tr>
<td>Median Gleason score</td>
<td>7 (6-9)</td>
</tr>
<tr>
<td>Mean cancer volume (cm³)</td>
<td>3.87 (0.51-16.52)</td>
</tr>
<tr>
<td>Cancer (n)</td>
<td></td>
</tr>
<tr>
<td>PZ</td>
<td>21</td>
</tr>
<tr>
<td>TZ</td>
<td>9</td>
</tr>
<tr>
<td>PZ &amp; TZ</td>
<td>4</td>
</tr>
<tr>
<td>Pathologic stage (n)</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>9</td>
</tr>
<tr>
<td>2c</td>
<td>16</td>
</tr>
<tr>
<td>3a</td>
<td>7</td>
</tr>
<tr>
<td>3b</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 1: Patient characteristics.

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Table 3: Intraclass correlation coefficient in cancer and benign tissue between precontrast and postcontrast

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<thead>
<tr>
<th></th>
<th>ICC ADC</th>
<th>ICC EADC</th>
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<tbody>
<tr>
<td>Cancer</td>
<td>0.894 (0.799, 0.946)</td>
<td>0.987 (0.804, 0.947)</td>
</tr>
<tr>
<td>Benign PZ</td>
<td>0.952 (0.907, 0.976)</td>
<td>0.948 (0.898, 0.974)</td>
</tr>
<tr>
<td>Benign TZ</td>
<td>0.902 (0.813, 0.950)</td>
<td>0.897 (0.804, 0.947)</td>
</tr>
</tbody>
</table>
Conclusion

On 3T-DWI, the ADC and EADC values in prostate cancers appear to be similar between precontrast and postcontrast images, without decreased imaging quality. However, the lesion-to-background contrast ratios might be decreased on post-contrast images. Further studies are needed.
Personal information

No conflict of interest.