Original Research

Differentiation of Noncancerous Tissue and Cancer Lesions by Apparent Diffusion Coefficient Values in Transition and Peripheral Zones of the Prostate

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Purpose: To compare the apparent diffusion coefficient (ADC) values of prostate cancer in both the peripheral zone (PZ) and the transition zone (TZ) with those of benign tissue in the same zone using echo-planar diffusion weighted imaging with a parallel imaging technique.

Materials and Methods: A total of 29 consecutive male patients (mean age 61.3 years, age range 53–88 years) with suspected prostate cancer were referred for MR imaging. All patients underwent transrectal ultrasound (TRUS)-guided biopsy of the prostate after MR imaging at 1.5T, including ADC. For each patient, seven to 10 specimens were obtained from the prostate, and regions of interest (ROIs) were drawn on the ADC map by referring to the urologist’s illustration of TRUS-guided biopsy sites. ADC values of cancerous tissue in both the PZ and TZ were compared to those of noncancerous tissue in the same zone.

Results: Out of 29 patients, 23 had cancer tissue. In the 23 patients with cancer, the mean ADC value of all cancer ROIs and that of all noncancer ROIs, respectively, were 1.11 ± 0.41 × 10⁻³ and 1.68 ± 0.40 × 10⁻³ mm²/second (values are mean ± SD) (P < 0.01). The mean ADC value of TZ cancer ROIs and that of TZ noncancer ROIs, respectively, were 1.13 ± 0.42 × 10⁻³ and 1.58 ± 0.37 × 10⁻³ mm²/second (P < 0.01).

Conclusions: ADC measurement with a parallel imaging technique showed that ADC values of prostate cancer in both the PZ and TZ were significantly lower than those of benign tissue in the PZ and TZ, respectively.

Key words: prostate neoplasm; magnetic resonance; apparent diffusion coefficient; peripheral zone; transition zone


EARLY DETECTION has been significantly improved using serum prostate-specific antigen (PSA) level as a tumor marker (1,2). Accurate preoperative staging is very important in selecting the method of therapy for prostate cancer (2,3). Magnetic resonance (MR) imaging and MR spectroscopic imaging have been gaining acceptance as tools in the evaluation of prostate cancer (4–13). Thus far, assessment using MR imaging and MR spectroscopic imaging has focused on the peripheral zone (PZ) of the prostate gland, except a few magnetic resonance spectroscopy (MRS) and dynamic MR studies (6,14). Although 65% of prostate cancers arise in the PZ, up to 30% arise in the transition zone (TZ) (15). Evaluation of the TZ with imaging, including both MR imaging and ultrasonography (US), is difficult because the TZ is the site of origin of benign prostatic hyperplasia (BPH), which can have a heterogeneous appearance (8,16). One study reported that dynamic MRI cannot differentiate central gland normal tissue and tumor (17), while another study reported that dynamic MR can differentiate carcinoma and normal tissue in the central gland (6). It has been shown that TZ cancer can be differentiated from central gland benign tissue by MRS if the lesion volume is at least 1 cm (3,14).

Histopathological examination by transrectal ultrasound (TRUS)-guided needle biopsy is important essentially for the establishment of prostate cancer diagnosis (14,18). However, false-negative results are not uncommon because most biopsies target the peripheral zone (14). Cancer lesions in the TZ are usually limited within the prostate gland and have favorable prognosis (14). Thus it is important to establish a method for the localization of prostate cancer, especially in the TZ to avoid false-positive biopsies.

An alternative approach can make use of diffusion-weighted imaging. There has been a report of a statistical difference in the mean apparent diffusion coefficient (ADC) values of normal and cancerous tissue imaged with pelvic phased-array coils (9). Although they showed that the ADC of cancer tissue was significantly lower than that of normal peripheral zone tissue, they did not compare the ADC values of tumor and...
benign tissue in the TZ. Another study using diffusion-weighted imaging reported no significant difference between ADC values of normal and cancerous tissue, although ADC values of cancerous tissue tended to be lower than those of normal tissue (19). In these two studies, a parallel imaging technique such as sensitivity encoding (SENSE) was not employed (20). The use of a parallel imaging technique can significantly improve the image quality of diffusion-weighted imaging acquired with a single-shot echo-planar sequence (21).

The purpose of this study was to compare the ADC values of prostate cancer in both the PZ and TZ with those of benign tissue in the same zone, using a parallel imaging technique.

MATERIALS AND METHODS

Patients

A total of 29 consecutive male patients (mean age: 61.3 years; age range: 53–88 years) with suspected prostate cancer were referred for MR imaging between May 2003 and January 2004. Patients with elevated serum PSA level (7.0–1300 ng/mL) were included in this study. All patients underwent TRUS-guided biopsy of the prostate after MR imaging.

This study was approved by the hospital ethics committee, and all participants signed written informed consent agreements regarding their participation.

Imaging Technique

All scans were performed before prostate biopsy on a 1.5-Tesla MR scanner (Symphony; Siemens AG, Erlangen, Germany) using an eight-channel body-coil phased array for signal reception. Its maximum gradient specifications were 30 mT/m for amplitude and 125 mT/m m/sec for slew rate.

The entire prostate gland and seminal vesicles were covered by axial T1-weighted spin-echo MR imaging with 600 msec/13 msec (repetition time/echo time), and both axial and coronal T2-weighted turbo-spin-echo MR imaging with 4000 msec/77 msec and an echo train length of 11. These conventional MR images were each obtained with a 7-mm slice thickness, 1.4-mm interslice gap, 250-mm field of view (FOV), and 253 × 384 matrix. Axial diffusion-weighted images (DWI) were obtained using a Stejskal-Tanner spin-echo echo-planar imaging (EPI) sequence with the following parameters: repetition time of 2700 msec, flip angle of 90°, echo time of 96 msec, and b-factors of 0, 300, and 600 second/mm². The bandwidth was 1184 Hz/pixel with a 119 × 192 matrix, and the FOV was 25 cm (square) for 13 7-mm-thick axial slices covering the entire prostate and seminal vesicles, with an interslice gap of 1.4 mm. Following the acquisition of b = 0 images, motion-probing gradients (MPGs) in three orthogonal orientations were applied sequentially. For each b-factor, three DWI acquisitions were averaged, giving a scan time of one minute and 16 seconds. An acceleration factor of two was applied using the modified sensitivity encoding (mSENSE) parallel imaging technique (20). The voxel size was 2.1 × 1.3 × 7.0 mm, equaling 19.11 mm³. The acquisition times were two minutes and 41 seconds for the T1-weighted images, and two minutes and 30 seconds for the axial and coronal T2-weighted images.

TRUS-guided biopsy was performed by a urologist using 18-G needles. Seven to 10 prostate specimens were obtained in each case, targeting not only the peripheral zone but also the transition zone.

Image Analysis

For each patient, biopsy sites were hand-drawn by the urologist on a prostate illustration. Referring to the illustration, regions of interest were specified on the T2-weighted turbo-spin-echo images. The landmarks used for region of interest (ROI) localization were the urethra, the border between PZ and TZ, and the capsule of the prostate gland. If there is a pseudocapsule of benign prostatic hyperplastic nodule, it is also used as the landmark. These ROIs were then manually positioned on echo-planar images acquired with b = 0, accounting for the distortion of the EPI images, then copied on ADC maps. Placement of ROIs was performed by a radiologist with five years of experience reading prostate imaging (C.S.) without knowledge of the pathological results. Each ROI was a circle with an area of 8–38 mm². An example of ROI placement is shown in Fig. 1.

The PZ was defined as the peripheral area of the prostate gland with high signal on T2-weighted turbo-spin-echo images surrounding the posterior part of the central low-signal area (TZ). If the peripheral area on one side had low signal on T2-weighted images, delineation of the PZ was estimated by referring to the other side.

Data and Statistical Analysis

Based on pathological diagnosis, the 29 patients were divided into two groups, 23 patients with cancer and six patients without cancer.

For the 23 patients with cancer, ROIs were separated into two groups, those containing cancer (104 ROIs) and those without cancer (84 ROIs).
In the 23 patients with cancer, the mean ADC value of all cancer ROIs (104 ROIs) and that of all noncancer ROIs (84 ROIs), respectively, were $1.11 \pm 0.41 \times 10^{-3}$ and $1.68 \pm 0.40 \times 10^{-3}$ mm$^2$/second (values are mean ± SD) ($P < 0.01$) (Fig. 2a).

In the 23 patients with cancer, the mean ADC value of PZ cancer ROIs (42 ROIs) and that of PZ noncancer ROIs (37 ROIs), respectively, were $1.08 \pm 0.39 \times 10^{-3}$ and $1.80 \pm 0.41 \times 10^{-3}$ mm$^2$/second ($P < 0.01$) (Fig. 2b).

In the 23 patients with cancer, the mean ADC value of TZ cancer ROIs (62 ROIs) and that of TZ noncancer ROIs (47 ROIs), respectively, were $1.13 \pm 0.42 \times 10^{-3}$ and $1.58 \pm 0.37 \times 10^{-3}$ mm$^2$/second ($P < 0.01$) (Fig. 2c).

In the six patients without cancer, the mean ADC values of TZ cancer ROIs (32 ROIs) and PZ ROIs (16 ROIs), respectively, were $1.68 \pm 0.26 \times 10^{-3}$ and $1.93 \pm 0.24 \times 10^{-3}$ mm$^2$/second ($P < 0.01$) (Fig. 2d).

As shown above, the mean ADC values of the cancer ROI were significantly lower not only in PZ but also in TZ.

**RESULTS**

The 23 cases with cancer were consisted by four cases of well-differentiated adenocarcinoma, 12 cases of moderately differentiated adenocarcinoma, two cases of poorly/moderately differentiated adenocarcinoma, and five cases of poorly differentiated adenocarcinoma. Table 1 contains a summary of the clinical and pathologic information from the 23 cancer patients included in this study. The PSA values were 7.0–9.2 ng/mL in the six cases without cancer.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>PSA value (ng/mL)</th>
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**Table 1**

Summary of Age, PSA Level, and Biopsy Results in the Patients With Prostate Cancer

Well = well differentiate adenocarcinoma, Mod = moderately differentiate adenocarcinoma, Poorly = poorly differentiate adenocarcinoma, Mod– poorly = moderately–poorly differentiate adenocarcinoma.

ADC imaging of organs in the body has been attempted (22); however, the images were degraded by motion of the organs and by distortion caused by local magnetic susceptibility-related inhomogeneity of the main field. Recent advances in MR technology such as high-performance gradient coils, parallel imaging techniques (20), and phased-array receiver coils have finally made diffusion-weighted imaging of the body feasible for clinical use.

Decreased ADC values in various malignant lesions, probably due to increased cellular density, have been reported (23,24). In the present study, ADC values of prostate cancer lesions were significantly lower than those of normal PZ and TZ tissues, but the cause of decreased ADC values in these lesions is still unknown. Further histological investigation following total prostatectomy is necessary to determine the cause conclusively.

ADC measurement of the prostate, including malignant tissue, has been attempted using single-shot EPI without parallel imaging (9,19), but there were discrepancies between the two studies. Gibbs et al (19) utilized eight b-values ranging from 0 to 720 seconds/mm$^2$ in eight normal volunteers and 12 patients, and found no significant difference in ADC between benign and malignant tissues. Issa (9) utilized six b-values (64, 144, 257, 401, 578, and 786 seconds/mm$^2$) in 7 normal volunteers and 12 patients, and found no significant difference in ADC between benign and malignant tissue, has been attempted using single-shot EPI. However, the images were degraded by motion of the organs and by distortion caused by local magnetic susceptibility-related inhomogeneity of the main field. Recent advances in MR technology such as high-performance gradient coils, parallel imaging techniques (20), and phased-array receiver coils have finally made diffusion-weighted imaging of the body feasible for clinical use.
The technique may also have contributed to the significant difference through reduction of image distortion.

For ADC measurement, we utilized only three b-values (0, 300, and 600 seconds/mm²). Actual ADC values of noncancer tissue in Issa’s study (9) were $1.63 \pm 0.30 \times 10^{-3} \text{ mm}^2/\text{second}$ in the TZ and $1.91 \pm 0.46 \times 10^{-3} \text{ mm}^2/\text{second}$ in the PZ, close to the values in our patients without cancer, $1.68 \pm 0.26 \times 10^{-3} \text{ mm}^2/\text{second}$ in the TZ and $1.93 \pm 0.24 \times 10^{-3} \text{ mm}^2/\text{second}$ in the PZ. These data suggest that computing ADC with the three b-factors used in our study is reasonable.

An important result of our study was that we showed a significant difference in the TZ between ADC values of cancer and noncancer tissue. This revealed a new possibility for localizing cancerous tissue in the TZ which is sometimes missed by TRUS-guided biopsy.

It has been suggested that patients with multiple negative biopsy results and an elevated PSA level should undergo biopsies in which the TZ is specifically targeted (25). Even when the TZ is specifically targeted, small tumors (<2 cm³) may be missed (26). Accurate imaging guidance may improve the accuracy of biopsy results. Cancers in the TZ are more likely to be confined within the prostate gland, have a lower Gleason score, and have higher biochemical cure rates than same-volume PZ tumors (16). Thus, if patients with TZ cancers can be correctly diagnosed based on ADC mapping, they may be candidates for alternative therapies or watchful waiting, depending on other clinical considerations. Furthermore, BPH shows very heterogeneous signal especially in transition zone of the gland on T2-weighted images. The value of ADC mapping is significant (8,16).

One of the limitations of the present study was that ROI measurements were performed based on illustrations of biopsy sites drawn by the urologist. In practice, the biopsies were performed in three-dimensional space, and thus biopsy sites may not have been completely contained within the ROI, or may not have completely traversed the plane of the ROI. Thus the reproducibility of the present study may be limited by the expertise of the radiologist and urologist. Correlation with a total histological specimen following radical prostatectomy is necessary to confirm the result of the present study.

The other limitation of the present study was that the ROI placement was performed referring to T2-weighted images first, then copied to ADC maps. Thus the incremental values of ADC maps over T2-weighted images

![Figure 2](image-url)

Figure 2. Box-whisker plots of ADC values. The center horizontal line indicates the median. The bottom and top edges of the box indicate the 25th and 75th percentiles. The vertical line indicates the range of data. a: ADC values of all ROIs with cancer and all those without cancer in 23 patients with prostate cancer ($P < 0.01$). b: ADC values of PZ ROIs with cancer and those without cancer in 23 patients with prostate cancer ($P < 0.01$). c: ADC values of TZ ROIs with cancer and without cancer in 23 patients with prostate cancer ($P < 0.01$). d: ADC values of TZ ROIs without cancer and PZ ROIs without cancer in six patients without prostate cancer ($P < 0.01$).
REFERENCES


