Original Article

J Korean Soc Radiol 2022;83(5):1059-1070
https://doi.org/10.3348/jksr.2022.0004
eISSN 2951-0805

JOURNAL of THE KOREAN SOCIETY of RADIOLOGY

Comparison of Computed Diffusion-Weighted Imaging b2000 and Acquired Diffusion-Weighted Imaging b2000 for Detection of Prostate Cancer

전립선암 발견을 위한 계산형 확산강조영상 b2000과 실제 획득한 b2000 영상의 비교

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Received January 7, 2022
Revised March 5, 2022
Accepted March 21, 2022

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Purpose To compare the sensitivity of tumor detection and inter-observer agreement between acquired diffusion-weighted imaging (aDWI) b2000 and computed DWI (cDWI) b2000 in patients with prostate cancer (PCa).

Materials and Methods Eighty-eight patients diagnosed with PCa by radical prostatectomy and having undergone pre-operative 3 Tesla-MRI, including DWI (b, 0, 100, 1000, 2000 s/mm^2), were included in the study. cDWI b2000 was obtained from aDWI b0, b100, and b1000. Two independent reviewers performed a review of the aDWI b2000 and cDWI b2000 images in random order at 4-week intervals. A region of interest was drawn for the largest tumor on each dataset, and a Prostate Imaging-Reporting and Data System (PI-RADS) score based on PI-RADS v2.1 was recorded. Histologic topographic maps served as the reference standard.

Results The study population's Gleason scores were 6 (n = 16), 7 (n = 53), 8 (n = 9), and 9 (n = 10). According to the reviewers, the sensitivities of cDWI b2000 and aDWI b2000 showed no significant differ-

ences (for reviewer 1, both 94% [83/88]; for reviewer 2, both 90% [79/88]; p = 1.000, respectively). The kappa values of cDWI b2000 and aDWI b2000 for the PI-RADS score were 0.422 (95% confidence interval [CI], 0.240–0.603) and 0.495 (95% CI, 0.308–0.683), respectively.

Conclusion cDWI b2000 showed comparable sensitivity with aDWI b2000, in addition to sustained moderate inter-observer agreement, in the detection of PCa.

Index terms Magnetic Resonance Imaging; Diffusion; Neoplasm Grading; Prostate Cancer; Gleason Score

INTRODUCTION

Prostate cancer (PCa) can be treated individually according to the degree of aggressiveness, staging, and risk of recurrence. For rational determination of individual treatment plans, efforts have been made for risk stratification. Given the sampling errors to which systematic biopsy is prone (1, 2), not to mention the complications that can result from such invasive approaches (3), an idea to evaluate tumor aggressiveness by using a non-invasive imaging modality such as MRI for risk stratification has emerged.

The usefulness of acquired diffusion-weighted imaging (aDWI) with a b value of b = 2000 s/mm^2 (hereafter, b2000) for detection of PCa has been studied. The sensitivity of aDWI b2000 was significantly enhanced compared to that of DWI b1000 (4), as was tumor conspicuity (5). According to Prostate Imaging-Reporting and Data System (PI-RADS) v2.1, high b value (> 1400 s/mm^2) DWI was recommended as mandatory in imaging acquisition, which can be either extrapolated from low- and intermediate-b value images or obtained in a separate acquisition (6).

However, aDWI b2000 needs additional time, about 4 minutes or more, for acquisition, though the exact time will depend on the specific parameters used in each institution. Furthermore, an advanced MRI machine such as a 3 Tesla (3T) scanner is required in order to obtain a high diffusion gradient. However, access to such equipment is limited worldwide. We hypothesized that if computed DWI (cDWI) b2000 derived from aDWI b0, 100, and 1000 could show comparable detection sensitivity to aDWI b2000 in tumor detection with sustained inter-observer agreement, it could replace aDWI b2000, with benefits accrued in terms of time savings and obviation of the need for high-end MRI machines.

Several studies have suggested that cDWI b2000 is superior to aDWI b2000 in image quality and tumor detection (7-10). However, those analyses were focused on image quality predominantly. Thus, detection sensitivity and inter-observer agreement have been less frequently mentioned (7). Moreover, systematic biopsy was used as a gold standard rather than whole mount histology sections from radical prostatectomy specimens, which made for suboptimal radiologic-pathologic correlation.

Therefore, the aim of this study was to compare the detection sensitivity in tumor detection and inter-observer agreement between aDWI b2000 and cDWI b2000 based on whole mount histology sections as the gold standard.

MATERIALS AND METHODS

The pertinent institutional review board approved this retrospective study. Informed consent from patients was waived (IRB No. 2021-02-019-001)

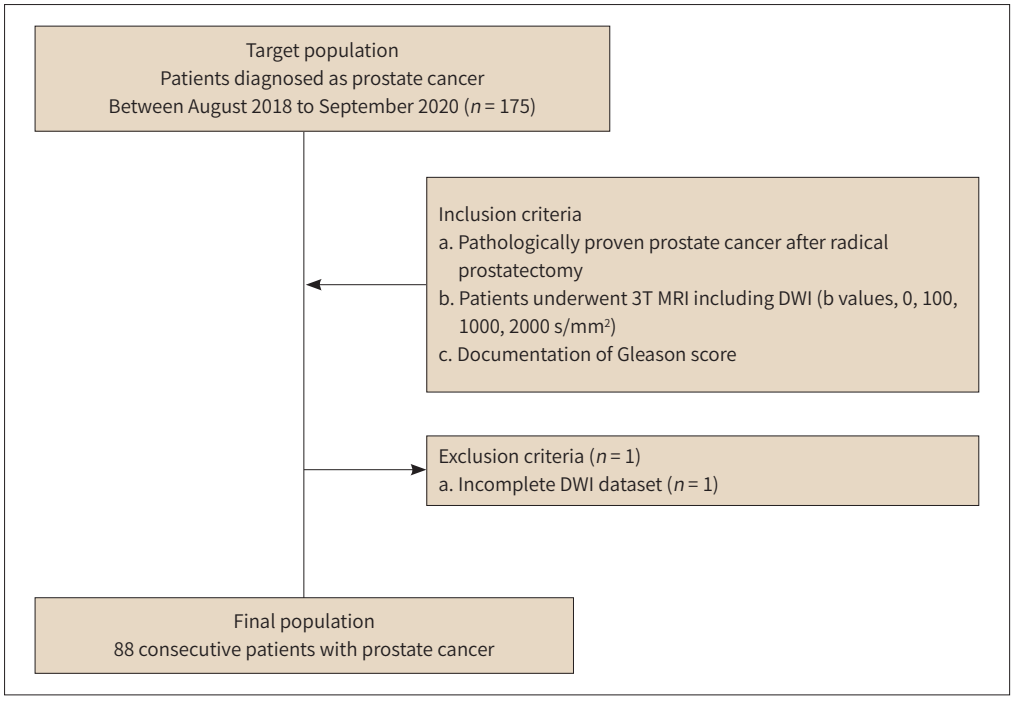
PATIENT SELECTION CRITERIA

A total of 175 patients who had been histologically diagnosed with PCa between August 2018 and September 2020 were declared initially eligible. Among them, 89 patients satisfying the inclusion criteria were included in the study. The inclusion criteria were as follows: 1) completed radical prostatectomy, 2) completed 3T-MRI including DWI (b values, 0, 100, 1000, 2000 s/mm^2), and 3) Gleason score (GS) documentation. Among the patients meeting these criteria, one was excluded due to an incomplete DWI dataset. Finally, 88 patients (mean age: 68.6 years, range: 47–82 years) were enrolled in the study. The case-accrual process is presented in Fig. 1.

MRI

All MRI examinations were performed using a 3T MR scanner (Achieva TX; Philips, Best, Netherlands) equipped with a parallel-array body coil (SENSE Torso/cardiac coil; USA Instruments, Gainesville, FL, USA). The scanning protocol consisted of axial, sagittal and coronal T2-weighted turbo spin-echo (T2WI) and axial DWI sequences (b = 0, 100, 1000, and 2000 s/mm^2). Apparent diffusion coefficient (ADC) map was generated from b values of 0, 100, 1000, and 2000 s/mm^2. The DICOM images of all DWI were transmitted from a picture archiving and

Fig. 1. Flowchart of the case-accrual process.



DWI = diffusion-weighted imaging, T = Tesla

Table 1. MRI Sequence Parameters

Parameter	T2-Weighted Axial, Sagittal, and Coronal TSE	DWI (b = 0, 100, 1000, and 2000 s/mm^2)
TR, msec	3327	5725
TE, msec	100	79
ETL	15	73
Slice thickness, mm	3	3
Slice gap, mm	0.3	0.3
Matrix size	316 × 255	120 × 118
NEX	1	b0, 2; b100, 3; b1000, 7; b2000, 14
FOV, mm^2	220 × 220	240 × 240
Acquisition time	2 min 15 sec, 2 min 22 sec, 2 min 24 sec, respectively	b0, 18 sec; b100, 51 sec; b1000, 2 min; b2000, 4 min
No. of slices	30	30

DWI was performed using the single-shot echo-planar imaging technique.
DWI = diffusion-weighted imaging, ETL = echo train length, FOV = field of view, NEX = number of excitations, TE = echo time, TR = repetition time, TSE = turbo spin echo

communication system (PACS) workstation (m-view; INFINITT Healthcare, Seoul, Korea) to a workstation with advanced diffusion analysis capability (IntelliSpace Portal, version 10.0, Philips) that could instantly make cDWI b2000 from aDWI b0, 100, and 1000 under a mono-exponential decay model. The detailed scan parameters are summarized in Table 1.

IMAGE ANALYSIS

In terms of tumor detection, two radiologists, both with 3 years of experience in reading prostate MRI, independently reviewed aDWI b2000 images first, then cDWI b2000 images with corresponding ADC maps after a 4-week interval to eliminate a recall bias. T2WI data with 3 planes also were presented for each review session. The order of patients was random. The two reviewers were blinded to the patients' clinical and pathologic information. However, they were aware that all of these patients had pathologically proven PCa. They manually drew regions of interest (ROIs) for the largest tumor on each aDWI b2000 and cDWI b2000 image. They were allowed to adjust the window setting to the width and level at which the lesion could be obvious to each reviewer.

INTER-OBSERVER AGREEMENT ON PI-RADS V2.1

The reviewers also recorded PI-RADS scores for the largest tumor on the aDWI b2000 and cDWI b2000 images based on non-contrast version of PI-RADS v2.1 (6).

IMAGE QUALITY

For independent assessment of the overall subjective image quality of the aDWI b2000 and

cDWI b2000 images, another two reviewers who both had 4 years of experience in reading prostate MRI and also blinded to the image information scored the grade based on a 5-point scale (1 = definitely unacceptable image quality, 2 = probably unacceptable, 3 = marginally acceptable, 4 = probably acceptable, 5 = definitely acceptable image quality for diagnostic tasks) adopted from the literature and considering anatomic clarity, background signal suppression, absence of distortion, and absence of ghosting (7). The image datasets were presented in random order.

For quantitative analysis, signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were calculated on aDWI b2000 and cDWI b2000. The SNR was defined as the signal intensity (SI) value of the prostate parenchyma divided by the standard deviation (SD) of the background noise. The CNR was defined as the absolute SI value of index tumor (SI value of the index tumor minus SI value of the prostate parenchyma) divided by the SD of the background noise. The third radiologist with 2 years of experience measured SIs of normal prostate gland, index tumor and background by placing a circular ROI at each area.

REFERENCE STANDARD

Dedicated urologists had performed the radical prostatectomies. A dedicated pathologist evaluated each pathological slide in accordance with the Gleason grading system (11) and made a whole mount histology section that served as the ground truth for tumor localization on MR images. When there were multiple lesions in a patient, the largest one was regarded as the index tumor. In terms of location, the radiologic-pathologic correlation and validation of the drawn ROIs with pathologic index tumor was done by the referee radiologist who had 13 years of reading experience on prostate MRI. Clinically significant cancer (CSC) was defined as GS $\geq$ 7, and non-CSC, GS 6 (12).

STATISTICAL ANALYSIS

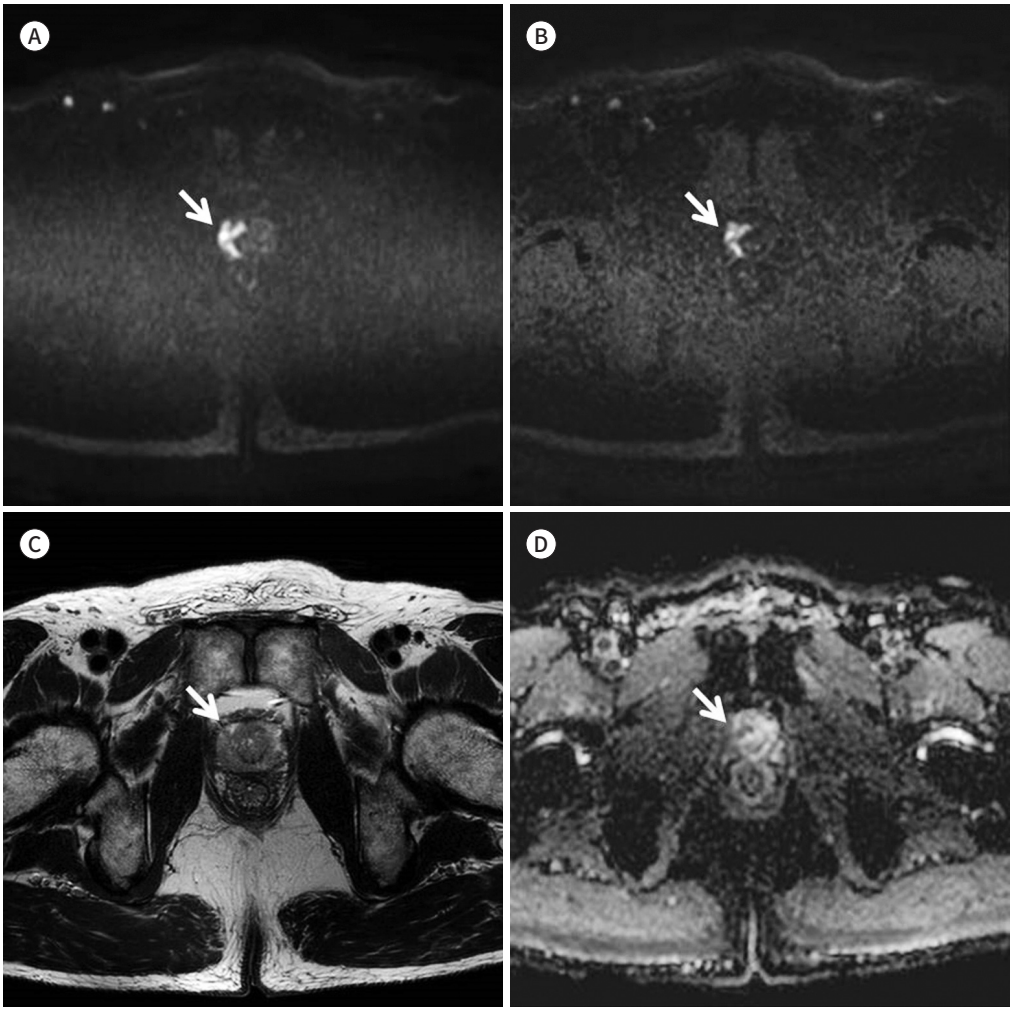
MedCalc software for Windows (MedCalc Software version 19.6.1, Mariakerke, Belgium) was used for the statistical analyses. When a *p* value was less than 0.05, the difference was regarded as significant. The tumor detection sensitivities of aDWI b2000 and cDWI b2000 were compared by the McNemar test. For inter-observer agreement regarding PI-RADS scores, the quadratic weighted kappa values were calculated. The strength of inter-observer agreement was defined as poor (< 0.20), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80), or excellent (0.81–1.00) (13). The overall image quality was compared by the Wilcoxon test. SNR and

Table 2. Demographics of the Study Population

Parameter	All	CSC (*n* = 72)	Non-CSC (*n* = 16)
Mean PSA, ng/mL [range]	21.5283 [0.02–149]	24.5603 [0.85–149]	7.8841 [0.02–20.4]
Tumor location, *n* (%)			
Peripheral zone	44 (50)	33 (46)	11 (69)
Transitional zone	25 (28)	20 (28)	5 (31)
Fibromuscular zone	4 (5)	4 (6)	0 (0)
Diffuse	15 (17)	15 (21)	0 (0)

CSC = clinically significant cancer (Gleason score $\geq$ 7), PSA = prostate-specific antigen

Fig. 2. A 66-year-old male with histopathologically proven prostate adenocarcinoma of Gleason score 6 (3 + 3) after radical prostatectomy.
A. aDWI (b = 2000 s/mm^2) shows a high SI lesion (arrow) in the right apex peripheral zone.
B. cDWI (b = 2000 s/mm^2) shows a similar high-SI lesion (arrow) at the corresponding location.
C. T2-weighted image shows intermediate-SI lesion (arrow) in the same area.
D. Apparent diffusion coefficient map generated from 2A shows reciprocal low-SI lesion (arrow) in the corresponding area.
aDWI = acquired diffusion-weighted imaging, cDWI = computed diffusion-weighted imaging, SI = signal intensity



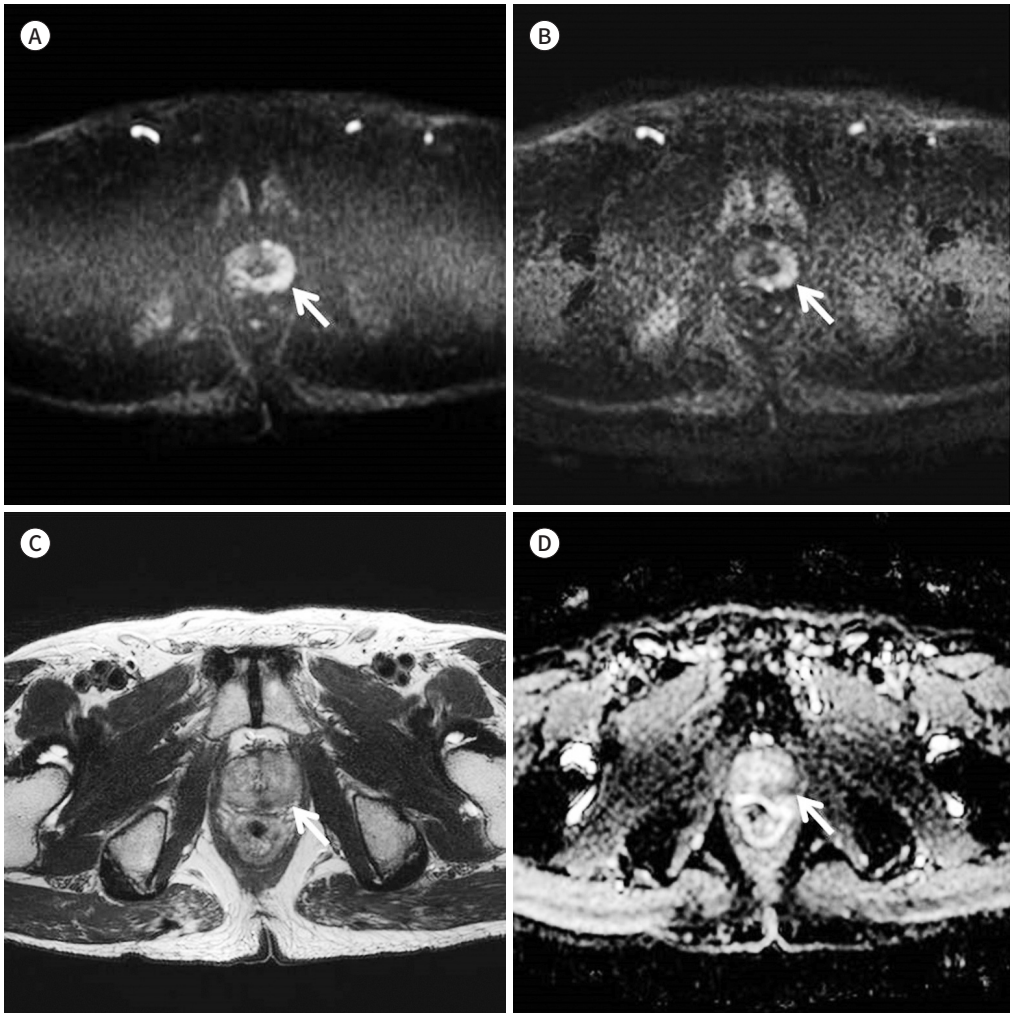
CNR between aDWI b2000 and cDWI b2000 were compared by the paired samples *t*-test.

RESULTS

PATIENT DEMOGRAPHICS

The study population comprised patients with GS 6 (n = 16), GS 7 (3 + 4, n = 30; 4 + 3, n = 23), GS 8 (n = 9) and GS 9 (n = 10). The mean interval between the radical prostatectomy and preoperative MRI was 30 days (range: 5–60 days). Their demographics are presented in Table 2.

Fig. 3. A 68-year-old male with histopathologically proven prostate adenocarcinoma of Gleason score 7 (3 + 4) after radical prostatectomy.
A. aDWI (b = 2000 s/mm²) shows a curvilinear high SI lesion (arrow) in the left middle peripheral zone.
B. cDWI (b = 2000 s/mm²) shows a similar high-SI lesion (arrow) at the corresponding location.
C. T2-weighted image shows intermediate-to-low-SI lesion (arrow) in the same area.
D. Apparent diffusion coefficient map generated from 3A shows reciprocal low-SI lesion (arrow) in the corresponding area.
aDWI = acquired diffusion-weighted imaging, cDWI = computed diffusion-weighted imaging, SI = signal intensity



COMPARISON OF DETECTION SENSITIVITY

For reviewer 1, the detection sensitivity between cDWI b2000 and aDWI b2000 showed, for all tumors (Fig. 2) and CSC (Fig. 3), no significant difference (p = 1.000, respectively). The sensitivities of cDWI b2000 and aDWI b2000 for detection of all PCa were both 94% (83/88); the false positive (FP) and false negative (FN) numbers for cDWI b2000 were both 5, and those for aDWI b2000 were 4 and 5, respectively. For CSC, the sensitivities were both 99% (71/72).

For reviewer 2, the detection sensitivity between the cDWI b2000 and aDWI b2000 also showed no significant difference for all tumors and CSC (p = 1.000, respectively). The sensitivities of cDWI b2000 and aDWI b2000 for detection of all PCa were both 90% (79/88); the FP

Table 3. Location of Each Region of Interest from both DWI Techniques

Location	Reviewer 1				Reviewer 2			
	aDWI		cDWI		aDWI		cDWI	
	CSC (*n* = 72)	Non-CSC (*n* = 16)	CSC (*n* = 72)	Non-CSC (*n* = 16)	CSC (*n* = 72)	Non-CSC (*n* = 16)	CSC (*n* = 72)	Non-CSC (*n* = 16)
Peripheral zone	33	8	33	8	30	9	30	9
Transitional zone	19	4	19	4	19	2	19	2
Fibromuscular zone	4	0	4	0	4	0	4	0
Diffuse	15	0	15	0	15	0	15	0

aDWI = acquired DWI, cDWI = computed DWI, CSC= clinically significant cancer (Gleason score ≥ 7), DWI = diffusion-weighted imaging

Table 4. Distribution of PI-RADS v.2.1 Scores between Image Sets

Location	PI-RADS 3				PI-RADS 4				PI-RADS 5			
	Reviewer 1		Reviewer 2		Reviewer 1		Reviewer 2		Reviewer 1		Reviewer 2	
	aDWI	cDWI	aDWI	cDWI	aDWI	cDWI	aDWI	cDWI	aDWI	cDWI	aDWI	cDWI
Peripheral zone	1	0	7	3	15	16	17	24	28	28	20	17
Transitional zone	0	1	4	5	7	7	7	9	18	17	14	11
Fibromuscular zone	0	0	0	0	0	0	1	1	4	4	3	3
Diffuse	0	0	0	1	0	0	0	0	15	15	15	14

aDWI = acquired diffusion-weighted imaging, cDWI = computed diffusion-weighted imaging, PI-RADS = Prostate Imaging-Reporting and Data System

and FN numbers for cDWI b2000 were 5 and 9, respectively, and those for aDWI b2000 were the same. For CSC, the sensitivities were both 94% (68/72). Location of each ROI was also compared from both DWI techniques and summarized in Table 3.

INTER-OBSERVER AGREEMENT ON PI-RADS V2.1

The kappa values of cDWI b2000 and aDWI b2000 for the PI-RADS scores were 0.422 (95% confidence interval [CI], 0.240–0.603) and 0.495 (95% CI, 0.308–0.683), respectively. These results indicated that both cDWI b2000 and aDWI b2000 showed moderate agreement. In addition, the inter-method agreement between the two image sets was good (0.619, 95% CI, 0.457–0.780) for reviewer 1 and moderate (0.533, 95% CI, 0.335–0.730) for reviewer 2. The distribution of PI-RADS scores between both image sets for each reviewer is summarized in Table 4.

IMAGE QUALITY

QUALITATIVE ANALYSIS

For reviewer 1, the overall image quality score of cDWI b2000 (median 4, interquartile range, 4.0–5.0) was higher than that of aDWI b2000 (median 4, interquartile range, 3.0–4.0) (p = 0.0001).

For reviewer 2, cDWI b2000 showed a higher image quality score (median 5, interquartile range, 3.5–5.0) than aDWI b2000 (median 4, interquartile range, 3.0–5.0) (p < 0.0001).

QUANTITATIVE ANALYSIS

The SNR of aDWI b2000 (95.683 ± 40.714) was higher than that of cDWI b2000 (52.266 ± 36.651) ($p < 0.0001$). Whereas, the CNR of cDWI b2000 (69.119 ± 59.795) was higher than that of aDWI b2000 (56.342 ± 39.136) ($p = 0.0226$).

DISCUSSION

Our study revealed that cDWI b2000 showed similar detection sensitivity to that of aDWI b2000 for detection of PCa. Our results correspond with those of previous studies (7-9). Jendoubi et al. (7) compared cDWI b2000 with aDWI b2000 for PCa detection rate. Out of 62 patients who underwent MRI-transrectal US (TRUS) fusion-guided biopsy, 44 were histo-pathologically diagnosed with PCa. Diagnostic performance for tumor detection was similar between cDWI b2000 (sensitivity: 75%–82%, specificity: 58%–74%) and aDWI b2000 (sensitivity: 73%–82%, specificity: 58%–74%). Kordbacheh et al. (8) reported that the diagnostic accuracies of cDWI b2000 and aDWI b2000 in the detection of CSC were comparable for 46 patients who had been pathologically confirmed by radical prostatectomy ($n = 11$) or TRUS-biopsy ($n = 35$). The areas under the curve (AUCs) of cDWI b2000 and aDWI b2000 for detection of CSC were 0.75 (95% CI, 0.60–0.87) and 0.71 (95% CI, 0.56–0.84), respectively, and the estimated accuracies were 77% (95% CI, 62%–89%) and 73% (95% CI, 57%–85%), respectively. Verma et al. (9) likewise observed that cDWI b2000 yielded comparable diagnostic performance to that of aDWI b2000 for detection of CSC. A total of 94 patients who had been pathologically confirmed as PCa by MRI-TRUS fusion-guided biopsy were included. The authors found that the AUCs of cDWI b2000 and aDWI b2000 for detection of CSC were 0.75 and 0.73, respectively, and that the corresponding estimated accuracies were 77% and 78%, respectively.

The reason for choosing b2000 in this study was based on the result of previous study (10). The investigators revealed that b2000 provided the best zonal anatomical delineation and less distortion among cDWI b values of 1500, 2000 and 3000. In addition, recently published study reported that the optimal b value of cDWI was within a range of 1700–1900 s/mm^2 through quantitative and qualitative analyses (14).

In order to obtain aDWI b2000, an advanced MR scanner equipped with the high gradient power of 3T is required in general; however, its accessibility is very limited worldwide. Furthermore, the mean acquisition time for aDWI b2000 (approximately 4 minutes or more) could be an obstacle to rapid image acquisition and enhanced productivity, though the exact time required will depend on the specific parameters used in given institutions. Based on the capability of transforming aDWI b values of 0, 100, and 1000 into the cDWI b2000 format under the mono-exponential decay model and the comparableness of diagnostic performance between cDWI b2000 and aDWI b2000 (as reported both herein and elsewhere) (7), we also suggest that cDWI b2000 could replace aDWI b2000, to the significant advantage of radiologists in terms of time savings and the non-necessity of high-end MRI machines. In our opinion, as PI-RADS v2.1 recommends DWI acquisition with at least two b values in predetermined ranges, including one low b value at 0–100 s/mm^2 (preferably 50–100 s/mm^2) and one intermediate b value at 800–1000 s/mm^2 (6), the extrapolated cDWI b2000 could be easily incorporated into routine practice instead of a separate acquisition of aDWI b2000.

With regard to PI-RADS scores, our study revealed moderate inter-observer agreement for both cDWI b2000 and aDWI b2000 based on PI-RADS v2.1. A recent study by Bhayana et al. (15) reported moderate inter-observer agreement (kappa = 0.42) based on 80 peripheral zone and transitional zone (TZ) lesions among 6 radiologists in cases of aDWI b1500. Meanwhile, other investigators reported good or substantial inter-observer agreement for evaluating TZ lesions by using aDWI b2000 based on PI-RADS v2.1 (16, 17). Wei et al. (16) evaluated PI-RADS scores for 355 patients with TZ lesions and found substantial agreement (kappa = 0.70). Tamada et al. (17) also observed good agreement (kappa = 0.645) for their cohort of 58 patients with TZ lesions.

In terms of image quality, our results showed that cDWI b2000 was better than aDWI b2000, which correspond well with other studies that found higher image quality for cDWI b2000 relative to aDWI b2000 (7, 9). They reported that cDWI b2000 had better overall image quality, better background signal suppression, better anatomic clarity, and less distortion compared with aDWI b2000 on a 5-point Likert scale ($p < 0.001$) (7), and that the overall subjective image quality of cDWI b2000 was superior to that of aDWI b2000 based on a similar 5-point scale ($p < 0.001$) (9). This qualitative result could be supported by the quantitative analysis. In our opinion, the higher CNR of cDWI b2000 could play a major role in the higher subjective image quality in spite of the lower SNR than aDWI b2000.

There are several limitations of this study. First, a single-center, retrospective study design could be considered. However, the use of whole mount histology sections as ground truth in the large study population would be merits to overcome the inherent limitation. Second, the level of experience of reviewers who took part in the diagnostic task was not that of experts. This level of experience might be one of reasons why the inter-observer agreements of current study are a bit low compared with previous studies (16, 17). However, the effect of reading experience on the task was beyond the scope of the study. Therefore, our observation could be valid in general radiologists or those with similar experience in reading prostate MRI. Third, sensitivity among the diagnostic predictive values was presented alone in the results section. However, it was inevitable because the study population consisted of patients who underwent radical prostatectomy.

In conclusion, cDWI b2000 showed comparable detection sensitivity and sustained moderate inter-observer agreement with aDWI b2000 for detection of PCa.

Author Contributions

Conceptualization, K.S.H.; data curation, K.S.H., K.Y.J.; formal analysis, K.S.H.; investigation, all authors; methodology, K.S.H.; project administration, K.S.H.; resources:, K.S.H.; software, K.S.H.; supervision, K.S.H.; validation, all authors; visualization, K.S.H., K.Y.J.; writing—original draft, all authors; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Funding

None

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JOURNAL of THE KOREAN SOCIETY of RADIOLOGY

전립선암 발견을 위한 계산형 확산강조영상 b2000과 실제 획득한 b2000 영상의 비교

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목적 계산형 확산강조영상 b2000과 실제 획득한 확산강조영상 b2000 사이에 전립선암 발견을 위한 민감도 및 관찰자 간 일치도를 비교하였다.

대상과 방법 근치적 전립선 절제술 및 확산강조영상(b, 0, 100, 1000, 2000 s/mm^2)을 포함한 수술 전 3 Tesla 자기공명영상을 통해 전립선암으로 진단받은 총 88명의 환자가 연구에 포함되었다. 계산형 확산강조영상 b2000은 실제 획득한 확산강조영상 b0, 100, 1000으로부터 단일 지수 감쇠 모델에 의해 계산되었다. 두 명의 독립된 검토자가 4주 간격으로 무작위 순서로 두 영상 세트를 검토하여, 가장 큰 종양에 대해 관심 영역을 그렸고, Prostate Imaging-Reporting and Data System 2.1에 기반한 점수를 기록하였다. 전층 절편 조직 검사가 참고 기준으로 제공되었다.

결과 연구에 포함된 환자의 글리슨 점수는 6 (n = 16), 7 (n = 53), 8 (n = 9), 9 (n = 10)로 구성되었다. 두 명의 검토자 모두 계산형 확산강조영상 b2000과 실제 획득한 확산강조영상 b2000 간 전립선암 발견에 대한 민감도 차이는 없었다(검토자 1, 모두 94% [83/88]; 검토자 2, 모두 90% [79/88], 모두 p = 1.000). 관찰자 간 PI-RADS 점수에 대한 일치도는 계산형 확산강조영상에서 0.422 (95% 신뢰구간, 0.240–0.603), 실제 획득한 확산강조영상에서 0.495 (95% 신뢰구간, 0.308–0.683)였다.

결론 계산형 확산강조영상 b2000과 실제 획득한 확산강조영상 b2000은 전립선암 발견 민감도에 차이가 없고, 관찰자 간 일치도는 유지되었다.

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