Computed diffusion-weighted imaging using 1.5-T magnetic resonance imaging for prostate cancer diagnosis.

Abstract

Computed Diffusion-Weighted MR Imaging (cDWI) is gradually known to be useful to detect the prostate cancer. We found that cDWIs (b=2000 s/mm2) were easily generated from measured DWIs (mDWIs) with image processing using Image J and a Windows-based calculation formula and that the contrast ratio (CR) of computed DWIs (b=2000) appeared to be higher than the CR of measured DWIs (b=1000 s/mm2) and measured DWIs (b=2000 s/mm2). The diagnostic ability of cDWI2000 for prostate cancer detection was equivalent to mDWIs 2000. There is a possibility that cDWI2000 can replace mDWIs 2000.

Abbreviations:

cDWI, Computed Diffusion-Weighted MR Imaging ; mDWI, measured Diffusion-Weighted MR Imaging ; DWI, Diffusion-weighted imaging ; MRI, magnetic resonance imaging ; T2-WI ,T2-weighted images ; ADC, apparent diffusion coefficient ; DICOM, Digital Imaging and Communications in Medicine ; ROIs, regions of interest ; SI, signal intensity ; ROC curve, Receiver operating characteristic curve ; Az , The areas under the curves ; Sen, sensitivity; Spe, Specificity ; PPV, positive predictive value ; NPV, negative predictive value; Acc, accuracy; PACS, Picture Archiving and Communication Systems

Keywords: Computed diffusion-weighted imaging, prostate cancer, contrast ratio, high b-value, MRI, 1.5T

Introduction

Diffusion-weighted and magnetic resonance imaging (DWI and MRI, respectively) are now being widely used in the body cancer imaging for detection, characterization, and assessment of treatment response [1–4].

It has been reported that DWI obtained with ultra-high b-values provide good contrast between cancerous and background tissue for a better prostate cancer detection [5–7]. Furthermore, some studies in particular have demonstrated the advantage of DWI obtained with a b-value of 2000 s/mm^2 rather than with 1000 s/mm^2 for prostate cancer diagnosis using either 1.5T or 3T MR systems [5–10].

The Computed DWI (cDWI) is an introduced computational technique that can produce any b-value images from DWI acquired with at least two different b-values [11,12]. Blackledge et al have reported that the cDWI technique allows higher b-value images to be obtained with a good SNR (signal noise ratio) at 1.5T MRI because it can suppress background noise while maintaining the original lesion signal[11,12].

The cDWIs of b=2000 s/mm^2 (cDWIs-2000) in MRI have gradually become known to be useful in detecting prostate cancer compared with measured original DWIs (mDWIs) of low b-value, using 3-T MR systems [10,12,13]. To our knowledge, there are few reports about cDWIs-2000 to detect prostate cancer using 1.5-T MR systems.

In this study, we aimed to compare the contrast ratio (CR) of cDWIs-2000 with mDWIs-1000 (i.e., b = 1000 s/mm^2) and mDWIs-2000 for prostate cancer and to evaluate the prostate cancer detection of computed diffusion-weighted images of cDWIs-2000 comparison with those of mDWIs using 1.5-T MR systems.

Materials and Methods

Patients

Our Institutional Review Board approved this retrospective study and waived the need for informed consent from the patients. According to the hospital's surgical-information system and radiology-information system, between October 2012 and September 2013, we found a total of 24 patients with prostate cancer underwent 1.5-T MR examinations, including DWIs (b=0, 1000, 2000 s/mm^2) of the prostate, followed by radical prostatectomy consecutively, in our hospital. We excluded the patients (n=6) whose MR examinations or prostatectomy were undergone in another hospital. The general exclusion criteria for MR imaging (e.g. claustrophobia, pregnancy, and implanted pacemaker) were applicable. Patients (n=5) with contraindications for hyoscine-N-butylbromide (Buscopan, Boehringer Ingelheim), including hypersensitivity to anticholinergic drugs, benign prostate hyperplasia, paralytic ileus, closed angle glaucoma, and

shallow anterior chamber, were also excluded.

MR technique

The MR scans were performed with the 1.5-T MR unit (Signa HDxt; GE Healthcare, Milwaukee, WI) using an 8-channel phased-array body coil for the signal. The endorectal coil was not used. A peristalsis was suppressed by intramuscular administration of 20 mg of scopolamine butylbromide (Buscopan; Nippon Boehringer Ingelheim, Tokyo, Japan) or 1 mg of glucagon (Glucagon-G Novo; Eisai Co. Ltd., Tokyo, Japan).

T2-weighted turbo spin-echo images, covering the entire prostate gland and seminal vesicles, were acquired in two orthogonal planes: axial and coronal. The acquisition parameters for T2-weighted images (T2-WI) and DWIs are shown in Table 1. Although T1-weighted images and dynamic contrast-enhanced images were also obtained for clinical examinations, they were not evaluated in this study.

Method for computed DWIs

The apparent diffusion coefficient (ADC) was calculated with ADC=ln [−Sm/S0] / (bm-b0) using two mDWI signals, S0 and Sm, based on a mono-exponential model. ADC maps were constructed according to this equation on the basis of a voxel-wise calculation. Next, the cDWI signal at b = bc was obtained by the equation Sc = S0 exp [− (bc-b0) ADC] [11]. Using the

Digital Imaging and Communications in Medicine (DICOM) data, cDWIs-2000 were generated from real mDWIs at b-values of 0 and 1000 with image processing using Image J and a Microsoft® Windows®-based calculation formula. Image J is well known as an open-source image-processing program designed for multidimensional scientific images [14,15].

Analysis and assessment

Quantitative assessment

The acquired images were anonymized and collected in the DICOM format. The circular regions of interest (ROIs) were placed on real mDWIs-2000, by the two genitourinary radiologists (_. _. had 11 years and _. _. had 18 years of experience in prostate MR imaging) in the consensus, within the malignant or normal lesions with reference to the histopathological findings of radical prostatectomy. For setting the ROIs with more precision, the ADC map using b=0 and 2000 s/mm^2 was also referenced. The same ROIs were then copied onto other DWIs acquired in the same axial section. The ROIs were created with the DICOM viewer (SDS DICOM Viewer; Techmatrix Ltd., Tokyo, Japan) and Image J. The mean signal intensity (SI) of both cancerous and non-cancerous lesions in the same zonal anatomy region on mDWIs-1000, mDWIs-2000, and cDWIs-2000 of all 24 patients was measured. Because DWIs were obtained with parallel imaging, the CR between cancerous and non-cancerous lesions was used to

quantify the analysis. Each CR was calculated as CR= (Sca - Snon-ca) / (Sca + Snon-ca) [16], where Sca is the average SI for the malignant lesion and Snon-ca is that for the non- malignant lesion. Finally, the CRs for the three DWIs (mDWIs-1000, mDWIs-2000, and cDWIs-2000) were compared statistically in each zone (peripheral zone [PZ] and transitional zone [TZ]) and in overall areas.

Detection Capability Assessment

To compare the capability of the DWIs for facilitating the detection, three combinations of images, protocol A (T2-WI + mDWIs-1000), B (T2-WI + mDWIs-2000), C (T2-WI +cDWIs-2000), were independently evaluated by the same two genitourinary radiologists (_. _. and _. _.) for the likelihood of the presence of cancer by prostatic region.

A five-point scale was used for evaluation: 5, definitely present; 4, probably present; 3, equivocal; 2, probably absent; 1, definitely absent. For region-specific comparisons among the protocols, the prostate was divided into the eight regions as for the pathological analysis. Each dataset was then independently reviewed by the two readers with a minimum interval of one month to avoid any decision threshold bias due to reading-order effect.

In addition, for both readers there was an interval of at least one month between quantitative and qualitative image analysis sessions. These assessments were performed before

the previously mentioned quantitative and qualitative image analyses. The criteria for the diagnosis of prostate cancer on each of the MR images were based on those used for several previous studies[6,8,17,18];on T2-WI, a lesion in the PZ was considered to be definitely malignant if it showed homogeneous low signal intensity with an irregular shape, unclear margin and diffuse extension with mass effect. For the TZ, a mass showing homogeneous low signal intensity on the T2WI accompanied by destruction of normal structures, such as the surgical capsule or anterior fibromuscular stroma without a capsule, was considered to be definitely malignant. A lesion detected on DWI was considered malignant if it showed high intensity relative to the background prostate parenchyma. We determined that the area with rank 4 or 5 were considered to be detectable by 1.5T MRI.

Pathological analysis

Prostate cancers in all 24 patients were proven histopathologically after radical prostatectomy. The Prostatectomy specimens were marked with ink, fixed overnight in 10% buffered formalin, and sliced from the apex to the base at 3- to 4- mm intervals. All glass slides obtained from the pathological step-section slices were reviewed by one experienced pathologist with 12 years of experience, who did not refer to the MRI findings. The locations of all tumor foci were recorded on a standardized diagram of the prostate. Finally, we compared the MRI findings directly using

step-section pathological maps for consensus. Specimens with malignant focal lesions were included in this study if the maximum diameter of the lesion was equal to or larger than 5 mm.

For region-specific comparisons among the protocols, the prostate was divided into the same eight regions as for the pathological analysis. Totally, we examined 192 regions in 24 patients.

For radiological–pathological correlation, a region was considered positive for cancer if it contained a cancer regardless of its diameter.

Statistical analysis

CRs between cancerous and non-cancerous lesions on mDWIs-1000, mDWIs-2000, and cDWIs-2000 were compared using the Tukey–Kramer's test.

For qualitative assessment of detection capability enhancement, inter-observer agreement on the likelihood of the presence of cancer was assessed by means of kappa statistics with quadratic weighting. A kappa value of up to 0.20 was considered to indicate slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement and 0.81 or greater almost perfect agreement [19].

Receiver operating characteristic (ROC) analyses were performed for comparison of detection capability accuracy for all protocols. The areas under the curves (Az) were estimated

non-parametrically for ordinal score assessments and the ROC analyses were used. Finally, sensitivity (Sen), specificity (Spe), positive predictive value (PPV), negative predictive value (NPV) and accuracy (Acc) of the protocols were compared by means of the McNemar's test. These analyses were performed for whole prostate of all patients.

IBM SPSS (version 22.0 for Windows, IBM, Japan) was used for all statistical analyses. The P value of < 0.05 was considered significant.

Results

The patients' characteristics are summarized in Table 2. The histopathological examinations identified a total of 46 cancer foci in 24 patients. Of 46 cancer nodules, 14 were in the TZ and 32 were in the PZ. There are 192 target areas totally in 24 patients.

Table 3 shows the CRs of cancerous compared with non-cancerous tumors in each zonal anatomy on mDWIs-1000, mDWIs-2000, and cDWIs-2000. The highest CR was obtained with cDWIs-2000. The CR of cDWIs-2000 was significantly higher than that of mDWIs-1000 and mDWIs-2000 ($P < 0.05$, Tukey–Kramer's test) in all of the prostate areas. The differences between CRs of mDWIs-1000 and CRs of mDWIs-2000 were not significant in all of the prostate areas. Representative examples are shown in Figure.

Table 4 shows the comparison of diagnostic performance of all methods. The area under the curve (Az) of ROC analyses by reader 1 (_._) was protocol A (0.73) , protocol B (0.75) and protocol C (0.78). And those by reader 2 (_._) was protocol A (0.71) , protocol B (0.76) and protocol C (0.77). The sensitivity of cDWI2000 was superior to that of mDWI, however the diagnostic performance of all methods did not differ significantly. The inter-observer agreement was rated as moderate agreement (0.435-0.521) for all protocols, A (T2-WI+ mDWIs-1000), B (T2-WI+ mDWIs-2000), and C (T2-WI+ cDWIs-2000).

Discussion

This study shows that the highest CR was obtained with cDWIs-2000 and the CR of cDWIs-2000 was significantly higher than that of mDWIs-1000 and mDWIs-2000 in all prostate areas and in each zonal anatomy, for the detection of prostate cancer using 1.5-T MR systems. However, cDWIs-2000 were not significantly superior or inferior to mDWIs in detecting prostate cancer even with the high contrast ratio using 1.5-T MR systems. Thus, this study indicates that cDWIs-2000 can be used as suitable substitute for mDWIs2000 using 1.5-T MR systems.

The DWIs and ADC map using a high b-value is generally known to be useful to detect prostate cancer on 3T-MRI and 1.5T-MRI [6,8]. High b-value on mDWI produce decreasing signal noise ratio (SNR) [8].Using mDWIs-2000 on 1.5T MRI unit, it need more time than only mDWIs-1000 in order to obtain the same image quality and mDWIs-2000 have the more noise problem. Therefore the high power field system with high SNR fit high b-value on mDWI. In results, cDWI-2000 is more effective on 1.5T MR system than on 3.0T MR system, because cDWI can benefit from the high SNR of the original lower b-value image sets due to lesser artifacts and more anatomical detail than mDWI-2000 on 1.5T MR system [20]. Furthermore cDWI-2000 do not need high power field system [20]. The 3.0T MR system is now widely used, however, there are many hospitals in which only 1.5T MR system is running.

The previous reports about the detectability of prostate cancer on 3T MRI using cDWIs showed that cDWIs are useful in detecting prostate cancer and are as valuable as mDWIs-2000[16,21]. In this study, the diagnostic performance of all methods did not differ significantly, however the sensitivity of cDWI-2000 was superior to that of mDWI. On the other hand, the specificity of cDWIs-2000 was inferior to that of mDWI. Because cDWIs had higher CR than that of mDWI, the readers might more easily detect abnormal signal intensity as a

prostate cancer. The cDWIs-2000 by adding the other sequences, such as ADC map and dynamic MRI, may be able to improve specificity.

If cDWIs-2000 has the same image quality as the real mDWIs-2000 and cDWI technique is more likely than acquired images to highlight differences in signal intensity between cancerous and non-cancerous tissue on images with high b-values, cDWIs-2000 would be appropriate as an alternative to mDWIs-2000. There is a possibility that cDWIs-2000 can replace mDWIs-2000.

The cDWI has several advantages. One is that images with high b-values can be obtained regardless of the MR system's ability. Moreover, cDWI can make high b-value images maintain tissue signal intensity without depending on TE. Another possible advantage is that distortion on images with high b-values would be reduced with cDWI. Images with high b-values for the MR system sometimes suffer from distortion because of the heterogeneity of the gradient field. Such distortion can be reduced with cDWI because images with lower b-values can be used for creating images with higher b-values. Moreover, we do not need special computers or special software to create cDWIs, which means that they do not need to cost extra. We can easily create cDWIs from another hospital's MR DICOM data, unaffected by imaging devices or magnetic forces.

There are some limitations to this research, such as the small number of cases in this single-institutional retrospective study. We must examine more cases, prospectively, comparing their CRs, and checking and evaluating the utility of the higher CR of cDWIs-2000 in the detectability of prostate cancer in clinical situations. If possible, the same patients are examined by 3T and 1.5T at the same time, we need to evaluate each image quality of the cDWI-2000, mDWI-1000 and mDWI-2000, in the further study. Second, in the cases that we could identify the cancer site, but we described the wrong major presence sites of cancer on MRI, because the prostate was a small organ, our answer of the interpretation did not match the correct answer in pathological findings. Therefore we may underestimate the possibility that the detection rate of cancer. Third, although there was more than one lesion per patient, the cluster analysis was not performed. Fourth, those who participated in this study have enough experience for the interpretation of prostate MRI. It will need to be examined whether the beginners of the prostate image interpretation can detect prostate cancer similarly using cDWIs-2000, in the future. Fifth the creation of cDWIs requires mDWIs taken with two or more different b-values and does not depend on the magnetic force of the MRI unit. In our hospital, the DWIs were obtained by b=0, 1000 and 2000. Therefore, this study did not include the influence of the combinations of b-values with the cDWIs for prostate cancer detection on 1.5T MR. Ueno et al reported the effect of the combinations of b-values on 3.0T MR [22]. They

reported the combinations of b-values influenced image quality and diagnostic ability of cDWIs for prostate cancer detection and the combinations of b > 100 and b > 500 smm-2, as well as b = 0 and b = 1000smm-2, were optimal in their study. We need to evaluate the influence of the combinations of b-values on each image quality using 1.5T MR in the further study. Sixth, in theory, we can make cDWIs from other hospitals' DICOM data; however, in this study we did not use trial images. Seventh, the image reconstruction using Image J is time-consuming in order to require the retrieval of the data of the Picture Archiving and Communication Systems (PACS). cDWIs-2000 for each patient case can be created in about 3 minutes. On this point, it is easy and convenient to create the cDWIs using Image J and a Windows-based calculation formula. However, in a clinical situation, it would be suggested the retrieval of the data from PACS and the making cDWI in all cases are time-consuming. We did not consider about what this process can conveniently be carried out routinely in clinical situation.

In conclusion**,** the cDWIs-2000 were easily generated from mDWIs with image processing using Image J and a Windows-based calculation formula. CRs of cDWIs -2000 appear to be higher than CRs of mDWIs-1000 and mDWIs-2000. The diagnostic ability of cDWI2000 for prostate cancer detection was equivalent to mDWIs-2000. There is a possibility that cDWI-2000 can replace mDWIs-2000.

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All authors have no conflict of interest to declare.

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Table 1 MR imaging parameters

Parameter	T2-WI	mDWIs1000	mDWIs2000
Acquisition plane	axial	axial	axial
TR/TE (ms)	6800/85	5200/72	6500/84
Flip angle (°)	90	90	90
ETL/EPI factor	14	96	96
ASSET factor	NA	2.0	2.0
Phase encoding direction	RL	AP	AP
b-values (s/mm2)	NA	0,1000	0,2000
Fat saturation	CHESS	SSRF	SSRF
FOV (mm)	220×220	300×300	300×300
Acquisition matrix	256×224	256×256	256×256
Slice thickness/gap (mm)	4.0/0.5	4.0/0.5	4.0/0.5
Number of slices	20-25	20-25	20-25
Number of excitations	2	7	6
Acquisition time (s)	160	151	163

Note:TSE: turbo spin-echo, TR: repetition time, TE: echo time, ETL:echo train length, EPI: echo-planar imaging, ASSET: array spatial sensitivity encoding technique, CHESS:chemical shift selective,SSRF:spectral special radio frequency, FOV: field of view

Table 2 Characteristics of the study subjects

Age (years)	Mean and SD		70.2 ± 6.0
	range		56 - 83
Initial PSA (ng/ml)	Mean and SD		9.17 ± 8.28
	range		3.29 - 45.31
Number of tumors per patient			
	Median		2
	range		1.0 - 4.0
Pathological stage			
	T2a		2 (8.3)
	T2c		15 (62.5)
	T3a		7 (29.2)
Number of Cancer nodule			46
	PZ cancer		32 (69.6)
	TZ cancer		14 (30.4)
Tumor size (mm)	All cancer nodules	Mean and SD	13.5 ± 8.5
		range	5 - 35
	PZ cancer	Mean and SD	14.3 ± 7.8
		range	5 - 35
	TZ cancer	Mean and SD	17.8 ± 9.7
		range	8 - 35
Highest Gleason Score	6 (3+3)		11 (23.9)
	7 (3+3,3+4)		32 (69.6)
	8 (4+4)		1 (2.2)
	9 (4+5,5+4)		2 (4.4)

Note: The figures in parentheses indicate percentage unless otherwise indicated.

Table 3：Contrast ratio of cancer nodules compared with non-cancer area

DWIs	Contrast ratio (mean ±SD)	
All cancer nodules		
mDWI 1000	0.115 ± 0.137	
mDWI 2000	0.126 ± 0.119	*
		]*
cDWI 2000	0.388 ± 0.188	
TZ cancer nodules		
mDWI 1000	0.126 ± 0.102	
mDWI 2000	0.109 ± 0.120	*
		]*
cDWI 2000	0.304 ± 0.200	
PZ cancer nodules		
mDWI 1000	0.111 ± 0.145	
mDWI 2000	0.150 ± 0.121	*
		]*
cDWI 2000	0.403 ± 0.183	

Note; * shows *P* values＜0.05.

Table 4.:Comparison of diagnostic performance of all methods

Protocol	Reader	Sensitivity	Specificity	Accuracy	PPV	NPV	Az
A：T2WI+mDWI1000	1	0.51	0.95	0.86	0.75	0.88	0.73
	2	0.44	0.98	0.86	0.86	0.87	0.71
B：T2WI+mDWI2000	1	0.59	0.91	0.84	0.65	0.89	0.75
	2	0.59	0.93	0.85	0.69	0.89	0.76
C：T2WI+cDWI2000	1	0.68	0.87	0.83	0.58	0.91	0.78
	2	0.61	0.93	0.86	0.71	0.90	0.77

Note: PPV: positive predictive value, NPV: negative predictive value, Az: area under the curve.

Figure Legend

Figure 1; A 67 years-old prostate cancer patient with Gleason score of 3+4=7, pT2a, initial PSA of 3.763 ng/ml. With T2-WI (a), the slightly low signal intensity lesion is shown in the right peripheral zone (arrow). With mDWI-1000 (b) and m-DWI2000 (c), abnormal signal intensity lesions are shown in the right peripheral zone (arrow). With c-DWI2000 (d), the abnormal signal of the right peripheral zone remains (arrow). Each CR were as follows, mDWI-1000 (b); 0.14, mDWI-2000 (c); 0.35 and cDWI-2000 (d); 0.40. (e) ADC map shows low spot in the same place (arrow). (f) The pathological specimen confirms prostate cancer in the right peripheral zone (asterisk).

Figure 2; A 75 years-old prostate cancer patient with Gleason score of 3+4=7, pT3a, initial PSA of 7.657 ng/ml. With T2-WI (a), the slightly low signal intensity lesion is shown in the transitional zone (arrow). With mDWI-1000 (b), mDWI-2000 (c) and cDWI-2000 (d), abnormal signal intensity lesions are shown in the same place (arrow), each CR were as follows, mDWI-1000 (b) ;0.31, mDWI-2000 (c) ; 0.45and cDWI-2000 (d) ;0.63.

(e) ADC map shows low spot in the same place (arrow). (f) The pathological specimen confirms prostate cancer in the anterior part of transitional zone (asterisk).