Diffusion-weighted whole-body imaging with background body signal suppression/T2 image fusion for the diagnosis of colorectal polyp and cancer

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Abstract. Diffusion-weighted whole-body imaging with background body signal suppression/T2 image fusion (DWIBS/T2) is useful for the diagnosis of cancer as it presents a clear contrast between cancerous and non-cancerous tissue. The present study investigated the limitations and advantages of DWIBS/T2 with regards to the diagnosis of colorectal polyp (CP) or cancer (CRC). The current study included patients diagnosed with CP or CRC following colonoscopy, who were subjected to DWIBS/T2 between July 2012 and March 2015. Patient records were analyzed retrospectively. Patients were subjected to DWIBS/T2 when they presented with abdominal cancers or inflammation. Colonoscopy was performed as part of screening, or if patients had suspected colon cancer or inflammatory bowel disease. A total of 8 male and 7 female patients were enrolled in the present study. All patients, with the exception of one who had been diagnosed with CRC following colonoscopy, had positive results and all patients diagnosed with CP following a colonoscopy, with the exception of one, had negative results on DWIBS/T2. Thus, CRC was detected by DWIBS/T2, while CP was not (P=0.0028). The diameter of CRC lesions was significantly larger than that of CP (P<0.0001) and that of lesions positive on DWIBS/T2 was significantly larger than that of negative lesions (P=0.0004). The depth of invasion tended to be greater for lesions positive on DWIBS/T2 compared with that of negative ones. This indicated that DWIBS/T2 may be suitable for the detection of CRC but not for detection of CP. The results of DWIBS/T2 may also be affected by lesion diameter and depth of invasion.

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Introduction

Colorectal cancer (CRC) develops from colorectal polyps (CP) as a consequence of the adenoma-carcinoma sequence (1). CRC is frequently encountered in clinical settings and has a poor prognosis (2). To improve the prognosis of patients with CRC, a prompt and accurate diagnosis is required. Preliminary screening for CRC is performed by fecal occult blood testing and colonoscopy is performed for the final diagnosis (3). However, despite being preferable over all other available diagnostic modalities in terms of practicability and affordability, fecal occult blood testing is not a reliable technique (4). Therefore, colonoscopy is currently the gold standard for the diagnosis of CRC (5,6).

Diffusion-weighted whole-body imaging with background body signal suppression (DWIBS) images are obtained using multiple-signal averaging, pre-pulse fat suppression and heavy diffusion weighting during free breathing (7). DWIBS is based on DWI that utilizes the random movement of water at the molecular level, known as Brownian motion (8,9). This imaging technique provides a strong contrast between cancerous tissue and the surrounding non-cancerous tissue, which is useful in the detection and staging of cancer (10). One major limitation of DWIBS is that anatomical assessment may be difficult (11,12). To overcome this, fusion images of DWIBS and T2-weighed images (T2WI) are created by overlapping DWIBS images with T2WI (DWIBS/T2) images using an Extended MR Workspace workstation (10,13,14).

DWIBS/T2 therefore clearly integrates functional and anatomical information.

The current study retrospectively analyzed DIWBS/T2 images from patients with CRC and CP to evaluate the advantages and limitations of this technique for the diagnosis of CRC and CP.

Materials and methods

Patients. Patient records from the Department of Gastroenterology at the National Hospital Organization Shimoshizu Hospital, including imaging results of patients from July 2012 until March 2015, were retrospectively analyzed. Each patient with suspected abdominal cancers or inflammation was subjected to DWIBS/T2 once for further examination, using magnetic resonance imaging (MRI), between July 2012 and March 2015. Colonoscopy was performed as part of screening or when patients had suspected colon cancer or inflammatory bowel disease. The enrolled patients were those who were subjected to colonoscopy and DWIBS/T2, and whose pathological diagnosis was available via biopsy, endoscopic mucosal resection, or surgical specimens. Patients were excluded from the present study when colonoscopy, DWIBS/T2, and pathological diagnosis were not available. A total of 15 patients were enrolled, comprising of eight male (mean age, 72.4±7.6 years) and seven female (mean age, 76.1±3.4 years) patients. Positron emission tomography/computed tomography (PET/CT) was performed for one patient with a colon polyp that was diagnosed as CRC via endoscopic mucosal resection. The present study was approved by the ethics committee of the National Hospital Organization Shimoshizu Hospital (Yotsukaido, Japan). The study was not considered a clinical trial since the procedures involved were performed as a part of routine clinical practice. Written, informed consent was obtained from all patients.

Diameter and depth of invasion. The diameter of the CP was measured using colonoscopy and the diameter of the CRC lesion was measured from surgical specimens using a ruler. Colonoscopy was performed using a CF-Q260A/I or PCF-Q260AI colonoscope (Olympus Corp., Tokyo, Japan). Therefore, the diameter of CRC lesions was only determined for patients who underwent surgery (n=5). Depth of invasion (mm) of the surgical specimen was determined by macroscopic examination by two pathologists.

MRI. All MRI studies were performed using a 1.5 Tesla scanner (Achieva, complementary software version 3.2.2; Philips Medical Systems, B.V., Eindhoven, The Netherlands). T1WI, T2WI and DWI were obtained with pulse sequences, as depicted in Table I. DWIBS/T2 images were constructed with an Extended MR WorkSpace (version 2.6.3.4; Philips Medical Systems). The DWI gradients were applied along the X, Y, and Z axes prior to and following a 180˚ inversion pre-pulse in order to obtain fat-saturated, isotropic images with DWI sensitivity. The following parameters were used for a single stack: b-value 0 and 800 sec/mm^2; repetition time, echo time and inversion recovery, 6,960.79 and 150 msec, respectively; acquisition matrix, 176x115 and reconstruction matrix, 256; field of view (FOV) right/left: 530 mm, anterior/posterior: 349 mm and feet/head: 226 mm; slice thickness, 6 mm; size of reconstructed voxel, 2.07x2.08x6 mm^3; four averages. One radiologist and one gastroenterologist analyzed the DWIBS/T2 images. To rule out T2 shine-through and distinguish malignant lesions from non-malignant causes of restricted diffusion, a positive apparent diffusion co-efficient (ADC) map was generated by ADC reduction (15).

PET/CT imaging. PET/CT was performed at the Diagnostic PET Imaging Center, Department of Radiology, Sannoh Medical Center (Chiba, Japan) (16). Patients fasted overnight or for at least 6 h prior to injection of 4.0 MBq/kg fluorodeoxyglucose (^{18}F-FDG). Images were obtained 60 min following the injection. Patients lay down in the supine position during the 60-min uptake period in order to minimize non-specific FDG uptake into the muscles. An integrated PET/CT system (Discovery ST; GE Healthcare Bio-Sciences, Pittsburg, PA, USA) was used for image acquisition. CT scanning was performed with 120 kV, 25 mA, a pitch of 1.75, a section thickness of 3.3 mm, a FOV of 50 cm and a matrix size of 512x512. Immediately following the unenhanced CT scan, a PET scan was performed with a section thickness of 3.3 mm, a matrix size of 128x128 and an acquisition time of 2.5 min. PET data sets were reconstructed iteratively using an ordered subsets expectation maximization algorithm and segmented attenuation correction (three iterations, 15 subsets) and the CT data. The standardized uptake value (SUV) was calculated using the following formula: SUV (g/ml) = regional radioactivity concentration (Bq/ml) / [injected dose (Bq) / body weight (g)] (17).

Colonoscopy. Colonoscopy was performed for patients with anemia, abdominal symptoms, a positive fecal occult blood test for screening or investigation of anemia, or for screening purposes. The devices used were CF-Q260A/I and PCF-Q260AL/I. Patients with CP were subjected to endoscopic mucosal resection as CP was considered to be a precancerous lesion. Submucosa was expanded via injection with physiological saline, and the mucosa was removed using a snare (SD-221U-25; Olympus Corp.) with a cushion of submucosa.

Statistical analysis. Values are expressed as the mean ± standard deviation unless otherwise specified. The χ^2 test was applied to evaluate the correlation between the diagnosis of CP or CRC obtained by colonoscopy and the results of DWIBS/T2. One-way analysis of variance was applied to the diameters of CP or CRC and the diameter of positive or negative results on DWIBS/T2. $P<0.05$ was considered to indicate a statistically significant difference. JMP 10.0.2 (SAS Institute, Inc., Cary, NC, USA) was used for statistical analyses.

Results

Clinicopathological characteristics. Patient clinicopathological characteristics are listed in Table II. A total of 7 patients were diagnosed with CRC and 8 patients were diagnosed with CP. All patients diagnosed with CRC following colonoscopy, with the exception of one, had positive results on DWIBS/T2. CRC presented with a clear signal in the horizontal (Fig. 1A)

Table I. Pulse sequences used in the present study.

Parameter	T1-weighted image	T2-weighted image	DWI (DWIBS)
Echo	GRE	Single-shot SE	EPI SE
TR, msec	Shortest	1,000	11,250
TE, msec	First: 2.3 (out-phase, second: 4.6 (in-phase)	90	83
Flip angle, ˚	75	90	90
NSA	1	1	4
Slice thickness, mm	8	8	5
Slice gap	1	1	0
Fat saturation	None	None	SPAIR
Phase encoding direction	Posterior-anterior	Posterior-anterior	Posterior-anterior

DWIBS, diffusion-weighted whole body imaging with background body signal suppression; GRE, gradient echo; SE, spin echo; EPI, echo planar imaging; SPAIR, spectral attenuated inversion recovery; NSA, number of signal averages; TE, echo time; TR, repetition time.

Table II. Clinicopathological characteristics of patients.

Patient no.	Gender	Age, years	Diagnosis	Pathological diagnosis	DWIBS/T2 findings	Diameter, mm	Depth of invasion	Depth of invasion, mm
1	M	67	CP	Well	(+)	15	M	3
2	M	73	CRC	Well	(+)	60	SS	12
3	F	78	CRC	Well	(+)	47	SS	12
4	M	74	CRC	Mod	(-)	30	SS	3
5	M	73	CRC	Well	(+)	63	SS	13
6	F	73	CRC	Well	(+)	55	SS	10
7	M	85	CRC	Well	(+)	N.A.	N.A.	N.A.
8	F	70	CRC	Well	(+)	N.A.	N.A.	N.A.
9	M	80	CP	Adenoma	(-)	4	N.A.	N.A.
10	F	76	CP	Adenoma	(-)	12	N.A.	N.A.
11	F	79	CP	Adenoma	(-)	5	N.A.	N.A.
12	M	63	CP	Adenoma	(-)	10	N.A.	N.A.
13	M	64	CP	Adenoma	(-)	5	N.A.	N.A.
14	F	78	CP	Adenoma	(-)	5	N.A.	N.A.
15	F	79	CP	Adenoma	(-)	7	N.A.	N.A.

M, male; F, female; CP, colorectal polyp; CRC, colorectal cancer; DWIBS/T2, diffusion-weighted whole body imaging with background body signal suppression; Well, well-differentiated adenocarcinoma; Mod, moderately differentiated adenocarcinoma; (+), positive result; (-), negative result; M, mucous membrane; SS, subserosa; N.A., not analyzed.

and coronal (Fig. 1B) sections. Surgical treatment was not performed for patients seven and eight, since they had advanced CRC. They received conservative treatment and the lesion diameter and depth of invasion were therefore not investigated for these two patients. All patients diagnosed with CP following colonoscopy, with the exception of one had negative results following DWIBS/T2: A specimen obtained from patient one by endoscopic mucosal resection revealed a well-differentiated adenocarcinoma (Table II).

Positive DWIBS/T2 is associated with CRC. Results of the χ^2 test revealed a significant association between the diagnosis of CP or CRC following colonoscopy and the results on DWIBS/T2 (P=0.0028; Table III). Seven patients diagnosed with CP had negative results, while six diagnosed with CRC had positive results following DWIBS/T2.

Greater lesion diameter is observed in CRC. To analyze the correlation between lesion diameter and detection of CP or CRC by DWIBS/T2, a scatter plot of lesion diameter in CRC and CP was generated (Fig. 2). The lesion diameter for CP (7.9±4.0 mm) was significantly smaller than that for CRC (51.0±13.2 mm; P<0.0001; Fig. 2). It was therefore implied that the diameter of the lesion may affect the detectability of CP or CRC when using DWIBS/T2.

Positive DWIBS/T2 is associated with lesion diameter. To determine the factors affecting the results of DWIBS/T2, scatter plots

Table III. Comparison between diagnosis of CP or CRC upon colonoscopy and results of DWIBS/T2.

Diagnosis on colonoscopy	DWIBS/T2 findings		Total
	Negative (n)	Positive (n)	
CP	7	1	8
CRC	1	6	7
Total	8	7	15

A χ^2 test was performed, indicating a significant association between the diagnosis of CP or CRC following colonoscopy and the results on DWIBS/T2 (P=0.0028). DWIBS/T2, diffusion-weighted whole body imaging with background body signal suppression/T2 image fusion; CP, colorectal polyp; CRC, colorectal cancer.

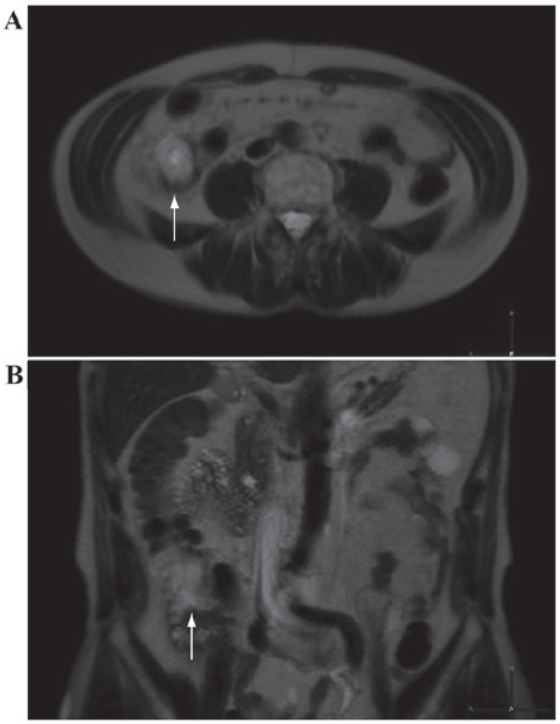

Figure 1. DWIBS/T2 images of an ascending colon cancer. DWIBS/T2 was performed for a 73 year-old man with ascending colon cancer (patient two Table II). The (A) horizontal and (B) coronal section present positive results (indicated by arrows) in the ascending colon. DWIBS/T2, diffusion-weighted whole body imaging with background body signal suppression/T2 image fusion.

of lesion diameter (Fig. 3A) and depth of invasion (Fig. 3B) were generated for lesions which were positive and negative on DWIBS/T2. The mean diameter of lesions with negative results (9.8±8.6 mm) was significantly smaller than that of lesions with positive results on DWIBS/T2 (48.0±19.4 mm; P=0.0004). Furthermore, the depth of tumor invasion of the lesions negatively diagnosed on DWIBS/T2 was at the lower margin of the range of the positively diagnosed lesion however, the statistical significance could not be analyzed as there was only one patient with a negatively diagnosed lesion (patient fou Table II).

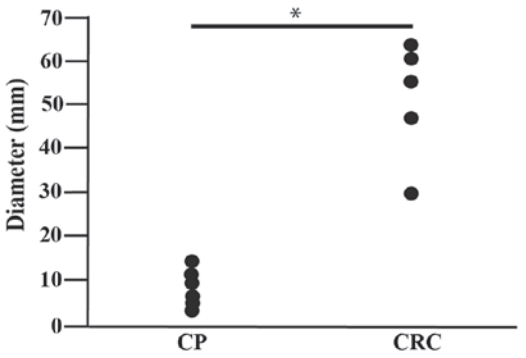

Figure 2. Scatter plot of lesion diameter (mm) of CP or CRC. The lesion diameter was plotted against CP or CRC. The mean lesion diameter in the CP group (7.9±4.0 mm) was significantly smaller than that in the CRC group (51.0±13.2 mm, P<0.0001). CP, colorectal polyp; CRC, colorectal cancer. *P<0.0001.

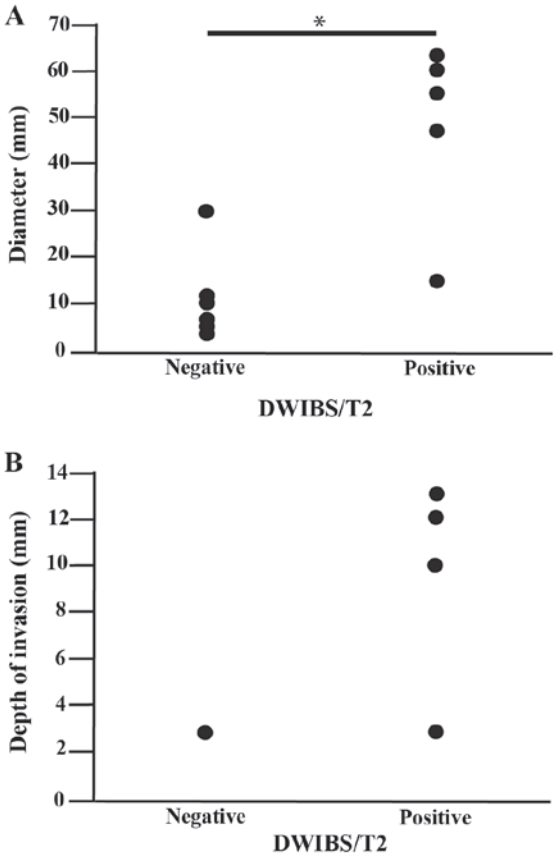

Figure 3. Scatter plot of diameter (mm) and depth of invasion (mm) of colorectal cancer. (A) Diameter (mm) and (B) depth of invasion (mm) were plotted against negative or positive results following diagnosis by DWIBS/T2. The mean diameter of lesions with negative results (9.8±8.6 mm) was significantly smaller than that of lesions with positive results on DWIBS/T2 (48.0±19.4 mm; P=0.0004). DWIBS/T2, diffusion-weighted whole body imaging with background body signal suppression/T2 image fusion. *P=0.0004.

Positive CP diagnosis with DWIBS/T2 and PET/CT. Patient one, who had been diagnosed with CP by colonoscopy (Fig. 4A and B) was positive on DWIBS/T2 (Fig. 4C). The PET/CT results for patient one were also indicative of CP (Fig. 4D). The patient's SUV of ^{18}F-FDG was 2.5, indicating

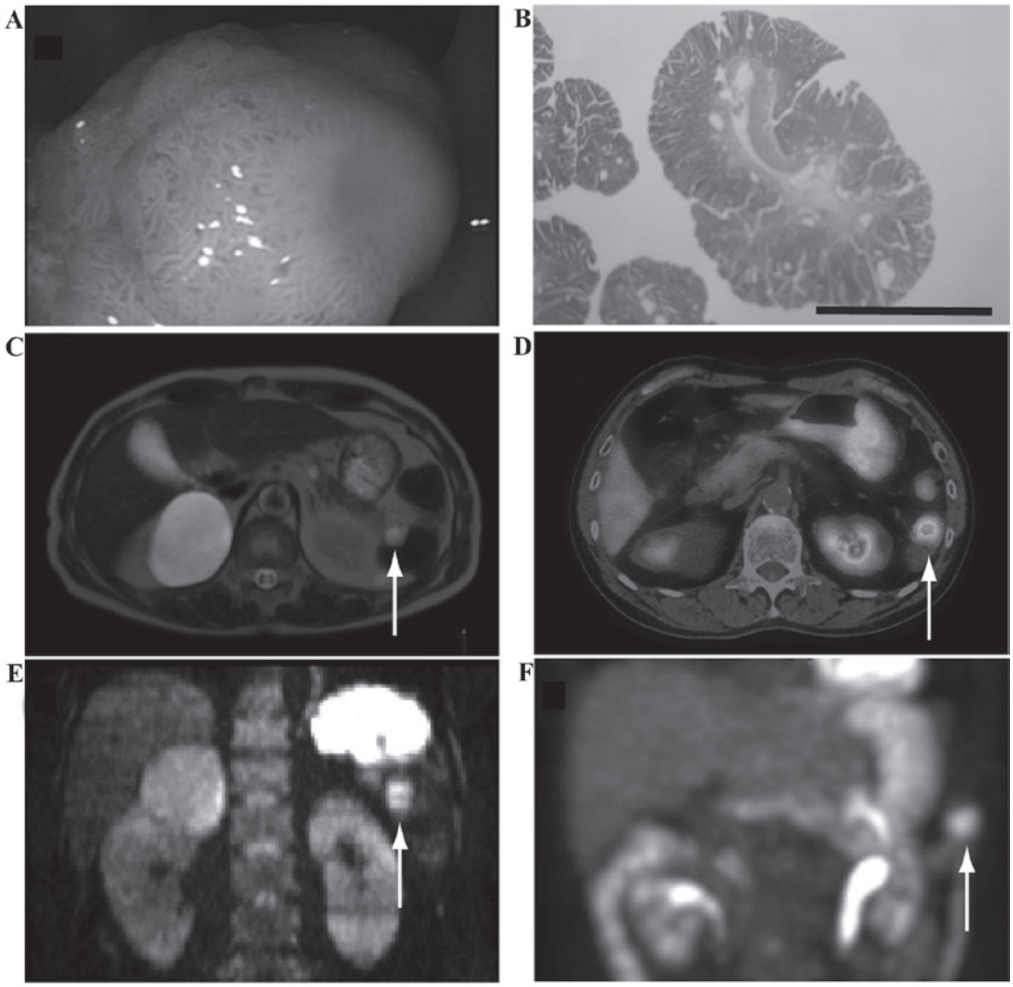

Figure 4. DWIBS/T2 and PET/CT images of a patient with CP. A 67 year-old man presented abdominal pain (patient one; Table II) and was subjected to DWIBS/T2 to investigate the presence of cancer in the abdominal cavity. Colonoscopy was performed to examine the colon and rectum. (A) CP was located, (B) endoscopic mucosal resection was performed and tissue was microscopically examined (scale bar, 5 mm). The horizontal section on (C) DWIBS/T2 and (D) PET/CT revealed positive results, indicated by arrows, in the descending colon. Coronal section on (E) DWI and (F) PET exhibited positive results, indicated by arrows. CP, colorectal polyp; DWIBS/T2, diffusion-weighted whole body imaging with background body signal suppression/T2 image fusion; PET/CT, positron emission tomography/computed tomography.

that uptake of ^{18}F-FDG in their CP was 2.5 times greater than the expected uptake in the whole body if ^{18}F-FDG was distributed equally. DWI (Fig. 4E) and PET findings (Fig. 4F) were similar.

Discussion

Conventional MRI has limitations with regard to tumor and node (N) staging, while DWI adds value, allowing for N staging (18). The ADC value is useful for distinguishing CRC from inflammatory bowel disease (19). Leufkens *et al* (20) performed DWI on patients who were scheduled for colonoscopy to evaluate the diagnostic accuracy of DWI for CP or CRC. It was demonstrated that for the detection of CRC or CP with a lesion diameter of >6 mm, the sensitivity and specificity of DWI were 80.0 and 72.7%, respectively (20). However, in the present study, DWIBS/T2 was able to distinguish between CRC and CP due to selectively detecting CRC. Furthermore, the mean lesion diameter in the CRC group was significantly larger than that in the CP group. Therefore, it was concluded that the lesion diameter may affect the results of DWIBS/T2. It has been indicated that the lesion diameter affects the results of ultrasonography for the diagnosis of CP and CRC (21).

It was also observed that the mean depth of invasion was greater in cases of CRC which were positively diagnosed on DWIBS/T2, compared with the depth of invasion in the one case that was negatively diagnosed; however, statistical significance could not be determined. It is therefore hypothesized that the pixel number may be a major factor affecting the diagnostic accuracy of DWIBS/T2.

For patient one, the results of DWIBS/T2, PET/CT, DWI and PET were similar. This indicated that DWIBS/T2 and PET/CT may be useful for detecting CP with well-differentiated adenocarcinoma, which is eligible for endoscopic mucosal resection. If the sensitivity of DWIBS/T2 for the diagnosis of large CP is proven to be superior to that of PET/CT, it may replace PET/CT as a diagnostic tool.

One limitation of the present study was the small sample siz therefore, further studies with larger samples are required to assess the correlation between the results of DWIBS/T2 and the depth of invasion.

In conclusion, lesion diameter and depth of invasion may affect the detectability of DWIBS/T2.

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