

Diagnostic accuracy of diffusion-weighted whole-body imaging with background body signal suppression/T2-weighted image fusion for the detection of abdominal solid cancer

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Abstract. Diffusion-weighted whole-body imaging with background body signal suppression (DWIBS) images show significant contrast for cancer tissues against non-cancerous tissues. Fusion of a DWIBS and a T2-weighted image (DWIBS/T2) can be used to obtain functional, as well as anatomic, information. In the present study, the performance of DWIBS/T2 in the diagnosis of abdominal solid cancer was evaluated. The records of 14 patients were retrospectively analyzed [5 patients with hepatocellular carcinoma (HCC), 4 with metastatic liver cancer, 3 with pancreatic cancer, 1 with renal cellular carcinoma and 1 with malignant lymphoma of the para-aortic lymph node]. T1WI and T2WI scans did not detect pancreatic cancer in certain cases, whereas DWIs and DWIBS/T2 clearly demonstrated pancreatic cancer in all cases. In addition, metastatic liver cancer and HCC were successfully detected with abdominal US and CECT; however, US did not detect pancreatic cancer in 1 case, while CECT and DWIBS/T2 detected pancreatic cancer in all cases. In conclusion, the diagnostic performance of DWIBS/T2 was the same as that of abdominal US and CECT in detecting primary

and metastatic liver cancer. DWIBS/T2 enabled the diagnosis of pancreatic cancer in cases where it was not detected with US, T1WI or T2WI.

Introduction

Diffusion-weighted whole-body imaging with background body signal suppression (DWIBS) is acquired using multiple signal averaging, prepulse fat suppression and heavy diffusion weighting during free breathing (1). This technique is based on diffusion-weighted imaging, which visualizes and assesses the random movement of water at the molecular level (also known as Brownian motion) (2). DWIBS significantly increases the signal-to-noise ratio and is useful for detecting and staging tumors, as well as monitoring the response to therapy (3,4). DWIBS is used to detect cancer in organs that are not influenced by respiration, such as in the breast (5). The existing literature regarding DWIBS mainly involves breast cancer, bone metastasis and malignant lymphoma (6-13). DWIBS is not commonly used to detect abdominal solid cancer, since the anatomical analysis of these tumors can be difficult and respiratory movement makes the image obscure (14,15). Sommer *et al* (16) reported on the use of DWIBS for detecting liver cancer; however, they mainly used it for the diagnosis of malignant lymphoma and breast cancer.

By overlapping a DWIBS image onto a T2-weighted image (T2WI) using a workstation, fusion of the DWIBS and T2WI (DWIBS/T2) can be performed (4,16,17). DWIBS/T2 clearly illustrates functional information through anatomic images, suggesting that DWIBS/T2 may enable the detection of cancer in the abdominal solid organs. Thus, DWIBS/T2 may be a

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potential diagnostic strategy for the diagnosis of abdominal solid cancer. The present study aimed to retrospectively analyze the performance of DWIBS/T2 in the diagnosis of abdominal solid (not-alimentary) cancer.

Materials and methods

Ethical statement. The present study was approved by the Ethics Committee of the National Hospital Organization, Shimoshizu Hospital (Yotsukaido, Japan). As procedures were performed as a part of routine clinical practice, written informed consent for inclusion into the study was waived. Patient records were anonymized and retrospectively analyzed. Written informed consent was, however, obtained from all patients who were subjected to contrast-enhanced computed tomography (CECT) and DWIBS/T2, due to an associated risk of adverse side effects. Informed consent was also obtained from patients who were subjected to abdominal ultrasonography (US), though written consent was waived as abdominal US is considered to be a safe and non-invasive therapeutic method (18).

Diagnostic procedure. Patients were subjected to abdominal US and CECT when they were suspected of malignancy in the abdominal cavity. DWIBS/T2 was performed to reveal the extent of the malignancy when the extent was not clear in the abdominal US or CECT images. DWIBS/T2 was also performed to accumulate information of positivity or negativity of the suspected lesion for more accurate diagnosis. It was expected that DWIBS/T2 showed the extent of the malignancy more clearly, due to the strong contrast of positive signals against the surrounding healthy tissues. These results were compared with the histological diagnosis or follow-up.

Inclusion criteria. Patient records, including imaging results, were analyzed retrospectively from patients admitted to National Hospital Organization, Shimoshizu Hospital between November 2012 and May 2014. Patients were enrolled in the present study if they were suspected to have abdominal cancer and had results available from abdominal US, CECT and DWIBS/T2 examinations. For patients referred to another hospital with suspicion of malignancy, the findings of other hospitals were received to confirm our diagnosis. Patients managed in the National Hospital Organization, Shimoshizu Hospital were followed-up with abdominal US, CECT and DWIBS/T2 examinations for up to 11 months.

Exclusion criteria. Patients were excluded from the current study when their abdominal US, CECT or DWIBS/T2 results were not available. In addition, patients referred to other hospitals were excluded when the response of the hospital was not available.

Abdominal US examination. Senior fellows of the Japan Society of Ultrasonics in Medicine (Tokyo, Japan) performed the abdominal US examination with an SSA-700A instrument (Toshiba Medical Systems Corp., Ohtawara, Japan) using a 3.75-MHz curved-array probe (PVT-375BT) (Toshiba Medical Systems Corp.).

CECT examination. CECT was performed using a 16-detector row CT scanner (SOMATOM Emotion 16; Siemens, Munich, Germany). Imaging parameters for three-phase contrast-enhanced images were as follows: Tube voltage, 130 kVp; gantry rotation speed, 0.6 rotations/sec; and maximum allowable tube current, 120 mA. Patients were administered the intravenous contrast medium (100 ml iopamidol; Konica Minolta Healthcare, Tokyo, Japan) at 3 ml/sec. CT images were acquired prior to injection of contrast medium and at 30, 70, and 180 sec later.

Magnetic resonance imaging (MRI) examination. All MRI studies were performed using a 1.5 Tesla scanner (Achieva software, version 3.2.2; Philips Medical Systems, Best, The Netherlands). The T1-weighted image (T1WI), T2WI and diffusion-weighted image (DWI) were obtained with pulse sequences as depicted in Table I. DWIBS/T2 images were constructed with the Extended MR WorkSpace 2.6.3.4 software (Philips Medical Systems). The DWI gradients were applied along the x-, y- and z-axes before and after a 180° inversion prepulse to obtain fat-saturated, isotropic images with DWI sensitivity using the following parameters for a single stack: b value, 0 and 800 mm²/sec; TR/TE/IR, 6960/79/150 msec; acquisition matrix, 176x115; reconstruction matrix, 256; field of view, 530 mm (right/left), 349 mm (anterior/posterior) and 226 mm (feet/head); slice thickness, 6 mm; size of reconstructed voxel, 2.07x2.08x6 mm³.

Staging. Staging of cancer tissue was determined according to guidelines of the American Joint Committee on Cancer classification (19). Briefly, the tumor stages assigned in the present study were as follows: For hepatocellular carcinoma (HCC): T2: Solitary tumor with vascular invasion or multiple tumors ≤5 cm, T3a: Multiple tumors >5 cm, T3b: Single tumor or multiple tumors of any size involving a major branch of the portal vein or hepatic vein. For pancreatic cancer: T3: Tumor extends beyond the pancreas but without involvement of the celiac axis of the superior mesenteric artery, T4: Tumor involves the celiac axis or the superior mesenteric artery. For renal cellular carcinoma: T1b: Tumor size >4 cm but not <7 cm in greatest dimension and limited to the kidney.

Results

Patients. A total of 14 patients were enrolled into the current study, including 5 males (mean age, 79.2±5.8 years) and 9 females (mean age, 73.0±4.7 years). The patients were diagnosed with abdominal US, CECT, T1WI, T2WI, DWI and DWIBS/T2. Of the 14 patients, 5 were diagnosed with HCC, 4 with metastatic liver cancer, 3 with pancreatic cancer, 1 with renal cellular carcinoma and 1 with malignant lymphoma of the para-aortic lymph node. No patients suffered from adverse side effects.

Diagnostic performance of DWIBS/T2 compared with T1WI and T2WI. To evaluate the diagnostic performance of DWIBS/T2, the detectability of abdominal cancer was compared among T1WI, T2WI, DWI and DWIBS/T2 (Table II). DWI and DWIBS/T2 indicated positive results in all the patients with a definitive diagnosis of abdominal

Table I. Pulse sequences in the present study.

Parameter	T1-weighted image	T2-weighted image	DWI and DWIBS/T2
Sequence	GRE	Single-shot SE	EPI SE
TR (msec)	182	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	No	No	SPAIR
Phase encoding direction	Posterior-anterior	Posterior-anterior	Posterior-anterior

DWI, diffusion-weighted image; DWIBS, diffusion-weighted whole-body imaging with background body signal suppression/T2-weighted image fusion; GRE, gradient echo; SE, spin echo; EPI, echo planer imaging; TR, time to repetition; TE, time to echo; NSA, number of signal averages.

Table II. Detection of cancer with magnetic resonance imaging.

Patient number	Final diagnosis	Stage ^a	T1WI	T2WI	DWI	DWIBS/T2
1	Hepatocellular carcinoma	T3a	(+)	(+)	(+)	(+)
2	Hepatocellular carcinoma	T2	(-)	(-)	(+)	(+)
3	Hepatocellular carcinoma	T3b	(+)	(+)	(+)	(+)
4	Hepatocellular carcinoma	T3b	(+)	(+)	(+)	(+)
5	Hepatocellular carcinoma	T2	(+)	(+)	(+)	(+)
6	Metastatic liver cancer	NA	(+)	(+)	(+)	(+)
7	Metastatic liver cancer	NA	(+)	(+)	(+)	(+)
8	Metastatic liver cancer	NA	(+)	(+)	(+)	(+)
9	Metastatic liver cancer	NA	(+)	(+)	(+)	(+)
10	Pancreatic cancer	T3	(+)	(+)	(+)	(+)
11	Pancreatic cancer	T4	(-) ^b	(-) ^b	(+)	(+)
12	Pancreatic cancer	T3	(-)	(-)	(+)	(+)
13	Renal cell carcinoma	T1b	(+)	(+)	(+)	(+)
14	Malignant lymphoma ^c	NA	(+)	(+)	(+)	(+)

^aAmerican joint committee on cancer classification (7th edition). ^bHead of pancreas slightly swollen without any difference in the intensity compared with the surrounding tissue. ^cOriginating from the para-aortic lymph node. T1WI, T1-weighted image; T2WI, T2-weighted image; DWI, diffusion-weighted image; DWIBS/T2, diffusion-weighted whole-body imaging with background body signal suppression T2-weighted image fusion; (+), positive results; (-), negative results; NA, not applicable.

cancer. In addition, the results of DWI were in accordance with those of DWIBS/T2. These results suggested that DWI and DWIBS/T2 had the same sensitivity of the detection of cancer. By contrast, T1WI and T2WI scans indicated negative results in 1 patient with hepatocellular carcinoma (HCC) and in 2 patients with pancreatic cancer. These results suggested that DWI and DWIBS/T2 were more sensitive than T1WI and T2WI in the detection of cancer.

Fig. 1 shows the representative case of a 73-year-old female who visited the National Hospital Organization, Shimoshizu Hospital with general malaise. HCC was detected in this patient as a space-occupying lesion with mixed enhancement using

CECT (Fig. 1A). However, T1WI (Fig. 1B) or T2WI (Fig. 1C) scans were negative for HCC. The lesion was clearly observed as a high signal in the DWIBS/T2 image (Fig. 1D). The lesion was finally diagnosed as HCC with ultrasound-guided fine needle biopsy. These findings suggested that DWIBS/T2 was more useful for the detection of HCC than T1WI and T2WI. Written informed consent was obtained from this patient prior to the use of her data in the present study.

Diagnostic performance of DWIBS/T2 compared with US and CECT. To evaluate ability of DWIBS/T2 to detect cancer, images were compared with abdominal US and CECT

Table III. Comparison of abdominal US, CECT and DWIBS/T2 findings.

Patient number	Final diagnosis	Stage ^a	Abdominal US	CECT	DWIBS/T2
1	Hepatocellular carcinoma	T3a	(+)	(+)	(+)
2	Hepatocellular carcinoma	T2	(+)	(+)	(+)
3	Hepatocellular carcinoma	T3b	(+)	(+)	(+)
4	Hepatocellular carcinoma	T3b	(+)	(+)	(+)
5	Hepatocellular carcinoma	T2	(+)	(+)	(+)
6	Metastatic liver cancer	NA	(+)	(+)	(+)
7	Metastatic liver cancer	NA	(+)	(+)	(+)
8	Metastatic liver cancer	NA	(+)	(+)	(+)
9	Metastatic liver cancer	NA	(+)	(+)	(+)
10	Pancreatic cancer	T3	(+)	(+)	(+)
11	Pancreatic cancer	T4	(+)	(+)	(+)
12	Pancreatic cancer	T3	(-)	(+)	(+)
13	Renal cell carcinoma	T1b	(+)	(+)	(+)
14	Malignant lymphoma	NA	(+)	(+)	(+)

^aAmerican joint committee on cancer classification (7th edition). US, abdominal ultrasound; CECT, contrast-enhanced computed tomography; DWIBS/T2, diffusion-weighted whole-body imaging with background body signal suppression T2-weighted image fusion; (+), positive results; (-), negative results; NA, not applicable.

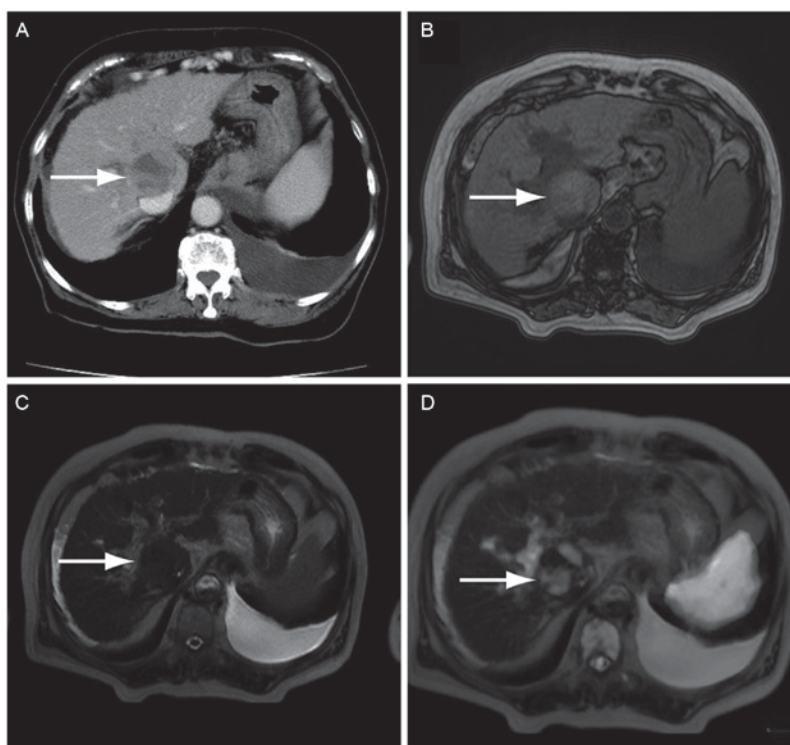


Figure 1. Imaging examination in the representative case of a 73-year-old patient diagnosed with hepatocellular carcinoma. The tumor was successfully detected with DWIBS/T2. (A) CECT scanning demonstrated a space-occupying lesion with mixed enhancement (arrow). (B) T1WI showed an unclear mass-like lesion. (C) Detection of the lesion was difficult in a T2WI when compared with the CECT scan. (D) DWIBS/T2 clearly showed a high signal. DWIBS/T2, diffusion-weighted whole-body imaging with background body signal suppression/T2-weighted image fusion; CECT, contrast-enhanced computed tomography; WI, weighted image.

(Table III). The detectability of HCC and metastatic liver cancer using DWIBS/T2 was the same as that of abdominal US and CECT, with the exception of 1 patient with pancreatic cancer who was not correctly diagnosed by abdominal US.

These results suggested that DWIBS/T2 had the same sensitivity as CECT. It was also suggested that DWIBS/T2 was more sensitive when compared with US for the detection of pancreatic cancer.

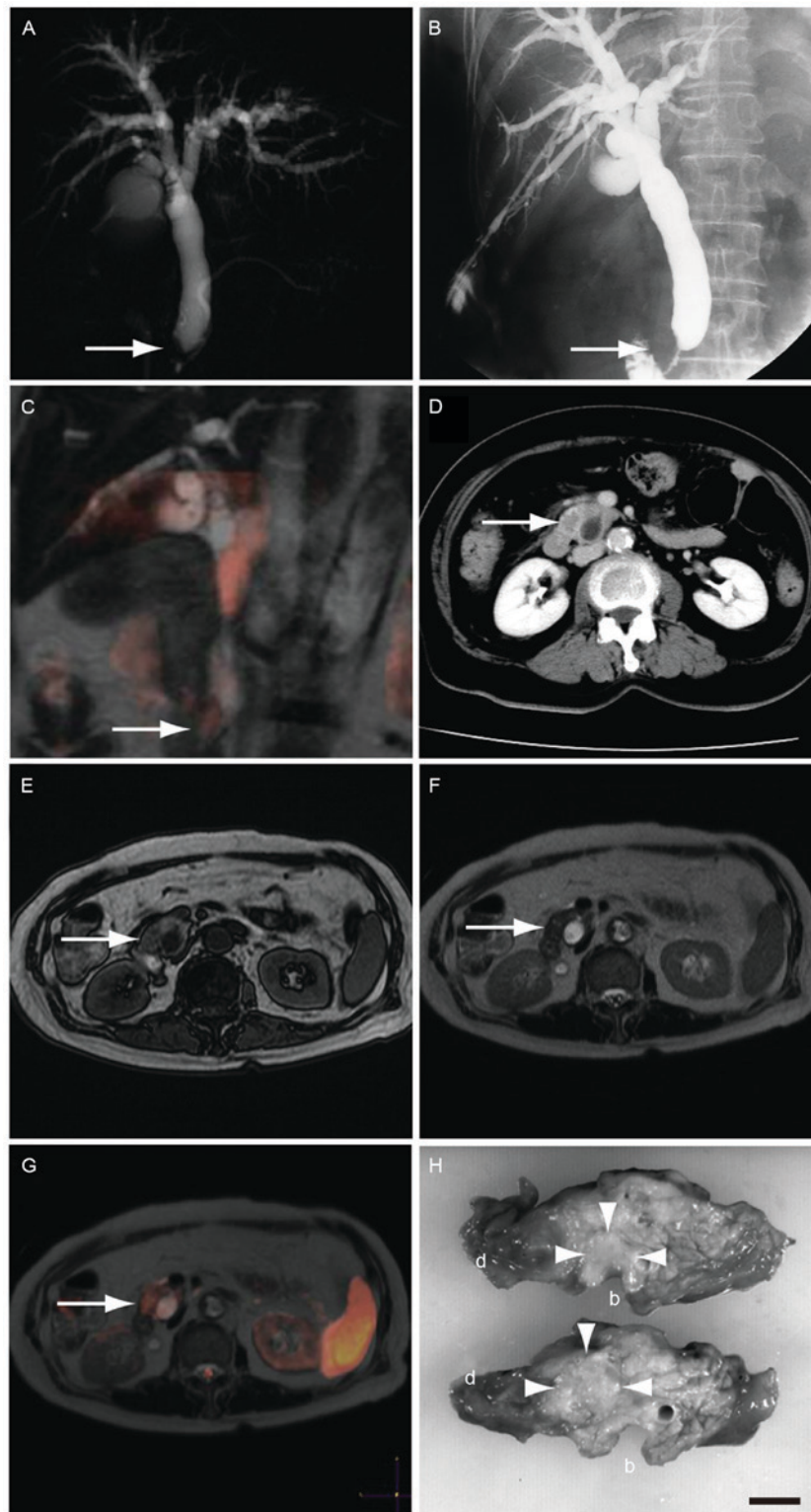


Figure 2. Imaging examination in the representative case of a 75-year-old female patient diagnosed with pancreatic cancer. The tumor was successfully detected by DWIBS/T2. (A) Magnetic resonance cholangiopancreatography showed obstruction of the common bile duct near the papilla of Vater (arrow). (B) Percutaneous transhepatic biliary drainage was performed. (C) A coronal section of DWIBS/T2 demonstrated a high signal on the obstruction. (D) CECT revealed an irregularly shaped low-density area in the head of the pancreas. (E) T1WI and (F) T2WI scans did not show clear presence of pancreatic cancer. (G) A transverse section of DWIBS/T2 demonstrated a high signal in the head of the pancreas. (H) Surgical specimens confirmed the diagnosis of pancreatic cancer in the head of the pancreas close to common bile duct (circled with arrowheads). Scale bar, 1 cm; b, common bile duct; d, duodenum; DWIBS/T2, diffusion-weighted whole-body imaging with background body signal suppression/T2-weighted image fusion; CECT, contrast-enhanced computed tomography; WI, weighted image.

Fig. 2 demonstrates the representative case of a 75-year-old female who visited our hospital with jaundice, and was diagnosed with pancreatic cancer. Cancer in the head of the

pancreas was shown as an obstruction of the common bile duct with magnetic resonance cholangiopancreatography (Fig. 2A). In order to reduce jaundice, percutaneous transhepatic biliary

drainage was performed (Fig. 2B). However, these images did not suggest the existence of pancreatic cancer. A coronal section of DWIBS/T2 examination clearly demonstrated a high signal in the head of pancreas (Fig. 2C), suggesting the presence of pancreatic cancer. In addition, CECT examination revealed a small unclear low density area (Fig. 2D). However, pancreatic cancer was not clear using T1WI (Fig. 2E) or T2WI (Fig. 2F). A high signal was shown in the head of pancreas with a transverse section of DWIBS/T2 (Fig. 2G). The diagnosis of pancreatic cancer was confirmed with a surgical specimen (Fig. 2H).

The aforementioned findings revealed that CECT detected pancreatic cancer, however with reduced contrast to the surrounding tissues when compared with DWIBS/T2. US failed to detect pancreatic cancer in 1 case, possibly due to the location of the cancer at the head of the pancreas, where it was surrounded by gas of the stomach and duodenum. These results suggested that DWIBS/T2 may be useful for the diagnosis of pancreatic cancer.

Discussion

CECT, T1WI, T2WI and DWI examinations have been demonstrated to have similar diagnostic performance for HCC (20). Among MRI sequences, no difference was observed for the detection of liver malignancy, including HCC and metastatic liver cancer (21,22). In the present study, DWI and DWIBS/T2 examination detected liver malignancy by differentiating the cancer as a region of strong contrast against the surrounding tissues. However, DWIBS/T2 images provided added anatomic information compared with DWI. Thus, the present study further investigated the use of DWIBS/T2 in the detection of abdominal cancer. The results indicated no difference in the diagnostic performance of CECT and DWIBS/T2 for liver malignancy. In addition, a previous study indicated that the diagnostic performance of contrast-enhanced MRI and non-contrast-enhanced MRI does not differ for liver malignancy (23). These previous findings along with the present study results suggest that DWBS/T2 may be more beneficial in the diagnosis of liver malignancy compared with CECT and contrast-enhanced MRI. DWIBS/T2 did not require contrast medium, and may avoid complications of CECT and MRI, including anaphylaxis (22).

US, CECT and MRI are used in the diagnosis of pancreatic cancer in routine clinical practice (24). Endoscopic US is essential for the diagnosis of pancreatic cancer with fine-needle aspiration (25). In addition, US is used as a screening method for pancreatic cancer; however, it is limited by field-of-view restriction, due to the presence of gas in the stomach and intestine (26). Therefore, US can fail to detect pancreatic cancer when the tumor is small or surrounded by gas. Diagnosis of pancreatic cancer by CECT may also be difficult due to insufficient contrast. In the present study, DWI and DWIBS/T2 clearly differentiated malignant tissues from the surrounding tissues, allowing easy detection. Furthermore, DWI and DWIBS/T2 did not require contrast enhancement. DWIBS/T2 provided additional anatomic information to DWI that is useful for the detection of pancreatic cancer (27). These results suggested that DWBS/T2 should be preferably performed prior to CECT examination.

The limitation of the present study was that it included a small number of patients. A larger sample size is required to confirm the results. HCC and pancreatic cancer should be diagnosed when the tumors are small for curative treatment (28,29). Thus, studies on the performance of DWIBS/T2 in detecting early-stage HCC and pancreatic cancer are needed.

In conclusion, the diagnostic performance of DWIBS/T2 was similar to that of US and CECT for the detection of primary and metastatic liver cancer. DWIBS/T2 enabled the diagnosis of pancreatic cancer, which was not detected by US, T1WI or T2WI examination. The findings suggest that DWIBS/T2 may be useful in the diagnosis of early-stage HCC and pancreatic cancer.

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