

Comparison of DWIBS/T2 image fusion and PET/CT for the diagnosis of cancer in the abdominal cavity

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Received January 24, 2016; Accepted February 1, 2017

DOI: 10.3892/etm.2017.4987

Abstract. Fusion images of diffusion-weighted whole-body imaging with background body signal suppression and T2-weighted image (DWIBS/T2) demonstrate a strong signal for malignancies, with a high contrast against the surrounding tissues, and enable anatomical analysis. In the present study, DWIBS/T2 was compared with ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) positron emission tomography/computed tomography (PET/CT) for diagnosing cancer in the abdomen. Patient records, including imaging results of examination conducted between November 2012 and May 2014, were analyzed retrospectively. In total, 10 men (age, 73.6±9.6 years) and 8 women (age, 68.9±7.1 years) were enrolled into the current study. Of the enrolled patients, 2 were diagnosed with hepatocellular carcinoma, 1 with cholangiocellular carcinoma, 1 with liver metastasis, 2 with pancreatic ductal adenocarcinoma, 1 with renal cell carcinoma and 1 with malignant lymphoma. Benign lesions were also analyzed, including adenomyomatosis of the gallbladder (5 patients), intraductal papillary mucinous neoplasm (4 patients) and right adrenal adenoma (1 case). All the patients with cancer showed positive results on DWIBS/T2 images. However, only 7 out of 8 patients were positive with PET/CT. One patient with right renal cellular carcinoma was positive with DWIBS/T2, but negative with PET/CT. All the patients with benign lesions were negative with DWIBS/T2 and PET/CT. In conclusion, DWIBS/T2 was more sensitive in

diagnosing cancer of organs in the abdominal cavity compared with PET/CT. Furthermore, negative results with DWIBS/T2 and PET/CT were useful for the diagnosis of benign lesions, such as adenomyomatosis of the gallbladder and intraductal papillary mucinous neoplasm.

Introduction

The abdominal cavity harbors solid organs, such as the liver, pancreas and kidneys. The liver is a common site of primary cancer, such as hepatocellular carcinoma (HCC) and cholangiocellular carcinoma (CCC), as well as of metastatic cancer (1). Renal cell carcinoma (RCC) can form in the kidney, while malignant lymphoma develops in the lymph nodes in the abdominal cavity. In addition, pancreatic ductal adenocarcinoma (PDA) occurs in the pancreas, and has a poor prognosis despite advances in treatment strategies, such as surgery, irradiation and chemotherapy (2-4). Furthermore, intraductal papillary mucinous neoplasm (IPMN) forms multiple cystic lesions in the pancreas (5), and may then result in intraductal papillary mucinous adenocarcinoma (6). In order to improve the prognosis of these diseases, early detection of pancreatic cancer is important (7).

¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) positron emission tomography/computed tomography (PET/CT) takes advantage of the Warburg effect (8), which suggests that cancer cells require more glucose than normal cells due to the activation of glycolysis. Therefore, cancer cells readily take up ¹⁸F-FDG, an analogue of glucose, which is then not metabolized and accumulates inside these cells to a much greater extent than in non-cancerous cells. Subsequently, PET/CT imaging is used to detect the signal of ¹⁸F-FDG and construct images of its uptake pattern. PET/CT has been established as a useful imaging modality for cancer diagnosis (9), and serves plays an important role in the evaluation of TMN staging of cancer and its metastasis to lymph nodes and distant organs (10,11). However, a possible disadvantage of

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Key words: computed tomography, endoscopic ultrasonography, pancreatic ductal adenocarcinoma, adenomyomatosis of the gallbladder, intraductal papillary mucinous neoplasm

PET/CT is that the patient is exposed to ionizing radiation from ^{18}F -FDG.

Diffusion-weighted whole body imaging with background body-signal suppression (DWIBS) is an imaging technique based on images that are created through analysis of the random movement of water at a molecular level (Brownian motion) and its diffusion through the tissues (12,13). Dense, highly cellular tumor tissue suppresses water diffusion, creating a strong DWIBS signal. DWIBS images are acquired with multiple-signal averaging, pre-pulse fat suppression and heavy diffusion weighting during free breathing (14).

One of the advantages of DWIBS is the strong contrast of positive signals against the surrounding tissues, thus DWIBS is useful for the detection and staging of cancer (15). However, a major limitation of DWIBS is that it is occasionally difficult to evaluate the positive signals in the context of the anatomical setting since the surrounding tissues are hard to observe due to the suppression of their signals. Fusion images can be created by overlapping DWIBS onto T2-weighted images (T2WI; DWIB/T2) (15-17). The image fusion is performed on a workstation, and DWIBS/T2 clearly enables functional analysis of DWIBS signals in the anatomical setting.

In the present study, the accuracy and clinical utility of DWIBS/T2 and PET/CT imaging for patients with cancer in the solid organs of the abdominal cavity were retrospectively compared.

Materials and methods

Ethical statement. The present study was approved by the Ethics Committee of the National Hospital Organization Shimoshizu Hospital (Yotsukaido, China). This study was not considered to be a clinical trial, as the procedures were performed as a part of routine clinical practice. Written informed consent for inclusion into the study was thus waived. Patient records were anonymized and retrospectively analyzed. Written informed consent was obtained from all patients who were subjected to DWIBS/T2, PET/CT, magnetic resonance cholangiopancreatography, endoscopic ultrasonography (US) and ultrasound-guided biopsy.

Diagnostic procedure. Abdominal ultrasonography and contrast-enhanced CT were typically performed for patients suspected of cancer in their abdominal cavity. Certain patients were also subjected to DWIBS/T2 to clarify the extent of cancer (15). PET/CT was performed in patients in which diagnosis was difficult with the aforementioned diagnostic imaging techniques. PET/CT was also performed to assess the staging of cancer. These results were compared with follow-up information, as a number of patients were assessed by histological analysis. Histological diagnosis was determined with surgical specimens or US-guided biopsy.

Inclusion criteria. Patients were enrolled into the present study when they met the following criteria: i) Suspected with cancer of the abdominal cavity, such as liver, pancreas or kidney cancer; ii) DWIBS/T2 results were available; and iii) PET/CT images were available. For patients referred to another hospital for the management of cancer, enrollment into the study was restricted to those whose reply was received to clarify their

final diagnosis. Patients were also enrolled when their final diagnosis was a benign lesion in order to evaluate the positivity of DWIBS/T2 and PET/CT for benign lesions.

Exclusion criteria. Patients were excluded when DWIBS/T2 or PET/CT results were not available. In addition, patients were excluded when they were diagnosed with alimentary tract cancer.

Study design. Patient records, including imaging results from patients managed in the National Hospital Organization Shimoshizu Hospital between November 2012 and May 2014, were analyzed retrospectively. The enrolled patients were subjected to both DWIBS/T2 and PET/CT, and diagnosed with malignant or benign lesions in the abdominal cavity with imaging diagnostics or pathological specimens obtained by surgery or US-guided biopsy. All patients with benign lesions were regularly followed-up with abdominal US and CT with or without contrast-enhancement in our hospital.

Magnetic resonance imaging (MRI). All MRI studies were performed using a 1.5 Tesla scanner (Achieva, software version 3.2.2; Philips Medical Systems, Best, The Netherlands). T1-weighted, T2-weighted and diffusion-weighted images (DWIs) were obtained with pulse sequences as depicted in Table I. DWIBS/T2 images were constructed with an Extended MR WorkSpace (Philips Medical Systems). The DWI gradients were applied along the x, y and z-axes before and after a 180° inversion pre-pulse to obtain fat-saturated, isotropic images with DWI sensitivity. The following parameters were used for a single stack: b-values, 0 and 800 mm²/s; repetition time, 6960 msec; echo time, 79 msec; inversion recovery, 150 msec; acquisition matrix, 176x115; reconstruction matrix, 256; field of view, right/left at 530 mm, anterior/posterior at 349 mm, and feet/head at 226 mm; slice thickness, 6 mm; size of reconstructed voxel, 2.07x2.08x6 mm³; four averages. A radiologist and a gastroenterologist analyzed the DWIBS/T2 images. To rule out the T2 shine-through effect or to differentiate malignant lesions from non-malignant causes of restricted diffusion, a decreased signal on the apparent diffusion coefficient (ADC) to determine a 'positive ADC map' (18). It took 20 min to perform both the DWIBS and T2-weighted imaging together.

PET/CT imaging. PET/CT was examined in Sannoh Hospital Medical Center. Patients were subjected to PET/CT in the Diagnostic PET Imaging Center, Department of Radiology, Sannoh Medical Center (Chiba, Japan) (19). Patients fasted overnight or for at least 6 h before injection of 4.0 mega Bq/kg of ^{18}F -FDG. At 60 min after the injection, images were acquired. Patients rested during the uptake of ^{18}F -FDG to minimize non-specific uptake in muscles. An integrated PET/CT (Discovery ST; GE Medical Systems, Milwaukee, WI, 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 field of view of 50 cm, and a matrix size of 512x512. Immediately after the unenhanced CT scan, a PET scan was performed with a 3.3-mm thick section, a matrix size of 128x128, and an acquisition time of 2.5 min. PET data sets were reconstructed iteratively with an ordered subsets expectation maximization algorithm and segmented

Table I. Pulse sequences used in the present study.

Parameter	T1-weighted image	T2-weighted image	DWI
DWIBS type	GRE	single-shot SE	EPI SE
TR (msec)	Shortest	1,000	11,250
TE (msec)	First: 2.3 (out of 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 imaging; DWIBS, diffusion-weighted whole-body imaging with background body signal suppression/T2 image fusion; GRE, gradient echo; SE, spin echo; EPI, echo planar imaging; TR, repetition time; TE, echo time; NSA, number of signal averages; SPAIR, spectral attenuated inversion recovery.

attenuation correction (three iterations, 15 subsets) and fused onto the CT data. The fused image of PET and CT allowed the evaluation of signals from PET in the anatomical settings. The standardized uptake value (SUV>2.5) was calculated as previously described (20), using the following formula: SUV (g/ml)=regional radioactivity concentration (Bq/ml)/[injected dose (Bq)/body weight (g)].

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

Abdominal and endoscopic US. Abdominal US was performed by senior fellows of the Japan Society of Ultrasonics in Medicine (Tokyo, Japan; www.jsuim.or.jp) in the US unit. The device used was an SSA-700A system (Toshiba Medical Systems Corp., Ohtawara, Japan). The probes used were a 3.75-MHz curved-array probe (PVT-375BT) or a 3-MHz sector-array probe (PST-308T; both from Toshiba Medical Systems Corp.). For patients with PDA, adenomyomatosis or IPMN, endoscopic US was also performed with a GF-UCT260 ultrasound gastrovideoscope (Olympus Corp., Tokyo, Japan) by senior fellows of the Japan Gastroenterological Endoscopy Society (www.jges.net).

Results

Patients. A total of 10 males (age, 73.6±9.6 years) and 8 females (age, 68.9±7.1 years) were enrolled into the present study. Of the enrolled patients, 8 were finally diagnosed with

malignant lesions, including 2 patients with HCC, 1 with CCC, 1 with metastatic liver cancer, 2 with PDA, 1 with RCC and 1 with malignant lymphoma surrounding the abdominal aorta. The remaining patients were diagnosed with benign lesions, which included 5 cases of adenomyomatosis of the gallbladder, 4 cases of IPMN and 1 case of right adrenal adenoma.

Diagnostic performance evaluation. To evaluate the diagnostic performance of DWIBS/T2, detection of cancer in the abdominal cavity was compared with the diagnostic ability of PET/CT (Table II). Positive results were obtained using DWIBS/T2 in all patients with malignancies. By contrast, only 7 out of 8 patients were positively diagnosed with PET/CT. These results suggest that DWIBS/T2 was more sensitive in the detection of cancer of the abdominal cavity.

Representative cases of PDA diagnosis. Images of PDA are demonstrated in Fig. 1, since the precise diagnosis of this cancer is important for patient management, but is occasionally difficult to diagnose. PDA was detected as a low echo lesion with abdominal US (Fig. 1A) and as an unenhanced area with contrast-enhanced CT (Fig. 1B). PDA was not clearly observed by T2WI (Fig. 1C). However, the contrast of PDA tissues was significantly higher when compared with the background tissues on DWIBS (Fig. 1D). Furthermore, DWIBS/T2 illustrated a high signal on the head of the pancreas (Fig. 1E), and enabled the evaluation of the high intensity area in the anatomical setting. Finally, PDA was also strongly positive with PET/CT (Fig. 1F), although it was difficult to evaluate the extent of PDA with this method. These figures demonstrated that DWIBS/T2 clearly showed the PDA lesion as a significantly high intensity area. It was also demonstrated that it was easier to evaluate the extent of PDA in the anatomical setting using DWIBS/T2 as compared with PET/CT.

RCC diagnosis. Contrast-enhanced CT provided positive results for 1 patient with right RCC (Fig. 2A and B). DWIBS/T2 also demonstrated positive results in this patient (Fig. 2C).

Table II. Diagnostic performance for malignant lesions.

Patient no.	Sex	Age (years)	Diagnosis	DWIBS/T2	PET/CT
1	F	73	HCC	(+)	(+)
2	M	83	HCC	(+)	(+)
3	F	57	CCC	(+)	(+)
4	F	74	Liver metastasis	(+)	(+)
5	F	67	PDA	(+)	(+)
6	M	83	PDA	(+)	(+)
7	F	81	RCC (right)	(+)	(-)
8	F	67	ML	(+)	(+)

DWIBS/T2, diffusion-weighted whole body imaging with background body signal suppression/T2 weighted image fusion; PET/CT, positron emission tomography/computed tomography; M, male; F, female; (+), positive results; (-), negative results; HCC, hepatocellular carcinoma; CCC, cholangiocellular carcinoma; PDA, pancreas ductal cancer; RCC, renal cellular carcinoma; ML, malignant lymphoma.

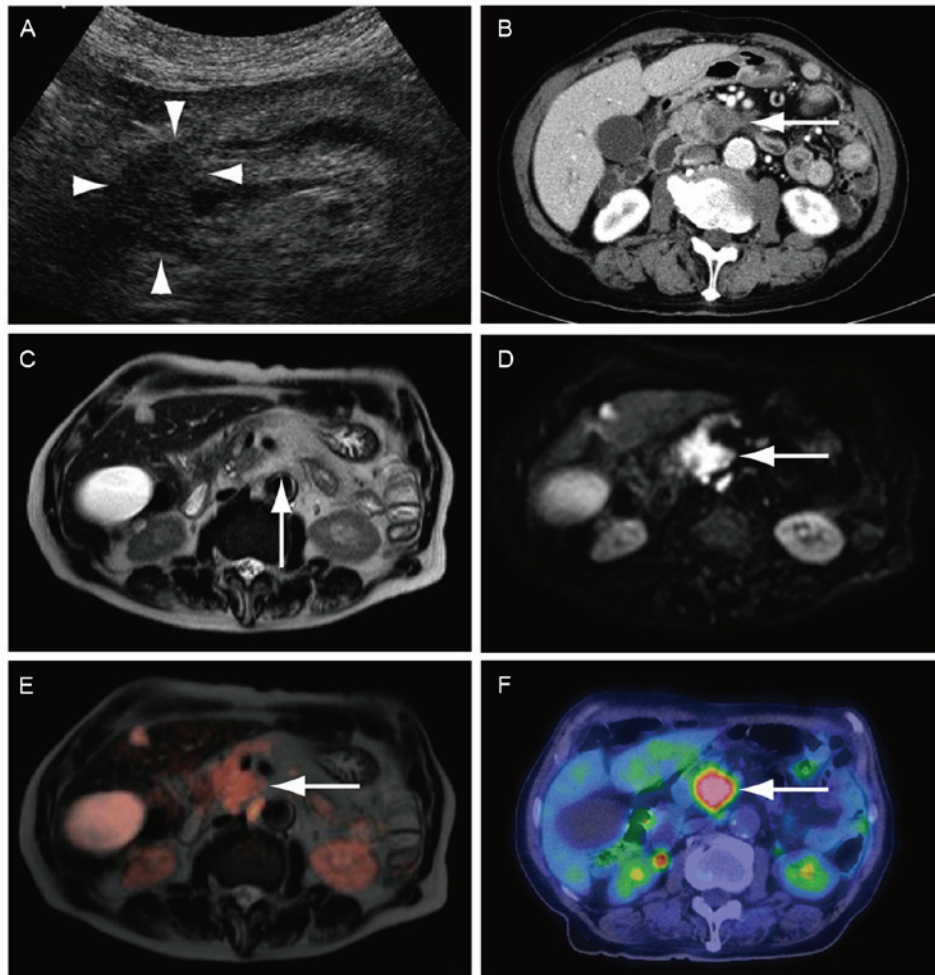


Figure 1. A representative case of pancreatic cancer in an 83-year-old man who presented with back pain. (A) Abdominal ultrasonography illustrates a low echo lesion (arrowheads) in the head of the pancreas. (B) Contrast-enhanced CT image demonstrating an unenhanced area (arrow). (C) T2-weighted image, which does not show an area with different intensity in the pancreas as compared with the surrounding tissues. (D) DWIBS demonstrating a significantly high intensity area (arrow). (E) DWIBS/T2 shows a high intensity area in the head of the pancreas. DWIBS clearly showed the extent of the cancer, while DWIBS/T2 enabled the evaluation of the extent of the cancer in the anatomical settings. (F) PET/CT shows a significantly high signal at the head of the pancreas; however, it was hard to evaluate the extent of the cancer with PET/CT. DWIBS, diffusion-weighted whole body imaging with background body signal suppression; DWIBS/T2, fusion of DWIBS and T2-weighted image; PET, positron emission tomography; CT, computed tomography.

By contrast, PET/CT was negative for RCC (Fig. 2D). These results suggest that PET/CT may occasionally give a negative

diagnosis in patients with cancer. It was also observed that DWIBS/T2 provided a positive diagnosis for cancer that was

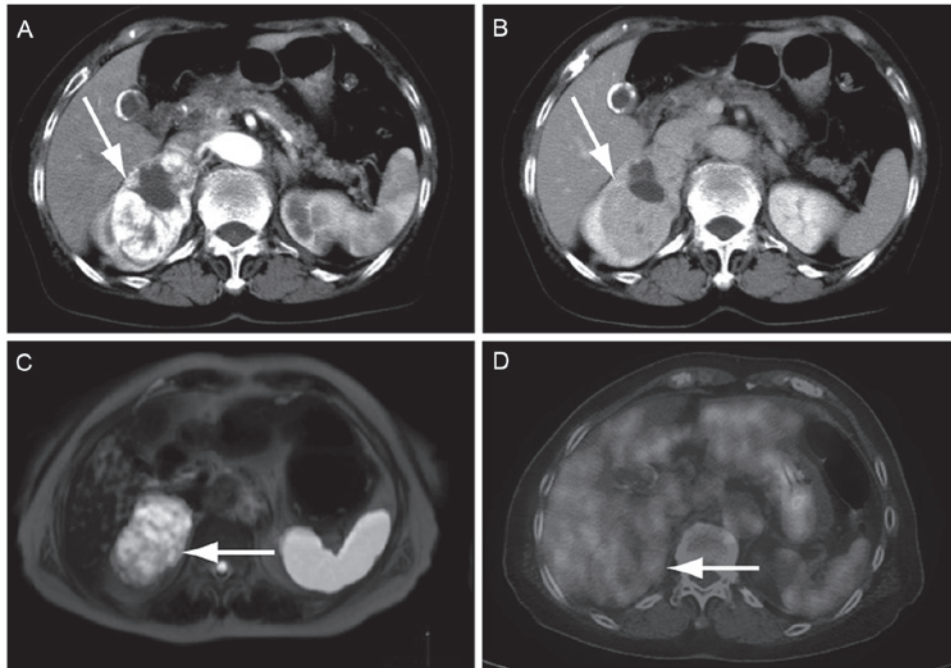


Figure 2. A representative case of renal cell carcinoma in an 81-year-old woman who visited our hospital with back pain and was diagnosed with acute cholangitis. (A) Contrast-enhanced CT image, demonstrating an enhanced tumor (arrow) in the right kidney at 10 sec after the administration of contrast medium. (B) The contrast enhancement agent was washed-out tumor at 180 sec. (C) DWIBS/T2 image, demonstrating a high intensity tumor. (D) The tumor is negative on the PET/CT image. DWIBS/T2, diffusion-weighted whole body imaging with background body signal suppression/T2-weighted image fusion; PET, positron emission tomography; CT, computed tomography.

negative with PET/CT. Thus, it is suggested that DWIBS/T2 was more sensitive compared with PET/CT.

Benign lesion evaluation. To evaluate the positivity of the signal of DWIBS/T2 in benign lesions, images were compared with PET/CT (Table III). All the patients with benign lesions had negative results upon DWIBS/T2 and PET/CT imaging (Table III). These results suggested that DWIBS/T2 and PET/CT provided negative results for benign lesions.

IPMN was demonstrated as a cystic lesion with magnetic resonance cholangiopancreatography (Fig. 3A). This lesion was further investigated with endoscopic US (Fig. 3B), and was seen as a high intensity signal on a T2WI (Fig. 3C). However, IPMN was negative in DWIBS and DWIBS/T2 (Fig. 3D and E), as well as in PET/CT images (Fig. 3F). These results clearly showed that DWIBS/T2 and PET/CT were negative for IPMN. It is also suggested that DWIBS/T2 enabled the evaluation of the negative results in the anatomical setting.

Discussion

In order to improve the anatomical analysis, fusion images of DWIBS with other images can be obtained. Manenti *et al* (21) reported that fusion images of DWIBS and contrast-enhanced CT had the same performance as PET/CT for the detection of primary site tumors and metastasis. As shown in Fig. 1, DWIBS/T2 enabled evaluation of the extent of PDA in the anatomical setting.

Cancer cells exhibit a positive signal with T2WI and DWI (15). However, with T2WI and DWI, positive signals are occasionally unclear, due to strong background signals. DWIBS suppresses these background signals and therefore, cancer

is easily detected using DWIBS with a strong positive signal against a low background. Wang *et al* (22) reported successful detection of HCC and CCC by DWIBS, but not of PDA. In the present study, PDA was successfully detected with DWIBS/T2, as well as PET/CT. The current data suggest that DWIBS/T2 has the same diagnostic performance for PDA as PET/CT. In addition, RCC was negative in PET/CT images in the present study, while it was positive in DWIBS/T2. However, PET/CT has been reported to typically provide a positive diagnosis for RCC (23). The negative results in the present study may be due to the biological characteristics and pathological features of the tumor (24,25). For instance, the glucose metabolism may have been low in the RCC of our patient (26). Notably, DWIBS/T2 provided positive diagnosis for RCC that was negative on PET/CT imaging. These results indicate that DWIBS/T2 was more sensitive for the diagnosis of cancer in the organs of the abdominal cavity.

In the present study, DWIBS/T2 and PET/CT were negative for all of the benign lesions, such as adenomyomatosis of the gallbladder and IPMN. A major issue with adenomyomatosis of the gallbladder is differentiating it from gallbladder cancer (27). Our previous study has already reported that IPMN was negative on DWIBS/T2 (28). The present study confirmed these negative results with PET/CT imaging. These previous and current findings suggest that negative results with DWIBS/T2 or PET/CT may indicate the presence of IPMN.

Overall, the current study results suggest that integrated assessment with DWIBS/T2 and PET/CT is beneficial for patients with cancer in the solid organs in the abdominal cavity (29). However, a major limitation of the study was that it was conducted on a small number of patients. Another limitation was that lymph node metastasis was not evaluated.

Table III Results of benign lesions.

Patient no.	Sex	Age (years)	Diagnosis	DWIBS/T2	PET-CT
1	M	60	Adenomyomatosis	(-)	(-)
2	M	63	Adenomyomatosis	(-)	(-)
3	M	70	Adenomyomatosis	(-)	(-)
4	F	65	Adenomyomatosis of the gallbladder	(-)	(-)
5	M	71	Adenomyomatosis of the gallbladder	(-)	(-)
6	M	85	IPMN	(-)	(-)
7	M	73	IPMN	(-)	(-)
8	M	64	IPMN	(-)	(-)
9	F	67	IPMN	(-)	(-)
10	M	64	Adrenal adenoma (right)	(-)	(-)

DWIBS/T2, diffusion-weighted whole body imaging with background body signal suppression/T2 weighted image fusion; PET/CT, positron emission tomography/computed tomography; M, male; F, female; (-), negative results; IPMN, intraductal papillary mucinous neoplasm.

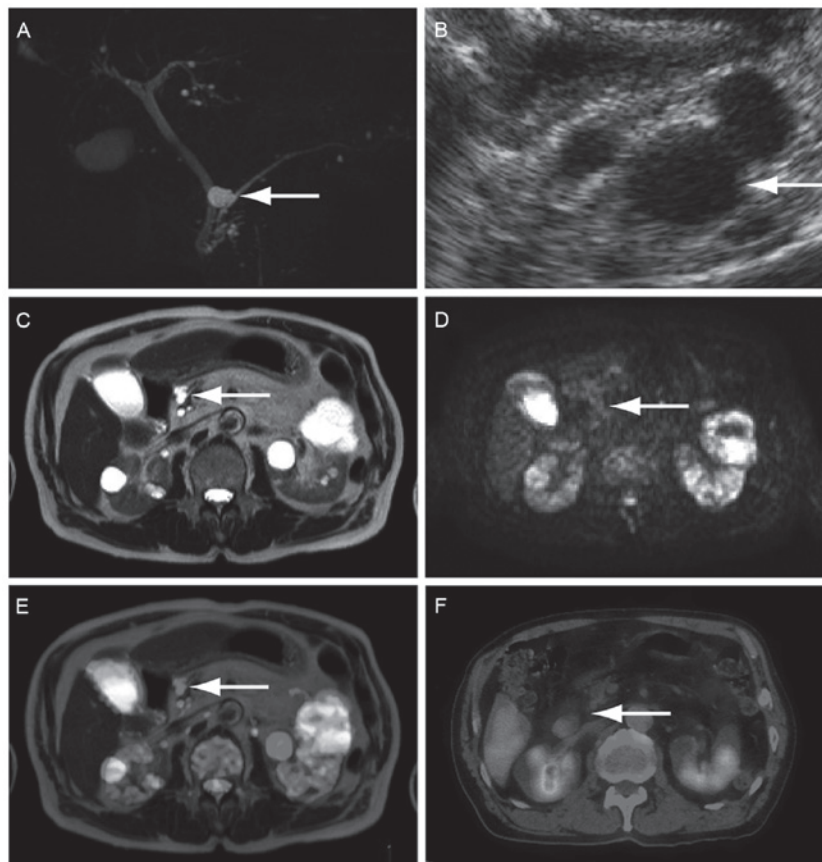


Figure 3. A representative case of intraductal papillary mucinous neoplasm in an 84-year-old man who was regularly followed-up for hepatitis B surface antibody (+). (A) Magnetic resonance cholangiopancreatography shows a cystic lesion (arrow) in the head of the pancreas. (B) Endoscopic US clearly shows a cystic lesion. (C) A T2-weighted image shows a high intensity area in the head of the pancreas. (D) The high intensity area is negative on the DWIBS image. (E) DWIBS/T2 image demonstrates no positive results in the head of the pancreas. (F) PET/CT is also negative for the cystic lesion in the pancreas head. The cystic lesion was finally diagnosed as an intraductal papillary mucinous neoplasm and the patient was followed-up for 30 months, with not evident changes. DWIBS/T2, diffusion-weighted whole body imaging with background body signal suppression/T2-weighted image fusion; PET, positron emission tomography; CT, computed tomography.

Furthermore, the present DWIBS/T2 analysis did not deal with whole body scans, but only evaluated abdominal cavity or pelvis. In the future, more patients should be studied to confirm the present results.

In conclusion, DWIBS/T2 was more found to be sensitive for diagnosing cancer of organs in the abdominal cavity as compared with PET/CT. In addition, negative results with DWIBS/T2 and PET/CT were useful for the diagnosis of

benign lesions, such as adenomyomatosis of the gallbladder and IPMN.

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