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PRACTICE

Diffusion-weighted imaging as a part of PET/MR for small lesion detection in patients with primary abdominal and pelvic cancer, with or without TOF reconstruction technique

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Abstract

Objectives To investigate the value of diffusion-weighted imaging (DWI) in detection of small lesions (≤ 10 mm) in patients with primary abdominal and pelvic cancer in hybrid PET/MR with or without time-of-flight (TOF) technique.

Materials and methods Twenty patients (11 females and 9 males, mean age 67.23 ± 12.90 years) with histologically confirmed primary abdominal and pelvic cancer underwent hybrid PET/MR examination. A total of 64 small lesions were included in this study, which were divided into two groups (≤ 10 mm and 10–30 mm). Visual scores of small lesion detection ability were rated by five-point ordinal scale. The visual scores and detectability of small lesions on TOF PET image, noTOF PET image, and DWI sequences of hybrid PET/MR examination with or without TOF technique were analyzed. Logistic regression model was established for analysis in the value of DWI in hybrid PET/MR examination with or without TOF technique in detection of the small lesions between two groups.

Results The visual evaluation revealed the small lesion (≤ 10 mm) visual scores of DWI (mean ± SD: 4.23 ± 1.41), TOF PET image (mean ± SD: 4.14 ± 0.89), and noTOF PET image (mean ± SD: 2.68 ± 1.13);.and the visual scores of small lesions (10–30 mm) on DWI (mean ± SD: 4.98 ± 0.15), TOF PET image (mean ± SD: 4.57 ± 0.59), and noTOF PET image (mean ± SD: 3.98 ± 1.05). The visual scores of all small lesions on DWI were higher than that on TOF PET data and noTOF PET data in both two groups (**$P < 0.01$). The missed diagnosis rates of small FDG avid lesions (≤ 10 mm) of DWI and noTOF PET image were 9.1% and 9.1%, respectively. However, the TOF PET-based clinical diagnosis detected all small lesions (≤ 30 mm). DWI was of great importance in detection of small lesions (≤ 10 mm) in the absence of TOF technique in PET/MR examination (**$P < 0.01$). DWI's effect on detection of small lesions(10-30 mm) has shown no difference between PET/MR examinations with TOF and without TOF techniques ($P > 0.05$).

Conclusion DWI has significant value in the detection of small lesions (≤ 10 mm) in hybrid PET/MR examination without TOF technique for patients with primary abdominal and pelvic cancer. However, it had less detection benefits in the small lesions (≤ 10 mm) in hybrid PET/MR examination with TOF PET image.

Keywords Diffusion-weighted imaging (DWI) · Hybrid positron emission tomography/magnetic resonance (PET/MR) · Time of flight (TOF) · FDG

Introduction

Hybrid positron emission tomography/magnetic resonance (PET/MR) improves the accuracy in assessment of tumor, based on the combined information of simultaneously obtained PET and MR images. Diffusion-weighted imaging (DWI) and PET are both functional modalities presenting biological characteristics of malignant tumor. PET/MR provides a new generation of multimodal imaging, combining PET data of tumor metabolism with structural and functional information of MRI [1, 2].

Not only the superior anatomic contrast of MR may help provide more accurate location of PET positive lesions, but also the functional information provided by MR, such as DWI and perfusion imaging, may further

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broaden the fields of the diagnostic value of the PET/MR. DWI is widely used to evaluate the microstructural characteristics of water diffusion in biological tissues in routine MR scans, especially for the diagnosis of neoplastic lesions, which yielded a significant improvement in terms of diagnostic confidence during MR examination [3]. PET reflects the metabolism changes in biological tissues, and features high sensitivity for the identification of the cancerous tissues.

Although many previous studies have reported the value of DWI or PET in the characterization of tumors [4–6], the investigation on the combined use of DWI and PET was not carried out widely. Several studies comparing the tumor staging performance of MRI alone (including DWI) and PET/MR could show better results for tumor detection with PET/MR, due to the additional metabolism information provided by 18F-FDG PET [7–9]. Previous studies in hybrid PET/MR scan showed no additional detection value of DWI, for restaging of breast cancer patients [10].

PET images with time of flight (TOF) technique can improve the detection of small lesions and greatly reduce artifacts [8, 11]. PET images with TOF technique has a better SNR than without TOF technique, especially for low-contrast lesions [9, 12].Comparable to the acquisition of PET/MR imaging with TOF technique, additional application of DWI in body integrated PET/MR examinations was debatable.

With the simultaneous TOF-PET/MR imaging being a novel technique, the detection benefit of DWI sequence on the small lesions (≤ 10 mm) in PET/MR imaging with TOF and without TOF technique should be further studied. Therefore, the aim of the present study was to evaluate the value of DWI in detection of the small lesions (≤ 10 mm) in hybrid PET/MR examination for patients with primary abdominal and pelvic cancer regardless of with or without the TOF technique.

Materials and methods

Patient population

Twenty patients (11 males and 9 females, mean age: 67.23 ± 12.90 years, BMI: 23.32 ± 2.85) with histopathological confirmed primary malignant abdominal and pelvic tumors (pancreas cancer: $n = 13$, rectal cancer: $n = 3$, gastric cancer: $n = 1$, ovarian cancer: $n = 1$, colon cancer: $n = 2$) between August 2015 and July 2018 were recruited consecutively for this retrospective study. The study was approved by ethics committee of our institution and written informed consent was obtained from all patients before the hybrid TOF-PET/MR imaging.

Small lesions

A totally of 64 small lesions (≤ 30 mm) were collected in these patients. Early stage hepatocellular carcinomas is defined as multiple tumors up to three tumors and ≤ 30 mm in diameter according to Milan criteria [13]. Most lesions were located in liver in this study, and therefore 30 mm was chosen as a cutoff value for the small lesion. All small lesions, located in the abdominal and pelvic cavities, were divided into two subgroups according to long-axis diameter, group 1 (diameter ≤ 10 mm) group and group 2 (diameter: 10–30 mm). All small lesions were confirmed by two experienced radiologists after reading the images of T2WI and T1WI +C. All these lesions included in the study were highly suspicious of malignant metastases, and all of them presented rim enhancement on the T1WI +C image and high signal in T2WI image. The long-axis diameter of 22 small lesions was smaller than 10 mm and that of 42 small lesions was between 10 and 30 mm. These small lesions were distributed in liver ($n = 38$), lymph node ($n = 25$) and right adrenal gland ($n = 1$). There were 24 small lesions located in liver and 15 lesions in lymph node in patients with pancreatic cancer. Fourteen lesions located in liver and 1 lesion in adrenal gland in patients with rectal cancer. Two lesions located in lymph node in patients with ovarian cancer. Five lesions located in lymph node in patients with gastric cancer, and 3 lesions located in lymph node in patients with colon cancer.

Hybrid PET/MR imaging

All patients were fasted for at least 6 h before integrated PET/MR examination. The injected dose of 18F-FDG for all subjects was 3.7 MBq/kg. All subjects underwent hybrid body PET/MR examination (mean time after tracer injection was about 40 min) by using PET/MR system (SIGNA, GE Healthcare, WI, USA), which features simultaneous PET imaging and 3.0T MR. Acquisition time of each bed position was 6 min. Four bed positions covered from the skull base to mid thighs. Figure 1 provided a workflow of simultaneous PET/MR imaging in this study.

The PET data of PET/MR were reconstructed with TOF and noTOF technique, and all PET images were reconstructed with ordered subsets expectation maximization algorithm (OSEM). The reconstruction parameters: 2 iterations, 28 subsets, Gaussian filter was 5 mm, matrix size was 192×192.

MR sequences of PET/MR included T2WI, DWI, MRAC (MR attenuation correction, MRAC), and T1WI +C sequences. The main parameters of MRI sequences were as follows, axial T2WI (TR = 8000 ms;

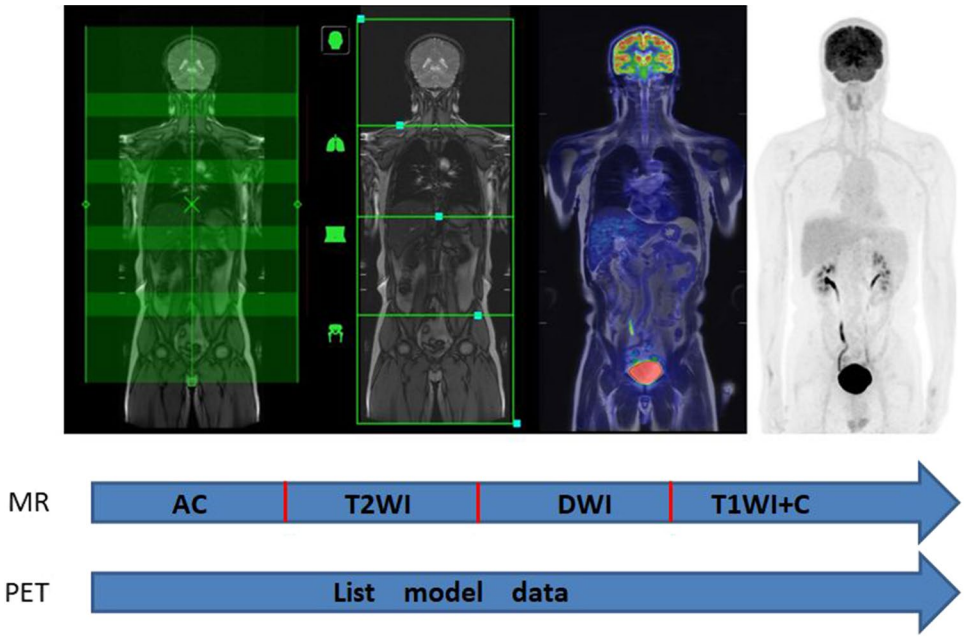

Fig. 1 PET/MR imaging workflow of this study. All MRI sequences and PET data were acquired simultaneously. The standard MR examination encompassed sequences for AC, and diagnosis sequences contained T2WI, DWI, and T1WI + C (Time bars)

TE = 78 ms; matrix = 288 × 288; slice thickness = 8 mm; FOV = 40 × 40 cm); axial DWI with fat saturation and respiratory triggering technique (TR = 6000 ms; TE = 60 ms; *b*-values = 50, 800 s/mm^2; slice thickness = 8 mm; FOV = 40 × 36 cm; axial T1WI contrast enhanced sequence (T1WI + C:TR, 5 ms; TE, 1.8 ms; matrix, 256 × 180; slice thickness, 4.8 mm; FOV, 40 × 32 cm). T1WI (LAVA-Flex) sequence for each bed position (TR = 4.045 ms, TE = 1.674 ms, slice thickness/space = 5.2/− 2.6 mm, FOV = 50 × 38 cm, Matrix = 256 × 128, NEX = 0.7) was acquired to serve as a template for MRAC, which was automatically generated based on the attenuation diagram of the four tissue (air, lung, fat and soft tissue) segments [14]. A total of PET/MR scan time was approximately 40 min.

Image analysis

A totally of 64 small lesions were reviewed by two radiologists and nuclear medicine doctors on a GE PET/MR advantage workstation (Version: AW4.6). Firstly, the small lesion visual scores of TOF PET data, noTOF PET data and DWI were rated by lesion contrast to background, sharpness of contours according to five-point ordinal scale (1 = unacceptable, 2 = poor quality, 3 = medium, 4 = good quality, 5 = excellent quality) (Table 1, Fig. 2). A circular region of interest (ROI) with the maximal diameter was positioned over the areas in the axial PET images [13]. In addition, ROIs (area is 192 mm^2) located in the right lobe of the liver as the background tissue in all subjects were selected. The ROIs were placed away from lesions and major blood vessels. Logistic regression model was established for evaluate the small lesion detection ability of DWI on small lesions in integrated PET/MR with or without TOF PET technique. In addition, SUV_{max} and SUV_{mean} of all small lesions and background tissue (liver) from PET image with TOF and noTOF technology were manually measured, respectively. All imaging datasets including TOF PET image, noTOF PET image, DWI of PET/MR were separately evaluated on the GE AW4.6 Workstation and independently analyzed by two doctors with 5 years of work experience in MR and molecular imaging.

Table 1 Five-point ordinal scale used for visual scores in rating small lesions

SCORE	Overall visual quality	Clarity of small lesion	Edge of small lesion
1	Unacceptable	Invisible	Invisible
2	Poor	Unclearness	Unclearness
3	Medium	Clearness	Unclearness
4	Good	Clearness	Clearness
5	Excellent	Sharpness	Sharpness

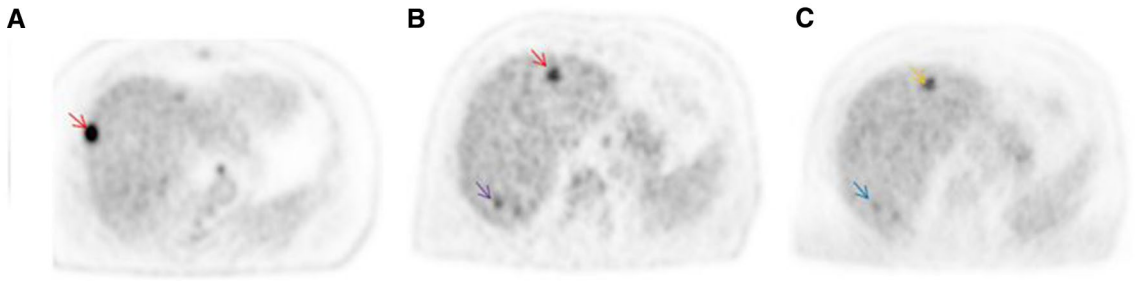

Fig. 2 Visual scores of small lesion. Score 5: red arrow; Score 4: red arrow; Score 3: yellow arrow; Score 2: purple arrow; Score 1: blue arrow

Statistical analysis

IBM SPSS 17.0 (IBM, Armonk, NY, USA) was used for statistical analysis. Analysis of Variance (ANOVA) was applied to test the differences in lesion visual scores of small lesions among TOF PET data, noTOF PET data and DWI image, which were acquired from hybrid body PET/MR examination. Furthermore, paired *T* test were performed to compare the differences in SUV_{max} and SUV_{mean} of all small lesions (≤ 10 mm and 10–30 mm) from PET image with TOF and noTOF technology. Generally, all values were expressed as mean ± SD. The consistency test was performed for the scores of the small lesions by the two readers. Logistic regression model was established for evaluating the detection value of DWI in the small lesions between ≤ 10 and 10–30 mm with application of TOF reconstruction or not in integrated PET/MR examination. *P* value < 0.05 was considered as statistically significant difference.

Results

Consistency test results

In this study, the consistency test was performed to analysis the consistency in the scores of small lesions between two readers, and found that the intergroup correlation coefficient was 0.989, It demonstrates that the evaluation in visual scores of small lesions between two readers was significant consistency.

The visual scores of small lesions on DWI, TOF PET and noTOF PET image

The visual evaluation revealed that the small lesions (≤ 10 mm, 8.59 ± 1.03 mm) visual scores of DWI (4.23 ± 1.41), TOF PET image (4.14 ± 0.89) and noTOF PET image (2.68 ± 1.13). The visual scores of small lesions (10–30 mm, 17.29 ± 4.77 mm) on DWI (4.98 ± 0.15), TOF PET image (4.57 ± 0.59) and noTOF PET image (3.98 ± 1.05). The visual scores of TOF image was higher than that of noTOF PET image in both two groups(**$P < 0.01$).The visual scores of all small lesions on DWI were higher than that on TOF PET and noTOF PET data in both two groups (**$P < 0.01$) (Table 2, Fig. 3).

Table 2 Visual scores of small lesion between PET data and DWI images

Small lesion (mm)	TOF PET	noTOF PET	DWI	*F* value	*P*
≤ 10	4.14 ± 0.89	2.68 ± 1.13	4.23 ± 1.41	12.230	0.000**
10–30	4.57 ± 0.59	3.98 ± 1.05	4.98 ± 0.15	21.883	0.000**
0–30	3.53 ± 1.22	4.42 ± 0.72	4.82 ± 0.89	25.596	0.000**

**$P < 0.01$

Detection ability of small lesions of DWI, TOF PET data and noTOF PET data

The present results show that the missed diagnosis rate of small lesions (≤ 10 mm) on DWI and noTOF PET image was 9.1% and 9.1%, respectively, but no small lesion (≤ 10 mm) was missed diagnosis on TOF PET image. There was no small lesion (10–30 mm) was missed diagnosis on DWI, noTOF PET and TOF PET image.

DWI's effect in detection of the small lesions in PET/MR examination with TOF and noTOF technology

The logistic model showed that DWI was of great importance in detection and specificity of the small lesions (≤ 10 mm) in the absence of TOF technique in PET/MR examination (**$P < 0.01$). However, there has been no significant effect in small lesions (10–30 mm) ($P = 0.995$), indicating that DWI's effect on small lesions (10–30 mm) recognition has not much different detection ability for lesions in PET/MR image with TOF and without TOF technique (Table 3).

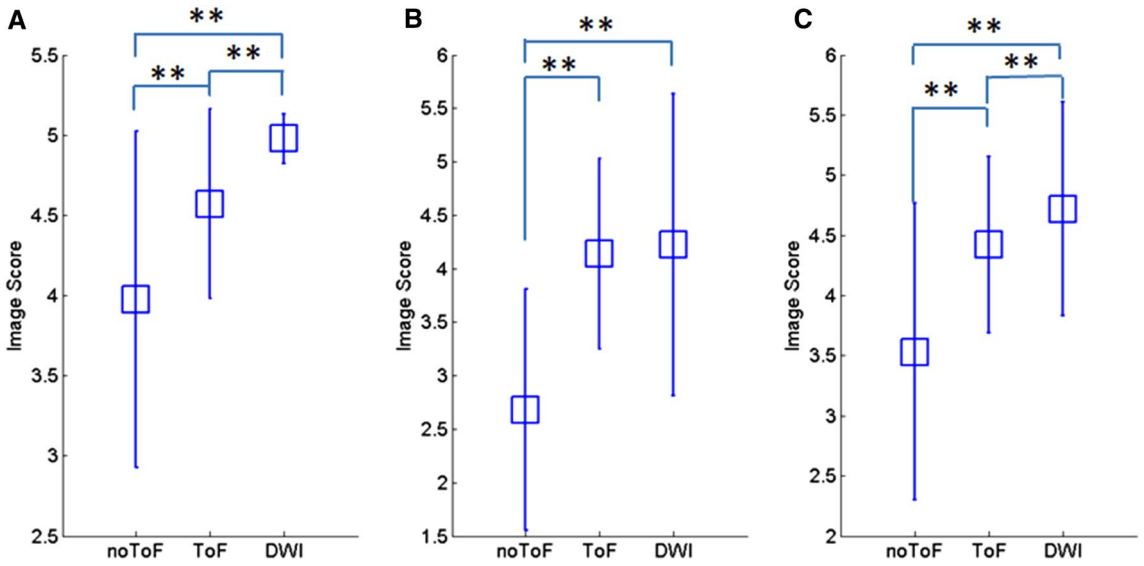

Fig. 3 Compare the difference in the visual scores of small lesions on DWI, TOF PET and noTOF PET images. **a** Visual scores of small lesions (≤10 mm) on DWI was higher than that on TOF PET data and noTOF PET image (**$P<0.01$). The visual scores of the small lesions of DWI, TOF PET data were all higher than that on noTOF PET data (**$P<0.01$). **b** The visual scores of the small lesions (10–30 mm) of DWI, TOF PET data were all higher than that on noTOF PET data (**$P<0.01$). There was no difference in small lesions (10–30 mm) between DWI and TOF PET image. **c** Visual scores of small lesions (≤30 mm) on DWI was higher than that on TOF PET data and noTOF PET image (**$P<0.01$). The visual scores of the small lesions of DWI, TOF PET data were all higher than that on noTOF PET data (**$P<0.01$)

Table 3 DWI's effect in detection of the small lesion in PET/MR examination with TOF and noTOF technique

TOF VS noTOF	*z* value	*P*
Small lesion (< 10 mm)	3.851	0.000**
Small lesion (10–30 mm)	0.007	0.995

**$P<0.01$

Table 4 SUV_{max} and SUV_{mean} of small lesions and liver

Small lesion	SUV	TOF PET	noTOF PET	*T* value	*P*
≤10 mm	SUV_{max}	9.44 ± 5.35	6.96 ± 4.91	0.971	0.000**
	SUV_{mean}	6.81 ± 3.89	5.61 ± 3.99	0.965	0.000**
10–30 mm	SUV_{max}	8.92 ± 3.67	7.81 ± 3.44	0.964	0.000**
	SUV_{mean}	6.41 ± 2.32	5.77 ± 2.27	0.963	0.000**
Liver	SUV_{max}	2.60 ± 0.65	3.27 ± 0.65	1.388	0.179
	SUV_{mean}	2.05 ± 0.51	2.04 ± 0.51	1.542	0.137

**$P<0.01$

SUV_{max} and SUV_{mean} of the small lesions and background tissue from TOF PET and noTOF PET image

Both SUV_{mean} and SUV_{max} of small lesions (≤10 mm, 10–30 mm and ≤30 mm) of TOF PET image were all significantly higher than that of noTOF PET image (**$P<0.01$), however, there was no significant difference in SUV_{max} and SUV_{mean} of background tissues (liver) ($P>0.05$) (Table 4, Fig. 4). It was demonstrated that the SUV of background tissues was not influenced by the application TOF technology to PET data.

Discussion

In this study, we investigated the value of DWI in the detection of small lesions smaller than 10 mm in process of hybrid PET/MR examination for patients with abdominal and pelvic cancer. We found that the visual scores of all small lesions (≤10 mm, 10–30 mm and 0–30 mm) of DWI was higher than that of TOF PET data and noTOF PET image. In addition, some small lesions (≤10 mm) were missed diagnosis on DWI and noTOF PET images (Fig. 5); however, no small lesions (≤10 mm) were missed in diagnosis of TOF PET images. All small lesions (10–30 mm) were found on TOF PET, noTOF PET and DWI images (Fig. 6). Meanwhile the logistic regression analysis was carried out and the results implied that DWI was a necessary sequence in detection of small lesions (≤10 mm) in hybrid PET/MR examination without TOF technology. However, no additional detection benefits of DWI was found in the lesions (10–30 mm) in hybrid PET/MR examination, no matter with TOF and without TOF technology.

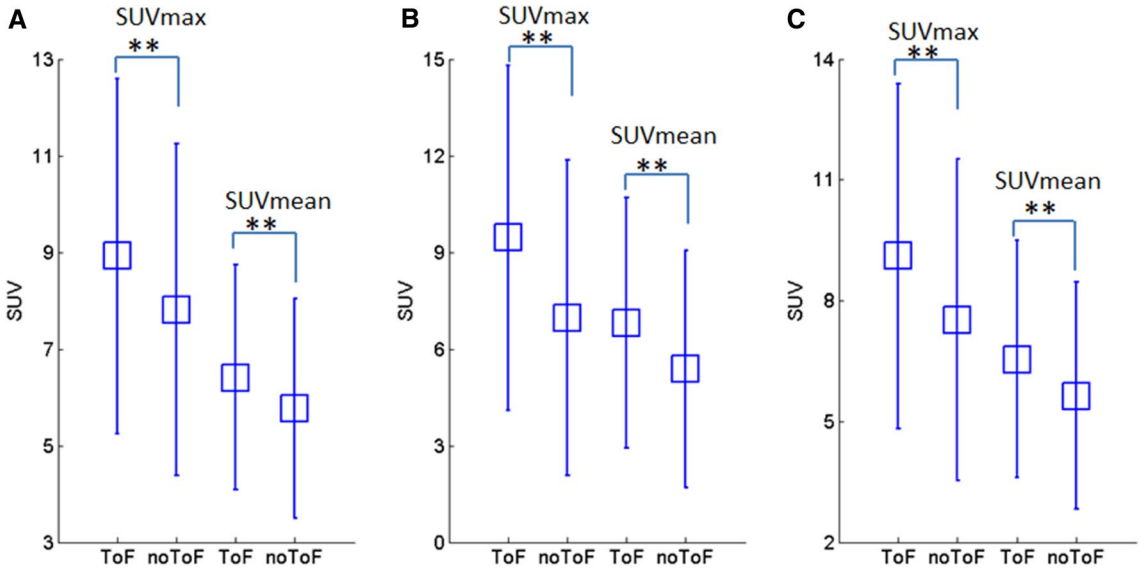

Fig. 4 Compare the difference in SUV_{max} and SUV_{mean} of small lesions between PET with TOF and noTOF PET technique. **a** (≤ 10 mm), **b** (10–30 mm) and **c** (≤ 30 mm). Both SUV_{max} and SUV_{mean} of small lesions (≤ 10 mm, 10–30 mm and ≤ 30 mm) on TOF PET image were all higher than that on noTOF PET image (**$P < 0.01$)

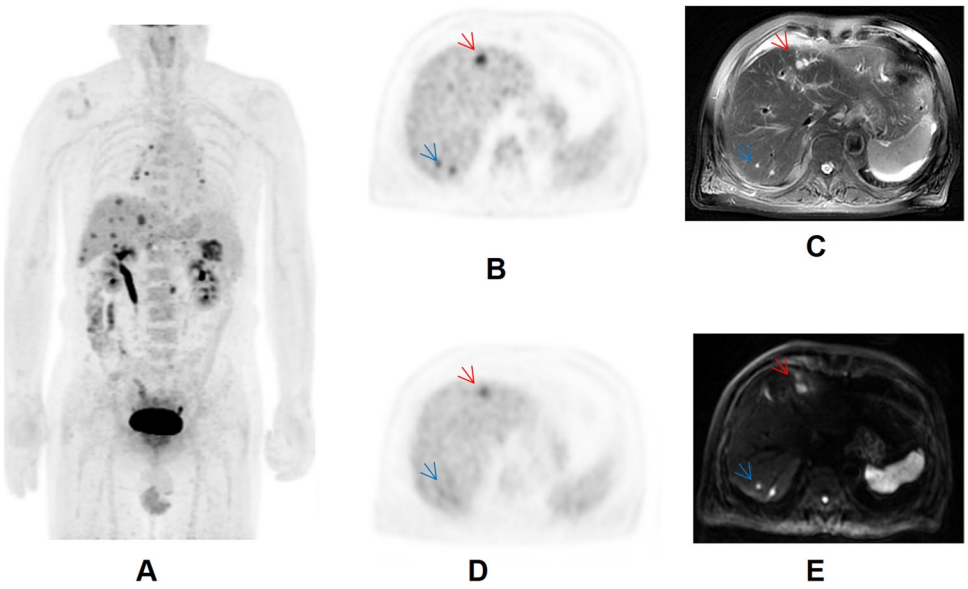

Fig. 5 Example of pancreatic cancer with multiple hepatic metastases. **a** MIP view of PET (PET/MR). **b** Axial TOF PET (PET/MR). **c** AXI T2WI. **d** Axial noTOF PET (PET/MR). **e** DWI. PET/MR showed multiple lesions in the liver. The image qualities of small lesion (red arrow) located in S3 from TOF PET data and DWI showed better than that of noTOF PET image. Two small lesions (≤ 10 mm) located in S7 (blue arrow) were visible on TOF PET image, T2WI and DWI. However, these small lesions (≤ 10 mm) were not detected on noTOF PET image

DWI provided good image quality and high sensitivity in the detection of focal liver lesions and was helpful in managing treatment in patients with colorectal cancer [15]. In addition, DWI was also very helpful in detection of lymph nodes metastasis in patients with cholangiocarcinoma [16]. And malignant tumors always show high signal intensity in DWI images and lower ADC values than nonmalignant lesions [17]. A previous study suggested that sensitivity of DWI in detection of focal liver lesions (≤ 10 mm) was 91.4%, and accuracy was 93.0% [18]. Another study found that free breathing DWI scores in detection of focal malignant liver lesions (≤ 10 mm) were 80% and 100% for the lesions (> 10 mm) [19]. The present study showed that DWI score in detection of focal liver lesions (≤ 10 mm) was 90.9%, and also has the same detection ability (100%) for the lesions (> 10 mm) as the previous study.

18F-FDG PET is valuable method for assessing the metabolic activity of tumors [20, 21]. Although DWI is a very useful sequence in finding small metastatic lesions for the conventional MR imaging, the additional detection value of it for integrated PET/MR imaging is controversial [22–24]. It was reported that DWI and PET/CT have considerable comparable in detection and characterization of tumors, such as gynecological malignant tumors [25–27]. It had been

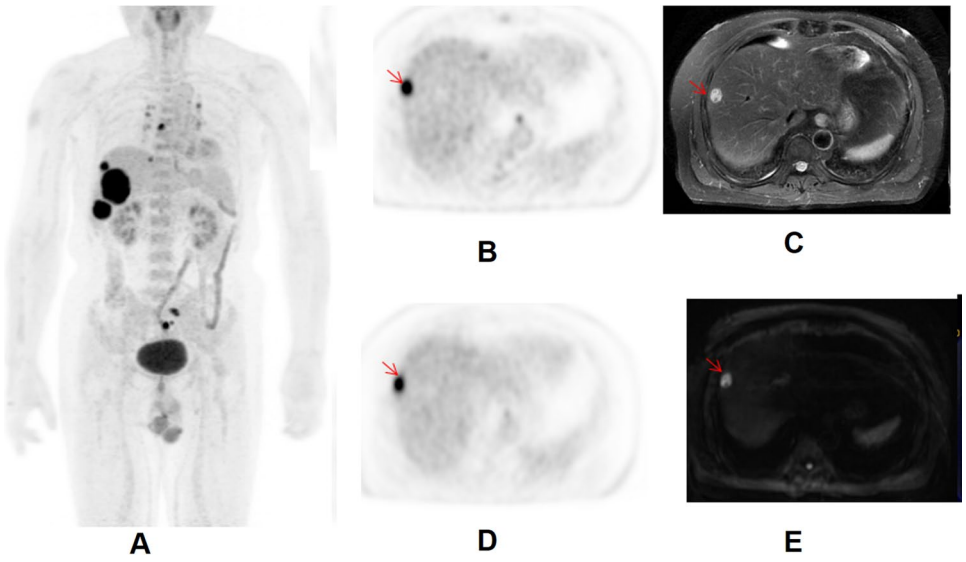

Fig. 6 Example of pancreatic cancer with multiple hepatic metastases (Red arrow). **a** MIP view of PET (PET/MR). **b** Axial TOF PET (PET/MR). **c** AXI T2WI. **d** Axial noTOF PET (PET/MR). **e** DWI. PET/MR showed multiple lesions in the liver. The small lesions (10–30 mm) located in S8 was shown excellent image quality on all images

found that DWI sequence of PET/MR imaging have no additional diagnostic value for systemic staging of patients with pelvic malignant tumors [28]. The visual score of noTOF PET image for the lesions (0–30 mm) was lower than that of TOF PET image and DWI image, which demonstrated that DWI and TOF PET images were significantly superior to noTOF images in display of these small lesions. Visual score of small lesions($\leq$10 mm) on noTOF PET image was lower than that of TOF PET images, which suggests TOF technology maybe significantly improve the detection ability of PET image in the small lesions ($\leq$10 mm). We also found that the obviously detection benefits of DWI sequence in detection of the small lesions ($\leq$10 mm) in hybrid PET/MR imaging without TOF technology for patients with primary abdominal and pelvic cancer, which is not reported in previous studies. It was also underlined that DWI could be a necessary sequence of PET/MR examination without TOF technology in the detection of small lesions ($\leq$10 mm).

TOF technique can improve the detection rate of small lesions [13]. It was also reported that TOF technology can help improve the spatial resolution and SNR of PET image, especially for low-contrast lesions [29]. TOF technique maximizes SUV_{max} of low-contrast lesions of liver metastases in patients with colorectal cancer [30].Shang et al. [31] also reported that application of TOF and PSF significantly increased the SUV value of small lesions in hybrid PET/MR images, potentially improving small lesion detectability. We also found that the SUV_{max} and SUV_{mean} of small lesions($\leq$10 mm and 10–30 mm) from PET image was increased by TOF technology, which demonstrated that lesion visibility for small lesions were improved by the application of TOF technology which was in consistent with previous studies [12, 14]. The present study also showed that all small lesions ($\leq$10 mm) were detected on TOF PET image, however, 9.1% of small FDG lesions ($\leq$10 mm) were missed in diagnosis on noTOF PET image, which supports the fact that TOF technique enhances visibility and detectability of small lesions ($\leq$10 mm) in hybrid body PET/MR scan. The present results also showed that the detection ability of small lesions (10–30 mm) were similarity in both DWI and PET image with or without TOF technology. It demonstrated that DWI sequence can't give additional benefits in detection of small metastases (10–30 mm) in hybrid PET/MR examination, no matter with or without TOF technique.

Conclusion

Overall, our findings demonstrated that DWI sequence is a necessary sequence in detection of the small lesions ($\leq$10 mm) in hybrid PET/MR examination without TOF technology for patients with primary abdominal and pelvic cancer. In other words, TOF technology of PET/MR is a valuable tool to detect a small lesions, especially for the small lesions which are smaller than 10 mm.

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Compliance with ethical standards

Conflict of interest These authors declared no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the insti-

tutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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