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ORIGINAL ARTICLE

The potential usefulness of ^{18}F-FDG PET/CT for detecting colorectal carcinoma and adenoma in asymptomatic adults

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Abstract
Objective The aim of this study was to evaluate the potential usefulness of ^{18}F-FDG PET/CT for detecting colorectal carcinoma and adenoma in asymptomatic adults.
Methods 614 subjects were enrolled in this retrospective study. They underwent both ^{18}F-FDG PET/CT and colonoscopy in the same day as part of a cancer-screening program. Small focal FDG accumulation along the colorectum on ^{18}F-FDG PET/CT images were compared with colonoscopy findings. Size of lesion was measured on colonoscopy and histology was determined by biopsy or polypectomy.
Results In 614 ^{18}F-FDG PET/CT images, 27 foci of FDG uptakes were observed in the colorectal area in 25 subjects. The overall sensitivity and specificity of ^{18}F-FDG PET/CT were 5.6 and 96.8 %, respectively, but sensitivity to detect lesions larger than or equal to 1 cm was 25.8 %. On the ROC analysis, the optimal cut-off value for differentiating premalignant and malignant lesions from other benign conditions was 5.0 (sensitivity = 50 %, specificity = 88 %, AUC = 0.643).
Conclusions Colonoscopic evaluation could be recommended by presence of focal colonic FDG uptake on ^{18}F-FDG PET/CT, especially when SUV_{max} is over 5.

Keywords FDG PET · Colorectal carcinoma · Adenoma · Colonoscopy

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Introduction

Colorectal cancer is one of the most common malignancies in Korea. Westernization of diet and an aging society are two major reasons for the ever-increasing incidence of colorectal cancer [1].

The concept that most colorectal carcinomas develop from preformed adenomatous polyp is widely accepted, which is referred to as adenoma–carcinoma sequence [2, 3]. It is well-known that only a minority of these adenomas undergoes malignant transformation, and it can take an average of approximately, 10 years for an adenoma, particularly one smaller than 1 cm in diameter, to transform into invasive cancer [3]. Therefore, the main targets of screening programs are adenomas with advanced pathologic features, i.e., high-grade dysplasia or early carcinoma. Detection and removal of adenomatous polyps are crucial for prevention and a potential cure. Colonoscopy is used to detect and remove adenomatous polyps.

Positron emission tomography (PET) using 2′-[^{18}F] fluoro-2′-deoxy-D-glucose (FDG) is well-accepted in the imaging workup of various malignancies. PET is recognized as a useful tool to manage colorectal cancer and was shown to have an additional value in the detection of recurrent colorectal cancer [4, 5]. The introduction of FDG PET/CT has paved the way for anatomic information

regarding FDG uptake. Accordingly, PET/CT has been carried out, even for health check-up, and some cases have been reported in which FDG colonic uptake revealed colonic adenomas or carcinomas [6–11].

This retrospective study was aimed to determine the usefulness of ^{18}F-FDG PET/CT scans compared with colonoscopy for the evaluation of colorectal (pre-) malignancy, such as adenomas and carcinomas in asymptomatic adults.

Materials and methods

Patient selection

Subjects of this retrospective study were 614 asymptomatic adults (427 men, 187 women; mean age ± SD, 51.45 ± 7.65 years) who had undergone both ^{18}F-FDG PET/CT and colonoscopy as part of our cancer-screening program between March 2010 and August 2011. Colonoscopy was performed after ^{18}F-FDG PET/CT in the same day.

^{18}F-FDG PET/CT imaging

The subjects fasted at least 6 h prior to the intravenous injection of ^{18}F-FDG(0.12 mCi/kg). Blood glucose levels were checked in all subjects prior to the injection of ^{18}F-FDG. A^{18}F-FDG PET/CT was performed only when blood glucose levels did not exceed 150 mg/dL (8.3 mol/L). ^{18}F-FDG PET/CT were acquired using Discovery LS PET/CT scanner (GE Medical Systems, Waukesha, WI). All studies were performed in three-dimensional mode with five to seven bed positions. The CT scan was performed immediately before the PET scan in the Discovery LS PET/CT scanner, using the multi-detector helical CT scanner. The imaging parameters were as follows: 140 kVp, 80 mA, 0.8 s per CT rotation, pitch of 6, and 22.5 mm/s table speed. The CT images were created in a matrix size of 512 × 512 but were reduced to a 128 × 128 matrix to correspond to the PET emission images. The emission data were acquired for 2.5 min in each bed position 60 min after the intravenous injection of ^{18}F-FDG. The PET images were reconstructed using CT for attenuation correction with the OSEM algorithm (2 iterations, 16 subsets).

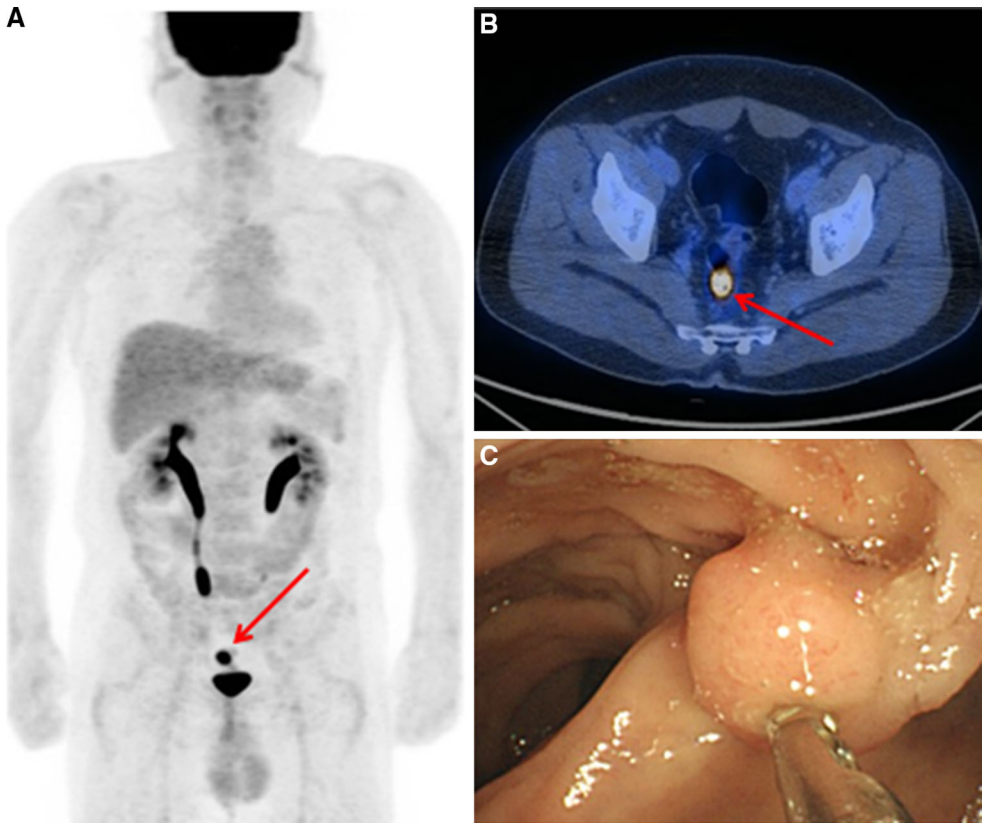

Fig. 1 Representative images of a 55-year-old man with tubulovillous adenoma are defined as true-positive. **a** and **b**, Intense focal FDG uptake (SUV_{max} = 16.3, *arrow*) located sigmoid colon was seen on FDG PET/CT images. **c** A 1.5 cm sigmoid colon polyp was seen in colonoscopy

Colonoscopy

Experienced gastroenterologists in our total healthcare center performed all of the flexible endoscopic procedures. All abnormal colonic lesions were described and biopsied. The locations of the abnormal colonic lesions were classified into 6 segments: cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum. The size of the polyp or mass was measured and compared with the width of a forceps.

Imaging data analysis and correlation with colonoscopy

The ^{18}F-FDG PET/CT images were reviewed by two experienced physicians in nuclear medicine. The readers analyzed the PET and fused images in both the axial and coronal planes without being informed of the endoscopic or surgical pathologic results. Any focal FDG uptake of colorectal area greater than what was seen in the normal hepatic parenchyma was considered intense focal bowel uptake. The attenuation-corrected PET component of the study was used to measure the maximum standardized uptake value (SUV_{max}) over the appropriate region of interest in the localized FDG activity. The specific localization of focal FDG activity in the colorectal area was compared to the site of endoscopic biopsy performed for histologic diagnosis. Contiguous diffuse FDG uptake in the intestine was not considered in this study because it is usually physiologic [12, 13].

In our study, the histopathologic diagnoses were grouped as primary carcinoma; premalignant lesions, which included adenoma with varying degrees of dysplasia; and benign lesions, such as hyperplastic polyps. A ^{18}F-FDG PET/CT result was considered true-positive when a FDG focus and a colonoscopic or surgical abnormality were situated in the same location, and pathologic result of this lesion was adenocarcinoma or adenoma (Fig. 1). False-positive results included benign condition such as diverticulitis and physiologic bowel uptake, which was defined as focal FDG uptake without a matching colonoscopic abnormality. When a mucosal lesion of any size was detected at endoscopy with no corresponding focal FDG

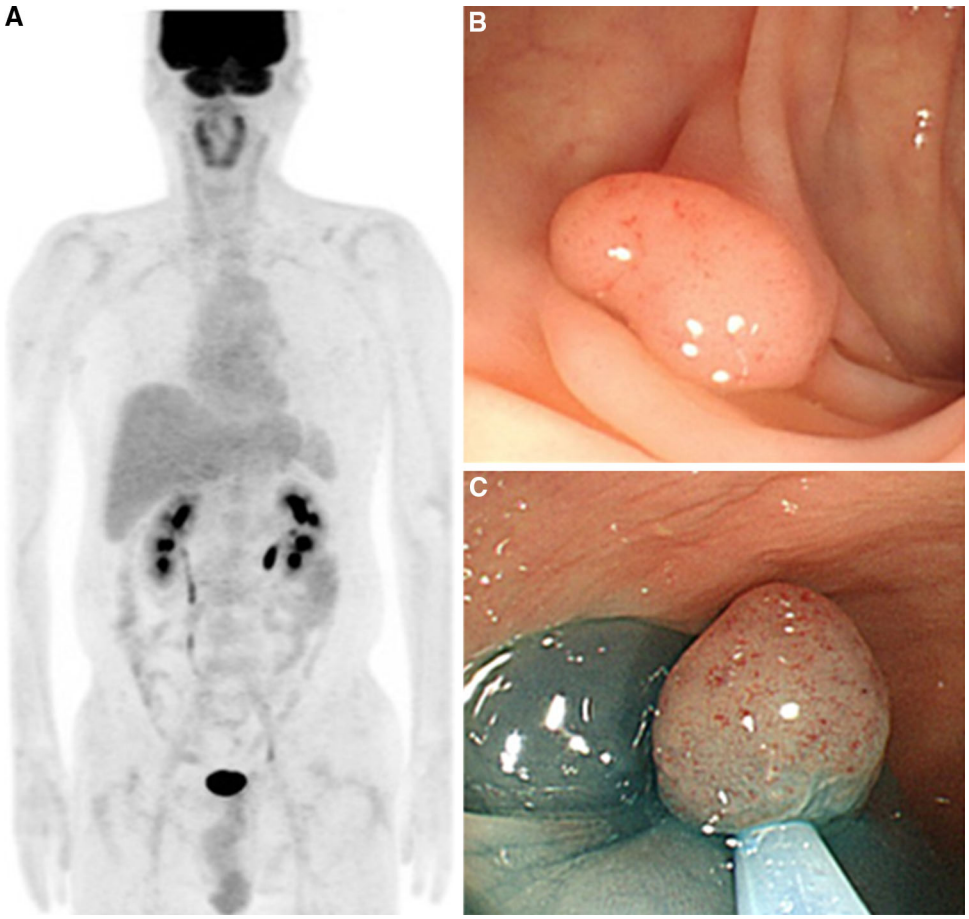

Fig. 2 Representative images of a 50-year-old man with tubular adenoma with low grade dysplasia are defined as false-negative. **a** Any focal FDG uptake was not seen on FDG PET image. **b** and **c** A 1.5 cm sigmoid colon polyp was seen in colonoscopy and performed polypectomy

uptake, the ^{18}F-FDG PET/CT result was interpreted as false-negative (Fig. 2).

Statistical analysis

FDG uptake of ^{18}F-FDG PET/CT was analyzed for sensitivity, specificity, accuracy, and positive and negative predictive values. MedCalc Version 7 was used to determine the optimal cut-off values for differentiating (pre-) malignant lesions from other benign lesions on the ROC analysis. Comparison between true and false positive FDG uptake was analyzed by Student's *t* test. Also, comparison between true positive lesions and false negative lesions on their size was analyzed by Student's *t* test. A p value <0.05 was considered statistically significant.

Ethics statement

This study was performed after obtaining approval from the Institutional Review Board of Kangbuk Samsung

Table 1 Colonoscopic findings and pathologic results for 25 subjects with focal FDG uptake

Patient no.	Location	True positive diagnosis			False positive diagnosis		False negative diagnosis	
		Final diagnosis	Size (cm)	SUV_{max}	Final diagnosis	SUV_{max}	Final diagnosis	Size (cm)
1	T-colon				Physiologic activity	5.0		
2	Cecum				Diverticulitis	3.2		
3	Rectum	TA with LGD	0.7	2.7				
4	Cecum				Physiologic activity	7.8		
5	Rectum	TA with LGD	1.5	4.5				
	A-colon						TA with LGD	0.7
6	A-colon						TA with LGD	0.7
	S-colon				Diverticulitis	5.0		
7	Rectum	Adenocarcinoma	2.0	6.6				
	T-colon						TA with LGD	0.3
8	T-colon				Physiologic activity	4.0		
9	A-colon				Physiologic activity	3.4		
10	A-colon				Physiologic activity	3.3		
11	A-colon				Physiologic activity	3.0		
12	Cecum				Physiologic activity	2.8		
13	Cecum				Physiologic activity	4.4		
14	A-colon	TA with LGD	1.2	3.1				
	S-colon	TA with LGD	1.2	8.3				
	S-colon	TA with LGD	0.9	6.8				
15	Rectum				Physiologic activity	8.5		
16	T-colon				Physiologic activity	5.0		
17	A-colon				Physiologic activity	3.1		
18	A-colon				Physiologic activity	4.8		
	T-colon						TA with LGD	0.5
	T-colon						TA with LGD	0.3
19	A-colon				Physiologic activity	4.5		
20	D-colon	TA with LGD	1.5	5.7				
	A-colon						TA with LGD	0.2
	A-colon						TA with LGD	0.5
21	S-colon	TA with LGD	1.0	4.5				
22	D-colon				Physiologic activity	3.0		
23	A-colon				Physiologic activity	4.0		
24	S-colon	Adenocarcinoma	6.5	24.1				
25	S-colon	Tubulovillous adenoma	1.5	16.3				
Mean ± SD			1.8 ± 1.7	8.3 ± 6.8		4.4 ± 1.6		0.5 ± 0.2

T-colon transverse colon, *A-colon* ascending colon, *S-colon* sigmoid colon, *D-colon* descending colon, *TA with LGD* tubular adenoma with low grade hyperplasia

Table 2 Comparison of ^{18}F-FDG PET/CT and endoscopy results (No. of lesions)

Pathology by colonoscopy	FDG uptake of PET/CT		
	True positive ($n = 10$)	False positive ($n = 17$)	No uptake ($n = 683$)
Adenocarcinoma ($n = 2$)	2	0	0
Tubulovillous adenoma ($n = 1$)	1	0	0
Adenoma with low grade dysplasia ($n = 177$)	7	0	170
Hyperplastic polyp ($n = 51$)	0	0	51
Other benign lesions ($n = 29$)	0	2	27
No mucosal lesion ($n = 450$)	0	15	435

Table 3 Comparison of ^{18}F-FDG PET/CT and endoscopy results for all lesions

PET findings	Colonoscopy results		Total
	Positive	Negative	
Positive	10	17	27
Negative	170	513	683
Total	180	530	

Table 4 Comparison of ^{18}F-FDG PET/CT and endoscopy results for lesions $\geq$ 1 cm

PET findings	Colonoscopy results		Total
	Positive	Negative	
Positive	8	17	25
Negative	23	513	536
Total	31	530	

Table 5 Comparison of ^{18}F-FDG PET/CT and endoscopy results for lesions <1 cm

PET findings	Colonoscopy results		Total
	Positive	Negative	
Positive	2	17	19
Negative	147	513	660
Total	149	530	

Hospital (IRB No. KBC12004). This study was waived of informed consent from the board.

Results

614 asymptomatic adults (427 men, 187 women; mean age ± SD, 51.45 ± 7.65 years) had undergone both ^{18}F-FDG PET/CT and colonoscopy in the same day. 435 of 614 subjects were negative on ^{18}F-FDG PET/CT and colonoscopy. 154 out of 614 subjects (248 lesions: 170 tubular adenoma with low grade dysplasia, 51 hyperplastic polyp, 11 polypoid colonic mucosal tissue, 8 chronic non-specific colitis, 2 carcinoid tumor and 6 others, size: 0.49 ± 0.31 cm) were negative on ^{18}F-FDG PET/CT and positive on colonoscopy. 25 out of 614 subjects (27 focal uptakes) were positive on ^{18}F-FDG PET/CT. Results of the 25 subjects with positive finding of ^{18}F-FDG PET/CT (27 focal uptakes) were summarized on Table 1. The number of true positive was 10 out of 27 focal uptakes (size: 1.8 ± 1.7 cm; 2 adenocarcinoma, 1 tubulovillous adenoma, 7 tubular adenoma with low grade dysplasia). The number of false positive was 17 out of 27 focal uptakes (15 physiologic bowel uptake, 2 diverticulitis). The mean size of colonoscopic lesions was larger in lesions with true positive uptake than those with false negative lesions (1.8 ± 1.7 vs. 0.49 ± 0.31 cm, $p < 0.0001$). The mean SUV_{max} of adenocarcinoma and adenoma were higher than those of physiologic bowel uptake and diverticulitis (8.3 ± 6.8 vs. 4.4 ± 1.6, $p = 0.032$).

Tables 2, 3, 4 and 5 compare the ^{18}F-FDG PET/CT results with the findings of endoscopy. ^{18}F-FDG PET/CT had sensitivity of 5.6 %, specificity of 96.8 % and accuracy of 73.6 %. The positive predictive value of ^{18}F-FDG PET/CT was 37.0 %, and the negative predictive value, 75.1 %. But, in the lesions ≥1 cm, sensitivity, specificity and accuracy of ^{18}F-FDG PET/CT were 25.8, 96.8 and 92.9 %, respectively. The positive predictive value of ^{18}F-FDG PET/CT was 32.0 %, and the negative predictive value, 95.7 %. In the lesions <1 cm, sensitivity, specificity and accuracy of ^{18}F-FDG PET/CT were 1.3, 96.8 and 68.5 %, respectively. The positive predictive value of ^{18}F-FDG PET/CT was 10.5 %, and the negative predictive value, 77.7 %.

On the ROC analysis, the optimal cut-off values for differentiating (pre-) malignant lesions from other benign lesions was $SUV_{max} > 5.0$ (sensitivity = 50 %, specificity = 88 %, AUC = 0.643, 95 % Confidence Interval 0.429–0.823, Fig. 3).

Discussion

The purpose of this retrospective study was to evaluate the potential usefulness of ^{18}F-FDG PET/CT compared with colonoscopy for detecting colonic (pre-) malignancy, such as adenomas and carcinomas in asymptomatic adults.

The overall sensitivity and specificity of ^{18}F-FDG PET/CT for detecting colonic carcinoma and adenoma were 5.6 and 96.8 %, respectively. Although overall sensitivity was very low, all of carcinoma ($n = 2$) and tubulovillous

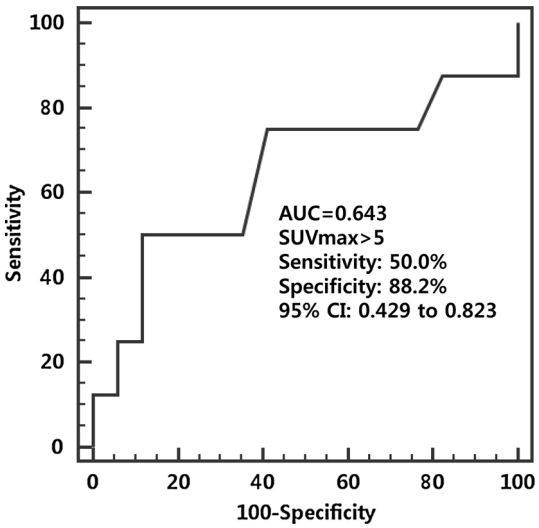

Fig. 3 On the ROC analysis, the optimal cut-off values for differentiating (pre-) malignant lesions from other benign lesions was 5.0 (sensitivity = 50 %, specificity = 88 %, area under the ROC curve = 0.643, 95 % Confidence interval 0.429–0.823)

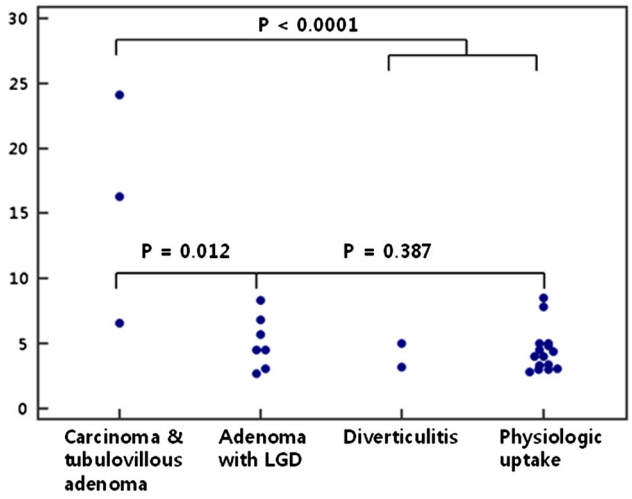

Fig. 4 The mean SUV_{max} of adenocarcinoma plus tubulovillous adenoma were significantly higher than those of adenoma with lower grade dysplasia ($p = 0.012$), and of physiologic bowel uptake and diverticulitis ($p < 0.0001$). There was no significant difference of SUV_{max} between adenoma with lower grade dysplasia and physiologic uptake ($p = 0.387$)

adenoma ($n = 1$), and 7 of 184 tubular adenoma with low grade dysplasia were detected on FDG PET/CT. Also, in the lesions ≥1 cm, sensitivity of ^{18}F-FDG PET/CT increased by 25.8 %.

Unlike our study, several previous studies revealed that the sensitivity of FDG PET for detecting (pre-) malignancy was 37–56 % [7–10]. Colon adenoma size and dysplasia grade have been reported to correlate with likelihood of detection by PET/CT [6, 9, 14]. When our colonoscopic and pathologic results (size and pathologic grade of polyps) were compared with previous studies, our study had smaller size and lower grade than those of previous studies. In our study, 154 out of 614 subjects (248 lesions: 170: tubular adenoma with low grade dysplasia, 51 hyperplastic polyp, 11 polypoid colonic mucosal tissue, 8 chronic non-specific colitis, 2 carcinoid tumor and 6 others, size: 0.49 ± 0.31 cm) were negative on FDG PET/CT, and these lesions consisted of 196 small size polyps (≤0.5 cm), 34 medium size polyps (0.6–0.9 cm) and 36 large polyps (≥1 cm). Because of these factors, we think that the sensitivity of FDG PET for detecting (pre-) malignancy in our study was lower than that of previous studies.

A correlation between SUV_{max} and colon neoplasm histology has not been demonstrated consistently. Although Gutman et al. [8] and Chen et al. [15] found that mean SUVs increased with higher grades of dysplasia with highest levels in patients with colon cancers, Israel et al. [7] did not observe such a progression in SUV values. In our study, the mean SUV_{max} of adenocarcinoma and adenoma were higher than those of physiologic bowel uptake and diverticulitis (8.3 ± 6.8 vs. 4.4 ± 1.6, $p = 0.032$). Especially, the mean SUV_{max} of adenocarcinoma plus tubulovillous adenoma were significantly higher than those of adenoma with lower grade dysplasia ($p = 0.012$, Fig. 4), and of physiologic bowel uptake and diverticulitis ($p < 0.0001$, Fig. 4). But, there was an overlap of FDG uptake between (pre-) malignancy and benign condition, and there was no significant difference of SUV_{max} between adenoma with lower grade dysplasia and physiologic uptake ($p = 0.387$, Fig. 4). It seems that mean SUV_{max} is not effective for differentiating between (pre-) malignancy and benign condition, because they all demonstrate increased FDG activity. Therefore, it seems that ^{18}F-FDG PET/CT will never completely replace colonoscopy for screening of colorectal (pre-) malignancy.

However, incidental colonic FDG uptake is not infrequent finding encountered during ^{18}F-FDG PET/CT. Although the sensitivity of ^{18}F-FDG PET/CT detecting (pre-) malignancy is low, we think that incidental colonic FDG uptake has clinical significance. Therefore, we think that one way improving the sensitivity of ^{18}F-FDG PET/CT detecting (pre-) malignancy is using the standardized PET cut-off value. Luboldt et al. [16] found that a standardized PET cut-off (e.g. $SUV_{max} \geq 5$) improved the accuracy of differentiating (pre-) malignancy and benign condition. In our study, the optimal cut-off values for differentiating (pre-) malignant lesion from other benign condition was 5.0 (sensitivity = 50 %, specificity = 88 %, AUC = 0.643).

In conclusion, colonoscopic evaluation could be recommended by presence of focal colonic FDG uptake on ^{18}F-FDG PET/CT, especially when SUV_{max} is over 5.

Conflict of interest The authors declare that they have no conflict of interest.

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