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The effect of oral contrast on large bowel activity in FDG-PET/CT

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Purpose: The purpose of this study was to determine the effect of oral contrast on FDG uptake in the colon and to determine the normal distribution of FDG in the colon. ***Methods:*** Sixty patients (30 patients in no contrast group and 30 patients in the received contrast group) underwent FDG-PET/CT scans. The pattern of FDG uptake was classified into 5 patterns (diffuse, segmental, single-nodular, multi-nodular, and other) in 5 segments (ascending, transverse, descending, and rectosigmoid colon). SUVs of the no oral contrast group were examined. The ratios of FDG uptake patterns were compared in the received contrast group and no contrast group to evaluate the effect of oral contast. The effect of attenuation correction on the uptake pattern was evaluated by comparison of the attenuation-corrected and non-attenuation-corrected PET images. ***Results:*** In the no contrast group, there was no significant uptake in 72 segments (59%) and a diffuse pattern was seen in 29 segments (24%), most frequently in the ascending colon and descending colon. A segmental pattern was seen in 15 segments (13%), most frequently in the rectosigmoid colon. A single-nodular pattern was seen in 3 segments (3%) and multi-nodular pattern in 1 segment (1%). A nodular pattern was seen only in the ascending colon. SUV_{max} of the ascending colon and that of the rectosigmoid colon were significantly higher than those of the transverse and descending colon. The frequencies of diffuse, multi-nodular and 'other' patterns were significantly higher in the received contrast group than in no contrast group. There was no significant difference between the frequency of the segmental pattern or the single nodular pattern in the two groups. There was no significant difference between the uptake patterns with attenuation correction and those without attenuation correction in either the received contrast group or no contrast group. ***Conclusion:*** Normal FDG uptake in the large bowel may show various degrees and patterns of uptake among the colonic segments. Oral contrast agent can cause focal or diffuse increased FDG uptake, which may be induced not only by the high CT density of oral contrast but also by an accelerated physiologic reaction of the large bowel.

Key words: FDG-PET/CT, oral contrast agent, colon, artifact

INTRODUCTION

COMBINED PET/CT systems were introduced about 3 years ago, and the technology is undergoing rapid evolution. CT contrast agents are now being used in PET/CT imaging and are being incorporated into clinical imaging protocols.[1–6] However, a high concentration of a high-density CT contrast agent can result in artifacts in CT-based attenuation-corrected PET images.[1,4,5] Since the introduction of a PET/CT system in our institute, we have sometimes observed high uptake areas in the bowels on CT-based attenuation-corrected PET images, with many of these high uptake areas showing increased uptake in non-attenuation-corrected PET images. We considered the possibility that the increased FDG uptake could be caused not only by a high CT value but also other factors like accelerated physiologic reaction, induced by oral contrast. Normal FDG uptake in the colon varies among the segments,[9] and we considered it important to know the

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normal FDG uptake pattern in the colon for image interpretation. The aims of this study were to determine 1) the normal physiologic FDG uptake pattern in the large bowel, 2) the effect of oral contrast agent on the large bowel FDG uptake pattern, and 3) whether the increased FDG uptake is caused by a physiological reaction induced in the presence of oral contrast or by a CT-based attenuation correction error.

PATIENTS AND METHODS

This study was approved by the Institutional Review Board of the University of Iowa.

Patient population

This retrospective study focused on 60 patients (30 patients in whom oral contrast was used and 30 patients in whom oral contrast was not used) who underwent PET/CT scans using a hybrid PET/CT system (Biograph, Siemens) during the period from August 2003 to February 2004. We selected patients who were examined at the University of Iowa Hospital and fulfilled the following criteria: 1) having undergone scanning of the whole abdomen and pelvis and 2) no history of bowel disease according to all available clinical information. We excluded any patients whose two sets of images fused incorrectly due to patients position change. No oral contrast group consisted of 15 male and 15 female patients with a mean age of 51 y (range, 17–81 y). The indication for the PET/CT study was lymphoma in 13 patients, breast cancer in 5 patients, head and neck lesions in 4 patients, characterization of pulmonary nodules in 3 patients, lung cancer in 2 patients, extragonadal germ cell tumor in 1 patient, follow-up study for post salivary excision due to stone in 1 patient, and neuroendocrine tumor in 1 patient. The received oral contrast group consisted of 17 male and 13 female patients with a mean age of 58 y (range, 18–90 y). The indication for the PET/CT study was lymphoma in 8 patients, lung cancer in 6 patients, characterization of pulmonary nodules in 6 patients, melanoma in 3 patients, malignant fibrous histiocytoma in 1 patient, uterine cervical adenocarcinoma in 1 patient, respiratory papillomatosis in 1 patient, malignant teratoma in 1 patient, carcinoid tumor in 1 patient, melanoma in 1 patient, and leiomyosarcoma in 1 patient.

Patient preparation and scans

The patients were asked to fast least 4 h before the examination. Blood glucose level of each patient was measured and confirmed to be below 150 mg/dl. We used 750 ml of 5% iodine-based oral contrast solution. The oral contrast agent was a mixture of 37.5 ml of Gastroview (367 mg iodine/ml, MD-Gastroview, Diatrizoate Meglumine and Diatrizoate Sodium Solution U.S.P, Mallinckrodt Inc.) and 712.5 ml of water. Just before the injection of FDG, 500 ml of oral contrast was given, and another 250 ml was given just before positioning on the table. The patients were typically positioned with their arms raised above their heads and supported with adequate aids for their head and knees. The PET/CT scan started with a topogram for an overview of the patient. The topogram is used to define the axial range of PET/CT imaging. After definition of the axial range, CT images were acquired with a 2-slice CT scanner. The technical parameters used on the CT part of PET/CT scans were 70 mAs, 130 kV, 5 mm acquired slice thickness, 4 mm collimation and 3.4 mm for reconstruction. After the completion of the CT images, the patient was advanced into the PET. PET images were obtained from 90 min after the injection of 370–555 MBq FDG in 3D mode. Our PET/CT scanner has 24 rings and the parameters used on the PET part were 16.2 cm of axial FOV, OSEM iterative reconstruction with 2 iterations and 8 subsets and 3.53 of pixel size. The emission time of PET imaging for an individual bed position was 3 min, and the combined scan was usually completed in 30 min. To minimize the difference due to movement of internal organs between CT and PET scans, PET images were obtained in the caudal to cranial direction. The patients breathed freely during the entire PET examination. During the CT imaging, patients also continued to breath freely. For muscle relaxation, Alprazolam (0.5–2 mg of Xanax) was given orally to 40–60 patients.

Image analysis

All of the images (CT, PET, PET/CT fused images) were displayed on the monitor in three orthogonal planes. For visual evaluation, the pattern of FDG uptake on both CT-based attenuation-corrected PET images and non-attenuation-corrected PET images was classified as one of the following patterns: diffuse, homogeneous uptake in longer than a half of the segment; segmental, homogeneous uptake but shorter than a half of the segment; single-nodular, single nodular shape uptake; multi-nodular, multiple nodular shape uptakes; other, not matching those patterns, including segments that cannot be separated from background. The segments evaluated were ascending, transverse, descending, and rectosigmoid colon. The degree of FDG uptake in these segments (except for the 'other' pattern) was graded as follows: grade 1 for uptake less than that in the liver, grade 2 for uptake similar to that in the liver, grade 3 for uptake higher than that in the liver, and grade 4 for intense uptake.

Quantitative analysis

For quantitative evaluation, a round-to-oval-shaped region of interest (ROI) of 3–27 cm^2 was put on the most intense area of each segment in CT-based attenuation-corrected PET images, and the highest standard uptake value of the ROI was determined as SUV_{max}. The degree of oral contrast was graded with CT image by assessing the volume of the agent in the lumen as follows: grade 0

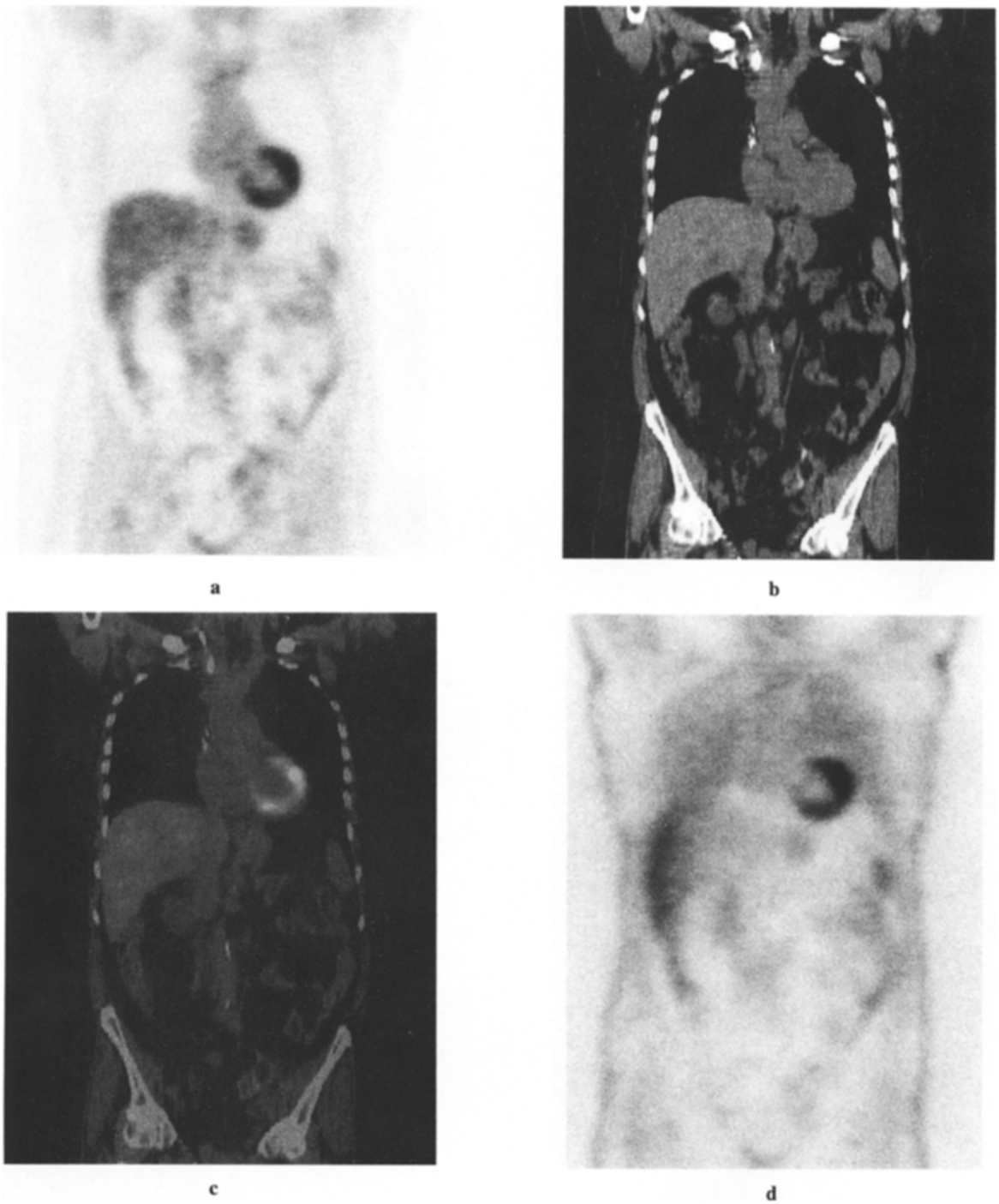

Fig. 1 Diffuse pattern (a: corrected PET image, b: CT image, c: fused image, d: uncorrected PET image). A 76-year-old female patient underwent a PET/CT study for restaging of non Hodgkin's lymphoma. Diffuse uptake is seen in ascending colon with both corrected and uncorrected PET images. Maximum SUV = 2.7, degree of uptake: grade 2, mean SUV of the liver = 2.7.

for none, grade 1 for filling less than half of the segment, grade 2 for filling greater than half of the segment.

Statistical analysis

To evaluate the difference in normal FDG uptake among the colonic segments, SUVs of no oral contrast group were examined using the paired t-test. The chi-squared test was used for comparison of the ratios of FDG uptake patterns in the received oral contrast group and no oral contrast group. For this analysis, only data for segments of the colon in which contrast agent was observed were used. The chi-squared test was also used for comparison of the

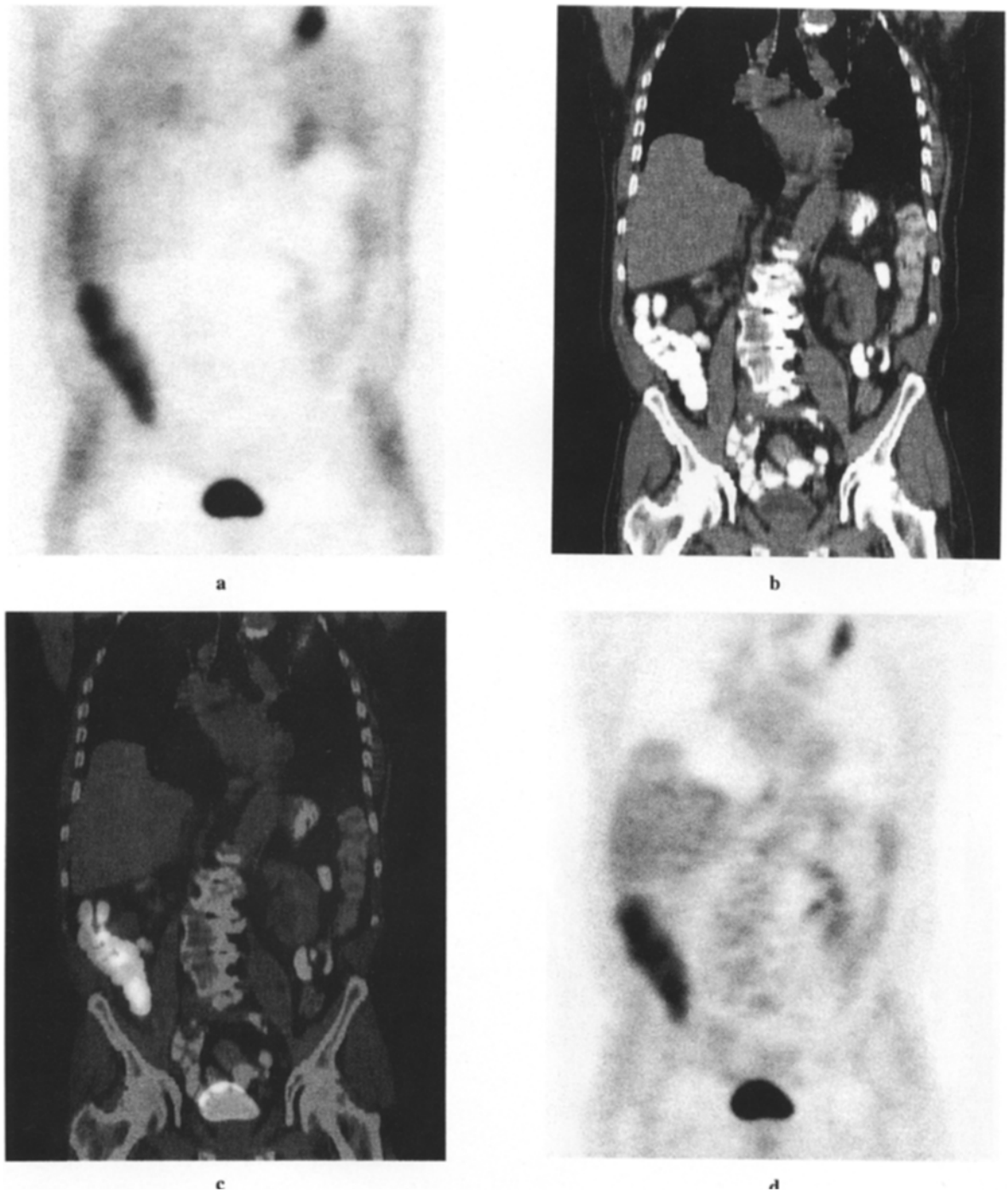

Fig. 2 Multi-nodular pattern (a: corrected PET image, b: CT image, c: fused image, d: uncorrected PET image). A 72-year-old male patient underwent a PET/CT study for characterization of left lung tumor. Multi-nodular pattern is identified in ascending colon (maximum SUV = 6.3, degree of uptake: grade 3, oral contrast volume: 2), and diffuse pattern is seen in descending colon (maximum SUV = 1.8, degree of uptake: grade 2) with both corrected and uncorrected PET images. Mean SUV of the liver = 2.1.

attenuation-corrected and non-attenuation-corrected PET images to determine the effect of attenuation correction on uptake pattern. P value < 0.05 was considered significant.

RESULTS

Images of diffuse pattern and multi-nodular pattern uptake are shown are in Figures 1 and 2, respectively. The liver shows honogeneous uptake in attenuation-corrected

Table 1 Summary of no oral contrast group. The numbers correspond to the patients that showed each FDG uptake pattern on CT-based attenuation-corrected PET images and non-attenuation-corrected PET images (in parentheses). Statistical analysis applied to SUV

	Pattern		Grade		
			1	2	3
Ascending*	Diffuse	11 (10)	2 (0)	9 (5)	0 (5)
SUV range; 1.1–5.5	Segmental	1 (1)	0 (0)	1 (0)	0 (1)
SUV mean ± SD; 2.0 ± 0.9	Single-nodular	3 (3)	0 (0)	1 (0)	2 (3)
	Multi-nodular	1 (1)	0 (0)	0 (0)	1 (1)
	Others	14 (15)	NA	NA	NA
		sum 30 (30)	2 (0)	11 (5)	3 (10)
Transverse	Diffuse	5 (5)	2 (0)	3 (4)	0 (1)
SUV range; 0.9–2.5	Segmental	0 (0)	0 (0)	0 (0)	0 (0)
SUV mean ± SD; 1.5 ± 0.5	Single-nodular	0 (0)	0 (0)	0 (0)	0 (0)
	Multi-nodular	0 (0)	0 (0)	0 (0)	0 (0)
	Others	25 (25)	NA	NA	NA
		sum 30 (30)	2 (0)	3 (4)	0 (1)
Descending	Diffuse	10 (10)	5 (1)	5 (1)	0 (8)
SUV range; 0.8–2.4	Segmental	2 (2)	1 (0)	1 (1)	0 (1)
SUV mean ± SD; 1.5 ± 0.4	Single-nodular	0 (0)	0 (0)	0 (0)	0 (0)
	Multi-nodular	0 (0)	0 (0)	0 (0)	0 (0)
	Others	18 (18)	NA	NA	NA
		sum 30 (30)	6 (1)	6 (2)	0 (9)
Rectosigmoid**	Diffuse	3 (3)	0 (0)	2 (1)	1 (2)
SUV range; 1.0–5.3	Segmental	12 (12)	4 (2)	4 (3)	4 (7)
SUV mean ± SD; 2.0 ± 0.8	Single-nodular	0 (0)	0 (0)	0 (0)	0 (0)
	Multi-nodular	0 (0)	0 (0)	0 (0)	0 (0)
	Others	15 (15)	NA	NA	NA
		sum 30 (30)	4 (2)	6 (4)	5 (9)

*: Ascending colon versus transverse colon, $p < 0.05$; versus descending colon, $p < 0.05$; versus rectosigmoid colon, difference not significant. **: Rectosigmoid colon versus transverse colon, $p < 0.05$; versus descending colon, $p < 0.05$. Transverse colon versus descending colon, difference not significant. NA: Not applied.

PET images. The lateral border of the liver showed more intense uptake compared to the medial aspect in non-attenuation-corrected PET images. None of the patients had a history of bowel disease or had any bowel lesion during the 8–14 month follow-up period by conventional CT and repeated PET/CT scans.

A summary of the no oral contrast group is shown in Table 1. There was no significant uptake in 72 segments (59%). Diffuse pattern was seen in 29 segments (24%), most frequently in the ascending colon and descending colon. Segmental pattern was seen in 15 segments (13%), most frequently in the rectosigmoid, especially in distal sigmoid colon. Single nodulat pattern was seen in 3 segments (3%) and multi-nodular pattern in 1 segment (1%). Nodular pattern was seen only in the ascending colon, and these nodular uptake areas were identified in both CT-based attenuation-corrected PET images and non-attenuation-corrected PET images. No tumor or abnormal wall thickening was seen in these three segments using CT images.

A summary of the received oral contrast group is shown in Table 2. There was no significant uptake in 52 segments (43%). A diffuse pattern was seen in 38 segments (32%), and a segmental pattern was seen in 11 segments (9%). These segments showed the same patterns in CT-based attenuation-corrected PET images and non-attenuation-corrected PET images. A nodular pattern was seen in 19 segments (16%) in the ascending and transverse colon, and 18 of 19 segments (95%) showed the same nodular pattern as that in non-attenuation-corrected PET images.

Since the ROI was set on the area of most intense FDG uptake for SUV analysis, no discrimination was made for the colon wall, contrast agent, substances in the colon or gas. SUVs ranged widely in the ascending colon and rectosigmoid colon compared to those in the transverse and descending colon. Average SUV_{max} of ascending colon and rectosigmoid colon was significantly higher than that of the transverse and descending colon. Two patients showed SUV_{max} over 5.0. One breast cancer patient had nodular uptake with 5.5 of SUV_{max} in the ascending colon. The other patient, who had a neuroendocrine tumor, had segmental uptake with SUV_{max} of 5.3 in

Table 2 Summary of the received oral contrast group. The numbers correspond to the patients that showed each FDG uptake pattern on CT-based attenuation-corrected PET images and non-attenuation-corrected PET images (in parentheses). Nodular pattern is more frequent compared to "no contrast" group. The number of diffuse patterns in transverse colon also increased

	Pattern		Grade			Oral contrast		
			1	2	3	0	1	2
Ascending	Diffuse	10 (10)	1 (0)	3 (2)	6 (8)	2	2	6
SUV range; 1.2–9.2	Segmental	1 (1)	0 (0)	0 (0)	1 (1)	0	1	0
	Single-nodular	1 (1)	0 (0)	0 (0)	1 (1)	0	1	0
	Multi-nodular	13 (13)	0 (0)	0 (0)	13 (13)	0	2	11
	Others	5 (5)	NA	NA	NA	5	0	0
		sum 30 (30)	1 (1)	3 (2)	21 (23)	7	6	17
Transverse	Diffuse	15 (13)	5 (0)	6 (5)	4 (8)	2	9	4
SUV range; 0.9–10.4	Segmental	0 (0)	0 (0)	0 (0)	0 (0)	0	0	0
	Single-nodular	2 (2)	0 (0)	1 (0)	1 (2)	0	1	1
	Multi-nodular	3 (2)	0 (0)	0 (0)	3 (2)	0	0	3
	Others	10 (13)	NA	NA	NA	9	1	0
		sum 30 (30)	5 (0)	7 (5)	8 (11)	11	11	8
Descending	Diffuse	11 (11)	6 (0)	3 (5)	2 (6)	2	5	4
SUV range; 0.8–4.8	Segmental	0 (0)	0 (0)	0 (0)	0 (0)	0	0	0
	Single-nodular	0 (0)	0 (0)	0 (0)	0 (0)	0	0	0
	Multi-nodular	0 (0)	0 (0)	0 (0)	0 (0)	0	0	0
	Others	19 (19)	NA	NA	NA	17	2	0
		sum 30 (30)	6 (0)	3 (5)	2 (6)	19	7	4
Rectosigmoid	Diffuse	2 (2)	1 (0)	0 (2)	1 (0)	1	1	0
SUV range; 0.8–3.5	Segmental	10 (10)	0 (0)	6 (5)	4 (5)	9	1	0
	Single-nodular	0 (0)	0 (0)	0 (0)	0 (0)	0	0	0
	Multi-nodular	0 (0)	0 (0)	0 (0)	0 (0)	0	0	0
	Others	18 (18)	NA	NA	NA	17	1	0
		sum 30 (30)	1 (0)	6 (7)	5 (5)	27	3	0

NA: Not applied.

Table 3 Analysis of the uptake patterns on CT-based attenuation-corrected PET images according to the presence/absence of oral contrast. This shows that the frequencies of the diffuse pattern and multi-nodular pattern were significantly higher in the received oral contrast group and that 'other' pattern was more frequent in the no oral contrast group. There was no significant difference between the frequency of the segmental pattern or the single nodular pattern in the two groups

Pattern	Received oral contrast		No oral contrast		p value
	Number of segments	%	Number of segments	%	
Diffuse	31	55	29	24	<0.05
Segmental	2	4	15	13	0.06
Single-nodular	3	5	3	3	0.35
Multi-nodular	16	29	1	1	<0.05
Others	4	7	72	59	<0.05
total	56	100	120	100	

the distal sigmoid colon.

The volume of oral contrast varied among the patients from none to totally filling in the lumen. The volume of contrast agent in the colon tended to be less in the direction of the ascending colon to the rectosigmoid colon; volumes in the ascending colon were grade 2 in 17 (57%) of the patients and grade 0 in 7 (23%) of the patients, whereas none of the cases were grade 2, and 27 (90%) of the cases were grade 0 in the rectosigmoid colon. Oral contrast had not reached the ascending colon in 7 patients (23%) by about 90 min after initiation of oral contrast administration.

Analysis of the uptake patterns according to the presence/absence of a contrast agent showed that the frequen-

Table 4 Analysis of the uptake patterns on non-attenuation-corrected PET images according to the presence/absence of oral contrast. Statistical results are the same as those of CT-based attenuation-corrected PET images

Pattern	Received oral contrast		No oral contrast		p value
	Number of segments	%	Number of segments	%	
Diffuse	31	55	28	23	<0.05
Segmental	2	4	15	13	0.06
Single-nodular	3	6	3	3	0.31
Multi-nodular	15	27	1	1	<0.05
Others	4	8	73	60	<0.05
total	55	100	120	100	

cies of the diffuse pattern and multi-nodular pattern were significantly higher in the received oral contrast group and that 'other' pattern was more frequent in the no oral contrast group. There was no significant difference between the frequency of the segmental pattern of the single nodular pattern in the two groups (Tables 3, 4).

There was no significant difference between the uptake patterns with attenuation correction and those without attenuation correction in either the received oral contrast group or no oral contrast group (the received contrast group: $p > 0.99$, no oral contrast group: $p > 0.99$).

DISCUSSION

In this study, normal FDG uptake in the large bowel and the effect of oral contrast agent on large bowel activity in PET/CT were demonstrated. We compared CT-based attenuation-corrected PET images and non-attenuation-corrected PET images to determine whether the increased FDG uptake was caused by a CT-based attenuation correction error.

Bowel uptake of FDG is a common finding in PET imaging. This study was an attempt to document the frequency and pattern of uptake in the normal bowel. Our study demonstrated that physiologic uptake is higher in the ascending colon and rectosigmoid colon and that diffuse or segmental uptake is more frequent than nodular uptake. There have been several reports on normal bowel uptake of FDG, but the exact mechanism has not been defined.[8–10] Bowel uptake has been considered to be influenced by many factors such as peristalsis, lymphoid tissue, water absorption, FDG excretion from the wall, and bacterial activity.[9,10] Kim reported that F-18 radioactivity was definitely present in patients' stools. This means that some FDG excreted into the bowel. Thus, it is reasonable that bowel uptake varies depending on the histologic and physiologic conditions. Two patients in this study had large bowel SUV_{max} of over 5.0. One breast cancer patient had nodular uptake with SUV_{max} of 5.5 in the ascending colon. The uptake corresponded to both bowel wall and lumen, and no tumor or abnormal wall thickening was observed using CT images. The other patient, who had a neuroendocrine tumor, had segmental uptake with SUV_{max} of 5.3 in the distal sigmoid colon. The segment was collapsed with no gas or stool in the lumen. The uptake corresponded mainly to the wall, and may have been related to contraction or peristalsis. We considered these two high uptake areas as normal physiological uptake, and no further examination was carried out for large bowels. These patients have shown no evidence of disease during a 1-year follow-up period. Three other subjects showed nodular patterns in ascending colon. No tumor or abnormal wall thickening was seen on CT images at that time. These patients were followed up for 4 to 5 months with no evidence of bowel lesion.

In this study, we focused on the effect of oral contrast agent on FDG uptake in the large bowel. We routinely use 5% iodine-based oral contrast agent, which is commonly used. Antoch et al. evaluated the effect of oral contrast in stomach and small bowel, and found that the contrast caused an overestimation of approximately 20% at clinically used concentrations.[4] Another study showed that clinically used contrast causes an only 4% overestimation in SUV.[3] Based on their results, the ratio of measured activity and true activity is 1.2 with 5% iodine-based oral contrast.

The motivation for this study was the fact that we frequency identified nodular uptake in the large bowel when using oral contrast to assist image interpretation. We felt it would be important to know the frequency of nodular or diffuse uptake pattern. To determine the difference in uptake patterns with and without oral contrast agent, we compared the FDG uptake patterns in the areas of the colon in which contrast agent was seen in the received oral contrast group and the FDG uptake patterns in the no oral contrast group, and we found that the ratios of the diffuse pattern and multi-segmental pattern were significantly higher in the contrast agent group. These results indicate that an oral contrast agent has an effect on the FDG uptake pattern. The sites of increased FDG uptake correlated highly with sites of oral contrast agent. In some patients, these areas of apparent increased FDG uptake overlapped with oral contrast agent, bowel wall and intraluminal stool.

We used liver uptake as an internal reference to grade colonic uptake. FDG uptake in the cirrhotic liver is less

than that in the normal liver.[12] There were no patients with cirrhosis or other diffuse liver disease in this study. In non-attenuation-corrected PET images, the lateral border of the liver usually showed intense uptake, and the medial aspect of the liver showed very mild uptake. Using the medial liver as the comparison standard had the effect of upgrading most areas when we used non-attenuation-corrected PET images.

Methods of CT-based attenuation correction are well established, and several studies on CT contrast agent-induced artifacts have been performed in phantoms and in clinical studies.[1–6] To obtain more information, oral and intravenous contrast agents are routinely used. Positive oral contrast agents, such as barium and iodine-based agents, and nonionic iodine-based intravenous agents increase CT attenuation. PET attenuation correction with CT data can be overcorrected in the presence of a positive contrast agent.[1,3,4] Thus contrast-enhanced structures may appear bright in CT-based attenuation-corrected PET images. High-density focal artifacts from intravenous bolus injection, which are sometimes seen in the superior vena cava, may be avoided by diluting with saline after the intravenous contrast injection.[1] Non-attenuation-corrected PET images can also be used to resolve these artifacts, because artifacts will be seen only on CT-based attenuation-corrected PET images. Another way to avoid artifacts induced by positive oral contrast agents is the use of negative oral contrast agents for PET/CT study.[11] These agents do not increase the CT density and cannot produce artifacts as do barium and iodine-based agents. It may be necessary to add different substances to prevent absorption of water in the gastrointestinal tracts when using water-based negative contrast agents.

If increased FDG uptake is caused by only the high CT density of oral contrast agent, we would expect the diffuse increased uptake to be milder and nodular uptake to disappear using non-attenuation-corrected PET images. However, there was no significant difference between the distribution of FDG uptake patterns on CT-based attenuation-corrected PET images and non-attenuation-corrected PET images. This result suggested that these sites of increased uptake arise not only from the CT density of oral contrast but also from other factors. We speculate that besides the high CT density of oral contrast, a normal physiological reaction such as concentration of intraluminal FDG due to water absorption, wall contraction and mucosal FDG excretion may be accelerated by the presence of oral contrast. Diffuse uptake may hide a tumor, and focal uptake mimics a neoplasm or inflammation. CT images of PET/CT can show the exact location and radiological features and are very helpful for interpretation, allowing us to exclude the presence of a tumor or abnormal wall thickening in all patients.

In conclusion, normal FDG uptake in the large bowel may show various degrees and patterns of uptake among the colonic segments. Oral contrast agent can cause focal or diffuse increased FDG uptake, which may be induced by not only the high CT density of oral contrast but also an accelerated physiologic reaction of the large bowel.

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