Comparison of the effect of positive and negative oral contrast agents on ^{18}F-FDG PET/CT scan

Abstract

Our *aim* was to compare the effect of orally taken 1% diatrizoate meglumine, 5% mannitol and water before positron emission tomography/computerized tomography (PET/CT) scan on gastrointestinal tract delineation and fluorine-18-fluorodeoxyglucose (^{18}F-FDG) uptake. *Our methods were as follows:* Sixty-one patients referred for PET/CT scan without gastrointestinal diseases were divided into three groups. One thousand mL of 1% diatrizoate meglumine was orally taken 50min before PET/CT scan in Group 1 (n=25), 1000mL 2.5% mannitol was orally taken before scan in Group 2 (n=20) and 1000mL water was orally taken before scan in Group 3 (n=16). Serum glucose and insulin were tested before and 45min after taking mannitol in Group 2 patients. Paired t test was used to compare the glucose and insulin changes. The degree of gastrointestinal filling and ^{18}F-FDG uptake were evaluated by three nuclear medicine physicians using a 4 grade classification standard. Kruskal-Wallis and Mann-Whitney none parametric test was used to compare the filling condition and ^{18}F-FDG uptake difference among the three groups and between each group. *Results:* the differences of serum glucose and insulin levels were not significant before and after contrast taken, in Group 2 patients. Group 2 patients had better gastrointestinal filling than patients of Group 1. Also, Group 2 patients' gastrointestinal filling was better than in Group 3 except in rectum. The jejunum, ascending, transverse and descending colon were better filled in Group 1 patients than in Group 3 patients. The degree of ^{18}F-FDG uptake in stomach, jejunum and ileum, in Group 2 were significantly lower than those of Group 3 ($P<0.05$). ^{18}F-FDG uptake in jejunum, in Group 1 was also lower than in Group 3 ($P<0.05$). ^{18}F-FDG uptake in ascending colon in Group 1 was higher than in Group 3 ($P<0.05$). ^{18}F-FDG uptake in transverse and descending colon, in both Group 1 and Group 2 was significantly higher than in Group 3 ($P<0.05$). ^{18}F-FDG uptake in rectum, in Group 2 was significantly higher than in Group 3 ($P<0.01$). The average maximum CT values in stomach, jejunum, ileum and ascending colon in Group 1 patients were: 132±23, 191±31, 313±47 and 374±53 Hounsfield units respectively (Mean±SD, $P<0.01$ between every two groups). *In conclusion,* patients who take iso-osmia mannitol have good gastrointestinal filling, less physiological ^{18}F-FDG uptake and may thus have better ^{18}F-FDG images displaying gastrointestinal abnormalities and differentiating pathological from physiological lesions.

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Introduction

Positron emission tomography (PET) and computerized tomography (CT) combined into a single scanner significantly increase diagnostic accuracy of lesion type and location compared with PET alone. If the CT component is used only for anatomic correlation however, the diagnostic potential of the combined scanning approach is not fully exploited. Image analysis of CT data in the abdomen is hampered by the similarity of CT densities of the bowel loops and other abdominal organs. Therefore, application of oral contrast media is a standard procedure to delineate intestinal structures from other retro- and intraperitoneal organs on CT, but in combined PET/CT, CT data are used for PET attenuation correction. Typical CT-based attenuation-correction algorithms are based on a two-step scaling method in which a threshold is set to separate soft tissue from bone. To obtain the corresponding attenuation map at 511keV, CT values are scaled with a scaling factor for either soft tissue or bone. Unlike to the PET annihilation quanta of 511keV, CT X-rays with energies of 70-140keV are attenuated substantially more by structures that contain elements with high atomic numbers, such as iodine and barium. If these differences in attenuation are not accounted for, contrast agents may lead to biases in the estimated attenuation coefficients, which may translate into artifacts in the corrected PET images. It was reported that oral contrast may cause SUV increase by about 4.4% [1]. Others reported that low-density barium does not cause significant artifacts and appears suitable for clinical use [2]. The concentration of the oral contrast agent in the gastrointestinal tract is not uniform because of water

absorption. In our previous study, we have shown that patients who had taken 1000mL 1% diatrizoate meglumine per os before PET/CT scan can increase the ^{18}F-FDG uptake in the colon more than patients who did not take the contrast [3]. Others reported that other physiological factors, besides the attenuation correction, may affect the increasing of intestinal ^{18}F-FDG uptake with the presence of oral contrast [4, 5].

Recently, iso-osmia mannitol solution was used as negative oral contrast agent in CT and magnetic resonance imaging (MRI). Reports have shown that this agent provides excellent bowel distention and avoids contrast material-induced PET artifacts [6]. The purpose of our study was to compare the difference in gastrointestinal delineation and ^{18}F-FDG uptake between patients who have taken positive and negative oral contrast agents.

Subjects and methods

Patients

Whole-body PET/CT examinations were performed in 61 patients, 47 males and 14 females 53±12.84 years old with different oncologic diseases or just for tumor screening. In these patients, 19 were healthy adults examined for tumor screening, 16 had lung cancer, 5 had elevated serum tumor markers, 6 had lymphoma, 5 had nasopharyngeal carcinoma, 4 had breast cancer and 6 had brain tumor. These patients were randomly assigned to three groups. Patients in Group 1 (n=25) orally took 1000mL 1% diatrizoate meglumine 50min before the PET/CT scan (800mL in 15min and 200mL before scan). Patients in Group 2 (n=20) and Group 3 (n=16) orally took 1000mL 2.5% mannitol and 1000mL water instead of diatrizoate meglumine respectively. Patients who had abdominal lesions with abnormal ^{18}F-FDG uptake were excluded from this study.

The study was approved by the Ethics Committee in our hospital and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and all subsequent revisions. All patients gave their informed consent prior to their inclusion in the study.

The PET/CT scan

The PET/CT scan was performed at 50min after intravenous injection of 5.55MBq/kg ^{18}F-FDG. Before administration of ^{18}F-FDG, blood glucose levels were determined in capillary blood samples. In Group 2 patients, additional capillary blood samples were obtained immediately before the scanning to demonstrate that blood glucose levels remained within the normal range. And, in these patients, serum insulin was determined before and 45min after the administration of mannitol. Scanning procedures were conducted with a dual-modality PET/CT scanner (GE Advance LS, USA). CT parameters were set to 200mAs, 140kV. Slice thickness was 4.25mm. The scanning range was set from the upper thigh to the head. PET scan started immediately after the CT scan. The time to scan one bed position was set to 5min. Depending on patients' size images were acquired in six to seven bed positions for whole-body coverage. Attenuation correction of the PET data was CT based. Ordered Subset Expectation Maximisation (OSEM, 28 subsets, 2 iterations) was used for PET reconstruction.

Data and statistical analysis

Gastrointestinal tract was divided into stomach, jejunum, ileum, ascending colon, transverse colon, descending colon, sigmoid colon and rectum for determining filling conditions, ^{18}F-FDG uptake and contrast uniformity. Gastrointestinal filling was determined according to CT images using a 4 grade visual analysis: none (0%-25% filling), mild (25%-50% filling), moderate (50%-75% filling) and high (75%-100% filling). The ^{18}F-FDG uptake degree was determined according to PET images. According to the highest ^{18}F-FDG uptake site, the ^{18}F-FDG uptake degree was evaluated as: none (background), mild (less than liver uptake), medium (equal to liver uptake) and high (much higher than liver uptake). Visual analysis was performed by three physicians independently and the final grading was in consensus with at least two physicians. In Group 1 patients, regions of interest were drawn in the highest density site of each organ and maximum CT values were recorded for contrast agent uniformity analysis. Kruskal-Wallis none parametric test was used to compare the filling and ^{18}F-FDG uptake difference among the three groups and Mann-Whitney test were used to compare the difference between every two groups.

The maximum CT values in Group 1 patients and serum glucose and insulin levels in Group 2 patients were analyzed using unpaired and paired t test, respectively.

Results

Ingestion of each contrast agent was well tolerated by all patients. Six patients who had ingested mannitol as the negative oral contrast agent reported watery diarrhea after the examination. There were no further side effects noted with any of the oral contrast agents. No blood glucose and serum insulin elevation were found after mannitol administration in Group 2 patients (Table 1).

Table 1. *Blood glucose and serum insulin levels before and 45min after mannitol taken in Group 2 patients (Mean ± SD, n = 10)*

Time	Blood glucose (mmol/L)	Serum insulin (IU/L)
Before mannitol	6.03±0.43	12.56±9.34
After mannitol	6.18 ±0.22	11.49±7.29

The filling and ^{18}F-FDG uptake in different parts of gastrointestinal tract in the three patients' groups were shown in Tables 2 and 3. Patients who had ingested mannitol (Group 2) had better gastrointestinal filling than those who ingested diatrizoate meglumine (Group 1) except jejunum, ileum (Fig. 1 and 2). Group 2 patients' tracts were all also better filled than in Group 3 except in rectum. The jejunum, ascending, transverse and descending colon were better filled in Group 1 patients than those in Group 3 patients.

In stomach, jejunum and ileum, ^{18}F-FDG uptake in Group 2 was significantly lower than in Group 3 (P<0.05). In jejunum, ^{18}F-FDG uptake in Group 1 was also lower than in Group 3 (P<0.05). In ascending colon, ^{18}F-FDG uptake in Group 1 was higher than in Group 3 (P<0.05). In transverse and descending colon, ^{18}F-FDG uptake in both Group 2 and Group 1 was significantly higher than in Group 3 (P<0.05). In rectum, ^{18}F-FDG uptake in Group 2 was significantly higher than in Group 3 (P<0.01).

The positive contrast was not uniformly distributed in gastrointestinal lumina. The average maximum CT values in stomach, jejunum, ileum and ascending colon in Group 1 patients were 132±23, 191±31, 313±47 and 374±53 respectively (Mean±SD, P<0.01 between every two groups).

Table 2. *The filling in different parts of gastrointestinal tract in three patient groups*

Location	Group	n	None	Mild	Moderate	High	Remarks
Stomach△	1	25	1	16	8	0	*
	2	20	0	0	18	2	‡
	3	16	2	13	1	0	
Jejunum△	1	25	0	0	23	2	*†
	2	20	0	0	6	14	‡
	3	16	0	3	13	0	
Ileum△	1	25	0	2	23	0	*
	2	20	0	0	6	14	‡
	3	16	0	5	11	0	
Ascending Colon△	1	25	5	13	7	0	*†
	2	20	0	0	20	0	‡
	3	16	11	5	0	0	
Transverse Colon△	1	25	14	9	2	0	*†
	2	20	0	0	20	0	‡
	3	16	15	1	0	0	
Descending Colon△	1	25	25	0	0	0	*†
	2	20	0	18	2	0	‡
	3	16	16	0	0	0	
Rectum△	1	25	25	0	0	0	*
	2	20	16	4	0	0	
	3	16	16	0	0	0	

Kruskal-Wallis: △: P<0.05; Mann-Whitney test: *: P<0.05, Group 1 vs Group 2; †: P<0.05, Group 1 vs Group 3; ‡: P<0.05, Group 2 vs Group 3

Table 3. *The ^{18}F-FDG uptake in different parts of gastrointestinal tract in three patient groups*

Location	Group	n	None	Mild	Moderate	High	Remarks
Stomach△	1	25	5	6	12	2	
	2	20	2	12	6	0	‡
	3	16	1	1	13	1	
Jejunum△	1	25	1	15	9	0	†
	2	20	0	12	8	0	‡
	3	16	0	1	15	0	
Ileum△	1	25	1	11	10	3	
	2	20	0	12	8	0	‡
	3	16	0	1	15	0	
Ascending Colon△	1	25	3	4	11	7	†
	2	20	0	10	10	0	
	3	16	8	1	7	0	
Transverse Colon△	1	25	6	4	11	4	†
	2	20	0	10	10	0	‡
	3	16	13	1	2	0	
Descending Colon△	1	25	10	4	6	5	†
	2	20	0	10	6	4	‡
	3	16	13	1	3	0	
Rectum△	1	25	12	6	7	0	
	2	20	0	12	8	0	‡
	3	16	13	1	2	0	

Kruskal-Wallis: △:P<0.05; Mann-Whitney test: *: P<0.05, Group 1 vs Group 2 ; †: P<0.05, Group 1 vs Group 3; ‡: P<0.05, Group 2 vs Group 3

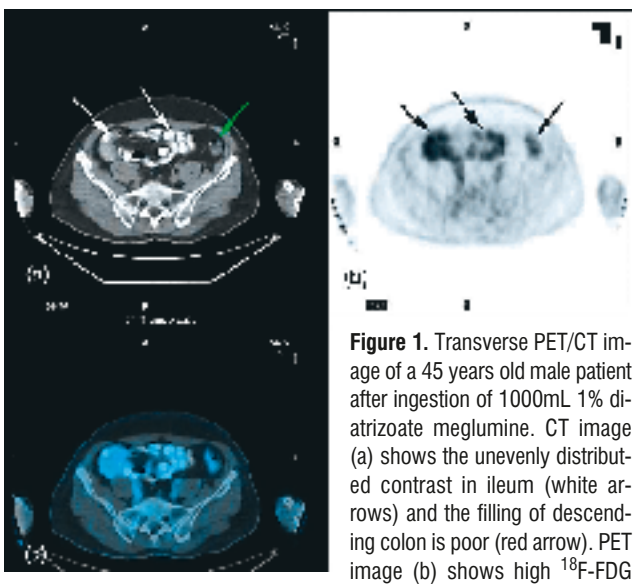

Figure 1. Transverse PET/CT image of a 45 years old male patient after ingestion of 1000mL 1% diatrizoate meglumine. CT image (a) shows the unevenly distributed contrast in ileum (white arrows) and the filling of descending colon is poor (red arrow). PET image (b) shows high ^{18}F-FDG uptake in ileum and colon (black arrows). (c) is the fusion image.

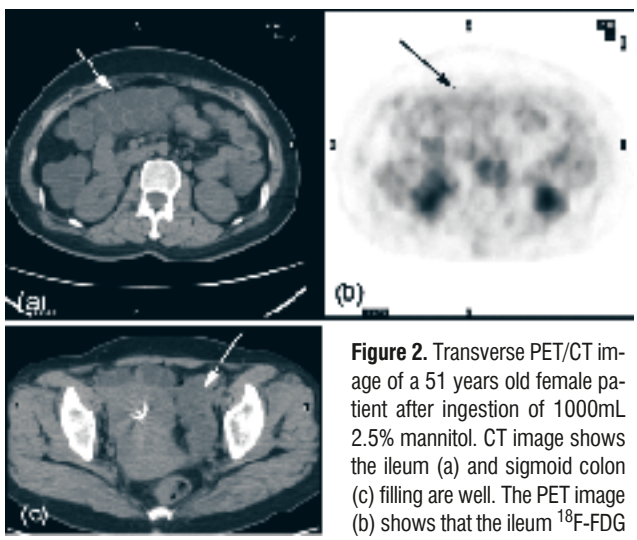

Figure 2. Transverse PET/CT image of a 51 years old female patient after ingestion of 1000mL 2.5% mannitol. CT image shows the ileum (a) and sigmoid colon (c) filling are well. The PET image (b) shows that the ileum ^{18}F-FDG uptake is relatively less.

Discussion

Using oral contrast agents one can delineate gastrointestinal tract from other abdominal organs. It can help better display the gastrointestinal abnormalities and differentiate pathological from physiological ^{18}F-FDG uptake. Patients who take iso-osmia mannitol have the best gastrointestinal filling. The second best is to take diatrizoate meglumine, and taking water is the worst. This may be because of the water absorption in gastrointestinal tract. Our results have shown that in patients who take diatrizoate meglumine, there is gradually increased contrast concentration from the upper to the lower tract.

The mechanism of ^{18}F-FDG uptake in gastrointestinal tract is not well elucidated. Reports have shown that positive contrast can produce artifacts of increased activity on the emission PET scan if CT-corrected emission data are used [1, 2]. These artifacts are caused by the energy differences between photons used for CT scanning and the 511keV photons used for PET scanning. The use of low-energy photons for transmission imaging results in increased attenuation coefficients in the presence of materials of high atomic number (metallic objects, high-density contrast material) compared with the use of high-energy 511keV photons. This increased attenuation for low-energy X-rays is caused by an increased probability of photoelectric interaction of low-energy photons with materials of high atomic numbers. Mathematic algorithms ideally should scale the attenuation coefficients obtained with low-energy photons to the energy level of 511keV photons. However, it appears that current and widely applied commercial scaling algorithms are not appropriate for high-density materials, causing an overestimation of attenuation coefficients in their presence and thus an overcorrection of the emission data resulting in an artifact of apparently increased tracer activity.

In our study, ^{18}F-FDG uptake in colon in Group 1 patients was significantly higher than in Group 2. This is consistent with the high contrast density in these sites. But in stomach, jejunum and ileum, ^{18}F-FDG uptake in Group 3 patients were higher than in Group 2. So, other ^{18}F-FDG uptake mechanisms may exist besides attenuation correction. The possible mechanisms are water absorption and peristalsis and tension of gastrointestinal muscles. Water absorption in the gastrointestinal tract is due to passive diffusion caused by osmotic pressure gradient. The formation of this gradient is an energy consuming procedure. It may cause increased glucose metabolism. In addition, the peristalsis and tension of smooth muscles also can cause increased glucose metabolism. The results of ^{18}F-FDG uptake in our study may have been caused by a combination of these three mechanisms: over attenuation, water absorption and peristalsis and tension of smooth muscles. In Group 3 patients, large amount of water was absorbed by the stomach, jejunum and ileum. In the same positions of Group 2, the concentration of diatrizoate meglumine was low and could not cause over attenuation correction. Also, the water absorption was slower than in Group 3 because of the high osmotic pressure of diatrizoate meglumine. So, the ^{18}F-FDG uptake was highest in Group 3 in upper gastrointestinal tract. Because there was no water absorption in Group 2, this group had the lowest ^{18}F-FDG uptake. In colon, the water absorption was not significant in all groups. The over attenuation correction in Group 1 became the main reason of ^{18}F-FDG uptake and the tension of smooth muscles in Group 2 was the second main reason. So, ^{18}F-FDG uptake in both Group 1 and Group 2 was higher than in Group 3.

Besides the over attenuation correction effect in patients who take positive contrast agents, other factors, such as water absorption or smooth muscle tension, may contribute to the gastrointestinal ^{18}F-FDG uptake.

In conclusion, patients who take iso-osmia mannitol have good gastrointestinal filling and less physiological ^{18}F-FDG uptake and may thus have better ^{18}F-FDG images displaying gastrointestinal abnormalities and differentiating pathological from physiological lesions.

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