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An analysis of the physiological FDG uptake pattern in the stomach

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The purpose of this study was to clarify the normal gastric FDG uptake pattern to provide basic information to make an accurate diagnosis of gastric lesions by FDG PET.

We examined 22 cases, including 9 of malignant lymphoma, 8 of lung cancer, 2 of esophageal cancer, and 3 of other malignancies. No gastric lesions were observed in any of the 22 cases on upper gastrointestinal examinations using either barium meal or endoscopic techniques. The intervals between FDG PET and the gastrointestinal examination were within one week in all cases. The stomach regions were classified into the following three areas: U (upper)-area, M (middle)-area, and L (lower)-area. The degree of FDG uptake in these three gastric regions was qualitatively evaluated by visual grading into 4 degrees, and then a semiquantitative evaluation was carried out using the standardized uptake value (SUV).

Based on a visual grading evaluation, the mean FDG uptake score in the U-, M-, and L-areas was 1.14 ± 0.96, 0.82 ± 0.96, and 0.36 ± 0.49 (mean ± S.D.), respectively. The FDG uptake scores obtained in the three areas were significantly different (Friedman test, $p < 0.05$). Furthermore, the rank order of the FDG uptake score in each case ($U \geq M \geq L$) was found to be statistically significant (Cochran-Armitage trend test, $p < 0.05$). The mean SUVs of 11 cases in the three areas were 2.38 ± 1.03, 1.91 ± 0.71, and 1.34 ± 0.44 (mean ± S.D.), respectively. The SUV in the U-area was significantly higher than that in the L-area (Friedman test, $p < 0.05$). A significant difference in FDG uptake was observed among the three gastric areas, and the FDG uptake extent in all cases was $U > M > L$. In conclusion, the physiological gastric FDG uptake was significantly higher at the oral end. A stronger gastric FDG uptake at the anal end may therefore be suggestive of a pathological uptake.

Key words: FDG PET, physiological uptake, stomach

INTRODUCTION

F-18-fluorodeoxyglucose (FDG) is likely to continue to be the most commonly used radiopharmaceutical for PET studies in oncology, cardiology, and neurology. This tracer is a substrate of energy metabolism; therefore, an increased FDG uptake is not limited to malignant tissue alone.[1,2] In addition to the abnormal FDG uptake associated with malignant tumors, both physiological and normal variant FDG uptakes are seen in various organs.[3] Interpretation of whole-body FDG PET requires a thorough knowledge of the normal patterns of the FDG uptake. The brain, heart, and urinary tract are the most prominent sites of FDG uptake. A relatively low FDG uptake is also seen in other organs and systems, such as the palatine tonsils, great vessels, liver, spleen, gastrointestinal tract, and skeletal muscles.

With respect to the gastrointestinal tract, FDG PET is considered to be useful for differentiating between postoperative changes and recurrence, and as a monitoring therapy for colorectal cancer.[4–6] On the other hand, the usefulness of FDG-PET for the diagnosis of gastric lesions has not been established, possibly because FDG

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uptake in the alimentary tract is physiologically observed, and the degree of FDG uptake is variable. The gastric FDG uptake is well known to vary widely in terms of intensity.[1,3,7] The normal gastric FDG uptake is usually somewhat greater than the hepatic FDG uptake and is readily identifiable on FDG PET images based on location and configuration. An intense gastric FDG uptake has been noted as occasionally recognized in the area inferior to the heart, and it can appear like a "second heart" below the diaphragm.[8] The gastric FDG uptake may appear as an FDG-avid mass that is indistinguishable from a malignant tumor. Although the FDG uptake in gastric lesions (e.g., in cases of gastric cancer,[9] malignant lymphoma,[10] Menetrier's disease,[11] and gastritis[8]) has been reported, gastric lesions cannot be reliably diagnosed by FDG-PET imaging studies alone. In order to utilize this technology to recognize pathologic gastric FDG uptake, it is crucial to first understand the pattern of normal gastric FDG uptake.

The purpose of this study was to clarify the physiological gastric FDG uptake patterns in order to obtain basic information that may be useful when identifying a pathological FDG uptake.

MATERIAL AND METHODS

Patients

Between January 2000 and April 2002, we examined 358 whole body FDG-PET studies. In the 358 FDG-PET studies, an upper gastrointestinal examination using either barium meal or endoscopic techniques was performed within one week in 36 studies. Gastric lesions were found in 14 patients. Finally, 22 patients without any gastric lesions were enrolled in this study. In this study, we examined 22 cases (male/female = 12/10; age range, 24–82 years; median age, 65 years), including 9 cases of malignant lymphoma, 8 cases of lung cancer, 2 cases of esophageal cancer, and 3 cases of other malignancies. The patient characteristics are shown in Table 1. All patients fasted for at least 4 hours before the examination and were not diagnosed to have diabetes mellitus. The blood glucose level was 104.8 ± 8.7 (mean ± S.D.) (range from 92.0 to 128.0) mg/dl upon administration of FDG. This study was approved by the Committee for the Clinical Application of Cyclotron-Produced Radionuclides at Kyushu University Hospital, and written informed consent was obtained from all patients before initiation of the study.

Table 1

Patient No.	Age	Sex	Diagnosis	Gastric FDG uptake					
				Score			SUV		
				U	M	L	U	M	L
1.	72	F	Rectal ca.	3	3	1	NA	NA	NA
2.	62	F	Eso ca.	3	3	1	3.30	3.14	1.78
3.	68	F	Lung ca.	3	1	1	4.55	2.73	2.03
4.	72	M	NHL	2	2	1	NA	NA	NA
5.	68	F	Lung ca.	2	2	0	2.87	2.84	1.63
6.	67	F	NHL	2	1	1	NA	NA	NA
7.	64	F	NHL	2	1	0	1.70	1.22	1.17
8.	62	M	Eso ca.	2	0	0	NA	NA	NA
9.	74	M	NHL	2	0	0	2.88	1.71	0.92
10.	60	M	Lung ca.	2	0	0	NA	NA	NA
11.	77	M	NHL	1	1	1	1.93	1.55	1.59
12.	56	F	ST Tumor	1	1	1	2.49	2.05	1.78
13.	51	F	NHL	1	1	1	NA	NA	NA
14.	74	M	Lung ca.	1	1	0	NA	NA	NA
15.	61	F	NHL	1	1	0	2.17	1.78	0.98
16.	74	M	Tongue ca.	1	0	0	2.34	1.71	0.86
17.	66	F	NHL	1	0	0	NA	NA	NA
18.	44	M	Lung ca.	1	0	0	NA	NA	NA
19.	82	M	Lung ca.	0	0	0	0.91	0.90	0.74
20.	64	M	Lung ca.	0	0	0	NA	NA	NA
21.	41	M	Lung ca.	0	0	0	1.09	1.39	1.31
22.	24	M	NHL	0	0	0	NA	NA	NA

Score: visual grading score referring to the liver uptake, U: upper region of the stomach, M: middle region of the stomach, L: lower region of the stomach, Rectal ca.: Rectal cancer, Eso ca.: Esophageal cancer, Lung ca.: Lung cancer, NHL: Non-Hodgkin's lymphoma, ST Tumor: Soft tissue tumor, Tongue ca.: Tongue cancer, NA: Not available

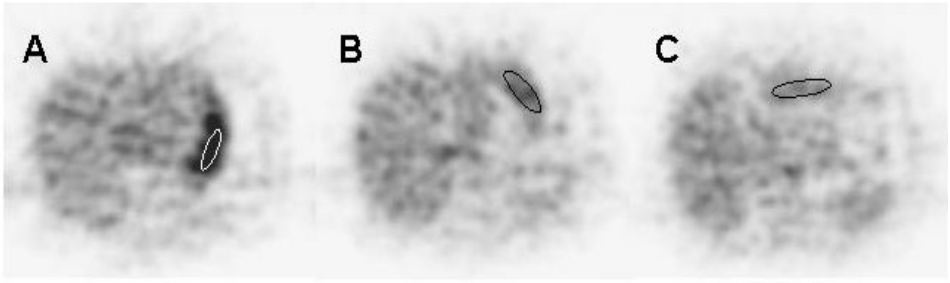

Fig. 1 An example of the regions of interest in a patient (patient No. 3). Elliptical regions of interest were placed on the Upper area (A), Middle area (B), and Lower area (C) of the stomach, and then the SUVs of each area were determined.

FDG-PET

Whole-body FDG PET was performed using ECAT EXACT HR$^+$ (Siemens, Knoxville, TN, USA). Intrinsic resolution was 4.6 mm full-width at half-maximum at the center. The data acquisition was initiated 60 minutes after the intravenous administration of FDG with 185 MBq. Emission scans were obtained in a 3-dimensional mode from the head to the thigh, using 9 bed positions with an acquisition time of 2 minutes each. The images without attenuation correction were reconstructed with a filtered back projection using a Hanning filter (cutoff = 0.4 cycle/pixel). In 11 cases, transmission scans were obtained in a 2-dimensional mode with an acquisition time of 2 minutes for each bed position after the emission scan using ^{68}Ga/^{68}Ge rod source. The 3 dimensional emission datasets were rebinned with the implementation of FORE into sets of 2D sinograms. Using the converted emission datasets and transmission datasets, the attenuation-corrected images were reconstructed with an ordered-subset expectation maximization (OS-EM) algorithm (16 iterations with 10 ordered subsets) using the segmentation attenuation correction method.

Data analysis

The gastric regions were classified into the following three areas: U (upper)-area, M (middle)-area, and L (lower)-area, according to the Japanese Classification of Gastric Carcinoma.[12] In brief, the upper, middle, and lower third of the gastric areas (regarding the length of both the greater and lesser curvatures) were referred to as the U-, M-, and L-areas, respectively. The locations of the three gastric areas (U-, M-, and L-areas) were determined based mainly on the coronal and axial images. X-ray CT and gastrointestinal examinations using either barium meal or endoscopy images were used to understand the rough location and configuration of the stomach. We determined the three gastric areas and put on the region of interest based mainly on the transaxial images of FDG-PET, referring to the coronal and sagittal images of FDG-PET and X-ray CT images. Using non-attenuation-corrected images, the degree of FDG uptake in the three gastric regions (i.e., the U, M, and L-areas) was visually graded while referring to the liver uptake: 0 indicated lower than the liver uptake, 1 was equal to the liver uptake, 2 was somewhat higher than the liver uptake, and 3 was much higher than the liver uptake. Because the FDG uptake in the surface of the liver on the non-attenuation corrected images was relatively higher than in the other regions, we determined the liver uptake to be the average of total liver uptake except for the surface area. The results were determined based on the consensus of three nuclear medicine physicians. In addition to the visual grading system, the standardized uptake values (SUVs) in each area were also examined in 11 cases for which the attenuation-corrected images were obtained. The elliptical regions of interest of the gastric wall, measuring from 3.68 cm^2 to 7.36 cm^2, were carefully placed based on visual comparisons with CT images (Fig. 1). The SUV was determined as the average radioactivity in the region divided by the injected radioactivity normalized to the body weight.

Statistics

The SAS computer package (SAS Institute, Cary, NC, USA) was used to perform all statistical analyses. A comparison of the visual graded scores among the three regions was carried out by Friedman's test. A two-way analysis of variance (ANOVA) with repeated measures was used to evaluate any differences in the SUVs. Multiple comparisons between each possible pair of regions were also evaluated by Bonferroni's method. A two-sided p-value of less than 0.05 was considered to be statistically significant. The rank order of the FDG uptake score in each case was evaluated by the Cochran-Armitage trend test.

RESULTS

By visual grading, the mean FDG uptake score in each gastric area was 1.41 ± 0.96 in the U-area, 0.82 ± 0.96 in the M-area, and 0.36 ± 0.49 in the L-area (Fig. 2). A significant difference in the mean FDG uptake scores among the three regions was found (Friedman test, $p < 0.001$ between the U-area and the M-area, and between

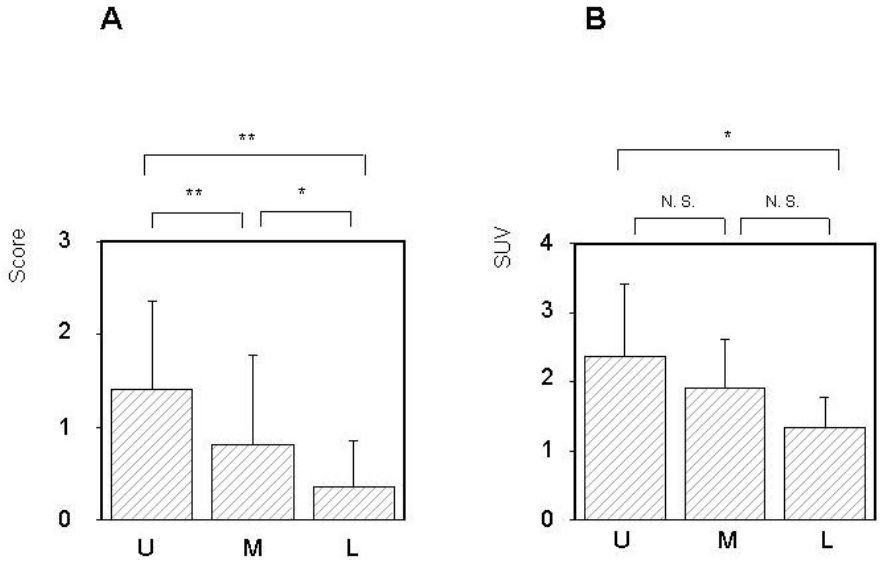

Fig. 2 The degree of the FDG uptake among the gastric regions in the normal stomach. (A) The mean ± S.D. The FDG uptake scores in the U- (1.41 ± 0.96), M- (0.82 ± 0.96), and L-areas (0.36 ± 0.49), as determined by visual grading, are shown. The FDG uptake score was significantly different (*$p < 0.05$, **$p < 0.001$) among the three areas. (B) The mean SUV ± S.D. in the U- (2.38 ± 1.03), M- (1.91 ± 0.71), and L-areas (1.34 ± 0.44) are shown. Among the three areas, the SUV in the U-area was significantly higher than that of the L-area (*$p < 0.05$), whereas the difference between the SUVs of the U-area and the M-area, and that between the SUVs of the U-area and L-area, were not significant.

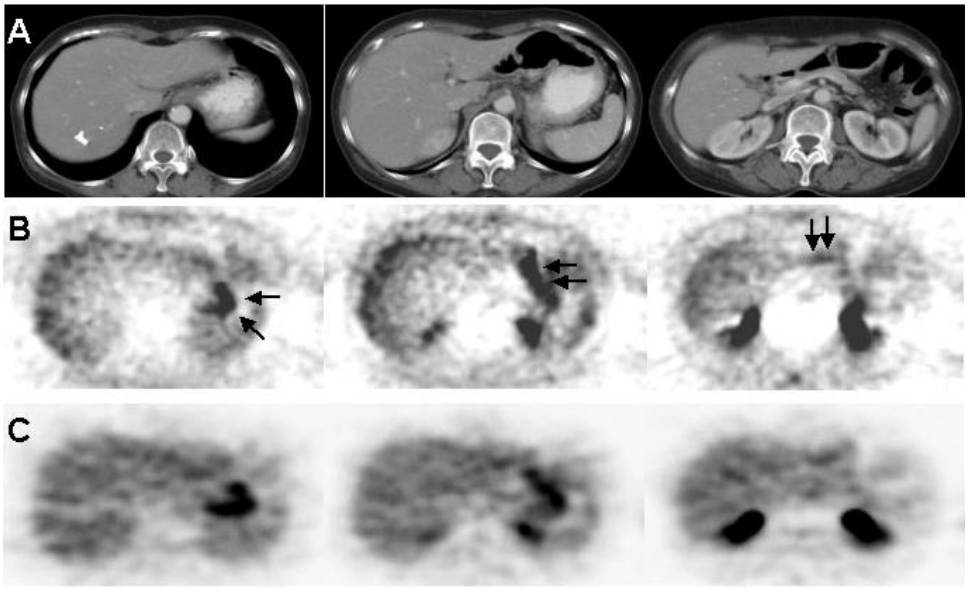

Fig. 3 A sixty-two-year-old female with esophageal cancer (patient No. 2). (A) Contrast-enhanced CT images of the stomach. (B) FDG PET axial images without attenuation correction. The arrows indicate areas of FDG uptake in the U-, M-, and L-areas of the stomach, respectively. The FDG uptake scores obtained by visual grading were 3 in the U-area, 3 in the M-area, and 1 in the L-area. (C) FDG PET axial images with attenuation correction of the U-, M-, and L-areas. The SUVs in the three areas were 3.30, 3.14, and 1.78, respectively.

the U-area and the L-area; $p < 0.05$ between the M-area and the L-area). In all 22 patients, the FDG uptake in the U-area was equal to or higher than that in the M- and L-areas, and that in the M-area was equal to or higher than that in the L-area. The rank order of the FDG uptake score in each case (U > M > L) was found to be statistically

significant (Cochran-Armitage trend test, $p < 0.05$).

By a semiquantitative analysis, the mean ± SD of the SUV of 11 cases in the three areas was determined to be 2.38 ± 1.03, 1.91 ± 0.71, and 1.34 ± 0.44, respectively. The SUV in the U-area was significantly higher than that in the L-area (Friedman test, $p < 0.05$). A rank order of the SUV in each case (U > M > L) was determined, except for in two cases (patients Nos. 11 and 21). Although the SUV in the M-area of patient No. 11 (1.55) was slightly lower than that in the L-area (1.59), and the SUV in the U-area of patient No. 21 (1.09) was slightly lower than that in both the M-area (1.39) and the L-area (1.31), these differences were quite small, and were not visually recognizable in either of these cases.

A representative case (patient No. 2) is shown in Figure 3. In this case, the FDG uptake scores according to the visual grading system were 3 in the U-area, 3 in the M-area, and 1 in the L-area. The SUVs in the three areas were 3.30, 3.14, and 1.78, respectively.

DISCUSSION

The mechanism of physiological gastric FDG uptake has not been clarified, although some hypotheses have been proposed. We proposed some hypotheses based on the functional and structural differences among the three gastric areas.

There are three different types of gastric glands: cardiac, oxyntic, and pyloric glands. Cardiac glands occupy a narrow zone (1–3 cm) around the gastroesophageal junction, oxyntic glands occupy the fundus (U-area) and corpus (M-area), and pyloric glands occupy the distal region of the stomach (L-area). In the oxyntic glands, the most conspicuous cells of the gastric mucosa are parietal cells that produce hydrochloric acid. The parietal cells possess a large number of mitochondria, thus reflecting their high rate of oxygen consumption for the purpose of acid secretion.[13] Therefore, glucose metabolism in parietal cells is considered to be high. In three gastric glands, abundant parietal cells are found in the oxyntic glands and occasionally in the pyloric glands.[13] Differences in the FDG uptake in these gastric areas may be associated with differences in the number of parietal cells in each region, as these cells require a large amount of energy.

It is possible that the observed differences in the FDG uptake may have been due to differences in the wall thickness among these respective gastric regions. Karantanas et al. showed that the mean thicknesses of the normal gastric wall in the fundus, body, and antrum was 2.40, 2.30, and 2.00 mm, respectively.[14] Although the wall thickness differed among the regions, such differences are not likely to account for these differences observed in the FDG uptake. The thickness of the gastric muscle does not differ among these regions. Furthermore, the thickest muscle is observed in the pyloric canal, where the FDG uptake is relatively low.

Motion and peristalsis of the stomach caused by the contraction of gastric smooth muscle may offer another explanation for these differences. The gastric muscle of the upper region exerts a continuous moderate tonic contraction, whereas the lower muscle is much more motile, with repeated peristaltic waves passing along this part of the stomach towards the pylorus.[15] However, because a high FDG uptake has been observed in skeletal muscle after exercise or when muscles are in a state of contraction,[16] our results showing that high FDG uptake was found in the upper region of the stomach are not thought to have been dependent on muscle motility.

In some types of neoplasm, the SUV has been reported to be potentially useful as a cutoff value for detecting malignant lesions. In order to differentiate between benign and malignant lesions, we previously reported a SUV of 3.20[17] for lung nodules, Hain et al. reported an SUV of 2.5 for the same purpose,[18] and Ho et al. reported an SUV of 2.5 for pancreatic masses.[19] However, it remains difficult to differentiate benign from malignant lesions in organs with a physiologically high FDG uptake. Stahl et al. reported that only 60% of locally advanced gastric cancers were detected by FDG PET.[20] Therefore, in our cases as well, it was difficult to accurately identify pathological FDG accumulation in the stomach based on the SUV alone, because the maximal SUV of the normal stomach was 4.55 in the U-area. On the other hand, our rank order of the FDG uptake score (U > M > L) may be of help in detecting pathological accumulations. If a higher focal gastric FDG uptake in the M- or L-area is clearly observed, then it is considered to be suggestive of a pathological uptake.

Our study suggests the possibility that a pathological uptake can be differentiated form a physiological uptake when a gastric high FDG uptake at the anal end including the M- and L-area is observed. However, using our results it is still considered difficult to differentiate a pathological uptake from a physiological uptake in cases with a somewhat high uptake in the U-area. To resolve this problem, other methods, for example, the addition of delayed images to assess the changes in the gastric FDG uptake pattern or a drug modification study using antispasmodic drugs, H2 blocker, or a proton pump inhibitor may be needed.

In conclusion, the normal gastric FDG uptake was significantly higher at the oral end of the organ. Although a high gastric FDG uptake is not always suggestive of an abnormal uptake, an increase in the FDG uptake above the average for the anal end may be indicative of an abnormality. Further examinations of patients with gastric lesions will thus be required to confirm the validity of this observation.

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