# Factors Influencing Physiological FDG Uptake in the Intestine

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The intestine is a well-known site of physiological <sup>18</sup>F-fluorodeoxyglucose (FDG) accumulation in positron emission tomography (PET). To identify factors influencing physiological FDG uptake in the intestine, the intensity of FDG uptake was evaluated in a total of 1,068 healthy adults. Non-attenuation-corrected whole-body PET images were obtained for all subjects and visually evaluated. Subjects were then classified into two groups according to the intensity of intestinal FDG uptake. Sex, age, presence or absence of constipation, and serum glucose, hemoglobin A<sub>1</sub>c, and free fatty acid levels were compared between the two groups. High intestinal FDG uptake was observed at an overall rate of 11.0%. Sex (female), age, and bowel condition (constipation) were found to affect intestinal FDG uptake. The factors we identified lead to further questions regarding the relationship between intestinal motility and glucose uptake that warrant further study.

Key Words: Positron emission tomography (PET), <sup>18</sup>F-fluorodeoxyglucose (FDG), Glucose metabolism, Intestine, Intestinal motility

# **INTRODUCTION**

Positron emission tomography (PET) with <sup>18</sup>F-fluorodeoxyglucose (FDG) has been used successfully in the diagnosis of various cancers. High FDG accumulation suggests the presence of malignant tumor. In the abdomen and pelvis, however, physiological intestinal FDG accumulation is occasionally noted on PET images, and this is problematic for the interpretation of images. This study was conducted to determine factors influencing physiological FDG uptake in the intestine.

## SUBJECTS AND METHODS

Subjects were members of our health club [6, 14] who underwent a PET study between January and December, 1996. Diabetic patients were not included, and five subjects with colonic activity later found to have colonic lesions were also excluded.

PET scans were obtained using a wholebody PET scanner (ECAT EXACT 47, Siemens/CTI, Knoxville, TN, USA). All subjects were asked to fast for at least 4 hours prior to examination. Forty-five to 60 minutes after injection of 260 MBq of FDG, emission scanning was undertaken from the level of the pelvis to the level of the maxilla. Transmission scanning for attenuation correction was not carried out [13].

Gray-scale hard copy images of transaxial sections were printed and visually evaluated by the same physician (S.Y.); images of coronal sections were also available. According to the intensity of intestinal FDG uptake, all subjets were classified into two groups: a bowel uptake positive (BU+) group and a bowel uptake negative (BU-) group. In the visual evaluation, activity in the liver and urinary tract were used as reference sites. If activity was present along the intestine, was higher than that of the liver, and was nearly equal to that of the urinary tract, the subject was classified into the BU+ group; otherwise the subject was classified into the BUgroup.

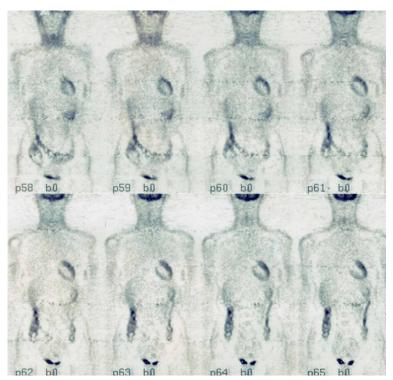
Sex, age, serum glucose, hemoglobin  $A_1c$ , and free fatty acid levels were compared between the two groups. All subjects were questioned about their bowel habits, and the presence or absence of constipation was also compared between the two groups.

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	Bowel uptake (+)	Bowel uptake (-)	Results
No. of subjects	117	951	
Sex, M : F	65:52	625:326	$P = 0.038^*$
Age (years)	$57.0 \pm 11.6$	$54.0 \pm 9.4$	$P = 0.0069^*$
Glucose (mg/dl)	$95 \pm 15.3$	$97 \pm 19.3$	NS**
Hemoglobin A <sub>1</sub> c (%)	$4.9 \pm 0.68$	$5.0 \pm 0.77$	NS
FFA (mg/dl)	$0.48 \pm 0.25$	$0.46 \pm 0.26$	NS
Constipation (+)	24/117 (20.5%)	115/951 (12.1%)	$P = 0.016^*$

Table Results of statistical analysis

\*: Statistically significant values, \*\*: Not significant, FFA: free fatty acid



**Figure** Eight consecutive coronal tomographic PET images of a 46-year-old woman. High FDG uptake is noted along the colon. Colonoscopy showed no abnormality in the colon. Normal FDG uptake is seen in the brain, myocardium, and urinary bladder.

Statistical analyses were performed using Student's t (two-sided) and  $\chi^2$  tests. P-values of less than 0.05 were considered significant.

# RESULTS

Total subjects eligible for the study were 1,068; 690 men and 378 women with a mean age of  $54.3 \pm 9.7$  years. The BU + group was comprised of 117 subjects, and the BU - group of 951 subjects.

In the BU + group, the ratio of women (52/117 = 0.44) was significantly higher than that (326/951 = 0.34) in the BU - group

(p=0.038). Similarly, the mean age was significantly higher in the BU+ group than in BU- group (p=0.0069). However, significant differences were not observed for serum glucose, hemoglobin A<sub>1</sub>c, and free fatty acid levels. Constipation was rather frequent among our study subjects. Twentyfour of the 117 (20.5%) BU+ subjects, and 115 of 951 (12.1%) BU- subjects showed constipation. This difference was significant (p=0.016).

Results of the statistical analysis are shown in the Table, and the Figure shows PET images of a 46-year-old woman that are representative of images in our series.

# DISCUSSION

The intestine is a well-known site of physiological FDG accumulation in PET [2, 3]. This intestinal FDG accumulation poses a practical problem in the reading of PET images; it can lead to misinterpretation or obliterate lesions. The cause is not well known, and methods of prevention have still not been established. Colonic lavage prior to examination is advocated in one report [10].

Previously, *in vivo* animal experiments using <sup>14</sup>C-deoxyglucose demonstrated glucose uptake in the intestine [4, 8]. It was estimated that the gastrointestinal tract accounted for up to 16% of the total rate of whole body glucose uptake in rats [8]. Glucose uptake by the small intestine or colon was significantly higher than that by the stomach, and glucose uptake in the intestine was approximately the same in the mucosa and muscle layer. Intravenously administered <sup>14</sup>Cdeoxyglucose was not detectable in the lumen of the small intestine [4].

FDG PET, an in vivo measurement of glucose metabolism, can depict hypermetabolic sites. In PET, images of the intestines vary. In our subjects, high intestinal uptake of FDG was noted at a rate of 11.0%. Sex, age, and bowel condition were factors influencing the uptake. Understanding the rate and factors may facilitate better interpretation of PET images.

Our study was limited by the fact that high intestinal FDG uptake may occur in patients with enterocolitis [9], pseudomembranous colitis [5], or Crohn's enterocolitis [1]. We identified a patient with ulcerative colitis and a patient with severe proctitis in whom high intestinal FDG uptake was observed. Because most subjects did not undergo intestinal examinations, it can not be ruled out that pathological FDG uptake associated with intestinal diseases was included in this study.

To our knowledge, our study is the first showing factors influencing intestinal uptake of FDG. The ultimate goal of our study is to find feasible methods to minimize intestinal activity. The mechanism of how sex or age affects intestinal activity is unknown, but the fact that constipation seemed to be associated with intestinal activity suggests a relationship between smooth muscle movements (intestinal motility) and glucose metabolism. It is well documented that skeletal muscle exercise is related to glucose metabolism [7, 11, 12]. The same mechanism may apply to the intestine. Further studies are neccessary to determine whether intestinal motility is related to intestinal FDG uptake.

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#### REFERENCES

- Bicik I, Bauerfeind P, Breitbach T, Schulthess GK, Fried M: Inflammatory bowel disease activity measured by positron-emission tomography. Lancet 350:262, 1997
- Cook GJR, Fogelman I, Maisey MN: Normal physiological and benign pathological variants of 18-fluoro-2-deoxyglucose positron-emission tomography scanning: potential for error in interpretation. Semin Nucl Med 26:308-314, 1996
- Engel H, Steinert H, Buck A, Berthold T, Huch Böni RA, Schulthess GK: Whole-body PET: physiological and artifactual fluorodeoxyglucose accumulations. J Nucl Med 37:441-446, 1996
- Hamar J, Hutiray G: In vivo determination of transport and metabolism of deoxyglucose in intestinal tissues. Pflügers Archiv 401:233-238, 1984
- Hannah A, Scott AM, Akhurst T, Berlangieri S, Bishop J, Mckay WJ: Abnormal colonic accumulation of fluorine-18-FDG in pseudomembranous colitis. J Nucl Med 37:1683-1685, 1996
- Ide M, Suzuki Y: A window on Japan: medical health club with clinical PET. Eur J Nucl Med 23:1677-1679, 1996
- Kostakoglu L, Wong JCH, Barrington SF, Cronin BF, Dynes AM, Maisey MN: Speech-related visualization of laryngeal muscles with fluorine-18-FDG. J Nucl Med 37:1771-1773, 1996
- Lang CH, Obith JCA, Bagby GJ, Bagwell JN, Spitzer JJ: Increased glucose uptake by intestinal mucosa and muscularis in hypermetabolic sepsis. Am J Physiol 261:G287-294, 1991
- Mayer MA: Diffusely increased colonic F-18 FDG uptake in acute enterocolitis. Clin Nucl Med 20:434-435, 1995
- 10) Miraldi F, Vesselle H, Faulhaber PF, Adler LP, Leisure GP: Elimination of artifactual accumulation of FDG in PET imaging of colorectal cancer. Clin Nucl Med 23:3-7, 1998
- 11) Yasuda S, Ide M, Takagi S, Shohtsu A: Elevated F-18 FDG in skeletal muscle. Clin Nucl Med 23:111-112,

1998

- 12) Yasuda S, Fujii H, Takahashi W, Takagi S, Ide M, Shohtsu A: High F-18 FDG uptake in the psoas muscle. Clin Nucl Med 23: 716-717, 1998
- 13) Yasuda S, Ide M, Takagi S, Shohtsu A, Mitomi T, Kobayashi S, Suzuki Y: Cancer detection with whole-

body FDG PET images without attenuation correction. KAKU IGAKU (Jpn J Nucl Med) 33:367-373, 1996

14) Yasuda S, Shohtsu A: Cancer screening with wholebody <sup>18</sup>F-fluorodeoxyglucose positron-emission tomography. Lancet 350:1819, 1997