PET/CT Detection of Unexpected Gastrointestinal Foci of ^{18}F-FDG Uptake: Incidence, Localization Patterns, and Clinical Significance

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Precise PET/CT localization of focal ^{18}F-FDG uptake in the gastrointestinal tract (GIT) may exclude malignancy in sites of physiologic activity but may also induce false-negative reports for malignant or premalignant lesions. The purpose of the present study was to retrospectively evaluate the nature and significance of unexpected focal ^{18}F-FDG uptake localized by PET/CT within the GIT. **Methods:** The files of 4,390 patients referred for ^{18}F-FDG PET/CT were retrospectively reviewed. The incidence of studies showing unexpected focal uptake of ^{18}F-FDG localized by PET/CT to the GIT was determined. The position of these foci along the GIT and their intensity were recorded. The etiology of the findings was confirmed histologically or by long-term follow-up. **Results:** Unexpected focal ^{18}F-FDG uptake in the GIT was found in 58 patients (1.3%). Follow-up data were available for 34 of these patients, including 4 with sites in the stomach, 2 in the small bowel, and 28 in the colon. GIT-related disease was confirmed in 24 patients (71%). There were 11 malignant tumors, 9 premalignant lesions, and 4 benign processes including 2 benign polyps, 1 case of active gastritis, and 1 abscess of the sigmoid. Ten patients (29%) had no further evidence of GIT abnormality, and the suggestive sites were considered to be physiologic uptake. Maximal standardized uptake value was 17.3 ± 10.2 in malignant lesions, 14.0 ± 10.5 in premalignant lesions, 18.0 ± 12.1 in benign lesions, and 11.1 ± 7.4 in foci of physiologic ^{18}F-FDG uptake in the GIT, with no statistically significant difference among the 4 subgroups. **Conclusion:** Incidental focal ^{18}F-FDG uptake localized by PET/CT within the GIT is of clinical significance in most patients. These findings should be followed up with appropriate invasive procedures guided by hybrid imaging results.

Key Words: gastrointestinal tract foci; ^{18}F-FDG; PET/CT; oncology; pitfalls

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PET using ^{18}F-FDG has successfully been implemented in the evaluation of malignant tumors. Diagnosis of cancer is based on the ability of ^{18}F-FDG PET to detect foci of tumors with increased glycolysis (*1,2*). Increased ^{18}F-FDG uptake, however, besides being present in malignant lesions, is present in benign, inflammatory, or granulomatous processes and in sites of normal, physiologic tracer biodistribution (*3,4*). These physiologic or benign sites of ^{18}F-FDG uptake may be falsely attributed to a cancerous etiology, and increased tracer activity in malignant lesions may be erroneously interpreted as unrelated to cancer (*2–6*). ^{18}F-FDG is excreted in part through the gastrointestinal tract (GIT), with uptake in the distal esophagus, stomach, small intestine, and large intestine representing normal patterns of tracer distribution (*3,4*). Diffuse increased ^{18}F-FDG uptake in the GIT can be defined as physiologic and unrelated to the malignant process with relatively high certainty. A focal, well-circumscribed intraabdominal area of increased ^{18}F-FDG uptake may, however, be interpreted as equivocal or suggestive of malignancy with an unclear location (*4,5*).

Hybrid PET/CT provides anatomic landmarks for better characterization of increased ^{18}F-FDG uptake (*7*). Initial literature reports have shown that the precise localization of hypermetabolic lesions by PET/CT may change the definition of focal intraabdominal ^{18}F-FDG uptake from an indeterminate or equivocal to a benign etiology and therefore improve the diagnostic accuracy of PET (*7,8*). This study was initiated by a series of cases in which focal intraabdominal ^{18}F-FDG uptake that had been localized by PET/CT to the GIT, which had no previously known morphologic lesions, was proven on follow-up to be of malignant or premalignant etiology. The purpose of the present study was to evaluate the frequency of incidental focal sites of increased ^{18}F-FDG uptake in the GIT and to assess the clinical significance of these unexpected findings.

MATERIALS AND METHODS

Patient Population

The files of 4,390 patients with known or suspected malignancy, who underwent whole-body ^{18}F-FDG PET/CT during the period September 2001 to March 2004, were retrospectively reviewed. All patients gave written informed consent for the PET/CT study and for evaluation of their clinical records for follow-up.

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TABLE 1
Incidental ^{18}F-FDG Foci in GIT: Diagnosis, Localization, and Intensity of Uptake

Parameter	Malignant	Premalignant	Benign	Physiologic
Foci (*n*)	11	9	4	10
Anatomic site				
Stomach	3	—	1	—
Small intestine	2	—	—	—
Colon	6	9	3	10
SUV_{max}				
Mean ± SD	17.3 ± 10.2	14.0 ± 10.5	18.0 ± 12.1	11.1 ± 7.4
Range	8.1–40.3	4.5–40	8.7–35.6	5.7–30.8

This analysis included PET studies showing a single site of focally increased abdominal ^{18}F-FDG uptake that was more intense than liver uptake and was localized by fused PET/CT to the GIT. The patients had no previous malignant involvement and no clinical or imaging suspicion of abnormalities in the same areas. Fifty-eight patients met these inclusion criteria, and they represented the group for calculating the incidence of unexpected focal ^{18}F-FDG uptake in the GIT on whole-body PET.

Of the 58 studies showing incidental focally increased ^{18}F-FDG uptake in the GIT, follow-up data were available for 34 patients, who represented the study group for further assessment of the clinical significance of these findings. There were 22 men and 12 women, with a mean age of 66 y (range, 27–88 y). The primary malignant tumors were colon cancer ($n = 9$), lymphoma ($n = 7$), lung cancer ($n = 6$), and metastatic cancer of unknown origin ($n = 2$). One patient each had sarcoma; malignant histiocytoma; and esophageal, gastric, or breast cancer. Five additional patients were evaluated for further characterization of single pulmonary nodules. PET/CT was performed on 14 patients assessed for diagnosis or staging, 5 patients assessed at restaging after initial treatment, and 15 patients assessed as part of routine follow-up or because recurrence was suspected.

Imaging Protocol

Patients were instructed to fast, except for glucose-free oral hydration, for 4–6 h before the injection of 370–555 MBq (10–15 mCi) of ^{18}F-FDG. After the tracer administration, patients remained lying comfortably and then voided immediately before PET/CT. The urinary bladder was not catheterized, and oral muscle relaxants were not administered. Whole-body PET and unenhanced CT images were acquired consecutively, 60–90 min after the injection, using a PET/CT system (Discovery LS; General Electric Medical Systems) combining a dedicated, full-ring PET scanner with bismuth germanate crystals and a third-generation multislice spiral CT scanner. The PET and CT devices were mechanically aligned back to back and shared a common table. The CT and PET images were registered using their shared positional information about the table and the patient.

Data obtained from CT were used for low-noise attenuation correction of the PET emission data and for fusion with attenuation-corrected PET images. PET images were reconstructed iteratively using ordered-subset expectation maximization software. PET, CT, and fused whole-body images displayed in axial, coronal, and sagittal planes were available for review. The PET data were also displayed in a rotating maximum-intensity projection.

Interpretation and Analysis of PET/CT Images

PET studies showing single, well-circumscribed foci of increased abdominopelvic ^{18}F-FDG uptake localized by PET/CT images to the GIT, including the esophagus, stomach, small intestine, or colon, were reviewed. The colon was further divided into ascending colon, descending colon, sigmoid, and rectum. The intensity of the ^{18}F-FDG uptake was measured as the maximal standardized value uptake of ^{18}F-FDG (SUV_{max}), using the software provided by the workstation manufacturer.

After PET/CT, 30 of the 34 patients underwent additional procedures for evaluation of the area of focally increased ^{18}F-FDG uptake. These included surgery in 8 patients, colonoscopy with biopsy in 11 patients, gastroscopy with biopsy in 4 patients, and ultrasound-guided fine-needle aspiration in 1 patient. Six patients underwent colonoscopy that revealed no abnormal findings, and

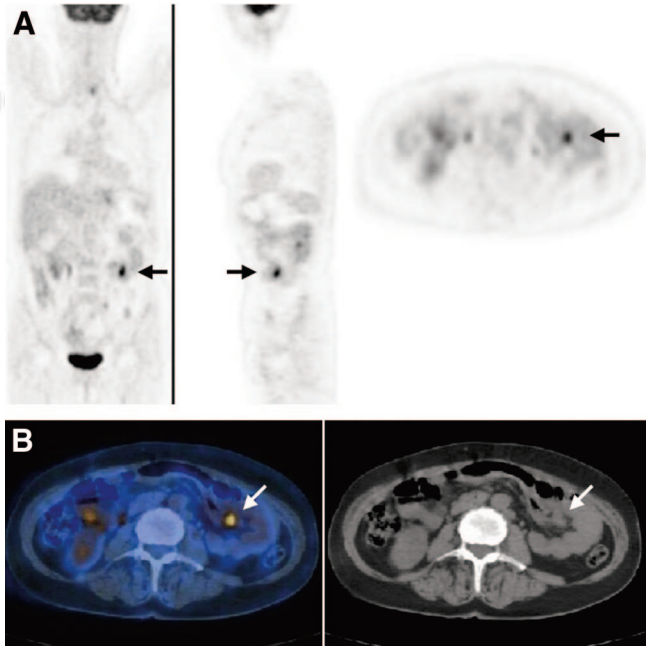

FIGURE 1. Focal ^{18}F-FDG uptake in 57-y-old woman who had undergone total gastrectomy for stomach cancer and was being evaluated for fatigue, abdominal pain, frequent vomiting, equivocal endoscopic findings at level of anastomosis, and negative findings on whole-body CT. (A) From left to right, coronal, sagittal, and transaxial PET slices show focus of increased ^{18}F-FDG uptake (arrows) in left lower abdomen. (B) Area of increased uptake (arrows) was localized by PET/CT (left panel) to small bowel, as seen on corresponding CT image (right panel). PET/CT-guided surgery revealed small-bowel metastasis originating from primary gastric cancer. No abnormal ^{18}F-FDG uptake was seen in region of anastomosis, and there was no further evidence of disease in this area.

TABLE 2
Localization and Etiology of 34 Foci of Incidental GIT Uptake of ^{18}F-FDG

PET/CT focus		Diagnosis		
Location	Patients (*n*)	On referral to PET/CT	After PET/CT	Patients (*n*)
Stomach	4	SPN	Gastric cancer	2
		Colon cancer	Second primary gastric cancer	1
		Colon cancer	Active gastritis	1
Small bowel	2	Stomach cancer	Metastasis	1
		Colon cancer	Metastasis	1
Colon	28	MCUO	Colon cancer	1
		SPN	Colon cancer	1
		Lung cancer	Second primary colon cancer	2
		Lung cancer	Metastasis	1
		Colon cancer	Metastasis	1
		Lymphoma	Villous adenoma	2
		Colon cancer	Villous adenoma	2
		Lung cancer	Adenomatous polyp with low-grade dysplasia	2
		Breast cancer	Adenomatous polyp with low-grade dysplasia	1
		Histiocytoma	Villous adenoma	1
		SPN	Tubular adenoma	1
		Lymphoma	Benign polyps (hamartomatous and serrated)	2
		Sarcoma	Abscess of sigmoid	1
		Lymphoma	Physiologic uptake	3
		Colon cancer	Physiologic uptake	3
		Esophagus cancer	Physiologic uptake	1
		Lung cancer	Physiologic uptake	1
		SPN	Physiologic uptake	1
		MCUO	Physiologic uptake	1

SPN = single pulmonary nodule; MCUO = metastatic cancer of unknown origin.

therefore no histologic specimens were obtained. Four patients had only clinical follow-up, for periods ranging from 12 to 31 mo.

Foci of increased tracer uptake in the GIT in patients with negative endoscopic findings, and with no further evidence of disease during a follow-up period of at least 12 mo, were considered to represent sites of physiologic ^{18}F-FDG activity.

The incidence of unexpected focally increased ^{18}F-FDG uptake in the GIT was calculated. The locations of suggestive foci were recorded. The intensity of the uptake was measured for the whole study population and compared among subgroups defined by histologic results and clinical follow-up. Differences in SUV_{max} among the 4 subgroups were assessed for statistical significance using 1-way ANOVA.

RESULTS

Focally increased ^{18}F-FDG uptake localized by PET/CT to the GIT was found in 58 of the 4,390 patients (1.3%). Of the 34 patients with confirmatory follow-up data, the focal ^{18}F-FDG uptake was in the stomach in 4 patients, the small intestines in 2, and the colon in 28. Of the 28 suggestive colonic sites, 13 were in the ascending colon, 6 in the descending colon, 7 in the sigmoid, and 2 in the rectum (Table 1).

Eleven (32%) of these 34 foci were found to be caused by malignant tumors. Tissue diagnosis after biopsy or surgery indicated the presence of 7 primary neoplasms in the colon ($n = 4$) or stomach ($n = 3$), with 3 of these tumors representing second primary malignancies. There were 4 metastatic lesions in the small bowel ($n = 2$), ascending colon ($n = 1$), or descending colon ($n = 1$), and these originated from colon ($n = 2$), stomach ($n = 1$), or lung cancer ($n = 1$) (Fig. 1 and Table 2). The mean interval between detection of the focal ^{18}F-FDG uptake and the histopathologic diagnosis was 3.3 mo (range, 1–13.5 mo).

For 13 sites (38%), histologic assessment of biopsy or surgical specimens showed no evidence of malignancy, indicating instead the presence of premalignant adenomatous polyps in the colon ($n = 9$) (Fig. 2) or benign lesions ($n = 4$). The 4 benign lesions included 1 case of active gastritis, 1 serrated polyp and 1 hamartomatous adenoma in the colon, and 1 abscess of the sigmoid. The mean interval between detection of the focal ^{18}F-FDG uptake and the final histopathologic diagnosis for these patients was 1.7 mo (range, 0.5–4 mo).

There was no further evidence of disease in 10 areas of focal ^{18}F-FDG uptake in the GIT (29%), localized to the ascending ($n = 7$) or descending colon ($n = 3$) (Fig. 3). Colonoscopy had negative results for 6 patients who also had no evidence of disease during a clinical follow-up period of 5–17 mo. No additional diagnostic procedures were performed on 4 patients who had an uneventful clinical follow-up period of 12–31 mo. These 10 foci were considered physiologic ^{18}F-FDG uptake in the bowel.

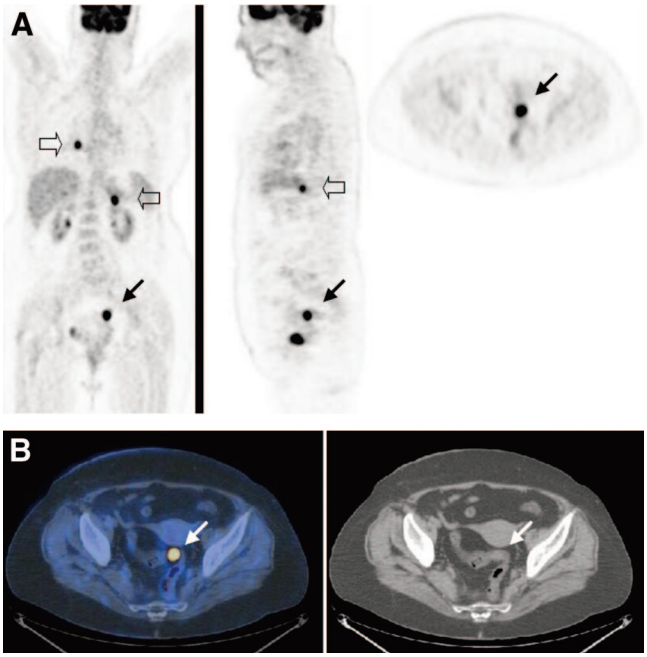

FIGURE 2. Focal ^{18}F-FDG uptake in 64-y-old woman who was being evaluated for staging of aggressive non-Hodgkin's lymphoma. (A) From left to right, coronal, sagittal, and transaxial PET slices show focus of increased ^{18}F-FDG uptake (arrows) in left pelvis. Coronal and sagittal PET images show additional areas of abnormal ^{18}F-FDG uptake in mediastinum and left upper abdomen (open arrows), consistent with sites of active lymphoma. (B) Pelvic area of increased uptake (arrows) was localized by PET/CT (left panel) to sigmoid, as seen on corresponding CT image (right panel). Villous adenoma was diagnosed from biopsy sample taken during colonoscopy.

SUV_{max} for the 34 foci of increased ^{18}F-FDG uptake in the GIT ranged from 4.5 to 40.3. Mean SUV_{max} was 17.3 (range, 8.1–40.3) for the 11 malignant lesions, 14.0 (range, 4.5–40) for the 9 premalignant lesions, 18.0 (range, 8.7–35.6) for the 4 benign lesions, and 11.1 (range, 5.7–30.8) for the 10 sites of physiologic activity. No statistically significant difference was found in the intensity of ^{18}F-FDG uptake among the 4 subgroups (Table 1).

The final histologic diagnosis, location, and intensity of focal ^{18}F-FDG uptake in the GIT are summarized in Tables 1 and 2.

DISCUSSION

Incidental foci of abnormal ^{18}F-FDG uptake, precisely localized by PET/CT to the GIT, were found in 1.3% of the present study population. Of these unexpected suggestive sites, follow-up data showed that 71% were caused by GIT-related pathology, with 59% representing malignant or premalignant lesions.

Physiologic ^{18}F-FDG uptake of variable intensity and localization patterns within the GIT has previously been described. Focal tracer uptake is frequently seen at the gastroesophageal junction; moderate uptake, in the stomach; low-intensity uptake, in the small bowel; and diffuse or focal uptake, in the colon (*3*). This physiologic tracer activity in the GIT has been attributed to uptake by smooth muscles (mainly in the bowel), swallowed secretions, or excretion and intraluminal concentration of ^{18}F-FDG (*9,10*).

PET using ^{18}F-FDG is more accurate than CT or other conventional imaging modalities for diagnosis of previously unknown recurrent or metastatic malignant foci (*11,12*). Focal colonic ^{18}F-FDG uptake has a high, 70%–80%, probability of showing corresponding abnormal histopathologic findings (*11–13*). Despite possible false-positive results, colonoscopy has therefore been recommended as the next diagnostic step for further evaluation of these findings (*14,15*). The present study found a slightly lower incidence, 64%, of clinically significant lesions in the colon, with a total of 71% throughout the whole GIT.

Although previous studies have evaluated the etiology of incidental ^{18}F-FDG PET findings in the colon (*13,15*), the clinical significance of abnormal foci in other parts of the GIT has not, to our knowledge, previously been addressed. In the present study, 6 of the 34 suggestive foci (18%) were in the stomach or small bowel, with all but 1 of these lesions proving malignant on further evaluation (Fig. 1).

Metastases have previously been considered to represent an unusual etiology for unexpected single sites of ^{18}F-FDG uptake in the GIT (*11*). In the present study population, 12%

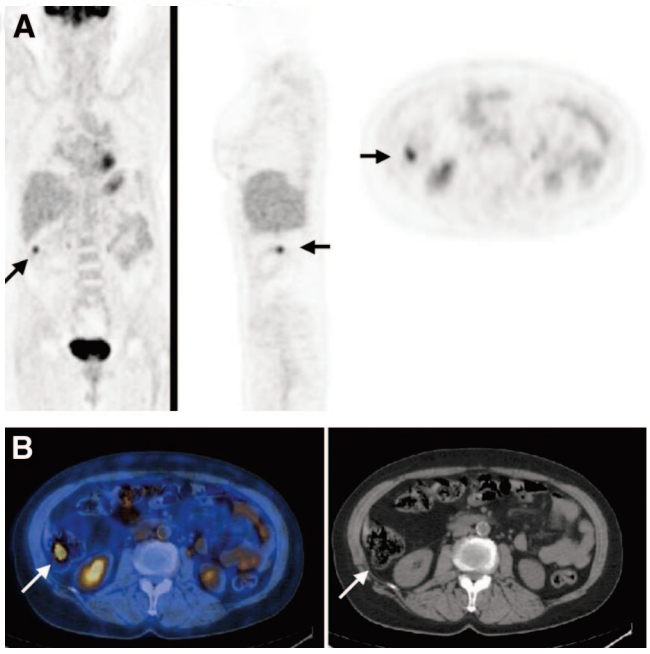

FIGURE 3. Focal ^{18}F-FDG uptake in 70-y-old woman with low-grade non-Hodgkin's lymphoma who was undergoing routine follow-up examination. (A) Coronal, sagittal, and transaxial PET slices show focus of increased ^{18}F-FDG uptake (arrows) in right upper abdomen. (B) Area of increased uptake (arrows) was localized by PET/CT (left panel) to ascending colon, as seen on corresponding CT image (right panel). Colonoscopy had negative findings, and patient showed no evidence of disease after 16 mo of follow-up. Focus of increased ^{18}F-FDG uptake was considered to represent physiologic bowel activity.

of incidental foci represented metastatic lesions, in addition to the 26% that were premalignant lesions and the 21% that were primary malignancies (Figs. 1 and 2).

Semiquantitative SUV measurements have been suggested as a tool to differentiate between potential etiologies of ^{18}F-FDG foci in the GIT (*16*). In the current series, a similar but wide range of ^{18}F-FDG uptake values was found in the different subgroups.

PET/CT has been advocated as a useful novel imaging tool leading to a decrease in the number of false-positive and false-negative PET findings in cancer patients (*5,7,11*). Despite this increase in confidence and decrease in the number of suggestive or equivocal lesions, the precise localization of increased ^{18}F-FDG foci using PET/CT cannot, at present, solve the diagnostic dilemma of abnormal tracer uptake in the GIT. Single sites of focally increased ^{18}F-FDG uptake, precisely localized by hybrid images to the GIT, warrant further evaluation using more invasive diagnostic procedures. Tissue sampling appears to be the only way to define the etiology and clinical significance of focal areas of ^{18}F-FDG uptake in the GIT in individual patients. In this clinical setting, however, PET/CT can play an important role in guiding further investigations, including biopsy or surgery, leading to a decrease in tissue-sampling errors and enhancing early, improved diagnosis and treatment.

CONCLUSION

The results of the present study indicate the need for further assessment and PET/CT-guided tissue sampling in patients with unexpected single areas of focal abnormal ^{18}F-FDG uptake in the GIT. Most of these incidental foci represent unexpected GIT-related abnormalities, such as second primary tumors, sites of unusual metastatic spread, or premalignant lesions.

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