# Focal fluorine-18 fluorodeoxyglucose accumulation in inflammatory pancreatic disease

Paul D. Shreve

Department of Nuclear Medicine, The Department of Veterans Affairs Medical Center, Ann Arbor, Michigan;
and Division of Nuclear Medicine, Department of Internal Medicine, The University of Michigan Medical Center, Ann Arbor, Michigan, USA

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**Abstract.** Focal 2-deoxy-2-[fluorine-18]fluoro-D-glucose (FDG) uptake on positron emission tomography (PET) in a pancreatic mass has been reported as a specific finding for pancreatic carcinoma. Inflammatory conditions of the pancreas and associated clinical circumstances yielding similar findings have not yet been fully defined. Among 42 patients studied by attenuation-corrected FDG PET for pancreatic disease, 12 with focal FDG uptake in the pancreas were identified as having no underlying neoplasm based on surgical findings, biopsy results, and long term clinical and imaging follow up. Focal FDG accumulation in the pancreas with standardized uptake values ranging from 3.4 to 11.2 on FDG PET was ultimately found to be related to inflammation rather than neoplasm. This occurred in pancreatic masses in which clinical and laboratory evidence of acute pancreatitis was equivocal or entirely lacking, as well as in the setting of acute pancreatitis and after recovery from acute pancreatitis. Inflammation can give rise to focal FDG uptake in the same intensity range as pancreatic neoplasm, even when clinical, laboratory and computed tomographic findings suggestive of an inflammatory etiology are equivocal or absent.

*Key words:* 2-Deoxy-2-[fluorine-18]fluoro-D-glucose – Pancreas – Pancreatitis – Inflammation

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## Introduction

Applications of positron emission tomography (PET) using the tracer 2-deoxy-2-[fluorine-18]fluoro-D-glucose (FDG) are rapidly expanding in clinical oncology. FDG PET has been shown to have greater diagnostic accuracy than anatomic imaging modalities in distinguishing scar from neoplasm and detecting small deposits of malignant neoplasm. Recently several investigators have reported improved diagnostic specificity for diagnosis of pancreatic mass using FDG PET. The presence of elevated FDG accumulation above background levels in a pancreatic mass was reported to be highly specific for neoplasm, while the absence of FDG uptake in a pancreatic mass correctly identified the scar tissue composition of the pseudomass of chronic pancreatitis [1–7].

Elevated FDG accumulation is not specific for neoplasm. Due to the increased glycolytic metabolism in activated leukocytes, inflammation can be associated with elevated FDG uptake [8, 9]. Thus, in the setting of pancreatitis increased FDG accumulation would be expected, and when focal, could be confounding in the assessment of a pancreatic mass for the diagnosis of pancreatic cancer using FDG PET. This article reports observations of focal FDG accumulation in the pancreas due to inflammation which in appropriate circumstances could be misinterpreted as neoplasm.

## Materials and methods

Among 42 patients studied by FDG PET for pancreatic disease, 12 with focal abnormal FDG uptake in the pancreas were eventually found to have no underlying neoplasm. All patients were male and ranged from 40 to 78 years of age, and gave written informed consent for the PET imaging in accordance with institutional human studies standards. A pancreatic mass identified on computed tomography (CT) was present in eight of these patients, while four of the patients were evaluated for suspicion of pancreatitis-related complications or underlying neoplasm in the setting of mild acute pancreatitis. Final diagnosis was obtained by surgical resection ($n$ = 4), core needle biopsy with long-term follow-up ($n$ = 2), and long-term (>18 months) clinical and CT follow-up.

PET imaging was performed using either Siemens ECAT 921 EXACT or ECAT 931 tomographs (CTI, Knoxville, Tenn., distributed by Siemens Medical Systems, Iselin, N.J.). The PET imaging was performed within 48 h of CT. Patients were fasted a minimum of 6 h prior to PET imaging, and had serum glucose levels of less than 150 mg/dl. All imaging was at one bed position with attenuation correction (12 min transmission scan prior to injection of tracer) and the 10 min emission acquisition used for image reconstruction was obtained 50–60 min following intravenous administration of 370 MBq of $^{18}$F-FDG. FDG PET images were

*Correspondence to:* P.D. Shreve, Division of Nuclear Medicine, UH B1 G412 Box 0028, 1500 E. Medical Center Drive, Ann Arbor, MI 48109-002, USA

reconstructed by filtered back projection using a 0.3 Hann filter. Images were interpreted using transaxial attenuation-corrected images viewed on a computer display using monochromatic and multicolor scales. Standardized uptake values (SUVs) were based on regions of interest of 8 pixels minimum, using average counts per pixel at 50–60 min post FDG administration, as well as maximum counts per pixel ($SUV_{max}$). SUV values were not corrected for partial volume averaging or lean body mass.

CT imaging was performed with a Picker PQ 1000 or 5000 (Picker Medical Systems, Cleveland, Ohio) using 5-mm spiral tomographic sections with pitch factor 1.3 obtained with oral and intravenous contrast enhancement. Dynamic imaging through the pancreas was performed in the arterial phase of bolus intravenous contrast injection of diatrizoate meglumine at 2 ml/s using a power injector.

## Results

Focal FDG uptake with SUVs ranging from 3.4 to 11.2 was observed in eight patients presenting with a pancreatic mass but with no, or equivocal, presenting evidence of pancreatitis (Table 1). These SUVs essentially span the entire range of SUVs reported for primary pancreatic carcinoma [3, 5–7], and in this series among patients with FDG-avid pancreatic cancer SUBs ranged from 3.5 to 8.2 with an average of 5.2±2.2 (average $SUV_{max}$ = 6.1±2.7). Among four patients presenting with clinical and laboratory evidence of mild acute pancreatitis and no pancreatic mass, focal FDG uptake with SUVs ranging from 3.1 to 5.4 was observed (Table 1). Amongst all patients with both inflammatory and neoplastic disease, liver SUV was 2.5±5 ($SUV_{max}$ = 3.3±9) while uninvolved pancreas SUV was 1.8±4 ($SUV_{max}$ = 2.5±6).

The most intense focal FDG uptake (SUV >7) occurred in two cases of pancreatic head-related inflammatory masses of mixed attenuation on CT (a phlegmonous mass) and a case of mass-forming pancreatitis with pseudocyst formation. The phlegmonous mass shown in Fig. 1 occurred in a 46-year-old male with a history of chronic pancreatitis and prior surgery including a partial pancreatectomy and choledochohepatoenterostomy, pre-

**Table 1**. Patient characteristics, imaging findings and clinical presentations

| Age (years) | Location of FDG uptake | SUV (SUVmax)[a] | CT findings | Clinical presentation and laboratory findings |
|---|---|---|---|---|
| 68 | Head (ametabolic center)<br>Celiac/SMA region<br>Parapancreatic node | 7.3±0.3 (7.9)<br>9.8±0.4 (10.6)<br>8.8±04 (9.5) | Pancreatic head mass, vessel encasement, biliary ductal dilatation, local lymph node enlargement | Abdominal pain and obstructive jaundice; amylase and lipase normal WBC = 14 k/μl |
| 46 | Porta hepatis and lateral pancreatic head | 11.2±0.9 (12.8) | Large heterogeneous mass extending from pancreatic head and into the porta hepatis region | History of chronic pancreatitis and abdominal pain. Amylase and lipase normal. WBC = 11.7 k/μl |
| 50 | Focal pancreatic head (heterogeneous) | 4.1–4.6±0.7 (5.2–5.7) | Homogenous pancreatic head mass | Abdominal pain and vomiting. Normal amylase, lipase, WBC |
| 42 | Focal pancreatic head | 4.2±0.3 (4.6) | Homogenous pancreatic head mass with bilary ductal dilatation | Abdominal pain, normal amylase and WBC; lipase = 56 IU/dl |
| 54 | Focal pancreatic head | 3.8±0.4 (4.4) | Heterogeneous pancreatic head mass with calcifications | History of pancreatitis WBC normal. Amylase = 161 IU/dl; lipase = 97 IU/dl |
| 40 | Focal pancreatic tail | 4.6±0.3 (5.0) | Diffuse gland enlargement | Acute pancreatitis. WBC normal Amylase = 349 IU/dl; lipase = 283 IU/dl |
| 64 | Head and tail segment | 5.4±0.6 (6.4)<br>4.7±0.5 (6.3) | Diffuse gland enlargement | Acute pancreatitis. WBC normal. Amylase = 379 IU/dl, lipase = 124 IU/dl |
| 72 | Three foci in tail | 3.1–3.3±02 (3.3–3.5) | Normal | post ERCP |
| 78 | Rim segment of pancreatic head mass | 3.4±0.4 (4.3) | Large cystic mass | Abdominal pain. WBC and Amylase normal; lipase = 22 IU/dl |
| 69 | Pancreatic head | 4.4±0.3 (4.8) | Resolved mild acute pancreatitis | Asymptomatic. Normal WBC, amylase and lipase |
| 66 | Pancreatic head | 5.3±0.3 (5.7) | Homogenous minimal head enlargement | Mild abdominal pain. Normal WBC, amylase and lipase |
| 48 | Caudal pancreatic head | 7.3±0.7 (8.6) | Heterogeneous pancreatic head mass | Abdominal pain. normal WBC, amylase and lipase |

WBC, Peripheral white blood cell count in thousand cells/microliter (k/μl)

[a] SUV, Standardized uptake value as average over region of interest, eight pixel minimum ($SUV_{max}$, SUV maximum pixel value in region of interest)

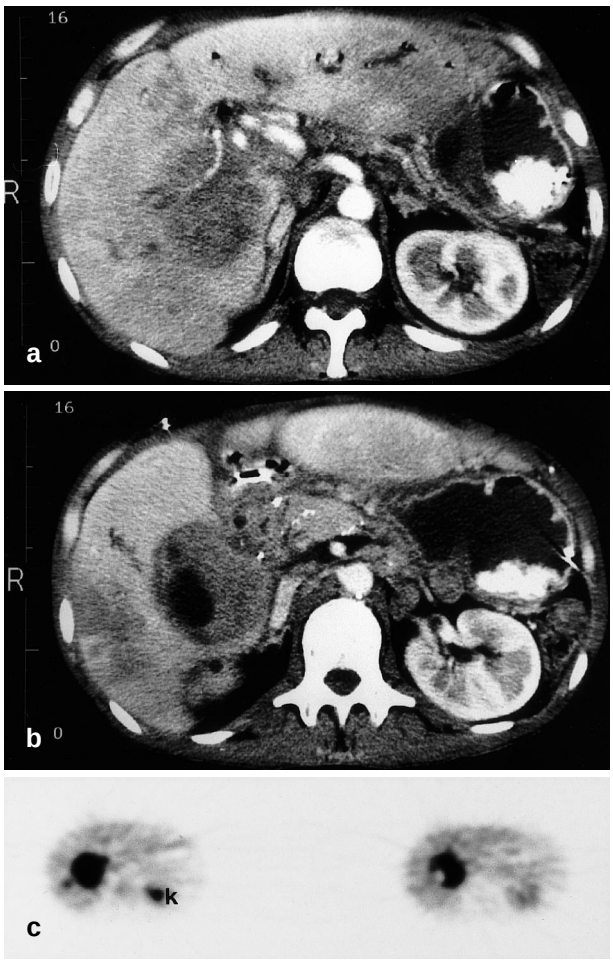


**Fig. 1a–c.** Phlegmonous mass. Patient had a history of chronic pancreatitis and chronic abdominal pain, and presented with weight loss and abdominal pain but no elevation of serum amylase or lipase. **a,b** Contrast-enhanced CT images of patient with a large mass extending from the pancreatic head into the porta hepatis region. **c** FDG PET at corresponding transaxial levels shows intense FDG accumulation in the mass (SUV = 11.2). *k* denotes renal urinary tracer

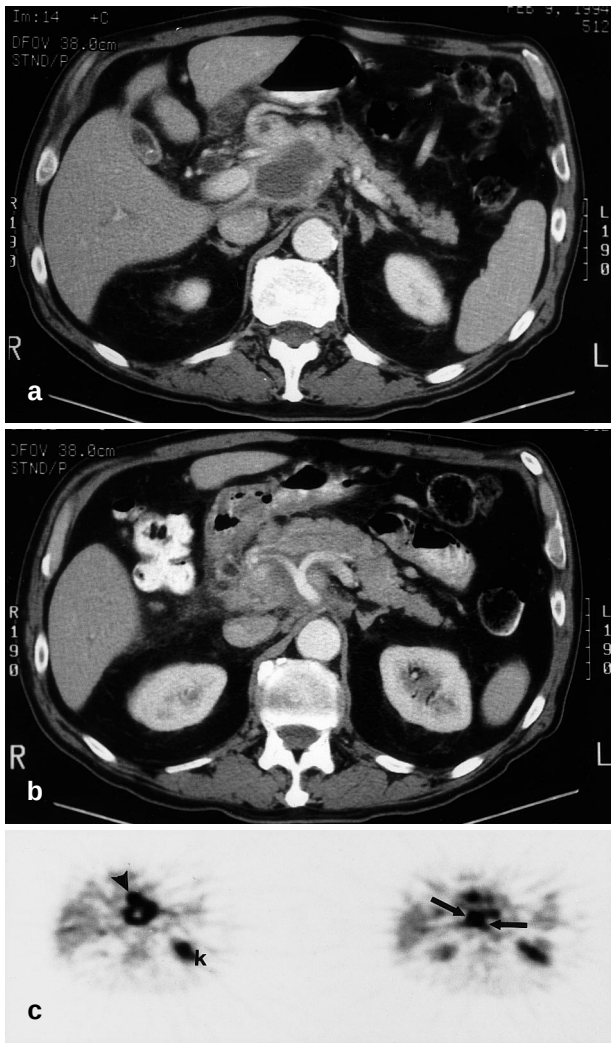


**Fig. 2a–c.** Mass-forming pancreatitis with pseudocyst formation and vessel encasement. Patient presented with abdominal pain and biliary tract obstruction and normal serum amylase and lipase. **a,b** Contrast-enhanced CT shows a pancreatic head mass with central low attenuation, an enlarged parapancreatic lymph node, and encasement of the celiac axis and superior mesenteric artery. **c** FDG PET at corresponding transaxial levels shows intense FDG accumulation (SUV = 9.8) in the mass surrounding an ametabolic center, and in an enlarged parapancreatic lymph node (*arrowhead*) and soft tissue vessel encasement (*arrows*). *k* denotes renal urinary tracer

senting with abdominal pain and normal serum amylase and lipase. Biopsy revealed acute and chronic inflammatory changes and no neoplasm. On serial follow-up CT scans the mass persisted, but was smaller 1 year later, at which time a core needle biopsy again revealed acute and chronic inflammatory changes. The mass continued to decrease in size over a subsequent yearly follow-up CT, and a final diagnosis of phlegmonous mass eroding into the porta hepatis was made.

The mass-forming pancreatitis with pseudocyst formation shown in Fig. 2 occurred in a 68-year-old male with no history of pancreatitis presenting with abdominal pain, normal serum amylase and lipase, and a white blood cell count (WBC) of 14 k/μl). On exploratory laparotomy extensive inflammatory changes were present, precluding definitive resection. On follow-up CT 6 months later, there was near-complete resolution of the mass and the follow-up CT performed nearly 2 years after initial presentation was normal.

Pancreatic head masses secondary to focal pancreatitis demonstrated both uniform and heterogeneous patterns of elevated FDG uptake. Figure 3b shows an example of heterogeneous uptake in a 50-year-old male with a history of chronic pancreatitis who presented with abdominal pain, vomiting, and a relatively homogeneous 5-cm pancreatic head mass on CT. FDG PET demonstrated heterogeneously elevated FDG uptake with an overall SUV of 3.2, but three discrete foci with SUVs of 4.1, 4.6, and 4.8; regions in the mass excluding the dis-

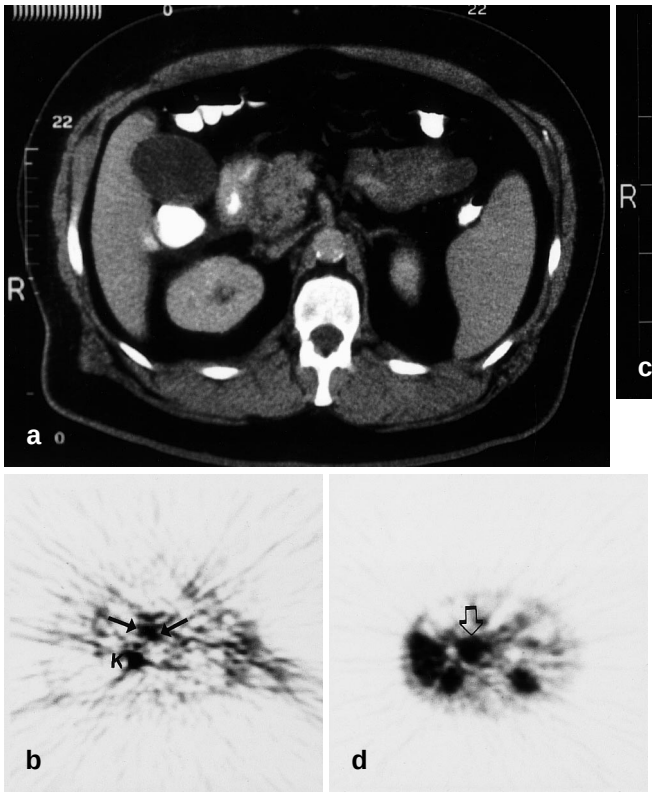


**Fig. 3a–d.** Pancreatic head enlargement due to focal pancreatitis. **a,b** Patient with a history of recurrent pancreatitis and presenting with equivocal evidence of active pancreatitis. **a** Contrast-enhanced CT shows enlarged pancreatic head. **b** FDG PET at the corresponding transaxial level demonstrated foci (*arrows*) of increased FDG uptake (SUV = 4.1–4.6) in the pancreatic head mass. This is a case of heterogeneous FDG uptake. *k* denotes renal urinary tracer. **c,d** Patient with a history of chronic pancreatitis and presenting with abdominal pain. **c** Contrast-enhanced CT shows calcifications in the pancreatic head and inhomogeneous enlargement of the lateral aspect of the pancreatic head. **d** FDG PET shows uniformly increased FDG uptake (SUV = 3.8) in the entire pancreatic head (*open arrow*). This represents a case of uniform FDG uptake

crete foci had an SUV of 2.7. At the time of imaging the serum amylase, lipase and WBC were all normal. ERCP and visceral angiography were negative for evidence of neoplasm, but the mass persisted on follow-up CT and was removed by Whipple procedure 2 months later. Acute and chronic inflammation with dense scar, but no neoplasm, was found in the mass. Similarly, enlarged regional lymph nodes were negative for neoplasm. Typical homogeneous uptake of focal pancreatitis is shown in Fig. 3d in a 54-year-patient with a history of chronic pancreatitis presenting with chronic abdominal pain and mildly elevated serum amylase and lipase.

Focal FDG uptake can also occur in the setting of mild acute pancreatitis where no corresponding mass on CT is present. Figure 4 shows a 40-year-old male with a history of pancreatitis, presenting with clinical acute pancreatitis and elevated serum amylase (349 IU/dl) and lipase (283 IU/dl). After resolution of clinical symptoms, subsequent FDG PET imaging was negative. Other cases had two or three discrete abnormal foci with SUVs as high as 5.4. Four months following complete recovery from an episode of acute pancreatitis with normal CT appearance of the pancreas and normal serum amylase, lipase and WBC, one patient nonetheless had a discrete focus of FDG uptake (SUV = 4.4) in the pancreas on FDG PET. No evidence of underlying neoplasm was found on follow-up CT 18 months later.

Among the patients studied without an underlying inflammatory etiology, 21 had neoplasms, including 17 with abnormal focal FDG uptake with an SUV greater than 3.0. These cases comprised 14 adenocarcinomas,

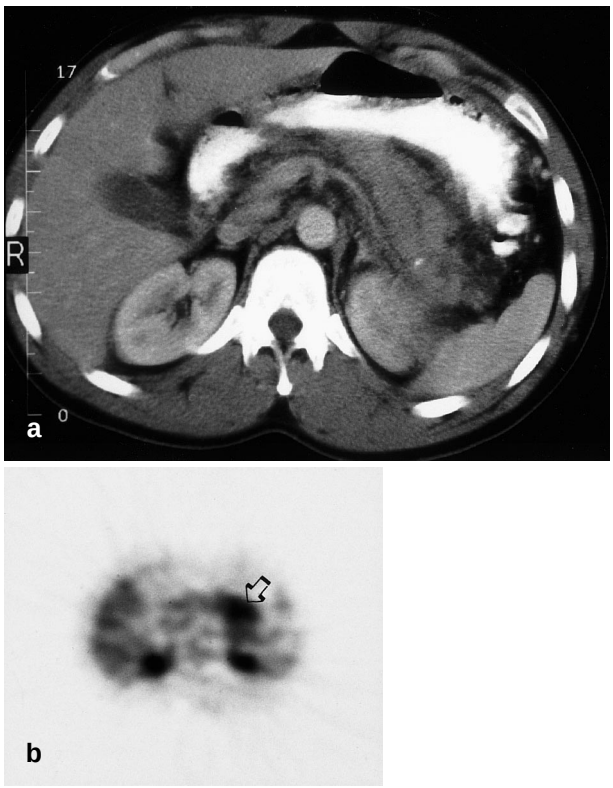


**Fig. 4a, b.** Focal FDG uptake associated with acute mild pancreatitis. Patient presented with clinical and laboratory evidence of acute pancreatitis. **a** Contrast-enhanced CT shows diffusely swollen pancreas typical of diffuse acute pancreatitis while FDG PET at the corresponding transaxial level (**b**) shows focal FDG accumulation (SUV = 4.6) in the tail only (*open arrow*)

one primary pancreatic lymphoma, one metastatic small cell carcinoma, and one pancreatic neuroendocrine (unspecified) neoplasm. Three patients with proven neoplasm of the pancreas had no identifiable abnormal FDG uptake and an SUV of less than 2.5. These cases included a cystic adenocarcinoma, a 1-cm poorly differentiated adenocarcinoma with associated fibrosis of chronic pancreatitis, and a 1.5-cm well-differentiated adenocarcinoma in a diabetic patient. In one patient, the apparent pancreatic mass with no associated abnormal FDG uptake was due to a portal vein thrombosis. Among eight patients with pancreatic mass due to chronic pancreatitis, SUVs ranged from 1.8 to 3.2, with an average of 2.8.

## Discussion

Differentiation of the pseudomass of chronic pancreatitis from pancreatic adenocarcinoma has been a persistent problem in patients with chronic pancreatitis [10]. Methods based on anatomic imaging including contrast enhanced CT and magnetic resonance imaging as well as transabdominal and endoscopic ultrasound have shown limited ability to reliably distinguish the scar tissue of the pseudomass of chronic pancreatitis from the neoplastic tissue of a focal pancreatic adenocarcinoma, necessitating either biopsy or surgical resection of suspected neoplasm. Recent reports suggest a more specific diagnosis is possible by metabolic tissue characterization of a pancreatic mass using FDG PET. FDG is not specific for neoplasm, however. Accumulation of this tracer also occurs in the leukocytic infiltration associated with inflammation and is a major source of false-positive diagnoses in the application of FDG PET in oncology [11]. Even the FDG uptake observed in neoplasm may, in part, reflect activated leukocytic cellular infiltration [12].

Diffuse edema and leukocytic infiltration (primarily neutrophilic) occur in mild acute pancreatitis. Accordingly, increased FDG accumulation throughout the gland and even in the peripancreatic fat, with SUVs in the 3–5 range, is observed in acute pancreatitis. Generally this diffuse pattern is recognized as acute pancreatitis [1] or chronic active pancreatitis [4], distinct from the focal FDG accumulation associated with neoplasm. As reported in this series, focal FDG uptake can occur in the setting of acute pancreatitis with CT findings of a normal pancreas or diffuse edema, but no anatomic correlate such as a mass or region of altered attenuation or contrast enhancement.

Such focal FDG uptake in the setting of acute pancreatitis (i.e., clinical and laboratory diagnosis) would generally not pose a diagnostic problem. Nevertheless, since a focus of neoplasm can be an underlying cause of pancreatitis due to mass effect obstructing the pancreatic duct or tributary, focal FDG uptake could be misinterpreted as evidence of underlying (and CT or sonographically occult) neoplasm rather than a normal variation in the FDG uptake associated with acute pancreatitis. The etiology of such focal uptake in the setting of apparently diffuse acute pancreatitis may well reflect inhomogeneity of the leukocytic infiltrate that is not commensurate with the edema revealed on anatomic imaging, or a focus or foci of residual inflammatory processes during resolution of pancreatitis. This phenomenon may be persistent as well. In one case in this series focal FDG uptake was present 4 months after the episode of acute pancreatitis had resolved clinically.

More potentially confounding in interpretation is focal FDG uptake associated with focal pancreatitis. Focal pancreatitis can occur in as many as 18% of cases of acute pancreatitis [13]. Focal pancreatitis can mimic anatomic imaging findings associated with pancreatic carcinoma such as obstructive jaundice or vascular encasement [10, 14]. Early series reported very few false-positives due to focal FDG uptake, and of those most were attributed to processes potentially associated with inflammation such as hemorrhagic pseudocyst, portal vein thrombosis, or presence of a stent [5], or were distinctive due to atypical location of the focal FDG uptake such as divisum or retroperitoneal fibrosis [1]. Kato et al [2] reported two cases of focal FDG uptake in a pancreatic mass which on histopathologic examination was found to be scar with leukocytic infiltration. In a recent larger series, Zimny and co-workers [7] observed five false-positive cases of focal FDG uptake due to acute inflammation superimposed on the chronic inflammation of chronic pancreatitis. Both groups of authors suggested that clinical and laboratory data should be consulted to exclude patients with evidence of acute pancreatic inflammation from FDG PET in order to minimize false-positive diagnoses for neoplasm [2, 7].

The cases reported here directly illustrate this limitation of FDG PET of the pancreas, particularly regarding the intensity of focal FDG uptake that can occur in inflammatory pancreatic processes. These cases also demonstrate that focal FDG uptake secondary to pancreatitis can be observed when clinical presentation and laboratory findings are only suggestive, or even not at all indicative, of an inflammatory etiology. This article does not attempt to prospectively determine the instances of false-positive FDG PET diagnoses in a population evaluated for pancreatic mass, but rather illustrates the range of conditions in which focal FDG uptake in the pancreas due to inflammatory processes occurs. In other series reporting on the diagnostic performance of FDG PET evaluation of a pancreatic mass, the paucity of false-positive diagnoses may well reflect appropriate patient preselection. The pseudomass of chronic pancreatitis is scar from prior focal inflammatory event(s) or low-grade, long-standing focal inflammation. If FDG PET is performed at a relatively quiescent period, when inflammatory activity is low, the mass will not be appreciably FDG avid and will be correctly classified as scar. Excluding patients with recent episodes of pancreatitis or any laboratory or CT findings suggestive of active pancreatitis would be expected to reduce the fraction of

false-positive (for neoplasm) FDG PET diagnoses. However as illustrated here, these considerations not entirely reliable. Patients may not be aware of, or relate, recent episodes of pancreatitis and may present with CT findings of pancreatic mass but equivocal or absent ancillary evidence of active pancreatitis at the time of imaging.

In summary, focal FDG uptake in the pancreas has been observed both in the setting of mild acute diffuse pancreatitis and in focal active pancreatitis associated with mass. Pancreatitis can give rise to focal FDG uptake in the same intensity range as pancreatic neoplasm, even when clinical, laboratory and CT findings suggestive of an inflammatory etiology are equivocal or absent.

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