PRELIMINARY NOTES

[^{11}C]Methionine Pancreatic Scanning with Positron Emission Computed Tomography

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By the use of [^{11}C] methionine and positron computed tomography (PCT), images of the pancreas were obtained in 32 patients. The injection of between 10 and 20 mCi of this product enables four to six transverse sections to be obtained. Seventeen of the patients studied had no exocrine pancreatic disease, and in all these cases the pancreas was clearly visible. In four cases of pancreatic carcinoma and one of retroperitoneal tumor, there were abnormalities visible. In five cases of chronic pancreatitis, no pancreatic uptake was observed. In a sixth case, concentration was visible, but only in the head of the pancreas. One case of acute pancreatitis, which showed no concentration during the acute phase, returned to normal after recovery. When visible, the pancreas was easily located and distinguishable from the intestinal image, except in two cases that were uninterpretable for technical reasons. No false positive or negative was observed, but a differential diagnosis between cancer and pancreatitis was impossible.

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The diagnosis of pancreatic diseases is difficult because of both the anatomic location of the gland and the fact that function must be seriously disturbed for exocrine-function tests to be modified.

Many tests have been devised to improve diagnostic accuracy: angiography (*1*), ultrasonography (*2*), endoscopic retrograde pancreatography (*3*), radionuclide scanning (*4*), and computerized tomography (*5*). Recent reviews have underlined the lack of specifity of the pancreatic scan (*6,7*). Poor results may be because Se-75 is a nuclide with long half-life, so the injected dose must be small. Furthermore, it is difficult in a frontal view with the gamma camera to distinguish the pancreatic shadow from the liver shadow and from intestinal activity. The use of amino acids labeled with C-11 or N-13—such as [^{11}C]methionine (*8*), [^{11}C]valine (*9*), or L-[^{13}N]tryptophane (*10*)—allows injection of large doses because of the short half-lives (20.4 min and 10.1 min) of these emitters. In addition, molecules labeled with C-11 retain their natural configuration, and we may expect a better ratio of activity between the pancreas and the liver.

The object of this study is the utilization of positron emission from C-11 to obtain transverse sections of the pancreas after injection of [^{11}C]methionine using positron computerized tomography (PCT) (*11*).

MATERIALS AND METHODS

Thirty-three scans were performed in 32 patients. The distribution by diagnosis is shown in the two columns at the left of Table 1.

A method for synthetizing [^{11}C]methionine by the action of $I^{11}CH_3$ on L-homocysteine has been described previously (*8*). A specific activity of 500-1000 mCi/μmol [^{11}C]methionine, with radiochemical purity of 100%, could be obtained by this method. No radiolysis was observed chromatographically for at least 1 hr after completion of the preparation.

The patients were injected intravenously with 15–20 mCi of [^{11}C]methionine. Patients had breakfast 4 hr before the examination and no stimulation tests were carried out. An initial examination was per-

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TABLE 1. DISTRIBUTION OF PATIENTS ACCORDING TO DIAGNOSIS. RESULTS OF PCT EXAMINATION AND OF OTHER TESTS ARE INDICATED

Diagnosis	No. of patients	PCT	Clinical, biologic, and radiologic findings	Ultrasound	Endoscopic retrograde cholangio-pancreatography	Duodenal intubation	Anatomic findings
Normal	11	normal 11	11	5 (1)*	—	1	3
Diabetes and liver disease	6	normal 5†	6	—	—	—	3
Chronic pancreatitis	6	no uptake 6‡	6	5 (1)*	3	1	4
Acute pancreatitis	3‖	no uptake 1 normal§ 2†	3	1	1	3	2
Duodeno-pancreatectomy	1	no uptake 1	—	—	—	—	1
Carcinoma of pancreas	4	localizing defect 3 no uptake 1	4	1	1	—	4
Retroperitoneal fibrosarcoma	1	abnormal 1	1	1¶	—	—	1

* Limited examination because of extensive bowel gas.
† One scan was of no diagnostic use for technical reasons.
‡ Localized defect in one case.
‖ Two scans were made in same patient.
§ Normal pancreas images were obtained after recovery.
¶ Echography revealed fluid in tail of pancreas.

formed using a positron emission tomographic instrument. Four or six adjacent slices, 2 cm thick were collected, starting 4 cm above the umbilicus and proceeding cephalad. Approximately 3 million counts were accumulated for each slice. The sequence was begun 8 min after injection, and transmission scans performed before injection were used to correct the emission data for attenuation. For comparison, a 300,000-count pancreatic image was obtained 40–50 min after injection using a conventional scintillation camera with high-energy collimator. Fifteen patients also underwent routine laboratory investigations, barium x-ray examination, and ultrasound. Pancreatic involvement was confirmed by endoscopic retrograde cholangiopancreatography and/or laparotomy as indicated in Table 1.

RESULTS

The images from 11 normal subjects provided an indication of normal structure. The head of the pancreas appeared in sections, 4 or 6 cm above the umbilicus, as a round or oval zone of high activity (Fig. 1). It projected along the midline or slightly to the right, but always within the ventral half of the section. The body and tail of the pancreas appeared in the higher sections in ten cases. The configuration corresponded to a "pistol" shape on the conventional scan obtained with a scintillation camera at the end of the examination. In one case the body and tail were located at the same level as the head, and the scintillation scan confirmed a vertical orientation. The pancreas was frequently narrowed at the junction between the head and body. Such normal patterns were also encountered in three patients with cirrhosis, two with diabetes mellitus, and one with a carcinoma of the hilum of liver.

In all cases the pancreatic image was distinguished from that of the gut by two characteristics: a high intensity of uptake, identical for the head and the body, and a form curving rearward around the rachis, which shows up as a nonradioactive zone. Intestinal images appeared as sinuous trails or small disseminated spots, especially in the left half of the section. The images obtained in a patient who underwent a total duodenopancreatectomy confirmed these findings.

No pancreatic uptake was found in five patients with chronic pancreatitis. In one patient the head was visible but not the body or tail, and surgery

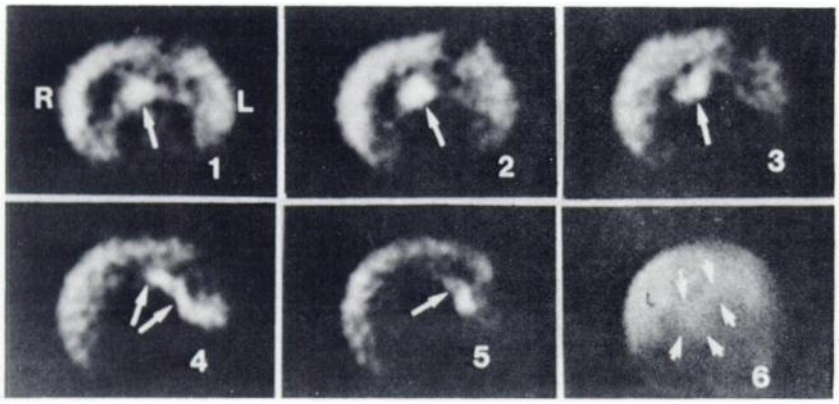

FIG. 1. Normal pancreas. Sections at various levels above umbilicus: 4 cm (1), 6 cm (2), 8 cm (3), 10 cm (4), and 12 cm (5). (L = left, R = right). Head of pancreas is visible in Sections 1, 2, and 3 (arrows). Body and tail can be seen in 4, and tail alone in 5. Image 6 is anterior scintiphoto, with pancreas indicated by arrows (L = liver).

revealed a pancreatitis localized to the body and tail. In a patient with an acute pancreatitis, the pancreas was not visible during the acute phase but became apparent 5 mo later after recovery. Normal pancreatic scans were also seen in two other patients 1 mo after the acute episode. Abnormal images were obtained in four cases of carcinoma of the pancreas. No uptake was seen in one case of carcinoma of the body, and local defects were observed in association with three other tumors: one of the tail, one of the body, and one of the head (Fig. 2). A retroperitoneal fibrosarcoma was visualized on the transverse sections (Fig. 3), but the pancreatic image was normal in an anterior view obtained with the scintillation camera.

DISCUSSION

Transverse and frontal views of the pancreas may be obtained after injection of 15–20 mCi of [^{11}C]methionine. The pancreas-to-liver activity ratio is not known for man but is approximately 2.5 in the mouse (*8*). Data recorded with a gamma camera and information-processing system, during 45 min after injection, have shown that a usable pancreatic image is visible from the eighth minute. The first tomographic section lasts approximatively 3 min; subsequent sections require progressively longer times because of the rapid decay of C-11. The total duration of the PCT study is around 20–30 min. Compared with the usual scintigraphy with [^{75}Se]selenomethionine, use of [^{11}C]methionine offers, a priori, certain advantages:

1. Fifteen to 20 mCi may be injected without danger; whole-body irradiation is about 180 mrads after injection of 20 mCi of [^{11}C]methionine (*12*), whereas it reaches 1600 mrads after injection of 250 μCi of [^{75}Se]selenomethionine (*13*).
2. Positron emission of C-11 allows transverse tomography.

The images thus obtained with PCT from both normal subjects and patients enable the differentia-

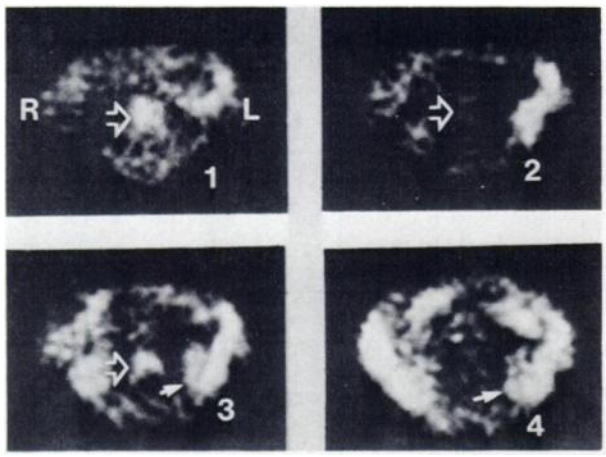

FIG. 2. Carcinoma of head of pancreas. Sections at 4 cm (1), 6 cm (2), 8 cm (3), and 10 cm (4) above umbilicus. Head is visible in Sections 1 and 3 (open arrow). Tumor is visible in 2 as area of low uptake (open arrow). Solid arrows indicate body and tail. Surgical findings: tumor, 5 cm in diameter, enlarged pancreatic head, which invaded and deformed the duodenal sweep.

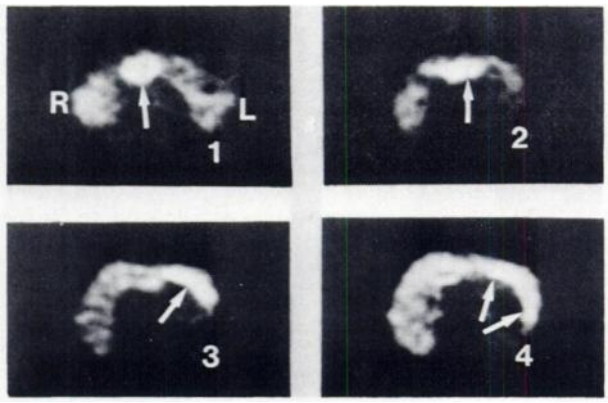

FIG. 3. Retroperitoneal fibrosarcoma. Sections are as in Fig. 2. Head of pancreas is visible in 1 and 2. In 3 and 4, body is displaced anteriorly and toward left (right of image) by extensive lesion in retroperitoneum.

tion of the pancreas from the small intestine. This may improve the diagnostic value of pancreatic scans in pancreatitis. The selenomethionine scan is difficult to interpret because high intestinal activity is present in most cases and may lead falsely to the conclusion of normal pancreatic uptake (*14*). In five cases of pancreatitis, the pancreas was not visible and the image was identical to that seen in a patient with duodenopancreatectomy; although three of these patients had pseudocysts, they could not be detected. The one patient with a normal uptake in the head of the pancreas was found, at operation, to have a fibrosis localized to the body and tail. Nonvisibility of the damaged pancreas during acute and chronic pancreatitis indicates that the uptake of [^{11}C]methionine in pancreatic tissue reflects exocrine pancreatic function.

These results parallel those obtained with [^{75}Se]selemethionine, with the difference of a clearly distinguished intestinal image (*15*). This advantage also appears in the case of a retroperitoneal tumor that presented the appearance of a normal pancreas in the conventional scintiphoto.

Early diagnosis of pancreatic carcinoma has not been possible with [^{75}Se]selenomethionine imaging. The ECAT can resolve 15-mm defects in phantoms, and thus provides a workable technique, though recent work indicates that longitudinal multiplane emission tomography using Se-75 improves sensitivity and specificity (*16*). The smallest tumor studied measured 4 cm in diameter.

These preliminary results indicate the potential value of pancreatic study with C-11 methionine and positron computed tomography. The examination provides anatomic information, such as is available with transmission computed tomography and ultrasound, but it also gives functional information, since it reflects uptake and incorporation of L-methionine in proteins.

We always obtained normal images from patients with no pancreatic disease. In patients with pancreatic disease, some abnormality was always visible—except in one case, which was uninterpretable for technical reasons. However, distinction between cancer and pancreatitis appears to be impossible, since both conditions result in a partial or total lack of uptake. A comparative study involving transmission computerized tomography, ultrasound, and positron computerized tomography with [^{11}C]methionine is thus justified to determine in which areas each technique can be of most benefit (*17*).

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