Diagnosis of pancreatic cancer by 2[¹⁸F]-fluoro-2-deoxy-D-glucose positron emission tomography

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Abstract

The detection of pancreatic cancer or the discrimination between pancreatic cancer and chronic pancreatitis remains an important diagnostic problem. The increased glucose metabolism in malignant tumours formed the basis for this investigation, which focused on the role of positron emission tomography (PET) with 2[¹⁸F]-fluoro-2-deoxy-D-glucose (FDG) in the detection of pancreatic cancer and its differentiation from chronic pancreatitis. Eighty patients admitted for elective pancreatic surgery received preoperatively 250-350 mBq FDG intravenously and emission scans were recorded 45 minutes later. Intense focal activity in the pancreatic region was taken at the time of scanning as showing the presence of pancreatic cancer. The presence of cancer was later confirmed by histological examination of the surgical specimens and histological findings were compared with the preoperative PET results. Forty one patients with pancreatic cancer (group I: n=42) had a focally increased FDG uptake in the pancreatic region. Two patients with a periampullary carcinoma (group II: n=6) failed to develop FDG accumulation. In 28 patients with chronic pancreatitis (group III: n=32) no FDG accumulation occurred. Overall sensitivity and specificity of PET for malignancy (group I+II) were 94% (45 of 48) and 88% (28 of 32), respectively. The standard uptake value of the patients with pancreatic carcinoma was significantly higher than in patients with chronic pancreatitis (3.09 (2.18) v 0.87 (0.56); p<0.001; median (interquartile range)). These findings show that FDG-PET represents a new and non-invasive diagnostic procedure for the diagnosis of pancreatic cancer and to differentiate pancreatic cancer from chronic pancreatitis. However, the diagnostic potential of this technique requires further evaluation.

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Among gastrointestinal cancers, pancreatic carcinoma has the worst prognosis: less than 20% of affected patients survive the first year after diagnosis. This poor outcome may result

from the frequent late diagnosis of the disease when it has reached stages III or IV, and the tumour has spread to lymph nodes or distant metastases, or both are already present.¹⁻³

Diagnosis of pancreatic cancer may be difficult, as clinical symptoms are rather unspecific and non-invasive imaging methods such as ultrasonography or contrast enhanced computed axial tomography (CAT) only detect indirect signs of the tumour such as a pancreatic mass or ductal abnormalities.

Positron emission tomography (PET) has recently been developed as a non-invasive imaging method for tissue characterisation based more on specific tissue metabolism rather than on imaging tissue mass, contour, echogenicity or x ray absorption. Thus, increased glucose utilisation, a metabolic hallmark of many malignant tumours,⁴ has been used for non-invasive identification of malignant primary or recurrent colorectal cancer, as well as cancer in the lung, head, neck, and brain.⁵⁻¹⁰ In these studies the glucose analogue 2[¹⁸F]-fluoro-2-deoxy-D-glucose (FDG) has been used to measure overall tumour glucose utilisation with PET.¹¹

In pancreatic disorders, PET with ¹¹C-labelled L-methionine cannot distinguish pancreatic cancer from chronic pancreatitis.¹² In contrast, previous studies show that FDG-PET seems to have a higher accuracy in the diagnosis of pancreatic cancer and to be effective in the differentiation of cancer from chronic inflammation.^{13 14} In addition, a general increase in the expression of genes associated with the inward transport of glucose and glycolysis has been shown in pancreatic adenocarcinoma.¹²⁻¹⁴ In this study we examined prospectively the performance of FDG-PET in the diagnosis of pancreatic cancer and assess the ability of the technique to differentiate pancreatic carcinoma from chronic pancreatitis in 80 consecutive patients undergoing elective pancreatic surgery.

Methods

Study protocol

The investigation was designed as a blind study (a) to evaluate the ability of FDG-PET to confirm the presence of cancer in patients with histologically confirmed pancreatic cancer (sensitivity) and (b) to define its specificity in patients with histological confirmed chronic pancreatitis. All patients were admitted to our hospital for elective pancreatic surgery and only those who gave written informed consent

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TABLE I Patient characteristics, tumour localisation, tumour stage, standard uptake value (SUV), tumour background ratio (T/B), and operative procedures in 42 patients with histological confirmed pancreatic cancer (patients 1–42) and six patients with histologically confirmed periampullary cancer (PC) (patients 43–48)

Patient	Sex	Age	Localisation	Stage	CAT	PET	SUV	T/B	FDG accumulation	Operation
1	M	78	Head	III	+	+	4.70	11.81	Head	Whipple
2	M	68	Head	II	+	–	3.91	7.90	Negative	Local recurrence after Whipple
3	M	55	Head	IV	+	+	1.20	3.98	Head	Biliary bypass
4	M	62	Head	II	+	+	2.22	5.57	Body	Local recurrence after Whipple
5	M	55	Head	IV	+	+	4.20	5.14	Body, liver	Local recurrence after Whipple
6	M	63	Body	IV	+	+	3.26	7.78	Body, lymph node	Laparotomy
7	F	73	Body	IV	–	+	3.35	7.43	Body	Laparotomy
8	F	63	Head	IV	+	+	5.65	21.27	Head, liver	Needle biopsy
9	M	64	Head	III	+	+	0.98	1.41	Head	Whipple
10	F	51	Head	III	–	+	2.11	4.09	Head	Whipple
11	M	50	Head	IV	+	+	3.16	3.60	Head, liver	Laparoscopy
12	M	50	Head	III	+	+	1.41	10.54	Head	Local recurrence after Whipple
13	F	52	Head	III	+	+	2.88	7.28	Head	Laparotomy
14	M	58	Head	III	–	+	1.54	3.10	Hepatic porta	Local recurrence after Whipple
15	M	71	Head	IV	+	+	1.19	2.67	Liver	Local recurrence after Whipple
16	F	55	Head	III	+	+	4.11	10.22	Head	Whipple
17	M	67	Head	IV	–	+	3.78	11.99	Head	Biliary and enteral bypass
18	M	59	Head	II	+	+	1.78	4.06	Pancreas	Whipple
19	F	62	Body	IV	+	+	2.41	4.43	Head	Laparotomy
20	F	66	Head	IV	+	+	5.22	16.30	Head	Whipple
21	M	79	Tail	IV	+	+	1.98	3.94	Tail	Laparoscopy
22	M	52	Body	IV	+	+	2.48	5.84	Head, liver	Laparotomy
23	F	69	Head	III	+	+	4.18	13.71	Head	Whipple
24	M	64	Head	IV	+	+	3.03	8.63	Head, liver	Biliary bypass
25	M	52	Head	III	+	+	2.00	5.40	Head	Whipple
26	M	50	Head	IV	+	+	5.52	14.58	Head	Whipple
27	M	58	Head	II	–	+	2.76	7.36	Head	Whipple
28	M	61	Head	III	+	+	1.44	5.50	Head	Whipple
29	M	64	Head	III	+	+	5.71	15.20	Head	Whipple
30	M	64	Head	III	+	+	0.85	2.10	Head	Whipple
31	M	52	Head	III	+	+	3.65	8.28	Head	Whipple
32	M	36	Head	IV	–	+	7.70	22.66	Head	Laparotomy
33	F	62	Head	III	+	+	2.29	4.88	Head	Whipple
34	F	55	Head	IV	–	+	5.66	10.86	Head	Biliary bypass
35	F	46	Head	II	–	+	1.27	2.19	Head	Whipple
36	M	62	Head	IV	+	+	3.45	8.80	Head, liver	Biliary bypass
37	M	58	Tail	III	+	+	3.47	8.52	Tail	Left resection
38	M	57	Head	III	+	+	2.38	6.34	Head	Whipple
39	M	60	Head	III	+	+	7.24	12.00	Head	Whipple
40	M	66	Head	III	+	+	4.70	12.20	Head	Whipple
41	M	52	Body	III	+	+	3.33	5.64	Body	Laparotomy
42	F	74	Head	II	–	+	2.22	5.15	Head	Laparotomy
43	M	42	PC	III	–	+	1.53	10.37	Head	Whipple
44	M	64	PC	III	+	+	1.47	2.65	Head	Whipple
45	F	62	PC	III	+	+	2.74	6.52	Head, lymph node	Whipple
46	F	53	PC	III	+	+	6.45	15.59	Head, lymph node	Cholecystectomy, lymph node dissection*
47	F	76	PC	I	–	–	1.14	2.11	Negative	Whipple
48	M	55	PC	II	–	–	0.64	1.70	Negative	Whipple

*Whipple resection was not possible because of intraoperative tachyarrhythmia and pulmonary insufficiency.

Whipple = Whipple's pancreatoduodenectomy. CAT: + = suspicious tumour mass with direct or indirect signs of malignancy, – = no pathological findings. PET: + = FDG accumulation in the tumour, suspicious for malignancy, – = no FDG accumulation in the tumour.

were included into this study. Staging of the pancreatic cancer was carried out according to the International Union against Cancer (UICC) classification.¹⁸ All patients had either surgery of the pancreas with subsequent histological examination of the surgical specimen or diagnosis was obtained by intraoperative fine needle biopsies. In addition, follow up in patients with chronic pancreatitis (7–25 months) after pancreatic surgery did not disclose any false diagnosis. The histological diagnosis was compared with the preoperative PET results. In addition in all patients, CAT was performed between four and 14 days before surgery and the results were compared with PET and the histological diagnosis of the patients.

Ethics

The protocol was approved by the institutional review board of the University of Ulm (human ethics committee). Informed written consent was obtained from each participant.

Patients

Eighty patients entered the prospective trial

between February 1992 and November 1993.

Group I – 42 patients (30 male, 12 female, median age: 60.5 years, range: 36–79) with pancreatic ductal cancer histologically confirmed at the time of surgery (Table I, patients no 1–42). The stages according to the UICC scale were: stage II: six patients, stage III: 19 patients, stage IV: 17 patients.

Group II – six patients (three male, three female, median age: 58.5 years, range: 42–76) with periampullary cancer histologically confirmed at the time of surgery (Table I, patients no 43–48). The UICC stages were: stage I: one patient, stage II: one patient, stage III: four patients.

Group III – 32 patients (27 male, five female, median age: 50 years, range: 25–74) with chronic pancreatitis histologically confirmed at the time of surgery (Table II).

Normal controls – 10 patients (six male, four female, median age: 51.5 years, range: 29–71) without gastrointestinal disease.

Radiopharmaceutical

FDG was synthesised according to the procedure described elsewhere.¹⁹ The

TABLE II Patient characteristics, standard uptake value (SUV), tumour background ratio (T/B), and operative procedures in 32 patients with histologically confirmed chronic pancreatitis

Patient	Sex	Age	CAT	PET	SUV	T/B	FDG accumulation	Operation
1	M	42	-	-	0.76	2.07	Negative	Cystojejunostomy
2	M	44	-	-	0.69	1.87	Negative	Necrosectomy, cholecystectomy
3	F	52	-	-	0.83	1.68	Negative	DPPHR
4	M	54	+	-	0.68	1.13	Negative	Whipple
5	M	38	+	-	0.73	1.57	Negative	Laparotomy
6	M	48	-	-	1.29	1.79	Negative	DPPHR
7	M	56	-	+	1.14	8.00	Head	Whipple
8	M	53	+	-	1.77	2.20	Negative	Whipple
9	M	44	-	-	1.20	3.06	Negative	DPPHR
10	M	37	+	-	0.83	3.21	Negative	DPPHR
11	M	49	-	+	2.29	3.89	Head	DPPHR
12	M	51	-	-	0.85	2.33	Negative	Necrosectomy
13	M	63	-	-	0.80	2.35	Negative	DPPHR
14	F	39	-	-	0.99	3.59	Negative	Cholecystectomy (gall stones)
15	M	31	-	-	1.25	3.30	Negative	Whipple
16	F	60	+	+	3.33	9.36	Head	Whipple
17	M	36	-	-	0.65	1.43	Negative	DPPHR
18	M	66	+	-	1.01	2.43	Negative	Left resection
19	M	56	-	-	0.69	1.13	Negative	DPPHR
20	M	64	-	+	1.93	4.13	Head, liver	DPPHR
21	M	35	-	-	0.88	1.70	Negative	DPPHR
22	M	54	+	-	0.75	2.78	Negative	Whipple
23	M	34	-	-	0.79	2.30	Negative	Whipple
24	M	56	-	-	1.98	7.80	Negative	Whipple
25	M	25	+	-	0.37	1.50	Negative	Whipple
26	M	47	-	-	1.51	3.99	Negative	DPPHR
27	M	58	-	-	0.90	2.10	Negative	DPPHR
28	M	59	-	-	1.23	2.19	Negative	DPPHR
29	M	40	-	-	0.70	1.89	Negative	DPPHR
30	F	74	+	-	1.36	1.50	Negative	Laparotomy
31	M	38	+	-	0.69	2.77	Negative	Whipple
32	F	53	-	-	0.46	1.70	Negative	DPPHR

DPPHR=duodenum preserving pancreatic head resection. Other abbreviations as Table I.

radiochemical purity was $98.5\% \pm (0.7\%)$, the specific activity was $> 10\,000$ Ci/mmol at the end of synthesis. Patients were injected 250–350 mBq within four hours of FDG synthesis.

Patient examination

PET was performed using an ECAT 931-08 scanner (Siemens-CTI, Knoxville, TN, USA), which produces 15 contiguous slices (slice thickness of 6.7 mm for both primary and secondary slices) per bed position.

Patients were fasted for at least six hours before the study. Emission scans were performed in three bed positions covering a field of view of 31.5 cm. The position of the pancreas was confirmed by ultrasonographic

localisation. By scanning 31.5 cm downwards from the liver dome the pancreatic bed was always located in the scanning area.

After transmission scanning with a Ge-68/Ga-68 ring source, 250–350 mBq FDG was injected into an antecubital vein and flushed with 10 ml saline. The patient was injected intravenously with furosemide (20 mg) and was instructed to urinate as often as possible to avoid unnecessary exposure of the bladder and to reduce measurement artifacts caused by high radioactivity in the urinary system. In preliminary studies without diuretic treatment, FDG contaminated urine in the urinary system was found in most cases to reduce image quality and analysis (data not shown). The patients had to leave the measurement area to urinate. Upon return they were carefully repositioned in the gantry using laser supported markings. We estimate that this led to a misalignment of maximum 1 cm in all directions, which in turn would cause an error of $\pm 20\%$ in the calculation of the standard uptake value (see later) assuming a change of 2 cm in the diameter of the target volume. Forty five minutes after FDG administration, emission scans were recorded for 10 minutes. Transmission scans were recorded to permit correction for photon attenuation. The acquisition time was 10 minutes per bed position and the count rate was $200\,000 \pm 15\%$ per second, resulting in a total of $120\,000\,000 \pm 15\%$ counts (random and scatter corrected true counts per acquisition).

Image reconstruction was performed by an iterative reconstruction algorithm modified according to Schmidlin *et al.*²⁰ The actual resolution was 7 mm for iterative reconstruction for full width at half maximum at the centre of the field of view.

Figure 1: Influence of plasma glucose concentrations on FDG standard uptake values (SUV) in 42 patients with pancreatic cancer, six patients with periampullary carcinoma, and 32 patients with chronic pancreatitis. Values for two patients with chronic pancreatitis (blood glucose 16.1 mmol/l, SUV 1.29; blood glucose 11.6 mmol/l, SUV 0.68), and one pancreatic cancer patient (blood glucose 12.1 mmol/l, SUV 2.29) are not shown.

TABLE III Standard uptake values (SUV) and tumour background ratio (T/B) in the pancreas and the liver of pancreatic cancer patients depending on blood glucose concentrations

Blood glucose		>6.66 mg/100 ml (n=8)	<6.66 mg/100 ml (n=34)	Mann-Whitney U test
Pancreas	(SUV)	3.07 (1.15)	3.10 (2.22)	NS
	(T/B)	6.46 (2.93)	7.39 (7.72)	NS
Liver	(SUV)	1.27 (0.42)	1.41 (0.38)	NS
	(T/B)	2.78 (1.08)	3.27 (1.30)	NS

Values are median (interquartile range), NS=not significant.

Images of the transversal, coronal, and sagittal image slices were evaluated by two independent observers who had no prior knowledge of the patients' clinical status. Pancreatic cancer was assumed if an intense focal activity accumulation was detected in the pancreatic region that exceeded the activity concentration in the liver.

Circular regions of interest were drawn on (a) the 'hot spots' of the pancreas, (b) corresponding regions of the head of the pancreas in patients without focal pancreatic activity, and (c) control regions. The size of the region of interests was 1500 (350) (mean (SD)) pixels. FDG accumulation was calculated using the standard uptake value:

$$\text{standard uptake value} = \frac{\text{activity concentration in region of interest} \times \text{body weight}}{\text{injected dose}}$$

Additional control regions (321 pixels) in the autochthonic skeletal muscle group of the back were chosen for the calculation of tumour/background ratios.

Statistics

The data are presented as median and interquartile range (median (interquartile range)). Blood glucose, standard uptake values, and tumour/background ratios of patients with pancreatic cancer and chronic pancreatitis were compared using the Mann-Whitney U test. Differences between proportions were analysed by the χ^2 test. Differences were considered statistically significant when p was <0.05 .

Figure 2: PET cross sections of the normal pancreas. Moderate glucose uptake in the liver, the renal parenchyma, and the urinary collecting system can be seen.

Results

All 80 patients of groups I to III had surgery eight days (range 1–54) after FDG-PET imaging. Median blood glucose concentrations were 5.19 (interquartile range: 1.94), 4.67 (interquartile range: 1.19), and 4.78 (interquartile range: 1.11) mmol/l, respectively in groups I, II, or III. No correlation between FDG uptake (as assessed by standard uptake value) and tumour/background ratio with plasma glucose concentrations were found (Fig 1).²¹ Blood glucose concentrations were obtained at the time of FDG injection in all patients. In eight of 42 patients with pancreatic cancer, the blood glucose concentrations exceeded 6.66 mmol/l. None of these patients, however, was false negative judged by visual analysis. Although all FDG uptake values were lower in a small group of patients with raised serum glucose concentrations, these differences were not significant (Table III).

Imaging

High quality FDG-PET images of the upper abdomen were obtained using the iterative reconstruction approach for imaging generation.²⁰ As known from previous PET studies in patients with various non-pancreatic cancers, glucose utilisation in the normal pancreas is very low in the fasting state and comparable with soft tissue background. As Fig 2 shows, the normal pancreas is not visualised by FDG-PET. There is moderate glucose uptake in the liver and some FDG uptake in the renal parenchyma and in the urinary collecting system. Using furosemide, FDG retention in the urinary system could be considerably reduced, thus improving image quality considerably (data not shown).

Qualitative evaluation

Figure 3 shows a typical FDG-PET image in a patient with pancreatic adenocarcinoma and stage III disease. The pancreatic mass noted in CAT had greatly increased FDG uptake. Similarly 41 of 42 patients with pancreatic cancer (group I) had a focally increased FDG uptake, amounting to a PET sensitivity of 98% for pancreatic cancer detection. The median standard uptake value was 3.09 (interquartile range: 2.18) in this group of patients (Fig 4, Table IV). The median standard uptake value was significantly higher than in group III (3.09 versus 0.87, $p<0.001$) (Fig 4, Table IV). Four of six patients with periampullary cancer were positive as judged by FDG-PET. Taking the cancer patients together the sensitivity was 94% (45 of 48). All patients with stage III and IV (pancreatic cancer and periampullary cancer) showed focally increased FDG accumulation in PET, compared with five of eight patients (63%) with stages I and II disease.

In 28 of 32 patients suffering from chronic pancreatitis, the pancreas was not visualised by FDG-PET, giving a specificity of 88% for a malignant lesion. The median standard uptake

Figure 3: PET cross sections in a patient with pancreatic cancer. Increase of FDG uptake in the malignant pancreatic tumour can be seen.

TABLE IV Standard uptake values in the pancreas and the liver of patients with pancreatic cancer, chronic pancreatitis, and normal controls

	Pancreatic cancer (n=42)	Chronic pancreatitis (n=32)	Normal controls (n=10)
Pancreas	3.09 (2.18)	0.87 (0.56)	0.73 (1.02)
Liver	1.38 (0.40)	1.25 (0.52)	1.27 (1.51)

Values are median (interquartile range).

the basic standard uptake value and the tumour/background ratios in patients of group I (pancreatic cancer) and group II (periampullary carcinoma) versus group III (chronic pancreatitis) was statistically significant ($p < 0.001$).

Diagnostic accuracy of CAT

Analysis of CAT for diagnosis of pancreatic cancer, performed in all patients preoperatively, yielded a sensitivity and specificity of 79% (33 of 42) and 69% (22 of 32), respectively.

Tumour stages I and II were present in two patients with periampullary carcinoma and six patients with pancreatic cancer. A suspicious tumour mass was detectable by CAT in three of these patients (38%). χ^2 analysis showed that PET had a significant higher sensitivity for pancreatic cancer detection than CAT ($p < 0.01$).

The positive and negative predictive values of CAT were 77% and 71%, respectively.

Discussion

This study shows that FDG-PET represents a new procedure for the diagnosis of cancer of the pancreas and the periampullary region with a sensitivity higher than 90%. FDG-PET also proved most successful in the differentiation of pancreatic cancer from chronic pancreatitis, in particular if in the second group the pancreatic head region is enlarged. The specificity of FDG-PET within this group of patients was 88%.

Cancer of the pancreas still has a very poor prognosis, unless it is diagnosed at an early and resectable stage.^{1-3 22} Our data show a relation between FDG accumulation and the size of the tumour. While all patients in advanced tumour stages (III-IV) had a focally increased accumulation in PET images, only five of eight patients in early stages showed increased FDG uptake.

Plasma glucose concentrations did not influence FDG uptake in the fasting state: standard uptake value and tumour/background ratio did not correlate with plasma glucose concentrations. Although there is evidence to suggest that diabetes mellitus may be responsible for false negative results,¹⁴ none of the three FDG-PET negative patients with a malignant tumour in the pancreatic region suffered from diabetes mellitus. Moreover, the size of the tumour seems to limit the diagnostic accuracy in our series of patients, as all had a tumour of stages I or II. The value of this diagnostic procedure, however, in the detection of small

value in chronic pancreatitis was 0.87 (interquartile range: 0.56). Of the patients with chronic pancreatitis who showed focally increased FDG uptake in the pancreatic head, one had received a nasobiliary probe to release common bile duct obstruction before FDG-PET. In a second patient BII resection had been performed 29 years previously. In addition, this patient had thrombosis of the portal vein with venous hypertension. In the third patient haemorrhage in a pancreatic pseudocyst was detected. The fourth patient had chronic pancreatitis without specific additional lesions or complications.

The positive and negative predictive values of FDG-PET were 91% and 98%, respectively.

Quantitative evaluation

Tumour/background ratios correlated highly with the corresponding standard uptake values ($r = 0.89$, $p < 0.001$). The difference between

Figure 4: FDG standard uptake (SUV) in pancreatic cancer (42 patients), periampullary cancer (six patients), and chronic pancreatitis (32 patients). SUV of patients with pancreatic cancer were significantly higher than in patients with chronic pancreatitis ($p < 0.001$). Horizontal bar=median, vertical bar=interquartile range.

malignancies was not the aim of this study. Larger study populations will be required for a definite evaluation of FDG-PET in this respect.

The standard diagnostic procedures to diagnose pancreatic cancer are ultrasonography, CAT, and ERCP.²³⁻²⁶ Ultrasonography represents the most widely used imaging procedure in patients presenting with a suspicious pancreatic mass.²³ However, the high percentage of inadequate results, the dependence upon experience of the investigator for satisfactory imaging, and its low sensitivity often require additional diagnostic procedures to be carried out. The ideal standard in the diagnosis of pancreatic cancer remains ERCP, which has accuracy rates of around 80–90%.^{25, 26} Only lesions that change the duct system, however, can be detected and often additional imaging procedures such as CAT are required to determine the size and the extent of the pancreatic lesion. The sensitivity of CAT to diagnose pancreatic cancer is between 50% and 90% and is based on an increase in pancreatic size, contour changes, obliteration of peripancreatic tissue or other signs of invasive or metastatic disease.²⁴ In addition, differential diagnosis between chronic pancreatitis and pancreatic cancer by CAT is extremely difficult.

In this study, the diagnosis of pancreatic cancer was based on functional changes in the pancreatic mass caused by tumour metabolism. This represents a new approach to the diagnosis of pancreatic malignancies. FDG-PET provides comparable diagnostic accuracy, but is less invasive than ERCP. In this series of patients its diagnostic accuracy in patients with histologically confirmed pancreatic carcinomas is definitely superior to CAT. The results of this investigation suggest a future complementary role of FDG-PET to other established techniques in the diagnosis of pancreatic cancer.

Our data support the recently published preliminary evidence of a high accuracy rate of PET in pancreatic cancer diagnosis.^{13, 14} The Aachen group had one of nine false positive PET results in chronic pancreatitis. Their false positive patient had previously undergone a BII resection.¹⁴ In this study, four of 28 patients with histologically confirmed chronic pancreatitis had FDG accumulation in the pancreas. Patient history showed BII resection and thrombosis of the portal vein with venous hypertension, the placement of a nasobiliary probe, and haemorrhage into a pancreatic pseudocyst in three of these patients. Unspecific granulation tissue might have contributed to the false positive accumulation of FDG in the pancreatic region in these patients. Therefore, the specificity of FDG-PET seems to be limited (a) in patients with chronic pancreatitis who previously had upper gastrointestinal surgery, (b) if pancreatitis related complications that can lead to unspecific FDG accumulation (intracystic haemorrhage) have occurred, or (c) if interventional techniques (stent, probe placement) have been used.

Although it was not the aim of this study to evaluate FDG-PET as a diagnostic procedure for correct staging of pancreatic cancer, liver metastasis could be identified in seven of 17 patients with a stage IV tumour. Lymph node involvement was detected in three patients. As no histological verification of this metastasis was obtained, however, definite conclusions on the value of FDG-PET for staging pancreatic cancer cannot be drawn.

In the few patients investigated thus far, PET technology using FDG provided a sensitivity of >90% in patients suffering from breast, colonic, liver, or brain cancer, and lymphoma.⁵⁻¹⁰ In our study, seven patients with pancreatic cancer that were negative by CAT showed FDG accumulation in the pancreatic tumour. In addition, three patients with pancreatic cancer in stage II could be detected by PET but not by CAT. Therefore, it seems probable that this technique might in the future contribute to the diagnosis of pancreatic cancer patients. The role of this technique, however, will be clearly defined in future larger oncological populations.

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1. Warshaw AL, Fernandez-Del Castillo C. Pancreatic carcinoma. *N Engl J Med* 1992; **326**: 455–65.
2. Neoptolemos JP, ed. *Cancer of the pancreas*. Baillieres Clin Gastroenterol, 1990.
3. Gudjonsson B. Cancer of the pancreas. 50 years of surgery. *Cancer* 1987; **60**: 2284–303.
4. Warburg O. On the origin of cancer cells. *Science* 1956; **123**: 309–14.
5. Langen KJ, Braun U, Rota Kops E, Herzog H, Kuwert T, Nebeling B, et al. The influence of plasma glucose levels on fluorine-18-fluorodeoxyglucose uptake in bronchial carcinomas. *J Nucl Med* 1993; **34**: 355–9.
6. Di Chiro G, Hatawawa J, Katz DA, Tizzoli HV, De Michele DJ. Glucose utilization by intracranial meningiomas as an index of tumor aggressivity and probability of recurrence: a PET study. *Radiology* 1987; **164**: 521–6.
7. Wahl RL, Cody RL, Hutchins GD, Mudget EE. Primary and metastatic breast carcinoma: initial clinical evaluation with PET with the radiolabeled glucose analogue 2-(F-18)-fluoro-2-deoxy-D-glucose. *Radiology* 1991; **179**: 765–70.
8. Yonekura Y, Benua RS, Brill AB. Increased accumulation of 2-deoxy-2-(F-18)fluoro-D-glucose in liver metastases from colon carcinoma. *J Nucl Med* 1982; **23**: 1133–7.
9. Okada J, Yoshikawa K, Itami M, Imaseki K, Uno K, Itami J, et al. Positron emission tomography using fluorine-18-fluorodeoxy-glucose in malignant lymphoma: a comparison with proliferative activity. *J Nucl Med* 1992; **33**: 325–9.
10. Strauss LG, Conti PS. The applications of PET in clinical oncology. *J Nucl Med* 1991; **32**: 623–48.
11. Gallagher BM, Fowler JS, Guttererson NI, MacGregor RR, Wan Ch-N, Wolf AP. Metabolic trapping as a principle of radiopharmaceutical design: some factors responsible for the biodistribution of (18-F)2-deoxy-2-fluoro-D-glucose. *J Nucl Med* 1978; **19**: 1154–61.
12. Syrota A, Duquesnoy N, Paraf A, Kellershohn C. The role of positron emission tomography in the detection of pancreatic disease. *Radiology* 1982; **143**: 249–53.
13. Zanzi I, Robeson W, Vinciguerra V. Positron tomography (PET) imaging in patients with carcinoma of the pancreas. *Proceedings of the American Society of Clinical Oncology* 1990; **9**: A434.
14. Klever P, Bares R, Fass J, Büll U, Schumpelick V. PET with fluorine-18 deoxyglucose for pancreatic disease. *Lancet* 1992; **349**: 1158–9.
15. Schek N, Hall BL, Finn OJ. Increased glyceraldehyde-3-phosphate dehydrogenase gene expression in human pancreatic adenocarcinoma. *Cancer Res* 1988; **48**: 6354–9.
16. Hiraki Y, Rosen OM, Birnbaum MJ. Growth factors rapidly induce expression of the glucose transporter gene. *J Biol Chem* 1988; **263**: 655–62.
17. Persons DA, Schek N, Hall BL. Increased expression of glycolysis-associated genes in oncogene-transformed and growth-accelerated states. *Mol Carcinog* 1989; **2**: 88–94.
18. Hermanek P, Scheibe O, Spiessl B, Wagner G, eds. *TNM Klassifikation maligner Tumoren*. Berlin: Springer, 1987.
19. Hamacher K, Coenen HH, Stöcklin G. Efficient stereospecific synthesis of no-carrier-added 2-[¹⁸F]-fluoro-2-deoxy-D-glucose using aminopolyether supported nucleophilic substitution. *J Nucl Med* 1986; **27**: 235–8.
20. Schmidlin P. Iterative Verfahren für die Emissionstomographie. *Nuklearmedizin* 1990; **3**: 155–8.

- 21 Lindholm P, Minn H, Leskinen-Kallio S, Bergman J, Ruotsalainen U, Joensuu H. Influence of the blood glucose concentration on FDG uptake in cancer – a PET study. *J Nucl Med* 1993; **34**: 1–6.
- 22 Poston GJ, Gillespie J, Guillou PJ. Biology of pancreatic cancer. *Gut* 1991; **32**: 800–12.
- 23 Campbell JP, Wilson SR. Pancreatic neoplasms: how useful is evaluation with US? *Radiology* 1988; **167**: 341–4.
- 24 Raptopoulos V, Schellinger D. Imaging of the pancreas with computed tomography. *Comput Tomogr* 1979; **3**: 37–47.
- 25 Freeny PC, Ball TJ. Endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) in the evaluation of suspected pancreatic carcinoma. *Cancer* 1981; **47**: 1666–78.
- 26 Stadelmann O, Safrany L, Löffler A. Endoscopic retrograde cholangiography in the diagnosis of pancreatic cancer. *Endoscopy* 1974; **6**: 84–93.

I would have preferred to find the references (some 3600 of them) after each chapter rather than all lumped together in 103 pages at the end of the book. It would have been easier to identify the overall bibliography for any one drug.

Among all the good things, hepatotoxicity due to unorthodox and particularly herbal remedies is clearly covered. Physicians often fail to question a patient on this aspect.

Hepatic granulomas are found in up to 10% of liver biopsy specimens. Drugs are believed to be responsible for up to one third where the cause is not evident. Twenty five foreign compounds that have been incriminated in hepatic granulomatous disease are tabulated. The authors rightly emphasise that in only a few can causality be established. The more important include allopurinol, carbamazepine, phenylbutazone, phenytoin, sulphonamides, and quinidine. The physician must be cautious in attributing hepatic granulomas to a drug reaction until the many other possibilities have been excluded.

The book is very well produced and easy to handle. Tables and figures are particularly clear and useful. It is an essential tool for hepatologists and gastroenterologists and should be available for reference in every medical library.

SHEILA SHERLOCK

NOTES

Sir Francis Avery Jones BSG Research Award 1996

Applications are invited by the Education Committee of the British Society of Gastroenterology who will recommend to Council the recipient of the 1996 Award. Applications (**eighteen copies**) should include:

- (1) A manuscript (2 A4 pages *only*) describing the work conducted.
- (2) A bibliography of relevant personal publications.
- (3) An outline of the proposed content of the lecture, including title.

(4) A written statement confirming that all or a substantial part of the work has been personally conducted in the UK or Eire.

Entrants must be 40 years or less on 31 December 1996 but need not be a member of the BSG. The recipient will be required to deliver a 40 minute lecture at the Spring meeting of the Society in 1996. Applications (**eighteen copies**) should be made to: The Honorary Secretary, BSG, 3 St Andrews Place, London NW1 4LB by 1 December 1995.

1995, in Pécs, Hungary. Further information from: Professor Dr G Mózsik, First Department of Medicine, Medical University of Pécs, PO Box 99, H-7643 Pécs, Hungary. Fax: 36-72-327-660.

Travel Fellowship

The Pancreatic Society awards annually a Travel Fellowship worth £1500 to young researchers in any field of pancreatology, to enable him or her to visit laboratories and hospitals in another country to further the Fellow's education. Applicants need not be a member of the Society.

Applications are invited from clinicians in any discipline, or basic scientists, who have demonstrated an interest and ability in pancreatic research. The purpose of the Fellowship is to visit other centres, and is not primarily designed to support research. Travel solely for the purpose of attending a conference is not supported. The closing date for applications will be 31 October 1995. Applicants should submit a curriculum vitae and a proposed itinerary. Selection will be based on an interview to be held during the Society's annual meeting on 24 November 1995. Further details from the Secretary: Mr Colin Johnson, University Surgical Unit, F Level, Centre Block, Southampton General Hospital, Tremona Road, Southampton SO16 6YD.

CORRECTION

An error occurred in the paper by Dr Friess and others (*Gut* 1995; 36: 771-7). The legends to Figures 2 and 3 have been transposed.

Gastrointestinal pharmacology

The International Union of Pharmacology (IUPHAR), Gastrointestinal Pharmacology Section, will hold a symposium on Biochemical Pharmacology as an Approach to Gastrointestinal Diseases on 12-14 October

Liver disease

The Sixth Manchester Liver Symposium will be held on 6 October 1995. Full programme and registration details are available from: Dr T W Warnes, Liver Unit, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL. Tel: 0161-276 4316.