Diagnosis of pancreatic cancer by 2\(^{18}\)F-fluoro-2-deoxy-D-glucose positron emission tomography

H Friess, J Langhans, M Ebert, H G Beger, J Stollfuss, S N Reske, M W Büchler

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\(^{18}\)F\)-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 periamillary 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) vs 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.

(Gut 1995; 36: 771–777)

Keywords: pancreatic cancer, positron emission tomography.

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 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\(^{18}\)F-fluoro-2-deoxy-D-glucose (FDG) has been used to measure overall tumour glucose utilisation with PET.11

In pancreatic disorders, PET with \(11\)C-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

Department of Visceral and Transplantation Surgery, University of Berne, Inselspital, Berne, Switzerland
H Friess
M Ebert
M W Büchler

Departments of Nuclear Medicine and Surgery
J Langhans
J Stollfuss
S N Reske
H G Beger

University of Ulm, Ulm, Germany

Correspondence to: Professor M W Büchler, Department of Visceral and Transplantation Surgery, University of Berne, Inselspital, CH-3010 Berne, Switzerland.
Accepted for publication 30 August 1994
were included into this study. Staging of the pancreatic cancer was carried out according to the International Union against Cancer (UICC) classification. All patients had either surgery of the pancreas with subsequent histological examination of the surgical specimen. The stage 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.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Localisation</th>
<th>Stage</th>
<th>CAT</th>
<th>PET</th>
<th>SUV</th>
<th>T/B</th>
<th>FDG accumulation</th>
<th>Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>78</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>4.70</td>
<td>11.81</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>68</td>
<td>Head</td>
<td>II</td>
<td>+</td>
<td>–</td>
<td>3.91</td>
<td>7.90</td>
<td>Negative</td>
<td>Local recurrence after Whipple</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>55</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>1.20</td>
<td>3.99</td>
<td>Head</td>
<td>Biliary lysis</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>62</td>
<td>Head</td>
<td>II</td>
<td>+</td>
<td>+</td>
<td>2.22</td>
<td>5.97</td>
<td>Body</td>
<td>Local recurrence after Whipple</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>55</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>4.20</td>
<td>5.14</td>
<td>Body, liver</td>
<td>Local recurrence after Whipple</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>63</td>
<td>Body</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>3.26</td>
<td>7.79</td>
<td>Body, lymph node</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>73</td>
<td>Body</td>
<td>IV</td>
<td>–</td>
<td>–</td>
<td>3.35</td>
<td>7.43</td>
<td>Body</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>63</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>5.65</td>
<td>21.27</td>
<td>Head, liver</td>
<td>Needle biopsy</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>64</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>0.98</td>
<td>1.41</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>51</td>
<td>Head</td>
<td>III</td>
<td>–</td>
<td>+</td>
<td>2.11</td>
<td>4.09</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>50</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>3.16</td>
<td>3.60</td>
<td>Head, liver</td>
<td>Laparoscopic</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>50</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>1.41</td>
<td>10.54</td>
<td>Head</td>
<td>Local recurrence after Whipple</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>52</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>2.88</td>
<td>7.28</td>
<td>Head</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>58</td>
<td>Head</td>
<td>III</td>
<td>–</td>
<td>+</td>
<td>1.54</td>
<td>3.10</td>
<td>Hepatic porta</td>
<td>Local recurrence after Whipple</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>71</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>1.19</td>
<td>2.67</td>
<td>Head</td>
<td>Local recurrence after Whipple</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>55</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>4.11</td>
<td>10.22</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>77</td>
<td>Head</td>
<td>IV</td>
<td>–</td>
<td>+</td>
<td>3.78</td>
<td>11.99</td>
<td>Head</td>
<td>Biliary and enteral bypass</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>59</td>
<td>Head</td>
<td>II</td>
<td>+</td>
<td>+</td>
<td>1.78</td>
<td>4.06</td>
<td>Pancreas</td>
<td>Whipple</td>
</tr>
<tr>
<td>19</td>
<td>F</td>
<td>62</td>
<td>Body</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>2.41</td>
<td>4.43</td>
<td>Head</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>20</td>
<td>F</td>
<td>66</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>5.22</td>
<td>16.30</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>21</td>
<td>M</td>
<td>79</td>
<td>Tail</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>1.98</td>
<td>3.94</td>
<td>Tail</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>22</td>
<td>M</td>
<td>52</td>
<td>Body</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>2.48</td>
<td>5.94</td>
<td>Head, liver</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>23</td>
<td>F</td>
<td>69</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>4.18</td>
<td>13.71</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>24</td>
<td>M</td>
<td>64</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>3.03</td>
<td>8.65</td>
<td>Head</td>
<td>Biliary lysis</td>
</tr>
<tr>
<td>25</td>
<td>M</td>
<td>55</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>2.00</td>
<td>5.40</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>26</td>
<td>M</td>
<td>50</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>5.52</td>
<td>14.58</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>27</td>
<td>M</td>
<td>58</td>
<td>Head</td>
<td>II</td>
<td>+</td>
<td>+</td>
<td>2.76</td>
<td>7.36</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>28</td>
<td>M</td>
<td>61</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>1.44</td>
<td>5.50</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>64</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>5.71</td>
<td>15.20</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>30</td>
<td>M</td>
<td>52</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>0.85</td>
<td>2.10</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>31</td>
<td>M</td>
<td>52</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>3.65</td>
<td>8.28</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>32</td>
<td>M</td>
<td>56</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>3.50</td>
<td>5.14</td>
<td>Head</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>33</td>
<td>F</td>
<td>62</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>2.29</td>
<td>4.88</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>34</td>
<td>F</td>
<td>55</td>
<td>Head</td>
<td>IV</td>
<td>–</td>
<td>+</td>
<td>5.66</td>
<td>10.86</td>
<td>Head</td>
<td>Biliary lysis</td>
</tr>
<tr>
<td>35</td>
<td>F</td>
<td>46</td>
<td>Head</td>
<td>IV</td>
<td>–</td>
<td>+</td>
<td>1.27</td>
<td>2.19</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>36</td>
<td>M</td>
<td>62</td>
<td>Head</td>
<td>IV</td>
<td>+</td>
<td>+</td>
<td>3.45</td>
<td>8.80</td>
<td>Head, liver</td>
<td>Biliary lysis</td>
</tr>
<tr>
<td>37</td>
<td>M</td>
<td>58</td>
<td>Tail</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>3.47</td>
<td>8.52</td>
<td>Tail</td>
<td>Left resection</td>
</tr>
<tr>
<td>38</td>
<td>M</td>
<td>57</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>2.38</td>
<td>6.34</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>39</td>
<td>M</td>
<td>60</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>7.24</td>
<td>12.00</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>40</td>
<td>M</td>
<td>66</td>
<td>Head</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>4.70</td>
<td>12.20</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>41</td>
<td>M</td>
<td>61</td>
<td>Body</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>3.33</td>
<td>5.64</td>
<td>Body</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>42</td>
<td>F</td>
<td>74</td>
<td>Head</td>
<td>II</td>
<td>–</td>
<td>+</td>
<td>2.22</td>
<td>5.15</td>
<td>Head</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>43</td>
<td>M</td>
<td>42</td>
<td>PC</td>
<td>III</td>
<td>–</td>
<td>+</td>
<td>1.53</td>
<td>10.37</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>44</td>
<td>M</td>
<td>64</td>
<td>PC</td>
<td>III</td>
<td>–</td>
<td>+</td>
<td>1.47</td>
<td>2.65</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>45</td>
<td>M</td>
<td>62</td>
<td>PC</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>2.74</td>
<td>6.52</td>
<td>Head, lymph node</td>
<td>Whipple</td>
</tr>
<tr>
<td>46</td>
<td>F</td>
<td>53</td>
<td>PC</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>6.45</td>
<td>15.59</td>
<td>Head, lymph node</td>
<td>Choledochectomy, lymph node dissection*</td>
</tr>
<tr>
<td>47</td>
<td>F</td>
<td>76</td>
<td>PC</td>
<td>III</td>
<td>+</td>
<td>+</td>
<td>1.14</td>
<td>2.11</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>48</td>
<td>M</td>
<td>55</td>
<td>PC</td>
<td>II</td>
<td>–</td>
<td>+</td>
<td>0.64</td>
<td>1.70</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
</tbody>
</table>

*Whipple resection was not possible because of intraoperative tachyarrhythmia and pulmonary insufficiency. Whipple=Whipple's pancreaticoduodenectomy. 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.

**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. The
radiochemical purity was 98.5\% \pm (0.7\%), the specific activity was \( > \) than 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. 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 1** Patient characteristics, standard uptake value (SUV), tumour background ratio (T/B), and operative procedures in 32 patients with histologically confirmed chronic pancreatitis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>CAT</th>
<th>PET</th>
<th>SUV</th>
<th>T/B</th>
<th>FDG accumulation</th>
<th>Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>42</td>
<td>-</td>
<td>-</td>
<td>0.76</td>
<td>2.07</td>
<td>Negative</td>
<td>Cystojejunostomy</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>44</td>
<td>-</td>
<td>-</td>
<td>0.69</td>
<td>1.87</td>
<td>Negative</td>
<td>Nephrectomy, cholecystectomy</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>52</td>
<td>-</td>
<td>-</td>
<td>0.83</td>
<td>1.68</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>54</td>
<td>-</td>
<td>+</td>
<td>0.68</td>
<td>1.13</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>38</td>
<td>+</td>
<td>-</td>
<td>0.73</td>
<td>1.57</td>
<td>Negative</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>48</td>
<td>+</td>
<td>-</td>
<td>1.29</td>
<td>1.79</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>56</td>
<td>+</td>
<td>-</td>
<td>1.14</td>
<td>8.00</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>53</td>
<td>+</td>
<td>-</td>
<td>1.77</td>
<td>2.20</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>44</td>
<td>+</td>
<td>-</td>
<td>1.20</td>
<td>3.06</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>45</td>
<td>+</td>
<td>-</td>
<td>0.83</td>
<td>3.21</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>49</td>
<td>+</td>
<td>-</td>
<td>2.29</td>
<td>3.89</td>
<td>Negative</td>
<td>Head</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>51</td>
<td>+</td>
<td>-</td>
<td>0.85</td>
<td>2.33</td>
<td>Negative</td>
<td>Nephrectomy</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>63</td>
<td>-</td>
<td>-</td>
<td>0.80</td>
<td>2.35</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>39</td>
<td>-</td>
<td>-</td>
<td>0.99</td>
<td>3.59</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>31</td>
<td>+</td>
<td>-</td>
<td>1.25</td>
<td>3.30</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>60</td>
<td>+</td>
<td>-</td>
<td>3.33</td>
<td>9.36</td>
<td>Head</td>
<td>Whipple</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>34</td>
<td>+</td>
<td>-</td>
<td>0.65</td>
<td>1.43</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>66</td>
<td>+</td>
<td>-</td>
<td>1.01</td>
<td>2.43</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>19</td>
<td>M</td>
<td>56</td>
<td>-</td>
<td>-</td>
<td>0.69</td>
<td>1.13</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>64</td>
<td>+</td>
<td>+</td>
<td>1.93</td>
<td>4.13</td>
<td>Head, liver</td>
<td>DPPHR</td>
</tr>
<tr>
<td>21</td>
<td>M</td>
<td>35</td>
<td>+</td>
<td>-</td>
<td>0.88</td>
<td>1.70</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>22</td>
<td>M</td>
<td>54</td>
<td>+</td>
<td>-</td>
<td>0.75</td>
<td>2.78</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>23</td>
<td>M</td>
<td>34</td>
<td>+</td>
<td>-</td>
<td>0.79</td>
<td>2.30</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>24</td>
<td>M</td>
<td>56</td>
<td>+</td>
<td>-</td>
<td>1.98</td>
<td>7.80</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>25</td>
<td>M</td>
<td>25</td>
<td>+</td>
<td>-</td>
<td>0.37</td>
<td>1.50</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>26</td>
<td>M</td>
<td>47</td>
<td>+</td>
<td>-</td>
<td>1.51</td>
<td>3.99</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
<tr>
<td>27</td>
<td>M</td>
<td>58</td>
<td>-</td>
<td>-</td>
<td>0.90</td>
<td>2.10</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
<tr>
<td>28</td>
<td>M</td>
<td>59</td>
<td>-</td>
<td>+</td>
<td>1.23</td>
<td>2.19</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>40</td>
<td>-</td>
<td>-</td>
<td>0.70</td>
<td>1.89</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
<tr>
<td>30</td>
<td>F</td>
<td>74</td>
<td>+</td>
<td>-</td>
<td>1.36</td>
<td>1.50</td>
<td>Negative</td>
<td>Laparotomy</td>
</tr>
<tr>
<td>31</td>
<td>M</td>
<td>38</td>
<td>+</td>
<td>+</td>
<td>0.69</td>
<td>2.77</td>
<td>Negative</td>
<td>Whipple</td>
</tr>
<tr>
<td>32</td>
<td>F</td>
<td>53</td>
<td>-</td>
<td>-</td>
<td>0.46</td>
<td>1.70</td>
<td>Negative</td>
<td>DPPHR</td>
</tr>
</tbody>
</table>

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

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

Additional control regions (321 pixels) in the autochthonous 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 \(\chi^2\) test. Differences were considered statistically significant when \(p\) was <0.05.

**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).

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

---

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

<table>
<thead>
<tr>
<th>Blood glucose</th>
<th>&gt;6.66 mg/100 ml</th>
<th>&lt;6.66 mg/100 ml</th>
<th>Mann-Whitney U test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas (SUV)</td>
<td>3.07 (1.15)</td>
<td>3.10 (2.22)</td>
<td>NS</td>
</tr>
<tr>
<td>Liver (SUV)</td>
<td>1.27 (0.42)</td>
<td>1.41 (0.35)</td>
<td>NS</td>
</tr>
<tr>
<td>Liver (T/B)</td>
<td>2.78 (0.98)</td>
<td>3.27 (1.30)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are median (interquartile range), NS = not significant.
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 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%). $\chi^2$ 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.\textsuperscript{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,\textsuperscript{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

**TABLE IV**

<table>
<thead>
<tr>
<th>Value</th>
<th>Pancreatic cancer (n=42)</th>
<th>Chronic pancreatitis (n=32)</th>
<th>Normal controls (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas (SUV)</td>
<td>3-09 (2-18)</td>
<td>0-87 (0-56)</td>
<td>0-73 (1-02)</td>
</tr>
<tr>
<td>Liver (SUV)</td>
<td>1-38 (0-40)</td>
<td>1-25 (0-52)</td>
<td>1-27 (1-51)</td>
</tr>
</tbody>
</table>

Values are median (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 ultrasono-
graphy, CAT, and ERCP. 23–26 Ultrasonogra-
phy represents the most widely used
imaging procedure in patients presenting with
a suspicious pancreatic mass. 25 However, the
high percentage of inadequate results, the
dependence upon experience of the investiga-
tor 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 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
癌症 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 meta-
bolism. 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 com-
plementary role of PET 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. 6–7 The
Aachen group had one of the few false positive
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. Unspecifictic
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 (intraepithelial
haemorrhage) have occurred, or (c) if inter-
vensional techniques (stent, probe placement)
have been used.

Although it was not the aim of this study to
evaluate 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 PET for staging pancreatic cancer
cannot be drawn.

In the few patients investigated thus far,
PET technology using FDG provided a sen-
titivity 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,
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.

The authors thank Dr A M Wheatley for correcting the
manuscript.

1 Warshaw AL, Fernandez-Del Castillo C. Pancreatic
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 H, Herzog H, Kuwert T,
Nebeling B, et al. The influence of plasma glucose levels
on fluorescence-18-fluorodeoxyglucose uptake in bronchial
6 Di Chiro G, Hataway J, Katz DA, Tazetti HV, De Micheile
DJ. Glucose utilization by intracranial meningiomas as an
index of tumor aggressivity and probability of recurrence:
7 Wahl RL, Cody RL, Hutchins GD, Mudgett EE. Primary and
metastatic breast carcinoma: initial clinical evaluation with
PET with the radiolabelled glucose analogue 2-F
(18)-fluorodeoxy-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
9 Okada J, Yoshikawa K, Iimai M, Imaeke K, Uno K, Itami J,
et al. Positron emission tomography using fluorine-18
fluoro-deoxyglucose in malignant lymphomas: a comparison
10 Stagner IG, Conti PS. The applications of PET in clinical
11 Gallagher BM, Fowler JS, Gutterton NJ, MacGregor RR,
Wan CH, 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.
12 Syrotu A, Duquesnoy N, Paraf A, Kellershohn C. The role
of positron emission tomography in the detection of
13 Zaniz I, Robeson W, Vinciguerra V. Positron tomography
(PET) imaging in patients with carcinoma of the
pancreas. Proceedings of the American Society of Clinical
with fluorine-18 deoxyglucose for pancreatic disease.
15 Schek N, Hall BL, Finn OJ. Increased glycerol-aldehyde-3-
phosphate dehydrogenase gene expression in human
16 Hiraki Y, Rosen OM, Birnbaum MJ. Growth factors rapidly
induced by fluorine-18 deoxyglucose transporter gene. J Biol
17 Perrons DA, Schek N, Hall BL. Increased expression of
glycogen-associated genes in oncogene-transformed and
19 Hamacher K, Coenen HH, Stecklen G. Efficient stereo-
specific synthesis of no-carrier-added 2-F(18)-fluoro-2-deoxy-
d-glucose by using aminopolyether supported
20 Schmidlin P. Iterative Verfahren für die
Diagnosis of pancreatic cancer by $^{18}$F-fluoro-2-deoxy-D-glucose positron emission tomography

25 Freney PC, Ball TJ. Endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) in the evaluation of suspected pancreatic carcinoma. Cancer 1981; 47: 1666-78.
Diagnosis of pancreatic cancer by 2[18F]-fluoro-2-deoxy-D-glucose positron emission tomography.

H Friess, J Langhans, M Ebert, H G Beger, J Stollfuss, S N Reske and M W Büchler

Gut 1995 36: 771-777
doi: 10.1136/gut.36.5.771
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 implicated 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.

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 1995, in Pécs, Hungary. Further information from: Professor Dr G Mózskó, 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. Applications 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.

Liver disease

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

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.