Preoperative Imaging of Pancreatic Cancer: A Management-Oriented Approach

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Imaging of pancreatic cancer involves both diagnosis and staging of the tumor. Accurate diagnosis allows the clinician to be frank with the patient and eliminates anxiety and uncertainty associated with a pancreatic lesion of unknown etiology. Accurate staging should facilitate clinical decision making and limit surgery to those who would benefit from laparotomy. Imaging includes nonoperative techniques, such as abdominal ultrasonography, CT scan, MRI, and angiography and a variety of invasive techniques, such as laparoscopy and laparoscopic or intraoperative ultrasonography. Operative imaging complements nonoperative imaging but is outside the scope of this article. The algorithm for use of nonoperative imaging techniques needs to be clearly defined, because rapid technologic development has resulted in increasing costs and a degree of confusion among clinicians. Recent reviews have focused on diagnosis of early pancreatic cancer in high-risk patients using a combination of biochemical markers and imaging or technical aspects of current imaging techniques without attempting to integrate them into a flexible management algorithm that can be tailored to the individual patient. This article attempts to relate these investigations directly to individual patient management. So patient factors, such as the need to assess stage, and establish a tissue diagnosis in certain categories of patient, factor into the choice of appropriate investigations.

The importance of the clinical examination cannot be understated. This has two objectives: to assess fitness for operation and to detect evidence of metastatic disease. If the patient is not fit enough to withstand abdominal surgery or has diffuse metastatic disease, surgery is contraindicated and more thorough investigation is not warranted. The presence of supraclavicular or umbilical nodes, peritoneal carcinomatosis on rectal examination, or ascites can provide evidence of diffuse malignant disease. It is a simple matter to confirm this with a lymph node biopsy or an ascitic tap. Clinically apparent disseminated disease is a contraindication to pancreatic resection because of its abysmal prognosis. But in the absence of signs, the clinician relies on imaging techniques to stage the disease.

Abdominal ultrasonography

Abdominal ultrasonography (US) is the initial screening technique because of its low cost and easy availability. In Europe, abdominal US is part of the routine surgical examination. US will confirm the presence of gallstones, assess the liver for metastatic deposits, detect abdominal ascites, and identify the level of biliary obstruction. In certain patients, ultrasonography can enable one to manage the patient without any further investigation. Patients with malignant ascites and liver deposits require confirmatory biopsy and no further investigation.

Rosch and colleagues demonstrated abdominal US to have a low sensitivity and specificity of 67% and 40%, respectively, in the diagnosis of pancreatic cancer. There are many limitations with abdominal US. Bowel gas obscures the image in up to 15% of patients, and US is notoriously operator-dependent and is not accurate in assessing central abdominal and retroperitoneal structures.

The combination of US with color Doppler ultrasonography (CDUS) can improve accuracy in assessing vascular invasion. Tomiyama and associates evaluated the relationship between tumor and surrounding arteries with CDUS in 33 patients. Imaging results were compared with angiographic, surgical, and pathologic findings. In 22 nonsurgical patients, CDUS agreed with angiography for the presence of invasion, absence of invasion, and overall resectability rate in 78%, 95%, and 88% of cases, respectively. Without surgical exploration...
as a definitive comparison, the validity of these figures is unclear. In the 11 surgical patients, a sensitivity of 60%, specificity of 93%, and accuracy of 87% for detection of arterial invasion were obtained. But the accuracy of CDUS was higher than CT (72%) and equal to angiography (91%). The noninvasive nature and safety of CDUS make it a popular modality, but experience with the technique is limited and its role awaits clarification.

Computerized tomography

CT scan has undergone a rapid evolution over the last two decades, with each new development enhancing the imaging capability of the technique and even threatening to overwhelm our current capability to process data.7-11 Conventional CT has been superceded by dynamic thin section CT, spiral CT, and multidetector CT (MDCT). These new techniques have dramatically improved the ability of CT to diagnose and stage pancreatic cancer. The rapid evolution of CT technology makes staging of pancreatic cancer a dynamic field.

Criteria predictive of unresectability with conventional CT include hepatic and distant metastasis and locally advanced disease (peripancreatic extension of tumor to locally contiguous structures, vascular encasement or invasion, and local lymphadenopathy). CT criteria for resectability include the absence of extrapancreatic disease, no evidence of arterial encasement, and a patent superior mesenteric-portal venous confluence.12,13 CT is most accurate in assessing extrapancreatic involvement, but it is of more limited value in assessing local vascular invasion and most efforts have been directed to improving its ability to assess this factor. Table 1 summarizes the findings of several authors regarding the reliability and accuracy of CT in the staging of pancreatic cancer. It is difficult to compare results from diverse centers because scanning techniques differ, and surgical definitions of resectability differ, with some surgeons resecting involved segments of the portal vein and others regarding portal vein invasion as nonresectable cancer.12

Ross and coworkers7 reviewed their experience with CT in staging pancreatic cancer in 66 patients. An independent radiologist reviewed the CT scans. Resectability was correctly predicted in only 38% of cases, and unresectability was accurately predicted in 93% of cases. An incorrect prediction of unresectability was made in three patients who eventually had curative resection (incorrect diagnosis of hepatic metastases, and locally advanced

<table>
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<th>Abbreviations and Acronyms</th>
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<td>CDUS</td>
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<td>EUS</td>
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<td>EUS-FNA</td>
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<td>FDG-PET</td>
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<td>UMRI</td>
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**Table 1.** Reported Accuracy of Conventional CT Scan

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<tr>
<th>Lead author, y</th>
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<th>PPV predicts unresectability (%)</th>
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<td>Retrospective CT only</td>
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<td></td>
<td>38</td>
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<tr>
<td>Freeny, 1988 (DCT)†</td>
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<td>Warshaw, 1990</td>
<td>Prospective MRI/SVA/ laparoscopy</td>
<td>88</td>
<td>Liver or lymphatic metastases/vascular invasion</td>
<td>45</td>
<td>92</td>
</tr>
<tr>
<td>Rosch, 1992</td>
<td>Prospective vs EUS/SVA</td>
<td>60</td>
<td>Portal vein involvement</td>
<td>97</td>
<td>91</td>
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| Fuhrman, 1994 (TSCE)† | Prospective vs surgery | 145 | Liver metastases                           | 88                            | —                               |
| McCarthy, 1998      | Retrospective vs surgery | 88  | Arterial encasement                        | 95                            | 100                             |
| McCarthy, 1998      | Retrospective vs surgery | 88  | Venous encasement                          | 95                            | 55                              |
| McCarthy, 1998      | Retrospective vs surgery | 88  | Lymph node metastases                      | 97                            | 91                              |
| McCarthy, 1998      | Retrospective vs surgery | 88  | Overall assessment                         | 77                            | 76                              |

*Dynam CT.
†Thin section contrast enhanced.
EUS, endoscopic ultrasonography; NPV, negative predictive value; PPV, positive predictive value; SVA, selective visceral angiography.
disease that did not preclude resection). Metastatic disease was an accurate predictor of unresectability. But CT assessment of local tumor invasion was not very accurate. The most common problem was unexpected invasion of visceral vessels. This is mainly from the small size of the vessels in relation to the large width of the cuts (5–10 mm). These authors believed that CT is not reliable in predicting unresectability on the basis of locally advanced disease and cautioned about the decision to embark on nonoperative treatment purely on the basis of a CT assessment.

Freeny and colleagues assessed the accuracy of dynamic CT in diagnosing and staging pancreatic adenocarcinoma. CT made the correct diagnosis in 91% of patients, with a false-positive rate of 8% and a false-negative rate of 1%. CT assessment of resectability was compared with angiography and surgery. CT was more accurate than angiography in demonstrating vascular involvement. No CT-determined unresectable tumors were found resectable during surgery, and only three of nine predicted resectable tumors were found to be unresectable. No patients with potentially resectable tumors were denied surgery. CT was deemed reliable in the assessment of resectability of pancreatic cancer.

Warshaw and coauthors prospectively compared the accuracy of contrast-enhanced CT, MRI, angiography, and laparoscopy in determining the resectability of pancreatic and ampullary adenocarcinoma in 88 consecutive patients. On its own, CT was 92% accurate in predicting unresectability but only 45% accurate in predicting resectability. Angiography predicted resectability in 54% of cases. When CT and angiography were used in conjunction, unresectability was predicted 87% of the time. But neither modality on its own was accurate in predicting resectability. The authors concluded that accurate staging of pancreatic cancer required a combination of CT, angiography, and laparoscopy.

McCarthy and associates reported their use of standard protocol for performing and reporting on CT scan. They retrospectively compared CT assessment of resectability with surgical findings over a 5-year period in 88 patients. The final sensitivity and specificity for CT prediction of resectability were 72% and 80%, respectively. Positive predictive value was 77% and negative predictive value 76%. Of concern were seven false-positive and nine false-negative scans. Although McCarthy's group believed that CT was reasonably accurate in predicting resectability, they cautioned that it could not be relied on entirely because some criteria of unresectability—such as venous encasement, dorsal extension, and lymphadenopathy—are relative and not absolute.

Despite the wide application of conventional CT scan in the assessment of resectability, it remains inaccurate in assessing local vascular invasion unless it is used in conjunction with complementary techniques. There also remains a concern that a subset of patients will erroneously be labeled unresectable and denied potentially curative operations. But the rapid evolution in CT technology has outdated conventional CT and has necessitated ongoing reappraisal of CT.

Fuhrman and colleagues assessed the predictive accuracy of thin section contrast-enhanced CT for resectability of pancreatic carcinoma. Of the patients with tumors deemed resectable by this technique, 88% underwent pancreaticoduodenectomy. The rest were found at laparotomy to be unresectable. They concluded that thin section contrast-enhanced CT scan was more reliable than first-generation CT scanners in predicting resectability of pancreatic cancer. This group had an aggressive surgical policy of resecting involved portal vein.

The advent of dual-phase thin-cut spiral CT scan has offered the potential of improved accuracy. Spiral CT allows rapid acquisition of three-dimensional data. An image is then reconstructed in multiple planes. Although a great deal of computer memory is required, there are distinct advantages over conventional contrast-enhanced CT. The whole pancreas can be imaged in a single breath-hold, allowing high-quality images to be taken in ill patients. The ability to reconstruct overlapping images and the elimination of artifacts from respiratory movement improve the detection of small lesions. Dual-phase scanning improves the detection of arterial and venous disease with good visualization of parenchymal lesions. A thin section, dual-phase spiral CT acquisition during optimal pancreatic, arterial, and portal venous enhancement, followed by a second acquisition during the hepatic phase, notably improves the accuracy of helical CT for the detection of pancreatic cancer. Spiral CT scan generates highly detailed images that enable a greater appreciation of the relationship between the tumor and surrounding vascular structures.

Several authors have shown spiral CT to be accurate for diagnosing pancreatic cancer and for predicting resectability. Table 2 summarizes these results. Bluemke and associates used single-phase spiral CT,
detected pancreatic cancer in 89% of patients, and demonstrated an overall accuracy for the assessment of resectability of 70%. Diehl and colleagues,\textsuperscript{16} using dual-phase spiral CT, predicted resectable disease in 79% of patients and unresectability in 96%. This technique allows pancreatic scanning during the phase of maximal vascular enhancement and during the phase of maximal hepatic enhancement. Dual-phase spiral CT demonstrated liver metastases in 75% of patients, distant lymph node involvement in 54%, extrapancreatic invasion in 85%, and vascular invasion in 88%. Gmeinwieser and coworkers\textsuperscript{17} found that spiral CT was 92.8% and 100% accurate in detecting portal venous and arterial involvement, respectively, in pancreatic cancer.\textsuperscript{17}

Lu and coauthors\textsuperscript{13} looked at involvement of visceral vessels on spiral CT scan as a criterion of unresectability. They prospectively established radiologic grading criteria for the diagnosis of unresectability. If the tumor surrounded more than half the circumference of a named vessel, the tumor was unresectable. But contiguity of the tumor to anything less than half the circumference of the vessel was nonspecific, and the tumor might still have been resectable.

The optimal technique of spiral CT scanning has not yet been established. Many authors advocated scanning the pancreas during the arterial phase. Because the pancreas is highly vascular, it should increase tumor conspicuity. But Graf and colleagues\textsuperscript{18} showed that images obtained during the portal-venous phase were superior to those obtained during the arterial phase.

In the latest advance in spiral CT technology, volume rendering of spiral CT data can be combined with a three-dimensional display and is referred to as MDCT. It allows the user to modify parameters to optimize visualization of structures. The viewing plane can be altered to allow inclusion of key elements of anatomy, which might have been missed. This provides CT angiography, which rivals the images obtained by conventional angiography. Visualization of the bile and pancreatic ducts is also optimized. Novick and Fishman\textsuperscript{11} have demonstrated in a pictorial essay the incredibly accurate images provided by MDCT. They believe that MDCT accu-

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<th>PPV predicts unresectability (%)</th>
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<tr>
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<td>Dufour, 1997</td>
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<td>Vascular invasion</td>
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<td>58</td>
<td>Extrapancreatic extension</td>
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<td>Legmann, 1998\textsuperscript{†}</td>
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<td>Metastatic nodes/liver metastases arterial invasion</td>
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<td>Diehl, 1998\textsuperscript{†}</td>
<td>Prospective vs surgery</td>
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<td>Size &gt; 5 cm/extrapancreatic, vascular invasion/liver node metastases</td>
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<td>Diehl, 1998</td>
<td>Prospective vs surgery</td>
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<td>Vascular invasion</td>
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<td>Midwinter, 1999</td>
<td>Prospective vs EUS</td>
<td>48</td>
<td>SMV and portal invasion</td>
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<td>Midwinter, 1999</td>
<td>Prospective vs EUS</td>
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*Single-phase spiral CT.
†Dual-phase spiral CT.

EUS, endoscopic ultrasonography; NPV, negative predictive value; NS, not stated; PPV, positive predictive value; SMA, superior mesenteric artery; SMV, superior mesenteric vein; UMRI, ultrafast MRI; US, ultrasonography.
rately assesses the patency of the superior mesenteric artery, coeliac axis, and portal venous system. Software for this is still not widely available, and a great deal of computing memory is required, but it is likely to become more widely applicable in the future. Its accuracy and reliability need to be proved.

Although it is difficult to make comparisons between these reports because study design, patient demographics, scanning protocols, and definitions of resectability and unresectability differ, there seems to be an overall trend and consensus that spiral CT is the most useful investigation tool in the assessment and staging of pancreatic cancer. Although it can reliably predict unresectability, there are limitations. Spiral CT has a sensitivity of 67% for detection of tumors less than 3 cm in diameter, and detection of peritoneal metastatic deposits, small liver metastases, and peritoneal micrometastases is similarly limited with spiral CT scan. Spiral CT cannot distinguish between reactive lymphadenopathy and malignant deposits. Thin-section helical CT scan with assessment of three-dimensional shape of the node might enable this distinction to be made. Concern remains about the potential for false positive diagnosis of unresectability and the inappropriate denial of potentially curative surgery. These limitations can be overcome either by using an operative imaging modality such as laparoscopic ultrasonography or by a trial of resection. Local expertise and resources will determine the optimal policy.

Magnetic resonance imaging

MRI was initially limited by image artifacts from respiration, aortic pulsation, bowel peristalsis, and a lack of suitable contrast material for the gut lumen, and has not yet replaced CT scan in the workup of pancreatic cancer. But it avoids the risks associated with intravenous contrast and ionizing radiation.

Steiner and colleagues evaluated 32 patients with proved pancreatic carcinomas with MRI and CT. They compared T1-weighted spin-echo and T2-weighted spin-echo pulse sequences. T1-weighted spin-echo pulse sequences have been shown to reduce motion artifacts from respiration. They found the T1-weighted spin-echo images superior to the T2-weighted images and comparable with—and in 22% of cases, better than—CT because it showed a signal intensity difference between the tumor and normal pancreatic tissue. MRI was slightly superior to CT in visualizing larger tumors. But this was not statistically significant, and the authors believed that MRI offered no notable advantage over CT in assessing pancreatic cancer.

The introduction of ultrafast MRI (UMRI), has increased the usefulness of the technique. Trede and colleagues prospectively evaluated the accuracy of UMRI in predicting surgical resectability in pancreatic tumors in 58 consecutive patients. Surgical assessment was correlated with US, UMRI, spiral CT, selective visceral angiography, and ERCP. UMRI was more accurate than both US and CT in predicting resectability, with sensitivity, specificity, and overall accuracy of 95.7%, 93.5%, and 80.4%, respectively, compared with a sensitivity, specificity, and overall accuracy of 85.1%, 87.2%, and 76.6% for CT and 74.4%, 87.2%, and 69.2% for US (Table 3). These authors concluded that UMRI was superior to other imaging modalities, avoiding endoscopy, vascular cannulation, allergic reactions, and ionizing radiation. Trede and coworkers have been criticized for including ampullary tumors in their cohort, which prevents meaningful conclusions from being reached.

The use of MRI to visualize the biliary system without the administration of intravenous contrast is known as magnetic resonance cholangiopancreatography (MRCP). Adamek assessed 124 patients with a strong clinical suspicion of pancreatic carcinoma with MRCP and ERCP. MRCP had a sensitivity and specificity of 84% and 97%, respectively, for the diagnosis of pancreatic carcinoma. This compared well with the results for ERCP of 70% and 94%. But Adamek believed that

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NPV, negative predictive value; PPV, positive predictive value; UMRI, ultrafast MRI; US, ultrasonography.
MRCP was not as accurate as spiral CT for assessment of resectability. MRI combines pancreatography and angiography in one sitting without any exposure to ionizing radiation and, as such, might well replace spiral CT scan as the imaging modality of choice in pancreatic cancer.

**Endoscopic ultrasonography**

Endoscopic ultrasonography (EUS) allows a high-frequency ultrasonographic probe to be placed in close proximity to the pancreas. This eliminates interference from overlying bowel gas and allows higher frequencies to be used, resulting in markedly improved resolution of images of the pancreas and surrounding structures. EUS is not as widely available as spiral CT and requires extensive experience and knowledge of pancreatic ultrasonographic anatomy. Its use tends to be limited to enthusiasts. Table 4 summarizes the experiences of several authors with EUS.

Rosch and colleagues\(^5\) compared EUS with US, CT, and angiography in 60 patients with pancreatic and ampullary cancer. The value of these procedures in determining resectability was assessed. In the 40 patients who were explored surgically, EUS was markedly superior to abdominal US and CT in determining tumor size, extent, and lymph node status. Involvement of the portal vein was correctly predicted by EUS in 95% of patients, compared with which angiography (85%), CT (75%), and abdominal US (55%) were less sensitive. In contrast, arterial encasement was less reliably detected by EUS.

Harrison and associates\(^23\) reviewed 19 patients who had CT and EUS performed for a pancreatic mass. All subsequently had an exploration. EUS identified pancreatic neoplasms in 17 of 19 patients, with two false positives. Node status was correctly predicted in 9 of 12 specimens. Nine of 12 tumors had accurate tumor staging by EUS. In all 19 patients, preoperative abdominal CT scan was obtained, but on six scans no pancreatic mass was detected. Both of these studies used conventional CT. More recent studies have compared spiral CT with EUS.

Howard and coworkers\(^24\) prospectively investigated 21 patients with periampullary tumors using spiral CT and EUS. All patients were subsequently explored. Spiral CT had a sensitivity of 63%, a specificity of 100% for detection of tumor, and an accuracy of 86% for the prediction of resectability. EUS had a sensitivity of 75%, a specificity of 77% for diagnosis of tumor, and an accuracy of 76% for prediction of resectability.

Dufour and associates\(^25\) compared spiral CT and EUS for diagnosis and staging of pancreatic carcinoma in 24 patients. They looked at existence of a pancreatic mass, diagnosis of malignancy, and vascular and lymph node involvement. For diagnosis of pancreatic mass, both methods had equivalent sensitivities for spiral CT (91.5%) and for EUS (87.5%). Two pancreatic masses smaller than 3 cm were seen only with EUS. Spiral CT was superior to EUS for diagnosis of malignancy (96% versus 71%). The accuracy of spiral CT for vascular involvement was superior to EUS (90% versus 40%). In the six patients with lymph node involvement, EUS was superior to helical-CT assessment. These authors concluded that spiral CT and EUS are complementary modalities. Legmann and coauthors\(^26\) compared dual-phase helical CT and EUS in 30 patients with suspected pancreatic tumours. Preoperative findings were compared with surgical and pathologic findings. Overall diagnostic sensitivity was 92% for dual-phase spiral CT and 100% for EUS. Overall accuracy for staging was similar.

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EUS, endoscopic ultrasonography; NPV, negative predictive value; PPV, positive predictive value; SMA, superior mesenteric artery; SMV, superior mesenteric vein; SVA, selective visceral angiography.
in both modalities (92%), and overall accuracy for predicting resectability was 90% for both modalities. The authors concluded that EUS does not offer much advantage over dual-phase helical CT. They believed that dual-phase spiral CT scan has faster scanning times, thin-section acquisition, and the ability to obtain multiple scans after administration of contrast, and consequently has much improved imaging of small pancreatic lesions. They concluded that dual-phase spiral CT was equal to EUS in the evaluation of pancreatic tumors.

Midwinter and colleagues subjected 48 patients with clinically suspected pancreatic carcinoma to spiral CT and EUS. Both radiologists and endoscopists were blinded to the results of the complementary investigation. Imaging results were compared with final laparotomy findings in 34 patients. EUS demonstrated 33 and spiral CT only 26 of the 34 primary lesions. Six of the tumors missed by CT scan were resectable. Five of these tumors were identified by EUS. EUS seems to be particularly useful in assessing small resectable tumors missed by spiral CT. The sensitivity and specificity of spiral CT and EUS for detecting involvement by the tumor of the superior mesenteric vein, portal vein, and lymph nodes were 56% versus 81% and 100% versus 86%, respectively. EUS was less effective at evaluating the superior mesenteric artery than spiral CT with sensitivities and specificities of 0.17% versus 50% and 67% versus 100%, respectively. There was no major difference in the detection of lymph node involvement between the two modalities (33% versus 44% and 86% versus 93%, respectively). The authors concluded that EUS has an advantage over CT scan in the detection of small lesions and recommended its use in patients suspected of having a pancreatic neoplasm in whom a CT scan has not demonstrated a lesion.

Although EUS gives superior results compared with conventional CT scan, it appears to be as good as spiral CT scan in detecting tumors larger than 3 cm and in assessing venous invasion and lymph node involvement. But its assessment of arterial invasion is limited. Its main advantage is the assessment of small tumors (<3 cm) that may be missed on CT scan. But EUS is an invasive procedure requiring sedation and monitoring and is highly operator dependent. Perhaps its real advantage lies in its ability to obtain accurate tissue for histologic diagnosis.

### Endoscopic ultrasonographically guided fine needle aspiration (EUS-FNA) and preoperative tissue diagnosis

A confident diagnosis of pancreatic malignancy can be made in most patients with noninvasive imaging. Previously, the high morbidity and mortality associated with pancreaticoduodenectomy meant that surgeons were reluctant to proceed to surgery without a tissue diagnosis. Several authors have reported excellent sensitivity and specificity for percutaneous FNA with minimal morbidity.

Warshaw raised the possibility of peritoneal seeding of malignant cells along the needle tract during percutaneous biopsy of pancreatic cancers and for this reason his group forego a preoperative biopsy in potentially resectable tumors. A negative FNA result does not absolutely exclude a malignancy.

EUS cannot reliably distinguish nodal metastases from inflammatory lymphadenopathy or differentiate focal pancreatitis from the tumor. EUS-FNA enables the clinician to accurately sample a localized lesion so a confident tissue diagnosis can be made. Numerous centers have confirmed the specificity and accuracy of the technique.

Chang and coauthors subjected 44 patients to EUS-guided FNA of pancreatic lesions and associated lymph nodes. Most lesions were in the pancreatic head. Adequate specimens were obtained in 94% of the pancreatic lesions and 100% of suspicious lymph nodes. The overall sampling adequacy was 95%. EUS-guided FNA had a sensitivity of 92%, specificity of 100%, and diagnostic accuracy of 95% for pancreatic lesions. For lymph nodes, the results were 83%, 100%, and 88%, respectively. EUS-FNA precluded surgery in 27% of cases, and in 57% of patients further tests were not required. This expedited therapy in 57% and influenced decisions in 68% of patients. The estimated savings was $3,300 per patient.

Williams and associates reviewed the experience with EUS-FNA of a large single center. Of 333 consecutive patients who underwent EUS-FNA, 144 had pancreatic lesions. A primary diagnosis of malignancy was obtained by EUS-FNA in 62% of patients with clinically suspicious lesions. The sensitivity, specificity, and accuracy of EUS-FNA for the diagnosis of malignancy were 84%, 96%, and 85%, respectively. In evaluating lymph nodes, EUS-FNA had superior accuracy and
specificity for diagnosing malignancy. Only one complication occurred. The authors concluded that EUS-FNA is safe and can readily obtain tissue specimens adequate for diagnosis. It provides accurate diagnosis of pancreatic malignancies, but the technique appears to be less useful for intramural lesions.

Many experienced pancreatic surgeons feel comfortable proceeding to resection without histology. If history, preoperative, and intraoperative findings are all consistent with diagnosis, then the chance that a cancer is present is extremely high. If cancer is not present, the next most likely diagnosis is chronic pancreatitis, and in specialized units with low morbidity and mortality, resection is still appropriate.35,36 But if neoadjuvant chemotherapy or radiotherapy is proposed, a firm tissue diagnosis is imperative. EUS-FNA is safe and reliable and improves the accuracy of noninvasive imaging techniques such as CT scan. EUS-FNA is an advance on EUS. EUS itself probably does not offer much more information than a good quality spiral CT scan, but the tissue sampling ability of EUS-FNA allows focal pancreatitis to be distinguished from a pancreatic neoplasm, preventing an unnecessary resection.

**Positron emission tomography**

Positron emission tomography (PET) provides an alternative in tumors less than 2 cm in diameter. In lesions of this size, it is often difficult to distinguish focal pancreatitis from tumor. EUS-FNA is only of diagnostic value if histology confirms a pancreatic tumor. The development of PET with 2-[18F]-fluoro-2-deoxy-D-glucose (FDG-PET) has made it possible to demonstrate sites of increased glycolysis from cancer. The glucose analogue FDG enters the cell in the same manner as glucose, is trapped after phosphorylation, and cannot be further metabolized. Intracellular FDG concentration reflects intracellular glucose metabolism.

Imdahl and associates37 performed FDG-PET in 48 patients with chronic and acute pancreatitis and pancreatic cancer. The results were compared with CT, US, ERCP, operative findings, and histology. FDG-PET predicted pancreatic cancer in 26 of 27 patients and predicted acute, chronic pancreatitis and normal pancreas in 100% of patients. In five cases, CT mislabeled a tumor as chronic pancreatitis; FDG-PET correctly diagnosed malignancy in these instances. In this study, ERCP mislabeled three patients with chronic pancreatitis as having a tumor and missed three patients with pancreatic cancer. Similarly, in the patients with benign disease, CT and ERCP were misleading in comparison with FDG-PET. FDG-PET had a positive predictive value for pancreatitis and tumor of 92% and 100%, respectively, compared with 70% and 91%, respectively, for CT. The authors concluded that PET is able to differentiate between otherwise unclear pancreatic masses and that an FDG-PET diagnosis of pancreatic cancer should be regarded as a true positive finding, making EUS-FNA redundant. FDG-PET was also shown to be superior to CT scan in distinguishing benign from malignant cystic neoplasms of the pancreas. FDG-PET correctly diagnosed 16 of 17 malignant tumors; only one false positive occurred in the 38 benign tumors. CT diagnosed only 12 of the malignant tumors, and there were 6 false positives in the benign group.

Hosten38 described a technique to superimpose images from CT and FDG-PET to help distinguish focal pancreatitis from tumor. Hosten reported a 66-year-old woman in whom this technique successfully identified a pancreatic tumor. CT had showed only atrophy, but no distinct lesion, and FDG-PET revealed several diffuse areas of increased uptake in the upper abdomen. Combining the two images allowed the tumor to be localized to the pancreatic head. This image overlay technique is experimental and requires sophisticated software. A combined scanner has been recently developed and described.39 Evaluation of its use in pancreatic cancer is in its infancy, but it would appear to have applications not only in diagnosis and in staging but also for monitoring the response to treatment.

**ERCP**

ERCP was and is widely used as a diagnostic tool in pancreatic cancer.40,41 It remains necessary when the patient presents with cholangitis, renal failure, or when there is doubt regarding choledocholithiasis as a highly effective way of alleviating biliary obstruction. It will remain the definitive treatment for most patients who present with established complications of obstructive jaundice (renal failure or cholangitis) but will not negate a subsequent operative approach. There are several flaws in its use for diagnosis. Parenchymal abnormalities can only be detected by inference and a normal pancreatogram does not entirely exclude malignancy.42 Potentially “silent areas” on ERCP are the uncinate process, the accessory duct, and the tail. Small tumors just below the papilla will dilate the entire duct and are often missed on
ERCP. It can be difficult to differentiate between chronic pancreatitis and pancreatic cancer on ERCP. Pancreatography might be frankly misleading in up to 13% of patients and might be unable to make a diagnosis in 7.6% of patients.42

Various techniques have been developed in an attempt to obtain tissue specimens during ERCP for pathologic assessment. Cytologic examination of pancreatic fluid obtained during ERCP with secretin stimulation has been reported to be highly specific and sensitive but has not been validated by other centers.4 Brush biopsy obtains cells that are better preserved than cells that have been exfoliated into the duct and are often degenerated.43,44 The use of these techniques might decline with the use of EUS to define and aspirate pathologic areas more accurately. Diagnostic ERCP always carries the risk of pancreatitis, but more importantly, in an obstructed system it might induce cholangitis by contaminating a nondraining biliary system.45,46 So ERCP should generally only be undertaken with therapeutic intent after the tumor has been thoroughly assessed noninvasively.47

In summary, this plethora of imaging modalities available demands that clinicians formulate a rational approach to the diagnosis and staging of pancreatic cancer. Investigations should be tailored to each individual patient. Paramount in the management decision tree is the establishment of a diagnosis, accurate staging of the tumor, and assessment of the individual patient’s comorbid factors.

Figure 1 outlines an approach. After a thorough clinical examination, an ultrasound provides useful information and might be the only investigation necessary to manage the patient with disseminated disease. With disease confined to the pancreas, a good-quality, dual-phase spiral CT scan will give an excellent idea of tumor resectability. The alternative UMRI is attractive because of its noninvasive nature, safety, and ability to image the tumor and the ductal system. But widespread availability of spiral CT scan has tended to limit the use of UMRI to specialized centers. In the majority of cases, these investigations are sufficient to allow the clinician to formulate a therapeutic approach for the patient. The individual’s comorbidity and the surgical unit’s philosophy and technical bias are major determinants in the final decision. These variables are hard to objectively quantify. ERCP is indicated if the patient presents primarily with cholangitis or renal failure. But, in general, ERCP should be reserved for therapy in those who, after detailed assessment of their tumor, are appropriate for endoluminal stenting.

Operator-dependent EUS and PET scanning have the ability to detect and differentiate small tumors from other pancreatic pathology and will be useful in selected patients. Despite the fact that CT more accurately predicts unresectability than resectability, it is important to ensure that no patient with a potentially curable tumor is denied a resection. An operative imaging modality such as laparoscopy or laparoscopic ultrasonography can confirm unresectability and avoid exploration in some, but for the fit individual a trial dissection will remain the final arbiter.
The rapid evolution of technology can be confusing and certainly increases the complexity of managing pancreatic cancer. Knowledge of the investigations allows their appropriate use according to patient factors so the clinician can decide on an optimal investigative and therapeutic plan for each patient.

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Study conception and design: Thomson
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Analysis and interpretation of data: Clarke
Drafting of manuscript: Clarke
Critical revision: Thomson, Madiba
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