



Pierre-Auguste Renoir. *The Skiff*, 1878.

*Endoscopic ultrasonography identifies patients unlikely to be cured by surgery due to vascular invasion or regional nodal metastasis.*

## Applications of Endoscopic Ultrasonography in Pancreatic Cancer

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**Background:** Accurate staging of pancreatic cancer is essential for surgical planning and for identification of locally advanced and metastatic disease that is incurable by surgery. Advances in endoscopic sonography (EUS), computed tomography (CT), and positron emission tomography have improved the accuracy of staging and reduced the number of incomplete surgical resections. Tissue acquisition is necessary in nonsurgical cases when chemoradiotherapy is considered. The complex regional anatomy of the pancreas makes cytologic diagnosis of malignancy at this region difficult without exploratory surgery. Although CT-guided fine-needle aspiration (FNA) is used for this purpose, reports of an increased risk of peritoneal dissemination of cancer cells and a false-negative rate of nearly 20% make this a poor choice. The ability to position the EUS-transducer in direct proximity to the pancreas by means of the stomach and duodenum, combined with the use of FNA, increases the specificity of EUS in detecting pancreatic malignancies.

**Methods:** The current literature regarding the accuracy of EUS with FNA in the evaluation of pancreatic cancer is reviewed.

**Results:** EUS accuracy ranges from 78% to 94% for tumor staging and from 64% to 82% for nodal staging. EUS also enables FNA of lesions that are too small to be identified by CT or MRI or too well encased by surrounding vascular structures to safely allow percutaneous biopsy. The accuracy for detecting invasion into the superior mesenteric artery and vein is lower than that for detecting portal or splenic vein invasion, especially for large tumors. EUS permits delivery of localized therapy such as celiac plexus neurolysis for pain control and direct intra-lesional injection of antitumor therapy.

**Conclusions:** EUS in combination with FNA is a highly accurate method of preoperative staging of pancreatic cancer, especially those too small to be characterized by CT or MRI, and it has the ability to obtain cytological confirmation of pancreatic cancer.

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## Introduction

Pancreatic cancer is the fourth-leading cause of cancer-related deaths in the United States, and its incidence appears to be increasing. Cancer of the pancreas develops in approximately 30,000 people in the United States annually. The disease is associated with a high mortality rate and a median survival of approximately 4 months in untreated patients. Data from the National Cancer Database show the 5-year survival rate after surgery to be 3%.<sup>1</sup> However, if surgery achieves clear margins and negative lymph nodes, the 5-year survival rate approaches 25%. Unfortunately, most patients diagnosed with pancreatic cancer present at an advanced stage of the disease when surgical cure is no longer possible. When unresectable, chemotherapy, radiation therapy, or a combination of the two may improve overall survival and quality of life.

The regional anatomy of the pancreas is complex, making procurement of cytologic samples difficult without exploratory laparotomy. Traditionally, computed tomography (CT)-guided fine-needle aspiration (FNA) has been used for biopsy of the pancreas. However, this technique is associated with a risk of peritoneal dissemination of cancer cells and has a false-negative rate of up to 20%.<sup>2,3</sup> Even endoscopic retrograde cholangiopancreatography (ERCP) brush cytology has a false-negative rate of nearly 30%.<sup>4</sup>

Endoscopic ultrasonography (EUS) was developed in the 1980s to overcome limitations of transabdominal US imaging of the pancreas caused by intervening gas, bone, and fat. The ability to position the transducer in direct proximity to the pancreas by means of the stomach and duodenum, combined with the use of high-frequency transducers, produces detailed high-resolution images of the pancreas that far surpass those of CT or magnetic resonance imaging (MRI). The high resolution of these

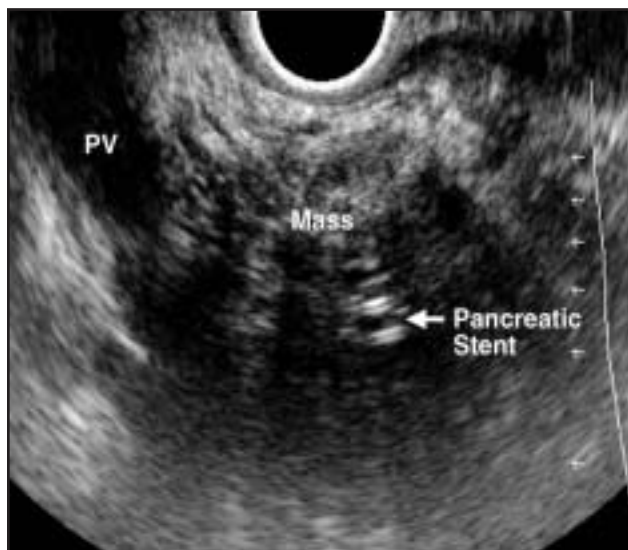


Fig 1. — EUS image of a patient with pancreatic head mass that invades the portal vein (PV).

images allows identification of lesions as small as 2 to 3 mm and their relationship to adjacent blood vessels such as the portal vein and mesenteric vasculature (Fig 1). An added advantage of EUS is the ability to perform FNA. Compared with other imaging modalities, the results of EUS-FNA of pancreatic masses are excellent, with a sensitivity of 85% to 90% and a specificity of virtually 100%.<sup>5,7</sup> The procedure is safe, with reported complication rates being less than 1%.<sup>8</sup>

With the availability of EUS and EUS-guided FNA procedures in major medical centers around the world, earlier diagnosis and more accurate staging have improved the management of pancreatic cancer. Furthermore, EUS-guided therapy, such as celiac plexus neurolysis for pain control, and direct injection of cytotoxins into malignant lesions are becoming important adjuncts in the management of patients with surgically unresectable disease. This review focuses on the role of EUS in diagnosis and staging of malignant pancreatic lesions.

## Pancreatic Adenocarcinoma

EUS staging of pancreatic and other tumors follows the TNM system of the American Joint Committee on Cancer (AJCC). In 2002, the AJCC modified the T staging system for pancreatic cancer to classify tumors invading the portal venous (superior mesenteric vein or portal vein) system as T3 (these were previously staged as T4) and tumors invading the celiac or superior mesenteric artery as T4. Although this change is likely to result in decreased reported accuracy for EUS, it remains unclear if surgical therapy is beneficial compared to radiochemotherapy for tumors invading the portal venous system. The literature reviewed below largely reflects the previous AJCC staging system in which all mesenteric vascular invasion (venous or arterial) is considered to be T4.

Many large series have found T stage accuracy to range from approximately 78% to 94% and nodal (N) stage accuracy between 64% and 82%.<sup>9-12</sup> However, lower accuracy has also been described. One such series, for example, included 89 patients in whom EUS was compared to surgical and histopathologic TNM staging.<sup>13</sup> The overall accuracy of EUS for T and N staging was only 69% and 54%, respectively. Furthermore, only 46% of tumors believed to be resectable by EUS were actually found to be resectable during laparotomy. Staging accuracy of EUS can be influenced by several factors, including the experience level of the endosonographer, imaging artifacts, and the endosonographer's knowledge of the results of previous imaging tests. In general, T stage accuracy for EUS is highest in patients with smaller tumors, whereas helical CT is more accurate in staging larger tumors.<sup>14-16</sup> The accuracy of EUS for detecting invasion into the superior mesenteric artery and vein is lower than that for detecting portal or splenic vein invasion.<sup>17,18</sup>

A recent review<sup>19</sup> that pooled data from four studies comparing the accuracy of EUS with helical CT in the evaluation of pancreatic cancer found that EUS detected more tumors (97% vs 73%), was more accurate for determining tumor resectability (91% vs 83%), and was more sensitive for detecting vascular invasion (91% vs 64%). However, when the data were interpreted individually, two of the reports concluded that CT and EUS were approximately equivalent in detecting the primary tumors,<sup>14,20</sup> while the other two found EUS to be superior.<sup>21,22</sup> Several features of the individual reports may account for these variable conclusions, including differences in the gold standards, variations in the specific techniques used for helical CT, and the proportion of patients with advanced disease in each study. A reasonable conclusion from these data and from clinical experience is that EUS and helical CT are complementary for staging pancreatic cancer. EUS is a more accurate modality for local T staging and for predicting vascular invasion, especially in tumors less than 3 cm, while helical CT is better for the evaluation of distant metastasis and for staging larger tumors. Similar to CT, studies comparing MRI with EUS suggest that EUS may be more sensitive for detecting small tumors while providing complementary information regarding resectability.<sup>23</sup>

Recent advances in CT technology, including the development of spiral scanners and more recently multi-detector CT (MDCT) scanners, and the development of three-dimensional (3D) imaging software have improved the ability of CT to image the pancreas and to evaluate a wide range of pancreatic pathology. In most of the published series, older dynamic scanners or single-row spiral scanners were used, and 3D imaging was not included. With the narrow collimation and faster scanning possibilities with new MDCT scanners, it is likely that the CT accuracy for detecting pancreatic tumor will improve. In a recently published study by McNulty et al<sup>24</sup> using MDCT, 27 of 28 pancreatic cancers were detected. This progress will continue as manufacturers introduce the



Fig 2. — EUS image of a 1.5-cm localized lesion in the uncinus process of the pancreas.

next generation of scanners, which can acquire up to 32 slices per second with even faster scan times. The impact of these new scanners on diagnostic accuracy will need to be carefully evaluated.

Several studies have compared the accuracy of angiography and EUS for determining vascular invasion.<sup>17,18,25</sup> Although the results varied, a general conclusion is that EUS is as accurate or more accurate for determining vascular invasion, with the exception of some tumors that invade the superior mesenteric artery. In a study of 21 patients with pancreatic cancer who underwent EUS and angiography prior to an attempt at curative resection, EUS was much more sensitive than angiography for detecting vascular invasion (86% vs 21%). The specificity and accuracy of EUS were 71% and 81%, respectively, compared with 71% and 38% for angiography.<sup>23</sup>

EUS has an important role in guiding a biopsy needle into lesions that are too small to be identified by CT or MRI or too well encased by surrounding vascular structures to safely allow percutaneous biopsy.<sup>26</sup> The impact of EUS-FNA was studied by Chang et al<sup>27</sup> in a series of 44 patients. EUS-FNA had an accuracy rate of 95% for pancreatic lesions and 88% for lymph nodes. Three patients had enlarged celiac nodes on EUS that showed malignancy on FNA. Overall, FNA precluded surgery in 41% of the patients, avoided the need for further diagnostic tests in 57%, and influenced clinical decisions in 68% of the patients, thus providing substantial cost savings. Gress et al<sup>26</sup> examined the role of EUS-FNA in patients with suspected pancreatic cancer after a negative CT-guided FNA or ERCP brush cytology. In 102 patients, 57 had positive cytology on EUS-FNA and 37 had negative cytology. The examination was inconclusive in 8 patients. After a median follow-up of 24 months, all 57 patients with positive cytology on EUS-FNA had verification of the diagnosis of pancreatic cancer. Of the 45 patients with negative or inconclusive cytology on EUS-FNA, 41 had no evidence of pancreatic malignancy at follow-up. One particularly important application of EUS-FNA is the detection of malignant lymph nodes. FNA has been demonstrated to increase the accuracy of lymph node staging and thereby reduce the number of unnecessary surgical explorations by identifying patients with surgically incurable disease.<sup>27</sup>

Lesions located in the uncinus process of the pancreas are the most difficult to puncture (Fig 2). To access a mass in the uncinus process, the echoendoscope must be advanced into the duodenal C-loop in the “long” position. This exerts substantial angulation and torque on the FNA needle. The needle is more difficult to advance and also causes a “bowed shape.” This altered shape can result in mistargeting. Also, lesions in the pancreatic isthmus pose a similar challenge in that the echoendoscope is usually in the “long” scope position with the tip in the gastric antrum. A transgastric approach can be more difficult than the transduodenal approach due to the laxity and redundancy of the gastric wall, as well as the capaciousness of the stom-

ach. Lacking anchorage, the echoendoscope tends to displace during advancement of the FNA needle.

A controversial issue is identifying who should undergo EUS-FNA (Table). There is general consensus that it is reasonable to obtain a tissue diagnosis in patients suspected of having pancreatic cancer who are poor surgical candidates. Histologic confirmation in such patients can be helpful in deciding on chemotherapy or radiotherapy. More controversial is the role of EUS-guided FNA in patients suspected of having pancreatic cancer who appear to be resectable on other imaging studies. One view is that a tissue diagnosis will not alter management and is therefore unnecessary. This argument is supported by the recognition that the sensitivity of EUS-guided FNA is in the range of 85% to 90%, potentially leading to false-negative results in up to 15% of patients. However, an argument can be made for EUS-guided FNA in such patients when the establishment of a histologic diagnosis before surgery may alter management since other types of malignancy involving the pancreas can mimic adenocarcinoma (eg, lymphoma). Therapy for these tumors may not include surgery. Some patients and physicians want to know definitively whether cancer is present before undergoing a surgical resection. When the FNA is negative, some patients may be willing to accept the 15% chance of missing a diagnosis of cancer rather than undergoing surgery. This is especially true with there is concurrent acute or chronic pancreatitis that may mimic a focal pancreatic cancer.

An emerging role for EUS is the detection of small, occult liver metastases in patients with pancreatic tumors. Although EUS is best suited for loco-regional staging, its high resolution and proximity to the left lobe and inferior right lobe of the liver has led to detection of small liver metastases. The ability to perform immediate EUS-FNA allows accurate distinction of benign from malignant lesions. We reported the results of EUS-FNA of liver lesions in 167 patients (including 62 with pancreatic can-

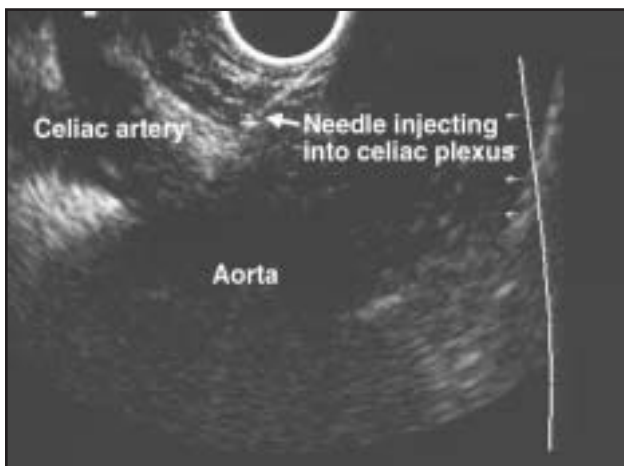


Fig 3. — Celiac plexus block being performed with the curvilinear array echoendoscope. The celiac artery is seen emerging from the aorta, and the needle is shown just above this point.

#### Indications for EUS-FNA

- To document a diagnosis of malignancy in a patient with an unresectable mass as a prerequisite for adjuvant chemotherapy or radiation therapy.
- To exclude other tumor types such as lymphoma, small-cell metastasis, or neuroendocrine cancer that may require a different management strategy.
- To determine a diagnosis in patients who are reluctant to undergo major surgery without a definitive diagnosis.
- To document the absence of malignancy when the pretest probability of malignancy is low.

cer), all of whom had negative or equivocal CT or US of the liver. EUS-FNA was highly accurate with a complication rate of 4%. One death occurred when EUS-FNA of a liver lesion was performed in the setting of an obstructed biliary stent, leading to cholangitis. Antibiotic prophylaxis and biliary drainage should be used in conjunction with EUS-FNA of liver lesions in the setting of obstructing pancreatic tumors.<sup>28</sup>

Another emerging role of EUS is the identification of small, occult pancreatic tumors in the patients with liver metastases of “unknown” primary. In the report by ten-Berge et al,<sup>28</sup> EUS identified a pancreatic tumor in 17 of 33 patients whose CT showed only metastatic tumor of unknown primary. The identification of a pancreas primary allowed pancreas-specific chemotherapy to be administered in each of these cases.

The safety of EUS-FNA for evaluating pancreatic lesions is well established.<sup>29,30</sup> Rare complications include pancreatitis, infection, and bleeding. In a multicenter study evaluating the safety of EUS-FNA of solid pancreatic masses, 14 of 4,958 patients developed pancreatitis.<sup>29</sup> In another study involving EUS-FNA of pancreatic cystic lesions, 1 of 81 patients developed an infected cystadenoma after EUS-FNA.<sup>30</sup> This patient did not receive prophylactic antibiotics prior to the procedure. Current standard of care includes routine administration of antibiotics for patients undergoing FNA of pancreatic cystic lesions.

Accurate staging of patients with pancreatic cancer is critical to avoid the expense, morbidity, and mortality related to unnecessary surgery. While several tests are available for assessing such patients, consensus has not been achieved on the optimal approach. Thus, the role of EUS and EUS-guided FNA varies among treatment centers. EUS has a more prominent role at our institution. We recommend that helical CT should be performed initially to evaluate for the presence of a pancreatic mass. EUS is most clearly indicated when no clear tumor or only equivocal changes are seen on CT. If metastatic disease is evident, EUS or CT-guided biopsy can establish the diagnosis. If the helical CT is negative for metastatic disease or an obvious mass, EUS should then be performed to further evaluate the pancreas (if the clinical suspicion is high for pancreatic cancer) followed by EUS-guided FNA of any apparent mass noted.

## Cystic Lesions of the Pancreas

Cystic lesions of the pancreas present a difficult clinical dilemma. They are often detected serendipitously and include completely benign, potentially malignant, and frankly malignant lesions. The only definitive management is surgical resection, often requiring pancreatoduodenectomy. The principal dilemma is how to accurately distinguish lesions of low malignant potential, such as pancreatic pseudocysts and serous cystadenomas, from neoplastic lesions with high malignant potential, such as mucinous cystadenoma, cystadenocarcinoma, and intraductal papillary mucinous tumors (IPMTs). A further surgical dilemma is deciding whether to perform extensive vs limited resections. Because of its high resolution and its ability to aspirate fluid and place internal cystgastrostomy or cystoduodenostomy tubes, EUS has become an important tool in pancreatic cyst management.

Occasionally, pancreatic cystic lesions can be distinguished by morphologic criteria alone, although no endosonographic features have proven to be useful for distinguishing benign from malignant lesions.<sup>31,32</sup> Mucinous cystic neoplasms are more common in women aged 40 to 60 years and are located more frequently in the body and tail of the pancreas. The endosonographic appearance is typically macrocystic with rare internal septations. Focal wall thickening raises a suspicion of malignancy. On the other hand, serous cystadenomas are typically microcystic. They are composed of multiple small, "honeycomb-like" compartments separated by thin-walled but sometimes vascular septae and have a characteristic (although not always preset) central calcification. Pancreatic pseudocysts often show echogenic debris with parenchymal changes. EUS findings of IPMTs include segmental or diffuse dilation of the main pancreatic duct, side branches, or both. Although not specific, a main pancreatic duct diameter greater than 10 mm, cystic lesion greater than 40 mm with thick, irregular septum in the branch-duct type IPMT, and the presence of mural nodules more than 10 mm in size suggest an underlying malignancy.<sup>33</sup> Among IPMT lesions, those arising from the main duct are more often malignant than those arising from side branches. A longitudinal study of branch-duct IPMTs without mural nodules showed no progression to malignancy over a median 33 months.<sup>34</sup> Sampling tissue or cyst fluid can be helpful in patients in whom the diagnosis is uncertain.<sup>35</sup> Intra- and extra-cellular mucin are seen in fluid aspirated from mucinous cysts. Glycogen-staining cells are seen in serous cystadenomas. Histiocytes are associated with pseudocysts. Amylase levels are increased in pseudocysts but variable in other types of cysts. Carcinoembryonic antigen (CEA) concentration is increased in the cyst fluid from mucinous cystadenomas whereas it is normal in those with pseudocysts and serous cystadenomas. The utility of CA19-9, CA125, and CA72-3 is under investigation. The

use of tumor marker CA72-4 may be of special significance.<sup>36</sup> The concentration of CEA and CA72-4 in fluid aspirated from mucinous cystadenomas is, on average, higher than the CEA and CA72-4 in fluid aspirated from serous cystadenomas. It is our current practice to send fluid for amylase, CEA, mucin stain, and cytology. The use of tumor markers in predicting the malignant potential of different pancreatic cystic neoplasms is being actively investigated. With further study in this area, recommendation for other fluid analyses may be forthcoming. Currently, none of the EUS imaging or fluid characteristics are sufficiently active to entirely exclude a diagnosis of a malignant or premalignant cyst. It is our practice to consider resection in all cases of complex cysts, in cases without a clear antecedent acute pancreatitis (and thus at risk for pseudocyst), and when the fluid contains mucin, suspicious cytology, or elevated CEA level (>200 ng/mL). It is reasonable to follow patients with suspected pseudocysts, those with small, side-branch type IPMTs in the absence of mural nodules, and those with a substantially elevated risk of surgery.

## Neuroendocrine Tumors

Pancreatic endocrine tumors are often small and hard to detect by radiologic techniques. Since the original description of gastrinomas in 1955 by Zollinger and Ellison,<sup>37</sup> multiple imaging modalities have been evaluated to localize pancreatic neuroendocrine lesions for surgical resection. Studies have shown that CT, MRI, and conventional US detect tumors in less than 50% of patients.<sup>38</sup> Somatostatin receptor scintigraphy (SRS) is reported to have the highest sensitivity for gastrinomas but is less accurate for detecting insulinomas.<sup>39</sup> The optimal algorithm for staging pancreatic neuroendocrine tumors is unknown. Issues important for clinical management include (1) is the tumor localized to the region of the pancreas (including gastrinoma triangle) or metastatic, (2) is it unifocal or multifocal within the pancreas, and (3) is it functional or non-functional, benign or malignant?

To determine whether a tumor is localized or metastatic, cross-sectional imaging and SRS are likely more accurate than EUS due to their ability to image broad areas.<sup>39</sup> For imaging within the pancreas, EUS provides superior resolution and accuracy relative to CT scan. In a study of 82 patients, Anderson et al<sup>40</sup> identified 100 tumors in 54 patients, emphasizing the frequency of multifocal tumors. EUS accurately localized the tumor in 93% of patients and had a specificity of 95%, which was higher than CT or transabdominal US. EUS was not reliable for detection of extrapancreatic tumors. Zimmer et al<sup>41</sup> compared EUS to CT, SRS, US, and MRI in 40 patients with neuroendocrine tumors. EUS had the highest overall accuracy for both gastrinomas and insulinomas but missed 50% of extrapancre-

atic tumors. In one report of patients who had negative ultrasonography and CT scans, EUS detected endocrine tumors in the pancreas with high sensitivity (82%) and specificity (95%).<sup>42</sup>

In patients with nonfunctioning neuroendocrine tumors where the risk of surgery is elevated, it would be useful to distinguish benign from malignant neuroendocrine tumors. In two studies,<sup>43,44</sup> EUS was able to accurately distinguish malignant lesions based on the presence of an irregular inhomogeneous hypoechoic mass or on invasion and obstruction of the pancreatic duct. Tumors without these features were almost always benign.

Intraductal endoscopic ultrasonography (IDUS) involves the insertion of an ultra-thin (2 mm) US probe directly into the pancreatic duct during ERCP. Preliminary experience suggests that it may be more accurate than standard EUS for the detection of neuroendocrine tumors. Although experience with IDUS is limited, initial data suggest that IDUS may improve the evaluation of these patients and lead to the identification of tumors arising within the pancreas that have gone unrecognized by other techniques.<sup>45,46</sup> In one study, IDUS was able to identify the presence of an islet cell tumor in 7 of 7 patients.<sup>45</sup> In 1 of these patients who had multifocal disease, IDUS accurately determined the number of tumors while EUS failed to detect all lesions. The distance from the tumors to the main pancreatic duct was accurately determined, thus aiding preoperative planning of wedge resection, which was possible in 2 patients.

EUS can also be useful for preoperative localization of pancreatic endocrine tumors by its ability to tattoo lesions by fine-needle injection using India ink.<sup>47</sup> This may shorten operative time because it obviates the need to localize the tumor by palpation and intraoperative US. This technique may have the potential to facilitate tumor resection by less invasive methods such as laparoscopic enucleation.

These data suggest that EUS serves an important role in localizing tumors within the pancreas, detecting multifocal tumors, and distinguishing benign from malignant tumors. In addition, EUS should be used with cross-sectional imaging and SRS to identify extrapancreatic tumors or metastases.

## Recent Advances

Pain related to pancreatic cancer and chronic pancreatitis is often poorly controlled. Celiac plexus neurolysis (CPN) is a chemical splanchnicectomy of the celiac plexus, which ablates the afferent nerve fibers that transmit pain from intra-abdominal viscera. CPN is most commonly used to palliate pain from pancreatic cancer, but it has also been used to relieve pain in chronic pancreatitis. EUS guidance offers the most direct access to the celiac plexus of all the CPN techniques short of surgical

intervention. The celiac ganglia are located at the origin of the celiac artery, which is easily identified at endosonography (Fig 3). The relative proximity of the celiac ganglia to the posterior gastric wall ensures an accurate passage of the injecting needle into the ganglia, thereby minimizing the risk of complications and potentially increasing the effectiveness of the block. Bupivacaine and absolute ethanol are commonly used for performing CPN. EUS-CPN performed for the palliation of pancreatic cancer pain appears to be as safe and effective as CPN performed by other techniques. An added advantage of the EUS approach is that it can be performed during staging and biopsy of the tumor.

In a pilot study, pain relief lasting for a median of 10 weeks was achieved in 88% of 25 patients undergoing EUS-CPN.<sup>48</sup> Similar results were observed in a later prospective study involving 58 patients; pain scores were significantly lower than baseline in 78% of patients 2 weeks after the procedure and were sustained for 24 weeks.<sup>49</sup> On multivariate analysis, the benefit of EUS-CPN was independent of morphine use, chemotherapy, and radiation. Direct antitumor therapy has recently been reported in phase I and II trials. Patients with unresectable tumors who underwent a single EUS-guided fine-needle injection of activated lymphocytes had minimal side effects and a median survival of 13 months, which was longer than historical controls.<sup>50</sup> Bedford et al<sup>51</sup> reported preliminary results of injection of a modified adenovirus capable of preferentially replicating in and destroying tumor cells. Injections of the virus were performed weekly for 8 weeks with concomitant gemcitabine therapy. Three patients had minor response (<50%) and 5 had stable disease. Long-term survival is unknown. Further trials evaluating the efficacy of other injectable local therapies are currently underway.

EUS-guided placement of inert brachytherapy seeds was performed in pigs under EUS and fluoroscopy guidance.<sup>52</sup> The procedure required approximately 20 minutes, and no immediate complications were observed. The seeds were placed accurately in 4 to 5 columns spaced 1 to 1.5 cm apart. No seeds were inadvertently placed outside the pancreas. Human trials are currently under investigation.

## Conclusions

EUS is now established as an accurate method for staging malignancies of the pancreas. The most valuable role of EUS is the ability to identify patients unlikely to be cured from surgical excision due to vascular invasion or regional nodal metastasis. The ability to obtain tissue confirmation plays a critical role in patients unsuitable for surgical therapy, and recent investigations into EUS-guided fine-needle injection therapy may further expand the armamentarium for treating unresectable tumors.

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