

# Endoscopic ultrasound–guided, 18-gauge, fine needle aspiration biopsy of the pancreas using a 2.8 mm channel convex array echoendoscope

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**Background:** Previous studies have reported on endoscopic ultrasound–guided, fine needle aspiration biopsy using 22- to 25-gauge needles. We evaluated the histologic and cytologic yield of endoscopic ultrasound–guided, fine needle aspiration biopsy of the pancreas using an 18-gauge, Menghini-type core needle.

**Methods:** Fine needle aspiration biopsy was performed in conjunction with a prototype 2.8 mm channel convex array echoendoscope. The core specimen was placed in formalin for cell block, and residual material was expelled on slides for cytology. Definitive diagnosis was established by surgery or clinical follow-up.

**Results:** Of 45 patients who underwent fine needle aspiration biopsy, the needle failed to penetrate indurated pancreatic lesions in five. An average of 2.6 passes were performed in the remaining patients. Sufficient material for a histologic and/or cytologic diagnosis was obtained in 40 patients (histologic and cytologic yield of 68% and 75%, respectively). Combining the results of histology and cytology, the sensitivity and specificity for detection of malignancy was 76% and 100%, respectively. Histology confirmed the cytologic findings in 35 patients, providing additional tissue specific information. In three cases histology established a diagnosis of malignancy where cytology was not conclusively malignant. However, in three cases of surgically confirmed malignancy histology failed to detect malignancy, whereas cytology showed suspicious or malignant cells. The sensitivity of histology and cytology alone in detecting malignancy was 53% and 70%, respectively. Mild pancreatitis occurred after pancreatic fine needle aspiration biopsy in one patient.

**Conclusion:** Core specimens for histology can be safely obtained using an 18-gauge needle. Histology provides tissue-specific information that complements cytology, but histology is less sensitive than cytology in detecting malignancy. (*Gastrointest Endosc* 1998;47:121-7)

Endoscopic ultrasound (EUS)–guided, fine needle aspiration biopsy is a novel method for tissue sam-

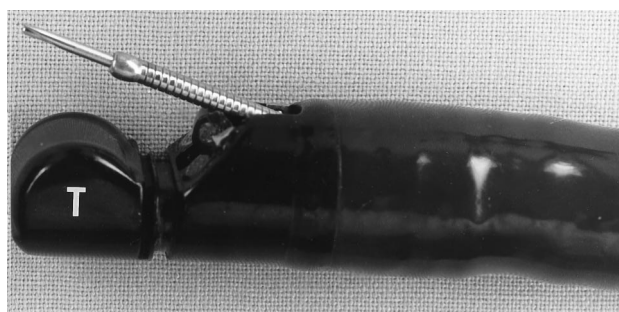
Received March 5, 1997. For revision July 7, 1997.  
Accepted September 15, 1997.

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pling of intramural and extramural gastrointestinal lesions. This procedure is performed in conjunction with an echoendoscope that produces a sector scan image oriented along the long axis of the endoscope, thus allowing the examiner to visualize the course of the needle as it is inserted into the imaging plane. Previously published studies have reported on the use of the Pentax convex array echoendoscope (FG-32 UA; Pentax Precision Instrument Corp., Orangeburg, N.Y.) for fine needle tissue sampling. This echoendoscope has a relatively small working chan-



**Figure 1.** Distal end of the Olympus convex array echoendoscope (GF-UC30P) with needle exiting through the biopsy channel for EUS-guided fine needle aspiration. T, Transducer

**Table 1.**  
**Technical specifications of the Olympus GF-UC30P convex array echoendoscope**

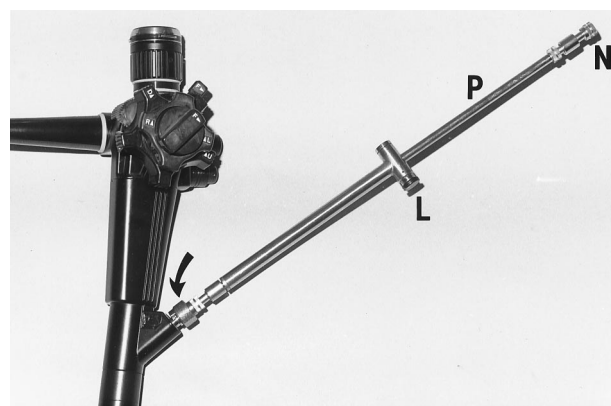
Angle of view (degrees)	85
Distal outer diameter	12.8 mm
Tip deflection	
Up/down	130/90
Right/left	90/90
Working length	1255 mm
Total length	1570 mm
Working channel diameter	2.8 mm
Elevator	Yes
Scanning angle (degrees)	180
Frequency	7.5 MHz
Display mode	M, B, Doppler

nel of 2.0 mm, thus limiting the size of the needle (22- to 25-gauge) that can be inserted through the channel. The aim of this study was to evaluate the results of fine needle aspiration using an 18-gauge needle in conjunction with a prototype 2.8 mm channel convex array echoendoscope. The procedure is referred to as fine needle aspiration biopsy (FNAB) in this study.

## PATIENTS AND METHODS

### Patients

During a 10-month period between August 1995 and June 1996, 45 patients (mean age 62 years, range 26 to 77 years) underwent FNAB of the pancreas. Patients were selected to undergo EUS-guided FNAB on the basis of their clinical history and findings of a mass lesion on preliminary endosonographic evaluation using an Olympus 360-degree radial scanning echoendoscope (GF-UM20; Olympus Optical, Inc., Tokyo, Japan). In all patients FNAB was judged to have potential impact on treatment strategy. Before FNAB, informed consent was obtained for the procedure in all cases. Bleeding parameters (coagulation studies and complete blood count) were performed before FNAB; an uncorrectable coagulation



**Figure 2.** Needle handle (own prototype) Luer-locked to the working channel of the echoendoscope (curved arrow). P, Piston; L, lock for piston; N, needle Luer-locked to piston.

profile was considered a contraindication to FNAB. Antibiotics were not administered routinely before or after FNAB. Patients were hospitalized 24 hours after FNAB and subsequently discharged if their clinical course was uneventful.

Patients who did not undergo operation underwent expectant observation. The following subjective and objective parameters were followed at 3-month intervals: clinical status (general condition, weight gain or loss), imaging studies (sonography or endosonography), and CA 19-9 tumor marker levels. The criteria for establishing a benign course of disease were a sense of well-being, an absence of weight loss, and no alteration of morphologic findings on imaging studies over a minimum of 6 months.

### Materials

FNAB was performed using a prototype convex array echoendoscope (GF-UC30P; Olympus). The echoendoscope is an oblique viewing fiberscope that incorporates an electronic convex array transducer at the tip (Fig. 1). Technical specifications are detailed in Table 1. A balloon is mounted over the transducer housing and is filled with water for acoustic coupling. The echoendoscope has a 2.8 mm working channel. An elevator allows adjustment of the exit angle up to a maximum of 40 degrees (with the elevator fully open, the needle exits at an angle of approximately 25 degrees). Any accessory passed through the working channel can be endoscopically visualized as it exits the working channel.

The echoendoscope is connected to a dedicated console unit with a B-mode sector display (Dornier AL52006, Germering, Germany). The focal length of the ultrasound beam is adjustable to provide optimal resolution of a specific region of interest. Color and pulsed Doppler capability are integrated into the console unit. After freezing an image, a cine-loop memory function allows the examiner to scroll through preceding images frame by frame.

For lesions located in the head and genu regions of the

**Figure 3. A,** Endosonographic images of a tumor mass in the pancreatic genu region; FNAB of the mass. The needle enters the mass from the right (*arrow* shows needle tip).

pancreas, biopsy specimens were obtained from the duodenum. For those located in the body and tail of the pancreas, biopsy specimens were obtained from the stomach. All FNAB procedures were performed with an institutionally manufactured needle catheter (Fig. 2). The needle has a short Menghini-type coring bevel. The needle was equipped with a blunt tipped stylet covered by a 118 cm protective metal spiral coil sheath. The needle could be advanced up to 12 cm from the spiral sheath. A safety catch on the handle served to lock the needle in the fully retracted position during insertion through the working channel. The handle was Luer-locked at the inlet of the biopsy port.

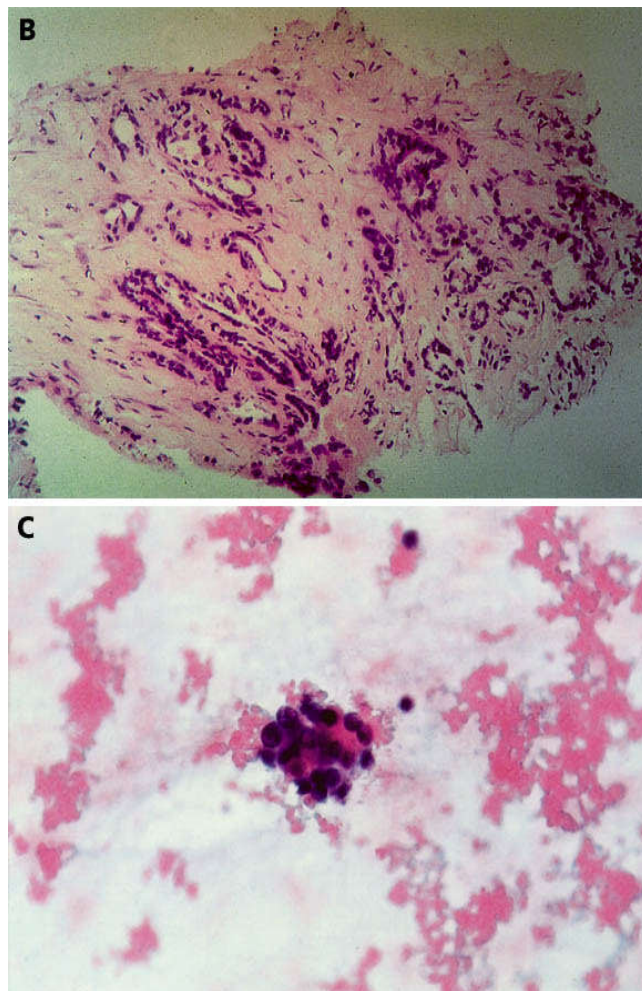
### Methods

All endosonographic examinations and FNAB procedures were performed by a single experienced endosonographer (K.F.B.).

The target lesion was endosonographically visualized and the region was scanned for vessels using color and pulsed Doppler. The needle catheter was passed through the instrumentation channel with the needle fully retracted within the protective metal coil sheath. The handle of the needle catheter was Luer-locked to the inlet of the biopsy channel. The needle was advanced approximately 1 cm beyond the sheath until the needle was sonographically visualized against the bowel wall. The needle appeared as a hyperechoic linear density structure and was readily identified by the artifactual acoustic reflections produced by the metal.

Before puncture, the stylet was withdrawn several millimeters thereby exposing the sharp needle tip. The needle was then advanced into the target tissue under endosonographic guidance (Fig. 3A).

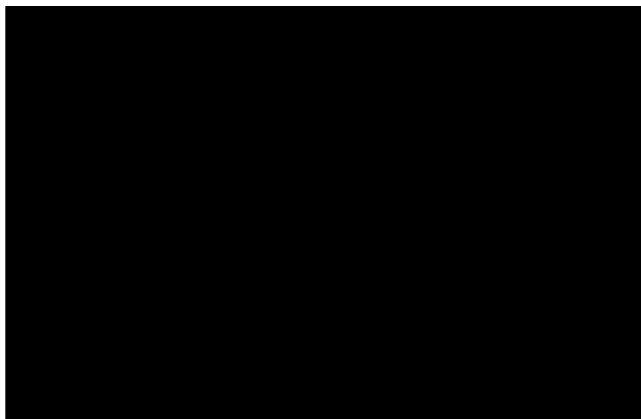
Once the lesion was penetrated, the stylet was advanced to the original position to "unplug" the needle. The



**Figure 3. (cont'd) B,** Histology of the FNAB specimen showing irregular glands with moderate nuclear atypia infiltrating desmoplastic stroma (adenocarcinoma) (hematoxylin and eosin, original magnification  $\times 100$ ). **C,** Cytology showing cellular atypia suspicious for but not confirming adenocarcinoma (Papanicolaou preparation, original magnification  $\times 630$ ).

stylet was then removed and suction was applied using a 10 mL syringe while moving the needle to and fro within the punctured lesion.

Before removing the needle, suction was released by disconnecting the syringe. The core specimen was expelled from the needle using a syringe and placed in formalin for a cell block. Residual material in the needle was smeared on glass slides for cytologic study. FNAB was repeated until a core specimen was obtained, limited to a total of five passes. A cytopathologist or cytotechnician was not present to determine the adequacy of specimens. Cytologic smears and histologic specimens were examined separately by a cytotechnician and cytopathologist, respectively. Both were blinded as to the diagnosis made by the other. All procedures were documented with thermal prints and video recordings.



**Figure 4.** Histology of an FNAB core specimen obtained from the pancreatic head showing marked interlobular and intralobular fibrosis without evidence of malignancy (hematoxylin and eosin, original magnification  $\times 25$ ). Cytology, however, showed pleomorphic cells diagnostic of malignancy. Surgical pathology confirmed adenocarcinoma.

Histology was categorized as adequate if it provided a coherent core tissue specimen from the target organ (Figs. 3B and 4). Cytology was categorized as adequate if it contained cells from the target organ (Fig. 3C). Inadequate specimens were not included in the statistical calculation of diagnostic accuracy.

## RESULTS

FNAB of pancreatic lesions was attempted in 45 patients. Lesions were located in the head in 28 patients, the body in 12 patients, and the tail of the pancreas in 5 patients. In 5 patients the needle failed to penetrate indurated lesions despite repeated attempts using different sites and angles to access the lesion. Four of these five patients subsequently underwent surgery; the surgical pathology demonstrated chronic calcifying pancreatitis in two patients and malignancy associated with chronic pancreatitis in the other two. In the remaining 40 cases an average of 2.6 needle passes were performed (range one to five passes). Adequate material for a histologic and/or cytologic diagnosis was obtained in all patients (Table 2). Core specimens ranged from 0.5 to 3 cm in length; histology showed normal exocrine pancreatic tissue in 9 cases, malignancy in 9 cases, and changes consistent with chronic pancreatitis in 13 cases (Fig. 3B). Cytology showed normal cells in 20 cases, inflammatory cells in 1 case, suspicious (atypical) cells in 7 cases, and malignant cells in 6 cases (Fig. 3C).

When the results of cytology and histology were combined, the sensitivity for detection of malignancy was 76% (13 of 17 lesions with a final diag-

**Table 2.**  
**FNAB results**

Diagnostic category	Cytology	Histology
Adequate	34	31
Normal	20	9
Inflammatory	1	13
Suspicious (cellular atypia)	7	—
Malignant	6	9

nosis of malignancy). The sensitivities of histology and cytology alone were 70% and 53%, respectively. Four patients had false-negative FNAB results (three patients had surgically confirmed adenocarcinomas and one patient died 2 months after FNAB and was therefore presumed to have a pancreatic malignancy [Table 3]). There were no false-positive results (specificity of 100%). The final diagnosis was established by surgery in 24 patients and clinical follow-up (median 11 months, range 7 to 16) in 21 patients.

Histology established a diagnosis of malignancy in nine cases (adenocarcinoma in seven patients, anaplastic carcinoma in one patient, and a neuroendocrine tumor in one patient). Of these, cytology showed malignant cells in five and cells that raised a suspicion of malignancy in three patients; in one patient the cytologic specimen was inadequate. Histology showed intralobular and interlobular fibrosis consistent with a diagnosis of chronic pancreatitis in 14 patients (Fig. 4). Of these, cytology showed benign cells in 11 patients, malignant cells in 1 patient, and "suspicious" (atypical) cells in 2 patients. Malignancy was surgically confirmed in the three patients who had malignant or "suspicious" cytology.

The only complication was post-procedural pancreatitis in one patient. This patient had a history of recurrent attacks of pancreatitis and underwent FNAB after a 3 cm hypoechoic lesion was identified in the body of the pancreas. The clinical course was uncomplicated and symptoms resolved with conservative treatment. None of the patients experienced clinically relevant bleeding (hematemesis, melena, drop in hemoglobin, or transfusion requirement). Perforation did not occur.

## DISCUSSION

Several studies have reported on EUS-guided aspiration to obtain tissue specimens for cytologic diagnosis of pancreatic lesions.<sup>1-5</sup> The investigators in these studies used 22- or 25-gauge needles that were inserted through the 2.0 mm working channel of the Pentax FG 32 UA convex array echoendo-

**Table 3.**  
**False-negative FNAB results**

Patient	Age (yr)	Cytology	Histology	ERCP finding	Computed tomography finding	EUS finding	CA 19.9 (normal <37 U/L)	Surgical pathology
1	69	Inadequate	Chronic pancreatitis	PD stenosis, head	Not done	Inhomogenous pancreatic head with microcysts	177	Adeno-CA, T2, N1
2	48	Normal pancreatic cells	Core specimen not obtained	PD stenosis, genu	Dilated pancreatic duct, no mass	2 cm pancreatic head mass	41	Adeno-CA, T2, N1
3	59	Normal pancreatic cells	Chronic pancreatitis	Double duct sign	Pancreatic head mass, dilated extrahepatic ducts	4 cm pancreatic head mass infiltrating CBD and portal vein	45	Adeno-CA, T3, N0
4	68	Insufficient material	Chronic pancreatitis	Not done	Pancreatic head mass	4 cm pancreatic genu mass	72	Patient died 2 months after FNAB

CA, Carcinoma; PD, pancreatic duct; CBD, common bile duct.

scope. The reported yield for adequate cytologic specimens has ranged from 82% to 91%. Two studies<sup>1,3</sup> mentioned that core biopsy specimens were occasionally obtained, but specific data regarding the histologic yield was not provided.

Harada et al.<sup>6</sup> recently reported the preliminary results of EUS-guided needle biopsy in 19 patients using a prototype 0.82 mm (21 gauge) needle in conjunction with a prototype electronic linear scanning echoendoscope (Toshiba Co., Tokyo, Japan). The authors reported a diagnostic histologic yield of 79% (15 of 19 patients). The majority of patients in this study had biopsy specimens obtained from submucosal tumors; attempts were made to obtain pancreatic biopsy specimens in only two patients. Histology in one of these patients was inadequate (showed gastric mucosa), and no further data are provided regarding the result of pancreatic biopsy in the other patient.

An 18-gauge needle was used in this present study in conjunction with a prototype 2.8 mm working channel convex array echoendoscope to obtain material for both histologic and cytologic study. An adequate core specimen for a histologic and cytologic diagnosis was obtained, respectively, in 68% and 75% of 45 cases. By combining the results of histology and cytology, an FNAB diagnosis was possible in 40 cases.

Our yield for cytology (75%) was low compared with that reported in other studies.<sup>1-5</sup> There are several explanations for this. First, there were

methodologic differences between our study and those of other authors. Our primary goal was to obtain a histologic specimen; accordingly, we first ejected the contents of the needle into formaldehyde by means of an air-filled syringe. Residual material was smeared on slides for cytologic analysis. Once a core specimen was obtained, further passes were not performed. Second, in contrast to the studies by Chang et al.,<sup>1</sup> Wiersema et al.,<sup>2</sup> and Gress et al.,<sup>5</sup> we did not have a cytologist or cytotechnician present during the procedure to verify the adequacy of specimens. Finally, we defined an adequate cytologic yield by the presence of cells of pancreatic origin. It is not clear from other studies whether the same criterion for cytologic yield was used.

A final diagnosis was established by surgery in 24 patients and clinical follow-up in 21 cases. Clinical follow-up has obvious drawbacks, compared with surgery, in establishing a final diagnosis. Nonetheless, we feel that the margin of error is small in this study given the relatively long follow-up period (median of 11 months), during which patients harboring a malignancy would be expected to demonstrate signs of clinical deterioration. The clinical outcome was found to be consistent with the FNAB diagnosis in all of the patients who did not undergo surgery. It must be emphasized that the FNAB results were weighed together with the clinical history, tumor marker levels, and findings on ancillary studies in determining the indication for surgery. In all of the patients with a benign FNAB diagnosis

who did not undergo surgery, the index of suspicion for pancreatic malignancy before FNAB was low and these patients continued to demonstrate a benign course of disease after FNAB.

The overall sensitivity of FNAB in diagnosing pancreatic malignancy was 76% (four false negatives). A relatively high rate of false negatives has also been reported for percutaneous ultrasound- and CT-guided FNAB.<sup>7,8</sup> This is explained by a marked desmoplastic reaction that typically accompanies pancreatic carcinoma. Of the four patients with false-negative FNAB results in our study, three had histology that showed fibrotic changes consistent with chronic pancreatitis (Table 3). Patients underwent surgery despite a negative FNAB result because the clinical history and endosonographic findings were believed to be strongly suggestive of malignancy.

Core biopsy specimens for histologic study complemented cytology in that they provided additional information regarding tissue origin, degree of tissue inflammation and fibrosis, tumor type, and differentiation grade. In three cases histology established a diagnosis of malignancy where cytology was not conclusively malignant (atypical cells were seen). In 11 cases histology established a diagnosis of chronic fibrosing pancreatitis where cytology revealed benign pancreatic cells.

Histology was not found to detect malignancy when cytology was benign. In fact, we found the reverse to be the case: in three cases of surgically confirmed malignancy, tissue fragment analysis failed to detect malignancy, but cytology showed malignant (one case) or atypical cells. These results argue strongly in favor of submitting a specimen for cytologic study, even when a tissue core specimen is obtained.

We encountered several technical problems using the 18-gauge needle. The increased diameter of the needle made penetration of indurated pancreatic lesions more difficult. Penetration was impossible in five patients, and the procedure was abandoned after repeated failed attempts. The increased needle stiffness posed two problems. First, it was difficult to pass the needle through the echoendoscope when the tip was angulated. For transduodenal FNAB, the echoendoscope tip had to be straightened, sometimes necessitating withdrawal of the echoendoscope back into the stomach. Second, having inserted the needle through the working channel, the bending section of the echoendoscope tip became stiffer, thereby limiting tip angulation. For transduodenal FNAB, this loss of tip angulation made it more difficult to visualize and access the lesion for

FNAB (loss of tip angulation was less of a problem for transgastric FNAB because the lesion could usually be visualized with minimal angulation of the echoendoscope tip). The stiffer needle also restricted the elevator function (loss of 5 to 10 degrees in range of motion). The increased needle stiffness did not result in any FNAB failures as this could be adequately compensated for by changing the position of the echoendoscope tip relative to the lesion. However, because of the more tangential approach, it was often the case that biopsy specimens could be obtained only at the periphery of the lesion.

Acute pancreatitis was the only procedure-related complication observed in our study. This occurred in a middle-aged woman with a history of recurrent attacks of pancreatitis who underwent FNAB of a discrete hypoechoic lesion in the body of the pancreas; after the procedure, the patient developed severe abdominal pain associated with markedly elevated serum amylase and lipase levels. Symptoms and enzyme elevation resolved with conservative treatment, and the patient was discharged after 3 days. Acute pancreatitis after EUS-guided FNAB was reported by Gress et al.<sup>5</sup> in 2 of 121 patients (2%) who underwent FNAB of pancreatic lesions. Both patients were discharged after 3 days. Although minor oozing was occasionally observed to occur after FNAB, clinically significant bleeding resulting in hematemesis, melena, or a decrease in hemoglobin greater than 2 gm% did not occur. Gress et al.<sup>5</sup> reported significant bleeding in two patients after EUS-guided FNA, one of whom had a fatal outcome. It is noteworthy, however, that a radial scanning echoendoscope (Olympus GF-UM20) was used for FNAB in both cases.

In conclusion, pancreatic core specimens for histologic examination can be safely obtained using an 18-gauge needle in conjunction with the prototype Olympus convex array echoendoscope. Histology and cytology should be regarded as complementary in the final diagnosis. Histology provides more tissue-specific information. However, it may fail to detect malignancy when cytology is positive. Thus, procurement of a core specimen for histology does not obviate the need for cytology. Further studies are required to determine the optimal strategy to maximize the yield and sensitivity of EUS-guided FNAB.

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