Indications and techniques for cytologic sampling of pancreatic and bile duct lesions

William R. Brugge, M.D.
Professor of Medicine
Harvard Medical School
Director, GI Endoscopy
Massachusetts General Hospital
Pancreatic Malignancies

Malignant

Solid

Adenocarcinoma

Benign

Solid

Neuroendocrine

Cystic

Intraductal papillary mucinous neoplasm

Cystic

Serous Cystadenoma
Pancreatic Cancer Development

Colon
Adenoma-Carcinoma Sequence:

Pancreatic
PanIN-Carcinoma Sequence:
Detection of Pancreatic Cancer

- **Key features on imaging**
  - Dual phase contrast
  - Early phase: arterial - pancreas
  - Late phase: venous - liver
  - Low attenuating mass - adenocarcinoma
Detection of Pancreatic Cancer

- Focal hypoechoic mass
- Invading and obstructing the CBD
- The appearance is not completely diagnostic of a malignancy
Differential Diagnosis of the Pancreatic Mass

- Autoimmune Pancreatitis
- Neuroendocrine tumor
- Chronic Pancreatitis
Pancreatic Neuroendocrine Tumor

- Most tumors are ‘non-functional’
- Histology: sheets of small cells
- Cytology: round secretory cells
- EUS: Doppler demonstrates hypervascular stroma
Autoimmune Pancreatitis

Diffuse infiltration of the pancreas

Focal plasma cell infiltration

Enlarged pancreas
Diagnosis: EUS-Guided FNA

- Translumenal FNA
- Patent UGI tract
- Cytologic diagnosis
- Risk of pancreatitis
- Excellent yield in adenoCA
- Poor yield in AIP

EUS imaging

Cytology

Animation cip
Indications for EUS

- **Strong indications**
  - Focal lesion in pancreas
  - Dilated pancreatic-biliary ducts
  - Recurrent pancreatitis

- **Weak indications**
  - Chronic abdominal pain
  - Hyperamylasemia
  - Malignant-appearing pancreatic mass
    - Not surgical-Oncology candidate

- **Tissue acquisition**
- **Diagnosis**
- **Staging**
Contraindications for EUS

- Results will not change management
- Active severe pancreatitis
- Coagulopathy
- Esophageal stenosis
- No stomach!
EUS FNA Needles

- FNA needles
  - Beveled tip
  - Stylet
  - Disposable
  - Suction-aspiration
  - Slide smears
EUS FNA core needle

- Tissue core for histology
- Autoimmune pancreatitis
- Lymph node
- Additional FNA tissue
  - Pancreatic mass
  - GIST
  - NET
Accuracy of Pancreatic EUS FNA

- 559 patients with 560 FNA-sampled lesions were included.
- The sensitivity of EUS-FNA in the diagnosis of pancreatic adenocarcinomas and PENs was 77% and 68%.
- Reclassification of atypical and suspicious cytologies as diagnostic of malignancy resulted in a sensitivity of 93%, in adenocarcinoma and 80% in PEN.
- The accuracy of the examination is significantly improved (94%) when atypical and suspicious samples are considered positive.

Accuracy of EUS FNA

- Method: Data extracted from EUS-FNA studies with a criterion standard (either confirmed by surgery or appropriate follow-up) were selected.

- Results: Data were extracted from 41 studies (N = 4766) which met the inclusion criteria. Pooled sensitivity of EUS-FNA in diagnosing the correct etiology for solid pancreatic mass was 86.8% (95% confidence interval [CI], 85.5–87.9).

- Conclusions: Endoscopic ultrasound–guided FNA is an excellent diagnostic tool to detect the correct etiology for solid pancreatic masses.
False Positive FNA

- 377 patients with positive or suspicious cytology underwent surgery. The FP rate was 20/377 (5.3%) and increased to 27/377 (7.2%) when FS cases were included. The incidence of discordance was higher in non-pancreatic FNA (15%) than pancreatic FNA (2.2%; p=0.0001).

- Two-thirds of the non-pancreatic FP cases involved sampling of perioesophageal or perirectal nodes in patients with luminal neoplasms or Barrett's esophagus.

- FP FNA is particularly likely when perioesophageal or perirectal nodes are aspirated in the setting of a luminal neoplasm or Barrett's oesophagus.

Customizing FNA

Adenocarcinoma

GIST

Neuro-endocrine

Lymph node
Cytology Criteria

Malignant

Serous

Morphology

Small, round, bland

Nuclear atypia

Mucinous

Mucinous epithelium

Inflammatory

Pseudocyst
Mucinous vs Non-mucinous

Mucinous

Macrocystic

Microcystic

MCN

Cyst with associated mass

Morphology

Serous

Pseudocyst / Inflammatory

Cavity
EUS-Guided Fine Needle Aspiration of Cystadenomas

- Transgastric or transduodenal FNA
- 22 gauge needle
- Stylet to prevent contamination
- Evacuate contents
- One passage
- Antibiotics
Malignant vs Benign IPMN

- Benign
- High Grade
- Low grade
- Malignant
Cyst Fluid Biomarkers IPMN

Glycoproteins
- CEA

DNA

RNA
-miRNA 21

Enzymes
- amylase

- Oncogene k-ras
  mutation detection in codon 12 & 13
EUS-Guided Liver FNA

- 132 cases of malignancy.
- The diagnostic accuracy of EUS/EUS-FNA and CT scan was 98% and 92%.
- In comparison to CT scan, EUS detected significantly higher number of metastatic lesions in the liver.

Types of Cholangiocarcinoma

- Mass forming
- Peri-ductal
- Intraductal
Endoscopic Diagnosis

- Imaging
- Staging
- Biopsy

EUS

Video

ERCP

IDUS
Bile Duct Strictures
morphology

- Symmetry
- Contour
- Texture
- Length
Recognition of Common Morphologies

Focal Strictures
- Pancreatic CA
- CHD Cholangio CA
- Hilar Cholangio CA

Multiple Intrahepatic strictures

Benign
Role of EUS

- 50 patients with obstructive jaundice
- 28 malignant (16 panc, 12 biliary), and 22 benign
- Sensitivity
  - ERCP-guided biopsy: 36%
  - ERCP-guided cytology: 46%
  - EUS-guided FNA: 43%
- Bile duct CA: ERCP-bx was more sensitive than EUS-FNA (75% vs 25%)
- Pancreatic CA: EUS-guided FNA was more sensitive than ERCP (60% vs 38%).
- Start with ERCP if a biliary malignancy is suspected
- Start with EUS if a pancreatic tumor is suspected

- Peroral pancreatoscopy or cholangioscopy in 11 patients with various pancreatobiliary diseases.

- The new peroral electronic pancreatoscope was inserted successfully into the pancreatic or bile duct in 9 of the 11 patients (82%). Direct visualization of lesion was successful in 8 of the 9 patients (89%).

- Visualization was excellent.

Initial experience with a new peroral electronic pancreatoscope with an accessory channel
Tadashi Kodama, MD, Yoshihide Tatsumi, MD, Hideki Sato, MD, Yoichi Imamura, MD,
Evaluate the yield of EUS-FNA and its impact on patient management for patients with suspected cholangiocarcinoma

28 pts underwent linear EUS with FNA

67% (14/21) had no definitive mass seen on prior abdominal imaging studies

The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 86%, 100%, 100%, 57%, and 88%, respectively

EUS-FNA had a positive impact on patient management in 84% of patients

Bile duct brushings in 131 patients
- FISH assay used a mixture of fluorescently-labeled probes to the centromeres of chromosomes
- 39 pts had cholangiocarcinoma, 19 had pancreatic carcinoma, and 8 had other types of malignancy.
- Sensitivity of cytology and FISH was 15% and 34% (p < 0.01), respectively.
- The combined sensitivity of FISH for aspirate and brushing specimens was 35%.
- The specificity of FISH and cytology brushings were 91% and 98% (p= 0.06), respectively.

Cytology: New Methods

- 100 patients, 56 strictures were malignant and 44 were benign
- Standard brush cytology sampling was performed twice (cytology and digital image analysis)
- DNA histograms were generated for aneuploidy
- Sensitivities of Digital Image Analysis and Routine Cytology were 39.3% and 17.9%
- The accuracy of DIA (56.0%) was equivalent to RC (53.0%) but DIA was less specific

A prospective study of 60 patients with bile duct stricture of unknown etiology

Patients underwent ERC with transpapillary biopsy and IDUS

All had surgical resection

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
<td>52%</td>
<td>100%</td>
<td>60%</td>
</tr>
<tr>
<td>IDUS</td>
<td>96%</td>
<td>20%</td>
<td>83%</td>
</tr>
<tr>
<td>Biopsy + IDUS</td>
<td>98%</td>
<td>100%</td>
<td>98%</td>
</tr>
</tbody>
</table>

Domagk et al. Gut 2002
Conclusions

- Pancreatic mass evaluation and FNA are critical patient care elements
- Maximize accuracy of FNA
  - Dedicated team
  - On-site cytology
  - Feedback analysis