**Definition**

**Endoscopic Ultrasound (EUS)**

A small, high frequency ultrasound transducer is incorporated into the distal end of the endoscope.
Objectives

• Outline the technical aspects and capabilities of endoscopic ultrasound (EUS)

• Review the indications for EUS, and outline its role in the diagnosis and management of neoplastic and non-neoplastic disease

• Outline peri-procedural management issues and risks
Technical Aspects and Capabilities
Historical background

- Hippocrates ‘reflective mirror’
- 18th century sword swallower in Vienna
- Fiberoptics
- Video endoscopy
- Endoscopic ultrasound (EUS)
Technical Advantages

**Conventional US**
- ‘From the outside in’
- Imaging compromised by intervening bowel gas
- Low frequency (2.5-3.5 MHz)
- High depth penetration
- Lower resolution

**Endoscopic US**
- ‘From the inside out’
- Image not compromised by intervening gases.
- Higher (7.5-30 MHz) frequency
- Superior resolution of target organs and structures.
- Lesions as small as 2-3 mm in diameter can be imaged.
EUS Equipment

Radial echoendoscope
• Introduced late 1980’s
• 360 degree field
• Image plane perpendicular to long axis of scope
• In axial orientation, image plane is that of a CT scan image
EUS Equipment

Linear echoendoscope

• Early 1990’s
• 180 degree field
• Image plane parallel to long axis of scope
• Fine needle aspiration (FNA) capability
• Exiting needle visible in image plane
Where EUS can go …

EUS Images the:
- Wall of the esophagus / stomach / duodenum
- Entire pancreas
- Extrahepatic bile duct, gallbladder, liver (75%)
- Vascular structures: Aorta, celiac axis, SMA, portal vein, splenic vein, SMV
- Regional lymph nodes
- Left kidney, spleen, left adrenal gland

Radial echoendoscope tip entering the stomach: The scanning plane (arrows) is perpendicular to the axis of the echoendoscope, providing cross-sectional views of the abdominal structures. Courtesy of Lyndon V. Hernandez, MD and Manoop S. Bhutani, MD.
Where EUS can go …

• Images of mediastinal structures

• Trans-esophageal biopsy of posterior mediastinal lesions, including subcarinal, aortopulmonary, and peri-esophageal lymph nodes
Where EUS can go …

Via rectal approach:

• Anal sphincters
• Rectal wall
• Perirectal lymph nodes
• Perirectal structures: prostate, seminal vesicles, GYN structures
• Left internal iliac region lymph nodes
Indications
Subepithelial GI tract lesions

• “Subepithelial Lesion“: An endoscopically visible bulge that is covered by normal or nearly normal mucosa.

  e.g. leiomyoma
  lipoma
  cyst
  extrinsic compression
EUS in Subepithelial GI lesions

- Intramural vs. extramural
- Tissue layer of origin
- Echo features of intramural lesions
- Size, Margins
- Solid vs. Cystic
EUS Wall Layer Imaging
Duodenal submucosal lipoma
Muscularis propria layer mass
EUS-FNA of Gastric Subepithelial Lesions

- **Diagnostic Yield**:
  - 83% sensitivity
  - 73% specificity
  - 80% accuracy

- 10-15% improvement in yield through use of **on site cytopathology**
EUS-FNA Evaluation of Gastrointestinal Stromal Tumor (GIST)

**EUS appearance**
- EUS alone 65% sensitive, 80% specific at defining malignancy
  - Size > 3-4 cm
  - Irregular borders
  - Echogenic foci
  - Cystic spaces
  - Ulceration of mucosa
  - LN’s > 10 mm

**EUS-FNA (FNB, TCB)**
- Cytologic assessment of GISTs
  - Mitoses per 50 HPF
  - Nuclear atypia
- Immunohistochemical staining of FNA specimen
  - c-kit (or CD-117)
  - DOG1
  - Ki-67
EUS evaluation of “large gastric folds”

• Hyperplastic
• Infiltrating Carcinoma
• Menetrier's disease
• Lymphoma
• Intramural varices
EUS In Luminal GI Malignancy

- Locoregional staging of GI malignancy is the best established indication for EUS.
  - Esophageal CA
  - Gastric CA
  - Rectal CA

- EUS accuracy 85% (compared to 40% for CT)
Progression of GI Tract Cancers

- Most GI tract cancers start in the mucosa, and grow to involve deeper layers
- Spread to regional lymph nodes
- Spread to distant lymph nodes and distant organs
TNM Staging Approach* to Luminal GI Cancers

- IMAGING to assess for distant metastasis (M)
- Endoscopic ultrasound (EUS) for locoregional staging:
  - Depth of invasion (T category)
  - Regional lymph node involvement (N category)

* Applies to Esophageal, Gastric, Rectal cancers
Case 1: Esophageal Adenocarcinoma

Endoscopic Findings

EUS Findings
Case 1: Esophageal AdenoCA

- Clinical Stage: uT3N1MX
- Preferred treatment is neoadjuvant chemoradiation therapy prior to surgery
Role of EUS in Esophageal CA

- Prognostication
- Neg. mucosal biopsy w/ high clinical suspicion
- EUS-FNA for nodes 85-95% sensitive
- Staging guides therapy:
  - T1 tumors (some) may be candidates for endo tx
  - T3 / Node positive tumors – neoadjuvant chemoradiation
  - T4 tumors inoperable (EUS > CT)
  - Identification of occult M1 disease (liver mets)

EUS in Barrett’s Esophagus

• Detect “missed cancer” in Barrett’s with high grade dysplasia (HGD)
  – Rate is as high as 43% \(^1\)
  – No proof that EUS can detect this

• *In Barrett’s with HGD, exclude regional LAN that could indicate metastatic disease – alters therapy*
  – *Generally not warranted in low grade dysplasia or no dysplasia*

• Evaluate a suspicious lesion within Barrett’s
  – Low sensitivity (50-60%) for early stage disease \(^2\)

\(^2\) AGA Tech Review, Gastroenterology, 2011.
Case 2: Rectal Adenocarcinoma
Abnormal Appearing Perirectal lymph node
Perirectal lymph node sampled with an endoscopic ultrasound-guided fine needle aspiration
EUS performance in staging rectal cancer

- T stage accuracy: 63-100%

- N staging
  - EUS: 64-86%
  - EUS-FNA: 76-82%
Rationale for EUS staging in rectal cancer

• High post surgical recurrence rates: 20-50%
• Preoperative XRT reduces recurrence in T3 and N1 tumors vs. postoperative XRT
  – 12% [preop XRT] vs. 21% [postop XRT]
• Swedish Rectal Cancer Trials showed a survival benefit with preoperative XRT for patients with advanced disease
  – T3N0, TxN1

¹ Pahlman, L. Ann Surg 1990
Rationale for EUS staging in rectal cancer, cont.

- Study of 80 patients with rectal CA
  - EUS changed management in 25 (31%) \(^1\)

- Recurrence-free survival better for EUS vs. non-EUS staged rectal cancer patients \(^2\)

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\(^1\) Harewood et al, Gastroenterology 2002.

\(^2\) Harewood et al, Journal of Gastro and Hepatology, 2004
Rectal Cancer – Pitfalls with EUS

• Stenotic tumors
• Tumors extending into the anal canal
• T2 tumors
  – Understaging due to microinvasion
  – Overstaging due to desmoplasia
• Lymph node evaluation
• Limited role in staging post XRT
EUS in Lung Cancer

- Most common neoplasm in Western world
- Management based on Type and Stage
- NSCLC prognosis correlates closely with presence of mediastinal LAN (28-38%)
- Patients with large subcarinal nodes or contralateral LAN are unresectable, with 5 yr survival < 5%
EUS in Lung Cancer

• Identification of the following involvement drastically alters management:
  – N2 (ipsilateral mediastinal &/or subcarinal LN)
    • Stage IIIA (some get surgery + chemo/XRT)
  – N3 (contralateral mediastinal LN)
  – T4 (invasion of mediastinal structures)
    • Stage IIIB (inoperable)
  – M1 (left hepatic lobe, left adrenal gland, celiac LN)
    • Stage IV (inoperable)
EUS-FNA of Mediastinal LN’s

All mediastinal LN’s that can be assessed from the esophagus.

EUS-FNA provides particularly good access to lower mediastinal nodes (7, 8, 9)

Left adrenal gland
Celiac nodes
Left hepatic lobe
EUS Underutilization in NSCLC


  “Knowledge of indications and utilization of EUS: a survey of oncologists in the United States”

- Utilization of EUS for staging NSCLC: 19 %

- “EUS has a role in staging NSCLC”: 61.5 %
Multimodality staging approach

- CT and PET scanning target which patients may benefit most from EUS-FNA (i.e. those with posterior mediastinal LN’s)

- EUS-FNA in posterior mediastinal LN’s
  - Sensitivity 88-96%, specificity 80-100%

- Alternative to mediastinoscopy or thoracoscopy

- EUS may identify advanced disease in up to 25% of patients with a “normal” mediastinum on CT
Routine use of EUS-FNA can spare futile thoracotomy

- Historically, 10-45% futile
- Larsen, SS et al, Lung Cancer 2005 Randomized Clinical Trial

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<td>Futile Thoracotomy</td>
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EUS in Non-Small Cell Lung CA

- NSCLC is the most prevalent malignancy for which EUS has a role in diagnosis, treatment, and prognosis.

- Mediastinal LN staging (N2/N3) and identification of metastases (stage III/IV) are critical determinants of therapy and prognosis for these patients.

- EUS-FNA is safe, and highly sensitive and specific for mediastinal LN involvement with NSCLC. EUS-FNA can dx metastases to Left Adrenal, Liver, and Celiac Nodes, and can spare futile thoracotomy.

- EUS-FNA compares favorably with alternative approaches to mediastinal staging, alone or in combination.

- EUS-FNA has a role in staging NSCLC patients even with radiologically negative mediastinum, and has a role in primary biopsy of centrally located lung lesions, as well as restaging of patients after chemo-XRT.
Other indications for EUS and EUS-FNA in the mediastinum

Benign

- Achalasia
- Duplication cyst
- Infection (Histo, TB)
- Sarcoidosis
- Extrinsic compression
- Portal hypertension

Malignant

- Pseudoachalasia
- Other mediastinal malignancies (lymphoma, breast cancer)
EUS in pancreatic disease

- **Neoplasia**
  - Solid tumors
    - Pancreatic ductal adenocarcinoma
    - Neuroendocrine tumors
    - Metastases (renal cancer, lung cancer, and lymphomas)
  - Cystic tumors
    - Serous and mucinous cystadenomas
    - Cystadenocarcinomas
    - Intraductal papillary mucinous neoplasm (IPMN)

- **Non-neoplasia**
  - Pseudocysts
  - Chronic pancreatitis
Pancreas Adenocarcinoma

Head Lesion

Body Lesion
EUS in pancreatic CA

• In clinically suspected cases (i.e. painless jaundice / biliary obstruction), EUS detects more tumors than CT (97 vs. 73%)
• EUS more accurate than CT for determining resectability, and more sensitive for vascular invasion
• CT better than EUS for evaluation of distant metastasis
EUS-FNA in pancreatic CA

• EUS-FNA useful for tissue confirmation in unresectable cases. Also useful to distinguish adeno CA from alternative solid tumors.
• EUS-FNA often diagnostic when other sampling techniques (ERCP, percutaneous biopsy) have failed
• EUS-FNA can sample lesions (including LN’s) too small to identify by other methods
• EUS-FNA traverses the intestinal wall (typically part of the resection specimen) thus reducing the risk of “tumor seeding”
The Incidental Pancreas Cyst

- Differential Diagnosis:
  - Pseudocyst
  - Simple Cyst
  - Pancreatic Cystic Neoplasm
  - Cystic degenerated solid neoplasm
    (primary / metastatic)
Pancreatic cystic neoplasms

- Up to 10% of pancreatic cystic lesions are neoplastic

Malignant

- Cystadeno-carcinoma

Malignant potential

- Mucinous cystadenoma

“Benign”

- Serous cystadenoma

IPMN

- Main duct

- Side Branch

Retention cyst
Pancreatic cystic neoplasms: Microcystic serous cystadenoma

Endoscopic Ultrasound

Surgical Specimen
Mucinous Cystadenoma of the Pancreas
Intraductal papillary mucinous neoplasm (IPMN)

CT scan appearance

EUS shows mural nodule
Role of EUS, EUS-FNA in pancreatic cystic tumors

- Imaging information / fluid analysis
- *No EUS features have proven consistently reliable to distinguish benign vs. malignant*

- Fluid sent for amylase, CEA, cytology, (+/- KRAS)
- Using a cutoff of 192 ng/mL, **CEA levels** were most accurate for differentiating mucinous versus nonmucinous cystic lesions (80% accuracy) *

- Mucinous lesions, or uncertain lesions, should be resected

Management of Asymptomatic Neoplastic Pancreatic Cysts (AGA Guidelines, 2015)

Cyst on Imaging

Two or more +ve features on MRI

+ve feature=dilated MPD, >= 3 cm cyst or solid component

No

Yes

Repeat MRI in 1 year
Then biennially to yr 5
+ve features on MRI at any point during 5 yr F/U

Yes

EUS + FNA

Concerning cytology and/or 2 features +ve

No

Repeat MRI in 1 yr then biennially to yr 5
Interval change of +ve features during 5 yr F/U

No

Yes

Stop surveillance
Repeat EUS + FNA

Concerning cytology then biennially to yr 5

Yes

Concern Consider Surgery
EUS in chronic pancreatitis

Function
- Direct hormonal stimulation tests
- Bentiromide test
- Serum trypsin-like immunoreactivity
- Fecal chymotrypsin or fecal elastase
- Quantitative fecal fat

Structure
- ERCP
- CT
- MRCP (+/- secretin)
- U/S
- Plain abdominal Xray
- EUS (+/- secretin)
EUS in chronic pancreatitis

- “Parenchymal” and “Ductal” criteria
- Sensitivity drops and specificity rises as a higher cutoff number of criteria “define” chronic pancreatitis
- Some criticize EUS as overly sensitive; some criticize other modalities as insensitive
- Age-related variations may limit usefulness
EUS for suspected gallstones

- Thorboll, J et al
  35 patients with biliary pain and neg U/S
  EUS
  18 w/stones  17 not
  15/17 verified
  13/15 asymp at 1 year
Case 3: Symptomatic gallstones

Likelihood of choledocholithiasis?

Low probability  
(Normal LFT’s)  
(Non dilated CBD)  
→ LAP CHOLE

Intermediate

→ Lap Chole w/ IOC
  → MRCP
  → EUS

High probability  
(Jaundiced)  
(Cholangitis)  
→ ERCP
EUS in choledocholithiasis

- Up to 95% sensitive, 98% specific
- MRCP 81-92% sensitive for stones >3mm
- Only EUS can detect sludge & microlithiasis with high accuracy, and provide simultaneous EGD.
EUS in Acute Recurrent Pancreatitis

• “Idiopathic”
• U/S and CT workup negative
• Causes include microlithiasis or biliary sludge, chronic pancreatitis, anatomic abnormalities (pancreas divisum, small tumors), Sphincter of Oddi dysfunction (SOD)
• EUS can diagnose all but SOD
• Studies indicate 68-78% diagnostic yield for EUS
EUS guided Celiac Plexus Intervention

- **Celiac Plexus Neurolysis**
  - Unresectable pancreatic CA
  - Refractory to narcotics
  - 78-88% effective palliation
  - Bupivicaine / dehydrated alcohol

- **Celiac Plexus Block**
  - Chronic pancreatitis
  - Less established / less favorable
  - Highly selected patients / appropriate consent
Peri-procedural management and Risks
Peri-procedural management

• Anti-platelet and anti-coagulant therapy managed as for other forms of endoscopy
• NPO status, bowel preparation (for per-rectum exams)
• Hospital based outpatient examinations
• Patients scheduled for EUS-FNA of a perirectal lesion or any type of cystic lesion receive prophylactic quinolone, continued for 2-5 days post procedure as outpatient
• Currently, Propofol sedation employed for diagnostic or ‘straight forward’ EUS-FNA exams. General ET anesthesia as indicated for prolonged / complex exams
• Intraprocedural consultation with cytopathology
Risks of EUS-FNA

• Three large published series, over 900 EUS-FNA’s of solid tissue structures, no biopsy-related complications
• Multicenter study of 554 mass or LN biopsies, five complications (about 1%), including 2 perforations, 2 fevers (cystic lesions), 1 hemorrhage
• Pneumoperitoneum has been reported when EGD performed within 2 days of EUS-FNA
• Pancreatitis risk is 0.3-0.6% for FNA of solid pancreatic masses, 1-3% in cystic lesions
• Bacteremia risk low. ? Risk of cystic lesion infection.
• Acute portal vein thrombosis reported after pancreatic mass FNA
• Risk of perforation with dilatation of esophageal malignancy to permit passage of echoendoscope
Future Directions

**Diagnostic**
- EUS-miniprobes for higher frequency
- Scope / image enhancements
- EUS elastography
- EUS cholangiography
- FNA / FNB needles
- 3 dimensional EUS

**Therapeutic**
- Directed chemo-sclerotheray
- Directed gene therapy
- Radiation seed implantation
- EUS-guided biliary-enteric anastomosis
- EUS-assisted NOTES
THANK YOU

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