EUS: Present and Future

BY RYAN O’CONNOR

3/12/15
Overview

- General
- Current indications
  - Upper
  - Lower
- Interventional/therapeutic
- Future
Ultrasound (US)

- **Sound** – *mechanical energy in the form of vibrations* that propagate through a medium (air, water, tissue)
  - Audible sound 20 – 20,000 Hz
  - US > 20,000 Hz
  - Bats 100,000 to 200,000 Hz
  - Medical applications 1,000,000 – 5,000,000 Hz

- Propagation of US results from the displacement and oscillation of molecules from their average position and the subsequent displacement and oscillation of molecules along the direction of the ultrasound wave
Anechoic

A structure that does not produce any internal echoes
Hypo-echoic:
An area that has decreased brightness of its echoes relative to an adjacent structure

Hyper-echoic
Hyper-echoic:
A structure which has increased brightness of its echoes relative to an adjacent structure

Shadowing (artifact):
Failure of the sound beam to pass through an object resulting in:
- Hyperechoic signal at the interface and no echo signal beyond the interface.
- Gallstones
- Pancreatic calcifications
Equipment

- Radial
- Linear
FNA Needle

- EUS-FNA Devices
  - 19G, 22G, 25G
  - Hollow needle
  - Removable stylet
  - Semi-rigid protective sheath
  - Handle with port
  - Syringe attachment
  - Suction
Needle Core Biopsy

- Hollow 19, 22G cutting sheath
- Needle with 5mm beveled tip, 18mm tissue tray
- Spring-loaded
- Trucut
Miniprosbes

- Range in size from 2-2.6mm
- Mostly mechanical radial
- Require additional motor drive unit
- Usually high frequency with shallow depth
- Good small mucosal/subepithelial lesions, and intraductal use
- Poor for staging esophageal tumors or large polyps
- Difficult to exclude air at sites of contact

Indications

- Staging cancers / FNA
- Mediastinal lymphadenopathy
- Confirming EMR potential
  - T1 disease, excluding sub-mucosal involvement
- Diagnosis and follow up of lesions
  - GIST, lipoma, cysts
- Investigating RUQ pain
- Investigating pancreatitis
- Possible CBD stone
- Fecal incontinence
- Therapeutics
  - Celiac neurolysis, Fiducials, Drainage procedures, fine needle injection therapy
Malignancy

- Assessment of operative risk
- Determination of T and N staging
  - In general EUS provides >85% accuracy
  - Staging Locoregional disease
    - EUS > PET CT or CT
    - GI luminal cancers
    - Pancreatic Ca
- Nodal staging
  - Lung/ Pancreatic/Rectal/Esophageal/Gastric
  - 75% accurate for predicting malignancy
Malignancy

- Shortcomings:
  - Poor for metastasis (unless mets are in Left lobe of the liver or adrenal gland)
  - Has not or cannot be used beyond mouth to duodenum and rectum
Mediastinum

- Subcarinal space
- Aorto-Pulmonary window
- LN
  - round shape, short-axis diameter greater than 10 mm, hypoechoic echotexture, and well-demarcated borders
  - Chance of malignancy is 80% to 100% if all 4 are present

Lung Cancer: A Brief Overview

- In the US, lung cancer is the most common cause of cancer deaths among both men and women.
- North Americans have the highest rates of lung cancer in the world.
- The 5-year survival rate for patients with lung cancer is only 14%.
- 50% of lung cancer patients have mediastinal lymphadenopathy at the time of diagnosis.

Non-small cell Lung Cancer

- CT and PET CT have low sensitivity and specificity
  - Negative CT results for mediastinal adenopathy is falsely negative 35%

- Advantages of EUS
  - Diagnostic accuracy is equal to surgical mediastinoscopy when used with EBUS
    - Reduces the number of mediastinoscopies and unnecessary thoracotomies
  - Can additionally evaluate for distant adenopathy and Left adrenal gland
  - LN sampling
    - Performed when management would change (i.e., LN contralateral to primary tumor)
    - Mediastinal lymph node metastases or mediastinal tumor invasion (stage III) are preferably treated with chemoradiation therapy
    - Without locally advanced disease - surgical resection

N-Staging

- N0 absence of any lymph node involvement
- N1 presence of cancer in the hilar lymph nodes
- N2 refers to an involvement of the mediastinal lymph nodes on the cancer side
- N3 cancers involve the lymph nodes on the other side of the chest or in the supraclavicular area

EUS Mediastinal Biopsies: Most Frequent Indications

- Bronchoscopy negative, but mediastinal adenopathy present (diagnosis)
- PET scan equivocal, i.e., “warm” spot in the mediastinum (staging)
Modalities

- Bronchoscopy: good for endobronchial lesions Subcarinal biopsies with Wang needle. Bleeding risk
- CT-guided transthoracic fine needle aspiration (FNA): limited by surrounding vascular structures, size of the targeted lesion. Pneumothorax risk
- Mediastinoscopy: invasive, requires general anesthesia. Subcarinal and subaortic (a-p window) nodes inaccessible
- Thoracoscopic biopsy (video-assisted thoracoscopy): limited to inferior mediastinum
- EUS-FNA

Varadarajulu S, Hoffman BJ, Hawes RH, Eloubeidi MA. EUS-guided FNA of lung masses adjacent to or abutting the esophagus after unrevealing CT-guided biopsy or bronchoscopy. Gastrointest Endosc 2004; 60:293.
Mediastinoscopy: Overused, Invasive, Limited Applications
Thoracoscopy: Limited To Inferior Mediastinum

Thoracoscopy is performed with a video monitor to allow diagnostic evaluation of a lung mass.
EUS: No Incision

Scans in plane parallel to axis of scope
Biopsy channel (with fine biopsy needle)

Scans in plane perpendicular to axis of scope
Transducer
Plane of imaging

EUS directed mediastinal lymph node biopsies are especially helpful for sub-carinal and subaortic lymph nodes.
Gastric Ca

- Useful for staging gastric cancer but ineffective for screening
  - Most important diagnostic procedure for local staging
  - Preoperative assessment of local tumor extent that will determine the choice of treatment
- Endoscopic mucosal resection (EMR) if:
  - Well differentiated and intramucosal
  - Superficial submucosa (<500μm), and the diameter of the tumor is less than 3cm
- T2 or T3 disease are treated surgically, T4 disease undergo palliative therapy
- Negative predictive value for metastatic disease in patients staged T1 or T2, N0 by EUS was 96%.
  - May negate laparoscopic staging

Esophageal Cancer

- 10\textsuperscript{th} leading cause of cancer death
- Fastest growing
- 15,000 diagnosed annually
- Prognosis and treatment dependent upon stage
  - TNM staging critically important
  - CT & EUS


Esophageal Cancer

- Survival based on stage
- Preoperative staging to consider operative risk
- CT to evaluate metastatic disease
- EUS for locoregional evaluation


Esophageal Ca

- Initial triage of patients to receive neoadjuvant therapy, immediate surgical resection or endoscopic mucosal resection
  - Nodal involvement - preoperative therapy
  - T1 or T2 tumors (without nodal involvement) - surgical resection
- EUS is superior to computed tomography and positron emission tomography in celiac and peritumoral lymph node detection
  - EUS fine-needle aspiration can document persistent lymph nodes in the celiac axis
- Downside:
  - Application of EUS after administration of chemoradiotherapy cannot accurately differentiate residual tumor from radiation effect

Limitations of EUS Staging

- Overstaging more frequent than understaging
  - Particularly T2 lesions
  - Peritumoral inflammation
- Restaging after chemoradiation frequently desirable but accuracy is limited
  - Difficult to differentiate post treatment fibrosis/inflammation from tumor

Endoscopic Mucosal Resection (EMR)

- Indications
  - Raised lesions
  - Focal area of dysplasia
  - Suspicion of malignancy
  - Barrett’s esophagus with dysplasia

Ell C, Gastroenterology 2000; 118:670-7
## CT vs EUS: Esophageal Ca

<table>
<thead>
<tr>
<th>Technique</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT - T stage</td>
<td>40-80</td>
<td>14-97</td>
</tr>
<tr>
<td>CT - N stage</td>
<td>40-73</td>
<td>25-67</td>
</tr>
<tr>
<td>EUS – T stage</td>
<td>71-100</td>
<td>67-100</td>
</tr>
<tr>
<td>EUS - N stage</td>
<td>60-97</td>
<td>40-100</td>
</tr>
</tbody>
</table>

Pancreatic Ca

- EUS is the most sensitive imaging modality for the detection of pancreatic masses
- EUS = CT in terms of staging Ca
- Can identify lesions missed on CT
  - Mets in left lobe of liver, perivascular cuffing by tumor, malignant involvement of celiac ganglia
  - Small pancreatic tumors that are missed on CT and likely are resectable
- Vascular involvement:
  - If visible on CT then EUS has comparable accuracy
- Tissue sampling
  - >85-95% accuracy with FNA, sensitivity 85-92% and specificity approaching 100%
    - Other lesions may be more difficult (pancreatic cysts, stromal tumors and autoimmune pancreatitis
      (?TruCut Biopsy)
    - FNA of liver metastases, ascites, or celiac adenopathy may avoid the need for surgical exploration.
- EUS is superior to CT and angiography for detection of tumor invasion of the portal vein or confluence. But CT superior to EUS for invasion of the mesenteric vessels and major arteries of the upper abdomen.
- Most accurate modality for pancreatic neuroendocrine tumors, smaller than 2.0 cm

Exocrine Pancreatic Cancer

- Poor survival (5yrs, 4%)
- 44,000 diagnoses annually
- 39,000 deaths annually
- Lifetime risk 1 in 71 (1.41%)
- Up to 85% unresectable at diagnosis


Pancreas Cancer

- Pancreatic resection 5 year survival
  - 25-30% Node negative disease
  - 10% Node positive disease
Computed Tomography (CT) scan

- Essential tool in diagnosis
- Risk of kidney toxicity from dye administration; risk of ionized radiation
- Multi Detector Row Helical CT with 3D reconstruction
- Sensitivity 100% tumors >2cm
- 77% tumors < than 2 cm

Bronstein et al. Detection of small pancreatic tumors with multiphasic helical CT. AJR 2004
MDCT

- Arterial phase - first 30 seconds
  - Celiac, SMA, peri-pancreatic arteries
- Pancreatic phase
  - After peak enhancement aorta
- Portovenous phase (60-70 seconds)
  - SMV, PV, hepatic mets

EUS Criteria for Vascular Invasion

- Peripancreatic venous collaterals in an area of a mass that obliterates the normal anatomic location of a major portal confluence vessel
- Tumor within the vessel lumen (Invasion)
- Abnormal vessel contour or irregular wall with loss of the vessel-parenchymal sonographic interface (adherence vs abutment)

EUS FNA

- Histologic diagnosis
- Any lesion visible only by EUS should undergo FNA
- Sensitivity approx 90%; Specificity 96%; Risk <1%
- No difference in the cytological yield between tertiary and community centers

Singh S, Purhoit T, Dhawan M, Morrissey S, Thakkar S. Digestive Disease & Endosc. In press
Neoadjuvant therapy

- Preoperative chemo and/or radiation therapy for treatment of borderline resectable cancers
- Goals
  - Shrink tumor - downstage
  - Rule out bad biology - rapid progressors
  - Early treatment micrometastasis

## Vessel Encasement

<table>
<thead>
<tr>
<th>Encasement</th>
<th>Likelihood of Invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>180°</td>
<td>40%</td>
</tr>
<tr>
<td>&gt;180°</td>
<td>80%</td>
</tr>
<tr>
<td>&gt;270°</td>
<td>≈100%</td>
</tr>
</tbody>
</table>

Pancreatic Cancer Staging

T1 < 2 cm
T2 > 2 cm

Invades stomach, spleen, colon, or large arteries

T3
Invades into duodenum, bile duct, major veins or peripancreatic tissues

T4
Neoadjuvant Therapy

- MD Anderson - 84pts Borderline resectable disease vascular criteria
  - 40% 5yr survival
- Single center institutional studies 38-100% R0 resections

Fiducials

- EUS-Guided Fiducial Placement for Treatment of Pancreatic Cancer with CyberKnife Stereotactic Radiosurgery

- Stereotactic radiosurgery uses 3-D target localization to treat tumors with minimal surrounding tissue damage

- Goal of three fiducials with an angle of at least 15 degrees and a distance of 2cm between any two fiducials

- Studies mainly focused on pancreatic cancer but fiducials can potentially be deployed into any intramural or extramural malignant tumor accessible by EUS

Conventional targeting
Reasons for movement:

- Gastric distension?
- Biliary drainage?
- Bowel/colon filling?
Fiducial markers
MV-CBCT showing fiducials
<table>
<thead>
<tr>
<th>Stage</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1, T2</td>
<td>Resection (Whipple or limited)</td>
</tr>
<tr>
<td>T3</td>
<td>XRT/Chemo</td>
</tr>
<tr>
<td>T4</td>
<td>Palliation</td>
</tr>
<tr>
<td></td>
<td>Pancreatico-Duodenectomy</td>
</tr>
</tbody>
</table>

**CT Scan**
- Palliation
- M1

**EUS**
- Local

**Extra-pancreatic**
- Palliation
- Stenting
- Pain Control
Fiducial markers used with MV-CBCT improve the accuracy of daily target delineation compared to localization using adjacent bony anatomy for pancreatic tumors.

Aligning to adjacent bony anatomy may miss a significant volume of tumor nearly 40% of the time.

The strategy of dose escalation and small conformal margins carries significant risk of geographic miss if careful attention to daily tumor motion is not given.

In effect, if systematically missing geographically, dose escalation strategies may actually result in dose “de-escalation,” possibly compromising local control.

Pancreatic Ca
Fiducials
Fiducial Placement

- 90% success rate
- 7% migration requiring second EUS
- Pancreatitis 2%

Complications of EUS

- No reliable data on patients with increased risk of bleeding
  - INR < 1.5
  - Platelets > 50,000
  - 22-25G needle
  - Minimize passes
  - Risk of perforation 0-0.4%
- Risk of infection 0.3% (9% without abx of cysts)
- Pancreatitis 0.3%-0.6%
- Track seeding, biliary peritonitis

Celiac Plexus Neurolysis
Celiac plexus neurolysis

- Ethanol, comes into contact with the ganglia and disrupts the ascending sympathetic ganglia
- Efferent nerves from the pancreas travel with the sympathetic chain
- Effect sustained for 24 weeks

Celiac Plexus Neurolysis
Rectal Ca
Accuracy of EUS for T and N staging in rectal cancer is 85% and 75%, with fine-needle aspiration the accuracy of nodal staging is 87%

EUS is recommended for all patients with newly diagnosed nonmetastatic rectal cancer (T3, T4N0, or TxN1 to TxN2 or stage II to III)

Reduction in recurrence rates among patients with locally advanced rectal cancer who undergo preoperative neoadjuvant therapy

Ampullary Tumors

- Ampullary tumors that are limited to the sphincter of Oddi and do not invade the duodenal submucosa should have curative endoscopic ampullectomy.
- EUS is the most reliable modality for local preoperative staging.
- EUS has been shown to be superior to CT, US, and angiography for evaluation of T and N staging and for determining resectability (95% accuracy assessing portal venous involvement).
- Ability to show intraductal infiltration.
- MRI was found not to be statistically superior to EUS for nodal staging.

GB disease

- Polyps
- Carcinoma
- Adenomyomatosis
- Diagnosing the nature of gallbladder polyps smaller than 2 cm, 86.5% were correctly diagnosed by EUS, compared with only 51.7% by US
- 19% to 29% of polyps between 5 and 10 mm in diameter correspond to adenomas
- Neoplastic polyps have a heterogeneous internal echo pattern on EUS
- EUS recommendations:
  - Some patients with gallbladder polyps (5 to 10 mm in diameter, or >10 mm in patients with poor operative status which may help define the therapeutic choice
  - If ? on US, EUS useful in differentiating benign from malignant lesions
  - EUS may also be helpful before surgery with suspected gallbladder cancer or in those with large polyps (>15 mm), to highlight criteria that can guide the surgical choice

Gallstones Missed on Conventional US

Sludge
Pancreatitis

- EUS preferred over MRCP in acute pancreatitis as symptomatic choledocholithiasis can often be secondary to small stones
- Idiopathic recurrent
  - 80% do not recur and more extensive workup is generally not needed
  - If first episode occurs at age greater than 40 y/o then malignancy should be ruled out
- Recurrent pancreatitis
- Divisum
- Except for calcifications all features of chronic pancreatitis can be seen in acute and thus usual recommendation is to wait 4-6 wks to check for chronic pancreatitis

CBD stones

- 98% specificity for CBD stones
- Can detect microlithiasis missed on other imaging studies


Chronic pancreatitis
Pancreatic cysts

- Most of these lesions are pseudocysts (80%), but detection of mucinous neoplasms is most important because these may be malignant or may have malignant potential.
- A combination of EUS features, fluid cytology, and carcinoembryonic or amylase levels.
- Congenital or simple cysts and other rarities account for approximately 10%.
- Cystic neoplasms: serous cystadenoma, mucinous cystadenoma, mucinous cystadenocarcinoma, and intraductal papillary mucinous neoplasia (IPMN)- remaining 10%

Pancreatic cysts
Subepithelial lesions
Balloon

Superficial mucosa / balloon interface

MM

Submucosa

Muscularis propria

Adventitia

EUS
Subepithelial lesions

- EUS can accurately differentiate a mural lesion from extrinsic compression against the gut wall.
- Any subepithelial lesion that appears to be larger than 1 cm on endoscopic examination, and is not regarded as a lipoma or cyst should be referred for EUS evaluation.
- Determination of the cause of an intramural lesion is based on its layer of origin and internal echo characteristics.
- Intact submucosal layer running deep to a mural lesion indicates that the lesion can be removed safely by endoscopic mucosal resection.
- Endoscopic views are limited, and standard biopsy techniques have a low yield.


Varices

- Small, round Anechoic
- 3rd layer
- Smooth margins
- Doppler flow
Varices
Varices
Varices

- Coil embolization of bleeding gastric varices vs cyanoacrylate therapy

Anal sphincter disease

- **Fecal incontinence** felt to be secondary to pelvic neuropathy studied under endosonography shows that anal sphincter disruption was present in many cases.

- Can be scheduled for surgical procedures that aim to restore integrity to the sphincter ring.

- Patients whose sphincters are intact, or whose muscles are thought to be of poor quality, can be directed toward conservative measures or alternative surgical approaches.

- **Tears and defects**
  - Determine muscular quality
    - Single most important investigation with anal incontinence.
  - Fistula-in-ano
    - Eus can predict likelihood of sphincter division with repair
      - Treatment of fistula involves cutting down on the fistula and avoiding division.

- **Abscesses**

Thymoma, Teratoma, Thyroid, Terrible Lymphoma?

EUS guided FNA biopsy
Other/ Future applications

- Pelvic abscess drainage
- Tx of pancreatic pseudoaneurysm
- Local delivery of chemotherapeutic agents (EUS-FNI)
- Cyst ablation
- EUS guided radiofrequency ablation
  - Delivery of radiation seeds under EUS guidance
- Cryoablation of intramural and extramural tumors
The Future

- EUS directed local therapy of non-resectable pancreatic cancer
  - DAB(389)EGF is a diphtheria toxin fused via a His-Ala linker to human epidermal growth factor (EGF), selectively toxic to EGFR-overexpressing cells

- EUS directed therapy of GERD
  - Implantable polymers
  - Role in post ablation patients

EUS Guided RFA

- Produces discrete zones of coagulation necrosis in the porcine pancreas

- Potential uses
  - Management of small neuroendocrine tumors
  - Palliation of unresectable pancreatic adenocarcinoma.

Gaidhane et al. Endoscopic Ultrasound-Guided Radiofrequency Ablation (EUS-RFA) of the Pancreas in a Porcine Model. Gastroenterology Research and Practice Volume 2012, Article ID 431451, 6 pages
Cyst Ablation

Table 1. Summary of previous reports of EUS-guided cyst ablations

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of patients</th>
<th>Ablative agent</th>
<th>Follow-up period</th>
<th>Complete resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gan et al</td>
<td>25</td>
<td>5%-80% ethanol</td>
<td>6-12 mo</td>
<td>35% (8/23)</td>
</tr>
<tr>
<td>Oh et al</td>
<td>14</td>
<td>80%/99% ethanol with paclitaxel</td>
<td>Median 9 mo (range 6-23 mo)</td>
<td>79% (11/14)</td>
</tr>
<tr>
<td>Oh et al*</td>
<td>10</td>
<td>99% ethanol with paclitaxel</td>
<td>Median 8.5 mo (range 6-18 mo)</td>
<td>60% (6/10)</td>
</tr>
<tr>
<td>DeWitt et al</td>
<td>42</td>
<td>85% ethanol</td>
<td>3-4 mo after second lavage</td>
<td>33% (12/36)</td>
</tr>
<tr>
<td>Oh et al†</td>
<td>47</td>
<td>99% ethanol with paclitaxel</td>
<td>Median 20 mo (range 12-44)</td>
<td>62% (29/47)</td>
</tr>
<tr>
<td>D’Maliet al</td>
<td>12</td>
<td>85% ethanol</td>
<td>12 mo after first lavage</td>
<td>38% (5/13)</td>
</tr>
</tbody>
</table>

*includes only patients with a solitary cyst
†includes study population of 2 preliminary reports
‡includes patients with multiple ablations

Oh H, Bruegge W. Gastroenterol Endosc. 2013; 526-533
Summary

- Intramural and Extramural malignancy
- Pancreatitis
- Biliary/GB disease
- Pancreatic cysts
- Subepithelial lesions
- Anal sphincter disease
- Interventional applications
- Future applications
Thank You