Novel Applications of EUS

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Clinical Updates in Gastroenterology, Hepatology, and Nutrition
Objectives

• Overview the benefits of EUS
• Review EUS-guided injection procedures
  ▫ Fiducial placement
  ▫ Celiac plexus neurolysis
  ▫ Tumor ablation
  ▫ Angiotherapy
• Discuss EUS-guided drainage procedures
  ▫ Fluid collection management
  ▫ Necrosis therapy
  ▫ Biliary access
Theoretical Benefits of EUS

- Less invasive than surgery
- Close proximity of the echoendoscope to the target lesion
- Ability to detect intervening vessels using Doppler imaging
- Use of continuous real-time imaging and enhanced image resolution
General Principles

• Technically challenging procedures
  ▫ Expertise in all interventional procedures (EUS, ERCP, stenting)
• Pts who are not candidates for other Tx
  ▫ Endoscopic, IR, surgical
• Any coagulopathy needs to be corrected
• Antibiotic prophylaxis
EUS-guided Injection
Fiducial Placement
Indication

- Radiation therapy has an impt role in Tx of locally advanced pancreatic cancer
  - Major challenge is respiratory organ motion
  - Fiducidal markers can used for localization
- Stereotactic body radiotherapy (SBRT)
  - Allows escalation of radiation doses targeted to tumors and minimizing exposure to normal tissue
Technique

- Preloaded delivery device or load into a 22G FNA needle
- Fiducial: radiopaque cylindrical gold seed
  - 10 mm long, 0.28 or 0.35 mm in diameter
  - 1-2 markers placed within the lesion or within 1 cm of a small target lesion
Clinical Outcomes

• EUS placement reported in:
  ▫ Mediastinal tumors
  ▫ Prostate cancer
  ▫ All GI tumors

• Most evidence for pancreatic cancer
  ▫ Technical success in >90%
  ▫ Failures
    • Unable to access tumor: post-surgical anatomy, gastric outlet obstruction
    • Unable to perform safe FNI: intervening vessels
Table 1  Efficacy and safety of endoscopic ultrasound-guided fiducial placement.

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (#)</th>
<th>Cancer (type)</th>
<th>Efficacy (%)</th>
<th>Adverse events ( # of patients)</th>
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<tr>
<td>Pishvaian AC et al. [3]</td>
<td>13</td>
<td>Mediastinal and abdominal malignancies</td>
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<td>Infectious complication (1)</td>
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<td>Varadarajulu Set al. [31]</td>
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<td>Ammar T et al. [27]</td>
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<td>Abdominal malignancies</td>
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<td>Park WG et al. [30]</td>
<td>57</td>
<td>Pancreatic cancer</td>
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<td>Needle malfunction (1), and minor bleeding (1)</td>
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<td>Sanders MK et al. [29]</td>
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<td>Mild pancreatitis (1)</td>
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<td>DiMaio CJ et al. [5]</td>
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<td>Majumder S et al. [21]</td>
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<td>Abdominal pain (3), vomiting (1), mild pancreatitis (1)</td>
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<td>Davila Fajardo R et al. [32]</td>
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<td>Pancreatic cancer</td>
<td>100</td>
<td>Minor bleeding (1)</td>
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</tbody>
</table>

Chavalithdhamrong Disaya et al. EUS-guided placement of fiducials...  Endosc Int Open 2015; 03: E373–E377
Celiac Plexus/Ganglia Neurolysis
Indications

• Definitions
  ▫ Plexus vs ganglia
  ▫ Neurolysis vs block

• Pain from intraabdominal malignancy
  ▫ Refractory
  ▫ Side effects from opioid medications
  ▫ ?use for prophylactic pain control in patients with metastatic or T4 disease
Technique

- Localize celiac artery takeoff from aorta
- Locate any visible ganglia
Technique

- Localize celiac artery takeoff from aorta
- Locate any visible ganglia
  - Higher response rate (73.5% vs 45.5% in RCT)
- Bilateral injection
  - 10 mL of 0.25% bupivacaine + 10 mL 98% alcohol
  - Several mL into each identified ganglia, the remainder around the plexus
- May have immediate pain response
Clinical Outcomes

• Improves pain relief in 70% of PCA pts
  ▫ Decrease in overall pain rating (no complete relief)
  ▫ Decrease in opioid consumption
• Temporary (3-6 months)
  ▫ May be sufficient for specific populations
  ▫ Benefit of repeat injections is unclear
• No survival or quality of life benefit

Fabbri C. WJG. 2014;20:8424
Complications

• Minor complications (typically transient)
  ▫ Orthostasis (IV hydration required)
  ▫ Diarrhea

• Major complications (1-2%)
  ▫ Lower extremity weakness/paralysis (2 cases)
  ▫ Retroperitoneal abscess
  ▫ Chronic gastroparesis
  ▫ Gastric/aortic necrosis

Fujii LL. Endosc. 2012;44:E265
Tumor Ablation
Ethanol ablation of pancreatic cysts

- **Technique:**
  - Puncture cyst with 22G FNA needle
  - Partial or total evacuation of cystic fluid
  - Inject a volume of ethanol equal to that aspirated
  - Maintain for 3-5 minutes
  - Reaspirate injected ethanol

EUS-guided local ablative procedures for pancreatic cystic neoplasms are not recommended outside experimental protocols.
Ethanol ablation of solid neoplasms

- Patients unsuitable for surgery
- Concentration ranges from 40-99% ethanol
- Total of 13 patients with insulinoma
  - Volume determined by hyperechoic blush within the tumor
    - Ranged from 0.3-8 mL
  - Resolution of symptoms and euglycemia in all
  - AE: mild pancreatitis, duodenal wall ulcer
- 2 patients with MEN1
  - Normalization of VIP and chromogranin A
  - AE: pancreatic necrosis
- More data is needed

Anti-tumoral agents

- Unresectable pancreatic cancer
- Different agents in pilot studies
  - Chemotherapy: gemcitabine
  - Cytoimplant
  - Dendritic cells
  - TNFerade
  - ONYX-015
  - Brachytherapy with I125 radiation seeds

Table 11: Endoscopic ultrasound-guided tumor ablation

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Design</th>
<th>Indications</th>
<th>Techniques</th>
<th>Type</th>
<th>Tumor response</th>
<th>Complications</th>
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<tr>
<td>Chang et al[206]</td>
<td>PS</td>
<td>Pancreatic cancer (n = 1)</td>
<td>Injection</td>
<td>Cytosmear</td>
<td>2 partial; 1 minor</td>
<td>None</td>
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<tr>
<td>Hecht et al[207]</td>
<td>PS</td>
<td>Pancreatic cancer (n = 21)</td>
<td>Injection</td>
<td>ONYX-015 and gemcitabine</td>
<td>2 partial; 2 minor; 6 stable; 11 progression surgical resection</td>
<td>2 sepsis; 2 duodenal perforations</td>
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<tr>
<td>Zhang et al[208]</td>
<td>RS</td>
<td>Pancreatic cancer (n = 1)</td>
<td>Injection</td>
<td>TNFerade and chemoradiotoc</td>
<td>1 complete; 5 partial; 4 minor; 12 stable</td>
<td>6 GI bleeding; 6 deep vein thrombosis; 2 pulmonary embolism; 2 pancreatitis; 6 cholangitis</td>
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<td>Iwasa et al[209]</td>
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<td>Pancreatic cancer (n = 7)</td>
<td>Injection</td>
<td>Immature dendritic cells</td>
<td>2 mixed; 2 stable; 3 progressive</td>
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<td>Hara et al[210]</td>
<td>PS</td>
<td>Pancreatic cancer (n = 9)</td>
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<td>EUS-guided</td>
<td>2 surgically resectable; 3 partial; 3 progressive</td>
<td>None</td>
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<tr>
<td>Chang et al[211]</td>
<td>PS</td>
<td>Esophageal cancer (n = 24)</td>
<td>Injection</td>
<td>BC-819 and chemoradiotoc</td>
<td>6 complete; 2 stable; 5 thromboembolic events (highest dose)</td>
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<td>Arredondo[212]</td>
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<td>Pancreatic cancer (n = 22)</td>
<td>Cryoablation</td>
<td>EUS-CTP</td>
<td>6 partial response (only 6 patients analyzed)</td>
<td>3 hyperamylasemia</td>
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<td>Maier et al[213]</td>
<td>PS</td>
<td>Head/neck cancer (n = 21)</td>
<td>Brachy</td>
<td>Ir-192 needles</td>
<td>4 null; 13 partial; 5 none</td>
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<td>Lah et al[214]</td>
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<td>Metastatic celiac lymph nodes (n = 1)</td>
<td>Brachy</td>
<td>I-125 seeds</td>
<td>Response;</td>
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<td>Martinez-Monge et al[215]</td>
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<td>Sun et al[216]</td>
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<td>Pancreatic cancer (n = 15)</td>
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<td>4 partial; 3 minor; 5 stable; 3 progressive</td>
<td>1 site infection; 3 hematologic side effects</td>
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<tr>
<td>Jin et al[217]</td>
<td>PS</td>
<td>Pancreatic cancer (n = 22)</td>
<td>Brachy</td>
<td>I-125 seeds</td>
<td>4 partial; 3 minor; 5 stable; 3 progressive</td>
<td>1 seed migration</td>
</tr>
</tbody>
</table>

RCT: Randomized controlled trial; PS: Prospective study; RS: Retrospective study; NR: Not reported; CTP: Cryoablation probe; GI: Gastrointestinal.

Angiotherapy
Indications

• Not candidates for endoscopic, surgical, IR therapy
• Varices
  ▫ Gastric > esophageal, duodenal, choledochal
• Nonvariceal GI bleeding
  ▫ GI tumors/polyps
  ▫ Dieulafoy lesions (identification and therapy)
  ▫ Refractory ulcers
Materials

- Coils +/- cyanoacrylate (glue)
  - Risk of glue embolization
  - Coils anchor the glue to the site of injection
  - MC experience: use glue after coil injection only with large (>8 mm) varices

Clinical Outcomes

- Limited to case series
- Variceal experience (n=152)
  - Gastric varices
  - Coil + cyanoacrylate injection
  - 93% obliteration of gastric varices on f/u EUS
    - 3% (3 patients) had rebleeding after obliteration
  - AE: 4 mild pain, 1 pulmonary embolism + PNA (1 week)
- Nonvariceal experience (n=17)
  - GIST, AVMs, Dieulafoy lesions, cancer, pancreatic pseudoaneurysms
  - Cyanoacrylate, hyaluornate, alcohol, epinephrine injection
  - 88% resolution of bleeding
  - No complications

Bhat YM. GIE. 2016;83:1173.
Law R. CGH. 2015;13:808
EUS-guided Drainage Procedures
Cyst Enterostomy
# Atlanta Classification of pancreatic collections

<table>
<thead>
<tr>
<th></th>
<th>Interstitial pancreatitis</th>
<th>Necrotizing pancreatitis</th>
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<tr>
<td><strong>Acute (≤4 wks)</strong></td>
<td>Acute peripancreatic fluid collection (APFC)</td>
<td>Acute necrotizing pancreatitis</td>
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<tr>
<td></td>
<td>- homogeneous</td>
<td>- heterogeneous</td>
</tr>
<tr>
<td></td>
<td>- pure liquid</td>
<td>- liquid + necrosis</td>
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<tr>
<td></td>
<td>- usually resolves</td>
<td>- usually resolves</td>
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<tr>
<td><strong>Chronic (&gt;4 wks)</strong></td>
<td>Pancreatic pseudocyst (PPC)</td>
<td>Walled off pancreatic necrosis (WOPN)</td>
</tr>
<tr>
<td></td>
<td>- pure liquid</td>
<td>- heterogeneous</td>
</tr>
<tr>
<td></td>
<td>- defined wall</td>
<td>- liquid + necrosis</td>
</tr>
</tbody>
</table>

Indications

• Symptomatic pseudocysts
  ▫ Luminal or biliary extrinsic compression
  ▫ Unexplained severe abdominal pain
• Infected cysts

• Prerequisites for EUS-guided drainage
  ▫ A well-defined mature wall is required
    • At least 6 weeks for pseudocysts
  ▫ Within 1 cm from gastric/duodenal wall
  ▫ Lack of duct disruption (ERCP preferable as first step)
Technique

- Find the ideal location for needle puncture
  - Intervening vessels, scope position
Technique

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- Advance needle into fluid collection
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- Dilate the tract (dilating catheters, balloons)
Technique

- Find the ideal location for needle puncture
  - Intervening vessels, scope position
- Advance needle into fluid collection
- Thread a guidewire into the collection under fluoroscopic guidance
- Dilate the tract (dilating catheters, balloons)
- Insert stent
Stents

- **Plastic stents**
  - Typically multiple double pigtail

- **Metal stents**
  - Self expanding metal stents (SEMS)
    - Biliary or enteral stents used
  - Lumen apposing metal stents (LAMS)
  - Shorter procedure time
  - May improve clinical success (larger fistula size)
Clinical outcomes

- **EUS vs surgical cyst gastrostomy**
  - Shorter mean LOS (2 vs 6 days)
  - Lower overall cost ($7,011 vs $15,052)
  - No difference in clinical outcomes
    - Treatment success (>95%)
    - Complications
    - Reintervention

- **Success rates**
  - Pseudocyst (>90%) > abscess (80-90%) > WOPN (73-92%)

Varadarajulu S. Gastroenterol. 2013;145:583
<table>
<thead>
<tr>
<th>Ref.</th>
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<th>Technical success</th>
<th>Clinical success</th>
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<td>Birolino et al.</td>
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</table>

| Total | 55 studies | 1867 | 97% (83%-100%) | 90% (69%-100%) | 8% (0%-23%) | 17% (0%-52%) |

1 Complications include early and late, procedural and stent related; Only patients with walled-off pancreatic necrosis. RCT: Randomized controlled trial; PS: Prospective study; RS: Retrospective study; NR: Not reported.
Complications

- Infection
- Bleeding
  - Severe bleeding with erosion of splenic artery, GDA, or visceral pseudoaneurysm
- Perforation
- Stent migration into the cyst
- Surgery required in 5-11% of patients
Pancreatic Necrosis Therapy
Technique

• Initial drainage is similar to fluid collections
• Requires additional necrosectomies
  ▫ Median of 4 additional procedures
  ▫ Baskets, snares, nets, grasper
Clinical outcomes

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Design</th>
<th>Cases</th>
<th>Technical success</th>
<th>Clinical success</th>
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<td>100%</td>
<td>20%</td>
<td>40%</td>
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<tr>
<td>Will et al⁹⁹</td>
<td>RS</td>
<td>18</td>
<td>100%</td>
<td>100%</td>
<td>11%</td>
<td>17%</td>
</tr>
<tr>
<td>Rische et al⁹¹</td>
<td>RS</td>
<td>22</td>
<td>100%</td>
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<td>36%</td>
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<tr>
<td>Yamamoto et al⁹³</td>
<td>RS</td>
<td>4</td>
<td>100%</td>
<td>50%</td>
<td>NR</td>
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<tr>
<td>Hritz et al⁹¹</td>
<td>RS</td>
<td>4</td>
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<tr>
<td>Yasuda et al⁹⁰</td>
<td>RS</td>
<td>57</td>
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<td>33%</td>
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<tr>
<td>Ang et al⁹⁰</td>
<td>RS</td>
<td>8</td>
<td>100%</td>
<td>87%</td>
<td>13%</td>
<td>None</td>
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<tr>
<td>Sarkaria et al⁹⁴</td>
<td>RS</td>
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<td>100%</td>
<td>88%</td>
<td>0%</td>
<td>6%</td>
</tr>
<tr>
<td>Total</td>
<td>16 studies</td>
<td>283</td>
<td>100% (97%-100%)</td>
<td>88% (50%-100%)</td>
<td>7% (0%-20%)</td>
<td>28% (0%-46%)</td>
</tr>
</tbody>
</table>

¹Complications include: early and late, procedural and stent related. RCT: Randomized controlled trial; PS: Prospective study; RS: Retrospective study; NR: Not reported.
EUS-guided Biliary Access
Indications

• Benign or malignant biliary obstruction
• Failed ERCP access (5%)
  ▫ Gastric/duodenal obstruction
  ▫ Anatomical variants (duodenal diverticulum)
  ▫ Surgically altered anatomy (BII, Whipple)
  ▫ Infiltrative ampullary/pancreatic cancer
Definitions

- Transpapillary/transanastomotic
  - Antegrade (EUS only)
  - Retrograde (EUS followed by ERCP)
- Transluminal
  - Antegrade (EUS only)
- Can gain access through either the intrahepatic or extrahepatic bile ducts
Technique: Retrograde
Technique: Retrograde
Technique: Retrograde
Clinical outcomes

- Technical success of 91%
- Treatment success of 88%
- EUS vs percutaneous drainage
  - Malignant distal biliary obstruction
  - Technical success rates higher in PTC
  - Clinical success rates similar
  - Lower AE and reintervention rates for EUS
Adverse Events

- Morbidity 29%
  - Intrahepatic > extrahepatic access
  - Antegrade > retrograde approach
  - Bile leak, penumoperitoneum, infection, pancreatitis, bleeding, stent migration
- Mortality 3%
Other Therapies

• Pancreatic duct access and drainage
• Drainage of non-pancreatic fluid collections
• Lumen apposing metal stent (LAMS)
  ▫ Gallbladder drainage
  ▫ Gastrojejunostomy
  ▫ EUS-guided transgastric ERCP access after ReY
Questions?
References