Title: Contrast enhanced EUS and elastography
Session No: 7

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Those who really know...
The issue

• Endoscopic ultrasound is superb for detection of even tiny lesions, given proximity to the upper GI tract (or rectum)
• EUS is less accurate for visual characterization
• FNA/FNB improves diagnostic accuracy, but the negative predictive value is still imperfect
  – Needle access
  – Sampling error
  – Sample acquisition/handling
• Additional image enhancement may be helpful
Contrast-enhanced EUS (CE-EUS)
CE-EUS - background

• Color doppler imaging allows visualization of significant vessels
  – Assessment of safe needle path
  – Distinction towards other ductal structures
  – Assessment of invasive growth

• Color doppler is suboptimal for assessment of tissue vascularization
  – Resolution issues
  – Blooming and flash artifacts
CE-EUS - principle

• Contrast medium inside vessels carry special characteristics allowing «harmonic imaging»
  – High echo from bubble interface
  – Removal of echo from «normal tissues»
• Different combination of mechanical index and focus of the ultrasound wave are used to optimize signal/noise ratio
  – «Harmonic» multiples of the original wave frequency emerge from the bubbles and can be singled out for detection.
CE-EUS- practical

- Normal preparation, sedation
- Identification of lesion, stable position
- Software switch to specialised EUS mode
- Bolus injection of contrast medium (e.g. Sonovue™)
- Continuous observation (and video recording) of sequential imaging
  - Wash-in (10-30 seconds)
  - Wash-out (30-120 seconds)
Neuroendocrine tumor
Adenocarcinoma of pancreas
Time-intensity curves
TIC in Submucosal lesions

• 17 subepithelial lesions, retrospect. study
• Sonovue 4.8ml
CE-EUS performance

Table 3. Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, and Accuracy of Standard EUS and CHE-EUS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoechoic lesion on standard EUS as a predictor of adenocarcinoma</td>
<td>86% (73%–94%)</td>
<td>18% (8%–34%)</td>
<td>58% (47%–69%)</td>
<td>59% (24%–76%)</td>
<td>57% (50%–64%)</td>
</tr>
<tr>
<td>Hypoenhancing lesion on CHE-EUS as a predictor of adenocarcinoma</td>
<td>96% (85%–99%)</td>
<td>64% (47%–78%)</td>
<td>78% (65%–87%)</td>
<td>93% (74%–99%)</td>
<td>82% (74%–85%)</td>
</tr>
<tr>
<td>Hyperenhancing lesion on CHE-EUS as an exclusion sign of adenocarcinoma</td>
<td>39% (30%–41%)</td>
<td>98% (92%–100%)</td>
<td>94% (74%–99%)</td>
<td>68% (63%–69%)</td>
<td>72% (65%–74%)</td>
</tr>
<tr>
<td>Hyperenhancing lesion on CHE-EUS as a predictor of NET</td>
<td>69% (46%–86%)</td>
<td>90% (87%–94%)</td>
<td>56% (33%–76%)</td>
<td>95% (87%–98%)</td>
<td>88% (81%–93%)</td>
</tr>
</tbody>
</table>

Fusaroli Clin Gastroenterol Hepatol 2010

<table>
<thead>
<tr>
<th>Final diagnosis (FNA / surgery / follow-up*)</th>
<th>n</th>
<th>Hypoenhancement, (FNA / surgery / follow-up*)</th>
<th>Hyper/isoenhancement (FNA / surgery / follow-up*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic adenocarcinoma (66 / 2 / 1)</td>
<td>69</td>
<td>66 (63 / 2 / 1)</td>
<td>3 (3 / 0 / 0)</td>
</tr>
<tr>
<td>NET (10 / 0 / 0)</td>
<td>10</td>
<td>0</td>
<td>10</td>
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<tr>
<td>Chronic pancreatitis (2 / 1 / 10)</td>
<td>13</td>
<td>2 (0 / 1 / 1)</td>
<td>11 (3 AIP) (2 AIP / 0 / 9)</td>
</tr>
<tr>
<td>Renal cancer metastasis (3 / 0 / 1)</td>
<td>4</td>
<td>–</td>
<td>4</td>
</tr>
<tr>
<td>Thyroid cancer metastasis (1 / 0 / 0)</td>
<td>1</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Smooth muscle tumor (1 / 0 / 0)</td>
<td>1</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Pseudosolid serous cystadenoma (2 / 0 / 0)</td>
<td>2</td>
<td>–</td>
<td>2</td>
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</tbody>
</table>

Napoleon Endoscopy 2014
CE-EUS- principal utility

• Adenocarcinoma: Hypovascular
• Pancreatitis: Hypervascular
• NE-tumors: Hypervascular
• Encouraging sens/spec/PPV/NPV values in early studies
• Utility in FNA-negative lesions
  – or even replacing FNA?
• Special case of chronic pancreatitis!
EUS elastography
Elastography - background

- Tissue characteristics differentiate between malignant/benign lesions
- EUS appearance (size/texture/delineation), as well as perfusion pattern guide diagnosis
- Tissue stiffness is yet another such feature
  - Malignant tissue is hard
  - Inflammatory tissue is soft
Elastography - principle

- Tissue stiffness is quantified by comparing response to compression with reference (normal) tissue.
Elastography - performance

Sensitivity: 92-100%
Specificity: 53-85%
Elastography pancreas - metaanalysis

Mei et al. GIE 2012
# Elastography lymph nodes - metaanalysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Study description</th>
<th>LN</th>
<th>SE</th>
<th>SP</th>
<th>PPV</th>
<th>NPV</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Giovannini, Endoscopy 2006</td>
<td>Qualitative</td>
<td>31</td>
<td>100</td>
<td>50</td>
<td>-</td>
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<td>FNA Surgery</td>
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<tr>
<td>Saftoiu, Ultraschall 2006</td>
<td>Qualitative Quantitative (cut-off ER=0.84)</td>
<td>42</td>
<td>91.7</td>
<td>95.8</td>
<td>94.4</td>
<td>94.4</td>
<td>Cytology Surgery Follow-up</td>
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<tr>
<td>Saftoiu, Gastrointestinal Endoscopy 2007</td>
<td>Quantitative (mean hue histogram values, cut-off=166)</td>
<td>78</td>
<td>85.4</td>
<td>91.9</td>
<td>92.1</td>
<td>85</td>
<td>Cytology Surgery Follow-up</td>
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<tr>
<td>Janssen, Endoscopy 2007</td>
<td>Qualitative (3 patterns)</td>
<td>66</td>
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<td>FNA</td>
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<tr>
<td>Hirooka, GIE 2009 (abstract)</td>
<td>Qualitative</td>
<td>55</td>
<td>96</td>
<td>89</td>
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<tr>
<td>Giovannini, WJG 2009</td>
<td>Qualitative (5 patterns), multicenter</td>
<td>101</td>
<td>91.8</td>
<td>82.5</td>
<td>88.8</td>
<td>86.8</td>
<td>FNA Surgery</td>
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<td>Knabe, Surg Endosc 2013</td>
<td>Qualitative (3 patterns) Quantitative (blue pixels)</td>
<td>40</td>
<td>100</td>
<td>64.1</td>
<td>75</td>
<td>-</td>
<td>Histology Cytology</td>
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<tr>
<td>Larsen, Ultraschall 2011</td>
<td>Interobserver agreement (5 scores, SR)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>FNA</td>
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<tr>
<td>Xu, Gastrointestinal Endoscopy 2011</td>
<td>Meta-analysis</td>
<td>431</td>
<td>88</td>
<td>85</td>
<td>91</td>
<td>-</td>
<td>FNA Surgery Follow-up</td>
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<tr>
<td>Larsen, Endoscopy 2012</td>
<td>Qualitative (5 patterns) Semi-quantitative SR (cut-off 4.5)</td>
<td>56</td>
<td>59</td>
<td>82</td>
<td>68</td>
<td>76</td>
<td>Histology</td>
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<td>Paterson, WJG 2012</td>
<td>Quantitative (SR ≥ 7.5)</td>
<td>53</td>
<td>83</td>
<td>96</td>
<td>95</td>
<td>86</td>
<td>FNA</td>
</tr>
</tbody>
</table>
EUS elastography – principal utility

• ...once more – mass lesions in the context of chronic pancreatitis
• May guide FNA/FNB for more accurate sampling.
• May guide selecting appropriate lymph nodes.
• Still needs standardization.
Conclusions

• EUS is excellent in detection of lesions, characterization may still improve
• CE-EUS as well as elastography both hold promise to expand the utility of EUS
• Both methods are operator dependent and standardization is still under way.