EUS in the Management of Pancreaticobiliary Cancers

Frank Gress, MD
Professor of Medicine and Chief Division of Gastroenterology and Hepatology
State University of New York Downstate Medical Center
Brooklyn, NY
• "EUS for the Diagnosis, Staging FNA and Celiac Neurolysis of Pancreatic Cancer"
Pancreatic Adenocarcinoma

• The fourth leading cause of cancer-related death in the U.S.
• At diagnosis only ~15% of patients are candidates for curative surgery
• Five-year survival following a Whipple procedure was only 25% for node-negative tumors and 10% for node-positive tumors

Pancreatic Cancer

• Late presentation, aggressive nature and lack of effective therapies all contribute to the poor prognosis.

• Early detection is crucial to improve the overall prognosis.

• Accurate Staging is vital for selecting the subset of patients who have potentially resectable tumors.
Common Indications for EUS

GI Tumor Staging

- Esophageal Cancer
- Gastric Cancer
- Rectal Cancer
- Ampullary Cancer
- Pancreatic Cancer
## Cancer Staging

### EUS Staging Accuracy Compared to Path

<table>
<thead>
<tr>
<th>Indication</th>
<th>n</th>
<th>T stage</th>
<th>N stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal CA</td>
<td>739</td>
<td>85%</td>
<td>79%</td>
</tr>
<tr>
<td>Gastric CA</td>
<td>1163</td>
<td>78%</td>
<td>73%</td>
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<tr>
<td>Pancreatic CA</td>
<td>155</td>
<td>90%</td>
<td>78%</td>
</tr>
<tr>
<td>Ampullary CA</td>
<td>94</td>
<td>86%</td>
<td>72%</td>
</tr>
<tr>
<td>Rectal CA</td>
<td>19</td>
<td>84%</td>
<td>84%</td>
</tr>
</tbody>
</table>
Clinical Applications for EUS

Pancreatic and Biliary Disease

- Tumor Staging
- Localization of Endocrine Tumors
- Detecting Choledocholithiasis
- Detecting Chronic Pancreatitis
EUS Indications for Staging

- Pancreatic Masses
  - Adenocarcinoma
  - Other malignancies/metastases

- Bile duct cancer (cholangiocarcinoma)
Clinical Applications for EUS

Current Indications

Pancreatic and Biliary Malignancies

1) Tumor staging primarily based on ability to assess for vascular invasion
2) Localization of Endocrine Tumors
3) Ability to sample lesions for diagnosis with >85% accuracy
Pancreatic Tumor Staging
<table>
<thead>
<tr>
<th>Transducer Location</th>
<th>Major Structures identified with EUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric Body</td>
<td>Confluence, Body/Tail of Pancreas, PD, Celiac Axis, Splenic vessels, SMA</td>
</tr>
<tr>
<td>Gastric Antrum</td>
<td>Gallbladder, Liver, Pancreas</td>
</tr>
<tr>
<td>Duodenum</td>
<td>Head of Pancreas, CBD, PD</td>
</tr>
<tr>
<td>Bulb</td>
<td>Head of Pancreas, SMA/SMV, Aorta, PD, Ampulla, Liver</td>
</tr>
<tr>
<td>2nd Portion</td>
<td></td>
</tr>
</tbody>
</table>
EUS Staging of Pancreatic Cancer

TNM Classification

**T Staging** is based on tumor size, depth of invasion and infiltration into major vessels.

**N Staging** assesses for nodal involvement.

**M Staging** denotes the absence/presence distant metastasis (EUS can detect hepatic metastasis).
T2 Pancreatic Mass
T3 Pancreatic Adenocarcinoma
T3 Pancreatic Tumor
Pancreatic Mass
<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV(%)</th>
<th>NPV(%)</th>
<th>Accuracy</th>
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<tbody>
<tr>
<td>Rosch, 1991</td>
<td>99</td>
<td>100</td>
<td>100</td>
<td>97</td>
<td>76</td>
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<tr>
<td>Snady, 1992</td>
<td>85</td>
<td>80</td>
<td>89</td>
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<tr>
<td>Yasuda, 1993</td>
<td>-</td>
<td>-</td>
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<td>Muller, 1994</td>
<td>94</td>
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<td>-</td>
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<td>Gress, 1997</td>
<td>93</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Baron, 1997</td>
<td>95</td>
<td>88</td>
<td>95</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Legmann, 1998</td>
<td>100</td>
<td>93</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Akahoshi, 1998</td>
<td>89</td>
<td>97</td>
<td>94</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>95</td>
<td>94</td>
<td>95</td>
<td>88</td>
<td>90</td>
</tr>
</tbody>
</table>
Pancreatic Cancer Staging by EUS

Pooled Data

• T staging accuracy ranges from 78 to 94%
• T staging accuracy is higher in patients with advanced lesions (T3 and T4)
• Vascular invasion accuracy was 82 to 93%
• N staging accuracy ranges from 64 to 82%
Diagnosis by EUS

- EUS provides improved imaging of small tumors not seen with other imaging modalities
- The detection of pancreatic tumors \( \leq 3 \text{ cm} \) in diameter was higher for EUS:
  - EUS (100%)
  - TUS (57%)
  - CT (68%)

Diagnosis by EUS

- The detection of pancreatic tumors < 2cm in diameter was higher for EUS:
  - EUS (100%)
  - ERCP (57%)
  - TUS (29%)
  - CT (29%)
  - Angiography (14%)

EUS Staging

Lower T and N staging accuracy has also been described:

- 89 patients with pancreatic cancer had EUS staging compared to surgery
- Overall accuracy for T staging was 69% and for N staging was 54%
- Only 46% of tumors designated by EUS as resectable actually were at laparotomy

Ahmad, et al. Gastrointest Endo 2000;52:46
Pancreatic Cancer

- Best modality for small lesions
- Diagnostic imaging and fine needle aspiration during single procedure
- Evaluate for chronic pancreatitis if not tumor found
- All pancreatic cancer has a dismal prognosis
Liver Metastasis
Liver

- EUS provides excellent imaging of the liver particularly the left lobe of the liver and some portions of the right lobe
- The left lobe is best seen from the gastric body and fundus
- The right lobe is best imaged from the antrum and duodenum
Clinical Utility of EUS FNA for Diagnosing Liver lesions

- Sensitivity of EUS-FNA for the diagnosis of malignancy ranged from 82 to 94%.
- When compared with benign lesions, EUS features predictive of malignant hepatic masses were the presence of regular outer margins (60% vs 27%; \( p = 0.02 \)) and the detection of two or more lesions (38% vs 9%; \( p = 0.03 \)).

EUS Indications
Cancer Staging

- Ampullary
  Most accurate locoregional staging
- Rectal
  Most accurate locoregional staging
- Other e.g. duodenal tumors, adenomas
T1 Ampullary Tumor
Limitations of EUS

- Factors influencing EUS staging accuracy:
  - Experience level of endosonographer
  - Imaging artifacts/Normal variants/Chronic Pancreatitis
  - Distinguishing vascular compression from tumor infiltration can be difficult in larger tumors
  - Accuracy for detecting invasion into the SMA and SMV is lower than that for PV or SV
EUS versus Helical CT

Contrast enhanced helical CT has been compared to EUS for detecting pancreatic tumors, predicting resectability and determining vascular invasion

Leggmann, et al; 1998
Midwinter, et al; 1999
Mertz, et al; 2000
Tierney, et al; 2002
**EUS versus Helical CT**

Pooled Data

<table>
<thead>
<tr>
<th>4 Studies n=164</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EUS</td>
</tr>
<tr>
<td>Detecting pancreatic tumors</td>
<td>97%</td>
</tr>
<tr>
<td>Predicting resectability</td>
<td>91%</td>
</tr>
<tr>
<td>Determining vascular invasion</td>
<td>91%</td>
</tr>
</tbody>
</table>

EUS versus Helical CT

- Several features of the individual studies may account for the disparity in the conclusions:
  - Differences in Gold Standard
  - Differences in Helical CT Technique
  - Number of patients with advanced disease
EUS versus Multidetector CT

• Prospective study comparing EUS and Multidetector CT for detecting and staging pancreatic cancer

120 patients with known pancreatic cancer

EUS was:
98% sensitive for tumor detection (86% for CT)
67% for tumor staging accuracy (41% for CT)
44% for nodal staging accuracy (47% for CT)

EUS versus Helical CT

Conclusions

• EUS and Helical CT are complementary for staging pancreatic cancer.

• EUS is a more accurate modality for T staging and predicting vascular invasion and CT is better for detecting distant metastasis.
EUS and Cancer Diagnosis

- Controversial whether pre-operative diagnosis is necessary
- Direct to resection when clinical suspicion is high vs.
- Pre-operative tissue diagnosis
Role of EUS in Recurrent Cancer after Whipple
EUS-FNA of Pancreatic Lesions

Not all pancreatic masses are cancer

Differential Diagnosis

- Adenocarcinoma
- Neuroendocrine tumor
- Lymphoma
- Chronic pancreatitis
Normal Pancreas

EG-3630UR
Normal Pancreas

GF-UM130

EG-3630UR
Pancreatic Cancer
Islet Cell Tumor
Chronic Pancreatitis

EG-3630UR
EUS-guided Fine Needle Aspiration

- Percutaneous or CT-guided biopsy has been the traditional approach for establishing the diagnosis of pancreatic cancer.

- EUS FNA was introduced ~10 years ago.

- The main advantage of EUS guided FNA biopsy is its ability to obtain tissue sampling of any suspicious mass found during EUS evaluation.
Fine Needle Aspiration
EUS FNA Needles
### Diagnostic Characteristics of EUS FNA for Pancreatic Mass Lesions

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giovannini</td>
<td>43</td>
<td>75</td>
<td>100</td>
<td>79</td>
</tr>
<tr>
<td>Cahn</td>
<td>50</td>
<td>88</td>
<td>100</td>
<td>87</td>
</tr>
<tr>
<td>Bhutani</td>
<td>47</td>
<td>64</td>
<td>100</td>
<td>72</td>
</tr>
<tr>
<td>Chang</td>
<td>44</td>
<td>92</td>
<td>100</td>
<td>95</td>
</tr>
<tr>
<td>Erickson</td>
<td>28</td>
<td>--</td>
<td>--</td>
<td>96</td>
</tr>
<tr>
<td>Faigel</td>
<td>45</td>
<td>72</td>
<td>100</td>
<td>75</td>
</tr>
<tr>
<td>Gress</td>
<td>12180</td>
<td>100</td>
<td></td>
<td>85</td>
</tr>
<tr>
<td>Wiersema</td>
<td>124</td>
<td>87</td>
<td>100</td>
<td>88</td>
</tr>
<tr>
<td>Binmoeller</td>
<td>5876</td>
<td></td>
<td>100</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>560</td>
<td>81%</td>
<td>100%</td>
<td>86%</td>
</tr>
</tbody>
</table>
### RESULTS OF EUS-GUIDED FNA BIOPSY IN PATIENTS WITH OR WITHOUT PANCREATIC CANCER

<table>
<thead>
<tr>
<th>EUS- Guided FNA BX</th>
<th>Patients with Pancreatic CA</th>
<th>Patients without Pancreatic CA</th>
<th>Likelihood Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive results</td>
<td>57/61 (93.%)</td>
<td>0/41 (0)</td>
<td>All values ≥</td>
</tr>
<tr>
<td>9.7+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative results</td>
<td>3/61 (4.9%)</td>
<td>34/41 (83%)</td>
<td>0.05 (0.02-0.15)</td>
</tr>
<tr>
<td>Inconclusive or</td>
<td>1/61 (1.6%)</td>
<td>7/41 (17.%)</td>
<td>0.096 (0.012-</td>
</tr>
<tr>
<td>nondiagnostic</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EUS-Guided FNA

Reported Complications:

- Infection (cysts >> solid mass)
- Pancreatitis (<1-2%)
- Bleeding
EUS-Guided FNA

Reported Complications:

Infection
Bleeding

- Pancreatitis (2-4%)

100 patients having EUS FNA of pancreas


- 2/100 developed clinical pancreatitis
- Transient Elevations in enzymes occur
Pancreatic Mass
Neuroendocrine Tumor
Advantages over CT-guided Biopsy

- Ability to sample lesions (including lymph nodes) too small to be identified by TUS, CT or MRI

- Minimizing the risk of needle track seeding

- Ability to obtain accurate local staging
# Diagnostic Characteristics of EUS FNA for Pancreatic Mass Lesions

<table>
<thead>
<tr>
<th>Accuracy (%)</th>
<th>n</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Giovannini</strong> [Endoscopy 1995;27(2)]</td>
<td>43</td>
<td>75</td>
<td>100</td>
</tr>
<tr>
<td><strong>Cahn</strong> [AJS 1996;172(5)]</td>
<td>50</td>
<td>88</td>
<td>100</td>
</tr>
<tr>
<td><strong>Bhutani</strong> [Endoscopy;1997;29(9)]</td>
<td>47</td>
<td>64</td>
<td>100</td>
</tr>
<tr>
<td><strong>Chang</strong> [GIE;1997;45(5)]</td>
<td>44</td>
<td>92</td>
<td>100</td>
</tr>
<tr>
<td><strong>Erickson</strong> [AFP 1997;55(6)]</td>
<td>28</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>Faigel</strong> [JClinOnc1997;15(4)]</td>
<td>45</td>
<td>72</td>
<td>100</td>
</tr>
<tr>
<td><strong>Gress</strong> [GIE1997;45(3)]</td>
<td>121</td>
<td>80</td>
<td>100</td>
</tr>
<tr>
<td><strong>Wiersema</strong> [Gastro 1997;112(4)]</td>
<td>124</td>
<td>87</td>
<td>100</td>
</tr>
<tr>
<td><strong>Binmoeller</strong> [GIE1998;47(2)]</td>
<td>58</td>
<td>76</td>
<td>100</td>
</tr>
</tbody>
</table>

Total: 560 | 81% | 100% | 86%
Diagnosis by EUS FNA

• 102 patients with suspected pancreatic cancer with negative CT-guided FNA and/or ERCP sampling underwent EUS-FNA
• EUS-FNA was positive in 57 patients (56%)
• 4 patients who had a negative EUS-FNA subsequently were found to have pancreatic cancer

Follow up Study of EUS FNA Accuracy in Suspected Pancreatic CA with prior negative CT/ERCP biopsies

(Harewood et al Am J Gastro 2002 97(6)

- 185 Subjects with known or suspected Pancreatic Cancer
  - 58 Negative CT FNA Biopsy
    - EUS FNA had 90% sensitivity for detecting malignancy with an overall 84% accuracy
  - 36 Negative ERCP Tissue Sampling
    - EUS FNA had 94% sensitivity for detecting malignancy with an overall 92% accuracy
Lymph Node FNA

Hitachi EUB-6000
## Diagnostic Characteristics of EUS FNA for Peri-intestinal Lymph Nodes

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Accuracy (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bhutani</strong> [GIE 1997;45(6)]</td>
<td>22</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td><strong>Chang</strong> [GIE 1997;45(5)]</td>
<td>14</td>
<td>83</td>
<td>100</td>
</tr>
<tr>
<td><strong>Erickson</strong> [AFP 1997;55(6)]</td>
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<td>100</td>
<td>100</td>
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<tr>
<td><strong>Gress</strong> [GIE 1997;45(3)]</td>
<td>56</td>
<td>-</td>
<td>-</td>
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<tr>
<td><strong>Wiersema</strong> [Gastro 1997;112(4)]</td>
<td>192</td>
<td>92</td>
<td>93</td>
</tr>
<tr>
<td><strong>Binmoeller</strong> [GIE 1998;47(2)]</td>
<td>43</td>
<td>91</td>
<td>100</td>
</tr>
<tr>
<td><strong>Reed</strong> [AJS 1999;67(2)]</td>
<td>57</td>
<td>72</td>
<td>97</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>398</td>
<td>90%</td>
<td>98%</td>
</tr>
</tbody>
</table>
Diagnosis by EUS FNA

- Molecular markers from EUS FNA can differentiate pancreatic neoplasia requiring surgery from benign conditions and chronic pancreatitis (Anderson, et al)

- EUS FNA of pancreatic duct fluid in the evaluation of pancreatic cancer (Davila, et al)
Metastatic Melanoma
Bile Duct Cancer

*Cholangiocarcinoma*

- Difficult to see a mass with EUS
- Difficult pathological diagnosis to make pre-operatively
- Sensitivity of EUS with FNA is low ~ 60%
Staging Cholangiocarcinoma with EUS

- Staging cholangiocarcinomas with EUS

- Role of intraductal US
EUS for Pancreatic Neoplasms

- Ductal adenocarcinoma
  - Diagnostic/Staging Accuracy
  - Negative Predictive Value
- Fine Needle Aspiration Biopsy
- Neuroendocrine tumors
- Miscellaneous: Lymphoma, Metastases
- Cystic Neoplasms
Normal Appearing Pancreas
Negative Predictive Value of EUS for Pancreatic Carcinoma

<table>
<thead>
<tr>
<th>Study Group</th>
<th>N</th>
<th>NPV</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaufman</td>
<td>25</td>
<td>87%</td>
<td>60%-98%</td>
</tr>
<tr>
<td>Baron</td>
<td>32</td>
<td>88%</td>
<td>71%-96%</td>
</tr>
<tr>
<td>Brown*</td>
<td>74</td>
<td>96%</td>
<td>88%-99%</td>
</tr>
</tbody>
</table>

* 5-yr follow up; CA developed in 2 patients

EUS features of chronic pancreatitis
T1 Pancreatic Head Carcinoma

16.3 mm x 13.1 mm
EUS for Detection of Pancreatic Cancer

- Panc CA: 4th leading cause of Ca death in men and women
- Overall 5-yr survival = 4%
- Survival is inversely proportionate to tumor size
- Small tumors, LN (-), Vascular Invasion (-) = 25% 5-yr survival
- EUS superior to CT/MR for lesions < 2-cm
- Accurate detection of small lesions impacts timing and type of therapy

T3 Pancreatic Cancer
## EUS T-Staging Accuracy

<table>
<thead>
<tr>
<th>Author</th>
<th># Staged by EUS</th>
<th># Surgical Patients</th>
<th>Staging Accuracy</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buscail 1999</td>
<td>73</td>
<td>26</td>
<td>19/26</td>
<td>73%</td>
</tr>
<tr>
<td>Gress 1999</td>
<td>151</td>
<td>75</td>
<td>64/75</td>
<td>85%</td>
</tr>
<tr>
<td>Ahmad 2000</td>
<td>na</td>
<td>89</td>
<td>55/79</td>
<td>69%</td>
</tr>
<tr>
<td>Total</td>
<td>190</td>
<td>138/180</td>
<td></td>
<td>77%*</td>
</tr>
</tbody>
</table>

* 95% CI = 70%-83%
# EUS N-Staging Accuracy

<table>
<thead>
<tr>
<th>Author</th>
<th># Staged by EUS</th>
<th># Surgical Patients</th>
<th>Staging Accuracy</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buscail</td>
<td>73</td>
<td>26</td>
<td>18/26</td>
<td>69%</td>
</tr>
<tr>
<td>Gress</td>
<td>151</td>
<td>71</td>
<td>51/71</td>
<td>72%</td>
</tr>
<tr>
<td>Ahmad</td>
<td>na</td>
<td>89</td>
<td>35/67</td>
<td>54%</td>
</tr>
<tr>
<td>Total</td>
<td>186</td>
<td>104/164</td>
<td></td>
<td>63%*</td>
</tr>
</tbody>
</table>

* 95% CI = 56%-71%
## EUS vs Helical CT for Pancreatic Cancer

<table>
<thead>
<tr>
<th>Series</th>
<th>Detection</th>
<th>Accuray of resectability</th>
<th>Sensitivity for vascular invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EUS</td>
<td>CT</td>
<td>EUS</td>
</tr>
<tr>
<td>Legman 1998</td>
<td>27/27</td>
<td>25/27</td>
<td>20/22</td>
</tr>
<tr>
<td>Midwinter 1999</td>
<td>33/34</td>
<td>26/34</td>
<td>25/30</td>
</tr>
<tr>
<td>Tierney 2001</td>
<td>30/31</td>
<td>30/31</td>
<td>25/31</td>
</tr>
<tr>
<td>Mertz 2000</td>
<td>29/31</td>
<td>16/31</td>
<td>16/16</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>97%</strong></td>
<td><strong>73%</strong></td>
<td><strong>91%</strong></td>
</tr>
</tbody>
</table>

When both EUS and MRI agree on resectability, 89% of cases were resectable

* P < 0.001
EUS Guided FNA for Pancreatic Tumors

- Sensitivity = 90%
- Specificity = 100%
- Accuracy = 94%
- For lesions as small as sub-cm
- Yield is enhanced with on-site cytopathologist
- May require up to 3-5 passes
- Biopsy primary, LNs, & liver lesions

## EUS for Pancreatic Neuroendocrine Tumors

<table>
<thead>
<tr>
<th></th>
<th>All Tumors</th>
<th>Gastrinomas</th>
<th>Insulinomas</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>75</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>93%</td>
<td>100%</td>
<td>88%</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>95%</td>
<td>94%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>PPV</strong></td>
<td>98%</td>
<td>95%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>NPV</strong></td>
<td>83%</td>
<td>100%</td>
<td>43%</td>
</tr>
<tr>
<td><strong>Accuracy</strong></td>
<td>93%</td>
<td>97%</td>
<td>89%</td>
</tr>
</tbody>
</table>

Pancreatic Lymphoma
EUS for Non-Pancreatic Primary Tumors

• Lymphoma
  – FNA diagnosis with flow cytometry
  – Good prognosis
  – Directed therapy

• Metastases
  – Breast
  – Renal Cell

Lewis et al. AJG 1998;93:834-6
Overview

• EUS
  – Anti-tumor therapy
  – Palliation of jaundice
  – Palliation of pain
EUS Guided radio-frequency or ETOH tumor ablation

Goldberg. GIE 1999;50:392
Barclay. GIE 2002;55:266
Immune Therapy

Background

• Tumors are immunosuppressive and block the host immune response

• Injection of lymphocyte culture ("Cytoimplant") directly into tumors may block tumor immunosuppression and enhance host immune response

• Phase I study using Cytoimplant performed on pancreatic cancer showed extended survival and no toxicity

Chang et al. Cancer 2000; 88:1325-1335
Phase II-III Studies of Cytoimplant

Results

- Multi center study
- Compared Cytoimplant to Gemcitibine
- Study stopped because interim analysis showed chemotherapy was better than Cytoimplant
EUS- guided injection of Onyx 015 for pancreatic cancer

- 18 pts
- Concomitant gemcitabine
- 3 minor responses (< 50% tumor reduction)
- 2 sepsis, 1 abscess, 2 duodenal perforations

Gene Therapy

TNF-α

- TNF-α → strong anti-tumor activity
- TNF-α → high toxicity with systemic administration
- TNFαrade-adenovirus vector carries the TNF-α gene
- Gene promoter is radiation inducible
- 37 Pts with locally advanced pancreatic Ca injected with TNFαrade followed by Chemo/XRT
- Tumor stable or decrease in size in 74% at 3 mo

Chang KC. Gastrointest Endosc. 2004
Farrell JJ. Gastrointest Endosc. 2006;63 AB93
Local Chemotherapy
Paclitaxel (OncoGel)

• OncoGel
  – Water soluble → hydrogel
  – Releases paclitaxel continuously up to 6 weeks
• Porcine model
• EUS guided injection of OncoGel
• High and sustained concentration in pancreas
• No toxicity

Matthes K. GIE 2007;65:448
Palliation of Jaundice

If ERCP fails, is there an alternative to PTC or surgical drainage?
Interventional EUS

*EUS-guided injection for diagnosis*

- **Cholangiography**
  - Wiersema et al., 1995 GIE
- **Pancreatography**
  - Gress et al., 1996 GIE
EUS GUIDED Hepatico-Gastrostomy

Sahai GIE 1998;47:AB37
Gastrointest Endosc. 2006 Jul;64:52
What is the best way to palliate pain in pancreatic cancer?

Narcotics? or Celiac Plexus Block?

How about chronic pancreatitis?
Chronic Abdominal Pain

- Can be a clinically challenging problem.
- Management of chronic pain can be difficult.
- There are many approaches to treating the patient with chronic pain:
  - narcotic analgesia
  - celiac plexus block
  - surgery (ie; ganglionectomy)
Why CPB or CPN?

- Pain relief
- Palliative
- Improve quality of life
EUS-Guided Celiac Plexus Block and EUS-Guided Celiac Plexus Neurolysis
Celiac Plexus Block
Fine Needle Aspiration
Celiac Plexus Block
EUS Guided Celiac Plexus Block
EUS-guided Celiac Plexus Neurolysis for Cancer

58 patients pancreatic cancer

Follow-up 6 mo

- Pain score reduction in 78% of patients
- Mean pain score decreased by 50%

Gunaratnam NT, GIE 2001;54:316
Relationship between pain and survival in pancreatic cancer

Pain correlates with resectability \( p=0.04 \)

- No pain before op \( 15 \text{ mo} \)
- Pain before op \( 5.7 \text{ mo} \) \( P=0.003 \)

Kelsen et al Surgery 1997;122(1):53-9
Effect of neurolysis on survival

137 pts randomized to intra-op neurolysis or placebo

- Neurolysis decreased pain scores and delayed or prevented onset of pain compared to placebo  \( p<0.05 \)
- In patients with pre-operative pain, neurolysis improved survival compared to placebo  \( p<0.0001 \)

Effect of Neurolysis on Pain, Survival and Quality of Life

100 Patients randomized to percutaneous celiac block or analgesic p.o. + sham block

<table>
<thead>
<tr>
<th></th>
<th>Neurolysis</th>
<th>Analgesic</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Pain reduction at 1 week</td>
<td>53%</td>
<td>27%</td>
<td>.005</td>
</tr>
<tr>
<td>% of patients with pain &gt; 5/10</td>
<td>14%</td>
<td>40%</td>
<td>.005</td>
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<tr>
<td>Survival at one year</td>
<td>16%</td>
<td>6%</td>
<td>.26</td>
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<tr>
<td>Quality of life</td>
<td>No difference</td>
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</table>

Meta Analysis of 5 RCT-302 patients

Narcotic use at 2 and 8 wks

Yan BM. Am J Gastroenterol. 2007;102:430
Meta Analysis of 5 RCT-302 patients

Survival at 8 wks

Yan BM. Am J Gastroenterol. 2007;102:430
CT vs. EUS CELIAC PLEXUS BLOCK FOR TREATMENT OF PAIN ASSOCIATED WITH CHRONIC PANCREATITIS

Bupivacaine + Triamcinolone

<table>
<thead>
<tr>
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<th>EUS</th>
<th>CT</th>
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<tr>
<td>N</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Pain benefit @ 8 wks</td>
<td>40%</td>
<td>25%</td>
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<tr>
<td>Pain benefit @ 24 wks</td>
<td>30%</td>
<td>12%</td>
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</tbody>
</table>

Gress. Am J Gastroenterol 1999;94:872-4
EUS-guided celiac plexus block for chronic pancreatitis

90 patients

• 55% experienced significant improvement in pain score
• Mean pain score @ 4 and 8 wks: 8 → 2  \( p < 0.05 \)
• 26% experienced benefit > 12 wks
• 10% experienced benefit > 24 wks

Age < 45 and prior pancreatic surgery predicted no benefit to EUS-Guided Celiac Block

Gress. Am J Gastroenterol 2001;96:409-16
Efficacy of EUS Guided Celiac Plexus Block (CPB) for Managing Abdominal Pain Associated with Chronic Pancreatitis (CP): A Meta-analysis

**Aim:** To evaluate the efficacy of EUS-guided CPB in alleviating chronic abdominal pain in CP

**Method:** A Medline database search was performed of the English literature for trials evaluating the efficacy of EUS-CPB for the management of chronic abdominal pain in CP
Efficacy of EUS Guided Celiac Plexus Block (CPB) for Managing Abdominal Pain Associated with Chronic Pancreatitis (CP): A Meta-analysis

- The diagnosis of CP was based on clinical presentation and a minimum of 4 EUS features of CP.
- Studies involving less than 10-patients were excluded.
- Data on pain relief was extracted, pooled, and analyzed.
- A Bayesian hierarchical model for the meta analysis was developed. A Markov Chain Monte Carlo algorithm was implemented in the analysis.
- **Results:** 6-relevant studies were identified comprising a total of 221 patients. EUS-guided CPB was effective in alleviating abdominal pain in 52.44% of patients (95% CI 31.64, 74.9).
<table>
<thead>
<tr>
<th>Study</th>
<th>Pain relief reported out of total patients</th>
<th>Observed proportion</th>
<th>Analysis for proportion</th>
<th>Quartiles</th>
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<tr>
<td></td>
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<td>Estimates</td>
<td>SE</td>
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<td>Gress et al 1999</td>
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<td>Levy et al 2007</td>
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<td>O’toole et al 2007</td>
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<td>0.65</td>
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<td>LeBlanc et al 2007</td>
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<td>0.0681</td>
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<td>Stevens et al 2007</td>
<td>16/26</td>
<td>0.62</td>
<td>0.6025</td>
<td>0.0887</td>
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<td><strong>Over All Studies</strong></td>
<td><strong>123/221</strong></td>
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<td><strong>0.5244</strong></td>
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</tbody>
</table>
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<table>
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<td>Summary</td>
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</table>
Efficacy of EUS Guided Celiac Plexus Block (CPB) for Managing Abdominal Pain Associated with Chronic Pancreatitis (CP): A Meta-analysis

Conclusion

- Meta-analysis demonstrates that EUS-guided CPB results in the reduction of abdominal pain due to CP in at least 50% of patients.
- Appropriate patient selection and refinement in technique will likely lead to better results. Further prospective randomized trials are needed.
Conclusions

• EUS
  – Can deliver targeted anti-tumor therapies
  – Can provide biliary and pancreatic drainage
  – Celiac plexus neurolysis should be considered first line therapy for in pancreatic Ca pain
  – Celiac plexus block has a limited role in selected patients with chronic pancreatitis

• ERCP with Direct Cholangioscopy
  – Direct visualization
  – Targeted biopsy
  – Therapy

Unlimited opportunities for the future