Histological diagnosis by EUS guided biopsy

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Can histology improve FNA diagnostic accuracy?
Who needs histological diagnosis than cytology

- Lymphoma
- Gastrointestinal stromal tumour
- Autoimmune pancreatitis
- Chronic pancreatitis
- Neuroendocrine tumour for staging
- Liver disease for liver biopsy
- Translational study for cancer
How to obtain histology

• Histology needle (ProCore – 25G, 22G, 20G, 19G)

• Needle with side port

• Big FNA needle such as 19G needle

• Direct biopsy through the lumen of 19G needle
Tissue core

✧ Conventionally defined as an architecturally intact piece of tissue measuring at least 550 micron in greatest axis
FNA and FNB needle
22G ProCore for pancreatic lesion

• Using 22G ProCore needles for pancreatic lesions (< 2 cm)

• 68 patients, The mean lesion size was 16.5 mm (range 5–20).

• 58 / 68 cases (85.3 %) adequate for pathological examination

• 36 / 68 cases (52.9 %) - presence of a tissue core

• Sensitivity 80%, specificity 100%, PPV 100%, NPV 40% and accuracy 42%.

Fabbri C, Surg Endosc 2015
25G FNA vs 22G FNB needle
56 patients with 61 solid pancreatic lesions.

Same lesion in same EUS session using 2 kinds of needles

The mean number of passes with FNA was 3.5 (ranges 1-8) vs core biopsy needle was 1.7 (ranges 1-5).

Adequate samples were 50/61 (81.9%) for FNA and 45/61 (73.8%) for core biopsy (P = 0.37).

The diagnostic yield was FNA 46/61 (75.4%), FNB 42/61 (68.9%) and both 47/61 (77.1%)
25G FNA needle vs 22G Core needle

- Agreement of 87.5% ($\kappa = 0.77; \ P < 0.001$) between core and FNA specimens.
- The sensitivity for the diagnosis of malignancy for FNA 68.1% and FNB 59.6%, ($P = \text{NS}$).
- Core needle missed 4 tumours, 3 in the head region.
- The specificity was 100% for both methods. The incremental increase in sensitivity and specificity by combining both methods are 1.5% and 0%, respectively.
Studies of 25G Procore needle
• Retrospective analysis. 50 patients.

• First pass cytologic analysis of malignancy – sensitivity of 83% (1st), 91% (2nd) and 96% (3rd).

• Visible core was reported in 46 patients (92%),

• Histologic core was seen in 16 patients (32%).
• Malignancy diagnosis in 29 patients on the 1\textsuperscript{st} pass, cumulative sensitivity of 63\% (1\textsuperscript{st}) and 87\% (1-4 passes).

• The sensitivity, specificity, and accuracy in combined cytologic and histologic results were 85\%, 100\%, and 86\% for single pass; and 96\%, 100\%, and 96\% on multiple passes.

• No complications were seen.
27 patients. Each lesion was punctured once by both a 25G EchoTip ProCore needle and a 22G standard needle (EchoTip; Cook Medical) with capillary sampling.

Blinded histocytologic analyses were conducted.

The final diagnosis was based on FNA findings of malignant cells, pathologic analysis of the surgical specimen, and/or radiologic and clinical follow-up of at least 7 months.
25G FNB needle vs 22G FNA needle

• 28 EUS-FNA procedures, pancreatic mass (n=19) and LN (n=9).
• No complications.
• Single-pass sensitivity for pancreatic and LN malignancy were equal for the needle types: 89.5% (95 %CI 66.82– 98.39) and 66% (95 %CI 24.1–94)
• EUS needle visualization (P=0.125), amount of blood contamination (P=0.705), macroscopic quantity of the material (P=0.858), quality of the cytology (P=0.438), and adequacy and accuracy of the cell block material (P=0.220).

Mavrogenis G, Endosc Int Open. 2015
Endoscopic ultrasound-guided sampling of solid pancreatic masses: 22-gauge aspiration versus 25-gauge biopsy needles

- Retrospective cohort. 38 22G FNA vs 38 25G FNB
- Technical success (100% for both), the mean number of needle passes (5.05 vs. 5.55, \( P = 0.132 \)), complications (0% for both)
- Cytological diagnostic accuracy (22G 97.4% vs. 25G 89.5%, \( P = \text{NS} \))
- Histological diagnostic accuracy (22G 34.2% vs. 25G 52.6%, \( P = \text{NS} \))
- Diagnostic cellular material present (22G 0.92 vs. 25G 1.32, \( P = 0.030 \))
- Retention of architecture (22G 0.97 vs. 25G 1.42, \( P = 0.010 \))
- The 25G FNB group showed a better histological diagnostic yield for specific tumor discrimination compared with the 22G FNA group (60% vs. 32.4%, \( P = 0.018 \)).

Yang MJ, BMC Gastroenterology 2015
Histologic diagnosis of pancreatic masses using 25-gauge endoscopic ultrasound needles with and without a core trap: a multicenter randomized trial

✧ 8 Japanese referral centers, N = 214
✧ 25G Procore (N= 106) vs 25G FNA (N=108)
✧ First pass comparison -
✧ Adequate for histologic evaluation - (Procore 81.1% vs. FNA 69.4%; P=0.048)
✧ Superior cellularity (rich/moderate/poor, 36%/27%/37% vs. 19%/26%/55%; P=0.003).
✧ Malignancy diagnosis: sensitivity (75.6% vs. 69.0 %, P=0.337) and accuracy (79.2% vs. 75.9 %, P=0.561)

Kamata K, Endoscopy 2016
N=56. randomly use each needle, 2 passes / needle

The mean pancreatic mass size was 35.3 ± 17.1 mm (range 14–122.3 mm).

28 patients (50%) had tumors at the pancreas head or uncinate process.

There were no technical failures or procedure-related adverse events.

Park SW, PLoS ONE 2016
<table>
<thead>
<tr>
<th></th>
<th>25G</th>
<th>22G</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procurement of histologic core, n(%)</td>
<td>49 (87.5%)</td>
<td>46 (82.1%)</td>
<td>0.58</td>
</tr>
<tr>
<td>Trans-duodenal, n(%)</td>
<td>27 (96.4%)</td>
<td>25 (89.3%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Trans-gastric, n(%)</td>
<td>22 (78.6%)</td>
<td>21 (75%)</td>
<td>0.75</td>
</tr>
<tr>
<td>Width of histologic core (mm) (Mean ± SD)</td>
<td>0.31 ± 0.2</td>
<td>0.38 ± 0.28</td>
<td>0.19</td>
</tr>
<tr>
<td>Length of histologic core (mm) (mean ± SD)</td>
<td>1.67 ± 3.86</td>
<td>2.99 ± 7.99</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Table 4. Histological diagnostic performance of both needles.

<table>
<thead>
<tr>
<th></th>
<th>25 G needle</th>
<th>22 G needle</th>
<th>25 G + 22 G needle</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Accuracy</strong></td>
<td>65.31% [95% CI, 51.11%–77.22%]</td>
<td>60.87% [95% CI, 46.25%–73.77%]</td>
<td>74.07% [95% CI, 60.85%–84.00%]</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>65.12% [95% CI, 49.07%–78.99%]</td>
<td>62.79% [95% CI, 46.73%–77.02%]</td>
<td>75.00% [95% CI, 60.40%–86.36%]</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>66.67% [95% CI, 22.28%–95.67%]</td>
<td>33.33% [95% CI, 0.84%–90.57%]</td>
<td>66.67% [95% CI, 22.28%–95.67%]</td>
</tr>
<tr>
<td><strong>Positive predictive value</strong></td>
<td>93.33% [95% CI, 77.93%–99.18%]</td>
<td>93.10% [95% CI, 77.23%–99.15%]</td>
<td>94.74% [95% CI, 82.25%–99.36%]</td>
</tr>
<tr>
<td><strong>Negative predictive value</strong></td>
<td>21.05% [95% CI, 6.05%–45.57%]</td>
<td>5.88% [95% CI, 0.15%–28.69%]</td>
<td>25.00% [95% CI, 7.27%–52.38%]</td>
</tr>
<tr>
<td>Diagnostic categories</td>
<td>25 G needle</td>
<td>22 G needle</td>
<td>25 G + 22 G needle</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>------------</td>
<td>------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Positive for malignancy (n)</td>
<td>26</td>
<td>23</td>
<td>33</td>
</tr>
<tr>
<td>Suspicous for malignancy (n)</td>
<td>25</td>
<td>26</td>
<td>18</td>
</tr>
<tr>
<td>Negative for malignancy (n)</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Non-diagnostic (n)</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>98%</td>
<td>95%</td>
<td>98%</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>98%</td>
<td>94%</td>
<td>98%</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>80%</td>
<td>57%</td>
<td>80%</td>
</tr>
</tbody>
</table>

Table 2. Cytological diagnostic categories of both needles.
RCT, 100 patients

Median of 1 pass was required to achieve on-site diagnosis of 19G 96% and 25G 92% (P = 0.68).

Technical failure (0% vs 2%, P = 0.99) or adverse events (2% vs 0%, P = 0.99) between 19G and 25G cohorts.

Histological core tissue procurement was better with 19G needle (88% vs 44%, P < 0.001)

Specimens were bloodier (severe bloodiness, 36% vs 4%; P < 0.001) in 19G needle.

Ramesh J, Pancreas 2015
• 120 patients with various pathology. Mean lesion size of $38 \pm 25$ mm (range 8-140 mm).

• Success rate 98.9%

• 116/119 (97.5%) - adequate samples for histological examination.

• A mean of $2.8 \pm 0.8$ passes per patient were performed.

• Sensitivity 91.8%, specificity 100%, PPV 100%, NPV 71.4%, accuracy 93.2%. 

Larghi A, Gastrointest Endosc 2011
Macroscopic on-site quality evaluation (MOSE) study of 19G FNA specimen

- 100 patients with 111 solid lesions, 83 malignancy, 28 benign
- MOSE revealed macroscopic visible core (MVC) in 91.1% with the median length of 8 mm.
- Histologic core was confirmed in 78.9%.
- MVC length of 4 mm – AUC of 0.893.
- MVC > 4mm with better histologic, cytologic, and overall diagnostic yields than in MVC <4 mm.
Reduce the need of on-site cytologist
FNB can reduce the need of rapid onsite evaluation (ROSE)

- 33 patients, 312 passes in 42 different lesions using FNB (SharkCore) without ROSE or FNA with ROSE

- Same patient, same operator, sequentially using FNA or FNB needles. 25G needle (27 times); 22G needle (15 times).

- Core tissue obtained from all FNB lesions, median length 15 mm (range, 5-25).

- Diagnosis of malignancy - FNB (72.7%) vs FNA (66.7%, P=.727),

- FNB vs FNA diagnose of cancer –sensitivities (88.9% vs 81.5%), specificities (both 100%), and accuracies for cancer 90.9% and 84.8% .

Rodrigues-Pinto E, Gastrointest Endosc 2016
FNB can reduce the need of rapid onsite evaluation (ROSE)

- Increasing the number of FNB sampling passes increased the likelihood of malignancy diagnosis (OR, 3.081; P = .049).
- Higher diagnostic yield that use 25G core needle (FNB 86.4% [19/22] versus FNA 45.5% [5/11]).
- EUS-FNB sampling provided a statistically significant advantage (87.9% [76%-100%] vs 27.3% [11%-43%], P < .001).
FNB can reduce the need of rapid onsite evaluation (ROSE)

FNB sampling provided qualitative information not reported on FNA, such as degree of differentiation in malignancy, metastatic origin, and rate of proliferation in neuroendocrine tumors.

Rodrigues-Pinto E, Gastrointest Endosc 2016
Histological diagnosis

- Lymphoma
- Gastrointestinal stromal tumour
- Autoimmune pancreatitis
- Chronic pancreatitis
- Neuroendocrine tumour for staging
- Liver disease for liver biopsy
- Translational study for cancer
EUS FNB for lymphoma using 19G needle

- EUS FNA can produce tissue for morphology, immunophenotyping, flow cytometric and cytogenetic analysis to subclassification of lymphoproliferative disorders

- 240 suspected patient, 152 (63%) diagnosed of lymphoma

- 147 patients (96.7 % ) were diagnosed by EUS-FNAB

Yasuda I, Am J Gastroenterol 2012
EUS FNB for lymphoma using 19G FNA needle

• Classification according to WHO is possible in 135 patients (88.8 %)

• Flow cytometry showed abnormal or unusual cell populations in 121 (79.6 %)

• In 114 (90.5 %) of the 126 patients diagnosed with B-cell lymphoma.

• Specific cytogenetic abnormalities were detected in 21 (13.8 %)

Yasuda I, Am J Gastroenterol 2012
Feasibility and Diagnostic Yield of EUS-FNB by 22G Procore needle in Gastric subepithelial Tumors ≥ 2cm

✧ N = 43, all successful puncture.
✧ EUS-FNB procedure results were diagnostic in 86.0%, suggestive in 4.7%, and nondiagnostic in 9.3% of cases.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Aspiration Cytology</th>
<th>Histology</th>
<th>Combined Cytology and Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal stromal tumor (%)</td>
<td>11 (64.7)</td>
<td>16 (94.1)</td>
<td>17 (100.0)</td>
</tr>
<tr>
<td>Leiomyoma (%)</td>
<td>4 (26.7)</td>
<td>14 (93.3)</td>
<td>15 (100.0)</td>
</tr>
<tr>
<td>Schwannoma (%)</td>
<td>0 (0.0)</td>
<td>1 (100.0)</td>
<td>1 (100.0)</td>
</tr>
<tr>
<td>Ectopic pancreas (%)</td>
<td>1 (50.0)</td>
<td>2 (100.0)</td>
<td>2 (100.0)</td>
</tr>
<tr>
<td>Lymphoma (%)</td>
<td>0 (0.0)</td>
<td>1 (100.0)</td>
<td>1 (100.0)</td>
</tr>
<tr>
<td>Metastatic carcinoma (%)</td>
<td>1 (100.0)</td>
<td>1 (100.0)</td>
<td>1 (100.0)</td>
</tr>
</tbody>
</table>

Lee M, Medicine 2015
Diagnostic efficacy of EUS guided needle sampling for upper GI subepithelial lesions: a meta-analysis

✧ 17 studies, 978 EUS-guided needle sampling

✧ Pooled diagnostic rate 59.9 %, with a heterogeneity I² of 55.2 %.

✧ Subgroup analysis showed no difference in diagnostic rate among FNA, TCB, and FNB

✧ Also no difference among 19-, 22-, and 25-G needles.

✧ Subgroup analysis and meta-regression suggested that the cell block method might be correlated with a higher diagnostic rate.

Autoimmune pancreatitis

• AIP is a systemic fibroinflammatory disorder, in which the pancreas is one of several potentially affected organs.
• Affect other organs - bile ducts, salivary glands, and retroperitoneal lymph nodes.
• In Asia, the prevalence of AIP that has been reported ranges from 5.4–6.0% of patients with idiopathic pancreatitis.
• Surgical cohorts - up to 26.5% histologically proved AIP
• M:F ratio 2:1
• Mean age at diagnosis is 60 (20 -70) years
Autoimmune pancreatitis

• Type 1 and 2.

• Lymphoplasmacytic infiltration

• Abundant immunoglobulin G4– positive plasmacyte infiltration (> 10/high-power field)

• Obliterative phlebitis, storiform fibrosis

• Granulocytic epithelial lesions (GEL)
AIP diagnosed by 19G FNA

✧ 41 patients.
✧ Lymphoplasmacytic sclerosing pancreatitis (N = 17)
✧ IgG4-positive plasma cells in 5
✧ 3 samples were positive for both
✧ No samples had granulocytic epithelial lesions.
✧ Therefore, 19 patients (43%) were diagnosed with AIP based on histologic analysis.

Iwashita T, Clin Gastroenterol Hepatol 2012
EUS features of chronic pancreatitis
EUS and pathological correlation

Albashir S, Am J Gastroenterol 2010
idiopathic chronic pancreatitis (ICP) - Pancreatic acinar structure is replaced by fibrosis with little lymphoplasmacytic infiltration. Obliterative phlebitis is not observed. No IgG4 (C)-positive plasma cells are apparent.

Mizuno N, J Gastroenterol 2009
Comparison of EUS-guided tissue acquisition using two different 19-gauge core biopsy needles: a multicenter, prospective, randomized, and blinded study

<table>
<thead>
<tr>
<th></th>
<th>19 FNB (n=44)</th>
<th>19 TCB (n=41)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of diagnostic histology</td>
<td>85%</td>
<td>57%</td>
<td>0.006</td>
</tr>
<tr>
<td>Accuracy</td>
<td>88%</td>
<td>62%</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean total length</td>
<td>19.4mm</td>
<td>4.3mm</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean complete portal triads from liver biopsy</td>
<td>10.4</td>
<td>1.3</td>
<td>0.0004</td>
</tr>
<tr>
<td>Cross over biopsy</td>
<td>2%</td>
<td>65%</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

DeWitt J, Endosc Int Open 2015
EUS guided liver biopsy

✧ 19-gauge Tru-cut biopsy needle (Quick-core) vs 19G Procore (PC)
✧ 75 patients, QC (n=45) or PC (n=30) needle.
✧ PC required fewer passes (median 2 vs 3; P < .0001), produced longer aggregate length (median 20 mm vs 9 mm; P < .0001) with more complete portal tracts (median 5 vs 2; P = .0003) and adequate specimens (P < .01).

Sey MS, Gastrointest Endosc 2016
### Table 3. EUS-guided core liver biopsy for parenchymal disease studies

<table>
<thead>
<tr>
<th>Design and size</th>
<th>Gleeson (Retrospective N = 9)</th>
<th>DeWitt (Prospective N = 21)</th>
<th>Gor (Retrospective N = 10)</th>
<th>Stavropoulos (Prospective N = 22)</th>
<th>Current study (Prospective N = 75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needle (19-gauge)</td>
<td>QC (core)</td>
<td>QC (core)</td>
<td>Expect† (FNA)</td>
<td>EchoTip‡ (FNA)</td>
<td>QC (core) PC (core)</td>
</tr>
<tr>
<td>No. complete portal tracts</td>
<td>7</td>
<td>2</td>
<td>8</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Median length, mm</td>
<td>13</td>
<td>9</td>
<td>13</td>
<td>37</td>
<td>9</td>
</tr>
<tr>
<td>Adequacy (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 complete portal tracts or &gt;15 mm</td>
<td>89</td>
<td>N/A</td>
<td>100</td>
<td>N/A</td>
<td>31</td>
</tr>
<tr>
<td>&gt;5 complete portal tracts and &gt;15 mm</td>
<td>33</td>
<td>29</td>
<td>30</td>
<td>91</td>
<td>16</td>
</tr>
<tr>
<td>Histologic diagnosis</td>
<td>100</td>
<td>90</td>
<td>100</td>
<td>91</td>
<td>73</td>
</tr>
<tr>
<td>No. complete portal tracts/mm</td>
<td>0.40</td>
<td>0.32</td>
<td>0.64</td>
<td>0.30</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Sey MS, Gastrointest Endosc 2016
19G vs percutaneous or transjugular liver biopsy

✧ Liver biopsy (LB) by EUS-LB (19G) vs TJ-LB(18-19G), and PC-LB (18-20G).

✧ Wilcoxon rank sum tests indicated that EUS-LB of both liver regions produced significantly more tissue in terms of both total specimen length (TSL) and complete portal triad (CPTs) compared with a PC-LB (P = .0000 and .0006).

✧ EUS-LB produced significantly longer TSL than TJ-LB (P = .01) and similar CPTs (P = .22).

Pineda JJ, Gastrointest Endosc 2016
Direct intracystic biopsy and pancreatic cystoscopy through a 19-gauge needle EUS (with videos)

Jose R. Aparicio, MD, Juan Martínez, MD, Maria Niveiro, MD, Antonio Cabezas, MD, Francisco Ruiz, MD, Enrique De Madaria, MD, Juan A. Casellas, MD

Alicante, Spain
Side port needle

- Multicenter, prospective, RCT for pancreatic mass
- N=154 patients (side-port 76, vs standard FNA 78)
- Diagnostic accuracy of histology (side-port, 87%, vs FNA, 82%; P=.51).
- Samples that enabled histologic interpretation – Side-port 64% vs FNA 43% (P =.009).
- No significant difference in blood contamination
Conclusion

✧ FNB needle appears better than FNA needle in providing tissue diagnosis.

✧ Certain disease groups require histology diagnosis

✧ Selective use of FNB needle is important to achieve diagnosis.