Prevalence of Pancreatic Cystic Neoplasms

- 300 consecutive autopsies – attn to panc
- 186 cystic lesions were found in 73 of 300 autopsies (24.3%)
- Epithelial atypia seen: normal (47.5); papillary hyperplasia (32.8); atypical hyperplasia (16.4); CA in situ (3.4); and invasive CA 0%.

1.2% of adult in US has a cyst in the pancreas

Spectrum of benign, malignant and borderline

Pseudocyst is the commonest cystic lesion

Serous cystadenomas are benign lesions

Mucinous neoplasms have malignant potential
Survival of Patients with Cystic Lesions of the Pancreas

- 30 pts retrospectively studied at Michigan
- 14 serous, 11 mucinous, 5 malignant
- 36% pts were asymptomatic
- All resected with morbidity rate 27% and mortality rate of 0%
- Actuarial 5-year survival
  - Serous 100%
  - Mucinous 100%
  - Malignant 33%

Pancreas Surgery At MGH 1990-2000

1988-1998 increase in cystic tumors from 16-30%
Fernandez-del Castillo C. Adv Surg 2000
## Precursor Lesions for Adeno CA

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Frequency of Malignant Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>High grade PanIN</td>
<td>100%</td>
</tr>
<tr>
<td>Mucinous Cystic Neoplasm</td>
<td>80% show premalignant/ malignant changes</td>
</tr>
<tr>
<td></td>
<td>35% show Invasive Cancer</td>
</tr>
<tr>
<td>Main Duct IPMN</td>
<td>35-50% show Invasive Cancer</td>
</tr>
<tr>
<td>Branch Duct IPMN</td>
<td>15% show Carcinoma-in-situ</td>
</tr>
</tbody>
</table>
Cystic lesions

- Pseudocyst post pancreatitis
- Cystic tumors
  - Serous
  - Mucinous cystic tumor
  - Intraductal Papillary Mucinous Neoplasm (IPMN)
- Other cystic tumors
  - SPEN
  - Necrotic solid tumor
- True Cyst
  - Incidental and VHL
Serous cystadenoma: 32-39%

Mucinous neoplasm: 10-45%

IPMN: 21-33%

>60% Mucinous
Cystic Degeneration in Solid Tumors

Neuroendocrine Solid and Pseudopaillary Neoplasm (SPEN)
Adenocarcinoma

< 10%
Cystic Lesion: Imaging Objectives

Morphologic details (pattern)

- Unilocular or Multilocular
- Microcystic
- Cyst communication with PD
- Extent of PD involvement

Sahani DV. ECNA 2005/Radiographics 2005/JACR 2009
Cystic Lesion: Imaging Objectives

Benign or Malignant

- Mural nodules
- Thick Septae
- Cyst/MPD size
- Metastases
MUCINOUS CYSTIC NEOPLASM (MCN)

- Middle age women
  - Tail location (85%) most common
- Single/few cysts (< 6 cyst) > 2cm
- Peripheral/septal Ca+/mural nodules
- No communication with PD
- Benign or malignant
- **10-20% are carcinoma**
MUCINOUS CYSTIC NEOPLASM
INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS (IPMN)

- Increasingly recognized
- Similar to MCNs—cystic tumor that secrete mucin
- Arise from a duct papillary epithelium
- Affect a mostly elderly men.
- Dilatation of the ducts as a result of tumor growth and mucin
- Upto 49% of IPMNs may be malignant

Ohhashi K et al Prog Dig Endosc 1982;20:348-351
IPMN Classification
Intraductal Papillary Mucinous Neoplasms of the Pancreas: An Analysis of Clinicopathologic Features and Outcome

[Original Articles]

D'Angelica, Michael MD*, Brennan, Murray F. MD, FACS*, Suriawinata, Arief A. MD†; Klimstra, David MD†; Conlon, Kevin C. MD, MBA, FACS*

From the *Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York, and the †Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, New York.

Spectrum from Benign, Borderline to Invasive

Hyperplasia          Adenoma          Ca-in-situ (PanIN)          Invasive

> 10 yrs
IPMN: HISTOPATHOLOGY

BENIGN

ATYPICAL CELLS

LOW GRADE DYSPLASIA
(Adenoma)

MOD. GRADE DYSPLASIA
(Borderline) > 50% Borderline

SEV. GRADE DYSPLASIA
Non-invasive (CIS)

AGGRESSIVE

NON-AGGRESSIVE

MALIGNANT
Divisum IPMN in Ventral duct
IPMN: MRCP

Main duct

Side-branch

Combined
SIDE BRANCH IPMN

- Communicate with the MPD
- 15-20% risk of malignancy
- Invasive Ca less common

Sahani DV et al. CGH 2009
MAIN DUCT
IPMN

• Higher risk of malignancy (60%)

• Surgery often needed for the management

Irie H et al. AJR 2000; 174: 1403-1408
Mucinous Cystic Neoplasms

MUCINOUS LESIONS

Macrocystic
<6 cysts, > 2 cm in size
Lobulated margins
± Calcification
± Mural nodule

SB IPMN

MD-IPMN
Differentiation of IPMN from Other Pancreatic Cystic Masses: MDCT VS. MRCP using ROC Analysis

- 53 patients with path confirmed cystic lesions evaluated by MDCT & MRCP.
- Two Radiologist evaluated cyst morphology features for diagnosis and predicting malignancy
- Diagnostic confidence compared using ROC

Song JS et al. JMRI 2007
Differentiation of IPMN from Other Pancreatic Cystic Masses: MDCT VS. MRCP using ROC Analysis

<table>
<thead>
<tr>
<th>Az Value</th>
<th>MRI</th>
<th>MDCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communication</td>
<td>0.94/0.91</td>
<td>0.79/0.87</td>
</tr>
<tr>
<td>IPMN</td>
<td>0.99/0.93</td>
<td>0.77/0.85</td>
</tr>
</tbody>
</table>

Differentiating IPMN from other cysts

| Differentiating IPMN from other cysts | 96/90% SN/SP | 80/86% SN/SP |

Song JS et al. JMRI 2007
Accuracy of CT: Cystic Lesions of the Pancreas

- 100 cystic lesions evaluated by 2 radiologists
- Categorize using morphologic features of CT
- Surgical pathology used to diagnose
- Serous cystadenomas were diagnosed with greatest accuracy and concordance
- Correct diagnosis made in 60%
- No diagnosis possible in 25%

Procacci: J Compt Assist Tomo 23:906 1999
Relative Accuracy of CT and MRI for Characterization of Cystic Lesions of the Pancreas

- 58 patients with cystic lesions evaluated
  - CT (n=40), MR (n=6) & both (n=12).
- Two Radiologist provided leading diagnostic certainty (0-100%) and likelihood of malignancy (0-100%)
- Surgical pathology used to diagnose

Visser BC et al AJR 2007
Relative Accuracy of CT and MRI for Characterization of Cystic Lesions of the Pancreas

- 36% (21/58) malignant
- CT and MR comparable in predicting Malignancy
  - (MR=0.91/0.85 & CT 0.82 and 0.76)
- Correct diagnosis made in 46% and 43%

Visser BC et al AJR 2007
### MDCT Accuracy – Cyst Characterization

<table>
<thead>
<tr>
<th>Lesion</th>
<th>MDCT Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtypes</td>
<td>70%</td>
</tr>
<tr>
<td>Mucinous v/s Non-mucinous</td>
<td>80%</td>
</tr>
<tr>
<td>Lesions &gt; 30 mm</td>
<td>83%</td>
</tr>
<tr>
<td>Lesions ≤ 30 mm</td>
<td>79%</td>
</tr>
</tbody>
</table>

Sahani et al. DDW 2007
### MGH Data: Prospective MDCT
**Size 7 – 100 mm (mean 32 mm)**

<table>
<thead>
<tr>
<th>TYPES</th>
<th>TOTAL</th>
<th>BENIGN</th>
<th>BORDERLINE</th>
<th>CIS</th>
<th>INVASIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MUCINOUS LESIONS</strong></td>
<td>64 (69%)</td>
<td>30</td>
<td>12</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>MD or C IPMN</td>
<td>36</td>
<td>8</td>
<td>8</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>SB-IPMN</td>
<td>16</td>
<td>12</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>MCN</td>
<td>12</td>
<td>10</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>NON-MUCINOUS LESIONS</strong></td>
<td>29 (31%)</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>SPPT</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SCA</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Benign cyst including pseudocyst</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Adenocarcinomas</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td><strong>TOTAL LESIONS</strong></td>
<td>93</td>
<td>50</td>
<td>12</td>
<td>11</td>
<td>20</td>
</tr>
</tbody>
</table>
Challenges in Cyst Characterization: Morphologic Overlap

Mucinous  Pseudocyst  IPMN

Cohen-Scali F et al. Radiolgy 2003
Khurana B et al. AJR 2003
Kim S et al. AJR 2006
Cyst Classification Challenges:
What are the problems?
Morphological Overlap

Radio MCN
Patho Lymphoepithelial Cyst

Radio MCN
Patho Enteric Duplication Cyst

Unilocular cyst comm. with PD may be pseudocyst or IPMN

Radio IPMN
Patho MCN
Features of Aggressive Biology In IPMN’s
Small Mural Nodule (< 5 mm) Detection

Irie et al Radiology 2002
Fukukura Y Acta Radiol 2003
Sahani et al Radiology 2005
## Pancreas Cyst: Features Predictive of Malignancy

<table>
<thead>
<tr>
<th>Features</th>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid mass</td>
<td>78-96%</td>
<td>67-92%</td>
</tr>
<tr>
<td>MPD &gt;10mm</td>
<td>92%</td>
<td>78%</td>
</tr>
<tr>
<td>Diffuse or multifocal MPD involvement</td>
<td>77-78%</td>
<td>56-93%</td>
</tr>
<tr>
<td>Calcified intraluminal content</td>
<td>77%</td>
<td>33%</td>
</tr>
<tr>
<td>Mural nodule</td>
<td>87%</td>
<td>56%</td>
</tr>
<tr>
<td>Side branch or combined &gt;5cm</td>
<td>94%</td>
<td>54%</td>
</tr>
<tr>
<td>Side branch &gt;3 cm</td>
<td>81%</td>
<td>67%</td>
</tr>
<tr>
<td>Peripancreatic haziness</td>
<td>77%</td>
<td>67%</td>
</tr>
</tbody>
</table>
Multifocal Lesions: ? Increased Risk of Malignancy
Small lesions: 122 patients  
Malignancy 13%

<table>
<thead>
<tr>
<th>ACCURACY</th>
<th>MDCT</th>
<th>MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septa</td>
<td>61 %</td>
<td>69 %</td>
</tr>
<tr>
<td>Mural Nodule</td>
<td>1 / 3</td>
<td>2 / 3</td>
</tr>
<tr>
<td>Duct Commu.</td>
<td>65 %</td>
<td>78 %</td>
</tr>
<tr>
<td>Histo Subtype</td>
<td>59 %</td>
<td>81 %</td>
</tr>
<tr>
<td>PPV Benignity</td>
<td>82 %</td>
<td>85 %</td>
</tr>
</tbody>
</table>
## MGH Experience: Malignancy Predictors

<table>
<thead>
<tr>
<th>MDCT FEATURES</th>
<th>PPV FOR MALIGNANCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mural Nodules (Cyst + Duct)</td>
<td>80</td>
</tr>
<tr>
<td>Septations</td>
<td>62</td>
</tr>
<tr>
<td>Significant MPD Dilatation (&gt;8 mm)</td>
<td>88</td>
</tr>
<tr>
<td>Mural Nodule + Significant MPD Dilatation (&gt;8 mm)</td>
<td>86</td>
</tr>
<tr>
<td>Septations + Mural Nodule</td>
<td>65</td>
</tr>
<tr>
<td>CBD dilatation</td>
<td>100</td>
</tr>
<tr>
<td>Size</td>
<td>82</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MDCT</th>
<th>OVERALL</th>
<th>LESIONS ≤ 30 MM</th>
<th>LESIONS &gt; 30 MM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity Malignant</td>
<td>65</td>
<td>45</td>
<td>87</td>
</tr>
<tr>
<td>Specificity Benign</td>
<td>80</td>
<td>82</td>
<td>87</td>
</tr>
</tbody>
</table>
Challenges with MDCT Predictors of Malignancy

- Differentiation of borderline and CIS changes (prevalent in mucinous lesions) is difficult on imaging

Called Malignant- Borderline
Called Benign Small, C IPMN
IS THERE A ROLE FOR PET CT?

Malignant

BL

Malignant
# PET CT

<table>
<thead>
<tr>
<th></th>
<th>MDCT</th>
<th>FDG-PET</th>
<th>Fused PET-CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant</td>
<td>80%</td>
<td>40%</td>
<td>90%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>92%</td>
<td>94%</td>
<td>94%</td>
</tr>
<tr>
<td>Specificity</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sahani et al. DDW 2007
Sainani RSNA 2008
WHAT IS THE ROLE OF EUS?

- Cyst fluid aspiration
  - Amylase
  - Tumor markers
    - CEA, CA 72-4, CA 125, CA 19-9, CA 15-3
- Biopsy suspicious areas
- Less risk of spillage of cyst contents

Cyst Fluid Analysis (CEA, amylase, cytology)

- CEA < 5
  - Serous cyst
  - Duplication

- CEA 5-200
  - Mucinous
  - Pseudocyst

- CEA 200-500
  - Mucinous

- > 500
  - Malignant

Non-mucinous cytology

Mucinous or inflammatory cytology

Mucinous cytology

Benign or malignant

Brugge W et al. AGA 2002
105/134 (78%) had FNA for cytological examination; results:

- Non-malignant epithelium: 37
- Unsatisfactory for evaluation: 29
- Atypical cells: 18; 3 had adenocarcinoma
- “Non-specific”: 15; 1 had adenocarcinoma
- Adenocarcinoma: 6; 4 were false-positive
Endoscopic US (EUS) FNA

- Sensitivity: 33%
- Specificity: 95%
- NPV: 95%
- PPV: 33%

MGH Experience
# MDCT/MR Vs. EUS/FNA: For Cyst Diagnosis & Biology

<table>
<thead>
<tr>
<th>Cyst Type</th>
<th>Overall performance</th>
<th>Cyst &lt;3 cm</th>
<th>Cyst &gt;3 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCN vs. Non-MCN</td>
<td>$\kappa$ Agreement</td>
<td>$\kappa$ Agreement</td>
<td>$\kappa$ Agreement</td>
</tr>
<tr>
<td>0.44</td>
<td>Moderate</td>
<td>0.24</td>
<td>Fair</td>
</tr>
<tr>
<td>Benign/ malignant</td>
<td>0.3 Fair</td>
<td>0.32</td>
<td>Fair</td>
</tr>
</tbody>
</table>
**MDCT/MR Vs. EUS/FNA: For Cyst Diagnosis & Biology**

<table>
<thead>
<tr>
<th>Cyst Size</th>
<th>&lt;3cm (N=57)</th>
<th>&gt;3cm (N=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Imaging</td>
<td>EUS/FNA</td>
</tr>
<tr>
<td></td>
<td>PPV</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Benign</td>
<td>97</td>
<td>82</td>
</tr>
<tr>
<td>Malignant</td>
<td>55</td>
<td>90</td>
</tr>
</tbody>
</table>
ALGORITHM FOR MANAGEMENT OF IPMN

CT/MR

Main duct IPMN
Mixed IPMN
Symptomatic branch duct IPMN

Risk/benefits for surgery

High risk
Old age, comorbidity

Low risk
Young patient, No comorbid factors

Resection

Asymptomatic branch duct IPMN
> 3 cm
2 - 3 cm

EUS

Benign
Follow-up with imaging

< 2 cm
No suspicious features*

* Suspicious features include presence of mural nodules, main duct dilatation, solid component, symptoms, thick wall/septations.
ALGORITHM FOR MANAGEMENT OF IPMN

CT scanning

> 3 cm cyst
MD-IPMN

Malignant

Risk / Benefit Assessment

EUS-FNA

Surgery

Cytology and CEA

Surgery

Monitoring

Observation

CEA>500
Atypia

CEA 10-500
Benign mucinous

CEA<10
Non-mucinous
Summary

• The majority of cystic neoplasms are incidentally-discovered (71%)

• >50% are operated on at the time of diagnosis

• 60% of those resected are either IPMN or MCN
Summary

- CT /MR remain moderately accurate in classifying cyst into various subtypes
  - Better for mucinous lesions > 80%
- IPMN morphology such as MD-IPMN, solid mass, enhancing wall, thick irregular separate or cyst > 3 cm have higher incidence of malignancy
SMALL IPMN/CYST (< 3 CM)

- Accurate diagnosis difficult with imaging.
- Most benign side branch IPMN
- MRCP better for small cyst morphology

Criteria for F/U
- No solid component
- No MPD involvement
- Clinical

Spinelli 2004
Fernandez del-castillo 2004
Sohn 2004
Sahani 2006
Sainani 2009
**Side-Branch IPMN Follow UP**

<table>
<thead>
<tr>
<th>Size</th>
<th>Interval</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 cm</td>
<td>1 year</td>
<td></td>
</tr>
<tr>
<td>1 - 2 cm</td>
<td>6 - 12 months</td>
<td>Resection</td>
</tr>
<tr>
<td>2 - 3 cm</td>
<td>6 months</td>
<td></td>
</tr>
</tbody>
</table>

- Increase in size > 3 cm
- > 1 cm growth per year
- Suspicious features*

* Suspicious features include presence of mural nodules, main duct dilatation, solid component, symptoms, thick wall/septations.
Cyst Follow-up

- May 2006
- August 2007
- Nov 2001
- June 2003
- August 2004
- Sept 2005

Worrisome

- 1 cm growth/year
- Solid mass
- PD ↑↑
Natural History of Small Cyst

- 119 patients SB-IPMN median follow-up of 33.9 months (7-140 months)
- The median initial cyst size was 13.3 mm
- Mean Growth 0.89 mm/year

<table>
<thead>
<tr>
<th>Factors</th>
<th>Growth mm/yr</th>
<th>Growth mm/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male 1.41</td>
<td>Female 0.56</td>
</tr>
<tr>
<td>P= 0.024</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>Smokers 1.40</td>
<td>Non-smokers 0.62</td>
</tr>
<tr>
<td>P=0.045</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid nodules</td>
<td>Nodules 1.71</td>
<td>No nodules 0.86</td>
</tr>
<tr>
<td>P&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2006

2009
Small Lesions: Follow-Up Interval

2002 2003 2003
ACKNOWLEDGEMENTS

- Nisha Sainani
- Michael Blake
- Peter Hahn
- Vikram Deshpande
- Mari Mino-Kenudson
- Stefano Crippa
- Stefan Fritz
- Carlos Fernandez-del Castillo
THANK YOU

Bulfinch Building, Massachusetts General Hospital