

The Role of Endoscopic Ultrasound in Diagnosis and Management of Pancreatic Cysts: Is there a Future?

Walter G. Park, MD, MS

Associate Professor of Medicine

Stanford University School of Medicine

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Disclosures

- No relevant disclosures related to this talk

Objectives

- The Role of EUS in Current Current Guidelines
- A Future role in Diagnosis and Risk Stratification

Guidelines – Radiological Surveillance

- First line imaging modality for all current surveillance guidelines for pancreatic cysts:
 - Revised Sendai Guidelines (Fukuoka) (2017)
 - American Gastroenterological Association Guidelines (2015)
 - American College of Radiology (2017)
 - American College of Gastroenterology (2018)
 - Canadian Association of Radiologists (2022)
- Relatively non-invasive
- Fairly standardized and reproducible
- Routinely used in all types of clinical practice

Are any of the following "high-risk stigmata" of malignancy present?
 i) obstructive jaundice in a patient with cystic lesion of the head of the pancreas, ii) enhancing mural nodule ≥ 5 mm, iii) main pancreatic duct ≥ 10 mm

Yes

Consider surgery, if clinically appropriate

No

Are any of the following "worrisome features" present?
Clinical: Pancreatitis ^a
Imaging: i) cyst ≥ 3 cm, ii) enhancing mural nodule < 5 mm, iii) thickened/enhancing cyst walls, iv) main duct size 5-9 mm, v) abrupt change in caliber of pancreatic duct with distal pancreatic atrophy, vi) lymphadenopathy, vii) increased serum level of CA19-9, viii) cyst growth rate ≥ 5 mm / 2 years

If yes, perform endoscopic ultrasound

Are any of these features present?
 i) Definite mural nodule(s) ≥ 5 mm ^b
 ii) Main duct features suspicious for involvement ^c
 iii) Cytology: suspicious or positive for malignancy

No

What is the size of largest cyst?

Inconclusive

<1 cm

CT / MRI in 6 months, then every 2 years if no change

1-2 cm

CT / MRI 6 months x 1 year yearly x 2 years, then lengthen interval up to 2 years if no change

2-3 cm

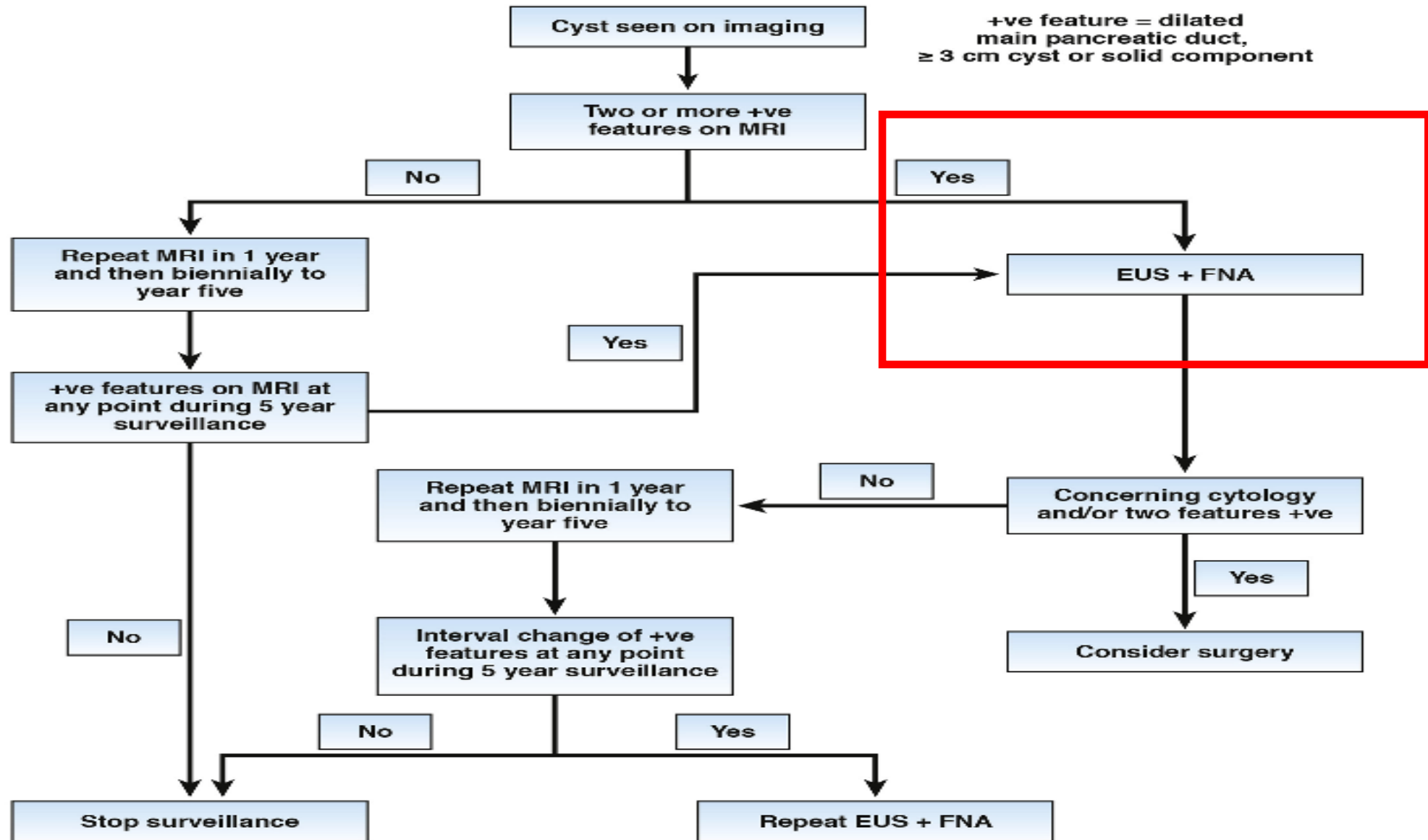
EUS in 3-6 months, then lengthen interval up to 1 year, alternating MRI with EUS as appropriate. Consider surgery in young, fit patients with need for prolonged surveillance

>3 cm

Close surveillance alternating MRI with EUS every 3-6 months. Strongly consider surgery in young, fit patients

Yes

AGA Guidelines



Endoscopic Ultrasound

- In all guidelines, Endoscopic Ultrasound is **currently** limited to evaluation and surveillance of cysts with **worrisome features** or **high-risk stigmata** after identified by MRI/CT imaging.



Endoscopic Ultrasound

Benefits

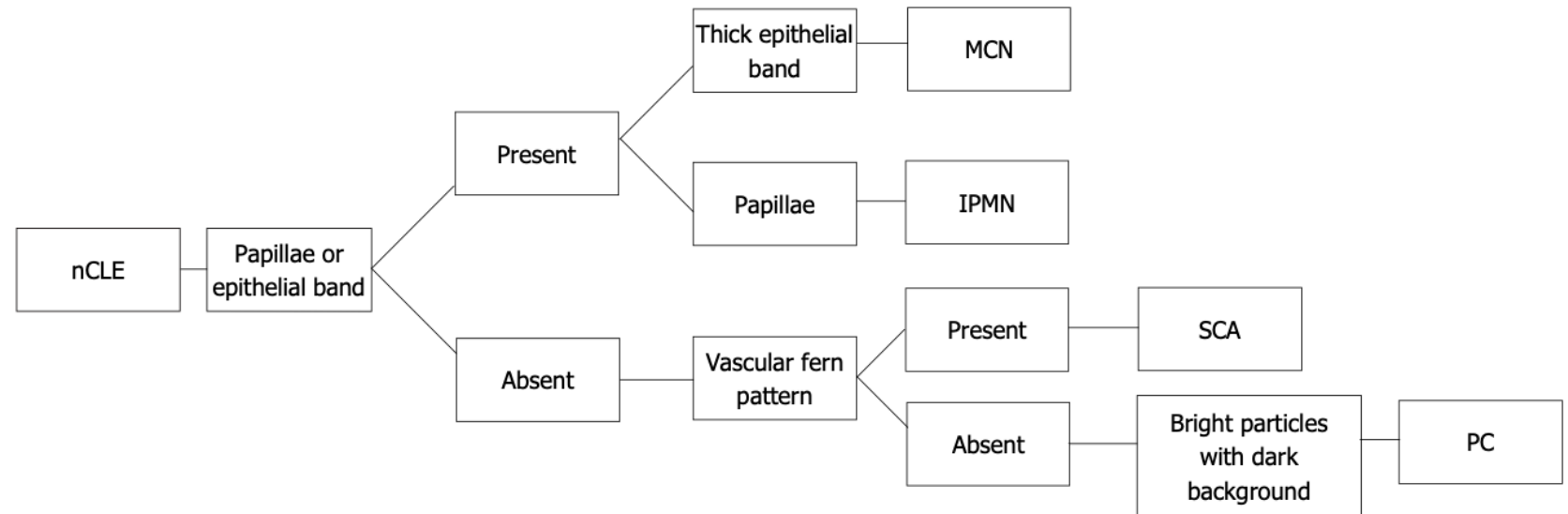
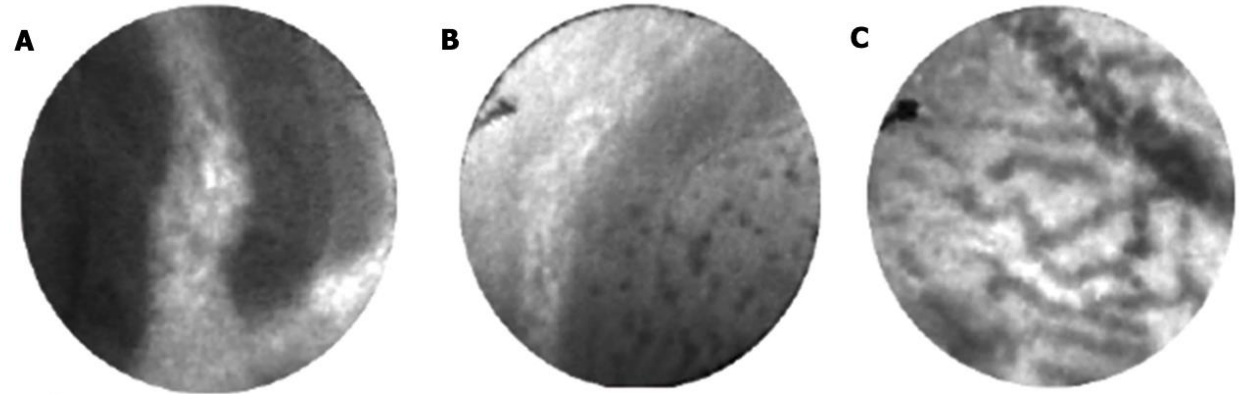
- High sensitivity for diagnosing malignant related mural nodules
- No Radiation
- FNA capabilities: DNA, tumor marker, and cytological analysis
- Platform for *in vivo* diagnostics and novel sampling devices
- Platform for therapeutics

Limitations

- Relatively invasive
- Inter-observer variability
- High Costs

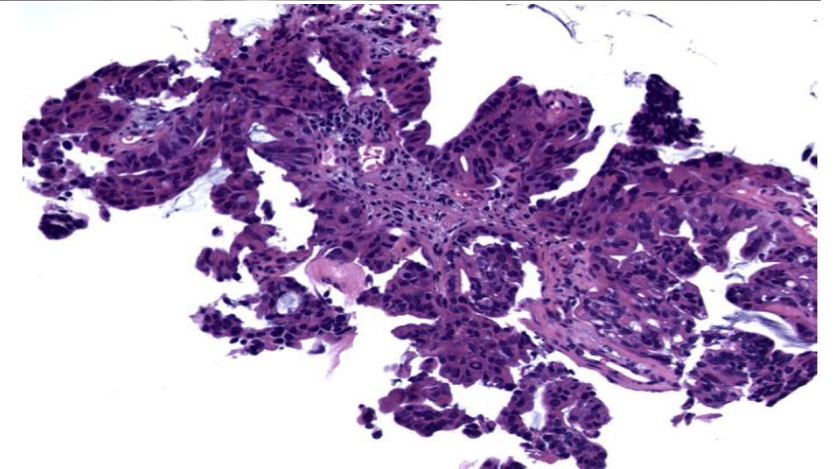
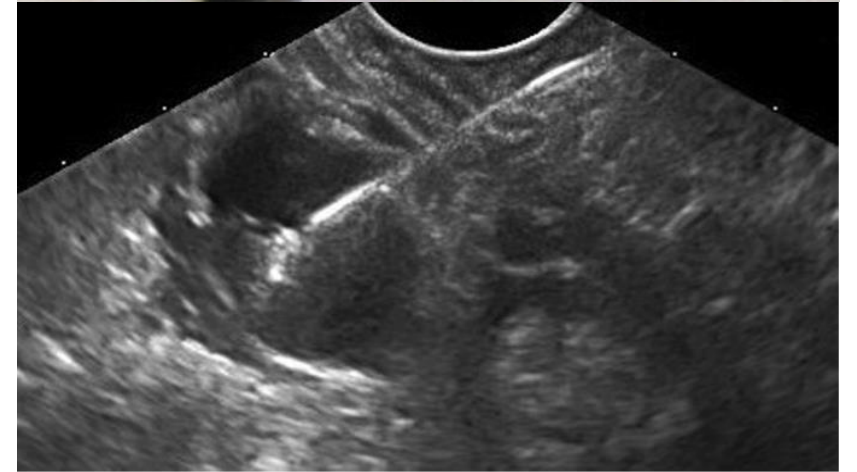
EUS-guided Needle-based Confocal Laser Endomicroscopy

- 19g FNA needle for real-time microscopic evaluation of pancreatic cyst epithelium
- Sensitivity – 59-91%
- Specificity – 95-100%
- Accuracy – 71-94%
- Limits:
 - Inter-observer
 - Cyst size
 - Cost
 - Pancreatitis 4%



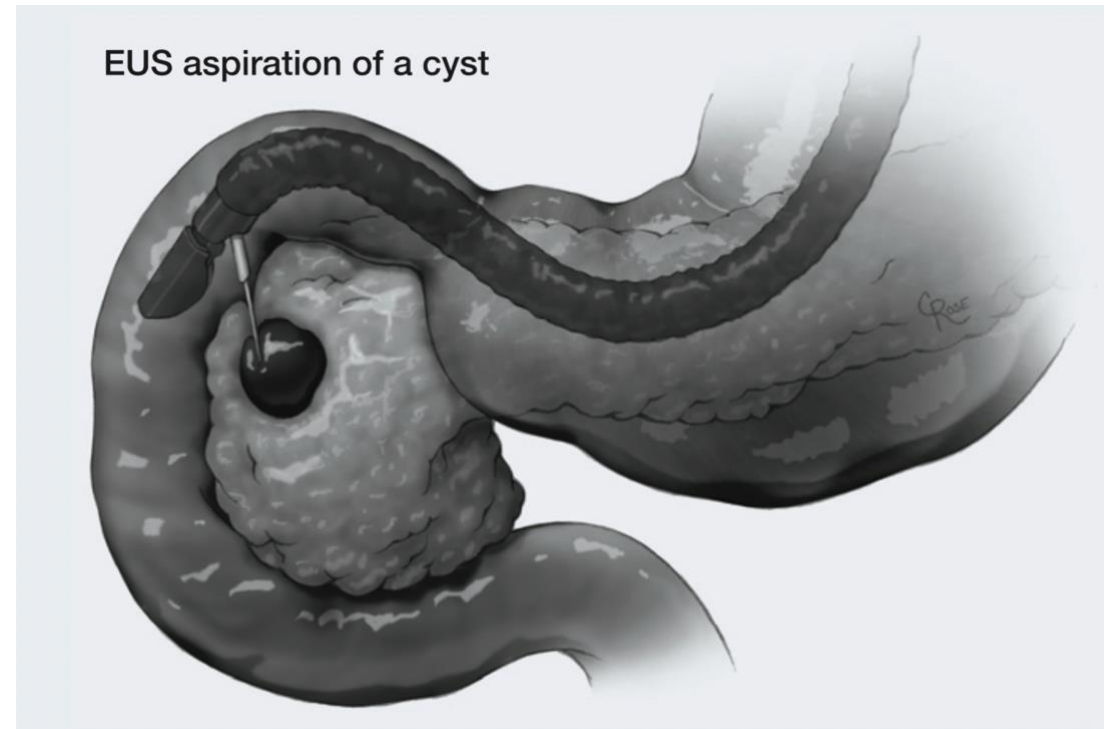
EUS-guided Microforceps

- 19 g microforceps biopsy
- Diagnostic yield 72%
- No difference with cytology for diagnosis mucinous or high-grade dysplasia
- Superior in diagnosing cyst type
- Limits:
 - Limited to fairly large cysts
 - Sampling of heterogeneous cyst wall

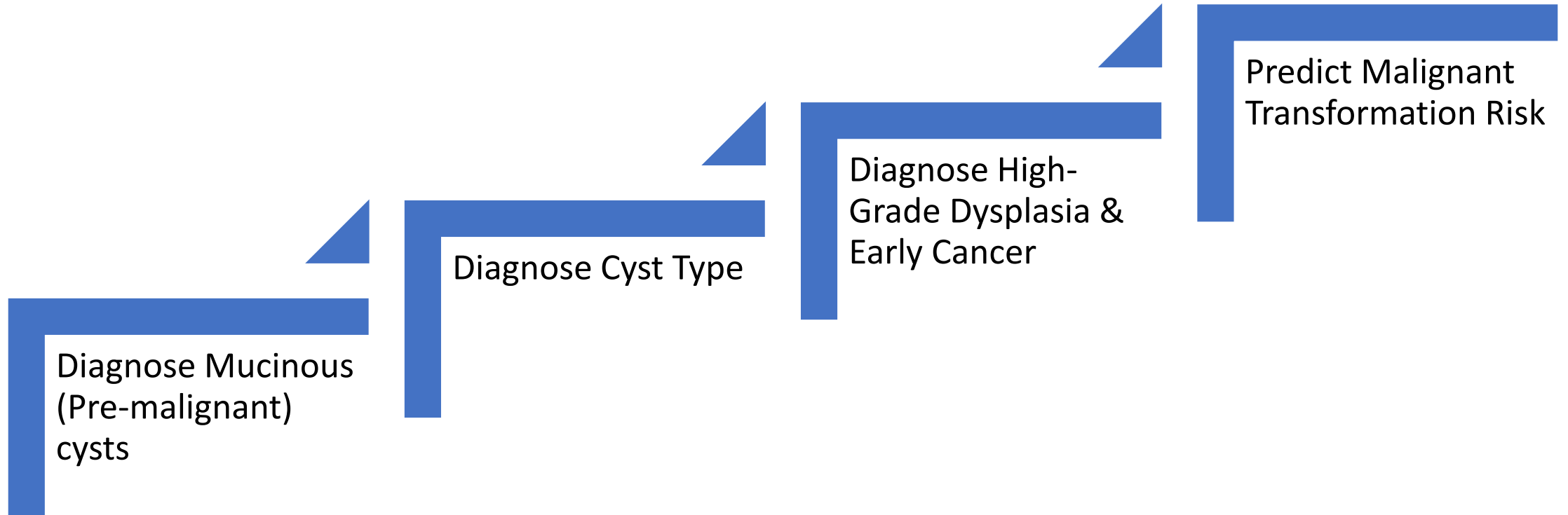


Pancreatic Cyst Fluid Biomarkers

- Relatively Protected Matrix
 - High concentration of secreted proteins, DNA, RNA, and metabolites related to tumor biology
- Highest Potential for Early Detection of High-Grade Dysplasia & early cancer
- Easily Accessible
- Safe



Hierarchical Goals of Cyst Biomarkers



Cyst Fluid Biomarker Landscape

Current

- Cytology
- Carcinoembryonic Antigen
- DNA Analysis
- Glucose

Investigational

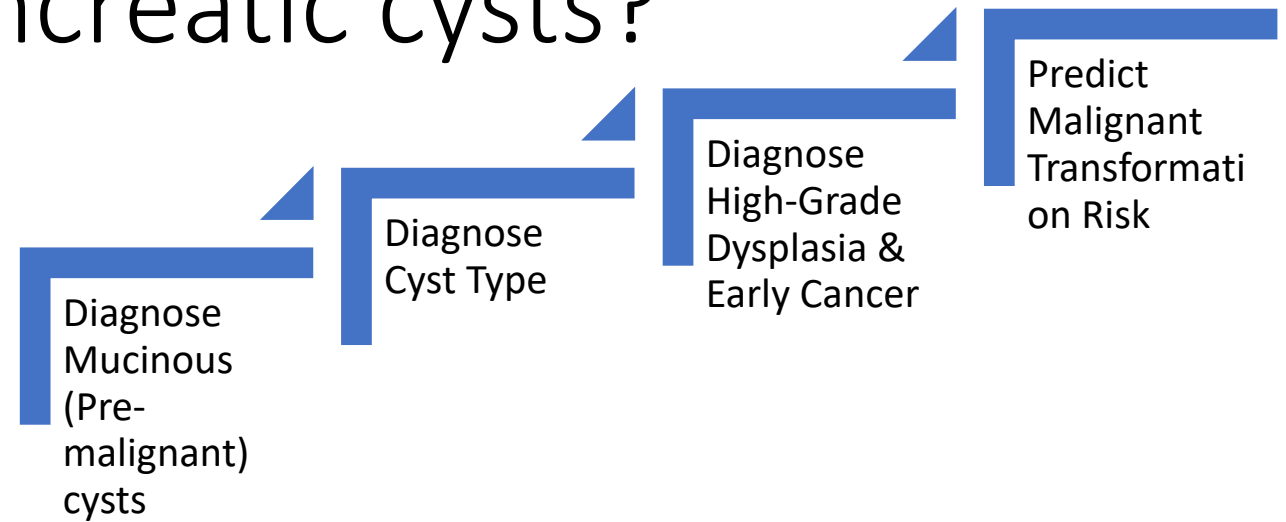
- DNA Methylation
- Monoclonal Ab Das-1
- VEGF-1
- Metabolomics
- Proteomics
- Etc.

Next Generation Sequencing DNA Analysis

| Parameter (n=102) | Sensitivity | Specificity |
|---|-------------|-------------|
| IPMN | | |
| KRAS and/or GNAS mutation | 100% | 96% |
| IPMN with Advanced Neoplasia | | |
| TP53, PIK3CA, and/or PTEN alterations | 88% | 95% |
| GNAS MAF > 55%, or TP53/PIK3CA/PTEN MAFs = GNAS/KRAS MAFs | 100% | 100% |
| IPMNs and MCNs | | |
| KRAS and/or GNAS mutations | 89% | 100% |
| IPMNs and MCNs with Advanced Neoplasia | | |
| TP53, PIK3CA, and/or PTEN alterations | 79% | 96% |
| GNAS MAF > 55%, or TP53/PIK3CA/PTEN MAFs = GNAS/KRAS MAFs | 89% | 100% |

- 626 EUS/FNA acquired cyst fluid samples from 595 patients, with 102 patients with surgical follow-up

Future of EUS in Pancreatic cysts?



- Current criteria are morphologically and macroscopically based
 - There is correlation but likely little precision to capture meaningful microscopic changes toward malignant transformation
- **Could serial cyst fluid analysis with current (and future) biomarkers provide earlier detection and prediction of malignant transformation?**

Goal: Identify cysts that harbor or are at high-risk of developing high-grade dysplasia or early cancer



AI & Radiomic Techniques in MRI/CT

Contrast-enhanced, confocal EUS imaging, shear wave elastography

FNA Technology: Core biopsy Micro-forceps

Precision Cyst Fluid Analysis

Endo
Tx

Thank you

wgpark@stanford.edu