ASCP 2020

VIRTUAL

DMT129-20 GIP: Sizzling Updates in the GI Tract: The New WHO and Beyond

The Rodger C. Haggitt GI Pathology Society

Dr. Wendy Frankel, OSU, Update on Hereditary Tumor Syndromes involving the Colorectum

Dr. Christopher Hartley, Mayo Clinic, Update on Pancreas

www.ascp.org/2020

Disclosures

I have no disclosures.

Funder Statement

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Objectives

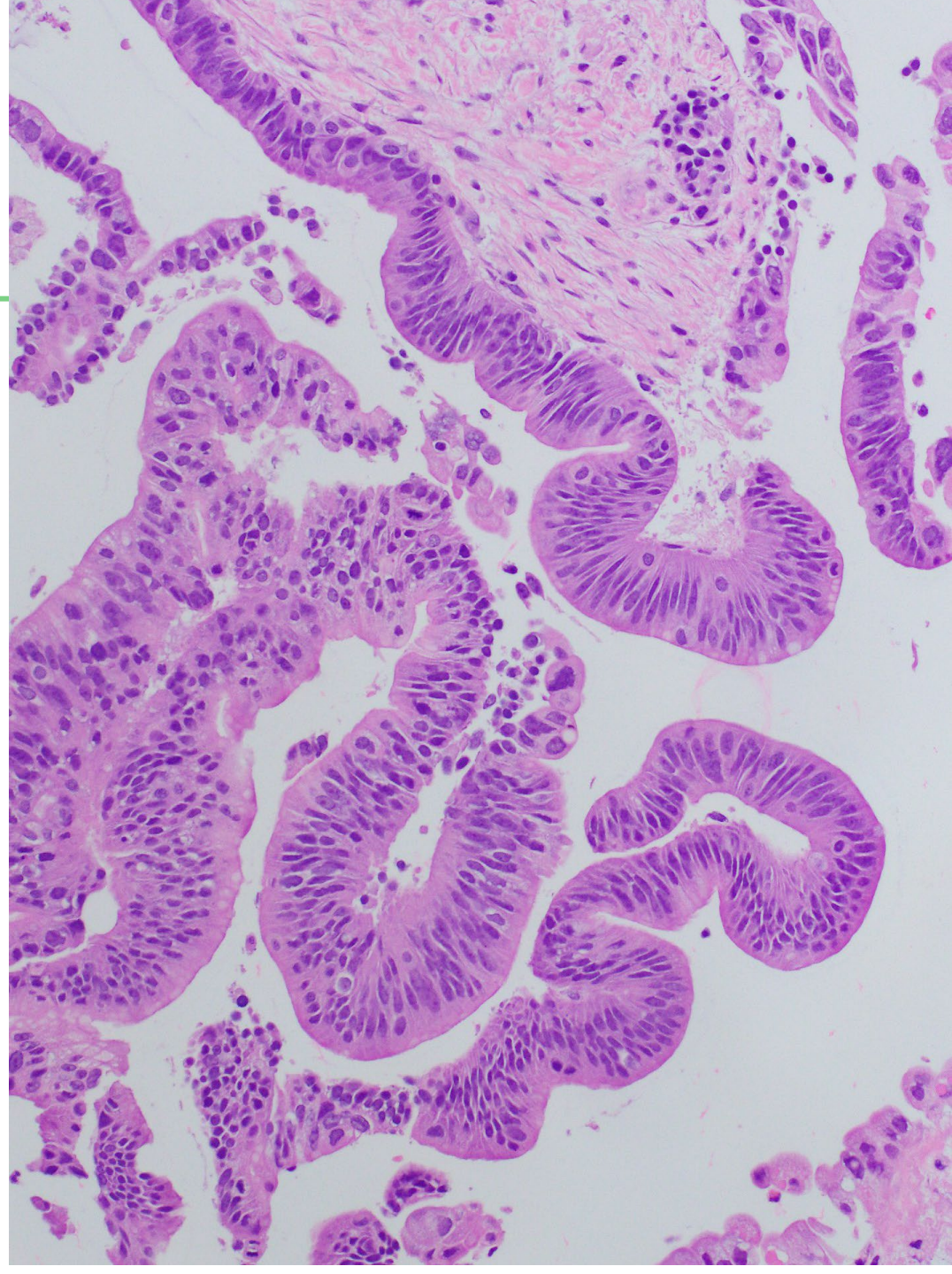
- To recognize and apply the simplified grading scheme for pancreatic intraepithelial neoplasia, and pancreatic mucinous neoplasms
- To recognize distinct subtypes of pancreatic precursor lesions and implications for gross and microscopic examination
- To implement recommended reporting guidelines (shorter reports!)

Scope and Terms

- **Pancreatic intraepithelial neoplasia (PanIN)**
  - High grade PanIN is the main precursor to PDAC
- **Intraductal papillary mucinous neoplasm (IPMN)**
- **Intraductal oncocytic papillary mucinous neoplasm (IOPN)**
- **Mucinous cystic neoplasm (MCN)**
- **IPMN/IOPN/MCN represent 4-5% of pancreatic neoplasms**

Size

- **PanIN (< 0.5 cm)**
- **IPMN (> 1.0)**
- **What if > 0.5 and < 1.0 cm?**
- **Incipient IPMN/IOPN**
  - If intestinal or oncocytic morphology



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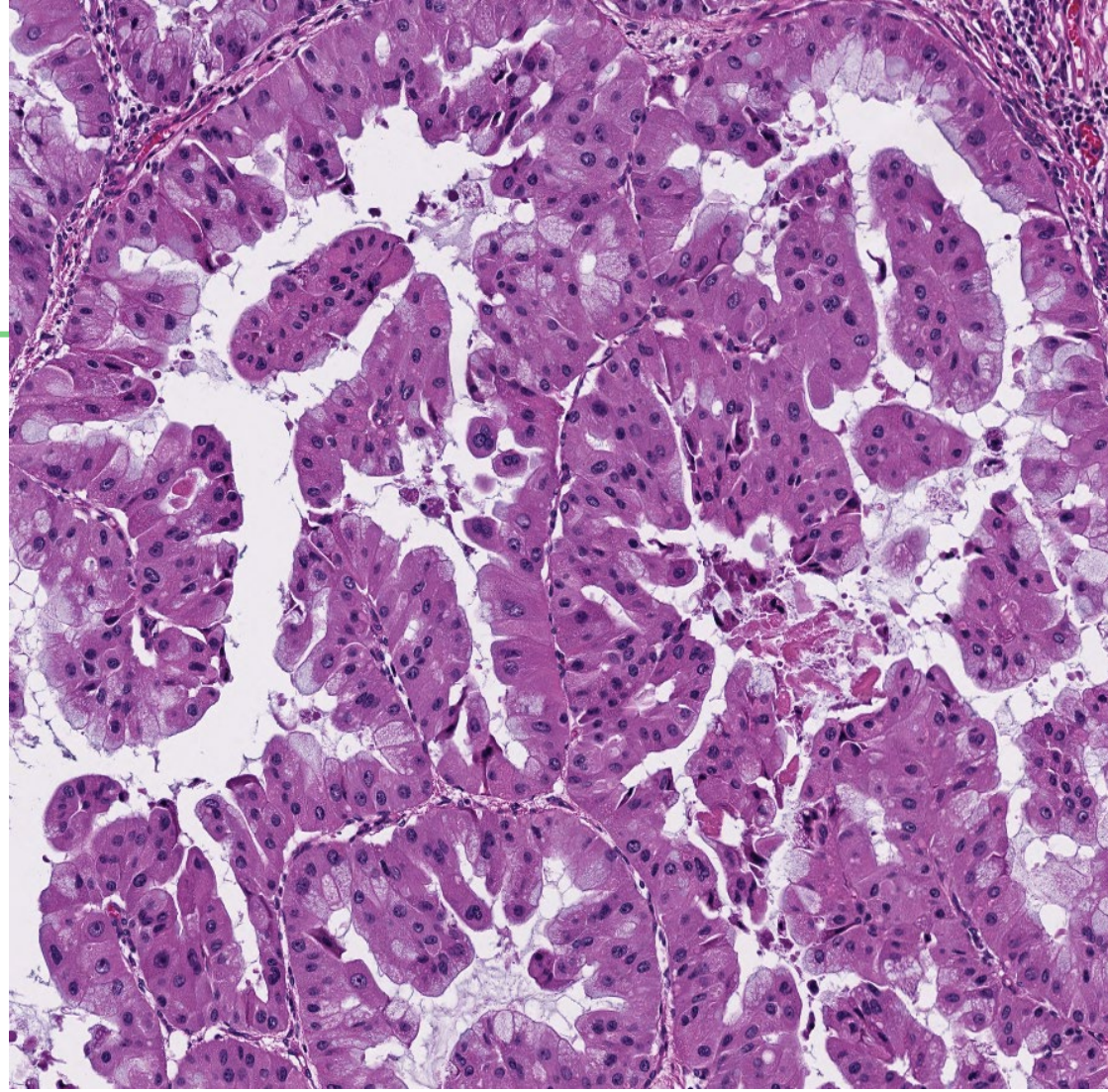

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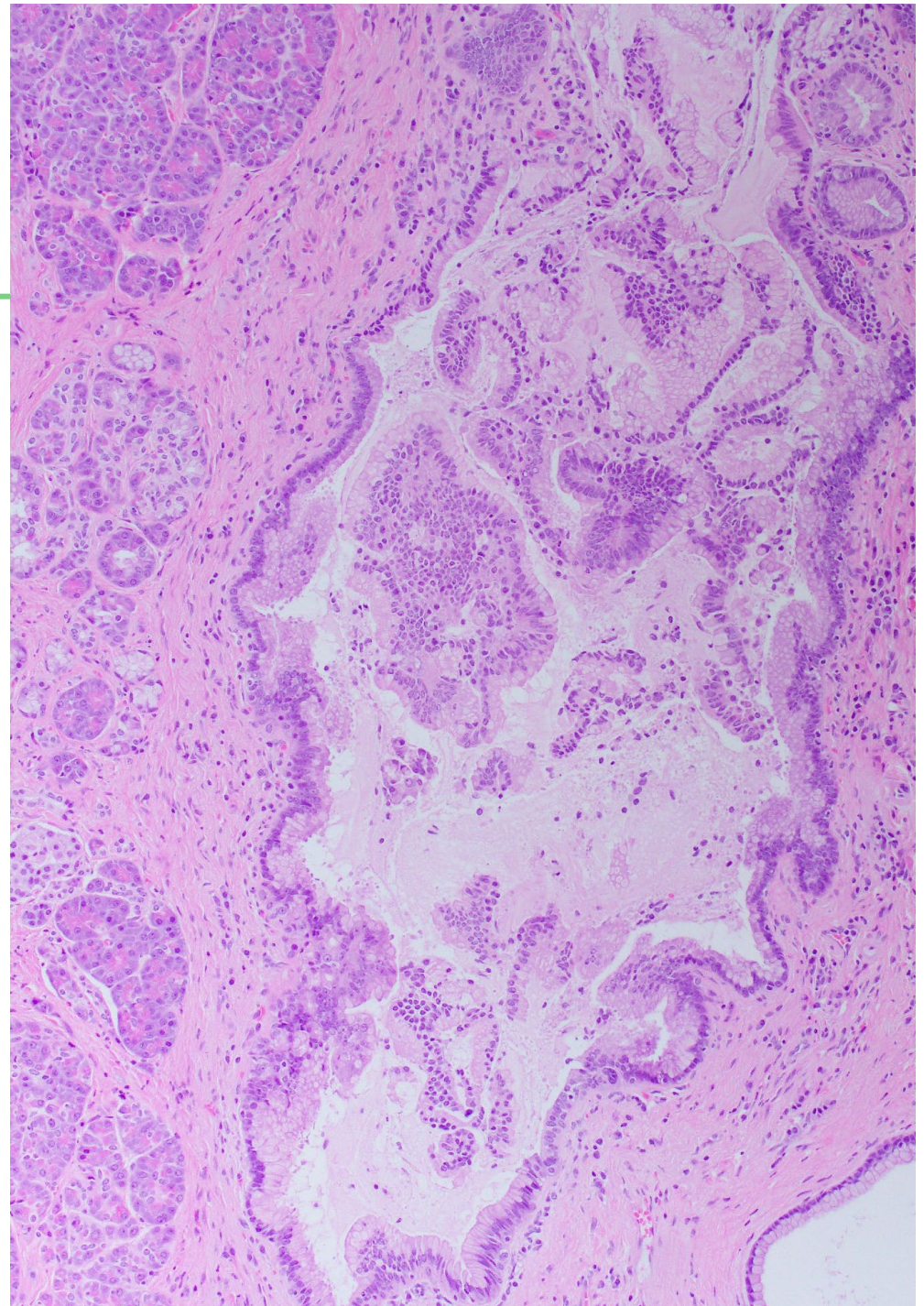
- **IPMN (> 1.0)**
- **What if > 0.5 and < 1.0 cm?**
- **Incipient IPMN**
  - If intestinal or oncocytic morphology
- **0.8 cm – this is a big PanIN**



No more PanIN-1A/1B/2/3 – only low/high grade PanIN

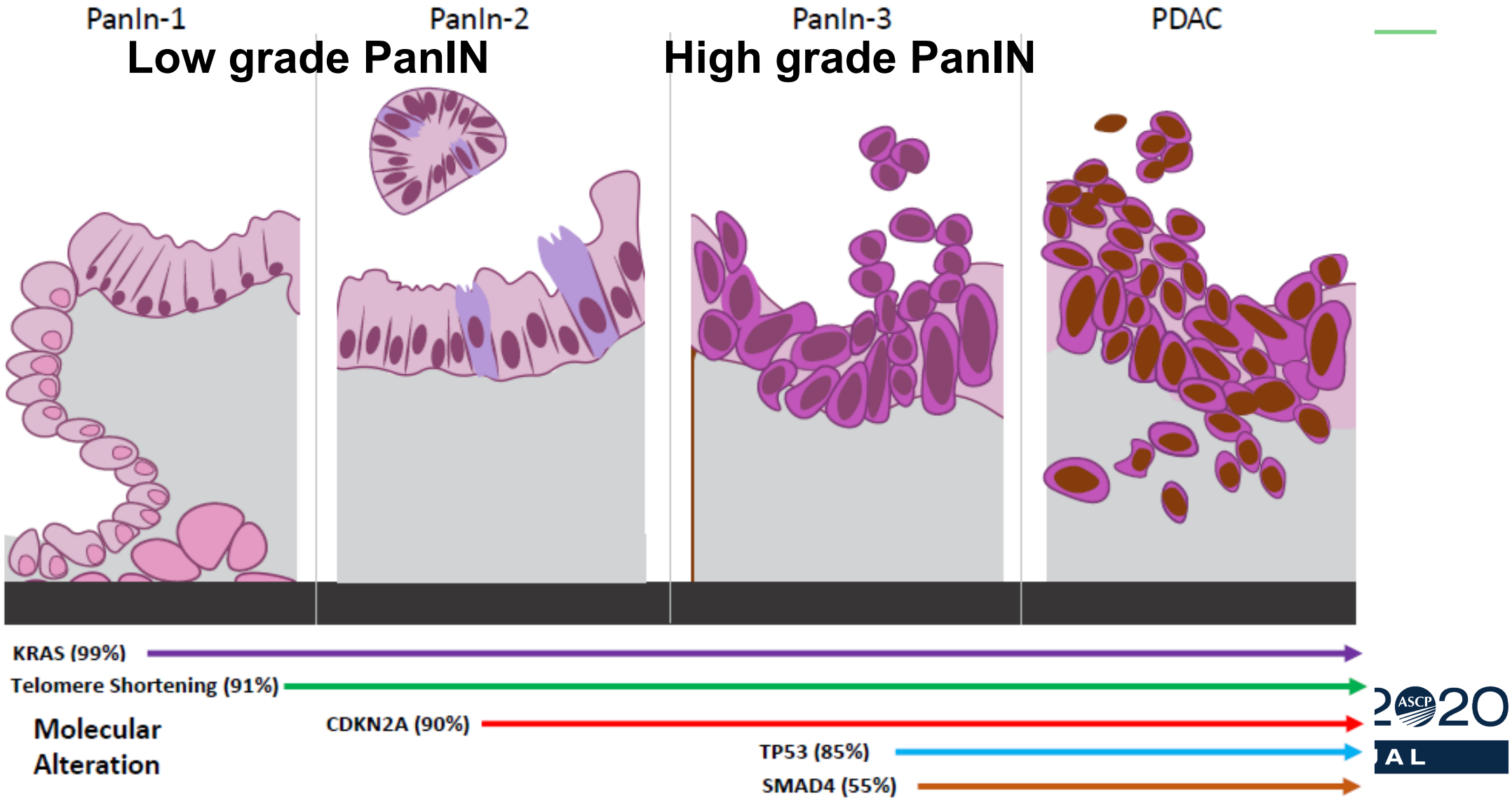


Figure adapted from Skoda (2016) and Guo., et al(2016)

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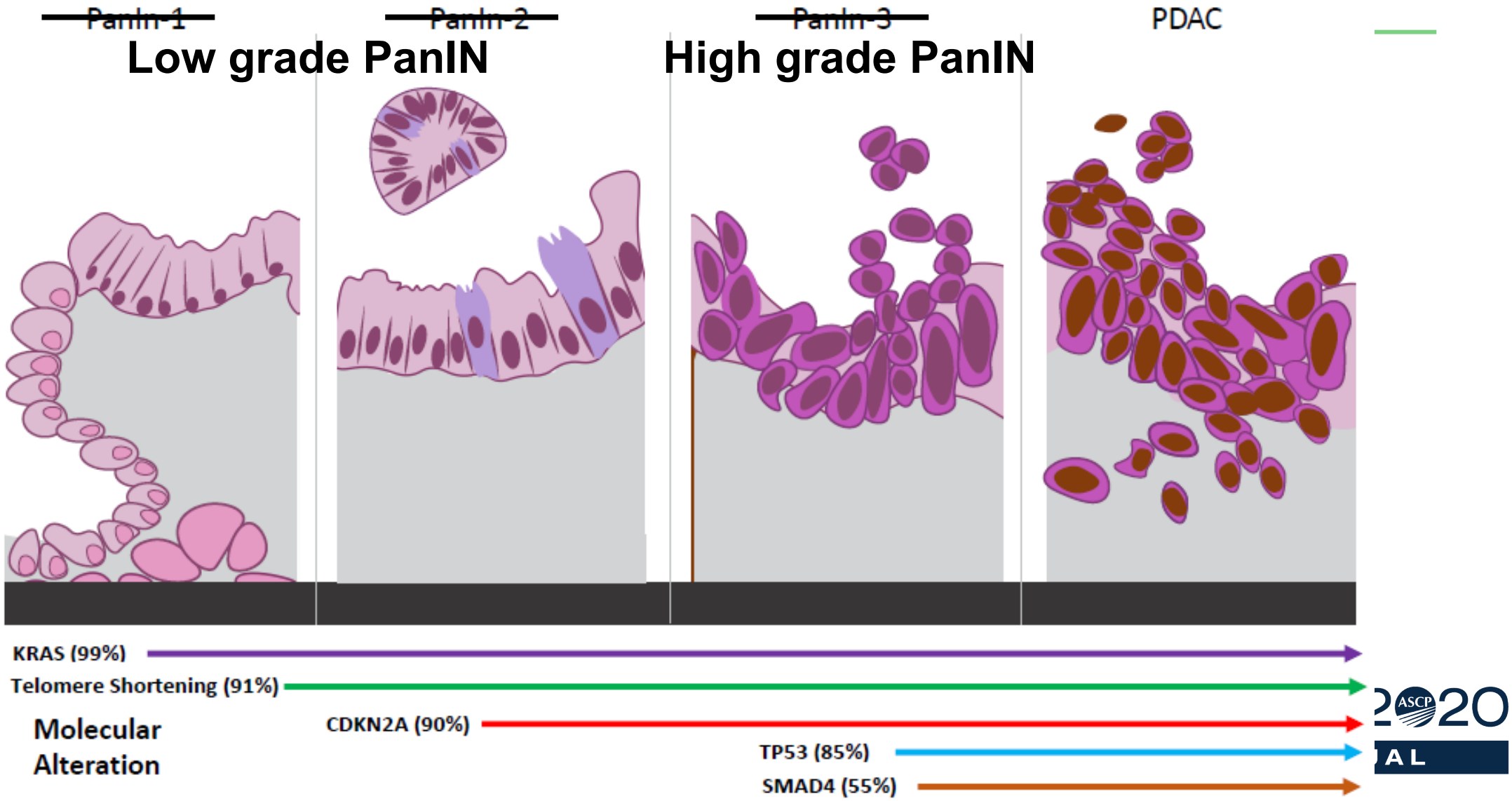

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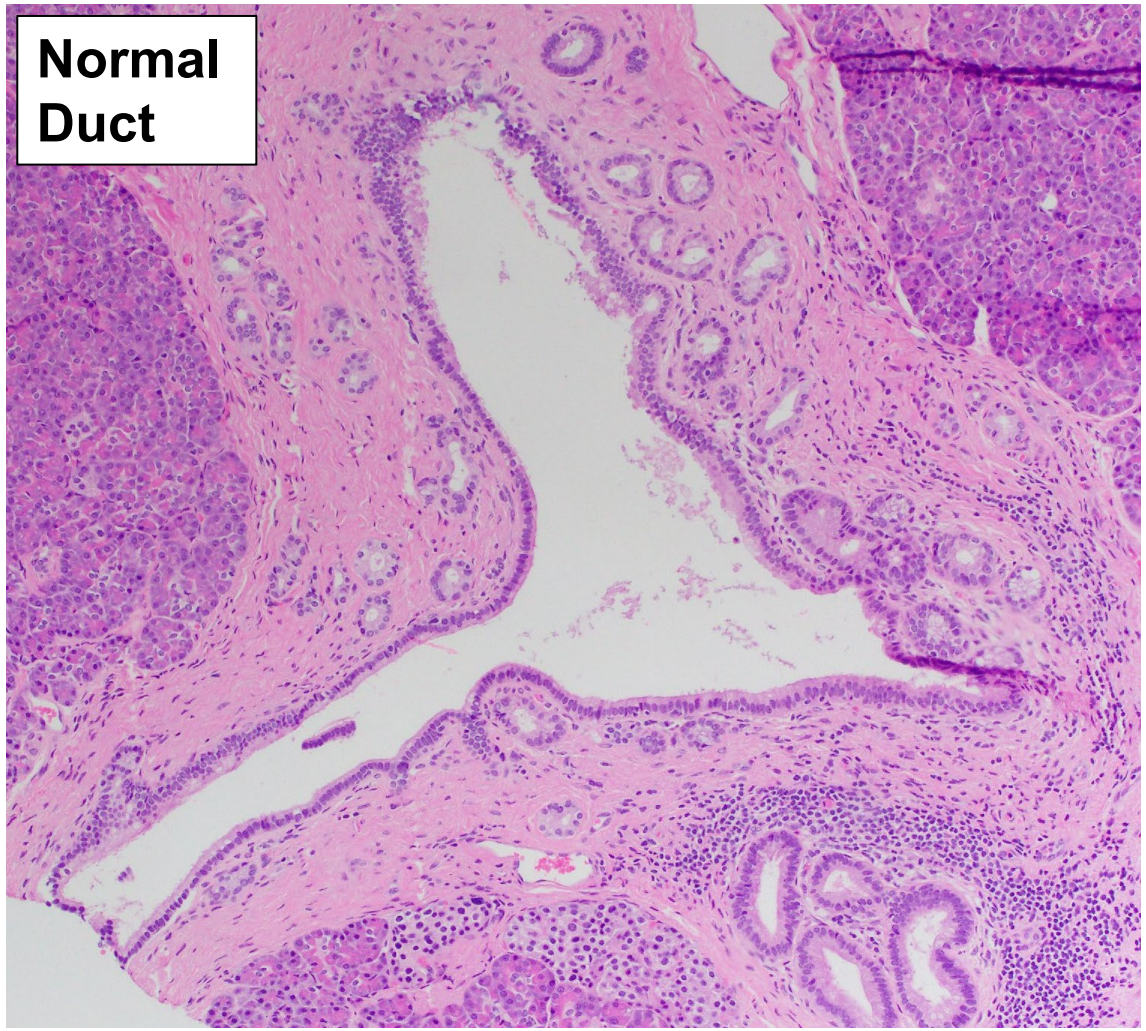
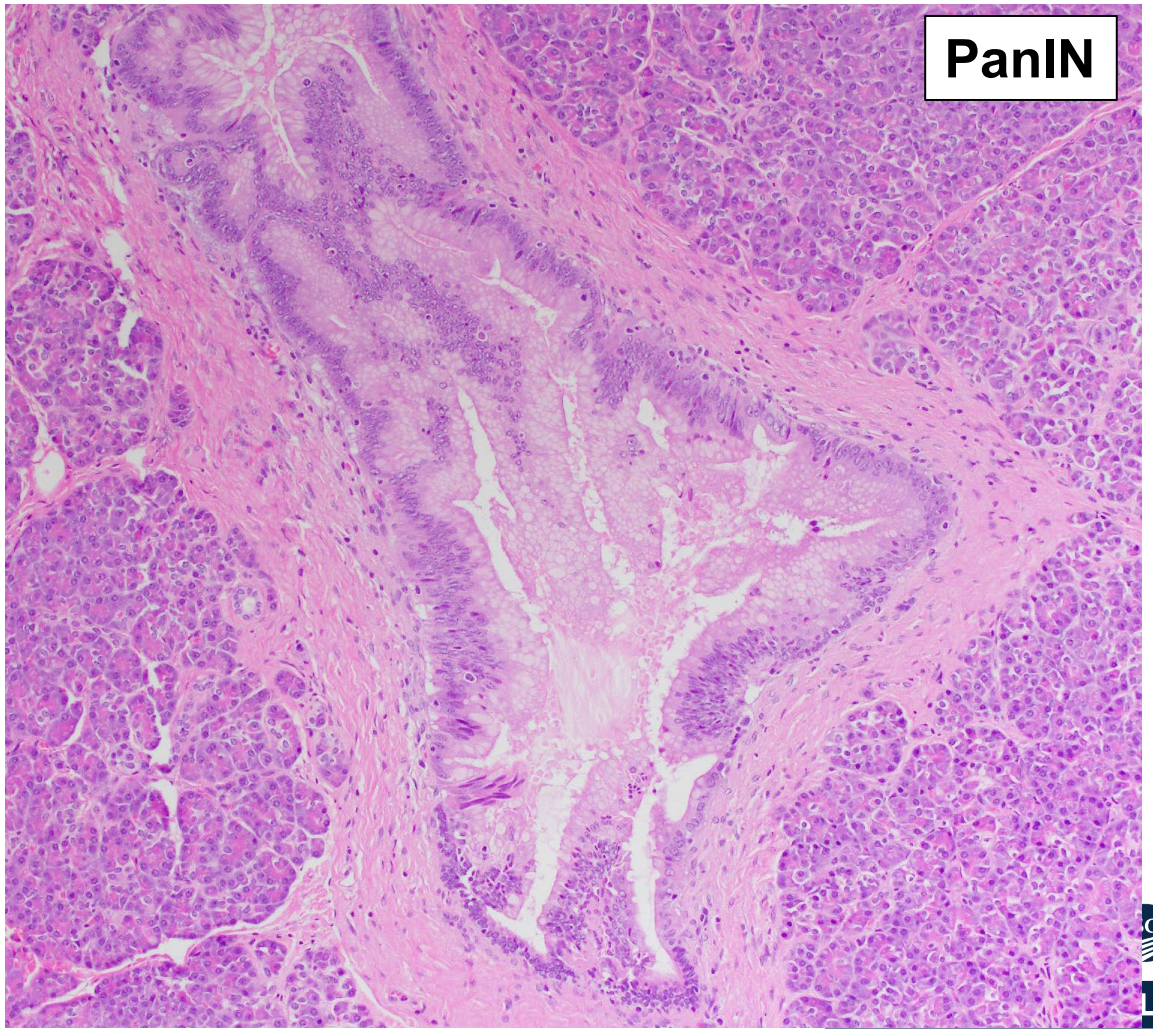
Does every pancreas have PanIN?





Does every pancreas have PanIN?

- Low-grade PanIN is a common incidental finding
- Present in more than half of individuals >50 years old*

FIGURE 2

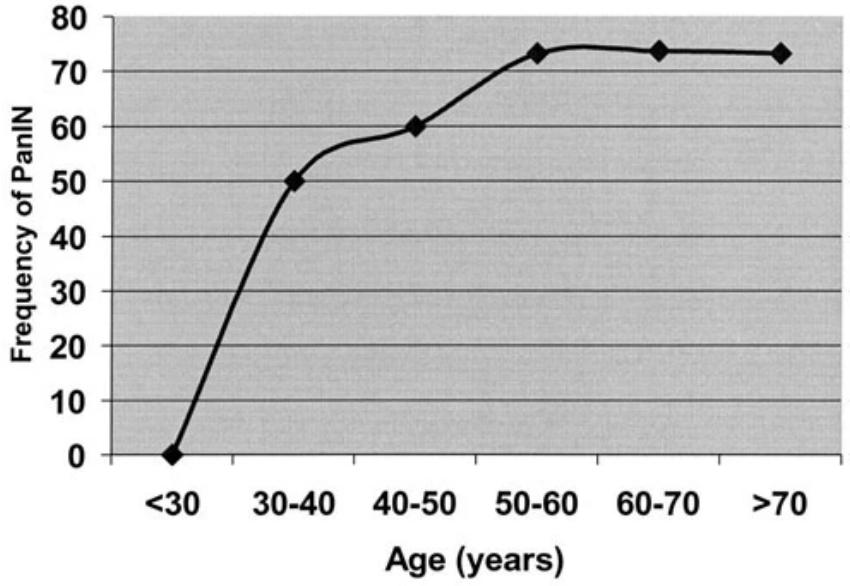
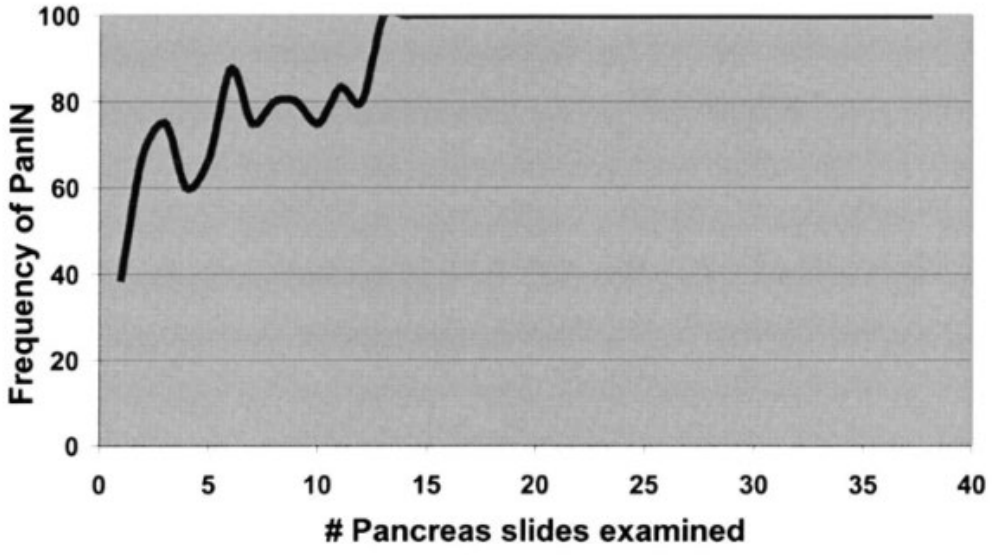


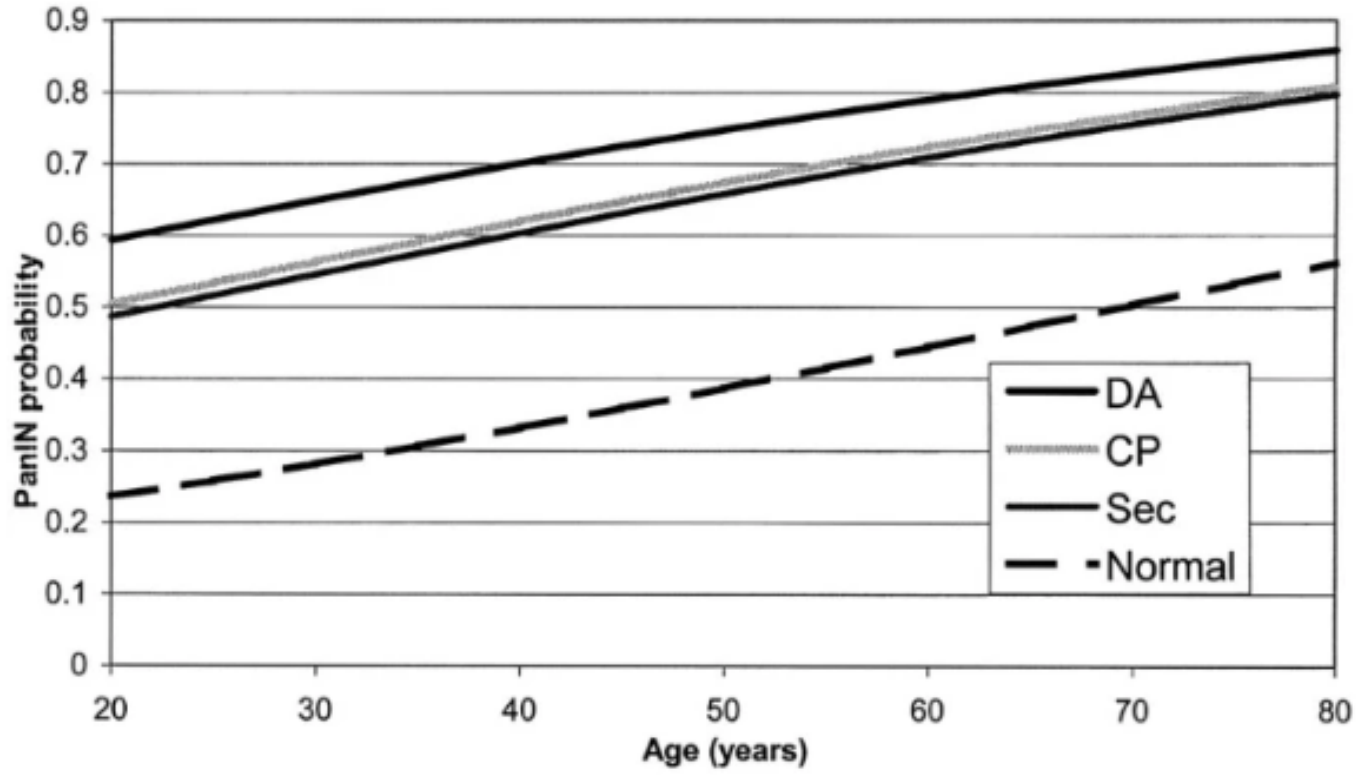
FIGURE 3



*Andea A, Sarkar F, and Adsay VN. Clinicopathological Correlates of Pancreatic Intraepithelial Neoplasia: A Comparative Analysis of 82 Cases With and 152 Cases Without Pancreatic Ductal Adenocarcinoma. *Modern Pathology*. 2003;16:996-1006.

Does every pancreas have PanIN?

FIGURE 4



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Brief history of PanIN: 70+ terms → 4 terms → 2 terms

- **1954:** Sommers et al. *Pancreatic duct hyperplasias and cancer. Gastroenterology* 1954; 72:629-640.
- ***1976:****Cubilla AL, Fitzgerald PJ . Morphological lesions associated with human primary invasive nonendocrine pancreas cancer. Cancer Res 1976; 36: 2690–2698.* ***100 autopsy controls***
- ***Several terms (approaching 100), several grading systems***
- **1994 "PanIN" coined:** Klimstra DS, Longnecker DS . K-ras mutations in pancreatic ductal proliferative lesions. *Am J Pathol* 1994; **145**: 1547–1550.
- **2001 PanIN 1A/1B/2/3:** Hruban RH, Adsay NV, Albores-Saavedra J, Compton C, Garrett ES, Goodman SN, *et al*. Pancreatic intraepithelial neoplasia: a new nomenclature and classification system for pancreatic duct lesions. *Am J Surg Pathol* 2001; **25:** 579–586.
- **2015 PanIN low/high:** Basturk O, Hong SM, Wood LD, et al. A Revised Classification System and Recommendations From the Baltimore Consensus Meeting for Neoplastic Precursor Lesions in the Pancreas. Am J Surg Pathol. 2015;39(12):1730-1741.

PanIN

Pancreatic Intraepithelial Neoplasia

A New Nomenclature and Classification System for Pancreatic Duct Lesions

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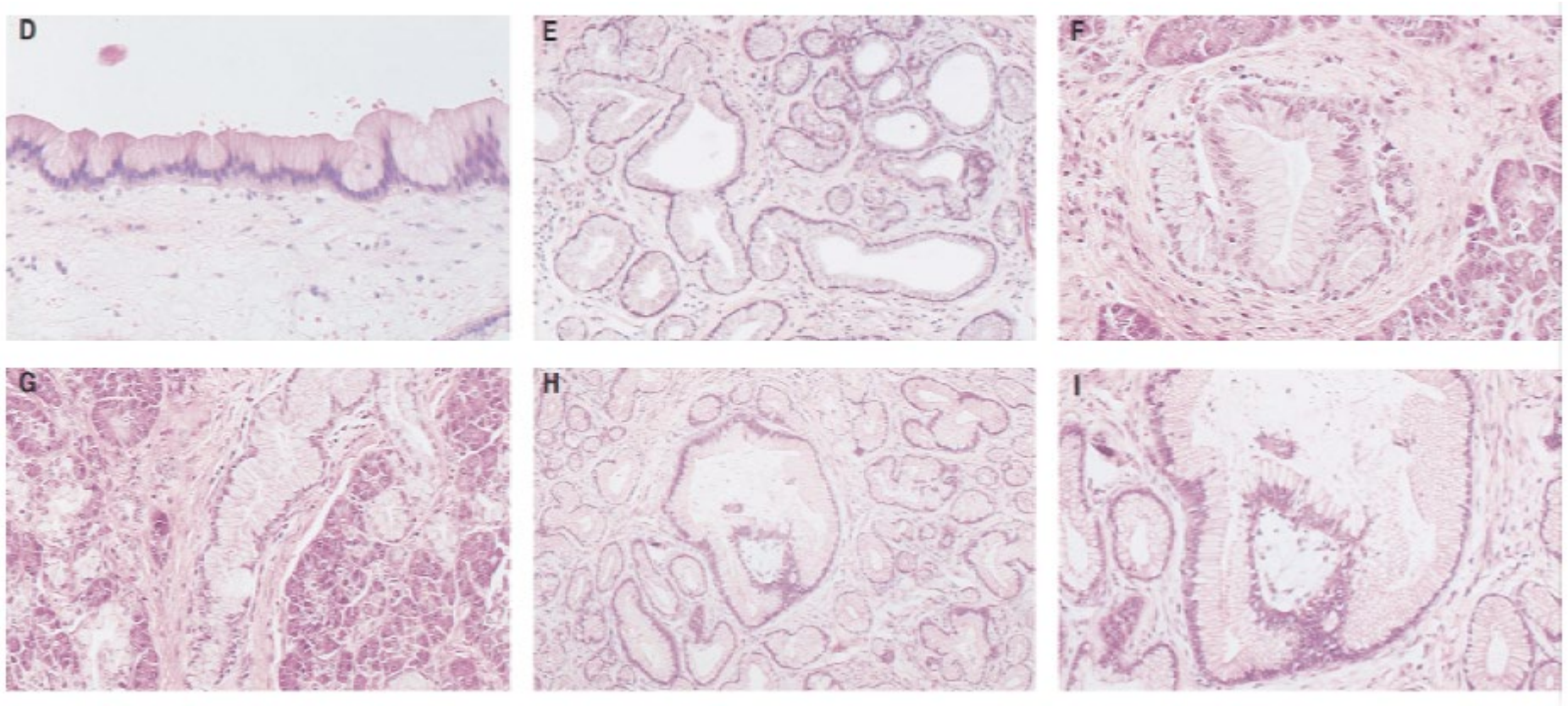
PanIN 1A



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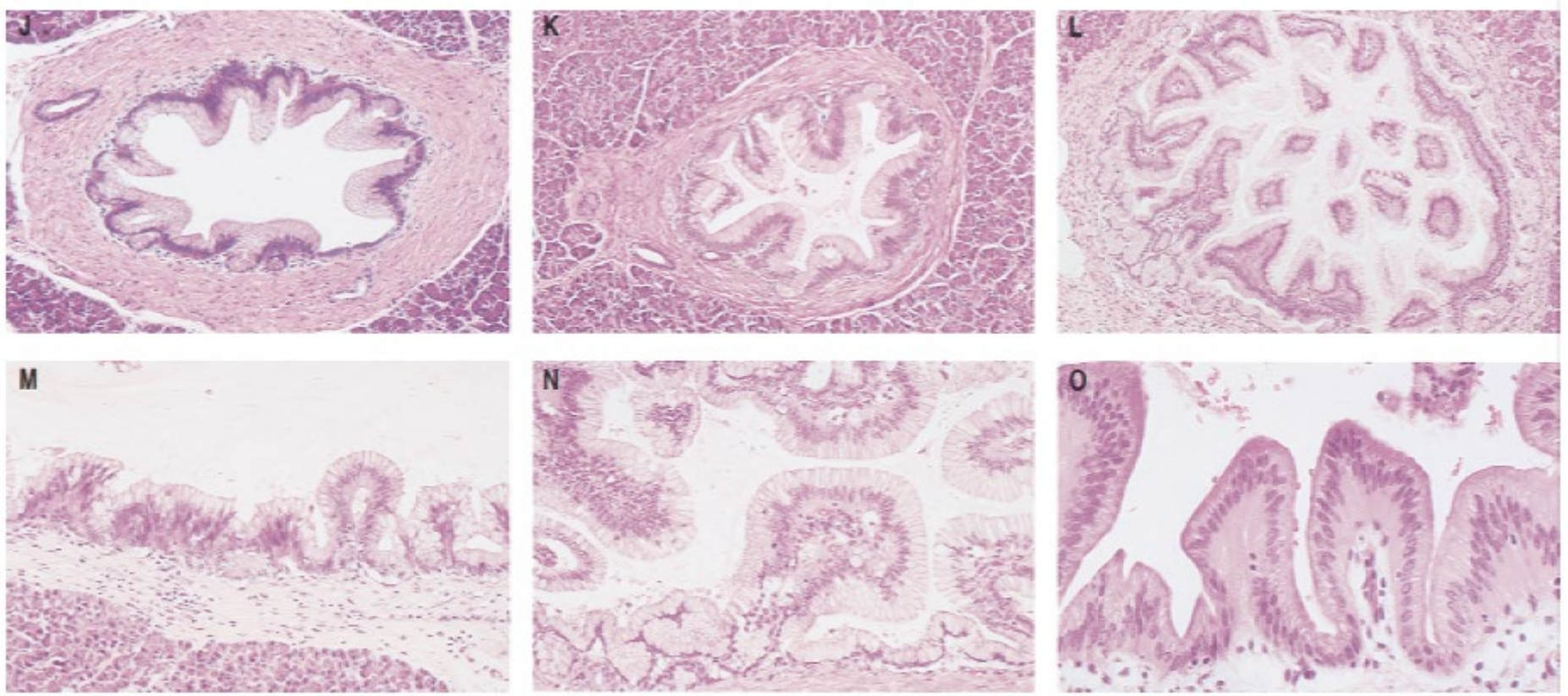
PanIN 1B



PanIN

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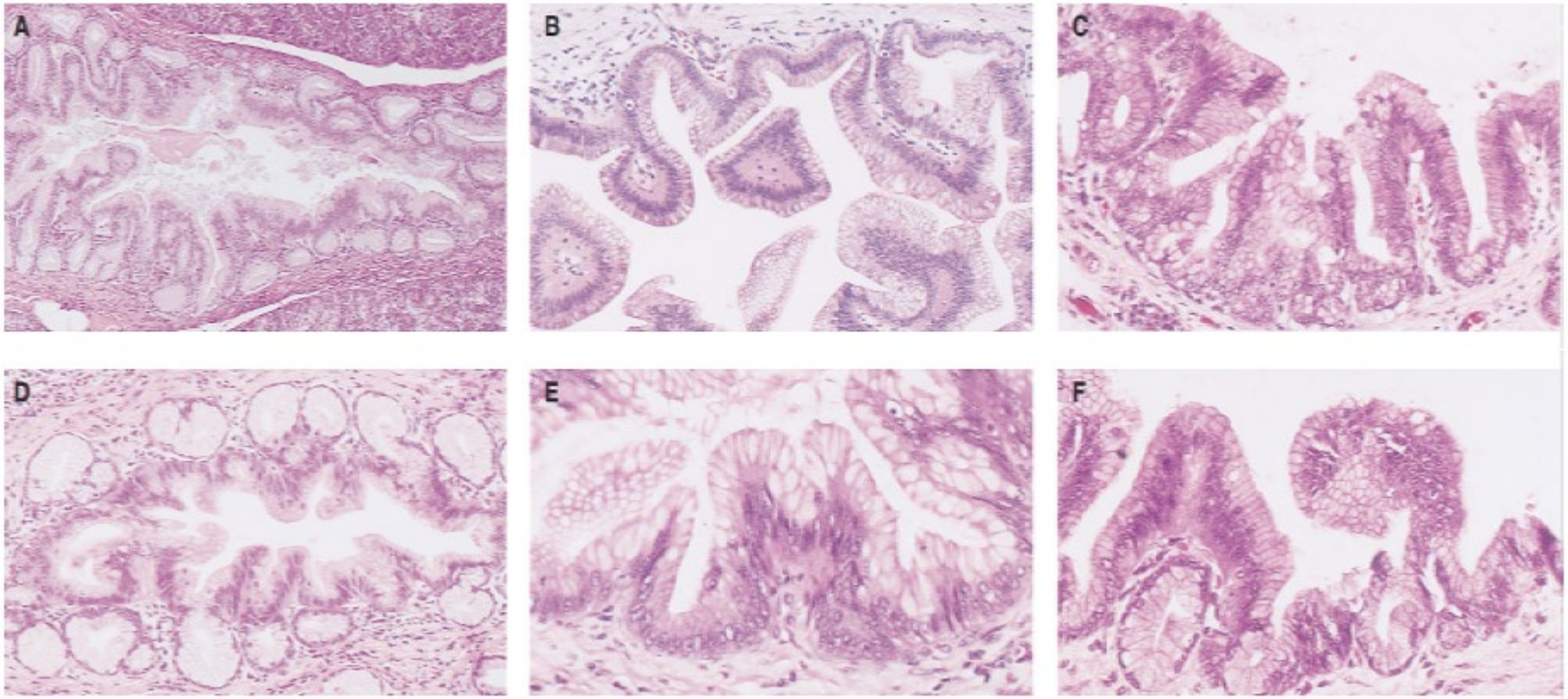
PanIN 2



PanIN

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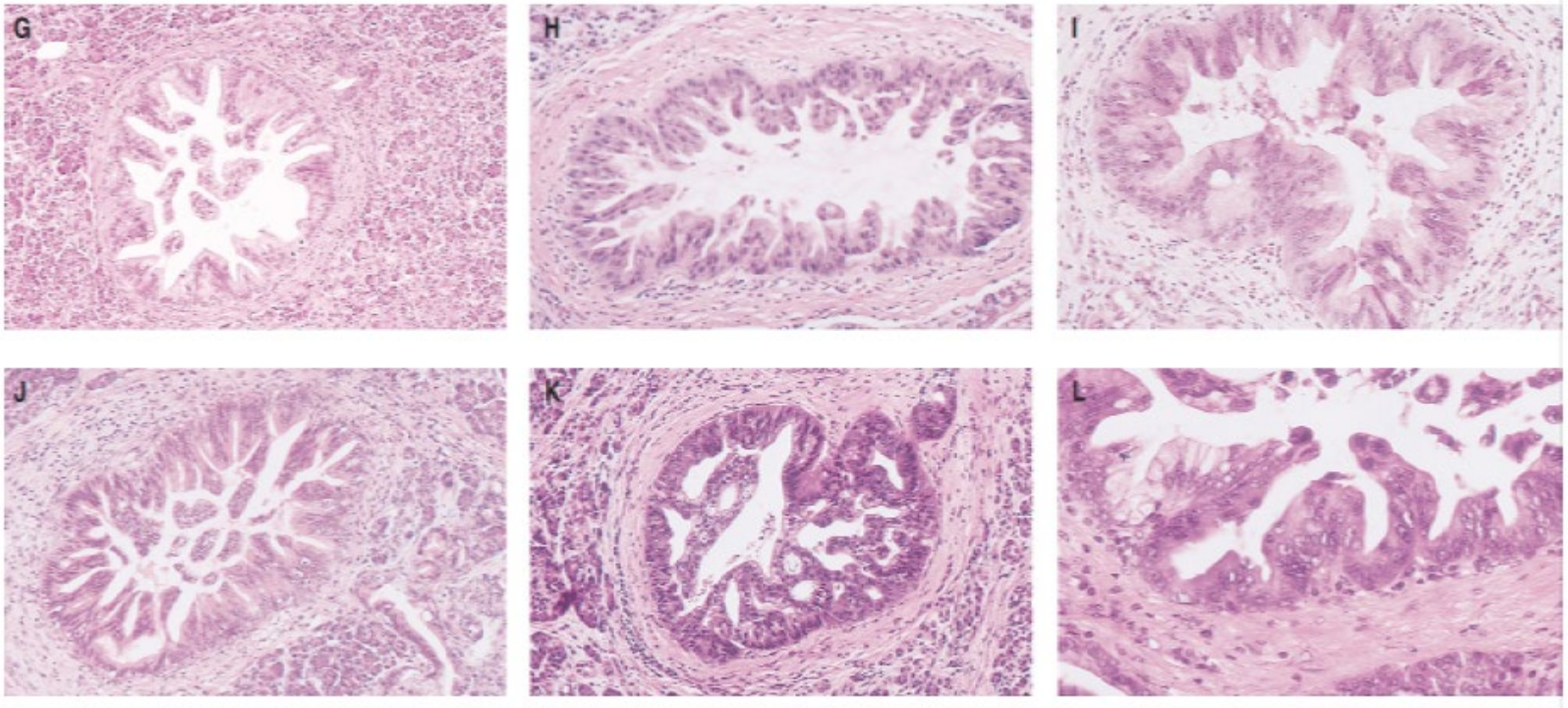
PanIN 3



Summary: Why simplify?

- Low grade PanIN common, incidental and of no clinical significance
- High grade PanIN is a surrogate for carcinoma

Simplifying PanIN: Challenge = PanIN 2 vs 3

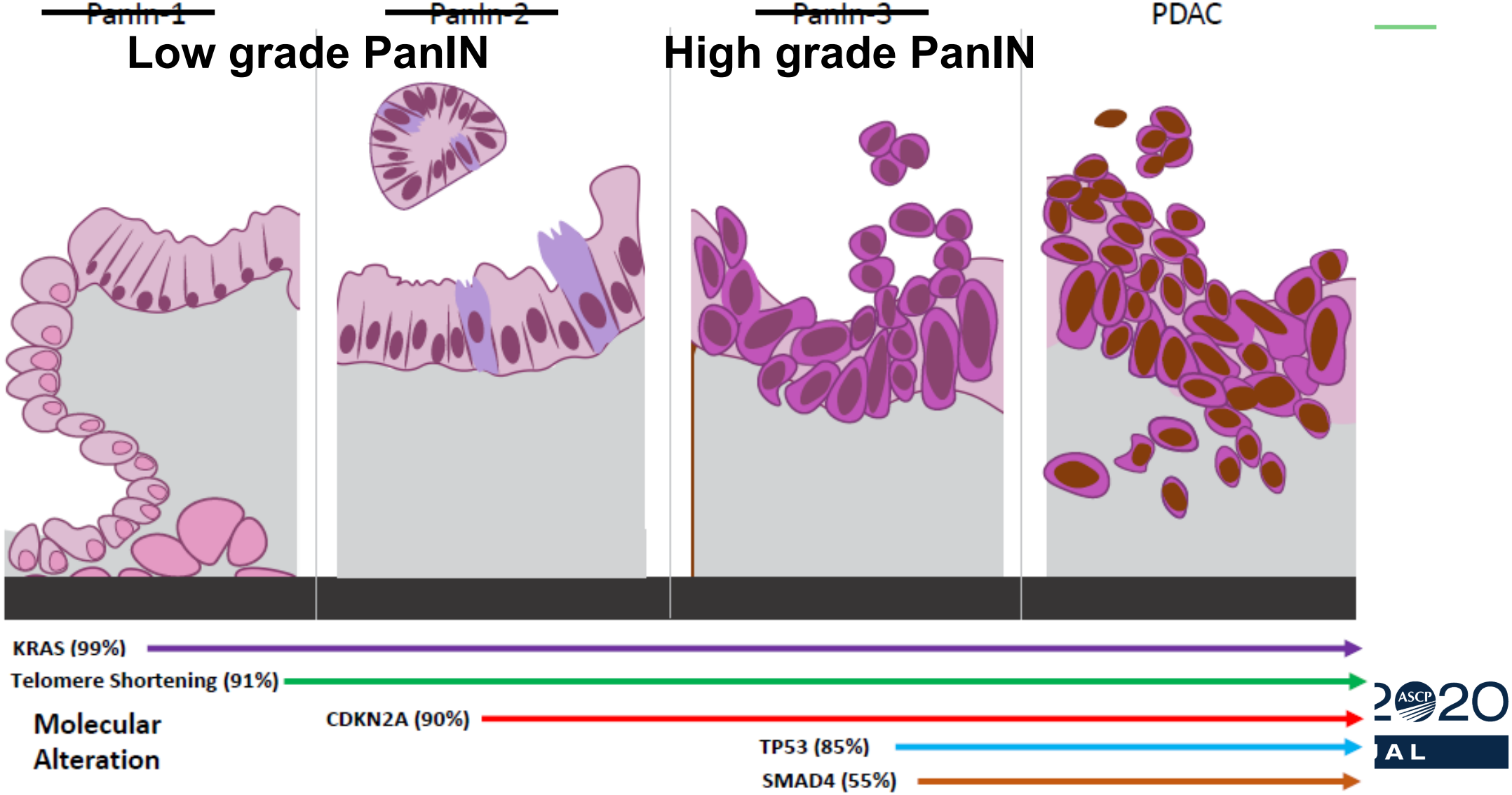
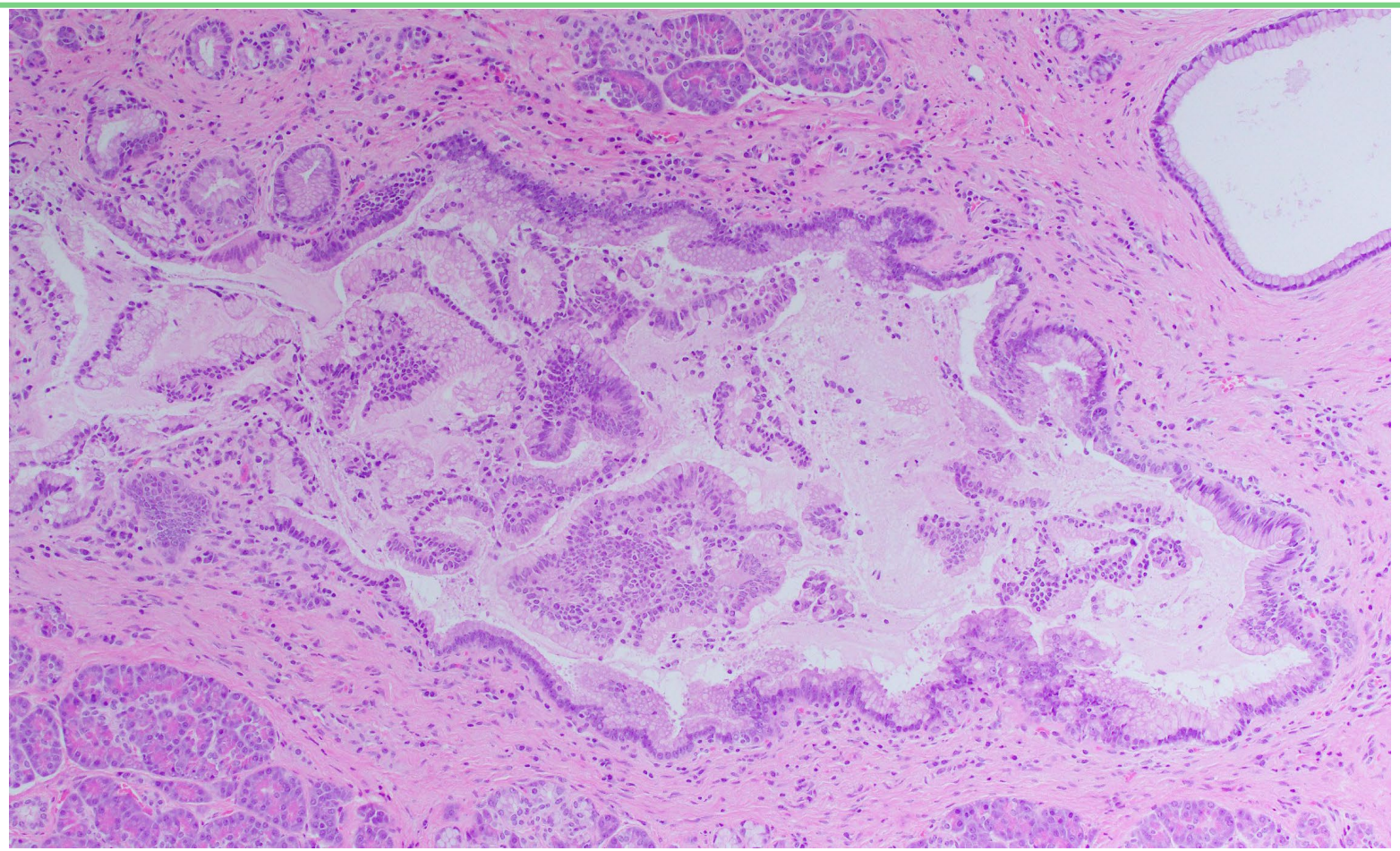


Figure adapted from Skoda (2016) and Guo., et al(2016)

Controversy: Pan-IN at the margin, cancer case

- **Low grade (don't report)**
  - "Pancreatic margin is negative for high grade dysplasia and carcinoma"
- **High grade (report)**
  - "R0" resection for adenocarcinoma (all margins negative for carcinoma)
  - **No evidence that high grade at the margin confers a worse prognosis in cancer cases**

Controversy: PanIN at the margin, cancer case



“Pancreatic margin is negative for high grade dysplasia and carcinoma”

A Convenience

- **Simplified cytoarchitectural low vs. high grade distinction translates to MCN and IPMN**

Reporting of Cases—The recommended terminology is:

- For PanIN:
  - Low-grade PanIN
  - *High-grade PanIN ("carcinoma in situ"*, according to local usage)
- For tumor-forming intraepithelial neoplasms (IPMN and MCN)
  - IPMN/MCN, low-grade
  - IPMN/MCN, high-grade
    - *IPMN (and MCN), high-grade* may be further classified with the relevant local usage such as "carcinoma in situ" in parenthesis.
- For cases that also have an associated invasive carcinoma
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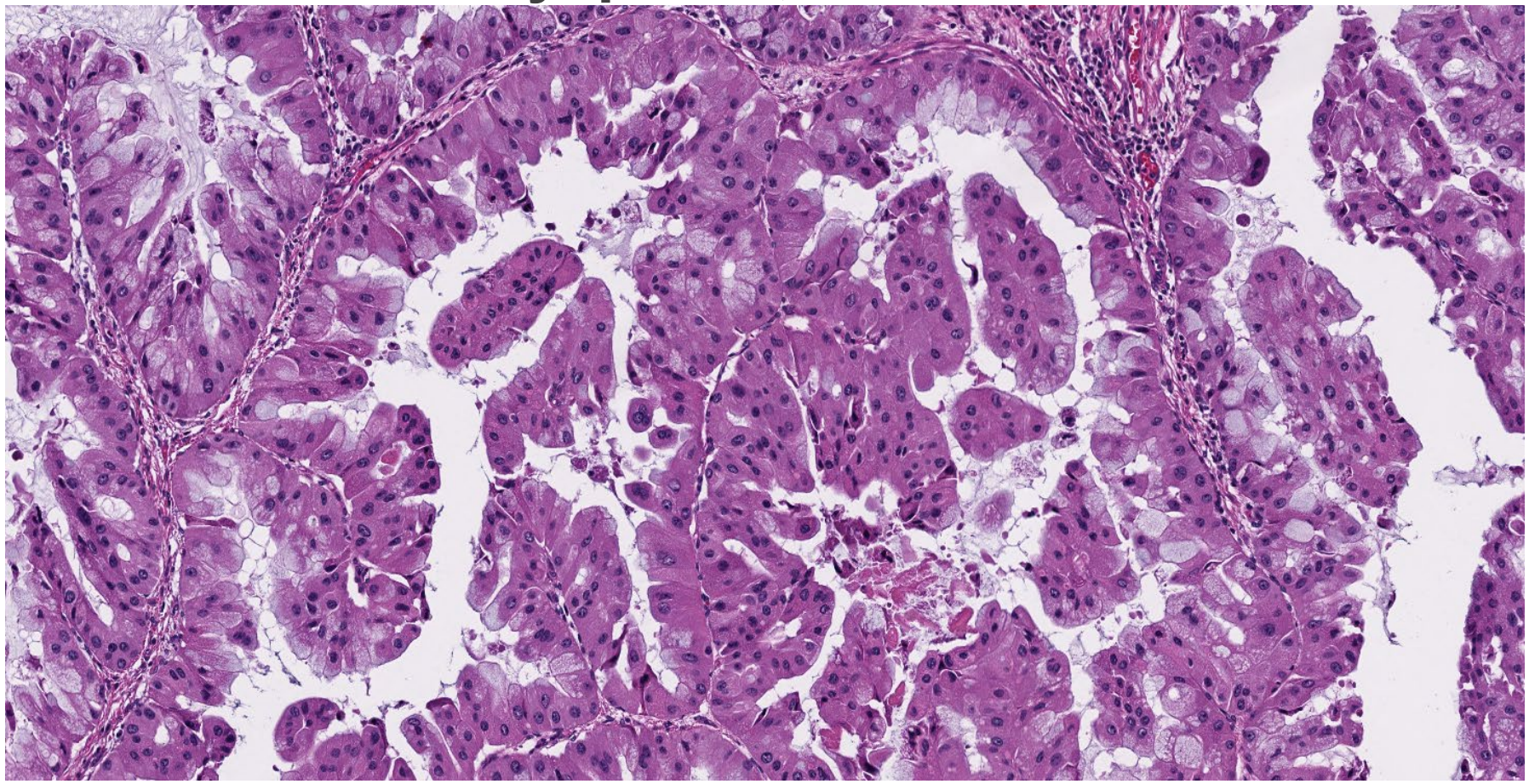
IPMN subtypes: what do they mean at signout?

- **Immunostains (don't, unless you must)**
- **Odds of high grade or carcinoma (HG/CA)**
  - Gastric (most common (70%)) – branch duct, HG/CA uncommon
  - Intestinal (20%) – main duct, HG common **(look harder)**
  - Pancreatobiliary (least common) – main duct, essentially all HG **(look harder)**
- **Submit it all, especially if you find HG**

Intraductal Oncocytic Papillary Neoplasm (IOPN) The New Old Tumor

- Essentially all IOPN have HG dysplasia, invasive carcinoma in about 30%



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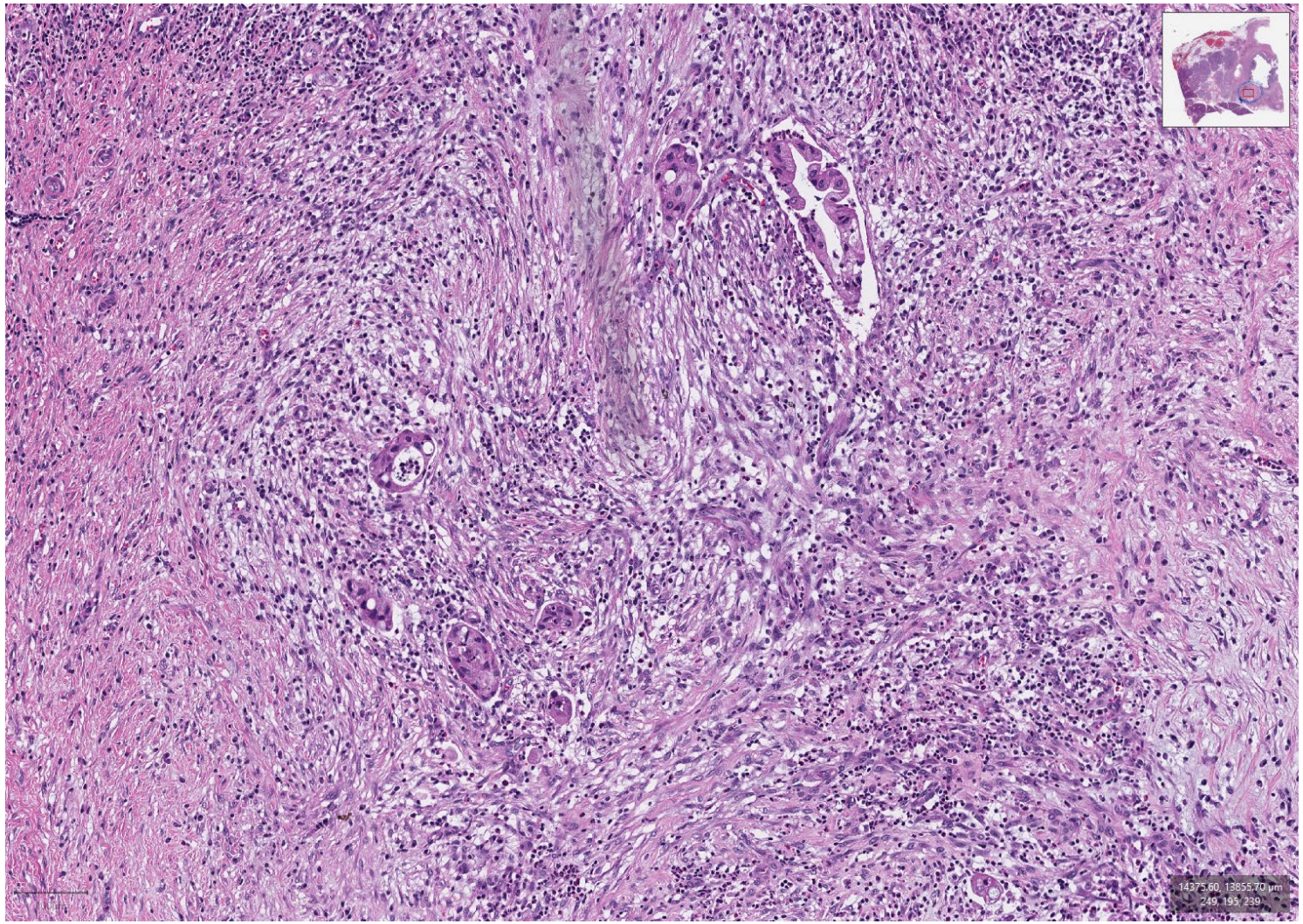

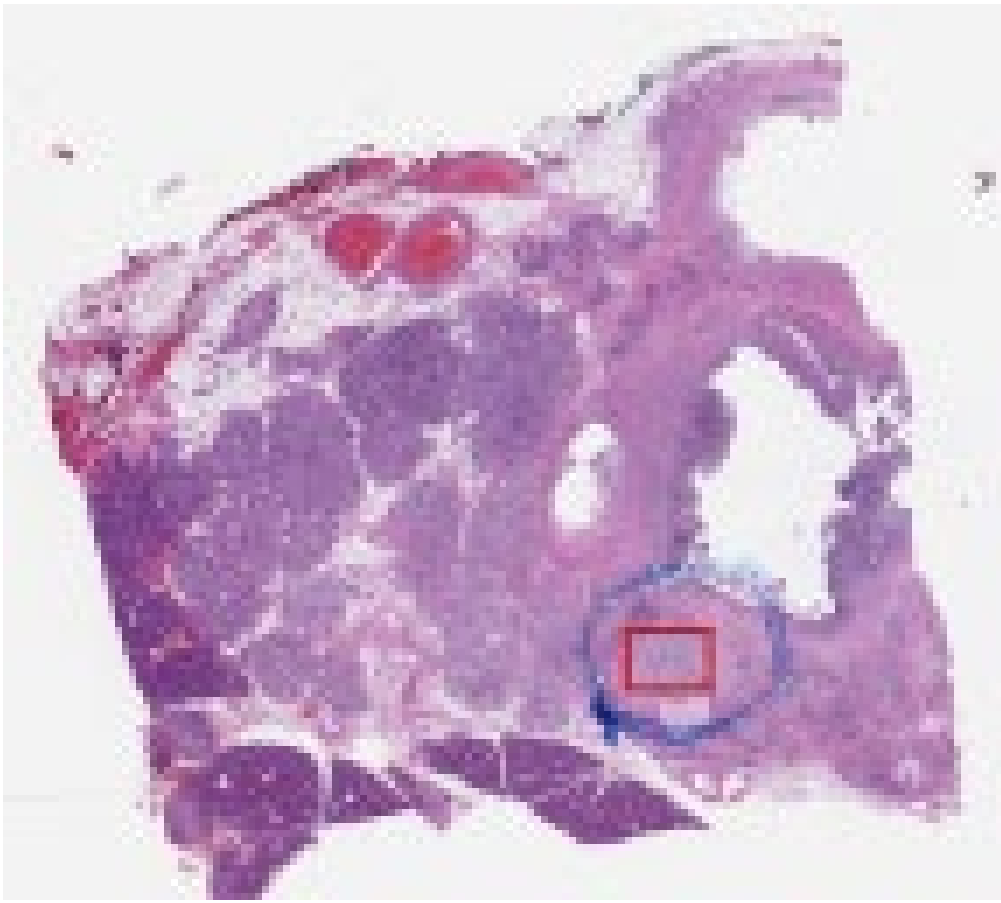

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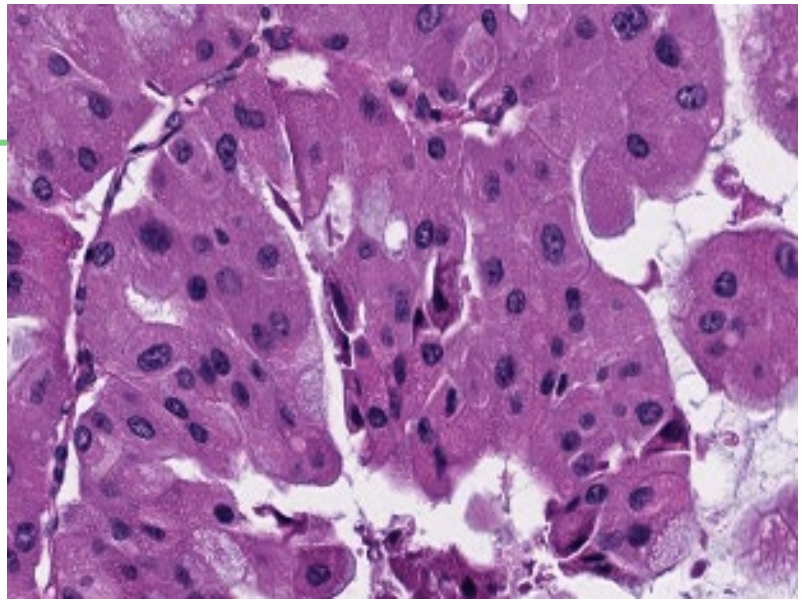


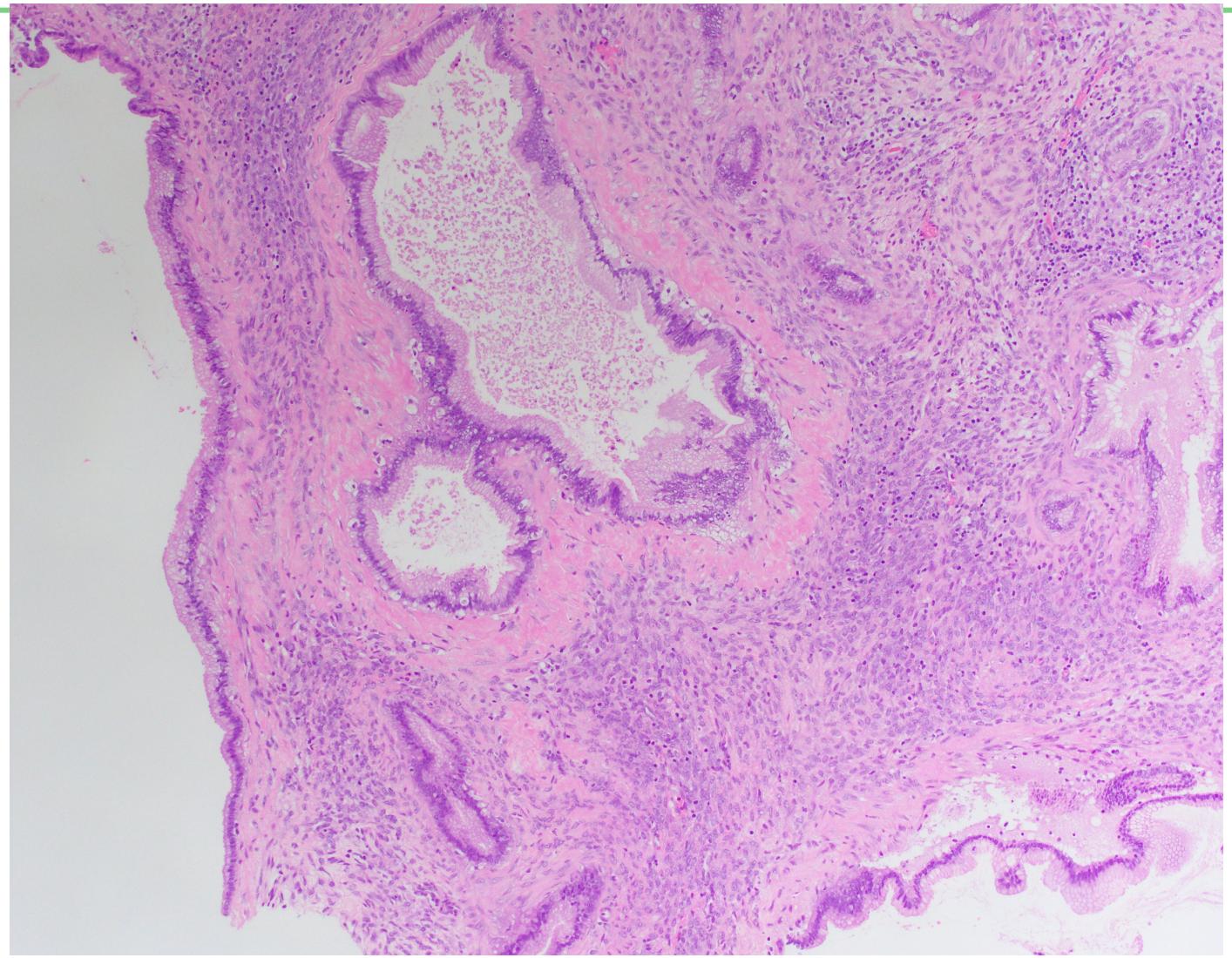
- **5% (4.5%) of intraductal neoplasms**
- **5% of 5% = 0.25% of all pancreatic tumors**
- **Lack KRAS, GNAS**
- **Few recurrent genes identified**
  - PRKACA and PRKACB mutations recently described*

*Singhi AD, Wood LD, Parks E, et al. Recurrent Rearrangements in PRKACA and PRKACB in Intraductal Oncocytic Papillary Neoplasms of the Pancreas and Bile Duct. *Gastroenterology*. 2020;158(3):573-582.e2.

Mucinous cystic neoplasm (MCN)

- >98% the body/tail
- Do not grow in the duct
- Women, average at 48 (14-95)
- Ectopic ovary/fetal periductal mesenchyme
- 15% have invasive CA

Mucinous cystic neoplasm (MCN)



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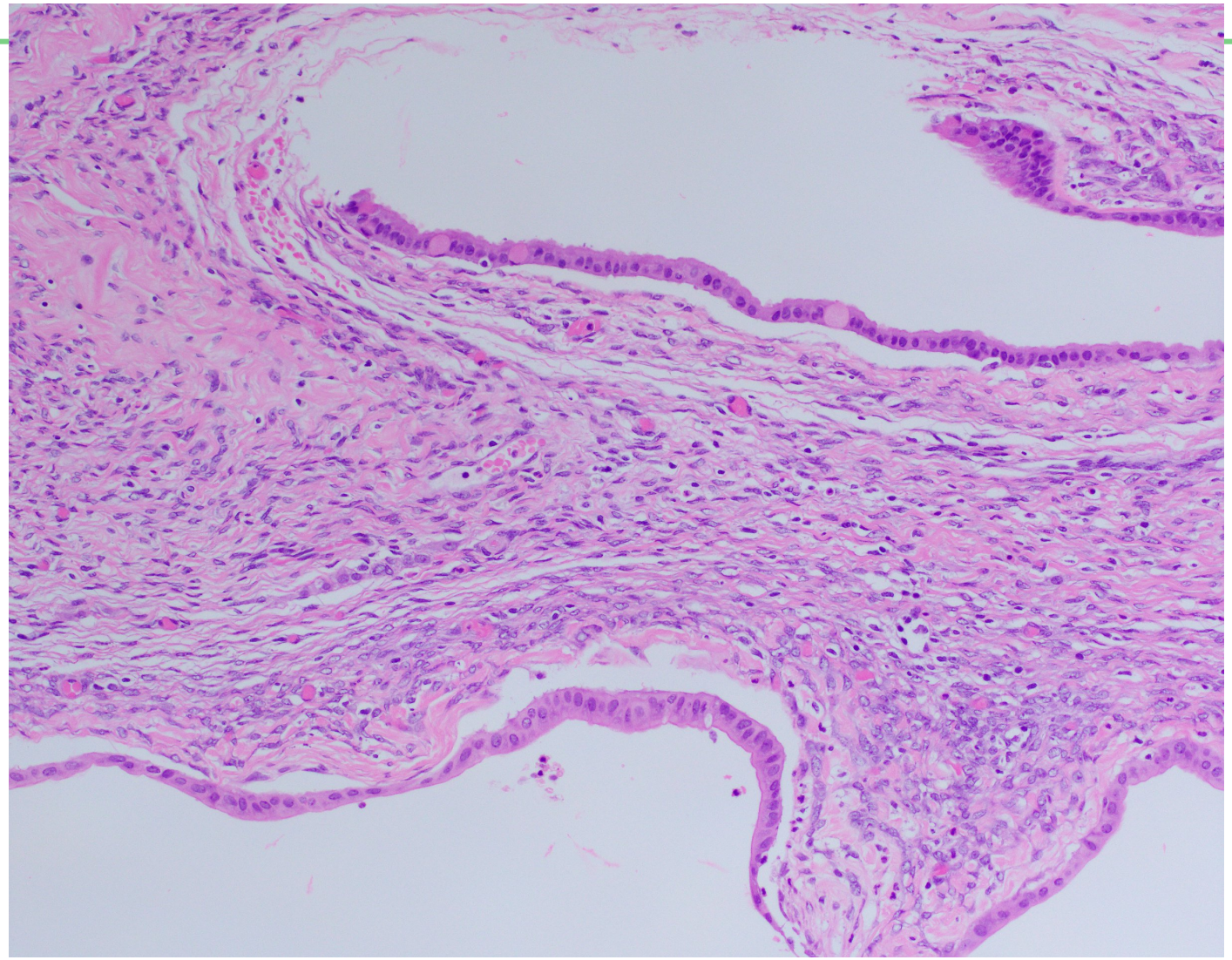

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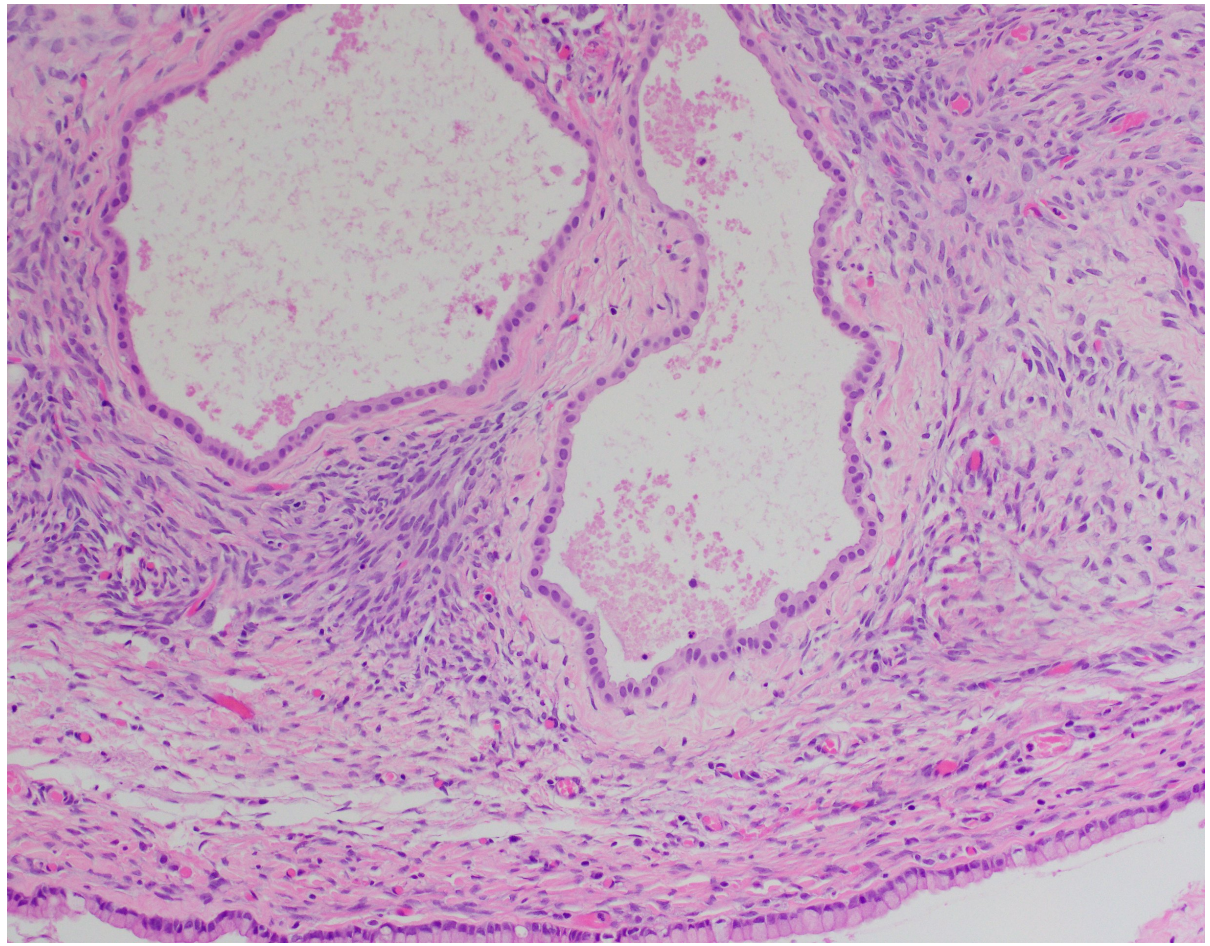

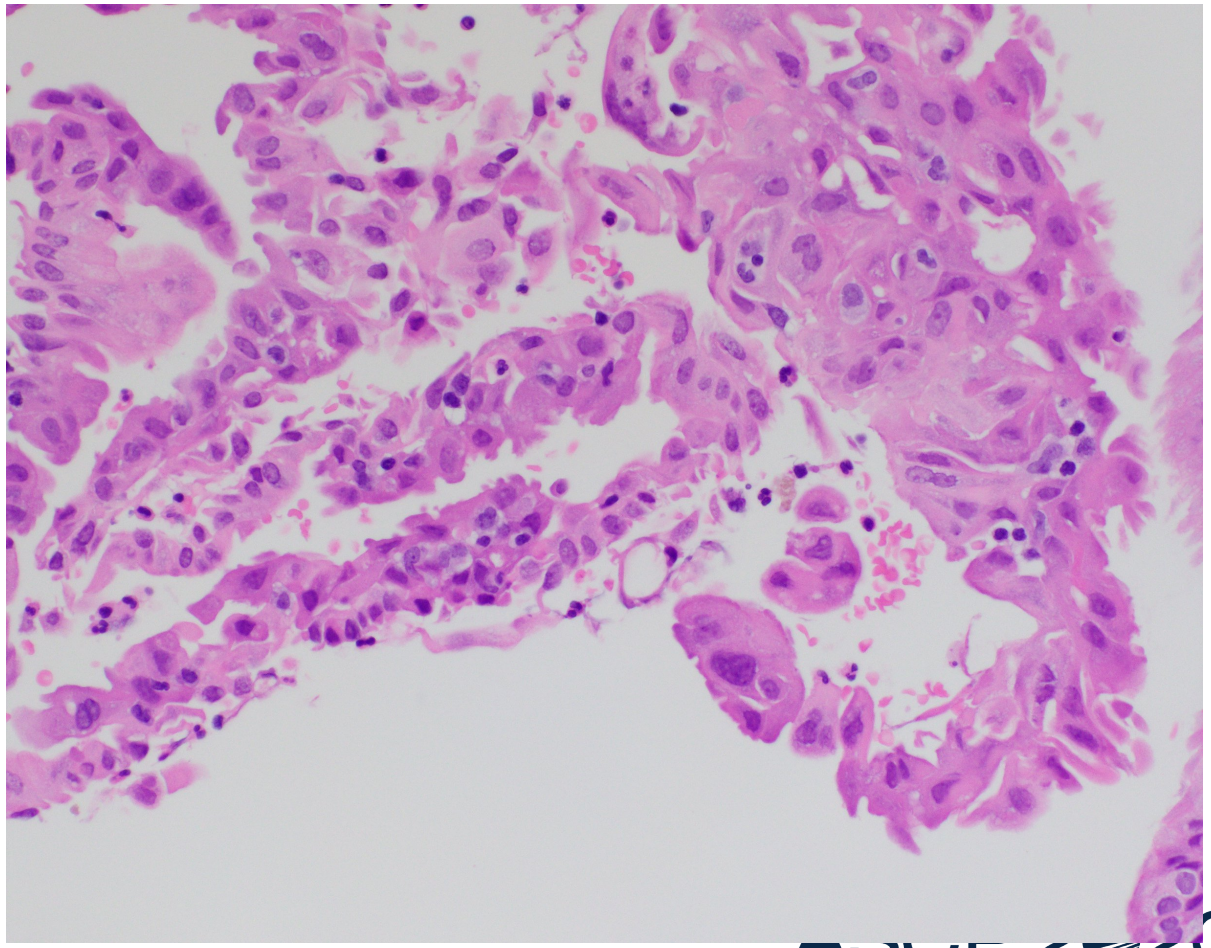

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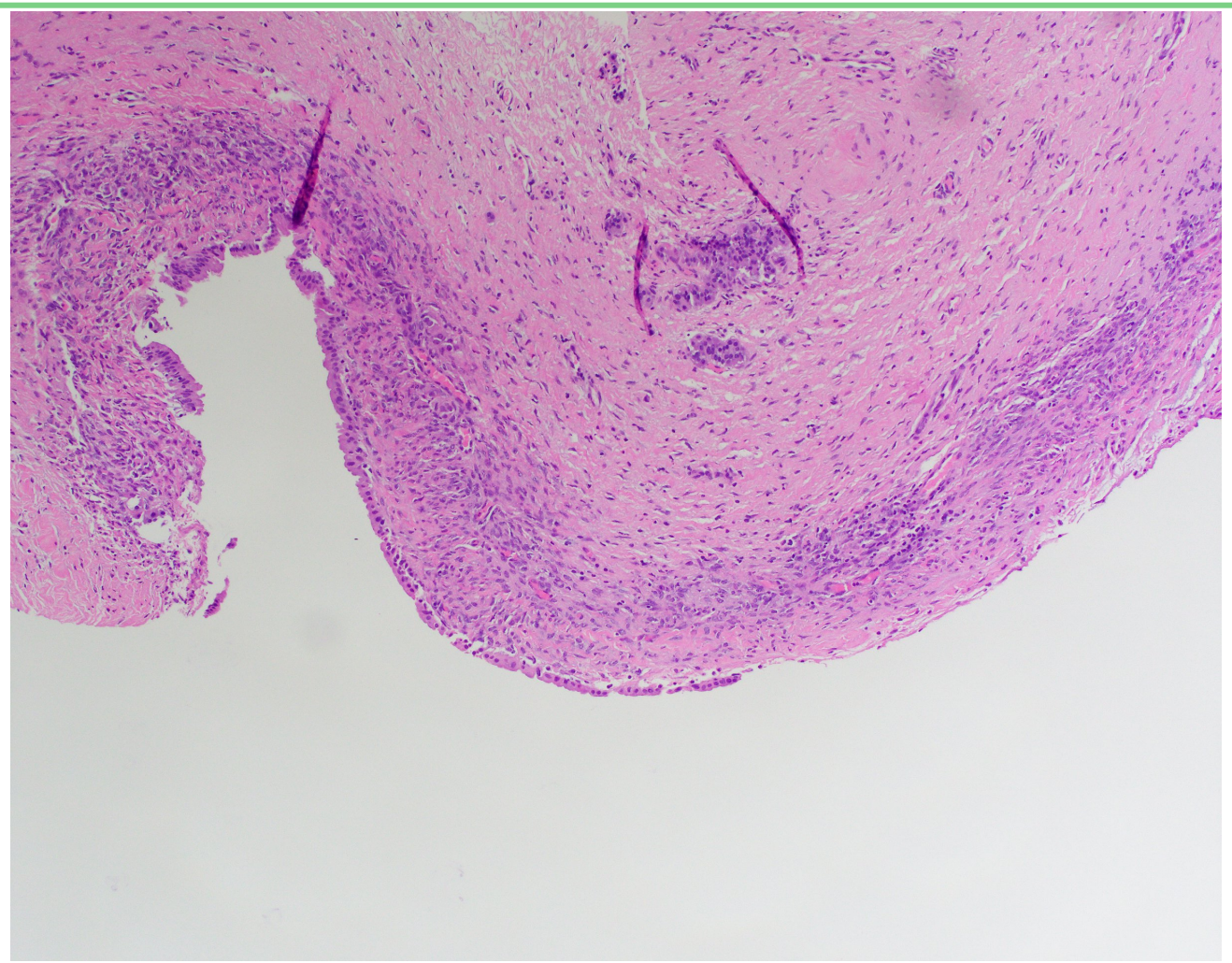

Controversy: Dysplasia at the margin, MCN/IPMN/IOPN

- Low grade (report)
- High grade (report)
- Significance of dysplasia at the margin in IPMN remains to be determined

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With regard to PanIN, IPMN/IOPN, and MCN

- **Grading is less nuanced**
- **Reports should be shorter (omit low grade Pan-IN)**
- **Reports should raise fewer alarms**
  - No more low grade PanIN present at the margin
  - High grade at the margin of a cancer case has not been shown to impact outcome (discuss locally)

Thank You

Questions?

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