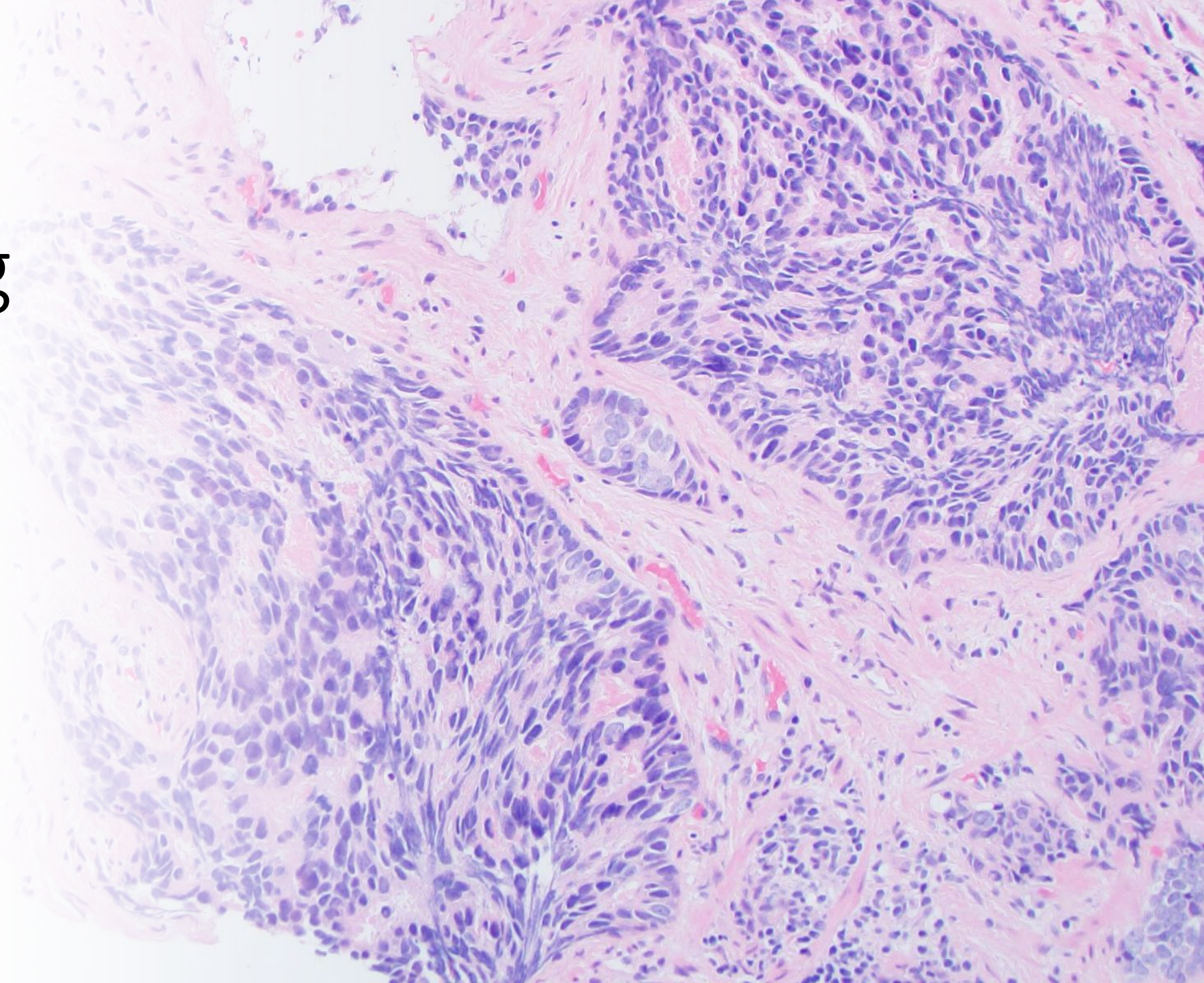


Interesting Cases in Prostate Pathology

Deepika Sirohi, MD

2/7/2023



- No disclosures

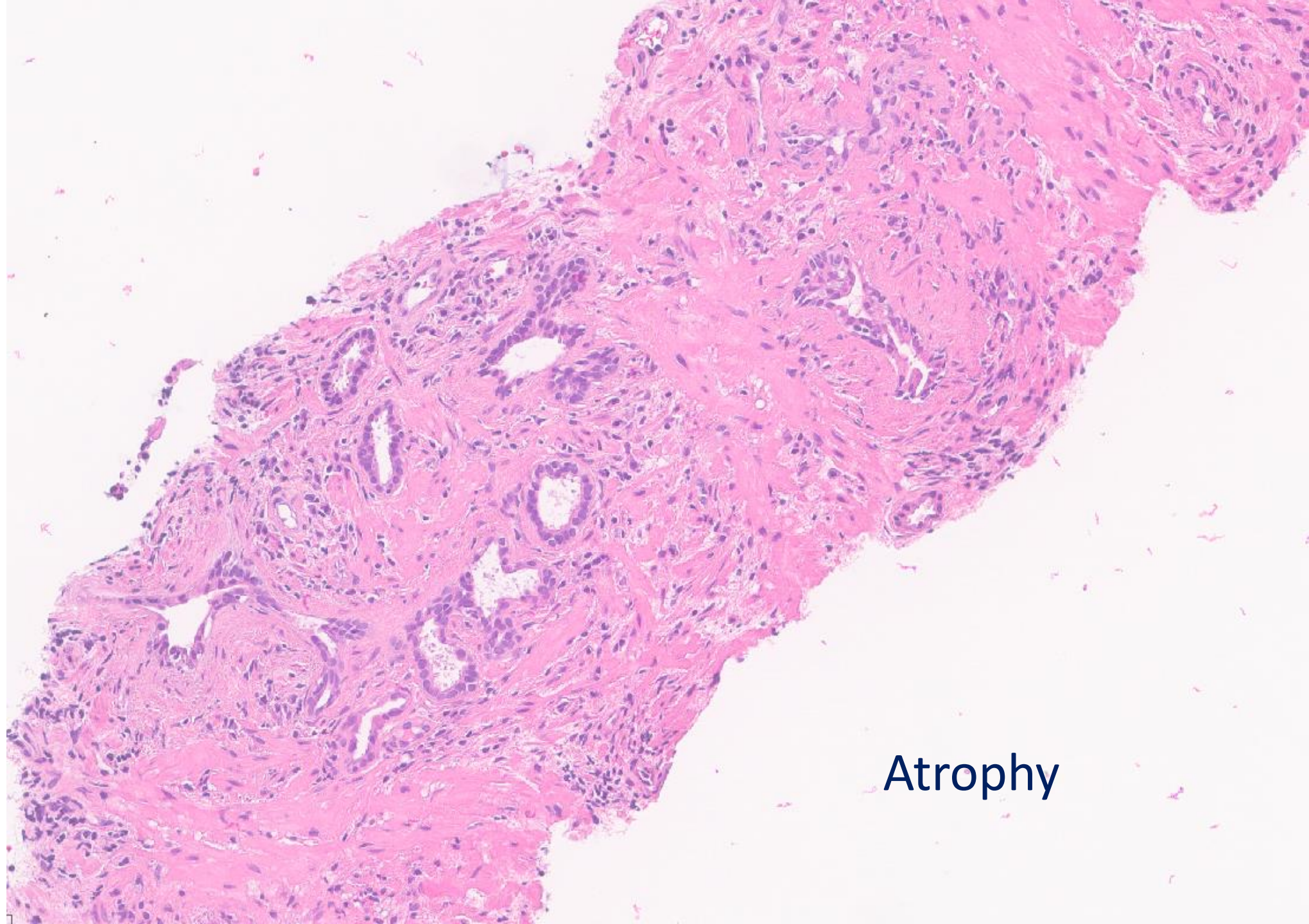
“Interesting Is a Non-Word. Be Specific.”

by mollyrookwood / 25 May 2021

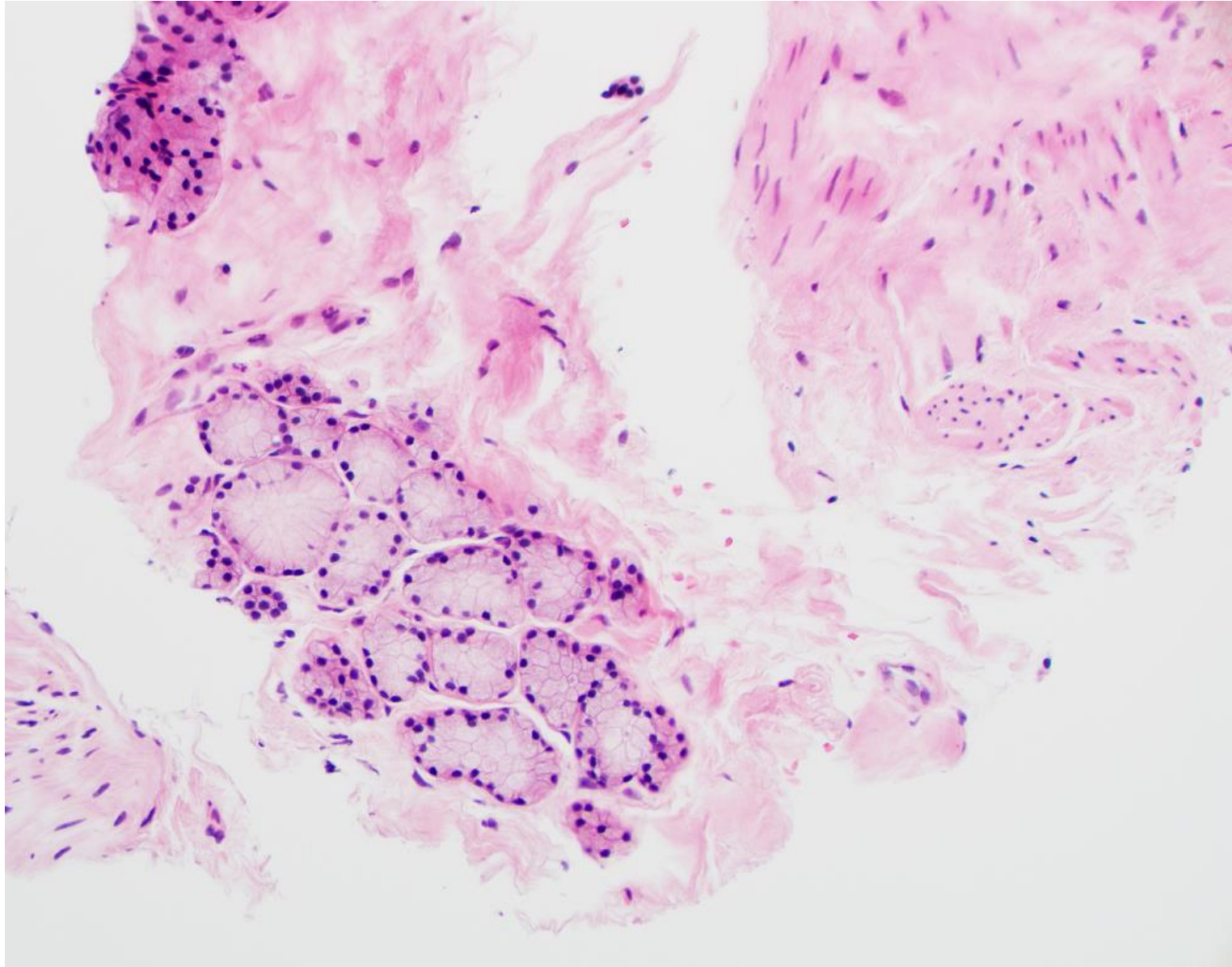


“Interesting” is a lazy word.

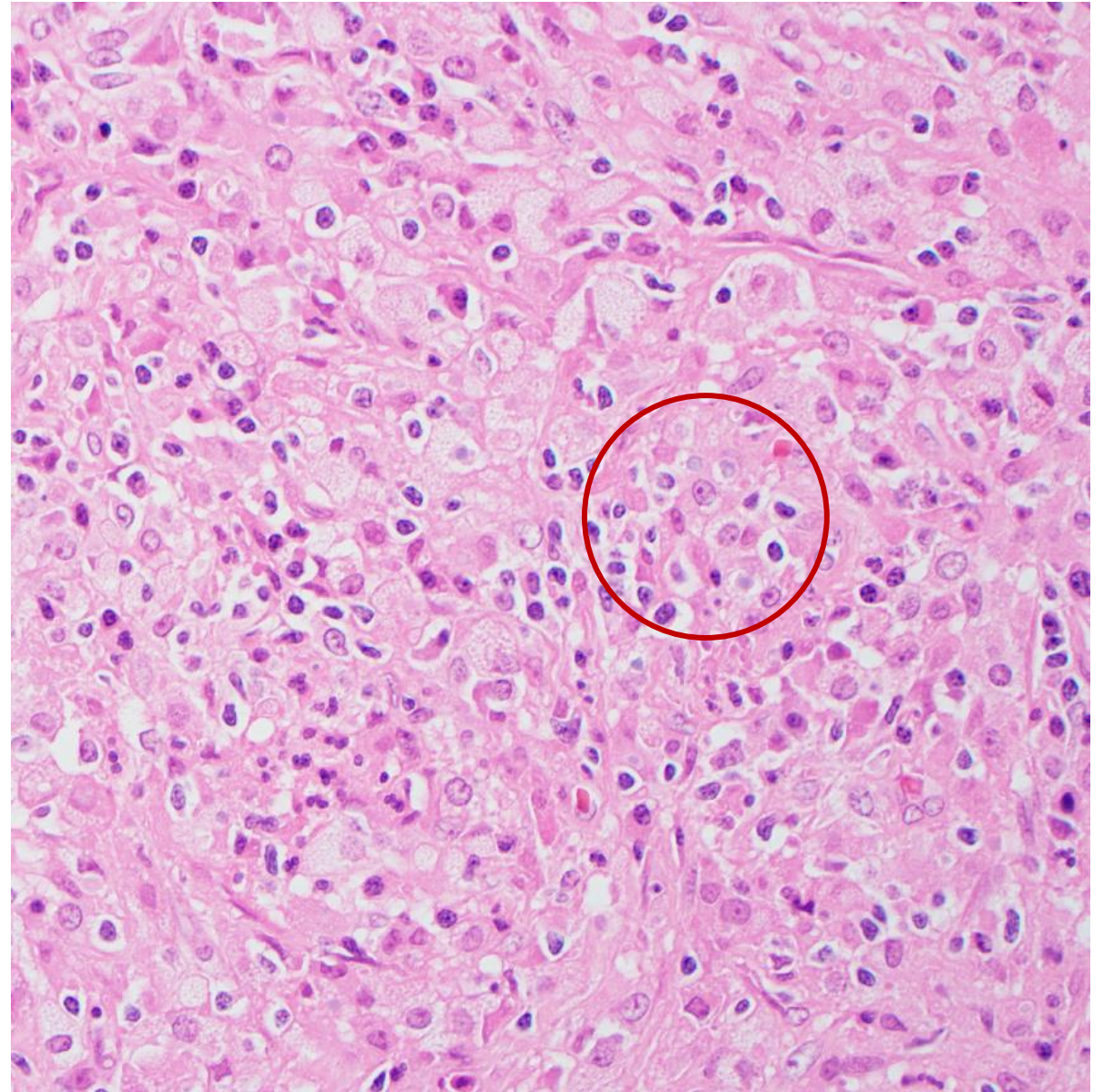
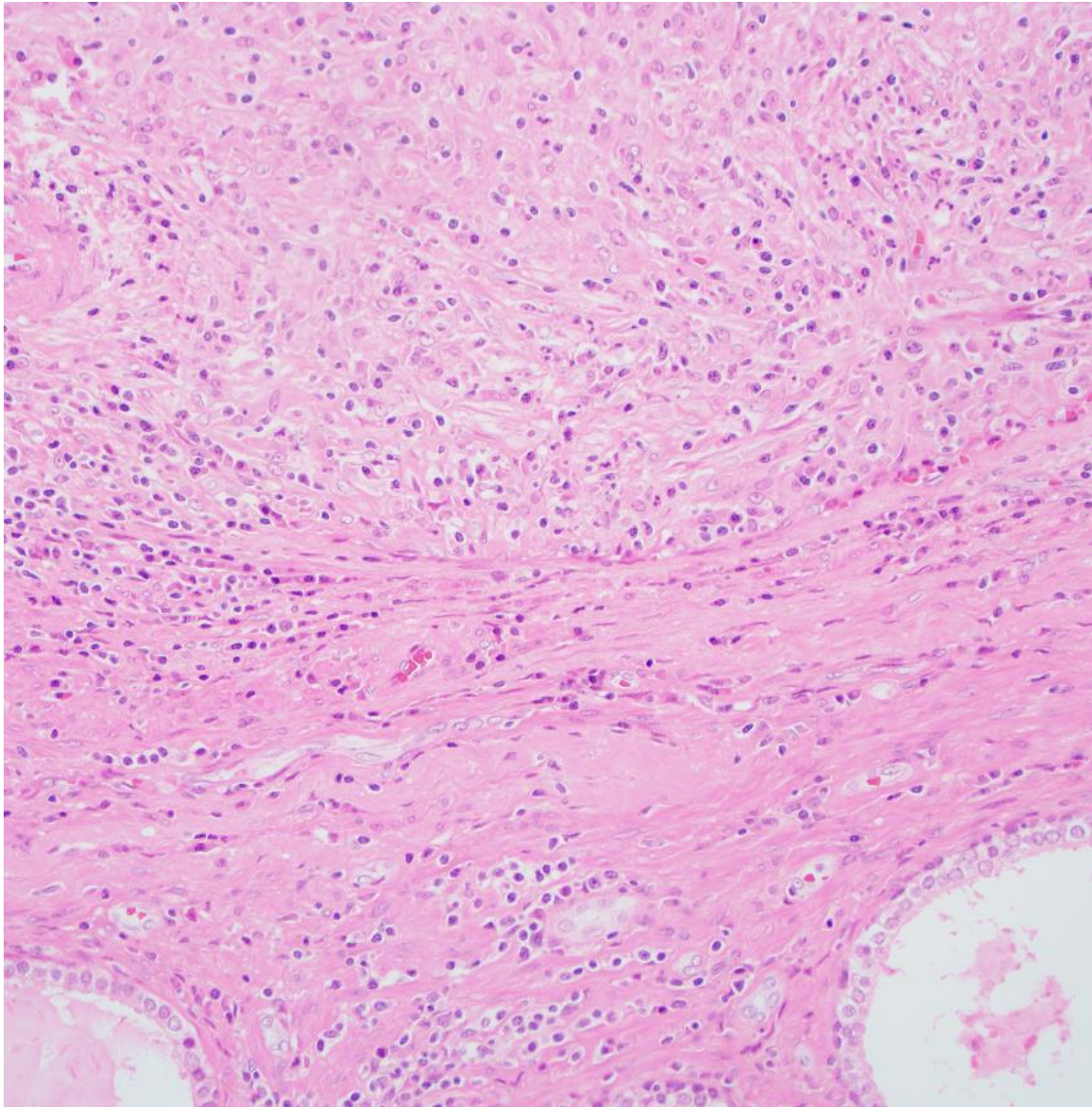
Case 1



Atrophy



Cowper's Glands

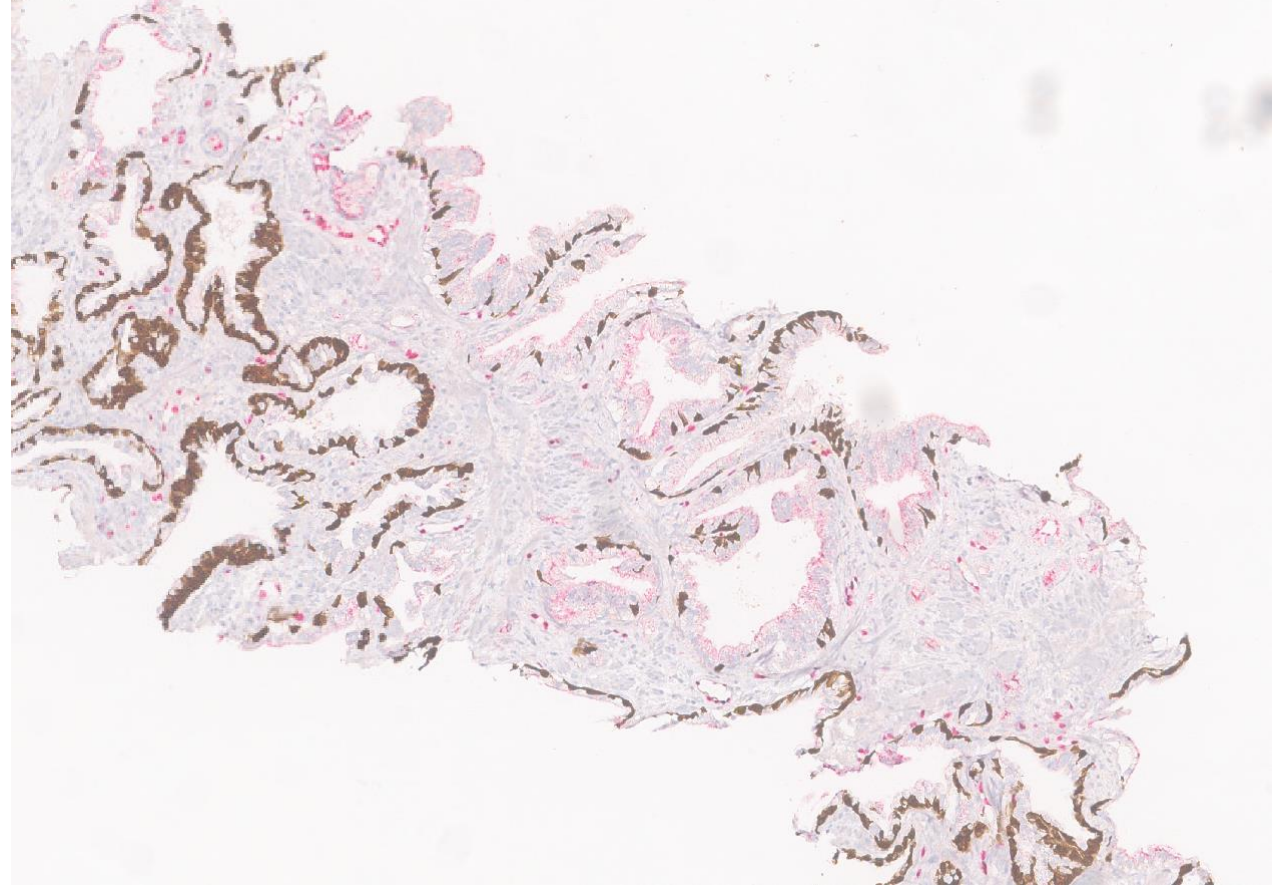
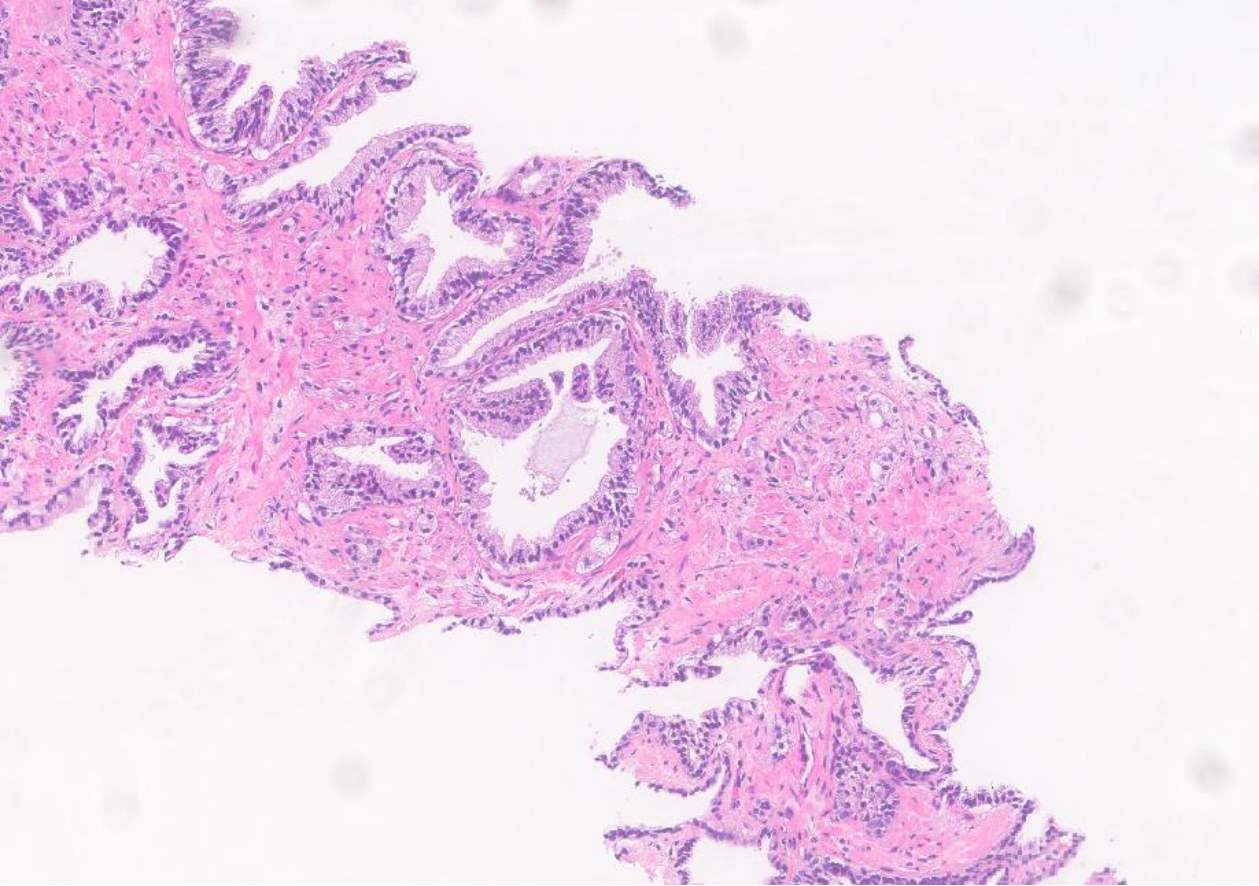


Malakoplakia

Benign Mimics of Prostate Carcinoma

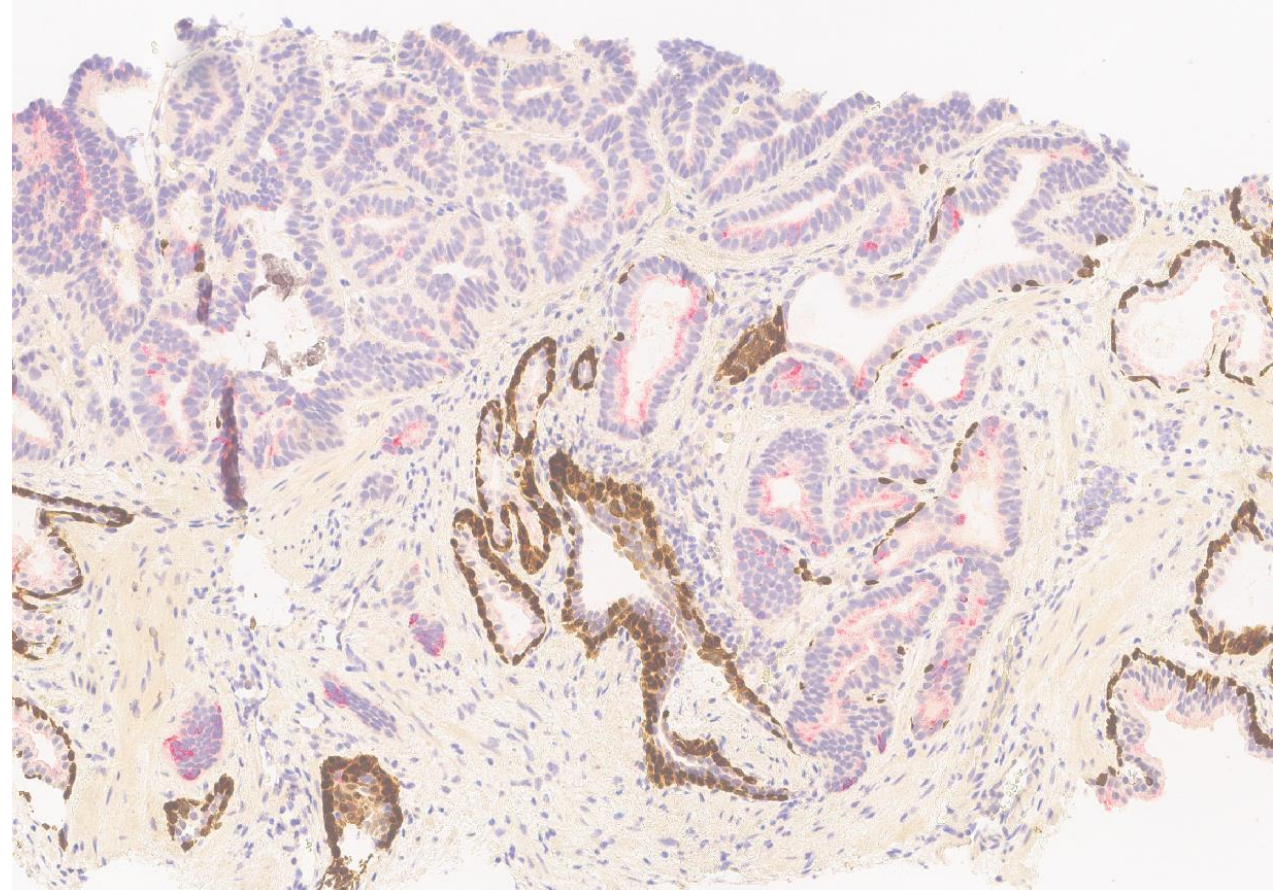
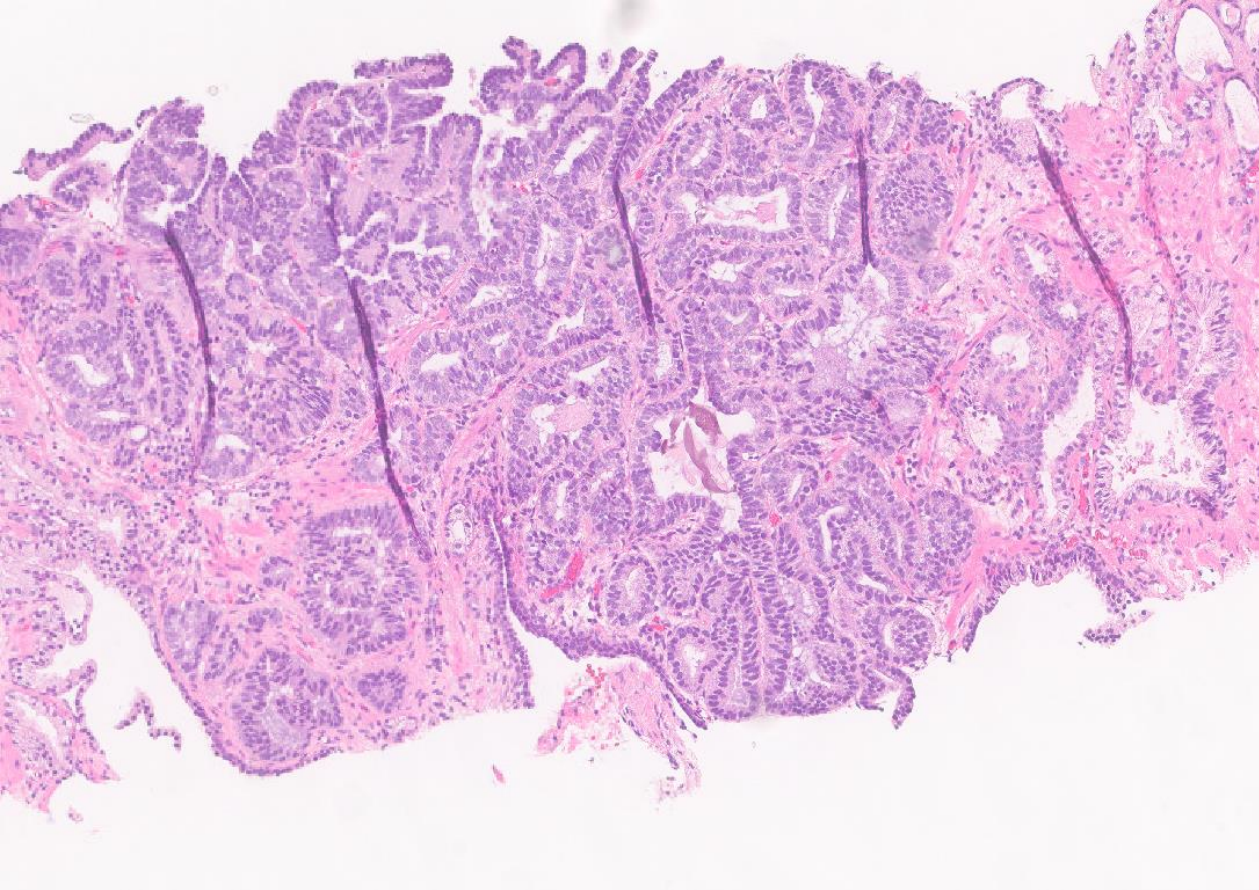
<i>Normal anatomy</i>	<i>Hyperplasia</i>
Seminal vesicles Cowper's glands Paraganglia	Basal cell hyperplasia Verumontanum gland hyperplasia Clear cell cribriform hyperplasia
<i>Atrophy</i>	<i>Metaplasia</i>
Simple Partial atrophy Postatrophic hyperplasia	Nephrogenic metaplasia Mucinous metaplasia
<i>Benign proliferations</i>	<i>Inflammatory process</i>
Adenosis (AAH) Sclerosing adenosis	Chronic inflammation Granulomatous prostatitis Malakoplakia

Case 2



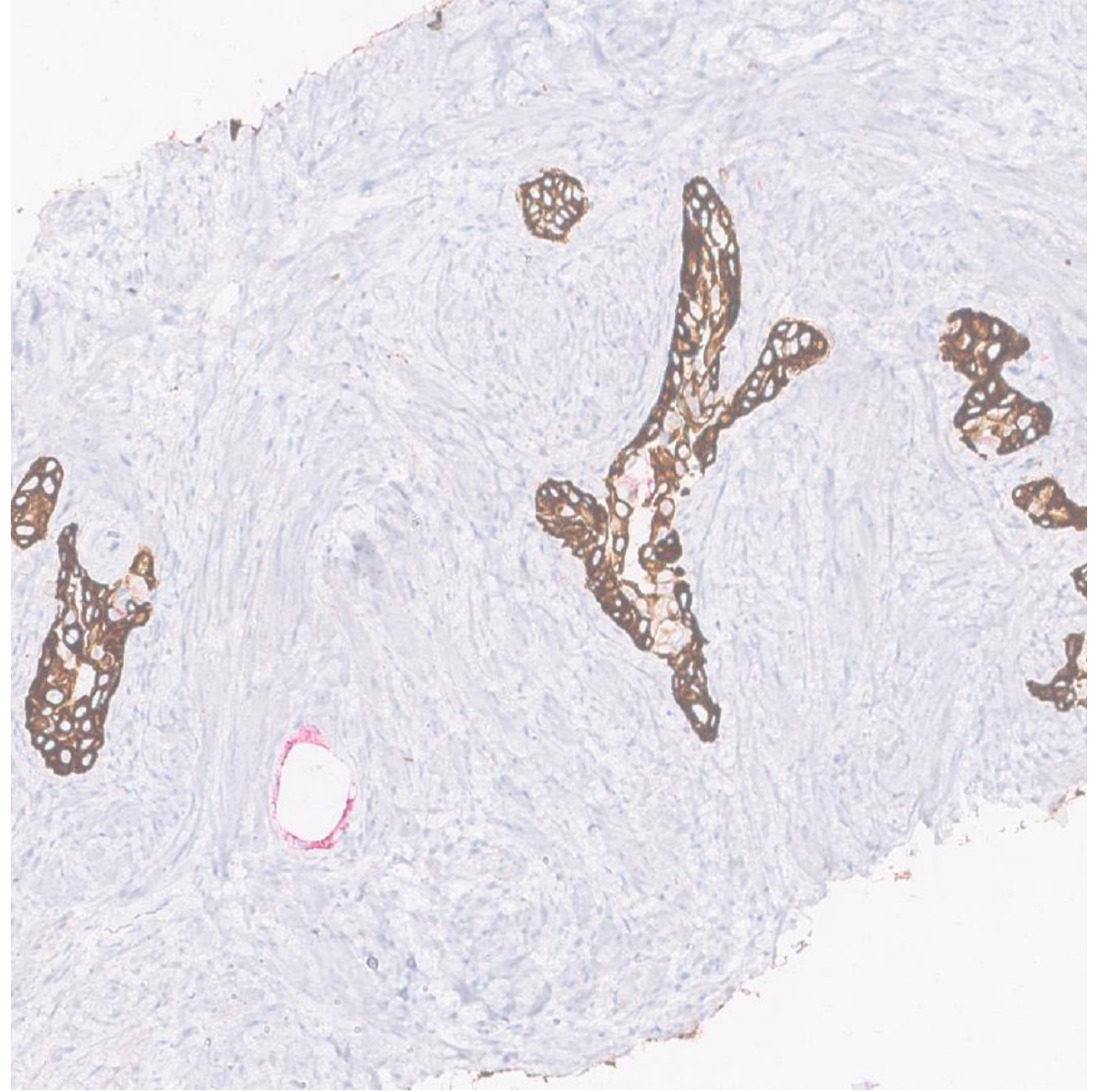
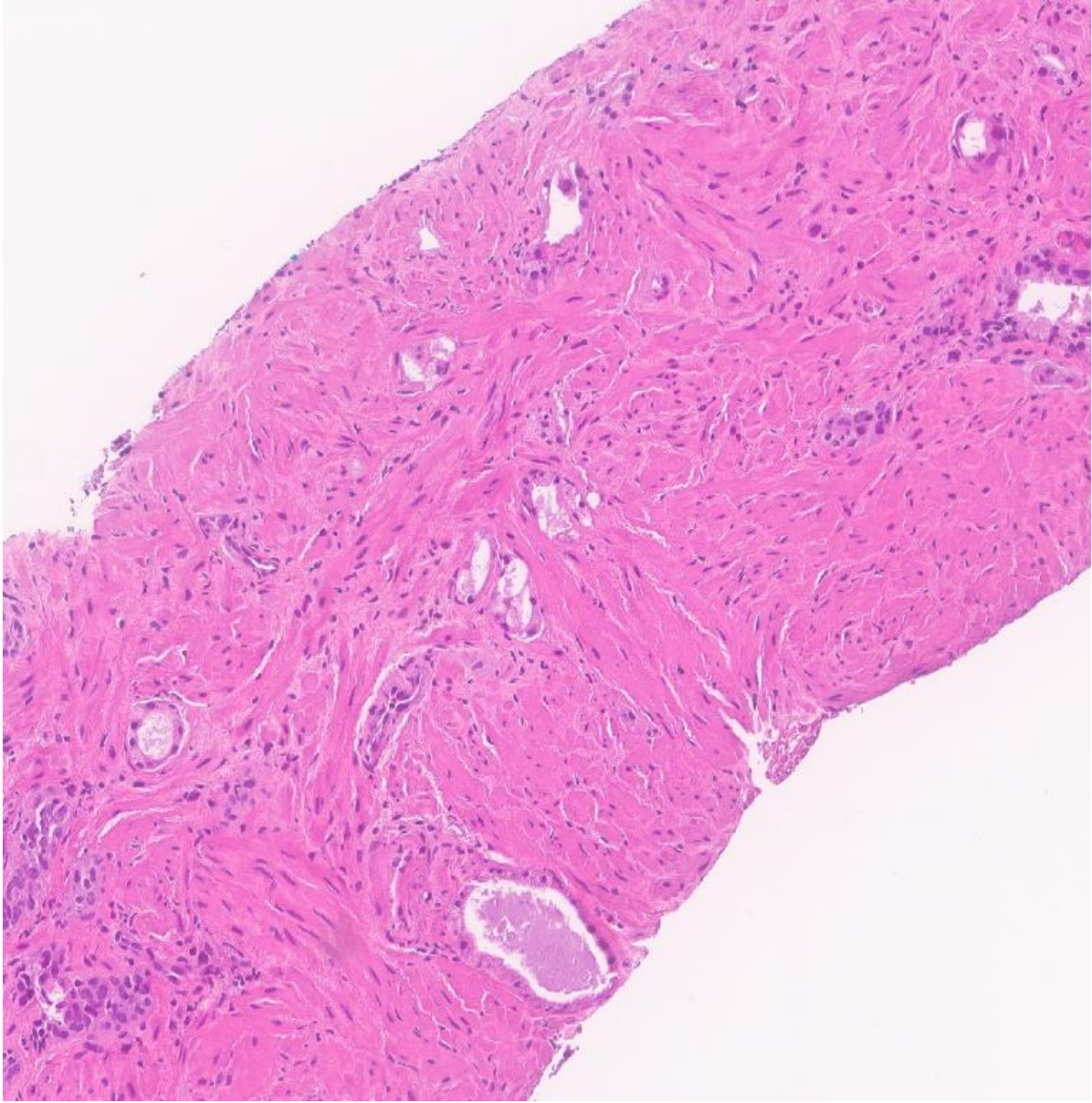
Atypical glands adjacent to a focus of high-grade PIN

Case 3



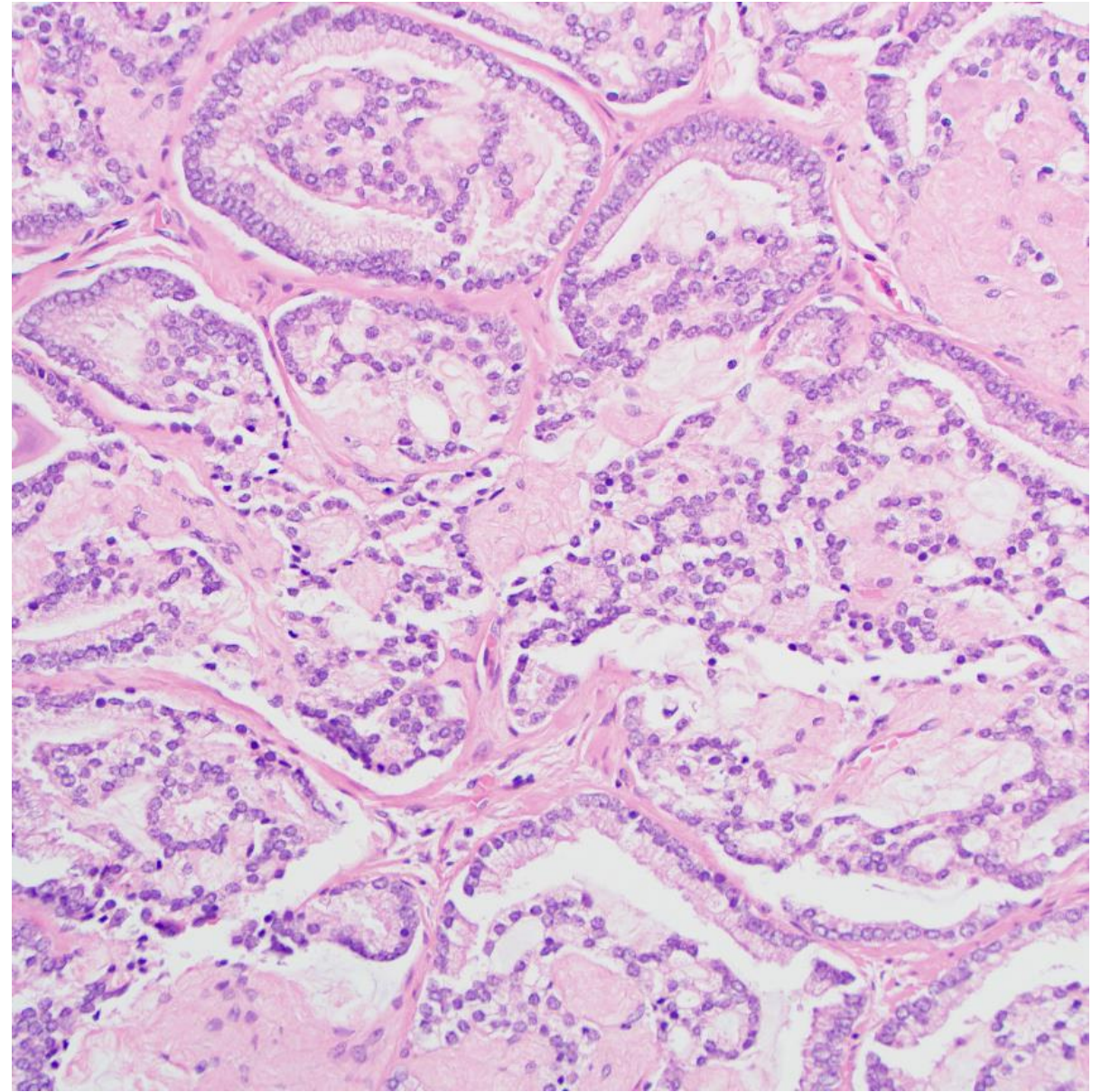
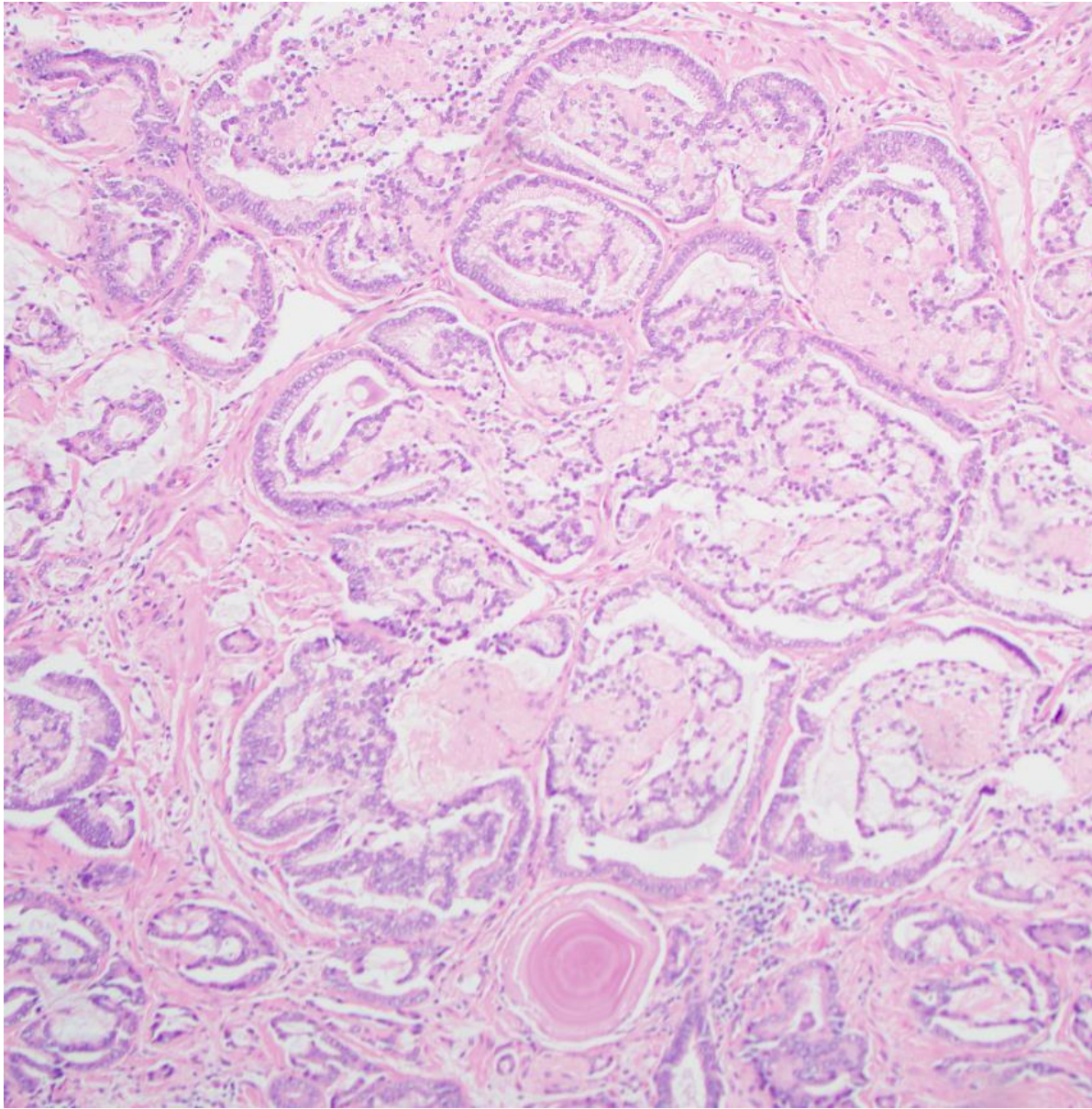
Atypical Focus: Low Grade Carcinoma Vs High grade PIN

Case 4



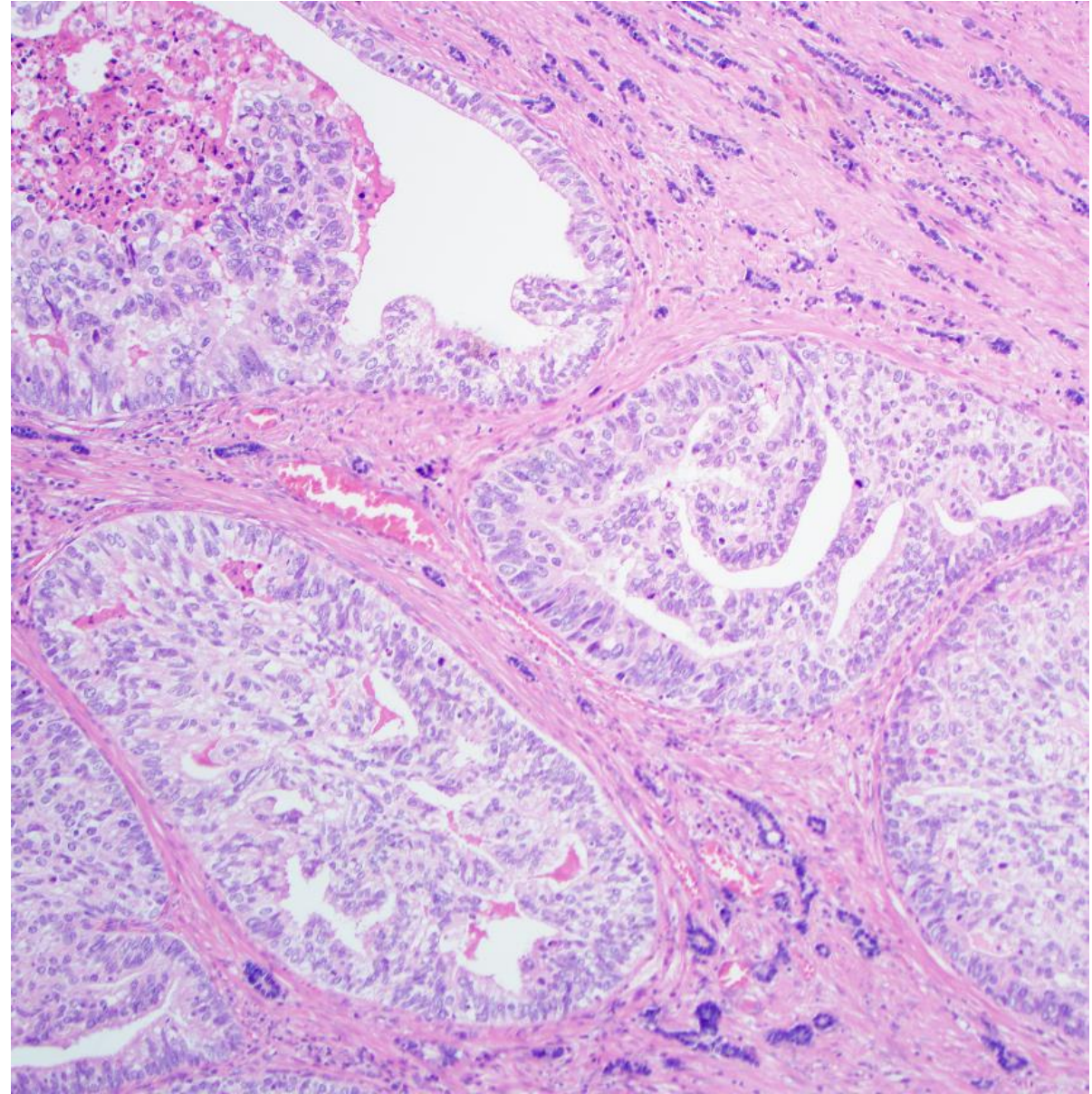
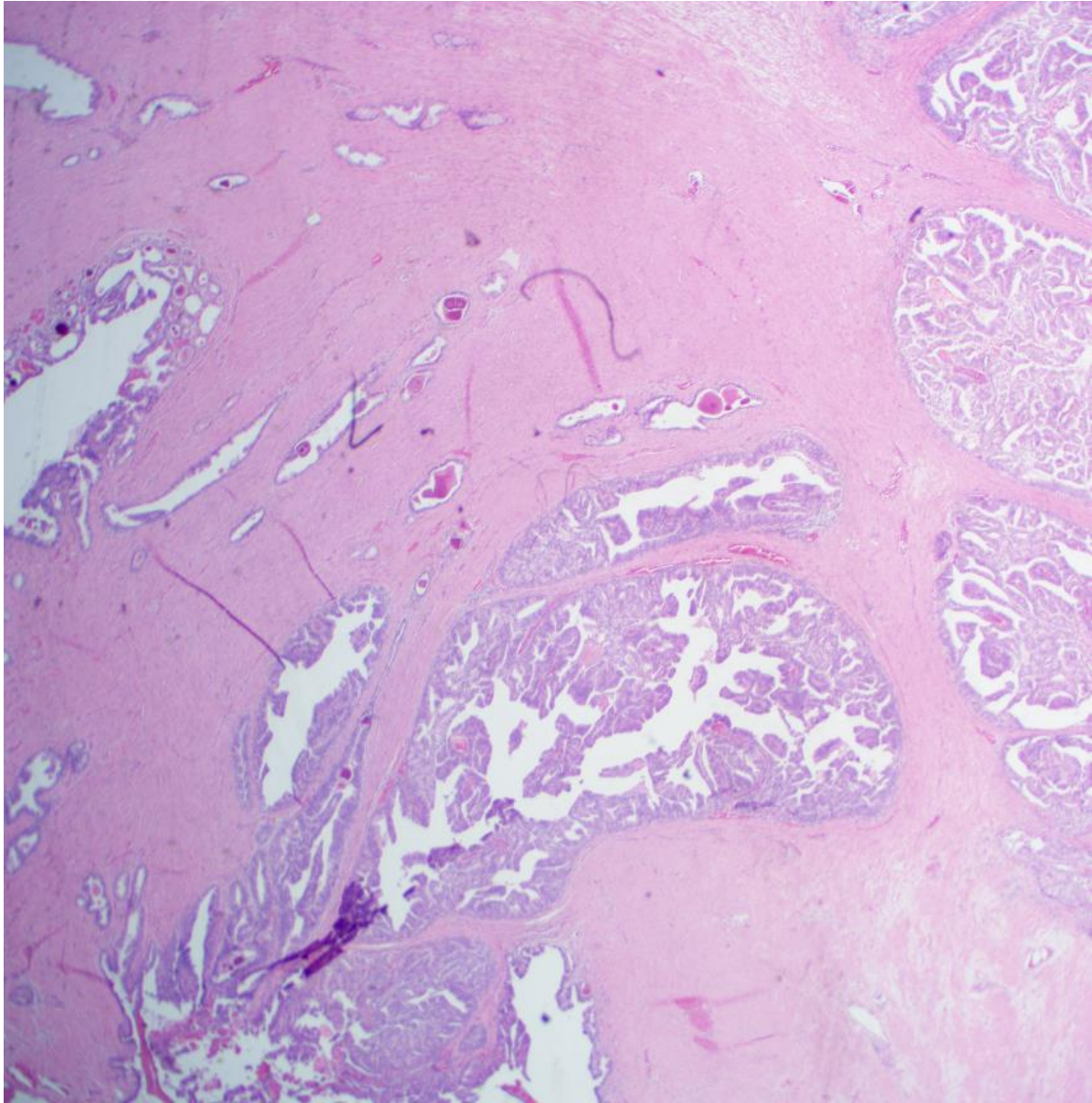
Post Radiation Carcinoma

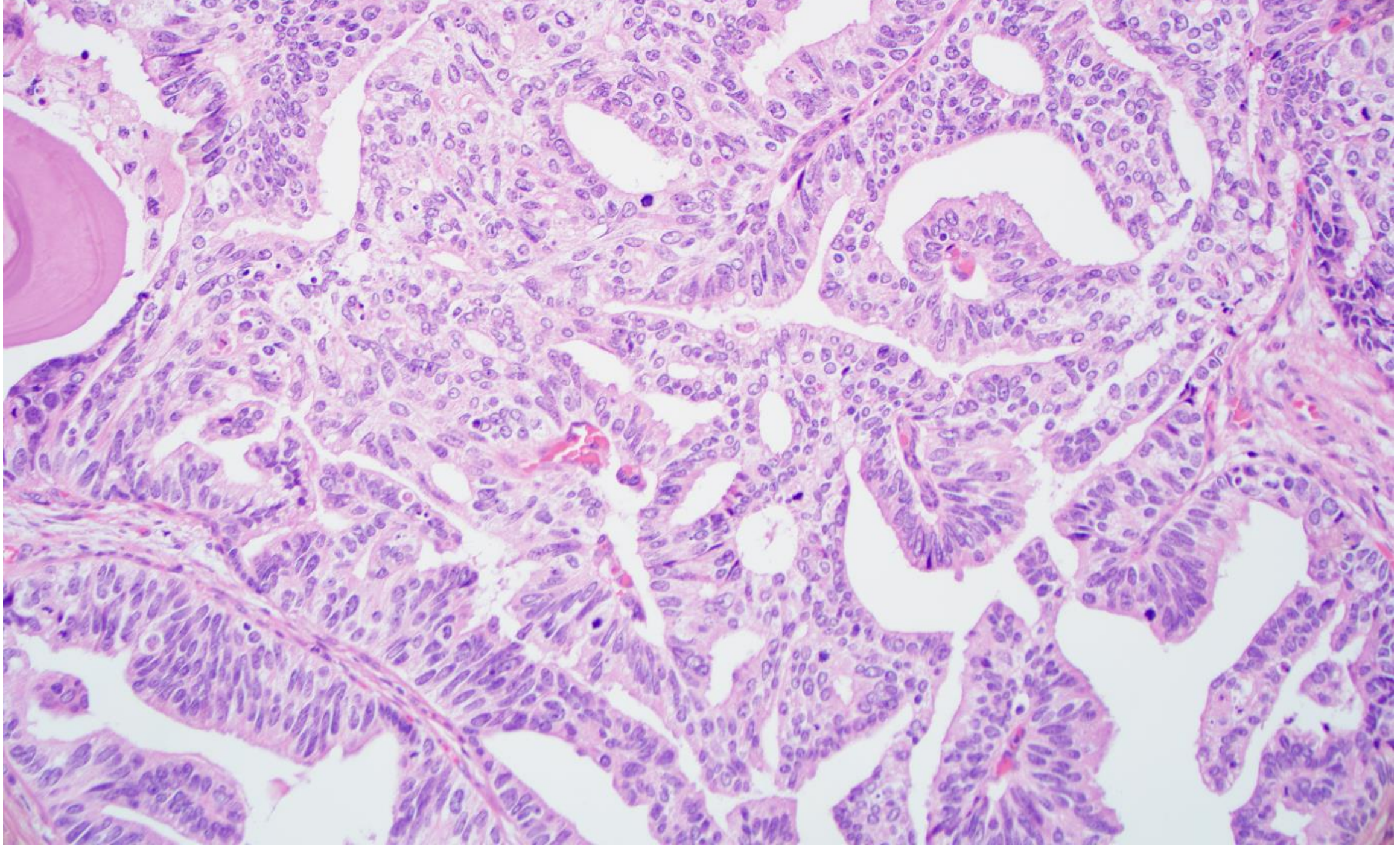
Case 5



Mucinous Fibroplasia

Case 6



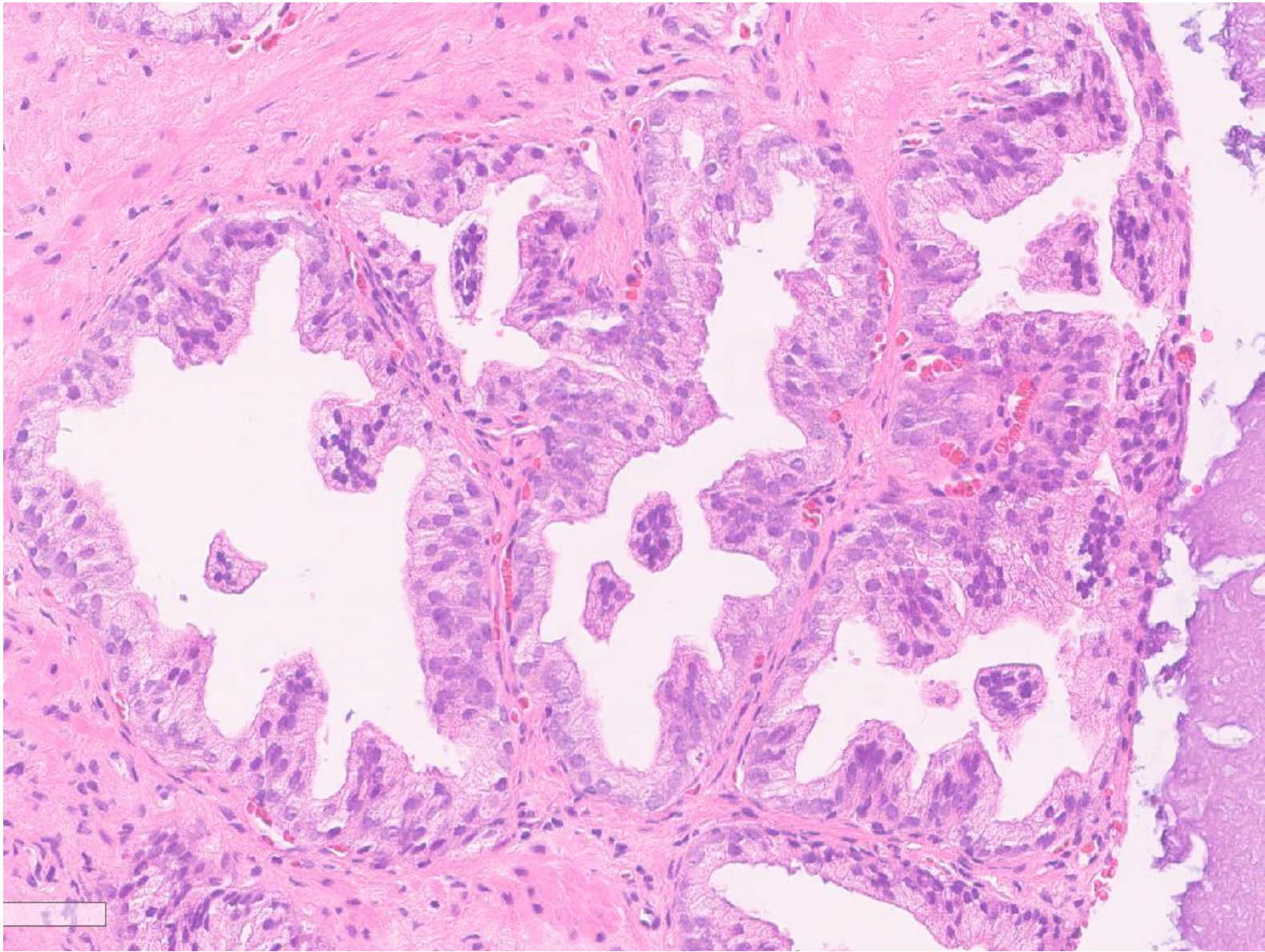


Ductal Carcinoma

- Frequently admixed with acinar
- WHO classification:
 - RP cases with >50% ductal morphology
 - Needle biopsies: Adenocarcinoma with ductal features
- More aggressive than acinar
- Distinct entity
- Prognosis similar to Gleason pattern 4
- Solid pattern with necrosis: grade as pattern 5
- PIN-like pattern: grade as pattern 3

Differential Diagnosis

- High grade prostatic intraepithelial neoplasia
- Atypical intraductal proliferation
- Intraductal Carcinoma
- Ductal Carcinoma
- Invasive cribriform pattern of Pca
- PIN-like carcinoma
- Intraductal Urothelial Carcinoma



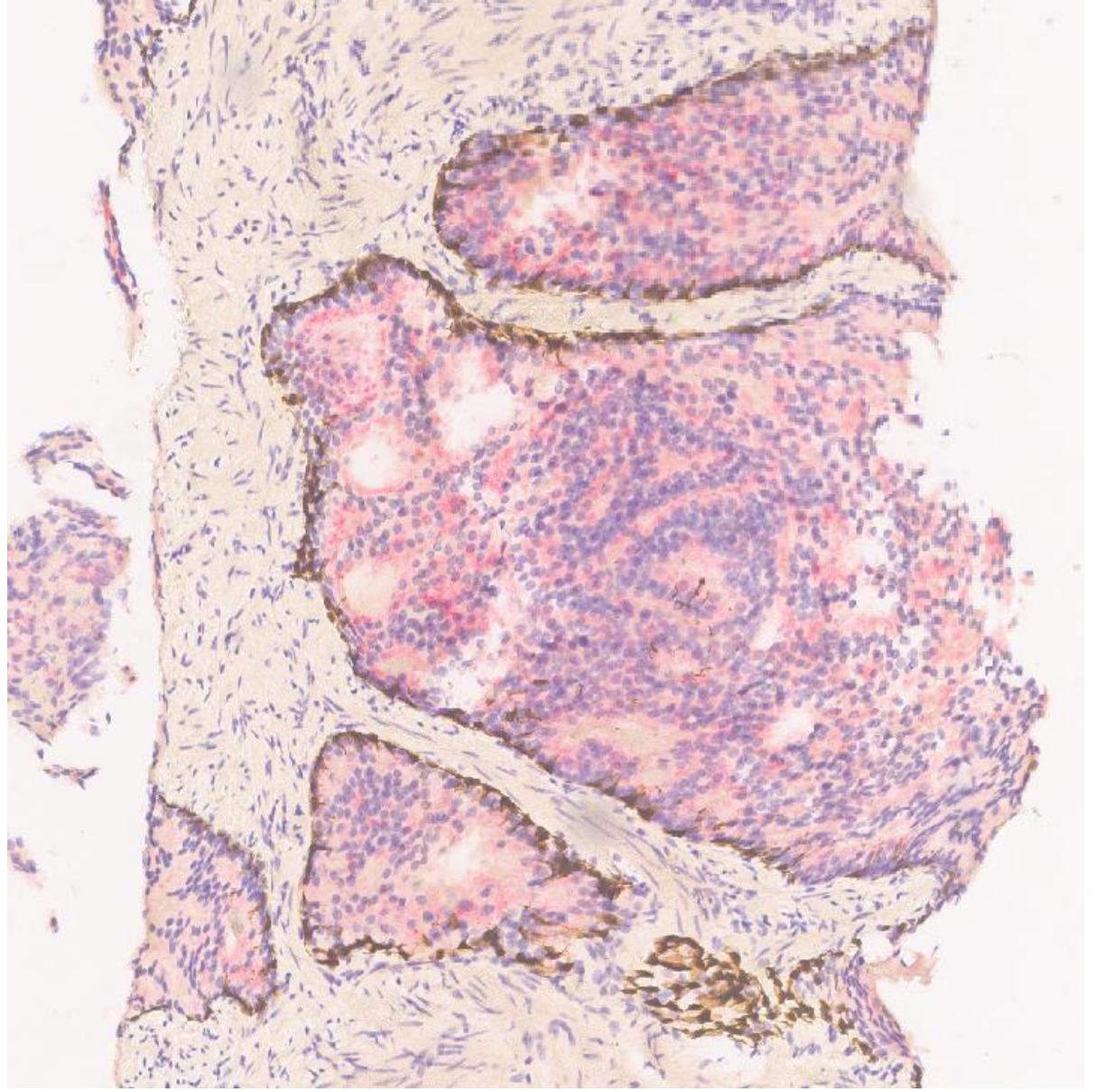
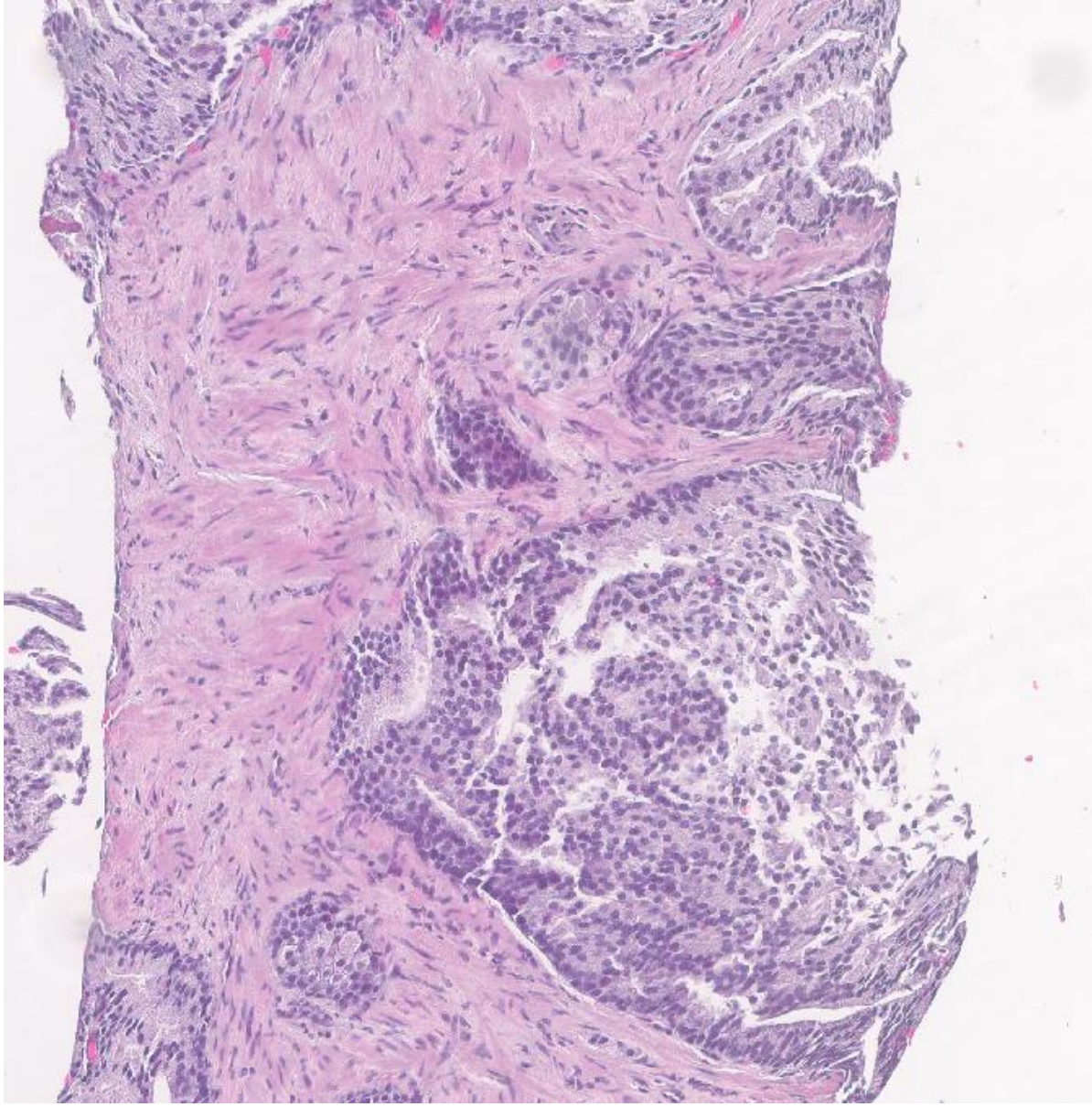
High Grade PIN

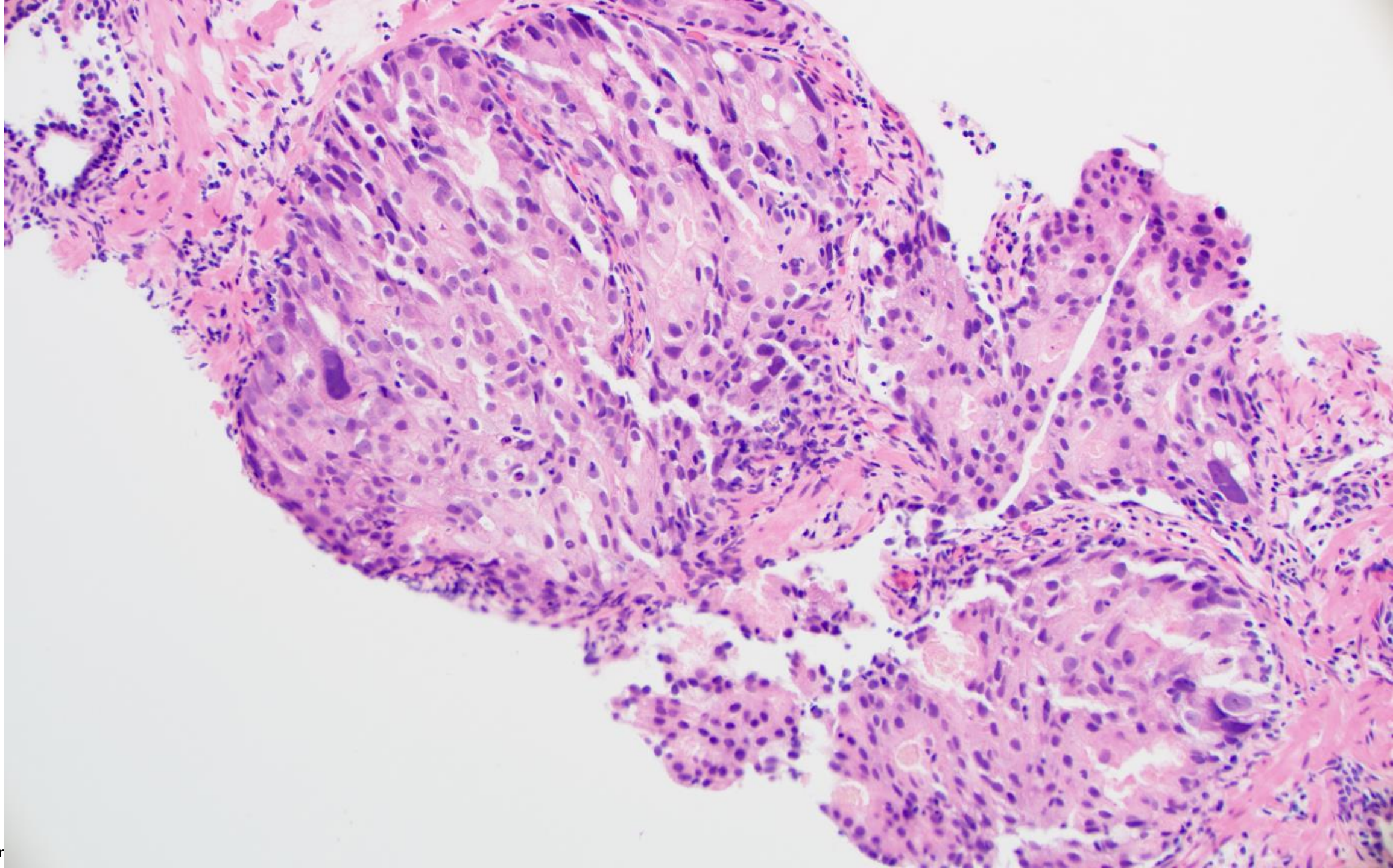
High Grade Prostatic Intraepithelial Neoplasia

- WHO 2022
 - Micropapillary, flat, tufted
 - Cribriform subtype
 - No longer considered HGPIN
 - Classify as IDC/AIP

Atypical Intraductal Proliferation

- Intraductal neoplastic proliferations fall short of either the architectural or cytological atypia required for a diagnosis of IDC-P but have more atypia than that usually seen in HGPIN.
- Suggests the presence of high-grade invasive carcinoma





Intraductal Carcinoma

- **Neoplastic** epithelial proliferation involving preexisting, generally expanded, duct-acinar structures and characterized by architectural and cytological atypia beyond what is acceptable for HGPIN
 - Colonization of existing ducts by invasive ca (retrograde spread)- majority
 - Precursor lesion (rare)
- Associated with high-grade prostate ca on RP
- With acinar ca: adverse prognostic factor
- Association with germline *BRCA2* (and other HRD mutations): controversial
- Do not grade pure IDC
- Pure IDC on biopsy: definitive treatment recommended

Intraductal Carcinoma

- Patterns
 - Solid
 - Dense cribriform
 - Loose cribriform/micropapillary with marked nuclear atypia or comedonecrosis
- Nuclear size (6x) not required

Essential criteria

- Expansile epithelial proliferation in the preexisting duct-acinar system
- Lumen-spanning solid, cribriform, and/or cribriform patterns
- Loose cribriform or micropapillary patterns with enlarged nuclei
- Residual basal cells

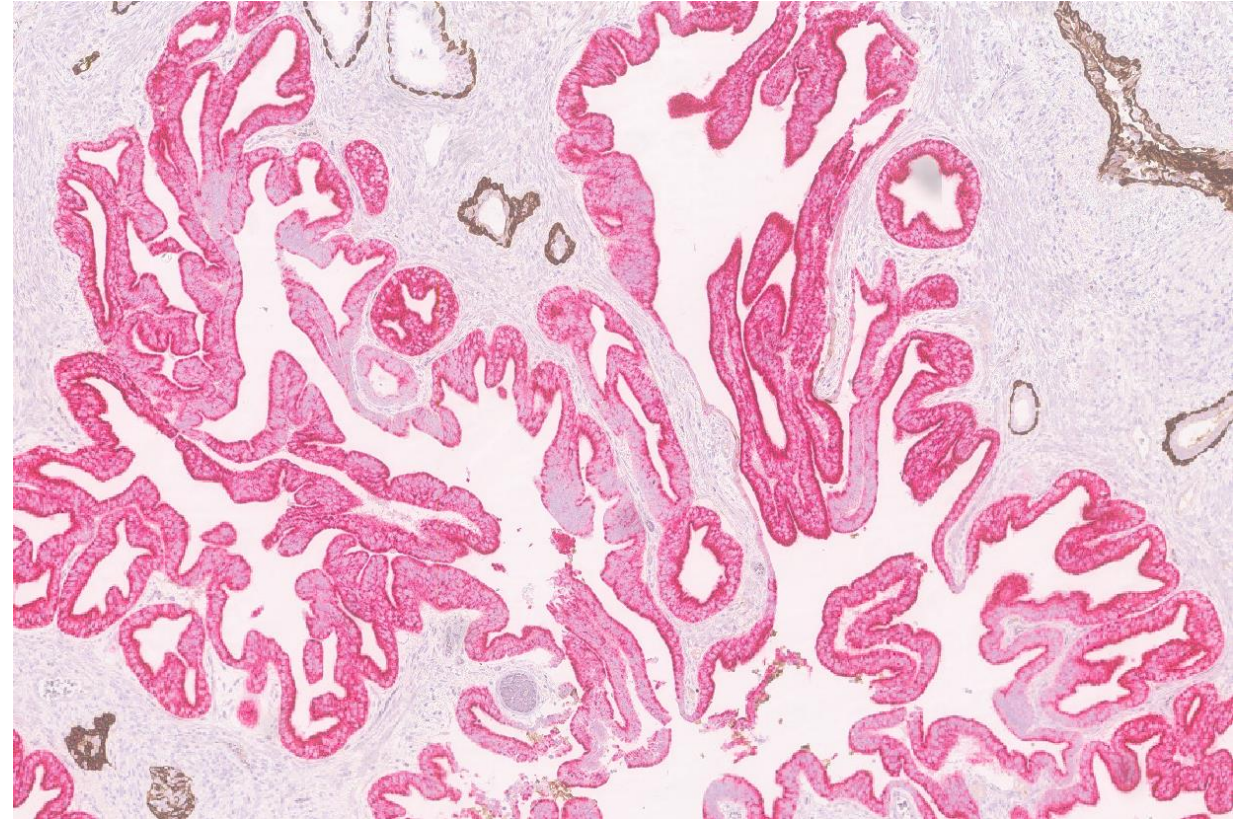
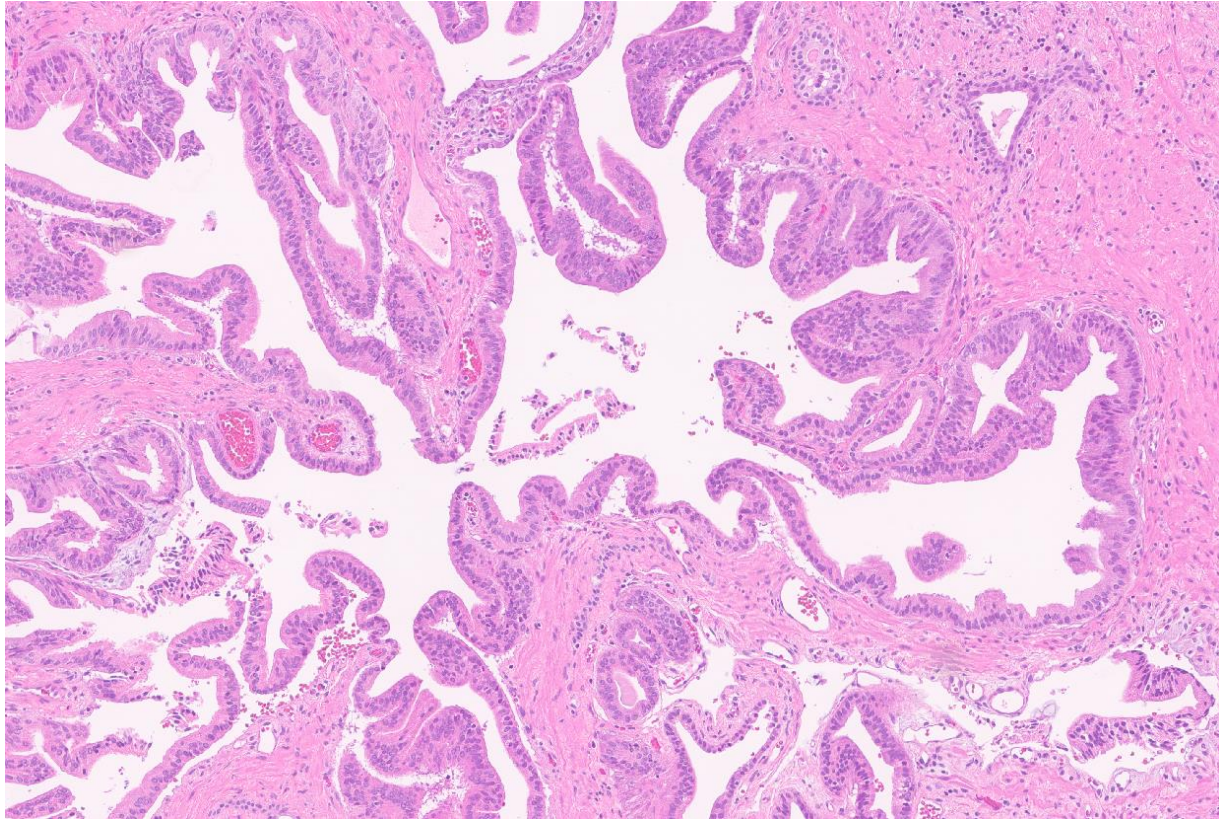
Desirable criterion

- Immunohistochemistry demonstrating at least partial basal cell retention
-

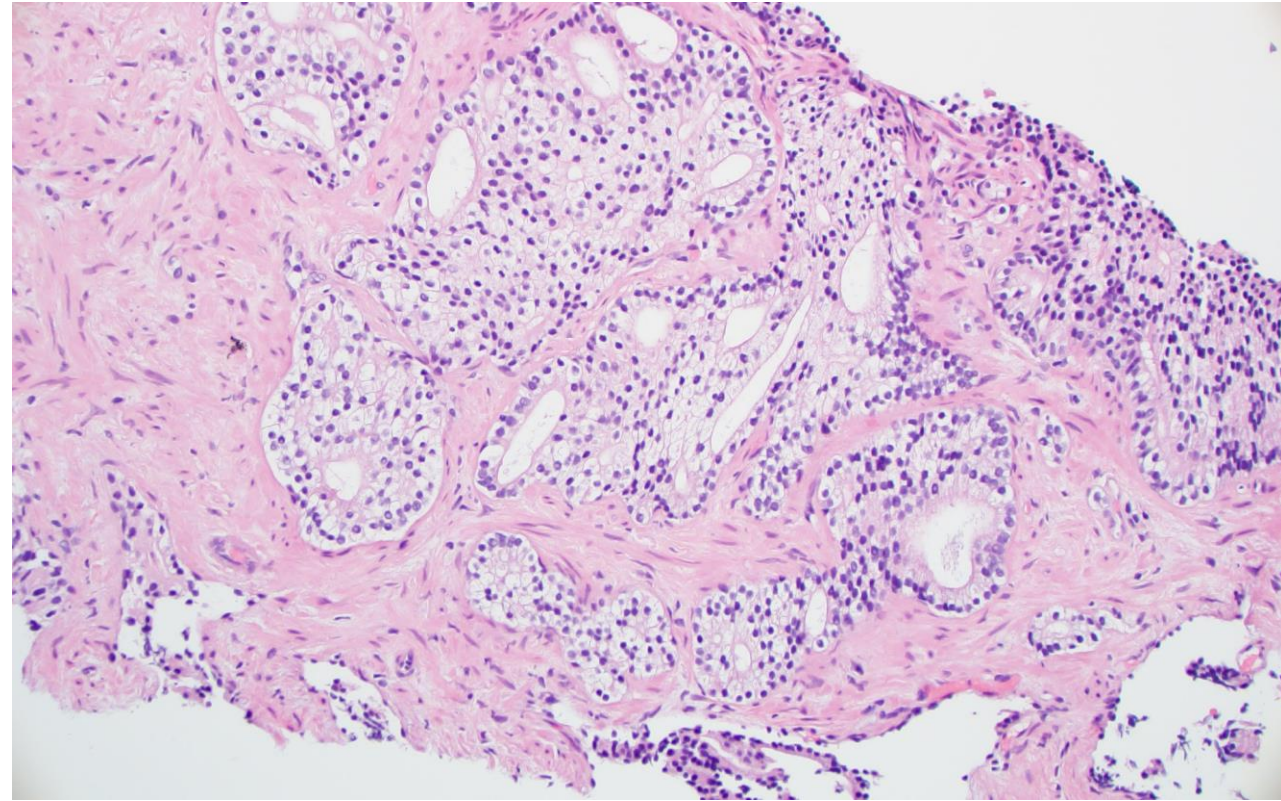
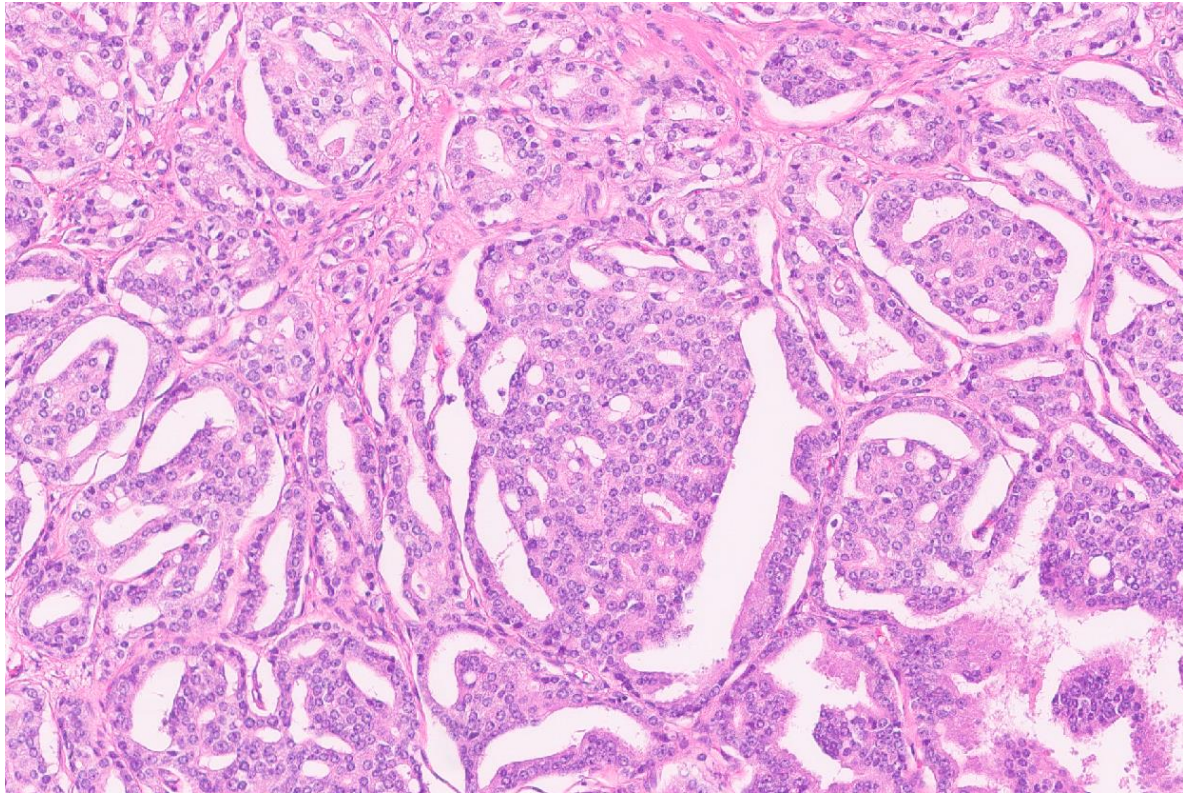
Grading of Intraductal Carcinoma

- To do (include) or not to do?

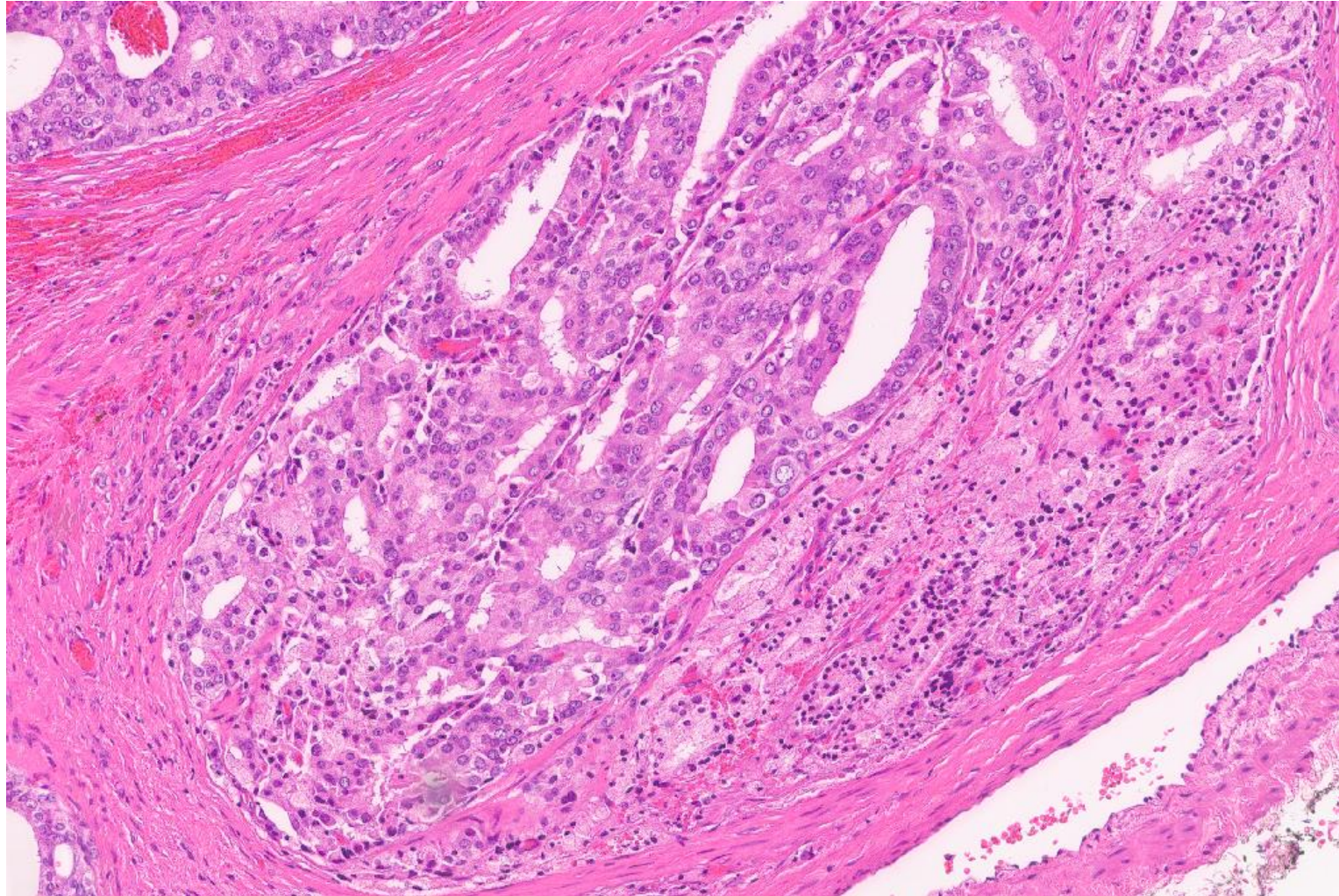
ISUP	GUPS
Include	Exclude
IDC: prognostic factor	Subset of IDC: precursor lesion
Score captures prognostic value	Rare change in GS
IHC only if impact on GG	



PIN Like Ca: Subtype of Acinar



Invasive Cribriform:
Gleason Pattern 4



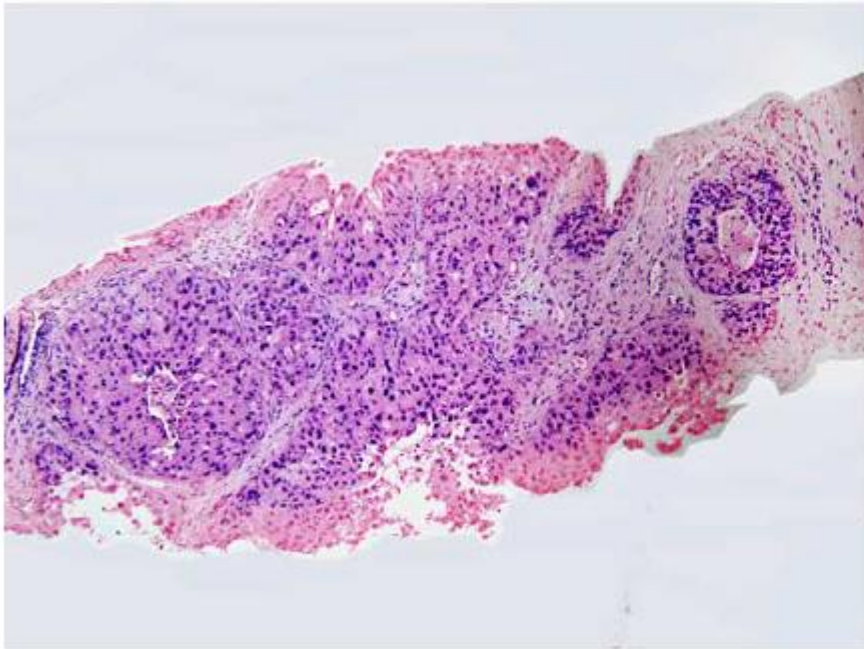
Cribriform mimic: back-to-back glands

Invasive Cribriform Pattern

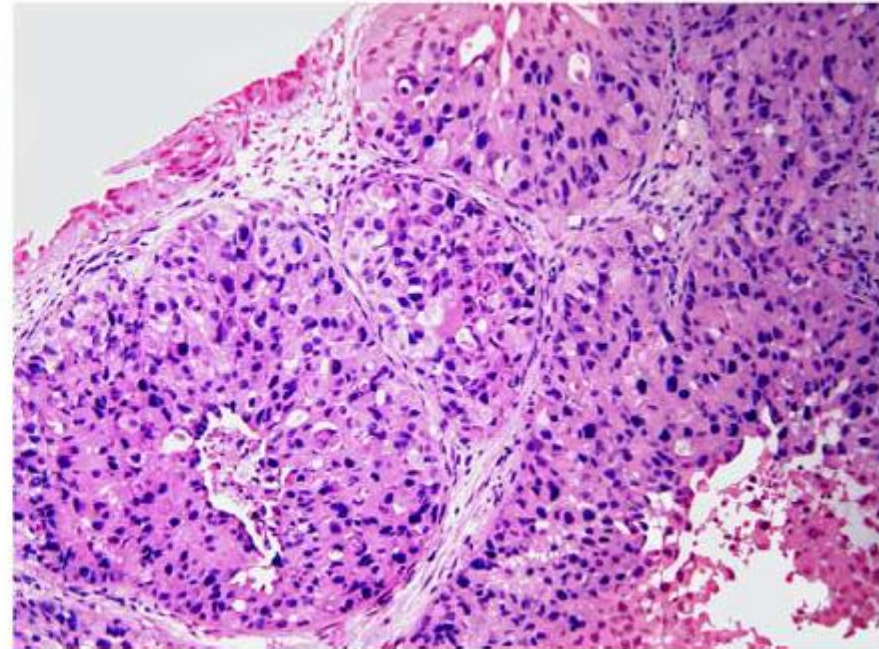
- A confluent sheet of contiguous malignant epithelial cells with multiple glandular lumina that are easily visible at low power (objective magnification x10)
- No intervening stroma or mucin separating individual or fused glandular structures.
- Invasive cribriform ca
 - Predictive of biochemical recurrence and Pca specific mortality

Intraductal Urothelial Carcinoma

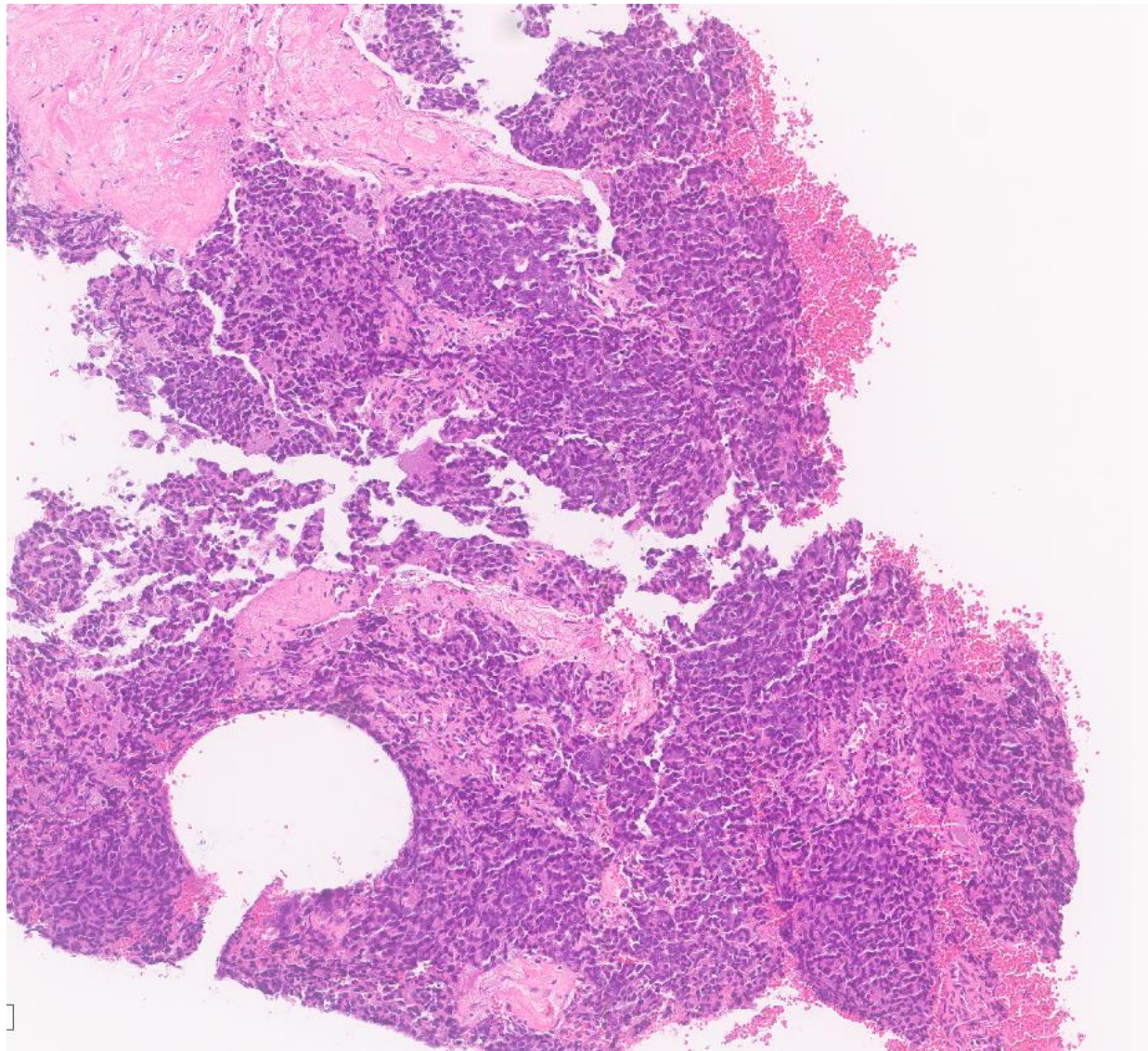
A



B



Case 7



Small Cell Carcinoma

Small Cell Carcinoma

- 40-50%: History of prostate ca
- Pure SCC: 50-60% at diagnosis
- Visceral metastasis, paraneoplastic syndrome
- Morphological diagnosis
- NE markers: 90%
- Prostate markers: 17-25%
- TTF-1: 50%

Am J Surg Pathol. 2014; 38(6): 756–767
Arch Pathol Lab Med. 2020;144:320–325

Small Cell Ca

- D/D: Small cell carcinoma of other sites.
- *ERG* by FISH or other molecular testing.
- IHC not reliable in this scenario.
- Prostate small cell carcinoma.
 - AR, PSA, membranous CD44 +

Am J Surg Pathol. 2014; 38(6): 756–767
Arch Pathol Lab Med. 2020;144:320–325

Neuroendocrine Cells in Prostate

- Scattered between epithelial cells, resting on the basal cells
- Variety of peptide hormones: endocrine, paracrine and autocrine effect
- Not readily recognizable on H&E
- Lack AR
- NE differentiation increases after ADT and in CRPC
- Lineage plasticity

Am J Surg Pathol. 2014; 38(6): 756–767

Transdifferentiation of Prostate Ca

- Epigenetic factors
- AR indifferent state
- Overexpression of epigenetic regulators

Am J Surg Pathol. 2014; 38(6): 756–767

Neuroendocrine Tumors of Prostate

- De novo (rare) <1%
 - After Androgen deprivation therapy (ADT) ~15%
-
- Prostate Ca: Androgen dependent
 - Androgen blockade
 - Therapeutic resistance
 - Continued AR signaling through alternate mechanisms
- Treatment related NE Pca
 - Low/absent AR expression
 - Small cell/NE morphology
 - Visceral/lytic bone metastases

Am J Surg Pathol. 2014; 38(6): 756–767

Treatment Related NE Prostate Ca

- Tumors with complete or partial NE differentiation after ADT
- 10-15% of CRPC, usually within 24 months of ADT, median survival ~7 months
- Small cell and large cell NE Ca
 - Primary or secondary
 - Mixed with conventional acinar Ca
 - Small cell component- not to be graded
 - Small cell: p53 and TTF-1 positive in 50%, few AR+, PSA, PSAP are negative

Am J Surg Pathol. 2014; 38(6): 756–767

WHO Classification

2004

- Focal NE differentiation in conventional Pca
- Carcinoid Tumor: Rare
- Small cell NE Ca

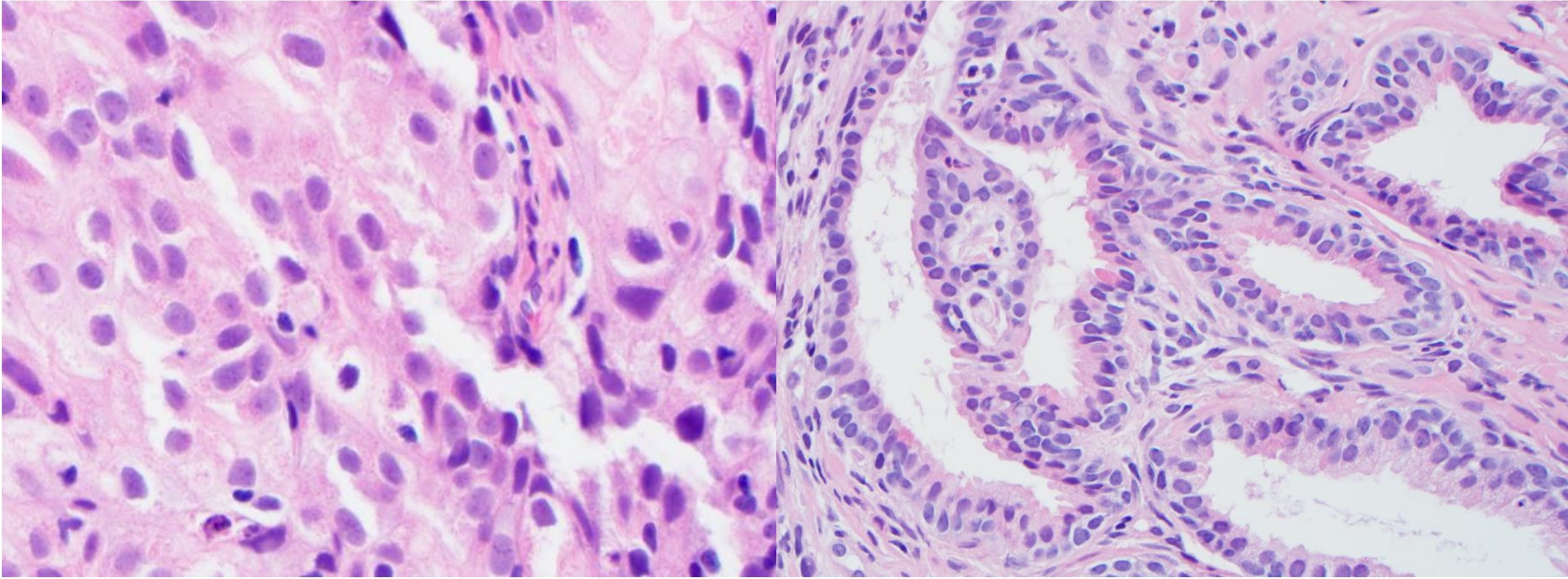
2014

- Usual Adenocarcinoma with NE differentiation
- AdenoCarcinoma with Paneth cell-like features
- Carcinoid Tumor
- Small cell Carcinoma
- Large Cell Carcinoma

Am J Surg Pathol. 2014; 38(6): 756–767

Usual Adenocarcinoma with NE Differentiation

- Acinar or ductal Prostate Ca with NE differentiation by IHC: IHC evaluation not recommended



Adenocarcinoma with Paneth Cell Like NE Differentiation

Adenocarcinoma with Paneth Cell Like NE Differentiation

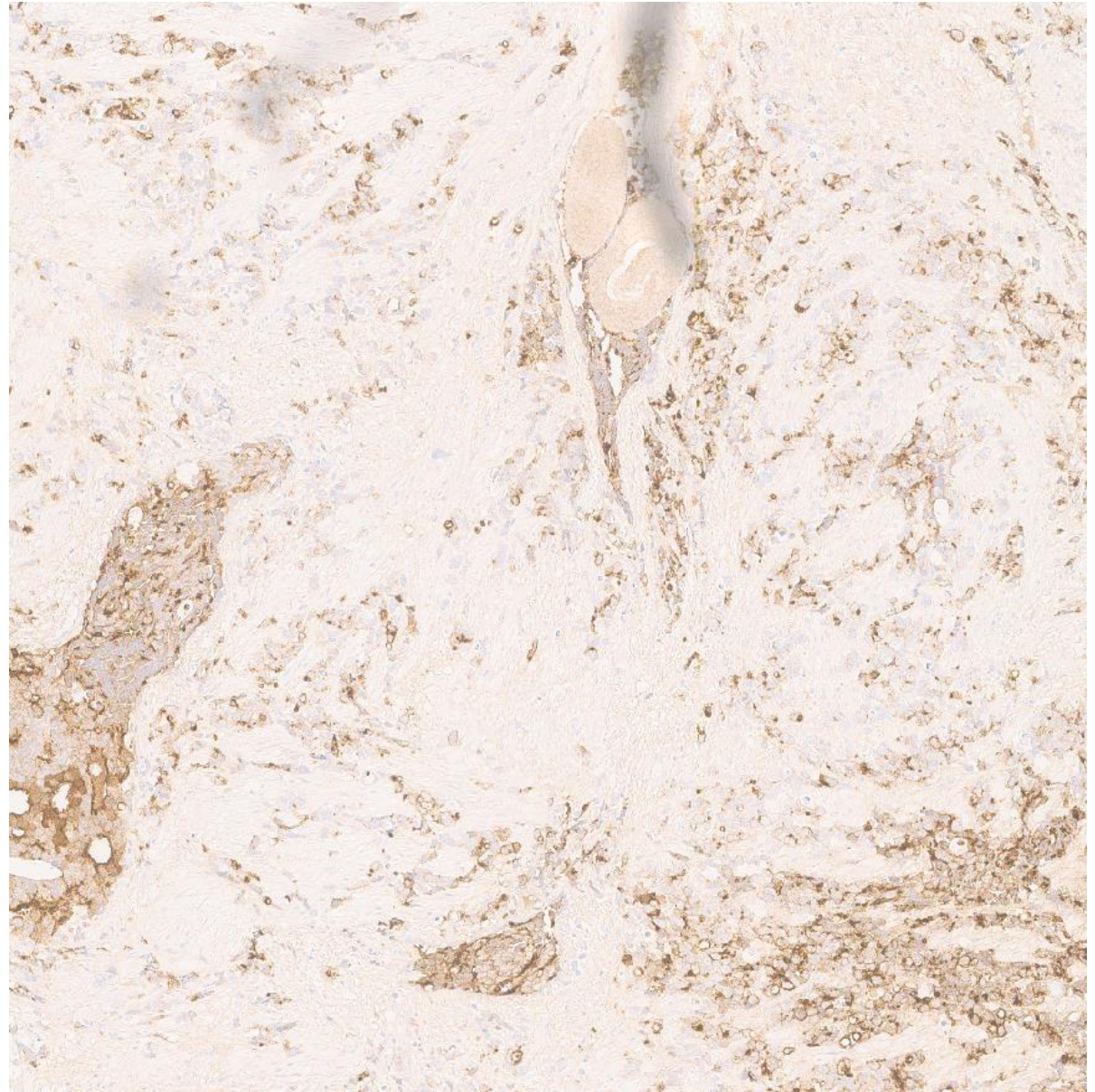
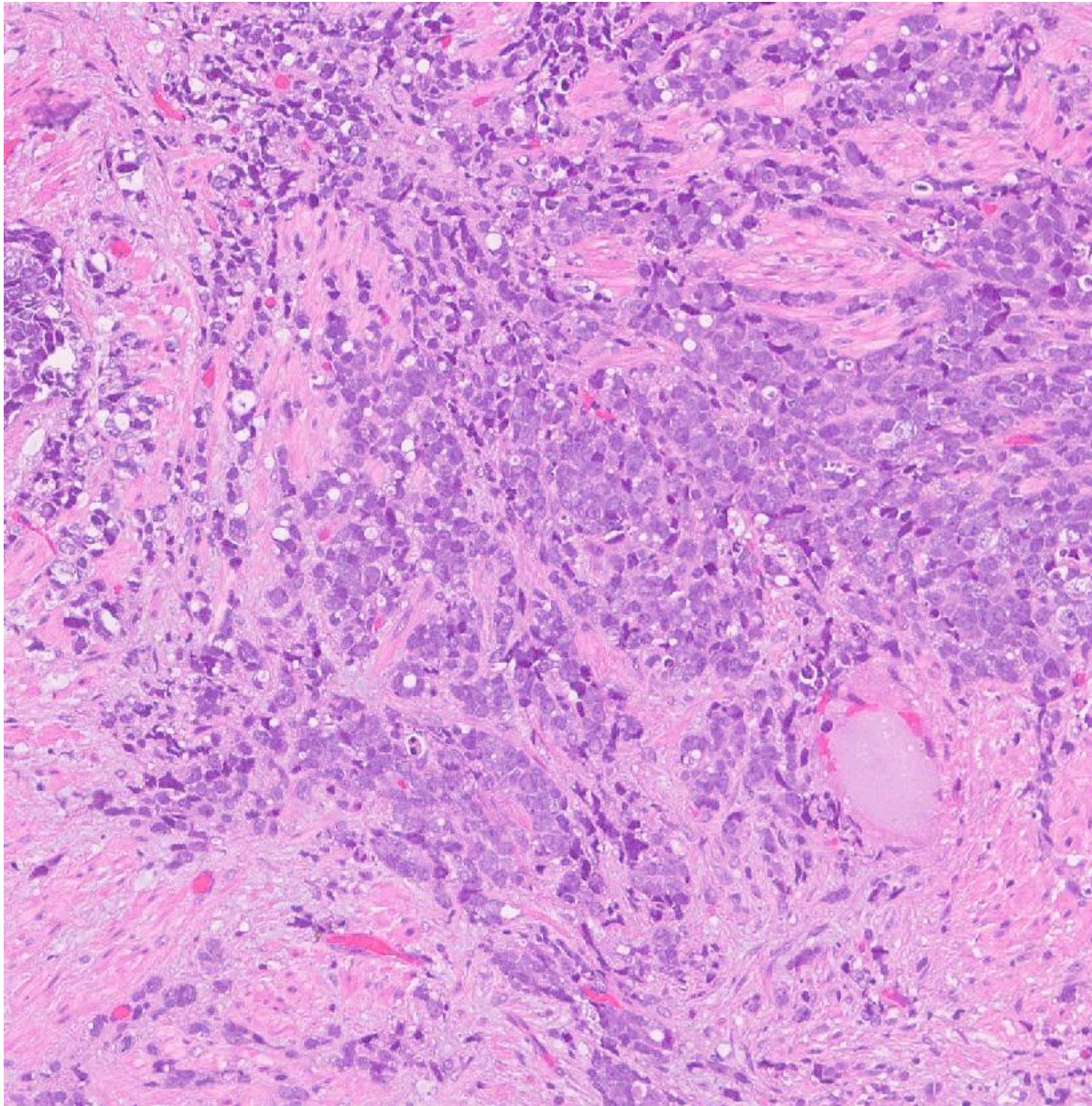
- Pca with prominent NE granules (Paneth cell-like)
- Resemble intestinal NE cell with prominent granules
- Not true Paneth cells
- NE marker +/- Lysozyme –
- Good prognosis
- Outcomes related to conventional prognostic features
- Do not upgrade single cell pattern of Paneth cells

Am. J. Surg. Pathol. 2006; 30; 980–985, Hum. Pathol. 2014;45; 2388–2393, Hum. Pathol. 2020; 102; 7–12.

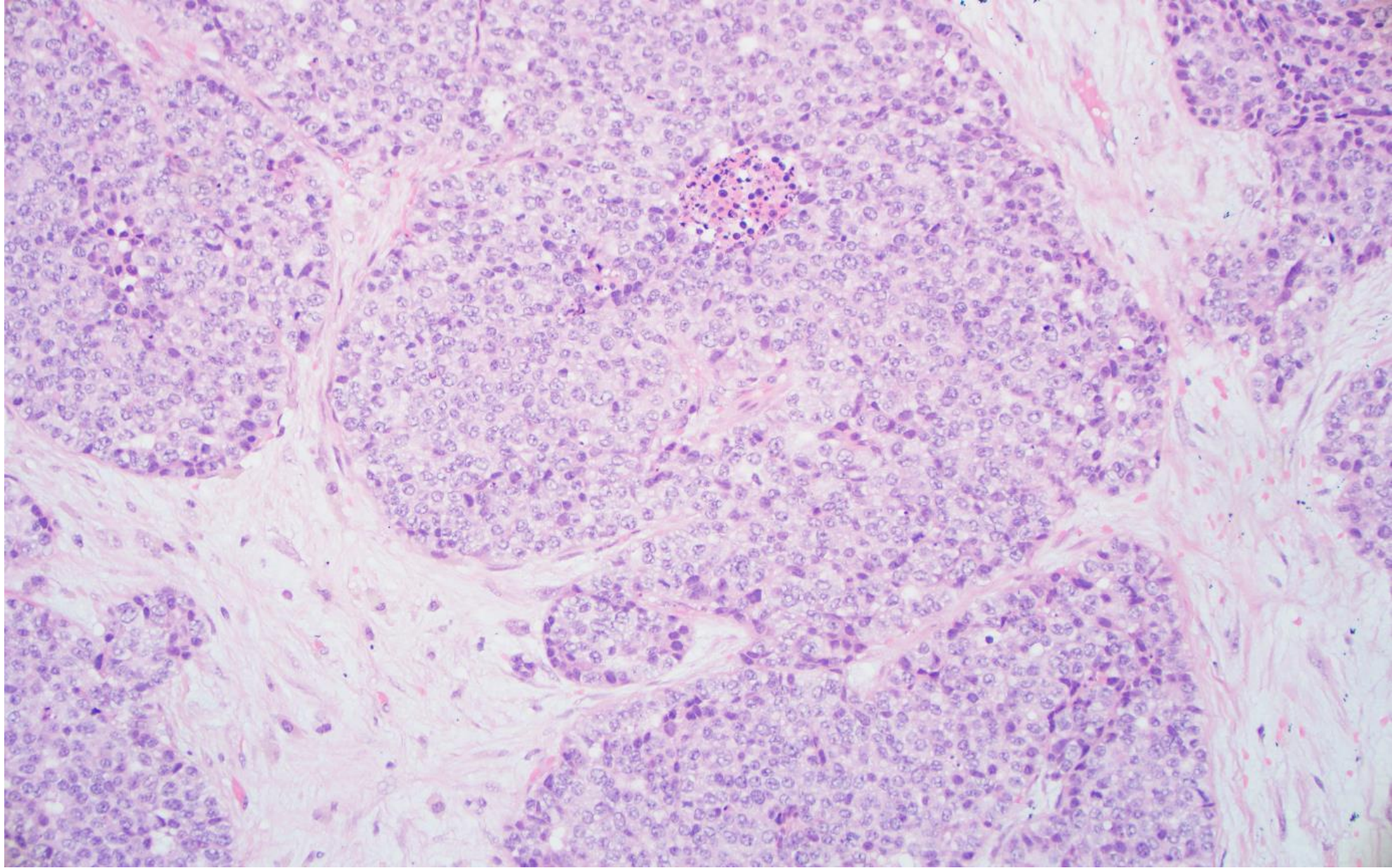
Mixed NE and Acinar Ca

- Biphasic: distinct conventional and NE components
- Adeno Ca: ductal/other variants
- Metastatic CRPC
- Cases with overlapping morphology and IHC profile

Am J Surg Pathol. 2014; 38(6): 756–767



Prostate Carcinoma: neuroendocrine carcinoma



Large Cell Carcinoma

Large Cell NE Ca

- Neuroendocrine differentiation
- Large nests with peripheral palisading and geographic necrosis
- Rare
- NE markers +. PSA/PSAP: negative/focal

Am J Surg Pathol. 2014; 38(6): 756–767

Carcinoid Tumor

- In prostate parenchyma (not urethra/bladder)
- Not closely associated with adenocarcinoma
- Positive for NE markers and negative for PSA
- Locally advanced disease
- Favorable prognosis
- Grade like GI carcinoids
- Investigate for MEN syndrome

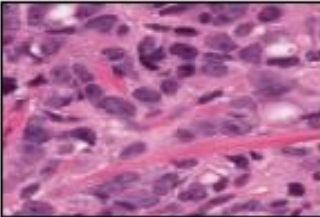
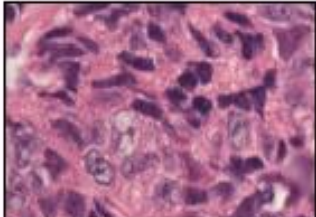
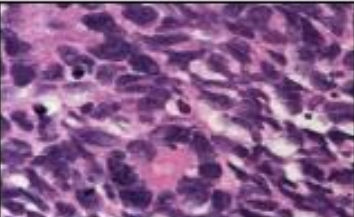
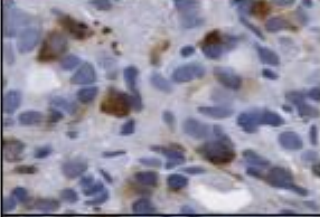
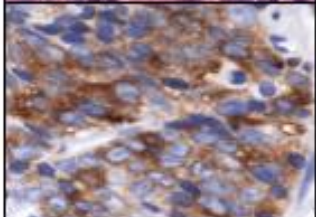
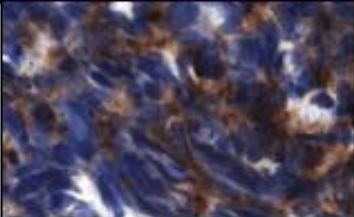
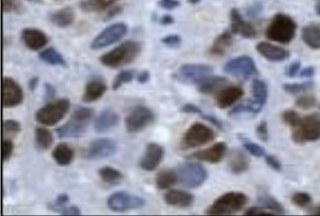
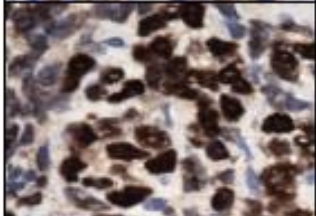

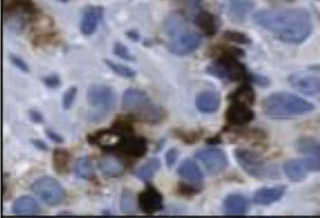
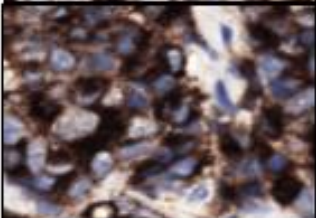

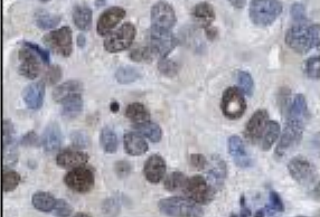
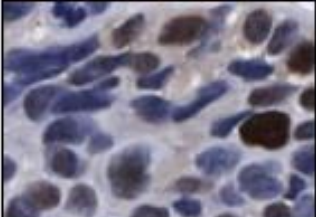

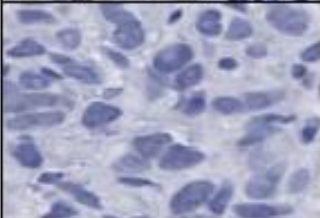

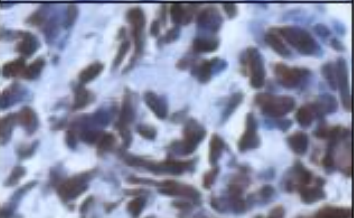
Am J Surg Pathol. 2014; 38(6): 756–767

Neuroendocrine Differentiation Primary Vs Metastatic (N=79)

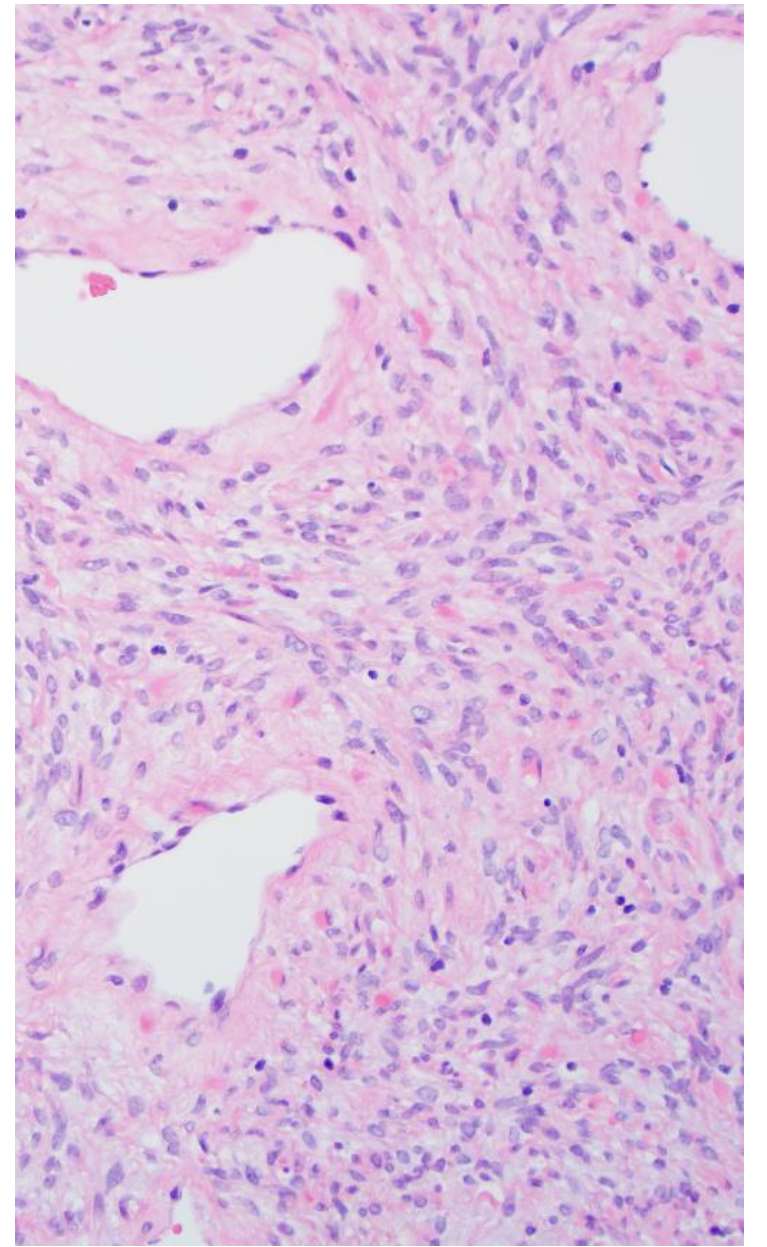
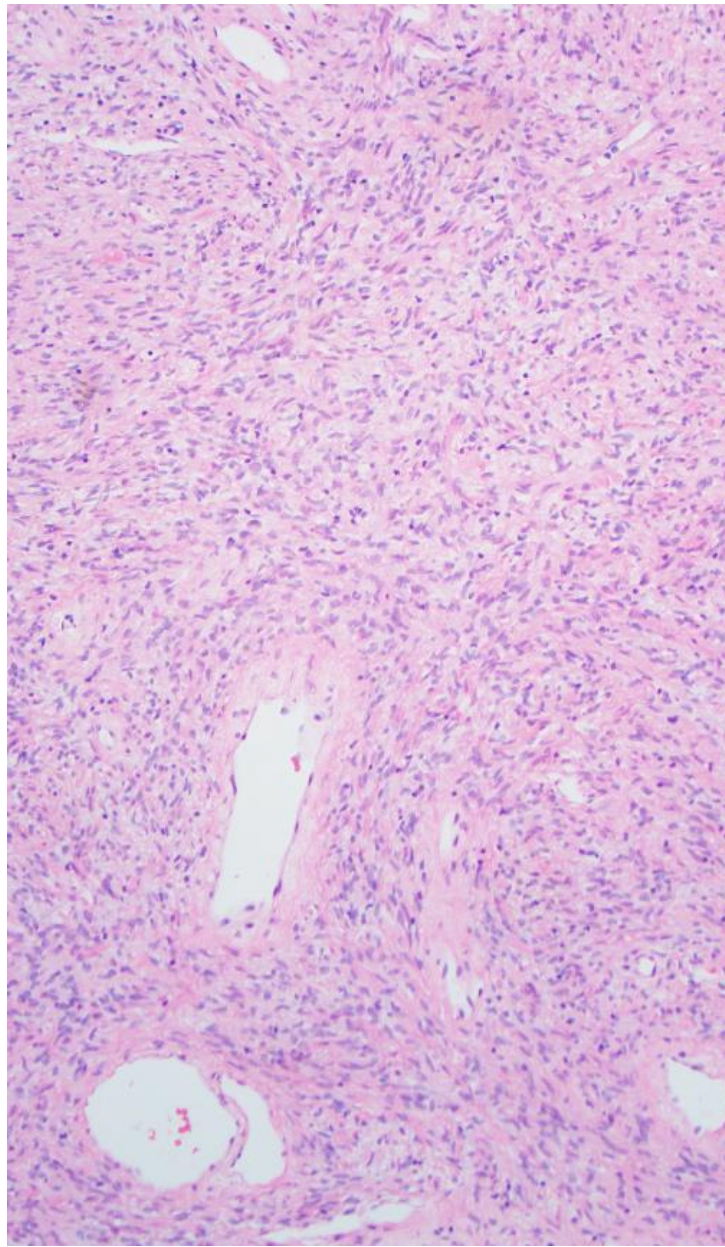
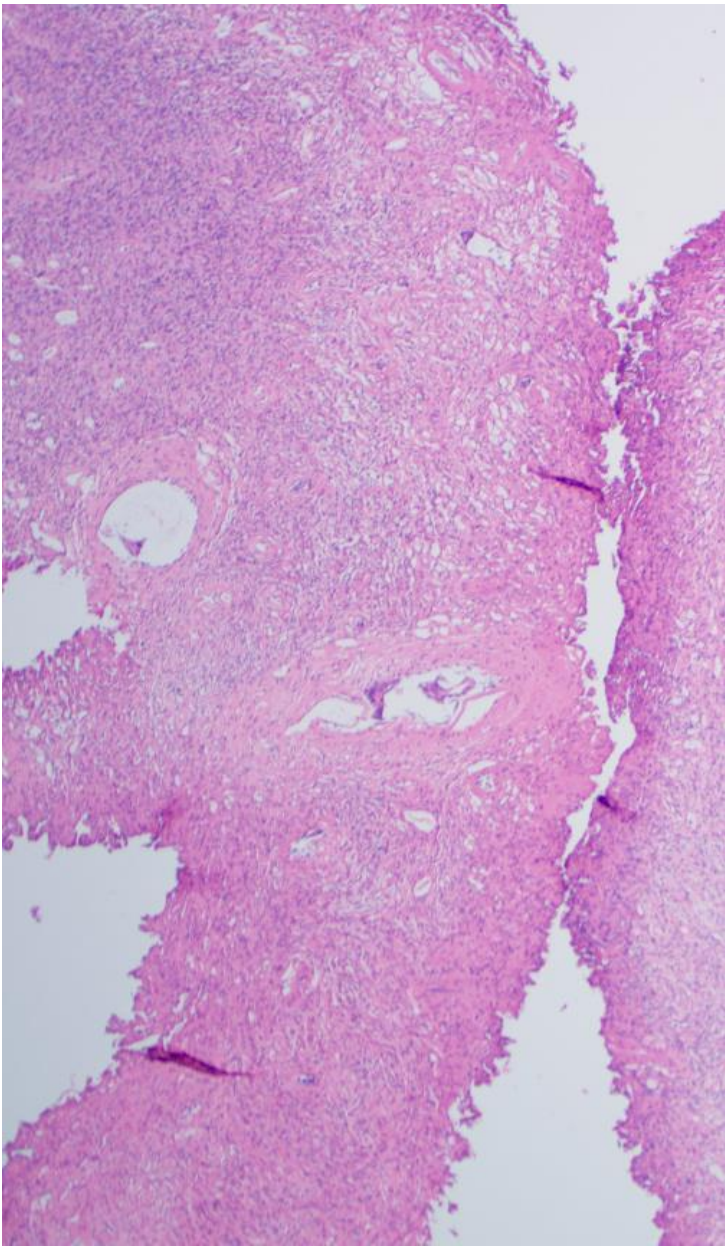
Category	Primary	Metastatic
Pure small-cell carcinoma / HGNEC	3/23	20/23
Combined adenocarcinoma + small-cell carcinoma / HGNEC	9/10	1/10
PCa with diffuse neuroendocrine differentiation	0/15	15/15
PCa with patchy neuroendocrine differentiation	5/11	6/11
PCa with isolated neuroendocrine marker positive cells	4/9	5/9
PCa with prominent neuroendocrine granules ('Paneth cell-like')	11/11	0/11
Total	32	47

HGNEC, high-grade neuroendocrine carcinoma; PCa, prostate cancer.

Histopathology 2022, 81, 246–254.

	Acinar with NED	Overlap PCa	Small Cell Ca
H&E			
Synapto physin			
AR			
PSMA			
Cyclin D1			
TTF-1			

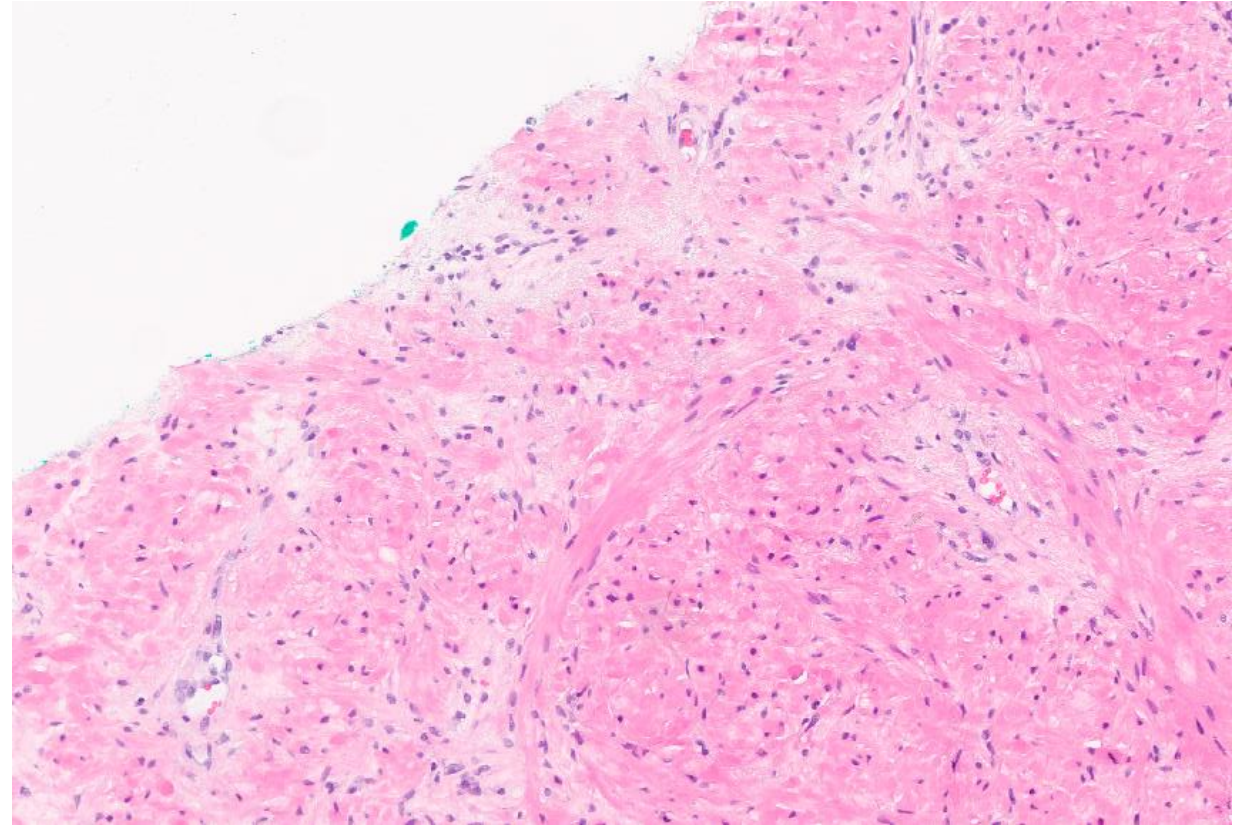
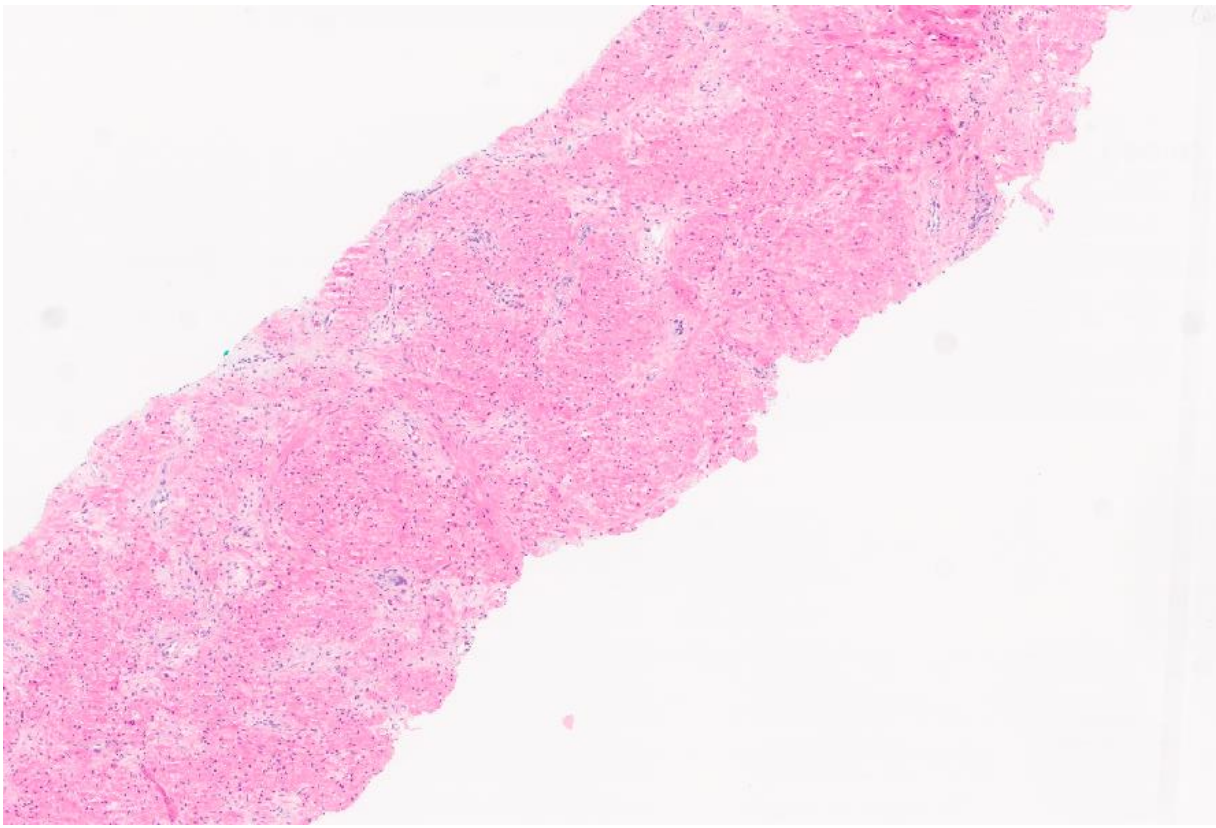
Case 8



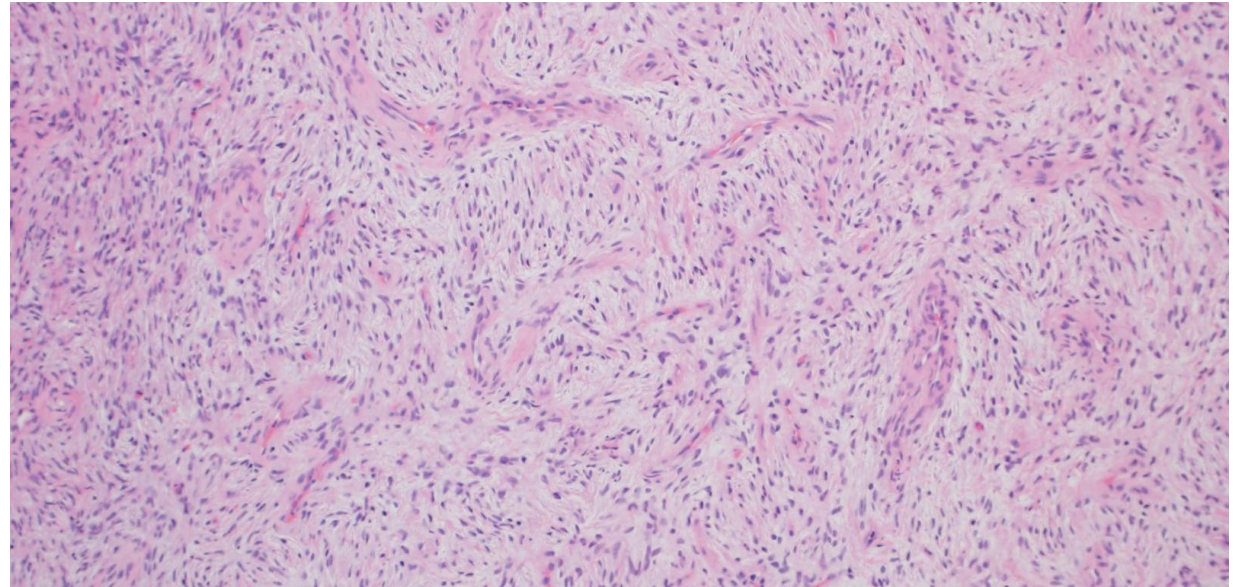
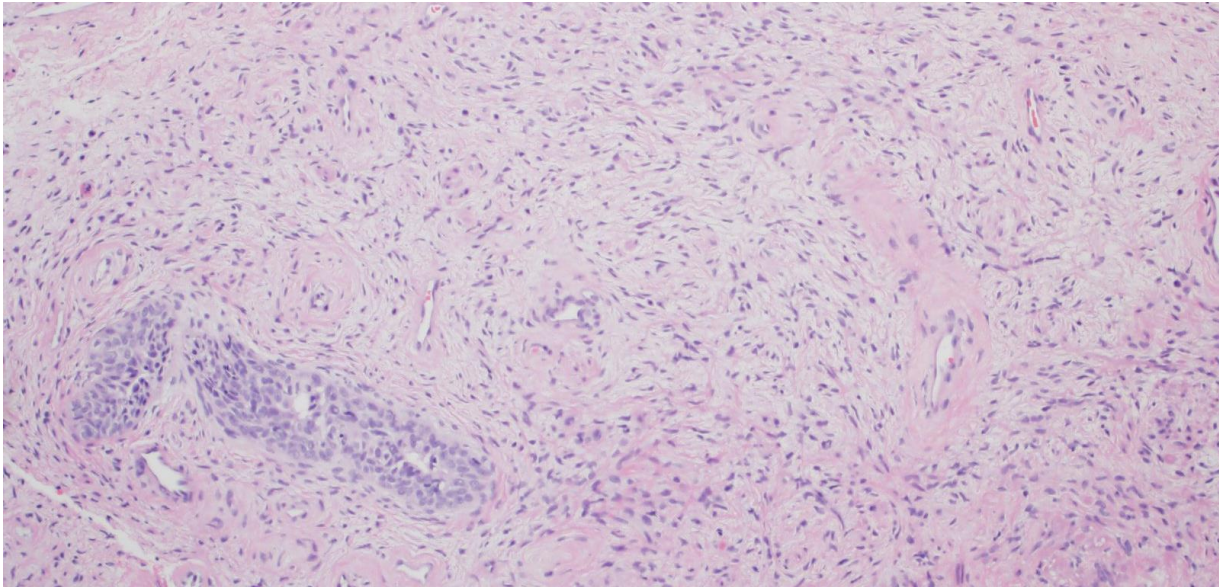
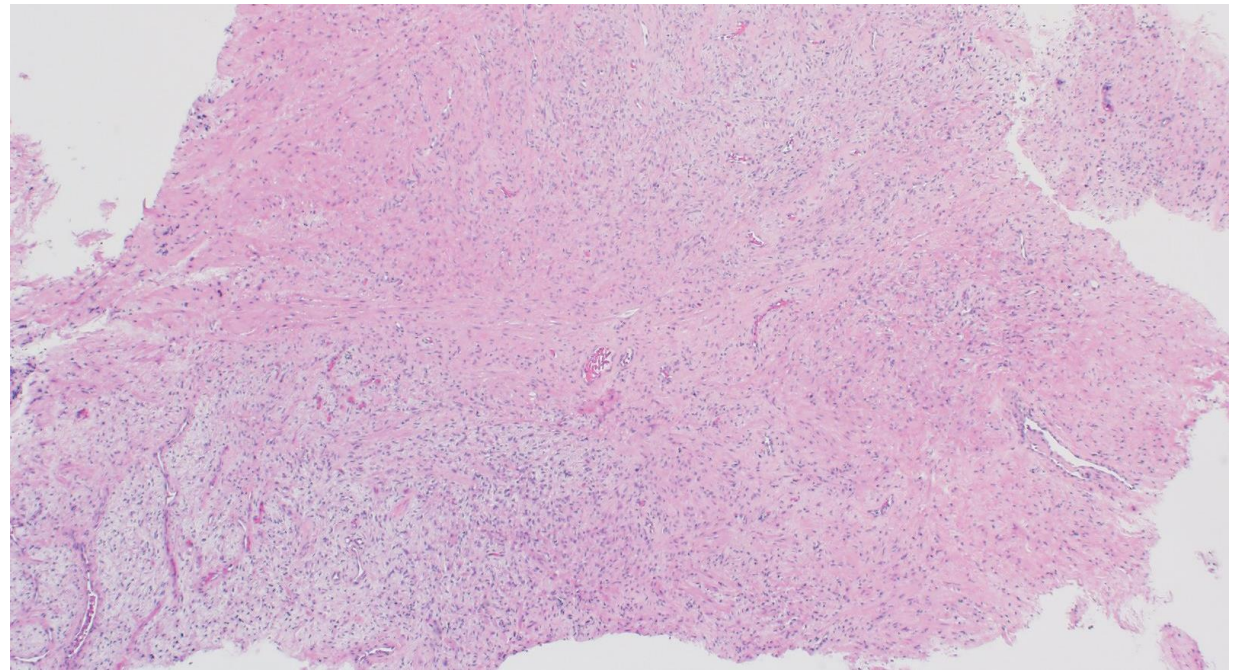
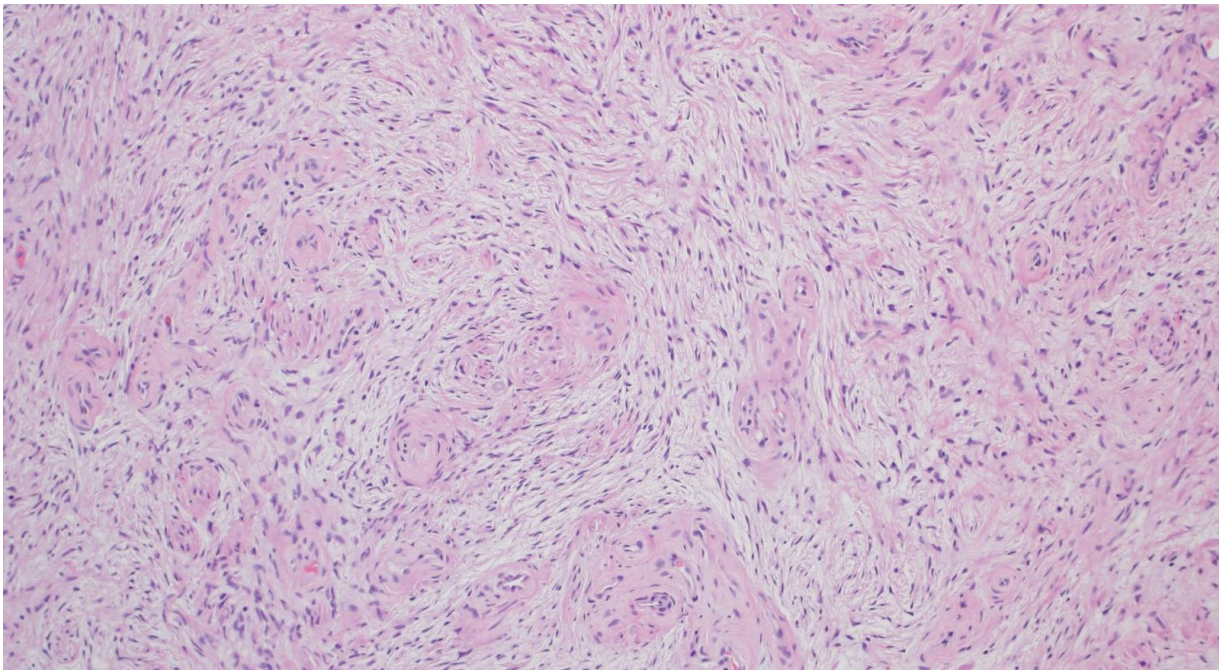
Benign Stromal Hyperplasia

Prostate Stromal Lesions: Differential Diagnosis

- Benign stromal hyperplasia
- Prostate stromal tumor of uncertain malignant potential (STUMP)
- Stromal sarcoma
- Other mesenchymal lesions
 - Gastrointestinal stromal tumor
 - Solitary fibrous tumor
 - Inflammatory myofibroblastic tumors
 - Smooth muscle tumors
 - Sarcomatoid carcinoma



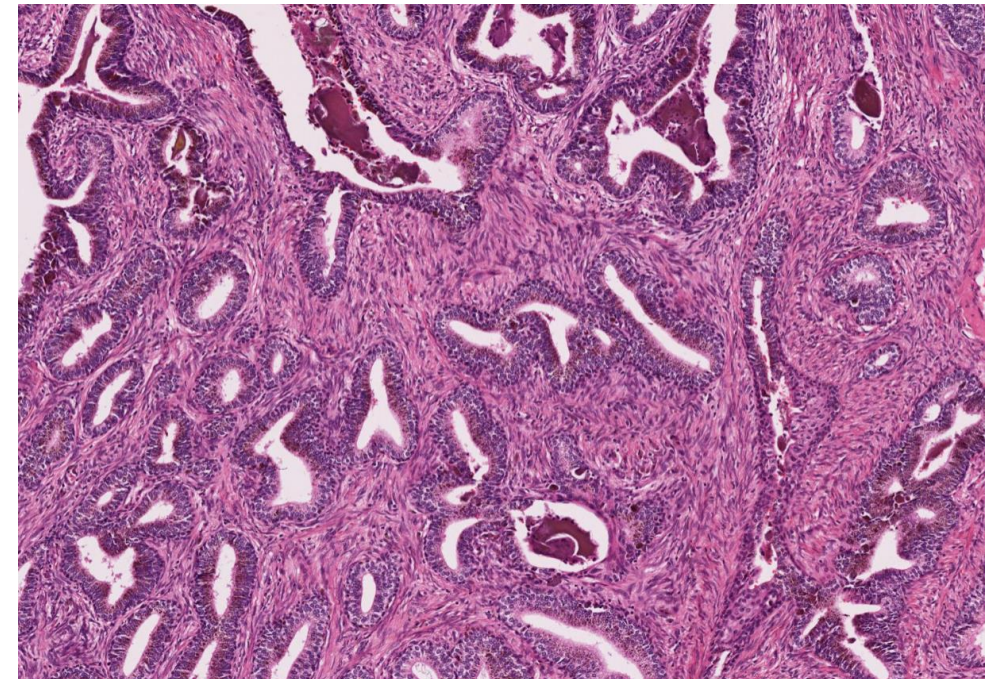
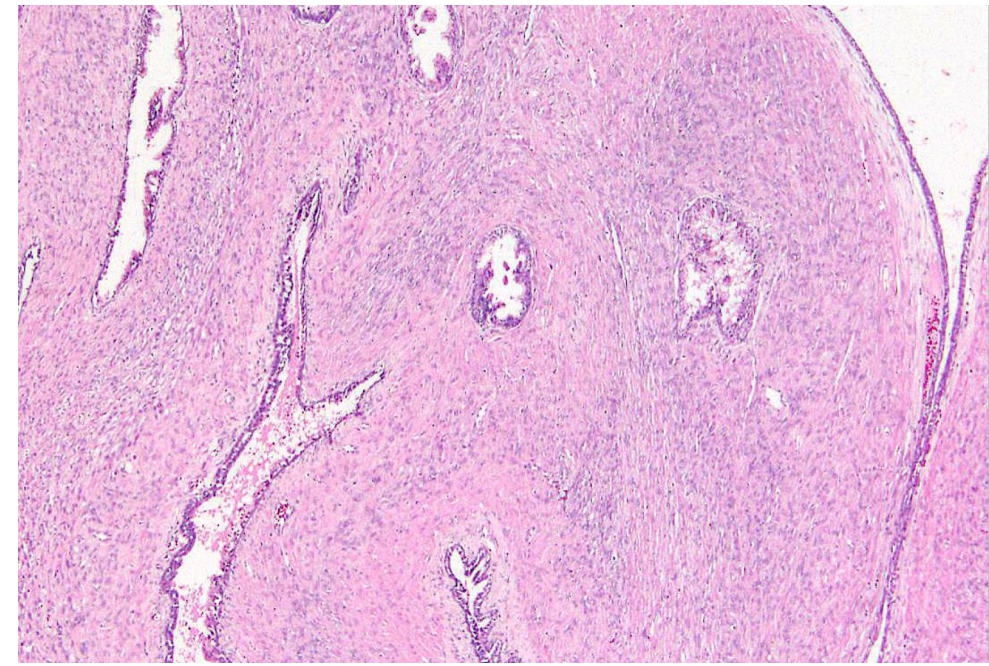
Benign Prostatic Stromal Hyperplasia



Benign Prostatic Stromal Hyperplasia

STUMP

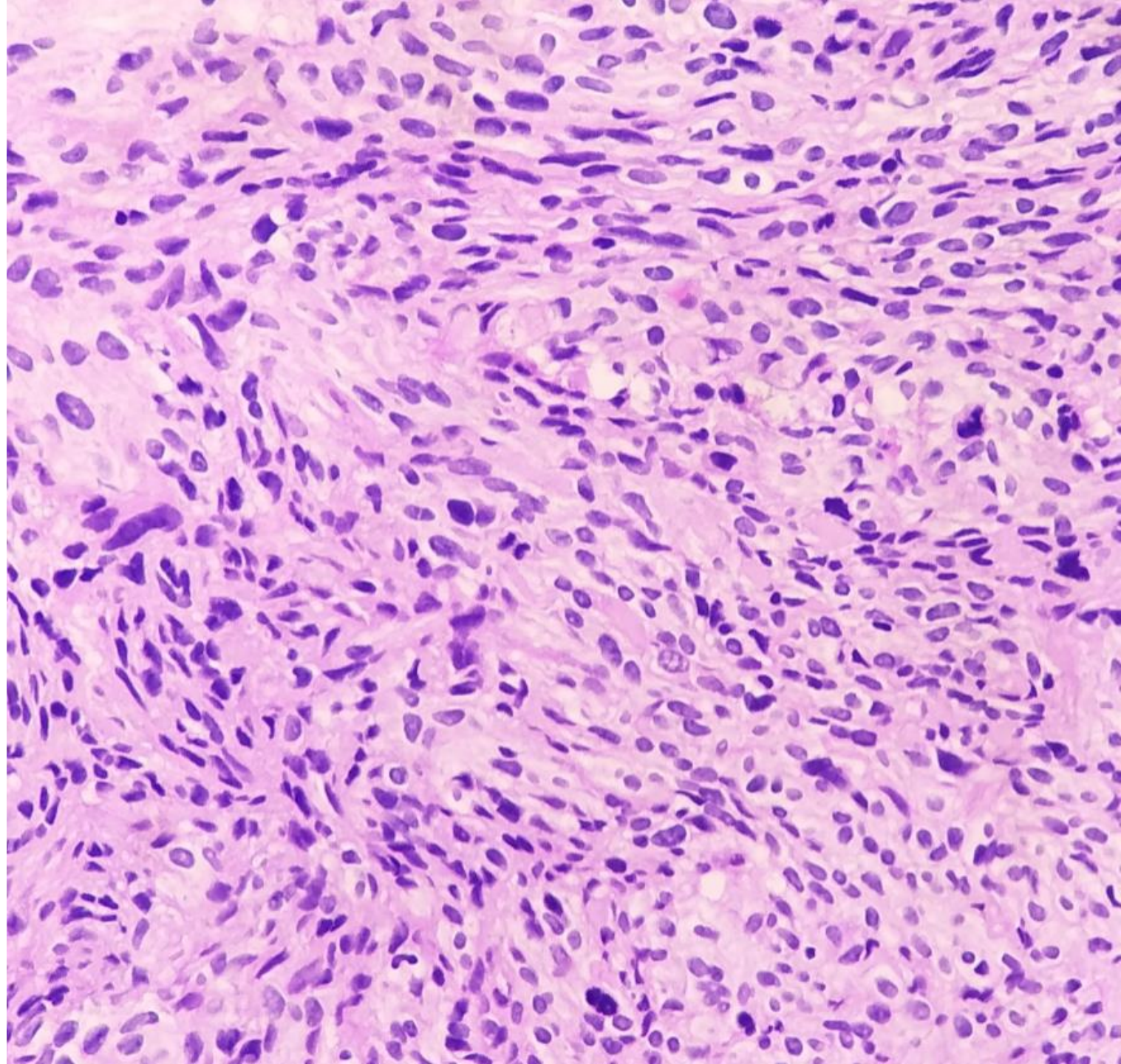
- Rare
- Median age: 57.5 y (25-68)
- Patterns
 - Hypercellular cells with scattered atypical cells admixed with benign glands
 - Hypercellular with bland spindle cells admixed with benign glands
 - Phyllodes pattern
 - Myxoid pattern
 - Epithelioid pattern
- Absence of nodularity and thick-walled vessels

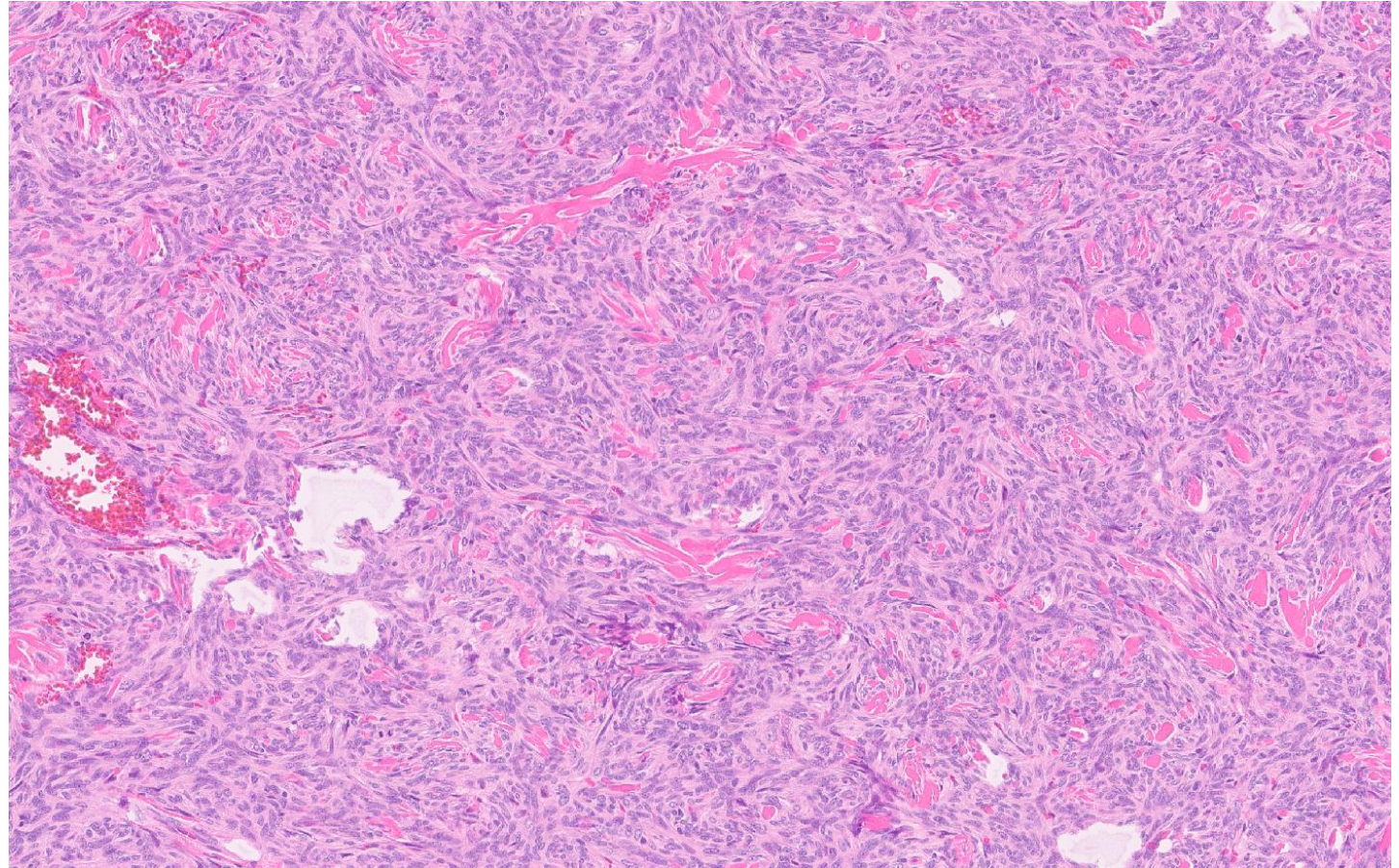
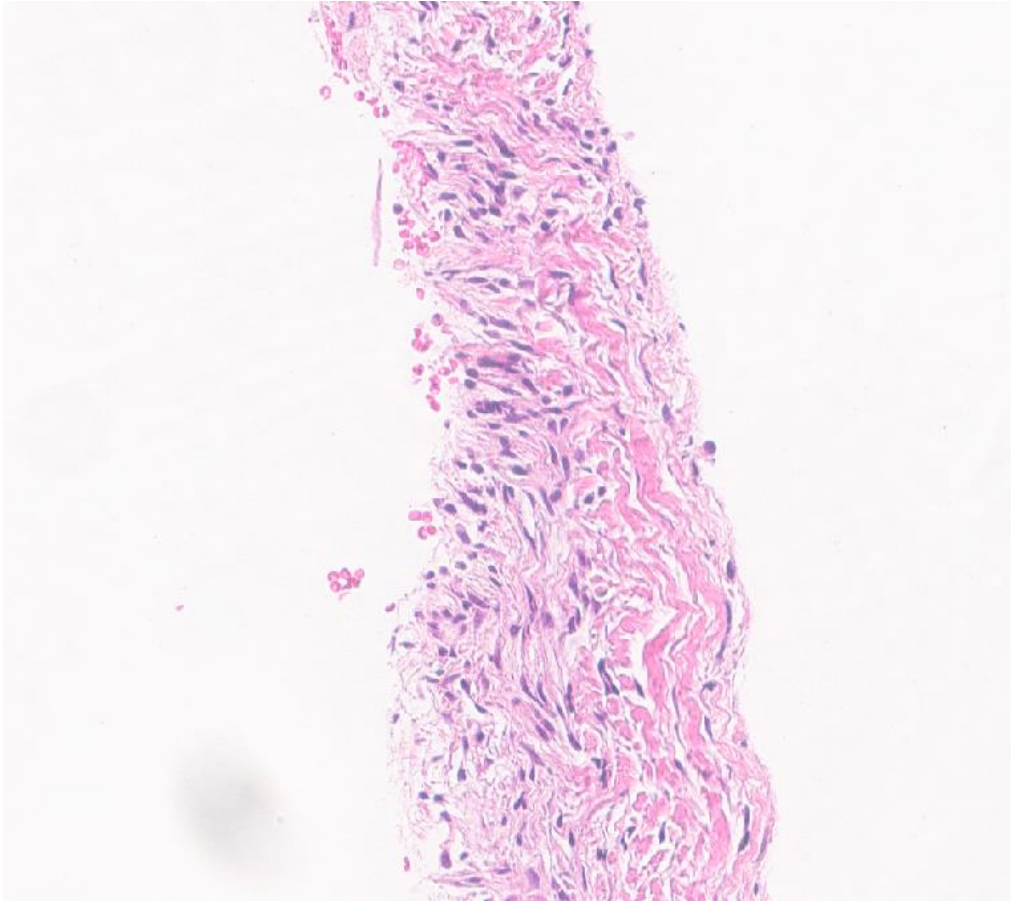


Stromal Sarcoma

- Marked hypercellularity
- Nuclear pleomorphism
- Necrosis
- Increased mitosis, atypical

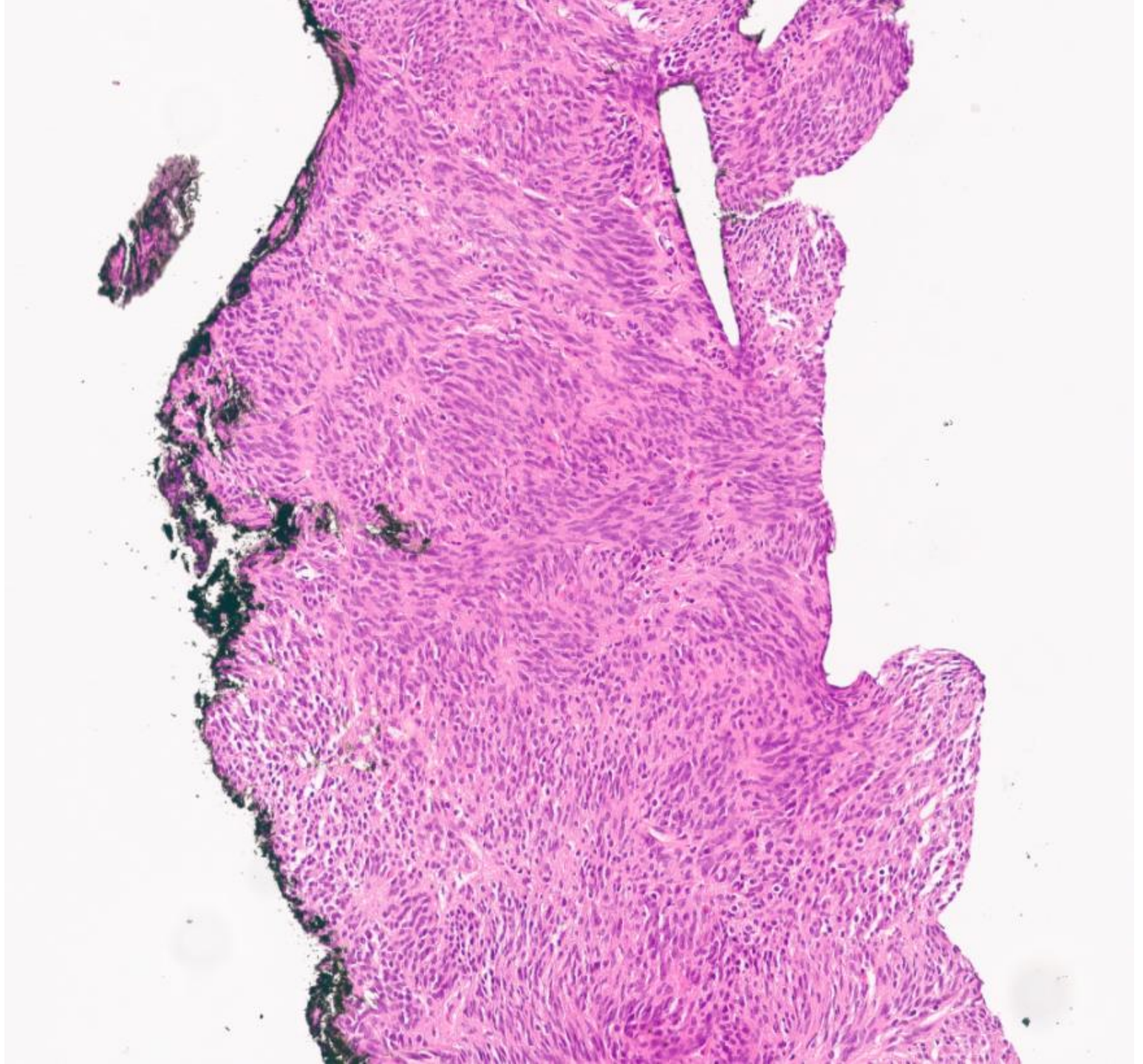
WHO Classification of Tumors of the Urinary System and Male Genital Organs, 2022



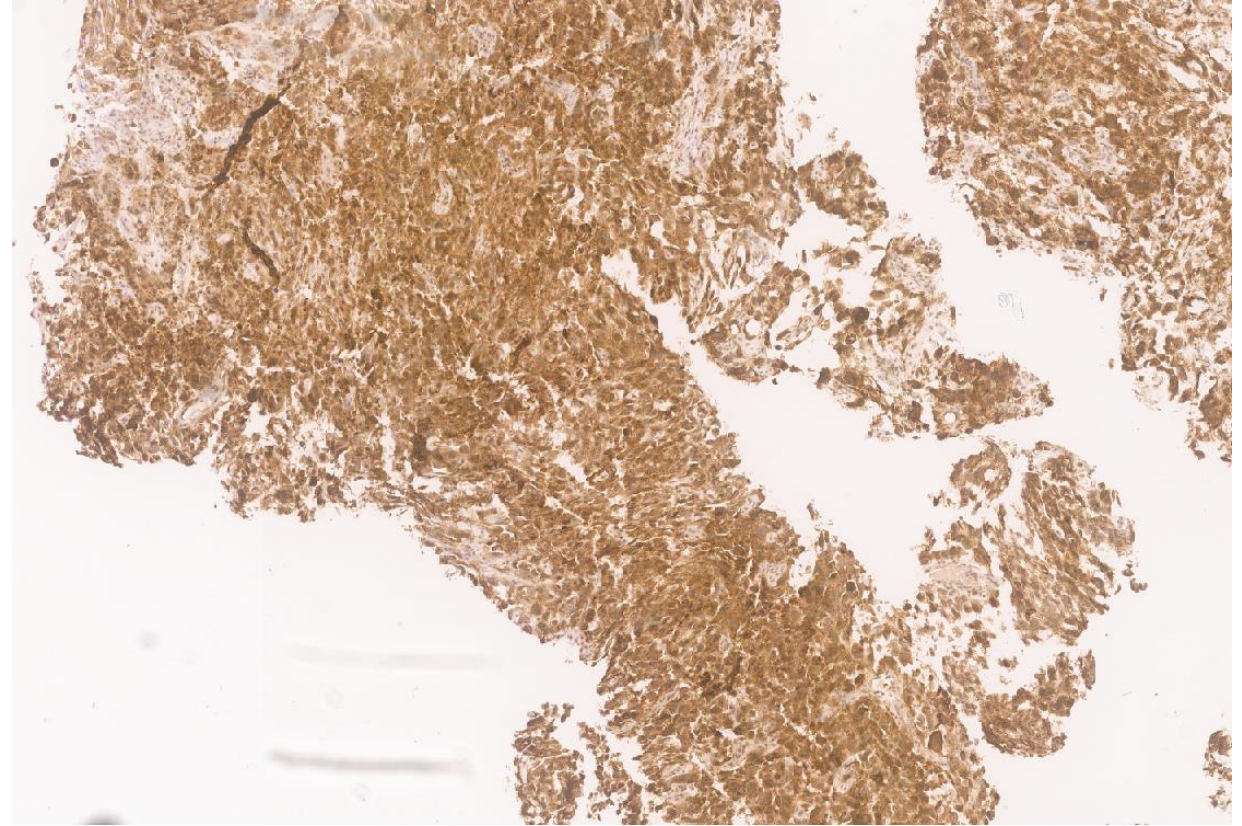
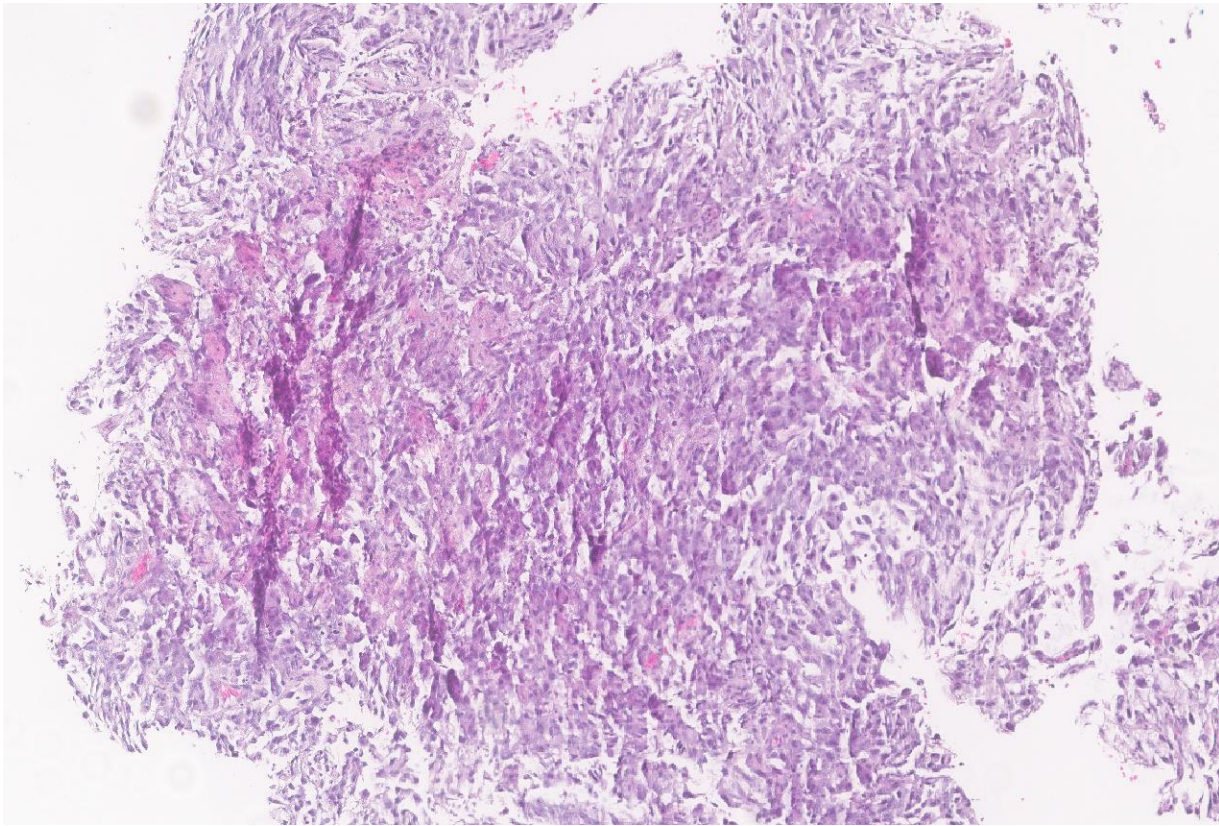


Solitary Fibrous Tumor

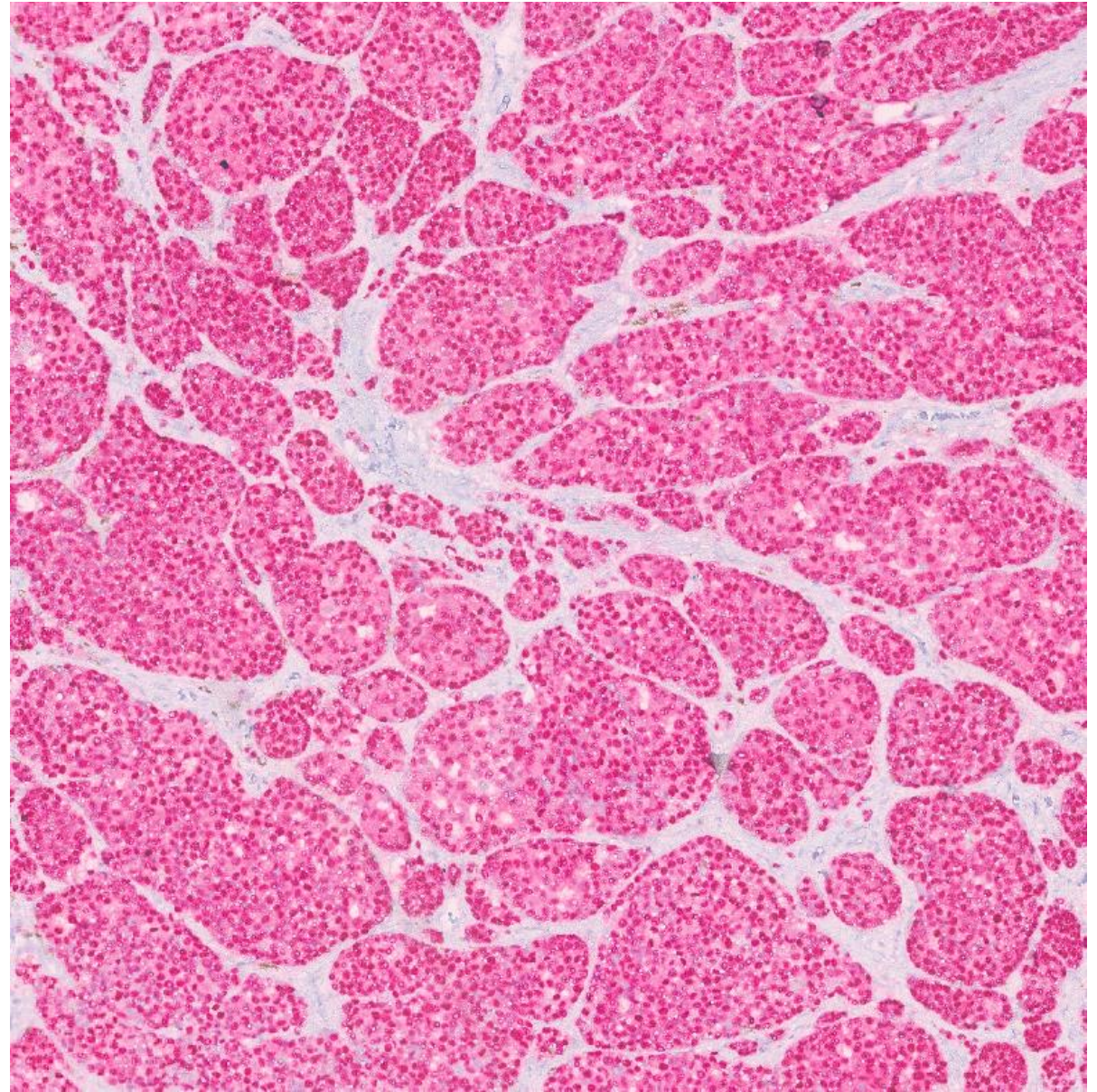
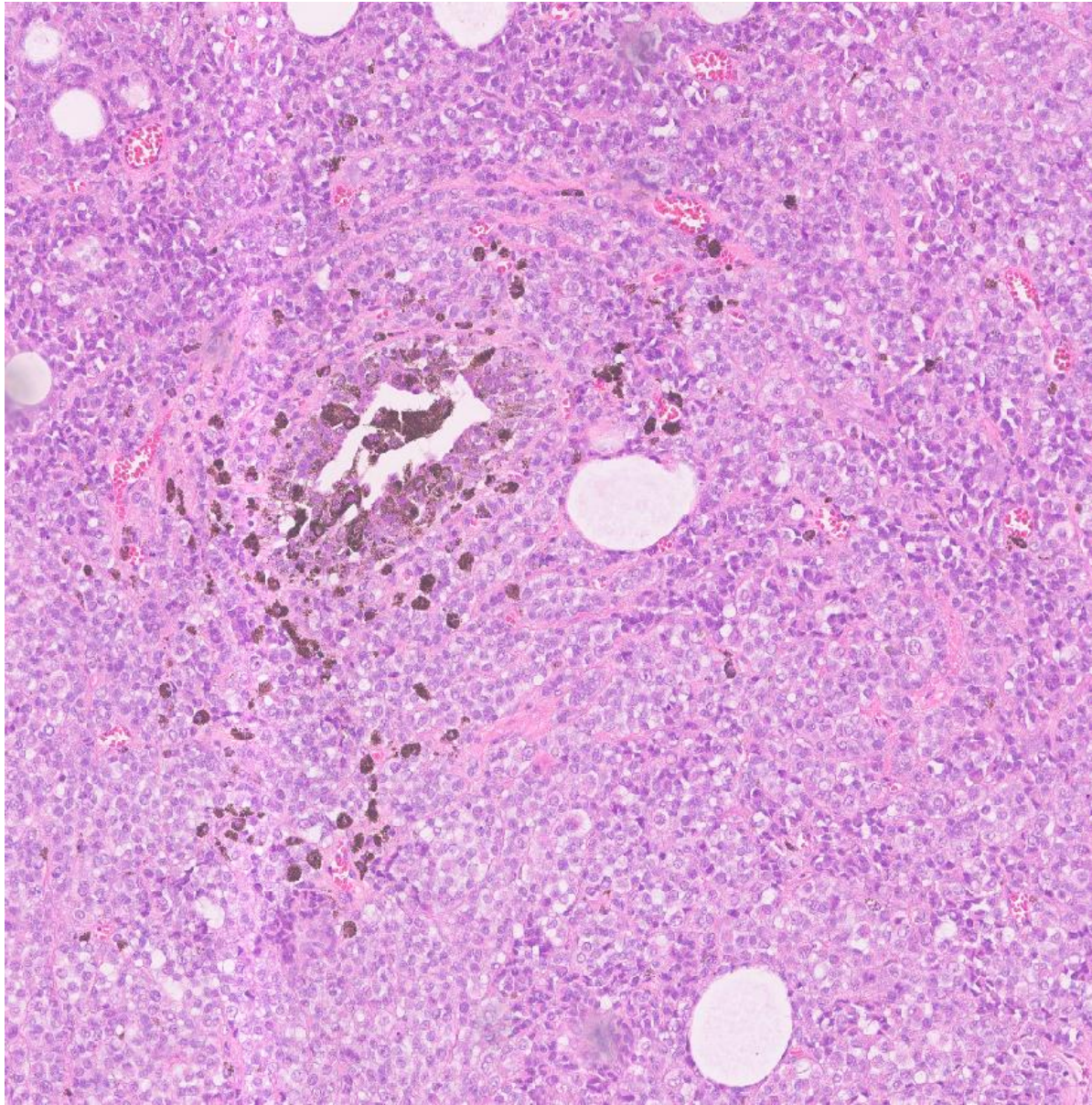
Prostate Gastrointestinal Stromal Tumor



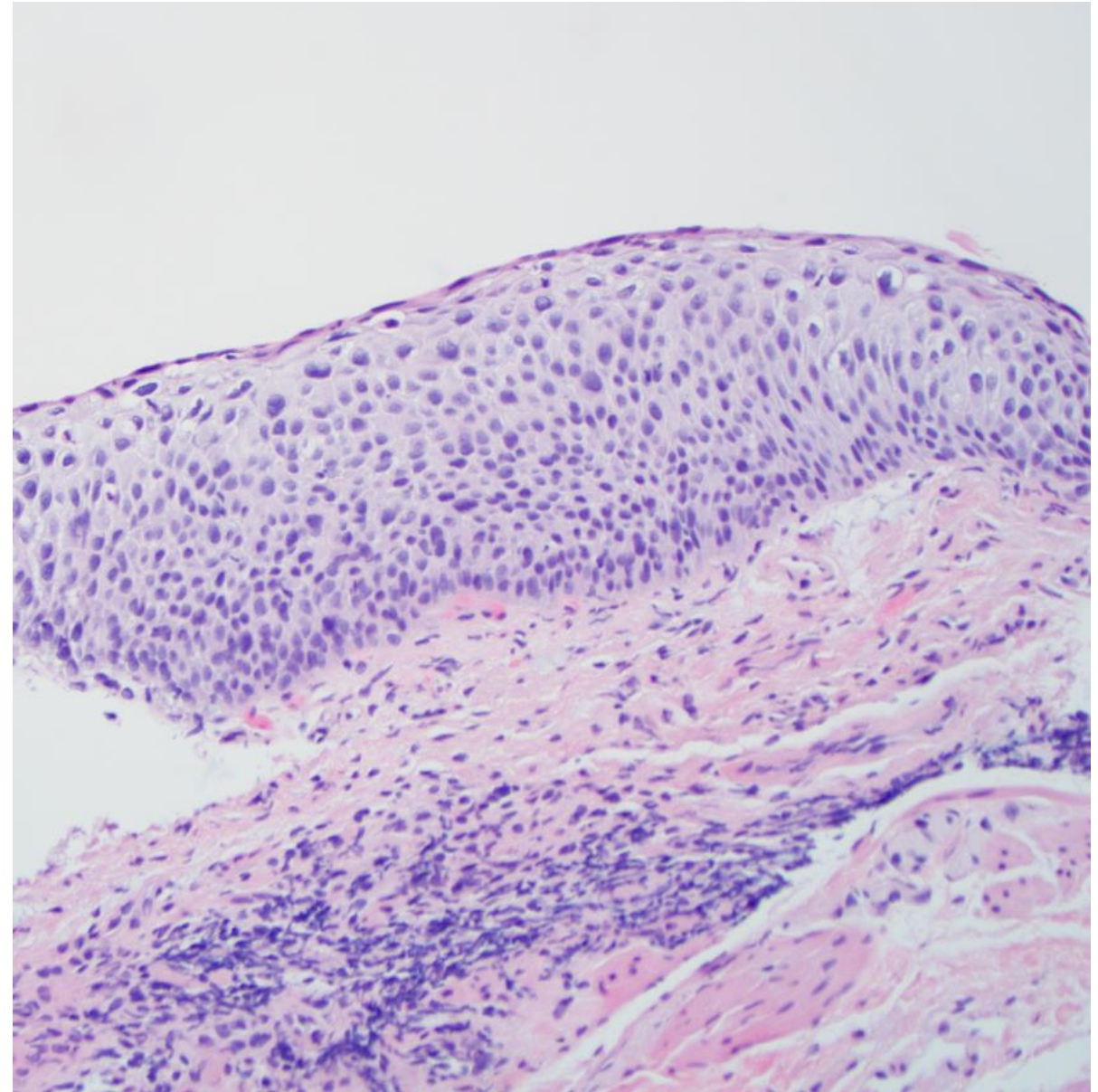
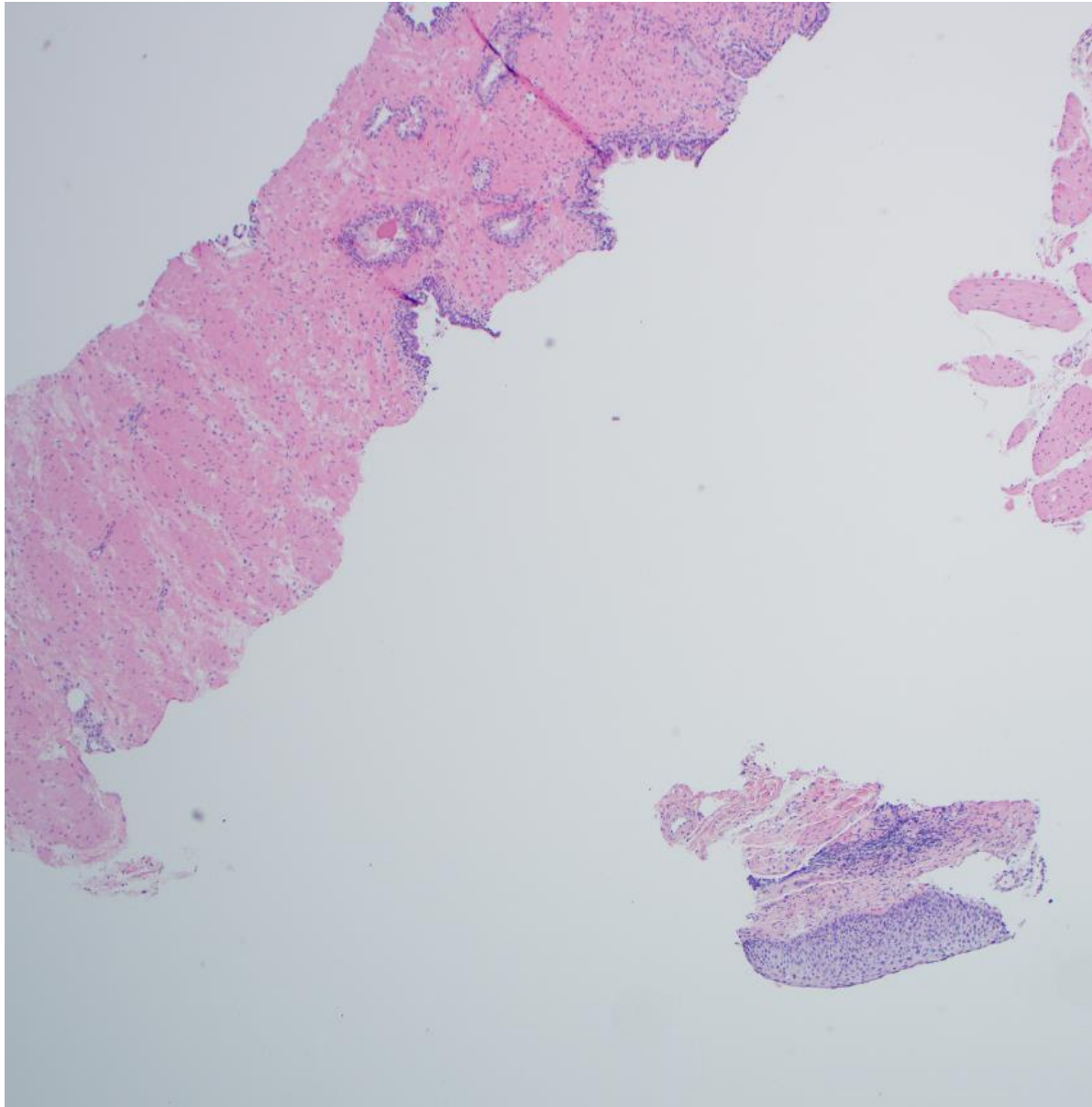
Case 9



Metastatic Yolk Sac Tumor



Metastatic Melanoma



Anal Intraepithelial Neoplasia



Signet ring-like
cells in Prostate
Carcinoma

Secondary Tumors

- Mean age 64 y
- Urothelial carcinoma
- Hematologic malignancies
- Presentation: like Pca
- Potential of misdiagnosis

TABLE 3. Summary of Tumor Types Among Metastatic Cases (N = 40)

Type of tumor	No. Cases (%)
Lung carcinomas	9 (22.5)
Colonic/rectal adenocarcinomas	7 (17.5)
Melanoma	6 (15)
Germ cell tumors	6 (15)
Pancreatobiliary adenocarcinoma	2 (5)
Renal cell carcinoma	2 (5)
Appendiceal adenocarcinoma	1 (2.5)
Appendiceal goblet cell adenocarcinoma	1 (2.5)
Esophageal adenocarcinoma	1 (2.5)
Gastric adenocarcinoma	1 (2.5)
Breast carcinoma	1 (2.5)
Merkel cell carcinoma	1 (2.5)
Squamous cell carcinoma	1 (2.5)
Well-differentiated neuroendocrine tumor (small bowel)	1 (2.5)

Type of spread	
Direct extension	36 (42)
Metastatic	40 (47)
Unclear/uncertain	9 (11)



Thank You

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