PROSTATE CANCER 2022: WHAT DO YOU NEED TO KNOW

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www.gupathsociety.org

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

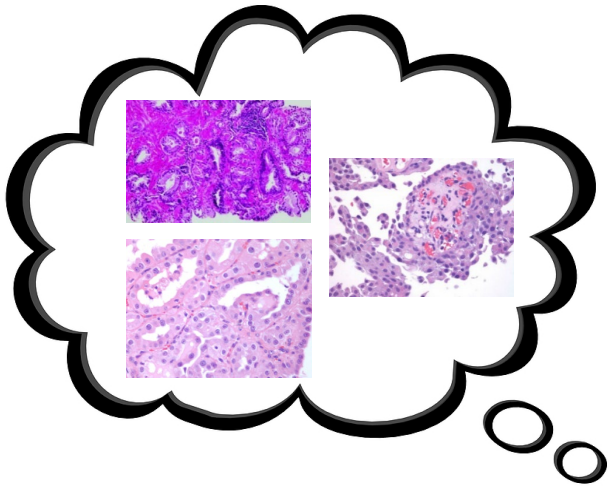
SCHOOL OF MEDICINE

I HAVE NO DISCLOSURES

OBJECTIVES

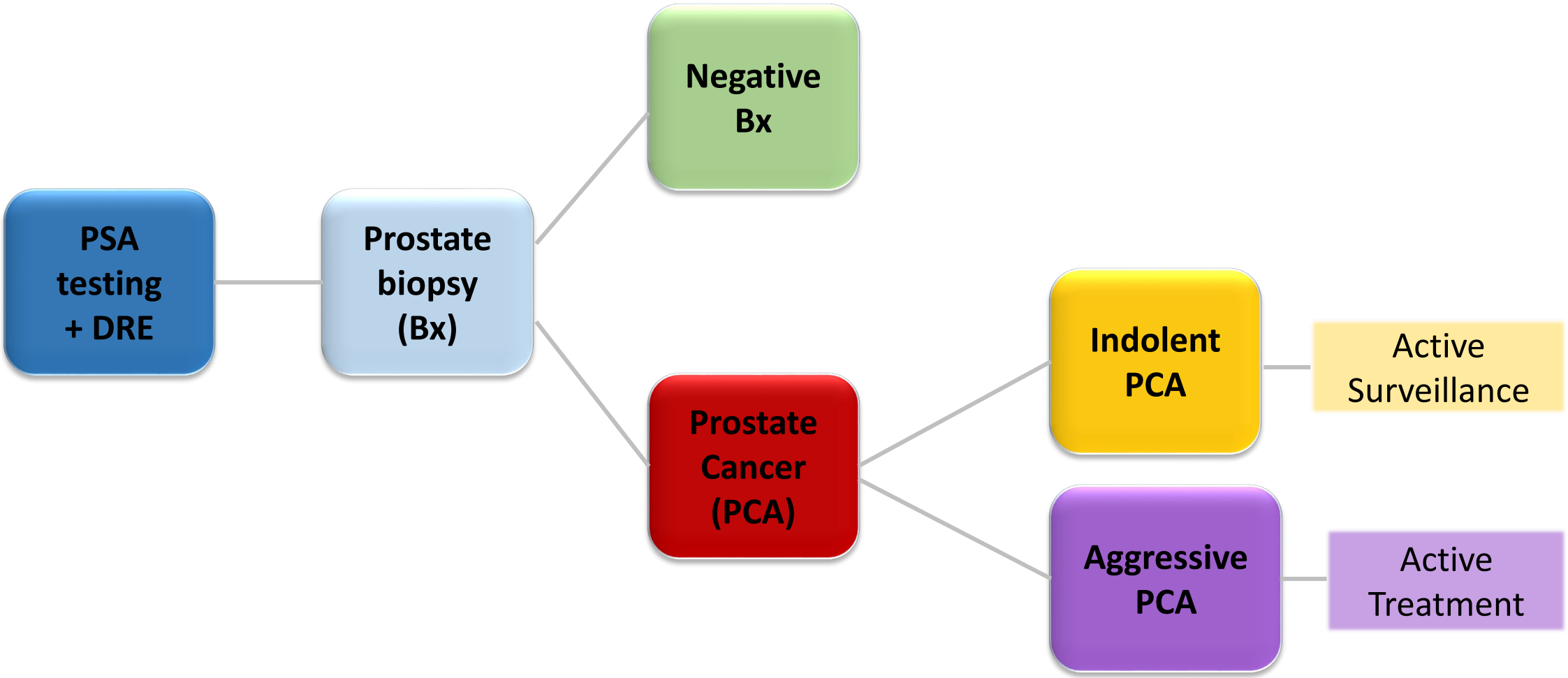
- Learn about recent changes/modifications of the prostate cancer (PCA) grading system
- Accurately grade and stage prostatic adenocarcinoma
- Recognize unfavorable pathologic features of prostate cancer and their impact on reporting

ROLE OF THE PATHOLOGIST: GUIDE PATIENT CARE

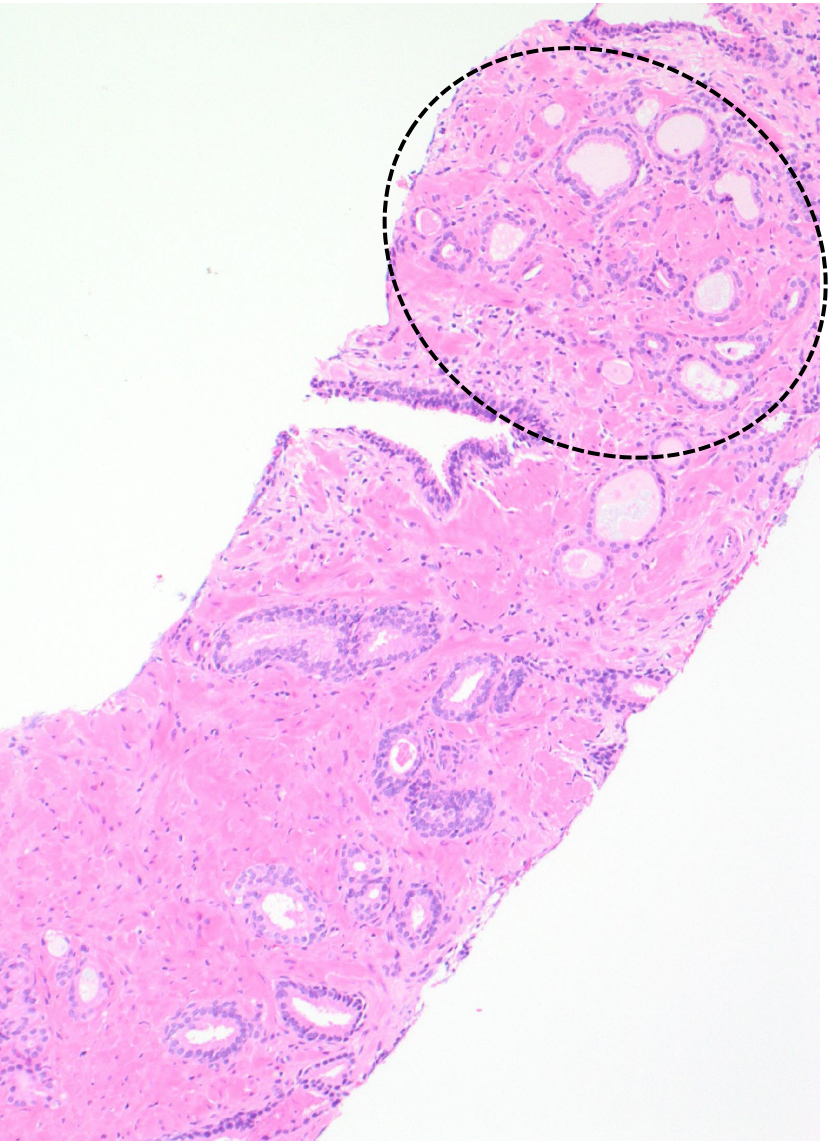


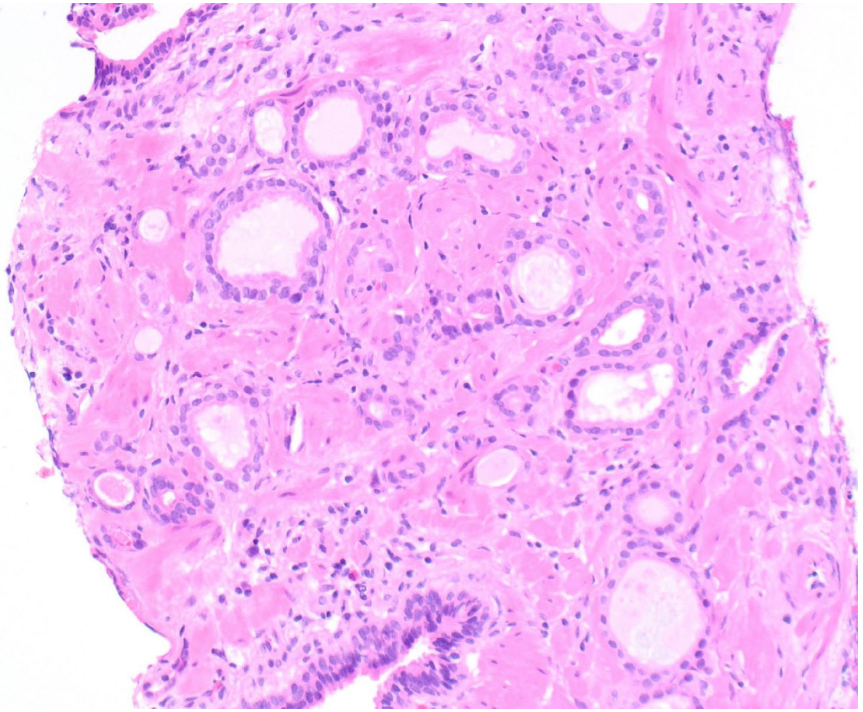
- Diagnosis
- Planning initial therapy
- Assessing prognosis
- Estimating likely benefit of adjuvant therapy
- Determine recurrent disease following treatment
- Understanding natural history of disease
- Integrating precision medicine

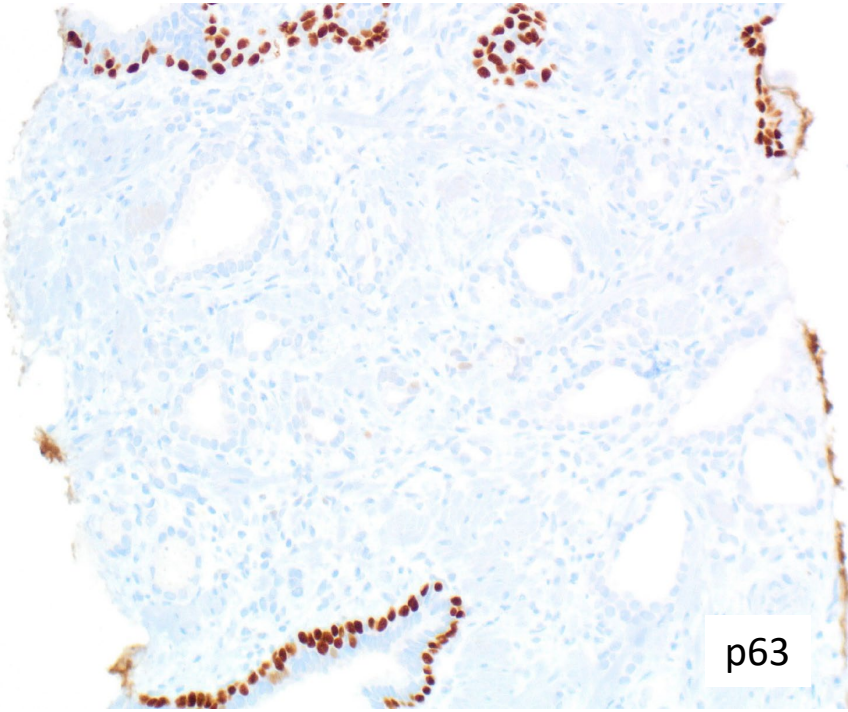
PROSTATE CANCER



PROSTATE CANCER - DIAGNOSIS







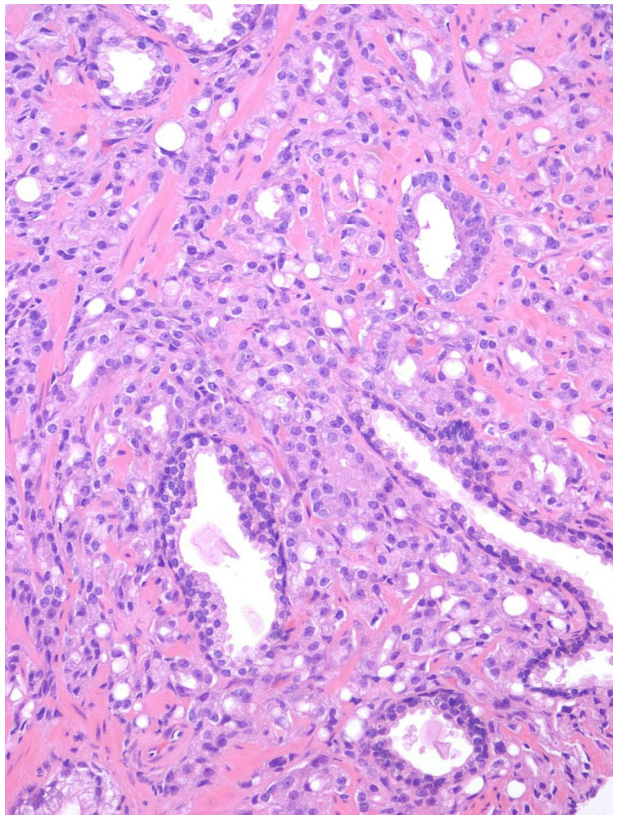
Prostatic adenocarcinoma, Gleason score 3+3=6 (Grade Group 1), involving 5% of one of one core and measuring 1 mm.

ESSENTIAL REPORTING PARAMETERS FOR CANCER-BEARING BX

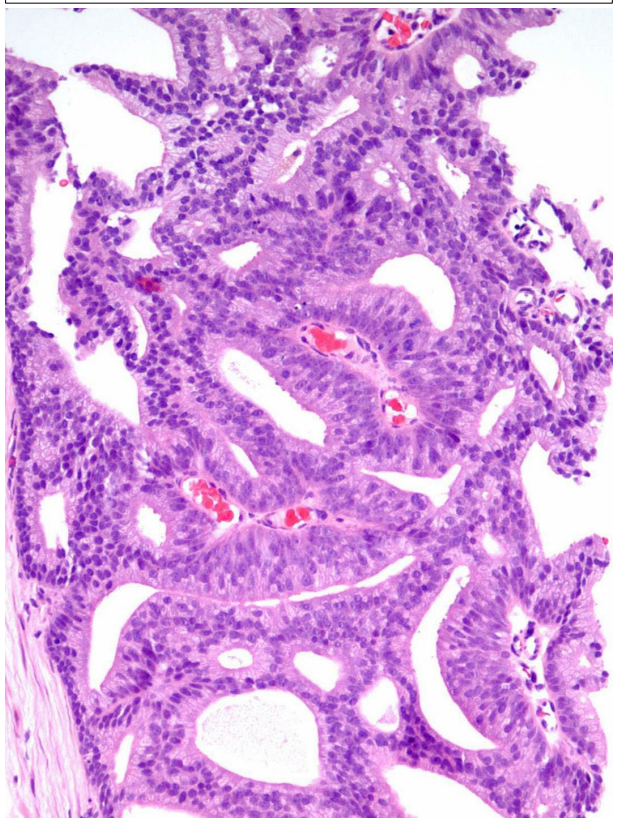
- Histologic type (acinar vs. nonacinar and other tumor types)
  - Ductal adenocarcinoma
  - Small cell carcinoma
  - Sarcomatoid carcinoma
  - Intraductal carcinoma
- Gleason Score & Grade Group
  - % pattern 4 (in 3+4=7 and 4+3=7)
  - Cribriform pattern 4 (present or absent)
- Location of positive cores (based on biopsy site)
- Tumor quantification:
  - # and % of positive biopsy cores
  - Linear % or length (mm) of core involved by prostate cancer
- Other (reported only if present)
  - Perineural invasion (PNI)
  - Extraprostatic extension (EPE)
  - Seminal vesicle invasion (SVI)

PROSTATE CANCER – HISTOLOGIC TUMOR TYPE

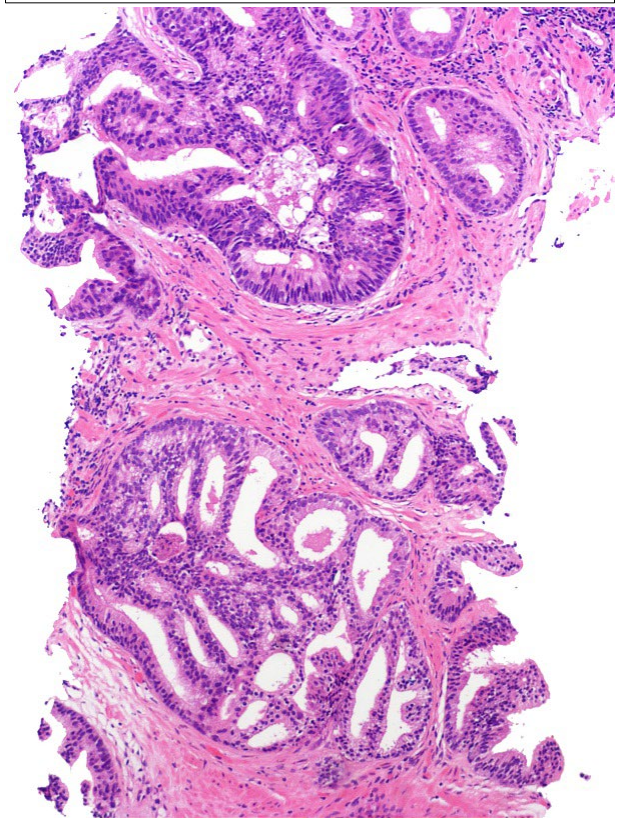
Acinar adenocarcinoma



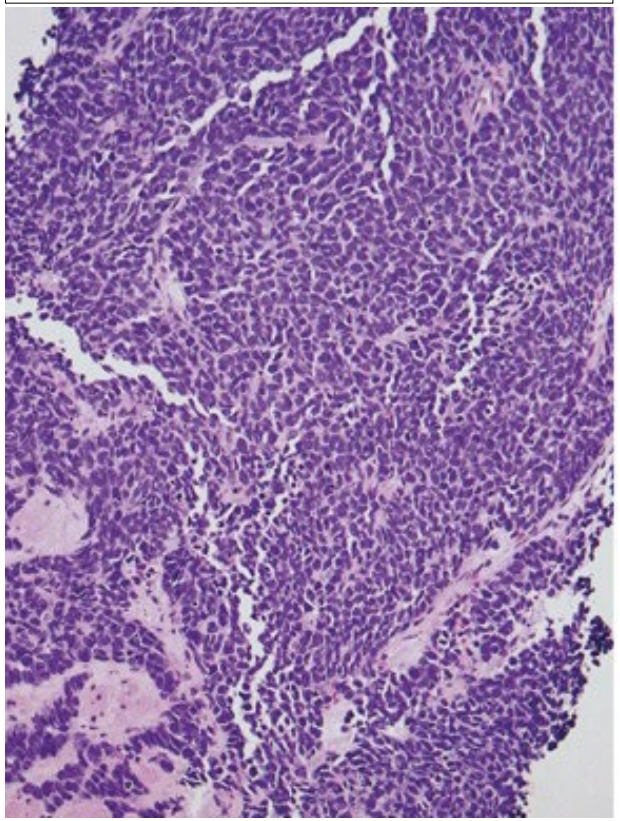
Ductal adenocarcinoma



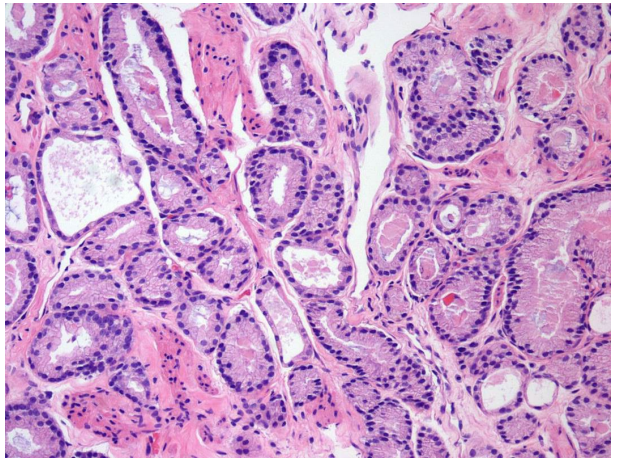
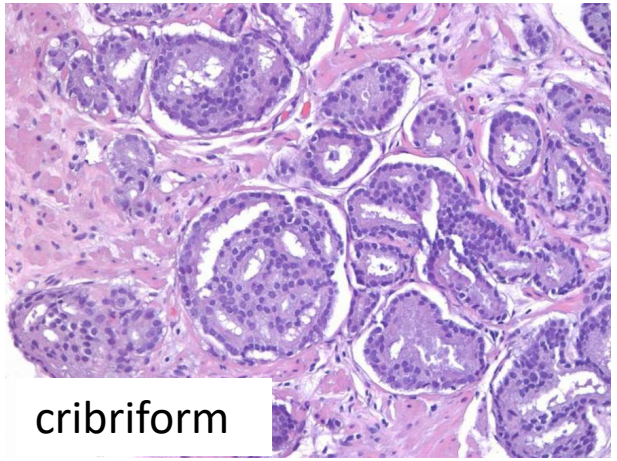
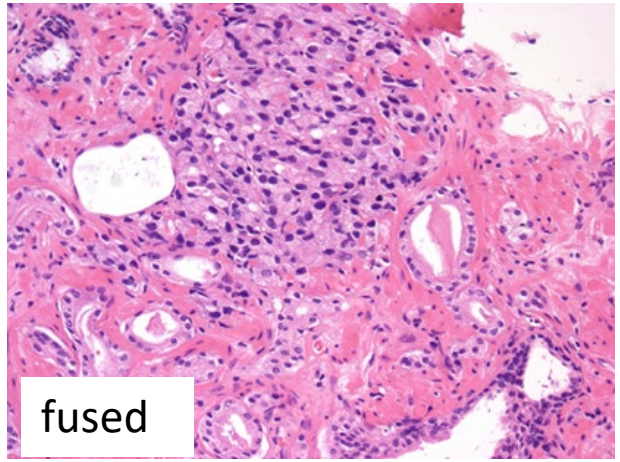
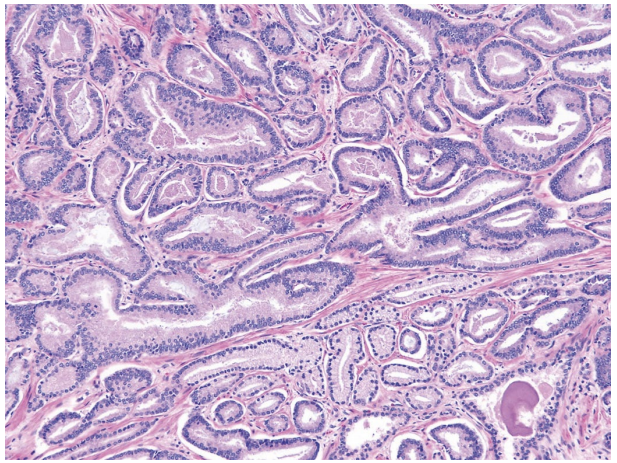
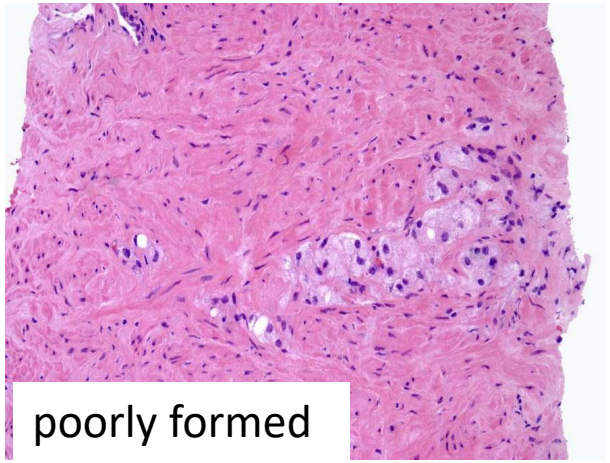
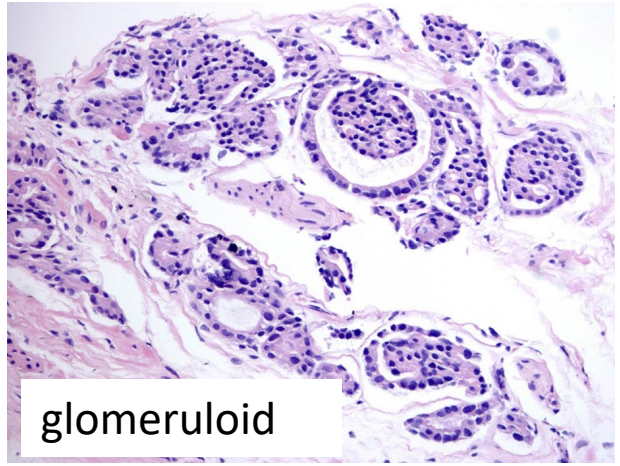
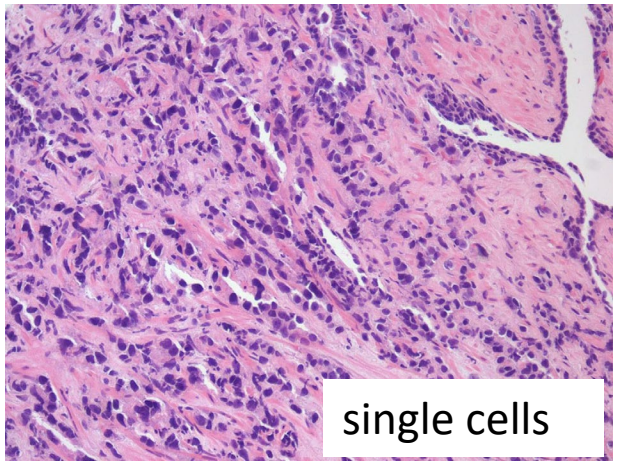
Intraductal carcinoma



Neuroendocrine CA



PROSTATE CANCER – TUMOR GRADING

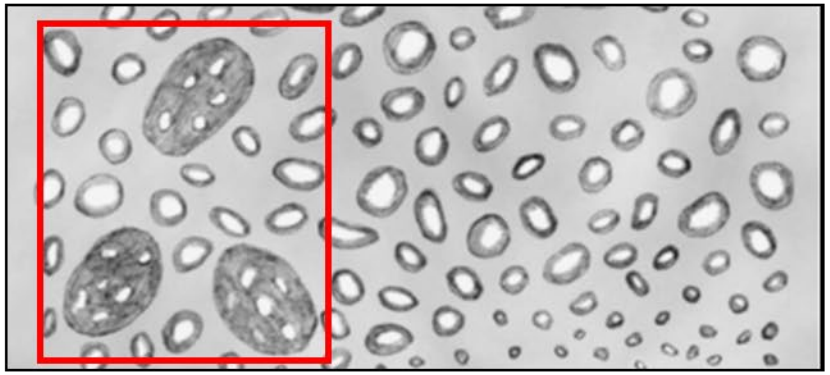
Pattern 3	Pattern 4		Pattern 5
	 cribriform	 fused	 solid sheets
	 poorly formed	 glomeruloid	 single cells

UPDATE ON GRADING

EVOLUTION OF GLEASON PATTERN 3

2005 ISUP modified

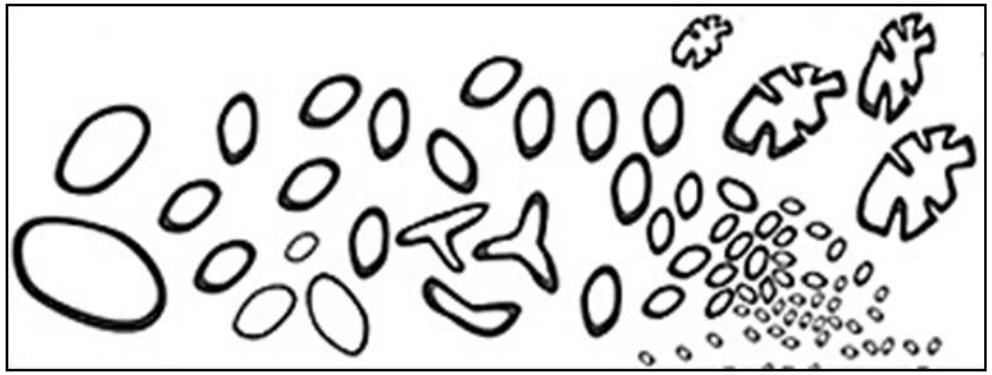
Epstein et al. AJSP 29, 2005



- Small well-formed glands
- Small cribriform lesions: exclude HGPIN with IHC
- ~~Medium to large sized cribriform glands eliminated~~

2014 ISUP modified

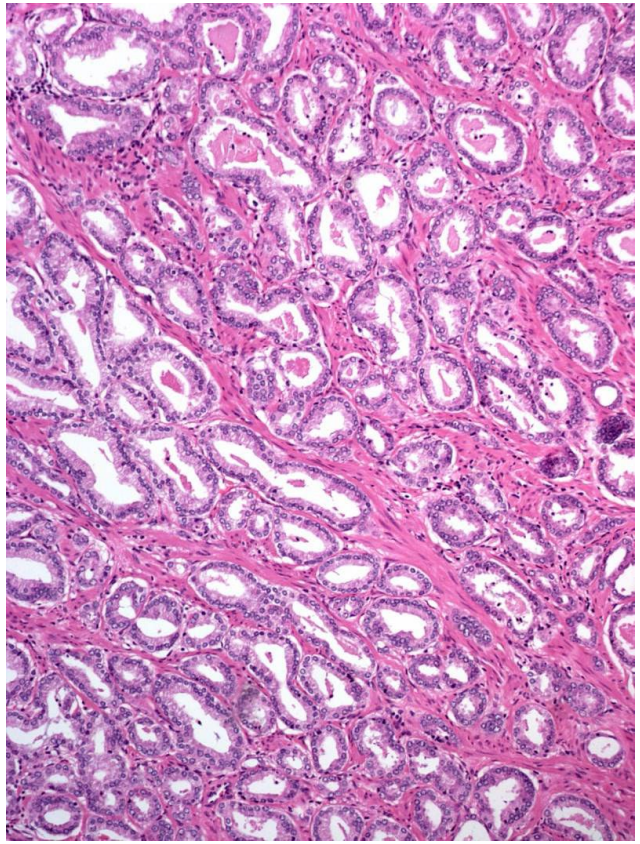
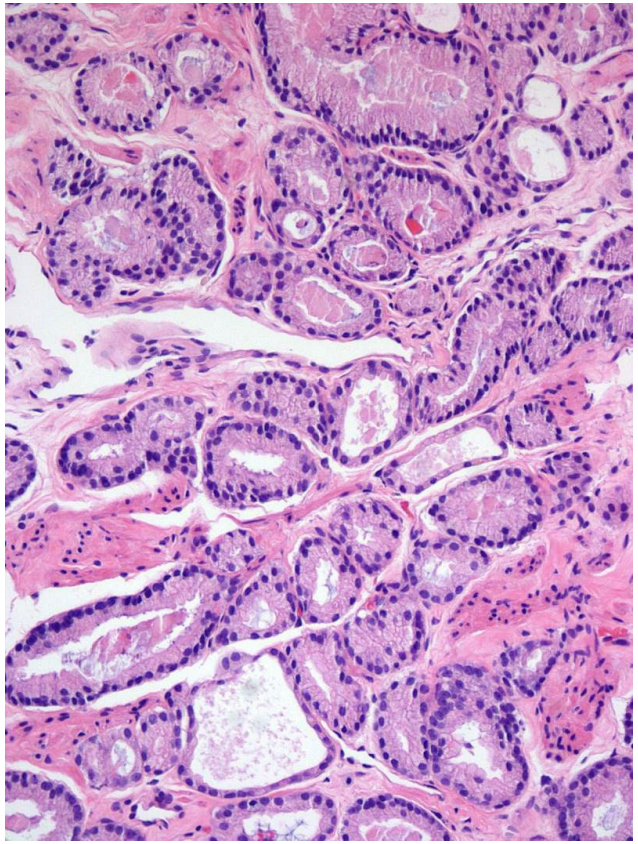
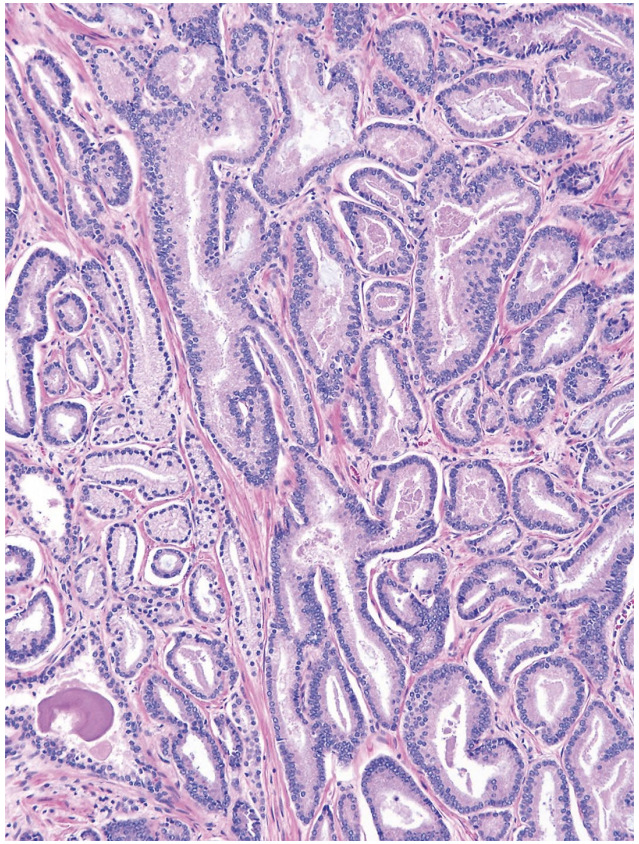
Epstein et al. AJSP 40, 2016



- Small well-formed glands
- Branched glands are allowed
- ~~Small cribriform glands~~

All cribriform glands should be graded as pattern 4 - ISUP, prostate cancer grading, Chicago, 2014 – 100% consensus

2014 ISUP MODIFIED GLEASON SYSTEM – PATTERN 3

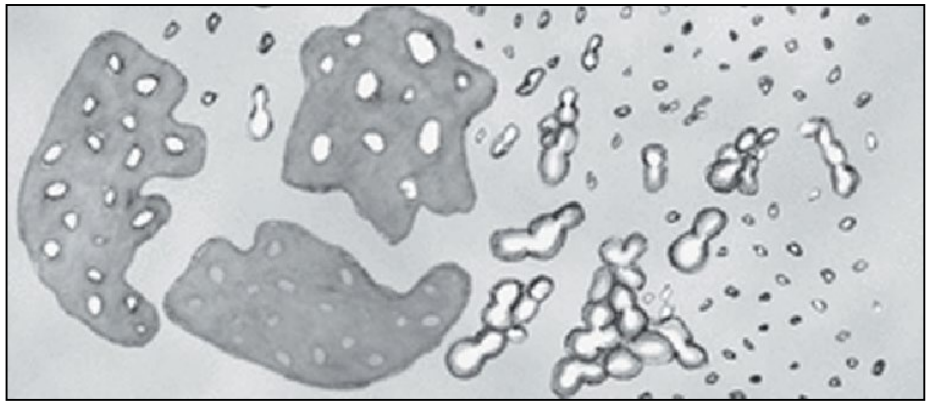
- Well-formed individual glands, discrete unit
- Variation is size and shape (microcystic and pseudohyperplastic)
- Branching glands are allowed in pattern 3

Paner et al. Arch Pathol Lab Med (2019)

EVOLUTION OF GLEASON PATTERN 4

2005 ISUP modified

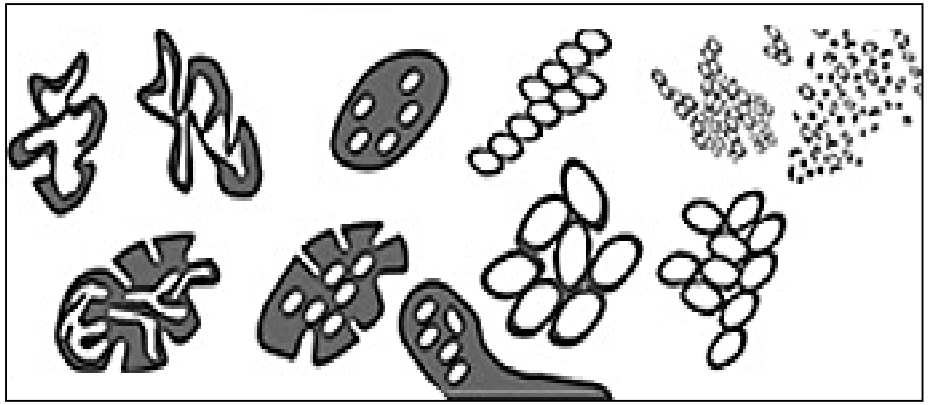
Epstein et al. AJSP 29, 2005



- Large cribriform glands
- Ill-defined glands with poorly-formed lumens
- Fused microacinar glands
- ~~Hypernephroma-like tumors~~

2014 ISUP modified

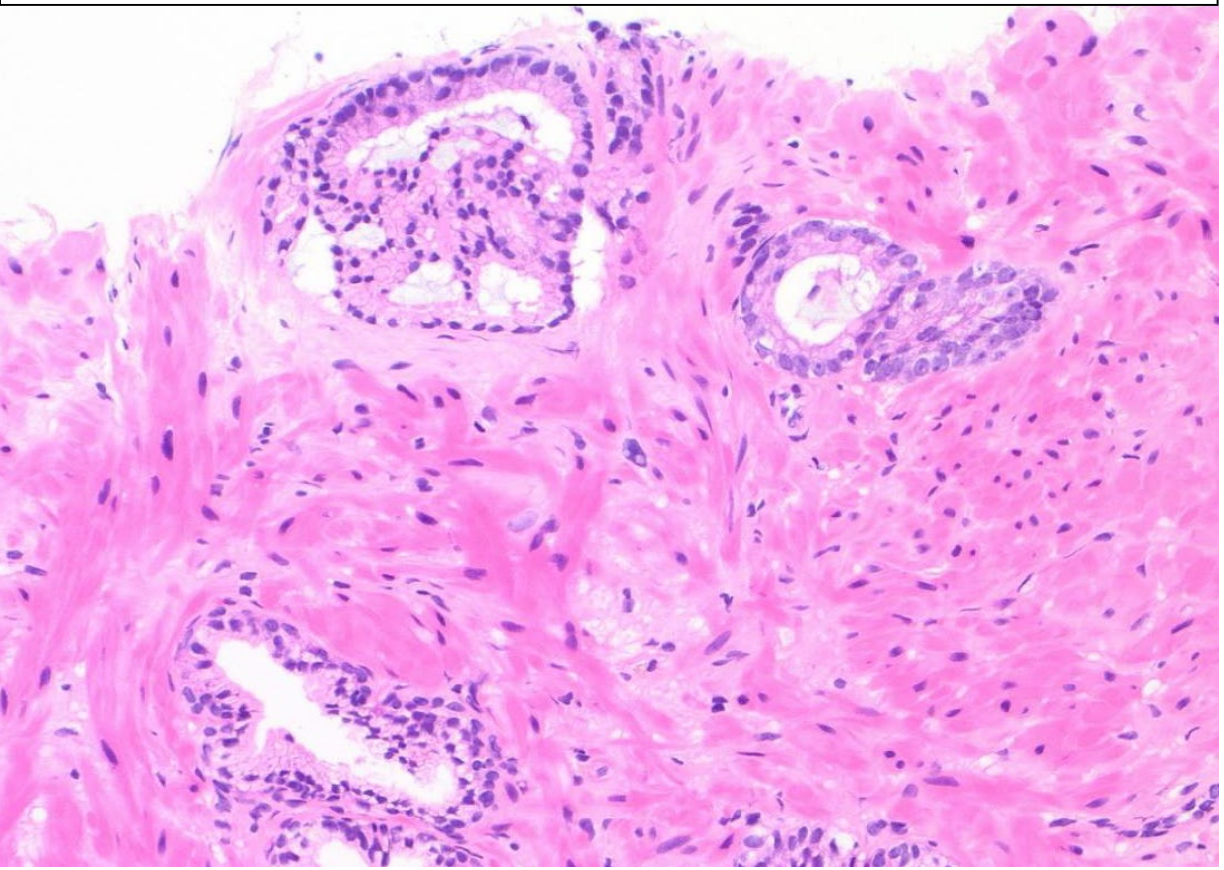
Epstein et al. AJSP 40, 2016



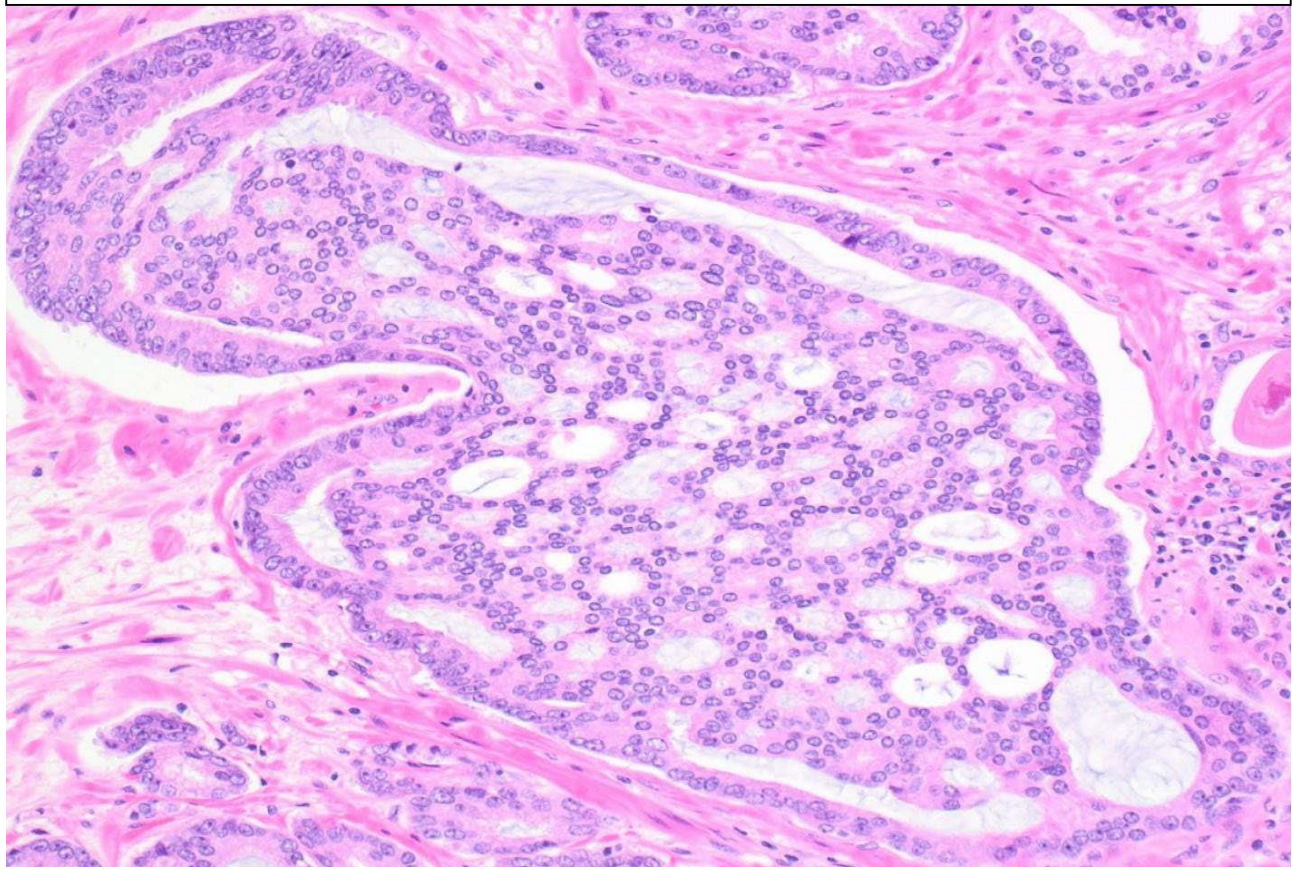
- Cribriform (small & large)
- Fused
- Poorly formed
- Glomeruloid glands

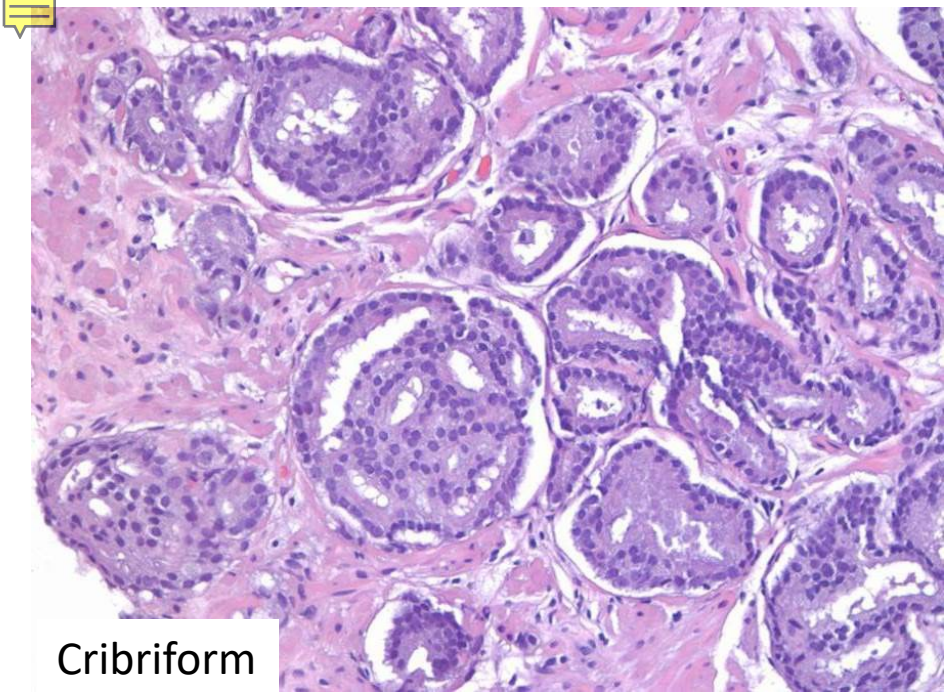
CRIBRIFORM GLEASON PATTERN 4

Small cribriform

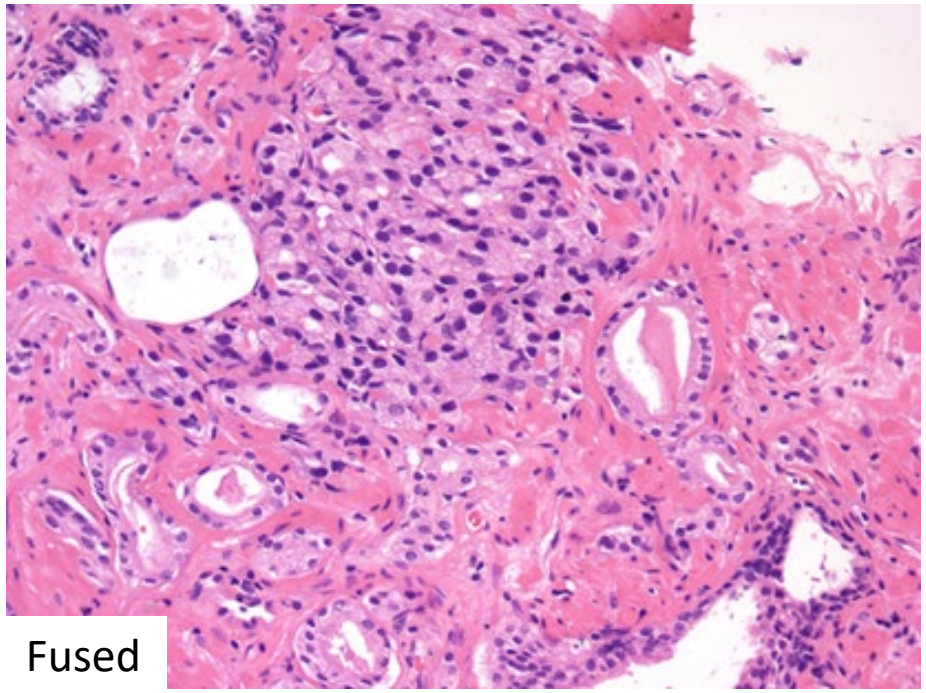


Large cribriform

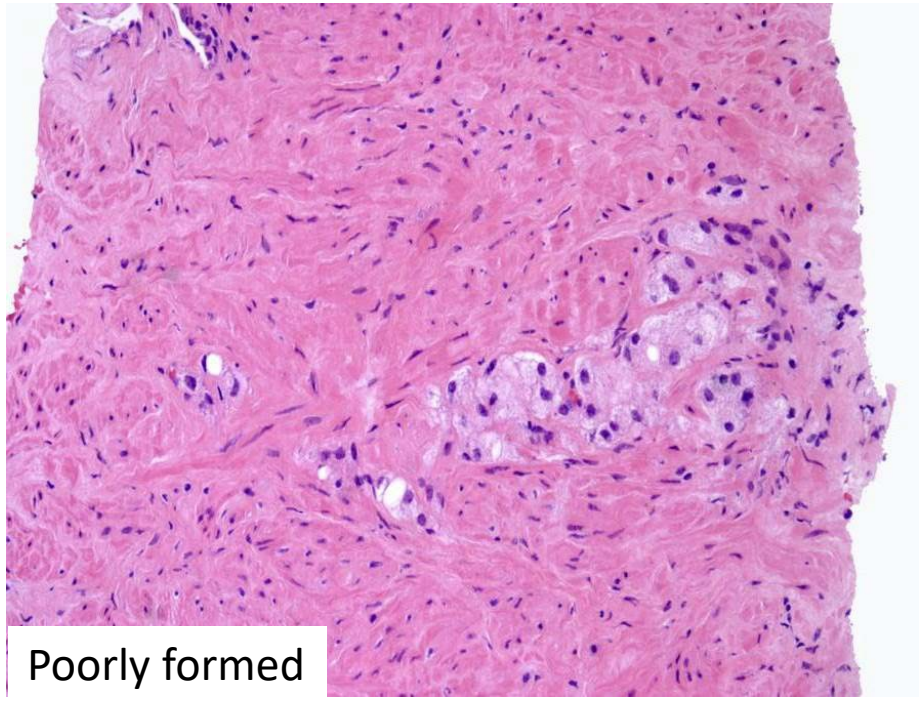




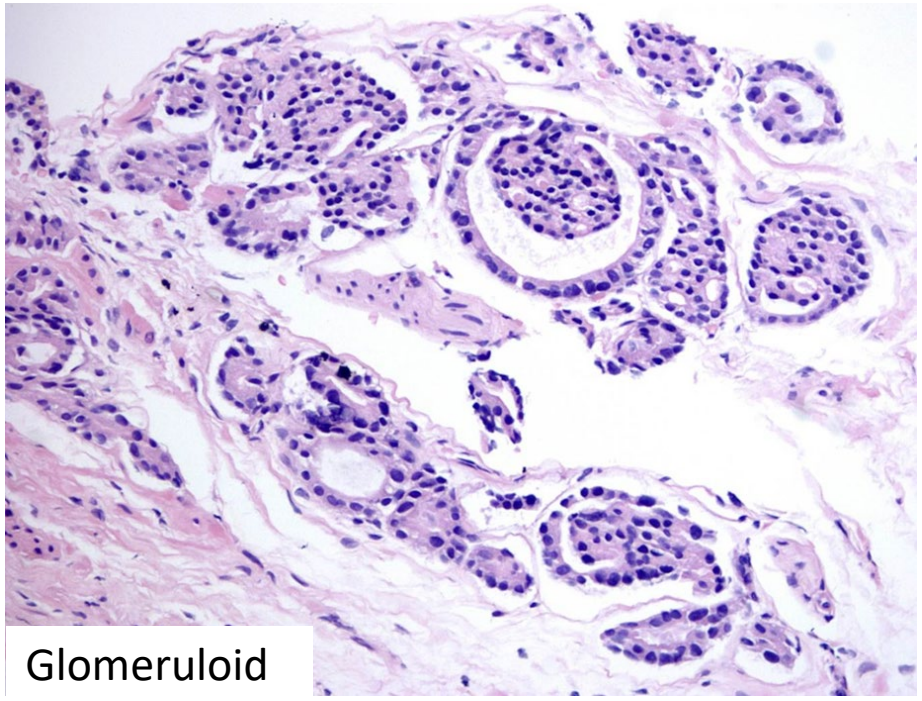
Cribriform



Fused



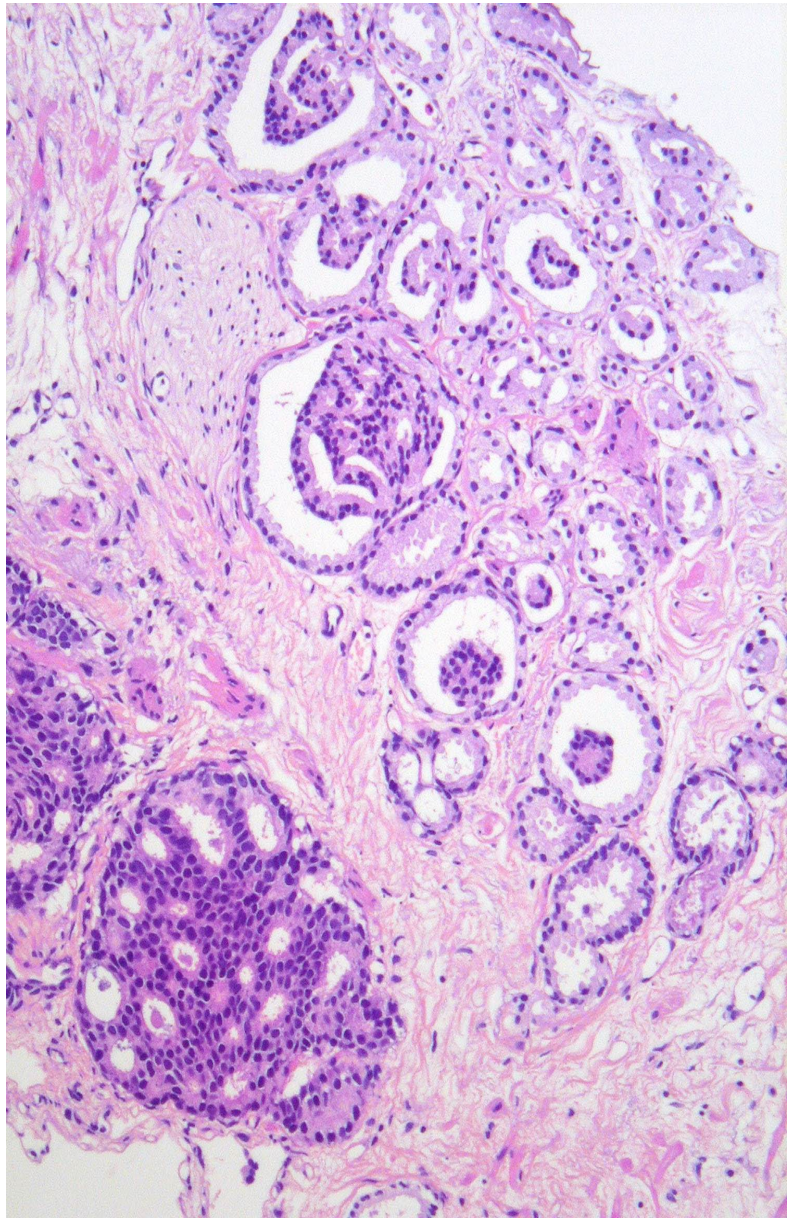
Poorly formed

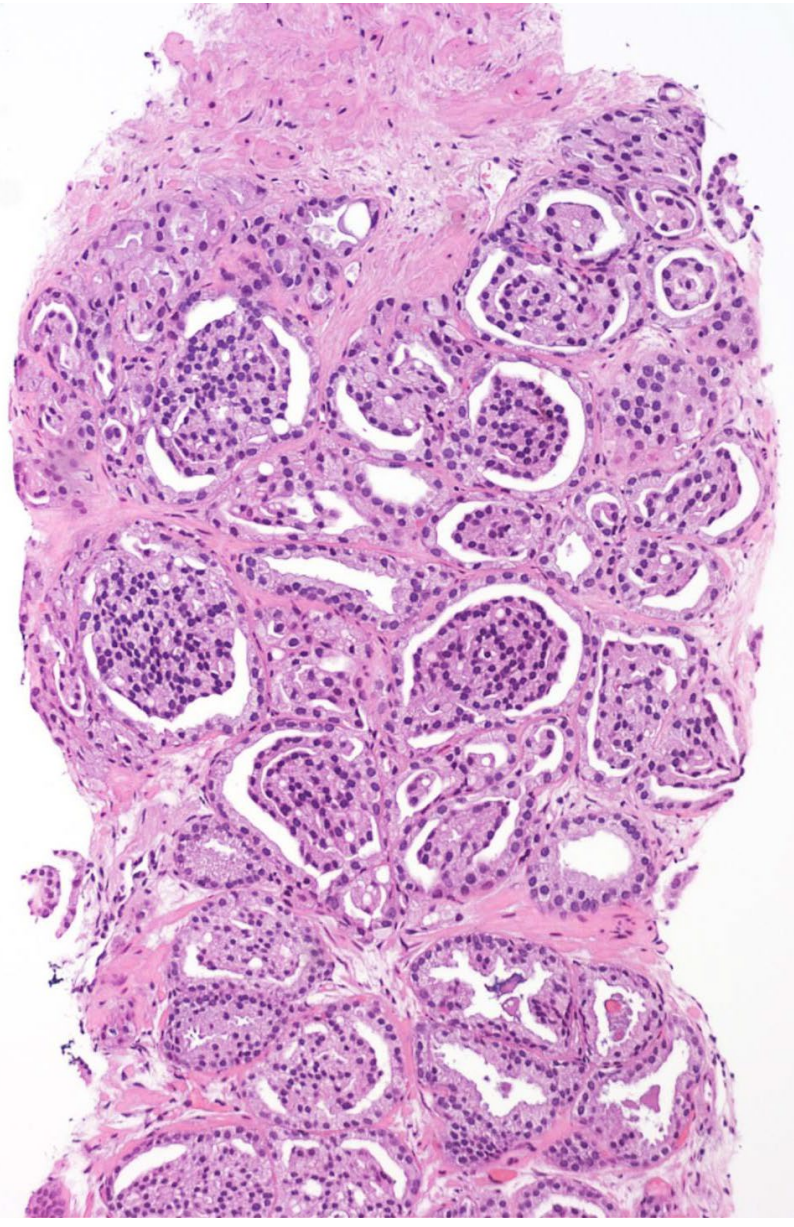


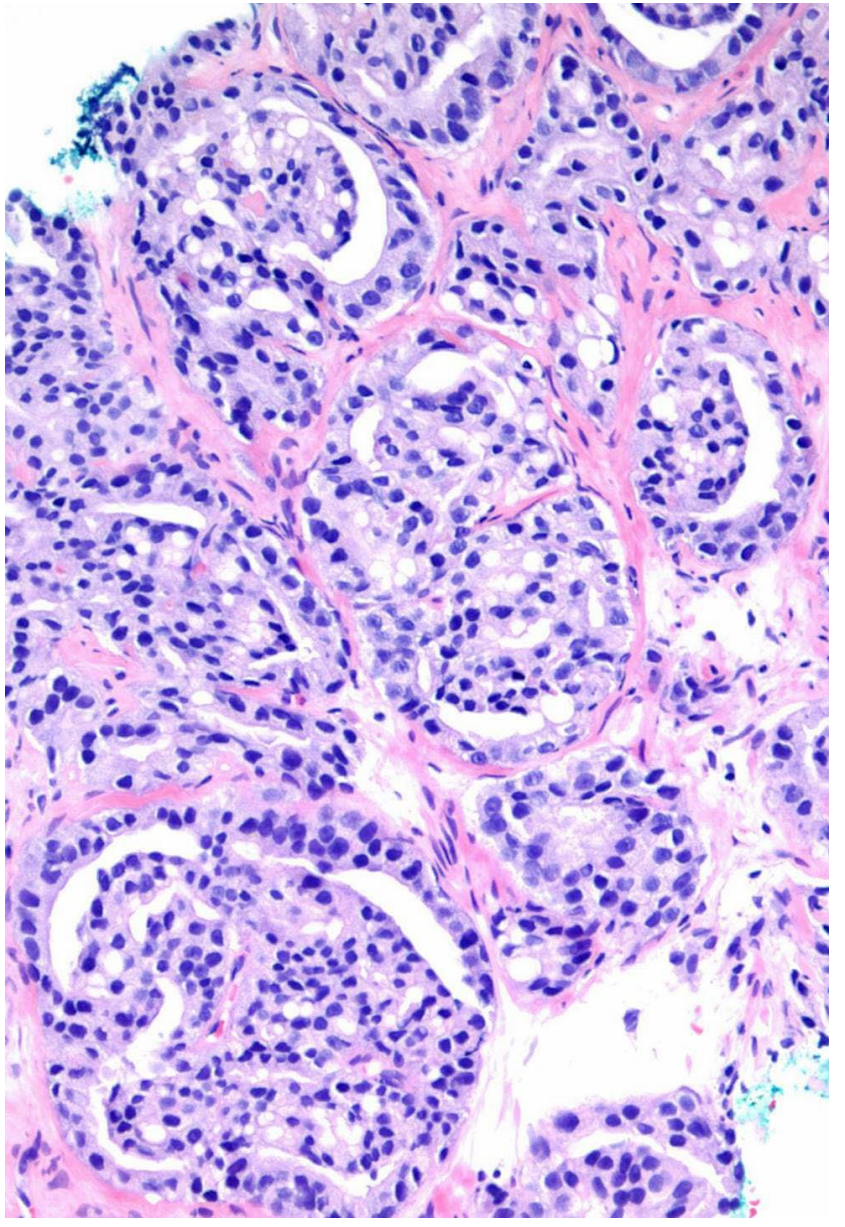
Glomeruloid

2014 ISUP modified Gleason pattern 4

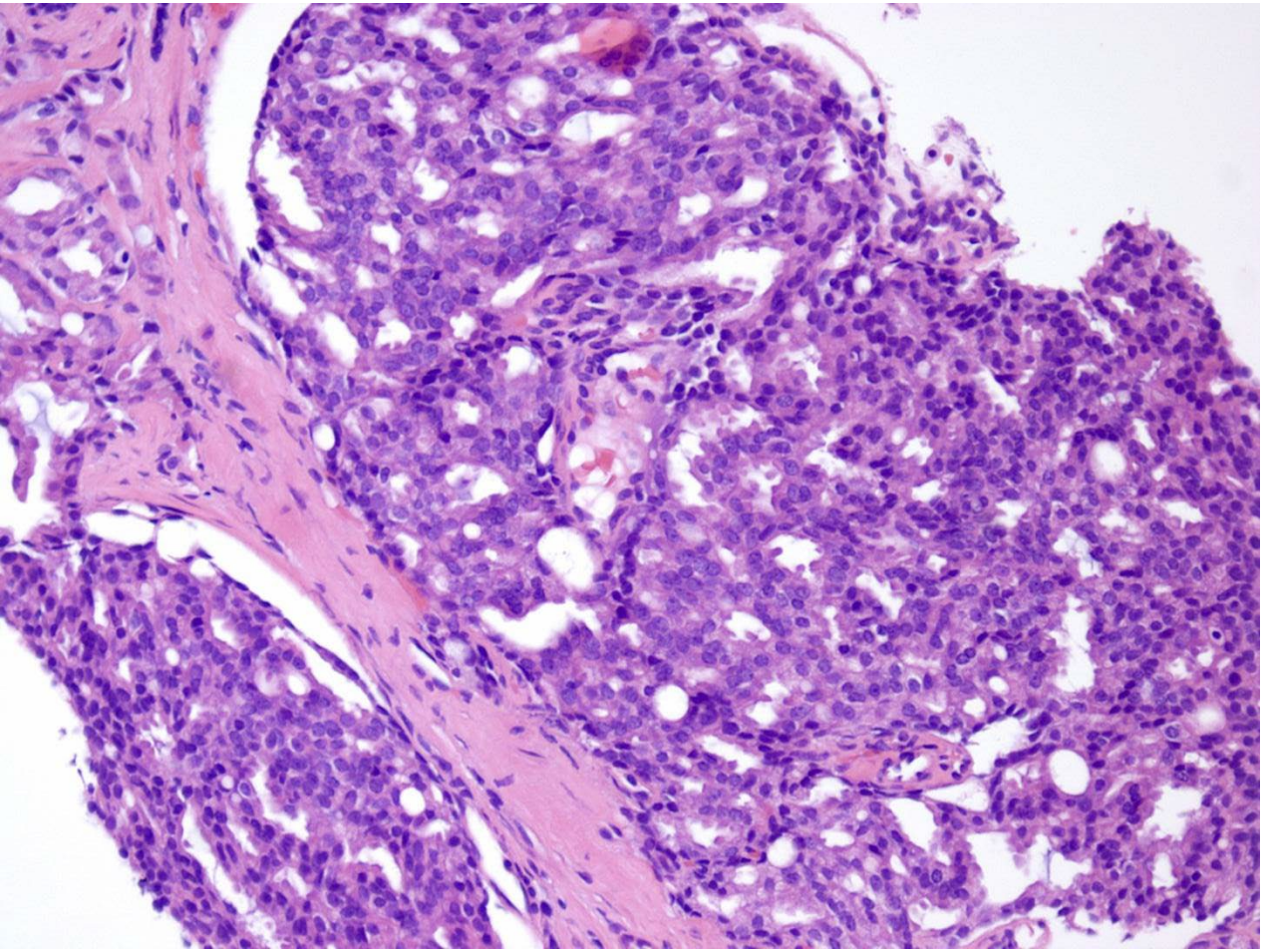
MODIFIED GP4 - GLOMERULOID & SMALL CRIBRIFORM



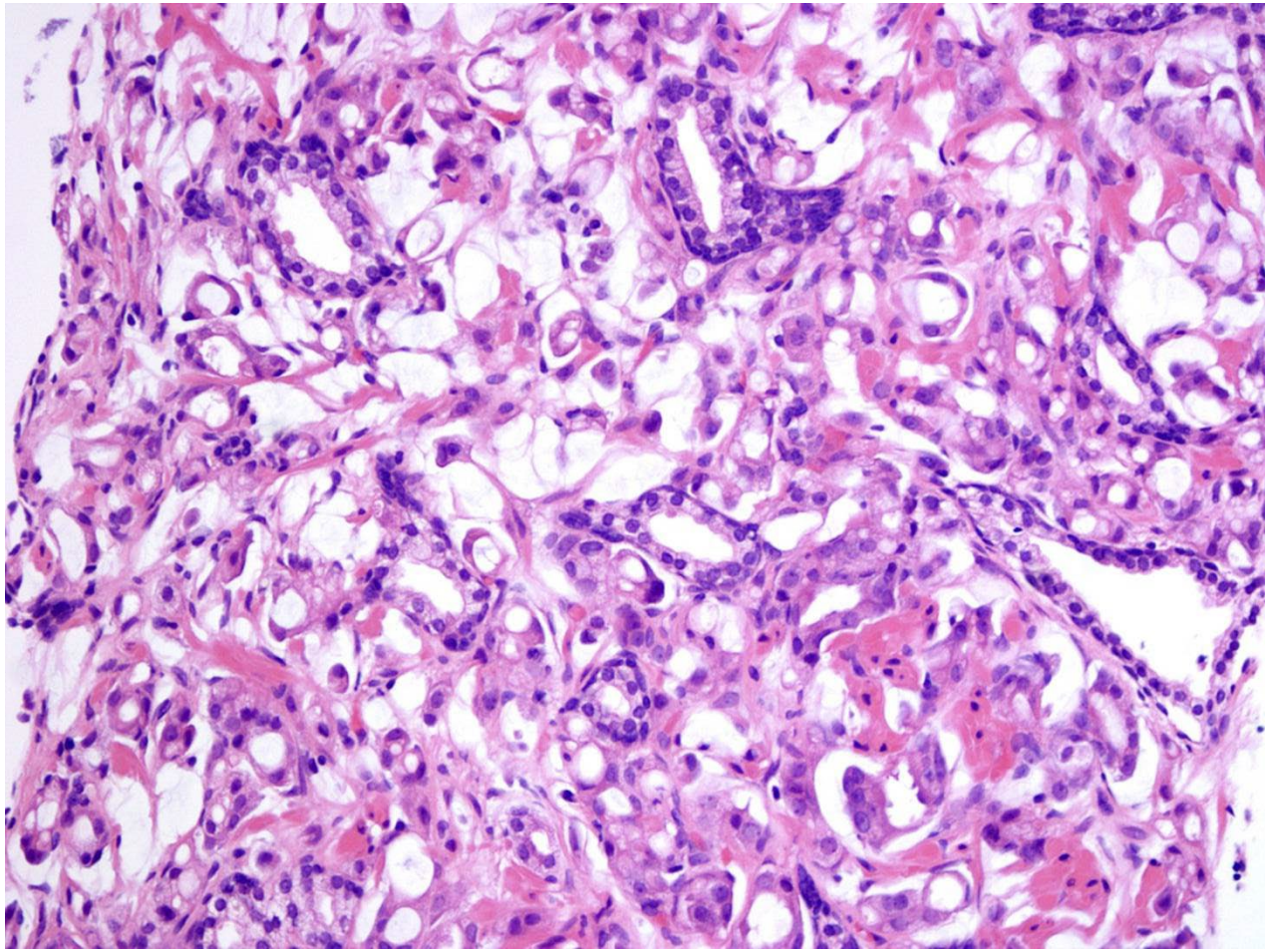




MODIFIED GP4 - LARGE CRIBRIFORM & FUSED GLANDS

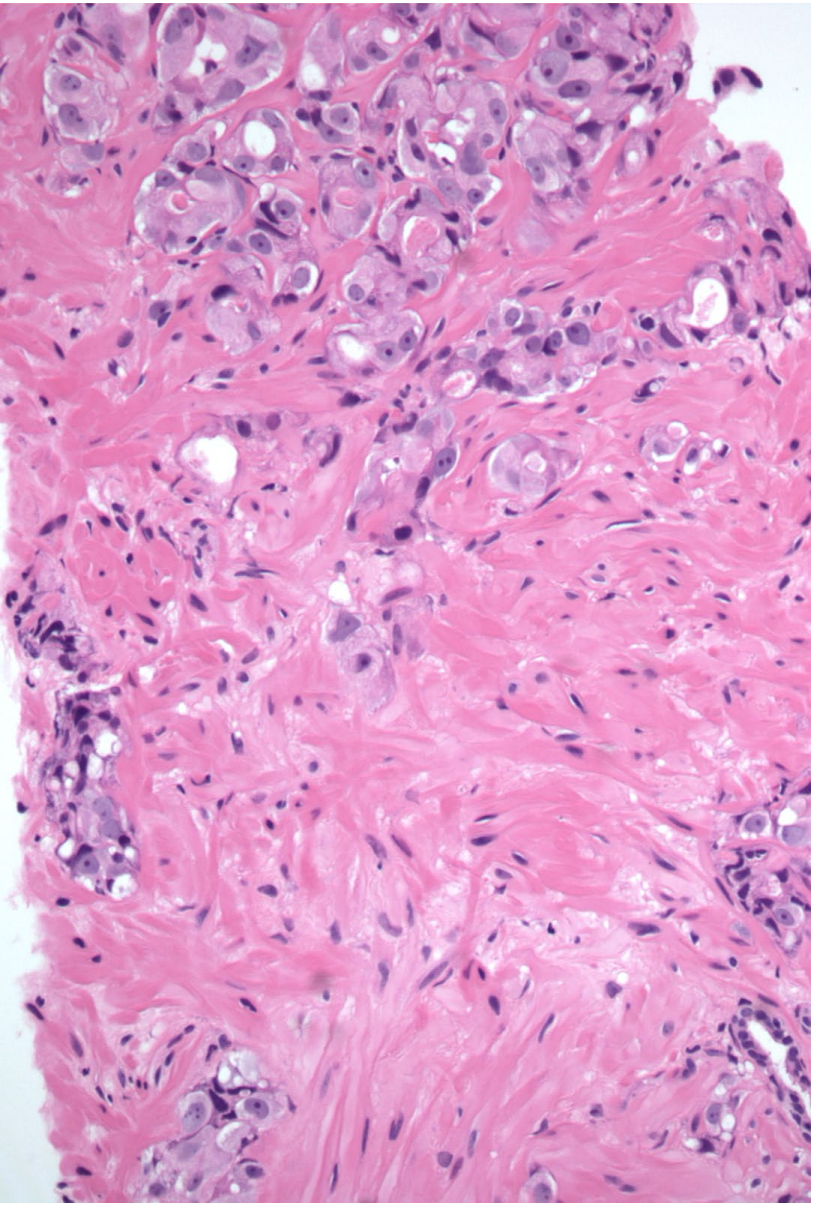


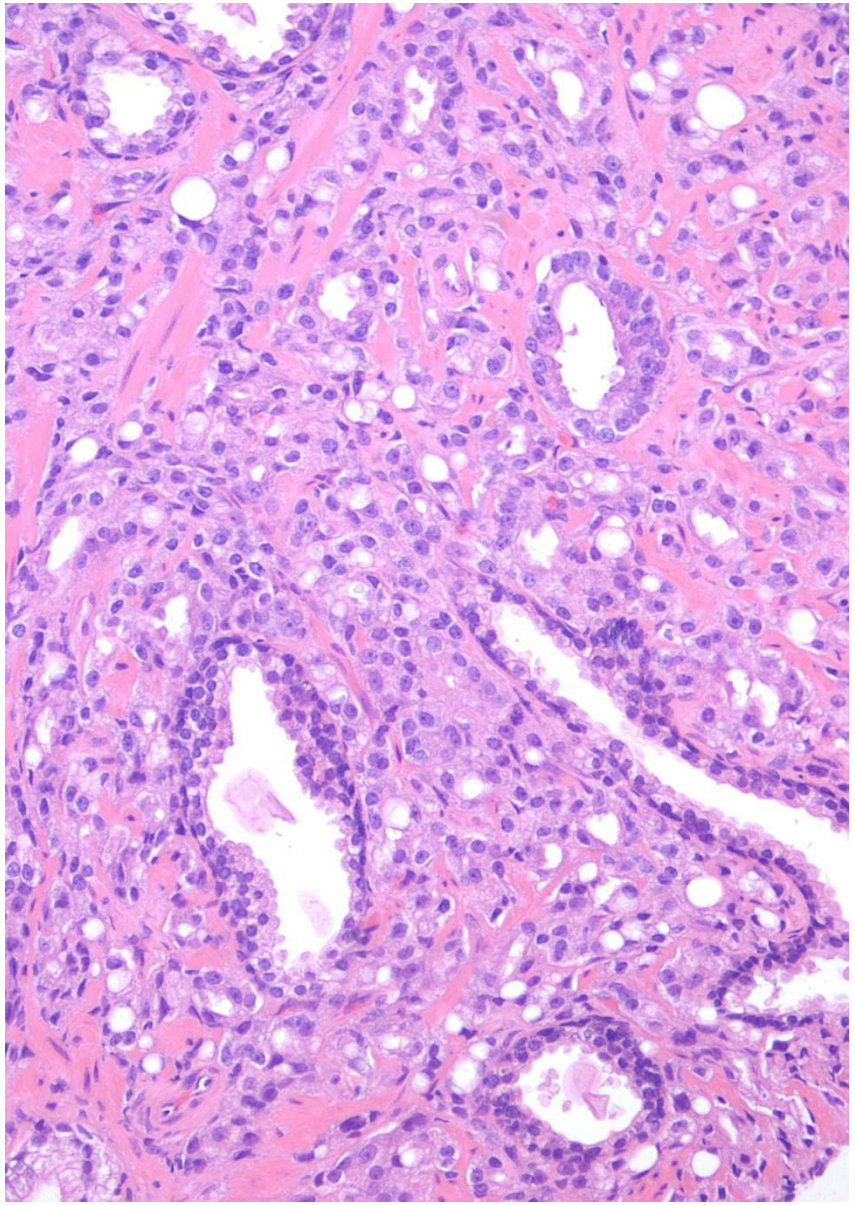
Large cribriform

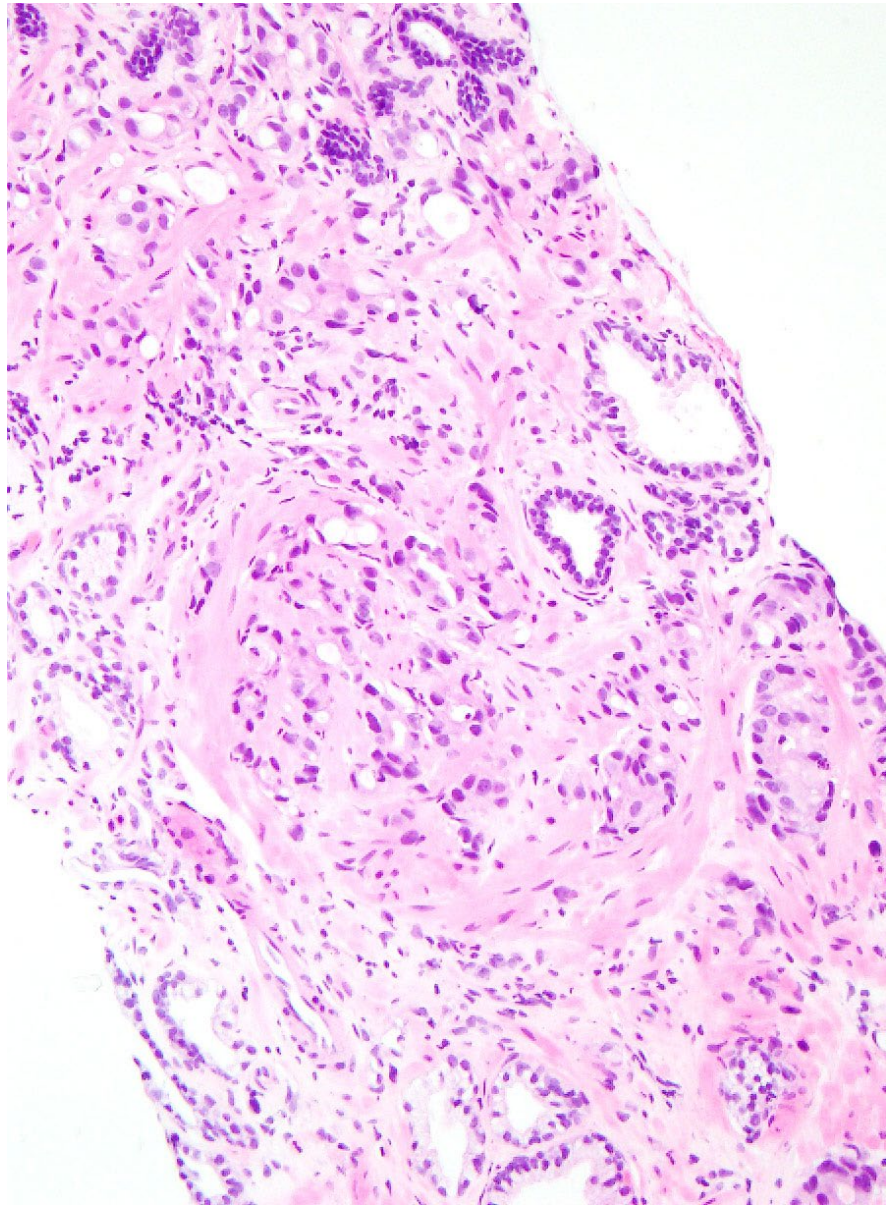


Fused microacinar

MODIFIED GP4 - POORLY FORMED GLANDS



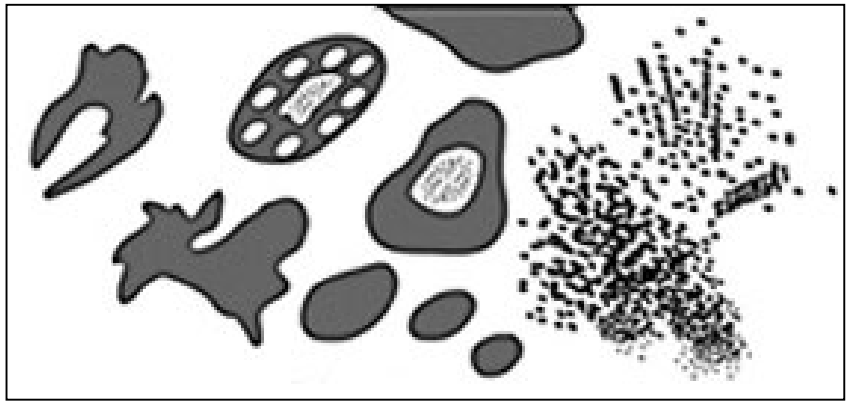




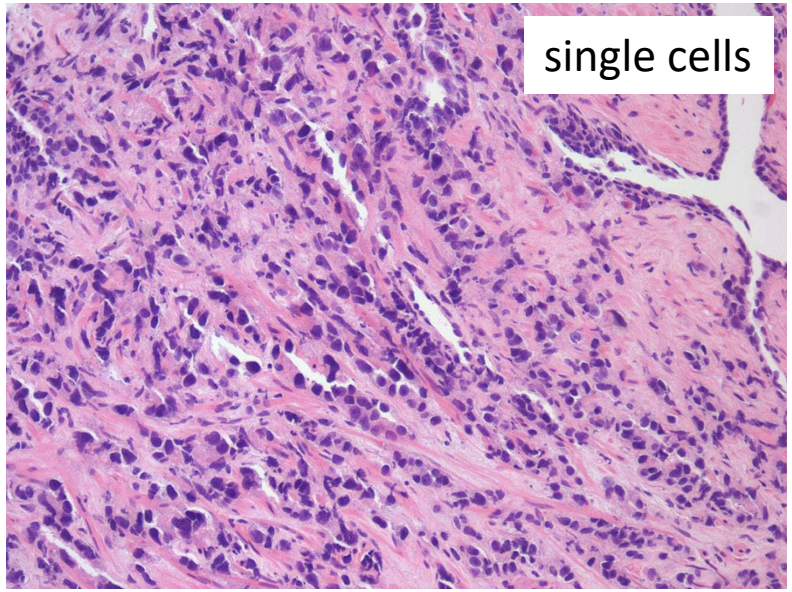
EVOLUTION OF GLEASON PATTERN 5

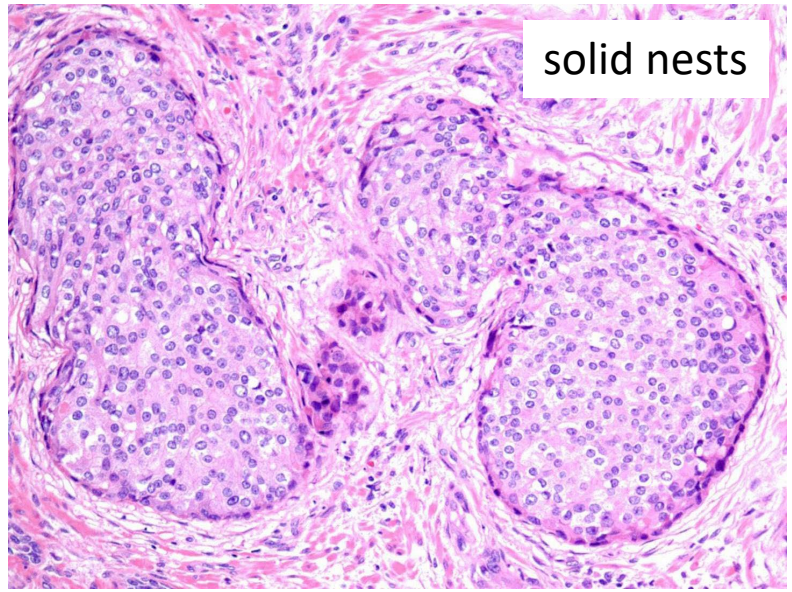
2014 ISUP modified

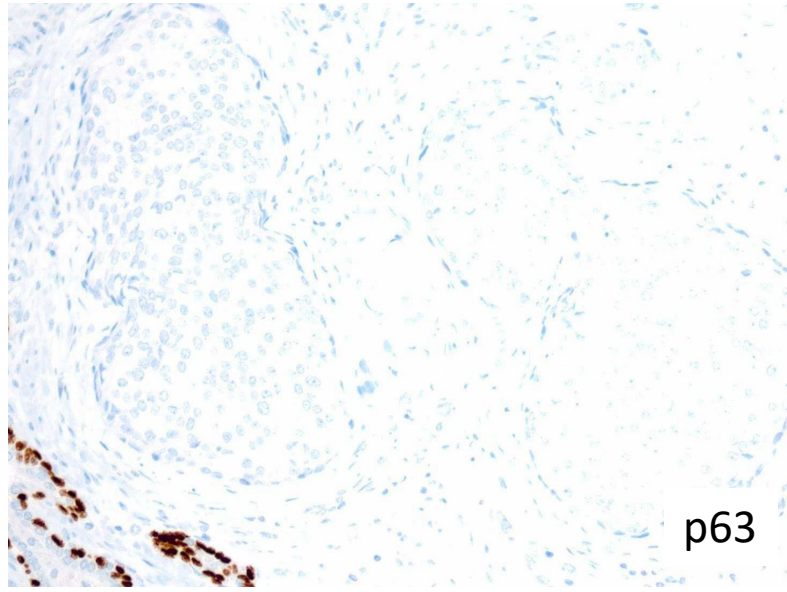
Epstein et al. AJSP 40, 2016



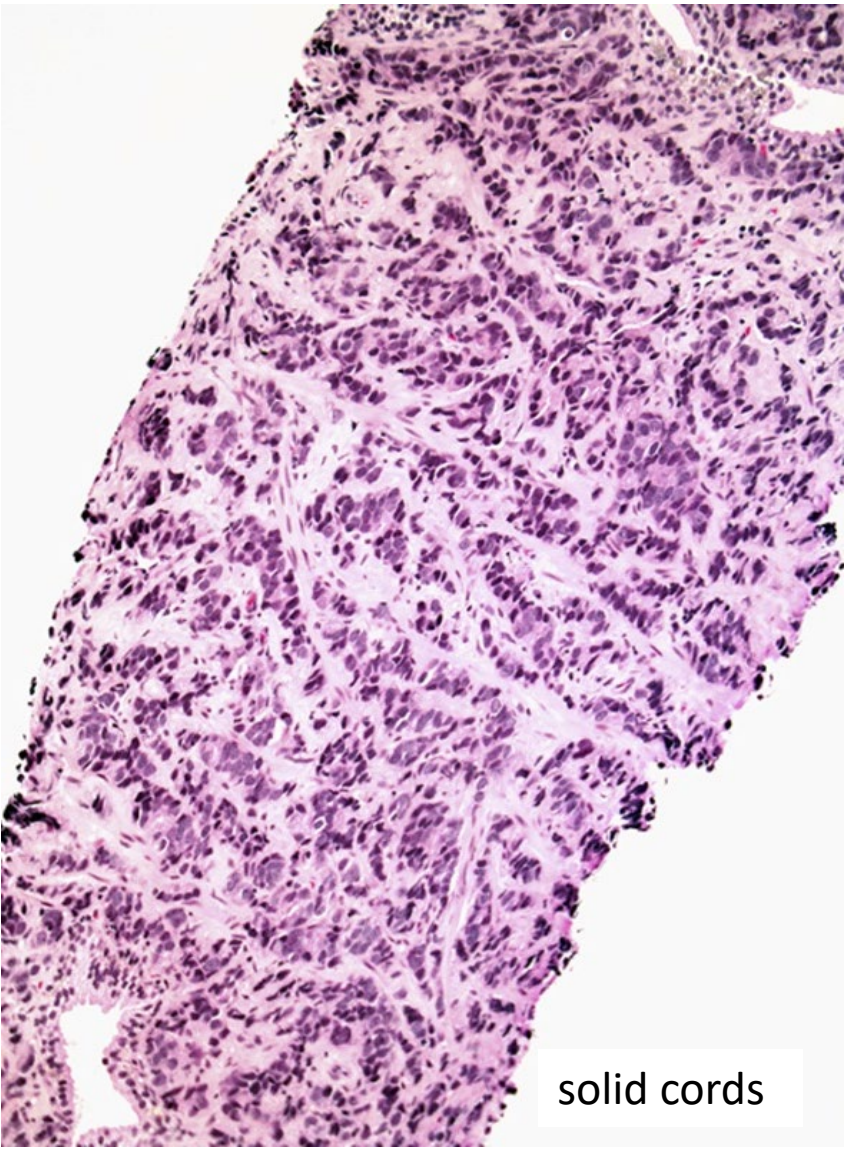
- Small solid cylinders
- Solid medium-to-large nests with rosette-like spaces
- Single cells
- *Unequivocal comedonecrosis*

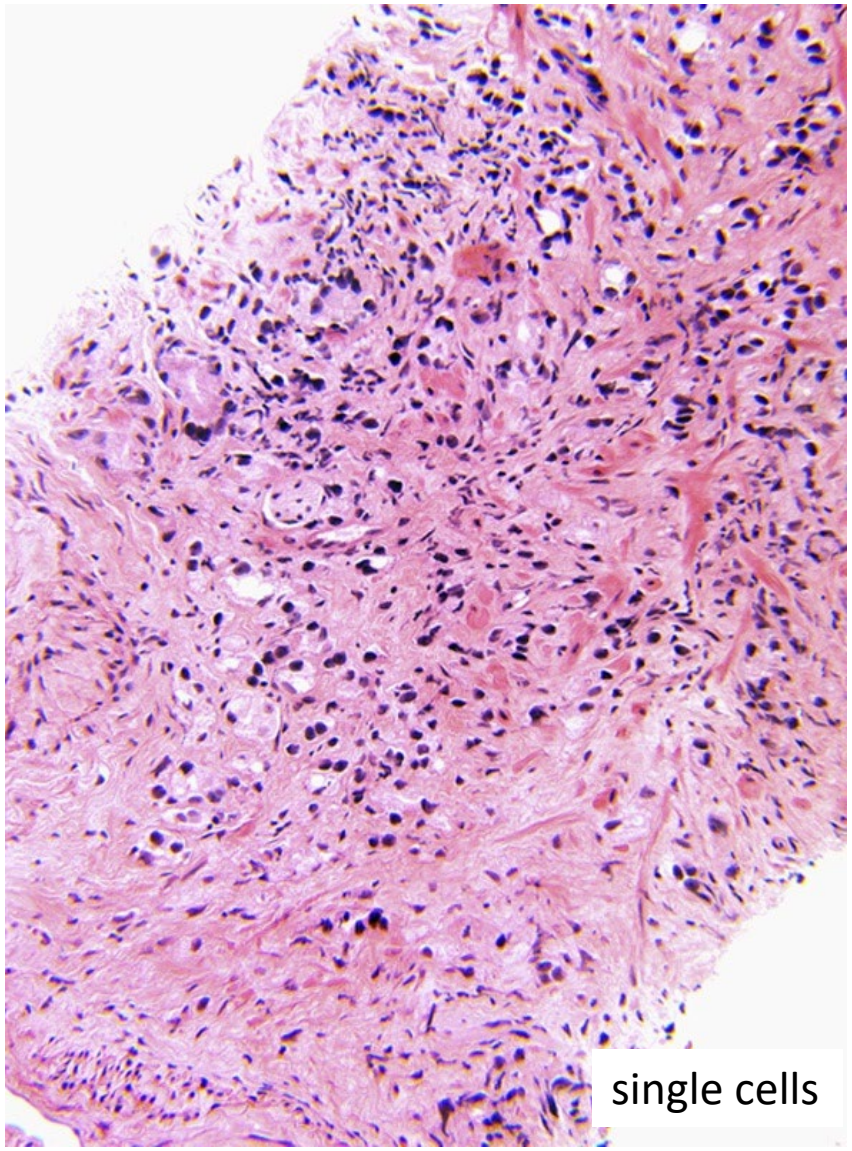


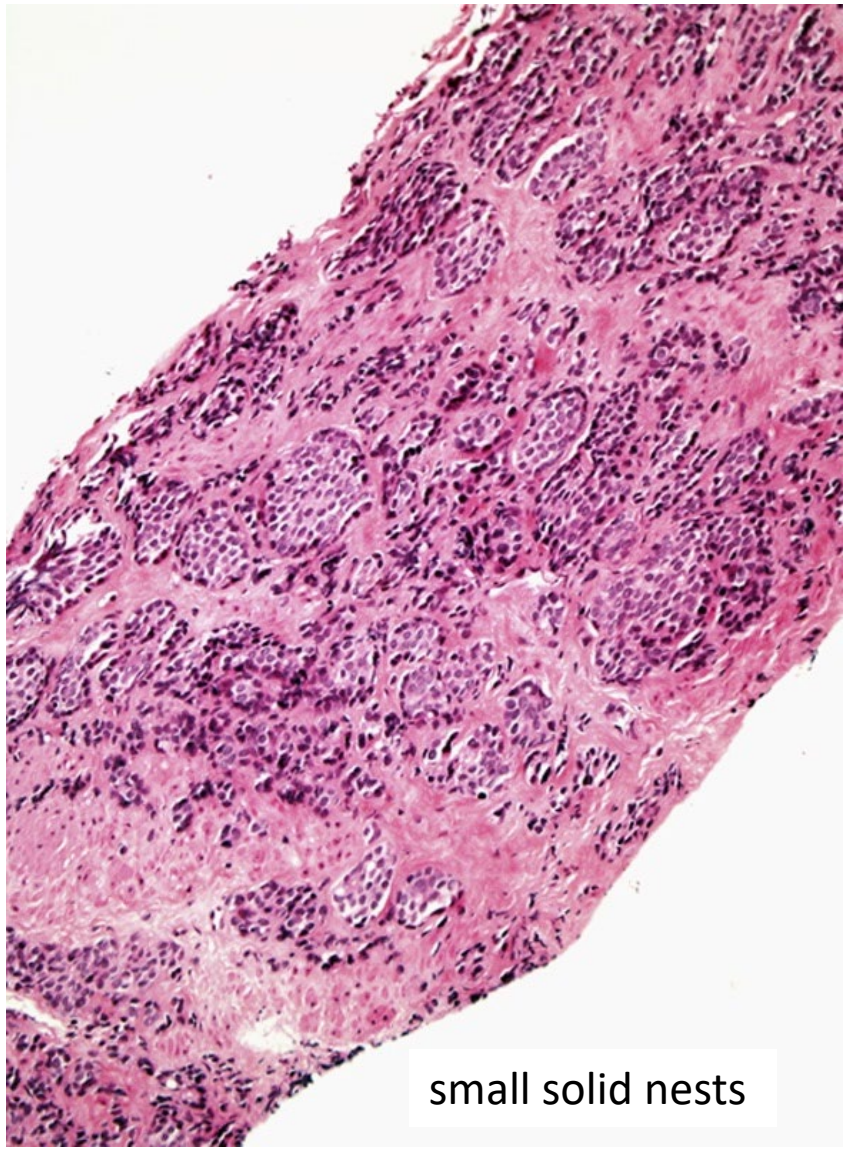




GLEASON PATTERN 5

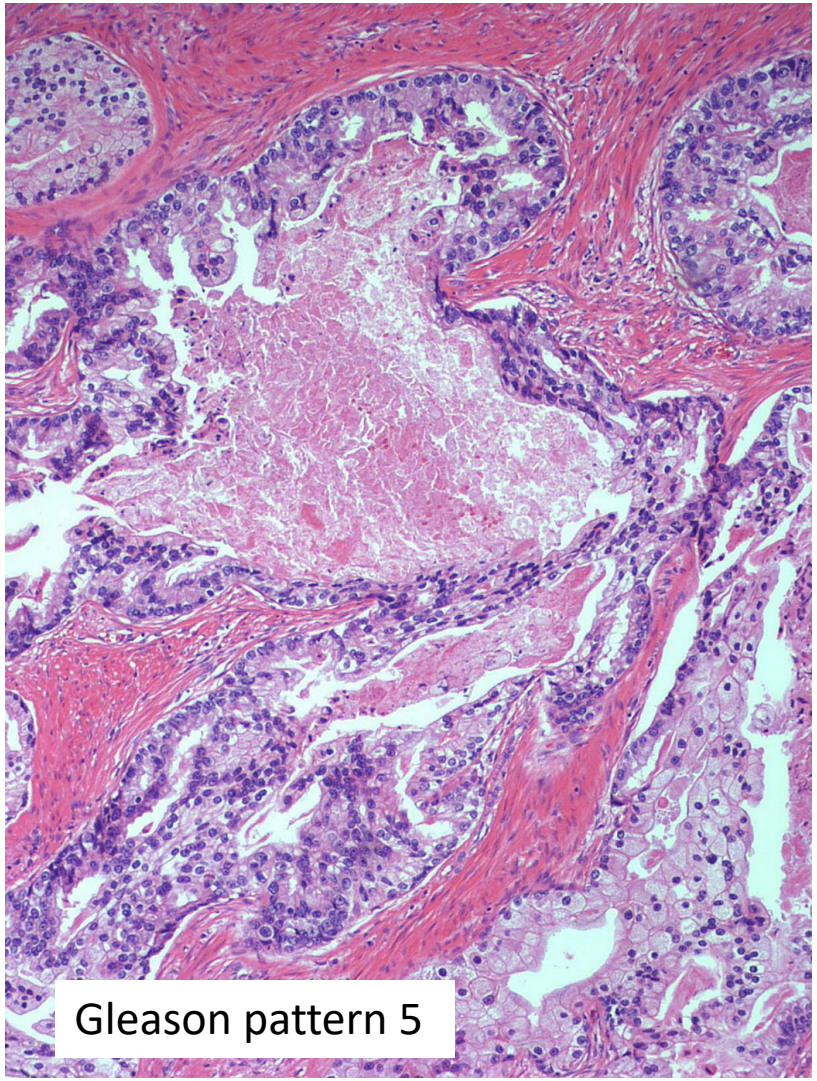

solid cords

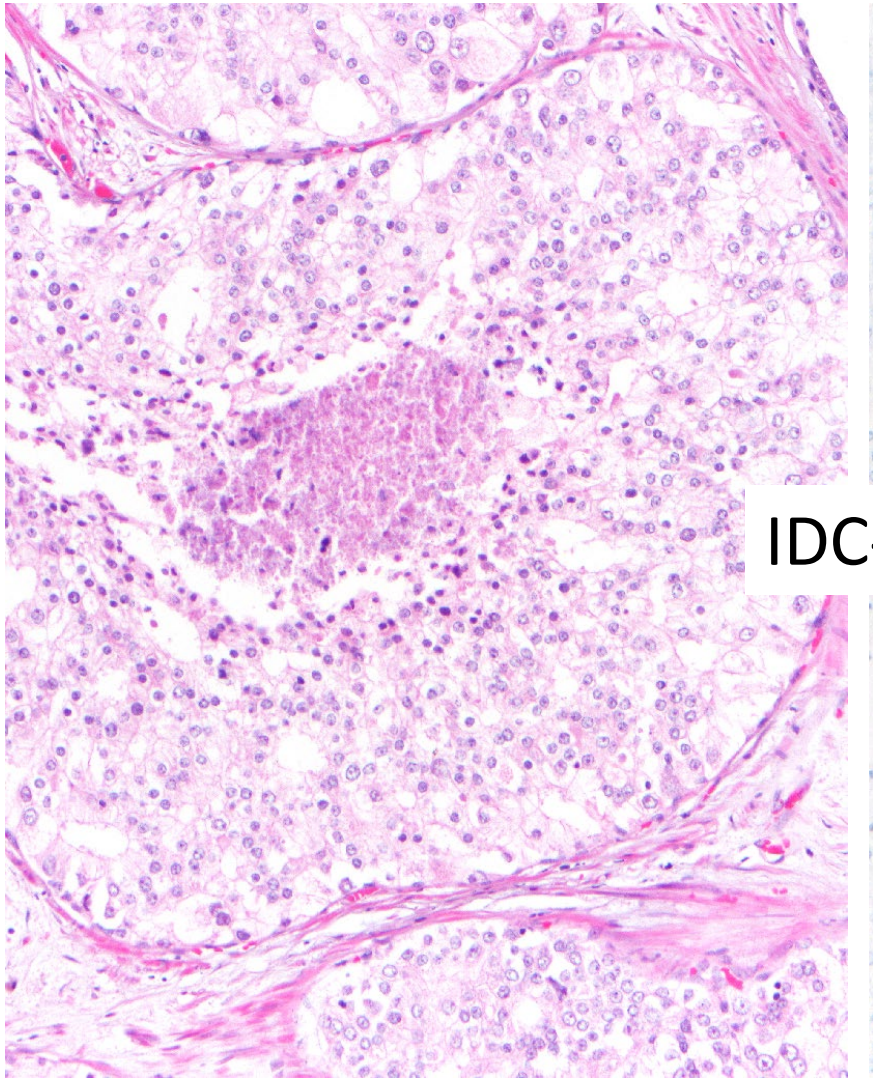

single cells

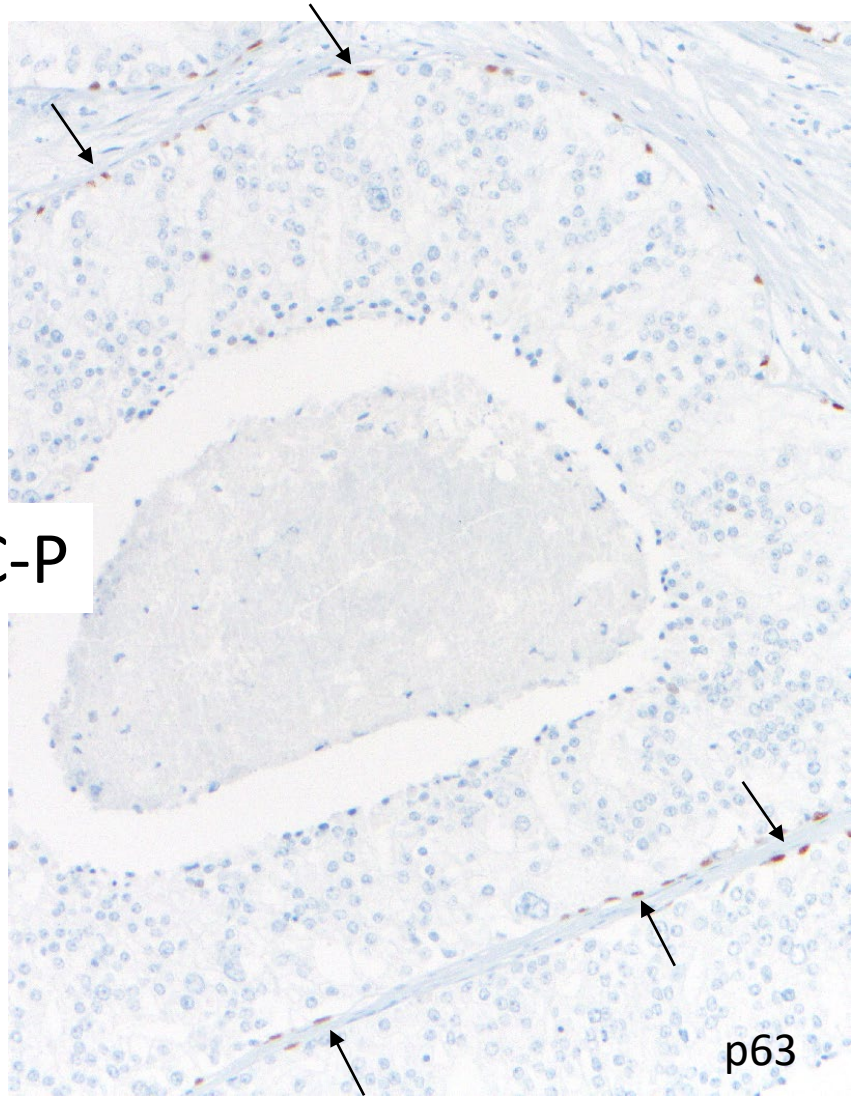

small solid nests

Gottipati et al. Am J Surg Pathol 2012

COMEDONECROSIS





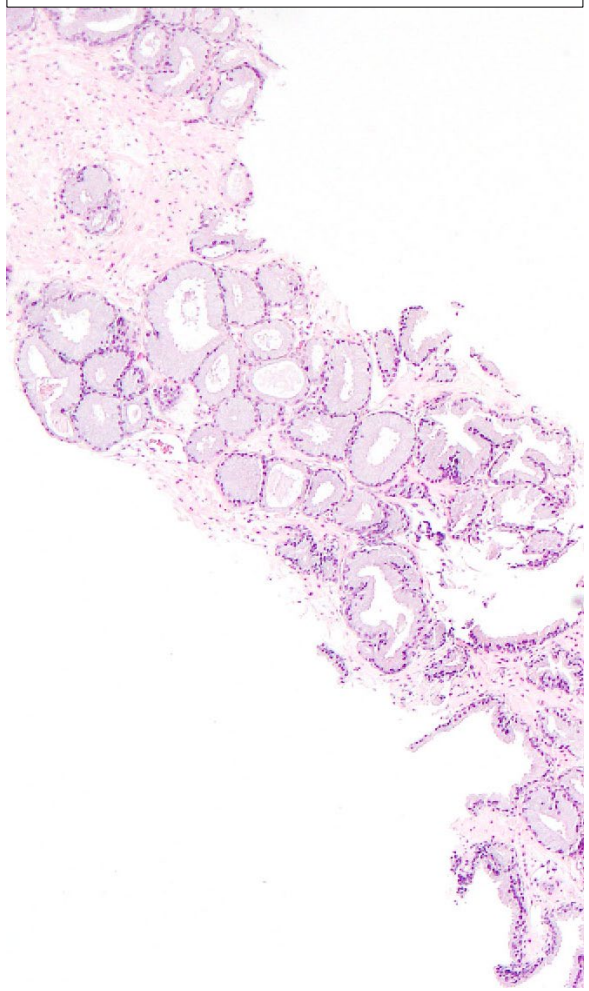


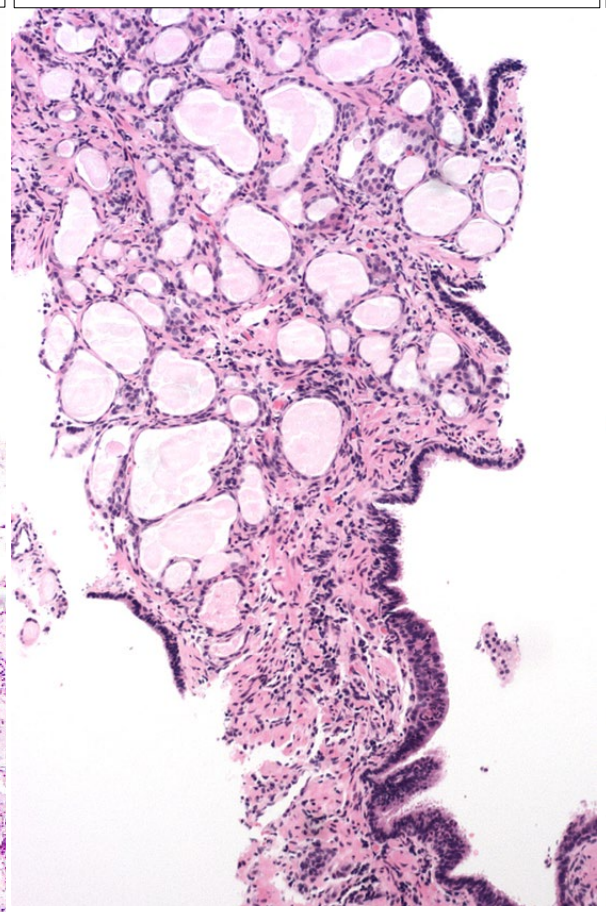
Fine et al. Am J Surg Pathol 2018; Madan et al. Histopathology 2019

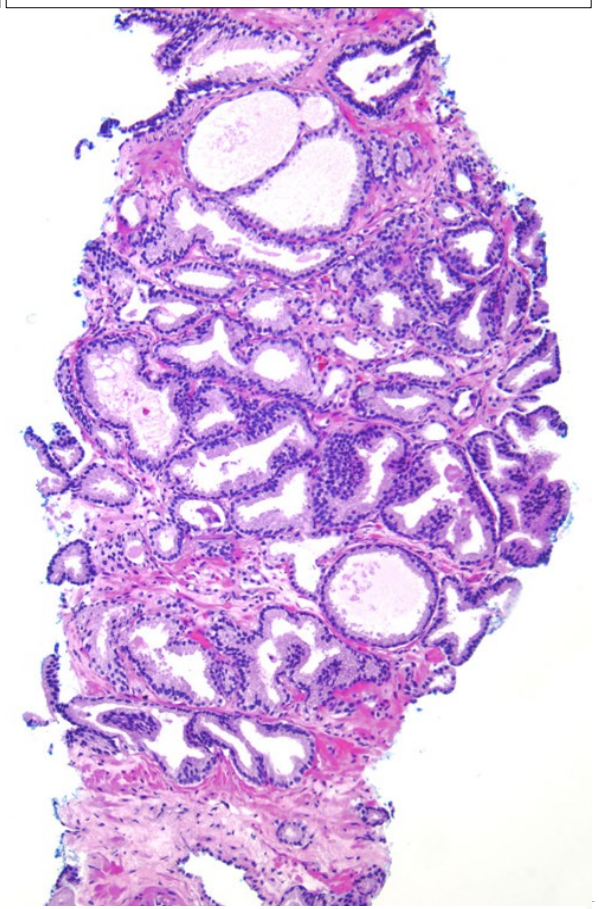
PROSTATIC ACINAR ADENOCARCINOMA

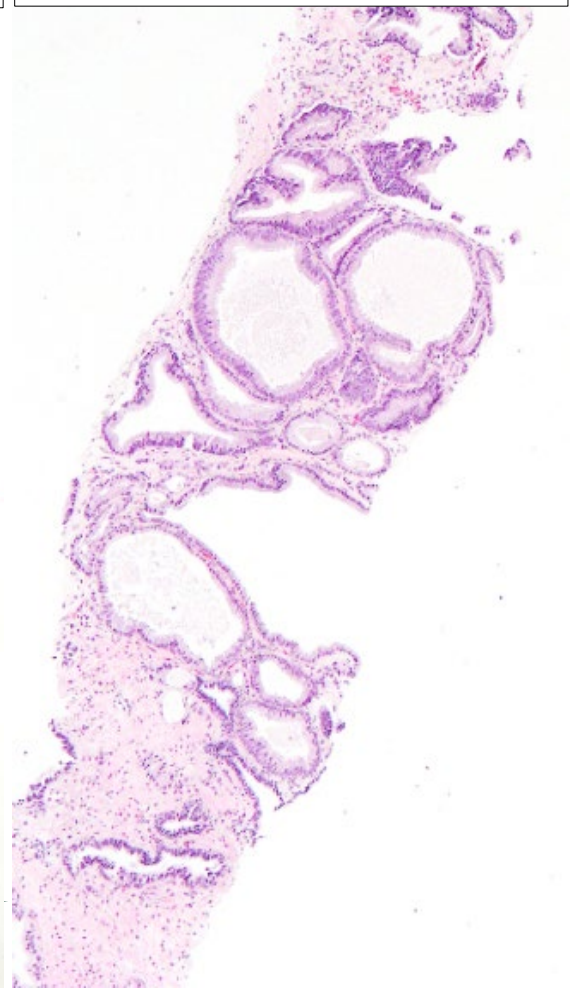
Unusual Histological Patterns

Foamy	Atrophic	Pseudohyperplastic	Microcystic





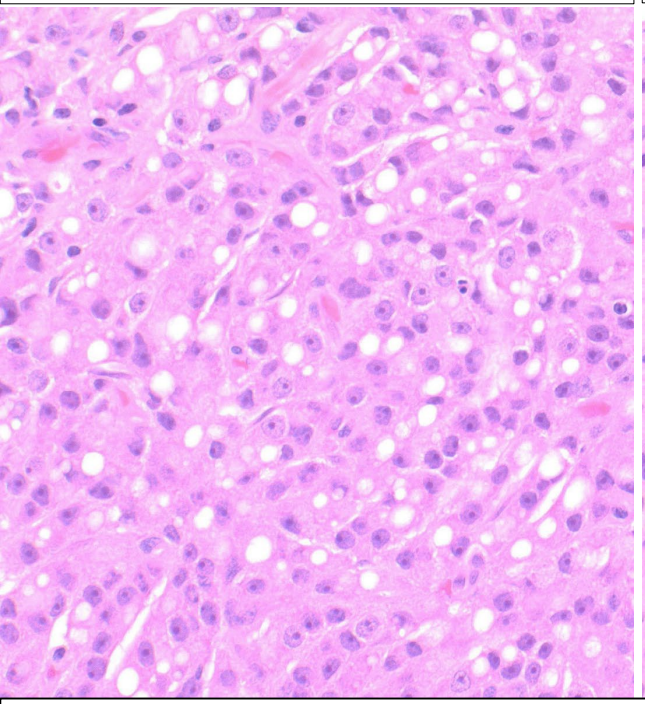
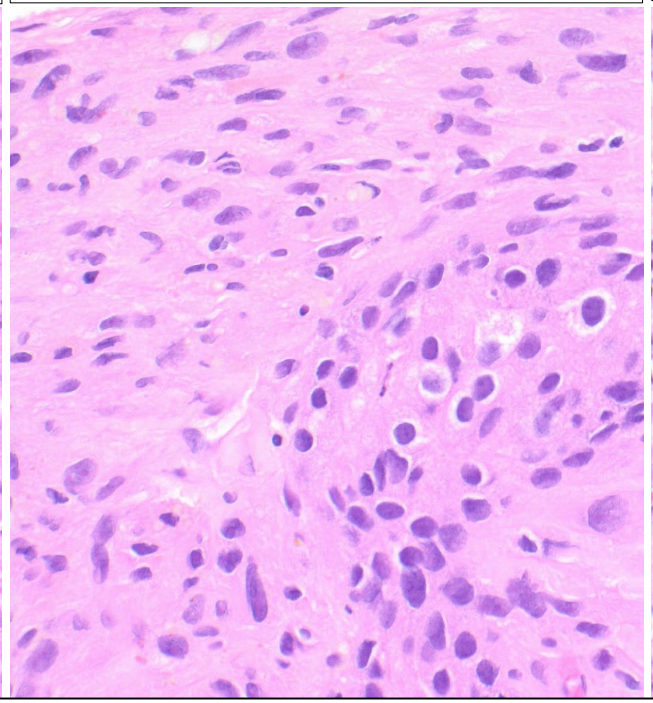
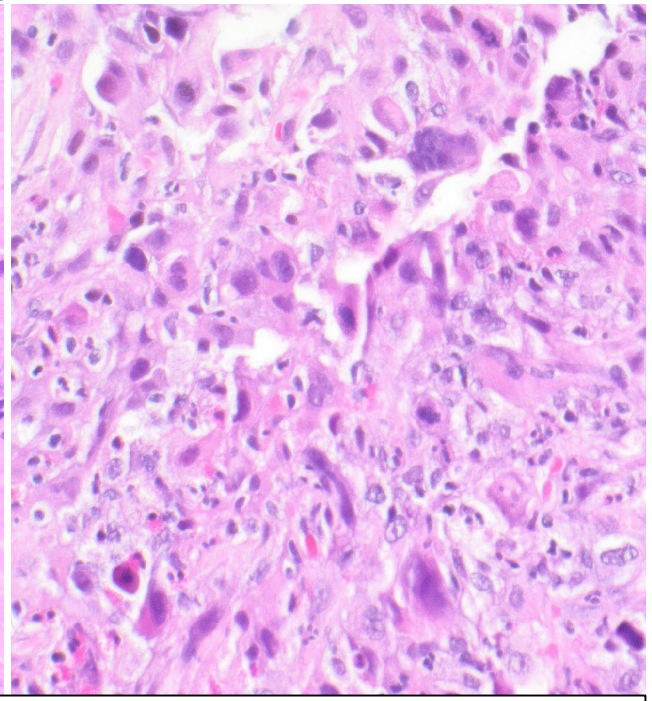
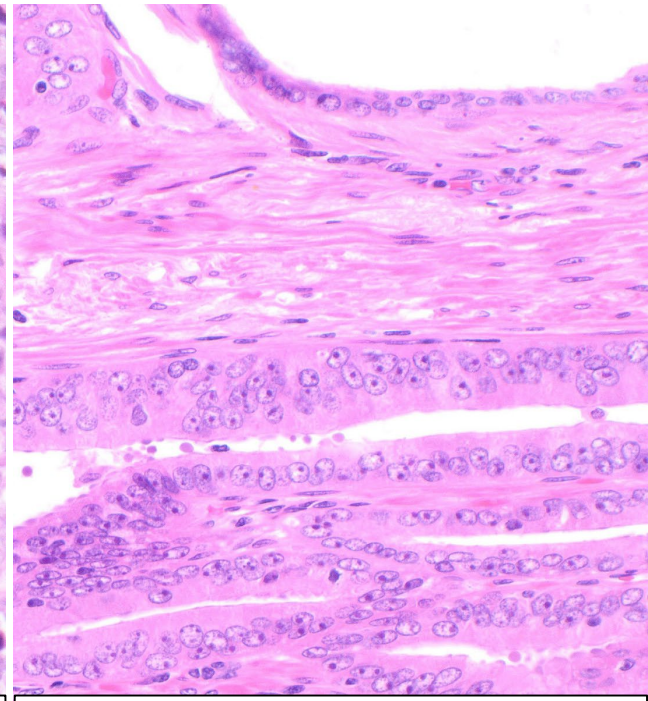




Gleason score 3+3=6 (WHO Grade Group 1)

PROSTATIC ACINAR ADENOCARCINOMA

Special Subtypes (morphologically distinct and have prognostic significance)

Signet ring-like cell	Sarcomatoid	Pleomorphic giant cell	PIN-like carcinoma
			
WHO Grade Group 5			WHO Grade Group 1

Previously a pattern of ductal adenocarcinoma

PITFALLS

- **Fused glands** (modified Gleason pattern 4):
  - May be under-graded when present in small foci
  - On the other hand, careful evaluation of multiple tissue levels may be necessary to determine whether few glands are truly fused or simply tangentially cut

- **Ill-defined or poorly formed glands**:
  - Ill-defined glands with poorly formed glandular lumina should be graded as pattern 4
  - Caution should be applied in distinguishing them from tangentially sectioned very small “well-formed” (Gleason pattern 3) glands

2014 ISUP CONSENSUS CONFERENCE ON GLEASON GRADING

Recommendations:

- For a diagnosis of Gleason pattern 4, it needs to be seen at x10 lens magnification

- Occasional/seemingly poorly formed or fused glands between well-formed glands is insufficient for a diagnosis of pattern 4

- In cases with borderline morphology between pattern 3 and 4 and crush artifacts, the **lower grade** should be favored

DIAGNOSIS OF "POORLY FORMED GLANDS" GLEASON PATTERN 4

Definition

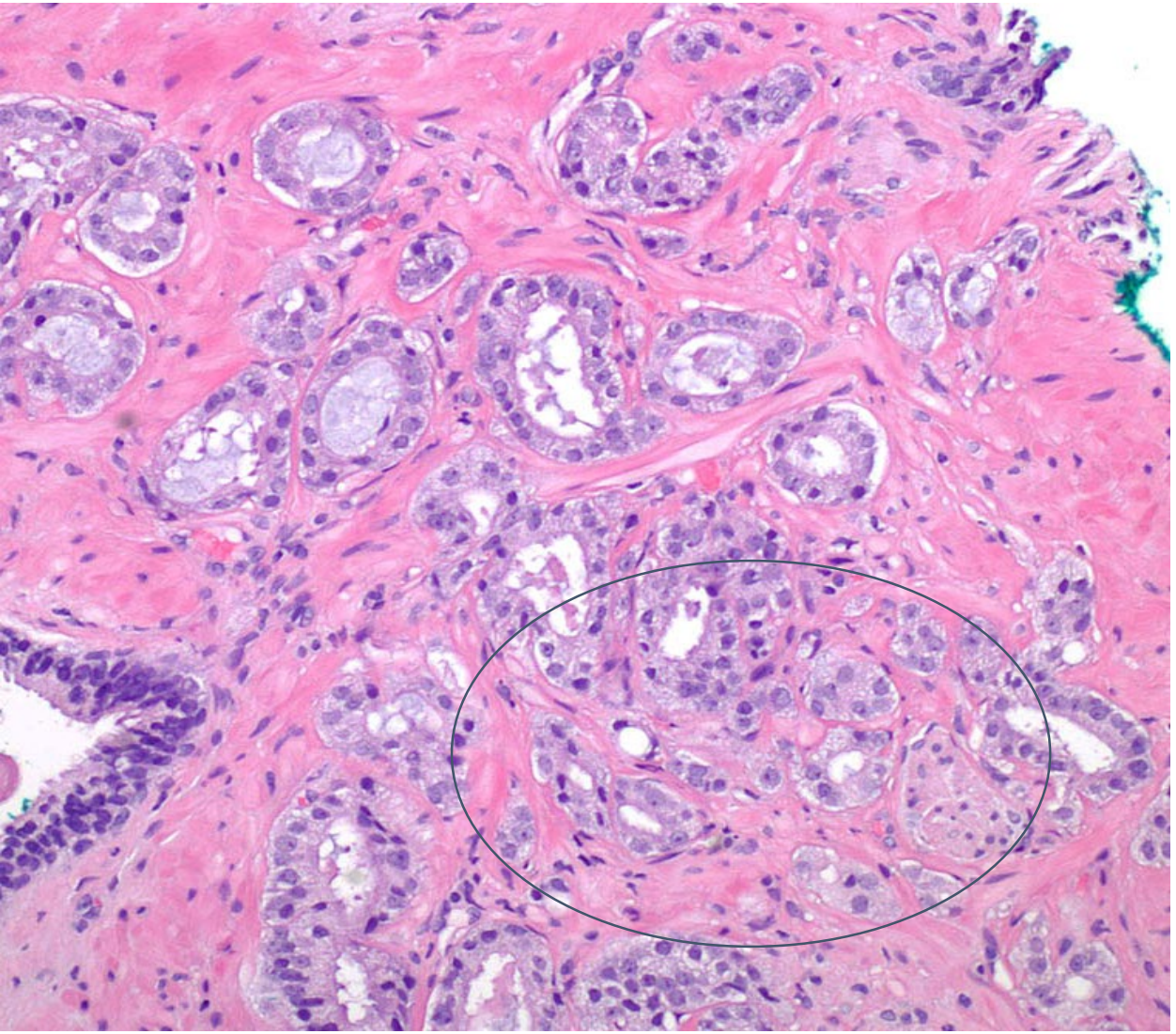
- Cancer glands with no or rare lumens
- Elongated compressed glands
- Elongated nests

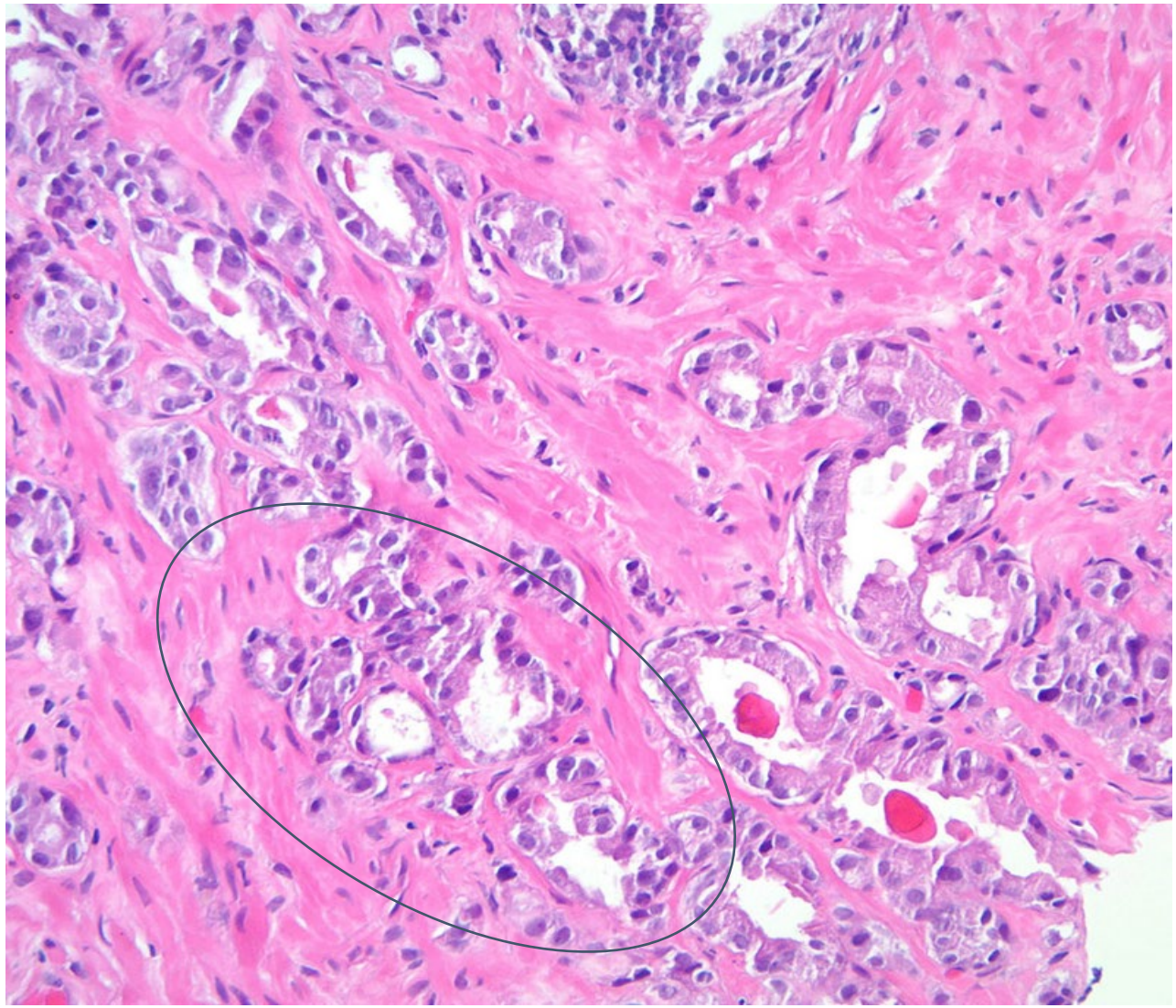
Consensus diagnosis (>70% agreement) was correlated with **quantitative** (≤5, 6-10, >10 glands) and **topographic** features (clustered, immediately adjacent to, and intermixed with other well-formed glands)

- Poorly formed glands immediately adjacent to well-formed glands regardless of number, and small foci of ≤5 poorly formed glands regardless of location were **not graded** as GP4
- Large foci of **>10 poorly formed glands** not immediately adjacent to well-formed glands were graded as GP4

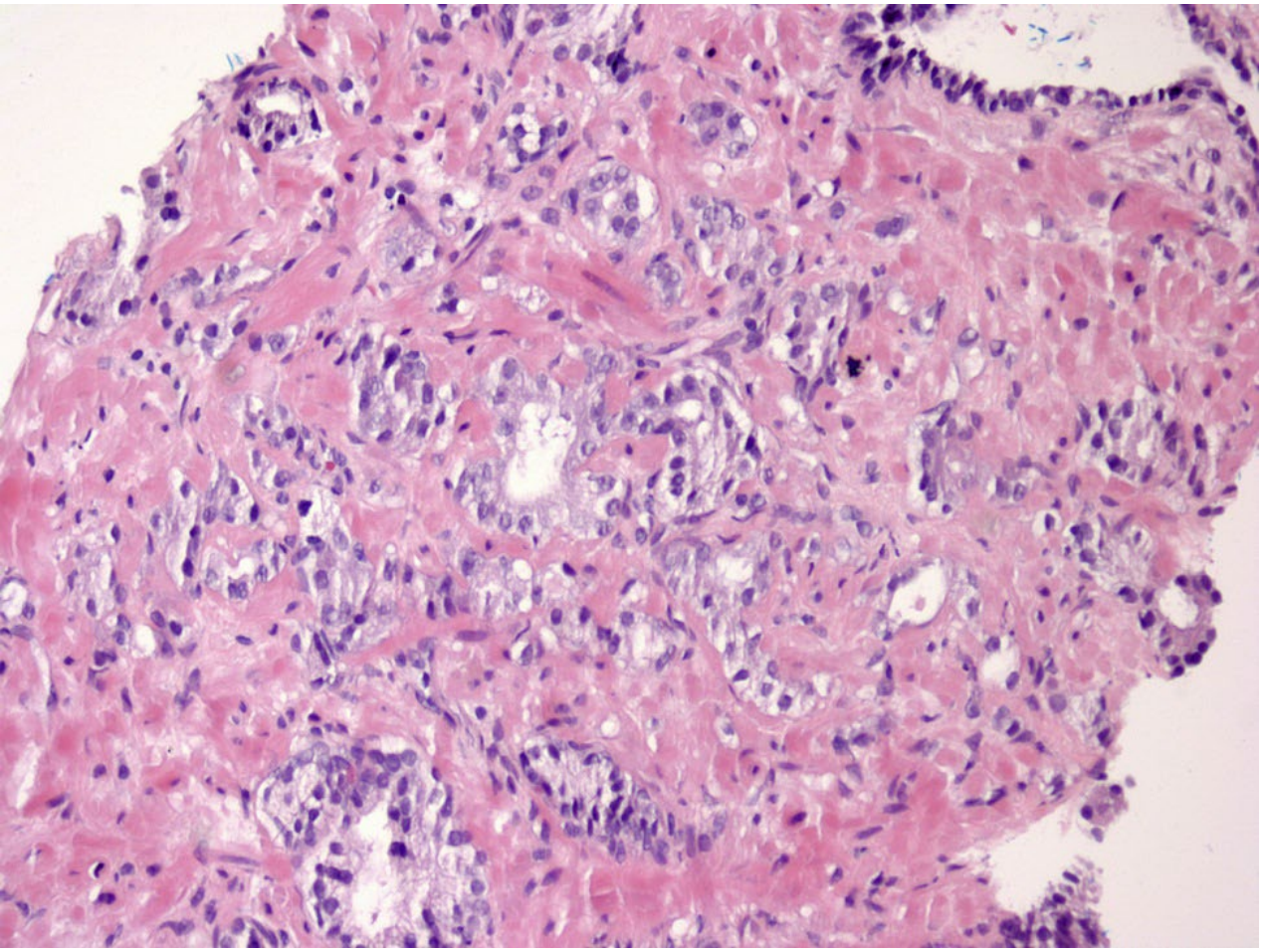
Zhou M et al. Am J Surg Pathol 2015

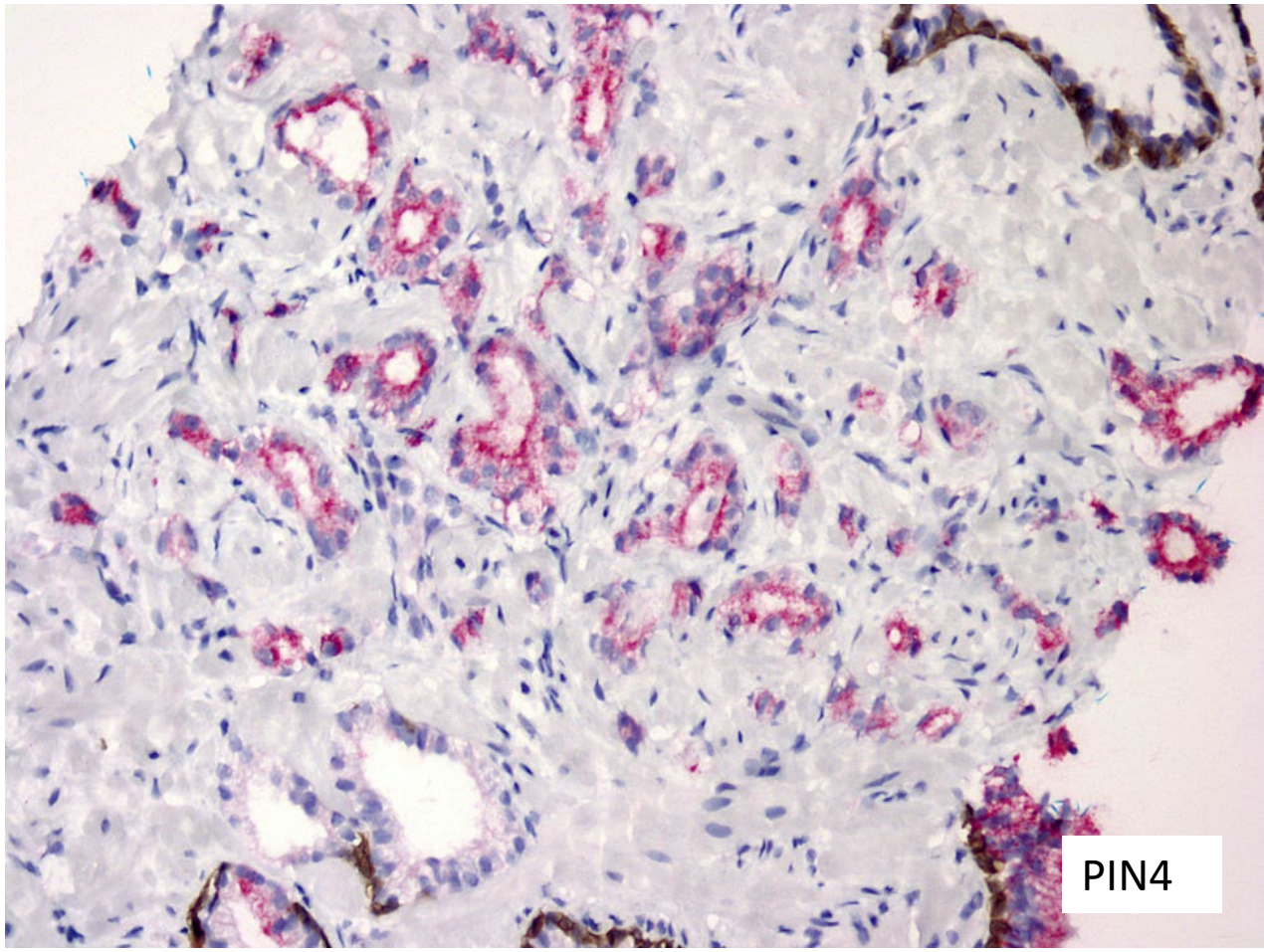
GLEASON SCORE 3+3=6



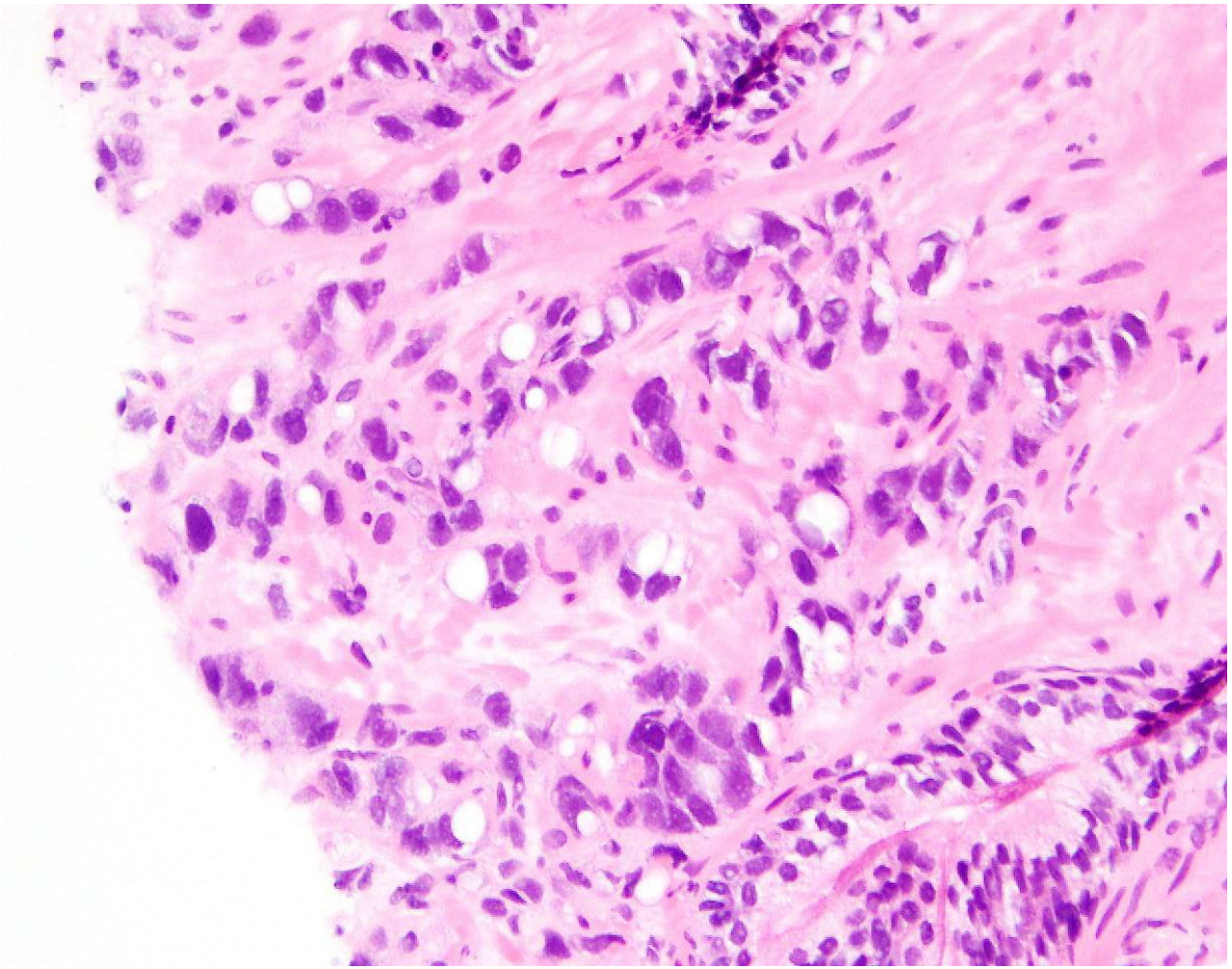


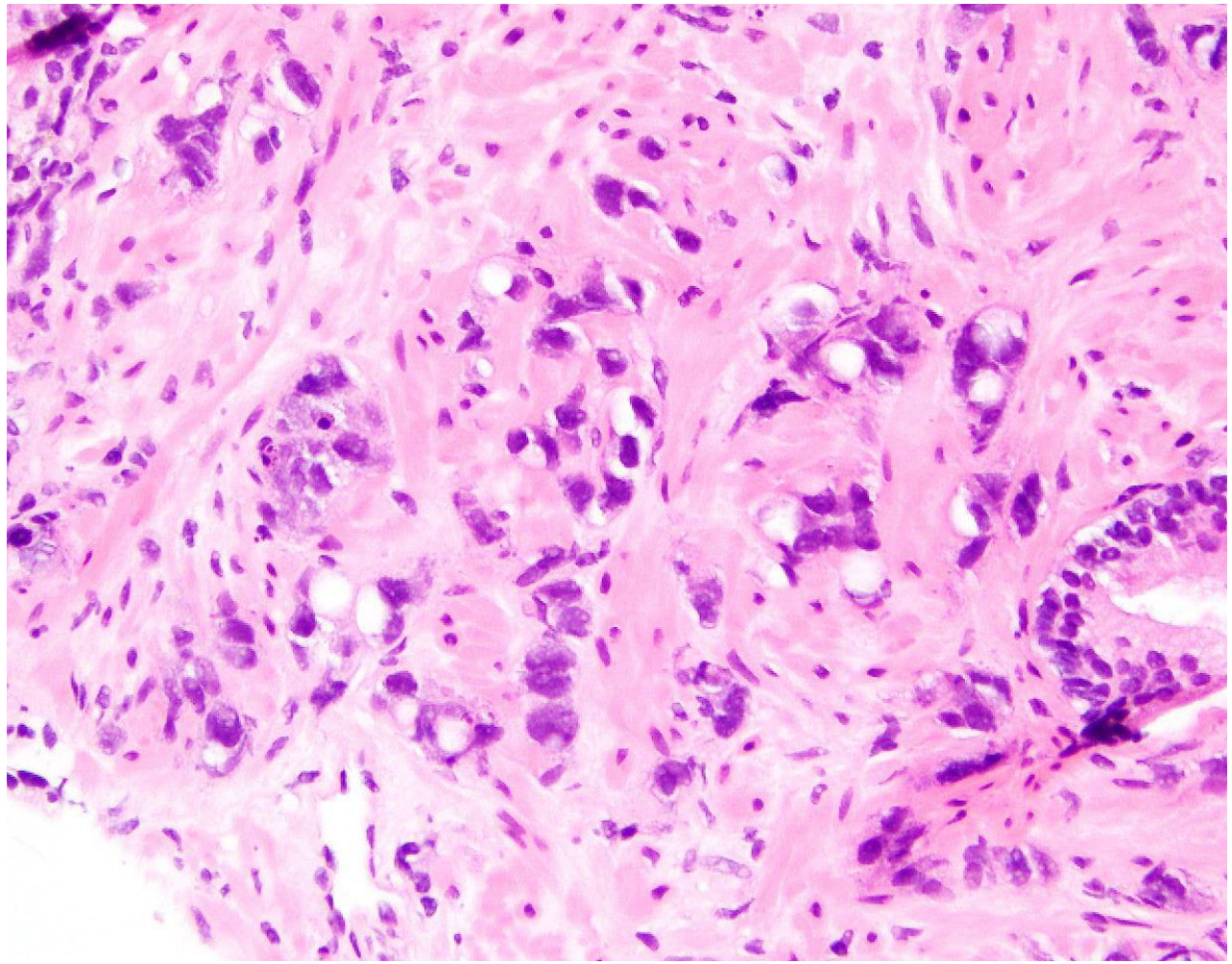
GLEASON SCORE 3+3=6 VS. **3+4=7**





POORLY FORMED GLANDS (PATTERN 4) V. SINGLE CELLS (PATTERN 5)?





Evaluate multiple levels!!!

CRITERIA FOR ACTIVE SURVEILLANCE

Institution (year)	Clinical stage	PSA	PSA density	Biopsy GS	# positive cores	% core involvement
Royal Marsden ('05)	T1-T2	≤15	--	≤3+4	≤50% total cores	--
U. of Toronto ('09)	T1c/T2a	≤10	--	≤6	--	--
PRIAS ('09)	T1c/T2	≤10	<0.20	≤6	≤2	--
UCSF ('08)	T1-T2	≤10	--	≤6	≤1/3 total	≤50%
MSK ('11)	T1-T2a	≤10	--	≤6	≤3	≤50%
U. of Miami ('10)	≤T2	≤10	--	≤6	≤2	≤20%
JHU ('06)	T1c	--	≤0.15	≤6	≤2	≤50%
Canary	T1/T2	any	any	≤7	any	

GRADE GROUP SYSTEM

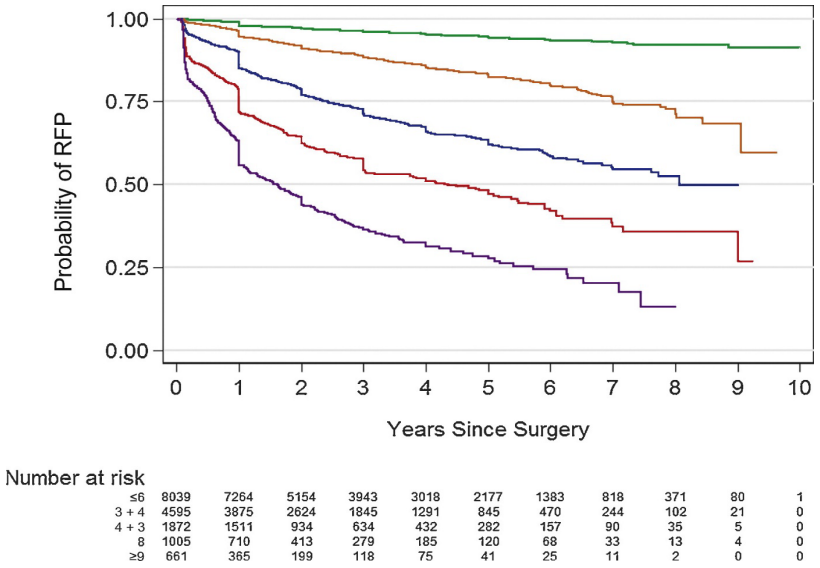
Grade Group 1	**GS ≤6**	Only individual discrete well-formed glands
Grade Group 2	**GS 3+4=7**	Predominantly well-formed glands with lesser component of poorly-formed/fused/cribriform glands
Grade Group 3	**GS 4+3=7**	Predominantly poorly-formed/fused/cribriform glands with a lesser component of well-formed glands
Grade Group 4	**GS 4+4=8** **GS 3+5=8** **GS 5+3=8**	Only poorly-formed/fused/cribriform glands Predominantly well-formed glands with a lesser component lacking glands Predominantly lacking glands with a lesser component of well-formed glands
Grade Group 5	**GS 9/10**	Lacks gland formation (or with necrosis) with or w/o poorly-formed/fused/cribriform glands

Pierorazio et al. BJU Int 2013; Epstein JI et al. AJSP 2016

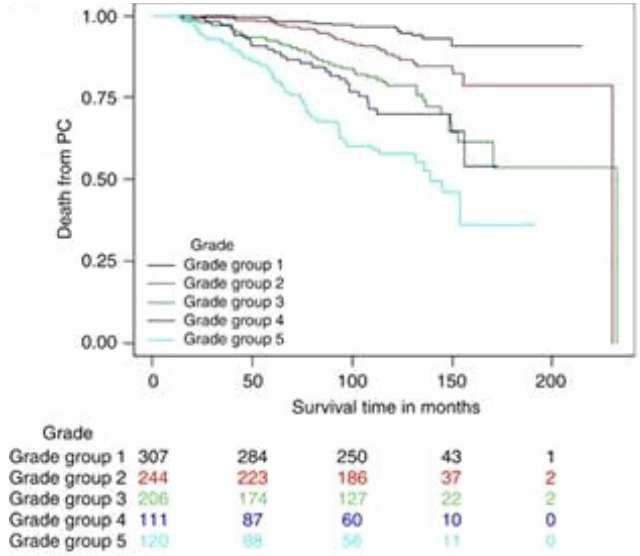
IMPACT OF THE MODIFIED GLEASON GRADING AND GRADE GROUPS

- Provides clearer labels for patient understanding
- Defines a more homogenous low-risk group (i.e. Grade Group 1)
- Distinguishes Grade Group 2 (**3+4=7**) (AS eligible) from Grade Group 3 (**4+3=7**) (AS non-eligible)
- Provides greater discrimination in prognosis than traditional Gleason classification

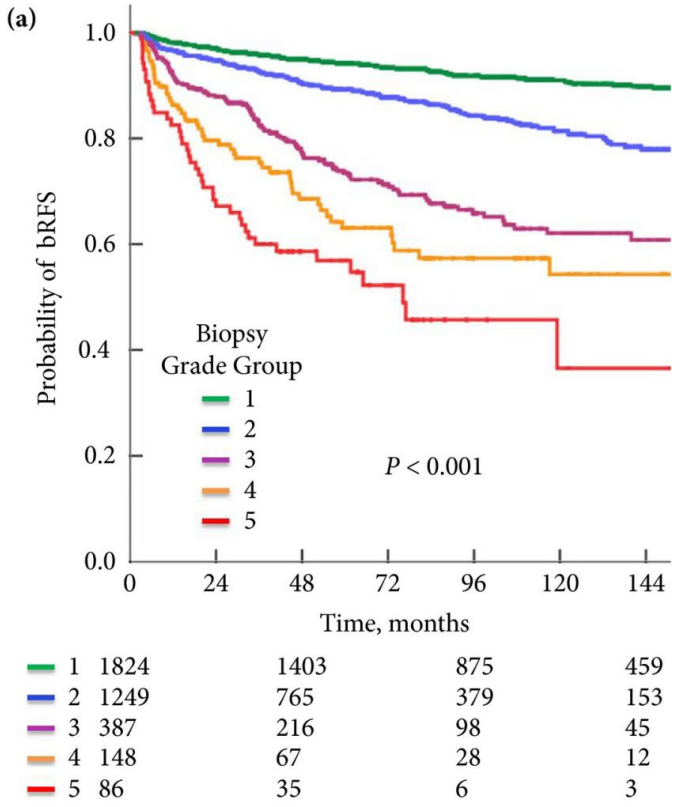
5-Grade Groups (GG) system validation



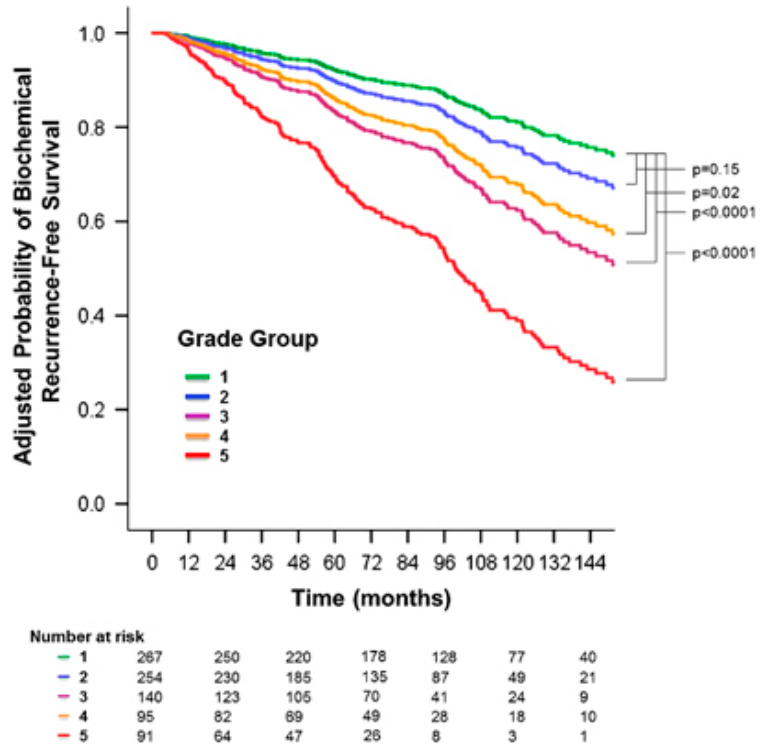
Epstein JI et al. Eur Urol 2016 (20,800 men)



Berney et al. British Journal of Cancer 2016 (988 men treated conservatively)



Spratt et al. BJUI 2016 (3,700 cases)



Spratt et al. Prostate Cancer Prostatic Dis 2016 (847 radiation-treated)

UPDATE ON REPORTING

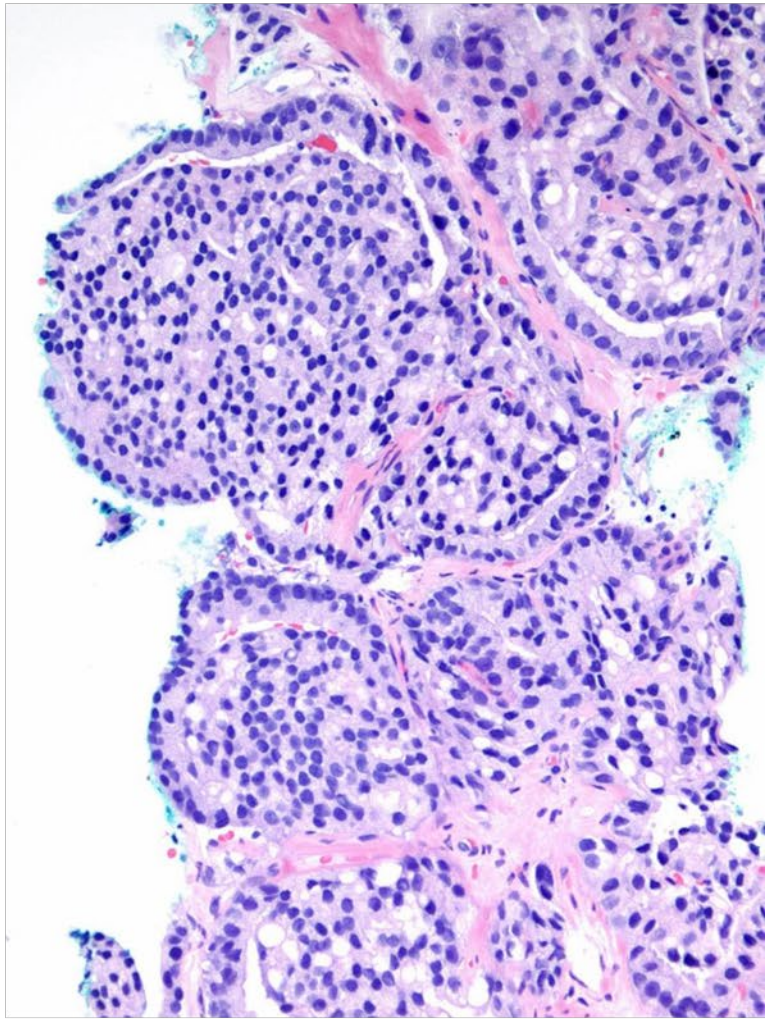
REPORTING % PATTERN 4 AND CRIBRIFORM MORPHOLOGY

- ISUP 2014 recommended reporting **% GP4** in **GS7 tumors** (implications for surveillance, XRT)
  - 3+4=7 PCA with <5% pattern 4 is associated with low-risk tumor on RP

  [Huang et al. AJSP 2014, Kir at al. Ann Diagn Pathol 2016]

- **Cribriform morphology** is associated with adverse outcome
  - meta-analysis of 14 publications determined an OR of 11.37 for adverse outcome in cribriform PCA

  [Luo X et al. Mod Pathol 2017, Iczkowski KA et al. Adv Anat Pathol 2017]



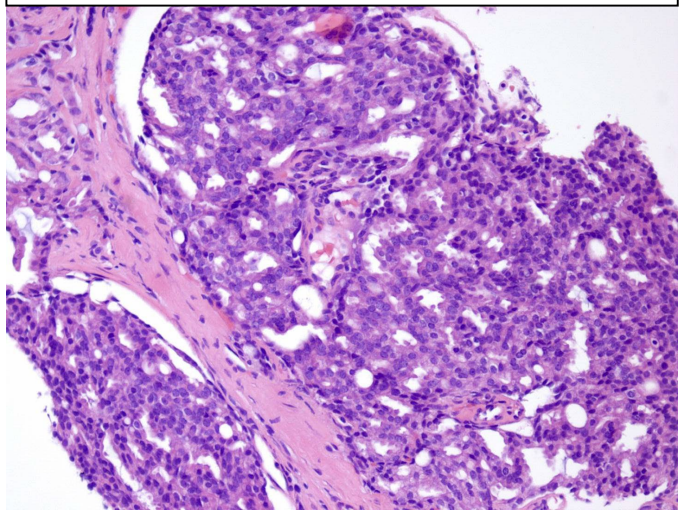
REPORTING PERCENTAGE PATTERN 4 IN GS7 TUMORS

Relationship between % GP4 and prognosis of PCA patients undergoing RP				
study [author, yr.]	**# of patients**	**specimen type**	**separation method of GP4**	**significance of RP %GP4**
Cheng et al. 2007	504	RP	0%/1-20/>20% (GP4, GP5, or both)	indep. predictor of CSS
Huang et al. 2014	256	Bx	≤5/6–50%	predictor of pT3 on RP
Choy et al. 2016	585	RP	1-5/6-10/11-20/2-30/31-40/41-50/51-60/61-70/71-80/81-90%	indep. predictor of BCR
Cole et al. 2016	1,691	Bx	1-9.9/10-19.9/20-39.9/40-59.9/60-79.9/80-100%	indep. predictor of BCR
Kir et al. 2016	372	Bx	<6/6–25/26/49/≥50%	indep. predictor of BCR
Sauter et al. 2016	12,823	Bx and RP	(I) ≤25/26-49/50-74/≥75&; (II) ≤5/6-10/11-20/21-30/31-49/50-60/61-80/>80%	predictor of BCR
Perlis et al 2017	1,255	Bx	1-5/6-10/11-20/21-49%	predictor of pT3 on RP

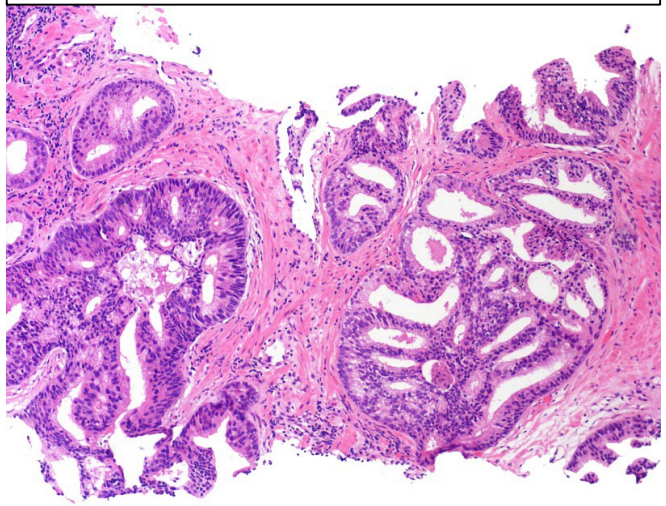
Sharma & Miyamoto Transl Androl Urol 2018

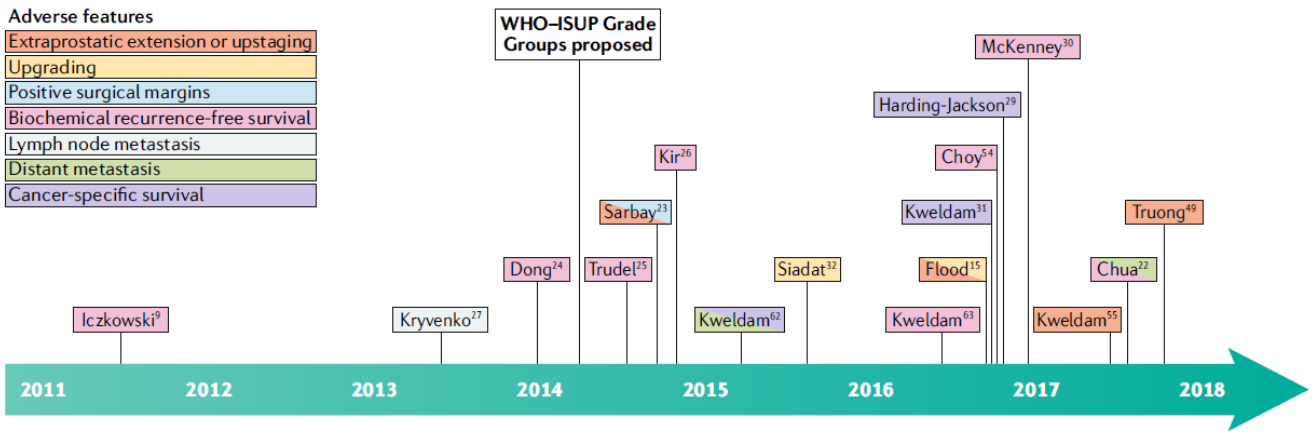
UNFAVORABLE PATHOLOGY

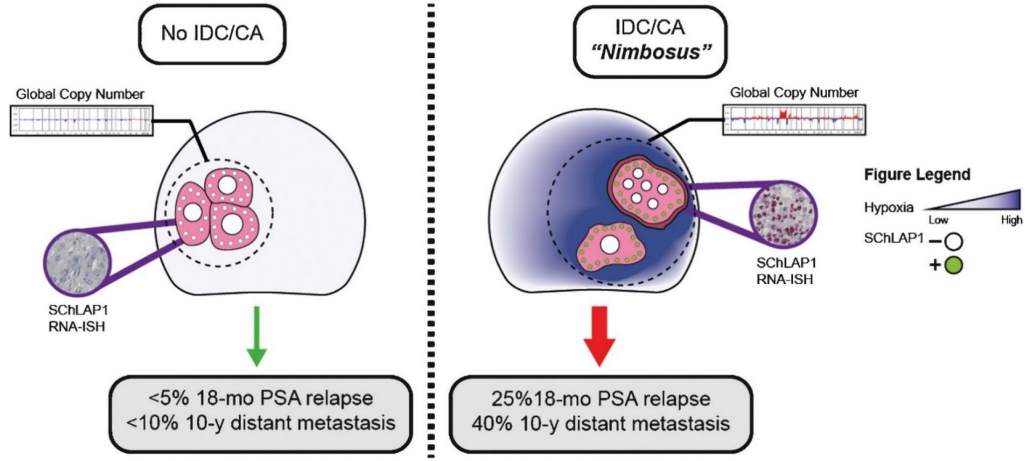
Cribriform morphology



Intraductal carcinoma







Truong et al. Nature Reviews. Urology 2018

Chua et al. Eur Urol. 2017

GUPS VS. ISUP RECOMMENDATIONS

PCA reporting	GUPS 2019 (Epstein et al. Arch Pathol Lab Med 2020)	ISUP 2019 (van Leenders et al. Am J Surg Pathol 2020)
Nomenclature	GG	ISUP GG or GG
%GP4 in GG2-3	Recommends reporting	Recommends reporting
%GP4 in GG2-3 if GG4 in other cores	Recommends reporting	No position
Reporting %GP4	<5%, 10% or <10%, 10% increments	No position
Reporting cribriform GP4	Report presence or absence of cribriform glands in GP4	Invasive cribriform PCA should be commented on in GG2-4
Isolated/pure IDC-P	Do NOT grade	Do NOT grade
IDC-P + invasive PCA	Do NOT grade IDC-P	Incorporating IDCP in GS

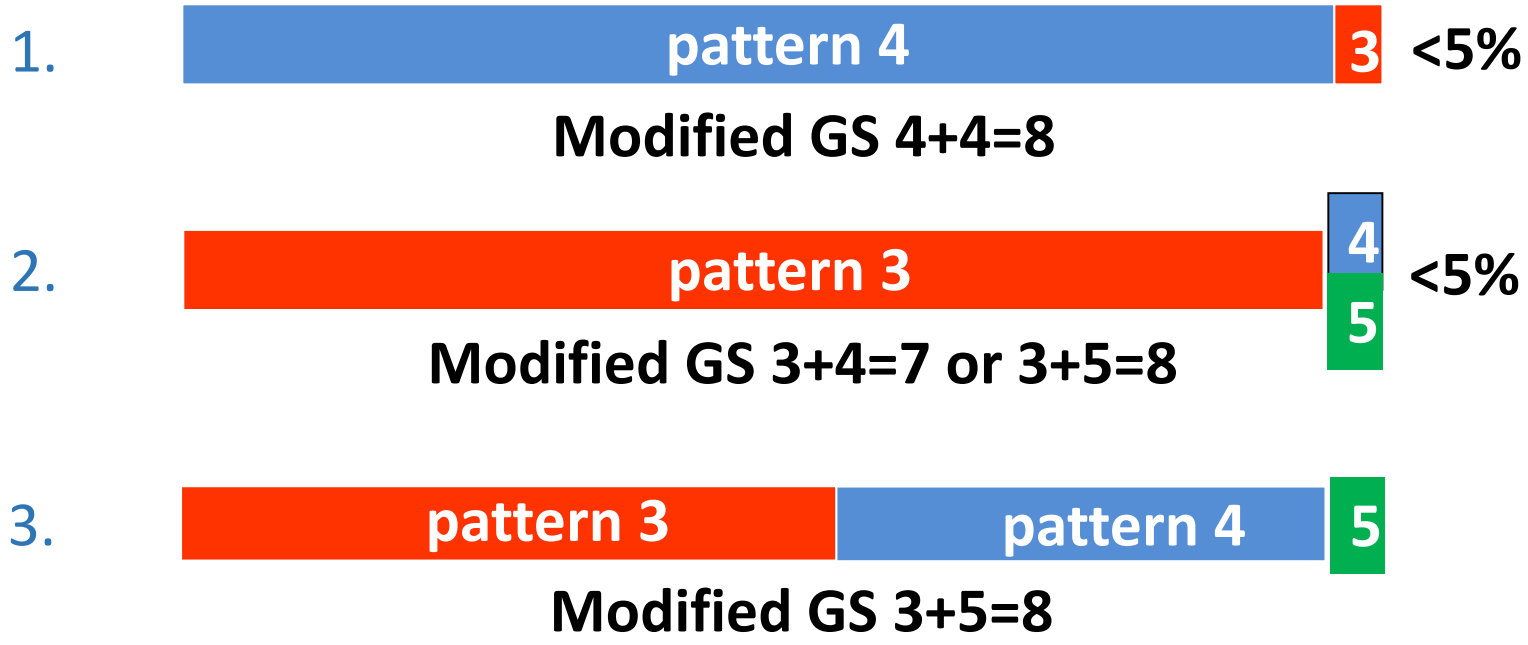
Epstein & Hirsch Am J Surg Pathol. 2021; Smith et al. Adv Anat Pathol 2020

REPORTING PCA ON NEEDLE BIOPSY

- Prostate, left base, biopsy (A) - Adenocarcinoma of the prostate Gleason score 3+4=7 (Grade Group 2), involving 10% of one of two cores and measuring 1 mm.
  - Gleason pattern 4 represents 5% of the tumor
  - Cribriform pattern 4 is not identified
- Prostate left mid, biopsy (B) - Benign prostatic tissue.
- Prostate, left apex, biopsy (C) - Adenocarcinoma of the prostate Gleason score 3+4=7 (Grade Group 2), involving 20% of one of two cores and measuring 2 mm.
  - Gleason pattern 4 represents 10% of the tumor
  - Cribriform pattern 4 is identified

REPORTING LIMITED SECONDARY PATTERNS OF LOWER AND HIGHER GRADE AND TERTIARY PATTERN ON BX

1. In a setting of high-grade PCA, ignore lower patterns if <5%
2. ANY quantity of high-grade tumor should be included within GS
3. In a setting of three patterns, most common (primary pattern) is added to highest



REPORTING MINOR HIGH-GRADE (TERTIARY PATTERN) ON RP

- If a minor high-grade pattern (pattern 5) is **>5%**, it is included in the Gleason score:
  - Gleason pattern 4 (60%) + pattern 3 (30%) + pattern 5 (10%) = **Gleason score 4+5=9**

- If a minor high-grade pattern (pattern 5) is **≤5%**, it is not included in the Gleason score, but reported as minor component:
  - Gleason pattern 4 (70%) + pattern 3 (25%) + pattern 5 (5%) = **Gleason score 4+3=7 with minor high-grade pattern 5**

- Minor high-grade pattern does not impact Grade Groups

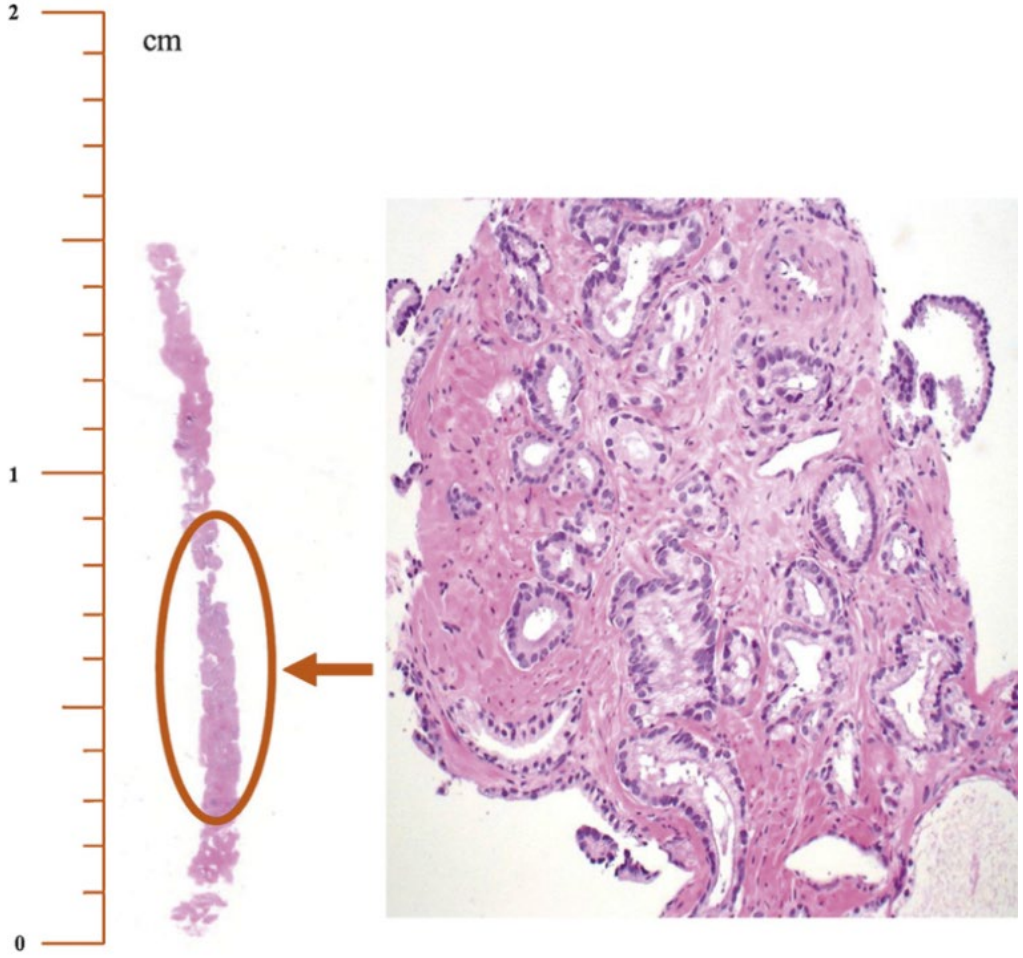
GUPS VS. ISUP RECOMMENDATIONS

PCA reporting	GUPS 2019 (Epstein et al. Arch Pathol Lab Med 2020)	ISUP 2019 (van Leenders et al. Am J Surg Pathol 2020)
Tertiary pattern 5 (tGP5) for GG2 and GG3 at RP	Recommends reporting	Recommends reporting
Minor/tertiary pattern, definition	A minor tertiary pattern exist when 3 patterns are present, with a minor tGP5 representing **≤5%**. If GP5 represents **>5%** it should be reported as secondary	Minor/tertiary may occur if 3 grades are present and highest grade is **<5%**; same applies for minor higher grade pattern if only 2 patterns are present; if any pattern is **≥5%** it should be reported as secondary pattern
Predominantly GP3 with minor GP4 at RP	3+4=7 (GG2) and record GP4	GG1 with minor/tertiary pattern 4
Predominantly GP4 with minor GP5 at RP	4+5=9 (GG5)	GG4 with minor/tertiary pattern 5

Epstein & Hirsch Am J Surg Pathol. 2021; Smith et al. Adv Anat Pathol 2020

TUMOR QUANTIFICATION ON PROSTATE BX

- # of positive cores involved by PCA out of total
- **Linear extent (% and/or mm) of cancer length in each core**
- Total % or length of cancer in all biopsy cores
- Greatest % or length of cancer involvement
- Amount of cancer in single core with largest amount of tumor



^fragmentation may preclude accurate assessment

From Montironi el al. Eur Urol 2012

REPORTING DISCONTINUOUS FOCI OF PCA

- Involvement by multiple PCA foci separated by BPT
- No consensus on quantification method:
  a. Adding foci, ignoring intervening BPT (additive quantification)
  b. Assessing discontinuous foci as single focus (linear quantification, end-to-end measurement)
- Both methods showed excellent correlation with tumor at RP; linear quantification improved prediction of PCA extent
- 78% of discontinuous tumors on PBx results from single tumor nodule

Schultz et al. AJSP 2013; Arias-Stella et al AJSP 2015

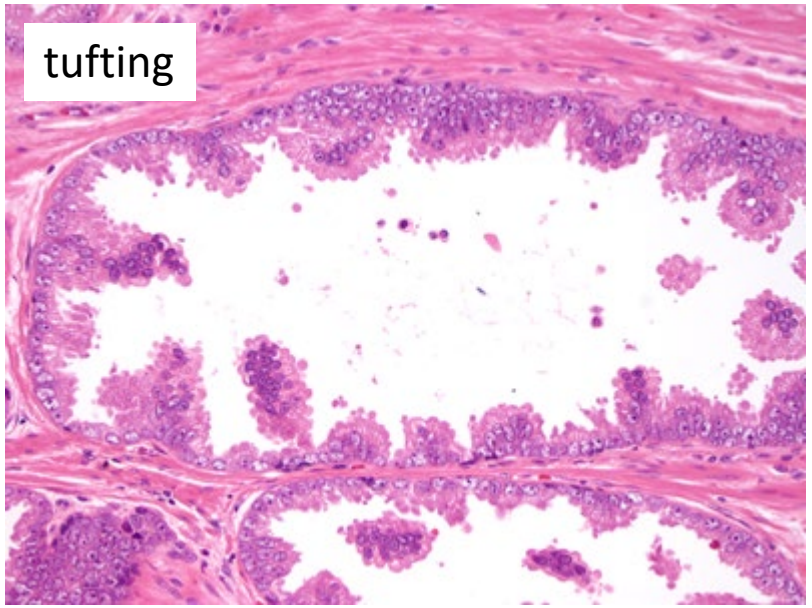
WHO 5TH EDITION UPDATE

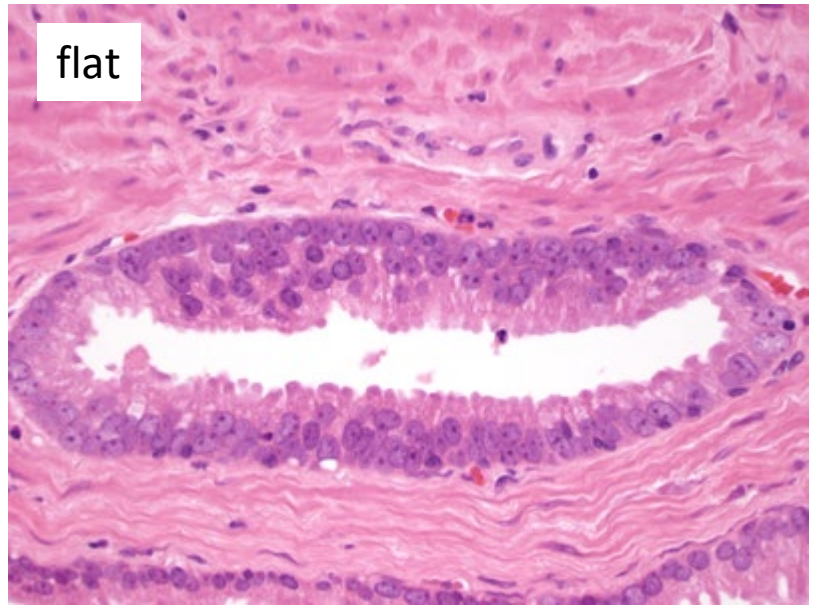
THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

HIGH-GRADE PROSTATIC INTRAEPITHELIAL NEOPLASIA

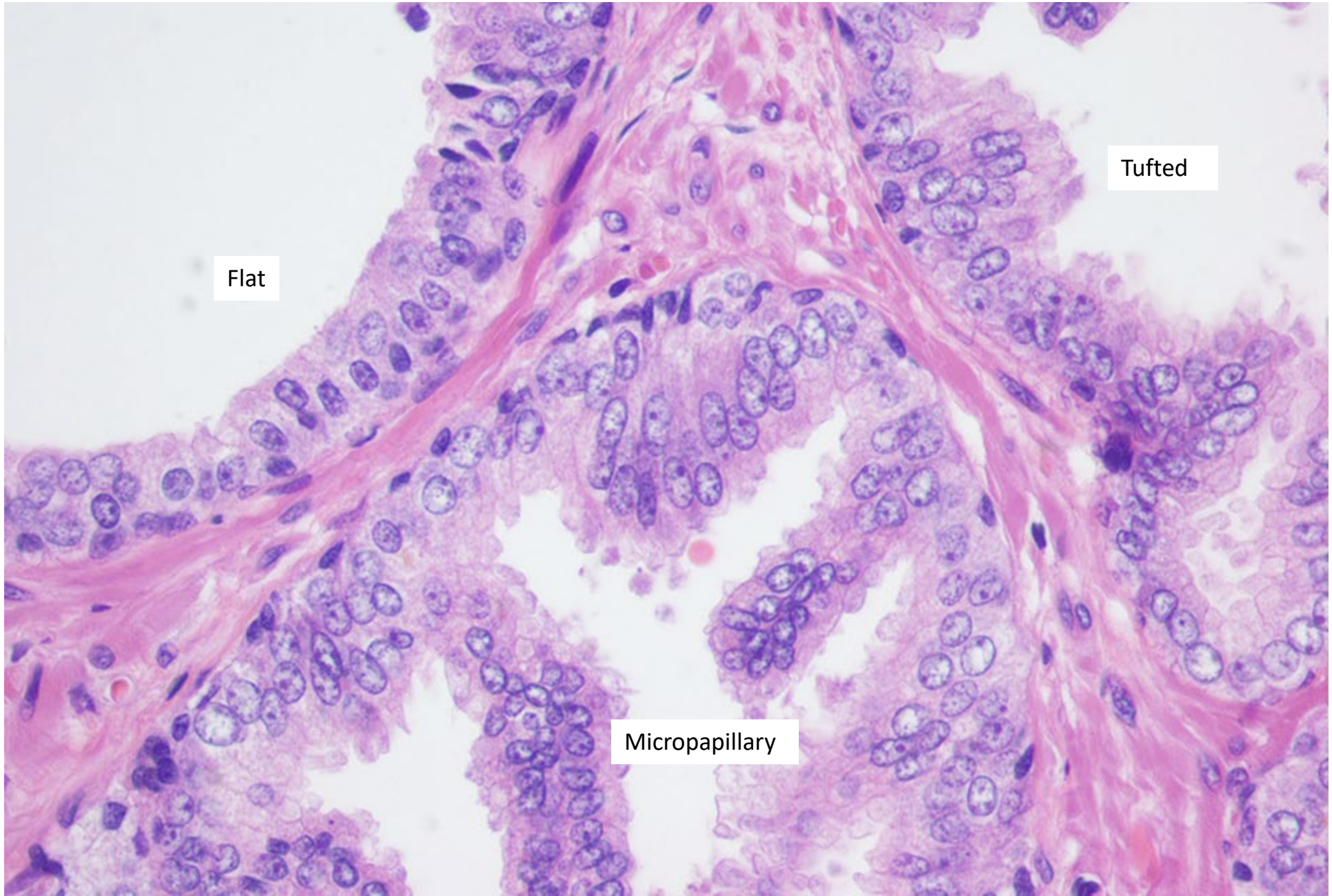
WHO 5th edition:

- Low grade PIN (LGPIN) and cribriform HGPIN are no longer regarded as distinct entities
- 3 main histologic patterns of HGPIN are recognized:





HGPIN

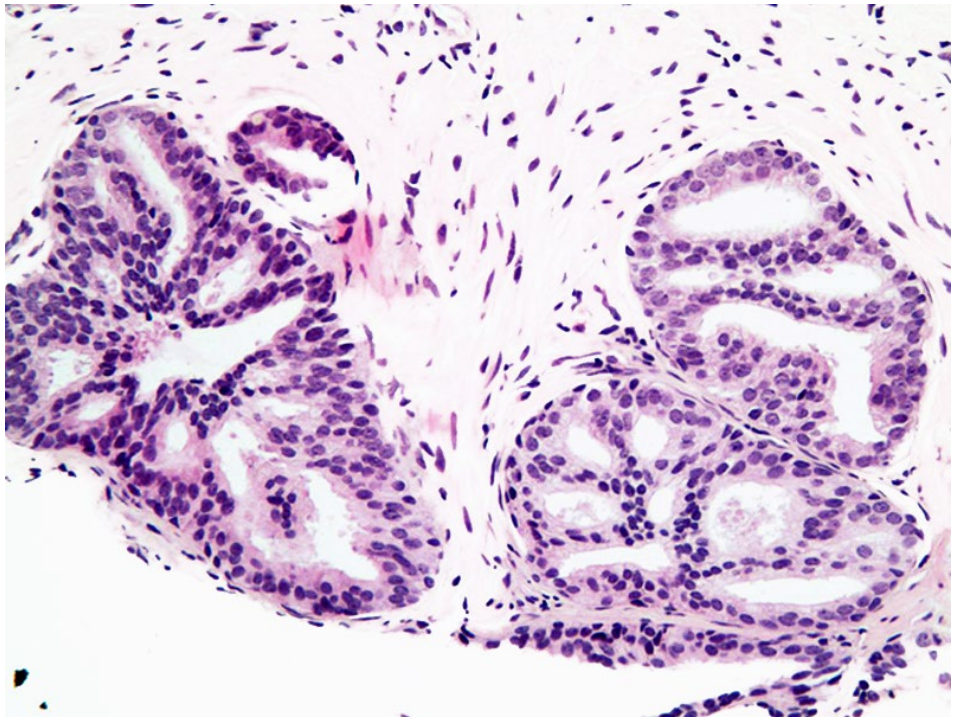


ATYPICAL INTRADUCTAL PROLIFERATION

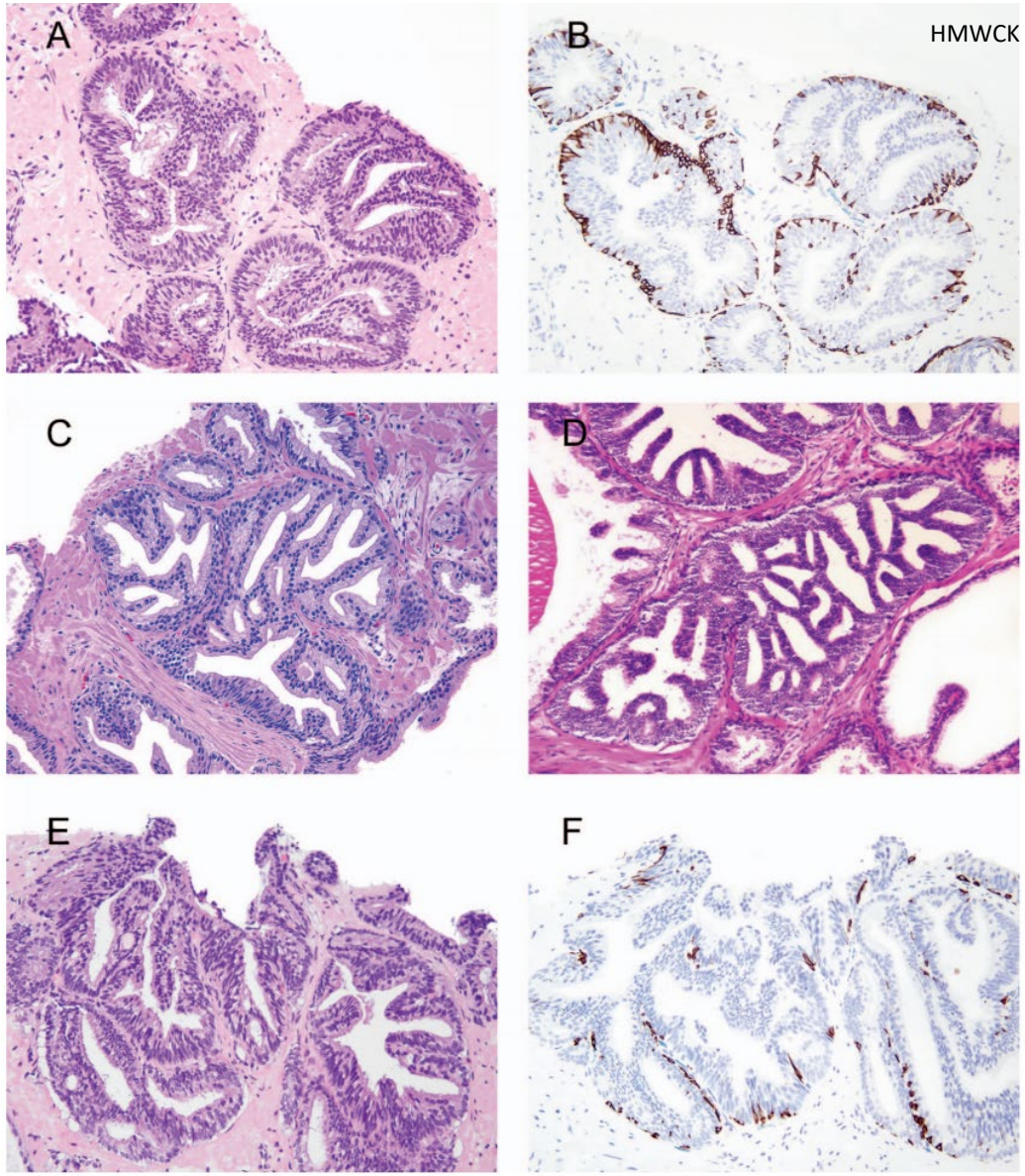
- Existence of a “cribriform” pattern of HGPIN is now controversial; its diagnosis is NOT recommended
- An intraductal proliferation architecturally and/or cytologically more complex than HGPIN, but which falls short of IDC-P, is referred to as:

  - **Atypical Intraductal Proliferation**

  (AIP)



Atypical Intraductal Proliferation



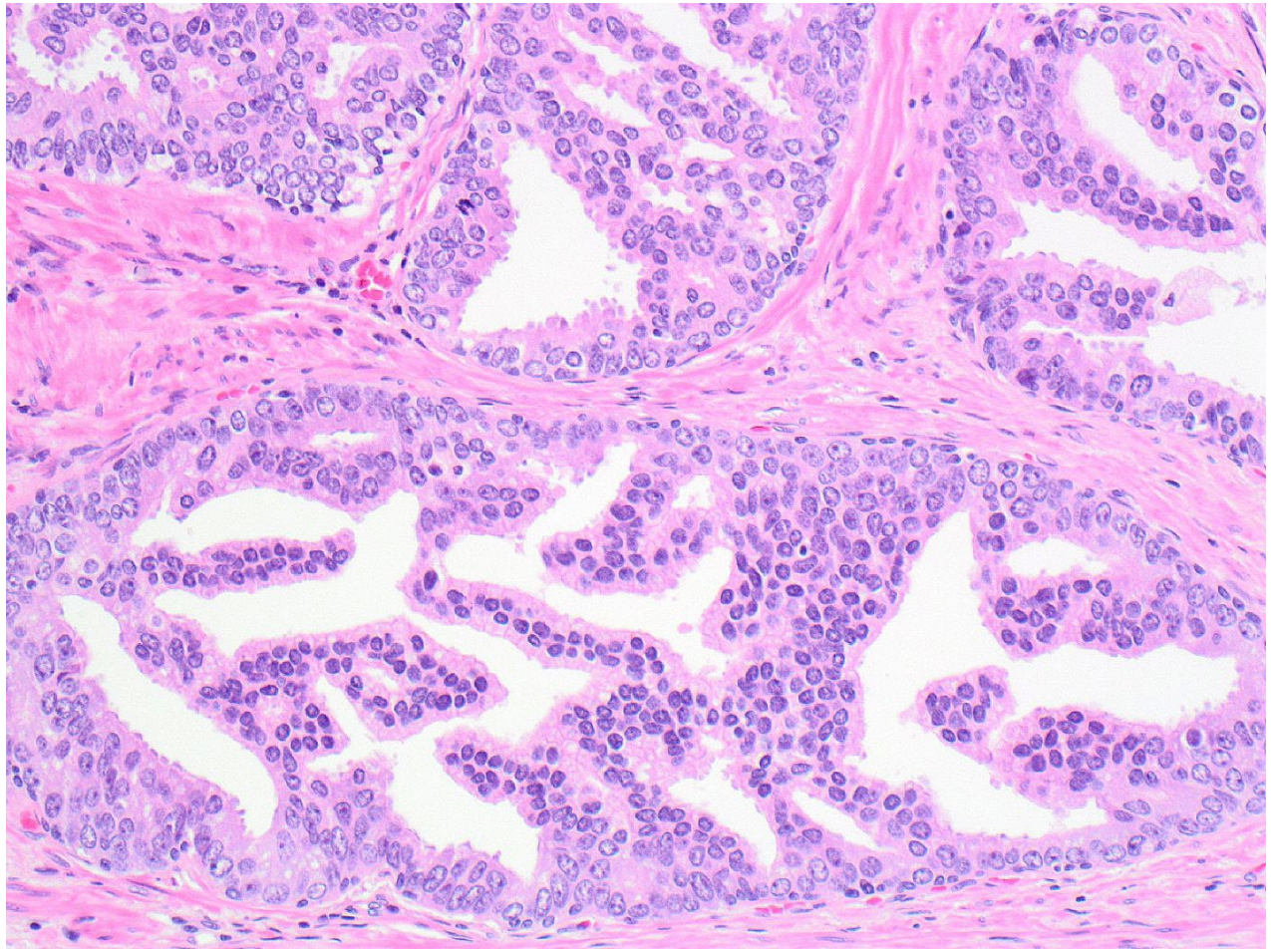
Loose cytologically atypical cribriform glands

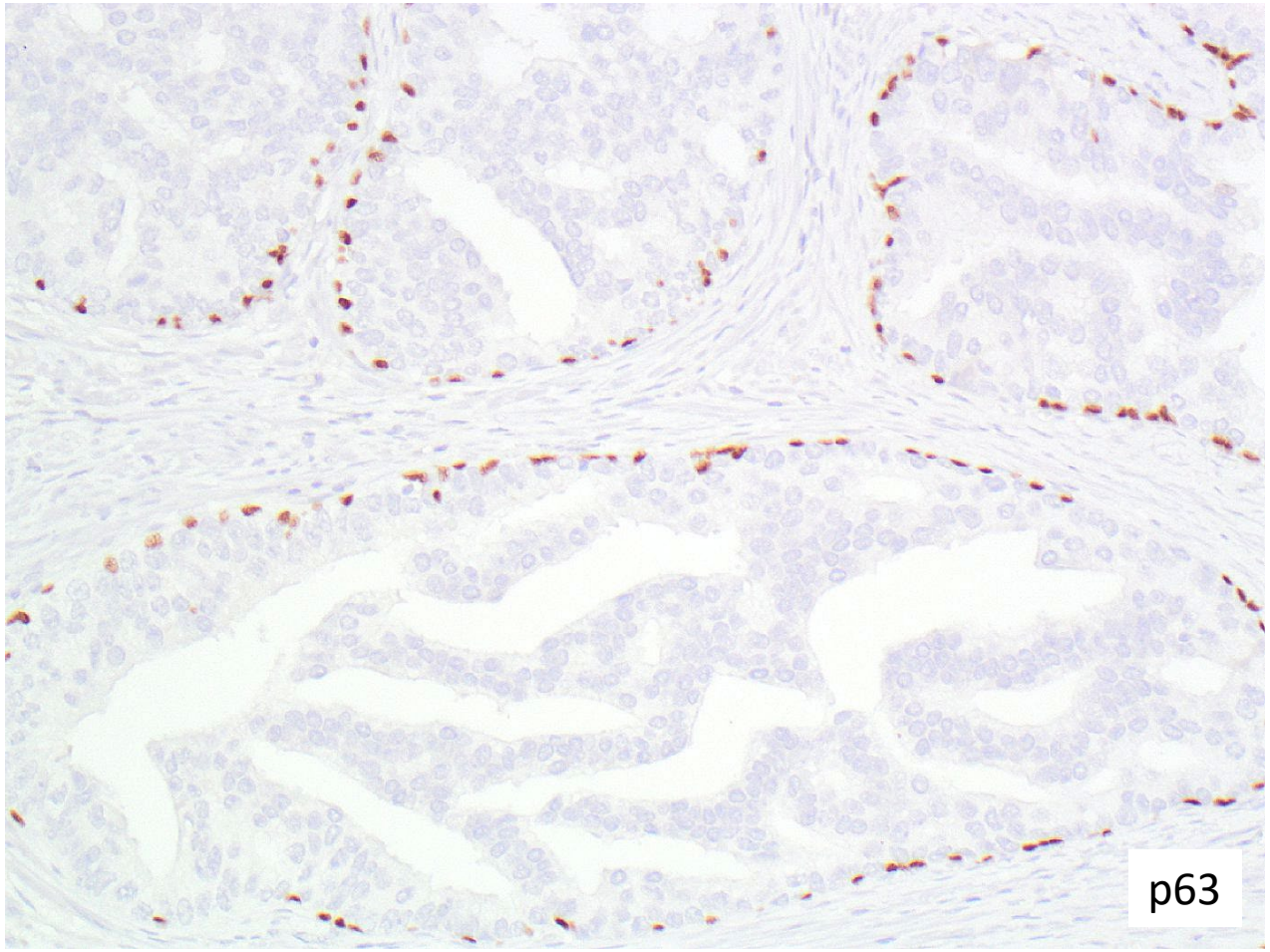
Loose cytologically bland cribriform glands

Loose cytologically atypical cribriform glands

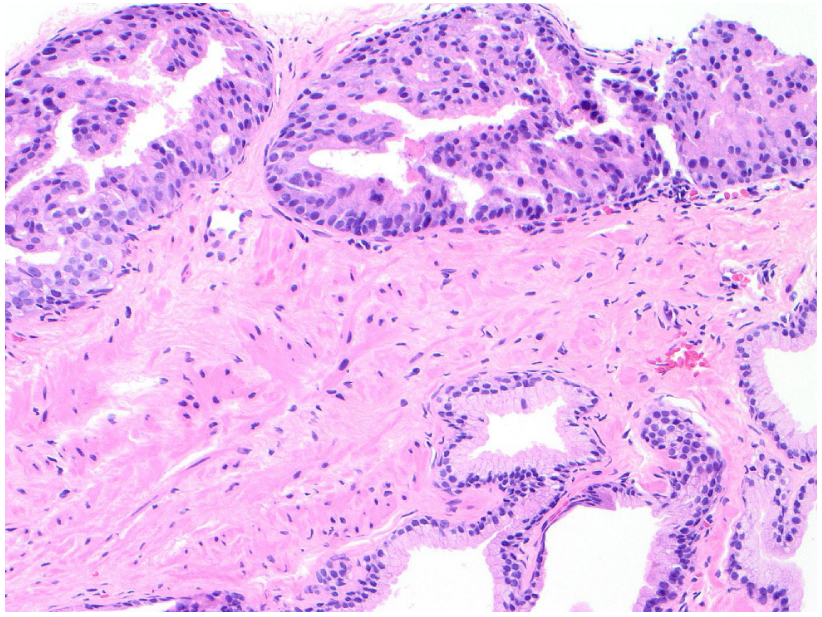
GUPS Grading of Prostate Cancer. Epstein et al. Arch Pathol Lab Med 2020

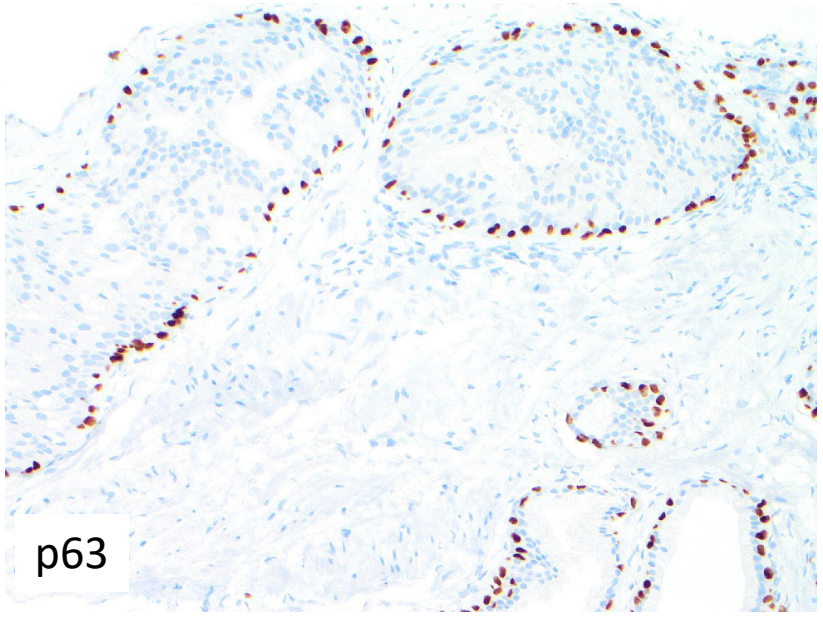
Atypical Intraductal Proliferation

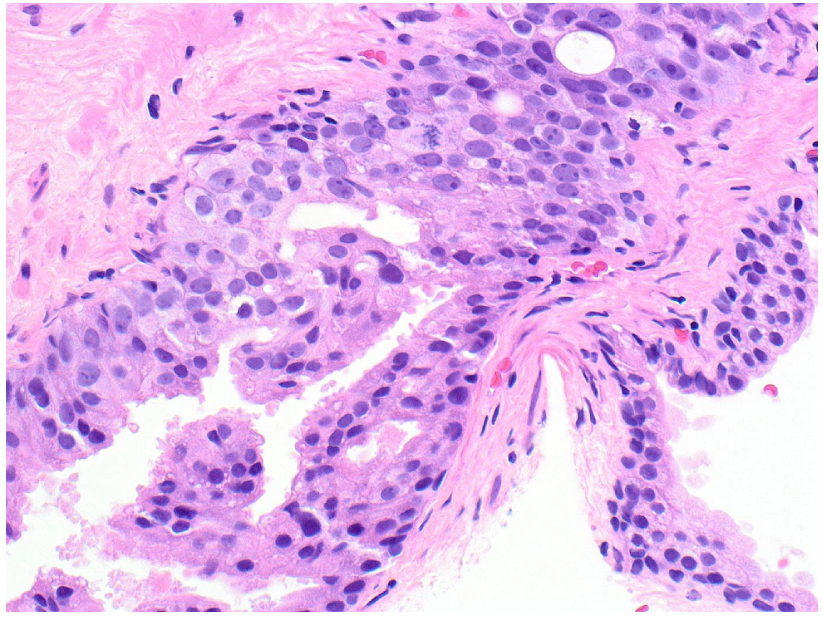


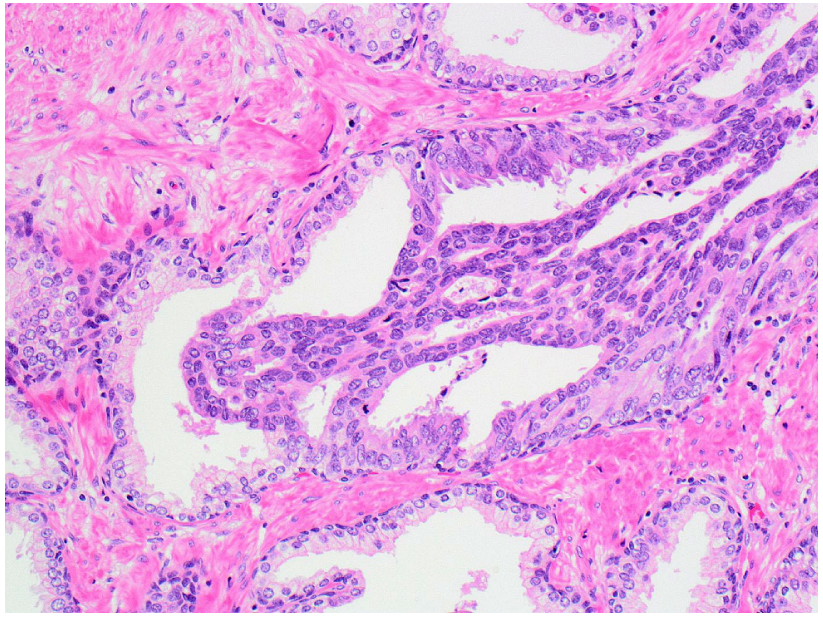


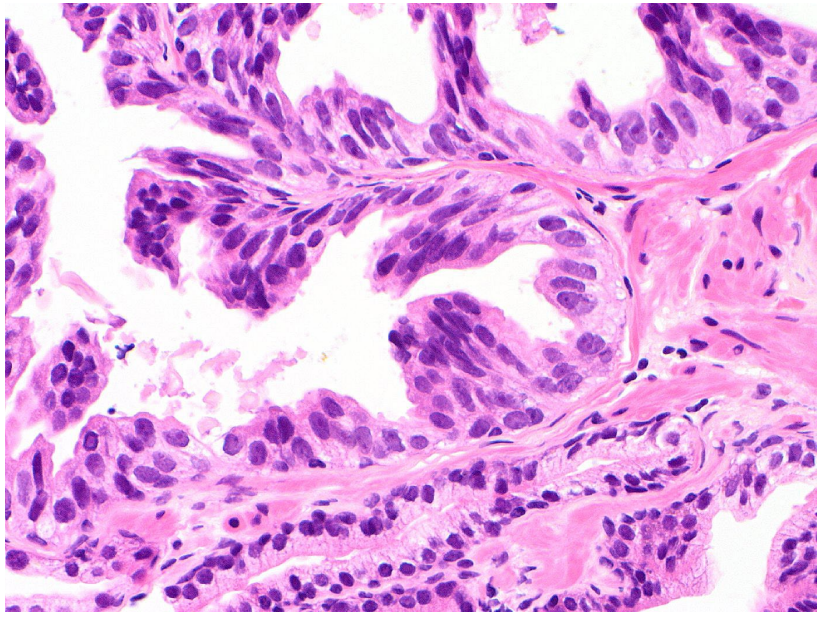
Atypical Intraductal Proliferation

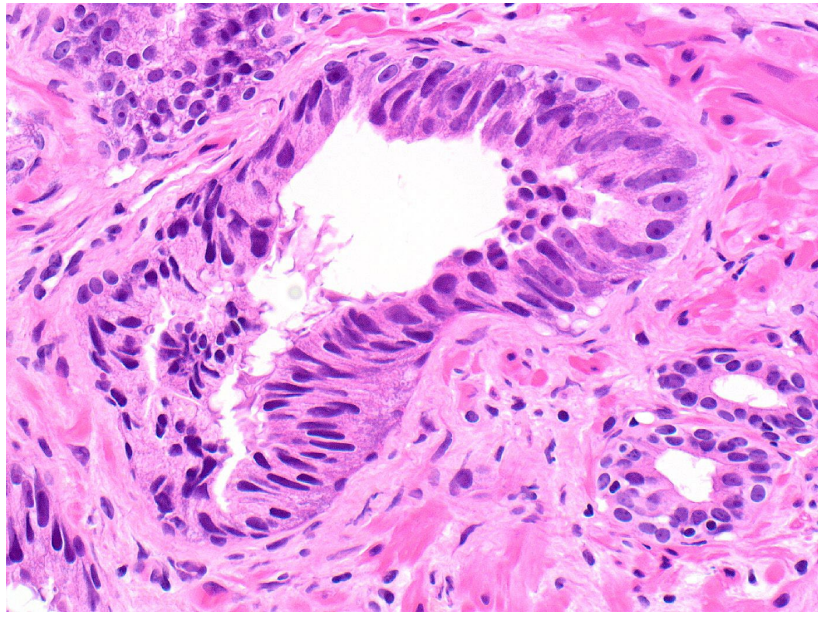






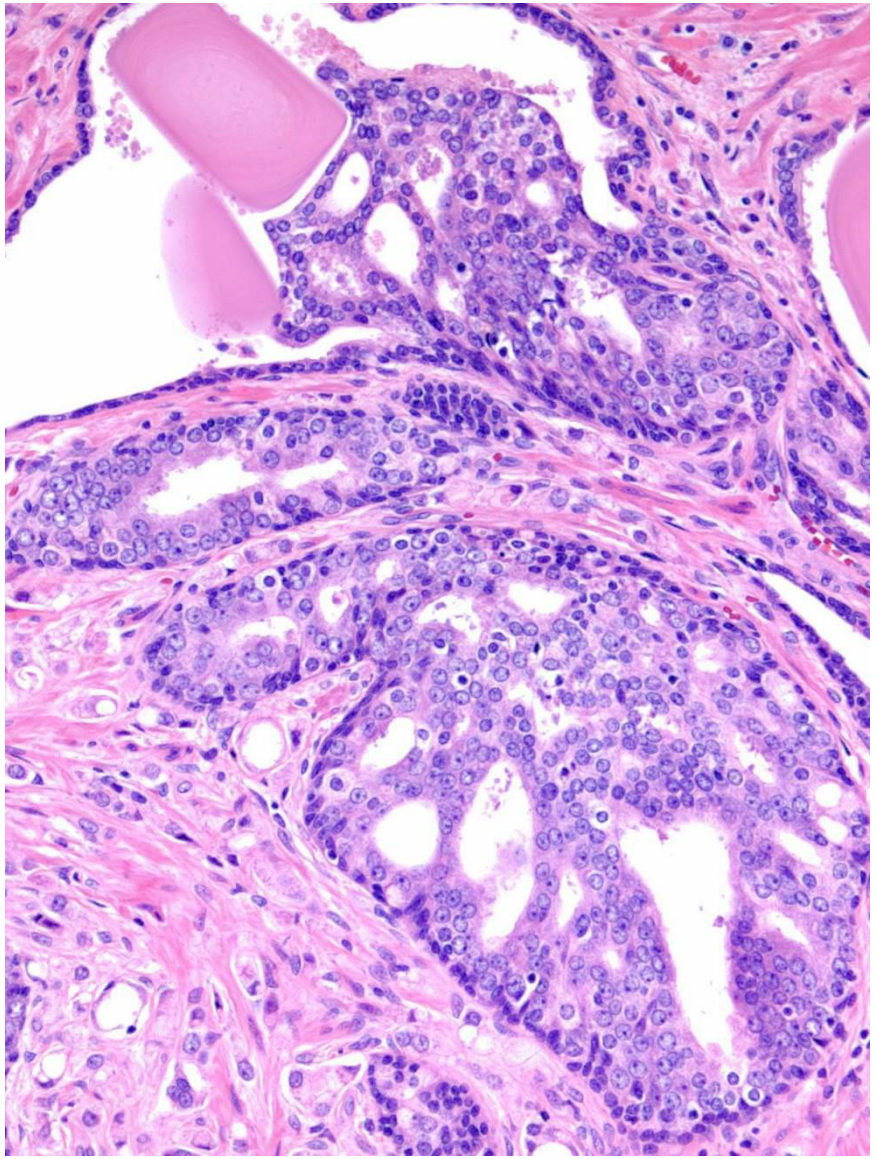




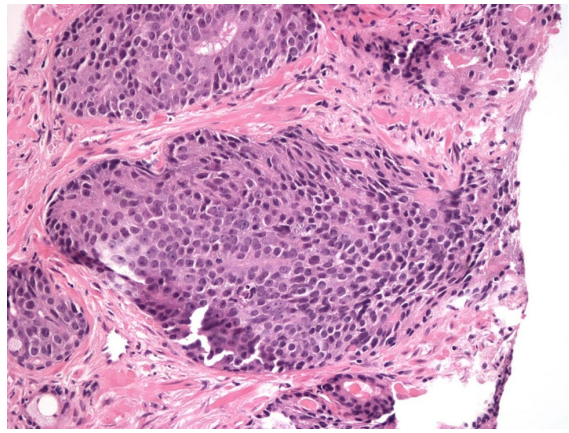


INTRADUCTAL CARCINOMA OF THE PROSTATE (IDC-P)

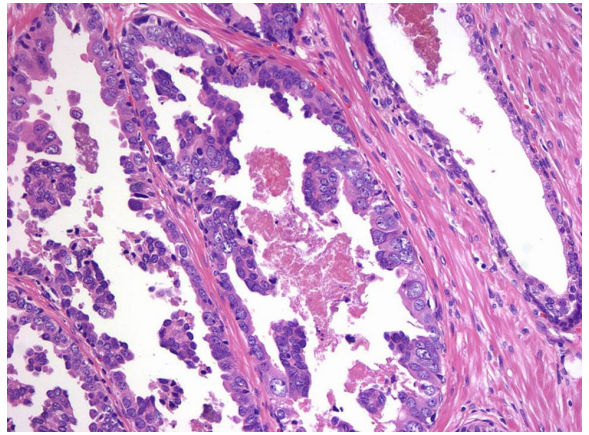
- Distinct entity in 2016 WHO
- Malignant secretory cells growing within and expanding prostatic ducts/acini:
  - Retrograde spread of PCA into prostatic glands
  - Precursor to PCA (rare cases)
- Associated with adverse prognostic features at RP:
  - High GS, large tumor, EPE, SVI, + margins
- Independent predictor of clinical outcome



IDC-P: Diagnostic Criteria



Spanning of large acini/ducts by malignant epithelial cells with **preservation of basal cells**



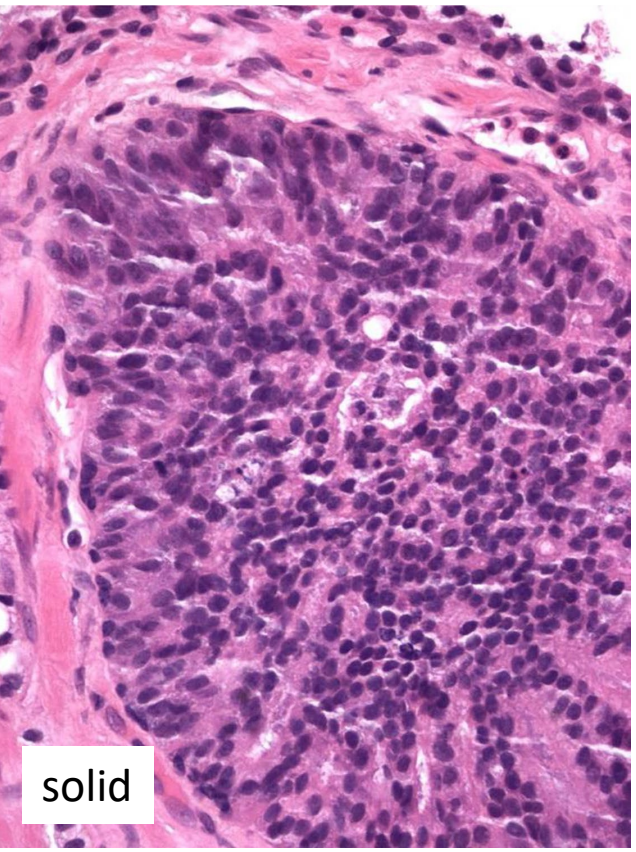
- **Solid**
- **Dense cribriform** (>50% epithelium)

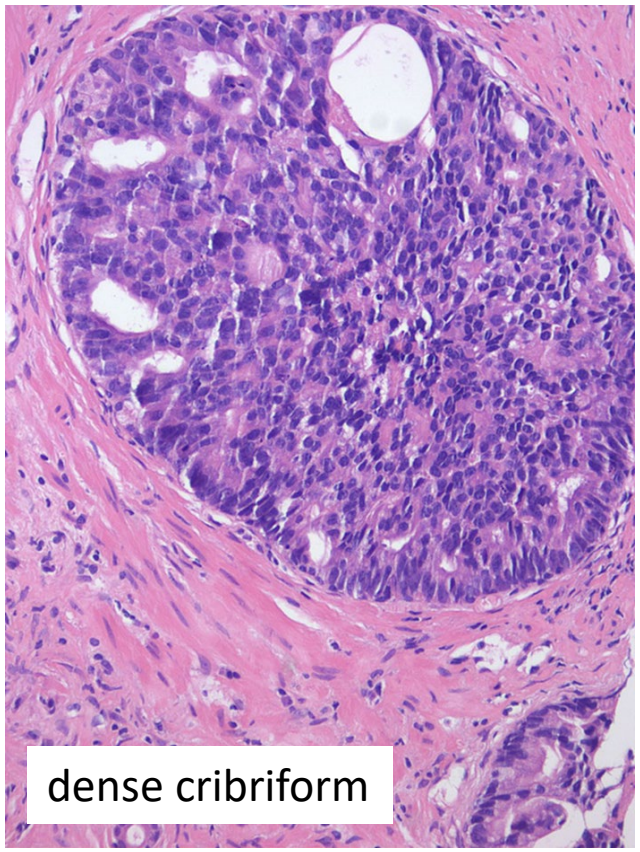
or

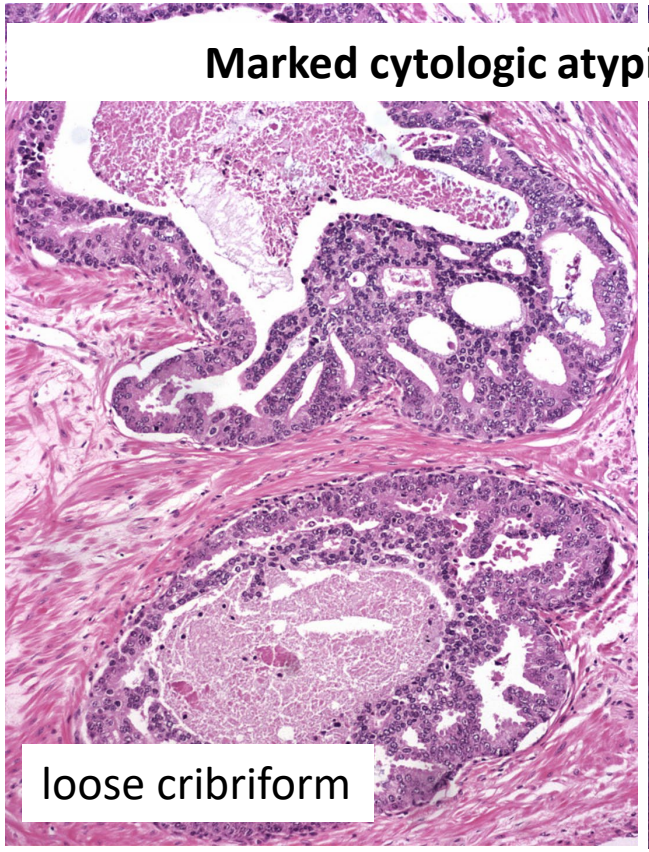
- **Loose cribriform** (<50%)
- **Micropapillary**
  - Comedonecrosis (non-focal)
  - Marked nuclear atypia (nuclear size ≥6x normal)

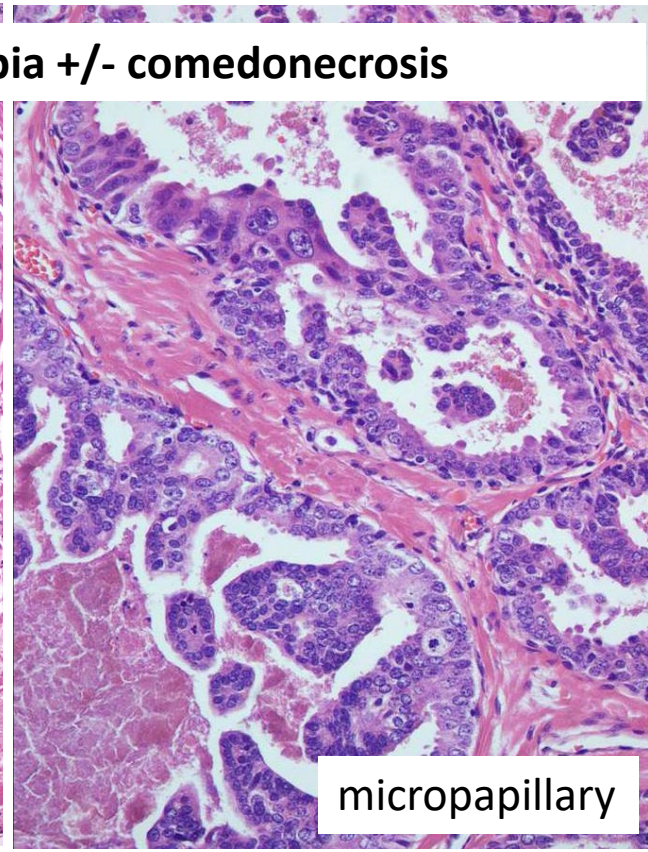
Guo & Epstein. Mod Pathol 2006

INTRADUCTAL CARCINOMA OF THE PROSTATE (IDC-P)



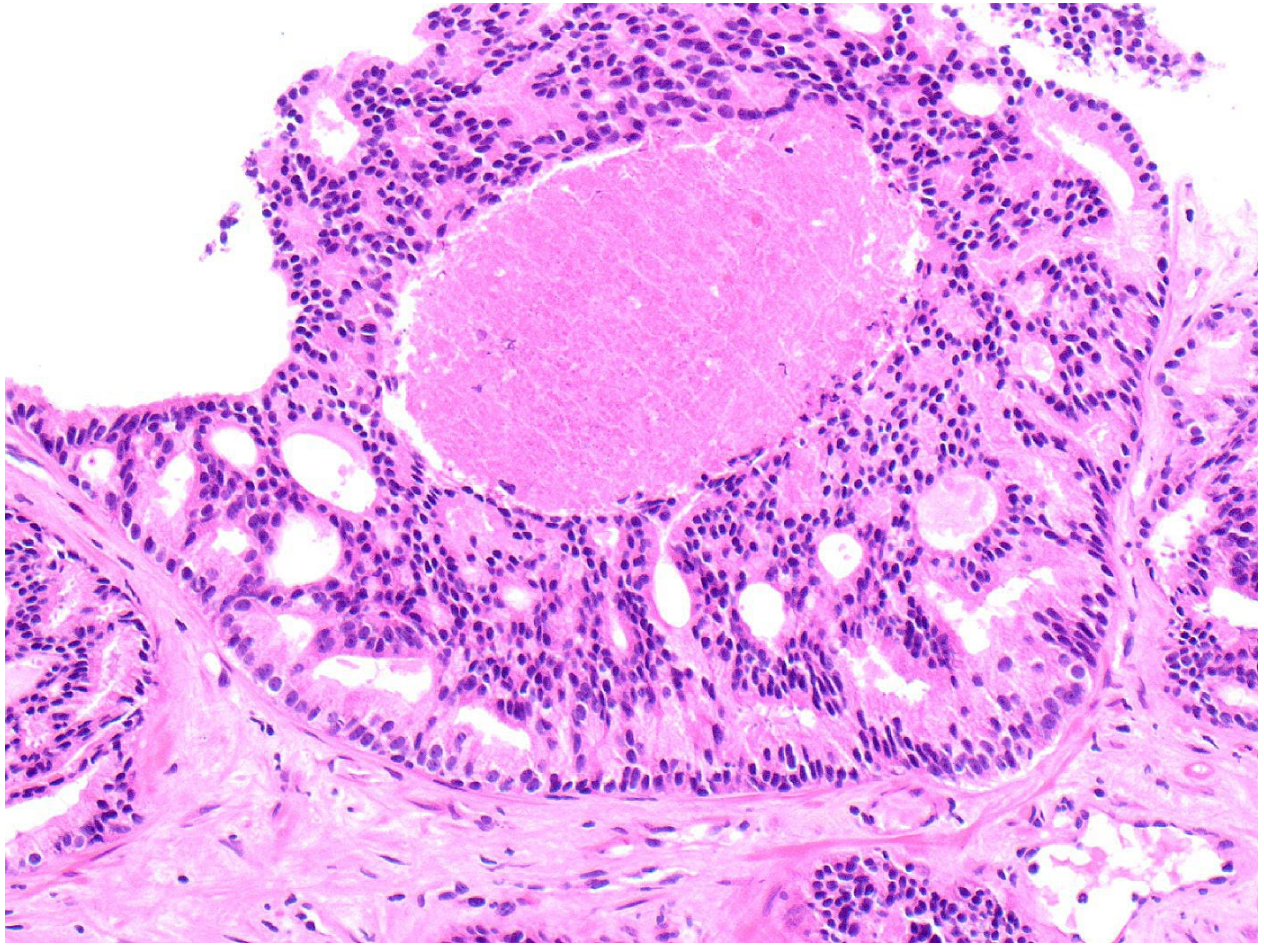


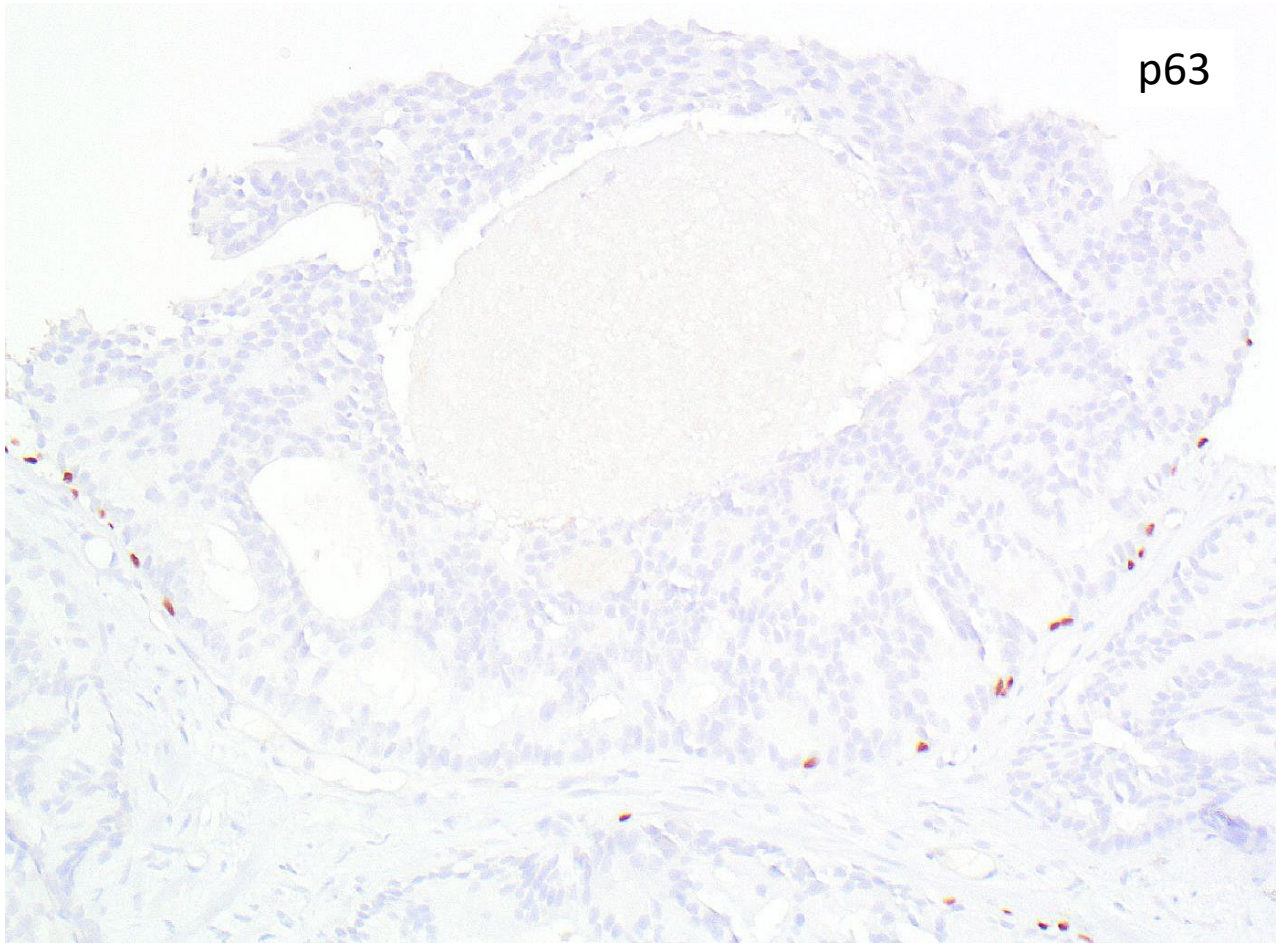




- Presence of IDC-P associated with invasive PCA **should be noted**
- Isolated IDC-P on PBx should **NOT** be **graded**
- Still **controversial** whether IDC-P should be <u>incorporated into PCA grading</u>

IDC-P with comedonecrosis



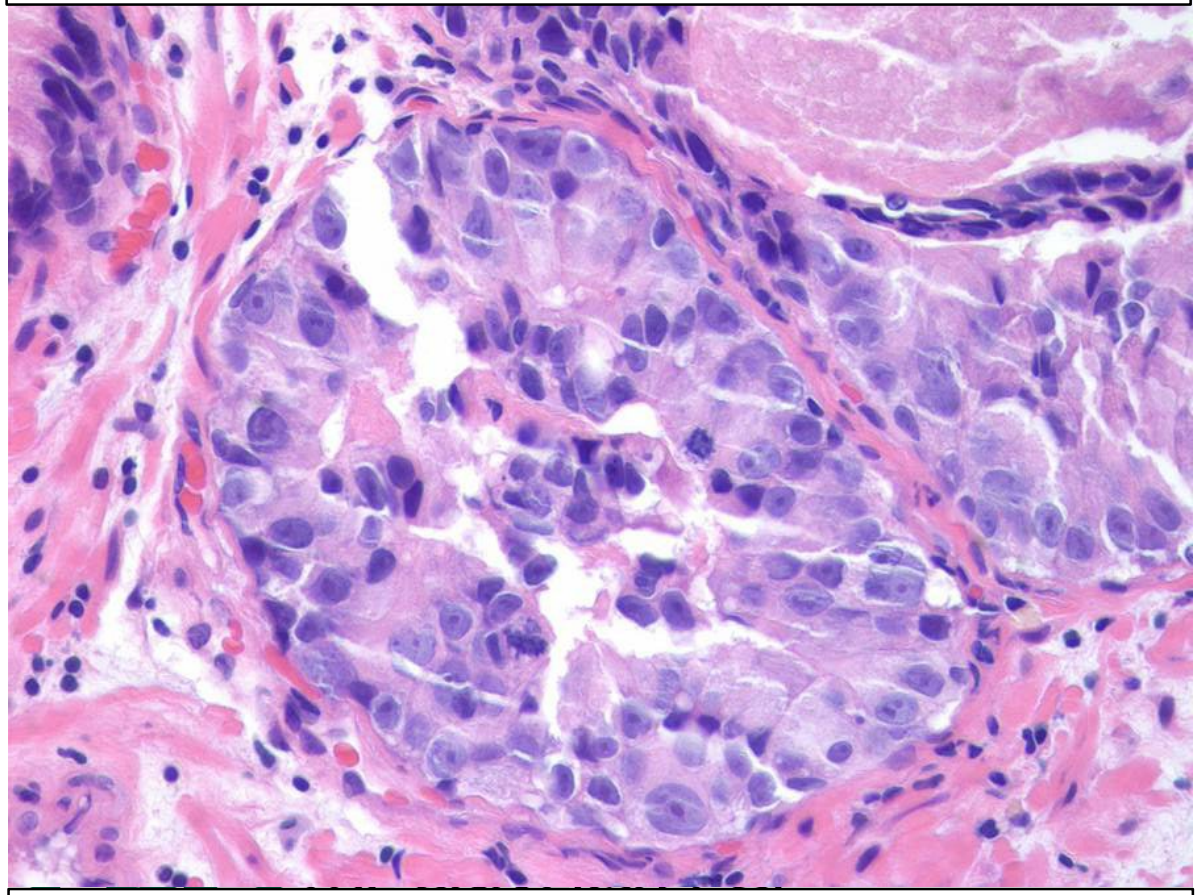


Fine et al. Am J Surg Pathol 2018; Madan et al. Histopathology 2019

INTRADUCTAL CARCINOMA OF THE PROSTATE (IDC-P)

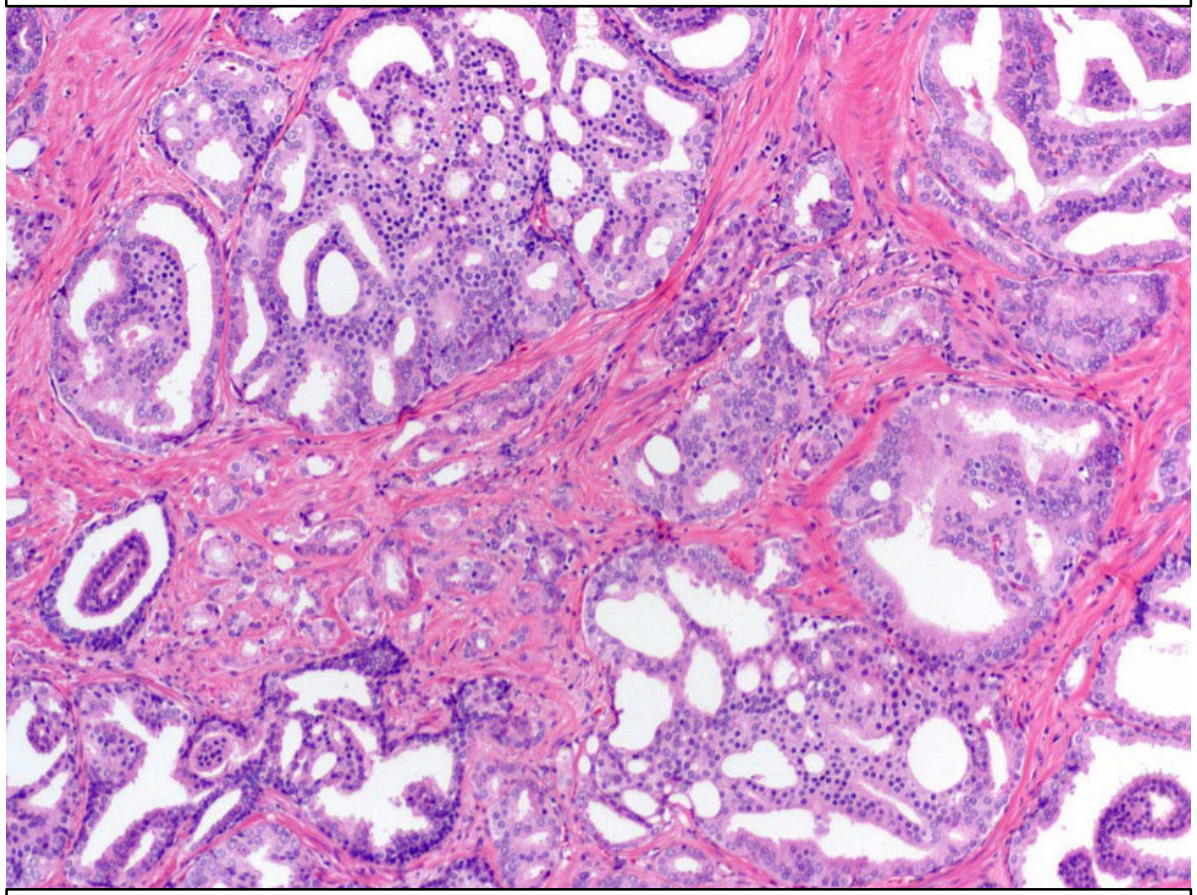
IDC-P represents two distinct entities

Isolated IDC-P (in situ) – small minority



Progression from HGPIN precursor

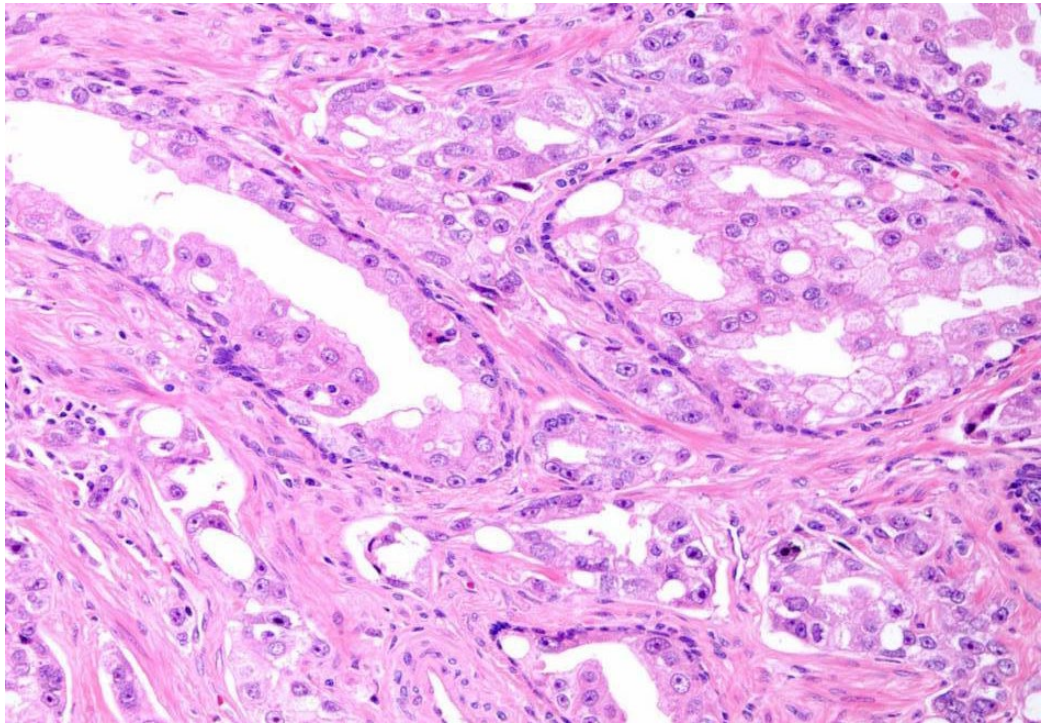
Invasive PCA spreads into benign ducts/acini

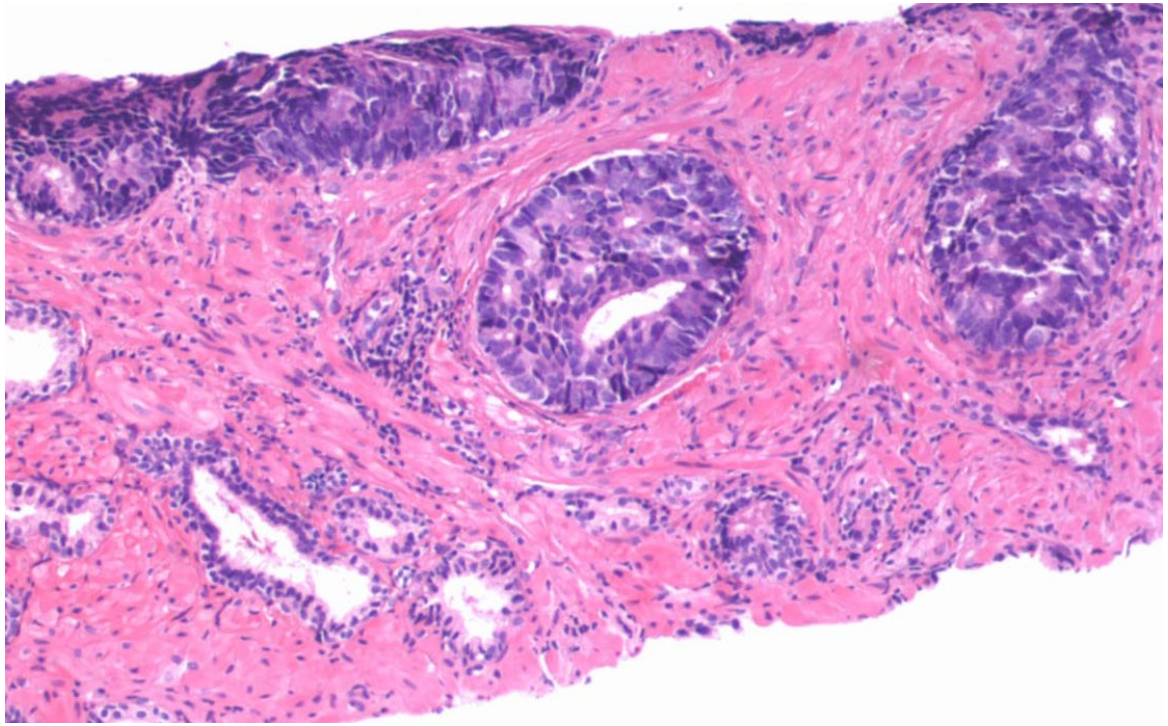


Late event in tumor progression

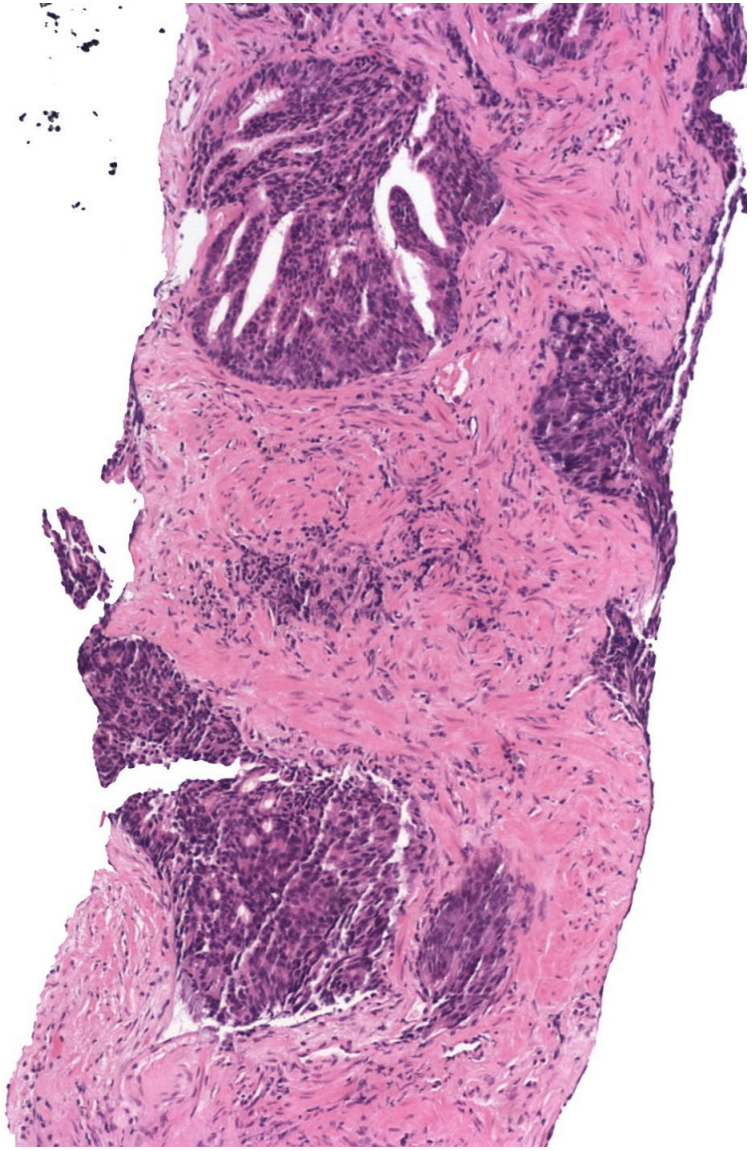
INTRADUCTAL CARCINOMA OF THE PROSTATE (IDC-P)

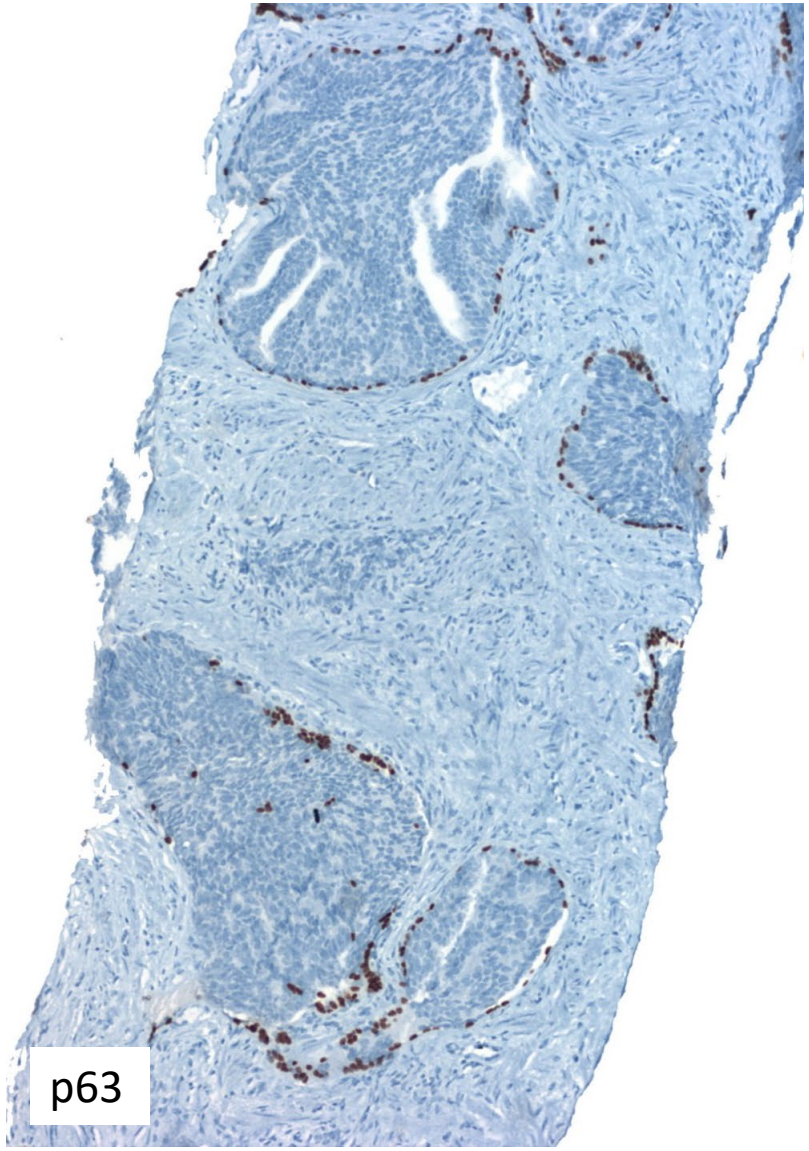
- 17% of RP cases
- 2.8% of PBx with high-grade carcinoma (mean GS 8)
- 0.1-0.3% of PBx without invasive carcinoma (isolated IDC-P)

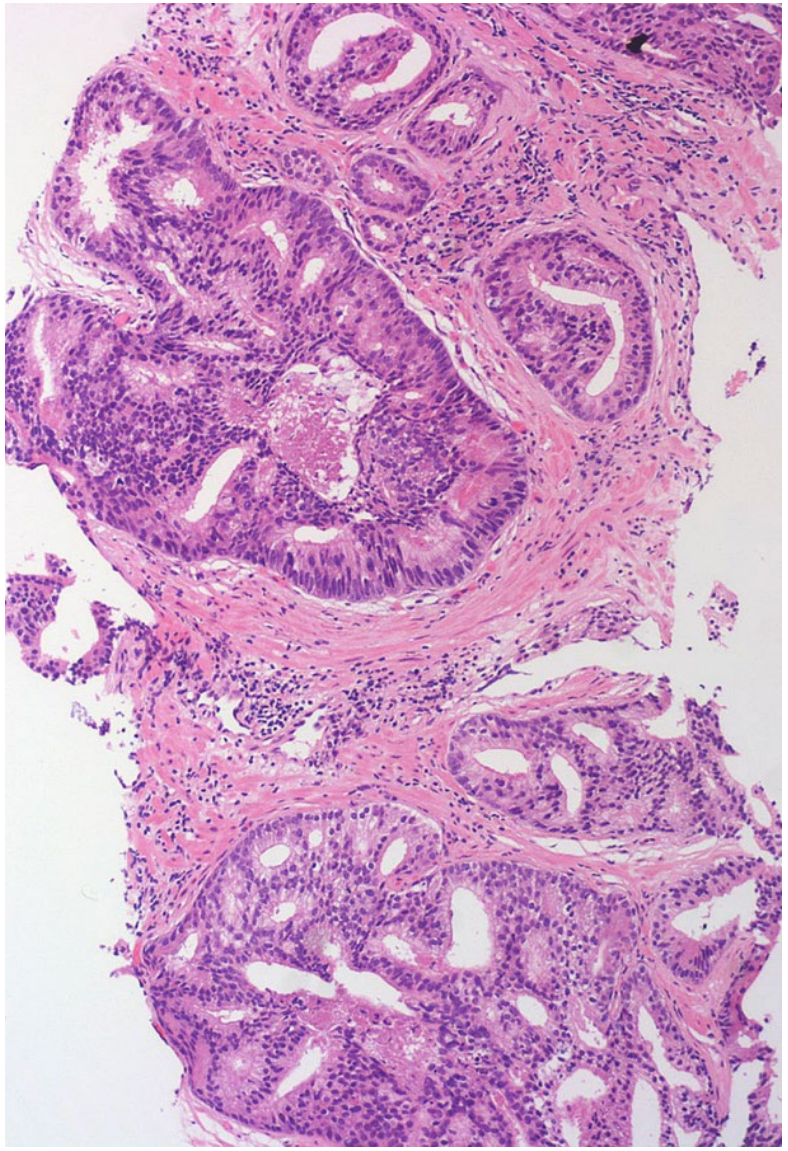




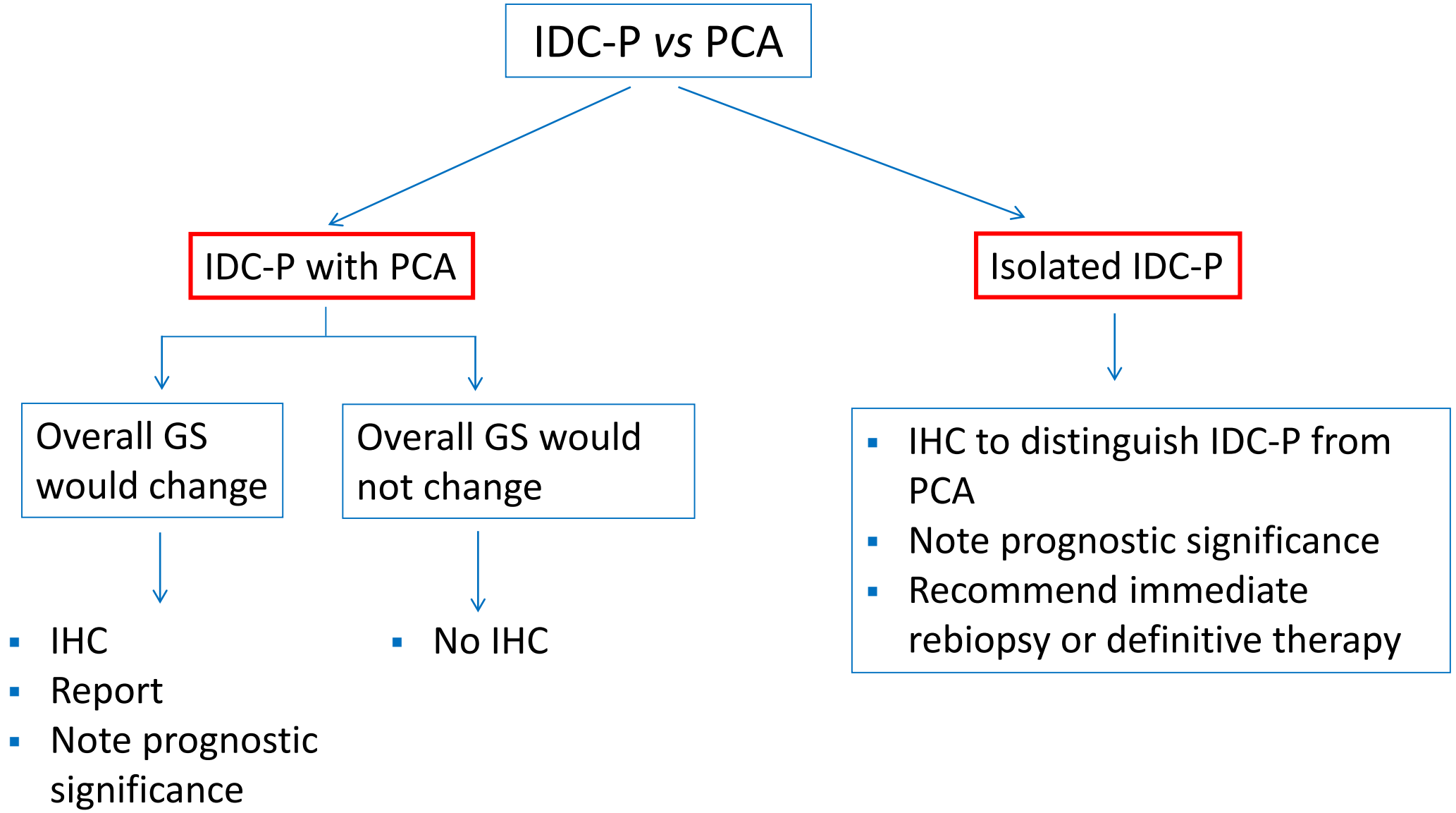
Isolated IDC-P





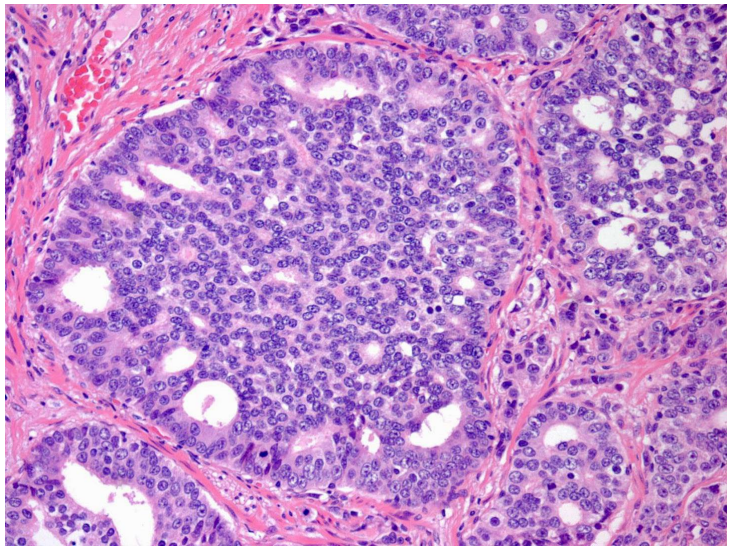


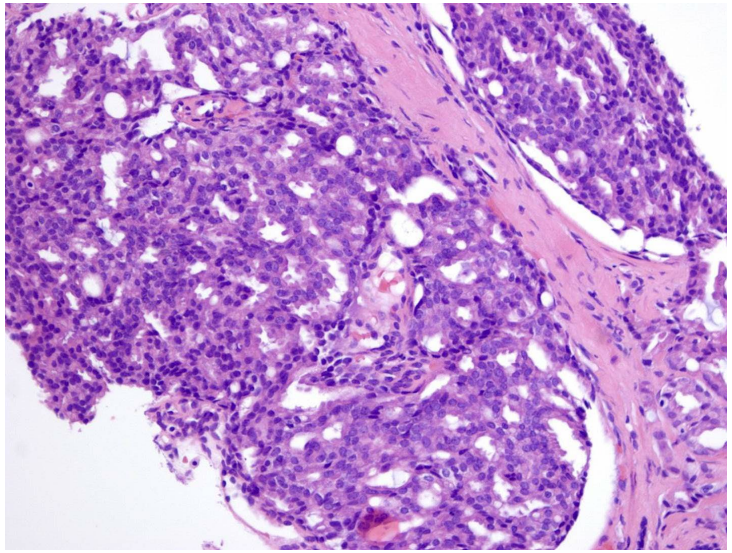
Working up/Reporting Atypical Lesions Suspicious for IDC-P in PBx



HEREDITARY TUMOUR SYNDROMES

- Homologous Recombination Repair (HRR) defects & Lynch Syndrome DNA mismatch repair (dMMR):
  - Germline (or somatic) alterations in DNA repair genes are present in 20% of aggressive primary and metastatic PCa
  - **IDC-P** and **cribriform** histology are more likely to harbor DNA repair genetic defect
  - Advanced PCa harboring **HRR** defects are likely to respond to PARP inhibitors
  - PCa with defected **dMMR** are offered immune checkpoint inhibitors

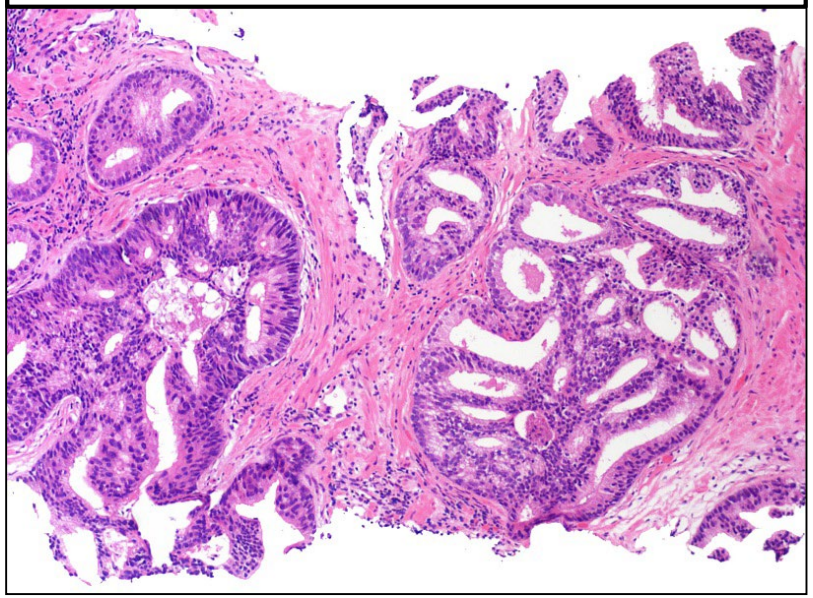




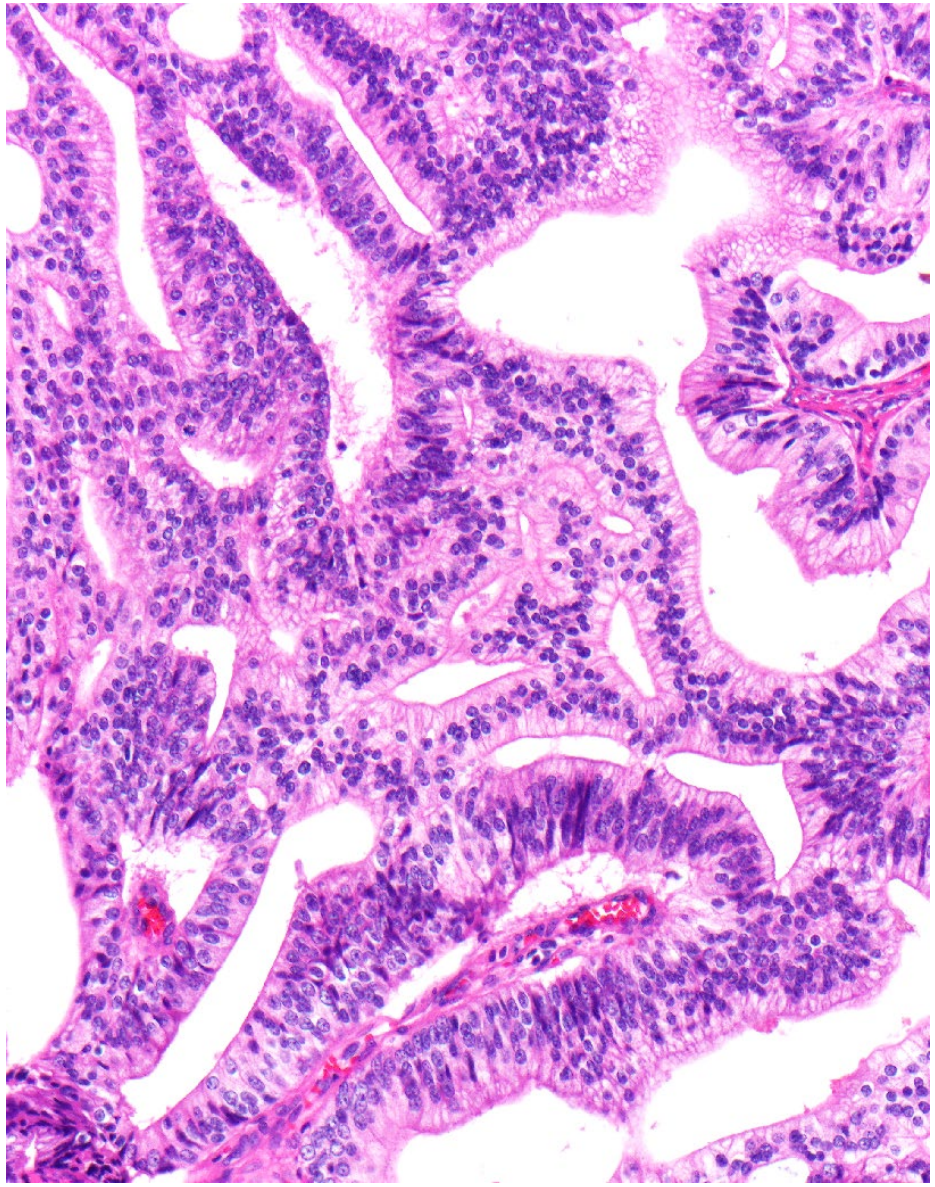
GENETIC TESTING RECOMMENDATIONS

- *Germline* genetic testing, with or without pretest genetic counseling, recommended for patients with PCA and any of the following:
  - Positive family history
  - High-risk, very-high-risk, regional, or metastatic PCA (regardless of family history)
  - Ashkenazi Jewish ancestry
  - **Intraductal histology**

Intraductal carcinoma

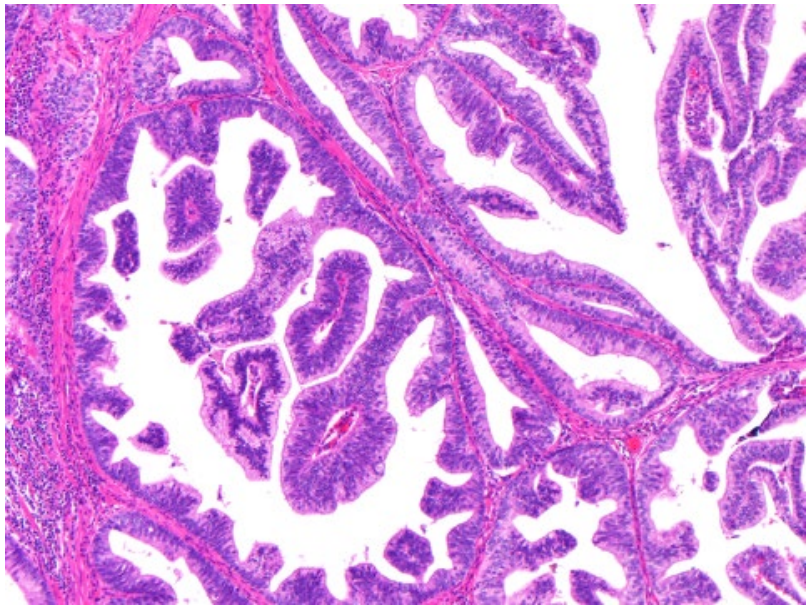


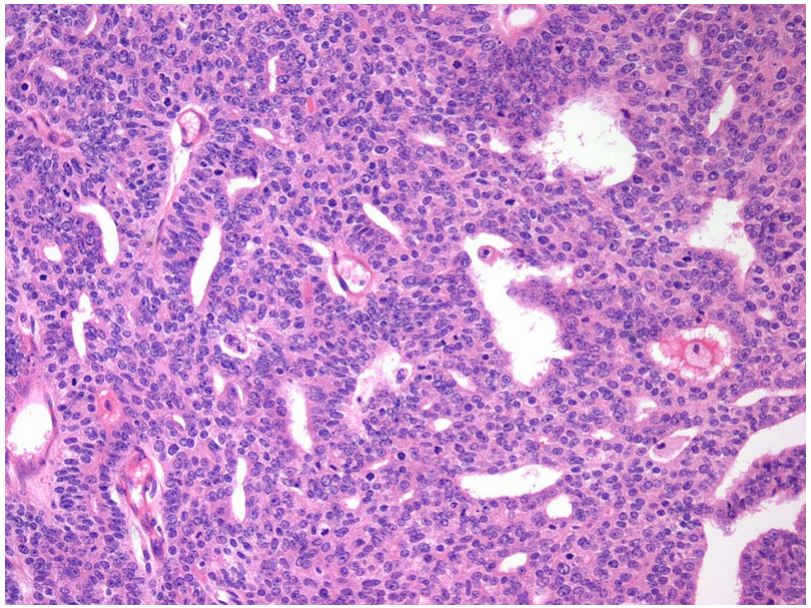
PROSTATIC DUCTAL ADENOCARCINOMA



- Uncommon (~3%) aggressive variant derived from prostatic glandular cells
- Clonally similar to acinar
- Defined morphologically by pseudostratified columnar epithelium
- 2 major architectural patterns:
  - Papillary: with true fibrovascular cores lined by stratified tall columnar cells
  - Cribriform: complex glandular arrangements with closely apposed acini showing slit-like lumina and multilayered nuclei

PROSTATIC DUCTAL ADENOCARCINOMA





- Enriched for germline or somatic pathogenic alterations in genes regulating DNA repair
- On RP, ductal is reserved for >50% ductal morphology
- On Bx, adenocarcinoma with ductal features is recommended
- Any proportion of ductal on Bx carries increased risk of BCF and metastatic disease
- Less responsive to ADT; higher propensity for visceral metastasis (mostly to lungs, liver, testis)
- Equivalent to **Gleason pattern 4 or 5**

UPDATE ON STAGING

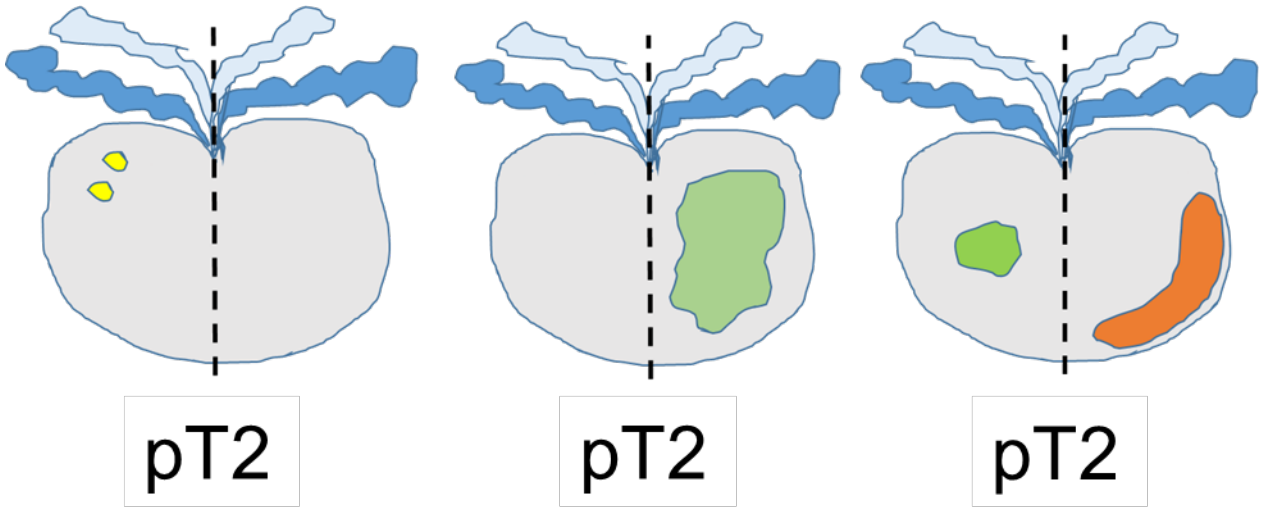
PROSTATE CANCER STAGING (AJCC 8TH EDITION)

Pathologic stage

Stage	Description
T0	No evidence of residual tumor
No T1	
T2	Tumor confined within prostate
T3	Tumor through prostate capsule
T3a	Extraprostatic extension
T3b	Seminal vesicle invasion
T4	Tumor invades adjacent structures
N1	Regional lymph nodes involvement
M1a	Non-regional lymph node involvement
M1b	Bone involvement
M1c	Visceral sites involvement

Organ-confined disease (pT2)

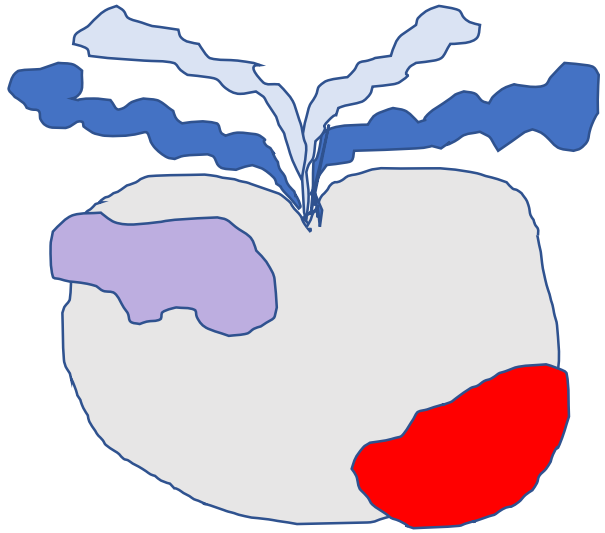
No longer subclassified by extent or laterality



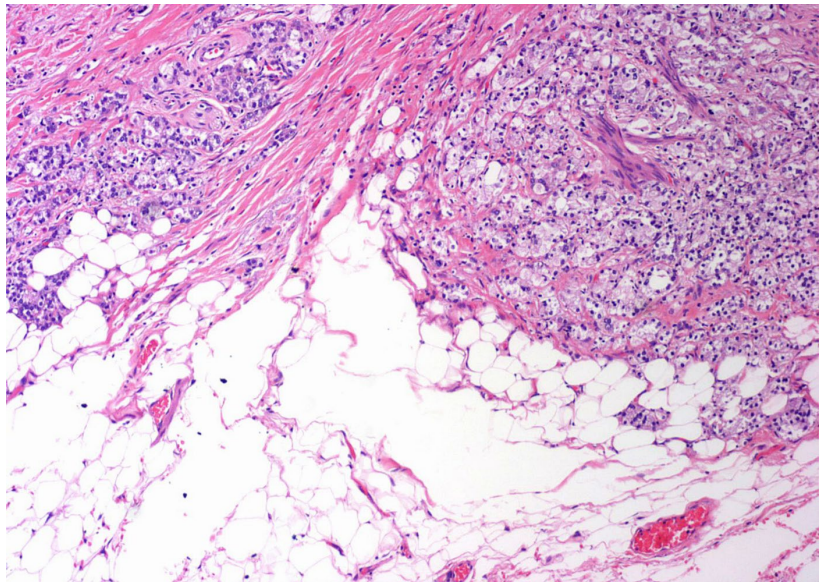
Nguyen DP et al. J Urol 2018; Bhindi B et al. J Urol 2017; AJCC 8th edition

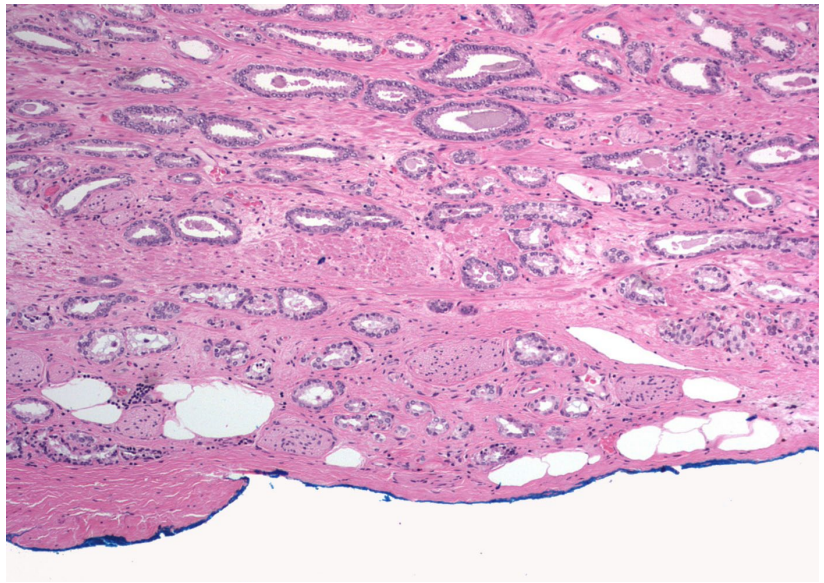
EXTRAPROSTATIC EXTENSION

- Tumor beyond confines of gland
- Admixed with periprostatic adipose tissue; easily recognized in posterolateral, posterior, lateral regions
- Tumor in skeletal muscle does **NOT** constitute EPE
- **Extent** (focal/nonfocal) and **location** of EPE should be documented



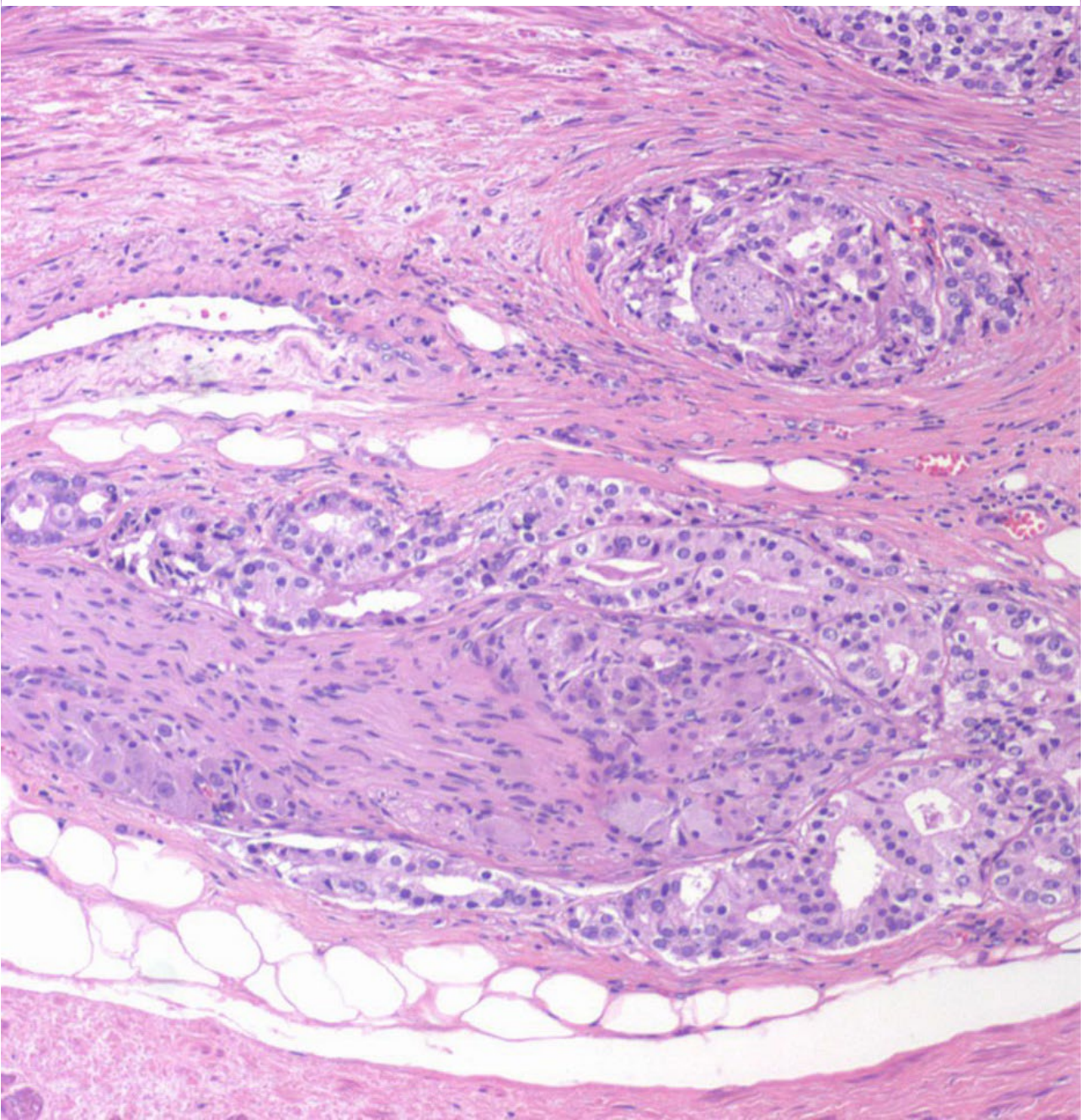
pT3a



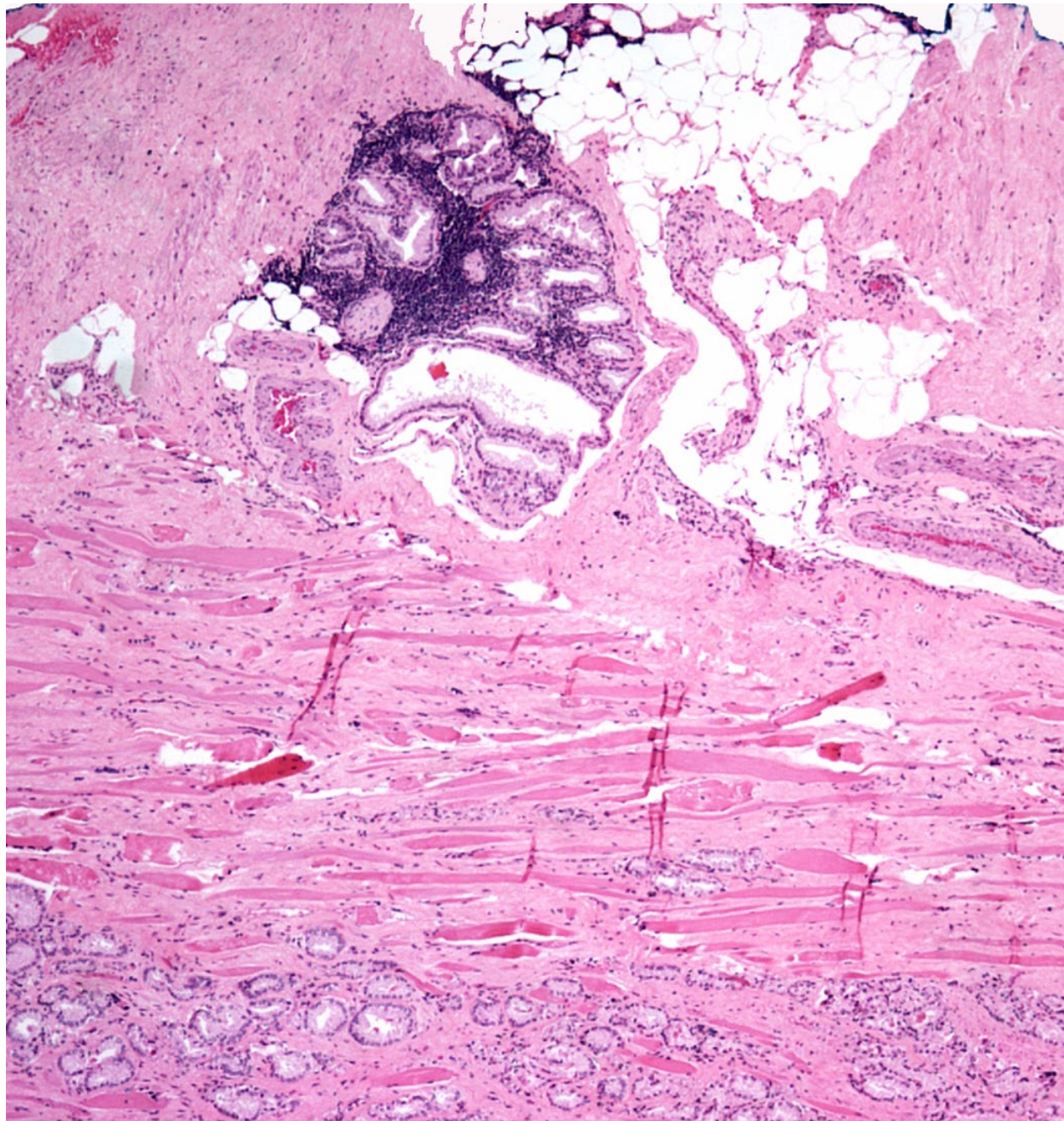


Magi-Galluzzi et al. Mod Pathol 2011

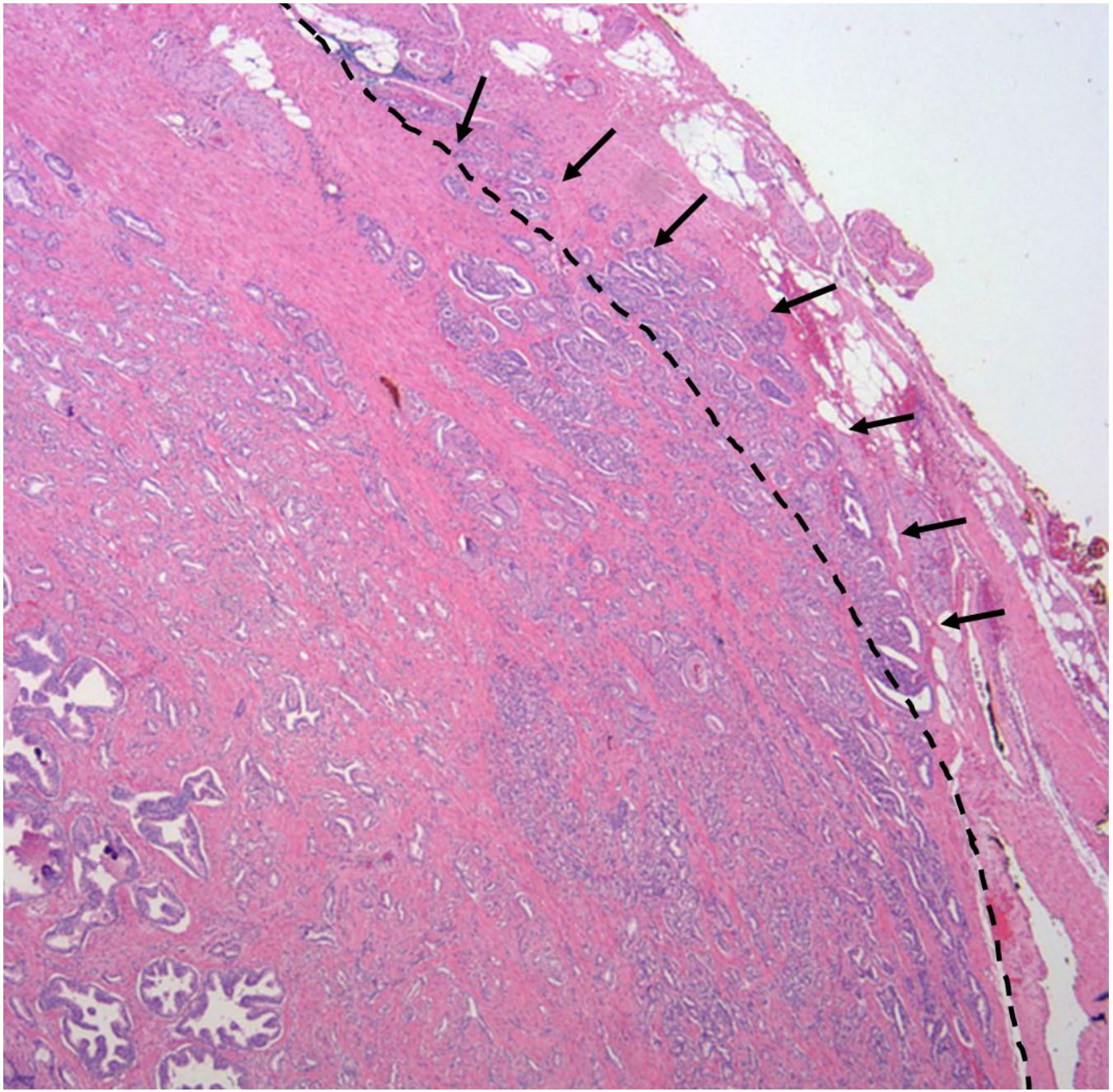
Tumor in perineural space

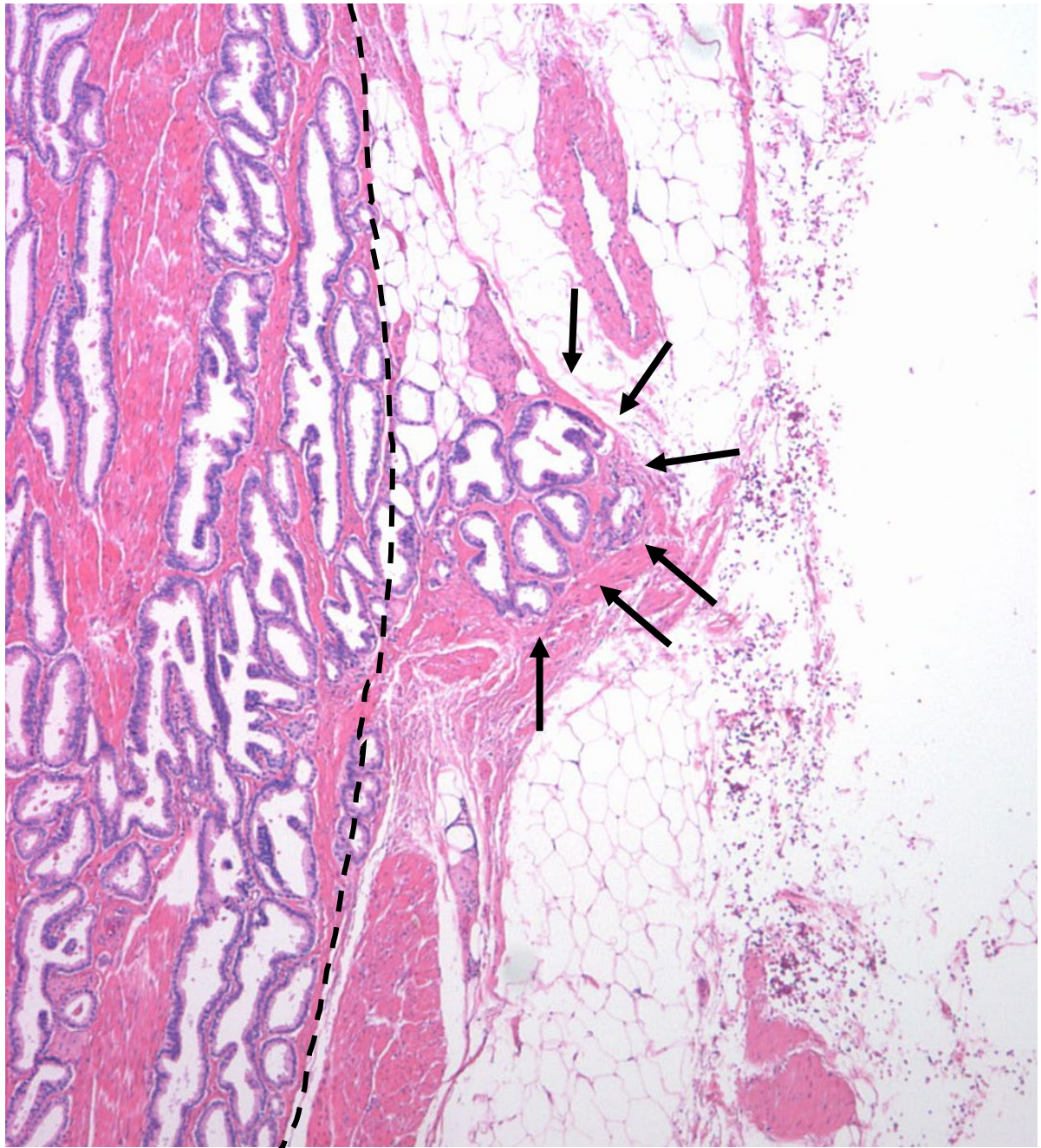


Tumor extends beyond prostate



Tumor bulges beyond prostate contour





Tumor in skeletal muscle

pT2

Microscopic bladder neck involvement

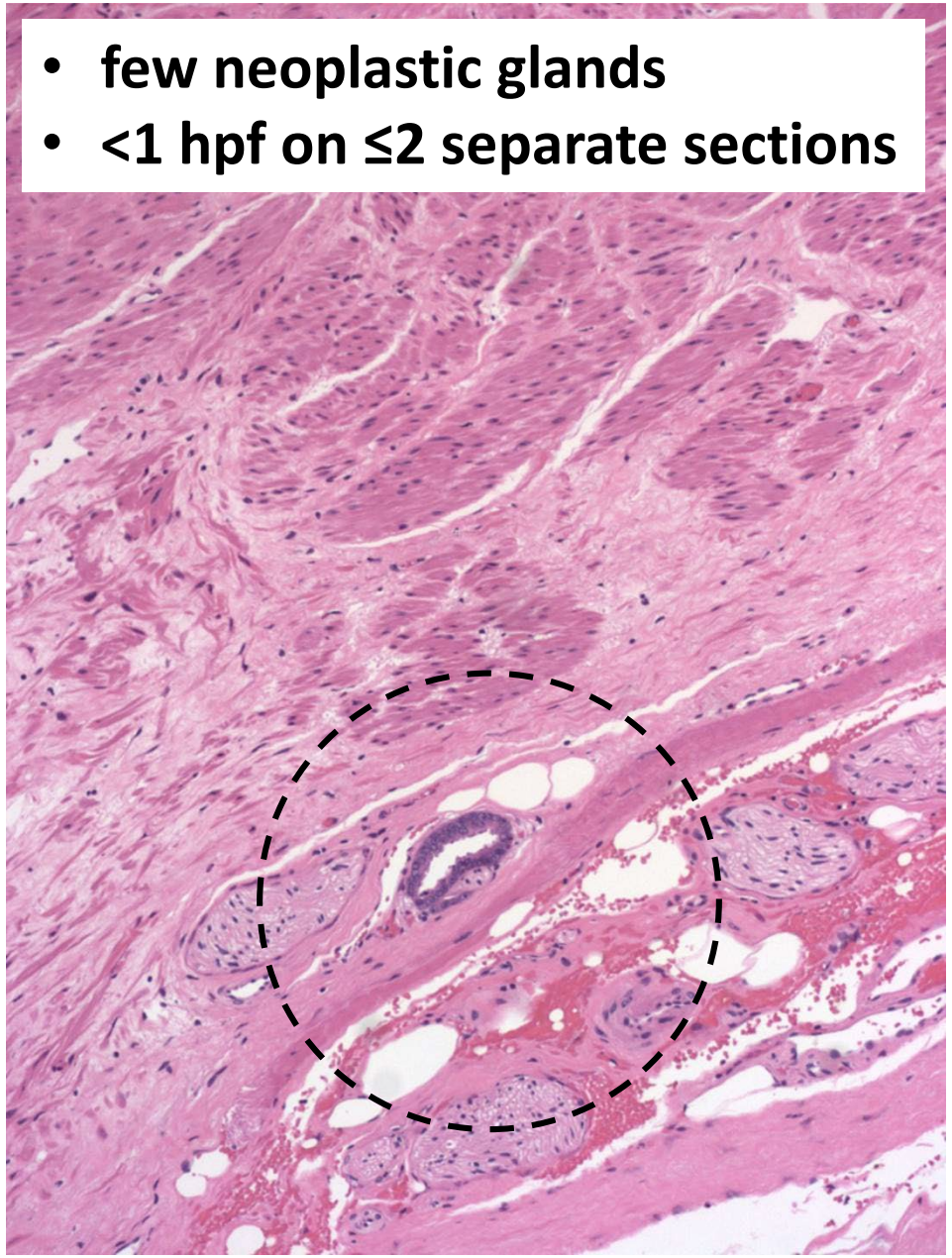
pT3a

Magi-Galluzzi et al. Mod Pathol 2011

Epstein Wheeler

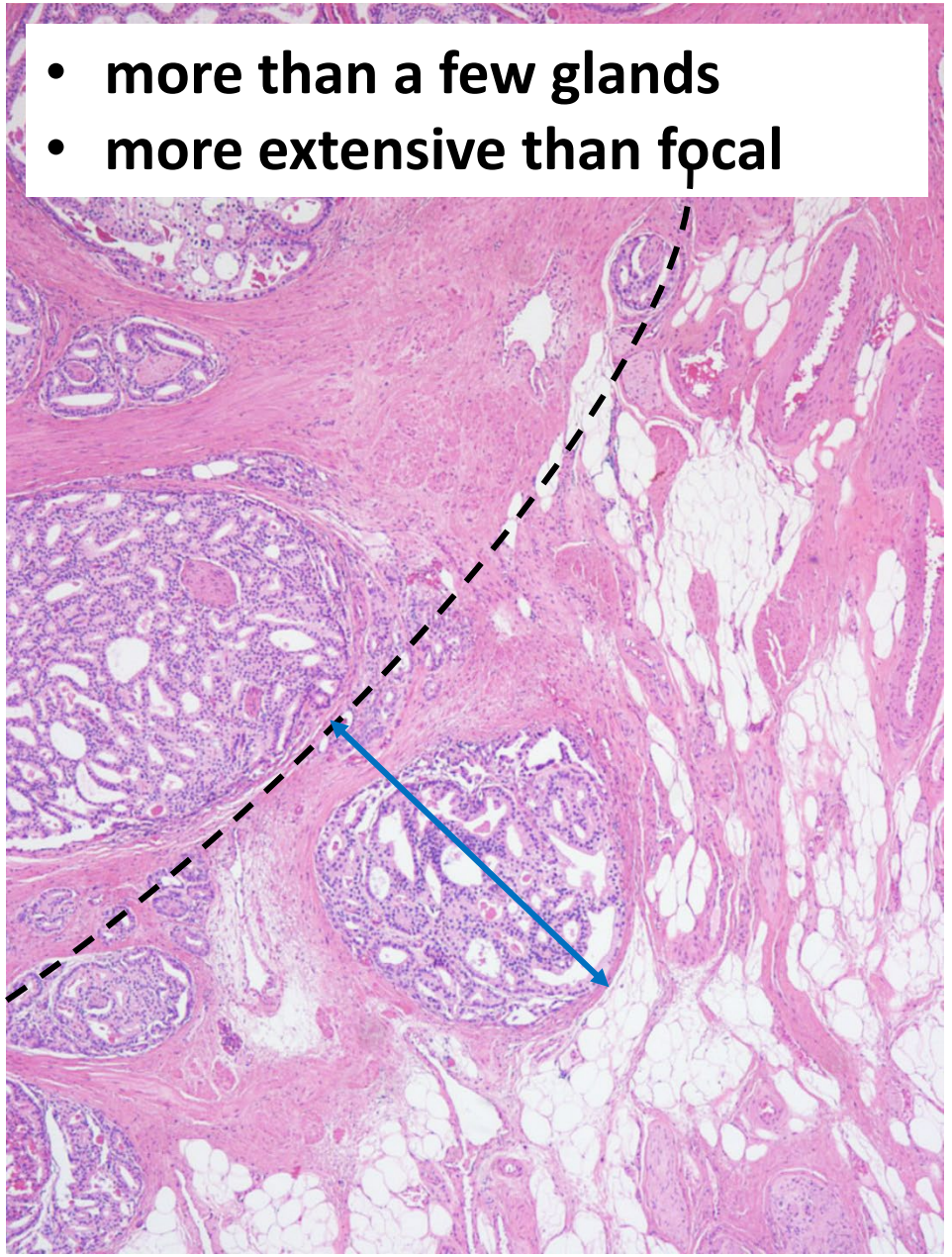
Focal EPE

- **few neoplastic glands**
- **<1 hpf on ≤2 separate sections**



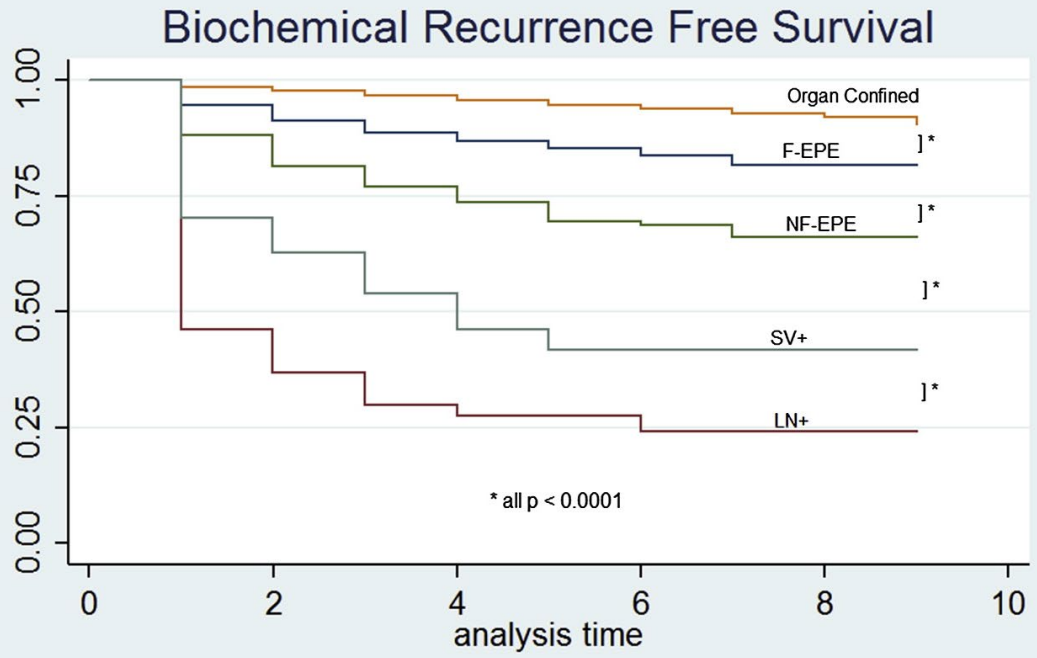
Nonfocal EPE

- **more than a few glands**
- **more extensive than focal**



RELATIONSHIP BETWEEN EXTENT OF EPE AND BCR-FREE SURVIVAL

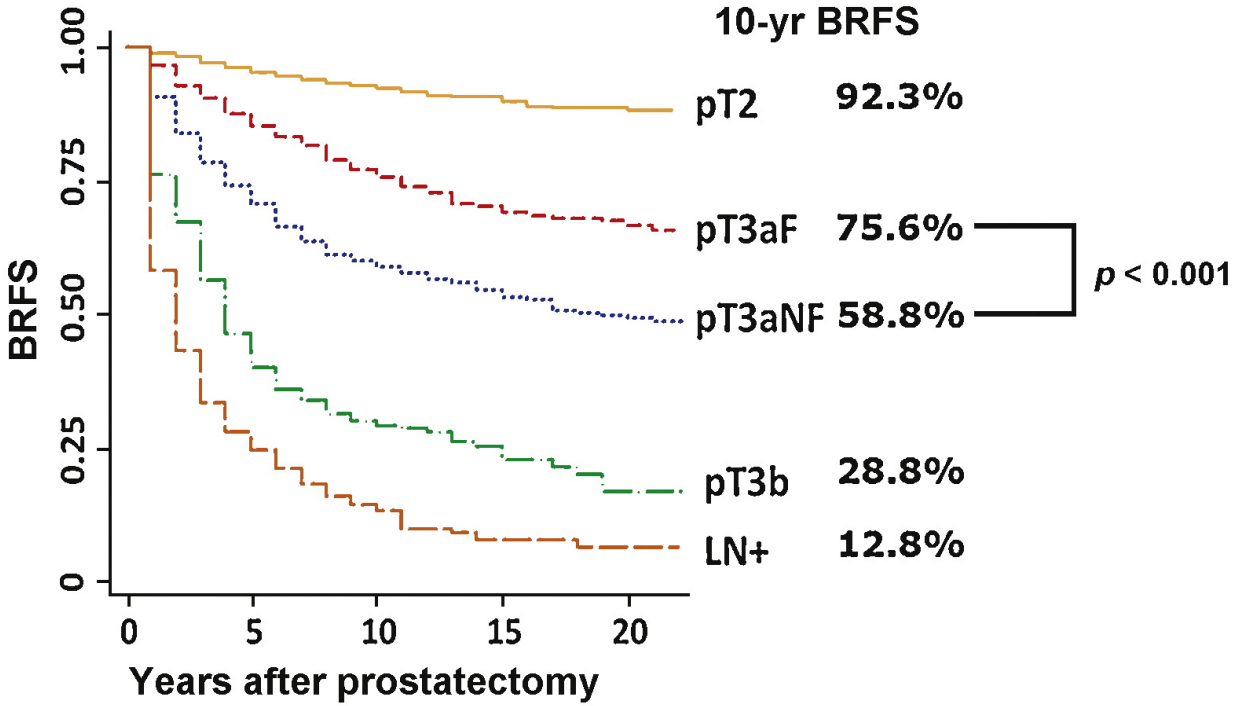
Ball et al. Urology 2015



Number at risk

Organ Confined	4411	2782	1518	786	251	0
F-EPE	683	428	236	120	36	0
NF-EPE	687	400	206	89	23	0
SV+	258	106	49	19	7	0
LN+	119	35	13	8	3	0

Jeong et al. Eur Urol 2015



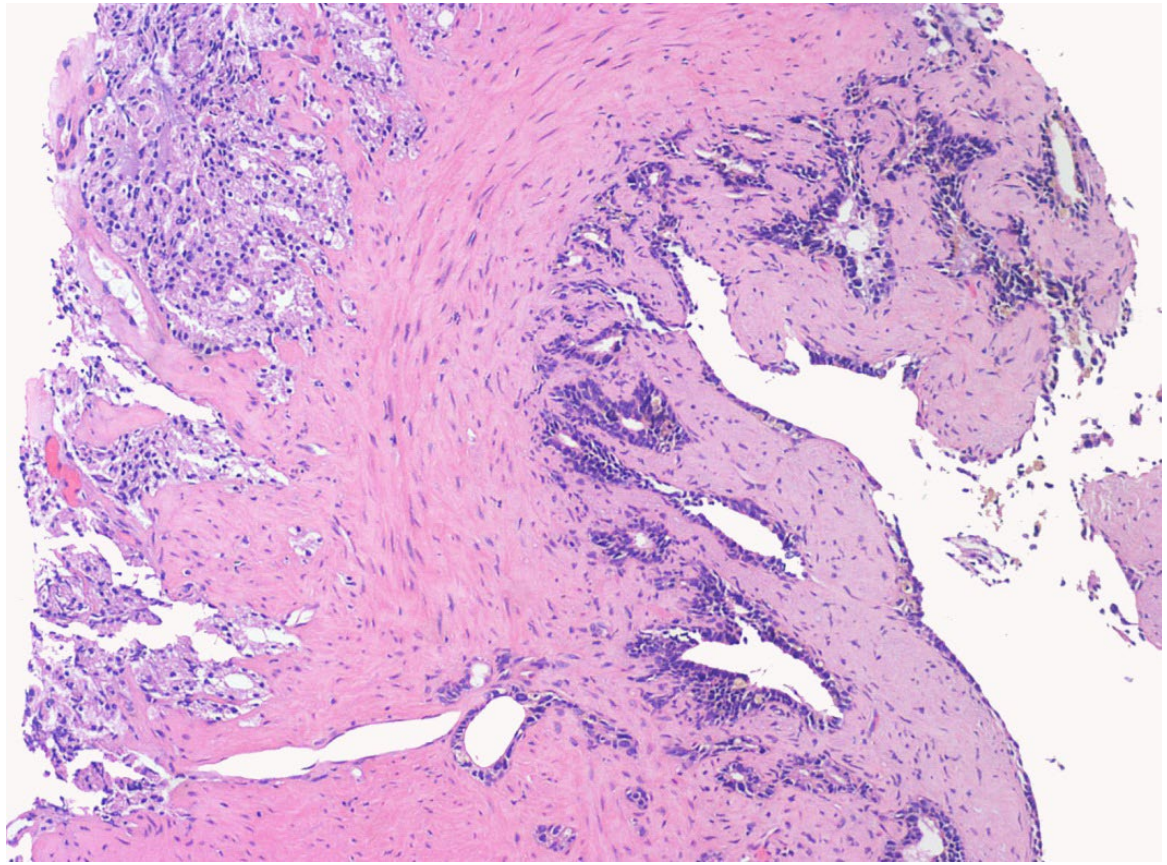
Number at risk

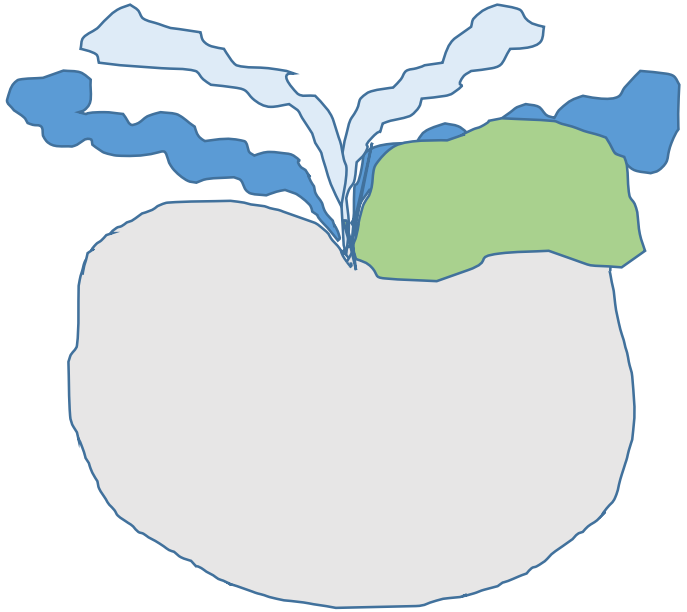
T2	10 365	4041	1947	692	212
T3aF	1869	852	467	231	90
T3aNF	2347	952	485	244	91
T3b	577	159	59	28	9
LN+	406	81	24	12	3

Subclassification of EPE extent improves correlation with BRFS

SEMINAL VESICLE INVASION

- Tumor invades muscular wall of extraprostatic portion of seminal vesicles





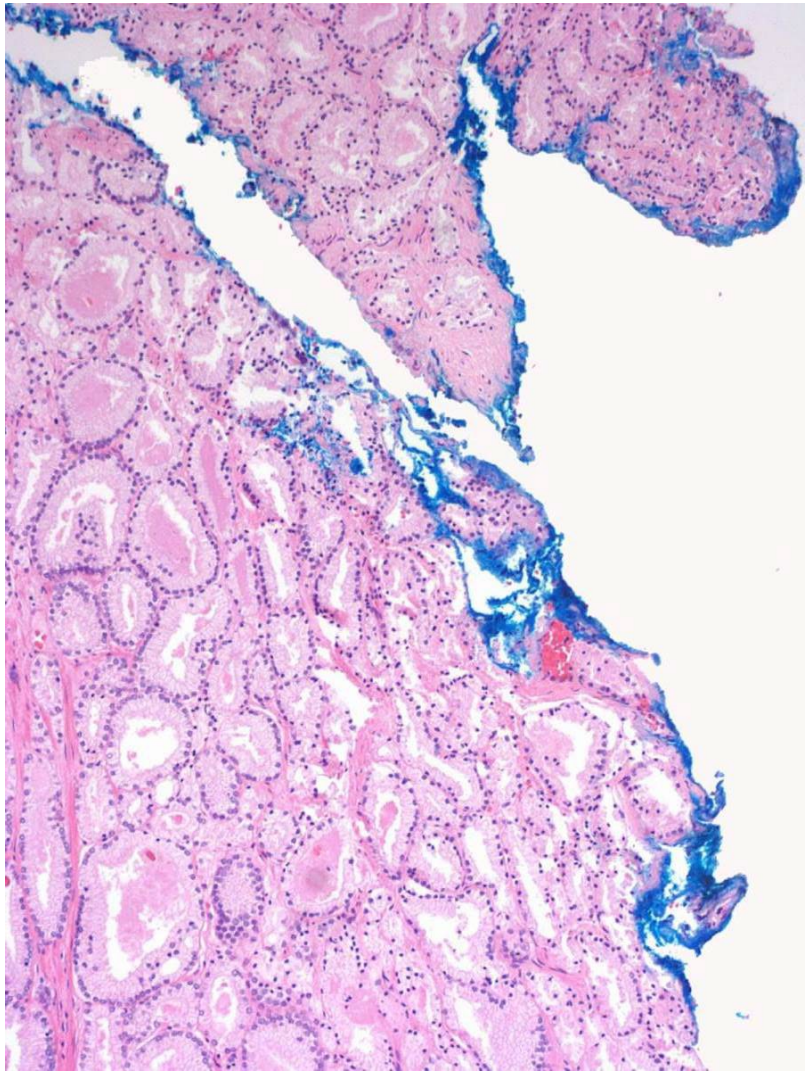
pT3b

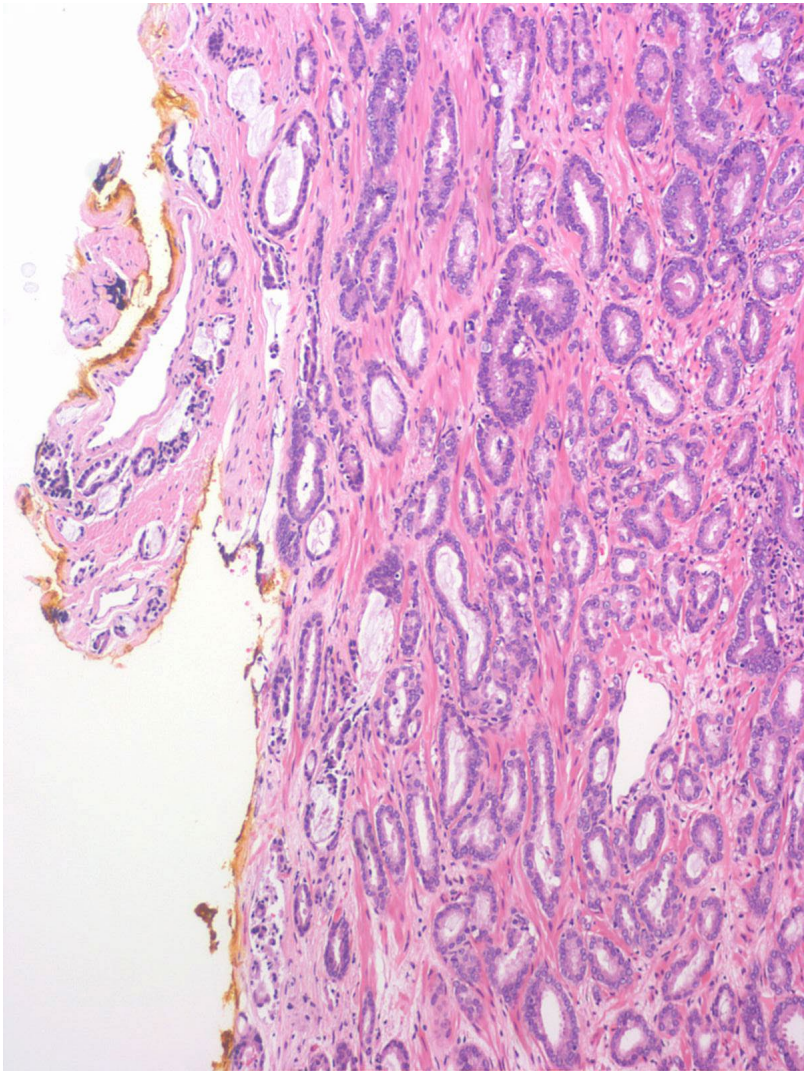
Berney et al. Mod Pathol 2011

SURGICAL MARGIN INVOLVEMENT (+SM)

- Tumor extends (extraprostatic or intraprostatic) to prostate inked surface

- For +SM document:
  - **Location**
  - **Extent** (limited: <3 mm or non-limited: ≥3 mm; linear length of +SM)
  - **Gleason pattern** @ +SM: pattern 3, 4, 5

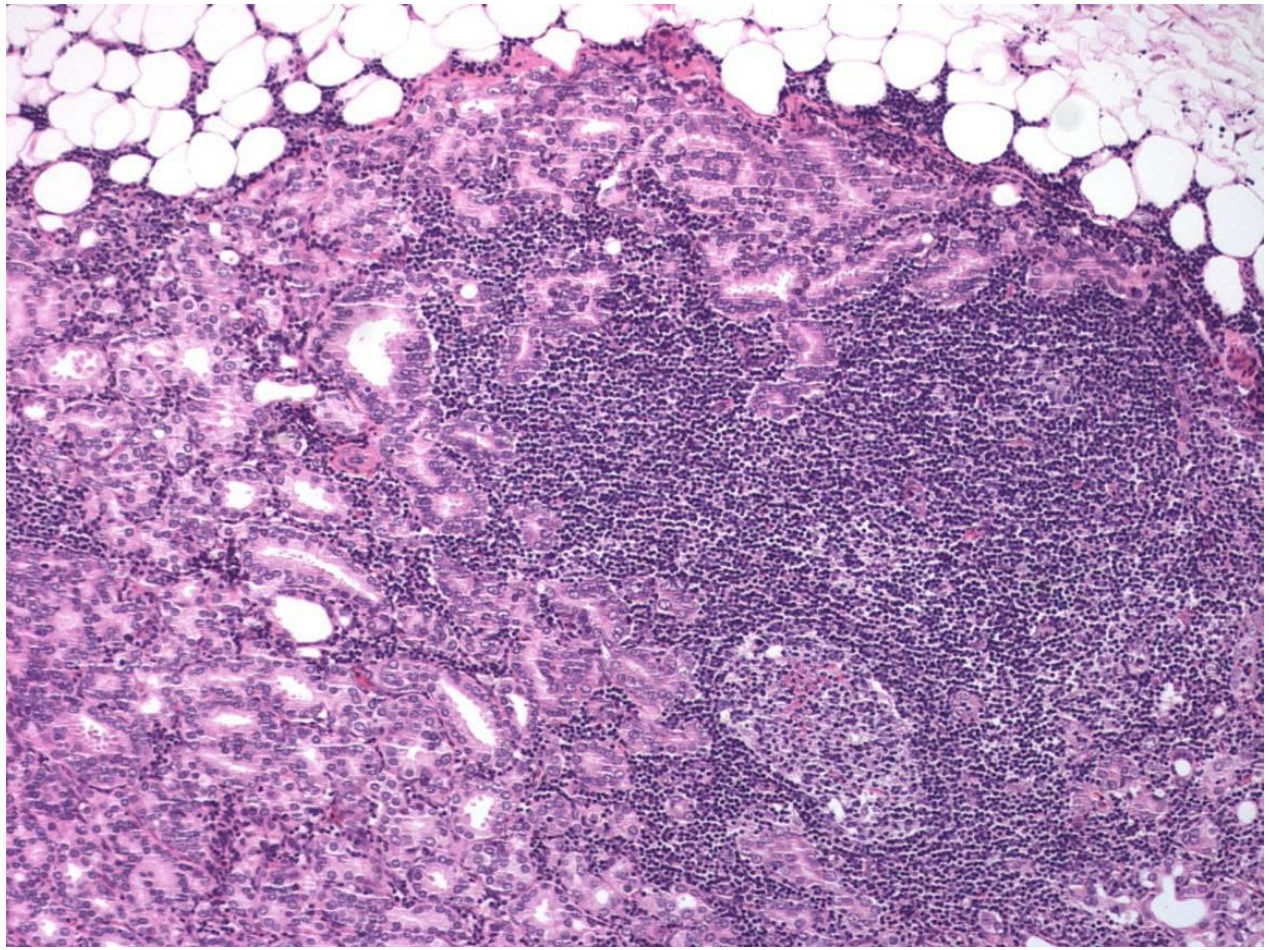




Tan et al. Mod Pathol 2011

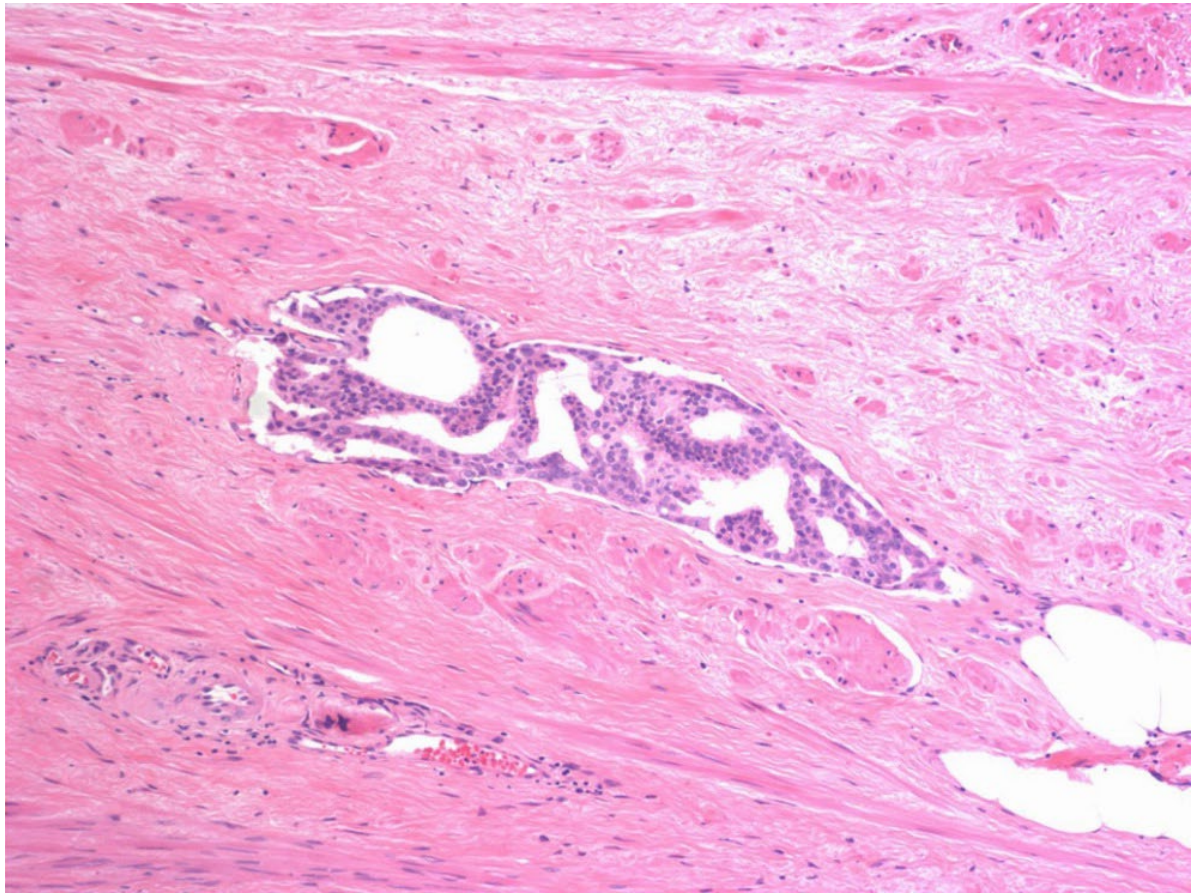
LYMPH NODE INVOLVEMENT (LNI)

- Important for adequate staging
- # and diameter of largest metastatic focus are independent predictors of early BCR [Passoni et al. BJU Int 2014]
- Extranodal extension is associated with significantly higher risk of BCR and “global” recurrence [Luchini et al. Sci Rep 2017]



LYMPHOVASCULAR INVASION (LVI)

- Significantly associated with adverse clinicopathologic features
- In pT3a and pT3b disease, LVI had 1.2 and 1.4-fold higher overall mortality than their counterparts without LVI [Jamil et al. Clin Genitourin Cancer 2021]
- Patients with LVI alone fared similarly to patients with LNI alone. Patients with LVI + LNI had worse OS than those with only LVI or LNI [Rakic et al. Urol Oncol 2021]



TAKE HOME POINTS

- In addition to accurate PCA diagnosis, pathology report should include essential elements to estimate tumor malignant potential
- Pathological parameters need to be:
  - Accurate
  - Reproducible
  - Consistently reported
- Unfavorable pathologic features (IDC, cribriform architecture, EPE, SVI, LVI) are important predictors of clinical outcome
- Genetic testing is recommended for patients with unfavorable features to guide precision therapy, active surveillance discussions and clinical trials eligibility

THANK YOU!

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SCHOOL OF MEDICINE