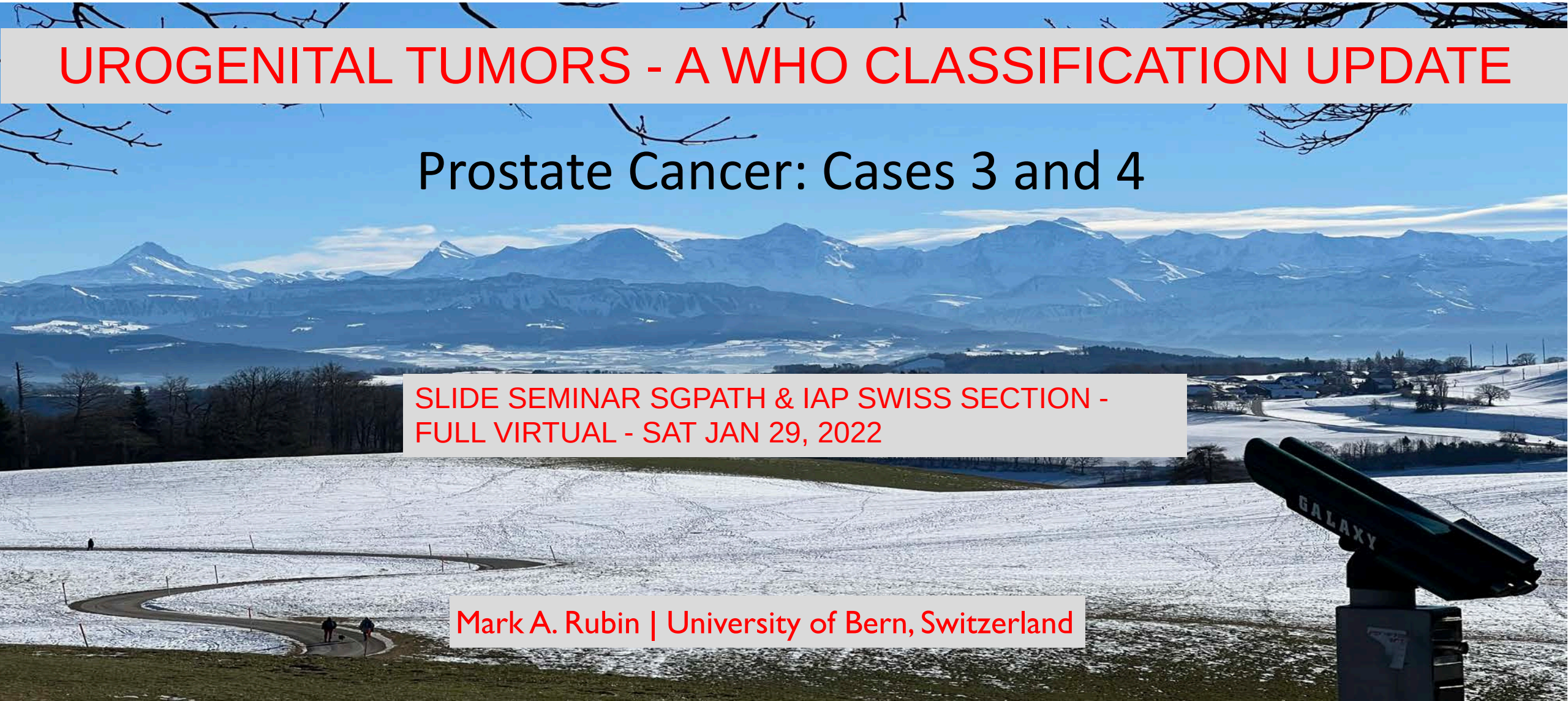
UNIVERSITÄT BERN

Bern Center FOR PRECISION MEDICINE

UROGENITAL TUMORS - A WHO CLASSIFICATION UPDATE

Prostate Cancer: Cases 3 and 4



SLIDE SEMINAR SGPATH & IAP SWISS SECTION - FULL VIRTUAL - SAT JAN 29, 2022

Mark A. Rubin | University of Bern, Switzerland

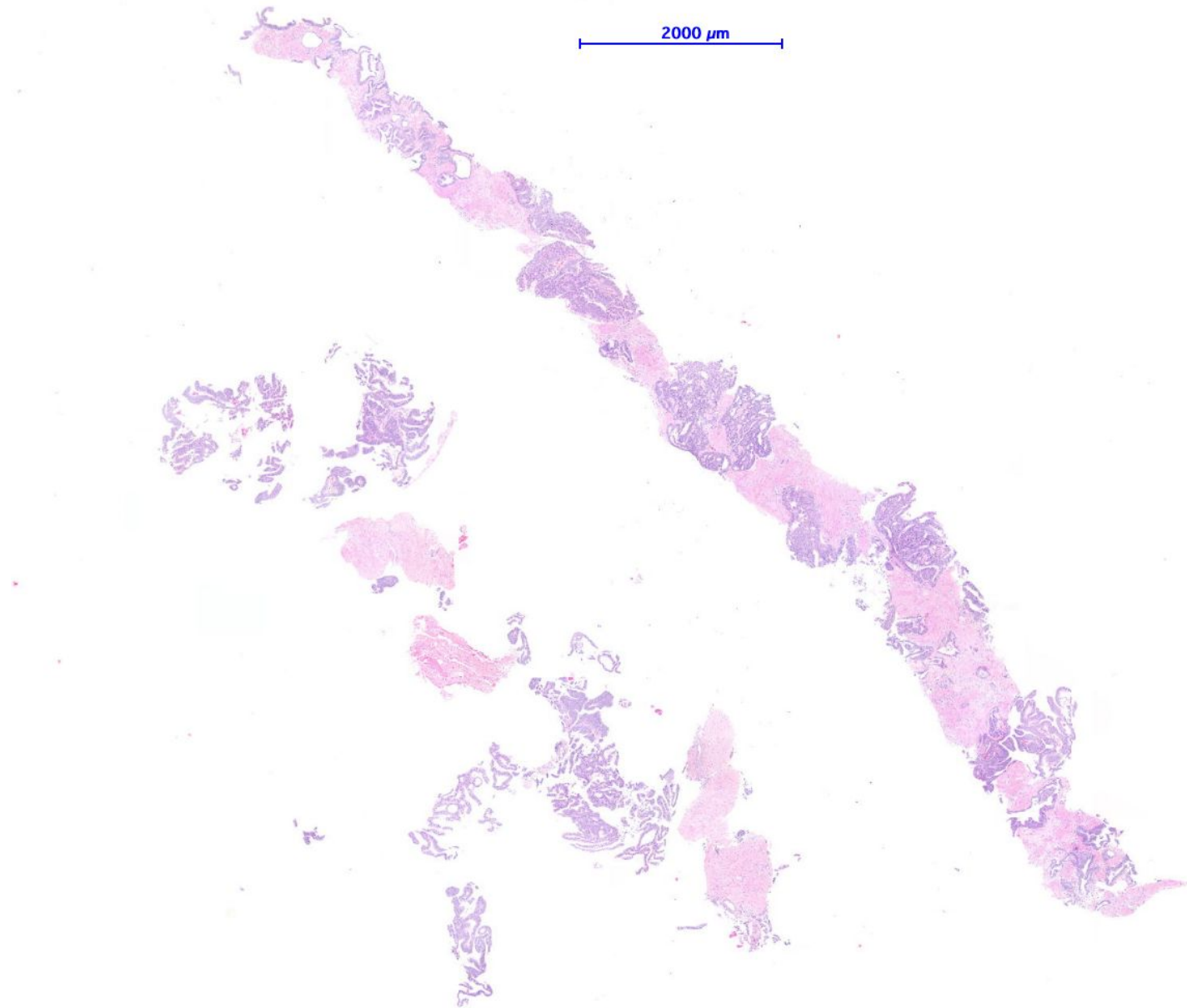
Case 3:
69 years old male patient. No further clinical information.

Case 4:
70 years old male patient. PSA 9, PIRADS 5.

Cases contributed by, José Antonio Rodríguez Calero
GU Pathologist, University of Bern and Inselspital

Case 3:
69 years old male patient. No further clinical information.

Case 4:
70 years old male patient. PSA 9, PIRADS 5.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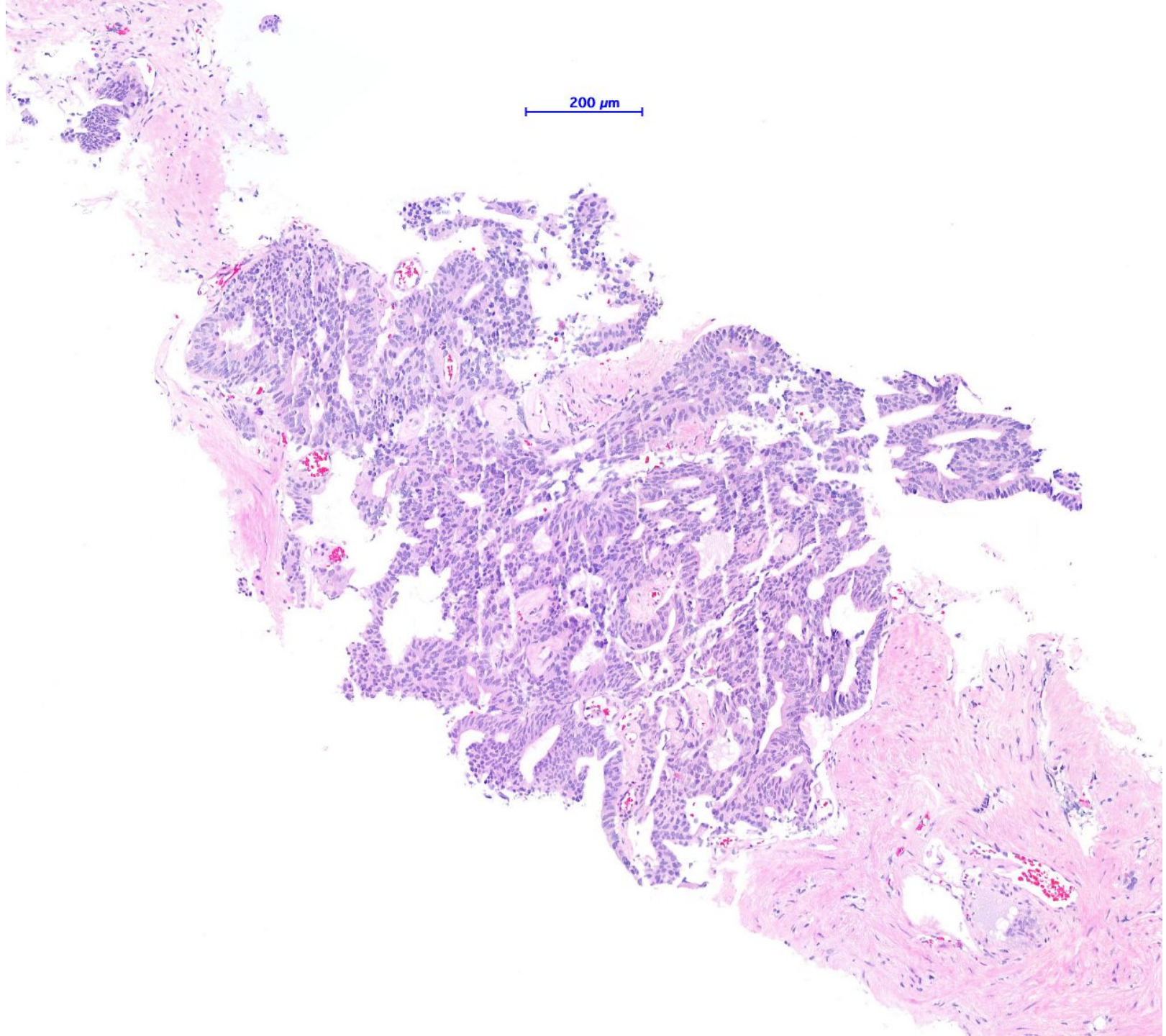
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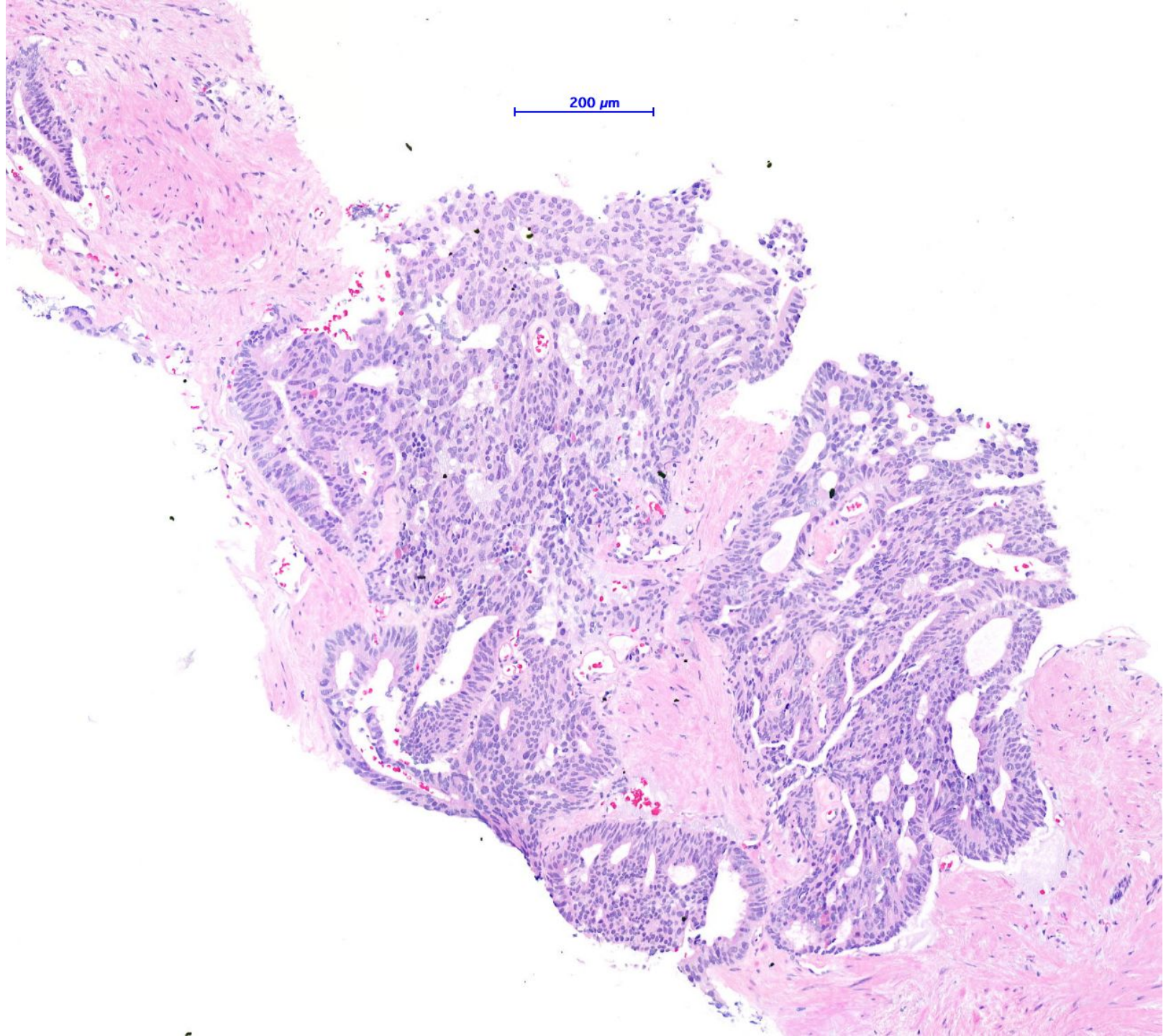
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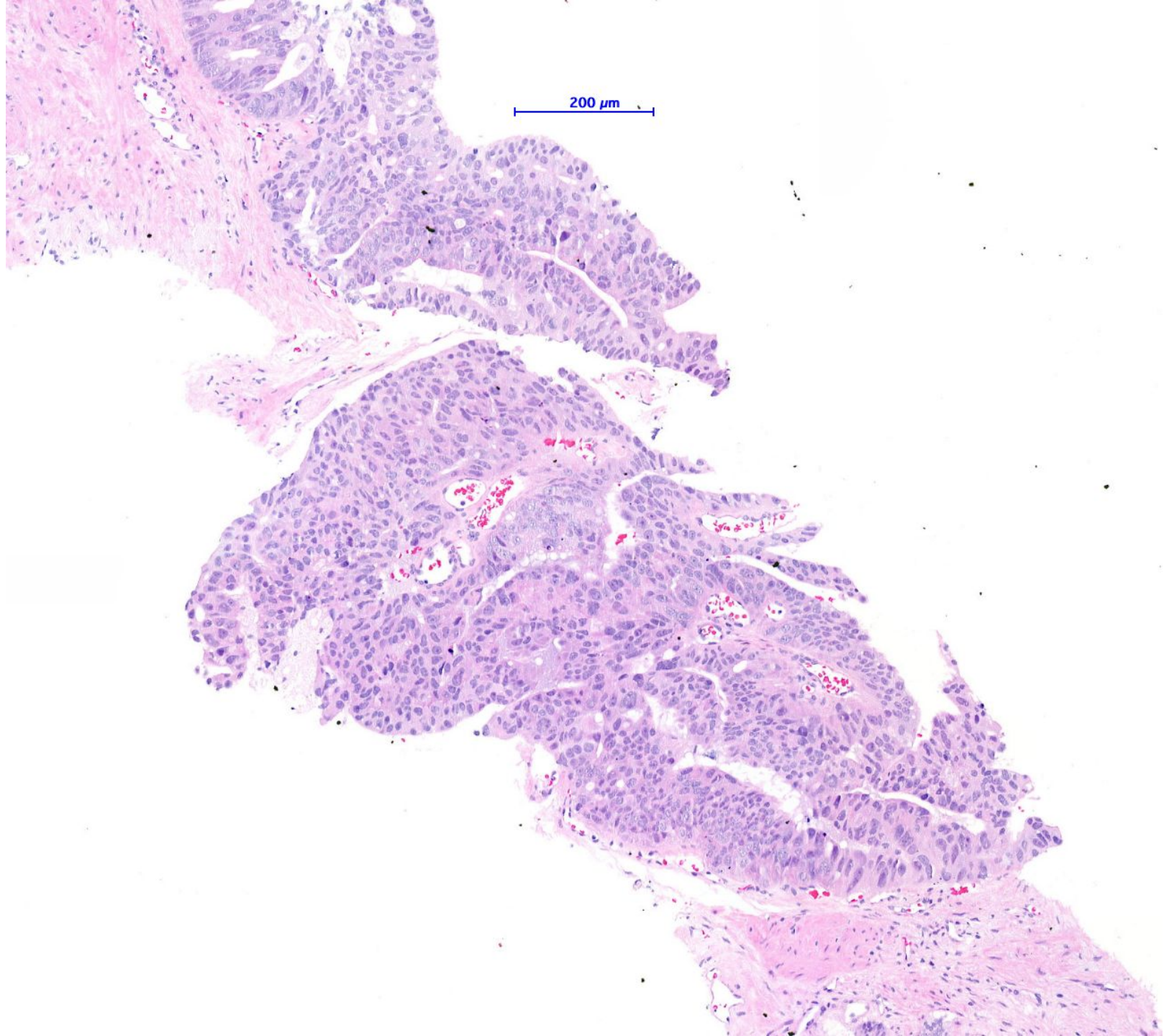
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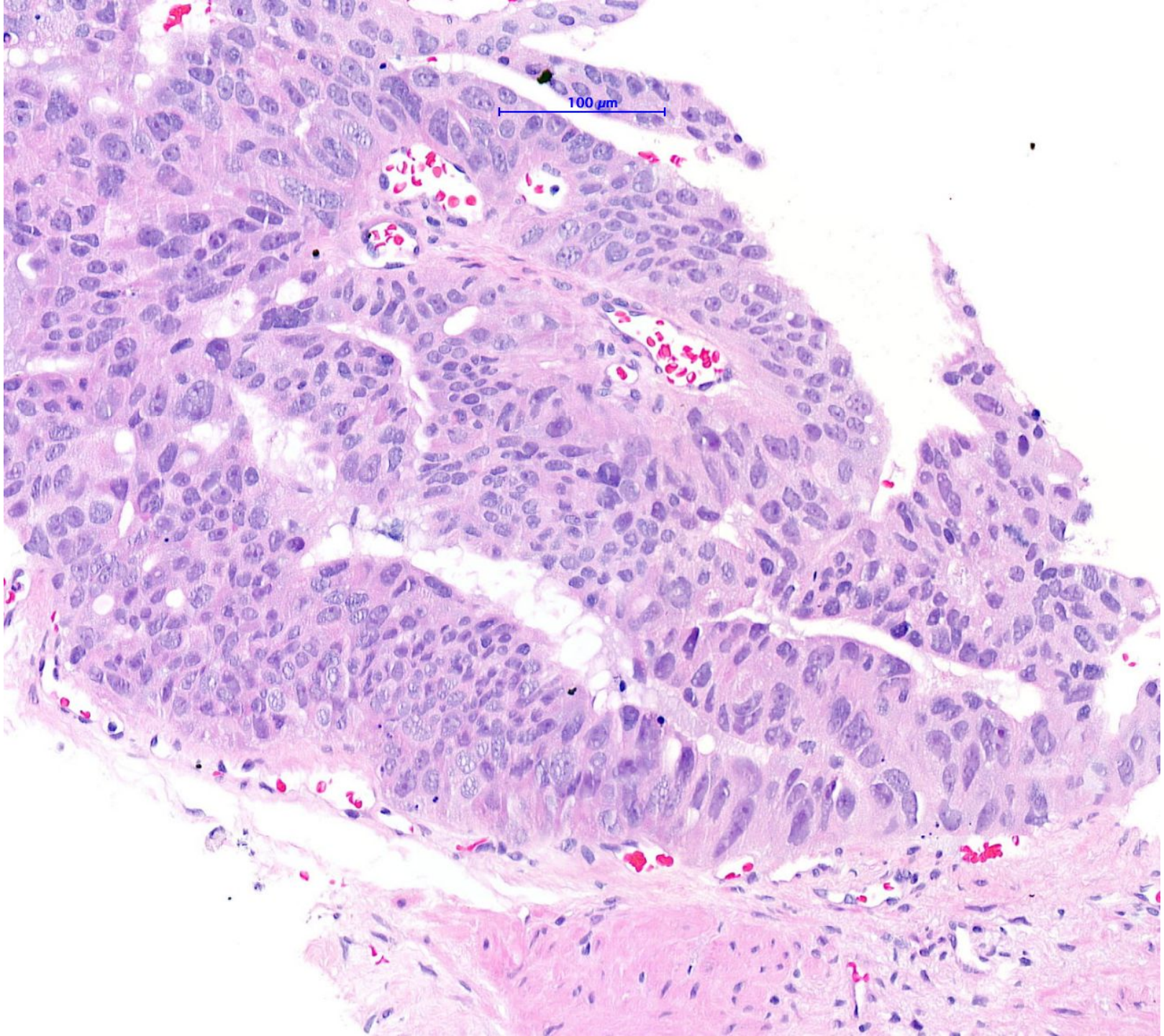
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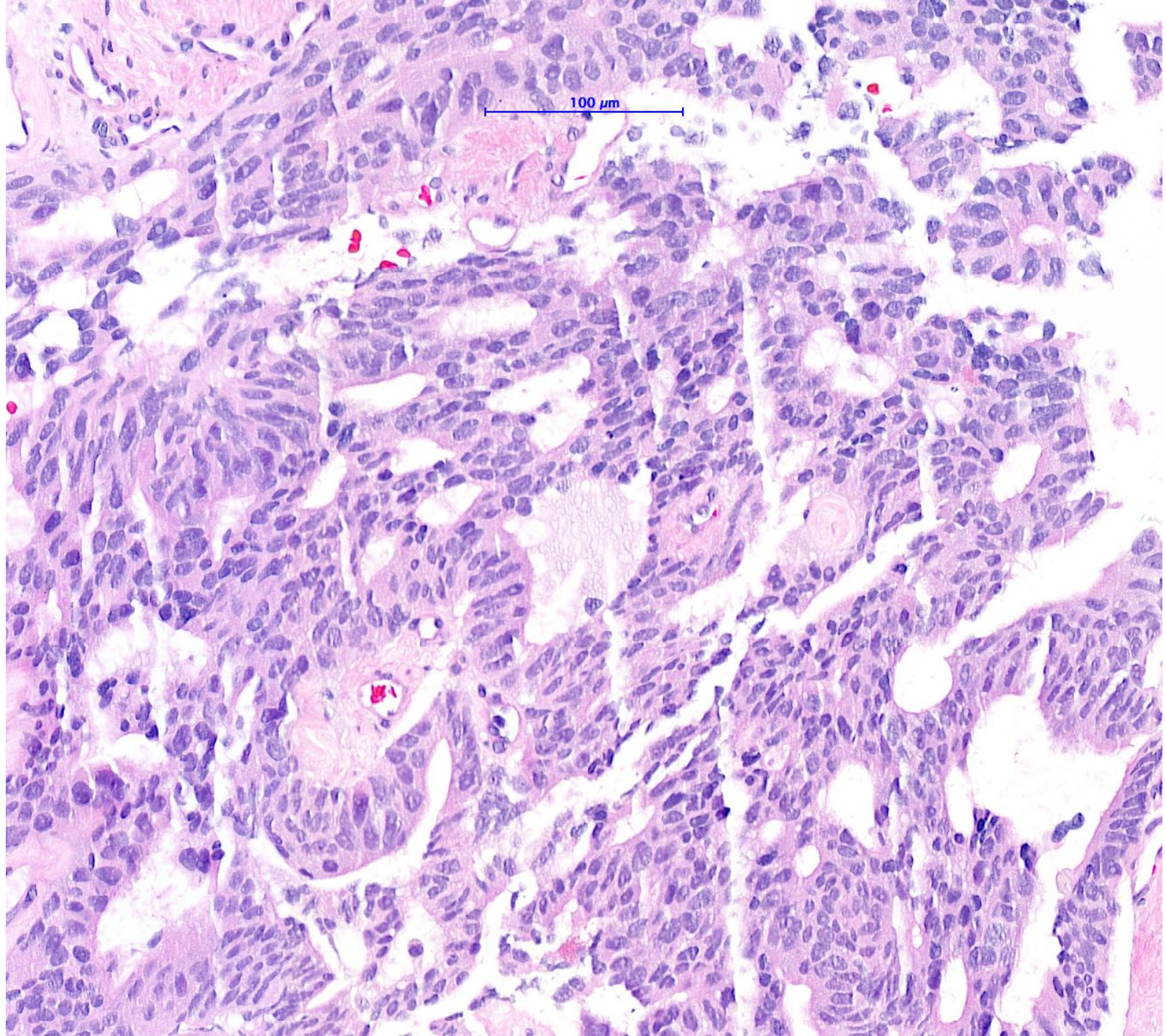
100 µm

Case 3:
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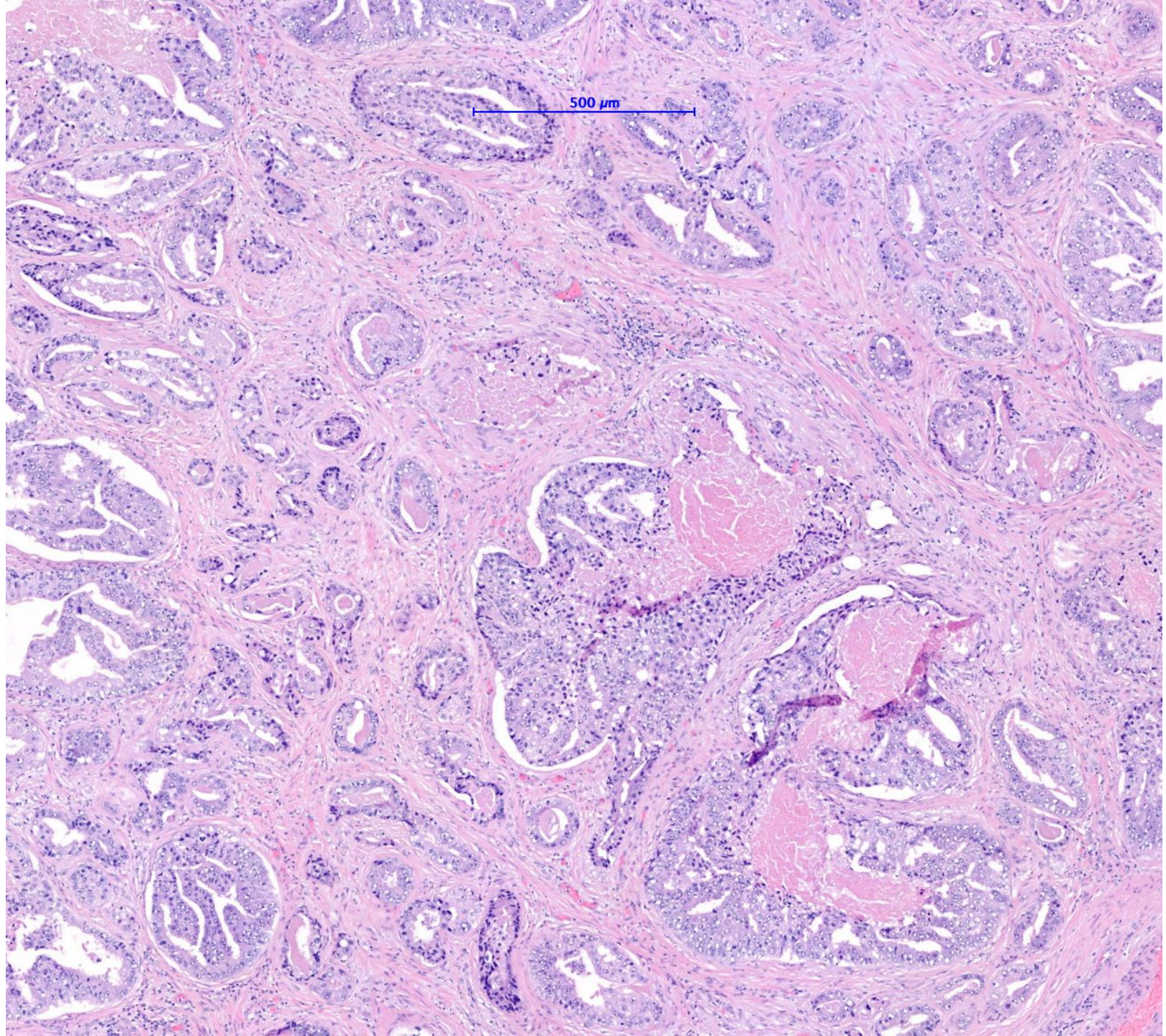
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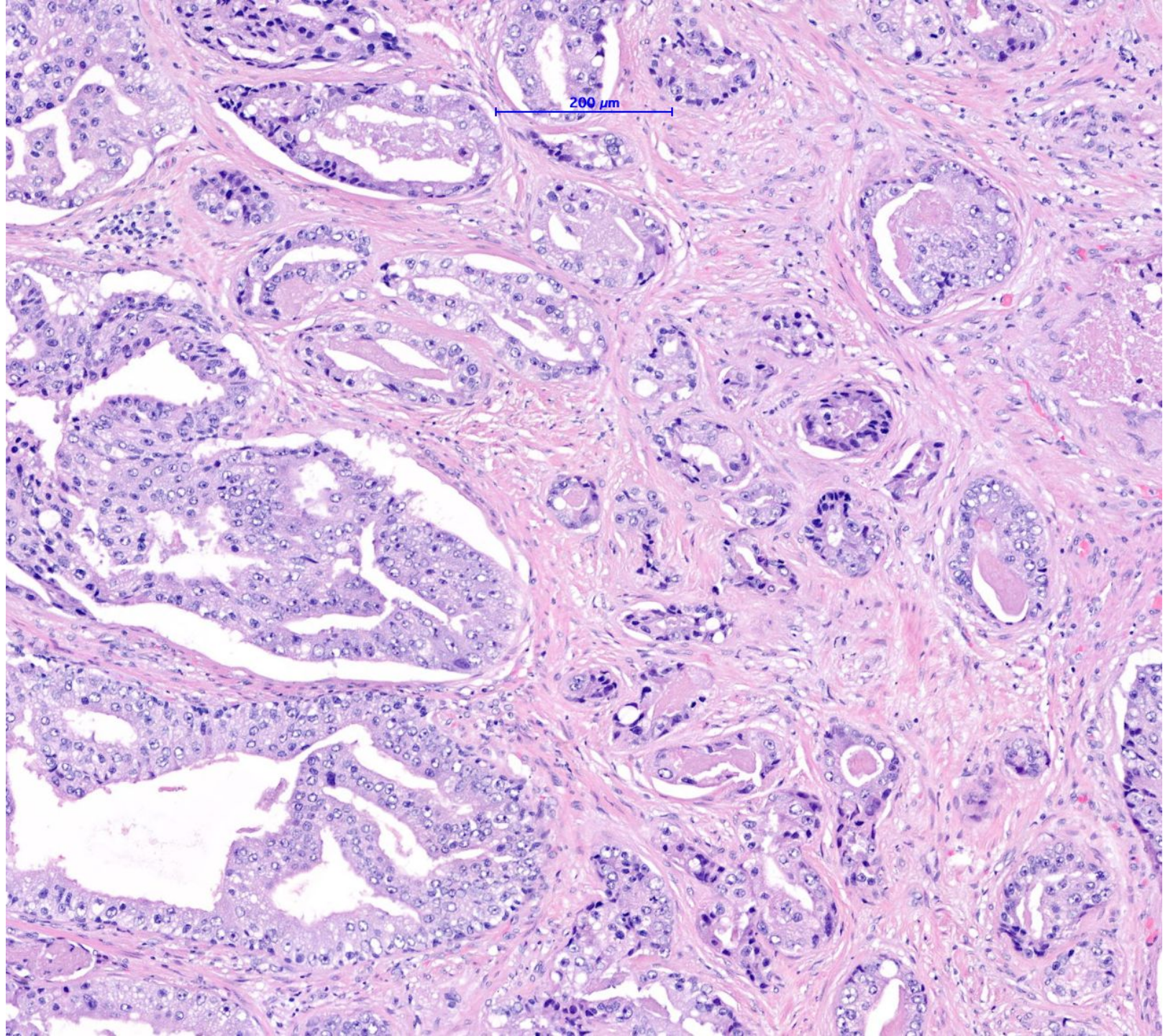
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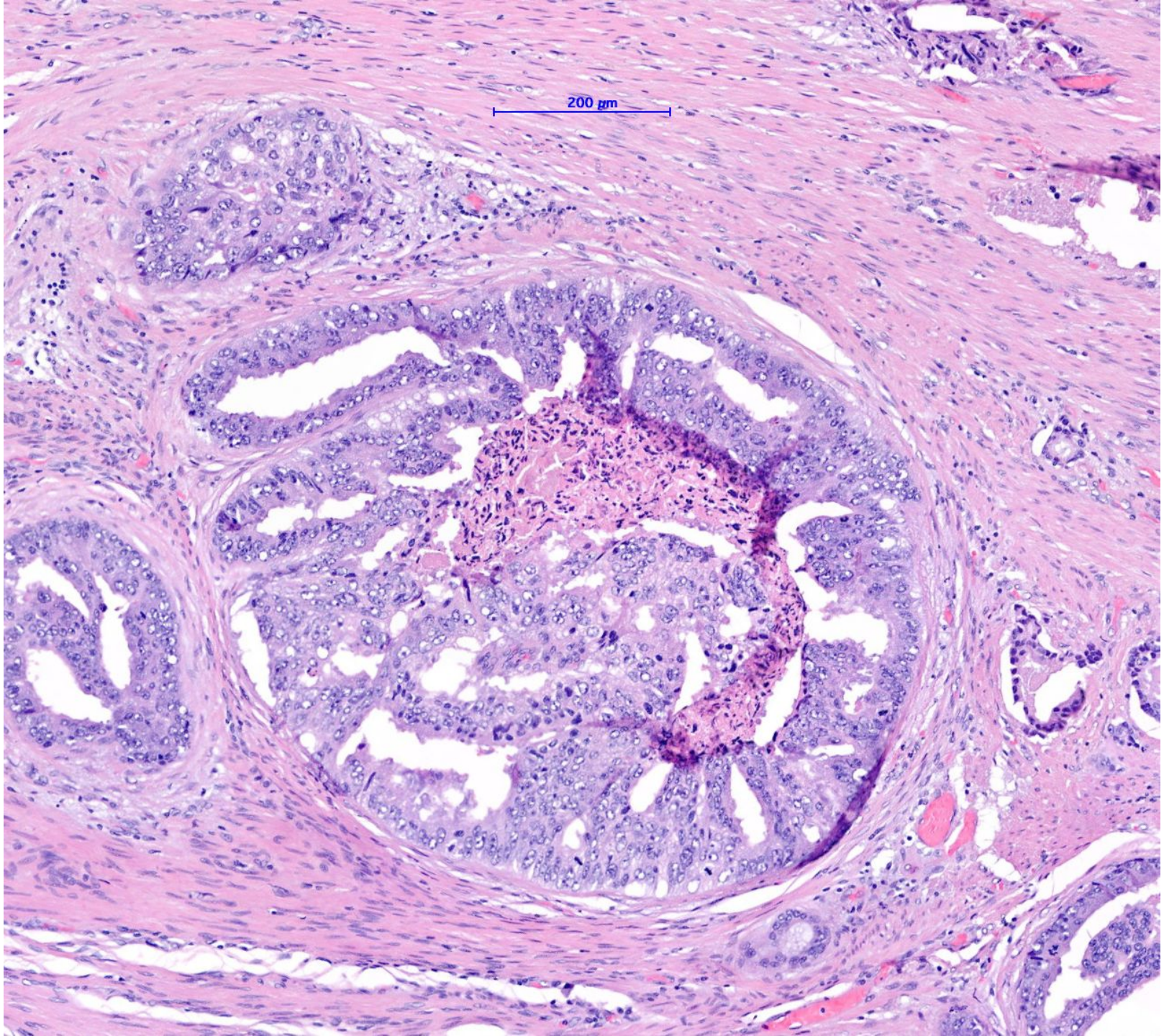
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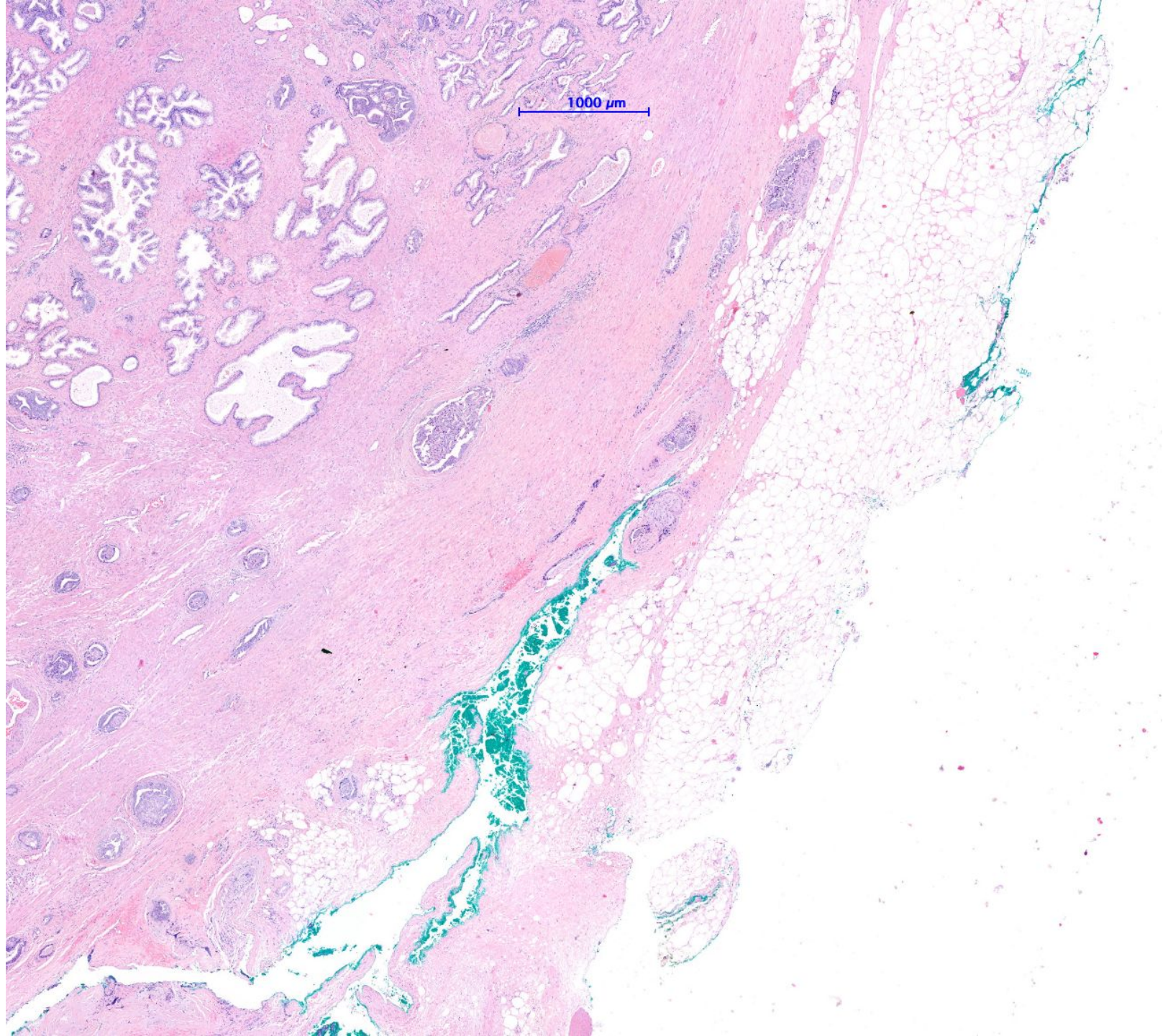
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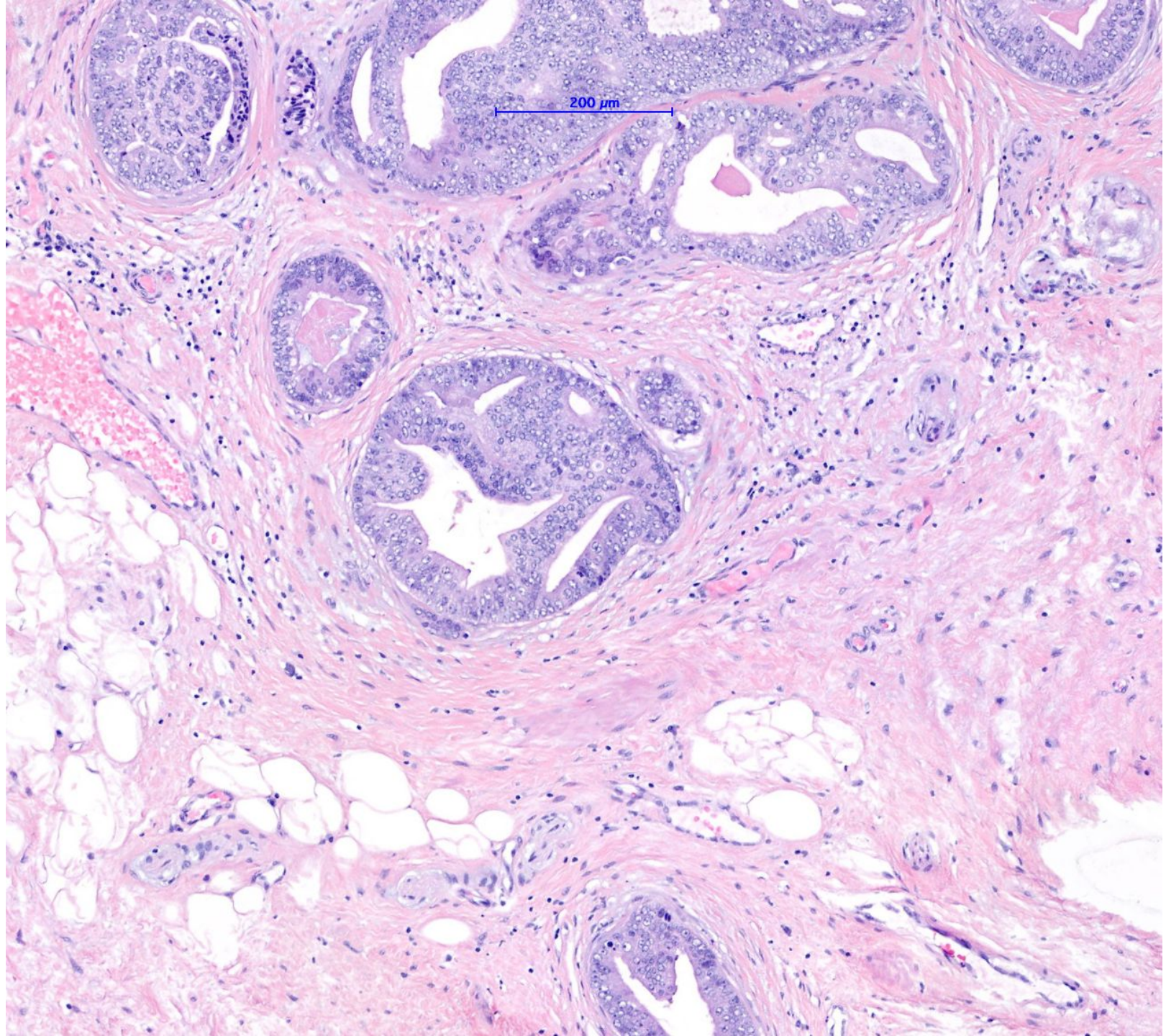
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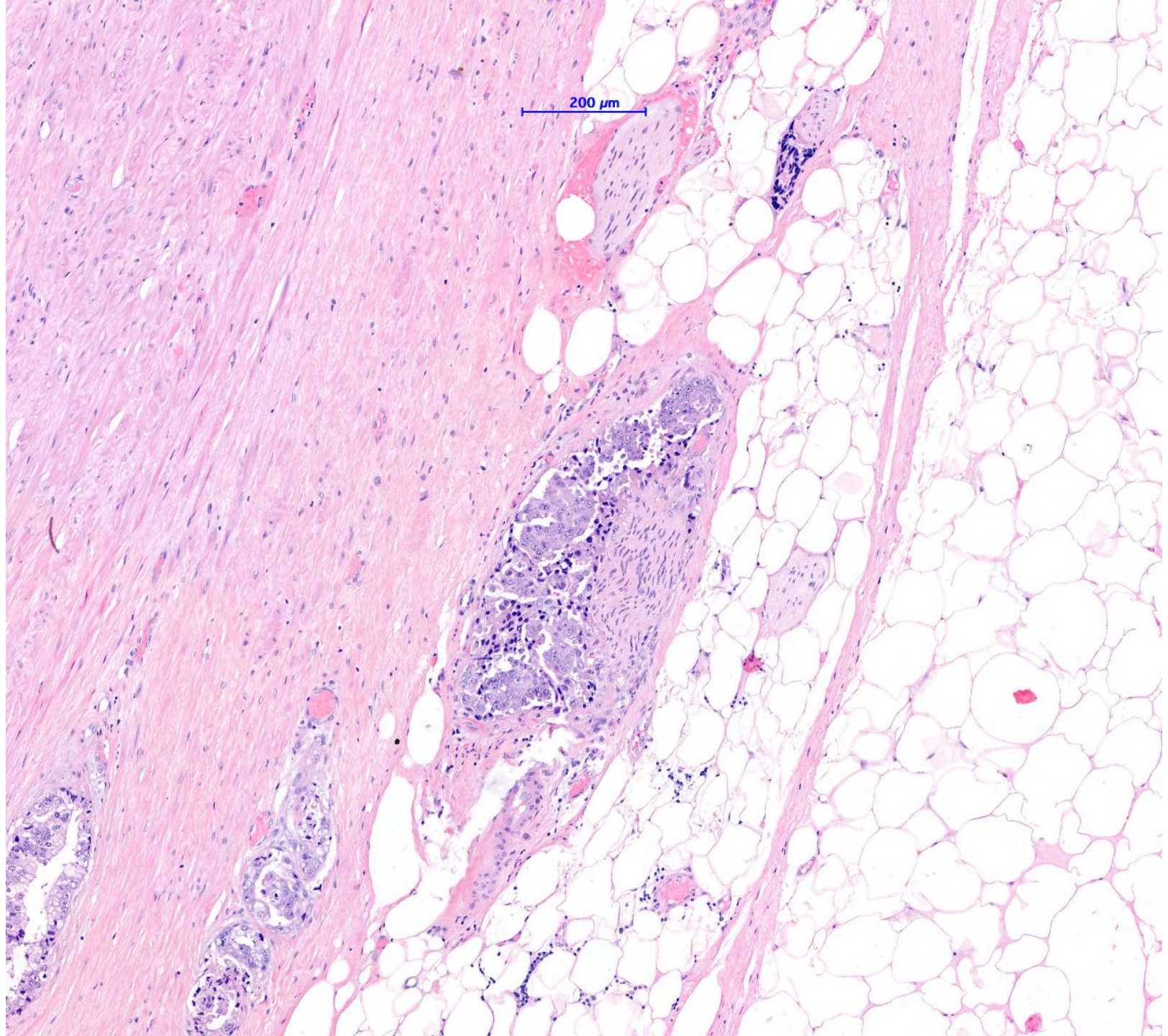
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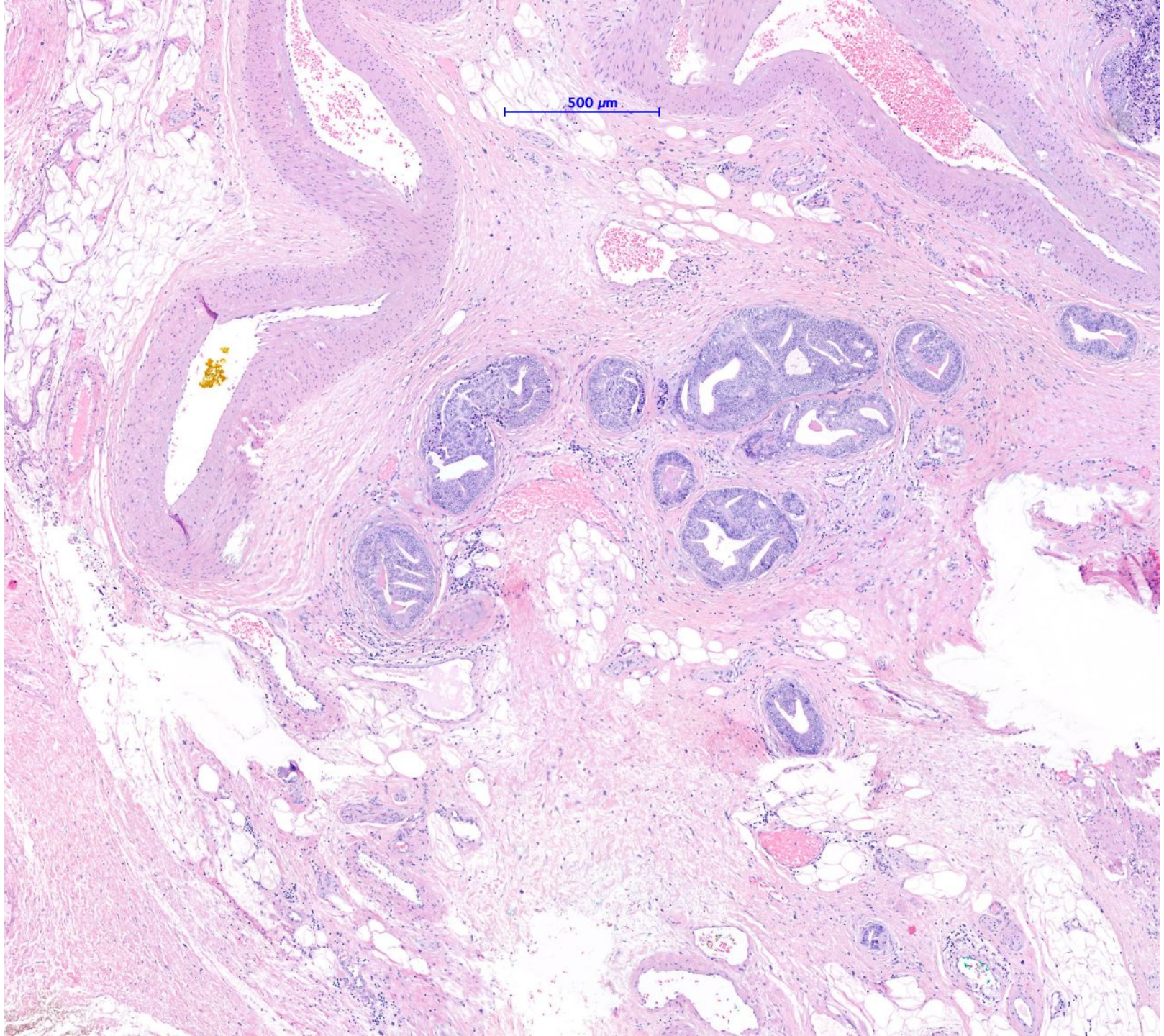
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Case 3:
Adenocarcinoma with ductal features. Gleason Score 4+4=8, Grade Group 4,
69 years old male patient. No further clinical information.

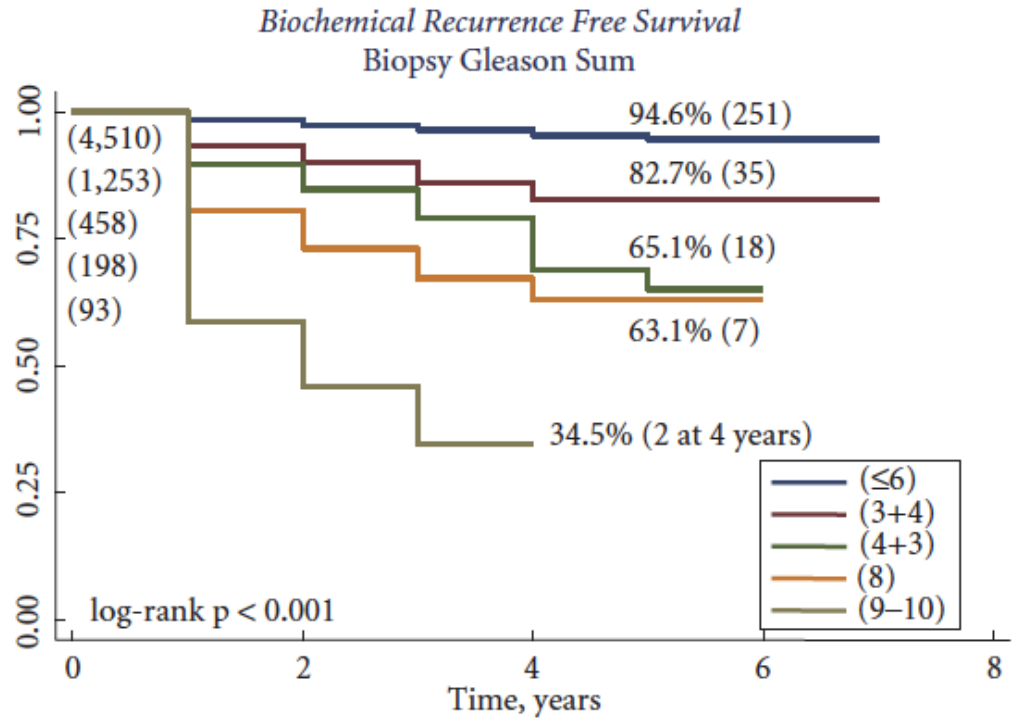
Case 4:
Adenocarcinoma with ductal features. Gleason Score 4+4=8, Grade Group 4.
70 years old male patient. PSA 9, PIRADS 5.

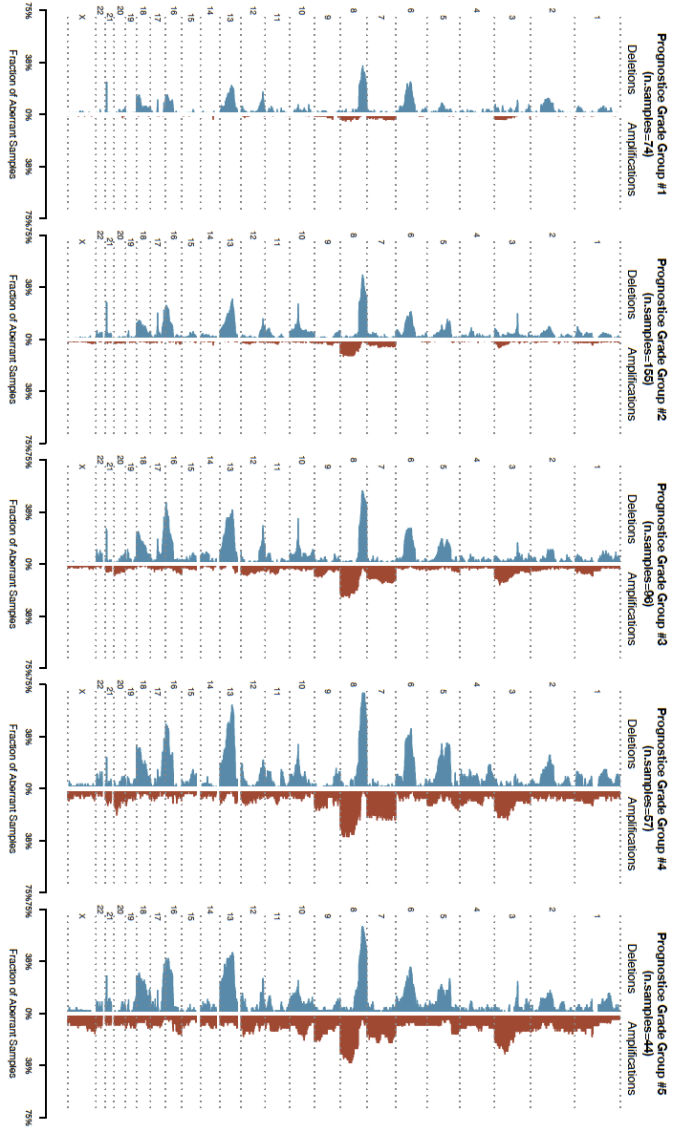
Primary Prostate Cancer

Prognostic Gleason grade grouping: data based on the modified Gleason scoring system

Phillip M. Pierorazio*, Patrick C. Walsh*, Alan W. Partin* and Jonathan I. Epstein*†‡

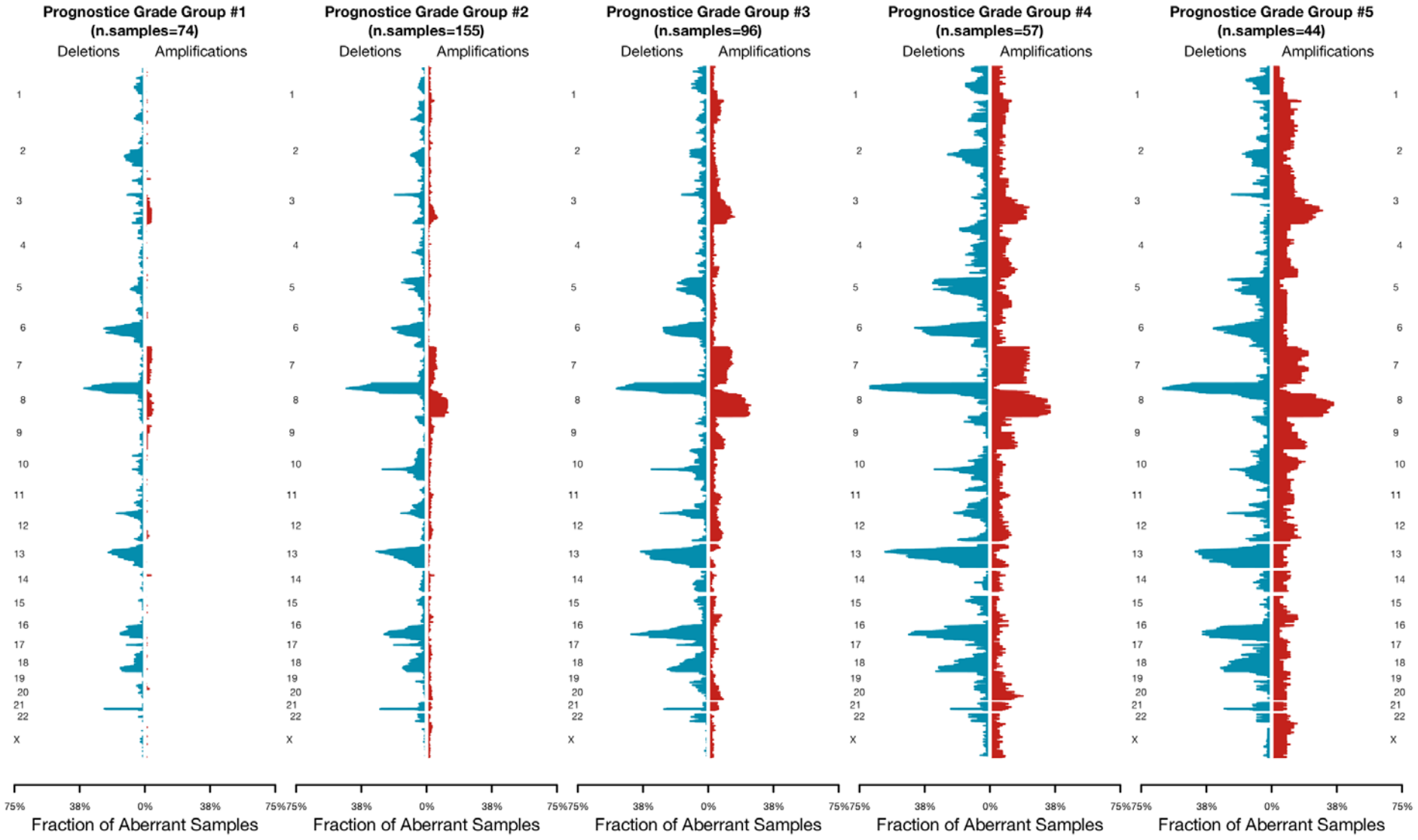
2013 BJU International





Rubin, Eur Urol 2016

SCNA in Prostate Cancer with Increasing Risk Groups



6 3/4 4/3 4/4 4/5+

Rubin, Eur Urol 2016

Case 3:
Adenocarcinoma with ductal features. Gleason Score ~~4+4=8, Grade Group 4,~~ 4+5=9, Grade group 5 (Area of cribriform growth with necrosis in another biopsy core)
69 years old male patient. No further clinical information.

Case 4:
Adenocarcinoma with ductal features. Gleason Score 4+4=8, Grade Group 4.
70 years old male patient. PSA 9, PIRADS 5.

Talk Overview*

1. Historic background—”*we’ve seen this before*”
2. Intra-ductal carcinoma-WHO Definitions
3. Prostatic ducal carcinoma-WHO Definitions
4. Clinical implications-Key practical implications
5. Summary

*Note: All slides available for private use at: ***https://www.rubinlab.com/presentations***

All references are given as PMIDs that are available on PubMed

ENDOMETRIAL CARCINOMA OF PROSTATIC UTRICLE (UTERUS MASCULINUS)

MEYER M. MELICOW, MD,* AND M. R. PACHTER, MD†

With the increased number of prostatic specimens submitted for pathologic examination, the variety of lesions discovered in the processed tissue has widened. In addition to the characteristic patterns of "benign prostatic hypertrophy" and the usual ones in primary adenocarcinoma of the prostate, other lesions not intrinsically prostatic have been observed. Some proved to be extensions from cancers of nearby structures such as the periurethral glandules, urethra, urinary bladder, seminal vesicles etc. It is important to be aware of these malignancies since their natural history and response to therapy differs from the usual prostatic cancer. The case presented here shows yet another pattern which is interesting and which may be the first of its kind to be reported. The patient was a normal genotypical, phenotypical man whose prostate was removed for what was thought to be "benign hypertrophy;" however, it revealed a malignancy which was of the endometrial variety and apparently arose from the region of the utricle; in other words, a carcinoma of the uterus masculinus.

Cancer 1967

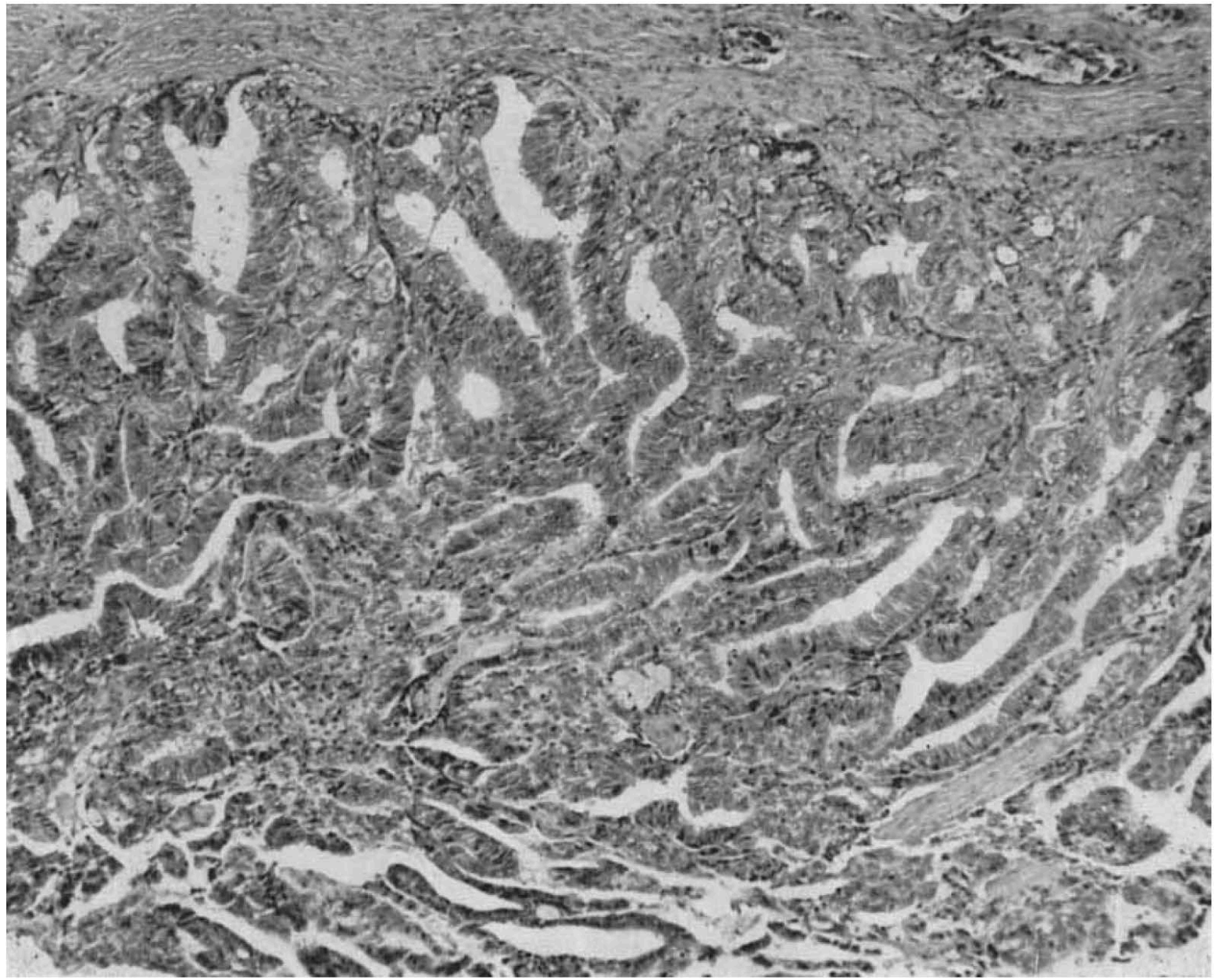


FIG. 1. Endometrial carcinoma of prostatic utricle (uterus masculinus). Note large columnar cells arranged in bands with infolding and pseudopapillary formations (×400).

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ENDOMETRIAL CARCINOMA OF UTERUS MASCULINUS (PROSTATIC UTRICLE). REPORT OF 6 CASES

MEYER M. MELICOW AND M. TANNENBAUM

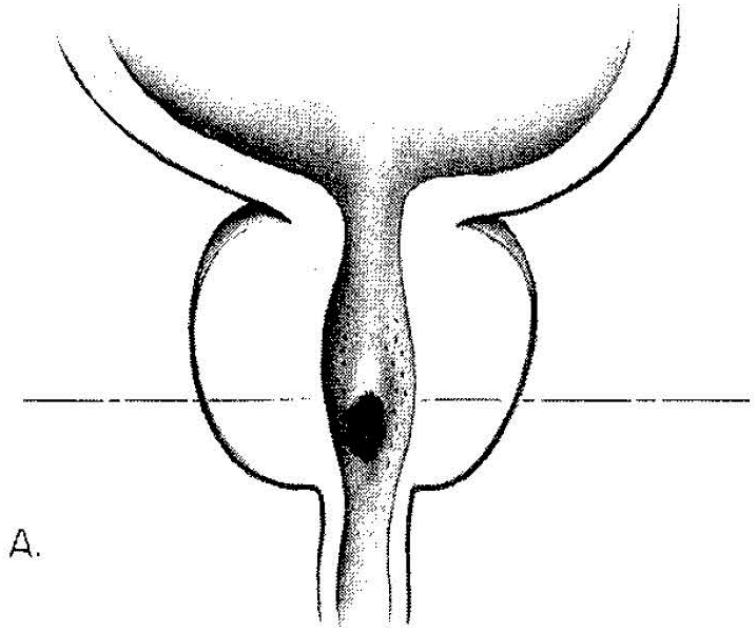
From Columbia University and the College of Physicians and Surgeons, New York, New York

In 1967 Melicow and Pachter reported on what was probably the first recognized case of endometrial carcinoma of the prostatic utricle (uterus masculinus).[1] The patient was not a male pseudohermaphrodite; buccal smear revealed a normal male pattern. The penis was well developed and the urethral meatus was located at the apex of the glans. The testes were intrascrotal and not abnormal. The neoplasm apparently had arisen in the utricle—a müllerian vestige present in normal male subjects. Since publication of this case, we have seen 5 additional cases (tables 1 to 3). All 6 cases are reported herein.

CASE REPORTS

present, which had apparently broken into the submucosa and infiltrated the gland (fig. 1, *c*). Diagnosis was adenocarcinoma of the utricle (uterus masculinus); orchiectomy was not performed and estrogens were not prescribed. Five years post-prostatectomy the patient is free of metastases.

Case 2. R. N., a 64-year-old man, was hospitalized on October 6, 1967 for evaluation of the prostate, which had been declared malignant. Orchiectomy had been advised but the patient declined. He complained of frequency and nocturia. The prostate was moderately enlarged and the right lobe was indurated. Seminal vesicles were not palpable. Serum acid and serum alkaline phosphatase levels were normal. Cystoscopy on



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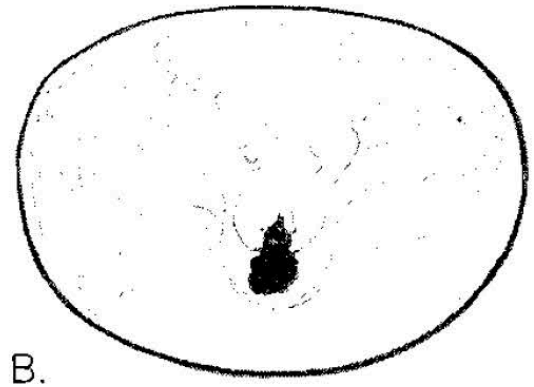

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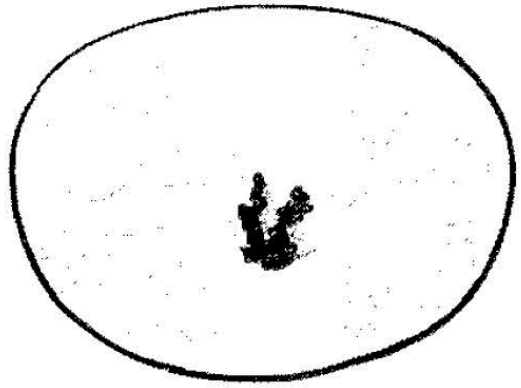

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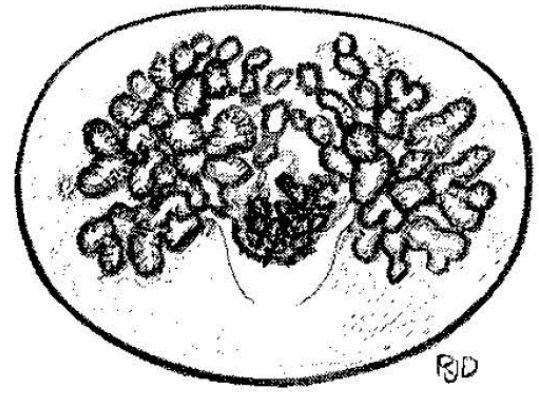

D.

DOUBLE PRIMARY PROSTATIC ADENOCARCINOMA*

HEIDRUN Z. ROTTERDAM, M.D.
MEYER M. MELICOW, M.D.

From the Departments of Pathology,
Columbia-Presbyterian Medical Center,
and Lenox Hill Hospital, New York, New York

ABSTRACT — Two cases of double primary prostatic adenocarcinoma are described. A periurethral papillary adenocarcinoma coexisted with the common acinar type of cancer, which tends to arise deep in the corpus of the gland. We are of the opinion that the patterns observed in these tumors are not mere variations of one neoplasm, but rather two dissimilar growths of diverse cell origin, varied histology, and possibly also of disparate biologic potential.

A number of articles have appeared in the recent medical literature which support the impression that the prostate gland can be the seat of parenchymal cancers of varied pathologic patterns.[1-9] We now report 2 cases of the simultaneous occ-

mal. Urine culture grew beta hemolytic streptococci.

Cystoscopy revealed a trabeculated, infected bladder with a prominent median bar. Papilliform projections were seen on the roof and floor of the

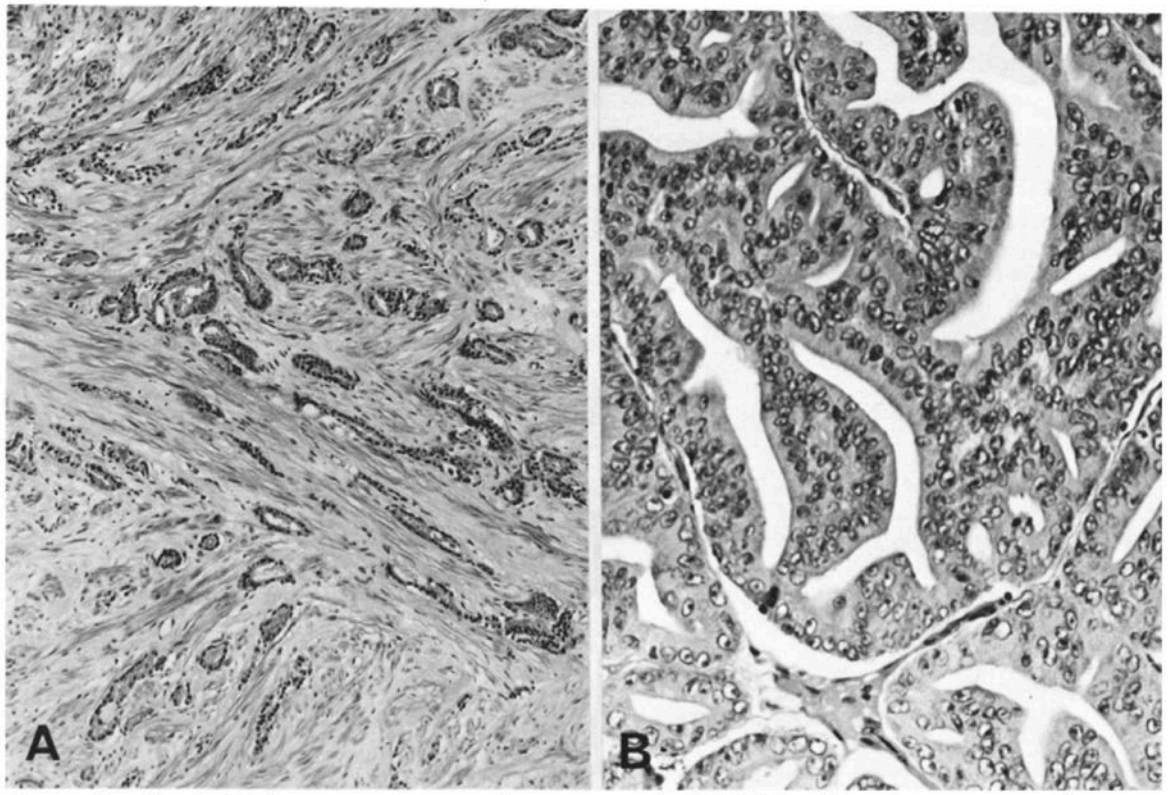

FIGURE 2. *Case 2. (A) Acinar-type prostatic adenocarcinoma (× 94). (B) Papillary adenocarcinoma of prostate, probably of ductal origin; note papillary fronds and cribriform pattern. Though columnar, the cells are not as tall as those in Case 1 and lack cilia (× 240).*

"…the occasional simultaneous occurrence of two histologically different primary adenocarcinomas in the same prostate."

Cribriform Carcinoma of the Prostate and Cribriform Prostatic Intraepithelial Neoplasia: Incidence and Clinical Implications

Rubin Mark A. M.D.; de La Taille, Alexandre M.D.; Bagiella, Emilia Ph.D.; Olsson, Carl A. M.D.; O'Toole, Kathleen M. M.D.

The American Journal of Surgical PathologyAmerican Journal of Surgical Pathology. 22:p 840-848, July 1998.

Author Information

From the Departments of Pathology (M.A.R., K.M.O.), Urology (A.T., C.A.O.), and Biostatistics (E.B.), College of Physicians and Surgeons, Columbia University, New York, New York, USA.

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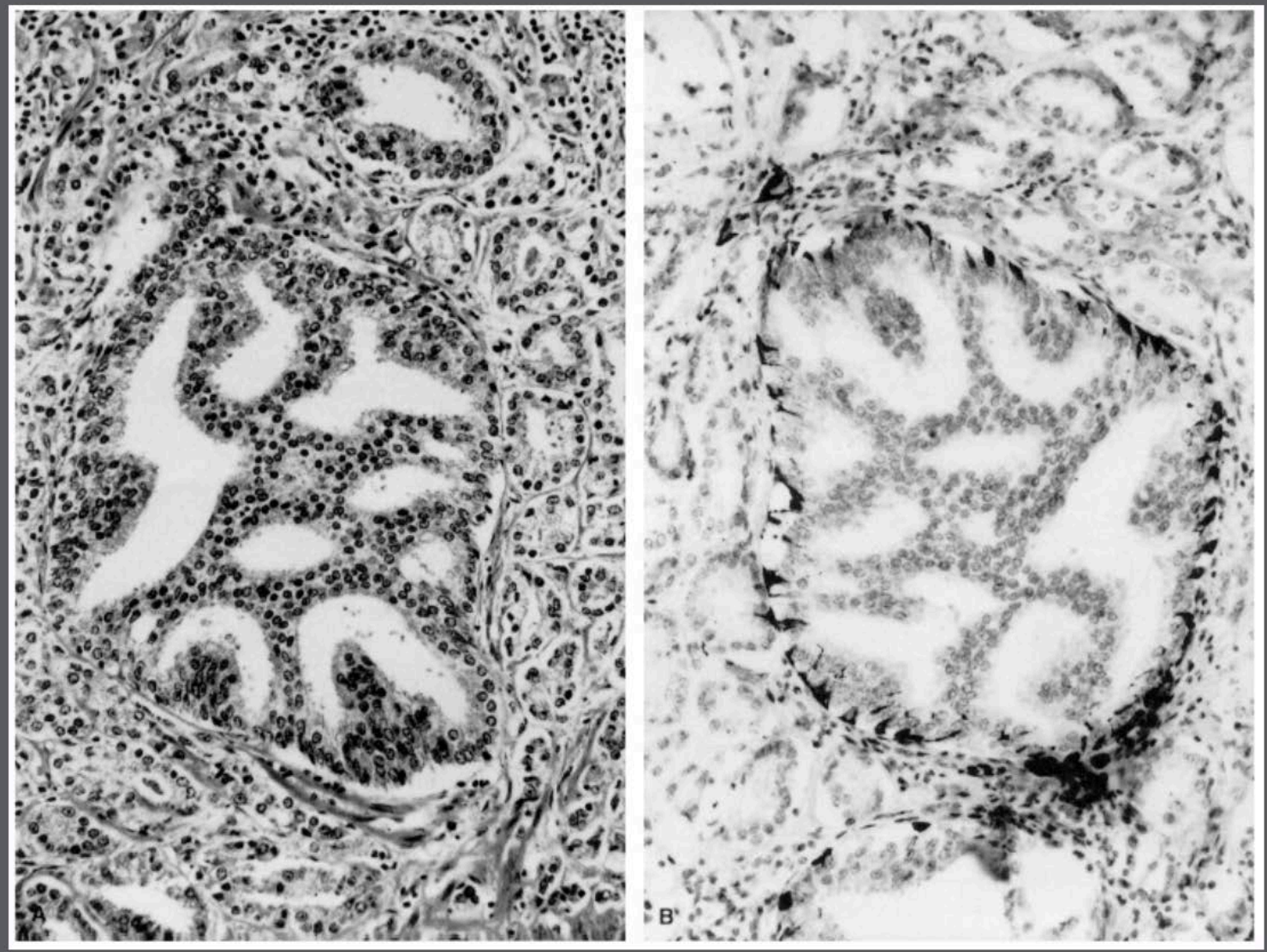
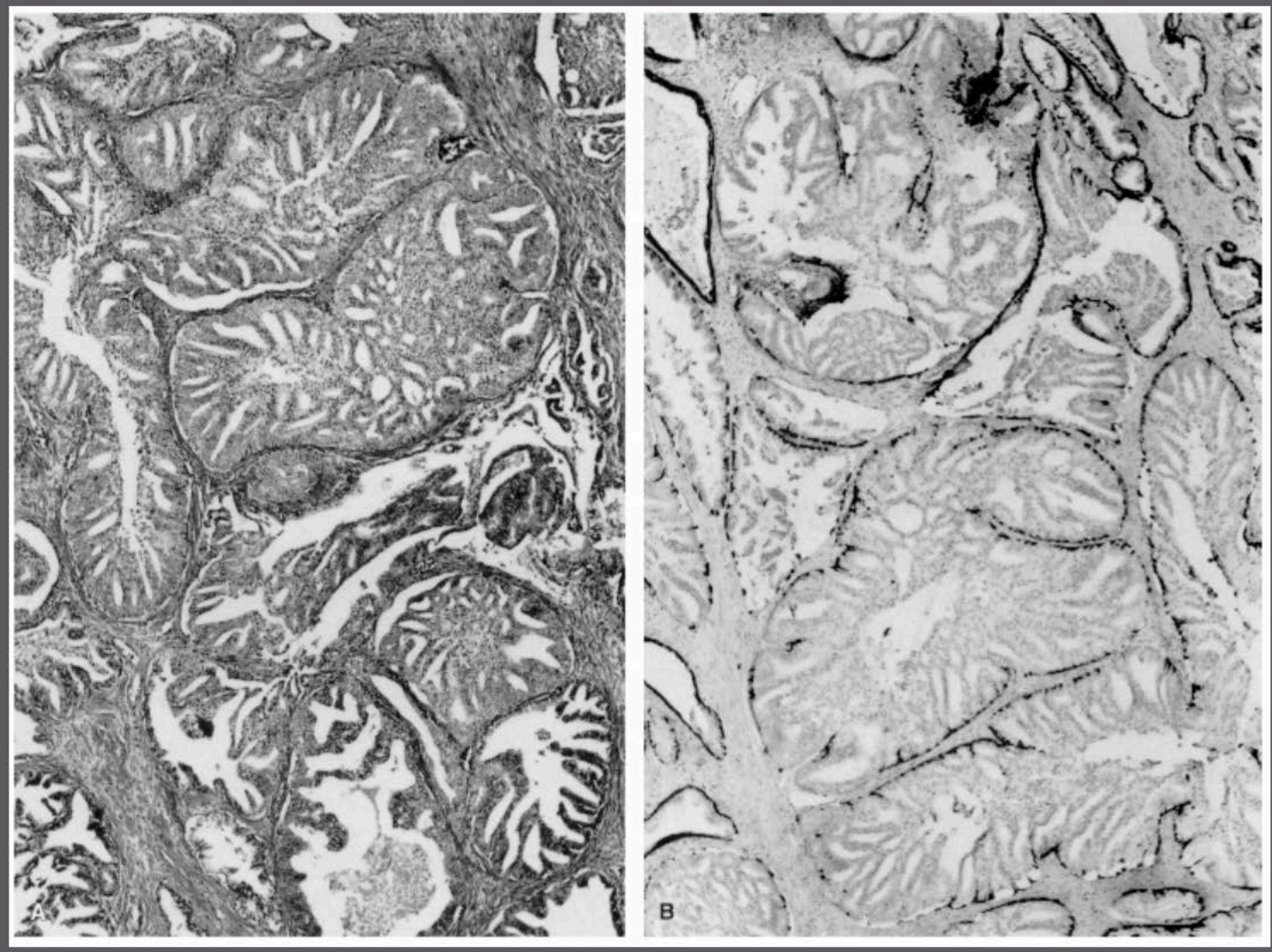
Abstract

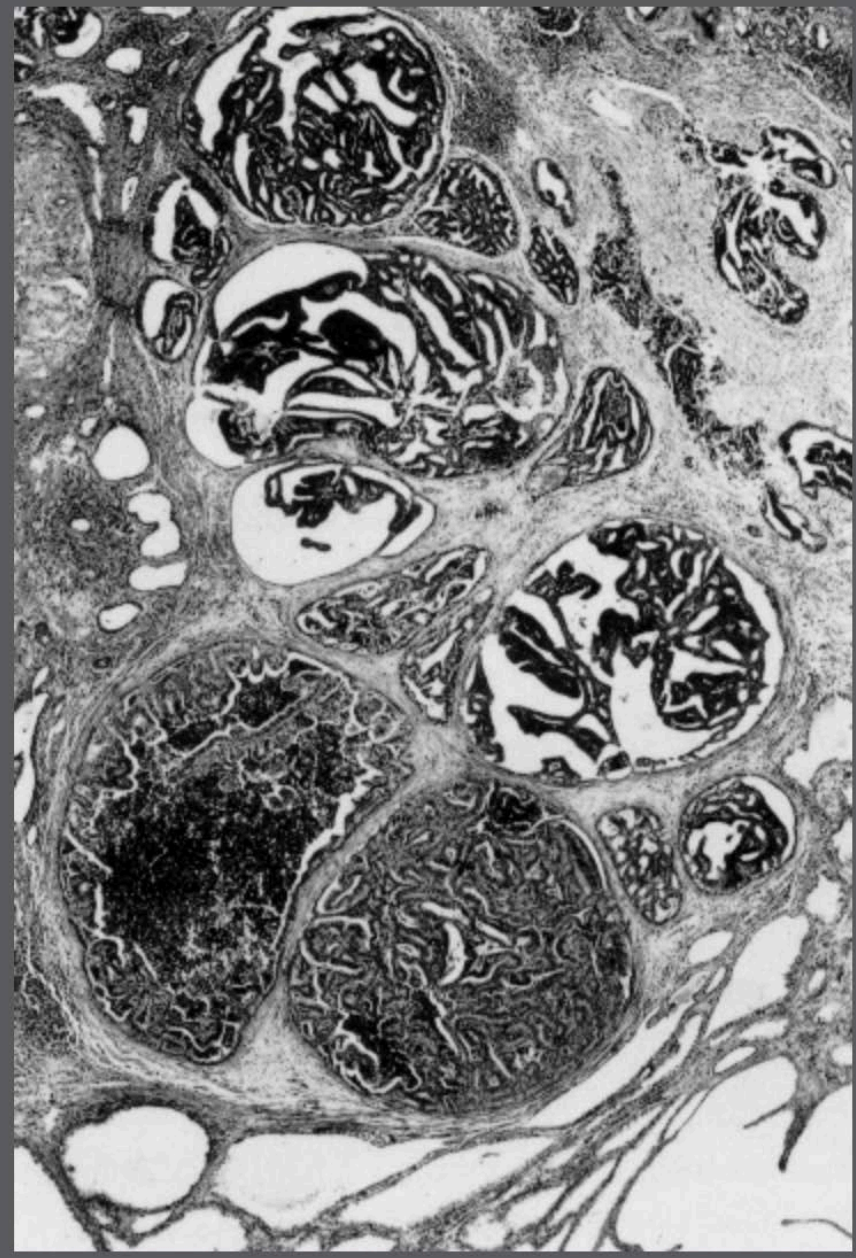


(A) High-grade cribriform prostatic intraepithelial neoplasia is seen in area with infiltrating acinar carcinoma (hematoxylin and eosin, 200×). (B) Immunostaining with 34 beta E12 shows a basal cell layer (34 beta E12 immunostain, 200×).

In none of these five cases could we show a basal cell layer.



(A) A florid example of high-grade cribriform prostatic intraepithelial neoplasia (hematoxylin and eosin, 50×). (B) Immunostaining with 34 beta E12 shows a basal cell layer (34 beta E12 immunostain, 50×).

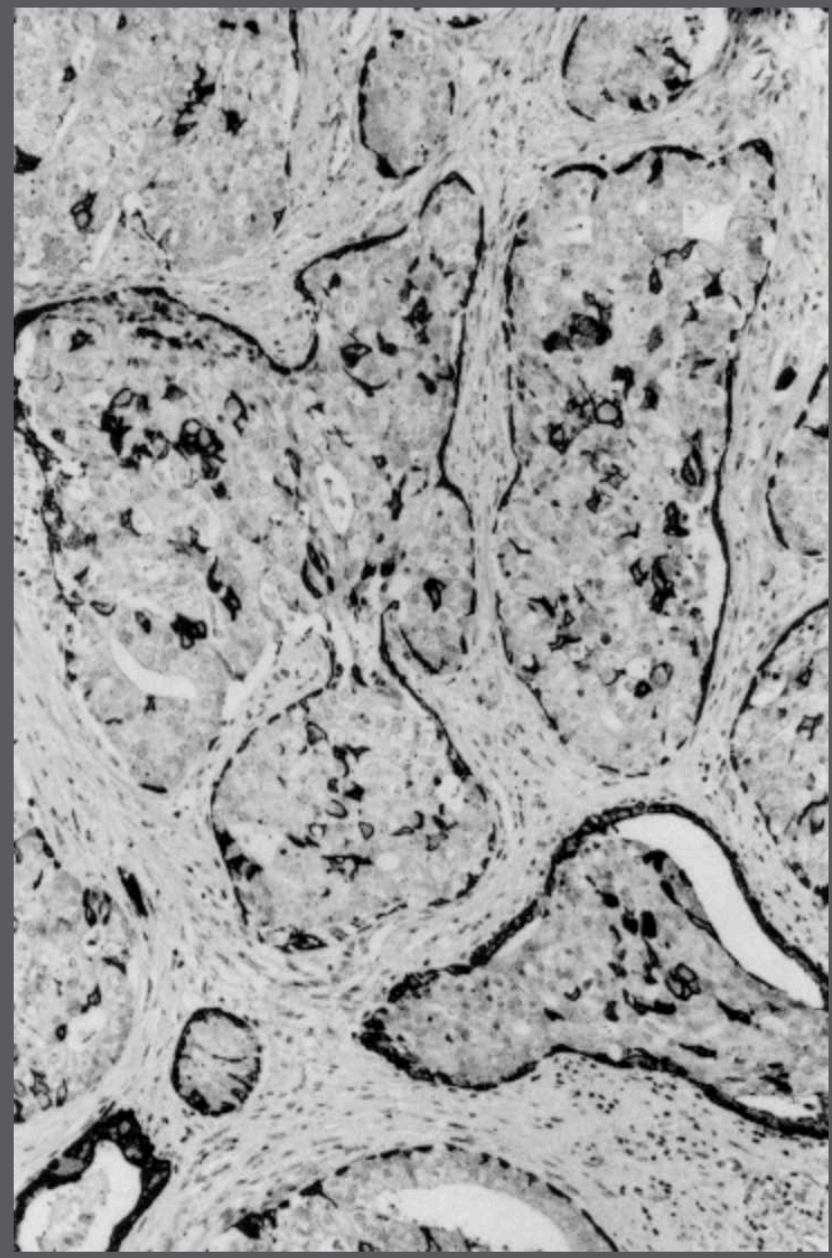


This case is an example of cribriform carcinoma; no basal cell layer could be shown (hematoxylin and eosin, 36×).

Histology	Count	%
Negative	71	62.2
CC	28	24.6
HGCP	15	13.2

CC, cribriform carcinoma; HGCP, high-grade cribriform PIN; PIN, prostatic intraepithelial neoplasia.
See text for details.

Presence of cribriform carcinoma and high-grade cribriform PIN (n = 114)



An example of basal cells making up part of the high-grade cribriform prostatic intraepithelial neoplasia (34 beta E12 immunostain, 125×).

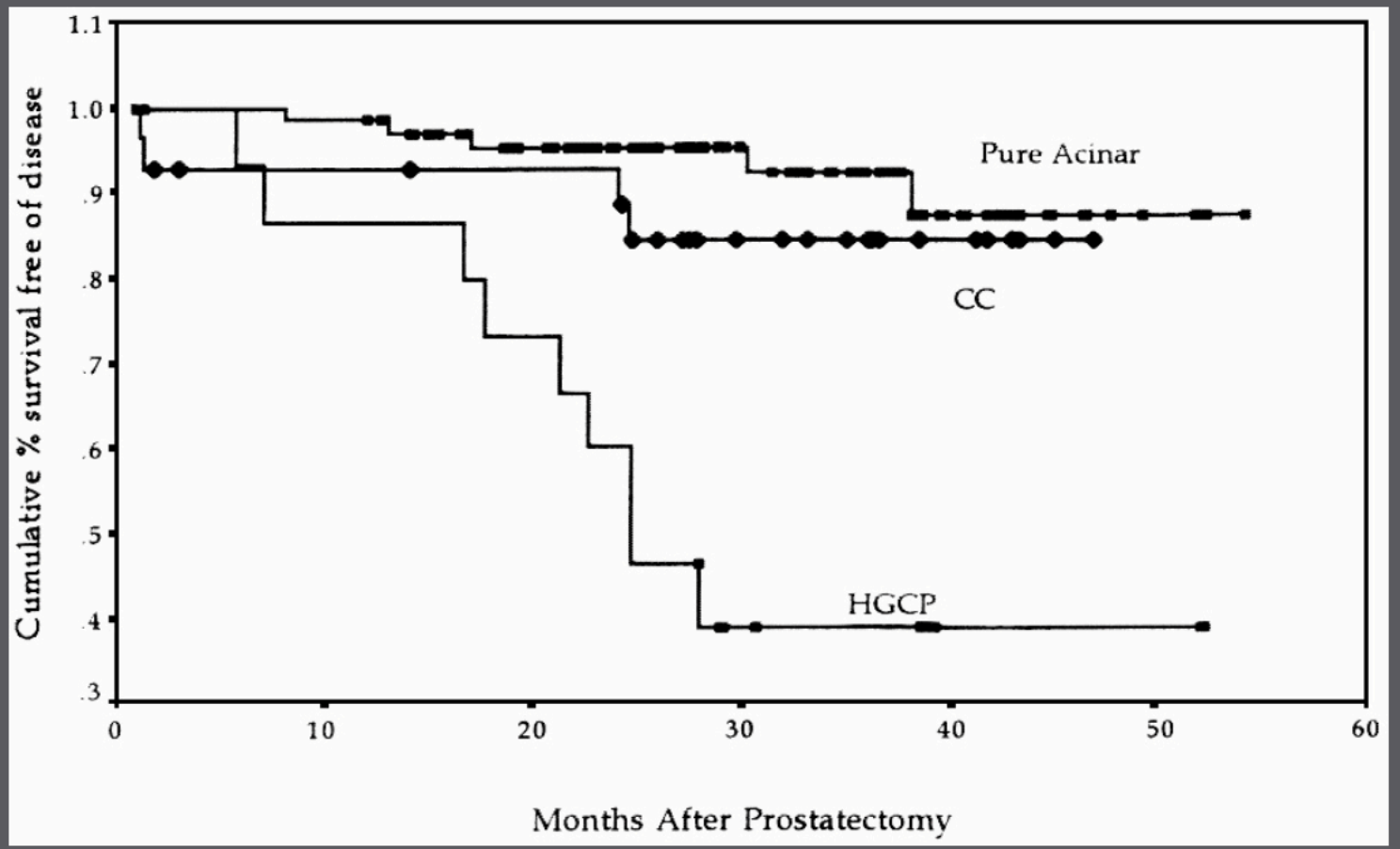
Variable	Risk ratio	95% CI	P value
GS	2.21	0.99–4.96	0.054
sPSA	1.05	1.00–1.10	0.042
Stage pT3 vs. pT2	3.12	0.83–11.68	0.091
Tumor Vol.	1.27	1.09–1.49	0.003

CI, confidence interval; EPE, extraprostatic extension; GS, Gleason sum; pT2, organ confined; pT3, either EPE or SV invasion.

Variable	Risk ratio	95% CI	P value
GS	2.07	0.87–4.94	0.099
sPSA	1.06	1.01–1.11	0.014
Stage pT3 vs pT2	2.40	0.54–10.67	0.2515
CC vs PAC	1.17	0.28–4.88	0.8296
HGCP vs PAC	4.66	1.22–17.78	0.0243

CC, cribriform carcinoma; EPE, extraprostatic extension; GS, Gleason sum; HGCP, high-grade cribriform carcinoma; PAC, pure acinar carcinoma (as defined in text); pT2, organ confined; pT3, either EPE or SV invasion.

Multivariate analysis model 2: Predictors of PSA failure



Kaplan-Meier analysis for the three histologic groups as described in the text: (1) pure acinar carcinoma, (2) cribriform cancer (CC), and (3) high-grade cribriform prostatic intraepithelial neoplasia (HGCP) ($p = 0.0001$, log-rank test).

Based on our present results and those of the others mentioned, HGCP does not appear to be a preinvasive neoplastic condition, but instead a late event in tumor progression, as suggested by its strong association to other poor prognostic factors, including tumor volume. Further supporting this view is the recent molecular evidence[13] that suggests that HGCP and Gleason pattern 5 carcinoma have similar genetic alterations. These findings support the view that HGCP represents intraductal spread of carcinoma within preexisting ducts and acini and should not be categorized as PIN.

A Proposal on the Identification, Histologic Reporting, and Implications of Intraductal Prostatic Carcinoma

Ronald J. Cohen, MBBCH, FFPATH, FRCPA, PhD; Thomas M. Wheeler, MD; Helmut Bonkhoff, MD; Mark A. Rubin, MD

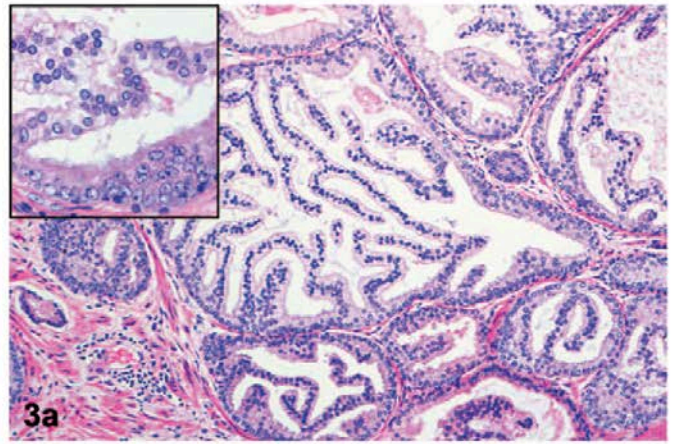
• ***Context.***—Prostatic adenocarcinoma growing within acinar-ductal spaces (intraductal carcinoma) in contrast to high-grade prostatic intraepithelial neoplasia (HG-PIN) impacts negatively on patient outcome. There is currently no generally accepted definition of this lesion nor is it classified in the current prostate cancer grading system (Gleason).

Objective.—To define intraductal carcinoma of the prostate (IDC-P) with major and minor diagnostic criteria that clearly separate it from HG-PIN. The implications of such a lesion are discussed with proposals to incorporate this entity into the Gleason grading system.

Data Sources.—We reviewed all published data referring to intraductal spread of prostate carcinoma. Articles discussing endometrial, endometrioid, and ductal carcinoma are included.

Conclusions.—Intraductal carcinoma of the prostate as defined by major criteria that include enlarged gland structures, neoplastic cells spanning the gland lumen, central comedonecrosis, and further supported by minor diagnostic criteria including molecular biological markers, separate this entity from HG-PIN. Despite its perimeter basal cells, IDC-P should be interpreted as biologically equivalent to Gleason pattern 4 or 5 adenocarcinoma. Several hypotheses are proposed as to the evolution of IDC-P, which is almost always a late event in prostate carcinoma progression. Diagnosis of IDC-P on needle biopsy should prompt therapeutic intervention rather than surveillance or repeat biopsy, as is the case for HG-PIN.

(*Arch Pathol Lab Med.* 2007;131:1103–1109)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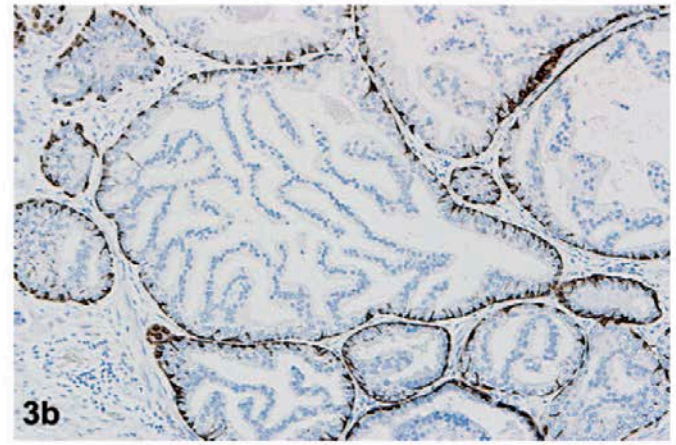
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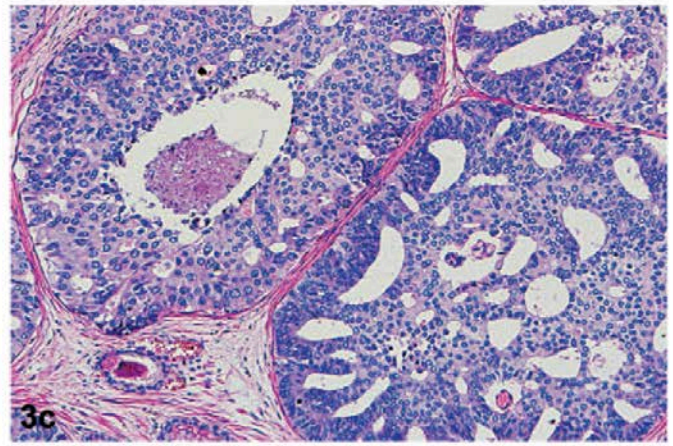
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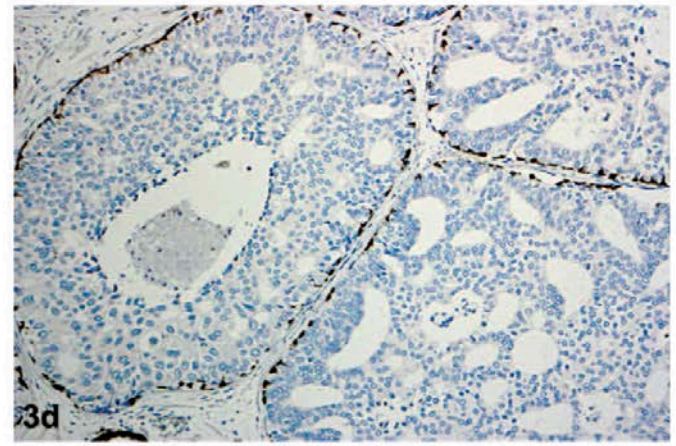
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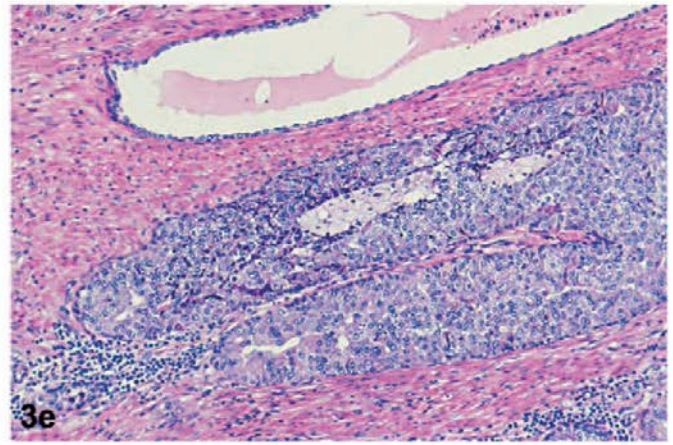
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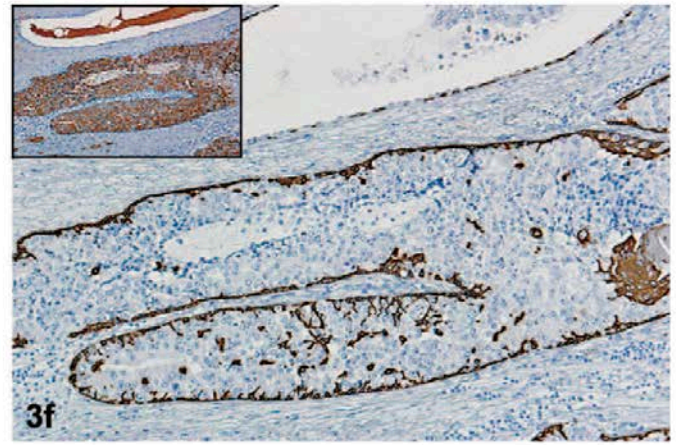
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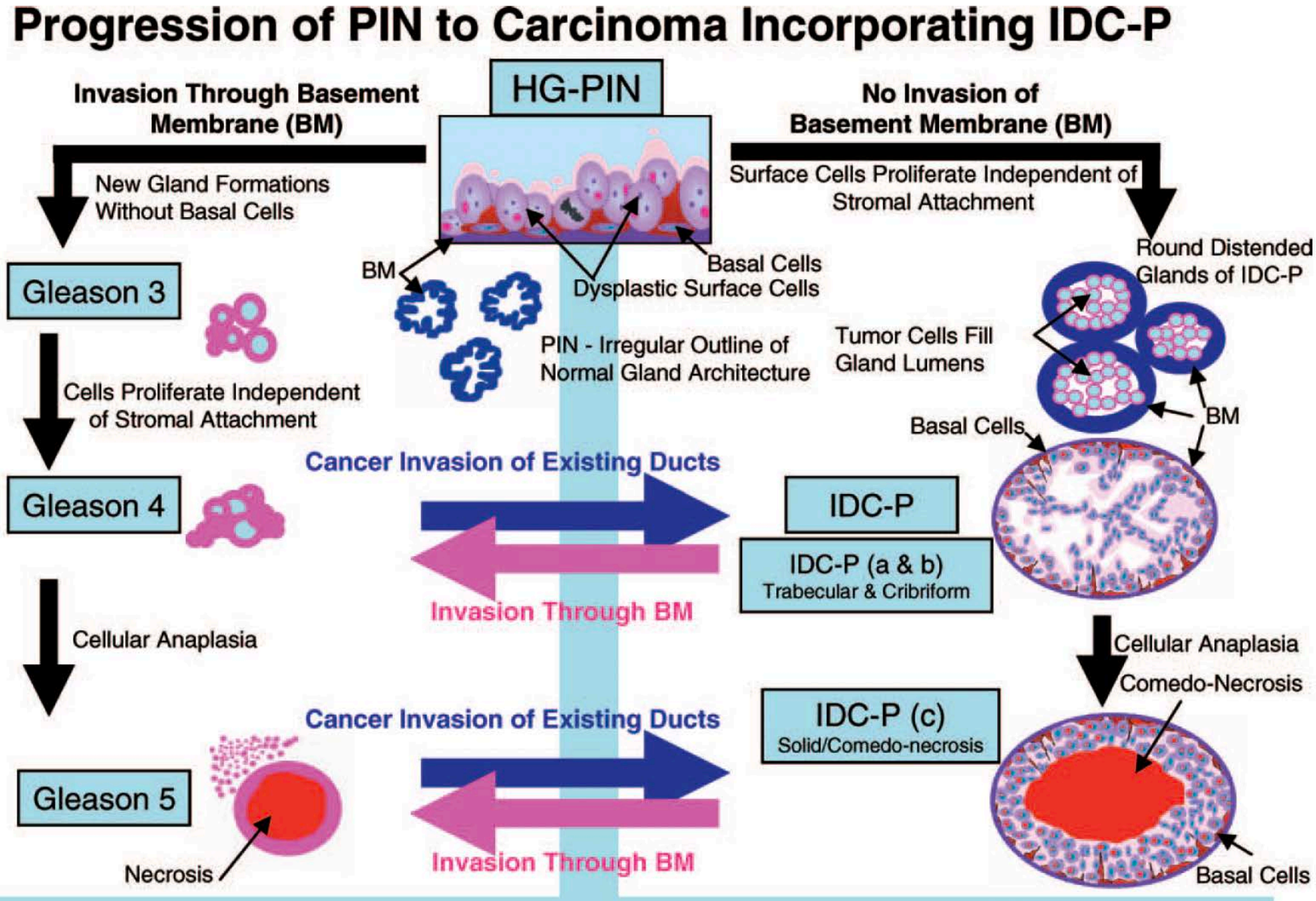
Progression of PIN to Carcinoma Incorporating IDC-P
HG-PIN
Invasion Through Basement Membrane (BM)
No Invasion of Basement Membrane (BM)
New Gland Formations Without Basal Cells
Surface Cells Proliferate Independent of Stromal Attachment
Round Distended Glands of IDC-P
BM
Basal Cells
Dysplastic Surface Cells
Gleason 3
PIN - Irregular Outline of Normal Gland Architecture
Tumor Cells Fill Gland Lumens
Cells Proliferate Independent of Stromal Attachment
Basal Cells
BM
Cancer Invasion of Existing Ducts
Gleason 4
IDC-P
IDC-P (a & b)
Trabecular & Cribriform
Invasion Through BM
Cellular Anaplasia
Cellular Anaplasia
Comedo-Necrosis
Cancer Invasion of Existing Ducts
IDC-P (c)
Solid/Comedo-necrosis
Gleason 5
Necrosis
Invasion Through BM
Basal Cells
2
STROMAL INVASIVE CARCINOMA
CARCINOMA CONFINED TO DUCTS

Intraductal

6.1.1.2: Intraductal carcinoma of the prostate

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Definition

Intraductal carcinoma of the prostate (IDC-P) is a neoplastic epithelial proliferation involving pre-existing, generally expanded, duct-acinar structures and characterized by architectural and cytologic atypia beyond what is acceptable for HGPIN. It is typically associated with high-grade and high-stage prostate carcinoma but in rare cases may represent a precursor lesion.

Epidemiology
IDC-P is seen in **15.4 to 31.1% of routinely processed radical prostatectomies {**24966964; 20182345; 31025722; 32542746; 28342640}. In a vast majority of cases, **IDC-P is seen associated with invasive prostate cancer**…IDC-P without concomitant invasive cancer is an **exceedingly rare finding** in radical prostatectomies {17617002; 30993692}. In prospective series, IDC-P has been identified in 2.8% of prostate biopsies {23931616} and in 14% of biopsies with invasive prostate cancer {32542746; 28342640}. **Isolated IDC-P without invasive prostate cancer has been reported in 0.06 to 0.26% of prostate biopsies** {16980940; 20723921; 23931616}.

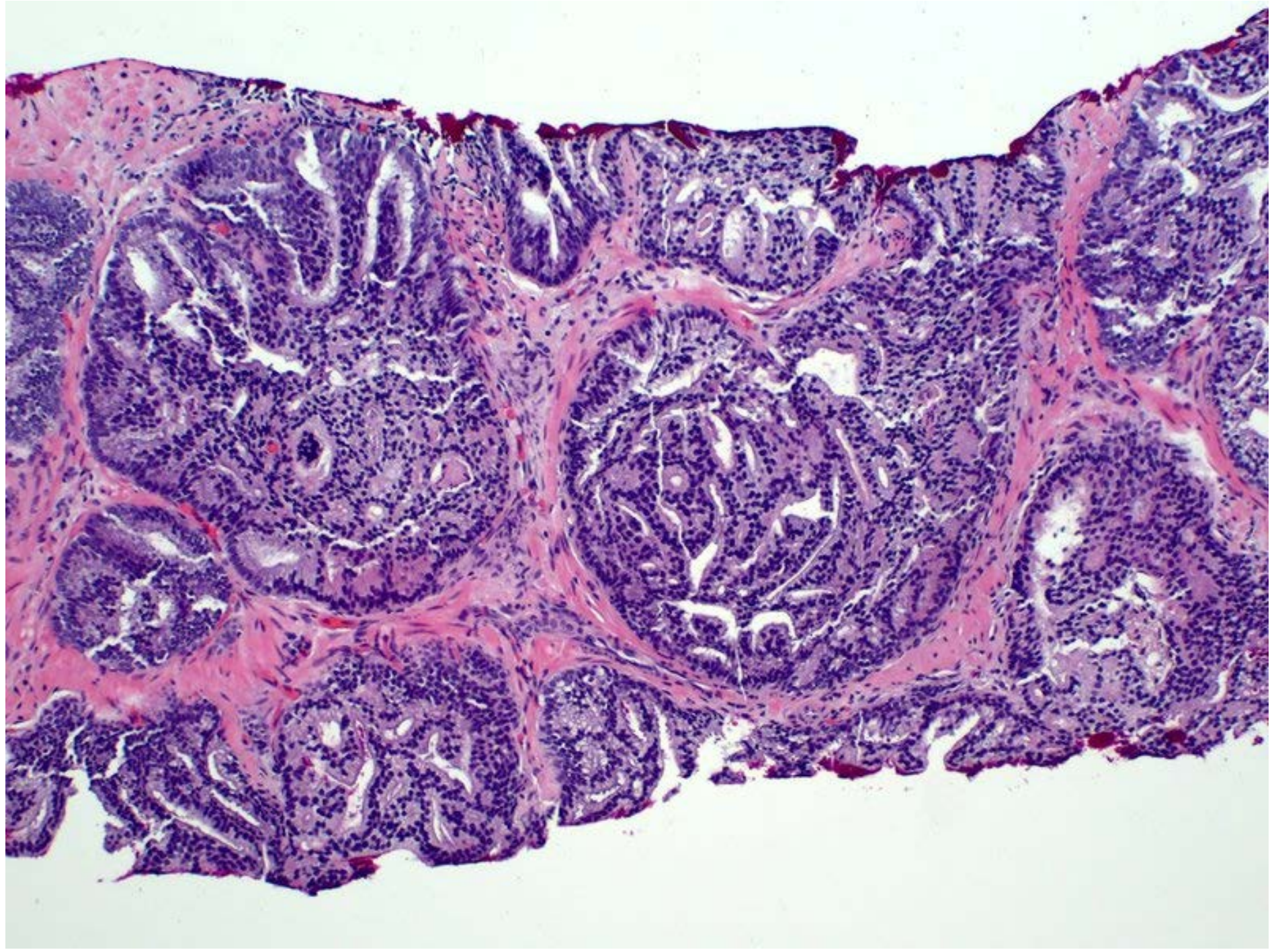
Etiology
As prostate adenocarcinoma. Bi-allelic *BRCA2* loss has been associated with primary prostate tumours, but the association of prostatic carcinomas with germline *BRCA2* mutations remains controversial {33626496; 32516092}.

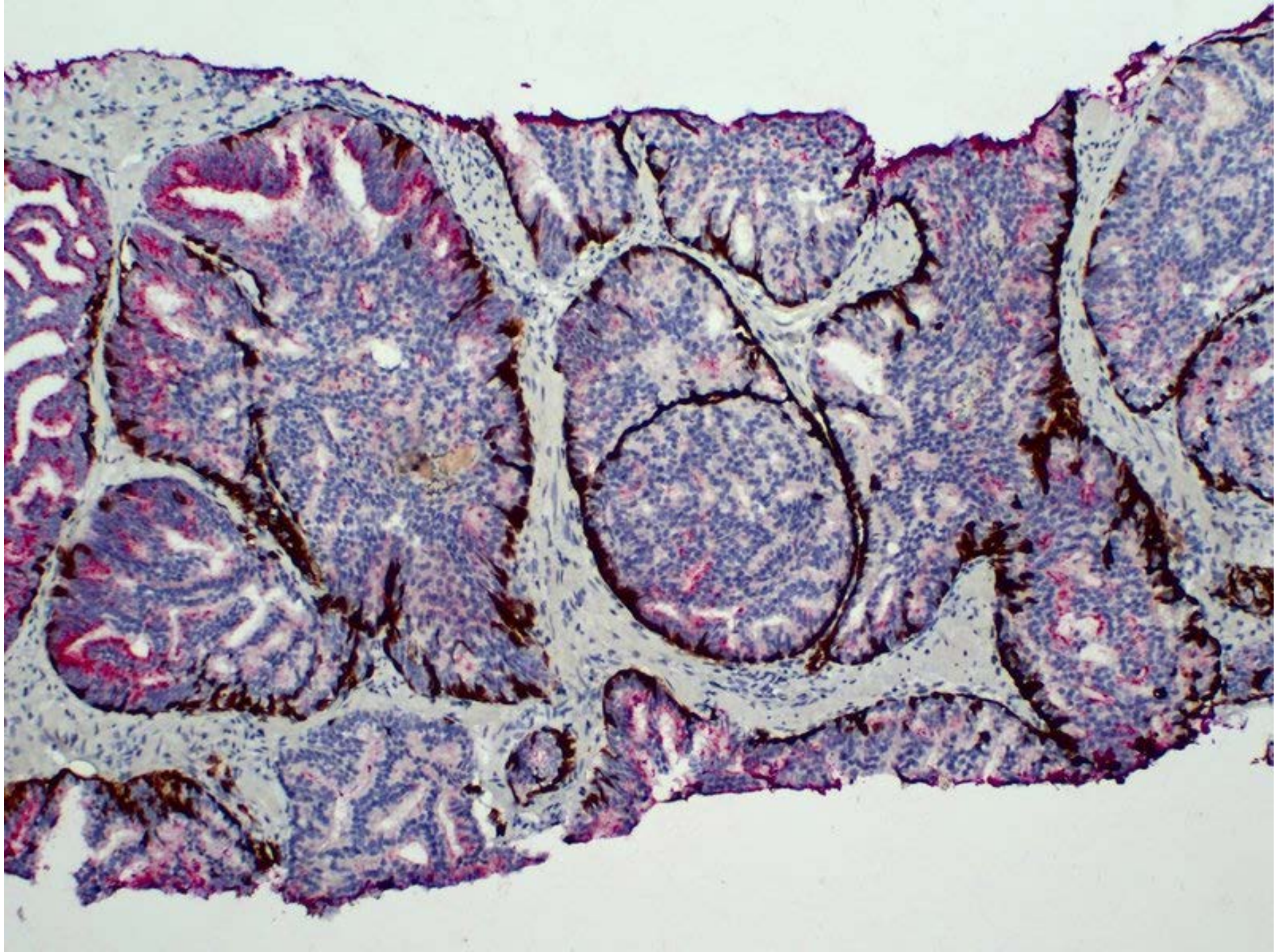
In prostate biopsies, lack of concomitant invasive prostate cancer generally **represents under-sampling**; follow-up radical prostatectomy specimens – when completely sampled – have virtually never displayed IDC-P alone.

Essential and desirable diagnostic criteria

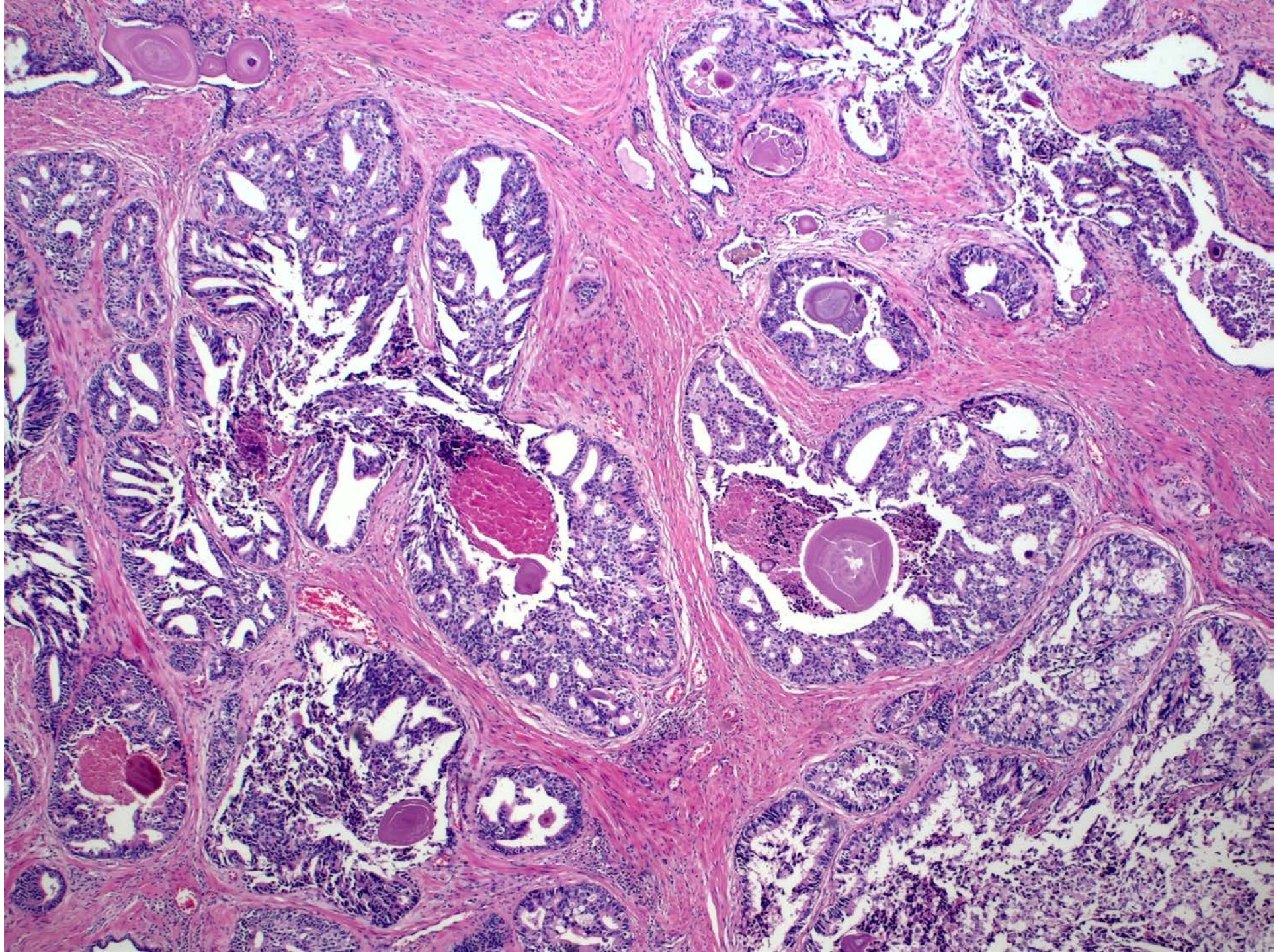
Essential: Expansile epithelial proliferation in pre-existing duct-acinar system; lumen-spanning solid, cribriform, comedo- patterns; loose cribriform or micropapillary patterns with enlarged pleomorphic nuclei; residual basal cells

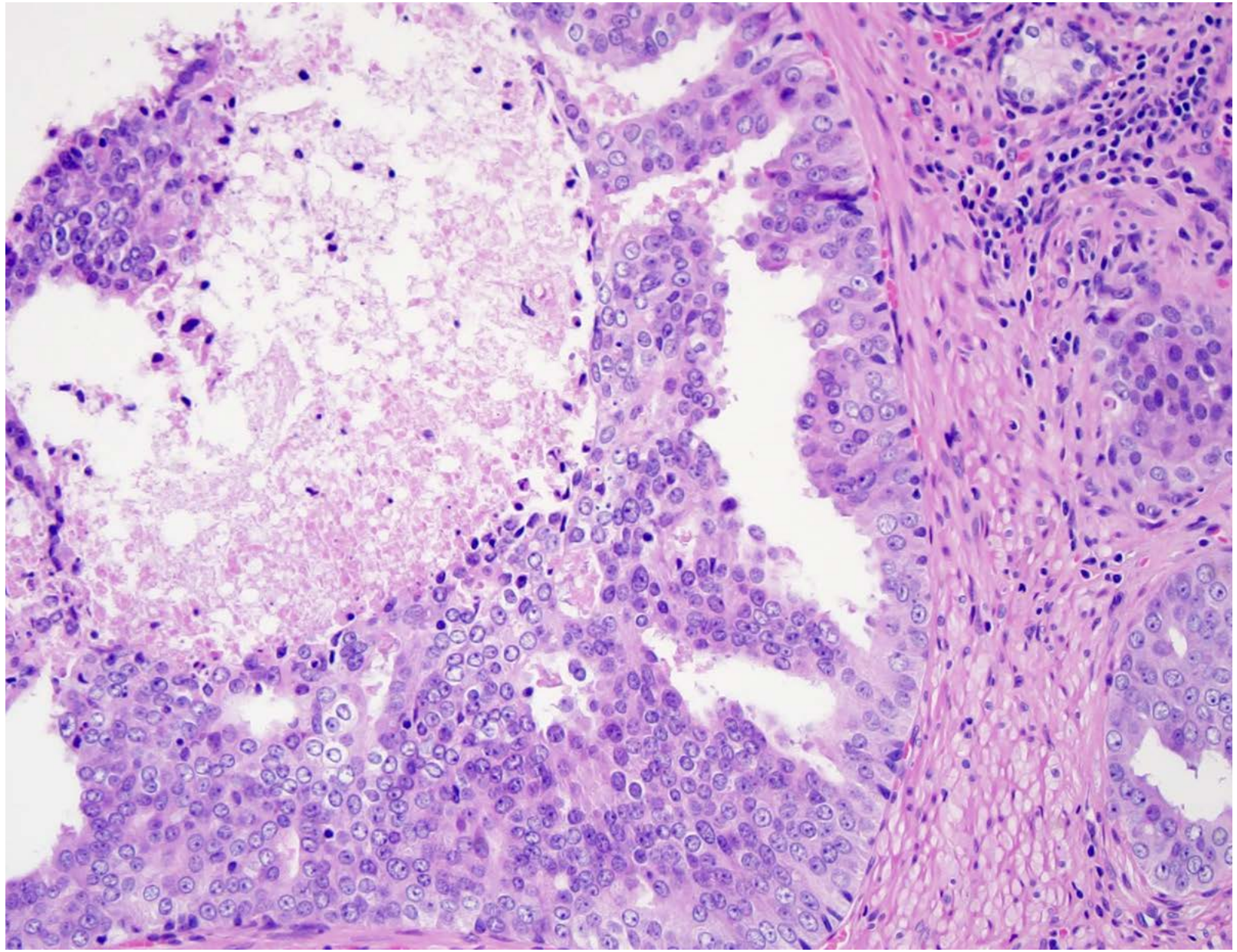
Desirable: Immunohistochemistry demonstrating at least partial basal cell retention.

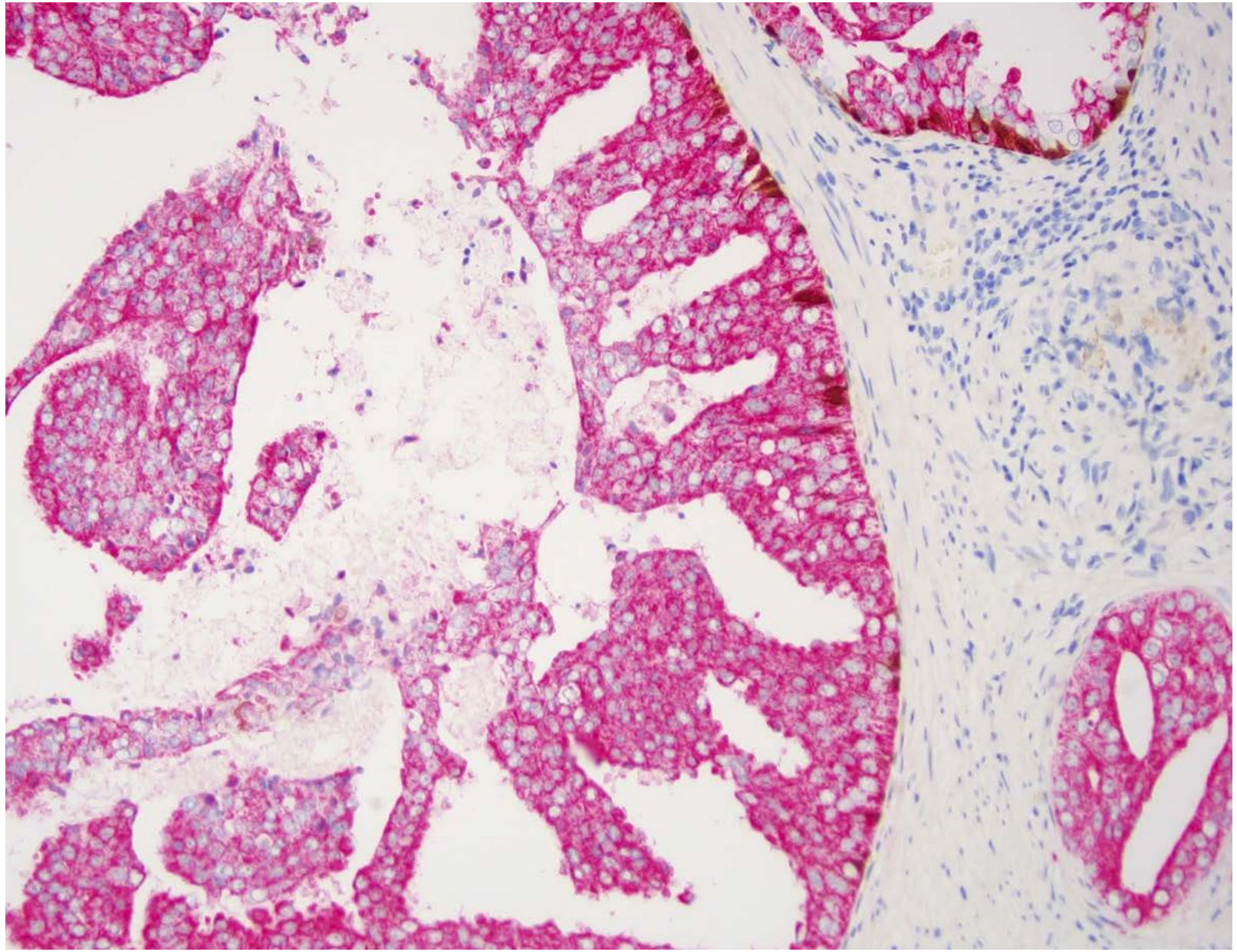


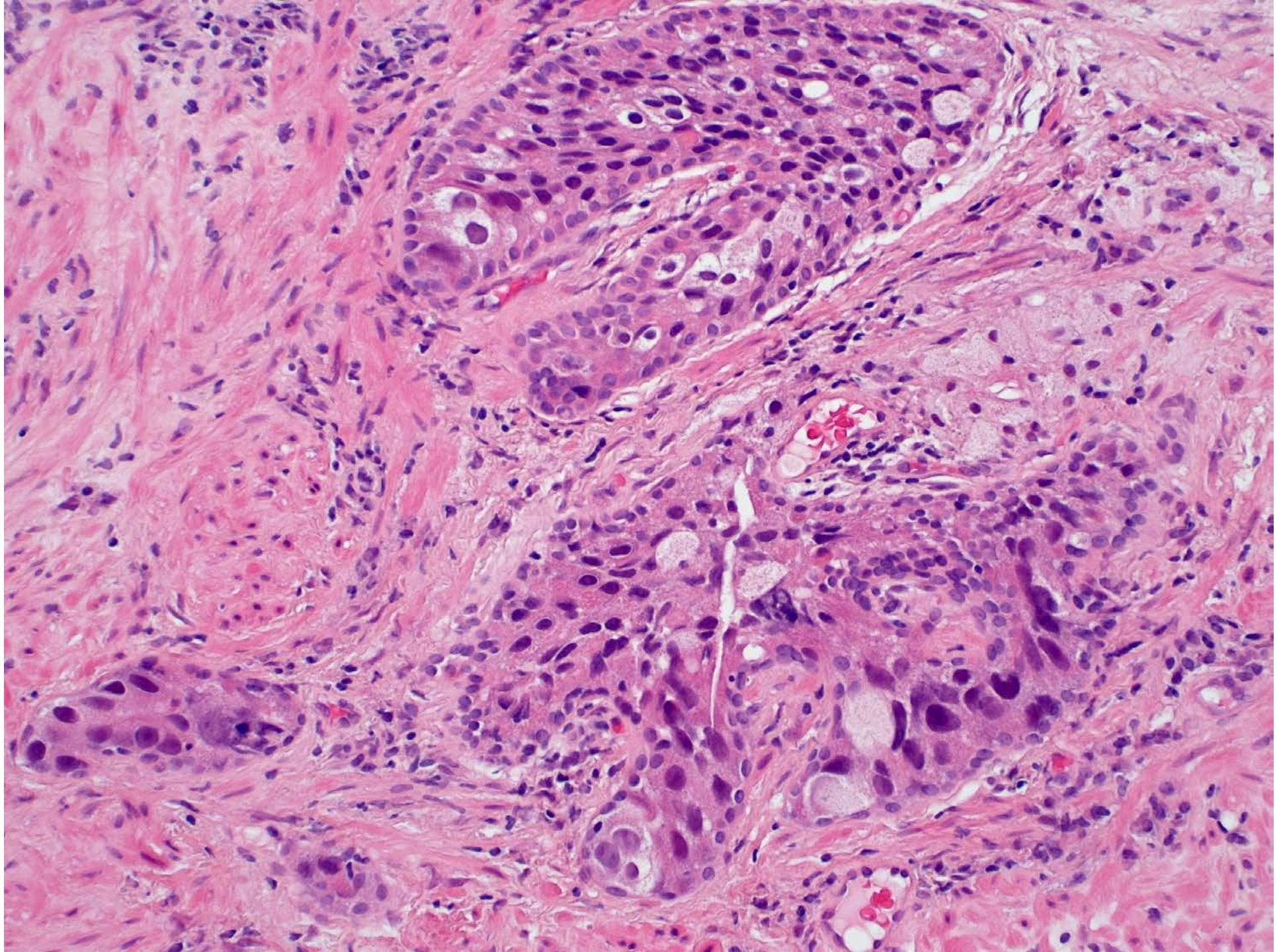


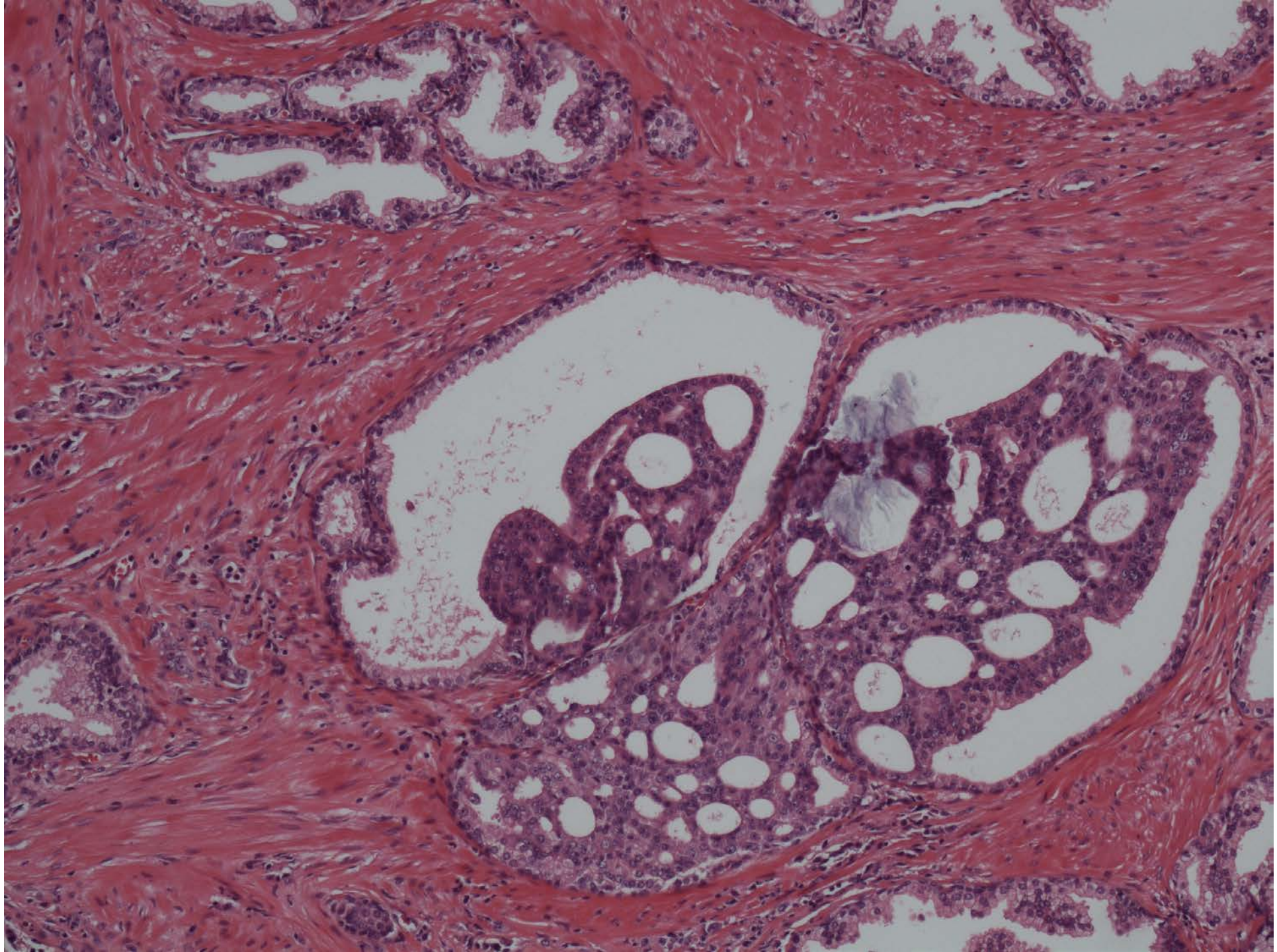
A current controversy is whether to perform immunohistochemical stains in biopsies containing invasive prostate cancer and cribriform/solid lesions that may represent IDC-P, when this determination impacts the assigned prostate cancer grade. **Immunohistochemistry is not considered necessary in cases when the distinction between IDC-P and invasive prostate cancer will not change the assigned prostate cancer grade**.











Prostatic Ductal Carcinoma

6.1.1.4: Prostatic ductal adenocarcinoma

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Definition

Ductal adenocarcinoma is composed of papillary structures and/or complex and cribriform glands lined by tall columnar pseudostratified cells.

Clinical features

Ductal adenocarcinomas of the prostate may present in an identical manner to acinar prostatic adenocarcinoma. However, the **peri-urethral tumours may project into the urethra leading to symptoms and signs of bladder outflow obstruction and gross hematuria** {24187500}. PSA levels are highly variable and may be lower than in acinar adenocarcinoma. When presenting as metastases, the diagnosis may be challenging as the tumour mimics other malignancies. **Ductal adenocarcinoma shows a predilection for unusual visceral metastases including penis and testis**{25025445;12173328;11939729}.

Epidemiology

In the majority of cases this subtype is mixed with acinar adenocarcinoma. However, its distinctive clinical behaviour and metastatic pattern have led it to be considered more than a subtype of acinar adenocarcinoma. While being present in 2.6 % of all prostatic adenocarcinomas {23443941}, **its pure form accounts for 0.2-0.4% only** {4091189; 2416422}.

Essential and desirable diagnostic criteria

Essential:

Identification of glandular structures with papillary and/or complex cribriform morphology lined by tall columnar pseudostratified cells; often (but not always) high grade nuclear atypia.

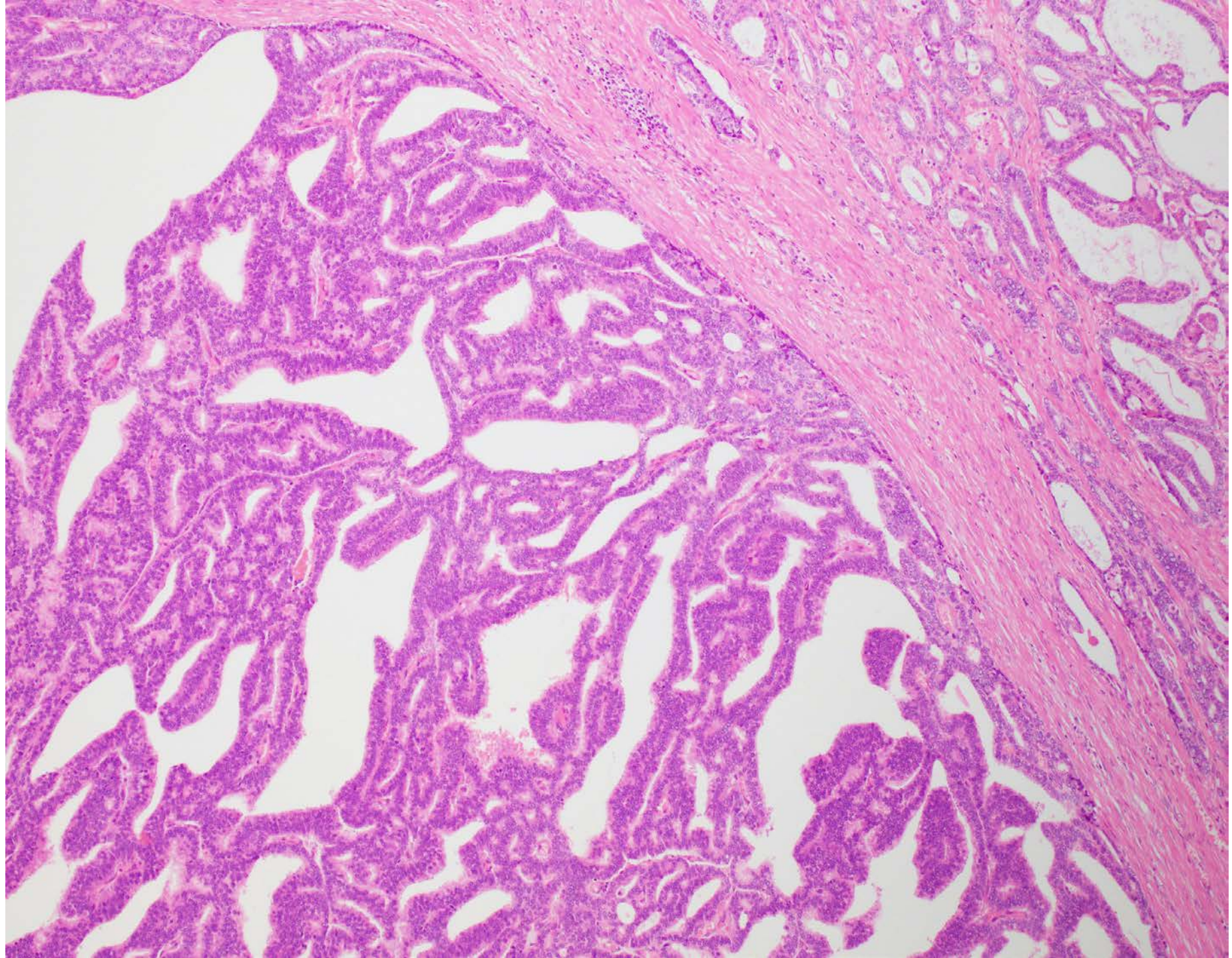
In Radical Prostatectomy: greater than **50% or pure histology** (and the percentage reported).

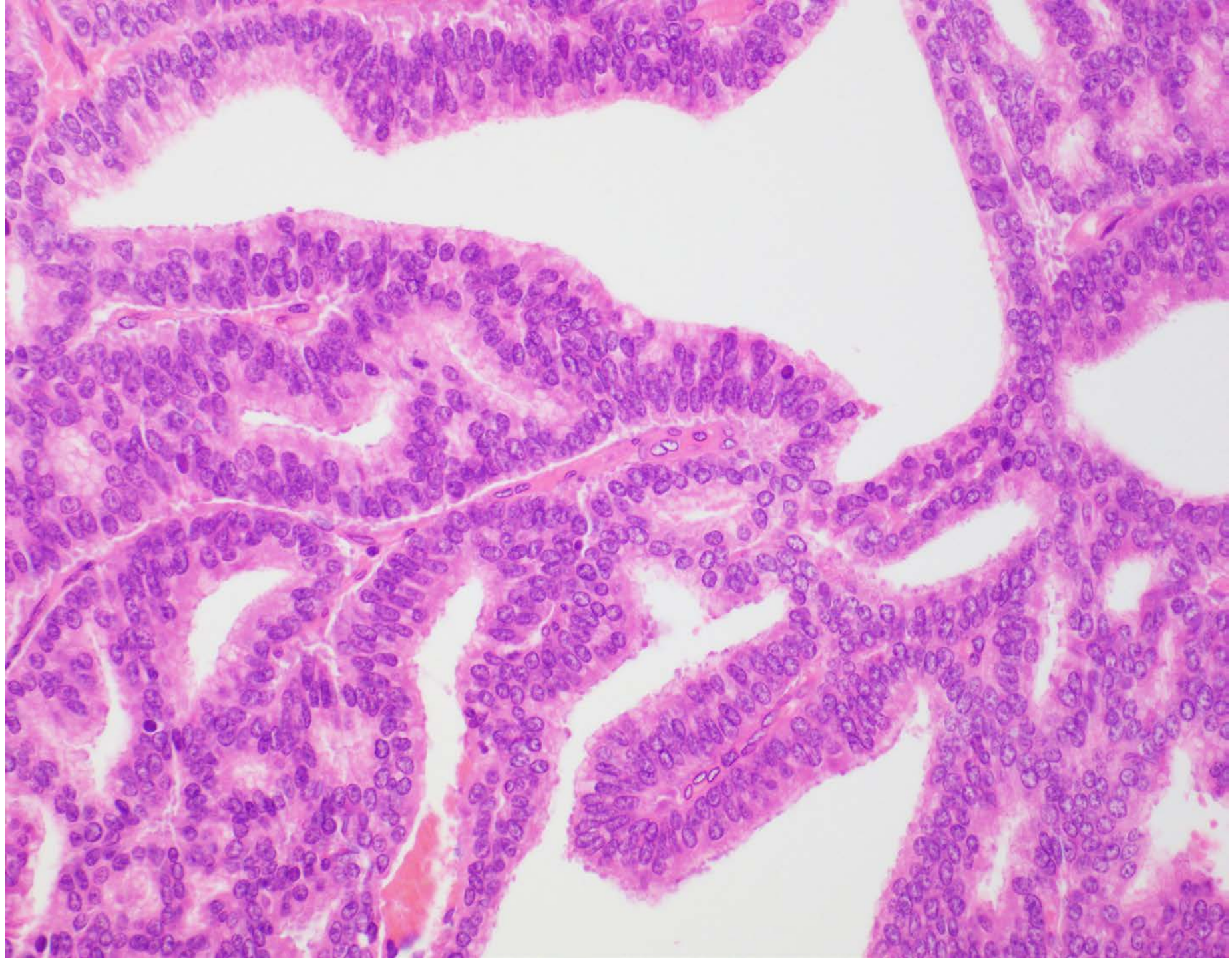
In needle biopsy: Even if pure - use terminology: Adenocarcinoma of prostate with ductal features.

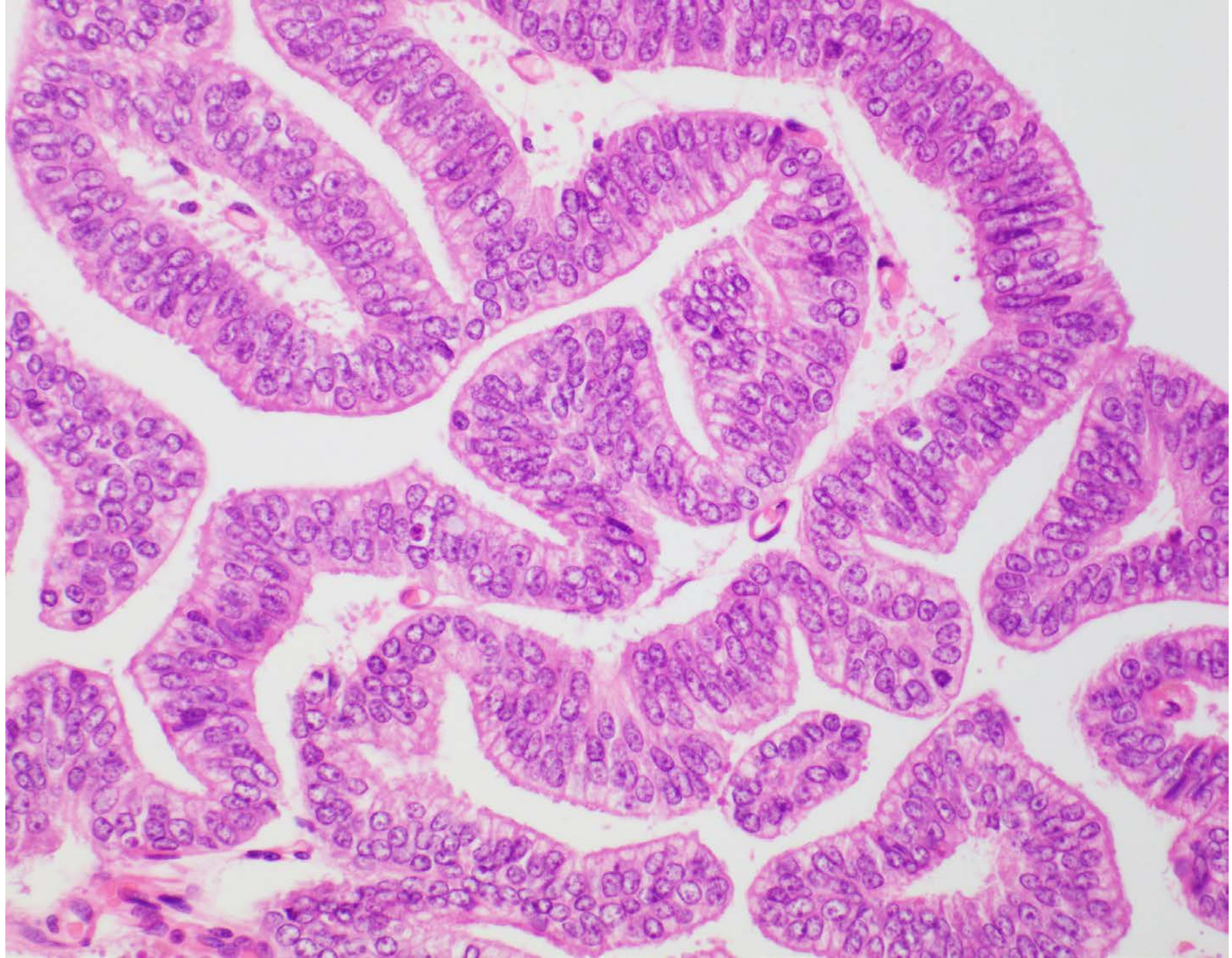
Desirable:

In urethral location and metastatic sites;

Immunohistochemical confirmation of prostatic epithelial origin.

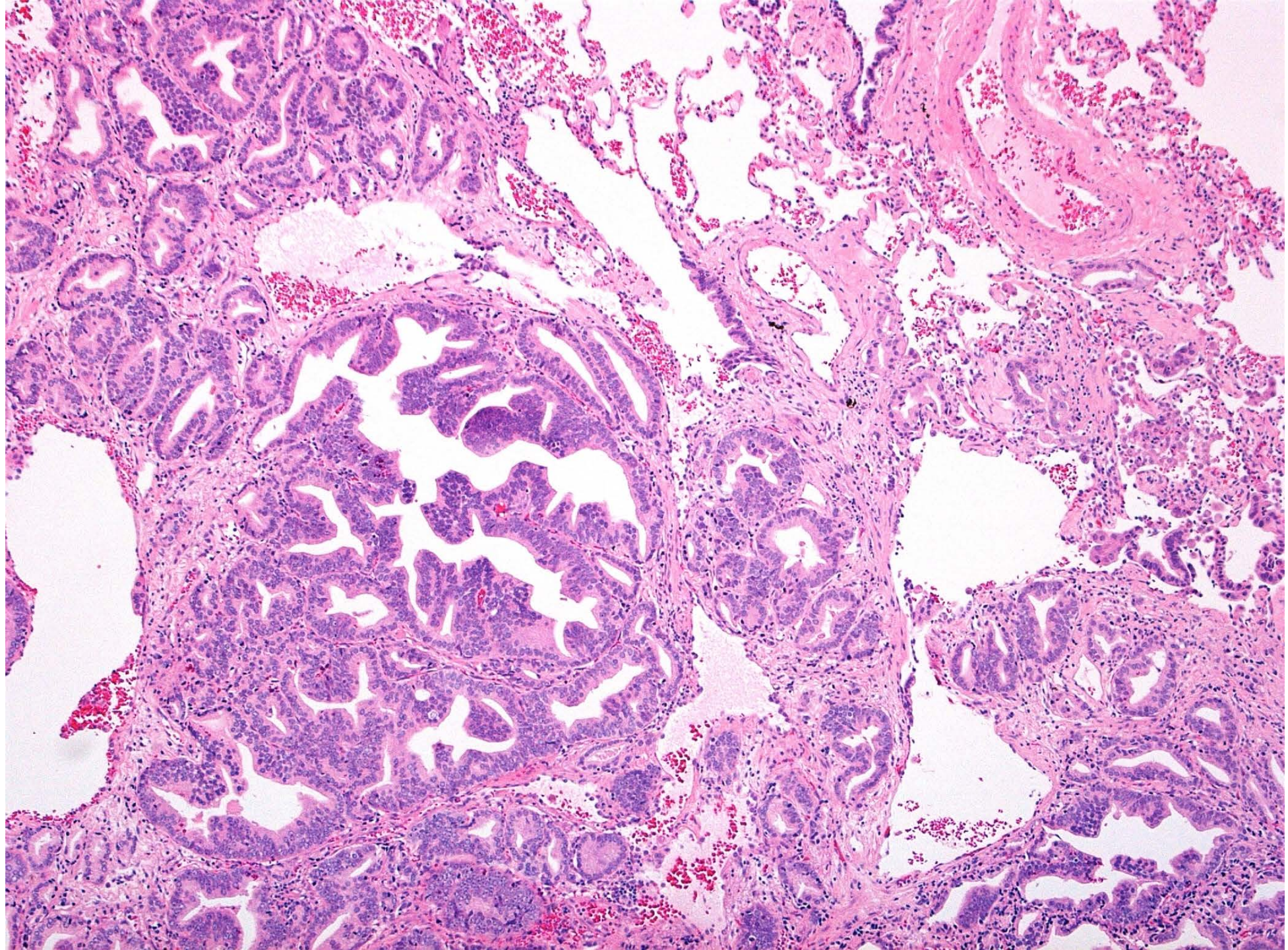






Grading Considerations

To take into account the architectural complexity and poorer prognosis of ductal adenocarcinoma, compared to Gleason score 6 acinar adenocarcinoma, the ISUP 2005 Consensus Conference recommended that **all ductal adenocarcinomas should be assigned pattern 4, except for those with comedonecrosis which are included in pattern 5 {16096414}.**



Case 1:
Adenocarcinoma with ductal features. Gleason Score 4+5=9, Grade Group 5,
69 years old male patient. No further clinical information.

Case 2:
Adenocarcinoma with ductal features. Gleason Score 4+4=8, Grade Groupe 4.
70 years old male patient. PSA 9, PIRADS 5.

National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Prostate Cancer

Version 3.2022 — January 10, 2022

NCCN.org

NCCN Guidelines for Patients® available at www.nccn.org/patients

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PRINCIPLES OF GENETICS AND MOLECULAR/BIOMARKER ANALYSIS

Germline testing is recommended *in patients with a personal history of prostate cancer* in the following scenarios:

- By Prostate Cancer Stage or Risk Group (diagnosed at any age)
  - Metastatic, regional (node positive), very-high risk localized, high-risk localized prostate cancer

- By Family History[a] and/or Ancestry
  - ≥1 first-, second-, or third-degree relative with:
    - ◊ breast cancer at age ≤50 y
    - ◊ colorectal or endometrial cancer at age ≤50 y
    - ◊ male breast cancer at any age
    - ◊ ovarian cancer at any age
    - ◊ exocrine pancreatic cancer at any age
    - ◊ metastatic, regional, very-high-risk, high-risk prostate cancer at any age
  - ≥1 first-degree relative (father or brother) with:
    - ◊ prostate cancer[b] at age ≤60 y
  - ≥2 first-, second-, or third-degree relatives with:
    - ◊ breast cancer at any age
    - ◊ prostate cancer[b] at any age
  - ≥3 first- or second-degree relatives with:
    - ◊ Lynch syndrome-related cancers, especially if diagnosed <50 y: colorectal, endometrial, gastric, ovarian, exocrine pancreas, upper tract urothelial, glioblastoma, biliary tract, and small intestinal cancer
  - A known family history of familial cancer risk mutation (pathogenic/likely pathogenic variants), especially in: ***BRCA1, BRCA2, ATM, PALB2, CHEK2, MLH1, MSH2, MSH6, PMS2, EPCAM***
  - Ashkenazi Jewish ancestry
- Personal history of breast cancer

Germline testing may be considered *in patients with a personal history of prostate cancer* in the following scenarios:

- By Prostate Cancer Tumor Characteristics (diagnosed at any age)
  - ◊ intermediate-risk prostate cancer with intraductal/cribriform histology[c]
- By prostate cancer[b] AND a prior personal history of any of the following cancers:
  - ◊ exocrine pancreatic, colorectal, gastric, melanoma, pancreatic, upper tract urothelial, glioblastoma, biliary tract, and small intestinal

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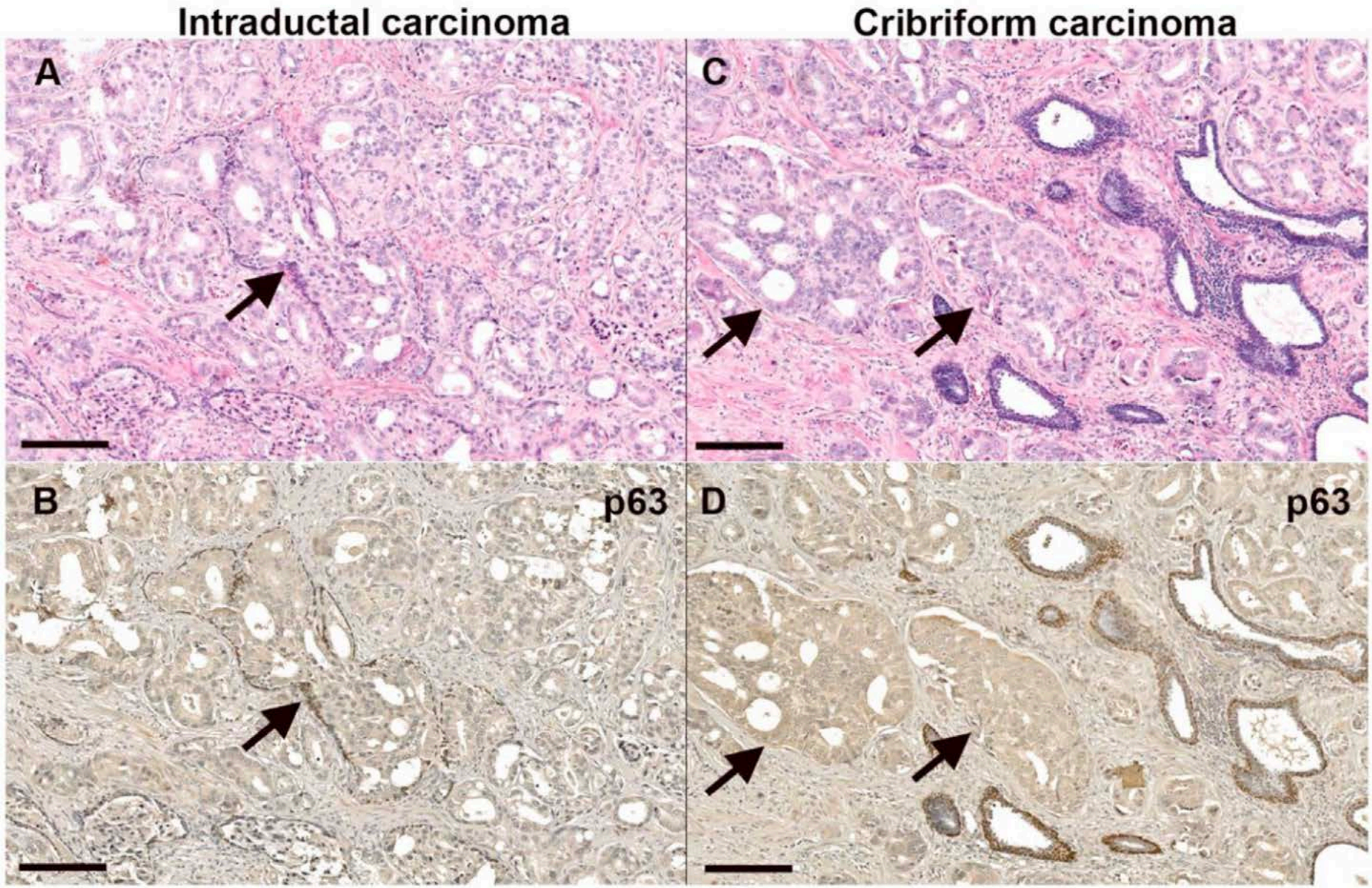
journal homepage: www.ejcancer.com

Original Research

Association between *BRCA2* alterations and intraductal and cribriform histologies in prostate cancer

Rebeca Lozano [a,b,1], Daniela C. Salles [c,1], Shahneen Sandhu [d], Isabel M. Aragón [a,b], Heather Thorne [d], Fernando López-Campos [a,e], José Rubio-Briones [f], Ana M. Gutierrez-Pecharroman [a,g], Laneisha Maldonado [c], Tomas di Domenico [h], Alejandro Sanz [a], Juan D. Prieto [i], Isabel García [i], María I. Pacheco [a], Teresa Garcés [a,b], Casilda Llacer [b,j], Nuria Romero-Laorden [k], Francisco Zambrana [l], Pedro P. López-Casas [a], David Lorente [a,m], Joaquin Mateo [n], Colin C. Pritchard [o], Emmanuel S. Antonarakis [p], David Olmos [a,b], Tamara L. Lotan [c,**], Elena Castro [a,b,j,*]


Intraductal carcinoma
Cribriform carcinoma
A
C
B
p63
D
p63

Conclusions: While we found **no association between gBRCA2 mutations and IDC or CRIB histologies,** bi-allelic BRCA2 loss in primary prostate tumours was significantly associated with both variant morphologies, independently of other clinical-pathologic factors.

Genomic Characterization of Prostatic Ductal Adenocarcinoma Identifies a High Prevalence of DNA Repair Gene Mutations

Michael T. Schweizer, MD[1,2]; Emmanuel S. Antonarakis, MD[3]; Tarek A. Bismar, MD[4]; Liana B. Guedes, MD[3]; Heather H. Cheng, MD, PhD[1,2]; Maria S. Tretiakova, MD, PhD[1]; Funda Vakar-Lopez, MD[1]; Nola Klemfuss, MHA[2]; Eric Q. Konnick, MD, MS[1]; Elahe A. Mostaghel, MD, PhD[1,2]; Andrew C. Hsieh, MD[2]; Peter S. Nelson, MD[2]; Evan Y. Yu, MD[1,2]; R. Bruce Montgomery, MD[1]; Lawrence D. True, MD[1]; Jonathan I. Epstein, MD[3]; Tamara L. Lotan, MD[3]; and Colin C. Pritchard, MD, PhD[1]

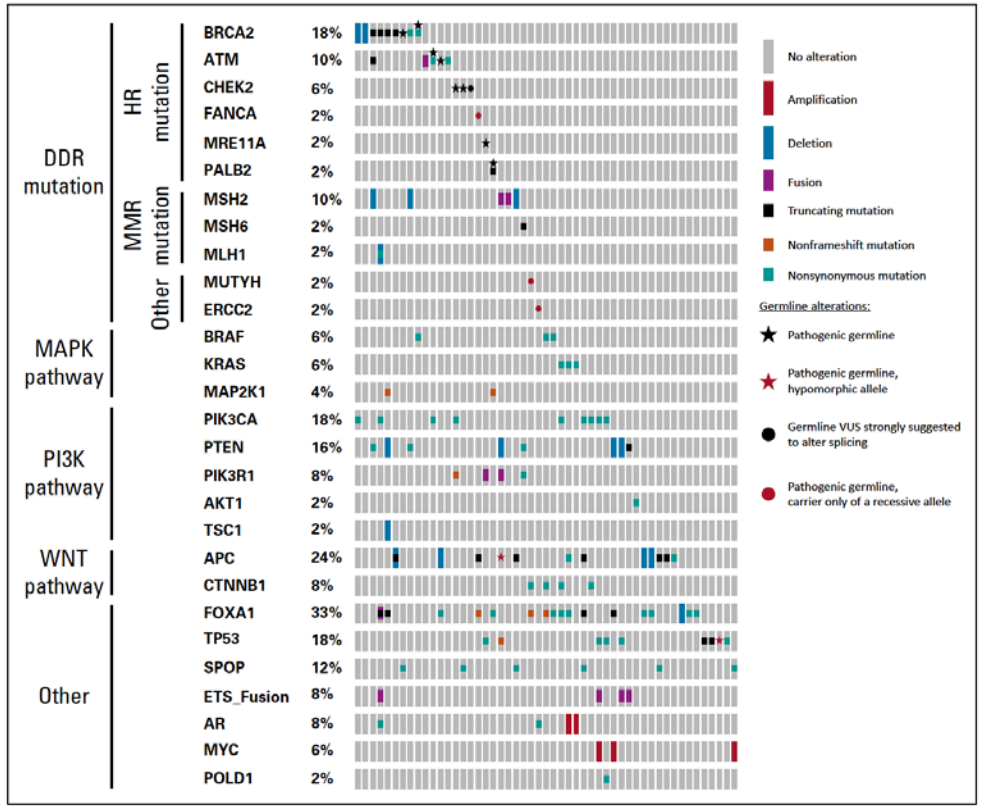


TABLE 2. Recurrent Genomic Alterations in Patients With Ductal Prostate Cancer Compared With Men With Spora Prostate Cancer [22,23]

	No. of Mutations (% of men)			Ductal Cohort Versus TCGA		Ductal Cohort Versus SU2C	
Gene/Pathway	Ductal Cohort (n = 51)	TCGA (n = 333)*	SU2C (n = 150)†	RR (95% CI)	*P*	RR (95% CI)	*P*
Any DDR	25 (49)	62 (19)	34 (23)	2.63 (1.84 to 3.77)	< .001	2.16 (1.44 to 3.25)	< .001
MMR alteration	7 (14)	11 (3)	3 (2)	4.16 (1.69 to 10.23)	.002	6.86 (1.84 to 25.55)	.004
MSH2	5 (10)	5 (2)	3 (2)	6.53 (1.96 to 21.77)	.002	4.90 (1.21 to 19.79)	.026
MLH1	1 (2)	1 (0.3)	1 (0.7)	6.53 (0.41 to 102.76)	.182	2.94 (0.18 to 46.17)	.443
MSH6	1 (2)	6 (2)	0	1.09 (0.13 to 8.85)	.937	—	.254
PMS2	0	4 (1)	0	—	1.00	—	—

2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

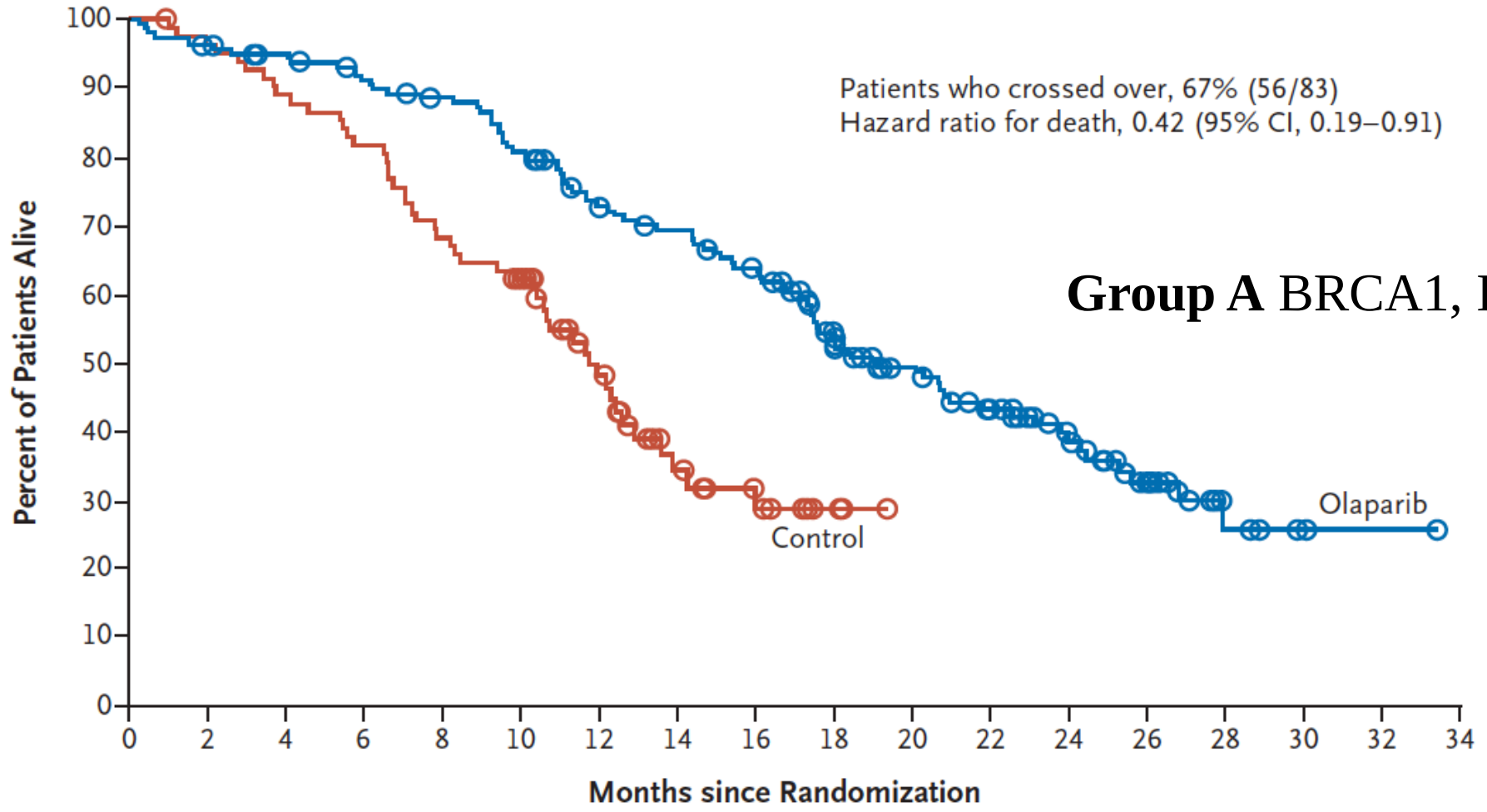
M. Hussain, J. Mateo, K. Fizazi, F. Saad, N. Shore, S. Sandhu, K.N. Chi, O. Sartor, N. Agarwal, D. Olmos, A. Thiery-Vuillemin, P. Twardowski, G. Roubaud, M. Özgüroğlu, J. Kang, J. Burgents, C. Gresty, C. Corcoran, C.A. Adelman, and J. de Bono, for the PROfound Trial Investigators*

Group A BRCA1, BRCA2, ATM

Group B: BRIP1, BARD1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D, and RAD54L

NEJM 2020

B Crossover-Adjusted Analysis of Overall Survival in Cohort A

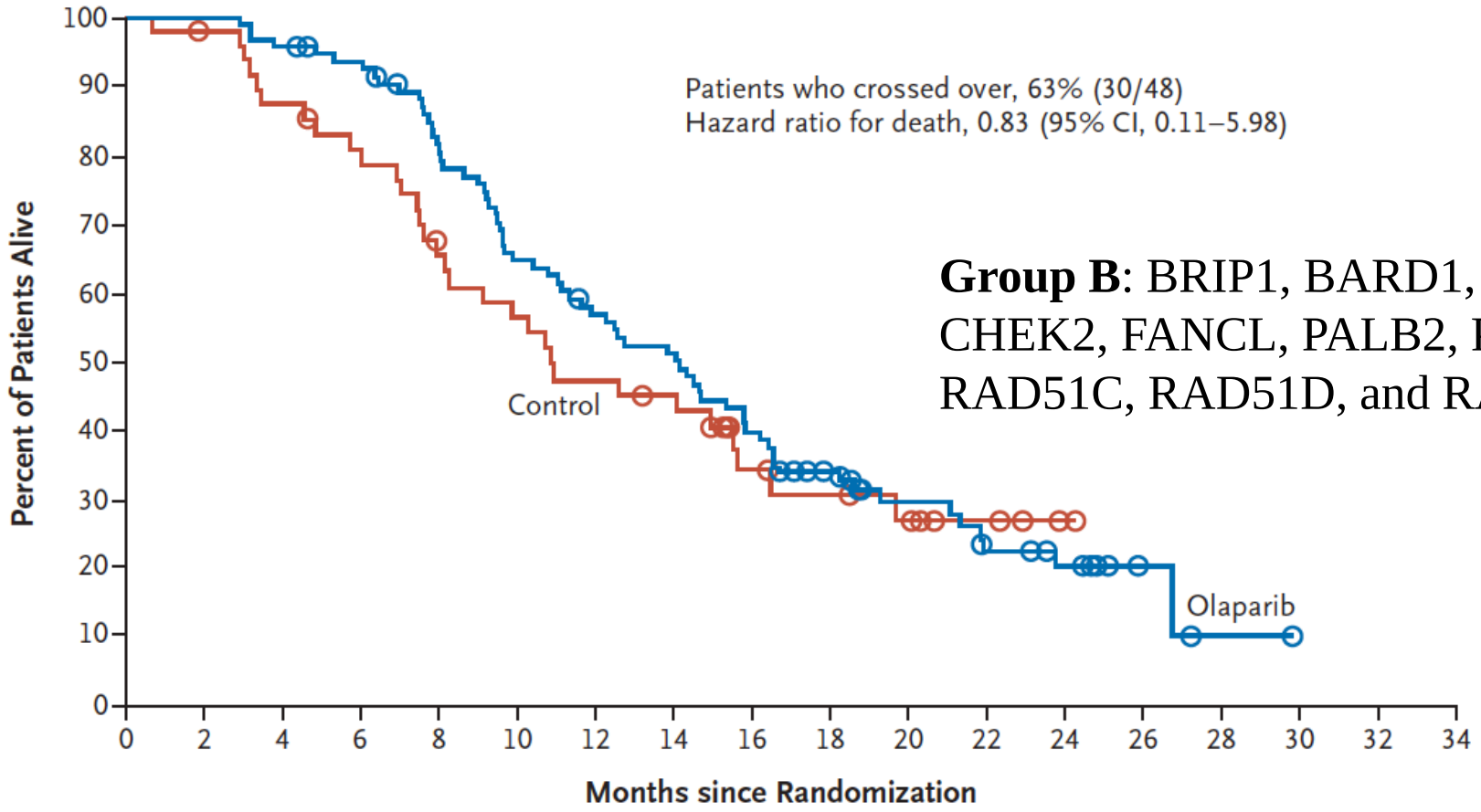


Group A BRCA1, BRCA2, ATM

No. at risk																		
Olaparib	162	155	150	142	136	124	107	101	91	71	56	44	30	18	6	2	1	0
Control	83	79	73	67	56	47	29	15	9	3	0	0	0	0	0	0	0	0

NEJM 2020

B Crossover-Adjusted Analysis of Overall Survival in Cohort B



Group B: BRIP1, BARD1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D, and RAD54L

No. at risk																		
Olaparib	94	94	90	86	73	58	50	45	35	25	17	12	9	4	1	0	0	0
Control	48	46	41	37	29	25	21	19	11	9	7	4	1	0	0	0	0	0

NEJM 2020

Practical handling of ductal lesions

1) Cribriform neoplastic growth-either cancer or cancer involving duct
2) If adenocarcinoma-no problem-grade the adenocarcinoma and note the ductal features
3) If no adenocarcinoma on biopsy –*Ducal Neoplasia with note that this is almost always associated with Invasive adenocarcinoma* (I would perform IHC for basal cell markers to rule out invasive lesion)
4) Pure Ductal Cacinoma is so rare that most of us will never see a case—therefore be careful about this diagnosis

*Note: All slides available for private use at: ***https://www.rubinlab.com/presentations***

All references are given as PMIDs that are available on PubMed

Summary

Ductal features are **commonly** identifed in prostate cancer

Intraductal/ductal features are **associated with other high-grade and stage** features including volume

Pure ductal prostate cancer is extremely **rare**

Diagnsosis of Ductal Adenocarcinoma can be made on prostatectomy (50% or greater) based on WHO classification. **Not on biopsy (sampling)**

Gleason pattern 4/5 for all cribriform/ductal cancer

Genetic testing based on intraductal/ductal prostate cancer **controvertial**