JOHNS HOPKINS
MEDICINE

UPDATE ON PROSTATE CANCER GRADING

Jonathan I. Epstein

Please Silence Your Cell Phones

Thank You

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Dr. Jonathan Epstein declares he has no conflict(s) of interest to disclose.

The International Society of Urological Pathology (ISUP) Consensus Conference on Grading of Prostatic Carcinoma

Chicago
November, 2014

Organizing Committee

Jonathan Epstein & Peter Humphrey (co-chairs)

Mahul Amin
Lars Egevad
Brett Delahunt
John Srigley

67 Pathology Experts in Prostate Cancer from 21 Countries

20 Urology, Oncology, and Radiation Oncology Experts

The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma

The American Journal of Surgical Pathology: Volume 29. September 2005 pp 1228-1242

Epstein, Jonathan I ; Allsbrook, William C Jr; Amin, Mahul B; Egevad, Lars L and the ISUP Grading Committee

Changes to the Gleason Grading System

1. **Poorly formed glands as Gleason pattern 4**

2. **Restricted criteria for cribriform pattern 4 vs. cribriform pattern 3**

Donald Gleason diagnosed only 10 of 270 (3.7%) cases with a primary grade pattern 4, and 20 of 270 (7.4%) cases with a secondary grade pattern 4 – currently the diagnosis of pattern 4 much more prevalent due to the above changes.

Changes to the Gleason Grading System

3. Ignore very small amounts of lower grade cancer on biopsy in the setting of extensive high grade cancer

4. Gleason patterns 1 and 2 not made on biopsy

Why the Need for Another Consensus Conference in 2014

1. **WHO book in GU Pathology scheduled to be finalized in December 2014. Last edition in 2004.**

2. **AJCC 8th ed. needs to be finalized by summer 2015 – Gleason part of the stage grouping.**

Why the Need for Another Consensus Conference in 2014

Update issues that in 2005 either:

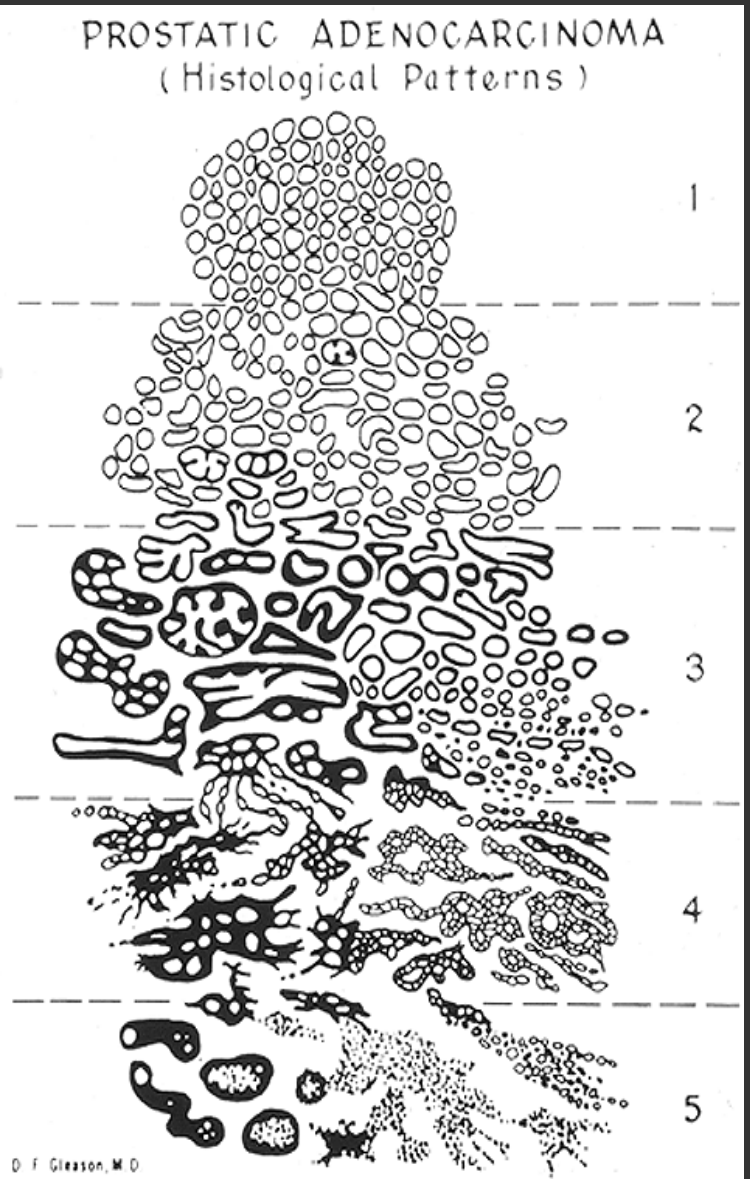
1. **Lacked consensus**
2. **Not discussed**
3. **Has since been modified**
4. **New research**

Topics

- Grading of cribriform carcinoma
- Grading of glomeruloid carcinoma
- Grading of mucinous carcinoma
- Grading of intraductal carcinoma
- Recording percent pattern 4
- New Grading System

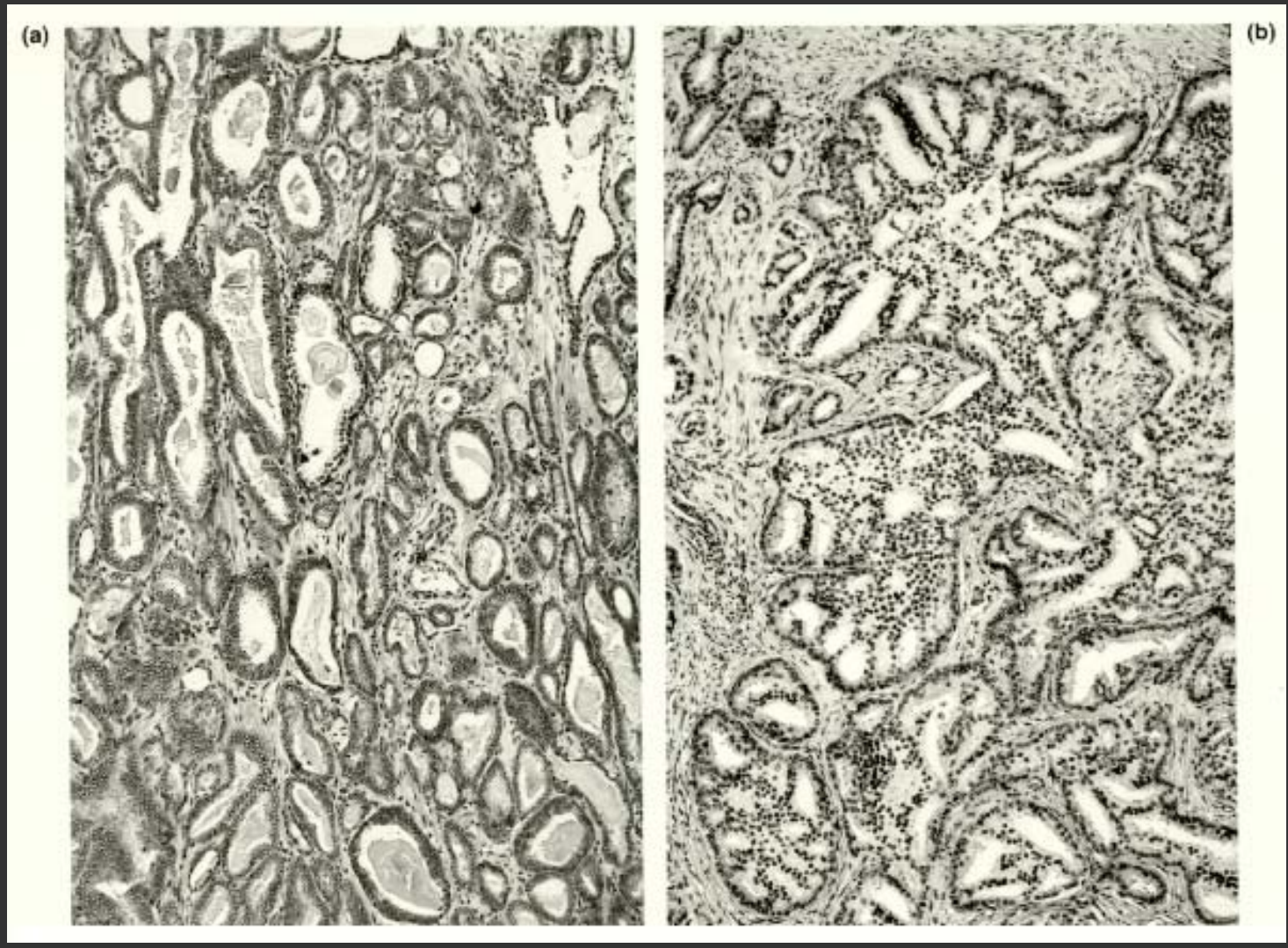
Grading of Cribriform Carcinoma

Cribriform Gleason Pattern 3
vs.
Cribriform Pattern 4



None of Gleason's studies addressed the prognostic differences between rounded cribriform glands and larger, irregular ones.

b. Gleason cribriform grade 3 prostatic adenocarcinoma.



McNeal J, Yemoto C. Am J Surg Pathol 1996; 20:802-14

Do Adenocarcinomas of the Prostate With Gleason Score (GS) $\leq$ 6 Have the Potential to Metastasize to Lymph Nodes?

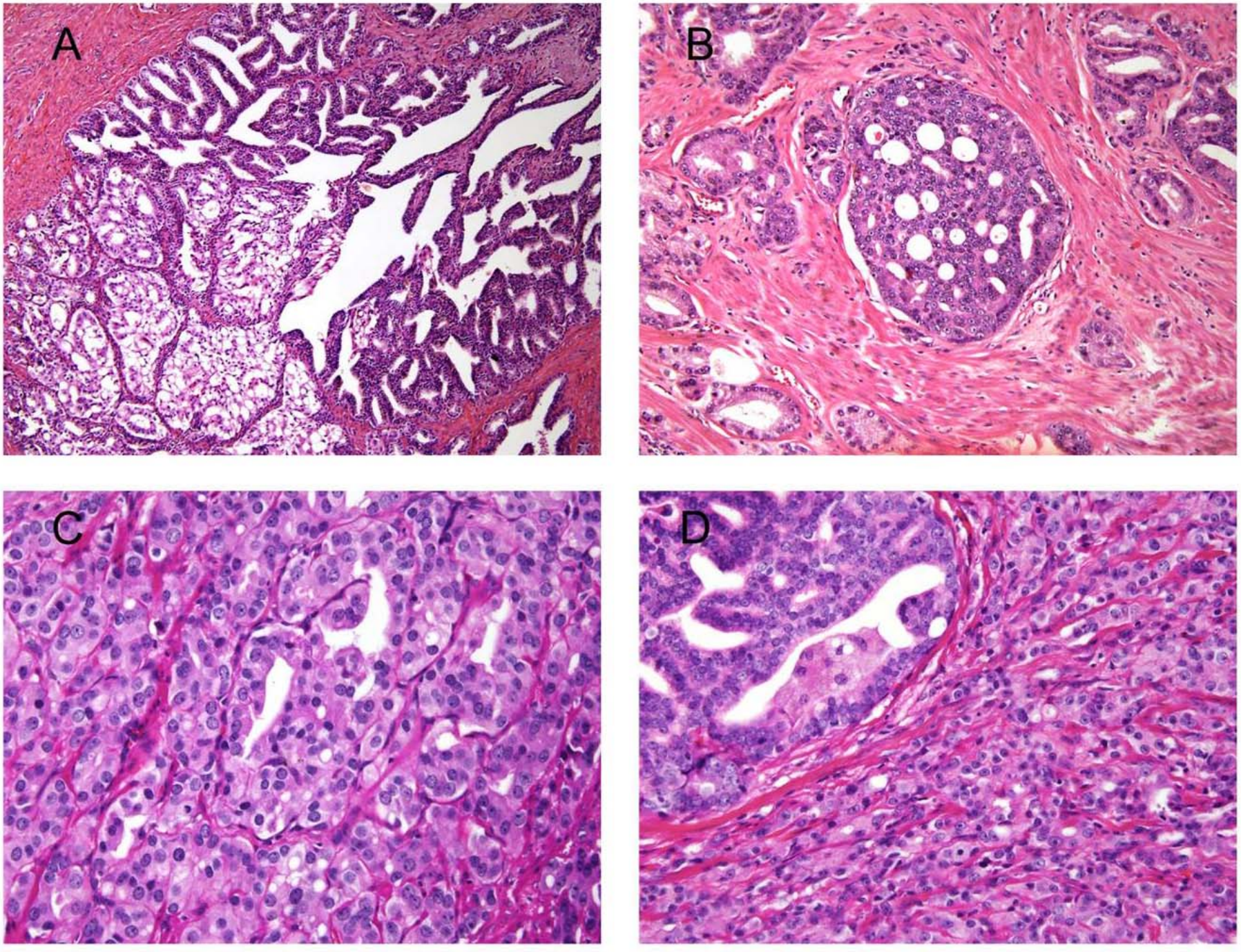
Hillary M. Ross, Oleksandr N. Kryvenko,† Janet E. Cowan,‡ Jeffry P. Simko,‡§ Thomas M. Wheeler,‖ and Jonathan I. Epstein, MD*¶#*

American Journal of Surgical Pathology 2012

- **Totally embedded RPs from 1975-2010 reported as GS ≤6 were identified from**

- **The Johns Hopkins Hospital**
- **Henry Ford Hospital**
- **University of California San Francisco (UCSF)**
- **Baylor College of Medicine.**

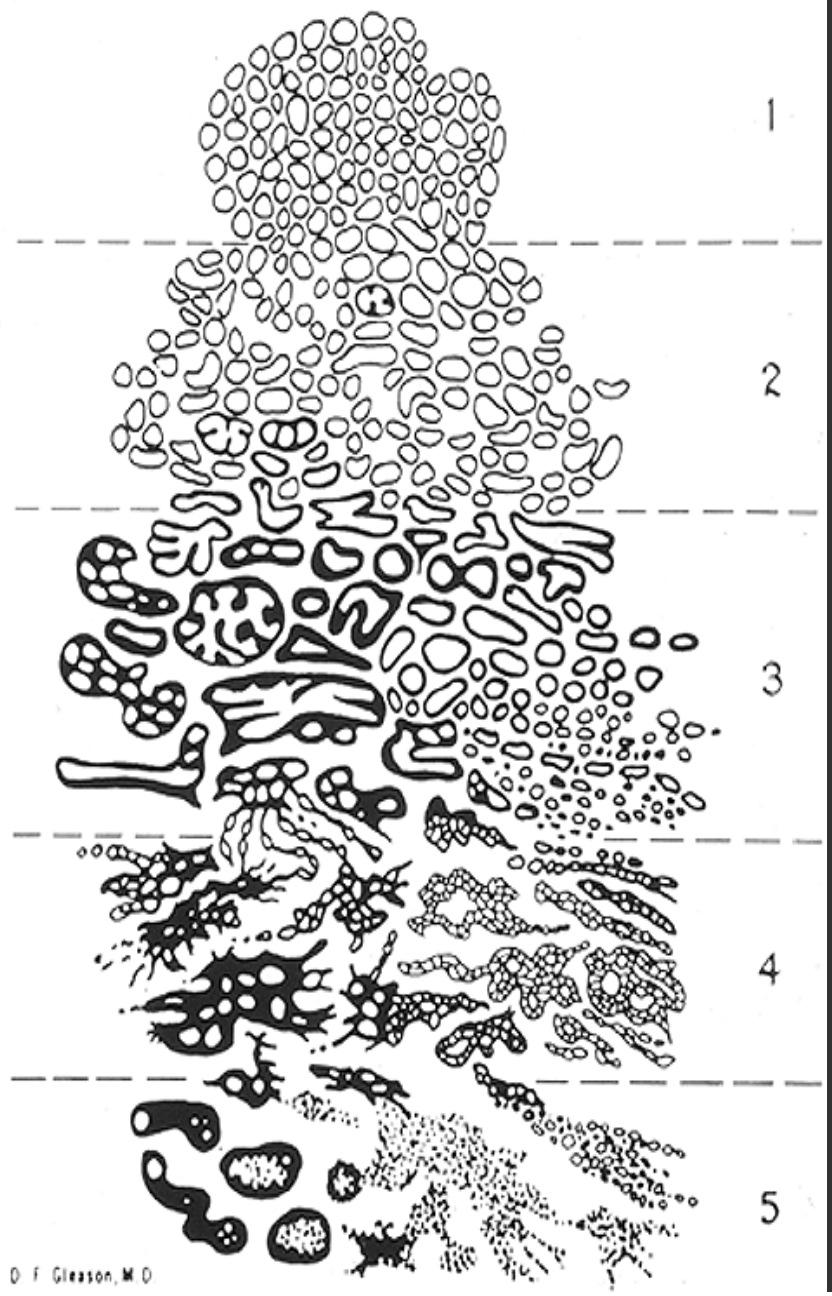
- **19 cases, mostly from the 1990s, diagnosed as GS≤6 with a positive LN**

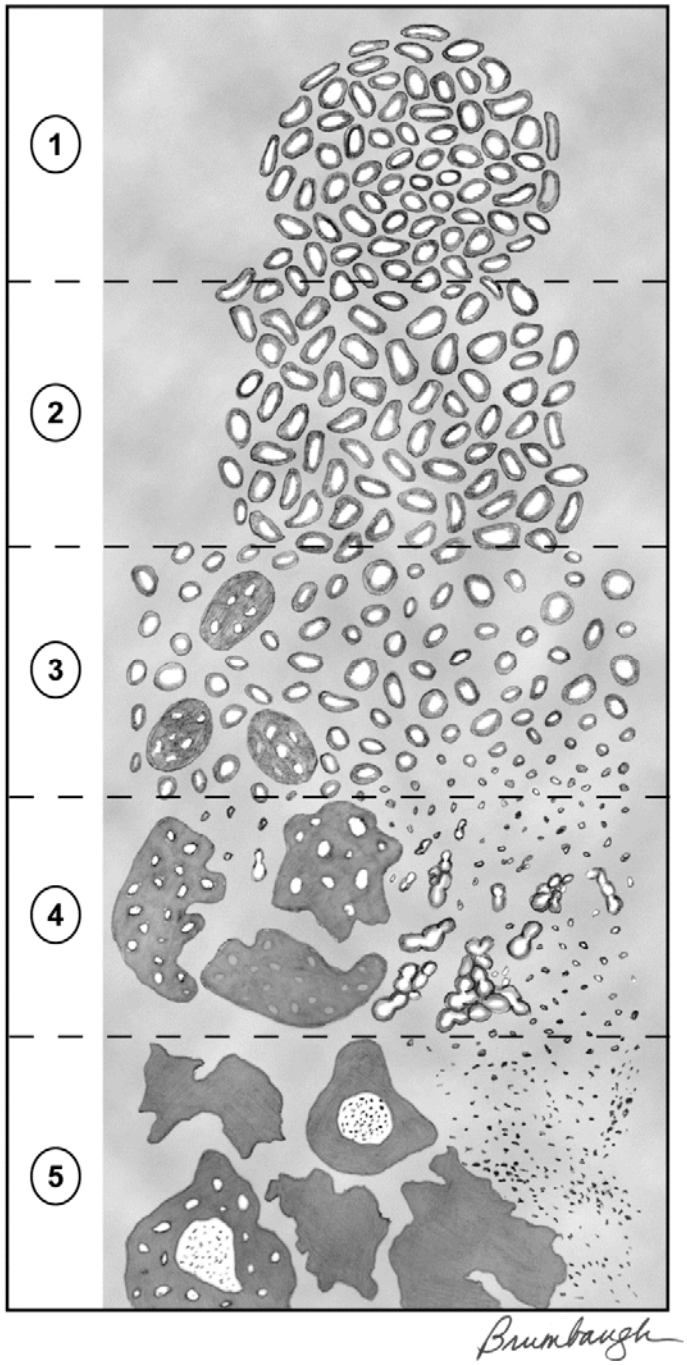

A
B
C
D

2005 - Cribriform Glands

- **More stringent criteria to help pathologists separate cribriform Gleason pattern 3 from pattern 4.**
- **Cribriform Gleason pattern 3 - individual small round glands with regular contour and large round evenly spaced lumens.**
- **Cribriform Gleason pattern 4 - larger glandular formations with irregular contour or jagged edges and/or smaller irregularly distributed lumens or slit-like lumens.**

PROSTATIC ADENOCARCINOMA
(Histological Patterns)





Grading of Invasive Cribriform Carcinoma on Prostate Needle Biopsy

An Interobserver Study among Experts in Genitourinary Pathology

Mathieu Latour, MD, Mahul B. Amin, MD,§ Athanase Billis MD,‖ Lars Egevad MD, PhD,¶ David J. Grignon, MD,# Peter A. Humphrey, MD, PhD,** Victor E. Reuter, MD,†† Wael A. Sakr, MD,‡‡ John R. Srigley MD,§§ Thomas M. Wheeler, MD,‖‖ Ximing J. Yang, MD, PhD,¶¶ and Jonathan I. Epstein, MD*†‡*

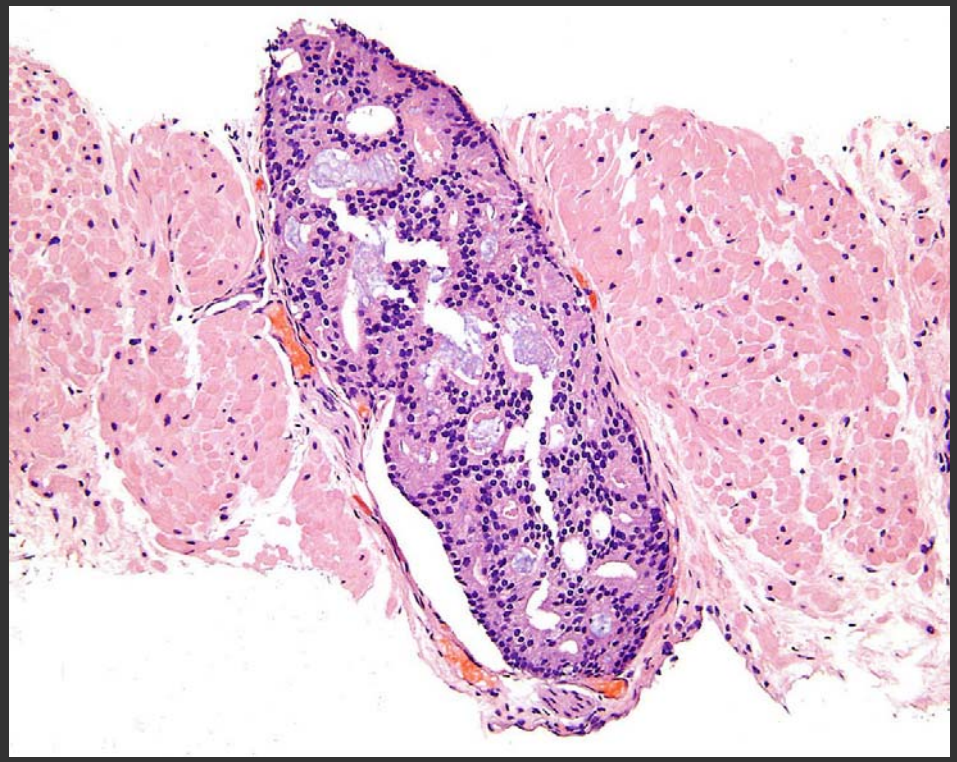
American Journal of Surgical Pathology - 2008

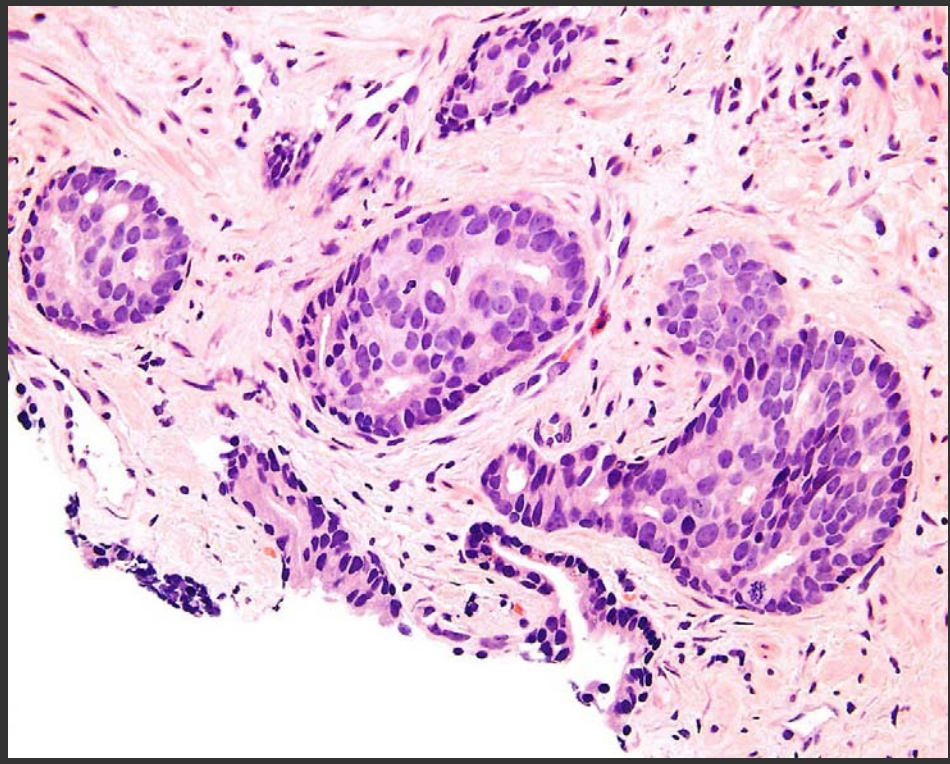
- **Out of 3590 prostate cancers sent to one of the authors over 7 months, 30 needle biopsy cases were selected that possibly represented cribriform Gleason pattern 3 cancer.**

- **Images sent to 10 experts – consensus 7 agreed**

- **Only 1 consensus Gleason cribriform pattern 3**

- **73% the cribriform foci were associated with more definitive pattern 4 elsewhere on the needle biopsy specimen**





Conclusion

Small cribriform cancer foci seen on needle biopsy should with exceedingly rare exception, be interpreted as Gleason pattern 4 and not pattern 3.

Post-2005 Studies

Numerous studies correlating cribriform glands with increased pathological stage, margins, biochemical recurrence after RP, metastases, and cancer-specific death.

Digital Quantification of Five High-Grade Prostate Cancer Patterns, Including the Cribriform Pattern, and Their Association With Adverse Outcome

Kenneth A. Iczkowski, MD,[1] Kathleen C. Torkko, PhD,[1] Gregory R. Kotnis, MD,[1] R. Storey Wilson, MS,[1] Wei Huang, MD,[2] Thomas M. Wheeler, MD,[3] Andrea M. Abeyta,[1] Francisco G. La Rosa, MD,[1] Shelly Cook, MD,[2] Priya N. Werahera, PhD,[1] and M. Scott Lucia, MD[1]

Am J Clin Pathol 2011: 136: 98-107

- **Multivariate analysis showed the cribriform pattern had the highest odds ratio for PSA failure - 5.89 (P < .0001).**

- **Both large and small cribriform patterns were significantly linked to failure.**

- **The cribriform pattern has particularly adverse implications for outcome.**

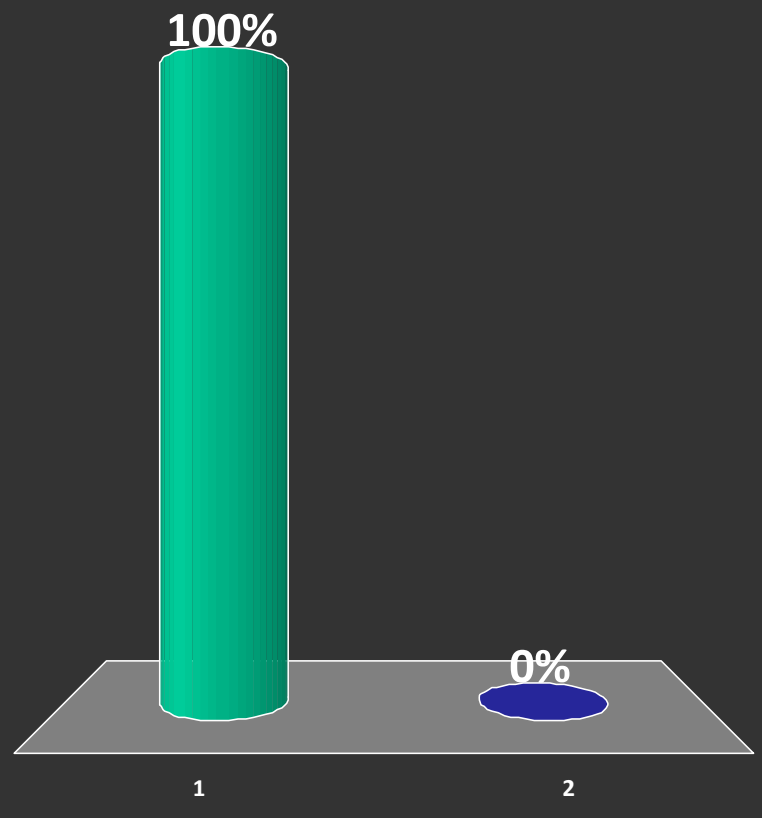
Conceptually

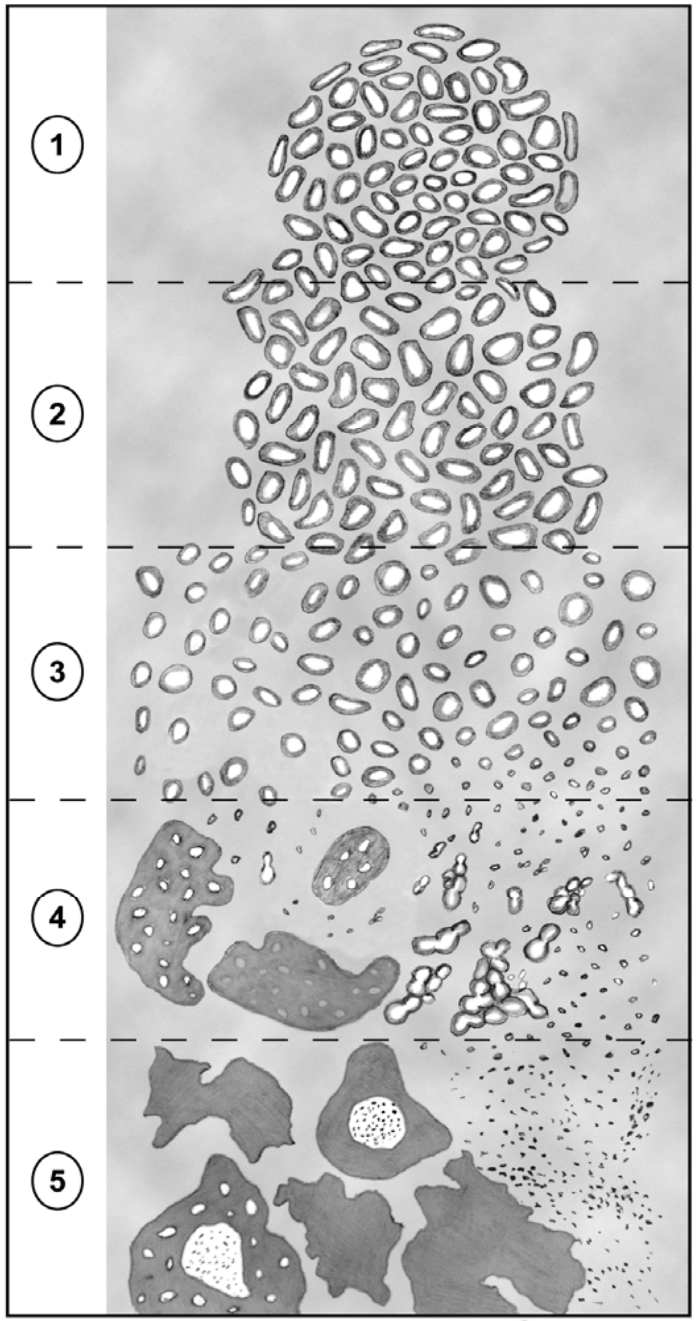
One would expect the change in grade from pattern 3 to pattern 4 to be reflected in a distinct architectural paradigm shift where cribriform as opposed to individual glands are formed rather than merely a subjective continuum of differences in size, shape, and contour of the cribriform glands.

VOTE

All cribriform glands should be graded as Gleason pattern 4 regardless of morphology.

1. Yes
2. No




1
2
3
4
5
Brumbaugh

Grading of Glomeruloid Glands

Glomeruloid Structures

- **Larger glomeruloid - Most agree pattern 4**
- **Small glomeruloid- ? pattern 3 or pattern 4.**
- **Not resolved in 2005 grading meeting**

Human Pathology (2009) **40**, 471–477

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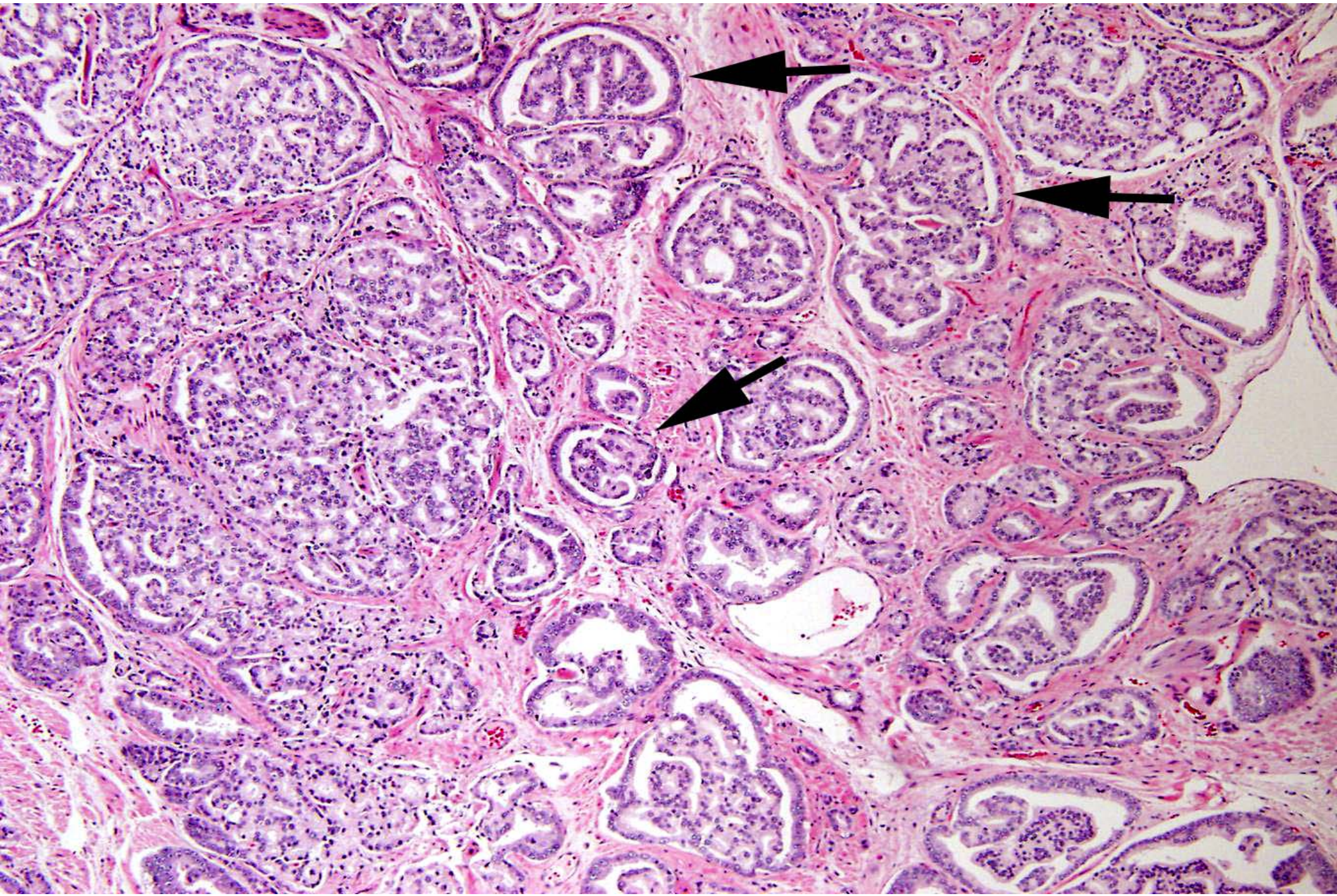
www.elsevier.com/locate/humpath

Original contribution

Gleason grading of prostatic adenocarcinoma with glomeruloid features on needle biopsy

Tamara L. Lotan MD[a], Jonathan I. Epstein MD[a,b,c,*]

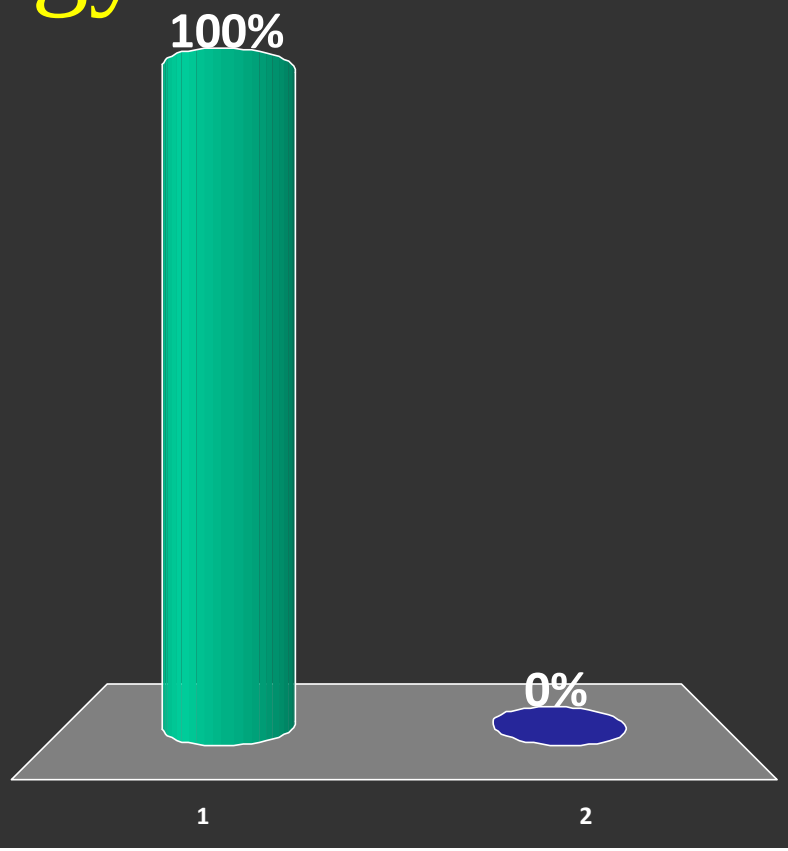
- **45 prostate needle biopsies containing carcinoma with glomeruloid features**
- **Associated with high-grade cancer on the same core, composed of either Gleason pattern 4 (80% of cases) or Gleason pattern 5 (4% of cases).**
- **Only a minority of glomerulations surrounded exclusively by pattern 3 cancer (16% of cases) on the same core.**
- **Transition could be seen among small glomerulations, large glomeruloid structures, and cribriform pattern 4 cancer.**



VOTE

All glomeruloid glands should be graded as Gleason pattern 4 regardless of morphology.

1. Yes
2. No



Grading of Mucinous Carcinoma

The American Journal of Surgical Pathology
9(4): 299–308, April
© 1985 Raven Press, New York

Jonathan I. Epstein, M.D.

Philip H. Lieberman, M.D.

Mucinous adenocarcinoma of the prostate gland

- **Of 1600 PCa. at MSKCC over 20 years, 6 mucinous carcinomas on TUR**
- **>25% extracellular mucin**
- **5/6 cribriform pattern predominated**
- **5/6 bulky palpable tumors treated with HT or RT with 5/6 developing mets.**

Mucinous Adenocarcinoma of the Prostate:

Histochemical and Immunohistochemical Studies

JAE Y. RO, MD, DAVID J. GRIGNON, MD, ALBERTO G. AYALA, MD,
PEDRO L. FERNANDEZ, MD, NELSON G. ORDONEZ, MD, AND
KENNETH I. WISHNOW, MD

Hum Pathol 1990; 21:593-600

- **12 patients treated with TUR**
- **Tumor stages were T3 (n=3), T4 (n=5), and unknown (n=4).**
- **Treatment was radiation, HT or a combination.**
- **7 patients died of disease (mean follow-up, 56 months), and 5 patients are alive with disease (mean, 32.2 months).**

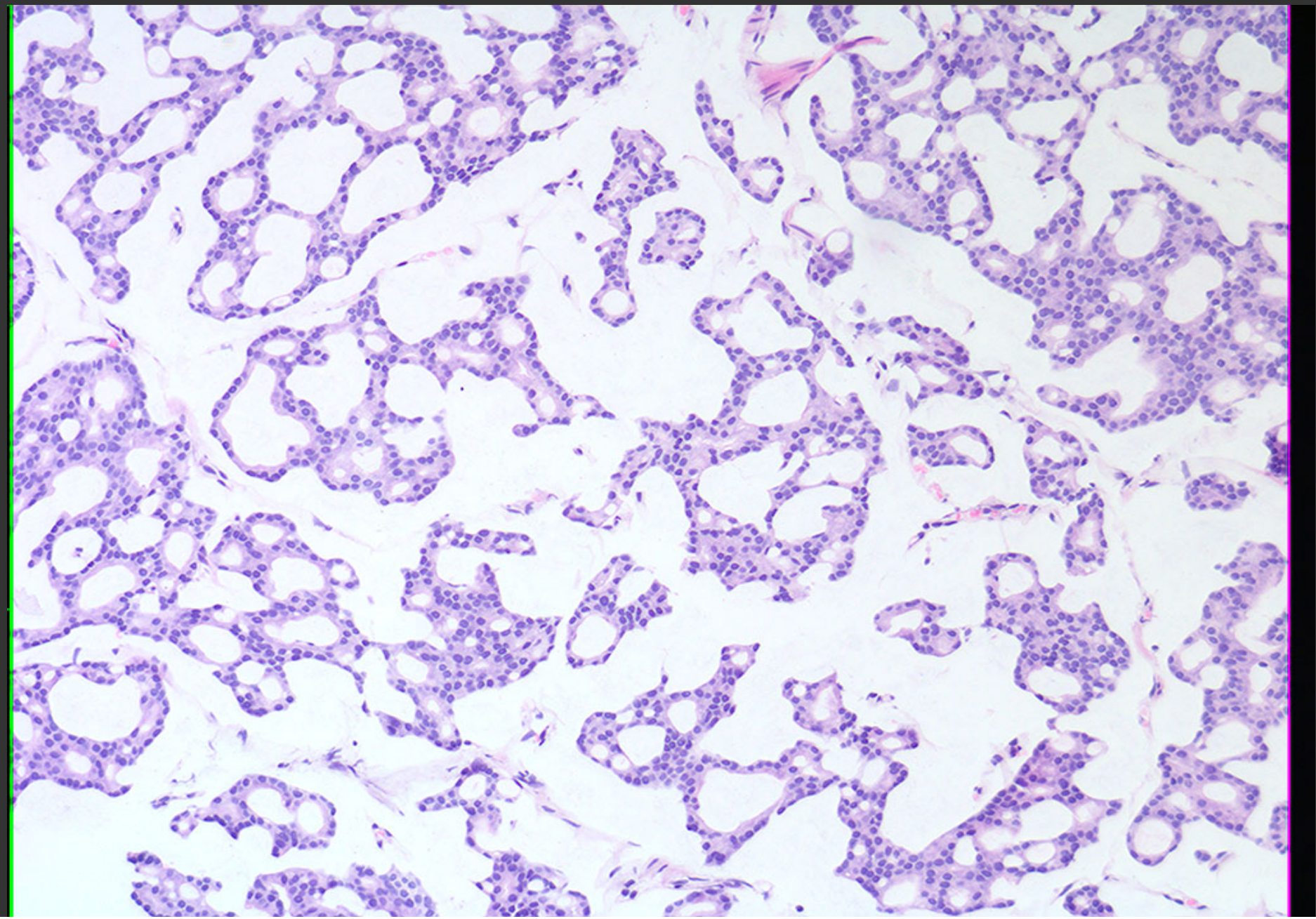
Colloid (Mucinous) Carcinoma

There is no consensus whether all colloid carcinomas should be assigned a Gleason score of 8, or that one should ignore the extracellular mucin and grade the tumor based on the underlying architectural pattern.

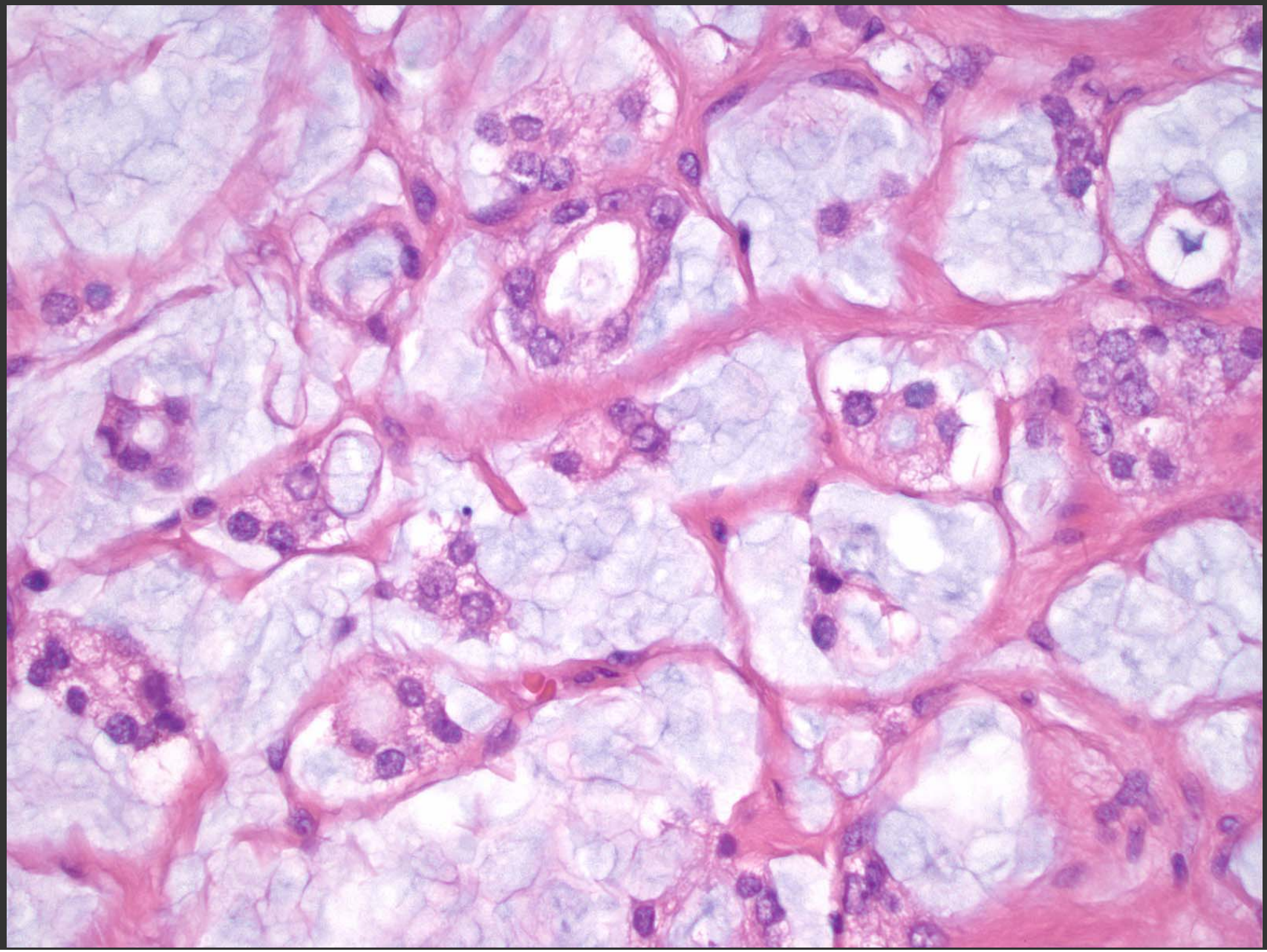
Most Gleason pattern 4

? Some Gleason pattern 3

Mucinous Cancer: Pattern 4



Mucinous Cancer: Pattern 3



MUCINOUS ADENOCARCINOMA OF THE PROSTATE DOES NOT CONFER POOR PROGNOSIS

BRIAN R. LANE, CRISTINA MAGI-GALLUZZI, ALWYN M. REUTHER, HOWARD S. LEVIN, MING ZHOU, AND ERIC A. KLEIN

Urology 2006: 68: 825-830

- **No patients with mucinous carcinoma or PCa. with focal mucin died of disease, and 11 (91.7%) of 12 patients with mucinous carcinoma and 9 (64.3%) of 14 patients with focal mucin were clinically and biochemically free of disease.**

- **No significant difference was found in BCR or overall survival between those with mucinous carcinoma or focal mucin and a matched group of patients with usual PCa.**

Prognosis of Mucinous Adenocarcinoma of the Prostate Treated by Radical Prostatectomy

A Study of 47 Cases

Adeboye O. Osunkoya, MD, Matthew E. Nielsen, MD,† and Jonathan I. Epstein, MD†‡§*

Am J Surg Pathol 2008: 32: 468-72

- **All together, taking into account both the mucinous and nonmucinous tumor, 20/47 cases (42.5%) had EEPE and 6/47 (12.7%) had positive margins.**

- **The 1 LN metastasis contained nonmucinous cancer.**

- **The mean follow-up for those without progression was 5.6 years (median 6 y, range: 1 to 15 y).**

- **One patient (2.1%) progressed 3 years after his RP (5 y actuarial progression-free risk 97.2%).**

- **Using the Kattan nomogram, the predicted mean 5-year PSA progression-free risk for nonmucinous prostate cancer with the same PSA and postoperative findings as in the current study was 85.4%.**

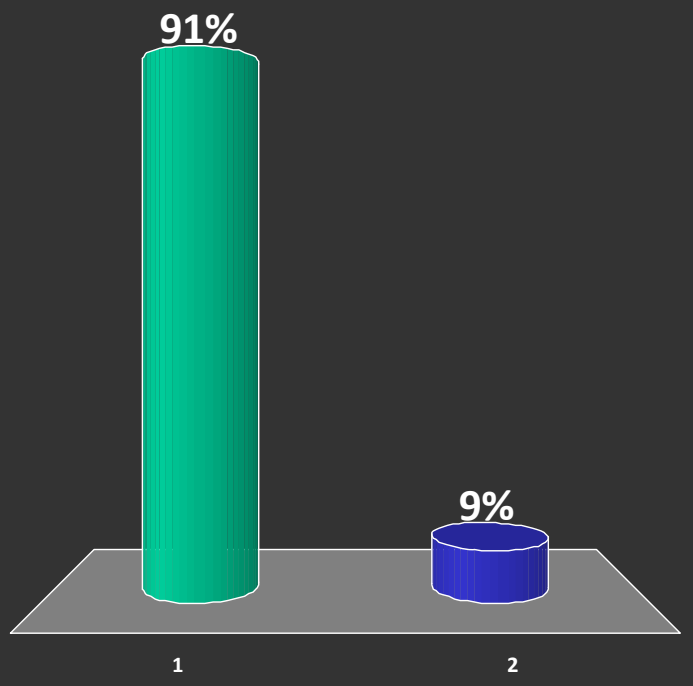
Conclusions

Mucinous adenocarcinoma of the prostate treated by RP is not more aggressive, and possibly even less aggressive than nonmucinous prostatic adenocarcinoma.

VOTE

Mucinous carcinomas should be graded based on their underlying growth pattern rather than grading them as all Gleason pattern 4.

1. Yes
2. No



Grading Variants of Prostate Adenocarcinoma

Same rule as grading usual prostate adenocarcinoma based on underlying grade pattern, except small cell carcinoma.

Foamy, Ductal, Vacuoles, Pseudohyperplastic

- **Individual well-formed glands**
- **Cribriform**
- **Individual cells or necrosis**

Grading of Intraductal Carcinoma

Ductal Spread in Prostatic Carcinoma

JOSEPH KOVI, MD, FRCPATH,* MARVIN A. JACKSON, MD,* AND MARTIN Y. HESHMAT, MD, DRPH†

Cancer 1985; 56: 1566-73

Spread of Adenocarcinoma Within Prostatic Ducts and Acini: Morphologic and Clinical Correlations

McNeal, John E. M.D.; Yemoto, Cheryl E. M. B.S., M.T.(A.S.C.P.)

Am J Surg Pathol 1996; 20: 802-4

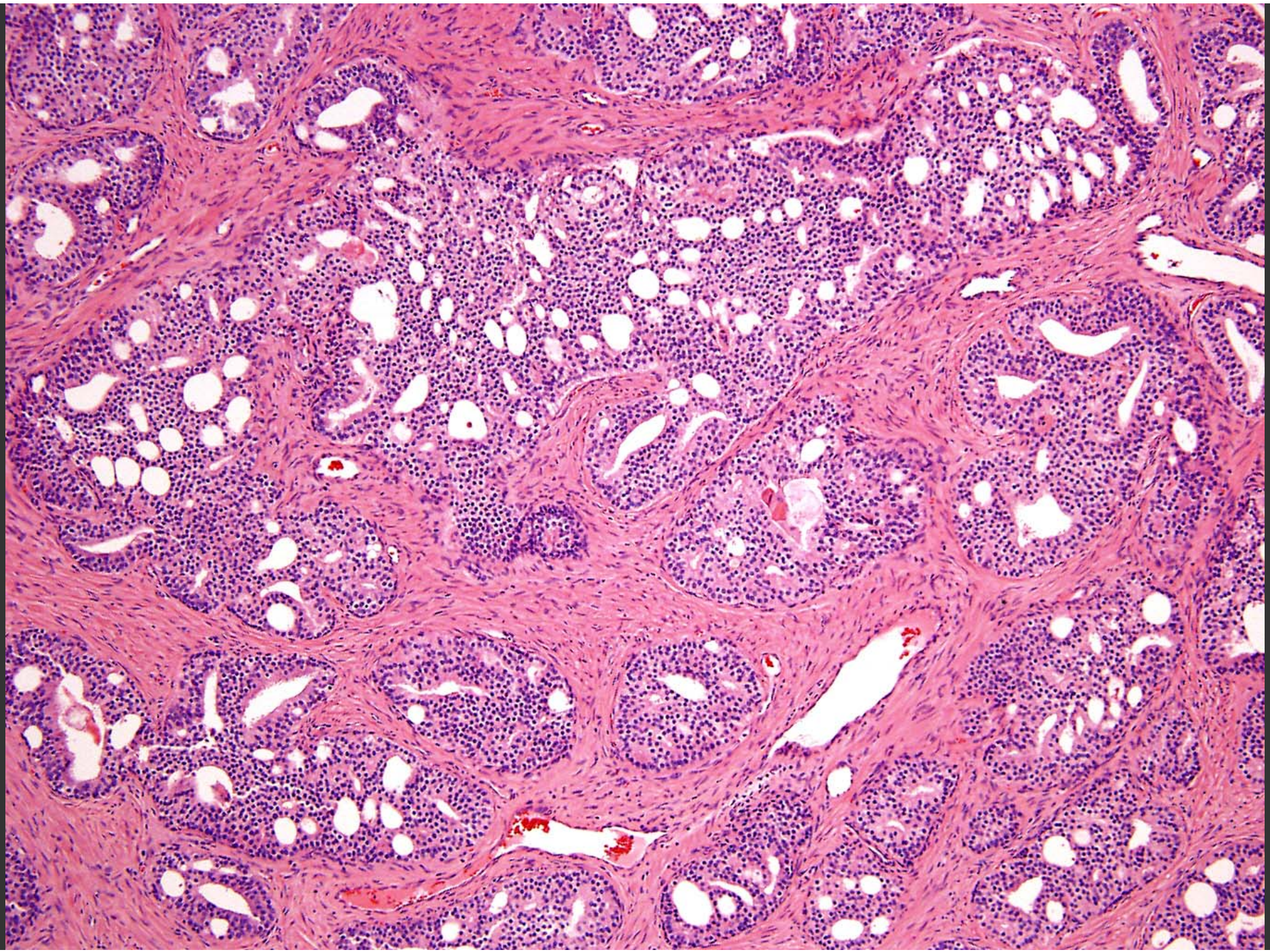
Modern Pathology (2006) 19, 1528–1535
© 2006 USCAP, Inc All rights reserved 0893-3952/06 $30.00
www.modernpathology.org

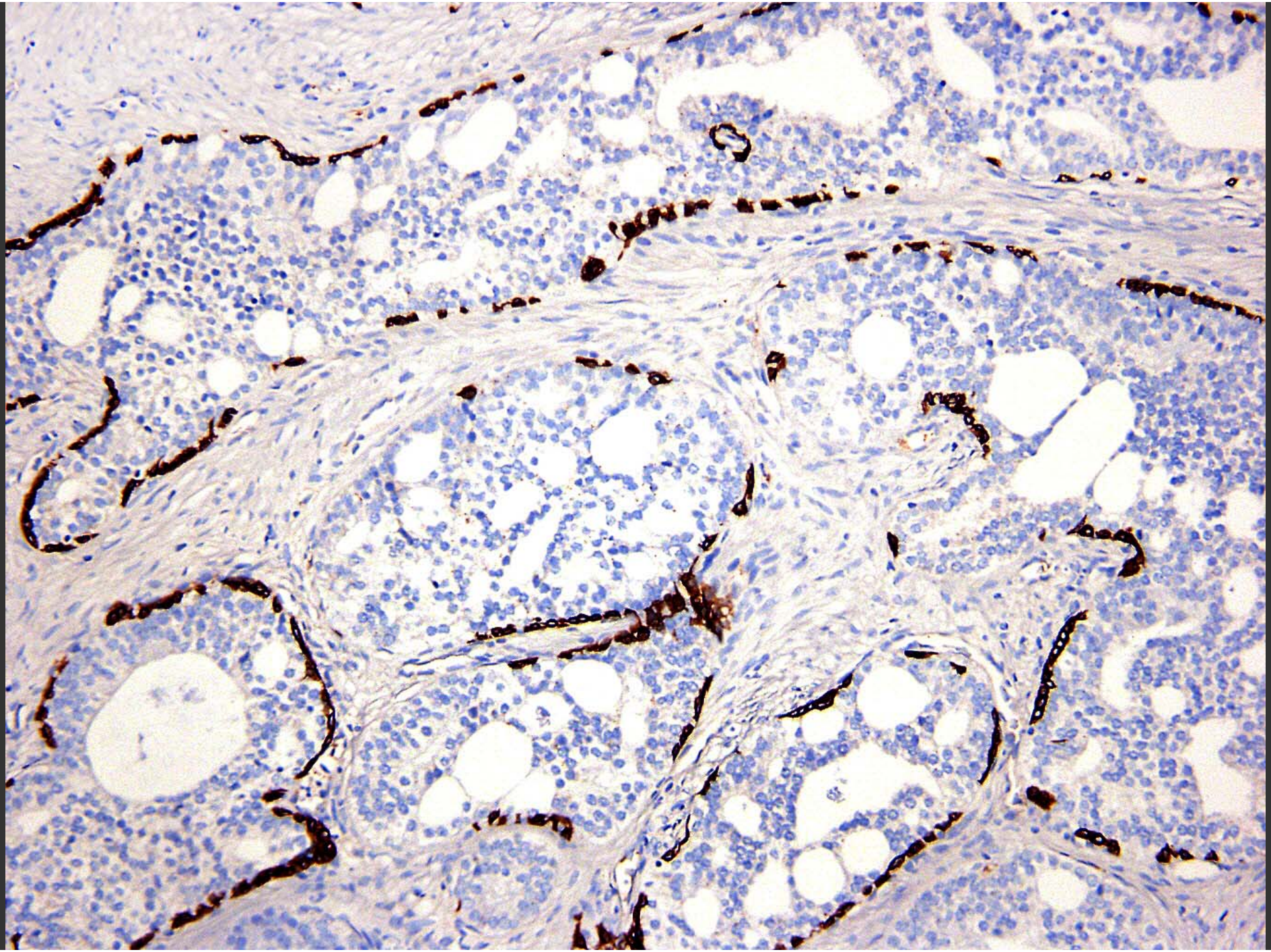
Intraductal carcinoma of the prostate on needle biopsy: histologic features and clinical significance

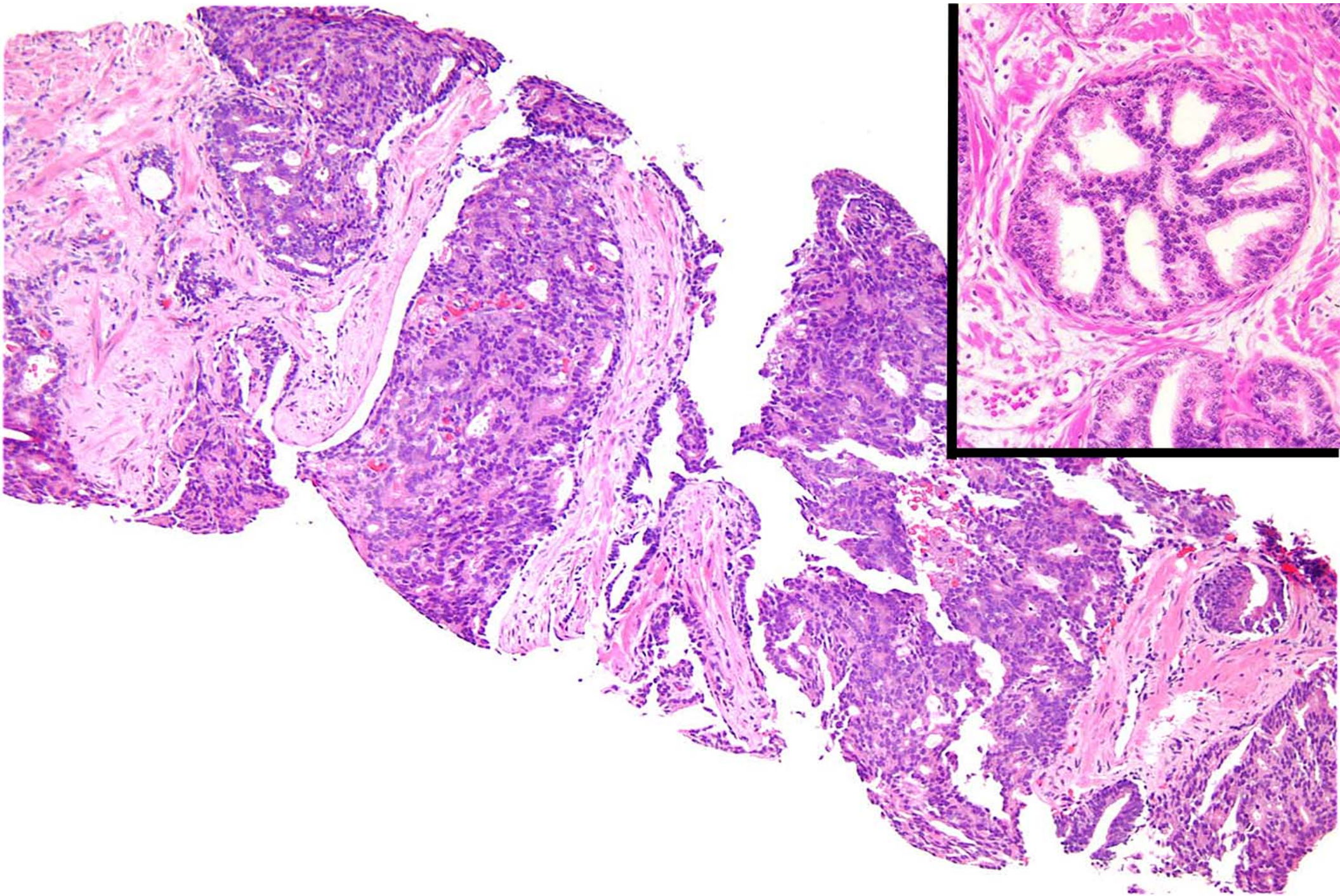
Charles C Guo[1] and Jonathan I Epstein[1,2,3]

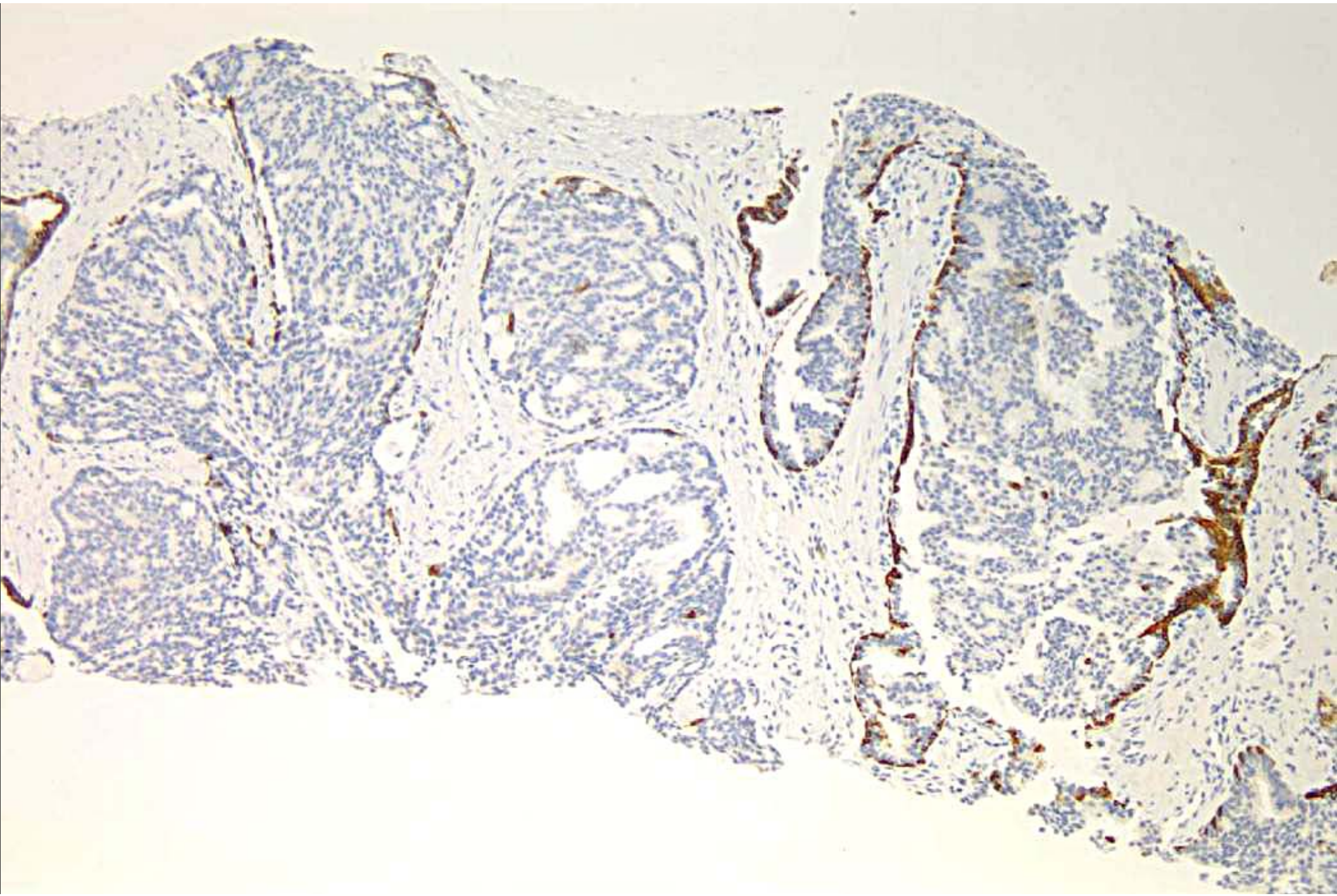
Intraductal Carcinoma

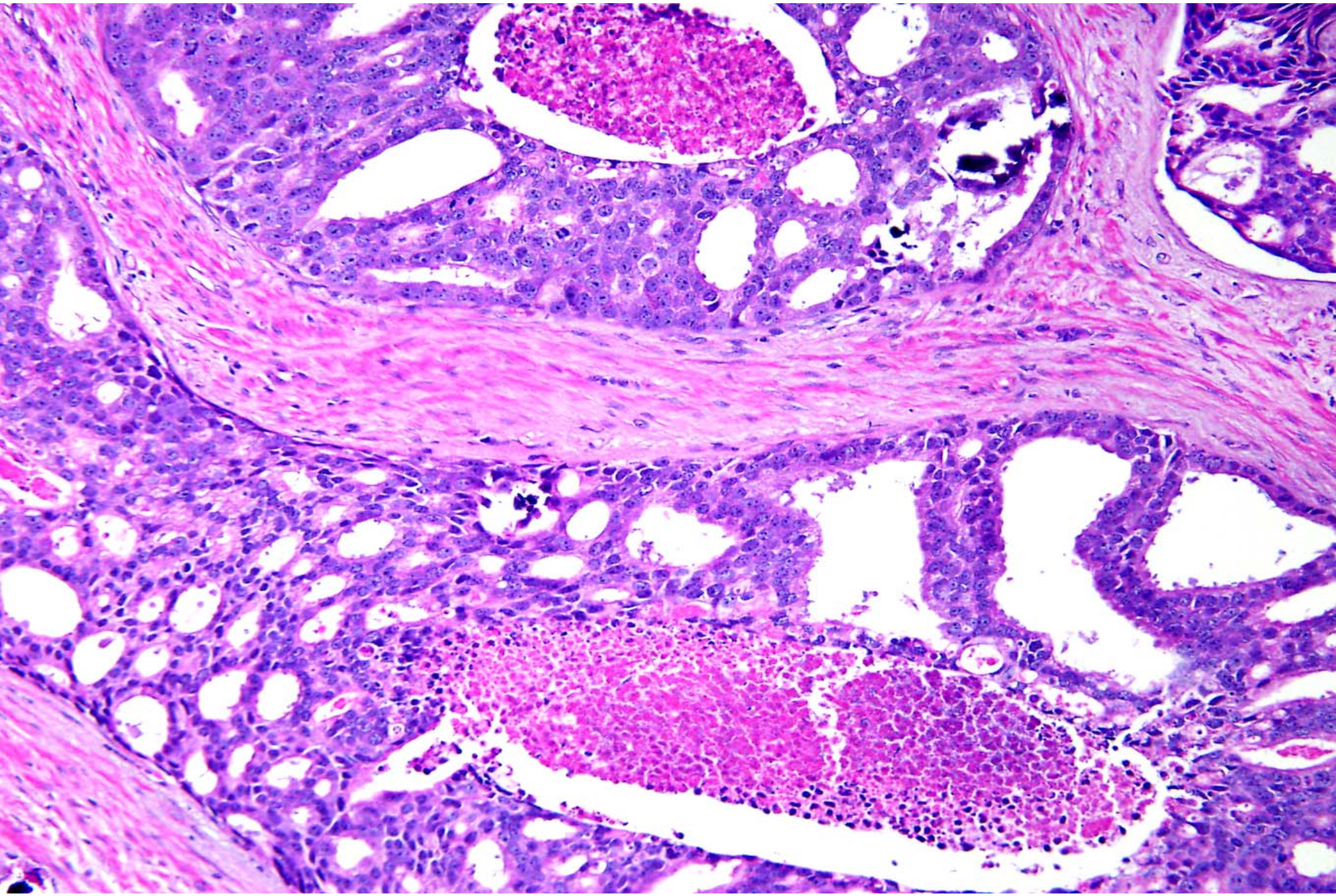
- **Solid or dense cribriform pattern**
- **Loose cribriform or micropapillary pattern with either**
  - **Marked nuclear atypia: Nuclei 6x normal**
  - **Necrosis**
- **Basal cell layer preserved**

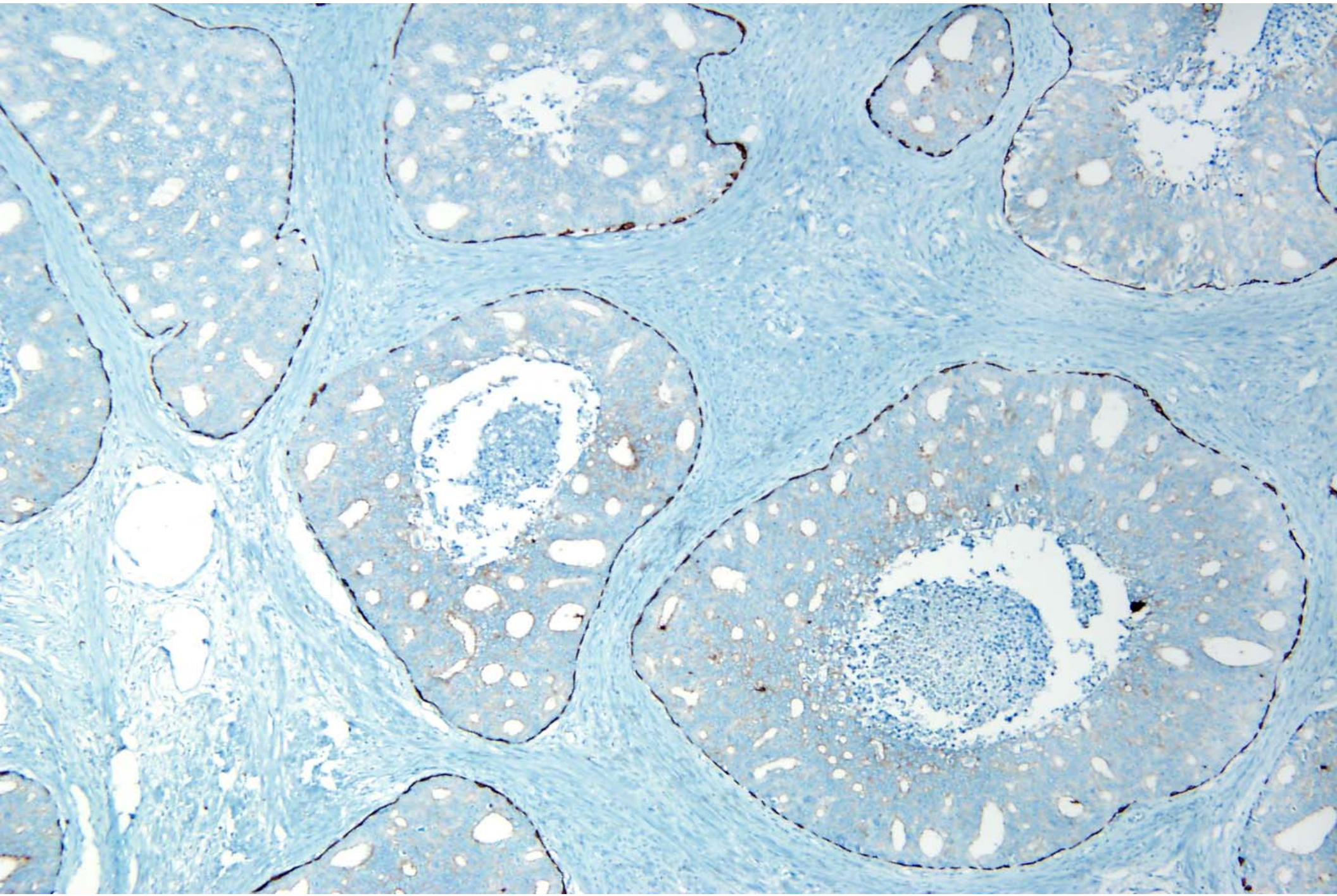


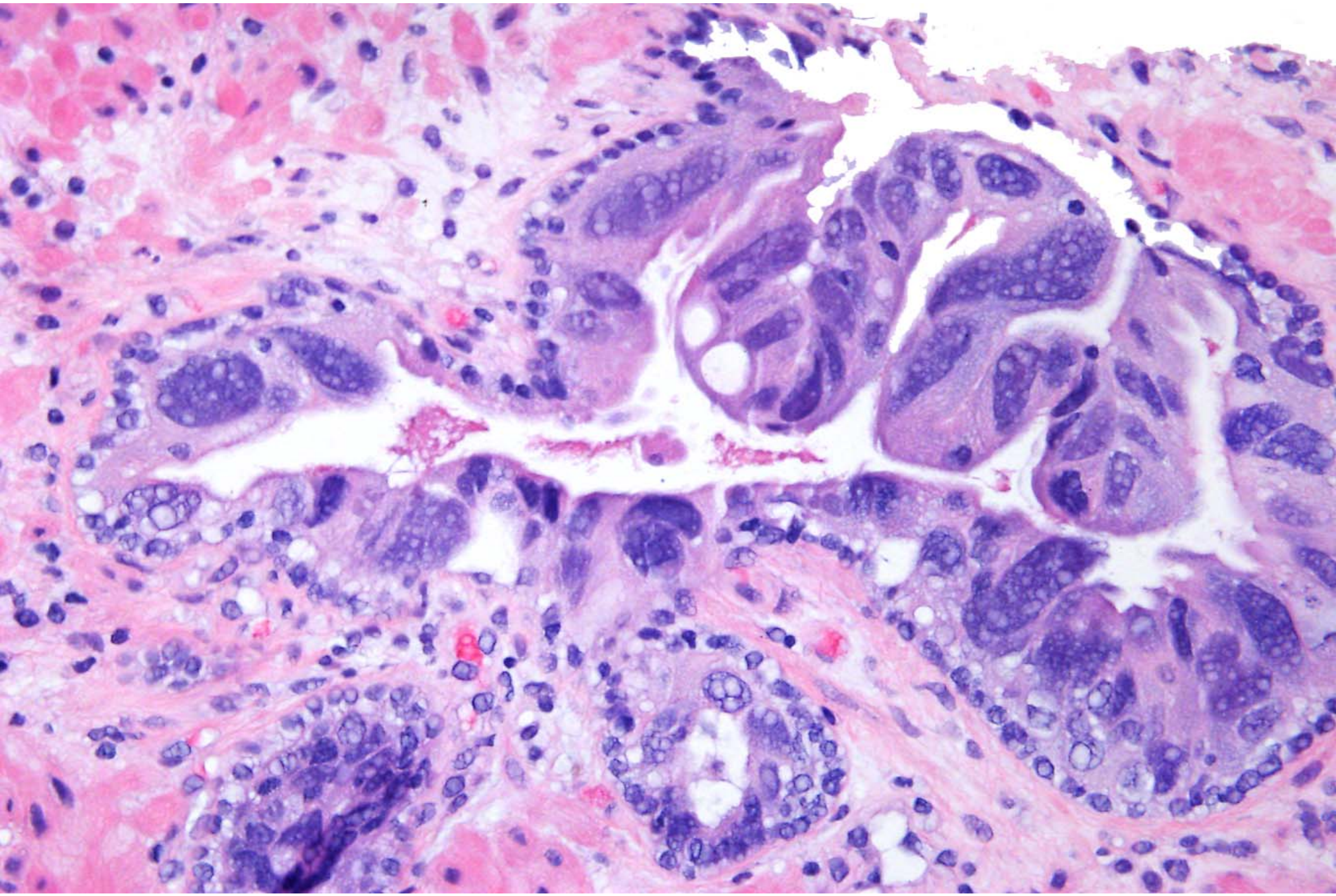












Int J Clin Exp Pathol 2014;7(2):2518-2526
www.ijcep.com /ISSN:1936-2625/IJCEP0000123

Original Article

Heterogeneous clinicopathological features of intraductal carcinoma of the prostate: a comparison between "precursor-like" and "regular type" lesions

Kosuke Miyai[1], Mukul K Divatia[1], Steven S Shen[1,3], Brian J Miles[2], Alberto G Ayala[1,3], Jae Y Ro[1,3]

- **Of 901 RPs, 141 had IDC with adjacent invasive carcinoma (regular IDC) and 14 (1.5%) showed IDC with cancer distant from IDC (precursor IDC)**

- **Regular IDC with cancer had significantly higher Gleason score, more frequent EPE and SVI, more advanced pathological T stage, and lower 5-year BCR than IDC w/o adjacent carcinoma.**

- **Prostate cancer with Gleason score $\geq$8 in the RP was observed in 73 (52%) cases with regular type IDC-P and in 3 (21%) cases with precursor-like IDC-P.**

IDC does not always represent intraductal spread of pre-existing high-grade invasive carcinoma, and at least a small subset of IDC could account for a precursor lesion of invasive carcinoma

Grading of IDC - Pro

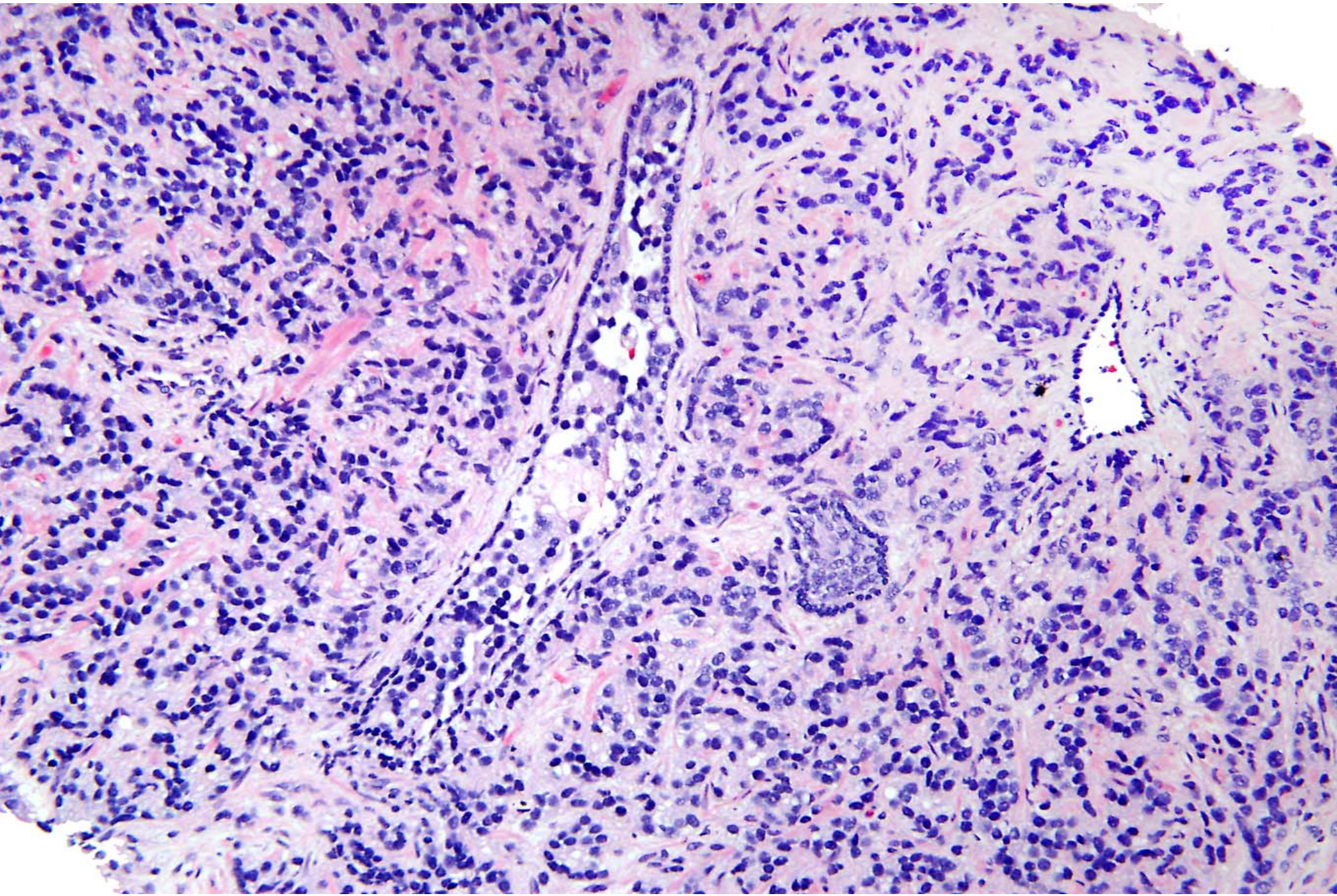
- **Even when IDC alone present on biopsy, 90% will have Gleason score ≥7 at RP**
- **When IDC and invasive cancer on biopsy, almost always Gleason score ≥7, so already Gleason pattern 4.**
- **Hard to tell IDC vs. cribriform Gleason pattern 4 cancer – ? Need to do IHC on multiple parts**
- **Several studies demonstrate correlation of IDC on biopsy with increased pstage and worse prognosis after either RP or RT.**

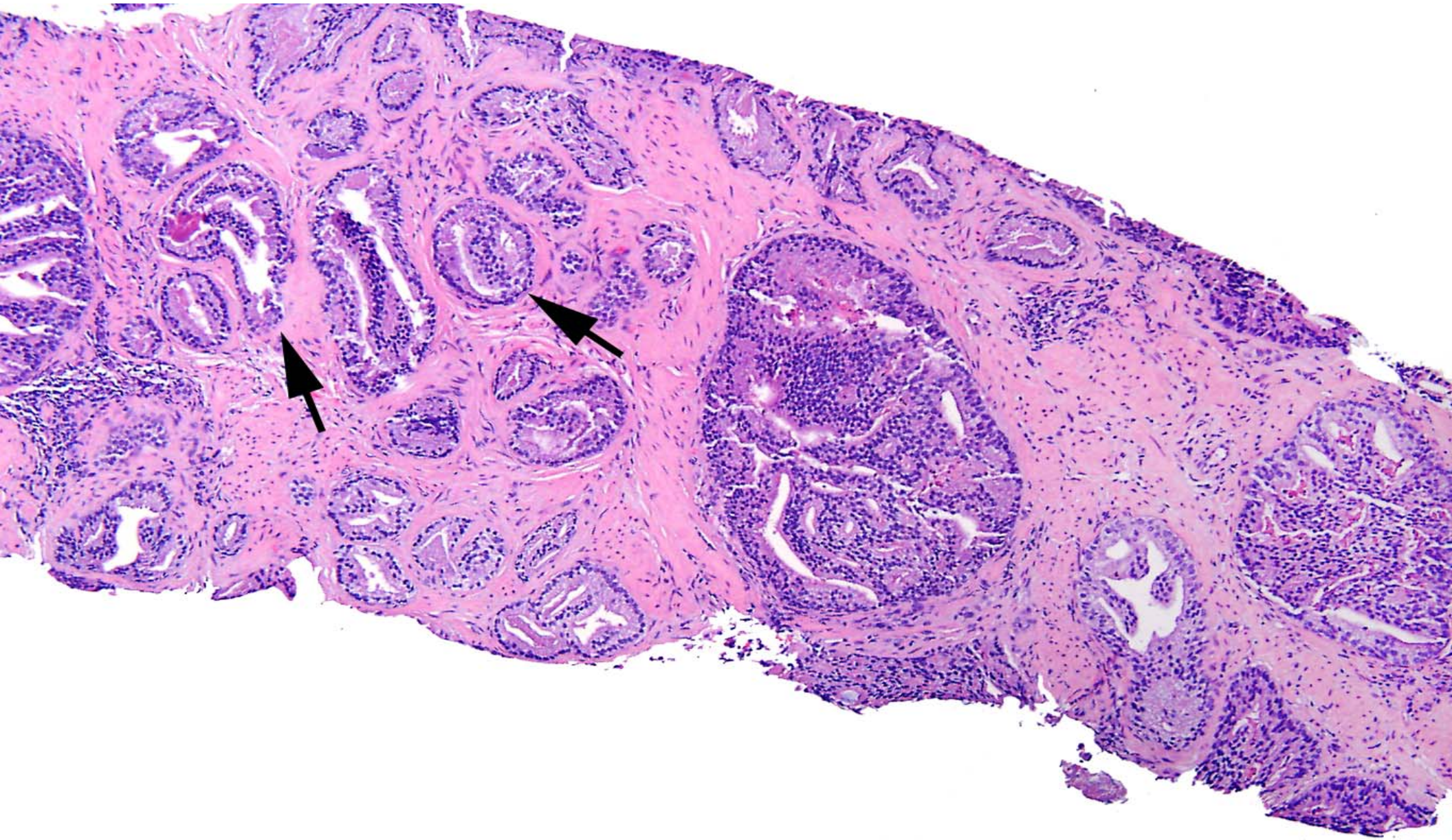
Grading of IDC - Con

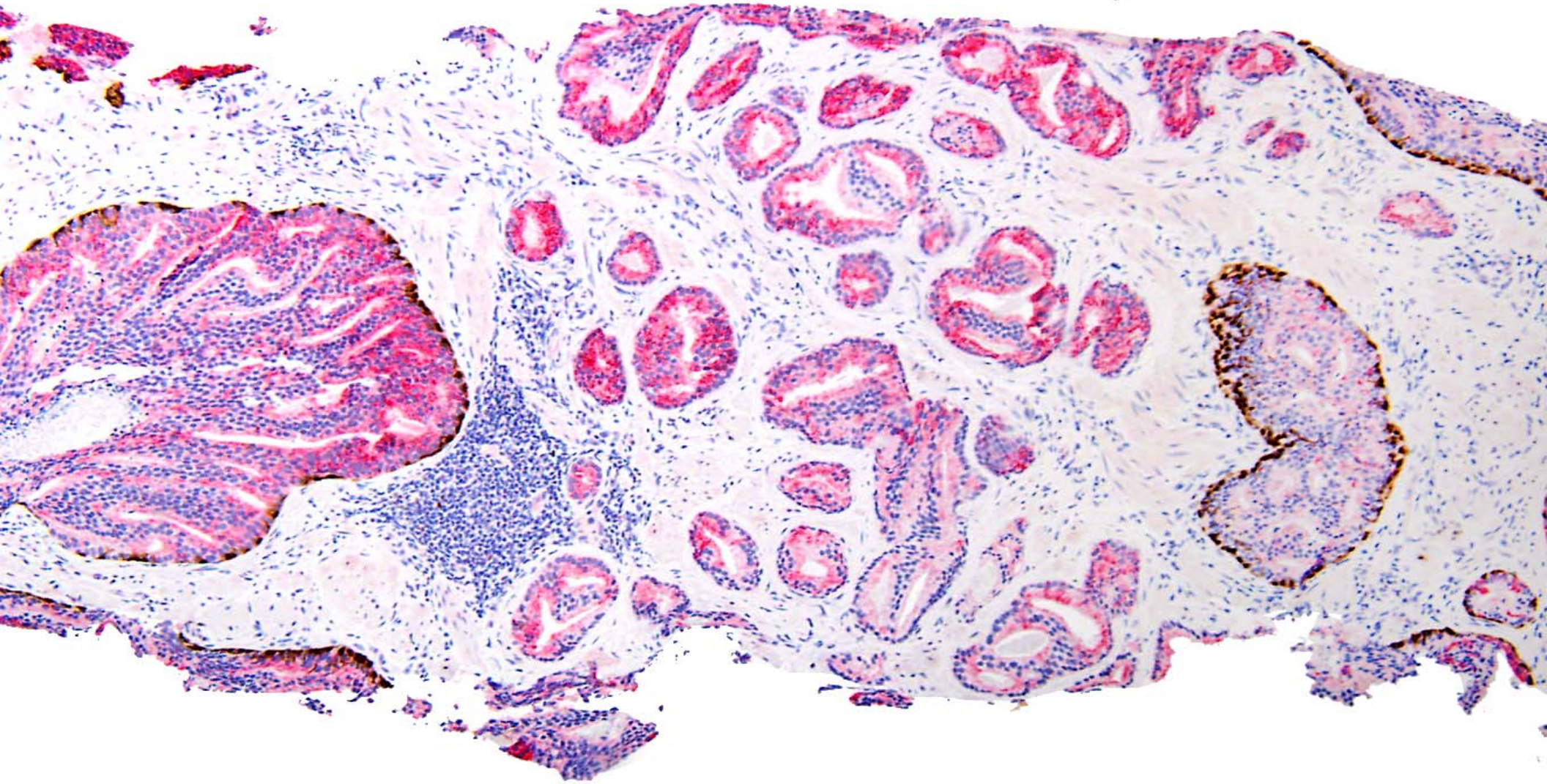
- **In the uncommon setting of IDC only on biopsy, 10% no invasive carcinoma at RP. If had called 4+4=8 on biopsy would have labeled the patient as having poor prognosis when in fact the patient is 100% cured with IDC only. Still justified to do the RP in these cases, as IDC may be precursor lesion with increased risk of more aggressive cancer.**

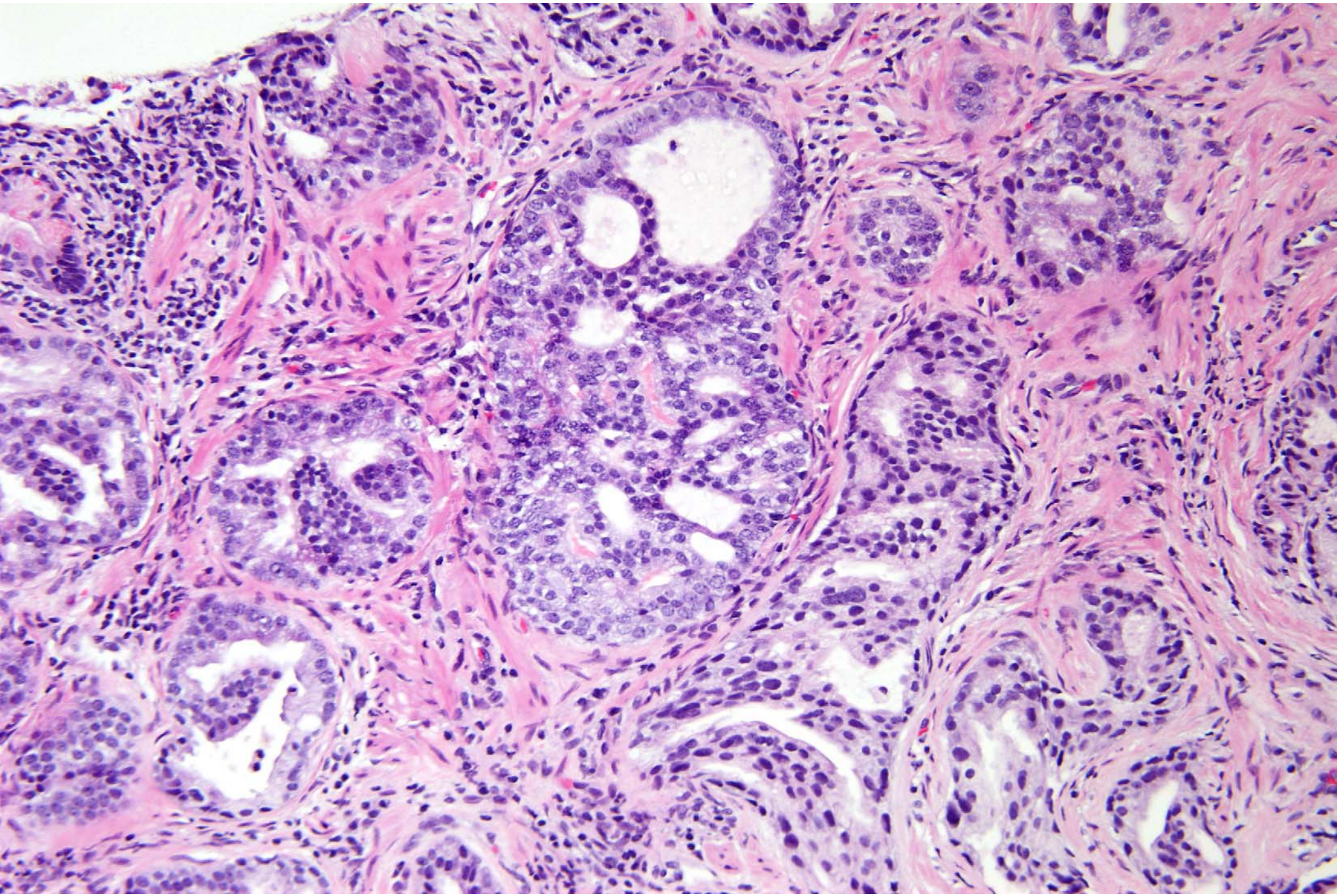
- **Uncommonly IDC and 3+3 on biopsy. 21% have Gleason 3+3=6 at RP along with IDC.**

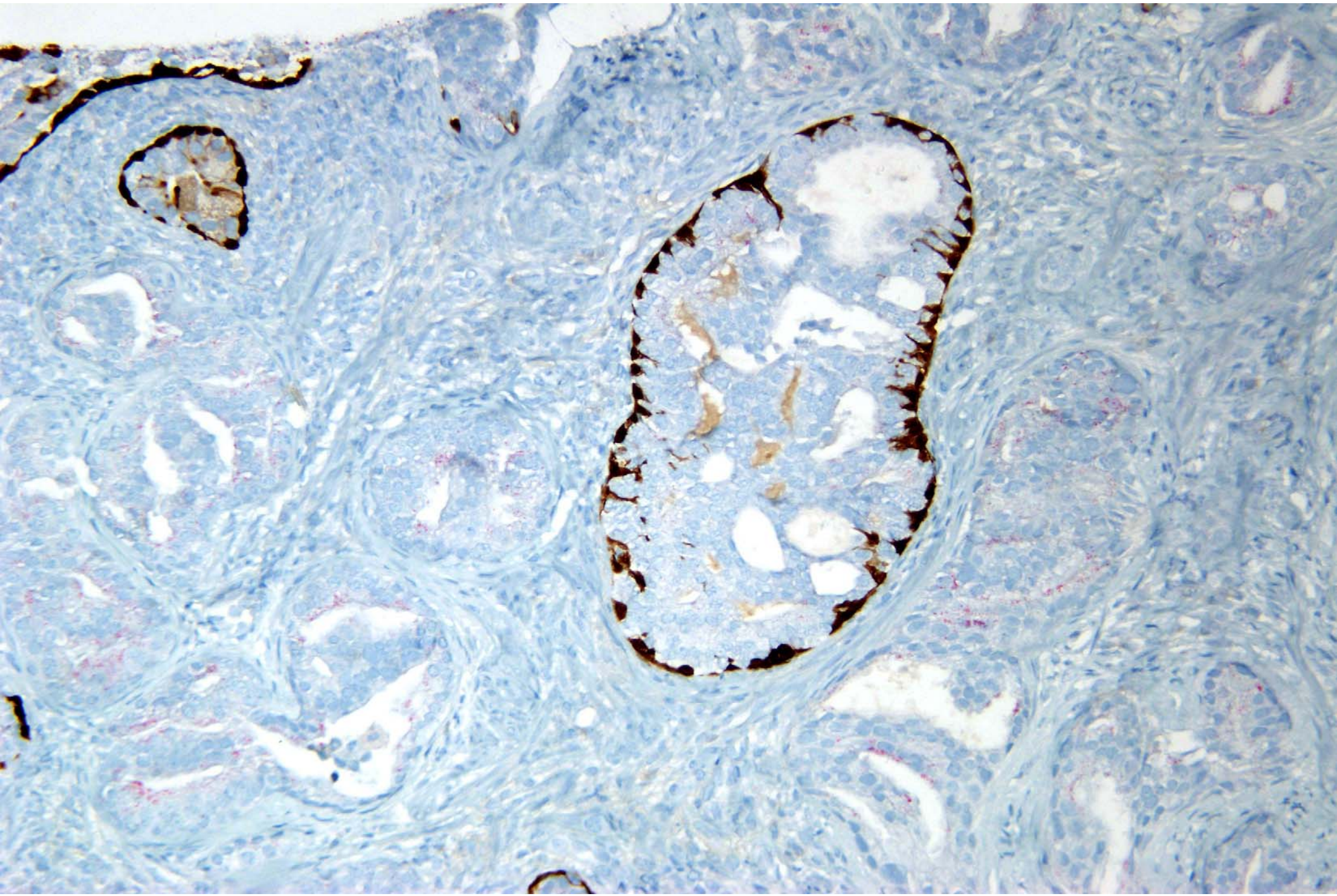
- **In other organ systems, we don't grade intraductal lesions using the same grading system as the invasive component.**

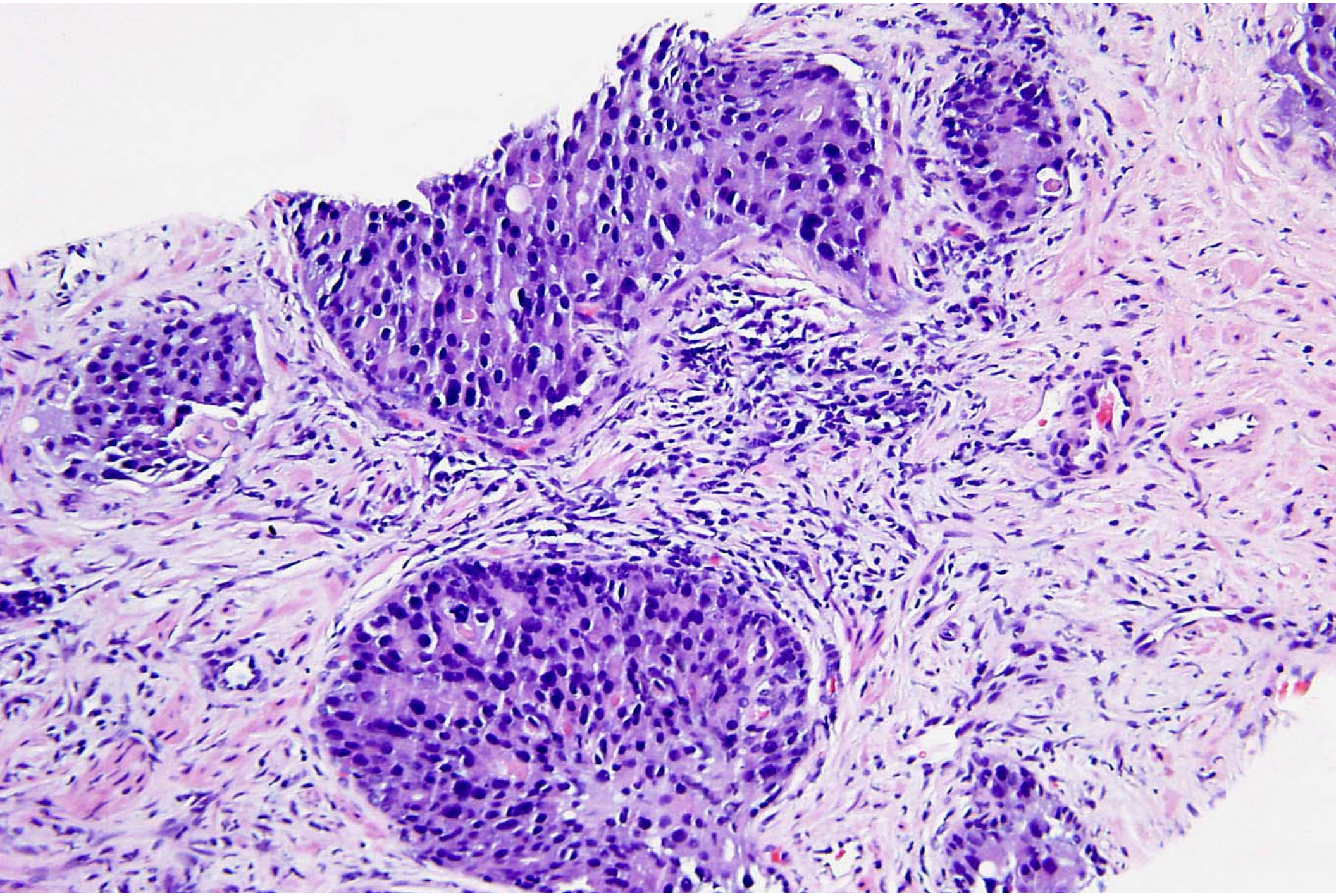


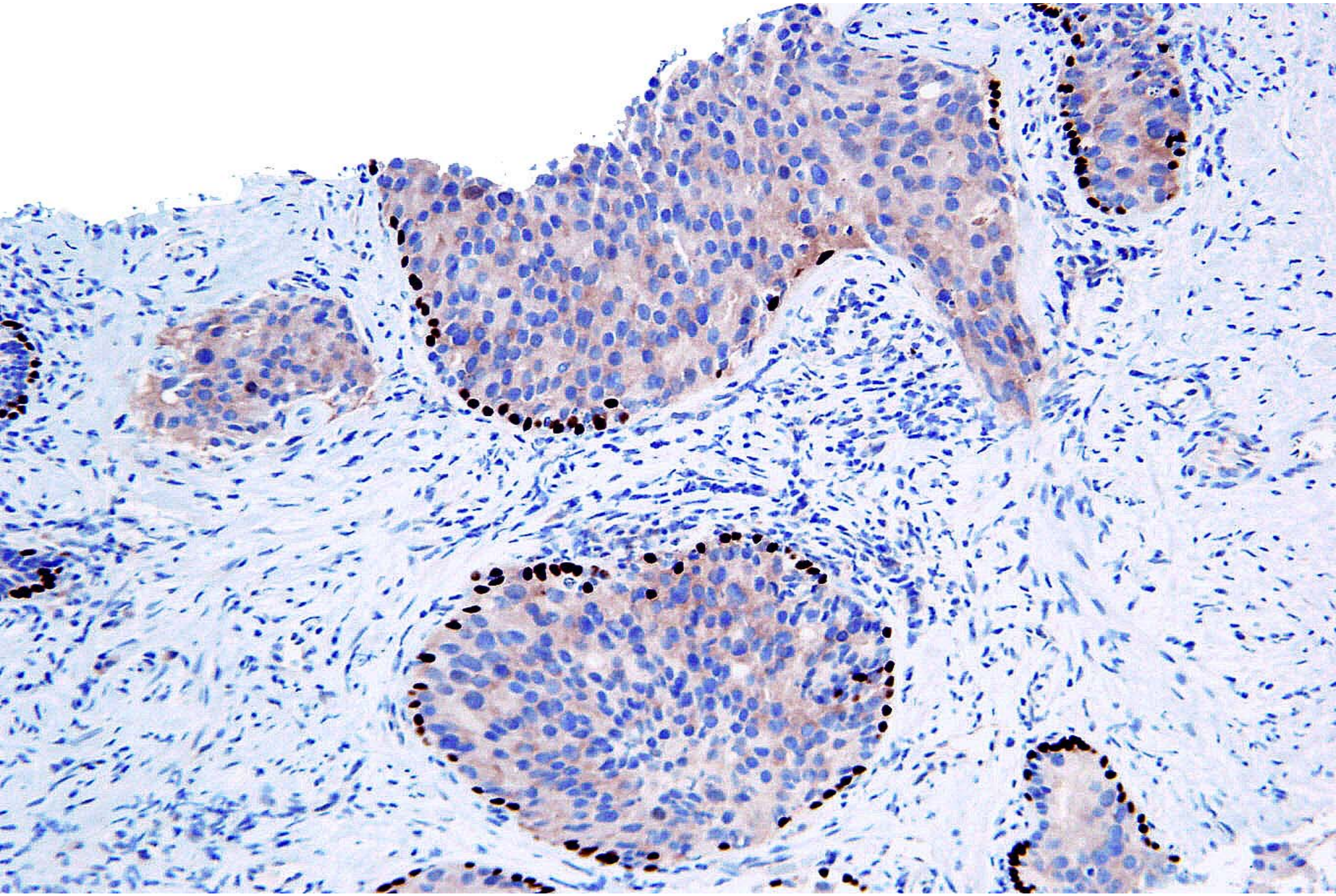


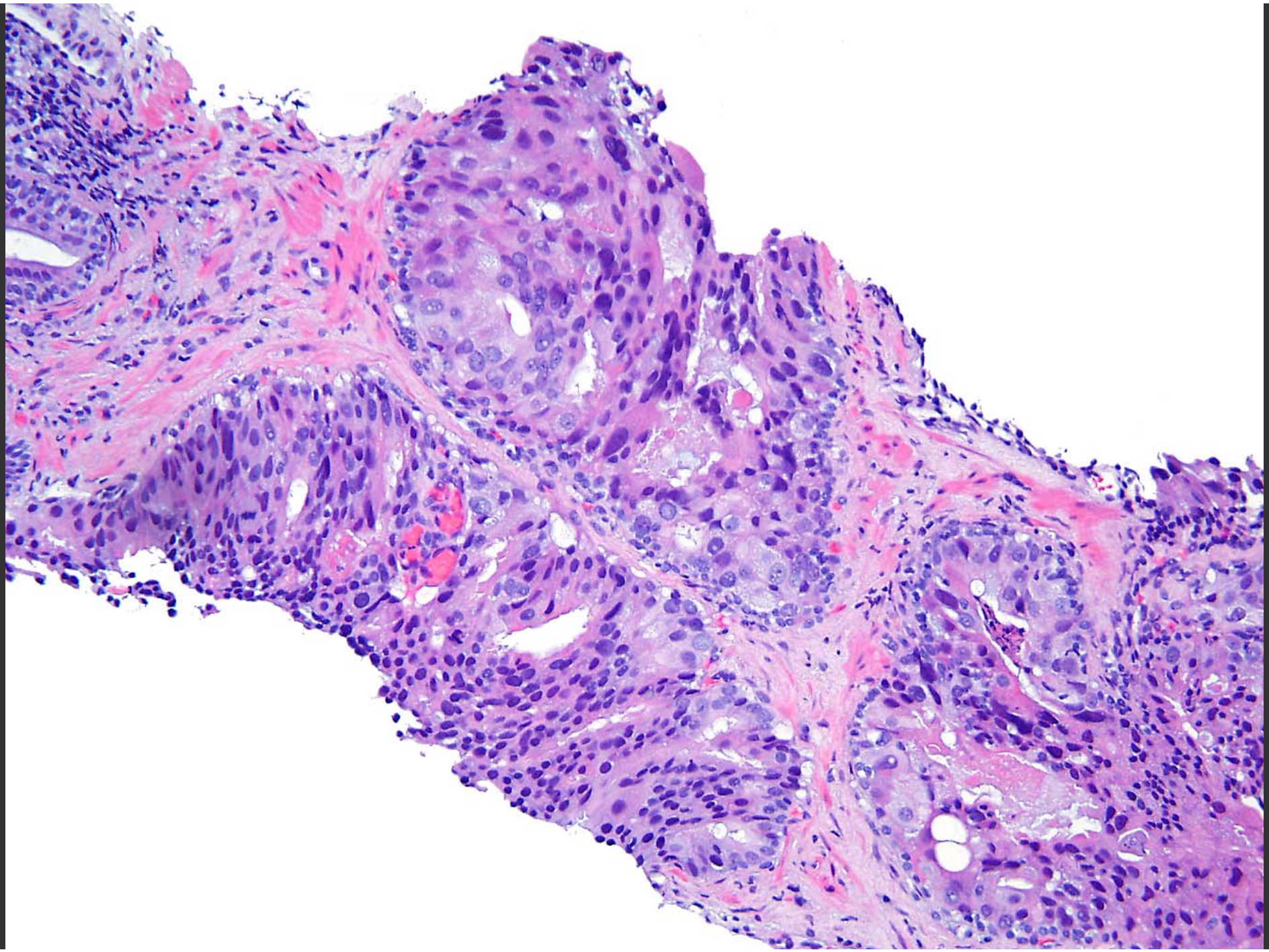


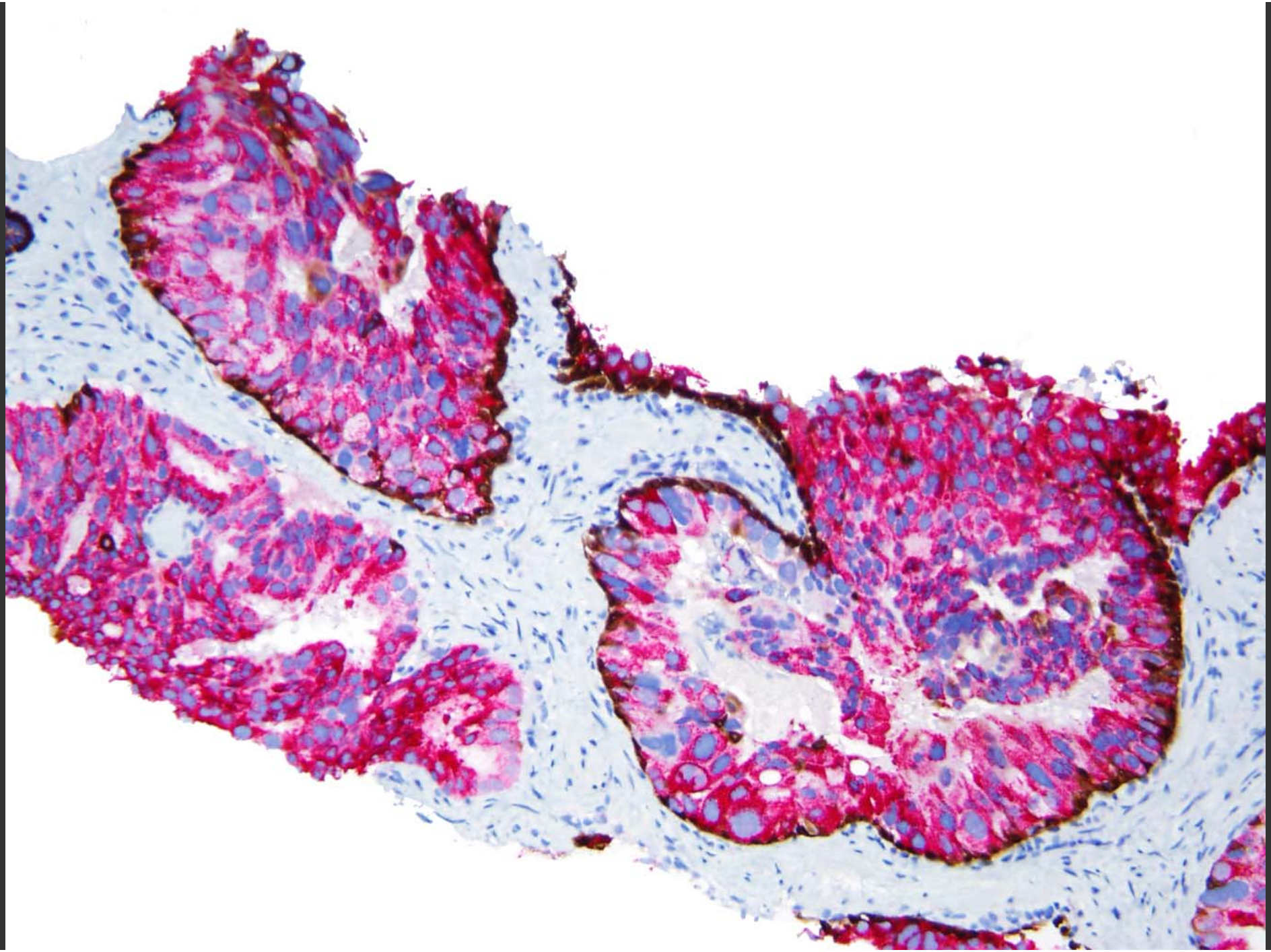








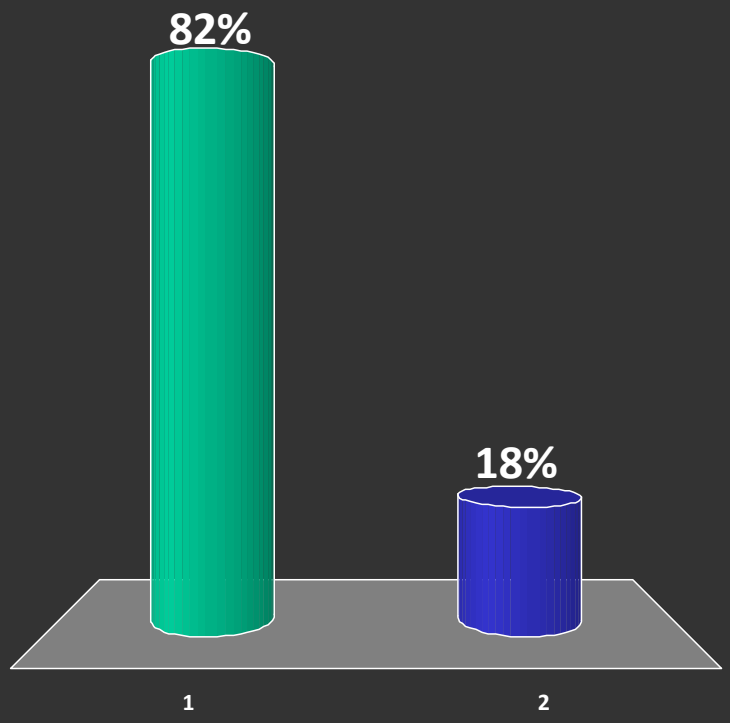




VOTE

IDC should not be graded as Gleason pattern 4 but should be noted typically correlated with aggressive behavior.

1. Yes
2. No



When to do IHC for Basal Cells on ?IDC-P

- **Do basal cell stains when it could make a difference if infiltrating cancer vs. IDC-P only**
- **Do basal cell stains if it could possibly make a difference in the grade**

Pros of Including %Pattern 4 on Needles & Radical Prostatectomy Specimens

BORDERLINE CASES

Borderline cases between 3+4 and 4+3 which currently we have to flip a coin to decide. If we record percent pattern 4, these ambiguous cases will be evident regardless if we call 3+4=7 with 40% pattern 4 or 4+3=7 with 60% pattern 4. There is greater transparency for the clinicians to decide therapy in ambiguous cases.

Having to record the percent poorly-formed/fused/cribriform glands in a borderline case between 3+3 and 3+4 is another way of having pathologists check again to specifically identify the foci which lack well-formed glands before verifying that there is pattern 4.

IMPROVED PATIENT CARE

The major advantage for patient care to record the percent pattern 4 on needle for Gleason 3+4=7 would be for active surveillance (AS). For the appropriate patient, Gleason 3+3=6 is accepted for men to undergo AS. However, there may be some men, depending on age, co-morbidity, extent of cancer, MRI findings, patient desire, etc, that could be a candidate for AS with 3+4=7 if the pattern 4 is limited. Currently, this information is not routinely available in pathology reports.

3. **The amount of pattern 4 is not only used for active surveillance but could be used for radiation therapy as well. Currently, there is different radiation therapy for 3+4 vs 4+3. In a case with borderline 3+4 vs 4+3 which would be apparent with recording the percent pattern 4 other factors (PSA, number of cores positive, etc.) could be used to make the call whereas now they would not know if it is 10% pattern 4 vs 90% pattern 4.**

PRACTICALITY

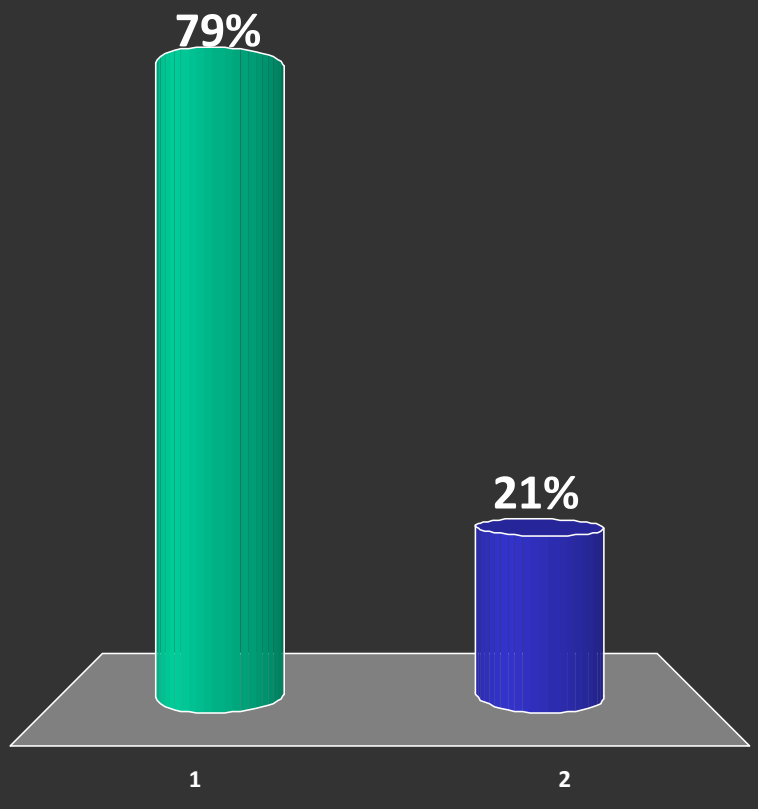
When a pathologist grades a specimen as 3+4 or 4+3, they already have to be deciding what tumor is pattern 4 or 3 such that to give a percent should not be that much extra effort.

Interobserver reproducibility of reporting percent GG4/5 on prostate biopsies is at least as good as that of reporting Gleason score.” (J Urol 2004; 171:664-7)

VOTE

Do you recommend reporting percent pattern 4 in Gleason score 7 biopsy and radical prostatectomy specimens?

1. Yes
2. No



Reporting Rules for Gleason Grading

Problems with “Tertiary” Patterns

- 3+3=6 with tertiary pattern 4; 4+4=8 with tertiary pattern 5
- Only used for RP and not for needles
- Confusing terminology as only 2 patterns
- Variability as to how pathologists report
  - Some report as 3+4=7 and some 3+3=6 with tertiary 4
  - Some require <5% pattern 4 and others allow greater percent as long as the 3rd most common pattern

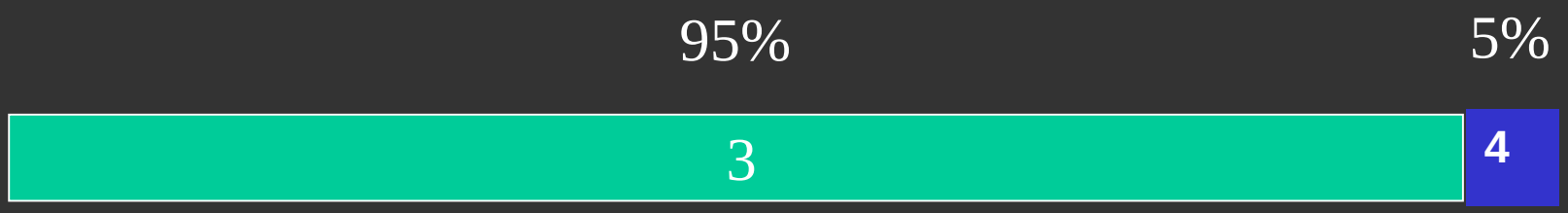
Tertiary Patterns

- **4+4=8 with tertiary pattern 5 behaves like 4+5=9 so now just called 4+5=9.**

- **3+3=6 with lesser amounts of pattern 4 will now be called 3+4=7 with recording the percent pattern ranging from 1%-50%.**

Reporting Minor High Grade Patterns Same Rules Needle & RP

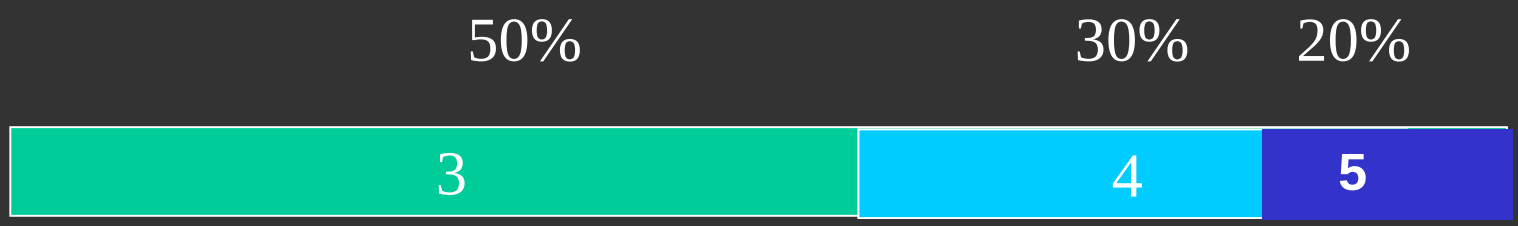
If only 2 patterns, record the HP even if very focal.



3 + 4 = 7

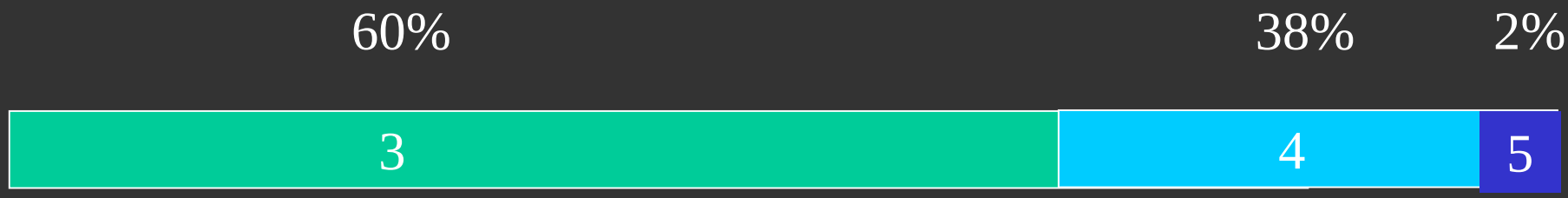
Reporting Minor High Grade Patterns Same Rules Needle & RP

If 3 patterns and the HP is the least common pattern yet still >5% then report the HP as the secondary grade.



3+5=8

Reporting Minor High Grade Patterns When 3 Patterns Different Rules Needle & RP



Needle - 3+5=8

RP - 3+4 with tertiary pattern 5

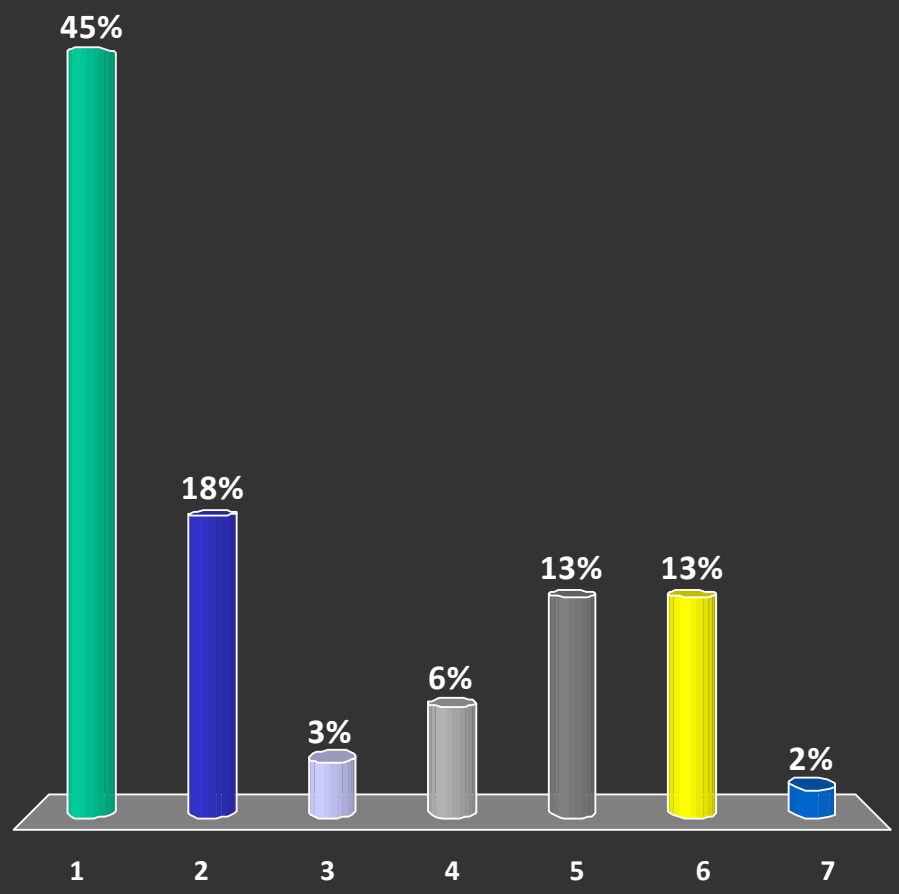
NEEDLE BIOPSY WITH DIFFERENT CORES SHOWING DIFFERENT GRADES

One should assign individual Gleason scores to separate cores as long as the cores were submitted in separate containers or the cores were in the same container yet specified by the urologist as to their location (ie. by different color inks).

Assigning a global (composite) score is optional.

Should we provide a grade for:

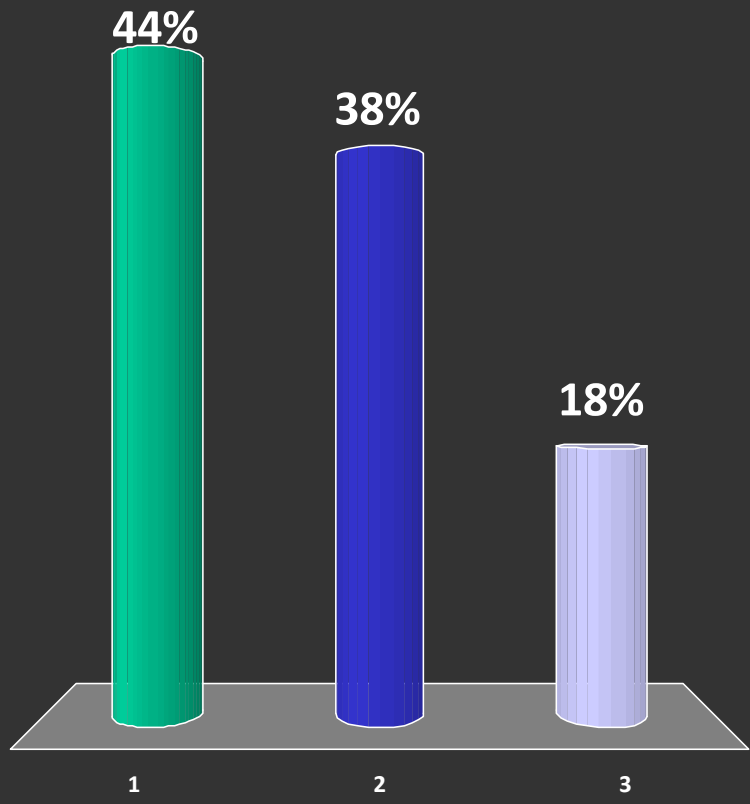
1. Each positive core
2. Each positive jar
3. Whole case
4. 1+2
5. 1+3
6. 2+3
7. 1+2+3



VOTE

How do we grade cases when multiple cores having different grades are present in the same specimen container:

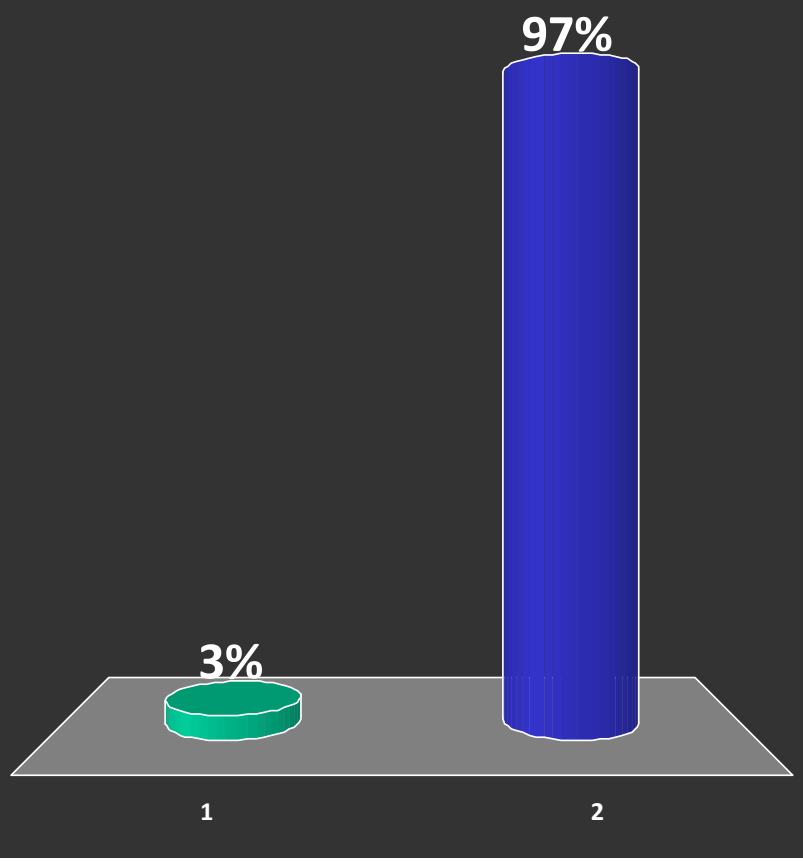
1. Assign grade to each +ve core
2. Give global grade for each specimen
3. Optional (1 and / or 2)



VOTE

How do we score fragmented cores received in a specimen container:

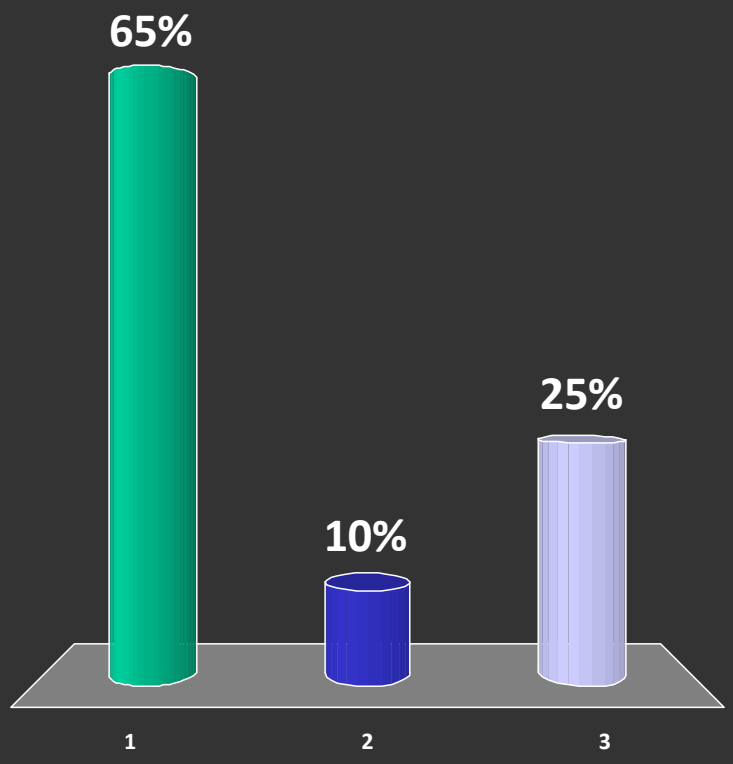
1. Assign grade to each core/fragment
2. Give global grade for whole specimen



VOTE

For purposes of clinical decision making which of the following grade(s) should be recorded in the pathology report:

1. Highest grade (any core)
2. Global grade for whole case
3. Optional (1 and / or 2)



Reporting of Gleason Grade in RPs

- **Each major tumor focus should be graded separately. For example: 2 tumor nodules – One left PZ 4+4=8 with larger right PZ 3+3=6. Give two scores and not call 3+4=7.**

- **Typically only the largest tumor foci are graded. Not necessary to report small multifocal lower grade cancer.**

- **Exception when there is a smaller tumor focus of higher grade, report this Gleason score.**

New Prostate Cancer Grade System

Impetus for a New Prostate Cancer Grading System

Movement to Rename Gleason Score 6 as not Cancer

The Word “Cancer” Drives Overtreatment

- **Fear of death from cancer likely plays some role, and removing the label “cancer” could reduce unnecessary treatment of low grade disease.**

- **Proposed name: IDLE (indolent lesion of epithelial origin) (Esserman, Lancet Oncol et al., 2013)**

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JOURNAL OF CLINICAL ONCOLOGY

COMMENTS AND CONTROVERSIES

Gleason Score 6 Adenocarcinoma: Should It Be Labeled As Cancer?

H. Ballentine Carter, Alan W. Partin, Patrick C. Walsh, Bruce J. Trock, Robert W. Veltri, William G. Nelson, and Donald S. Coffey, *The Johns Hopkins University and Johns Hopkins Hospital, Baltimore, MD*
Eric A. Singer, *National Cancer Institute, National Institutes of Health, Bethesda, MD*
Jonathan I. Epstein, *The Johns Hopkins University and Johns Hopkins Hospital, Baltimore, MD*

When is Prostate Cancer Really Cancer?

David M. Berman, MD, PhD[a], Jonathan I. Epstein, MD[b,*]

Urol Clinics of N Am 2014; 41:339-46

Arguments in Favor of Retention of Gleason Score 6 Cancer

- Morphological
- Molecular
- 20% undersampling of higher grade cancer with Gleason 6 on biopsy
- Patients will be lost to follow-up if called IDLE tumor

Gleason Score 6 Prostatic Adenocarcinoma Should Still be Called "Cancer"

- **Rather there is a need to change what patients think when they hear they have Gleason score 6 cancer.**
- **Urologists need to reassure and educate patients.**
- **Modify how we report prostate cancer grade to more accurately reflect their behavior.**

Problems with Gleason System: Scale

- **6 is the lowest grade reported although the scale goes from 2-10**
- **Patients are told they have a Gleason score of 6 out of 10 and logically but incorrectly think that they have a tumor in the middle of the grade spectrum, contributing to the fear of cancer**

Problems with Gleason System Grouping

- **Gleason 7 is not homogeneous: 4+3=7 has a much worse prognosis than 3+4=7**
- **Gleason 8-10 is often considered as one group - high grade disease**

Problems with Gleason System: Inconsistent & Inaccurate Grouping

Various combinations have been used in the literature including some of the highest impact clinical trials:

Prostate Cancer Outcomes Study (NEJM): 2-4; 5-7; 8-10

Scandinavian Prostate Cancer Group Study (NEJM): 2-6, 7; 8-10

Prostate Cancer Intervention vs. Observation (NEJM): 2-6; 7-10

Prostate Cancer Prevention Trial (NEJM): 2-6; 7-10

D’Amico Risk Classification Stratification

- **Low Risk: T1C/T2a & PSA≤10 & Gleason ≤6**
- **Intermed. Risk: T2b or PSA 10-20 or Gleason 7**
- **High Risk: T2c or PSA>20 or Gleason 8-10**

Problems with Gleason Grading
Too Many Grades with Similar Prognoses

- 1+1; 1+2; 1+3; 1+4; 1+5; 2+1; 2+2; 2+3; 2+4; 2+5; 3+1; 3+2; 3+3; 3+4; 3+5; 4+1; 4+2; 4+3; 4+4; 4+5; 5+1; 5+2; 5+3; 5+4; 5+5

- 25 potential grades!

- What are the least number of grades with a similar prognosis?

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*†‡

BJU International 2013; 111:753-60

New 5 Grade System

- **Grade Group 1 (3+3)**

  Only individual discrete well-formed glands

- **Grade Group 2 (3+4)**

  Predominantly well-formed glands with lesser component of poorly- formed/fused/cribriform glands

- **Grade Group 3 (4+3)**

  Predominantly poorly formed/fused/cribriform glands with lesser component of well-formed glands

- **Grade Group 4 (4+4/3+5/5+3)**

  Only poorly-formed/fused/cribriform glands or

  Predominantly mix of well-formed and lack of glands

- **Grade Group 5 (4+5/5+4/5+5)**

  Lack gland formation (or with necrosis) with or w/o poorly formed/fused/cribriform glands

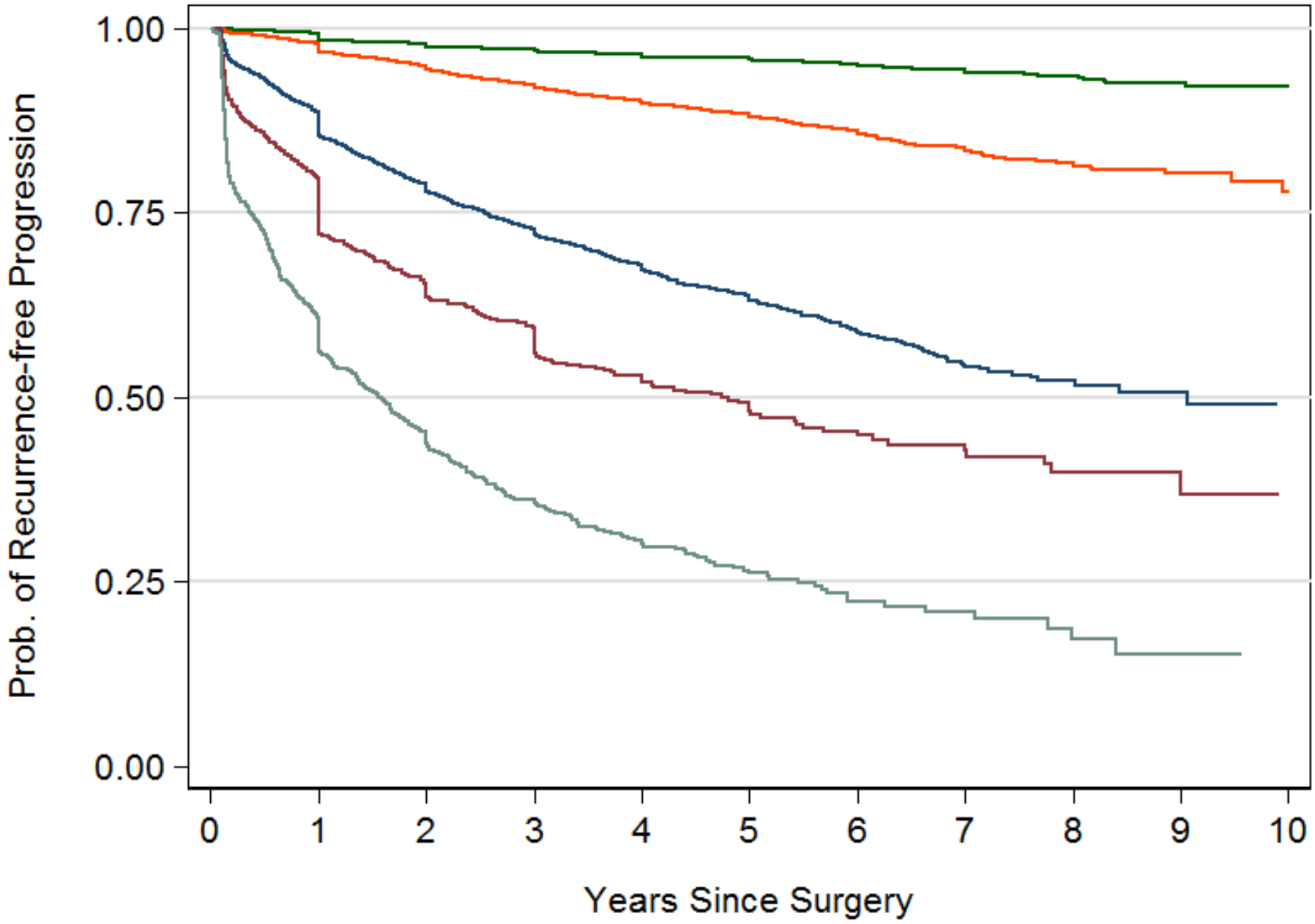
2014 - RP Data From 5 Institutions

- **Since 2005 – Modified Gleason grades**

- **University of Pittsburgh – J. Nelson, A. Parwani**
- **MSKCC – V. Reuter, S. Fine, A. Vickers, J. Eastham, D. Sjoberg**
- **CCF – C. Magi-Galluzzi, E. Klein, J. Ciezki, C. Reddy**
- **Karolinska – L. Egevad, P. Wiklund, T. Nyberg**
- **Johns Hopkins – J. Epstein, M. Han**

RP Grade Meta-Analysis

Hosp	Freq.
Pittsburgh	2,102
Karolinska	3,763
Hopkins	6,137
Memorial	6,673
CCF	2,170
Total	20,845


Prob. of Recurrence-free Progression
1.00
0.75
0.50
0.25
0.00
0
1
2
3
4
5
6
7
8
9
10
Years Since Surgery

RP Grade
Hazard Ratios Relative to Grade Group 1

Grade Group 1	**1.0**
Grade Group 2	**2.7**
Grade Group 3	**9.9**
Grade Group 4	**16.8**
Grade Group 5	**33.2**

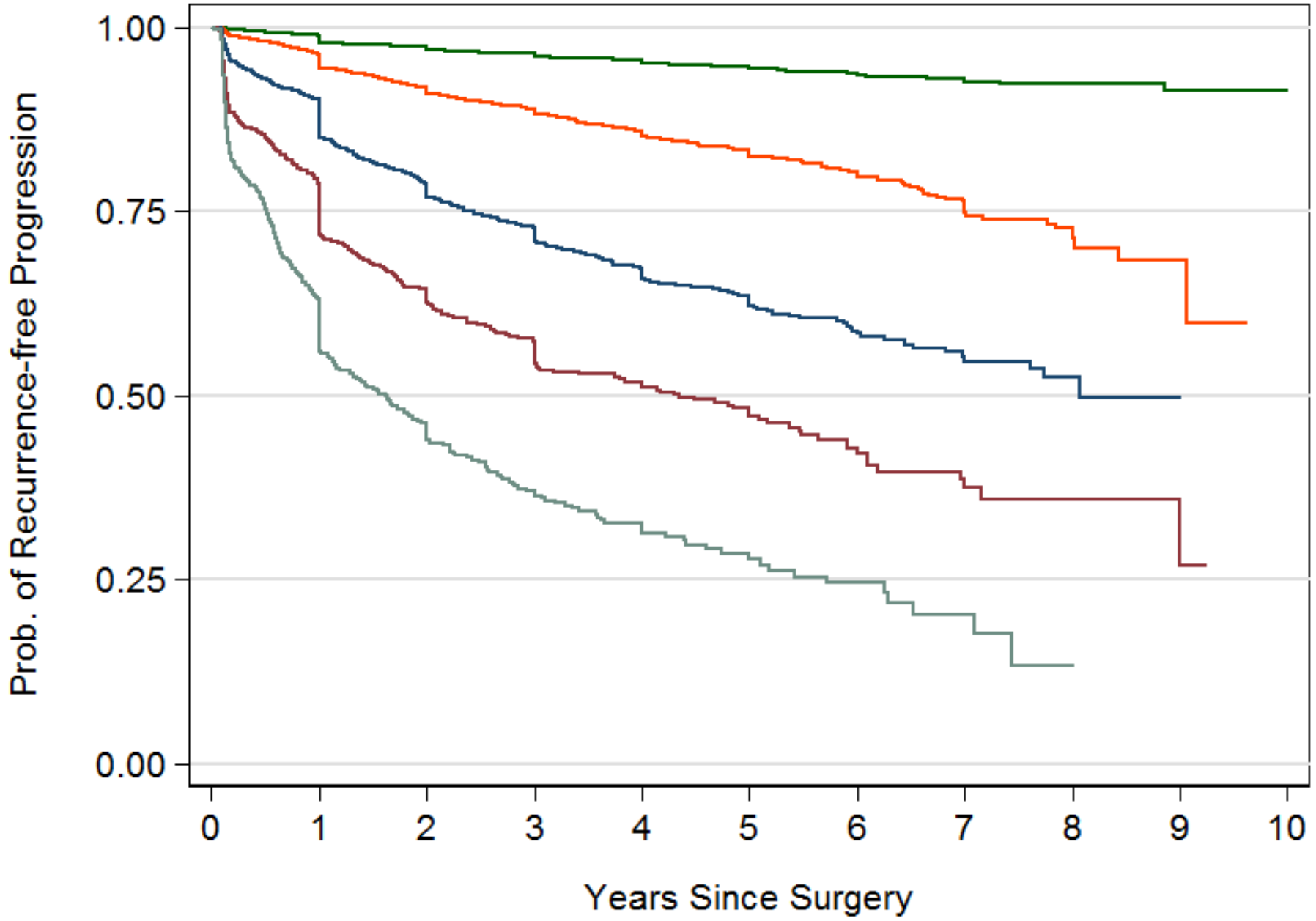
All curves significantly different by $p<0.00001$

RP Grade
5 Year Biochemical Risk Free Survival

Grade Group	Gleason	BRFS	95% Confidence Intervals
1	3+3=6	96%	94%-95%
2	3+4=7	88%	87%-89%
3	4+3=7	63%	61%-65%
4	4+4=8	48%	44%-52%
5	9-10	26%	23%-30%

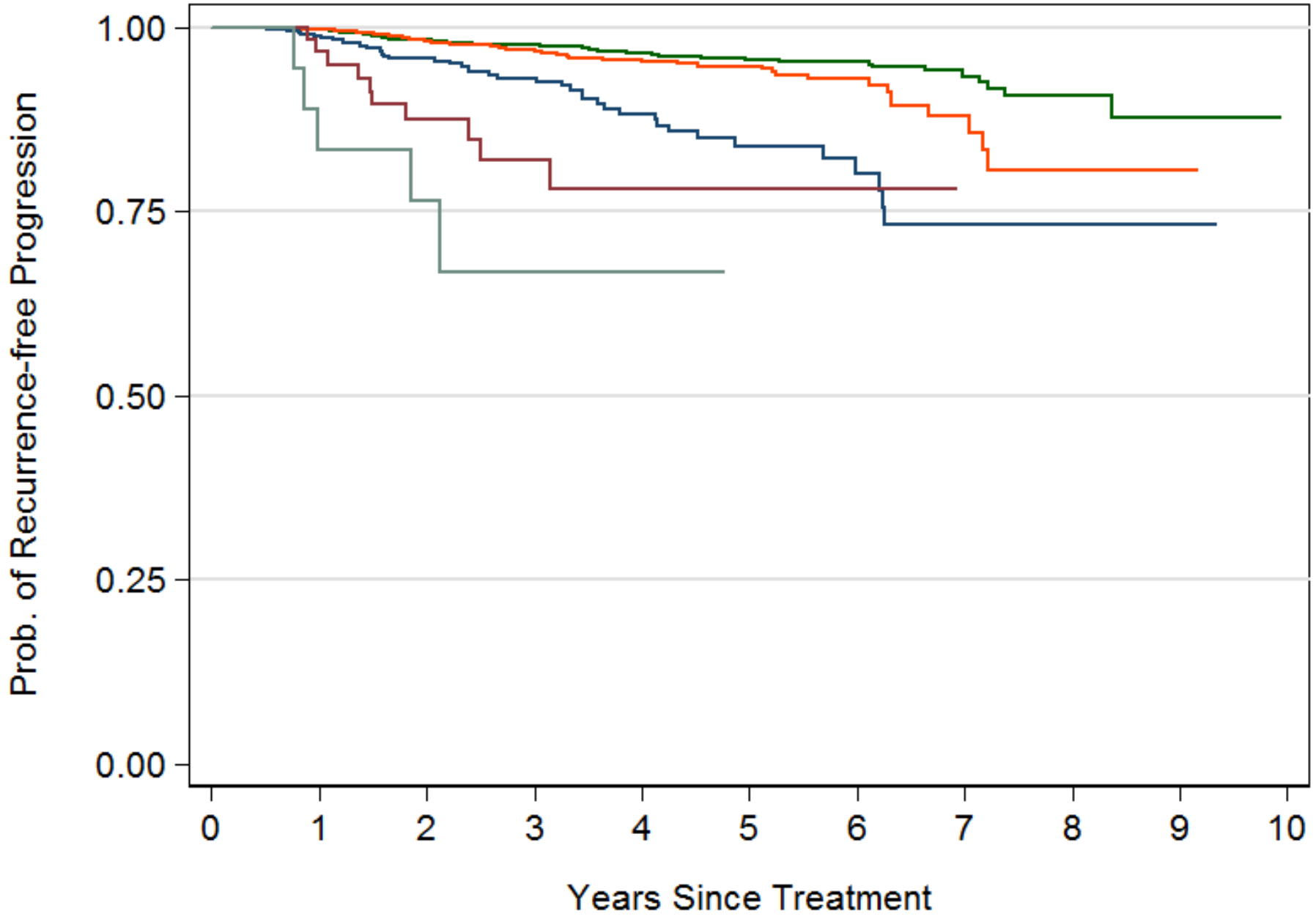
Biopsy Grade Meta-Analysis

Hosp	Freq.
Pittsburgh	2,102
Hopkins	6,137
Memorial	5,791
CCF	2,146
Total	16,176


Prob. of Recurrence-free Progression
1.00
0.75
0.50
0.25
0.00
0
1
2
3
4
5
6
7
8
9
10
Years Since Surgery

Radiation Therapy

CCF	**2495 (45%)**
MSKCC	**3006 (55%)**
Brachy	**3361 (61%)**
EBRT	**2140 (39%)**
Peri-RT	**1845 (34%)**
HT	


1.00
0.75
0.50
0.25
0.00
Prob. of Recurrence-free Progression
0
1
2
3
4
5
6
7
8
9
10
Years Since Treatment

More Accurately Reflects Biology of Disease than Current System

Grade Group 1 (as opposed to 6/10): Excellent prognosis – no metastases. Avoids issues of GS<6

Grade Group 2 (as opposed to 7/10): Very good prognosis – rare metastases

Grade Group 3 (4+3 and 3+4 both = GS7 – D'Amico): Greater distinction from grade 2

More Accurately Reflects Biology of Disease than Current System

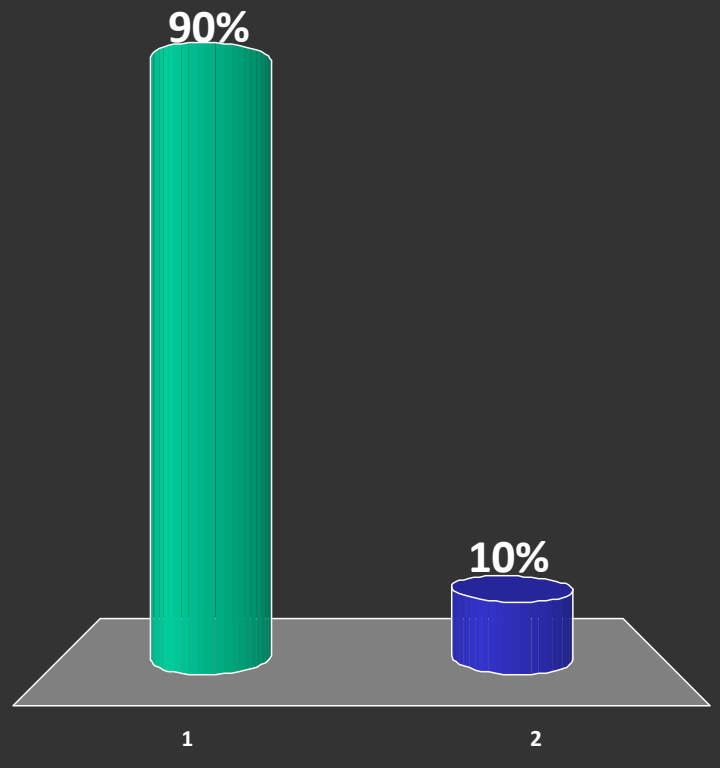
Grade Group 4 (as opposed to combined 8-10): Better prognosis than 9-10.

Grade Group 5: No need to distinguish 9 vs 10.

VOTE

A new grading system for prostate cancer should be adopted ranging from 1-5, initially used in conjunction with Gleason.

1. Yes
2. No



Following publication of the new grading system, will recommend its usage in parallel to the Gleason grading system

1. **Left Apex: Adenocarcinoma of the prostate Gleason score 3+3=6 (Grade Group 1) involving 20% of 1 core.**

2. **Left Mid: Adenocarcinoma of the prostate Gleason score 4+3=7 (Grade Group 3) involving 60% of 1 core (70% pattern 4).**

The new grading system and other findings presented in today's talk were recently accepted by the World Health Organization (WHO) and will be included in the 2016 edition of:

Pathology & Genetics:

Tumours of the Urinary System and Male Genital System

Questions?

Details on the study forming part of the basis of the new grading system will be presented Monday at the Genitourinary Proffered Paper session at 9 am and specific questions relating to that study can be addressed at that time.

Important Information Regarding CME/SAMs

The Online CME/Evaluations/SAM claim process will only be available on the USCAP website until October 2, 2015.

No claims can be processed after that date!

After October 2, 2015 you will NOT be able to obtain any CME or SAMs credits for attending this meeting.

Thank you!

Please go to the USCAP website to complete your Evaluation of the course and claim CME and/or SAMs Credits.