

PROSTATE CANCER GRADING:

An Update from the 2014
ISUP Consensus
Conference

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Disclosures

- None

Prostate Cancer Grading

- Review of Evolution of Prostate Cancer Grading
 - ▣ 1966 Gleason Grading System for Prostate Cancer
 - ▣ 2005 ISUP Modified Gleason Grading
- Proposal for New Grade Grouping
 - ▣ ISUP Nov 2014: Prostate Cancer Grading Panel, Chicago
 - Clarification of Previous ambiguous grading issues
 - Intraductal carcinoma
 - New Grade Grouping

Gleason Grading System

- 1966 Donald F. Gleason
- Based solely on architectural pattern
- Overall grade (Gleason score) based on sum of 2 most common patterns
- 86% had advanced disease
- PNB Sampling limited to a couple of large core biopsies directed to palpable abnormalities
- Before immunohistochemical stains that would highlight basal cells

PROSTATIC ADENOCARCINOMA (Histological Patterns)

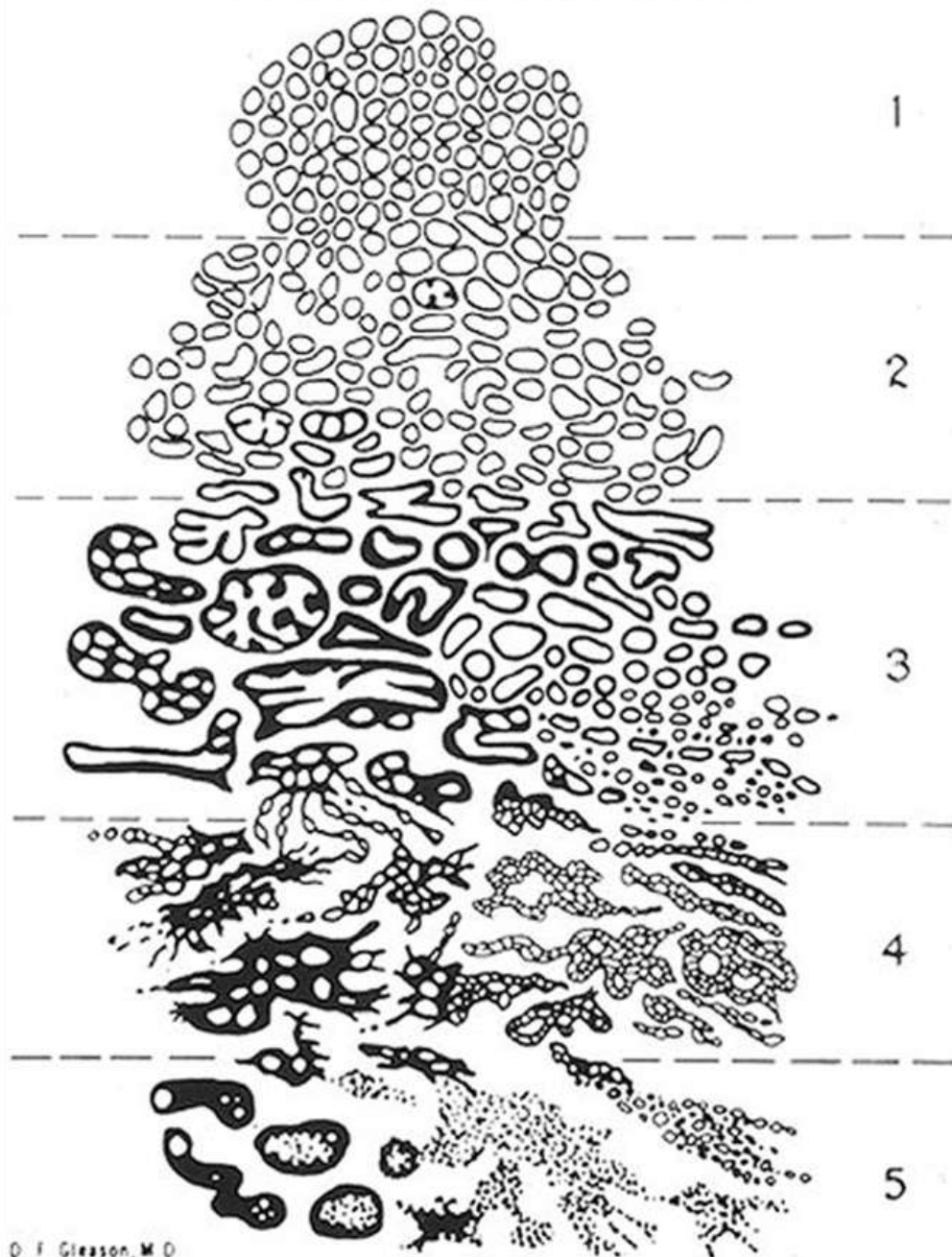


TABLE 1. Gleason System

Original Gleason System: 1966 & 1967

Pattern 1: Very well differentiated, small, closely packed, uniform, glands in essentially circumscribed masses

Pattern 2: Similar (to pattern 1) but with moderate variation in size and shape of glands and more atypia in the individual cells; cribriform pattern may be present, still essentially circumscribed, but more loosely arranged

Pattern 3: Similar to pattern 2 but marked irregularity in size and shape of glands, with tiny glands or individual cells invading stroma away from circumscribed masses, or solid cords and masses with easily identifiable glandular differentiation within most of them

Pattern 4: Large clear cells growing in a diffuse pattern resembling hypernephroma; may show gland formation

Pattern 5: Very poorly differentiated tumors; usually solid masses or diffuse growth with little or no differentiation into glands

Gleason's Modifications: 1974 & 1977

Patterns 1 & 2: Unchanged

Pattern 3: Adds to earlier description: may be papillary or cribriform (1974), which vary in size and may be quite large, but the essential feature is the smooth and usually rounded edge around all the circumscribed masses of tumor (1977)

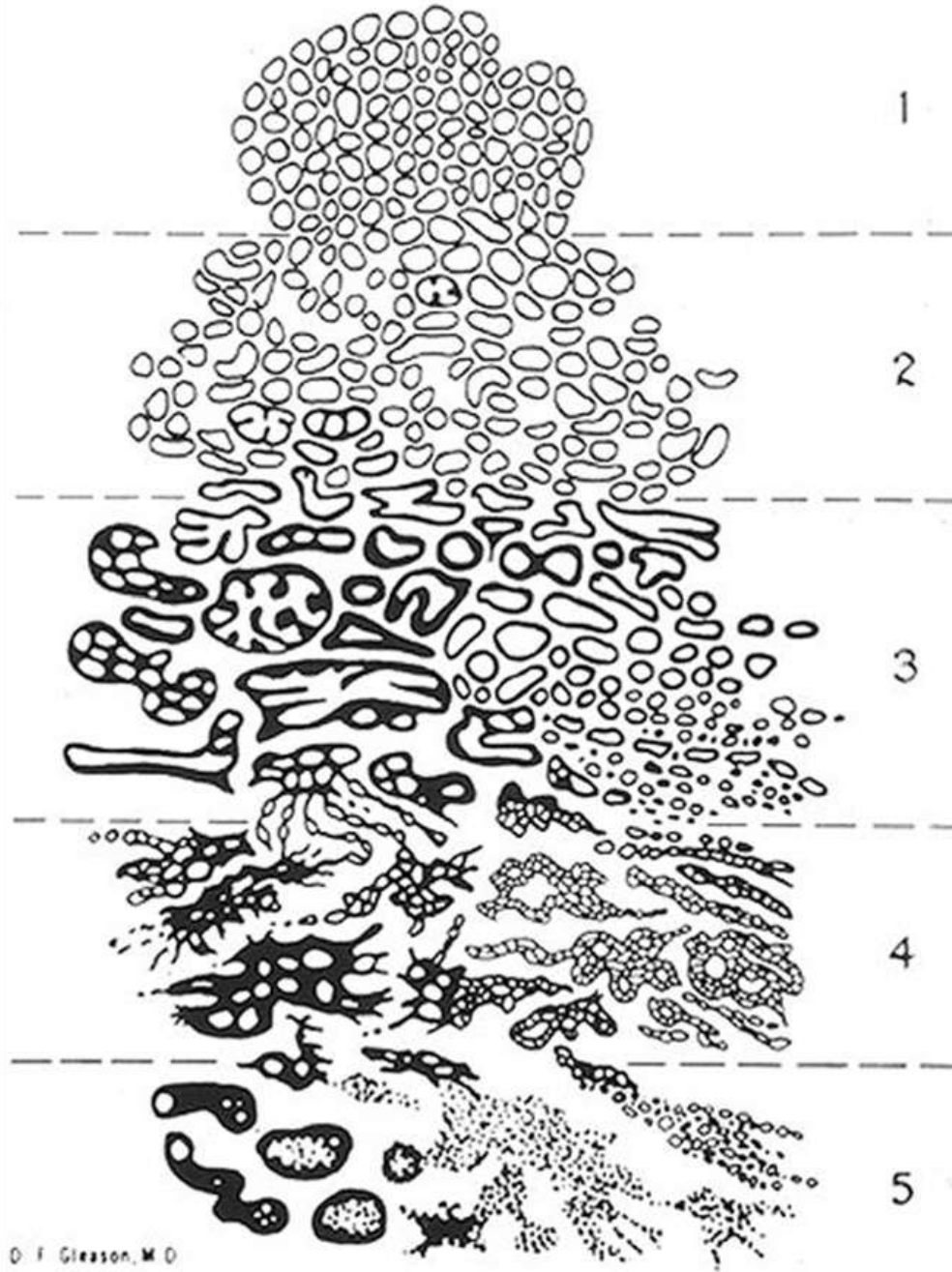
Pattern 4: Adds to earlier description: raggedly infiltrating, fused-glandular tumor (1974); glands are not single and separate, but coalesce and branch (1977)

Pattern 5: Adds to earlier description: can resemble comedocarcinoma of the breast (1977); almost absent gland pattern with few tiny glands or signet cells (1977)

PROSTATIC ADENOCARCINOMA (Histological Patterns)

Many cases
are adenosis
(mimic of PCa)

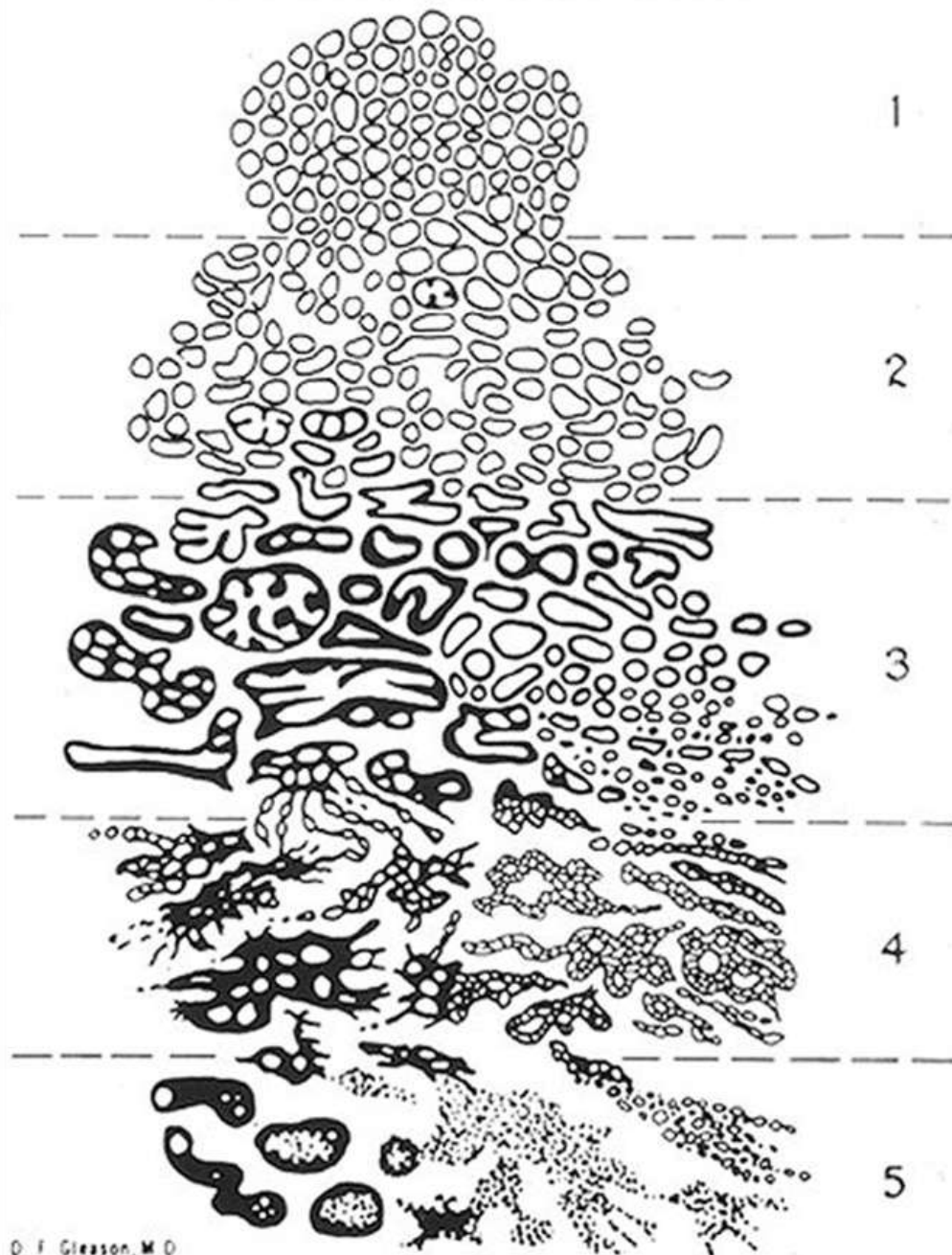
Some cases
HGPIN



ISUP 2005: Gleason Grading

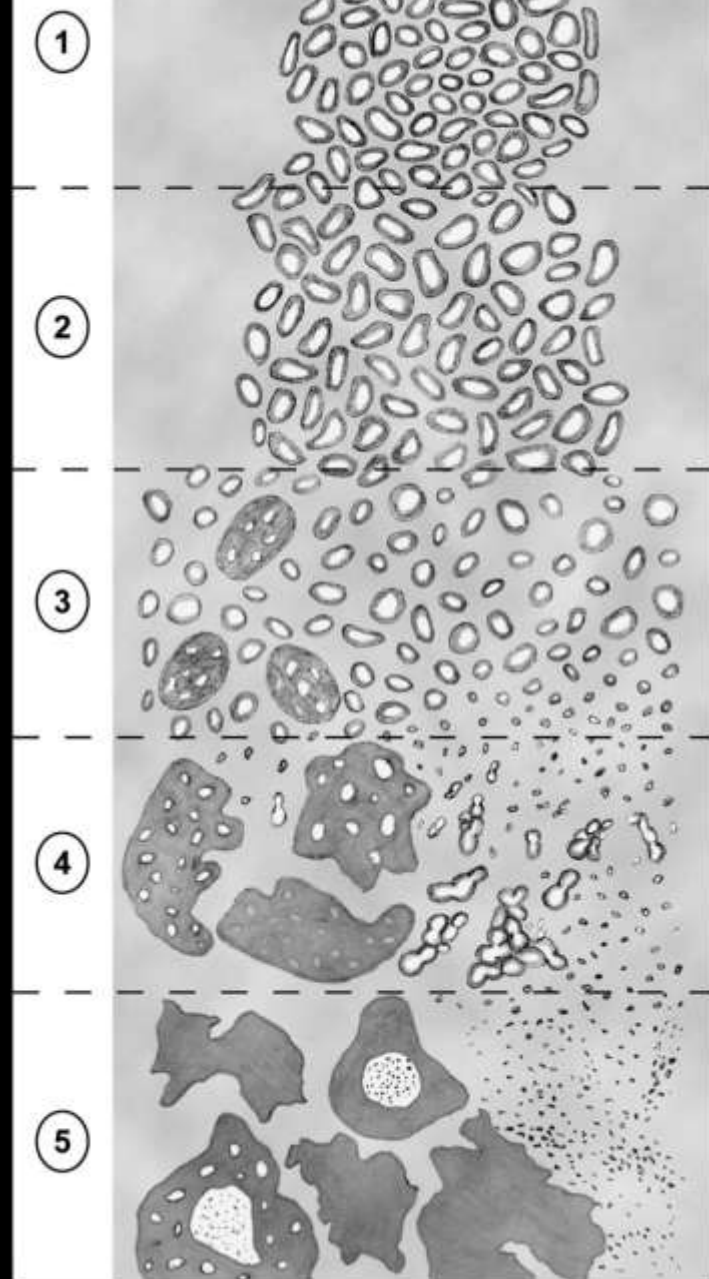
- International group of more than 70 leading urological pathologists
- Attempt to achieve consensus in controversial areas related to the Gleason grading system
- New tools for grading prostate cancer:
 - ▣ Diagram
 - ▣ Written descriptions
 - ▣ Reference images

PROSTATIC ADENOCARCINOMA (Histological Patterns)



D. F. Gleason, M.D.

2005



Brumbaugh

TABLE 3. 2005 ISUP Modified Gleason System

Pattern 1:

Circumscribed nodule of closely packed but separate, uniform, rounded to oval, medium-sized acini (larger glands than pattern 3)

Pattern 2:

Like pattern 1, fairly circumscribed, yet at the edge of the tumor nodule there may be minimal infiltration

Glands are more loosely arranged and not quite as uniform as Gleason pattern 1

Pattern 3:

Discrete glandular units

Typically smaller glands than seen in Gleason pattern 1 or 2

Infiltrates in and amongst nonneoplastic prostate acini

Marked variation in size and shape

Smoothly circumscribed small cribriform nodules of tumor

Pattern 4:

Fused microacinar glands

Ill-defined glands with poorly formed glandular lumina

Large cribriform glands

Cribriform glands with an irregular border

Hypernephromatoid

Pattern 5:

Essentially no glandular differentiation, composed of solid sheets, cords, or single cells

Comedocarcinoma with central necrosis surrounded by papillary, cribriform, or solid masses

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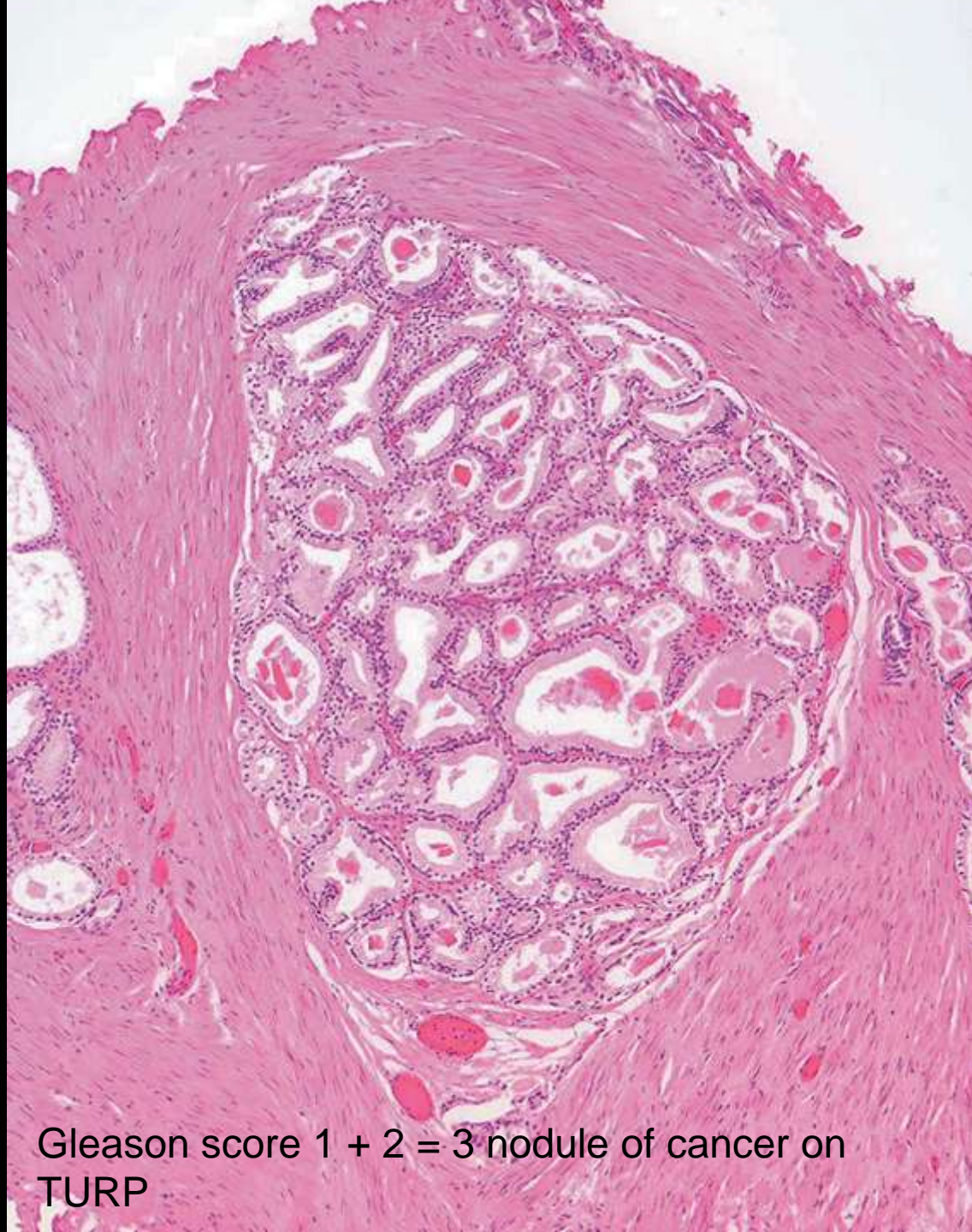
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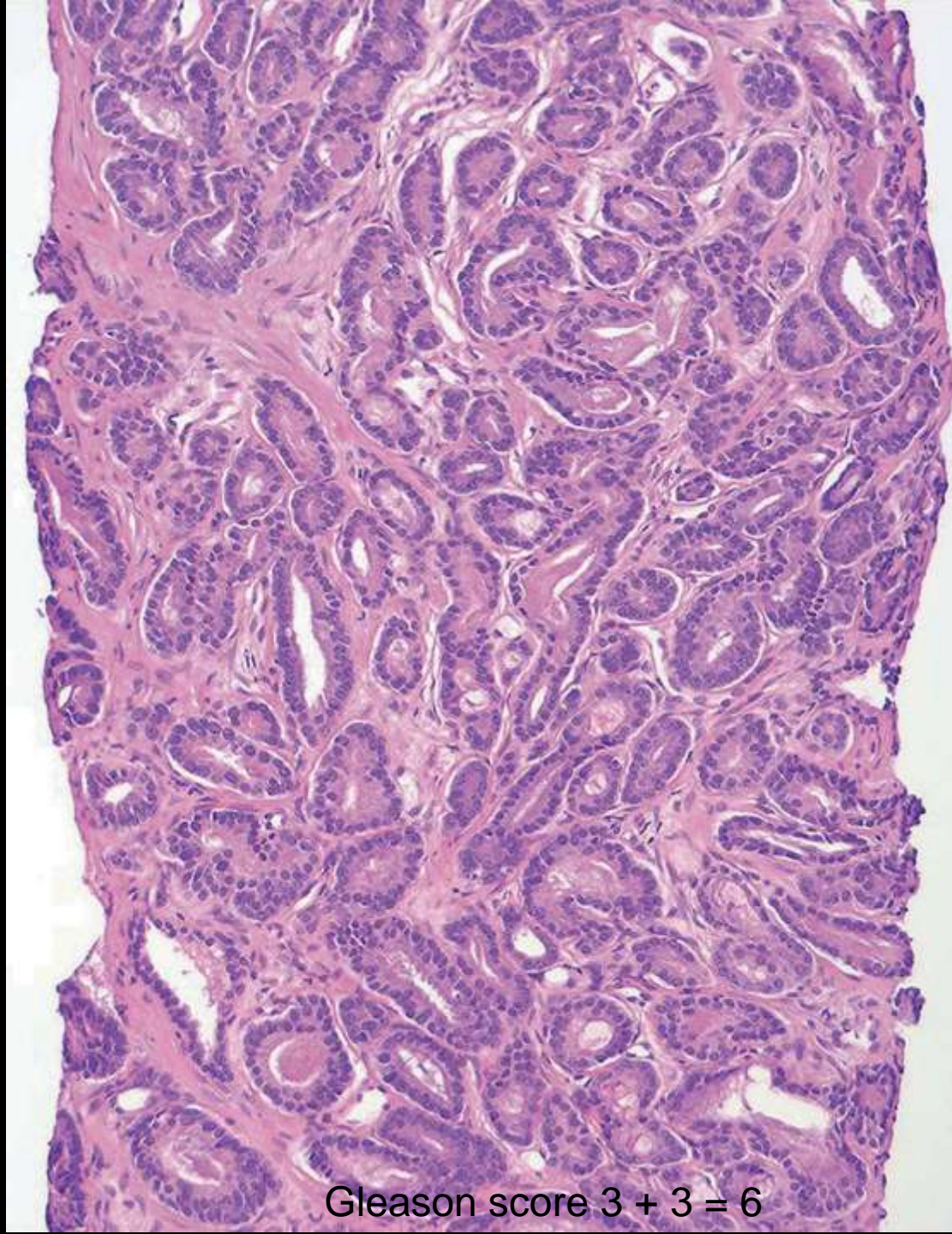
Comedocarcinoma with central necrosis surrounded by papillary, cribriform, or solid masses



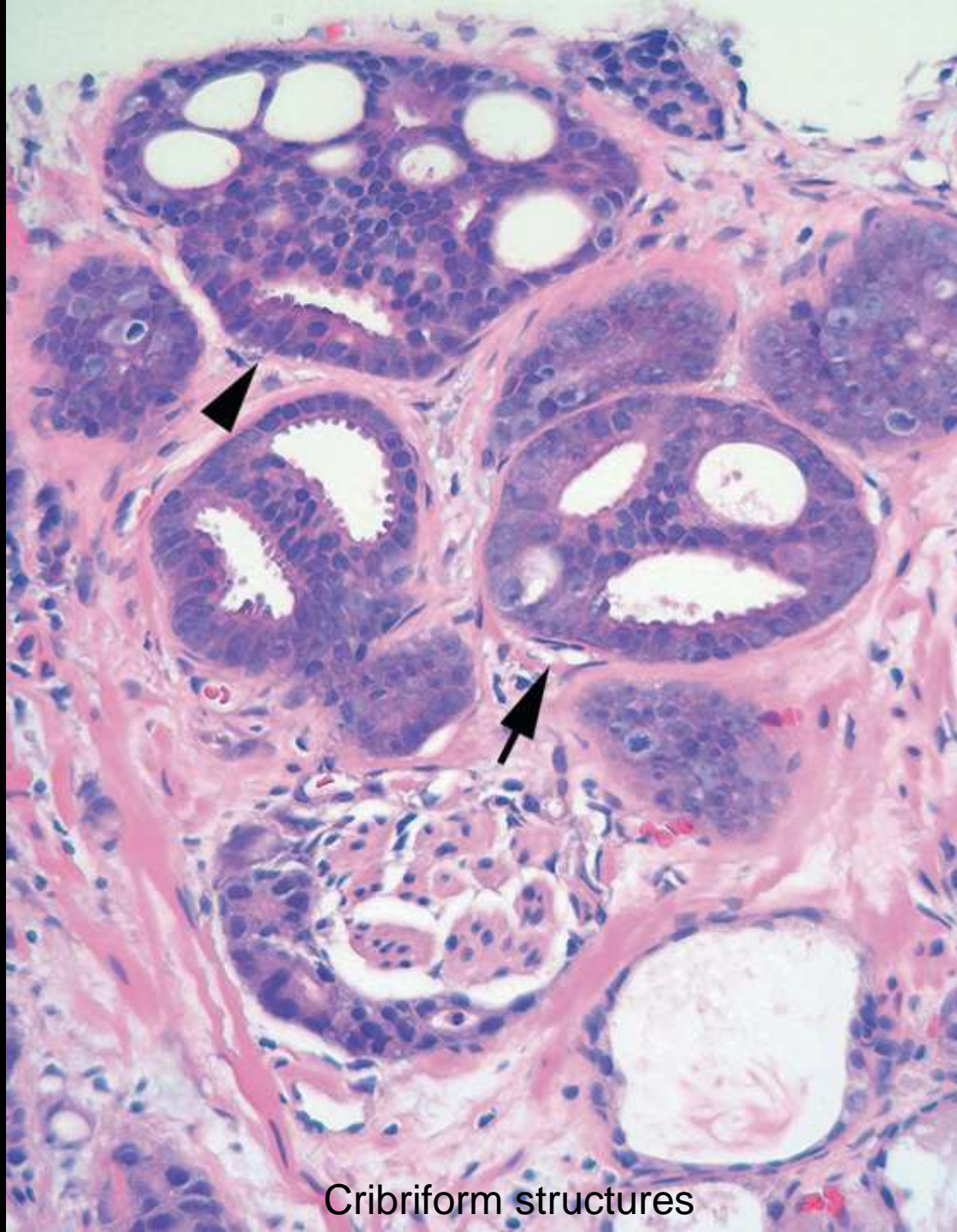
Gleason score 1 + 2 = 3 nodule of cancer on TURP



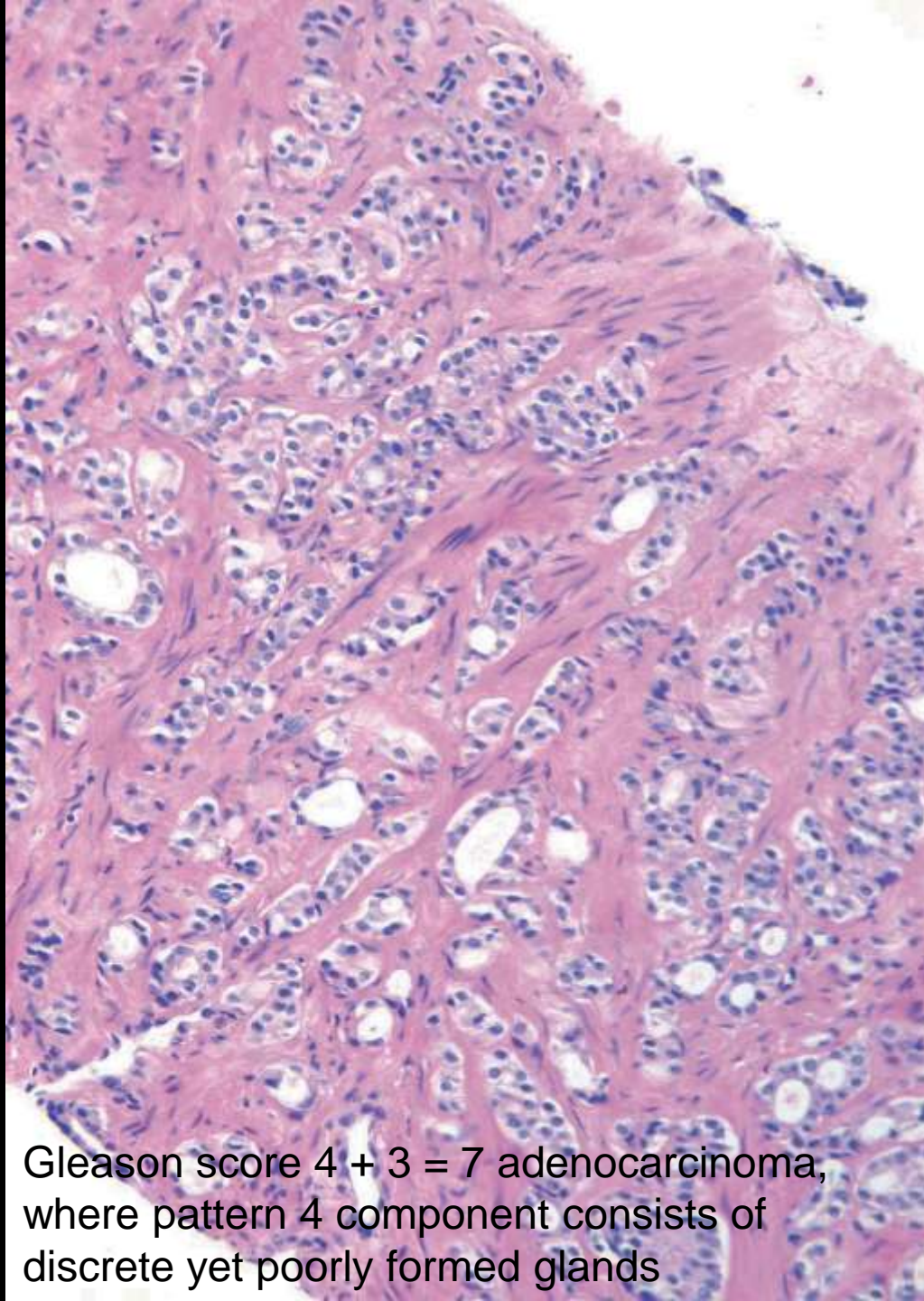
Gleason score 2 + 3 = 5 adenocarcinoma on
needle biopsy



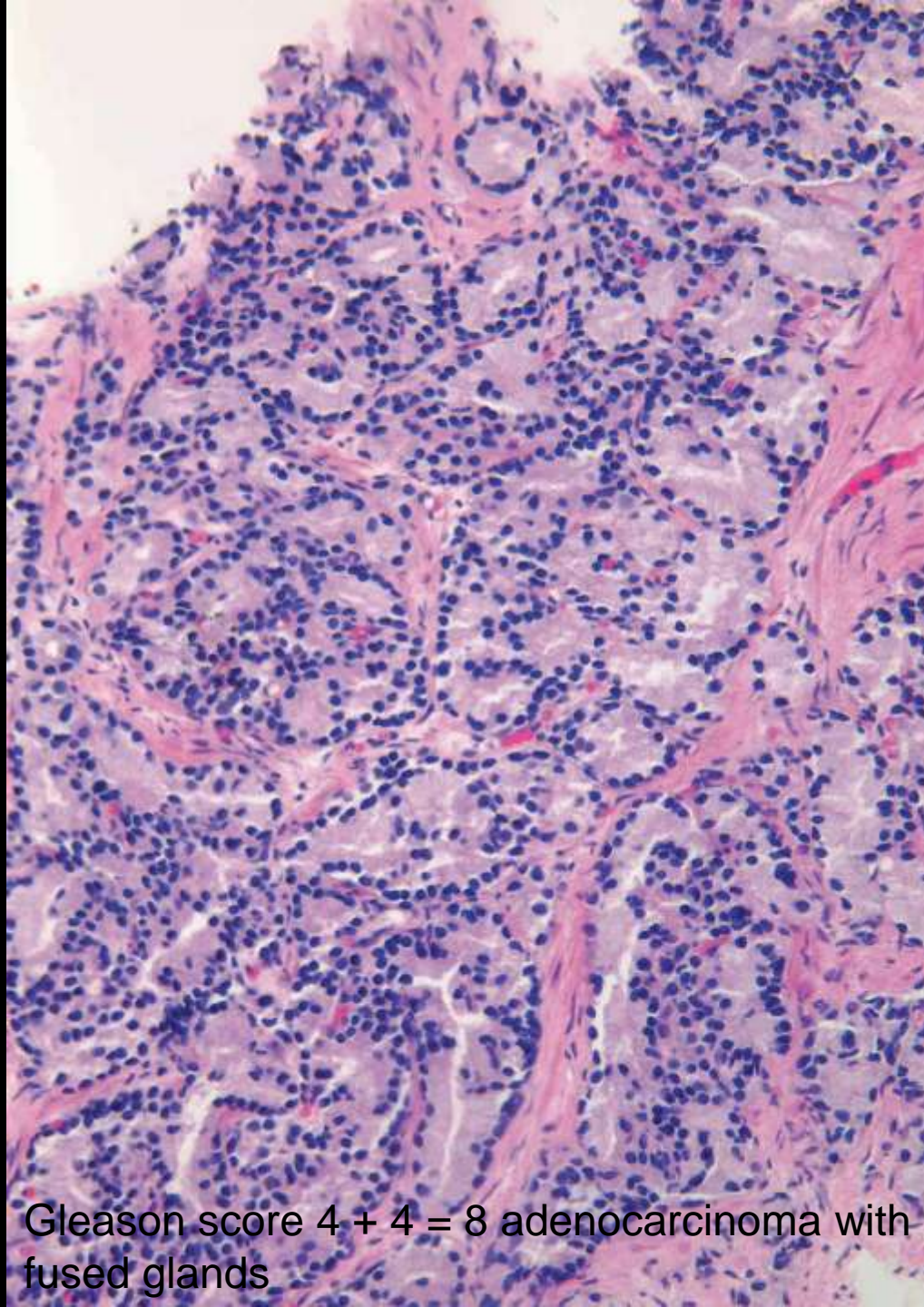
Gleason score 3 + 3 = 6



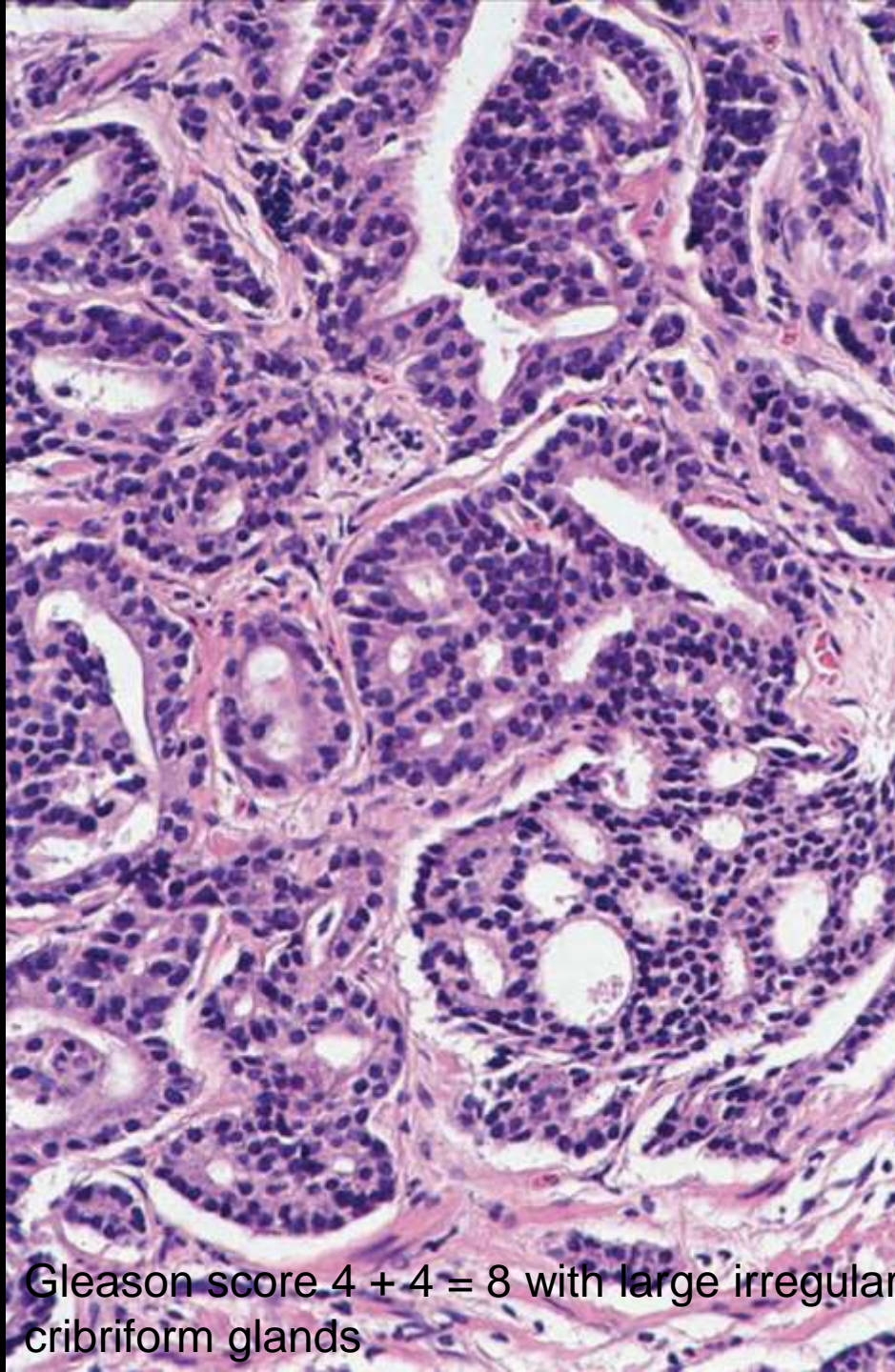
Cribriform structures



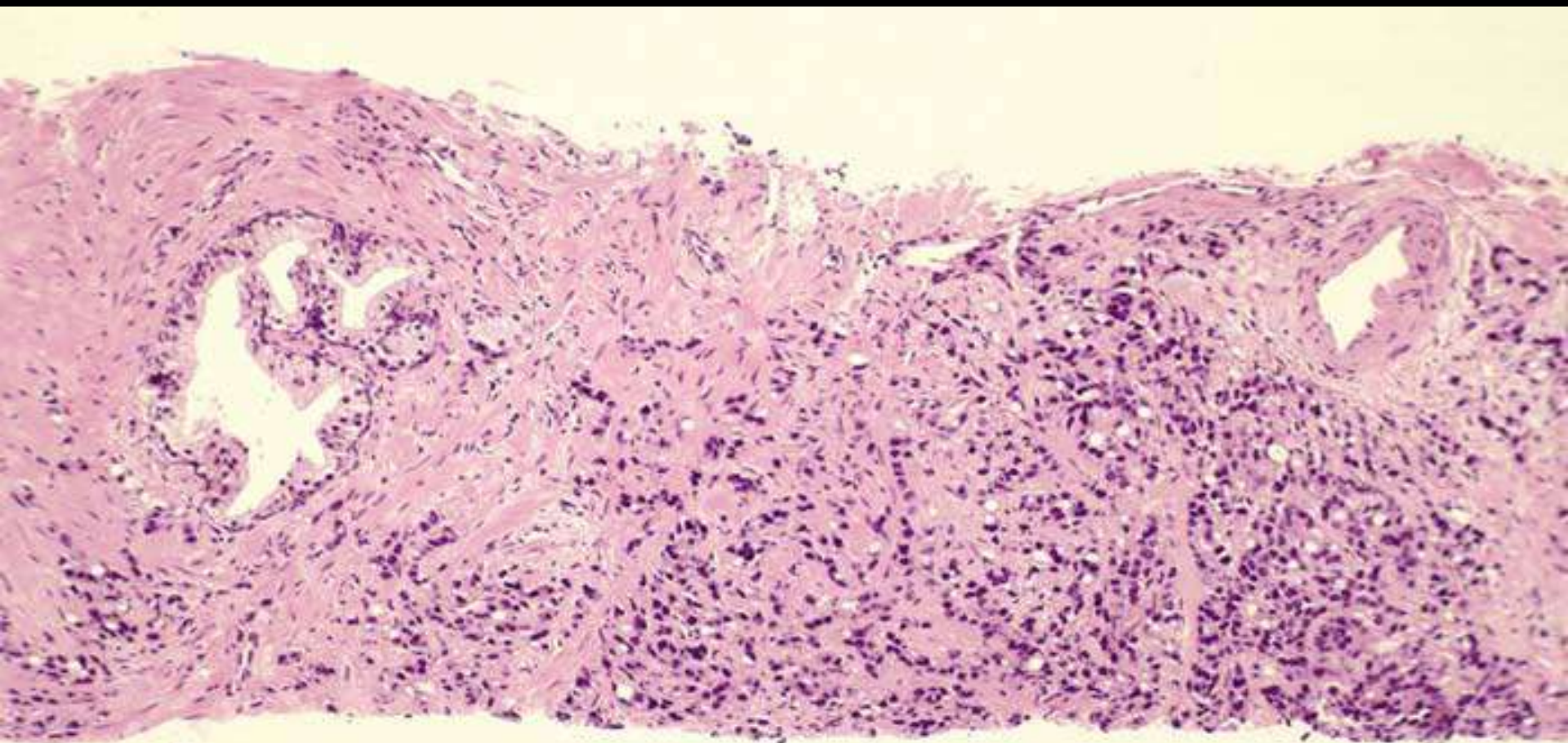
Gleason score $4 + 3 = 7$ adenocarcinoma, where pattern 4 component consists of discrete yet poorly formed glands



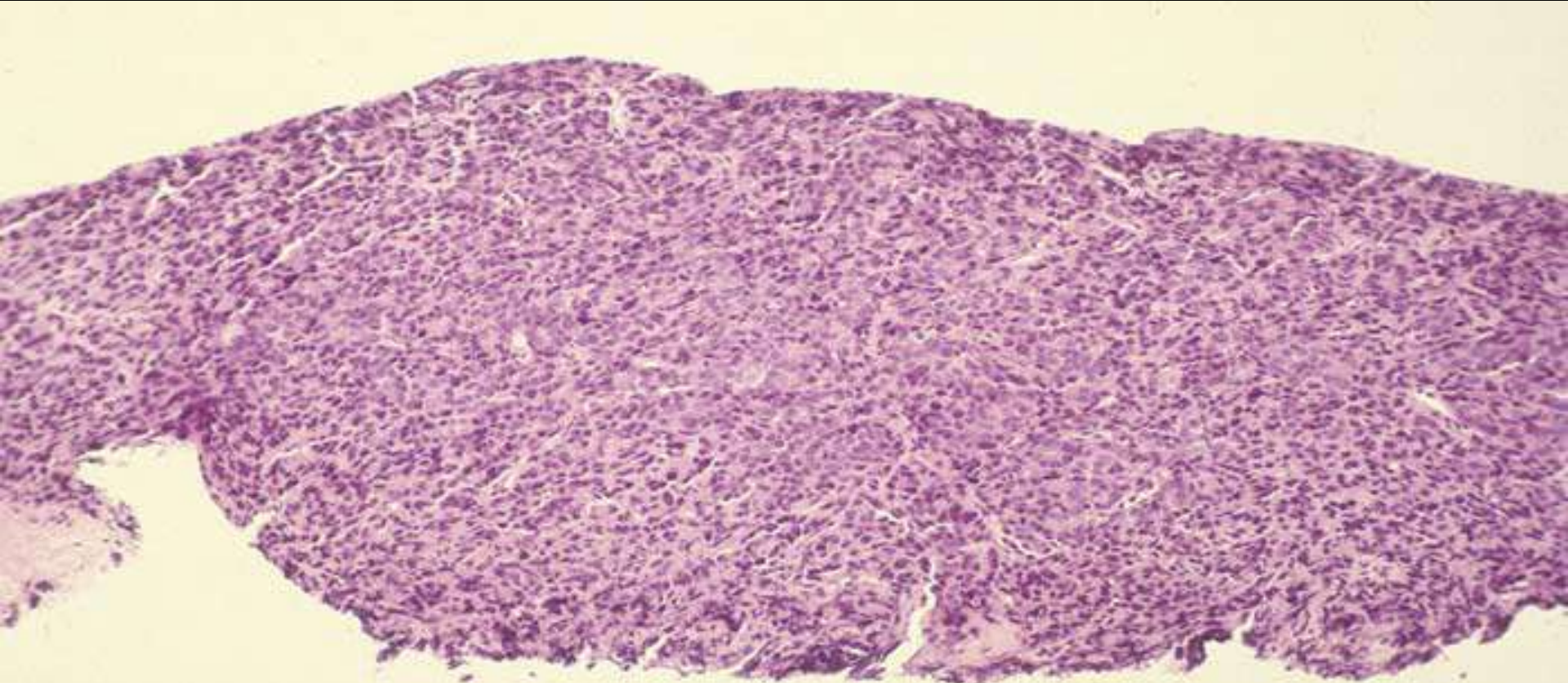
Gleason score $4 + 4 = 8$ adenocarcinoma with fused glands



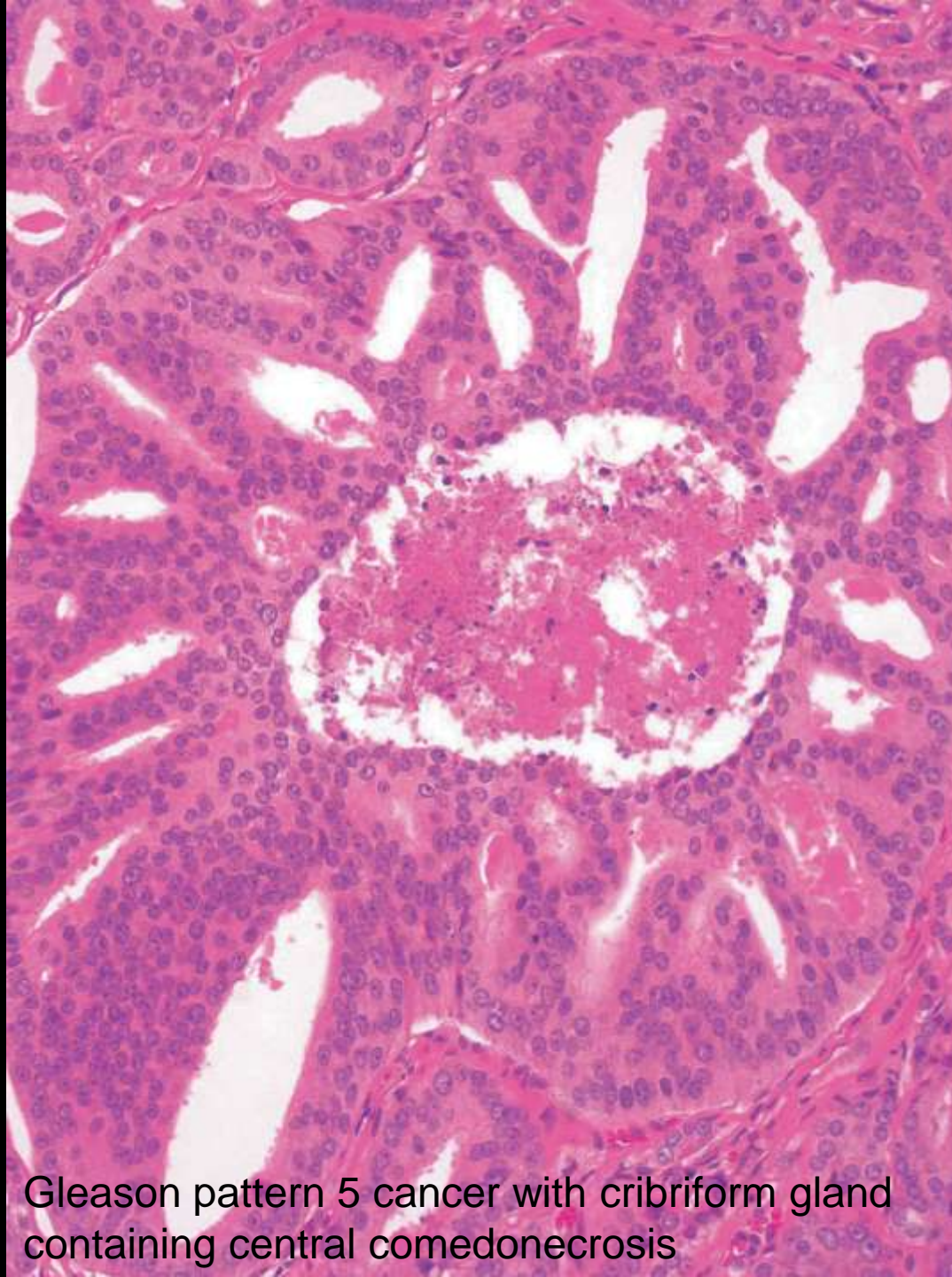
Gleason score 4 + 4 = 8 with large irregular cribriform glands



Gleason grade 5+4 = score of 9 adenocarcinoma



Gleason grade 5+5 = score of 10



Gleason pattern 5 cancer with cribriform gland containing central comedonecrosis

Assigning Gleason Score

- Primary pattern is the one that is predominant in area, by simple visual inspection
- Secondary pattern is the second most common pattern
- If only one pattern is in the tissue sample, that grade is multiplied by two to give the score
- If the secondary pattern is less than 5% of the total tumor and a lower grade, it is ignored, and the primary grade is again doubled to give the Gleason score

Assigning Gleason Score

- Tertiary pattern is the third most common pattern and in many situations it is < 5%
- On **PNB**, highest Gleason pattern must be incorporated into the score
 - ▣ Tumor composed of patterns 3 (60%), 4 (35%) and 5 (<5%) → Gleason score = 3+5=8
- On **RP**, if tertiary pattern is <5% of the tumor and a higher Gleason pattern; report as tertiary pattern
 - ▣ Tumor composed of 3 (60%), 4 (35%) and 5 (<5%) → Gleason score = 3+4=7 with a tertiary pattern 5
- On **RP**, if tertiary pattern is a significant percentage of the tumor (>5%), include it in the score
 - ▣ Tumor composed of 3 (50%), 4 (30%) and 5 (20%) → Gleason score = 3+5=8

TABLE 1. ISUP 2005 Modifications to Grading of Prostate Cancer

Poorly formed glands were classified as Gleason pattern 4

Restricted criteria were defined to distinguish cribriform pattern 4 vs. cribriform pattern 3

In needle biopsy specimens, the primary pattern + worst (not secondary) pattern were recommended to be included in the needle biopsy score

In needle biopsy specimens, very small amounts of lower-grade cancer occurring in the setting of extensive high-grade cancer were recommended to be ignored when assigning the score

Codified that the diagnosis of Gleason patterns 1 and 2 were not to be made in biopsy specimens

Discussed and recommended grading of existing variants of prostate cancer and variations in prostate cancer—small cell; mucinous; ductal; signet ring cell-like; and newly described variants—foamy; pseudohyperplastic; cancers with treatment effect

Provided recommendations of handling tertiary patterns in RP specimens

Provided recommendations of grading multiple cores from different sites

Provided recommendation of handling nodules of different grades in RP specimens



2014 ISUP Prostate Cancer Grading Panel

2014 Chicago ISUP Consensus Meeting

- Why further modifications?
 - ▣ Lack of consensus regarding certain grading issues at 2005 meeting
 - ▣ Some grading issues not covered in 2005
 - ▣ New pertinent research and data since 2005
 - ▣ Changes in prostate cancer practice has led some clinicians to challenge the existing grading system

Chicago ISUP Consensus Meeting

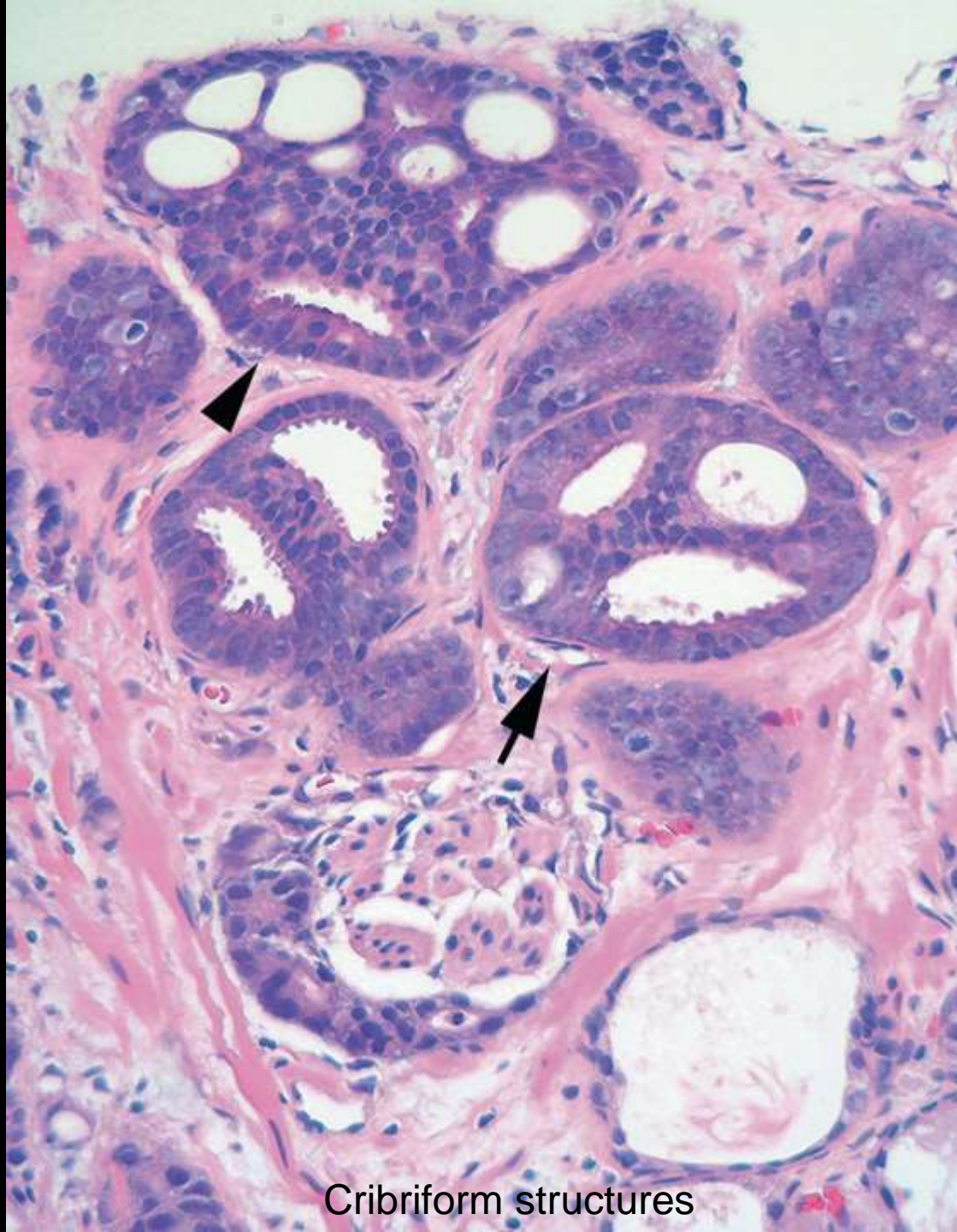
- November 1, 2014
- 65 prostate cancer pathology experts from 19 countries
- 17 clinical leaders (urologists, radiation oncologists, medical oncologists)
- Different issues:
 - ▣ Grading cribriform glands
 - ▣ Grading glomeruloid glands
 - ▣ Grading intraductal carcinoma
 - ▣ Grading mucinous carcinoma

2014 ISUP Prostate Cancer Grading Panel

- Cribriform pattern adenocarcinoma
 - ▣ Pattern 3 vs Pattern 4 ?

2005 Modified Criteria

- ▣ Pattern 3:
 - Small cribriform glands with regular contour and round evenly spaced lumina
- ▣ Pattern 4:
 - Large cribriform glands or cribriform glands with an irregular border



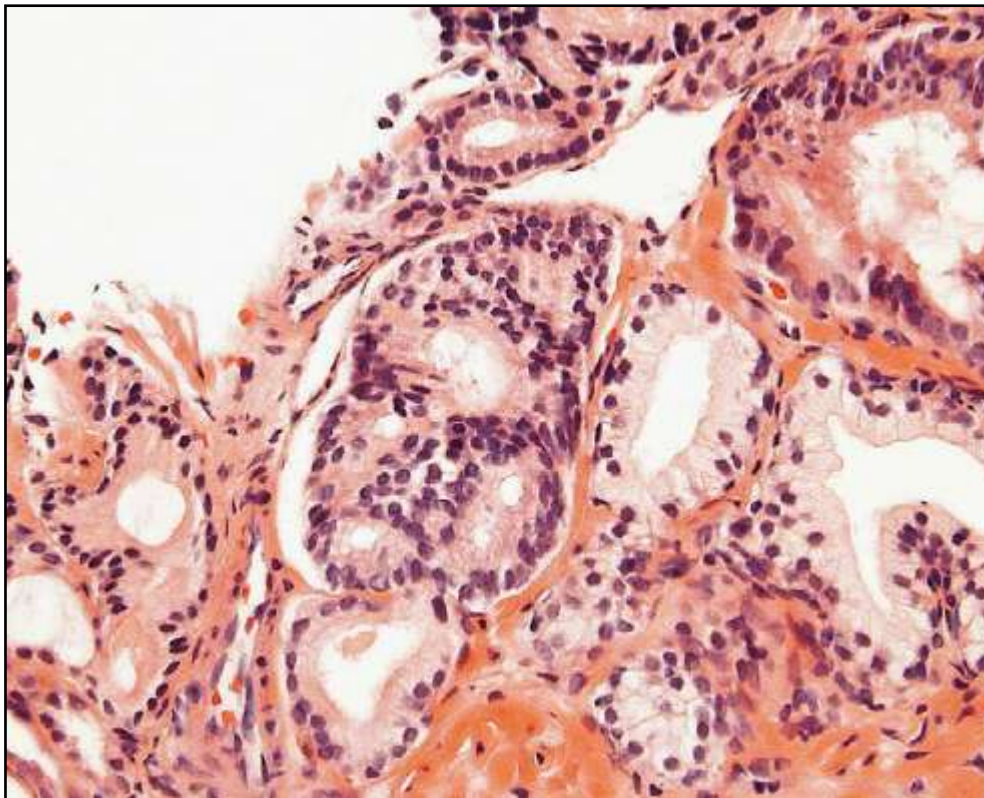
Cribriform structures

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* † ‡*

(Am J Surg Pathol 2008;32:1532–1539)

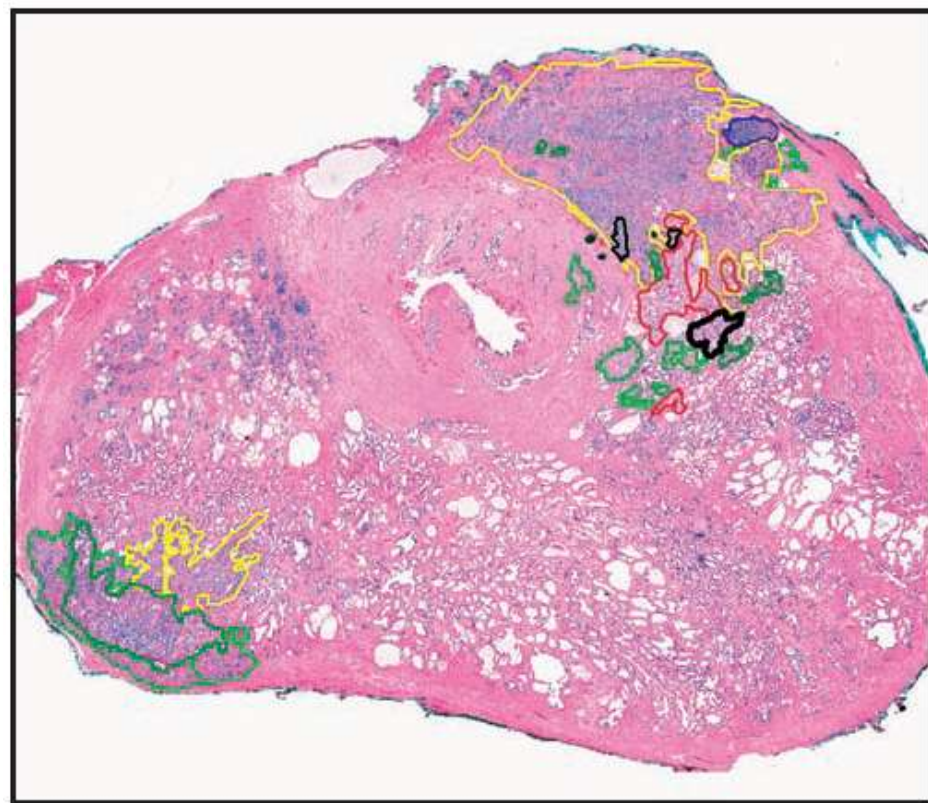
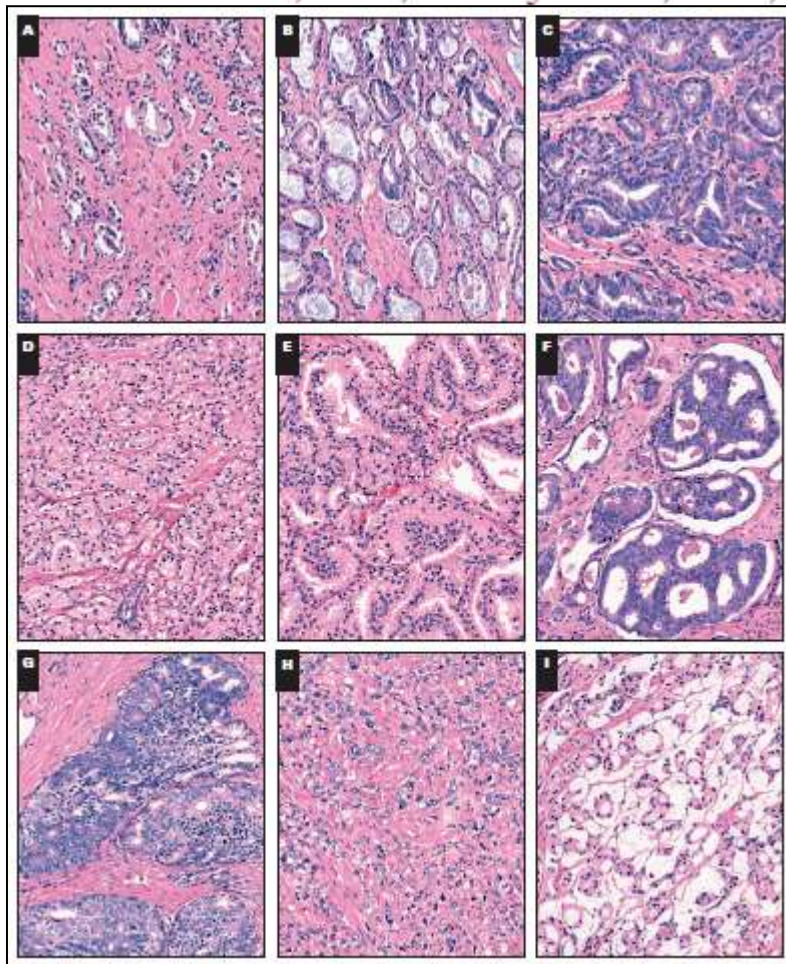


- On one (1) of 3590 cases of prostate cancer was there consensus agreement of Gleason pattern 3 cribriform growth among experts

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, MD¹

Am J Clin Pathol 2011;136:98-107
DOI: 10.1309/AJCPZ7WBU9YXSJPE



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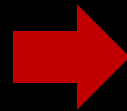
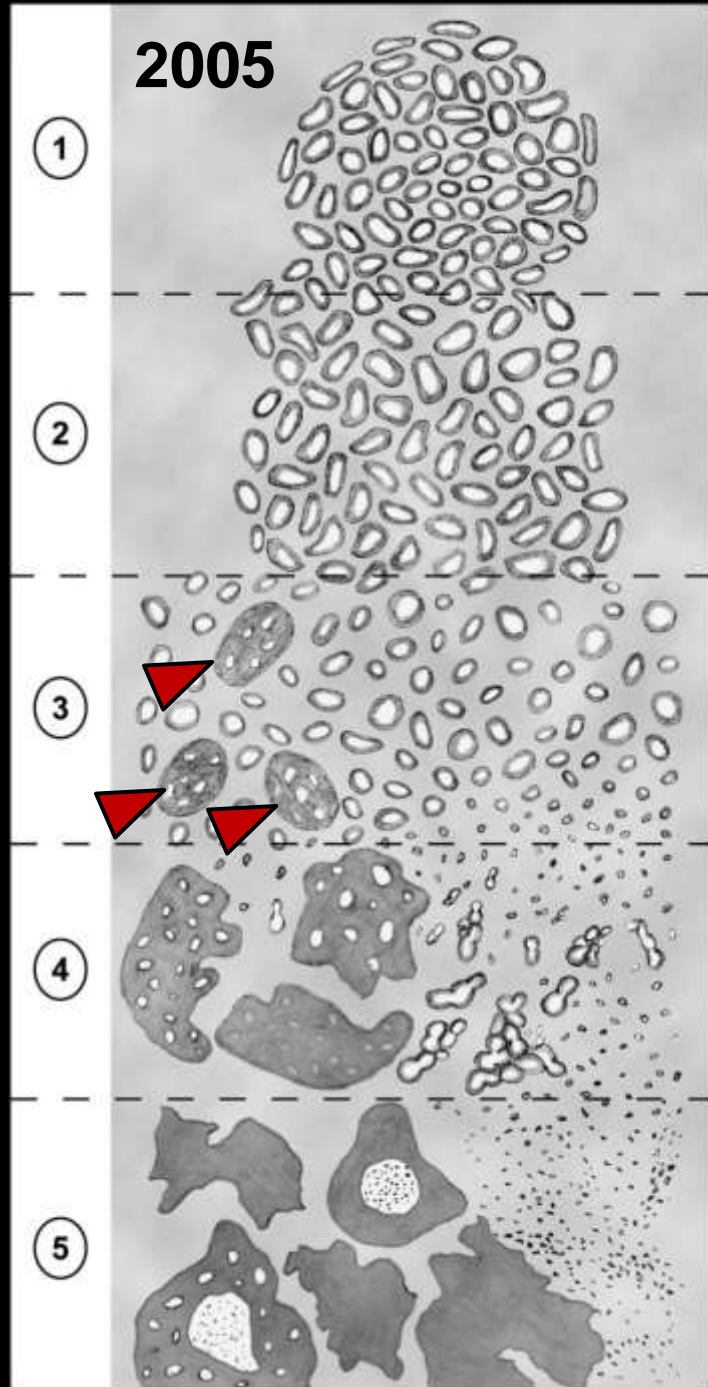
- Cribriform pattern had the highest OR for PSA failure at 5.89
- Both large and small cribriform patterns linked to failure
- Every mm² of cribriform pattern increased the OR for PSA failure

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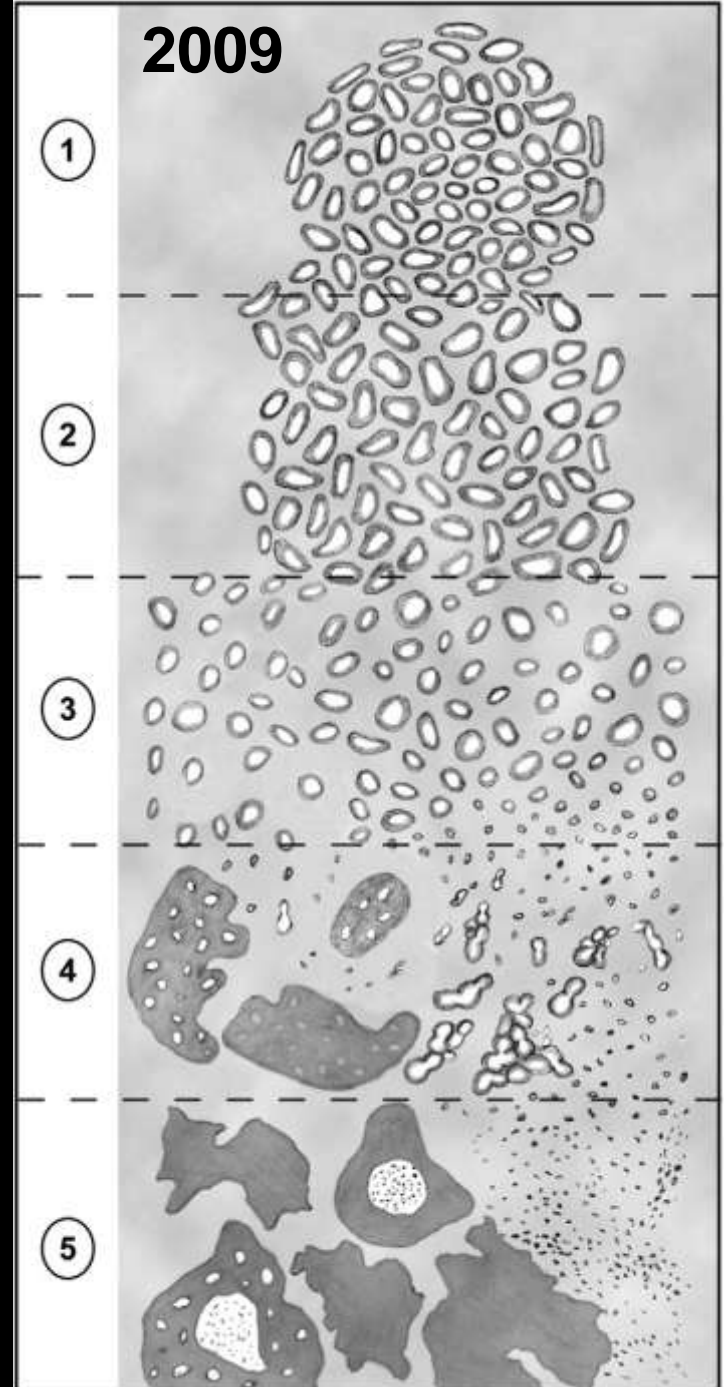
- Cribriform pattern adenocarcinoma associated with earlier biochemical recurrence, metastases and death
- ▣ All cribriform patterns graded as pattern 4

(Eur J Cancer 2014;50:1610-6. Am J Surg Pathol 2013; 37:1855-6)

2005

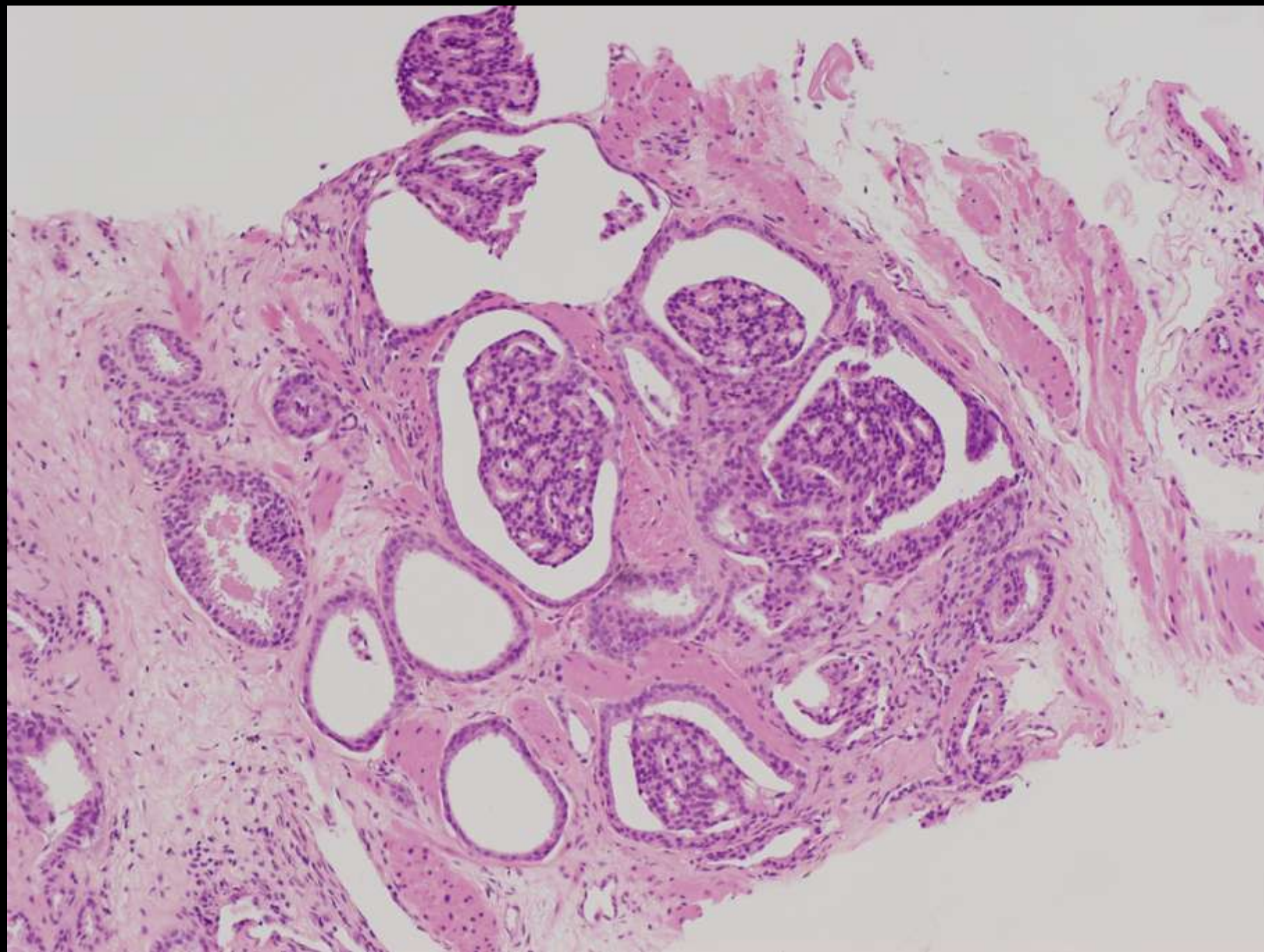


2009



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- Glomeruloid structures
 - ▣ Pattern 3 vs pattern 4
 - ▣ No consensus reached in 2005



Gleason grading of prostatic adenocarcinoma with glomeruloid features on needle biopsy

Tamara L. Lotan MD^a, Jonathan I. Epstein MD^{a, b, c, *}

Human Pathology (2009) 40, 471–477

- 45 needle biopsies with glomeruloid features
- 84% of cases associated with Gleason pattern 4 or 5 on the same core

2014 ISUP Prostate Cancer Grading Panel

- Glomeruloid structures
 - ▣ Favored to be early cribriform structures, therefore graded as pattern 4

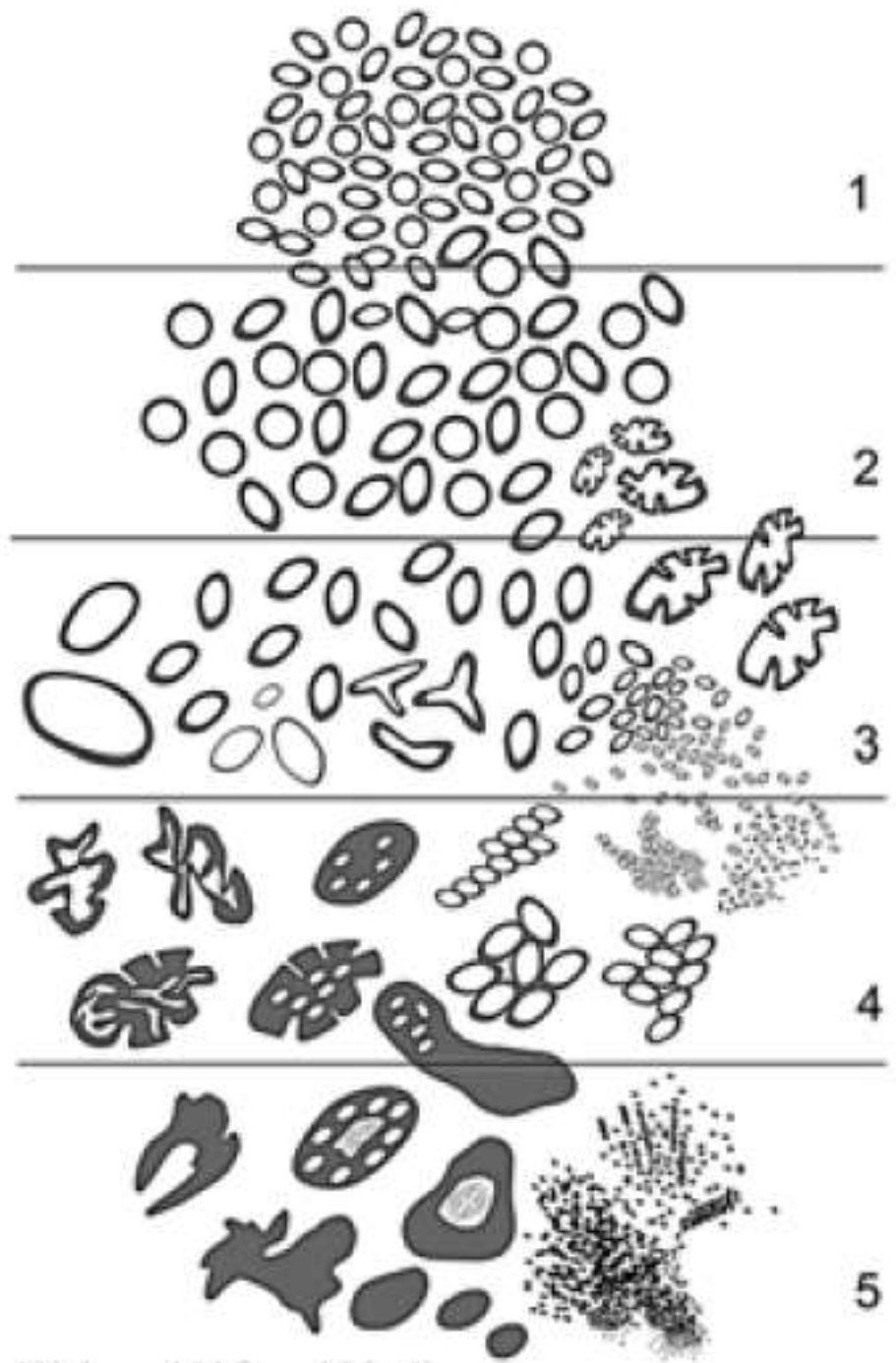
2015 Modified ISUP Gleason Patterns

The 2014 International Society of Urological Pathology
(ISUP) Consensus Conference on Gleason Grading of
Prostatic Carcinoma

Definition of Grading Patterns and Proposal for a New Grading System

Jonathan I. Epstein, MD, Lars Egevad, MD, PhD,† Mahul B. Amin, MD,‡ Brett Delahunt, MD,§
John R. Srigley, MD,|| Peter A. Humphrey, MD, PhD,¶ and the Grading Committee*

Am J Surg Pathol • Volume 00, Number 00, ■■ 2015



2014 ISUP Prostate Cancer Grading Panel

Other discussions and recommendations

- Mucinous carcinoma should be graded based on underlying pattern; not more aggressive than non-mucinous carcinoma
- Retire “hypernephromatoid” term

2014 ISUP Prostate Cancer Grading Panel

Other discussions and recommendations

- How do we report and grade intraductal growth?

Intraductal Carcinoma of the Prostate

Intraductal spread of conventional/acinar type prostatic adenocarcinoma

- Not prostatic duct carcinoma
- Not high grade prostatic intraepithelial neoplasia
- Not cribriform pattern (GP 4) of conventional/acinar type carcinoma

Intraductal Carcinoma of the Prostate

- Spread of prostatic adenocarcinoma within prostatic ducts
 - ▣ Kovi et al. *Cancer* 1985;56:1566-73
- Diagnostic criteria formalized
 - ▣ Guo, Epstein. *Mod Pathol*. 2006;19:1528-35

TABLE 2. Criteria for IDC²⁰

Malignant epithelial cells filling large acini and prostatic ducts, with preservation of basal cells and:

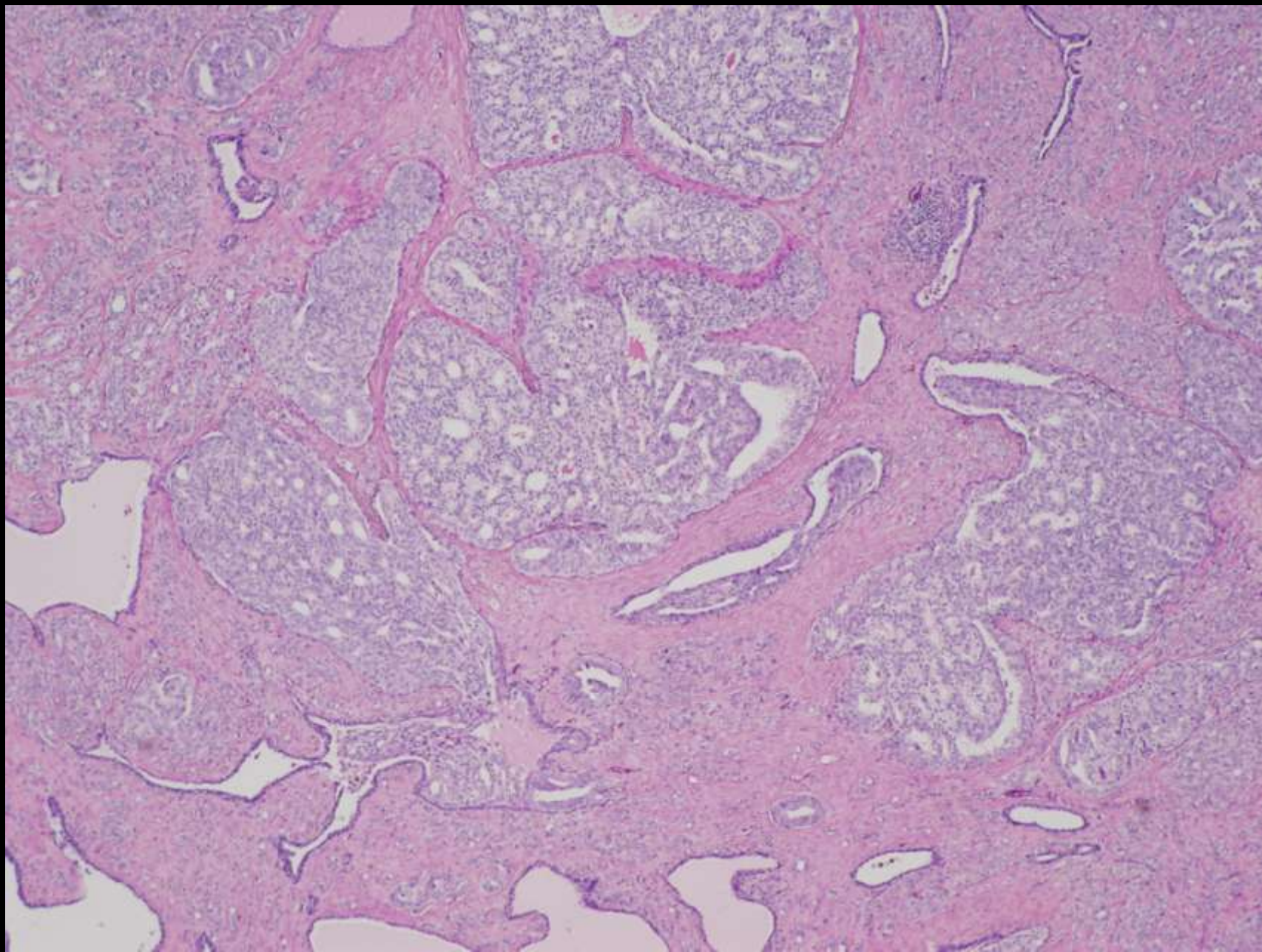
Solid or dense cribriform pattern

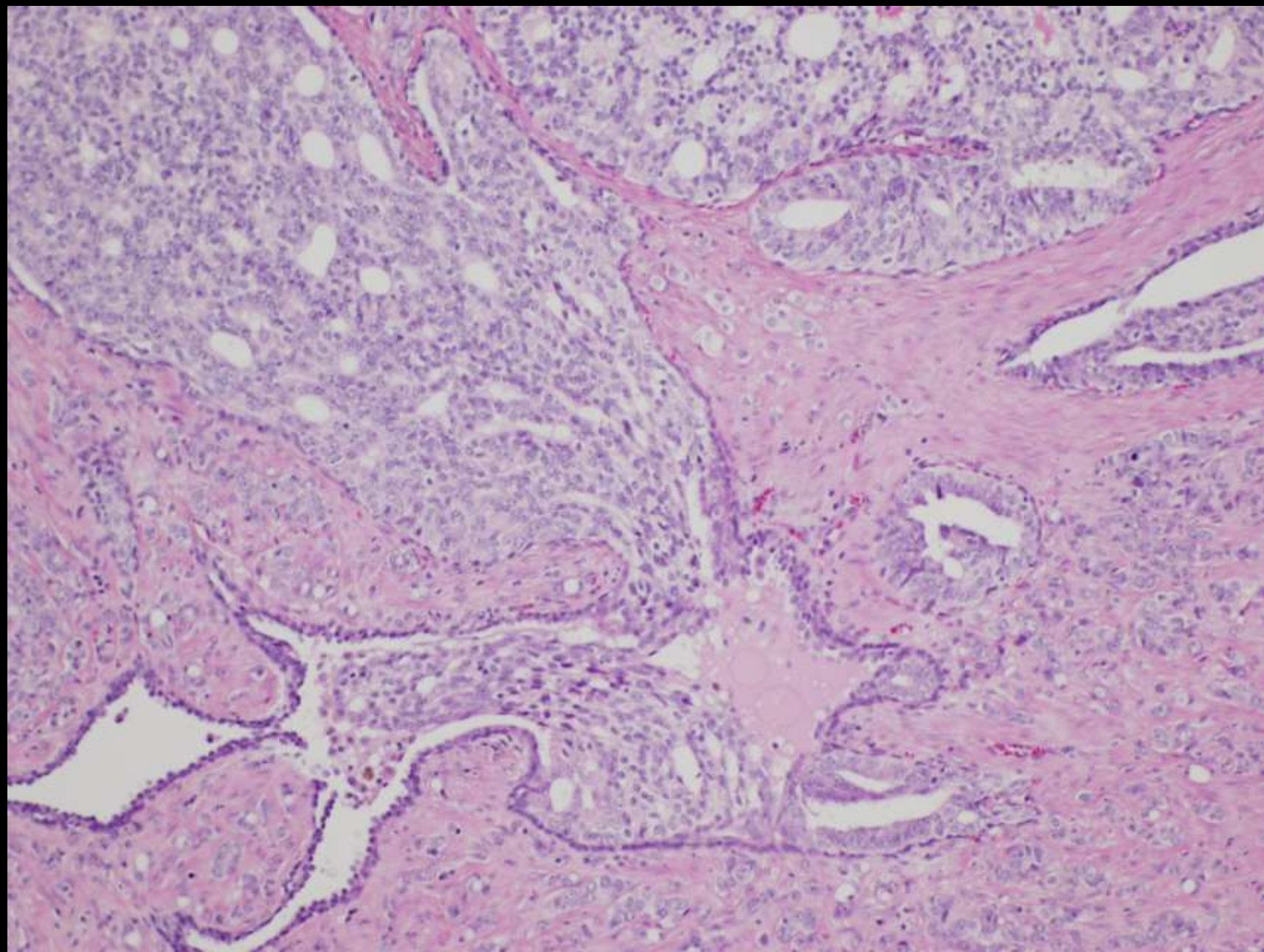
Or

Loose cribriform or micropapillary pattern with either:

Marked nuclear atypia: nuclear size $6 \times$ normal

Necrosis

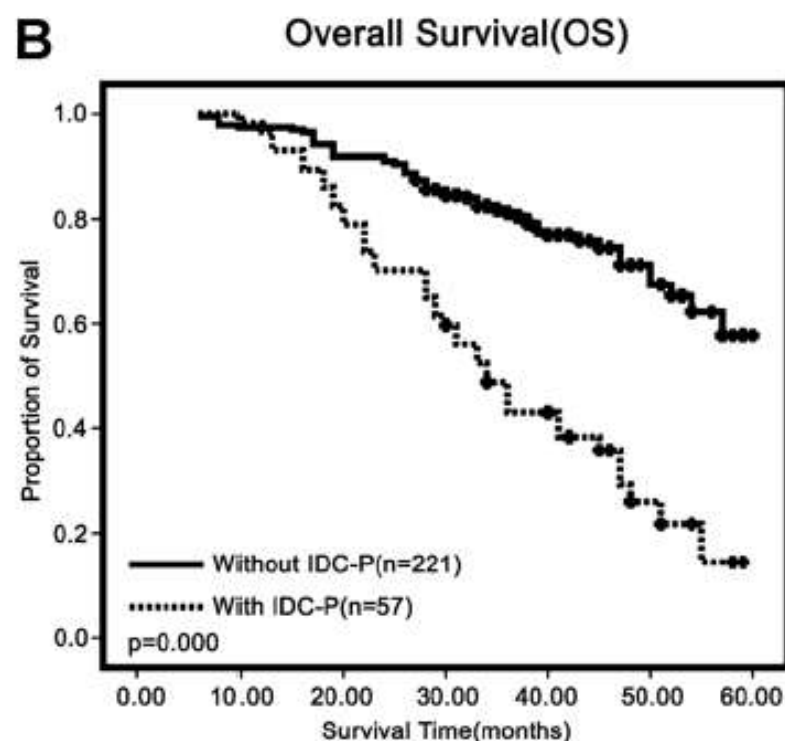
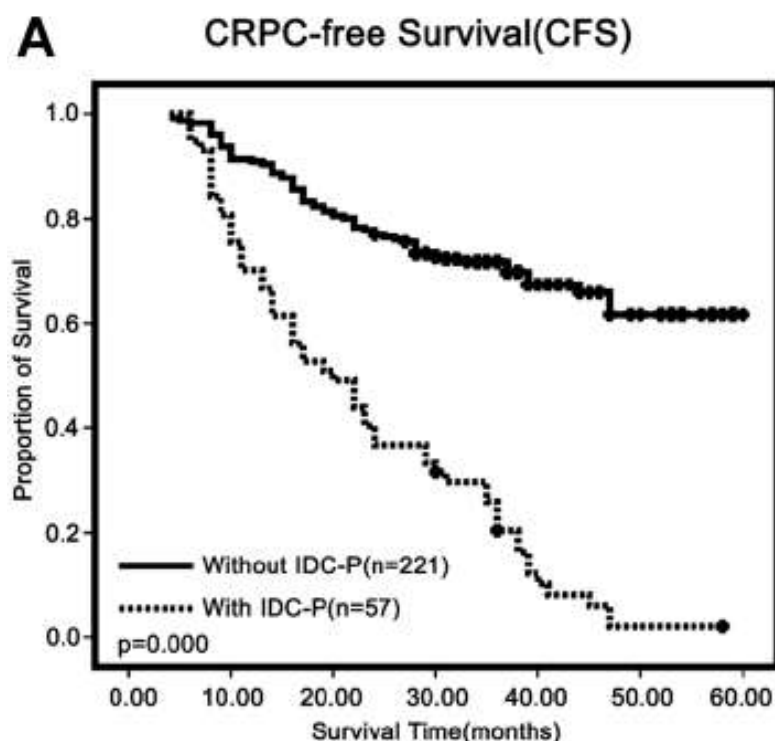




Is There any Prognostic Impact of Intraductal Carcinoma of Prostate in Initial Diagnosed Aggressively Metastatic Prostate Cancer?

Tao Zhao,¹ Banghua Liao,¹ Jin Yao,² Jiyan Liu,³ Rui Huang,⁴ Pengfei Shen,¹ Zhufeng Peng,¹ Haojun Gui,¹ Xueqin Chen,⁵ Peng Zhang,¹ Yuchun Zhu,¹ Xiang Li,¹ Qiang Wei,¹ Qiao Zhou,⁵ Hao Zeng,^{1*} and Ni Chen^{5*}

The Prostate 75:225–232 (2015)

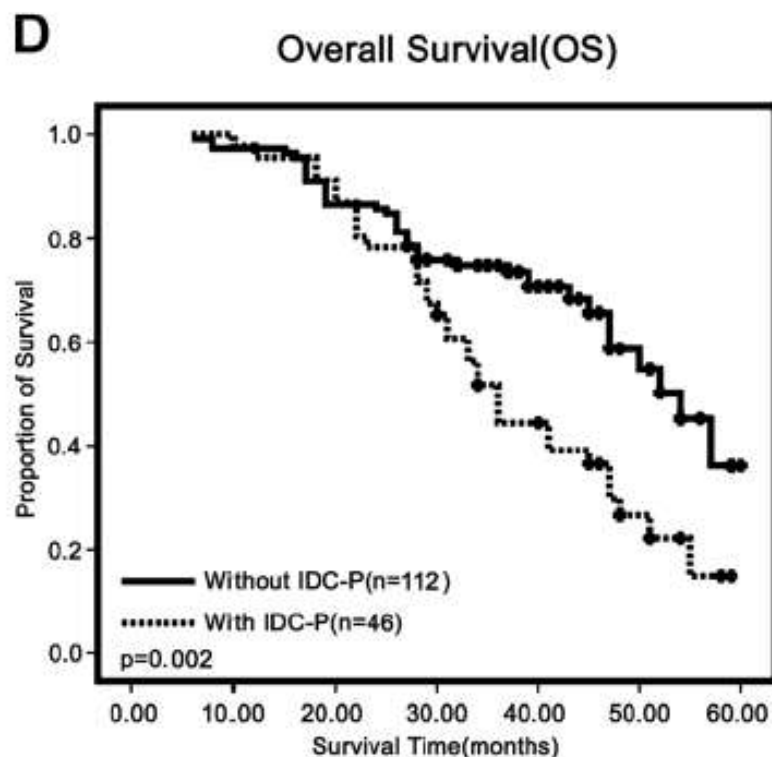
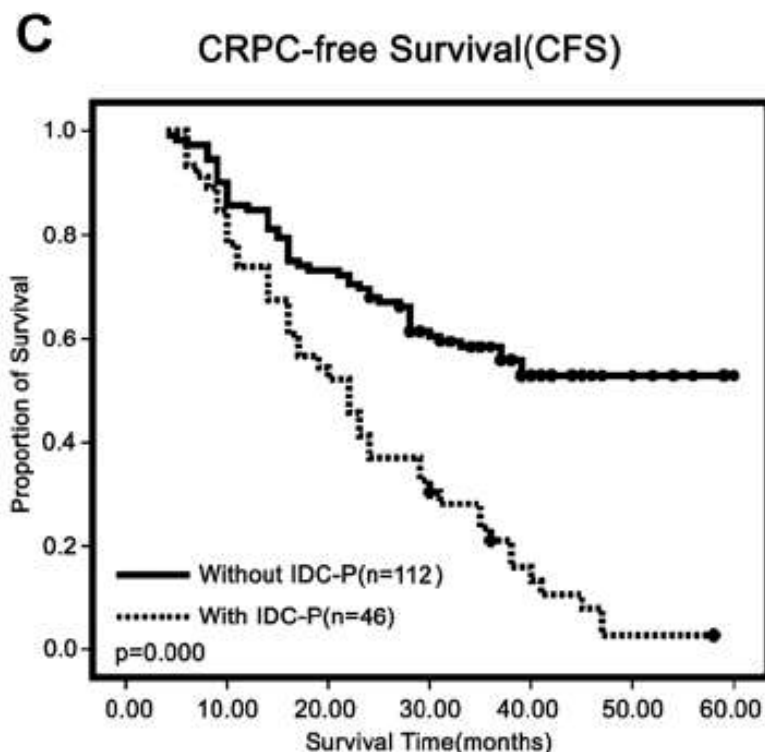


The prognostic value of IDC-P in metastatic prostate cancer

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The Prostate 75:225–232 (2015)



The prognostic value of IDC-P in metastatic prostate cancer with higher Gleason score(8-10)

Biopsy diagnosis of intraductal carcinoma is prognostic in intermediate and high risk prostate cancer patients treated by radiotherapy

T. Van der Kwast et al. / *European Journal of Cancer* 48 (2012) 1318–1325

T. Van der Kwast^{a,*}, N. Al Daoud^a, L. Collette^b, J. Sykes^c, J. Thoms^c, M. Milosevic^c, R.G. Bristow^c, G. Van Tienhoven^d, P. Warde^c, R.-O. Mirimanoff^e, M. Bolla^f

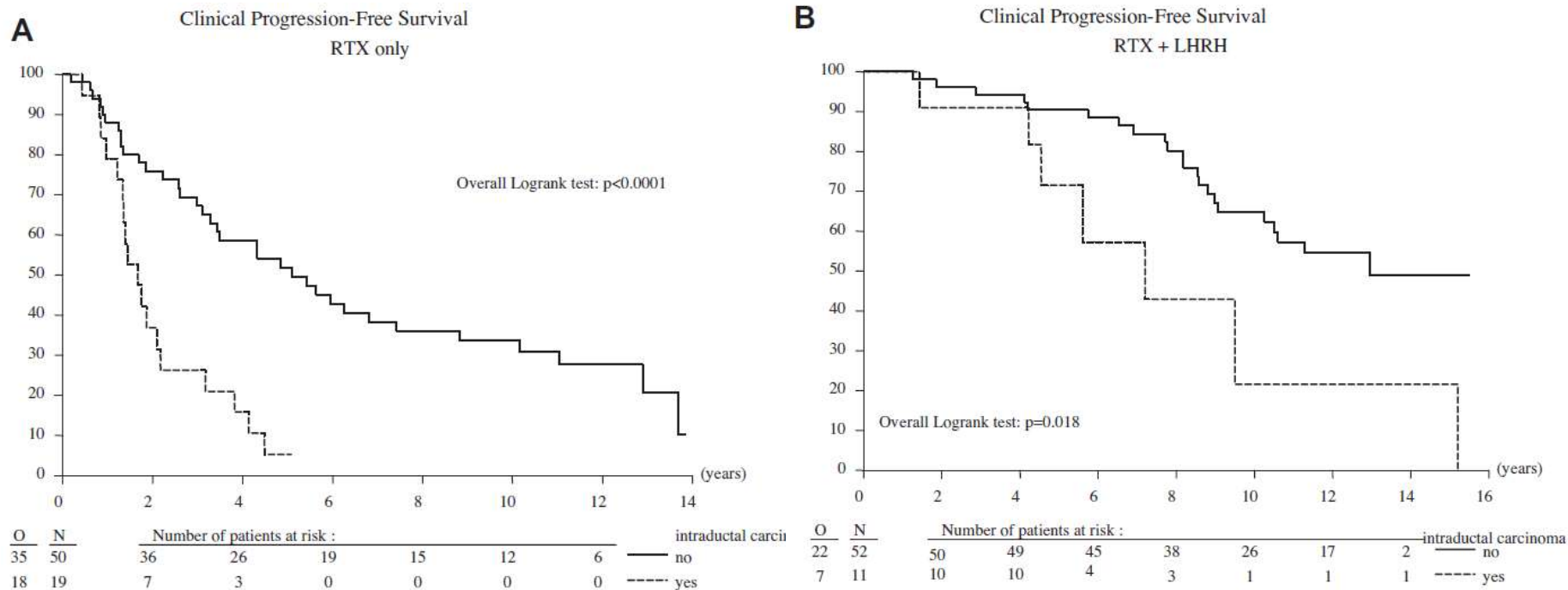
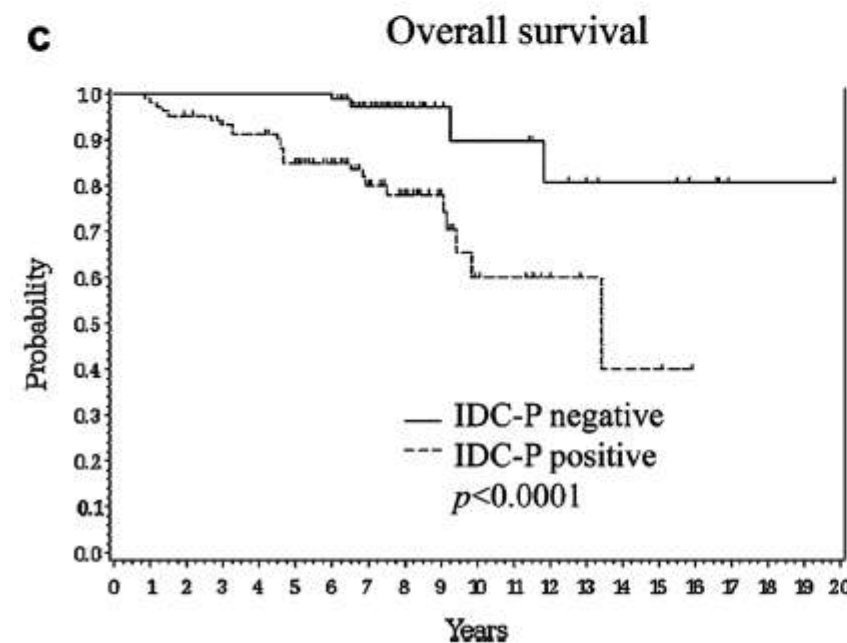
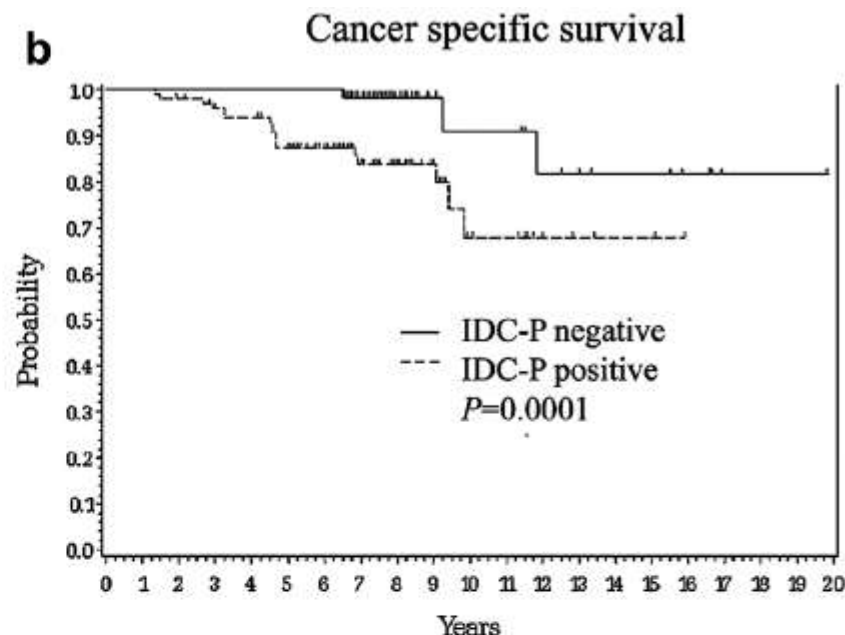
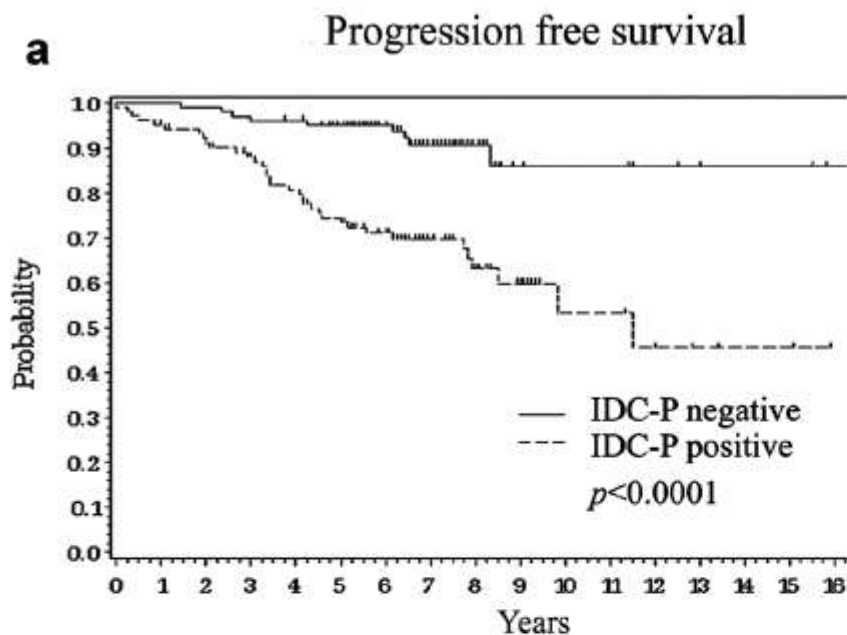


Fig. 4. Intraductal carcinoma as a prognostic factor in the radiotherapy arm (A) of the EORTC trial and the radiotherapy plus long term androgen deprivation arm (B).



Prognostic Value of Intraductal Carcinoma of The Prostate in Radical Prostatectomy Specimens

Kyosuke Kimura,¹ Toyonori Tsuzuki,² Masashi Kato,³ Akiko M. Saito,⁴ Naoto Sassa,³
Ryo Ishida,⁵ Hiroki Hirabayashi,⁶ Yasushi Yoshino,³ Ryohei Hattori,⁷ and Momokazu Gotoh³

The Prostate 74:680–687 (2014)

How do we report and grade intraductal growth?

TABLE 3. Pros and Cons of Grading IDC-P

Pros

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 and may need to do immunohistochemistry on multiple parts to distinguish
Several studies demonstrating correlation of IDC with increased stage and prognosis

Cons

Approximately 10% of IDC found at RP are not closely associated with invasive carcinoma and appear to be a precursor lesion as opposed to invasive cancer extending into ducts

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

In the uncommonly setting of IDC and $3 + 3$ on biopsy, approximately 20% have $3 + 3 = 6$ only at RP and would have been incorrectly labeled as having pattern 4 on biopsy

In other organ systems, intraductal lesions are not graded with the same grading system as the invasive component

How do we report and grade intraductal growth?

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In other organ systems, intraductal lesions are not graded with the same grading system as the invasive component

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How do we report and grade intraductal growth?

- Intraductal carcinoma without invasive carcinoma in the background, should not be assigned a Gleason grade
- Report presence of intraductal carcinoma and comment on its invariable association with aggressive prostate cancer
- Eg
 - ▣ Invasive prostatic adenocarcinoma, conventional type with intraductal growth; Gleason score 8/10 (4,4) [see comment]
 - ▣ Intraductal carcinoma [see comment]



Proposal for New Prostate Cancer Grading System

Why a “New” Grading System?

- Problems with Gleason grading system scale
- Use of inaccurate grade combinations for prognosis and therapy
- Response to proposals to redefine Gleason score 6 as “not cancer”

Problems with the Gleason Grading System

- Original scores: 2-10
- Reporting of GS 2-5 has virtually disappeared
 - ▣ Gleason's original data – 27.9% (*Recent Results Cancer Res* 1977; (60):61-72)
 - ▣ Pathologists' reporting of GS 2-4:
 - 24% in 1991 vs 2.4% in 2001 (*Eur Urol* 2005;47:196-201)
 - ▣ Biopsy assignment of GS 2-4:
 - 22.3% in 1994 vs 1.6% in 2003 (*J Urol* 2008;179:1335-8)
 - ▣ Biopsy assignment of GS 2-5
 - GS2-4: 2.7% (1996-2000) vs 0% (2005)
 - GS5: 12.2% (1996-2000) vs 0.3% (2005)

(*Virchows Arch* 2006;449:62-627)

Problems with the Gleason Grading System



- GS 2-5 are virtually nonexistent and cannot be diagnosed on biopsies
- GS 6 is the lowest score currently assigned
- GS 6/10 may imply an intermediate risk disease in patient's mind.

Use of inaccurate grade combinations for prognosis and therapy

- In literature and for therapeutic purposes, various scores have been grouped together (prognostic models/nomograms/risk stratification models) with the assumption that they have a similar prognosis
- 2-4; 5-7; 8-10
 - ▣ Prostate Cancer Outcomes Study; *N Engl J Med* 2013; 368: 436-445
- 2-6; 7-10
 - ▣ Prostate Cancer Prevention Trial & Prostate Cancer Intervention vs Observation Trial; *N Engl J Med* 2014; 370: 932-942
- 2-6; 7; 8-10
 - ▣ Scandinavian Prostate Cancer Group Study; NCCN; D'Amico classification system

Use of inaccurate grade combinations for prognosis and therapy

- **2-4; 5-7; 8-10**

- ▣ Prostate Cancer Outcomes Study; *N Engl J Med* 2013; 368: 436-445

- **2-6; 7-10**

- ▣ Prostate Cancer Prevention Trial & Prostate Cancer Intervention vs Observation Trial; *N Engl J Med* 2014; 370: 932-942

- **2-6; 7; 8-10**

- ▣ Scandinavian Prostate Cancer Group Study; NCCN; D'Amico classification system

GS 2-4 virtually never exists

Use of inaccurate grade combinations for prognosis and therapy

- 2-4; **5-7**; 8-10

- ▣ Prostate Cancer Outcomes Study; *N Engl J Med* 2013; 368: 436-445

- 2-6; 7-10

- ▣ Prostate Cancer Prevention Trial & Prostate Cancer Intervention vs Observation Trial; *N Engl J Med* 2014; 370: 932-942

- 2-6; 7; 8-10

- ▣ Scandinavian Prostate Cancer Group Study; NCCN; D'Amico classification system

Combining GS 6 (Excellent prognosis) with GS 7

Use of inaccurate grade combinations for prognosis and therapy

- 2-4; **5-7**; 8-10

- ▣ Prostate Cancer Outcomes Study; *N Engl J Med* 2013; 368: 436-445

- 2-6; **7-10**

- ▣ Prostate Cancer Prevention Trial & Prostate Cancer Intervention vs Observation Trial; *N Engl J Med* 2014; 370: 932-942

- 2-6; **7**; 8-10

- ▣ Scandinavian Prostate Cancer Group Study; NCCN; D'Amico classification system

No distinction between 3+4 and 4+3

Urology 2000;56:823-827. Urology 2006;67:115-119. J Urol 2001;166:1692-1697

Use of inaccurate grade combinations for prognosis and therapy

- 2-4; 5-7; 8-10

- ▣ Prostate Cancer Outcomes Study; *N Engl J Med* 2013; 368: 436-445

- 2-6; **7-10**

- ▣ Prostate Cancer Prevention Trial & Prostate Cancer Intervention vs Observation Trial; *N Engl J Med* 2014; 370: 932-942

- 2-6; 7; 8-10

- ▣ Scandinavian Prostate Cancer Group Study; NCCN; D'Amico classification system

Combining GS 7 with GS ≥ 8

Use of inaccurate grade combinations for prognosis and therapy

- 2-4; 5-7; **8-10**

- ▣ Prostate Cancer Outcomes Study; *N Engl J Med* 2013; 368: 436-445

- 2-6; 7-10

- ▣ Prostate Cancer Prevention Trial & Prostate Cancer Intervention vs Observation Trial; *N Engl J Med* 2014; 370: 932-942

- 2-6; 7; **8-10**

- ▣ Scandinavian Prostate Cancer Group Study; NCCN; D'Amico classification system

Combining GS 8 with GS 9-10

Response to proposals to redefine Gleason score 6 as 'not cancer'

- Proposal to consider GS 6 as not cancer
 - ▣ Excellent prognosis
 - ▣ Ameliorate the fear associated with the term 'cancer'
 - ▣ Response to frequent overtreatment of GS 6
- Proposed term IDLE (indolent lesion of epithelial origin) (*Lancet Oncol* 2014;15:e234-242)

Response to proposals to redefine Gleason score 6 as 'not cancer'

Addressing overdiagnosis and overtreatment in cancer: a prescription for change

Laura J Esserman, Ian M Thompson, Brian Reid, Peter Nelson, David F Ransohoff, H Gilbert Welch, Shelley Hwang, Donald A Berry, Kenneth W Kinzler, William C Black, Mina Bissell, Howard Parnes, Sudhir Srivastava
Lancet Oncol 2014; 15: e234–42

When is Prostate Cancer Really Cancer?

David M. Berman, MD, PhD^a, Jonathan I. Epstein, MD^{b,*}

Urol Clin N Am 41 (2014) 339–346

Collaborative Review – Prostate Cancer

The Contemporary Concept of Significant Versus Insignificant Prostate Cancer

EUROPEAN UROLOGY 60 (2011) 291–303

Guillaume Ploussard^{a,b,*}, Jonathan I. Epstein^c, Rodolfo Montironi^{d,e}, Peter R. Carroll^f, Manfred Wirth^g, Marc-Oliver Grimm^h, Anders S. Bjartellⁱ, Francesco Montorsi^j, Stephen J. Freedland^k, Andreas Erbersdobler^l, Theodorus H. van der Kwast^m

Response to proposals to redefine Gleason score 6 as ‘not cancer’

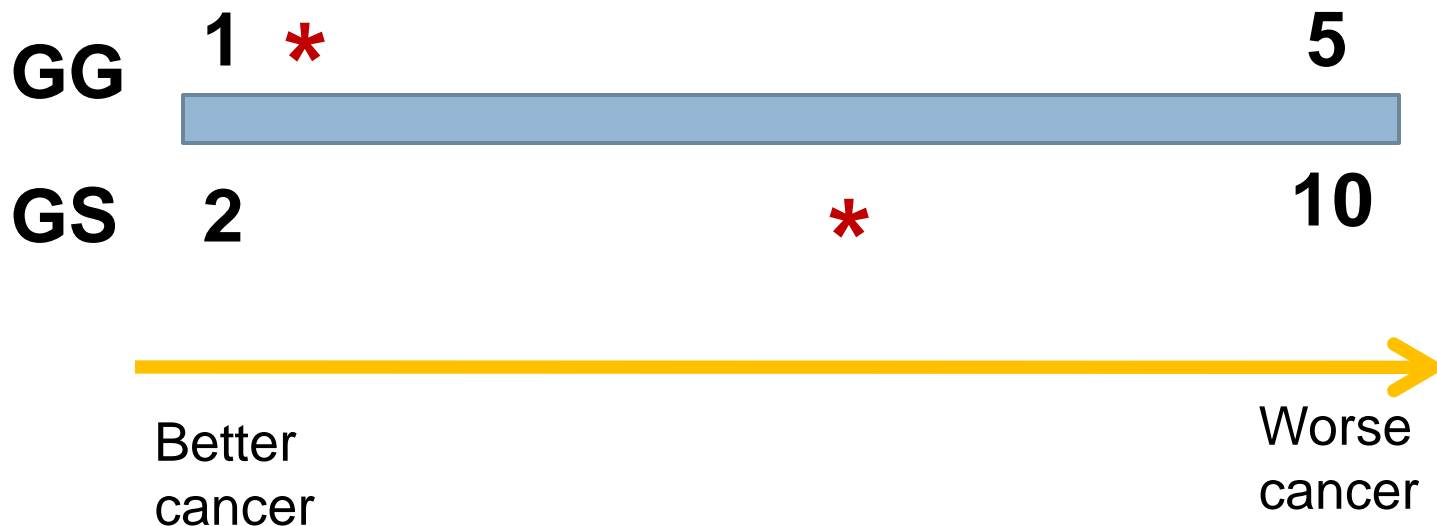
- “Indolent lesion of epithelial origin – IDLE
- Remove the term “cancer” from indolent, low malignant potential lesions or minimal risk lesions detected by screening
- Prevent overtreatment since although small volume, well-diff PCa has a 5 and 10yr survival of 99 and 97%, over 90% of patients receive surgery and/or radiation

2014 ISUP Prostate Cancer Grading Panel

- Issues with removing the “cancer” label
 - ▣ 20-25% of Gleason 6 PCa on biopsy are upgraded on the RP
 - Ie. Some may be “significant” cancers
 - ▣ Risk of patients being lost to follow-up when labeled with “IDLE”

2014 ISUP Prostate Cancer Grading Panel

- It may be easier to discuss surveillance options with patients if they are in ..
 - Grade Group 1 [Range 1-5]
 - vs Gleason Score 6/10 (3,3) [Range 2-10]



Grouping Gleason Scores

2-6 vs 7-10	Epstein 1993; Hanks 1995
2-5 vs 6-7 vs 8-10	Pilepich 1987
2-4 vs 5-7 vs 8-10	Russel 1991; Catalona 1994
2-4 vs 5-6 vs 7-10	Freedland 2000
2-6 vs 7 vs 8-10	D'Amico 1998; Tefilli 1999
2-5 vs 6 vs 7 vs 8-10	Bagshaw 1990
2-3 vs 4-6 vs 7 vs 8-10	Zagars 1995
2-4 vs 5-6 vs 7 vs 8-10	Ohori 1994; Epstein 1996
2-4 vs 5 vs 6 vs 7 vs 8-10	Partin 1997
2-3 vs 4-5 vs 6 vs 7-8 vs 9-10	Gleason 1977
2-6 vs 3+4 vs 4+3 vs 8-10	Makarov/Partin 2007
2-6 vs 3+4 vs 4+3 vs 8 vs 9-10	Eifler/Partin 2012

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*^{†‡}

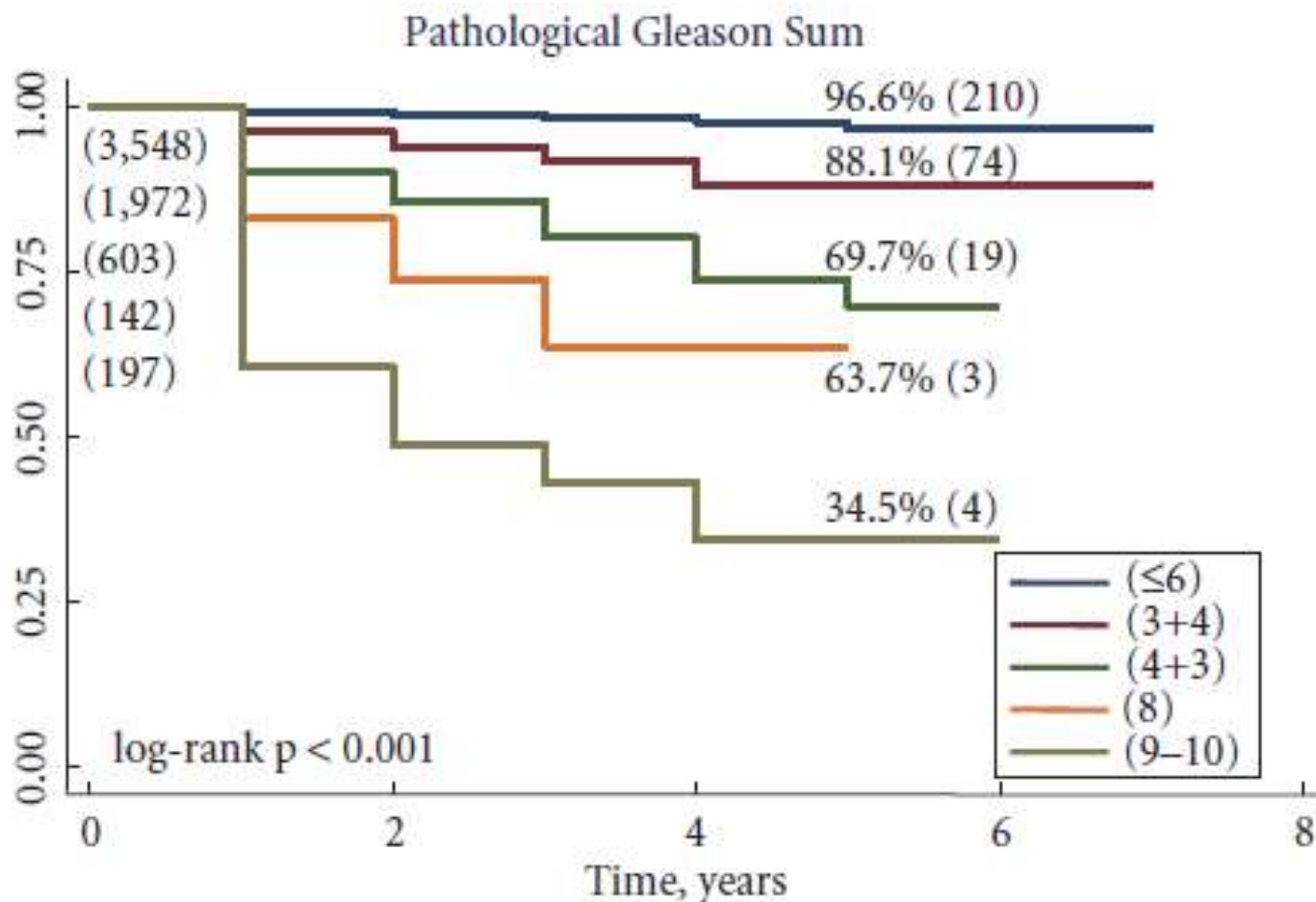
Departments of *Urology, [†]Pathology and [‡]Oncology, The Johns Hopkins Medical Institutions and The James Brady Buchannan Urological Institute, Baltimore, MD, USA

© 2013 BJU International | 111, 753–760

Table 5 Reporting of Gleason score Prognostic Grade Groups.

The overall Gleason score for this case is based on the core with the highest Gleason score. Gleason scores can be grouped and range from Prognostic Grade Group I (most favorable) to Prognostic Grade Group V (least favorable).	
Gleason score ≤ 6 :	Prognostic Grade Group I
Gleason score $3 + 4 = 7$:	Prognostic Grade Group II
Gleason score $4 + 3 = 7$:	Prognostic Grade Group III
Gleason score 8:	Prognostic Grade Group IV
Gleason score 9–10:	Prognostic Grade Group V

Fig. 1 Kaplan-Meier analysis of Gleason score at biopsy and RP pathological analysis. BFS at 2 and 4 years is shown. The number at risk is shown in brackets after each percentage surviving at a given time interval.



New Grading System (Novel Grouping)

- ▣ Grade Group 1 (GS $3+3=6$)
 - Excellent prognosis with no risk of lymph node mets (*AJSP* 2012;36: 1346-1352)
- ▣ Grade Group 2 (GS $3+4=7$)
 - Very good prognosis, rare mets
- ▣ Grade Group 3 (GS $4+3=7$)
 - Significantly worse prognosis
- ▣ Grade Group 4 (GS 8)
 - Bad prognosis, significantly better than group 5
- ▣ Grade Group 5 (GS 9-10)

Gleason Grade Grouping

The 2014 International Society of Urological Pathology
(ISUP) Consensus Conference on Gleason Grading of
Prostatic Carcinoma

Definition of Grading Patterns and Proposal for a New Grading System

Jonathan I. Epstein, MD, Lars Egevad, MD, PhD,† Mahul B. Amin, MD,‡ Brett Delahunt, MD,§
John R. Srigley, MD,|| Peter A. Humphrey, MD, PhD,¶ and the Grading Committee*

Am J Surg Path 2016; 40 (2): 244-252

Gleason Grade Grouping

TABLE 5. Histological Definition of New Grading System

Grade Group 1 (Gleason score ≤ 6) – Only individual discrete well-formed glands

Grade Group 2 (Gleason score $3 + 4 = 7$) – Predominantly well-formed glands with lesser component of poorly- formed/fused/cribriform glands

Grade Group 3 (Gleason score $4 + 3 = 7$) – Predominantly poorly-formed/fused/cribriform glands with lesser component of well-formed glands†

Grade Group 4 (Gleason score $4 + 4 = 8$; $3 + 5 = 8$; $5 + 3 = 8$)

Only poorly-formed/fused/cribriform glands *or*

Predominantly well-formed glands and lesser component lacking glands†† *or*

Predominantly lacking glands and lesser component of well-formed glands††

Grade Group 5 (Gleason scores 9-10) – Lacks gland formation (or with necrosis) with or w/o poorly formed/fused/cribriform glands†

†For cases with $> 95\%$ poorly-formed/fused/cribriform glands or lack of glands on a core or at RP, the component of $< 5\%$ well-formed glands is not factored into the grade.

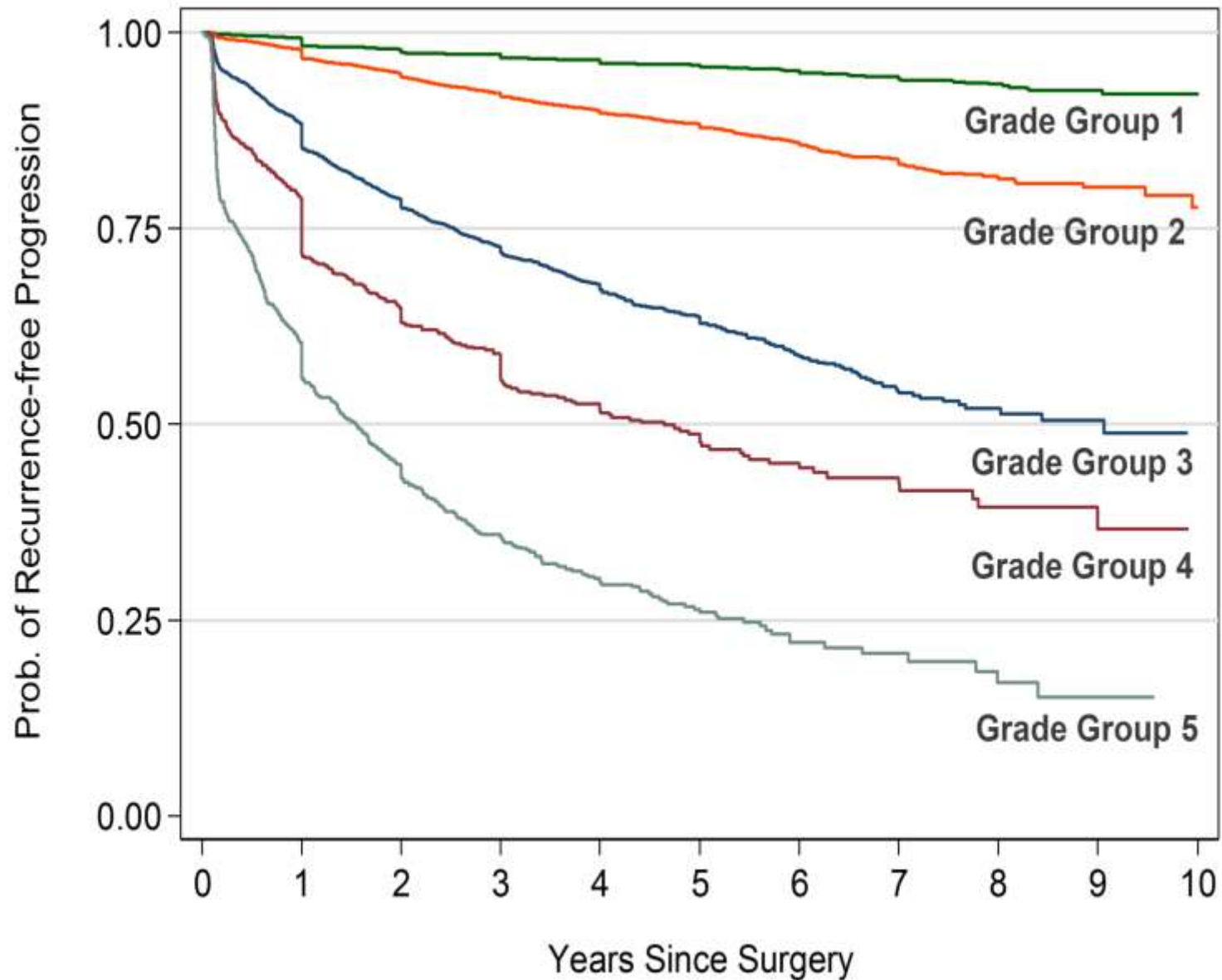
††Poorly-formed/fused/cribriform glands can be a more minor component.

RP data from five institutions



- Total 20845 RPs
 - Pittsburg
 - Karolinska
 - Hopkins
 - MSKCC
 - CCF

Biochemical Recurrence-Free Survival after Radical Prostatectomy



Gleason Grade Grouping

Grade Group	Hazard Ratio	5-Year Biochemical Recurrence-free Survival
Grade Group 1		96%
Grade Group 2	2.2	88%
Grade Group 3	7.3	63%
Grade Group 4	12.3	48%
Grade Group 5	23.9	26%

Gleason Grade Grouping

- Founded on the 1967-1973 Gleason system with many differences in the definitions and application of original system
 - ▣ Disappearance of GS 2-5
 - ▣ Poorly formed glands = GG4
 - ▣ All invasive cribriform glands = GG4
 - ▣ Summing Gleason patterns on RP vs PNB
- “New grading system” vs “novel grouping” of a modified Gleason grading system

Gleason Grade Grouping

Advantages

- More accurately reflects prostate cancer biology (eg 3+4 vs 4+3; 8 vs 9-10)
- Lower number of grade categories
 - ▣ 2, 3, 4, 5, 6, 7 (3+4), 7 (4+3), 8, 9, 10 vs 1-5
- Lowest grade is Grade group 1 vs Gleason score 6/10 when discussing cancer grade with patients
 - ▣ Even though many patients will have an excellent prognosis, the decision to go on active surveillance involves other factors than only Gleason score/Grade group (eg extent, PSA)
 - ▣ 20% may have unsampled higher grade disease

Gleason Grade Grouping

- 90% of participants in Chicago meeting: Yes
- Accepted by the WHO for the 2016 edition
 - ▣ Pathology and Genetics: Tumours of the Urinary System and Male Genital Organs
- Used in conjunction with the Gleason system
 - ▣ Gleason score $3+3=6$ (ISUP Grade Group 1)

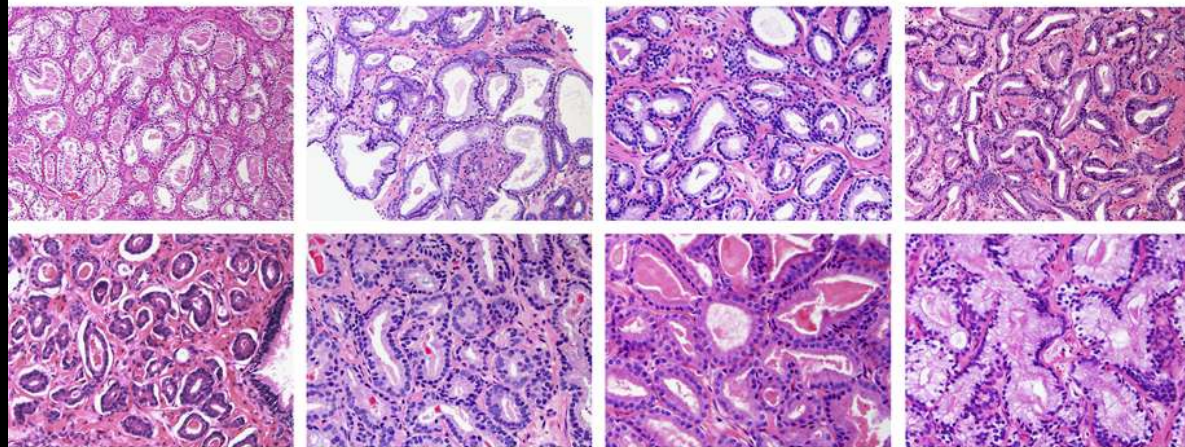
Prostate Cancer Grading

- Review of Evolution of Prostate Cancer Grading
 - ▣ 1966 Gleason Grading System for Prostate Cancer
 - ▣ 2005 ISUP Modified Gleason Grading
- Proposal for New Grade Grouping
 - ▣ ISUP Nov 2014: Prostate Cancer Grading Panel, Chicago
 - Clarification of previous ambiguous grading issues
 - Intraductal carcinoma
 - New Grade Grouping

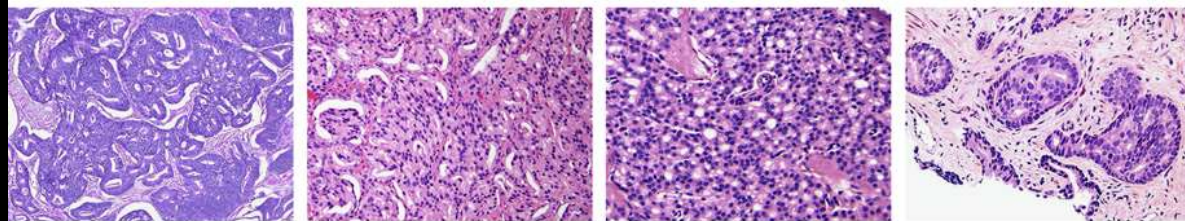
Prostate Cancer Grading: A Contemporary Photomontage

Jl Epstein
AJSP 2016 40:137-8

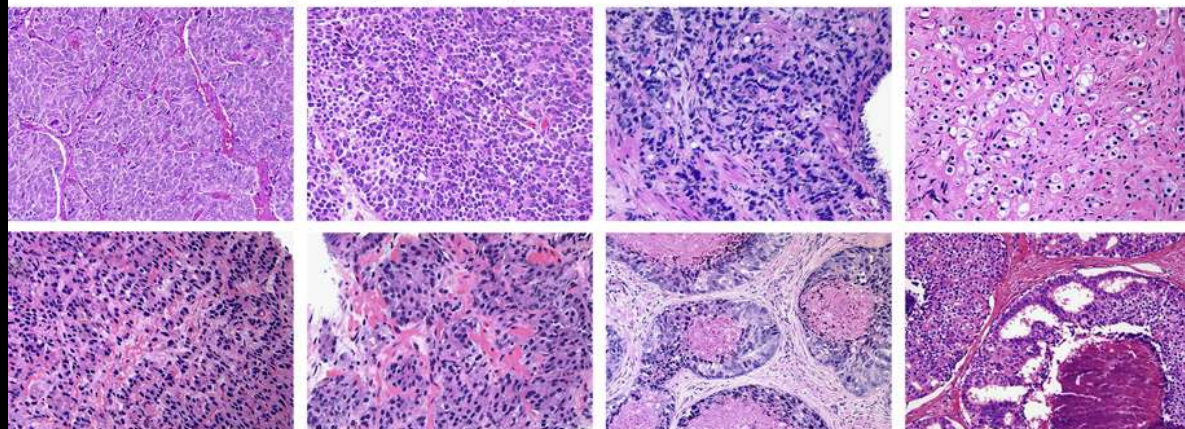
Discrete Well-formed Glands (Gleason Patterns 1-3)



Cribriform/Poorly-formed/Fused Glands (Gleason Pattern 4)



Sheets/Cords/Single Cells/Solid Nests/Necrosis (Gleason Pattern 5)



PROSTATE CANCER GRADING: An Update from the 2014 ISUP Consensus Conference

Dr. J. Merrimen
Associate Professor
Depts of Pathology and Urology
Dalhousie University

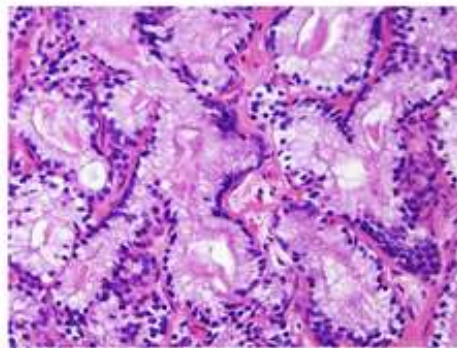
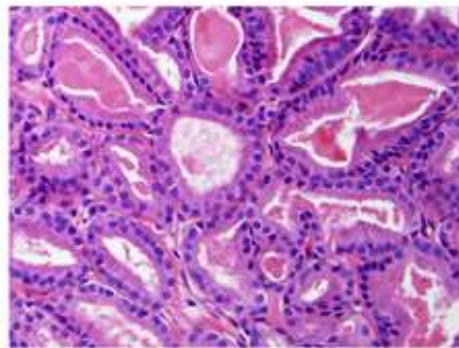
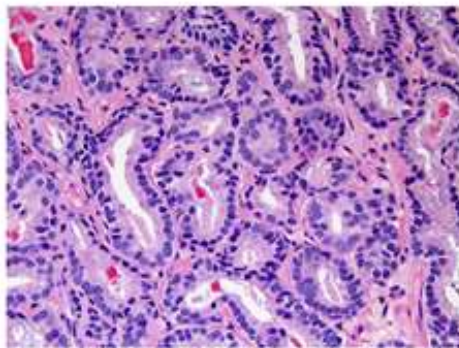
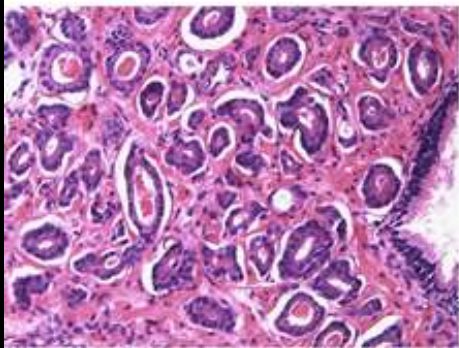
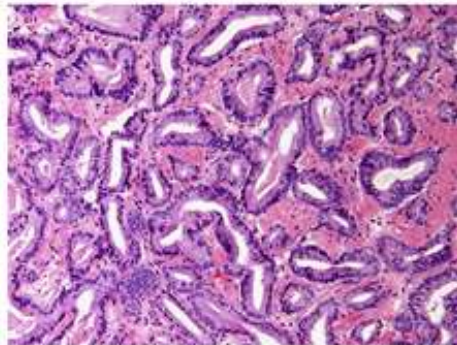
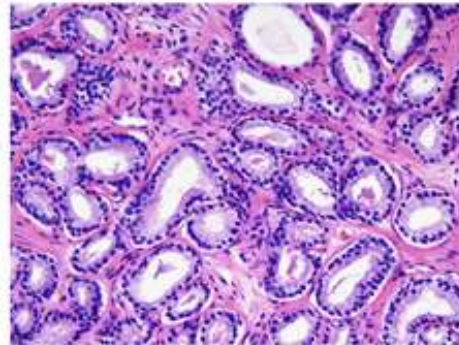
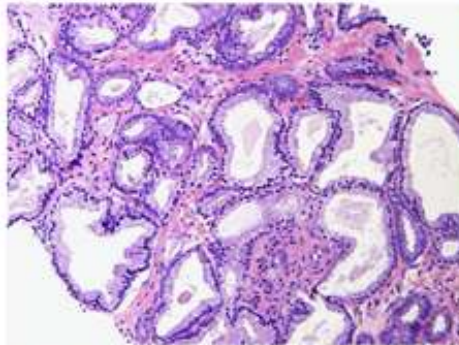
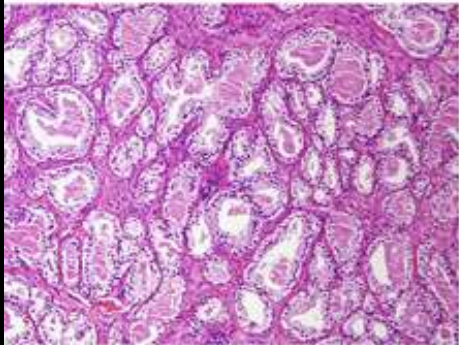
how do you make
the face for "yay"?

Am I
doing it?

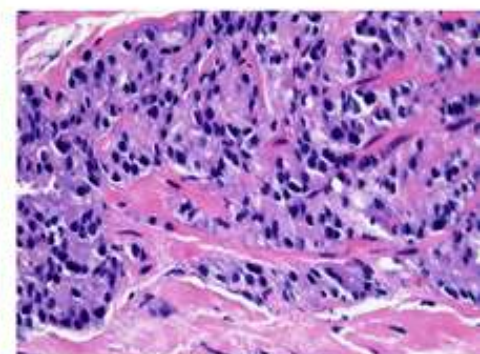
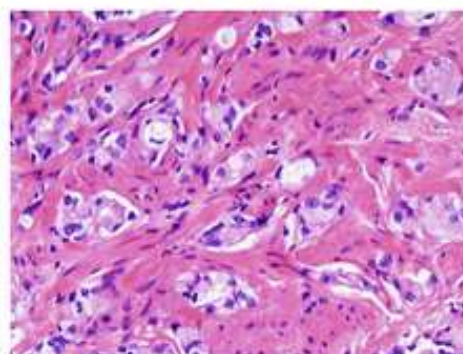
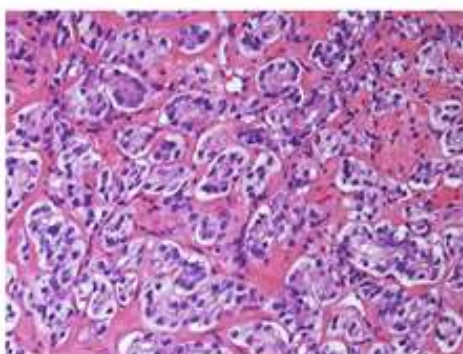
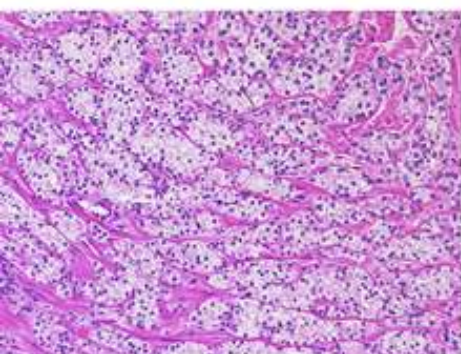
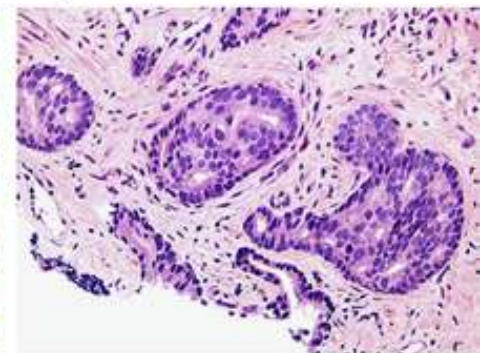
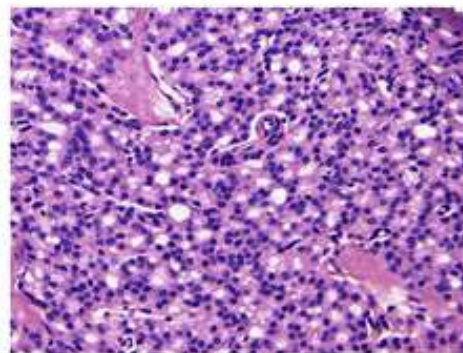
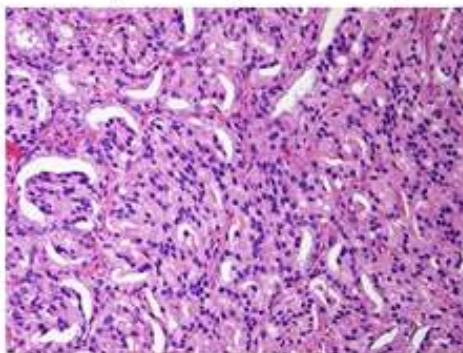
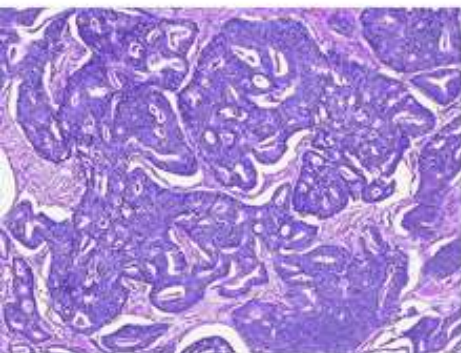
I hope
I'm doing
it.



Discrete Well-formed Glands (Gleason Patterns 1-3)



Cribriform/Poorly-formed/Fused Glands (Gleason Pattern 4)



Sheets/Cords/Single Cells/Solid Nests/Necrosis (Gleason Pattern 5)

