2017 Annual Meeting | September 14-17 | Deerhurst Skyline Resort | Huntsville, Ontario

Update on Reporting Prostate Cancer Pathology

COLLEGE of AMERICAN PATHOLOGISTS

Cancer Care Ontario

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Disclosures

- None

Learning Objectives

- Identify sources of data sets for reporting prostate specimens containing cancer
- Review recommended and optional items to be reported in prostate biopsies and prostatectomy specimens
- Discuss practical issues concerning recent changes to reporting guidelines, Gleason scoring and the application of Grade Groups in contemporary practice
- Review emerging topics of prognostic significance in prostate pathology.

CANCER PROTOCOL TEMPLATES

www.cap.org/

Protocol for the Examination of Specimens From Patients With Carcinoma of the Prostate Gland

Version: Prostate 4.0.0.0 **Protocol Posting Date:** June 2017

Includes pTNM requirements from the 8th Edition, AJCC Staging Manual

Revised Cancer Protocols and Electronic Cancer Checklists now available

The revised protocols now incorporate changes to tumor stage classification from the AJCC 8th edition Cancer Staging Manual and updated WHO classifications.

READ MORE »

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Protocol for the Examination of Specimens From Patients With Carcinoma of the Prostate Gland

Version: Prostate 4.0.0.0 **Protocol Posting Date:** June 2017
Includes pTNM requirements from the 8th Edition, AJCC Staging Manual

CAP Prostate Protocol Revision History

Summary of Changes
The following changes have been made since the June 2012 release.

This is a major revision to the protocol. Extensive changes have been made throughout the document.

Note: The Needle Biopsy case summary has been divided into 2 case summaries: specimen level and case level.

- Gleason score – Grade Group (ISUP Grade)
  - case level (composite) or specimen level *for biopsies*
  - % pattern 4 and/or 5
- intraductal carcinoma
- no more sub-staging of pT2 *for radical prostatectomy specimens*

INTERNATIONAL COLLABORATION ON CANCER REPORTING

Prostate Cancer Histopathology Reporting Guide
Radical Prostatectomy Specimen

Prostate Core Needle Biopsy Histopathology Reporting Guide
Part 1 - Clinical Information/Specimen Receipt

Prostate Core Needle Biopsy Histopathology Reporting Guide
Part 2 - Specimen Level Reporting

Cancer Care Ontario

https://www.cancercare.on.ca/

Performance of Needle Biopsy of the Prostate for Men with Suspected or Established Prostate Cancer

Report Date: September 2017

Recommendation Report

A special report developed by the Surgical Oncology Program at

Cancer Care Ontario in conjunction with the Prostate Biopsy Expert Panel

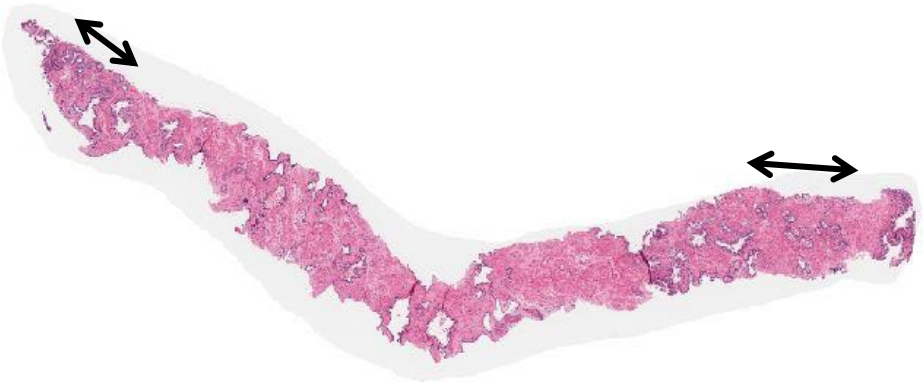
- Ordering of Prostate Biopsy
- Pre- and Peri-Biopsy Management
- Biopsy Technique
- Pathology
- Human Resources and Training
- Facility Requirements

This report was developed by Dr. Rajiv Singal (Chair), MD; Dr. Joseph Chin, MD; Dr. Christopher Morash, MD; Dr. Roland Sing, MD; Dr. John Srigley, MD; Dr. Andrew Evans, MD; Dr. Ants Toi, MD; Leigh McKnight, HBMSc; Dr. Alice Wei, MD; and Dr. Robin McLeod, MD.

Prostate Biopsies: Recommended Elements

- **Histologic type -** acinar-type adenocarcinoma (99.5%)
- **Histologic grade - Gleason Score**
  - ✓ Gleason primary (predominant)
  - ✓ Gleason worst remaining
  - ✓Grade Group
  - ✓ % pattern 4 for Gleason score 7/10 (3+4)
- **Tumour quantitation**
  - ✓ Number positive cores/total number of cores
  - ✓ % core involvement for each positive core
  - ✓ *total mm cancer/total mm prostate tissue*
- **Periprostatic fat invasion -** (yes/no)
- **Seminal vesicle/ejaculatory duct invasion -** (yes/no/not applicable)

Extent Involvement in Active Surveillance: The Devil is in the Details!



Active Surveillance

- Observation with curative intent
- Regular follow-up:
  - PSA
  - DRE
  - serial biopsies
  - imaging (prostate MRI)
- Treatment as soon as low-risk cancers become higher risk/progress
- Avoid negative impacts of overtreatment for disease that remains low-risk

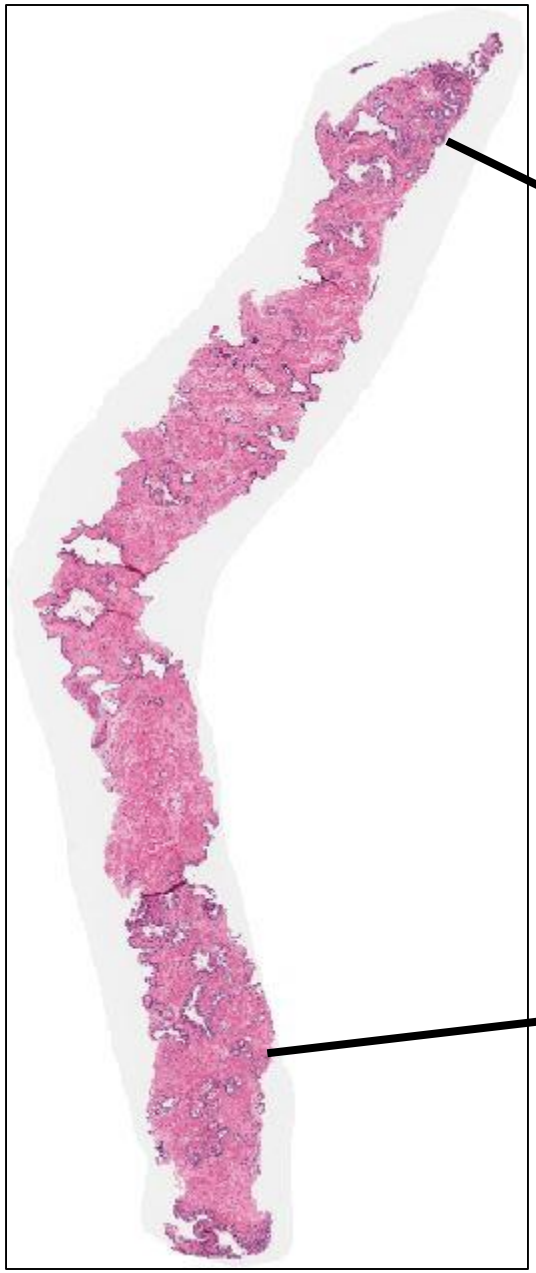
Special Article

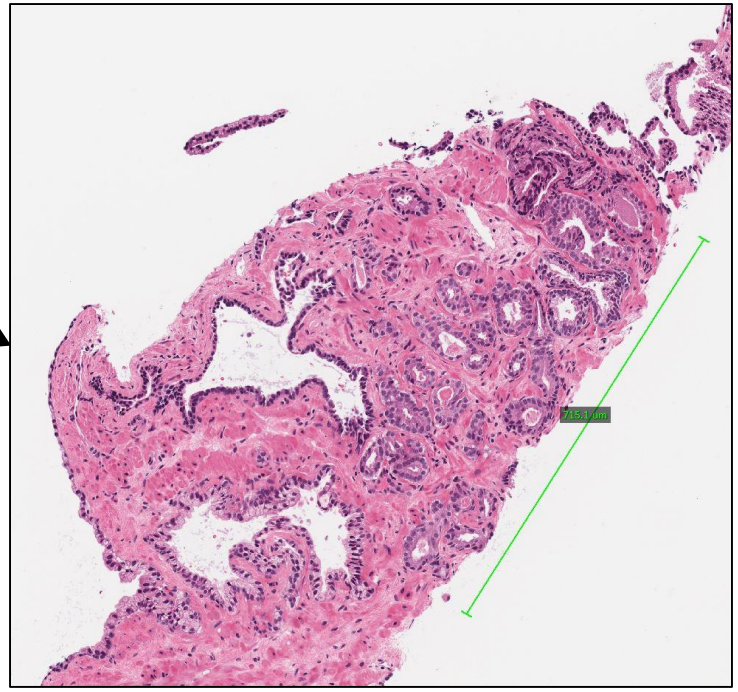
The Critical Role of the Pathologist in Determining Eligibility for Active Surveillance as a Management Option in Patients With Prostate Cancer

Consensus Statement With Recommendations Supported by the College of American Pathologists, International Society of Urological Pathology, Association of Directors of Anatomic and Surgical Pathology, the New Zealand Society of Pathologists, and the Prostate Cancer Foundation

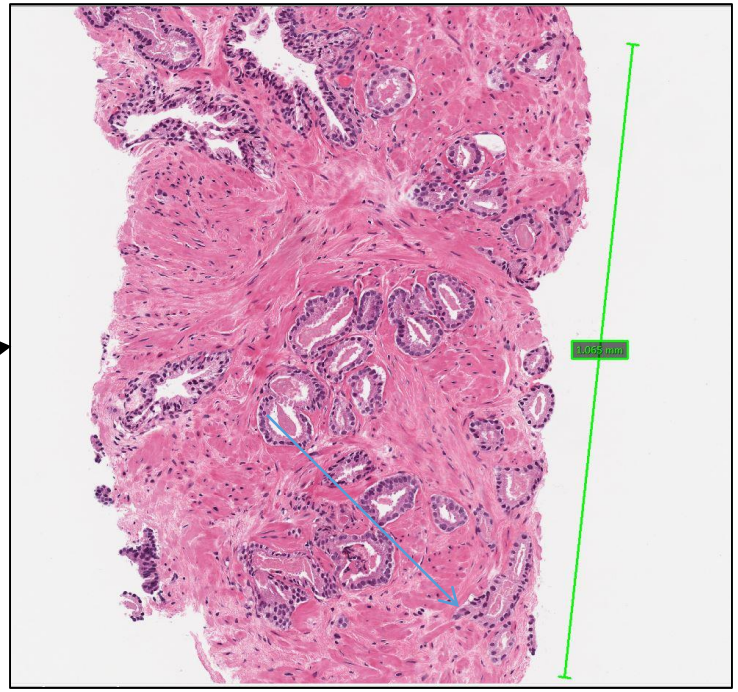
Mahul B. Amin, MD; Daniel W. Lin, MD; John L. Gore, MD, MS; John R. Srigley, MD, FRCPC, FRCPath; Hema Samaratunga, MBBS, FRCPA; Lars Egevad, MD; Mark Rubin, MD; John Nacey, MD; H. Ballentine Carter, MD; Laurence Klotz, MD; Howard Sandler, MD; Anthony L. Zietman, MD; Stuart Holden, MD; Rodolfo Montironi, MD, FRCPath, IFCAP; Peter A. Humphrey, MD, PhD; Andrew J. Evans, MD; Jonathan I. Epstein, MD; Brett Delahunt, MD; Jesse K. McKenney, MD; Dan Berney, MD; Thomas M. Wheeler, MD; Arul M. Chinnaiyan, MD, PhD; Lawrence True, MD; Beatrice Knudsen, MD, PhD; M. Elizabeth H. Hammond, MD

Arch Pathol Lab Med. 2014;138:1387–1405

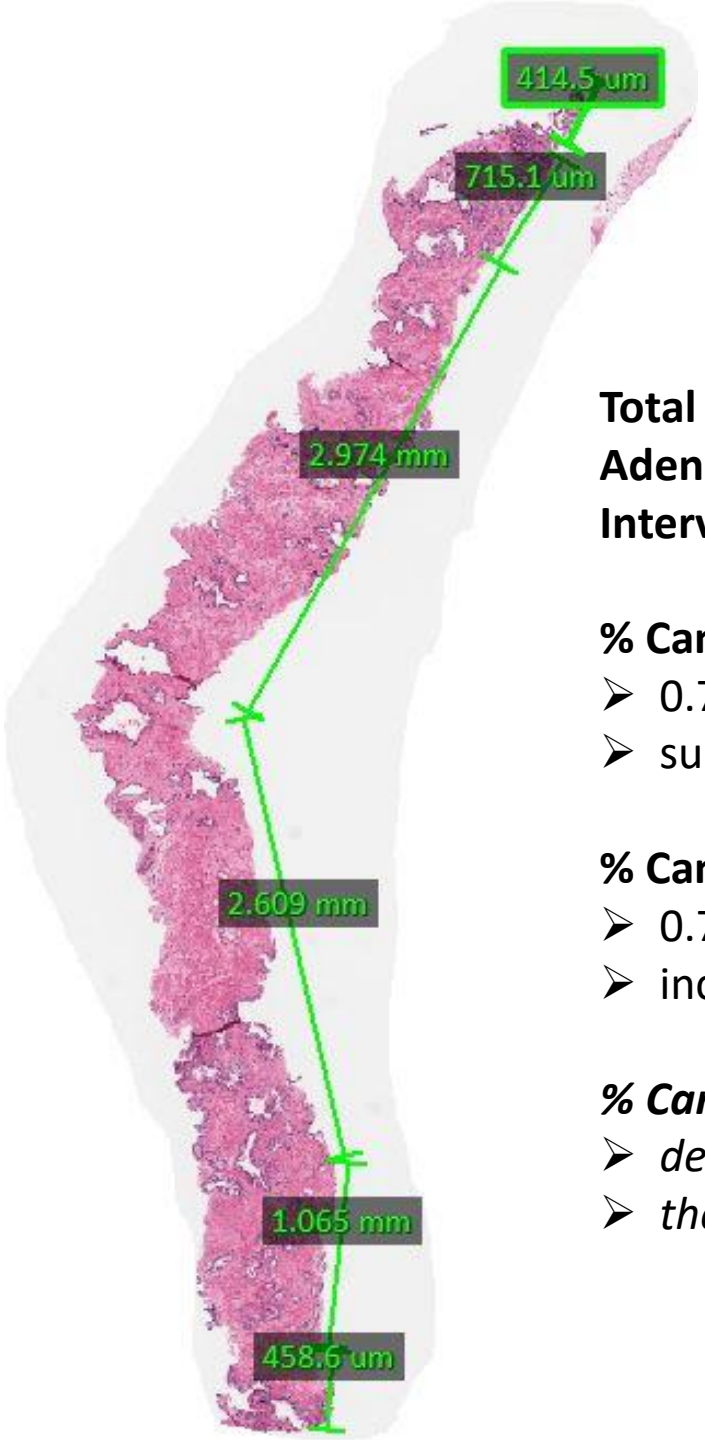




0.7 mm



1.1 mm



Total core length = 8.2 mm
Adenocarcinoma = 1.8 mm
Intervening benign tissue = 5.6 mm

% Cancer Option 1 = 20%

- 0.7 + 1.1 mm
- subtracting intervening benign tissue

% Cancer Option 2 = 90% (discontinuous involvement)

- 0.7 + 3.0 + 2.6 + 1.1 mm
- including intervening benign tissue

% Cancer Option 3

- *descriptive reporting*
- *the "compromise" option*

Bottom Line on Reporting Discontinuous Core Involvement

- Be consistent in how you handle benign intervening stroma
- Make sure your clinical colleagues are aware of how you do this
- Descriptive reporting option:
  - ✓ 2 discontinuous foci measuring 1.8 mm in total
  - ✓ involvement of 20% of the core and spanning 90% of the core

Should Intervening Benign Tissue Be Included in the Measurement of Discontinuous Foci of Cancer on Prostate Needle Biopsy? Correlation With Radical Prostatectomy Findings

Sarah Karram, MD, Bruce J. Trock, PhD,† George J. Netto, MD,*†‡ and Jonathan I. Epstein, MD*†‡*

(*Am J Surg Pathol* 2011;35:1351–1355)

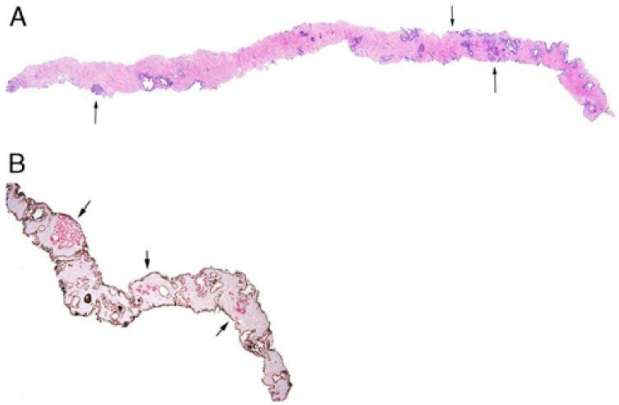


FIGURE 1. A, Several small foci of adenocarcinoma (arrows) discontinuously involve 80% of the length of the core (measured at Johns Hopkins), compared with 7% core involvement (excluding benign tissue) recorded at the outside institution. B, Different case from Figure 1A with triple stain consisting of p63 and high-molecular weight cytokeratin (brown chromogen) and racemase (red chromogen) showing 3 discontinuous foci of adenocarcinoma with lack of basal cells and positivity for racemase (arrows). The tumor discontinuously involved 50% of the core length (measured at Johns Hopkins), compared with 15% when intervening benign tissue was discounted (measured at outside institution).

TABLE 1. Maximum Percentage of Cancer per Core per Case

	Hopkins (%)	Outside Institutions (%)
Mean	64.2	28.8
Median	70	23
Range	20-100	1-80

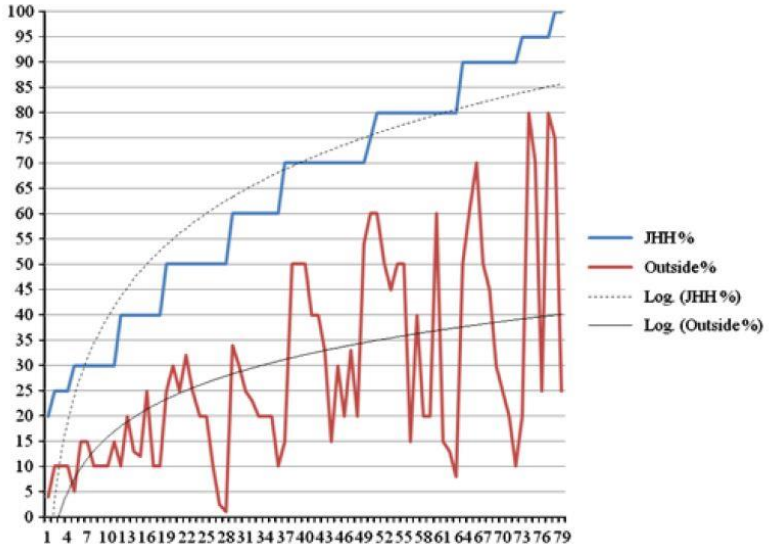


FIGURE 2. A case by case comparison between the maximum percentage of cancer per core per case reported at Johns Hopkins (JHH %) (upper curve) compared with that of the outside institutions (outside %) (lower curve).

JHH Experience:
Including intervening benign tissue better predicted pT and surgical margin status

TABLE 2. Association of Preoperative Parameters With Organ-Confined Disease

	Organ Confined	Nonorgan Confined	*P*
Mean PSA (ng/mL)	4.7	6.7	0.017
Mean JHH max %	59.7%	75.2%	0.004
Mean outside max %	25.7%	36.4%	0.027
Clinical stage			0.851
T1c	41 (76%)	17 (74%)	
T2	13 (24%)	6 (26%)	

JHH indicates the Johns Hopkins Hospital; Max %, maximum percentage of cancer per core per case.

TABLE 3. Association of Preoperative Parameters With Surgical Margins

	Positive Surgical Margins	Negative Surgical Margins	*P*
Mean PSA (ng/mL)	7.3	4.8	0.013
Mean JHH max %	79.3	61.0	0.004
Mean outside max %	34.5	27.6	0.238
Clinical stage			0.755
T1c	11 (79%)	47 (75%)	
T2	3 (21%)	16 (25%)	

JHH indicates the Johns Hopkins Hospital; Max %, maximum percentage of cancer per core per case.

One Tumour or Two?

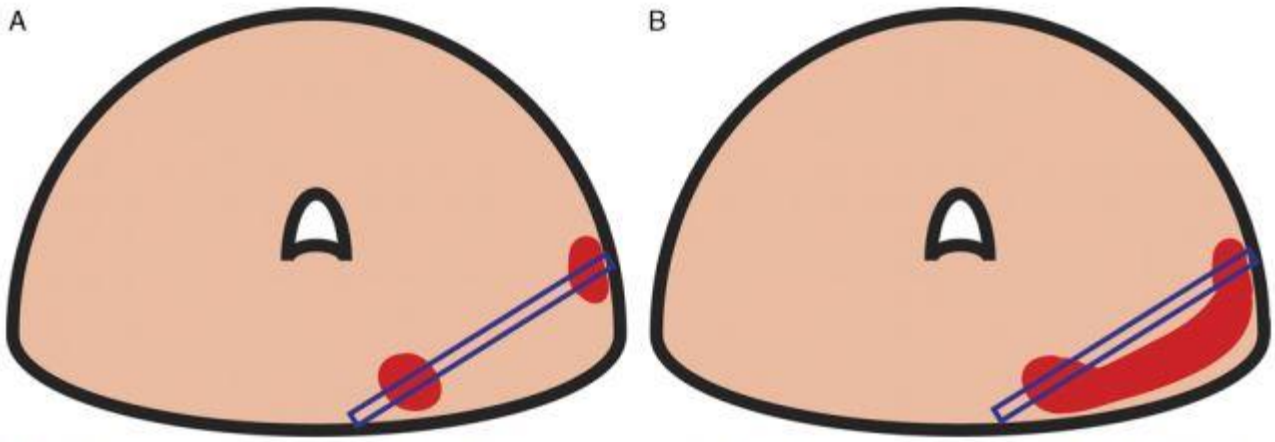
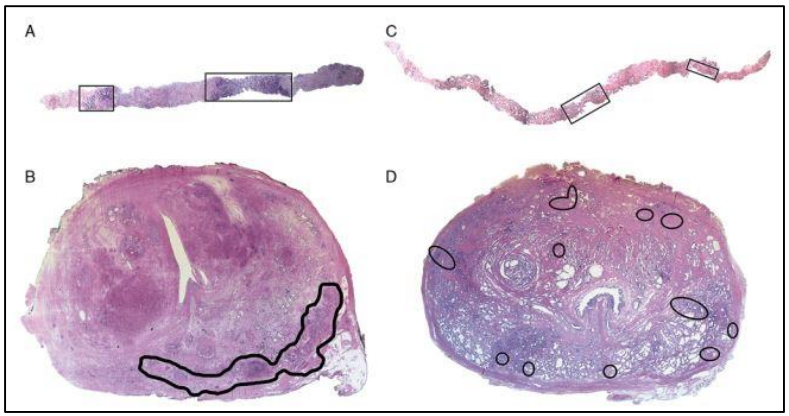


FIGURE 1. Diagrammatic representation of hypothesized tumor configurations in the prostate gland that could yield a discontinuously positive core needle biopsy. A, Two small (potentially clinically insignificant) tumor foci located in the right posterior peripheral zone are sampled by a single core biopsy with benign intervening tissue. B, A large, crescent-shaped tumor focus is present in the same region of the prostate gland and intersects the core biopsy path at 2 different points, separated by benign intervening tissue.

Does Discontinuous Involvement of a Prostatic Needle Biopsy Core by Adenocarcinoma Correlate With a Large Tumor Focus at Radical Prostatectomy?

Javier A. Arias-Stella, III, MD, Kavita R. Varma, MD,* Diego Montoya-Cerrillo,*†*
Nilesh S. Gupta, MD, and Sean R. Williamson, MD**

(*Am J Surg Pathol* 2015;39:281–286)

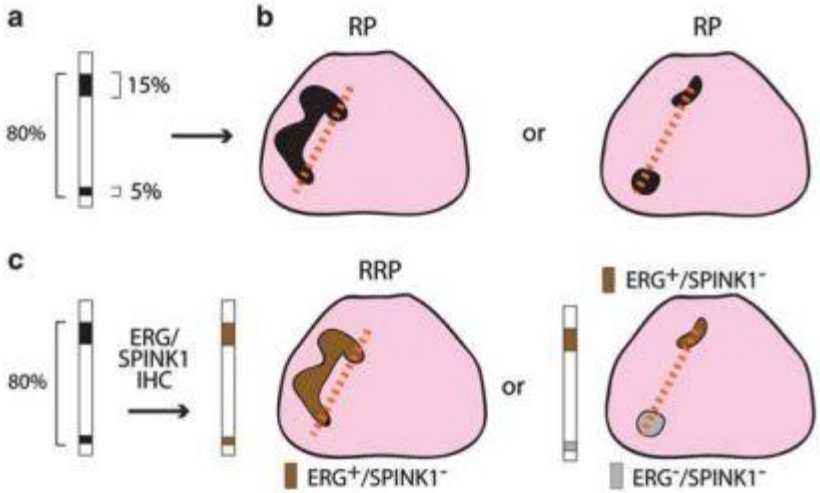


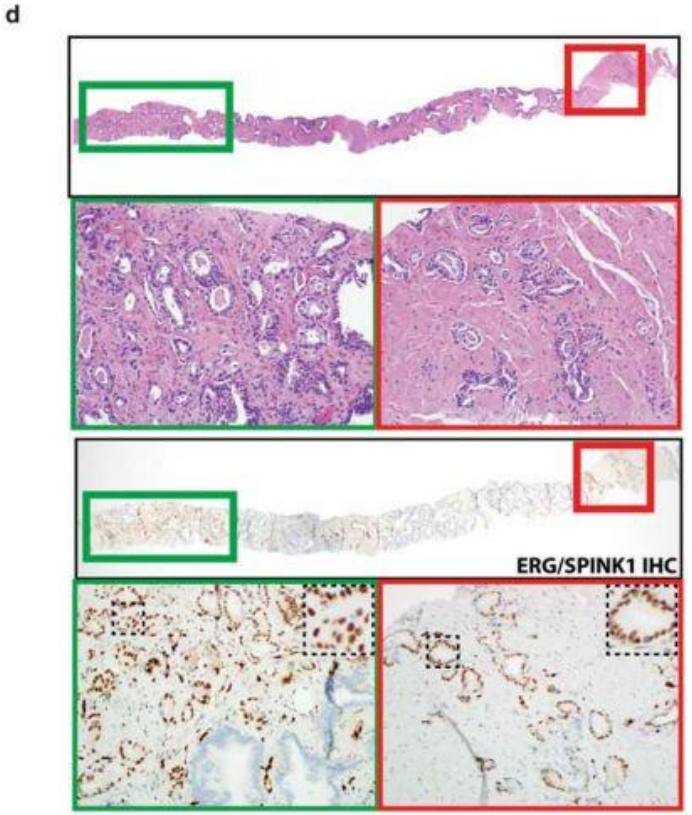
- 40 biopsy-radical prostatectomy pairs
- biopsy core with highest % involvement showing discontinuous involvement (≥ 2 mm gap of intervening benign tissue)
- 31/40 (78%) cases were associated with a single large focus at radical prostatectomy (often irregularly shaped)

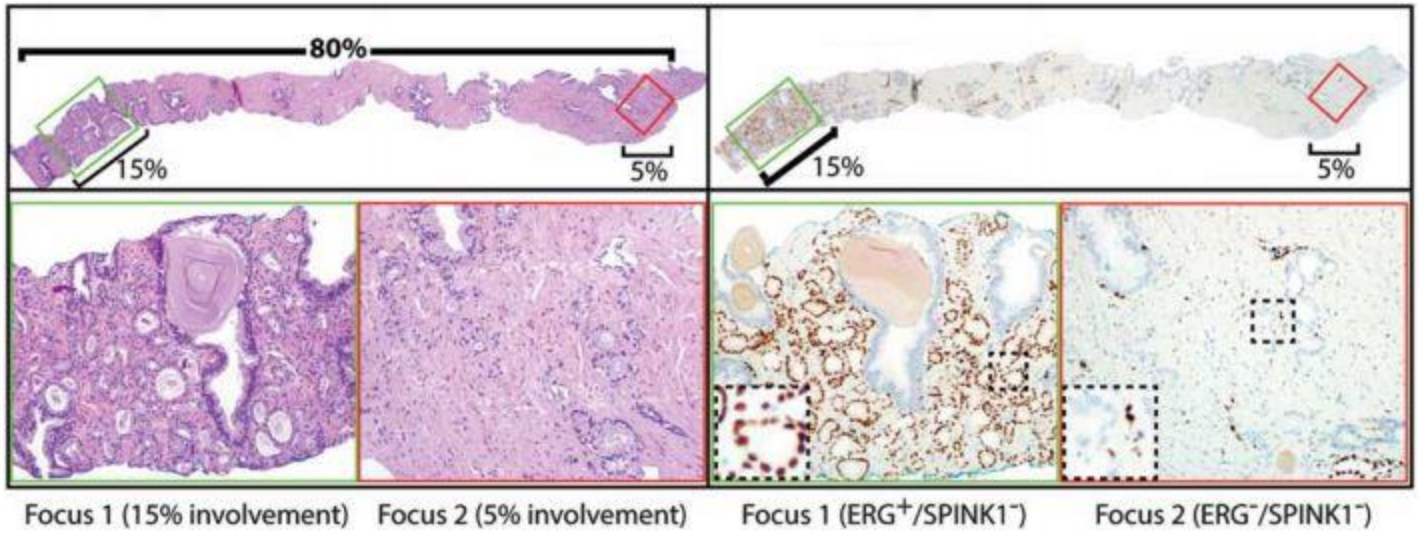
Clonal evaluation of prostate cancer foci in biopsies with discontinuous tumor involvement by dual ERG/SPINK1 immunohistochemistry

MODERN PATHOLOGY (2016) 29, 157–165

Jacqueline Fontugne[1,2,6], Kristina Davis[3,6], Nallasivam Palanisamy[3,7], Aaron Udager[3], Rohit Mehra[3,4], Andrew S McDaniel[3], Javed Siddiqui[3,4], Mark A Rubin[1,2], Juan Miguel Mosquera[1,2,8] and Scott A Tomlins[3,4,5,8]







- Dual ERG/SPINK1 immunohistochemistry (IHC)
- Discrepant staining between foci = different clones/tumours

- 97 biopsies (80 patients) with at least 2.5 mm intervening benign prostate between foci
- Gleason scores 6-9/10
- 20-100% core involvement (including intervening benign prostate)

- **25% of cores with discontinuous involvement harbour distinct cancer clones - <u>exclude</u> intervening benign prostate in these cases when reporting % core involvement.**

Prostate Biopsies: Optional Elements

- **% Gleason pattern 4 and 5** for Gleason score $\geq$ 7/10 (4+3)
- **Intraductal carcinoma -** (yes/no)
- **Lymphovascular invasion -** (yes/no)
- **Perineural invasion -** (yes/no)
- **Additional findings**
  - ✓ None identified
  - ✓ HG PIN
  - ✓ Adenosis
  - ✓ Inflammation - specify type
  - ✓ Other

Prostate Biopsies: Specimen vs Case Level

- **Specimen level** - individual diagnostic line for each part
- **Case level** - summary (synoptic) for all parts

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In situations where a case level summary is used and specimen level summaries are not used, the Gleason patterns, score, grade group and tumor extent should be documented for each positive specimen (container) in the line diagnosis. The essential information could be conveyed with a simple diagnostic line such as, "Adenocarcinoma, Gleason grade 3 + 4 = score of 7 (Grade group 2), in 1 of 2 cores, involving 20% of needle core tissue, and measuring 4 mm in length." (Note A.)

Prostatectomy: Recommended Elements

- **Histologic type -** acinar-type adenocarcinoma (99.5%)
- **Histologic grade - Gleason score**
  - ✓ Gleason primary (predominant)
  - ✓ Gleason secondary
  - ✓ Gleason tertiary - *≤ 5% not incorporated into Gleason score*
  - ✓ Grade Group
- **Tumour quantitation**
  - ✓ Estimated % involvement
  - ✓ Size of "dominant" nodule (if present)
- **Extraprostatic extension -** (no/yes)
  - ✓Focal or non-focal

Prostatectomy: Recommended Elements

- **Urinary bladder neck invasion -** (no/yes)
- **Seminal vesicle invasion -** (no/yes/no seminal vesicle present)
- **Surgical margins**
  - ✓ Uninvolved
  - ✓ Involved
    - Limited (≤ 3 mm) or non-limited (≥ 3 mm)
- **Treatment effect**
  - ✓ Hormone therapy - no Gleason score
- **Regional lymph nodes**
  - ✓ No lymph nodes submitted/found
  - ✓ Number involved/number examined
  - ✓ *Size of lymph nodes/metastatic deposits – optional*
  - ✓ *Extranodal extension - optional*

Prostatectomy: Optional Elements

- **% pattern 4 and/or 5 -** for Gleason score > 7/10
- **Intraductal carcinoma -** (no/yes)
- **Extraprostatic extension -** location(s)
- **Surgical margins**
  - ✓ Linear extent(s) in mm
  - ✓ Unifocal or multifocal
  - ✓ Gleason pattern at a positive margin
- **Margin positivity at a site of extraprostatic extension**
- **Lymphovascular invasion**
- **Perineural invasion**

Prostatectomy: Pathologic Staging (pT)

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Primary Tumor (pT)[#]

___ pT2: Organ confined
___ pT3: Extraprostatic extension
___ pT3a: Extraprostatic extension (unilateral or bilateral) or microscopic invasion of bladder neck
___ pT3b: Tumor invades seminal vesicle(s)
___ pT4: Tumor is fixed or invades adjacent structures other than seminal vesicles such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall

[#] *Note: There is no pathologic T1 classification.*

CAP Laboratory Accreditation Program Protocol Required Use Date: March 2018*

** Beginning January 1, 2018, the 8th edition AJCC Staging Manual should be used for reporting pTNM.*

2014 ISUP Consensus Conference: Are More Revisions to the Gleason System Really Necessary?

International Society of Urological Pathology

ISUP Consensus Conference: Chicago, November 1, 2014

- Recognized need for further modifications
  - lack of consensus on specific grading issues
  - some grading issues not covered in 2005
  - changes in prostate cancer management
- 67 urological pathologists (17 countries)
- 17 clinical leaders
- Presentations/discussions on key issues
  - voting on evidence-based recommendations

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 and the Grading Committee*

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

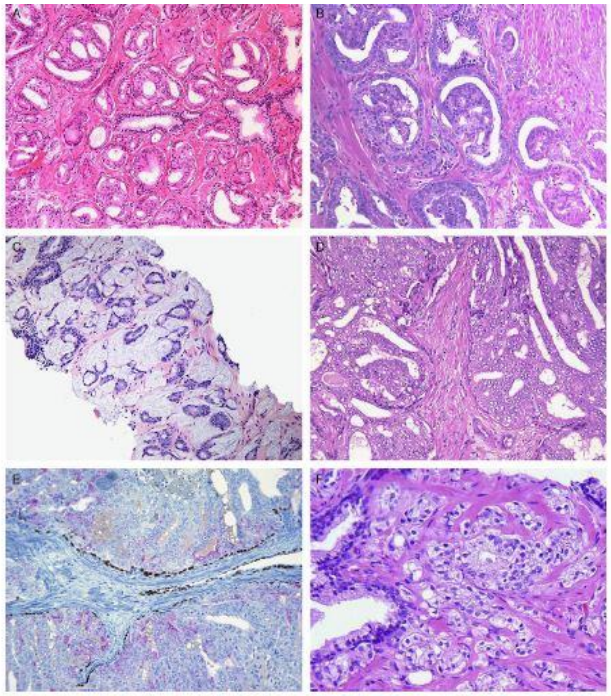

FIGURE 1. A, Gleason pattern 4 consisting of small round cribriform glands; before the 2014 consensus conference these were variably graded as either Gleason pattern 3 or 4. B, Small glomeruloid glands graded as Gleason pattern 4; there was no consensus as to how to grade in the 2005 conference. C, Mucinous carcinoma composed of discrete well-formed glands of Gleason pattern 3; before the 2014 consensus conference there was controversy how to grade. D, IDC with dense cribriform glands, which is not assigned a grade, an issue not discussed in the 2005 conference. E, Same case as (D) with p63-positive basal cells (brown chromogen) verifying carcinoma is intraductal. F, Predominantly poorly formed glands of Gleason pattern 4.

TABLE 4. Morphologies Within Gleason Patterns

1. Gleason pattern 4 includes cribriform, fused, and poorly formed glands.
   VOTE: 100% Yes
2. The term hypernephromatoid cancer should not be used.
   VOTE: 78% Yes
3. For a diagnosis of Gleason pattern 4, it needs to be seen at ×10 lens magnification.
   VOTE: 78% Yes
4. Occasional/seemingly poorly formed or fused glands between well-formed glands is insufficient for a diagnosis of pattern 4.
   VOTE: 85% Yes
5. All glomeruloid glands should be graded as Gleason pattern 4 regardless of morphology.
   VOTE: 100% Yes
7. In cases with borderline morphology between Gleason pattern 3 and pattern 4 and crush artifacts, the lower grade should be favored.
   VOTE: 98% Yes
8. Branched glands are allowed in Gleason pattern 3.
   VOTE: 94% Yes
9. Small solid cylinders represent Gleason pattern 5.
   VOTE: 87% Yes
10. Solid medium to large nests with rosette-like spaces should be considered to represent Gleason pattern 5.
    VOTE: 88% Yes
11. Presence of unequivocal comedonecrosis, even if focal is indicative of Gleason pattern 5.
    VOTE: 94% Yes
12. Rarely, discrete glands (otherwise pattern 3) with necrotic debris within the lumens represents Gleason pattern 5.
    VOTE: 49% Yes

Voting Summary

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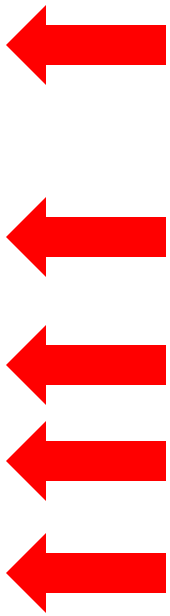
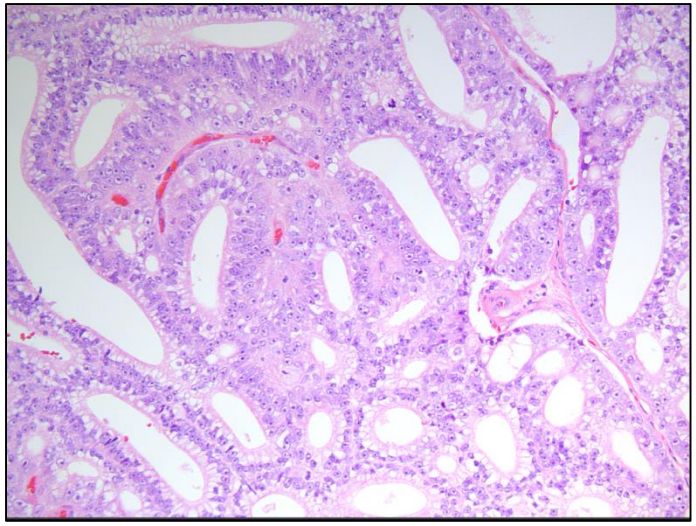


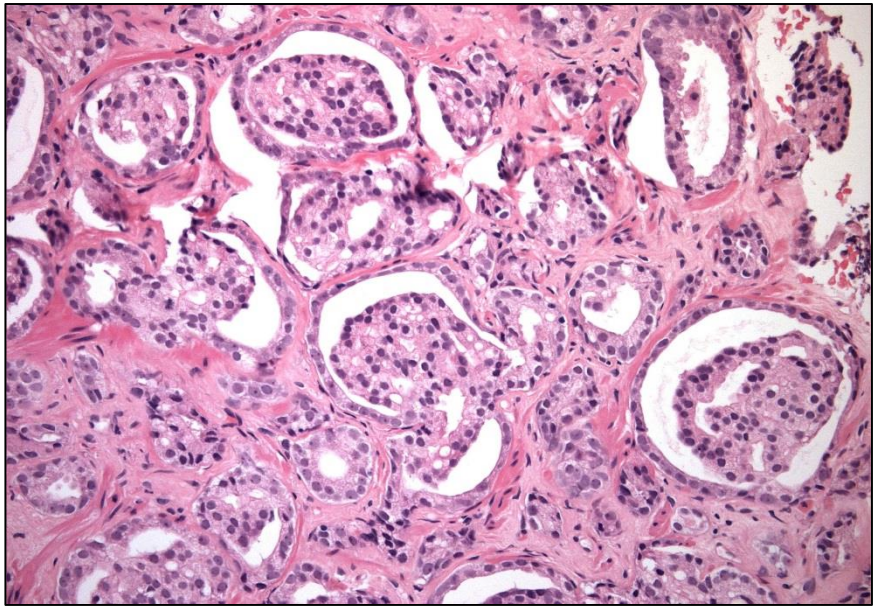
All Cribriform Glands = Pattern 4

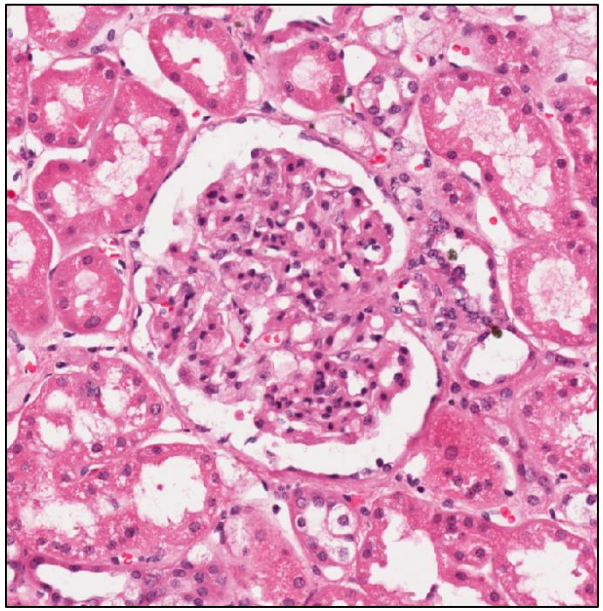


Sieve-like architecture (glands within glands)

- Original and 2005 modified Gleason allowed cribriform pattern 3
- 2008 - poor reproducibility for small cribriform glands
- 2011-2014 - cribriform glands (large and small) in prostatectomy specimens associated with biochemical failure

Glomeruloid Glands = Pattern 4

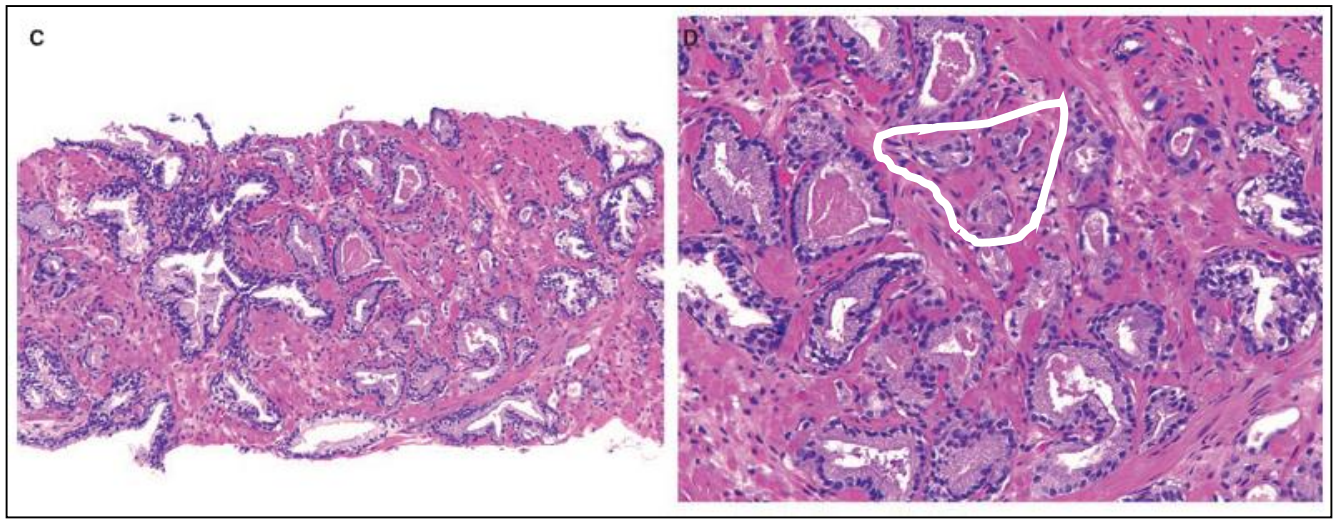




- No consensus in 2005
- 2009 - glomeruloid glands associated with higher grade cancer (> 80% of cases on biopsy)

Borderline Pattern 3 vs 4?

- Tangential sectioning, crush artifact, occasional poorly-formed glands
- Choose the lower pattern



Histopathology

Histopathology 2013, **62**, 247–256. DOI: 10.1111/his.12008

Standardization of Gleason grading among 337 European pathologists

Lars Egevad,[1] Amar S Ahmad,[2] Ferran Algaba,[3] Daniel M Berney,[4] Liliane Boccon-Gibod,[5] Eva Compérat,[6] Andrew J Evans,[7] David Griffiths,[8] Rainer Grobholz,[9] Glen Kristiansen,[10] Cord Langner,[11] Antonio Lopez-Beltran,[12] Rodolfo Montironi,[13] Sue Moss,[2] Pedro Oliveira,[14] Ben Vainer,[15] Murali Varma[8] & Philippe Camparo[16]

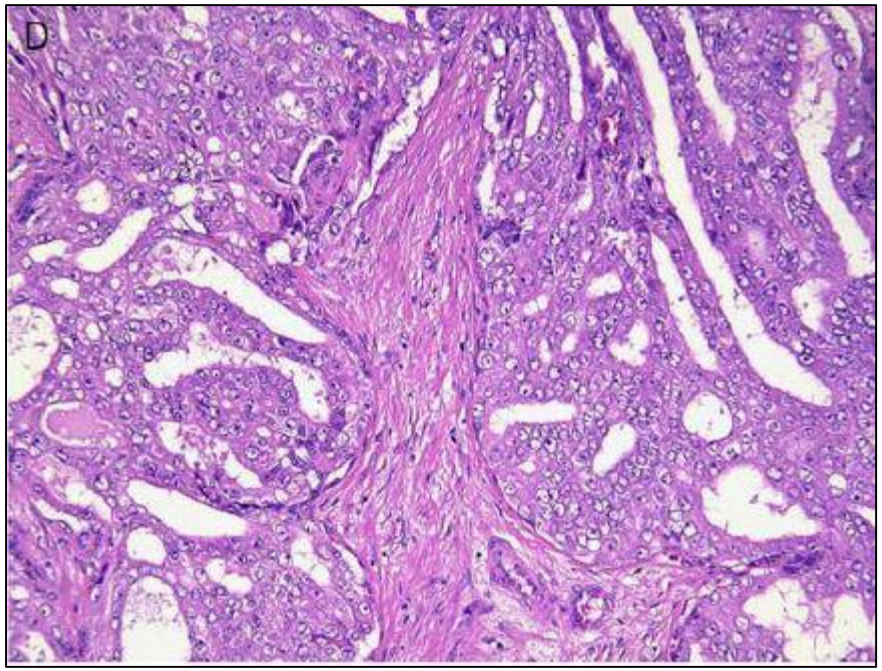
- **Main Problem Area**
  - threshold for minute components of pattern 4
  - especially challenging with small poorly-formed glands
  - <u>assumption that “experts” always go with higher grades</u>

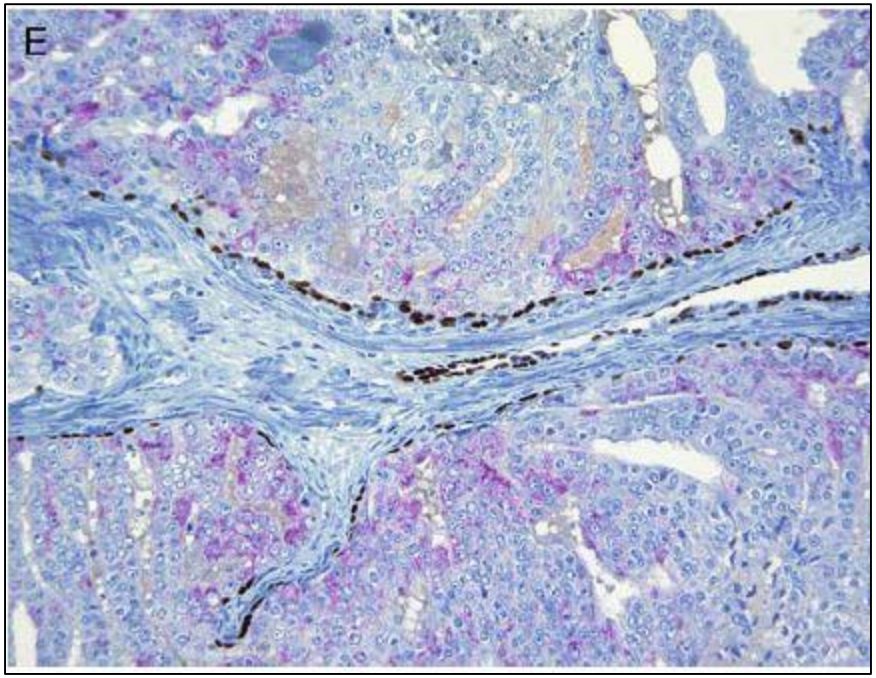
Intraductal Carcinoma (IDC)

TABLE 2. Criteria for IDC[20]

Malignant epithelial cells filling large acini and prostatic ducts, with preservation of basal cells and:
- Solid or dense cribriform pattern

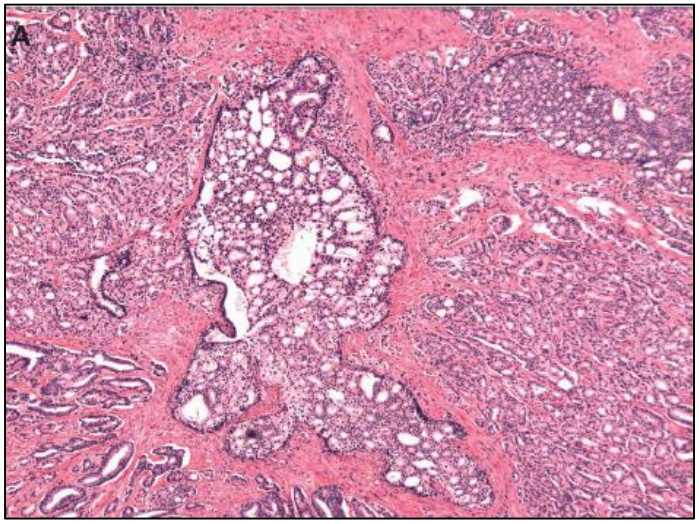
Or
- Loose cribriform or micropapillary pattern with either:
  - Marked nuclear atypia: nuclear size 6 × normal
  - Necrosis

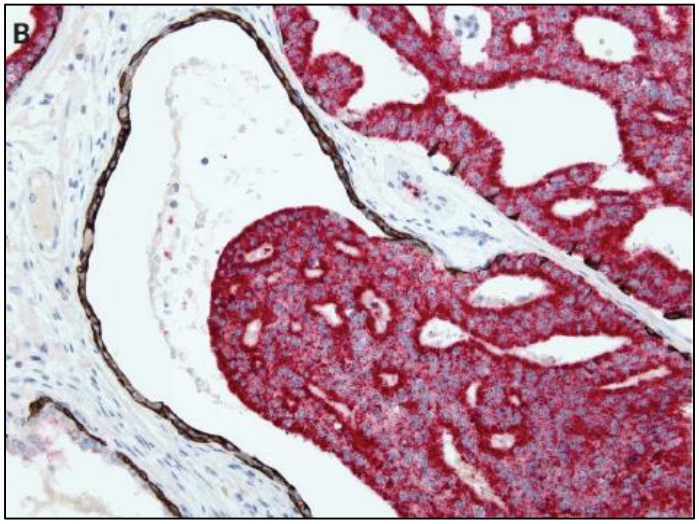




Intraductal Carcinoma is NOT Graded

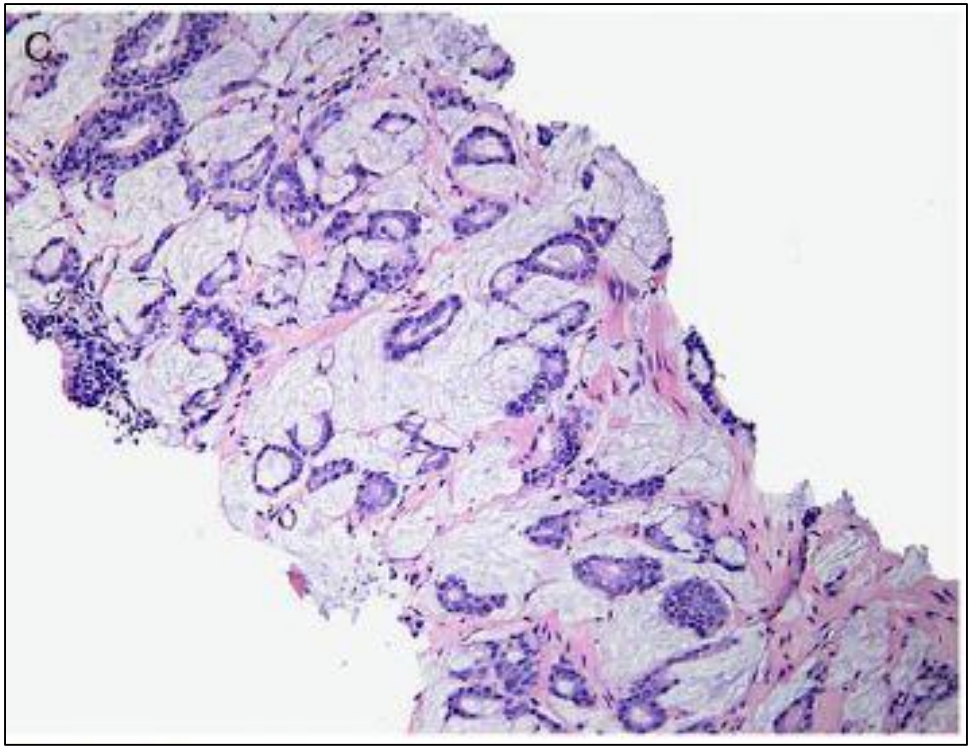
- Issue not addressed in 2005
- IDC (not ductal variant carcinoma)





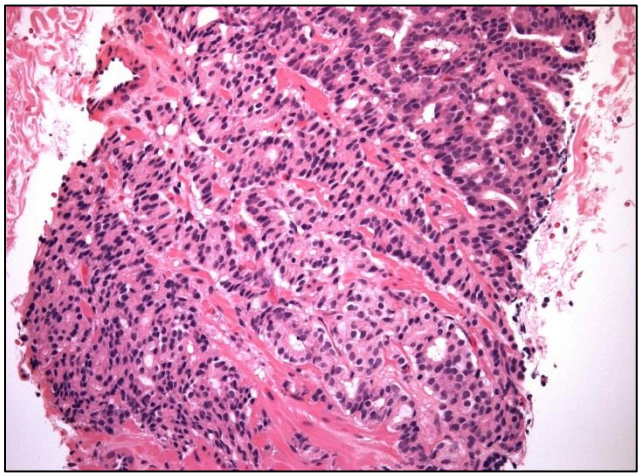
- Adverse prognostic indicator across all risk groups regardless of treatment modality

Mucinous Carcinoma

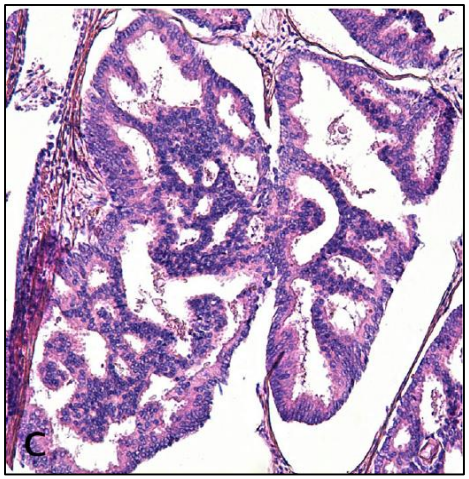


- 2005 no consensus on how to grade - default pattern 4 regardless of architecture???
- Biochemical free and overall survival same or better than conventional acinar carcinoma
- 2014
  - pattern 4 if cribriform
  - pattern 3 if discrete well-formed glands

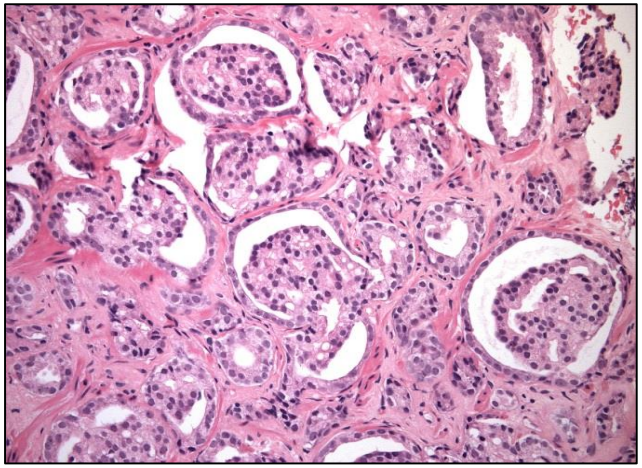
Pattern 4



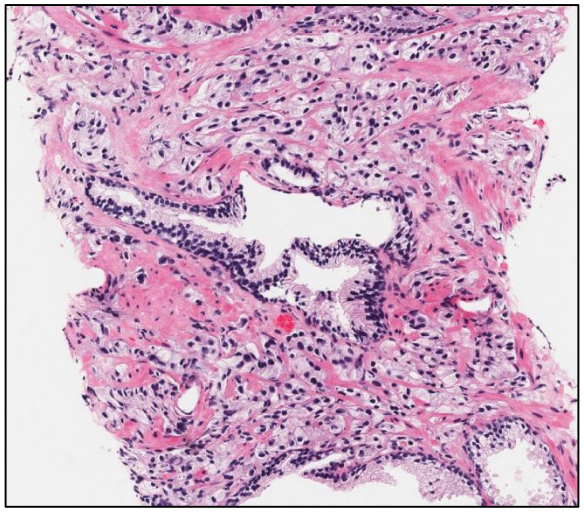
Fused Glands



Cribriform

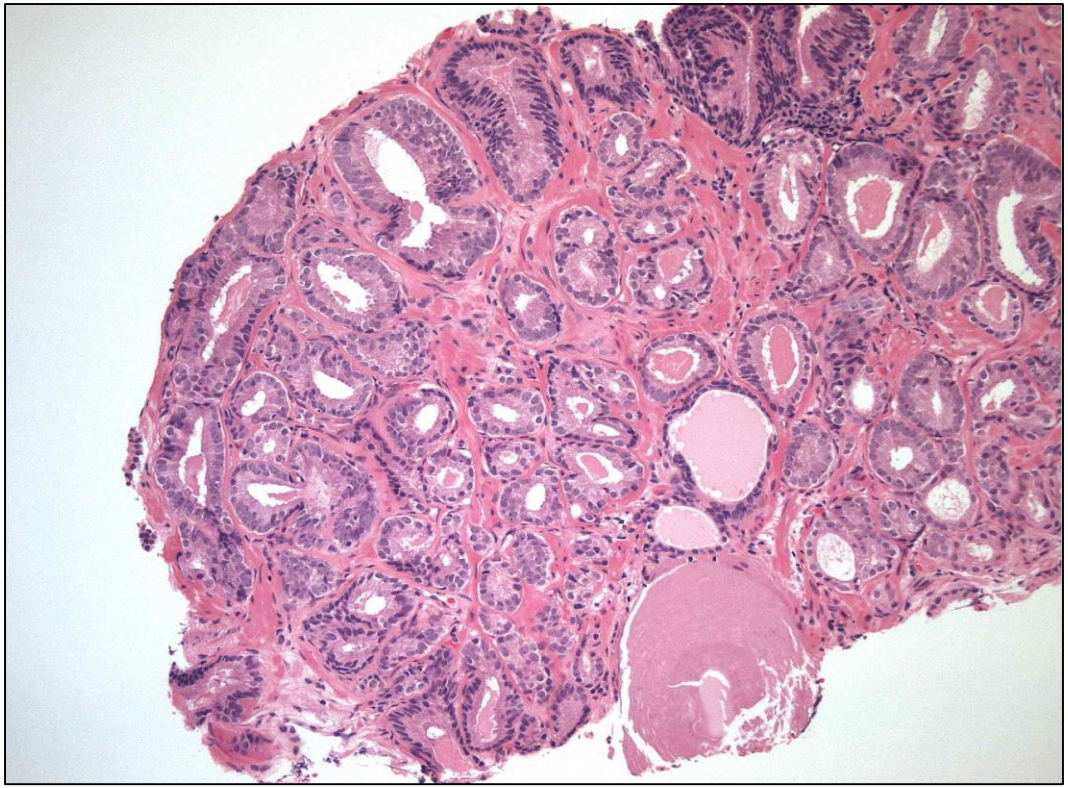


Glomeruloid



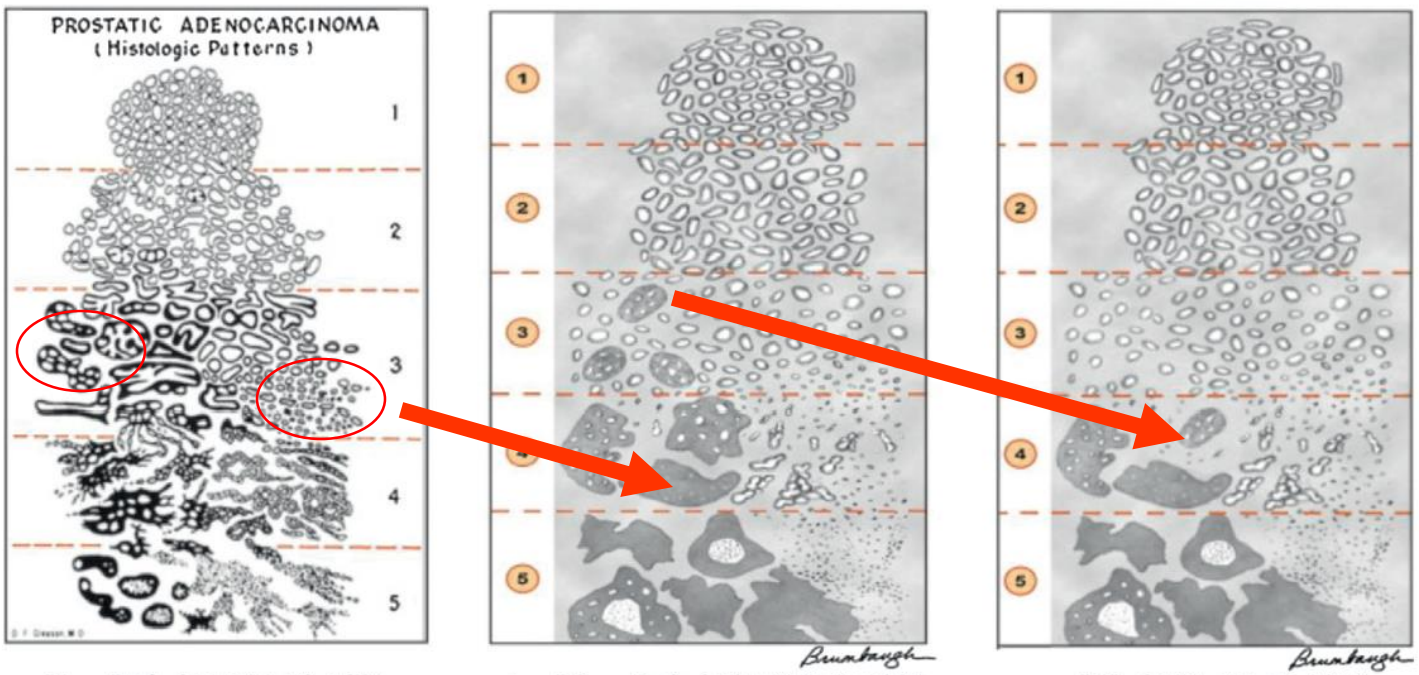
Poorly-Formed Glands

Homogenization of Pattern 3



- Individual, discrete, well-formed glands

Evolution of the Gleason Diagram



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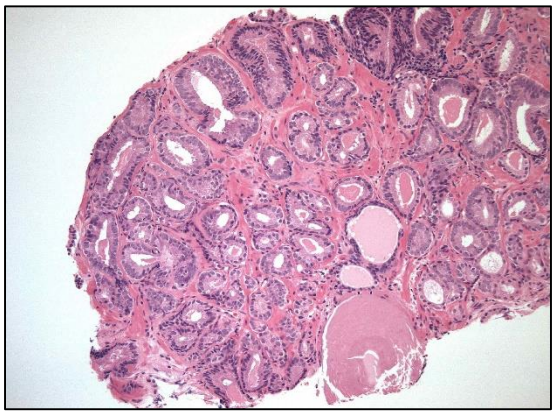
Question from Clinicians: Is Gleason 6 Still a "Cancer"?

- "Indolent lesion of epithelial origin" (IDLE)
- "Prostatic epithelial neoplasm of insignificant significance"



- Metastatic potential for pure Gleason 6 is negligible (but NOT zero)
  - 0.48% of 21920 prostatectomies have lymph node metastases (Liu et al, Pathology 2014:306-10)
- Still meets clinical, morphologic, immunohistochemical and molecular criteria for "cancer".

Concept of Grade Grouping

- **Rationale:**
  - Gleason $\leq$ 5/10 has all but disappeared
  - **Gleason 6/10 is "low risk" - tough for patients**
  - **Gleason 7/10 can be (3+4) or (4+3)**
  - Gleason 8-10 is "high-risk" and split into (4+4), (4+5), (5+4) and (5+5)

Grade Groups: Chicago 2014

- 5 groups
  - **Group 1** – Gleason 6/10 (3+3) or less
  - **Group 2** – Gleason 7/10 (3+4)
  - **Group 3** – Gleason 7/10 (4+3)
  - **Group 4** – Gleason 8/10 (4+4), *(3+5)*, (5+3)**
  - **Group 5** – Gleason 9-10/10 (any combination of pattern 4 and 5)

- Still Gleason grading (as per modifications from Chicago 2014)

A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score

Accepted June 29, 2015

Jonathan I. Epstein [a,*], *Michael J. Zelefsky* [b], *Daniel D. Sjoberg* [b], *Joel B. Nelson* [c], *Lars Egevad* [d], *Cristina Magi-Galluzzi* [e], *Andrew J. Vickers* [b], *Anil V. Parwani* [c], *Victor E. Reuter* [b], *Samson W. Fine* [b], *James A. Eastham* [b], *Peter Wiklund* [d], *Misop Han* [a], *Chandana A. Reddy* [e], *Jay P. Ciezki* [e], *Tommy Nyberg* [d], *Eric A. Klein* [e]

[a] *The Johns Hopkins Medical Institutions, Baltimore, MD, USA;* [b] *Memorial Sloan Kettering Cancer Center, New York, NY, USA;* [c] *University of Pittsburgh Medical Center, Pittsburgh, PA, USA;* [d] *Karolinska Institute, Stockholm, Sweden;* [e] *Cleveland Clinic, Cleveland, OH, USA*

- 5 centres
- 20,845 radical prostatectomies (2005-2014)
- 16,172 pre-prostatectomy biopsies*
- 5,501 treated by radiotherapy* (2005-2014)

Table 3 – Discrimination of varying Gleason grade categorizations

	RP biopsy Gleason grade		Post-RP Gleason grade		RT Gleason grade	
	Univariate	Multivariable	Univariate	Multivariable	Univariate	Multivariable
≤6 vs 7 vs ≥8	0.760	0.805	0.744	0.830	0.662	0.729
≤6 vs 3 + 4 vs 4 + 3 vs ≥8	0.781	0.811	0.791	0.842	0.684	0.736
≤6 vs 7 vs 8 vs ≥9	0.762	0.806	0.747	0.831	0.666	0.729
≤6 vs 3 + 4 vs 4 + 3 vs 8 vs ≥9	0.783	0.813	0.793	0.842	0.687	0.737

RP = radical prostatectomy; RT = radiation therapy.
Multivariable biopsy Gleason Cox model includes preoperative prostate-specific antigen (PSA) and clinical stage (T1 vs T2 vs T3/4), and post-RP Cox model includes preoperative PSA, surgical margin status, and pathology stage (pT2 vs pT3a vs pT3b vs pT4). The C-index has been corrected for optimism using 10-fold cross-validation.

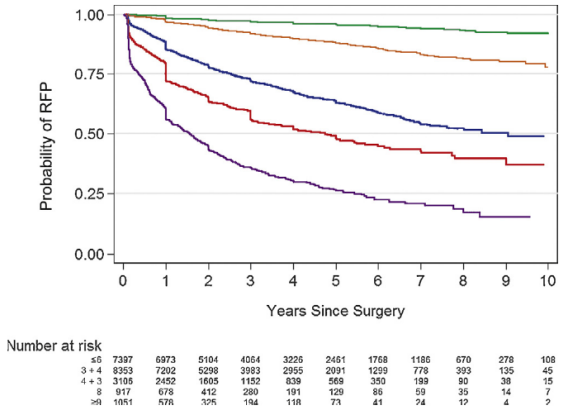


Fig. 1 – Recurrence-free progression following radical prostatectomy stratified by prostatectomy grade. Green line: Gleason score ≤6, grade group 1. Orange line: Gleason score 3 + 4, grade group 2. Dark blue line: Gleason score 4 + 3, grade group 3. Red line: Gleason score 8, grade group 4. Purple line: Gleason score ≥9, grade group 5.
RFP = recurrence-free progression.

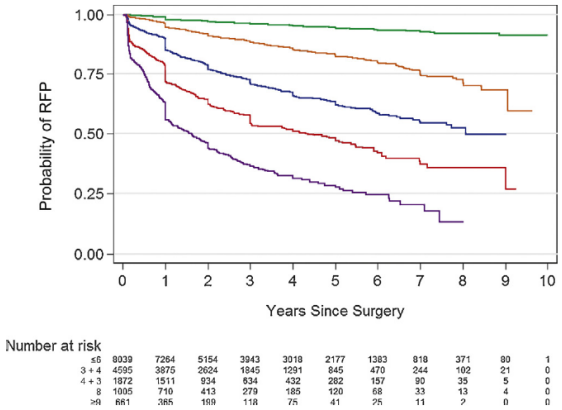
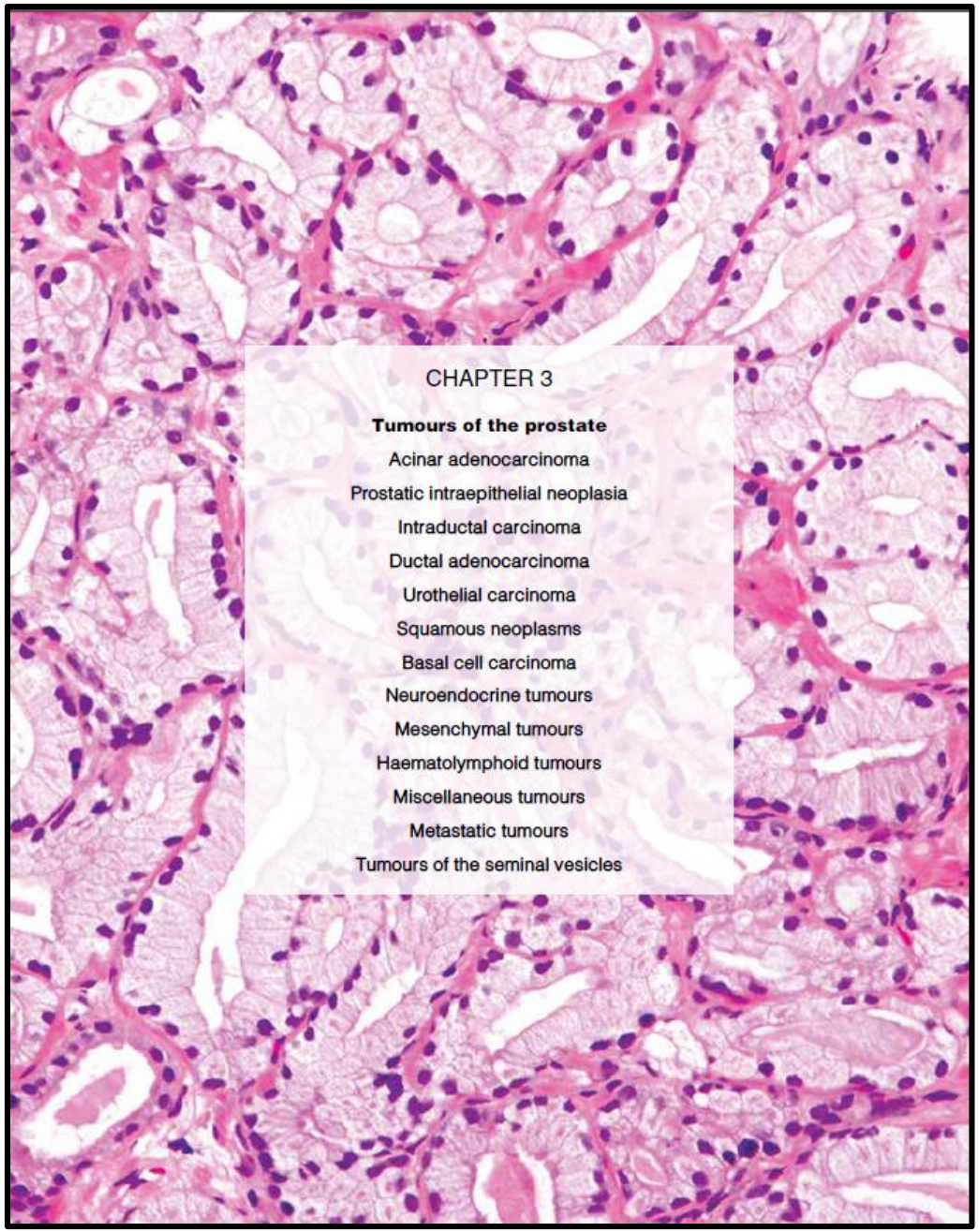


Fig. 2 – Recurrence-free progression following radical prostatectomy stratified by pre-prostatectomy biopsy grade. Green line: Gleason score ≤6, grade group 1. Orange line: Gleason score 3 + 4, grade group 2. Dark blue line: Gleason score 4 + 3, grade group 3. Red line: Gleason score 8, grade group 4. Purple line: Gleason score ≥9, grade group 5.
RFP = recurrence-free progression.



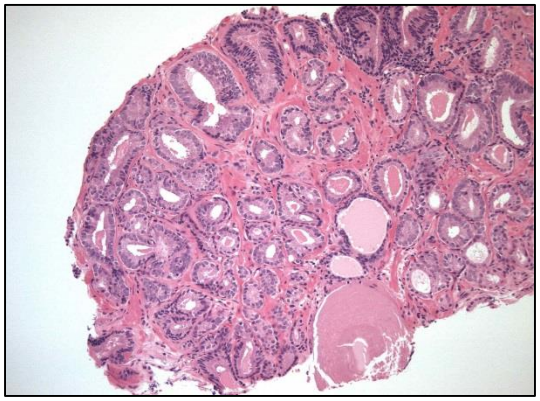
WHO 2016 Edition
GU Tumor Blue Book

Table 3.03 Grade groups

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 Lack gland formation (or with necrosis) with or without 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
From Epstein JI et al. {807B}, with permission.

Grade Group 1



- Lowest grade possible - reassuring to patients
- Metastatic potential negligible (but not zero)
- Potential to reduce over-treatment of indolent disease
- But, follow-up required re: possibility of un-sampled higher grade cancer

Grade Groups in Practice

1. Needle biopsy of prostate (right lateral):
   - Adenocarcinoma, Gleason score 6/10 (3+3), involving 1 of 1 core and 30% of the core.

Grade Group 1

2. Needle biopsy of prostate (right medial):
   - Adenocarcinoma, Gleason score 6/10 (3+3), involving 1 of 1 core and 50% of the core.

Grade Group 1

3. Needle biopsy of prostate (left medial):
   - Negative for malignancy.

4. Needle biopsy of prostate (left lateral):
   - Adenocarcinoma, Gleason score 7/10 (3+4), involving 1 of 1 core and 20% of the core.

Grade Group 2

Synoptic:

Histologic type – usual acinar

Overall Gleason Score – 7/10 (3+4)

Grade group – 2

% Gleason pattern 4 – 10%

Distribution – bilateral

Number of positive cores – 3

Number of cores total – 4

% tissue involvement – 25%

% involvement for most involved core – 50%

Perineural invasion – not identified

Contemporary Gleason Grading of Prostatic Carcinoma

An Update With Discussion on Practical Issues to Implement the 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma

Jonathan I. Epstein, MD, Mahul B. Amin, MD,† Victor E. Reuter, MD,‡ and Peter A. Humphrey, MD, PhD§*

(*Am J Surg Pathol* 2017;41:e1–e7)

- Reporting percent pattern 4 in biopsies and radical prostatectomies
- Reporting minor high-grade patterns in biopsies and radical prostatectomies
- Grading "core vs jar vs case" level
- Grading separate tumour nodules in radical prostatectomies

- Main goal of consensus conferences - uniformity in reporting of prostate cancer grade

Reporting % Pattern 4

- **Uniform reporting** of grade regardless of specimen type – avoids confusion created by different rules for biopsy vs RP
- **Active surveillance** patient selection - ≤ 10% pattern 4 may be suitable (CCO PEBC, ASCO guidelines)
- **Radiation therapy** approaches can differ for (3+4) vs (4+3) - "(3+4) with pattern 4 approaching 50%"
- **Quality assurance** - < 5% pattern 4 should stimulate intradepartmental QA review

Reporting % Pattern 4

Platinum Priority – Prostate Cancer
Editorial by XXX on pp. x–y of this issue

Clinical Utility of Quantitative Gleason Grading in Prostate Biopsies and Prostatectomy Specimens

Guido Sauter[a,], Stefan Steurer[a], Till Sebastian Clauditz[a], Till Krech[a], Corinna Wittmer[a], Florian Lutz[a], Maximilian Lennartz[a], Tim Janssen[a], Nayira Hakimi[a], Ronald Simon[a], Mareike von Petersdorff-Campen[a], Frank Jacobsen[a], Katharina von Loga[a], Waldemar Wilczak[a], Sarah Minner[a], Maria Christina Tsourlakis[a], Viktoria Chirico[a], Alexander Haese[b], Hans Heinzer[b], Burkhard Beyer[b], Markus Graefen[b], Uwe Michl[b], Georg Salomon[b], Thomas Steuber[b], Lars Henrik Budäus[b], Elena Hekeler[a], Julia Malsy-Mink[a], Sven Kutzera[a], Christoph Fraune[a], Cosima Göbel[a], Hartwig Huland[b], Thorsten Schlomm[b,c]*

[a] *Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany;* [b] *Martini-Klinik, Prostate Cancer Center, University Medical Center Hamburg-Eppendorf, Germany;* [c] *Department of Urology, Section for translational Prostate Cancer Research, University Medical Center Hamburg-Eppendorf, Germany*

Table 1 – Patient cohort

	No. of patients (%)	
	Study cohort (n = 12 823)[a]	Biochemical relapse among categories
Follow-up (mo)		
n	12 150	2389 (19.7%)
Mean	38.3	–
Median	36.0	–
Age (yr)		
≤50	440 (3.4%)	51 (11.6%)
51–59	2882 (22.5%)	506 (17.6%)
60–69	7045 (54.9%)	1299 (18.4%)
≥70	2456 (19.2%)	533 (21.7%)
Pretreatment PSA (ng/ml)		
<4	1551 (12.1%)	189 (12.2%)
4–10	8002 (62.5%)	1146 (14.3%)
10–20	2354 (18.4%)	640 (27.2%)
>20	893 (7%)	413 (46.2%)
pT stage (AJCC 2002)		
pT2	8582 (67%)	788 (9.2%)
pT3a	2602 (20.3%)	732 (28.1%)
pT3b	1588 (12.4%)	845 (53.2%)
pT4	45 (0.4%)	24 (53.3%)
Gleason grade		
≤6	2277 (17.8%)	91 (4%)
3 + 4	6849 (53.4%)	815 (11.9%)
3 + 4 TG5	655 (5.1%)	139 (21.2%)
4 + 3	1176 (9.2%)	438 (37.2%)
4 + 3 TG5	1060 (8.3%)	466 (44%)
8	72 (0.6%)	32 (44.4%)
9-10	734 (5.7%)	408 (55.6%)
pN stage		
pN0	7777 (88.3%)	1457 (18.7%)
pN+	1028 (11.7%)	585 (56.9%)
Surgical margin		
Negative	10 442 (82.8%)	1493 (14.3%)
Positive	2171 (17.2%)	820 (37.8%)
Cancers with matched preoperative needle biopsies		
n	2971	

AJCC = American Joint Committee on Cancer; PSA = prostate specific antigen.
[a] Numbers do not always add up to 12 823 in the different categories because of cases with missing data.

- Measure linear extent of cancer in biopsies
- Estimate % pattern 4 and/or 5
- Subdivide Gleason 7 cancers by % pattern 4:
  - 1-24% (low)
  - 25-49%
  - 50-74%
  - 75-95% (high)

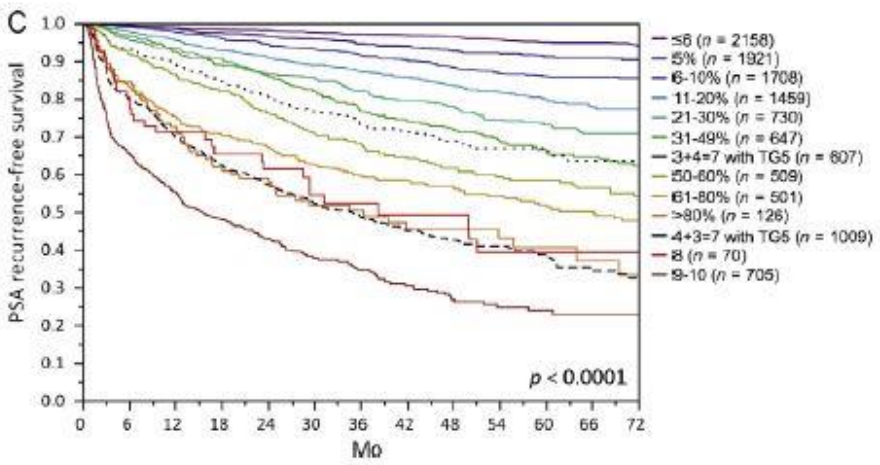
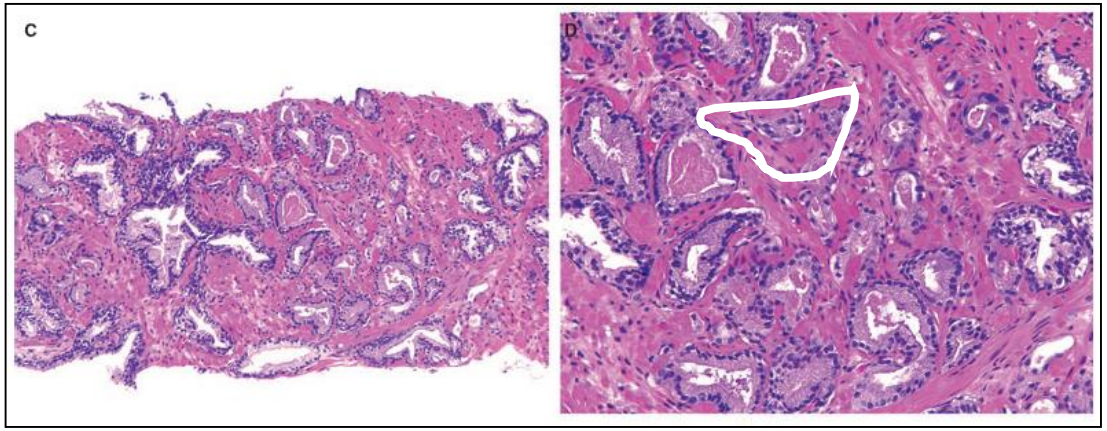


Fig. 1 – Impact of the Gleason pattern on patient prognosis (time to biochemical recurrence). (A) Gleason categories with Gleason 7 separated into 3 + 4 and 4 + 4; (B) further subdivision of Gleason categories 3 + 4 and 4 + 3 into cancers with low and high fractions of Gleason 4, with 3 + 4 low = ≤25% Gleason 4, 3 + 4 high = 26-49% Gleason 4, 4 + 3 low = 50–74% Gleason 4 and 4 + 3 high = ≥75% Gleason 4; and (C) "quantitative" Gleason with patient groups defined by the fraction of Gleason 4.
PSA = prostate specific antigen.

Implications for Active Surveillance

- Low % pattern 4 Gleason 7/10 (3+4) on biopsy
  - 5-10% pattern 4 cases have the same risk of unfavourable Gleason score as Gleason 6/10 (3+3) at prostatectomy
- Negate effect of interobserver variability for small amounts of pattern 4, allowing low % pattern 4 cases to enter active surveillance.



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Active surveillance for the management of localized prostate cancer: Guideline recommendations

Chris Morash, MD, FRCSC;[*] Rovena Tey;[†] Chika Agbassi, MBBS, MSc, CCRA;[†] Laurence Klotz, MD, FRCSC;[¥] Tom McGowan, MD, FRCPC;[±] John Srigley, MD, FRCPC;[§] Andrew Evans, MD, PhD, FRCPC[£]

[*]Division of Urology, University of Ottawa, Ottawa, ON; [†]Program in Evidence-based Care, Cancer Care Ontario, McMaster University, Hamilton, ON; [¥]Division of Urology, Sunnybrook Health Sciences Centre, Toronto, ON; [±]The Cancer Centre Bahamas & The Cancer Centre Eastern Caribbean; [§]Credit Valley Hospital, Mississauga, ON; [£]Department of Pathology and Laboratory, Faculty of Medicine, University of Toronto, Toronto, ON

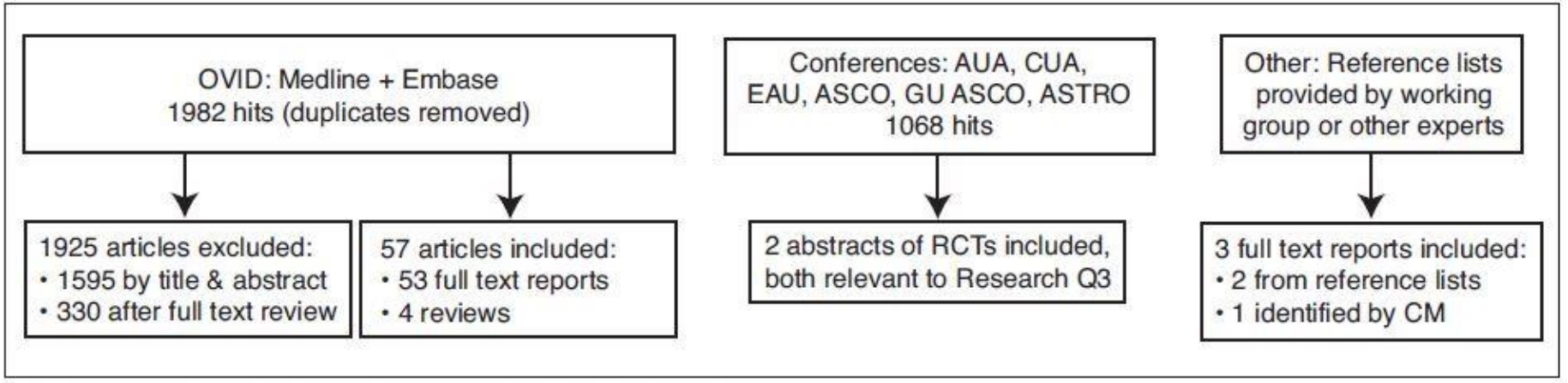


Fig. 1. Schematic diagram showing results from the primary literature search.

Recommendation 2

RECOMMENDATION 2: Active treatment (RP or RT) is appropriate for patients with intermediate-risk (Gleason score 7) localized prostate cancer. For select patients with low-volume Gleason 3+4=7 localized prostate cancer, AS can be considered.

- Need to report estimate of % pattern 4

Reporting Minor High-Grade Patterns in Prostatectomies

- (3+3) with < 5% pattern 4 = (3+4) not (3+3) with "tertiary pattern 4".
- (4+4) with < 5% pattern 5 = (4+5) not (4+4) with "tertiary pattern 5".
- Use "minor" high-grade pattern - not tertiary
- Is there an upper limit to % pattern 5 as a minor pattern?
  - all evidence is based on minor high-grade $\leq$ 5%
  - 50% -3 + 30%-4 + 20%-5 will have worse behaviour

TABLE 2. Vote at the 2014 Consensus Meeting on Should We Provide a Grade for: (Multiple Choice)

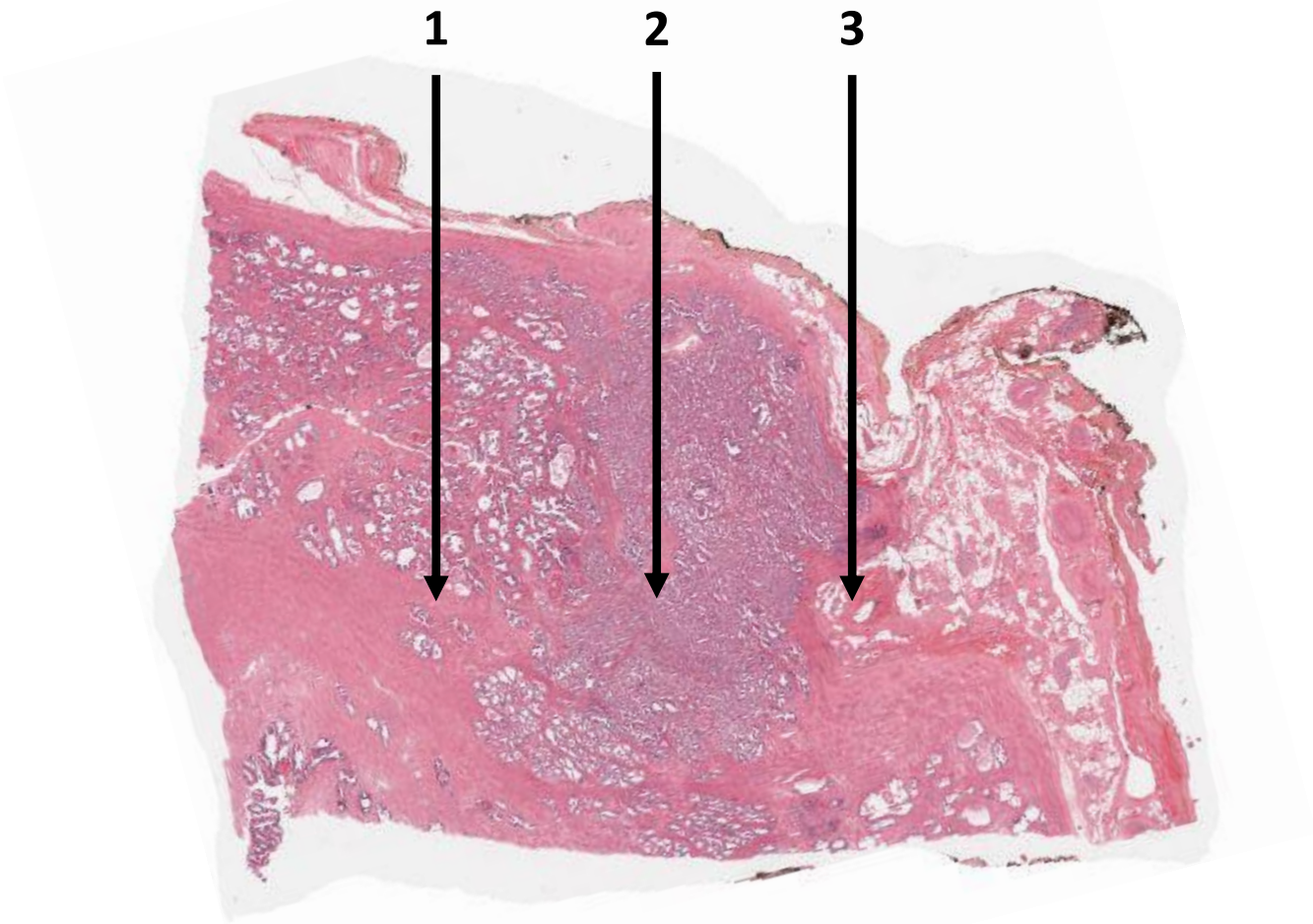
	Responses [n (%)]
Each positive core	28 (45.2)
Each positive specimen jar	11 (17.7)
Whole case overall (global grade)	2 (3.2)
1 + 2	4 (6.5)
1 + 3	8 (12.9)
2 + 3	8 (12.9)
1 + 2 + 3	1 (1.6)
Total	62 (100)

- 1 core per container - only 1 score
- 2-3 cores per container from the same site - global score for all cores
- Multiple cores from different sites per container - to be avoided

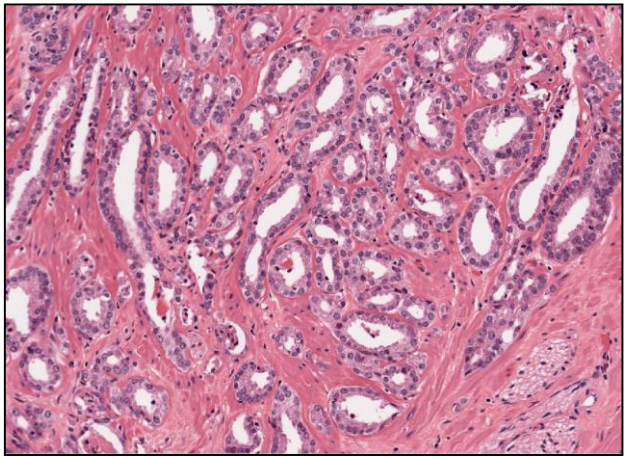
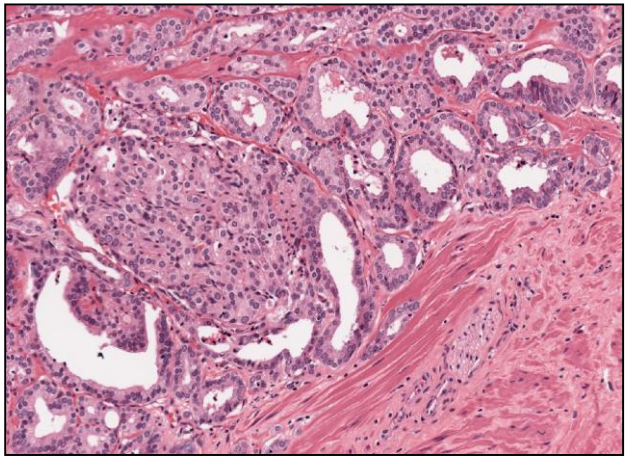
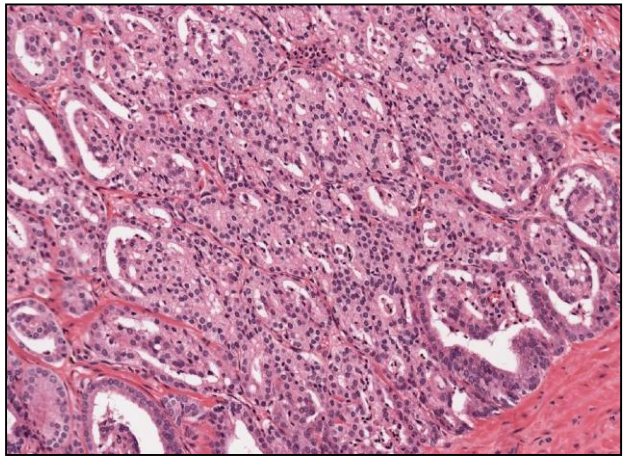
- Different cores can have different scores/grade groups
- Some clinicians use the core with the highest score for treatment planning - others consider where the cores came from
  - ipsilateral sites
  - contralateral sites

Sampling Issues on Prostate Biopsy: Interpreting Gleason Scores – Highest vs Composite?

Sampling Issues: Case 1



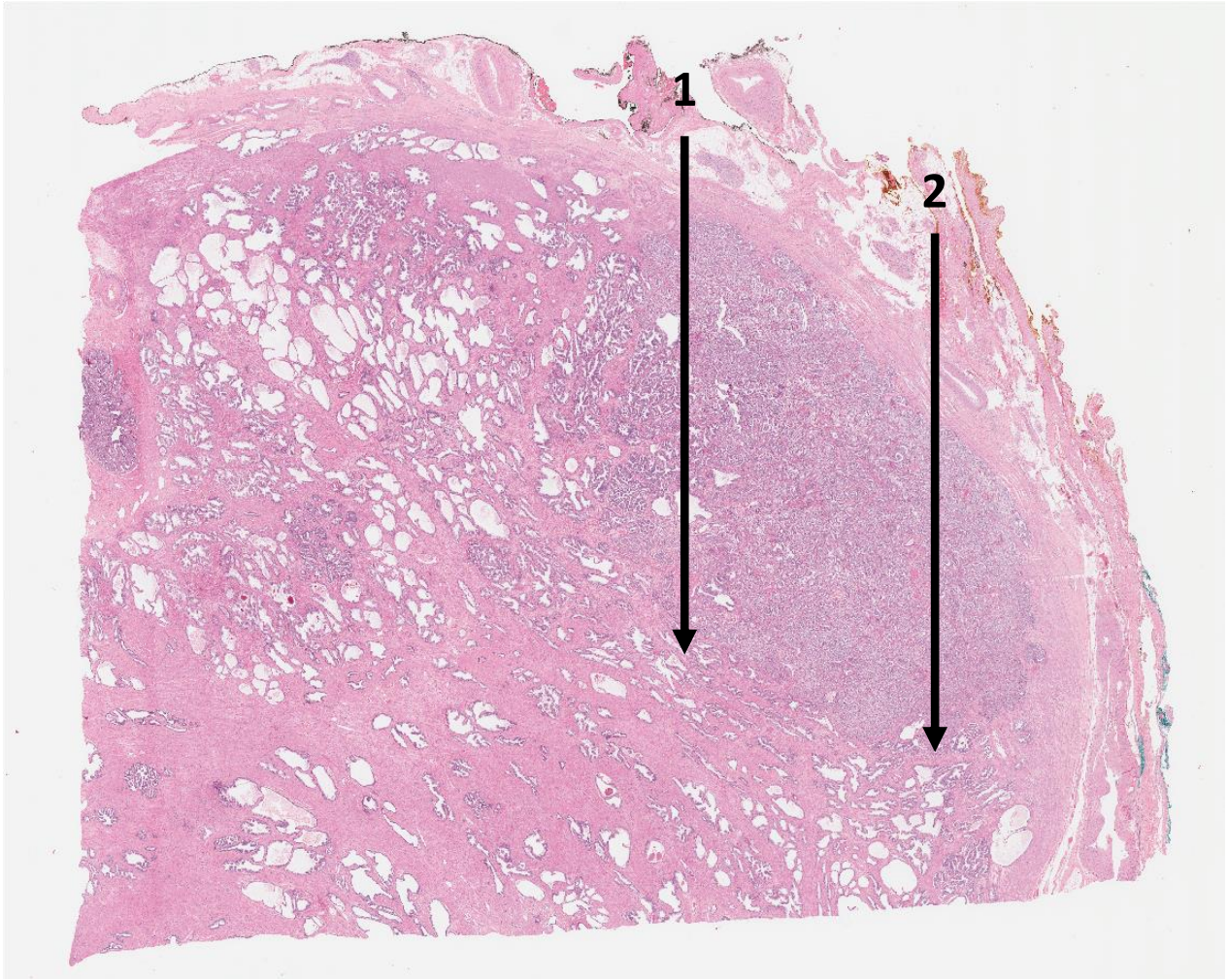
- 8 x 7 mm left posterior nodule
- 3 cores – 1) mid, 2) left medial, 3) left lateral

Mid	Left Medial	Left Lateral
		
6/10 (3+3) 1 of 1 core 15% involvement (% pattern 4 - 0)	7/10 (3+4) 1 of 1 core 80% involvement (% pattern 4 - 10)	8/10 (4+4) 1 of 1 core 5% involvement (% pattern 4 - 100)

Synoptic Report: Composite Gleason Score: Case 1

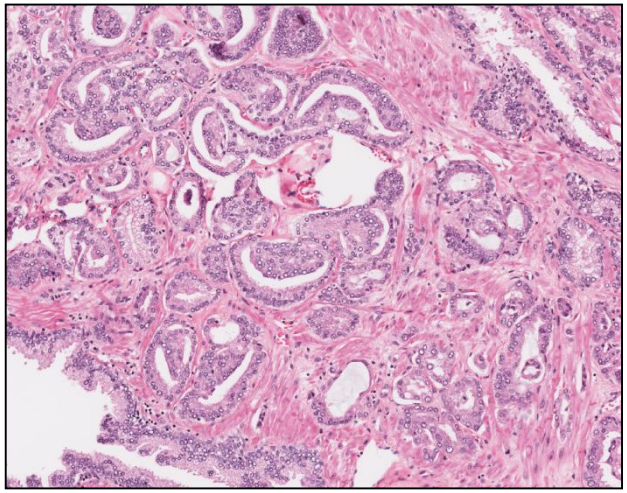
- Histologic type – adenocarcinoma, usual acinar type
- **Overall Gleason Score – 7/10 (3+4) (not 8/10 (4+4))**
- **Grade group – 2 (not Group 4)**
- **% Gleason pattern 4 – 10%**
- Distribution – unilateral, left
- Number of positive cores – 3
- Number of cores total – 12
- % tissue involvement – 8%
- % involvement for most involved core – 80%
- Perineural invasion – not identified
- Intraductal carcinoma – not identified

Sampling Issues: Case 2



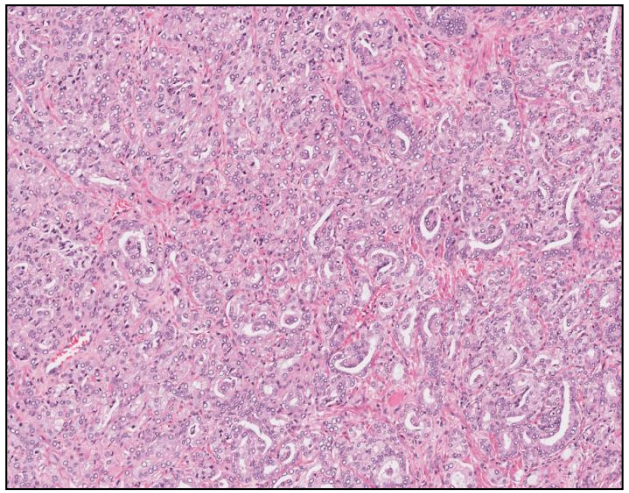
- 12 x 7 mm left posterolateral nodule
- 2 cores – 1) left medial, 2) left lateral

Left Medial



7/10 (3+4)
1 of 1 core
80% involvement
(% pattern 4 - 30)

Left Lateral



8/10 (4+4)
1 of 1 core
60% involvement
(% pattern 4 - 100)

Right medial - 6/10 (3+3), 1 of 1 core, 30%
Right transition zone - 6/10 (3+3), 1 of 1 core, 20%
Right lateral - 6/10 (3+3), 1 of 1 core, 10%

Synoptic Report: Composite Gleason Score: Case 2

- Histologic type – adenocarcinoma, usual acinar type
- **Overall Gleason Score – 7/10 (4+3) (not 8/10 (4+4))**
- **Grade group – 3 (not Group 4)**
- **% Gleason pattern 4 – 70%**
- Distribution – bilateral
- Number of positive cores – 5
- Number of cores total – 10
- % tissue involvement – 20%
- % involvement for most involved core – 80%
- Perineural invasion – present
- Intraductal carcinoma – not identified

Prostate Biopsy and Radical Prostatectomy Gleason Score Correlation in Heterogenous Tumors

Proposal for a Composite Gleason Score

Javier A. Arias-Stella, III, MD, Alpa B. Shah, MD, MPH,* Diego Montoya-Cerrillo,*† Sean R. Williamson, MD,* and Nilesh S. Gupta, MD**

(*Am J Surg Pathol* 2015;39:1213–1218)

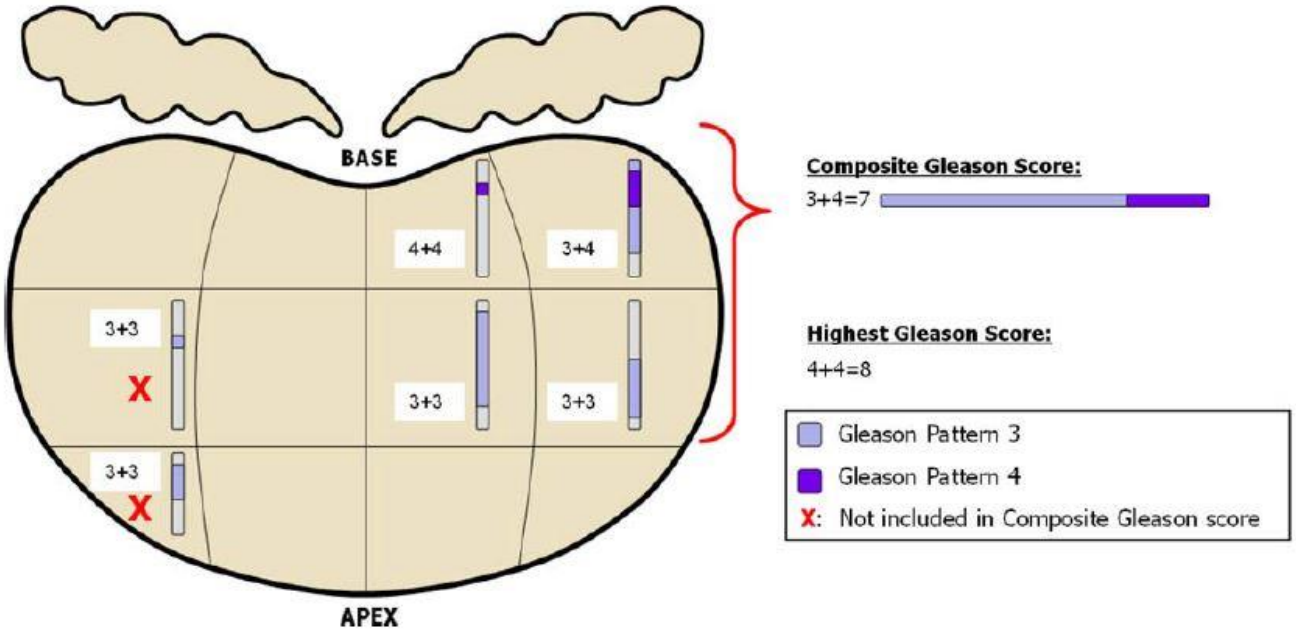


FIGURE 1. Comparison between HGS and CGS. Diagram showing a 12-core prostate biopsy with 6 total positive biopsy cores, of which 4 contiguous positive biopsy cores with highest tumor volume and grade represent the presumed dominant nodule. A CGS is assigned by measuring all Gleason patterns and estimating the percentage using the sum of all positive cores from the presumed the dominant nodule.

Cases

- 197 patients with biopsies showing:
  - ❖ > 2 Gleason scores (3+3, 3+4, 4+3)
  - ❖ > 1-step difference in Gleason score (3+4, 4+4, no 4+3)
- 100 underwent radical prostatectomy
- Radical prostatectomy Gleason score (higher, same or lower) was compared to biopsies using:
  - ❖ composite biopsy Gleason score
  - ❖ highest biopsy Gleason score

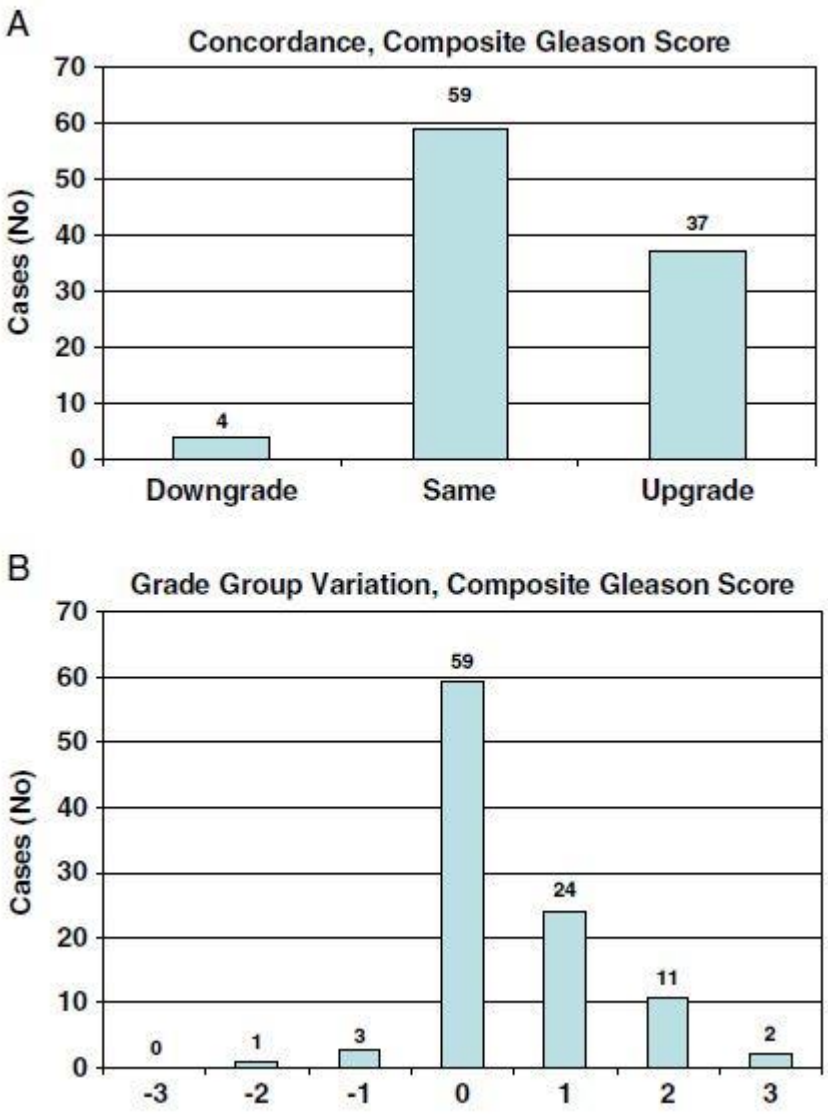
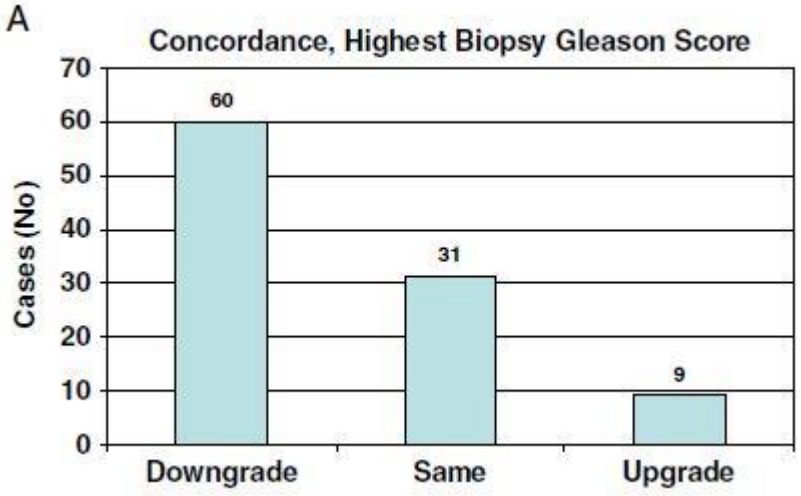


FIGURE 3. A, Using the proposed CGS method, the RPGS was predicted accurately in the majority of patients, although upgrading was more common when compared with HGS. B, Most patients had the same grade group when comparing CGS with RPGS. A smaller number of patients were upgraded to a higher-grade group category, usually by 1 step.

Composite Biopsy Gleason Score

- 59% had same score at RP
- 41% had a different score at RP
  - 10% downgraded
  - 90% upgraded (typically 1-step)



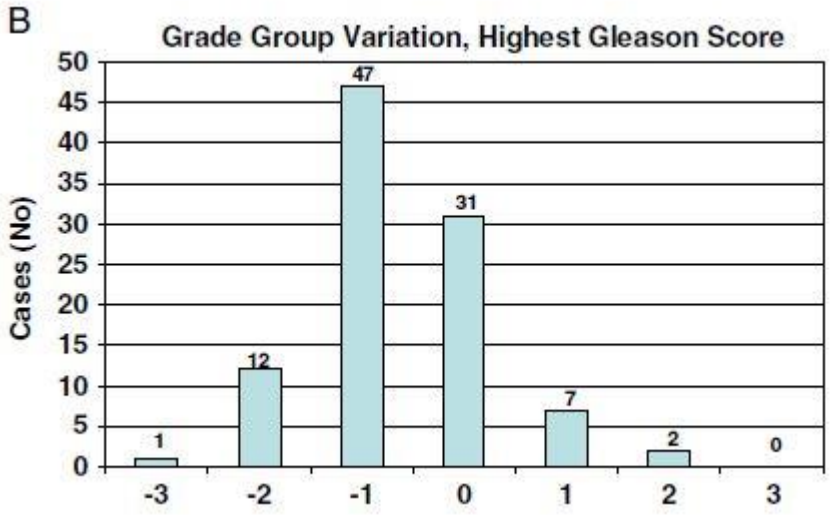


FIGURE 2. A, Using the HGS as representative of the tumor overall, most patients were downgraded to a lower GS at RP. B, Most patients had a 1-step downgrade in grade group when comparing the highest biopsy GS with RPGS.

Highest Biopsy Gleason Score

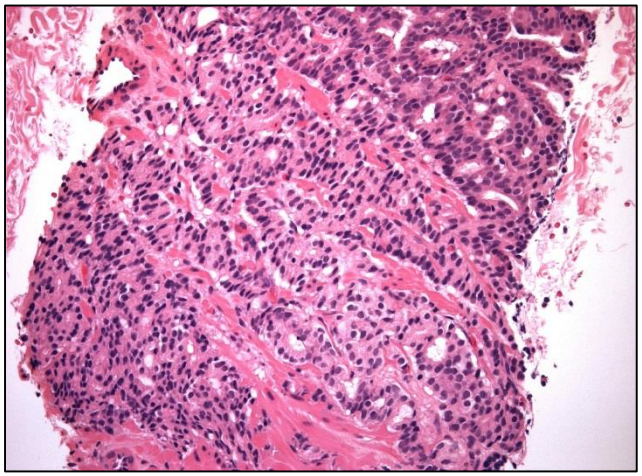
- 31% had same score at RP
- 59% had a different score at RP
  - 87% downgraded
  - 13% upgraded

Take Home Points

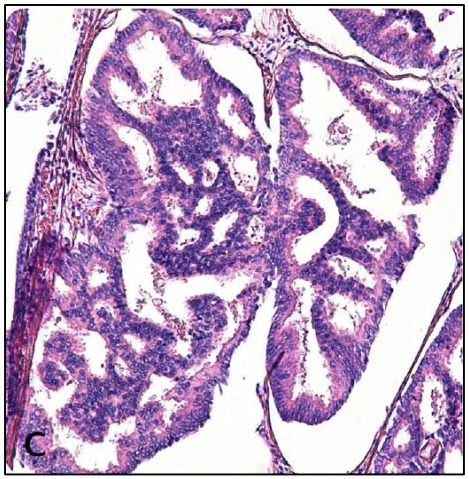
- There will always be assumptions/risks when interpreting biopsies with different Gleason scores.
  - ❖ not to mention sampling issues and pathologist factors

- Using the highest biopsy Gleason score to assess risk category will tend to overestimate the true grade (ie: downgrading at RP)
- Using composite Gleason score will be more accurate, but has a risk of underestimating the true grade (ie: upgrading at RP)

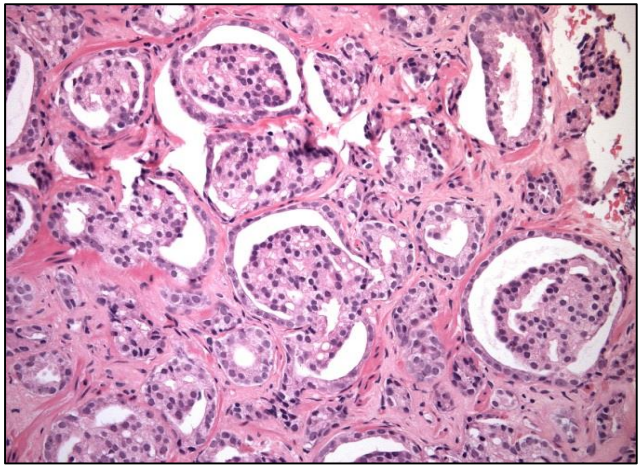
Emerging Topic: Types of Pattern 4



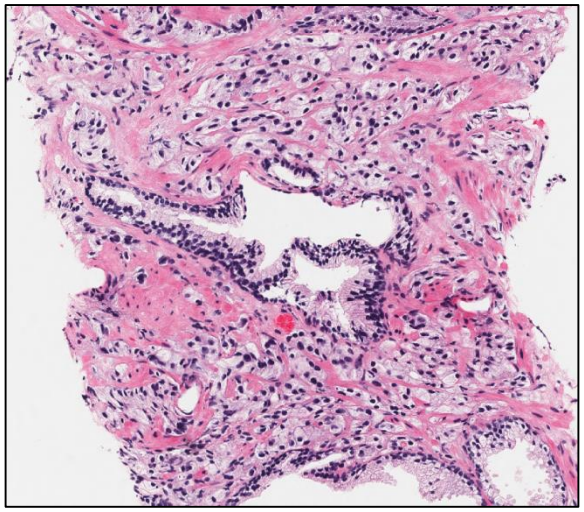
Fused Glands



Cribriform

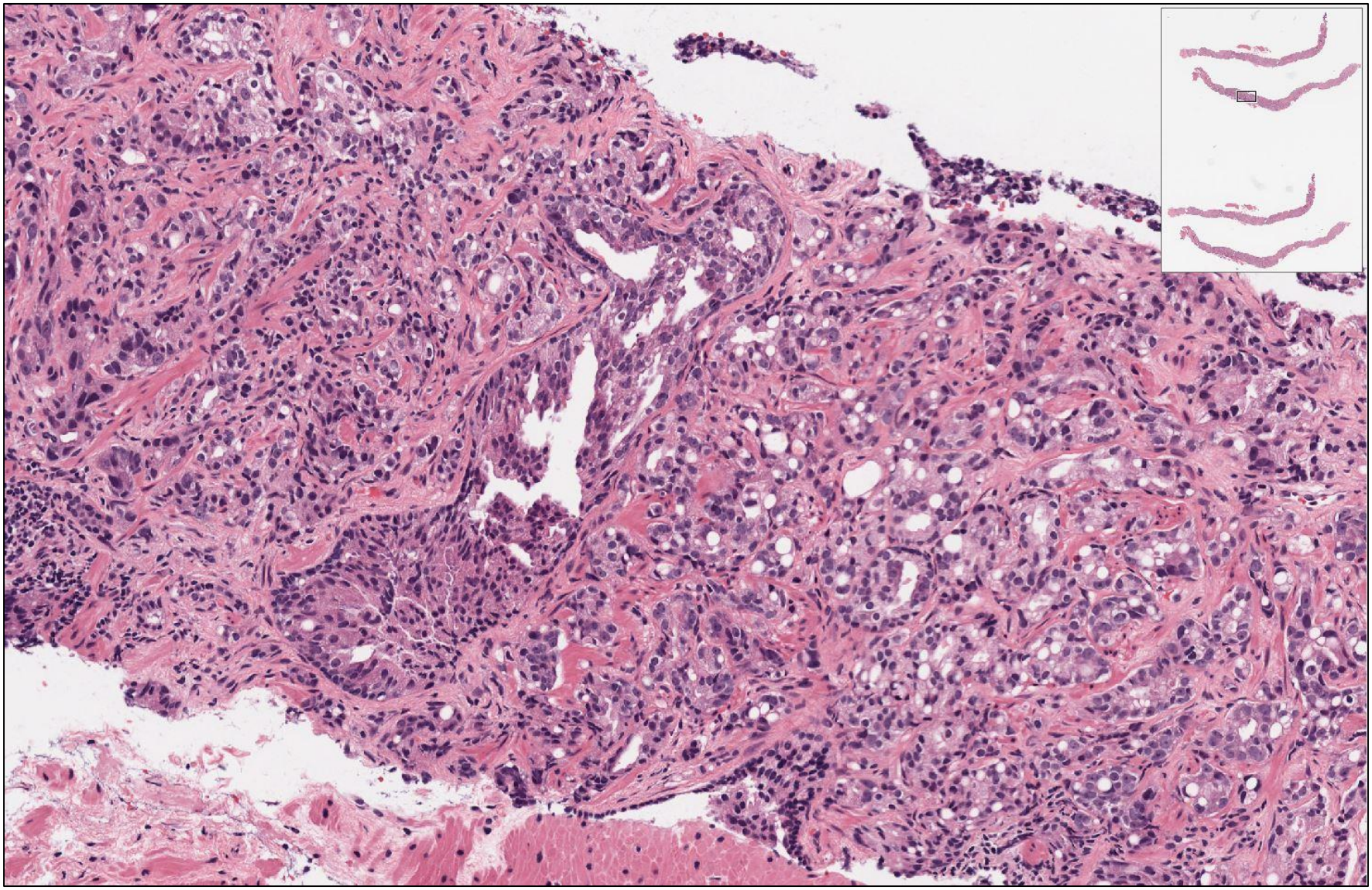


Glomeruloid



Poorly-Formed Glands

Which Pattern 4 Morphologies Predict Aggressive Behaviour? Are They All the Same?



The Prostate 75:1277–1284 (2015)

Not all Gleason Pattern 4 Prostate Cancers Are Created Equal: A Study of Latent Prostatic Carcinomas in a Cystoprostatectomy and Autopsy Series

Farshid Siadat,[1]* Jenna Sykes,[2] Alexandre R. Zlotta,[3] Najla Aldaoud,[4] Shin Egawa,[5] Dmitry Pushkar,[6] Cynthia Kuk,[3] Robert G. Bristow,[7] Rodolfo Montironi,[8] and Theodorus van der Kwast[9]

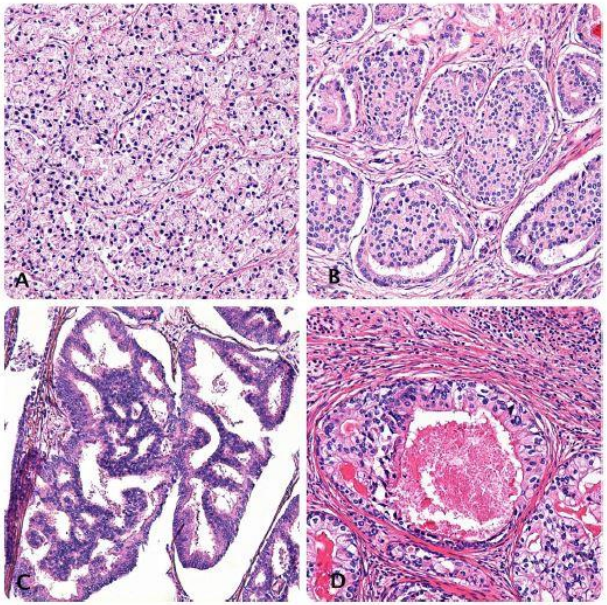
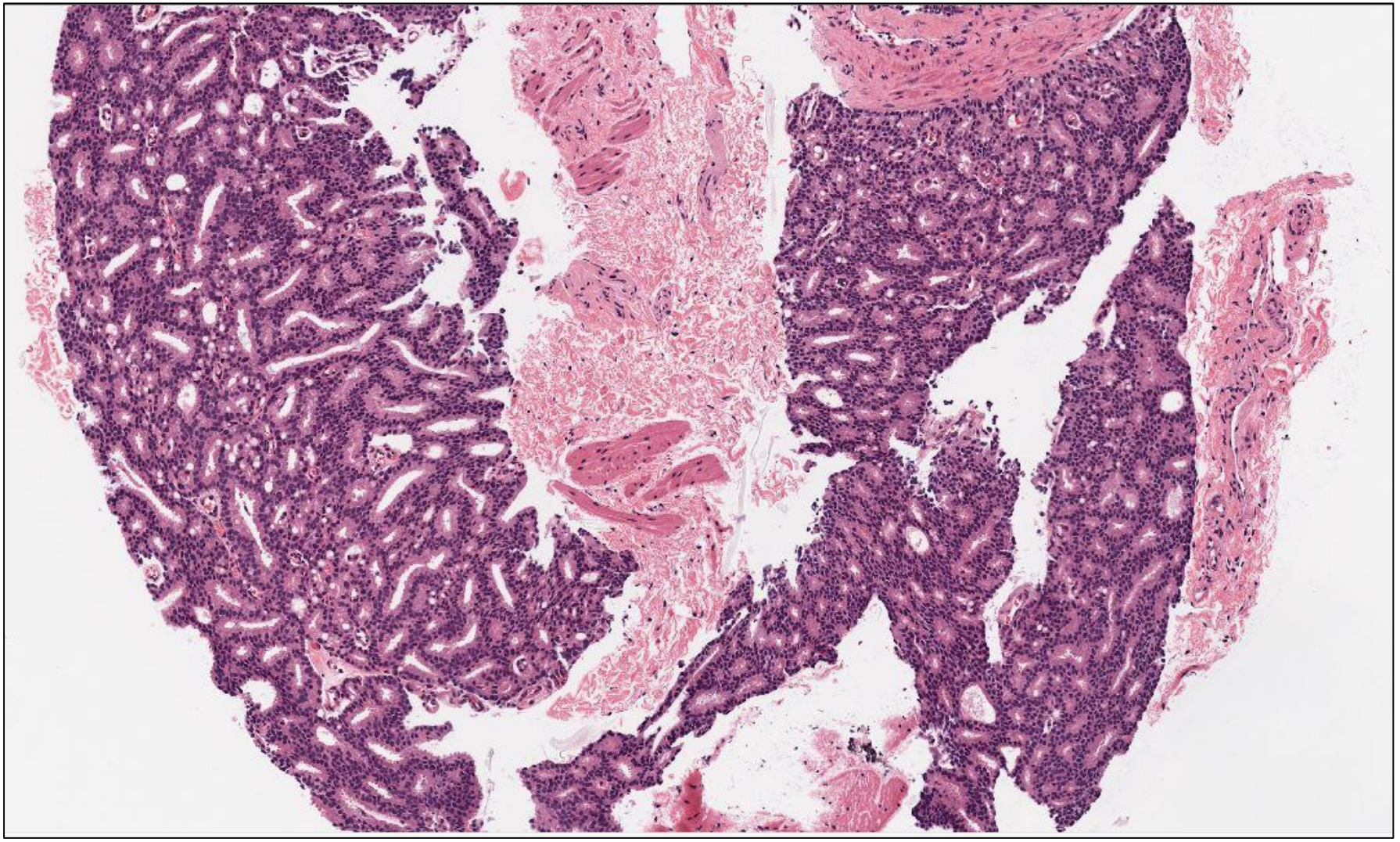


Fig. 1. Selected architectural patterns in Gleason grade 4 cancer and intraductal carcinoma. (**A**) small fused glands, (**B**) small cribriform, (**C**) large cribriform, and (**D**) intraductal carcinoma.

TABLE IV. Univariable Association of Architectural Pattern With EPE in the Autopsy Series

	Autopsy (n = 37)	
	OR (95%CI)	*P*-value
Small fused glands	0.15 (0.03, 0.75)	0.02
Poorly formed glands	0.91 (0.21, 3.94)	0.9
Small cribriform	4.38 (0.78, 24.45)	0.092
Large cribriform	20.83 (2.04, 212.97)	0.01
Intraductal carcinoma	10 (1.54, 64.75)	0.016
Cribriform architecture	9.62 (1.89, 48.93)	0.0063

Large Expansile Cribriform Pattern 4



MODERN PATHOLOGY (2015) 28, 457–464

Cribriform growth is highly predictive for postoperative metastasis and disease-specific death in Gleason score 7 prostate cancer

Charlotte F Kweldam[1], Mark F Wildhagen[2,3], Ewout W Steyerberg[4], Chris H Bangma[3], Theodorus H van der Kwast[5] and Geert JLH van Leenders[1]

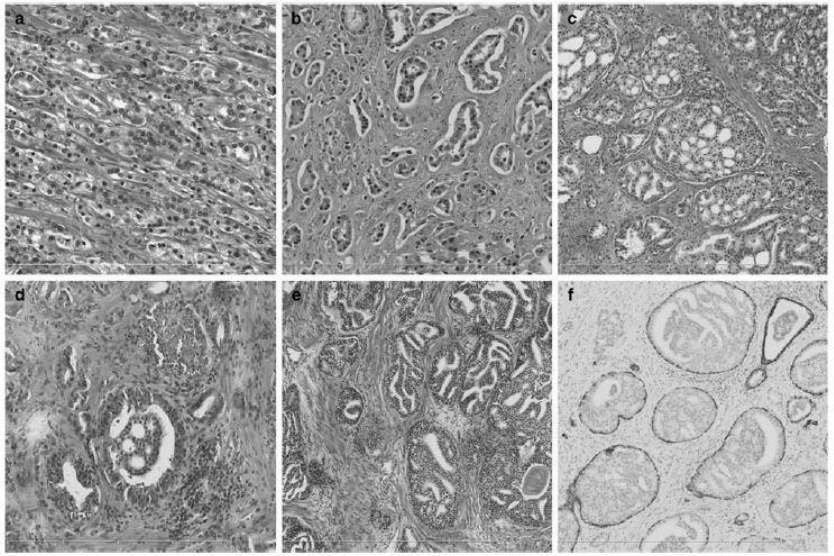
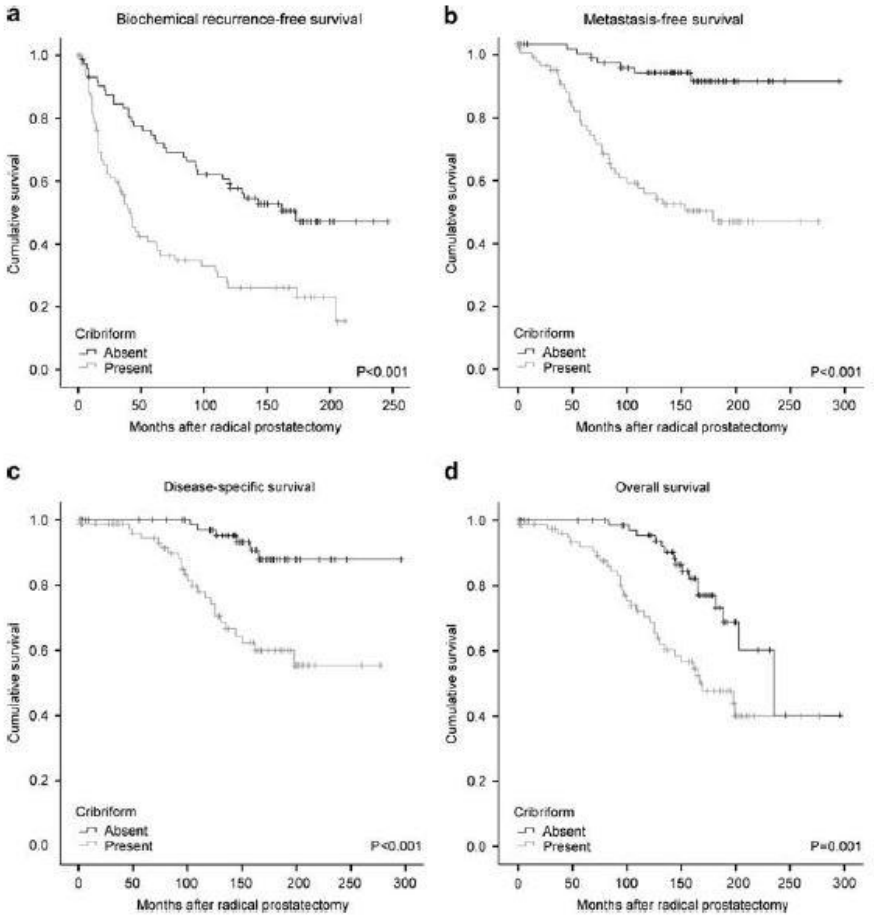


Figure 1 Gleason grade 4 patterns and intraductal carcinoma. (**a**) Fused glands; (**b**) ill-defined glands; (**c**) cribriform glands; (**d**) glomeruloid gland; (**e**) intraductal carcinoma; and (**f**) 34BE12 immunohistochemistry, demonstrating the presence of basal cells supportive for intraductal carcinoma.



MODERN PATHOLOGY (2016), 1–7

Disease-specific survival of patients with invasive cribriform and intraductal prostate cancer at diagnostic biopsy

Charlotte F Kweldam[1], Intan P Kümmerlin[1], Daan Nieboer[2], Esther I Verhoef[1], Ewout W Steyerberg[2], Theodorus H van der Kwast[3], Monique J Roobol[4] and Geert J van Leenders[1]

[1]*Department of Pathology, Erasmus Medical Centre, Rotterdam, The Netherlands;* [2]*Department of Public Health, Erasmus Medical Centre, Rotterdam, The Netherlands;* [3]*Laboratory Medicine Program, University Health Network, Toronto, ON, Canada and* [4]*Department of Urology, Erasmus Medical Centre, Rotterdam, The Netherlands*

Table 1 Patient and tumor characteristics ($N = 1031$)

	Mean (median, IQR) or n (%)					
	Gleason score 6 (n = 486)	*Gleason score 3+4 = 7 (n = 310)*	*Gleason score 4+3 = 7 (n = 104)*	*Gleason score 8 (n = 64)*	*Gleason score 9–10 (n = 67)*	*P-value*
Age at diagnosis (years)	66 (66, 61–70)	66 (67, 62–71)	68 (69, 65–71)	68 (69, 66–72)	67 (67, 64–71)	< 0.001[a]
PSA level at diagnosis (ng/ml)	5.8 (4.7, 3.5–6.9)	8.8 (5.8, 4.0–9.0)	15 (8.6, 4.7–18)	19 (11, 6.2–17)	16 (9.4, 5.4–16)	< 0.001[a]
Percentage of positive cores (%)	31 (29, 17–43)	2.9 (3.0, 2.0–4.0)	50 (43, 29–71)	55 (50, 40–71)	62 (57, 43–86)	< 0.001[a]
Tumor percentage (%)	24 (17, 9.5–33)	43 (44, 27–57)	51 (51, 33–68)	51 (52, 33–66)	56 (56, 41–74)	< 0.001[a]
Gleason grade 4 patterns						
Ill-formed		227 (73)	63 (85)	51 (80)	64 (96)	< 0.001[b]
Fused		153 (49)	46 (62)	32 (50)	39 (58)	0.07[b]
Cribriform		24 (7.7)	38 (37)	23 (36)	26 (39)	< 0.001[b]
Glomeruloid		33 (11)	14 (19)	13 (20)	11 (16)	0.02[b]
Gleason grade 5 patterns						
Single cells and strands				35 (55)	61 (91)	< 0.001[b]
Solid				3 (4.7)	16 (24)	0.002[b]
Intraductal carcinoma	4 (0.82)	41 (13)	44 (42)	18 (28)	32 (48)	< 0.001[b]
CR/IDC+ status	4 (0.82)	54 (17)	60 (58)	33 (52)	42 (63)	< 0.001[b]
Primary treatment						
Radical prostatectomy	216 (44)	129 (42)	33 (32)	14 (22)	14 (21)	< 0.001[b]
Radiotherapy	188 (39)	154 (59)	66 (63)	48 (75)	52 (78)	< 0.001[b]
Endocrine treatment	2 (0.41)	3 (0.97)	1 (0.96)	1 (1.6)		
Watchful waiting	80 (17)	23 (7.4)	3 (2.8)	1 (1.6)	1 (1.5)	< 0.001[b]
Radiotherapy and endocrine treatment			1 (0.96)			
Unknown		1 (0.27)				
Prostate-cancer-specific deaths	8 (1.6)	14 (4.5)	17 (16)	14 (22)	19 (28)	

[a]Kruskal-Wallis test. [b]Pearson's chi-square (χ^2) test.

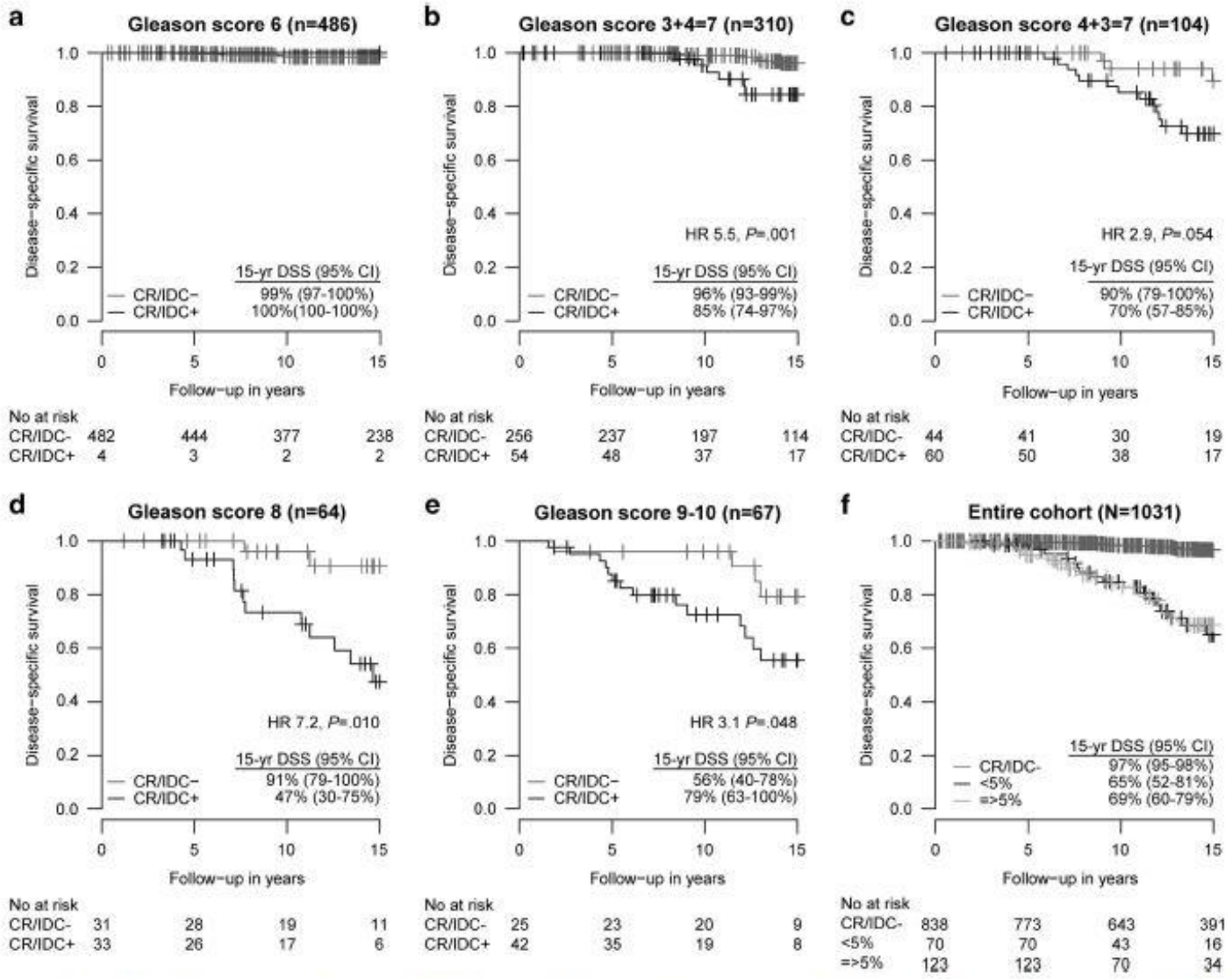


Figure 1 Kaplan-Meier disease-specific survival (DSS) according to Gleason score and CR/IDC status. (**a**) Gleason score 6. (**b**) Gleason score 3+4 = 7. (**c**) Gleason score 4+3 = 7. (**d**) Gleason score 8. (**e**) Gleason score 9–10. (**f**) DSS probabilities according to percentage of CR/IDC glands.

ONCOLOGY LETTERS 14: 390-396, 2017

Distinct DNA methylation alterations are associated with cribriform architecture and intraductal carcinoma in Gleason pattern 4 prostate tumors

EKATERINA OLKHOV-MITSEL[1,2], FARSHID SIADAT[3], KEN KRON[4], LIYANG LIU[1,2], ANDREA J. SAVIO[1,2], JOHN TRACHTENBERG[5], NEIL FLESHNER[5], THEODORUS VAN DER KWAST[2,6] and BHARATI BAPAT[1,2,6]

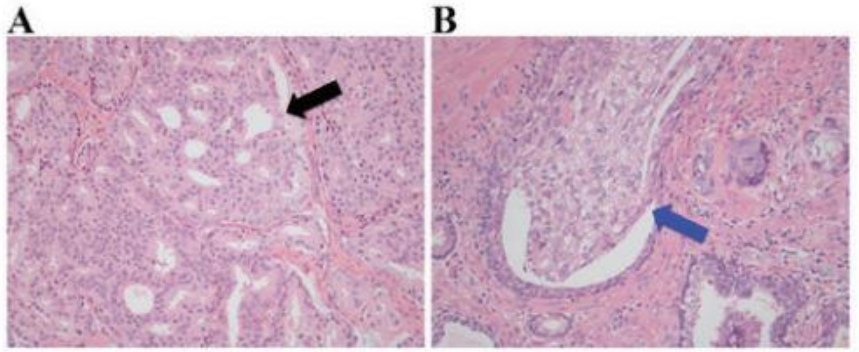


Figure 1. Representative hematoxylin and eosin stains of prostate cancer Gleason pattern 4 tissues with (A) cribriform architecture (marked with a black arrow) and (B) intraductal carcinoma (marked with a blue arrow). Magnification, x100.

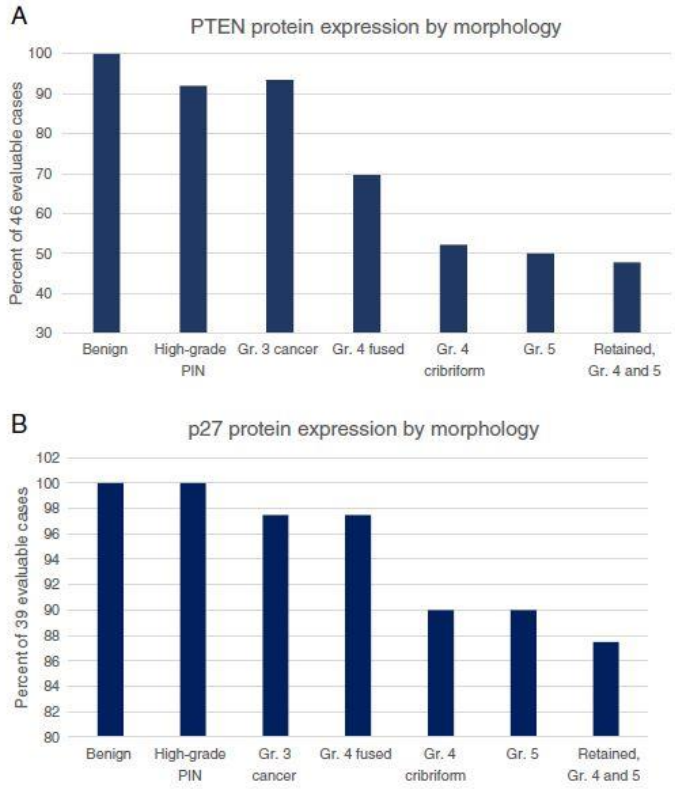
- 91 Gleason 7 prostatectomies
  - cribriform - 61/91 (67%)
  - IDC - 21/91 (23%)
- gene-specific methylation assay

- *APC*, *RASSF1A*, *TBX15* significantly higher % methylation ratio with cribriform and IDC

PTEN loss and p27 loss differ among morphologic patterns of prostate cancer, including cribriform☆,☆☆

Shira Ronen MD[a], Daniel W. Abbott MD[a], Oleksandr Kravtsov MD[a], Amrou Abdelkader MD[a], Yayun Xu MS[b], Anjishnu Banerjee PhD[b], Kenneth A. Iczkowski MD[a,*]

Human Pathology (2017) **65**, 85–91



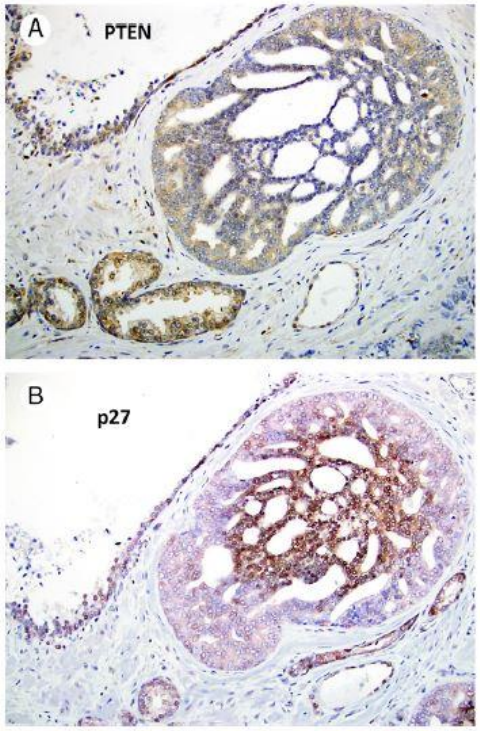


Fig. 3 This cribriform cancer shows predominant PTEN loss centrally (A) and p27 loss peripherally (B).

UHN Toronto General Toronto Western Princess Margaret Toronto Rehab

New Synoptic Reporting Items at UHN

- **Grade group -** 1 to 5
- **% pattern 4 or 5** (as a global % of all carcinoma)
- **Cribriform morphology**
  - Present
  - Absent
  - Indeterminate
- **Intraductal carcinoma**
  - Present
  - Absent
  - Indeterminate

Issues With Poorly-Formed Glands

- Moved to pattern 4 by ISUP consensus 2005
  - ✓ *clinical outcome evidence to support the move???*
- Frequently encountered in biopsies
- Suffer from high interobserver variability
- Frequent cause of grief for pathologists re: active surveillance patient selection (is it 6 or 7?)

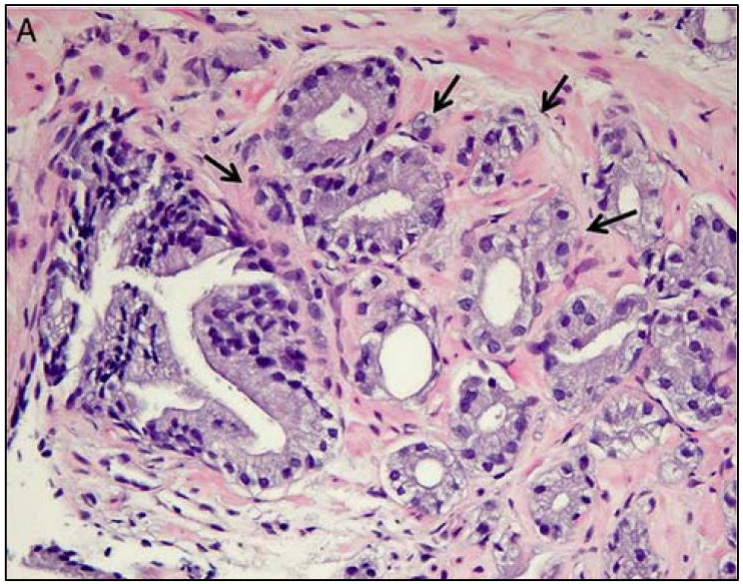
- Not predictive of upgrading/upstaging
- Ki67 labelling index closer to pattern 3

Diagnosis of "Poorly Formed Glands" Gleason Pattern 4 Prostatic Adenocarcinoma on Needle Biopsy

An Interobserver Reproducibility Study Among Urologic Pathologists With Recommendations

Ming Zhou, MD, PhD, Jianbo Li, PhD,† Liang Cheng, MD, PhD,‡ Lars Egevad, MD,§ Fang-Ming Deng, MD,* Lakshmi Priya Kunju, MD,‖ Cristina Magi-Galluzzi, MD, PhD,† Jonathan Melamed, MD,* Rohit Mehra, MD,‖ Savvas Mendrinos, MD,¶ Adeboye O. Osunkoya, MD,# Gladell Paner, MD,** Steve S. Shen, MD, PhD,†† Toyonori Tsuzuki, MD,‡‡ Kiril Trpkov, MD,§§ Wei Tian, MD,¶ Ximing Yang, MD, PhD,‖‖ and Rajal B. Shah, MD¶*

(*Am J Surg Pathol* 2015;39:1331–1339)



- Tangentially sectioned pattern 3?
- Poorly formed glands pattern 4?
- K = 0.34 (fair agreement)

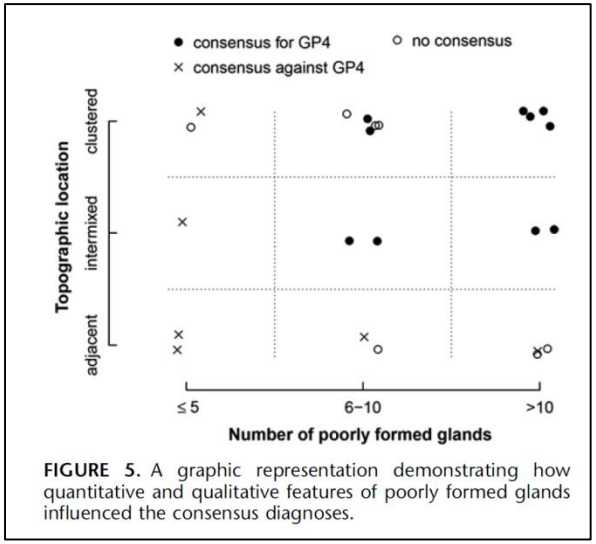


FIGURE 5. A graphic representation demonstrating how quantitative and qualitative features of poorly formed glands influenced the consensus diagnoses.

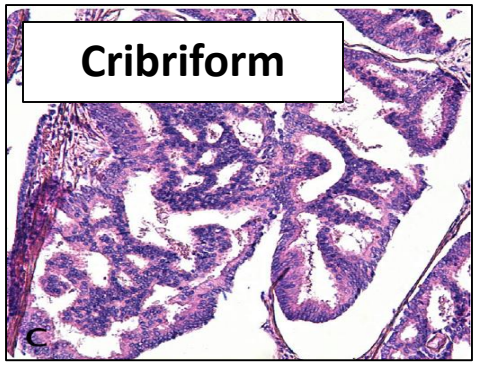
TABLE 4. Histologic Features That Are Diagnostic of and Against GP4 Poorly Formed Glands by Urologic Pathologists

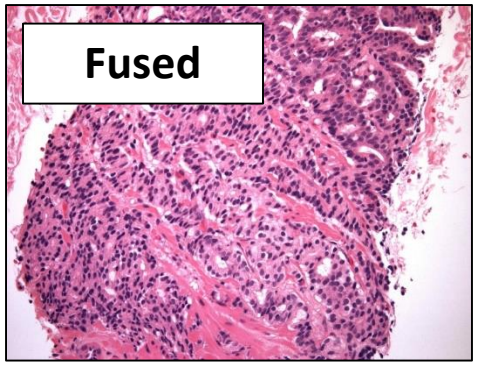
Histologic features that are "diagnostic of" GP4 "poorly formed glands"
> 10 poorly formed glands that are not immediately adjacent to other well-formed glands
Histologic features that are "against" GP4 "poorly formed glands"
Poorly formed glands intermixed with and immediately adjacent to (with < 1 gland distance from) well-formed glands regardless of their number
≤ 5 poorly formed glands regardless of their location

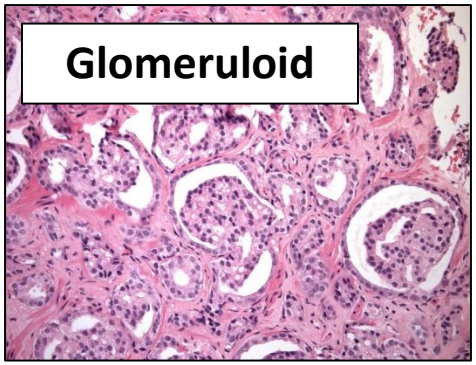
Poorly-Formed Glands: Do They Belong in Gleason Pattern 4?

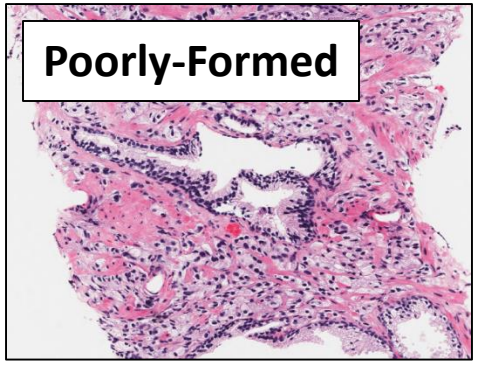
- **Outcomes** for Gleason 7 patients on active surveillance
  - types/amount of pattern 4 at initial biopsy
  - types/amount of pattern 4 after risk re-classification on follow-up biopsies after initial Gleason 6/10 (3+3).
    - ❖ *my experience that poorly formed glands are the most common reason for risk re-classification when pattern 4 = 5-10% of total carcinoma.*
- **Molecular characterization** vs pattern 3 and other forms of pattern 4

Active Surveillance for Gleason 7 Patients < 10% Pattern 4: My Predictions









- Definitely not suitable
- Most likely not suitable
- Suitable - like pattern 3 (especially cases < 10% pattern 4)

2014 ISUP Consensus Conference: Are More Revisions to the Gleason System Really Necessary?

Stay tuned for more!


Thank You!