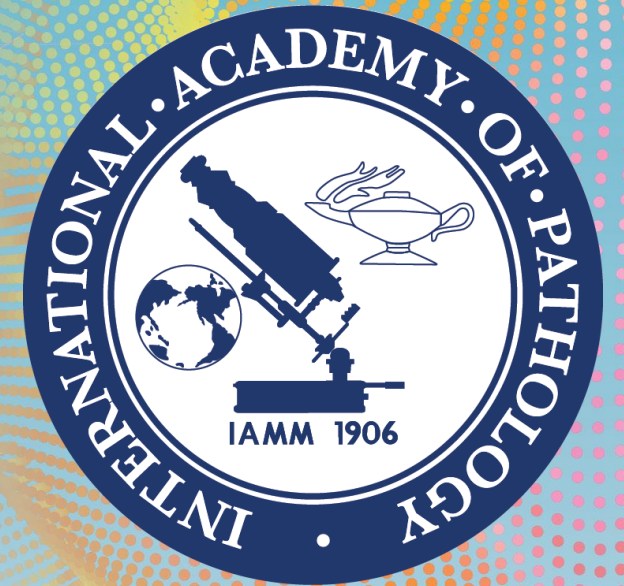


What's new in prostate pathology:
Update on morphologic aspects
**Emphasis on the poorly
formed gland**

Nicole Swarbrick

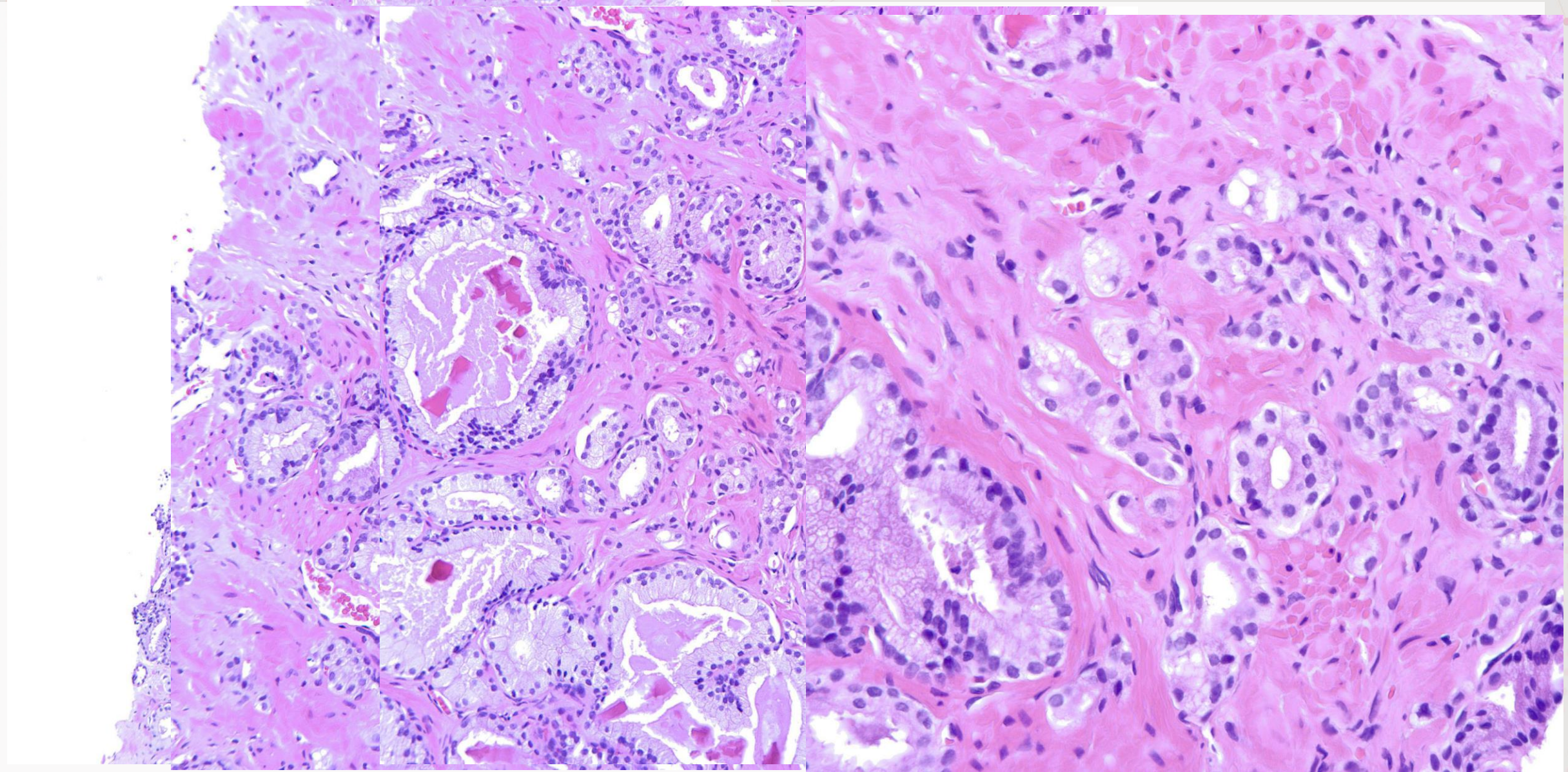
PathWest



Disclosure of Relevant Financial Relationships

No relevant financial relationships





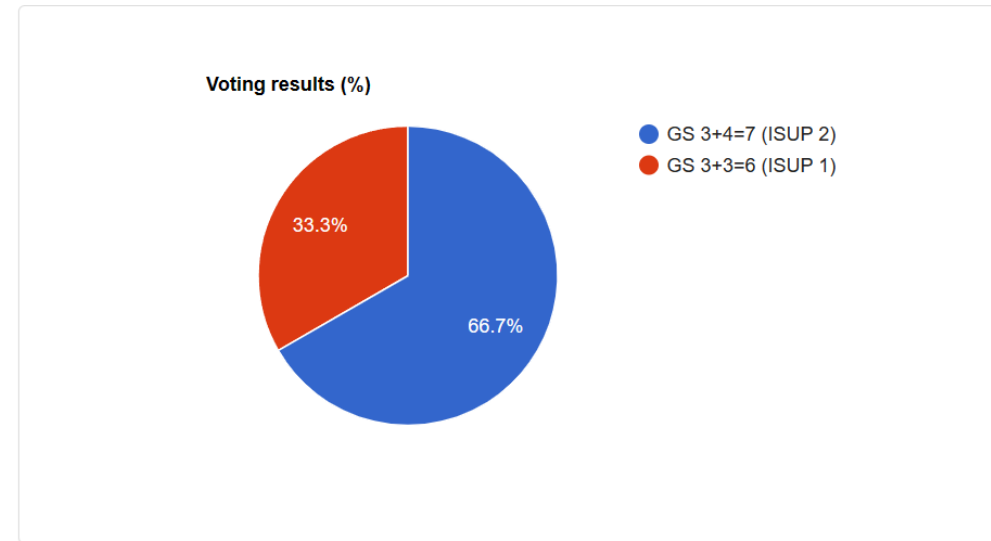


PATHOLOGY IMAGEBASE

An ISUP reference image library

Consensus grade: **GS 3+4=7 (ISUP 2)**

Show diagnosis by expert panel members



Reproduced with kind permission from Prof L Egevad

The extent of the problem

Distinguishing tangentially sectioned Gleason pattern 3 from Gleason pattern 4 amongst 11 pathologists

- Interobserver reproducibility - only fair (Light's κ 0.27).
- Intra-observer reproducibility ranged from 65% to 100% (mean 81.5%).

The Potential Impact of Reproducibility of Gleason Grading in Men With Early Stage Prostate Cancer Managed by Active Surveillance: A Multi-Institutional Study

Jesse K. McKenney,* Jeff Simko,† Michael Bonham, Lawrence D. True, Dean Troyer, Sarah Hawley, Lisa F. Newcomb, Ladan Fazli,‡ Lakshmi P. Kunju, Marlo M. Nicolas, Funda Vakar-Lopez, Xiaotun Zhang, Peter R. Carroll,§ James D. Brooks and the Canary/Early Detection Research Network Prostate Active Surveillance Study Investigators

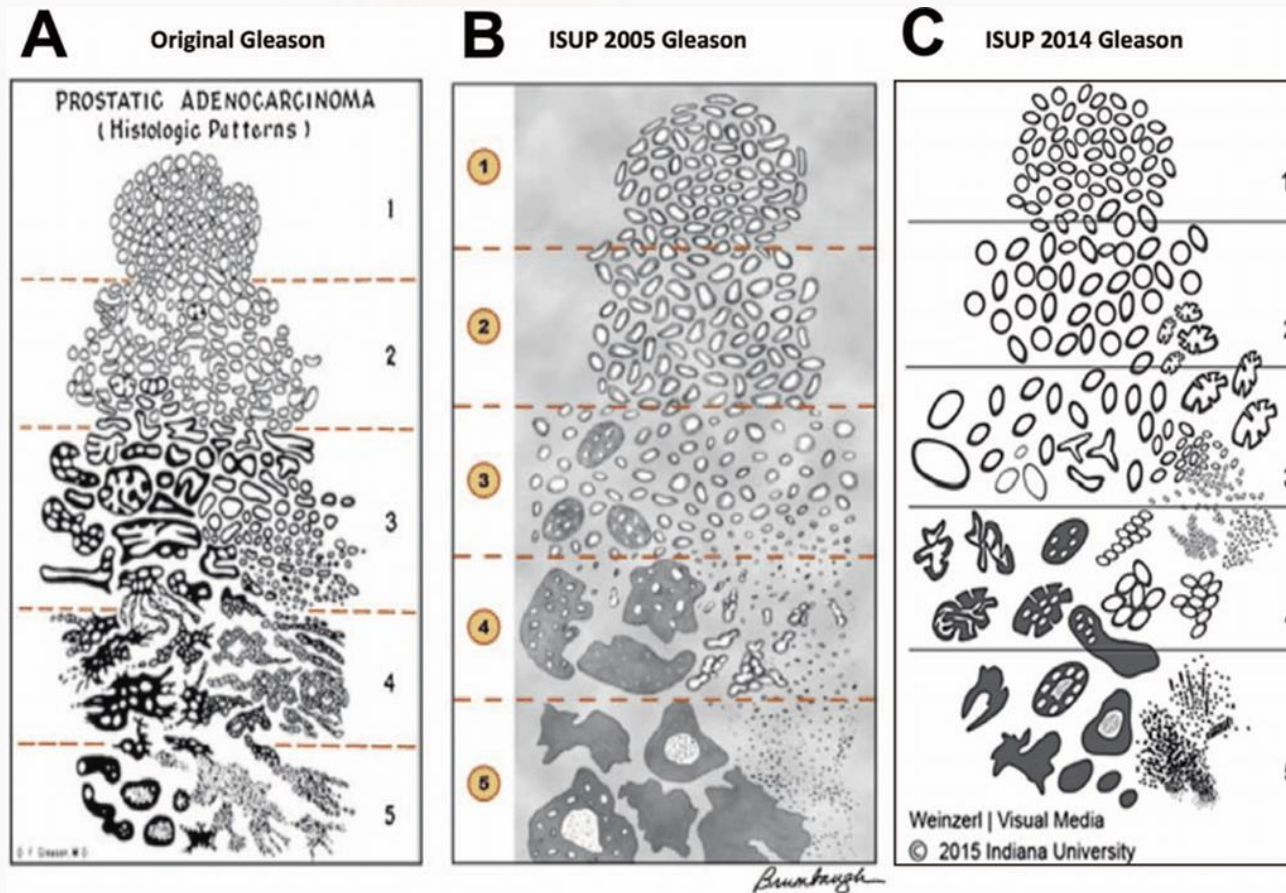
J Urol. 2011 Aug;186(2):465-9

Why does this matter?

Eligibility for active surveillance:

- Grade group 1
- Subset of Grade group 2
 - Low volume (number of cores involved/percent cancer involvement of involved cores)
 - Low percentage Gleason pattern 4
 - Absence of cribriform pattern/IDC
 - Family history/known germline mutations
 - MRI findings

The history



First added in ISUP consensus conference in 2005:

“ill-defined glands with poorly formed glandular lumens”

Ill-defined glands with poorly formed glandular lumina

“only a cluster of such glands, where a tangential section of Gleason pattern 3 glands cannot account for the histology , would be acceptable as Gleason pattern 4”

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

Jonathan I. Epstein, MD, William C. Allsbrook, Jr, MD,† Mahul B. Amin, MD,‡
and Lars L. Egevad, MD, PhD,§ and the ISUP Grading Committee[¶]*

Am J Surg Pathol • Volume 29, Number 9, September 2005

“high-grade tumor of any quantity on needle biopsy ... should be included within the Gleason score”

*as long as it was identified at low to medium magnification

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

Jonathan I. Epstein, MD, William C. Allsbrook, Jr, MD,† Mahul B. Amin, MD,‡
and Lars L. Egevad, MD, PhD,§ and the ISUP Grading Committee¶*

Am J Surg Pathol • Volume 29, Number 9, September 2005

- For a diagnosis of Gleason pattern 4, it needs to be seen at x 10 lens magnification.
- Occasional/seemingly poorly formed or fused glands between well-formed glands is insufficient for a diagnosis of Pattern 4.
- In cases with borderline morphology between Gleason pattern 3 and pattern 4 and crush artefacts, the lower grade should be favoured.

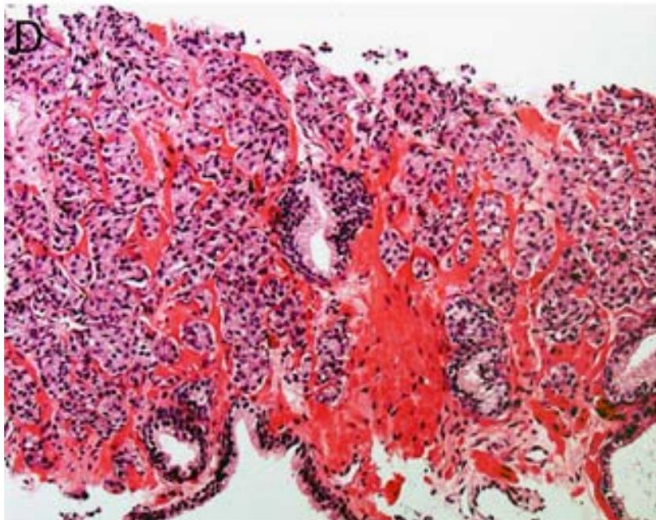
The 2014 International Society of Urological Pathology
(ISUP) Consensus Conference on Gleason Grading of
Prostatic Carcinoma

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 40, Number 2, February 2016

- Only cancer glands with no or rare luminal formation be considered “poorly formed.”
- A minimum of 10 “poorly-formed” glands constituting a separate tumour area in an otherwise Gleason pattern 3 tumour would be required to assign a pattern 4 .
- Poorly formed glands intermingled with bona-fide pattern 3 glands should not, in their view, lead to an upgrading of the biopsy.
- When there is uncertainty, recommend default to GP3.



K=0.34

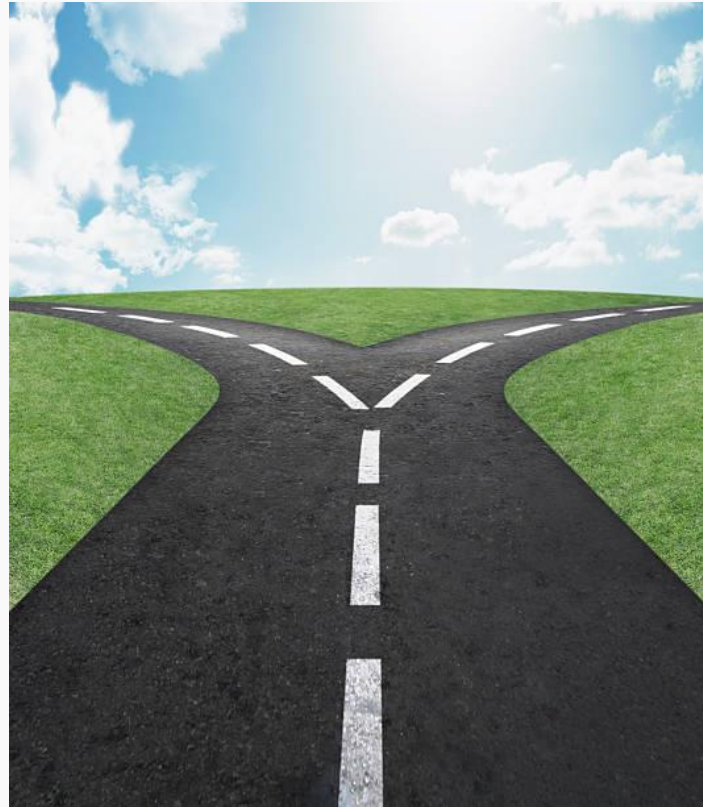
Diagnosis of “Poorly Formed Glands” Gleason Pattern 4
Prostatic Adenocarcinoma on Needle Biopsy
*An Interobserver Reproducibility Study Among Urologic Pathologists
With Recommendations*

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 • Volume 39, Number 10, October 2015

Where to from here?

Educate further within
the system we have



Look at the problem
from a different
perspective

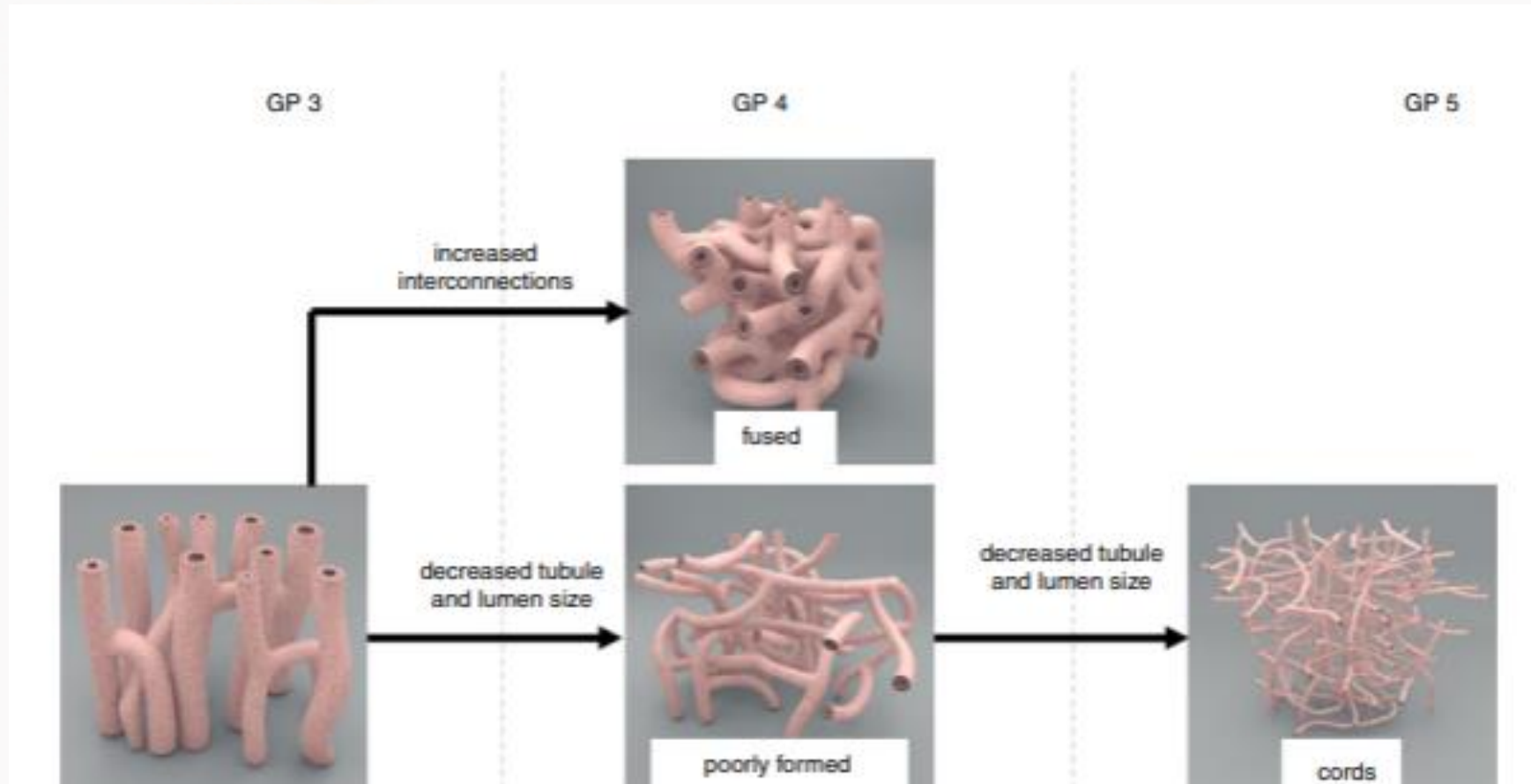
Three-dimensional architecture of prostate cancer growth patterns

Two distinct architectural subgroups

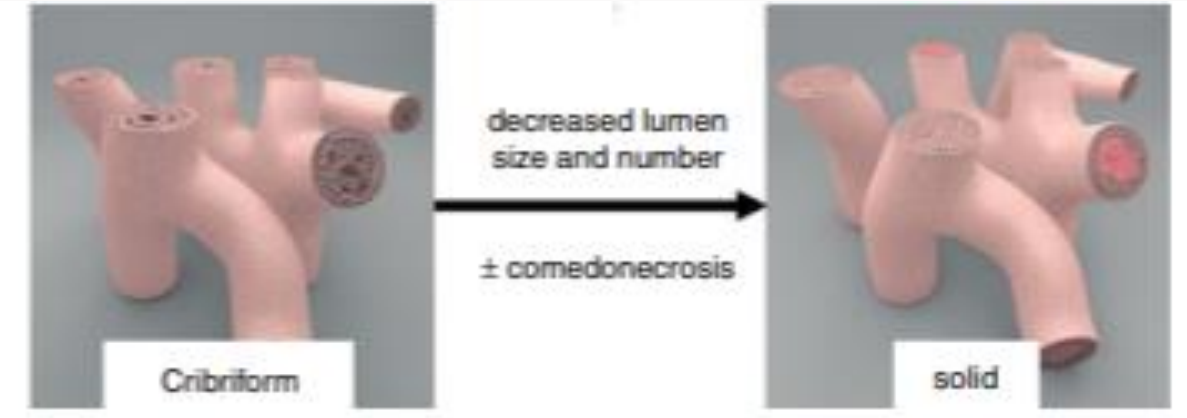
1. Prostate cancer with tumour cells in contact with stroma
2. Prostate cancer with tumour cells **not** in contact with stroma

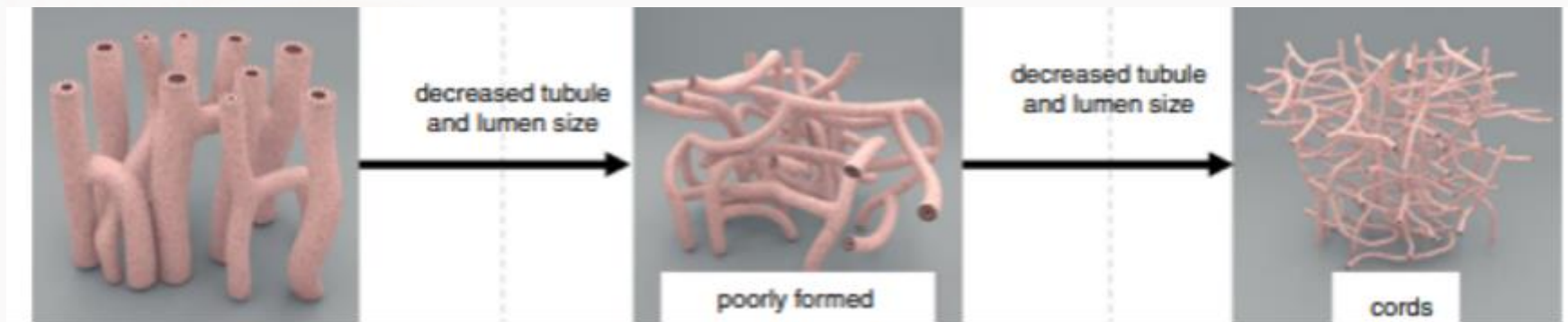


1. Tumour cells in contact with stroma



2. Tumour cells not in contact with stroma





Cribriform carcinoma/intraductal carcinoma


Greater risk of

- Extraprostatic extension
- Seminal vesicle invasion
- Positive surgical margins
- Biochemical recurrence
- Cancer specific mortality

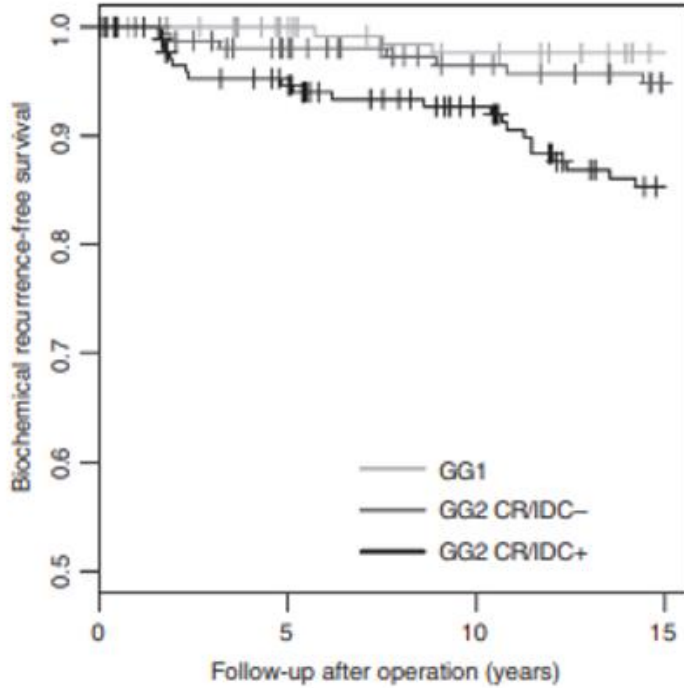
Böttcher et al. *BMC Cancer* (2018) 18:8
DOI 10.1186/s12885-017-3976-z

BMC Cancer

RESEARCH ARTICLE Open Access

Cribriform and intraductal prostate cancer are associated with increased genomic instability and distinct genomic alterations 

René Böttcher^{1†}, Charlotte F. Kweldam^{2†}, Julie Livingstone³, Emilie Lalonde^{3,4}, Takafumi N. Yamaguchi³, Vincent Huang³, Fouad Yousif³, Michael Fraser⁵, Robert G. Bristow^{4,5,6}, Theodoros van der Kwast⁷, Paul C. Boutros^{3,4,8†}, Guido Jenster^{1†} and Geert J. L. H. van Leenders^{2†}

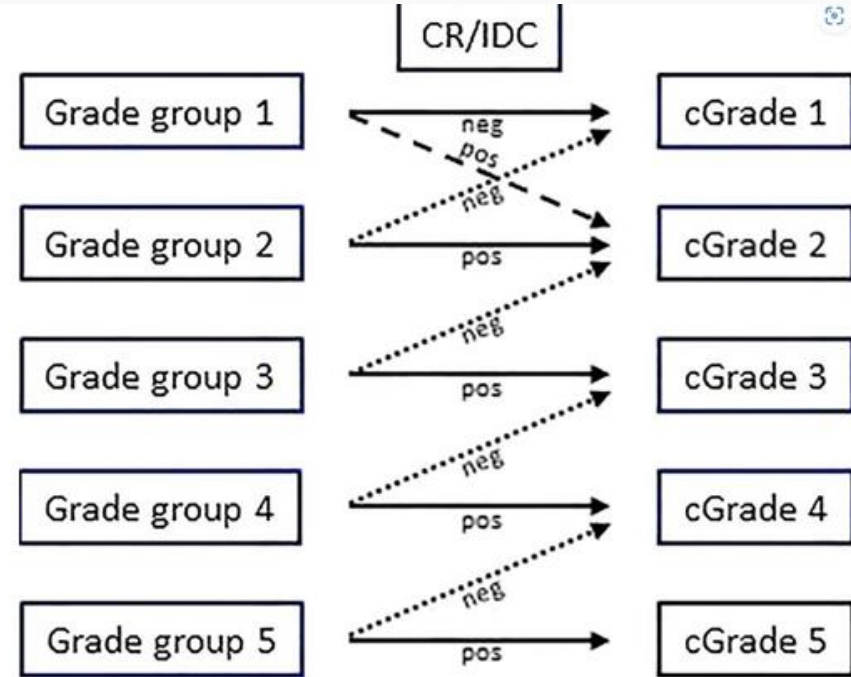


Histopathology

Histopathology 2020, 76, 755-762. DOI: 10.1111/his.14064

Clinical outcome comparison of Grade Group 1 and Grade Group 2 prostate cancer with and without cribriform architecture at the time of radical prostatectomy

Eva Hollemans,¹ Esther I Verhoef,¹ Chris H Bangma,² John Rietbergen,¹ Monique J Roobol,² Jozien Helleman² & Geert J L H van Leenders¹



EUROPEAN UROLOGY 77 (2020) 191-198

Improved Prostate Cancer Biopsy Grading by Incorporation of Invasive Cribriform and Intraductal Carcinoma in the 2014 Grade Groups

Geert J.L.H. van Leenders^{a,*}, Charlotte F. Kweldam^a, Eva Hollemans^a, Intan P. Kümmerlin^a, Daan Nieboer^{b,c}, Esther I. Verhoef^a, Sebastiaan Remmers^b, Luca Incrocci^d, Chris H. Bangma^b, Theodorus H. van der Kwast^e, Monique J. Roobol^b

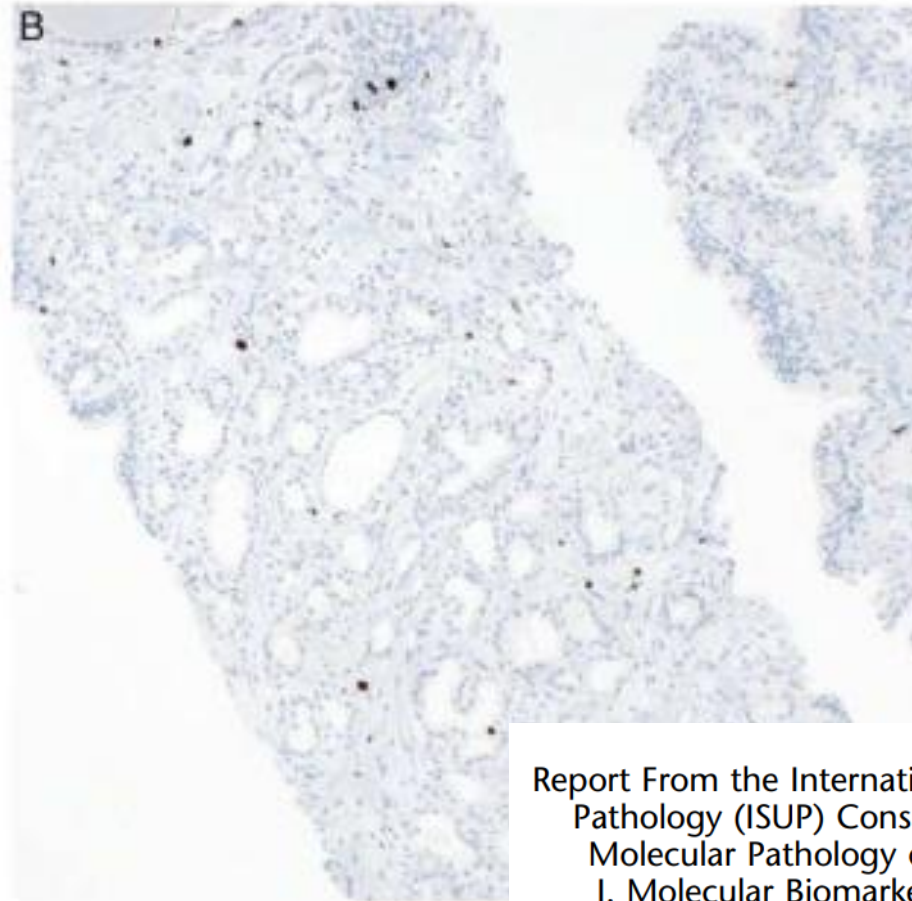
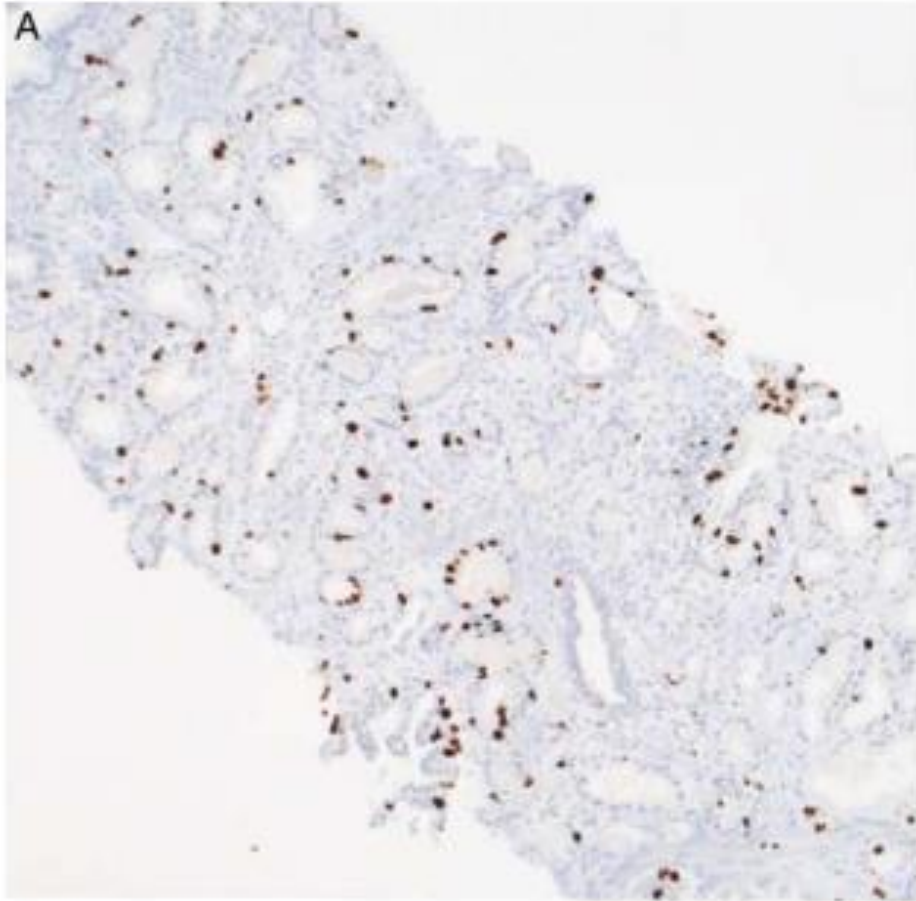
Sampling

40% of men with Grade Group 2 prostate cancer on biopsy were false-negative for invasive cribriform and/or intraductal carcinoma.



Use of tissue-based biomarkers in the prostate biopsy

- mRNA-based genomic signature testing
eg Decipher, Oncotype Dx
- Immunohistochemistry – Ki67, PTEN



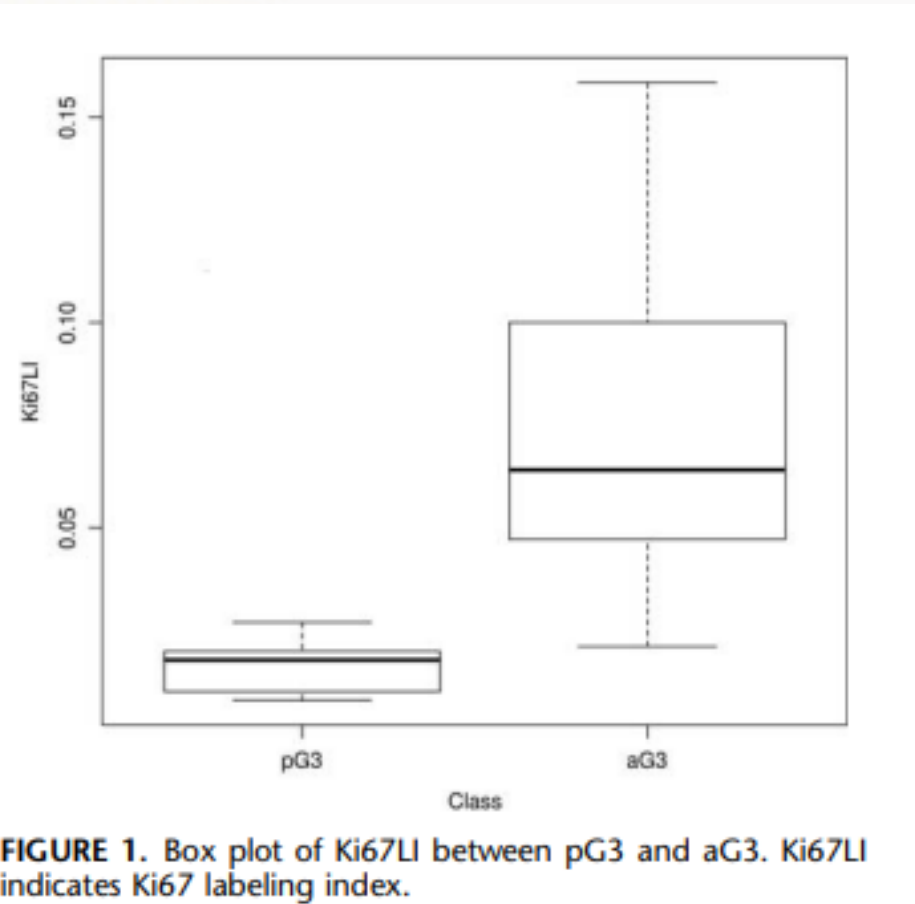
“Ki67 is a robust prognostic marker... particularly useful for patients considered for AS.”

Report From the International Society of Urological Pathology (ISUP) Consultation Conference on Molecular Pathology of Urogenital Cancers.
I. Molecular Biomarkers in Prostate Cancer

Tamara L. Lotan, MD,†‡ Scott A. Tomlins, MD, PhD,§ Tarek A. Bismar, MD,||
Theodorus H. Van der Kwast, MD, PhD,*¶ David Grignon, MD,# Lars Egevad, MD,**
Glen Kristiansen, MD,†† Colin C. Pritchard, MD, PhD,‡‡ Mark A. Rubin, MD,§§
and Lukas Bubendorf, MD|||*

Am J Surg Pathol • Volume 44, Number 7, July 2020

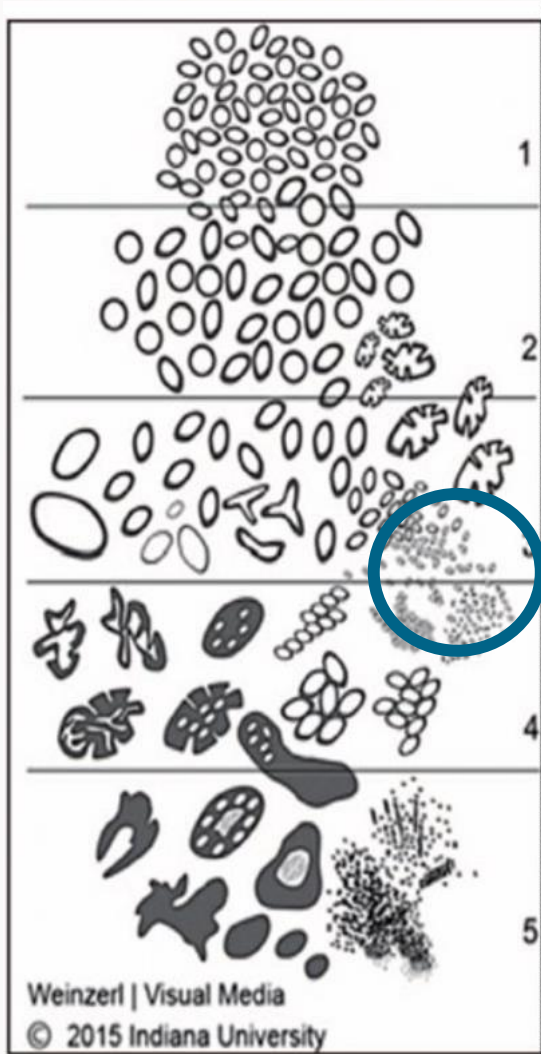
Ki67



Ki67 in Gleason Pattern 3 as a Marker of the Presence of Higher-Grade Prostate Cancer

Alessandro Caputo, MD, Antonio D'Antonio, MD, PhD,† Domenico Memoli, BS,† Francesco Sabbatino, MD, PhD,* Vincenzo Altieri, MD, PhD,*† and Pio Zeppa, MD, PhD*†*

Appl Immunohistochem Mol Morphol • Volume 29, Number 2, February 2021



Significant inter- and intra-observer variation remains.

Biologic continuum exists.

Cribriform carcinoma/IDC are different.

To overcome sampling error on prostate biopsy, ancillary testing may have merit.

Thank you

