

2° Convegno Nazionale

# IL TEAM INTERDISCIPLINARE NEL CARCINOMA DELLA PROSTATA

NEGRAR DI VALPOLICELLA 6-7 DICEMBRE 2019

Sala Perez - IRCCS Ospedale Sacro Cuore Don Calabria



Istituto Don Calabria  
IRCCS Ospedale

**Sacro Cuore Don Calabria**

PRESIDIO OSPEDALIERO ACCREDITATO - REGIONE VENETO

## Illustrazione del Nuovo Sistema di Grading

Enrico Munari

Anatomia Patologica  
IRCCS Sacro Cuore Don Calabria  
Negrar di Valpolicella (VR)



Cancer Care Center

Numero Verde

**800 143 143**

Numero per la Cura del Tumore

Coordinatori: STEFANIA GORI - FILIPPO ALONGI - STEFANO CAVALLERI

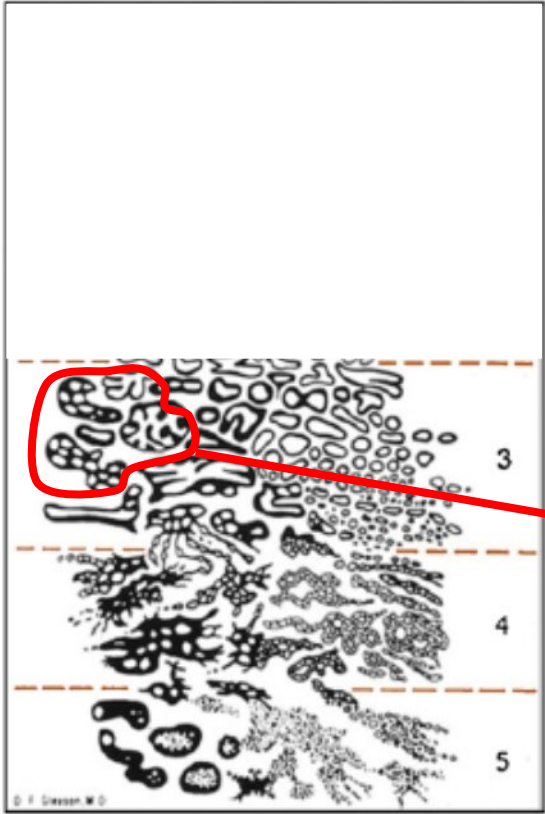
# Outline

- From Gleason to Grade Groups
- Problematic areas
- The cribriform pattern
- Beyond the single gland evaluation

# From Gleason to Grade Groups: pattern evolution

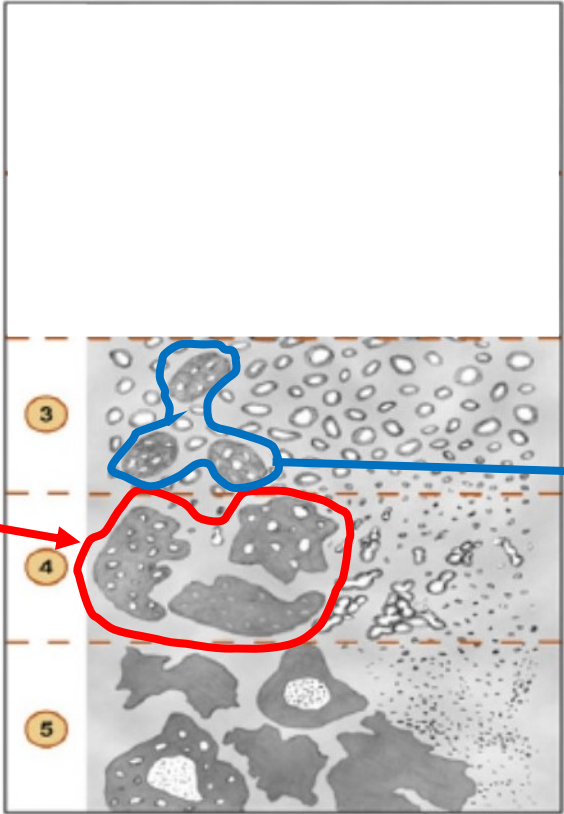
## Evoluzione del Gleason Score

Original Gleason



Gleason 1992 Hum Pathol

ISUP 2005 Gleason



Epstein 2005 Am J Surg Pathol

ISUP 2014 Gleason



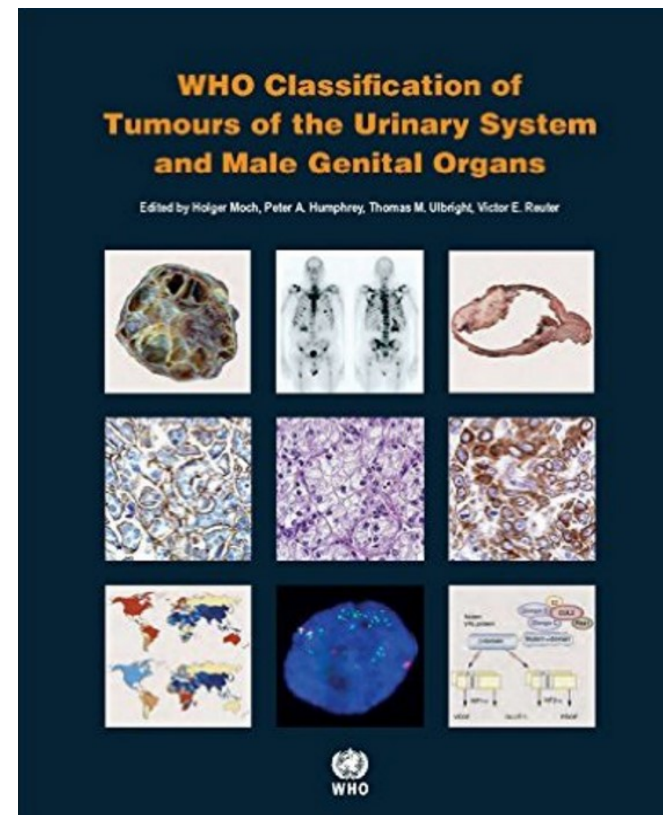
Epstein 2016 Am J Surg Pathol

Weinzerl | Visual Media  
© 2015 Indiana University

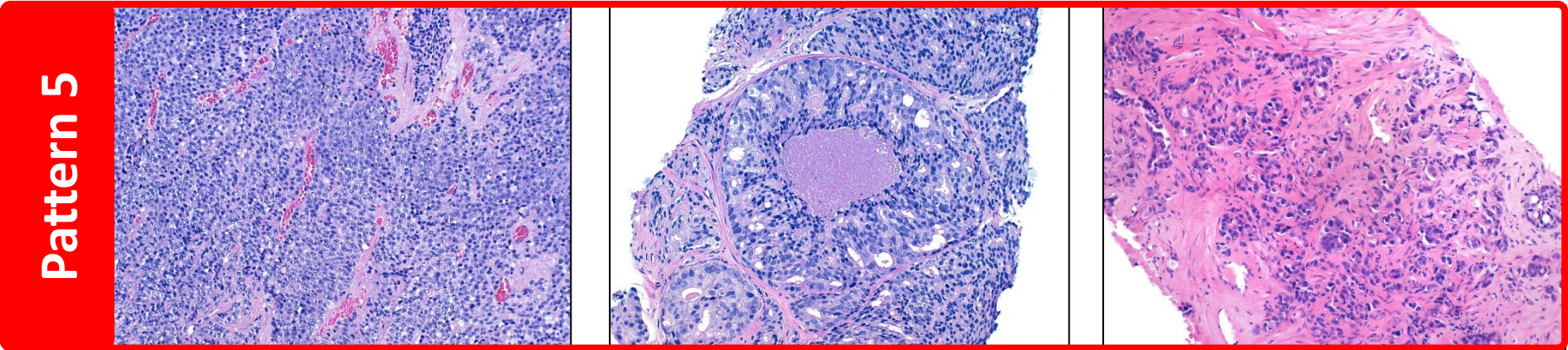
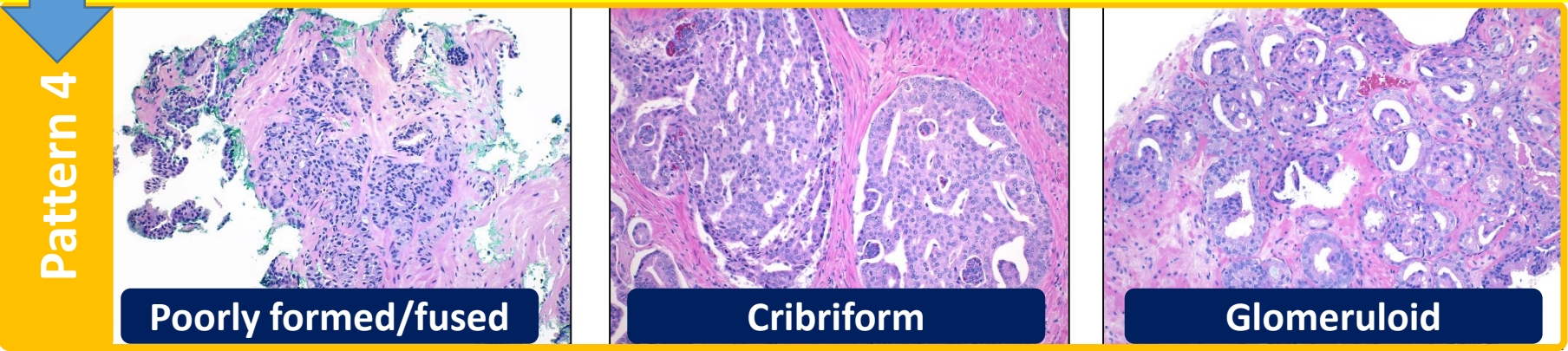
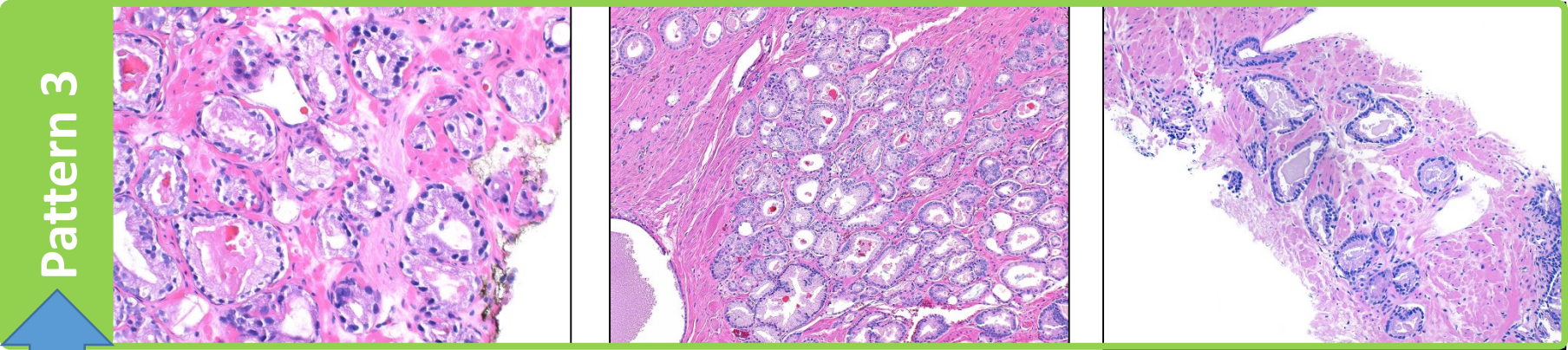
# From Gleason to Grade Groups: limits of GS

- 1+1; 1+2; 1+3; 1+4...25 scores possible!!
- 6 is the lowest score in a 2-10 interval
- With a GS 6 the patient thinks to have a bad prognosis
- GS 7 is not homogeneous:  $3+4 \neq 4+3$
- GS 8  $\neq$  GS 9-10

Grade Group	Gleason score
1	$\leq 6$
2	$3+4=7$
3	$4+3=7$
4	8
5	9-10

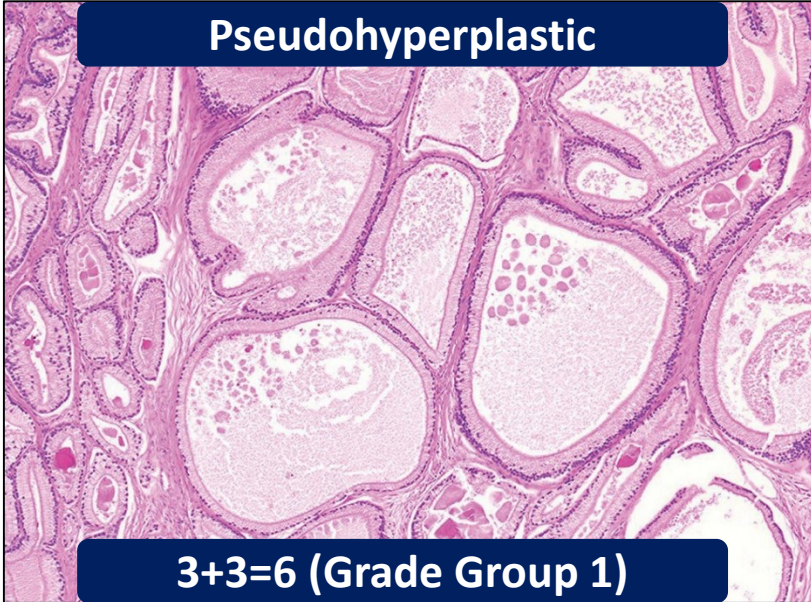


# From Gleason to Grade Groups: pattern morphology



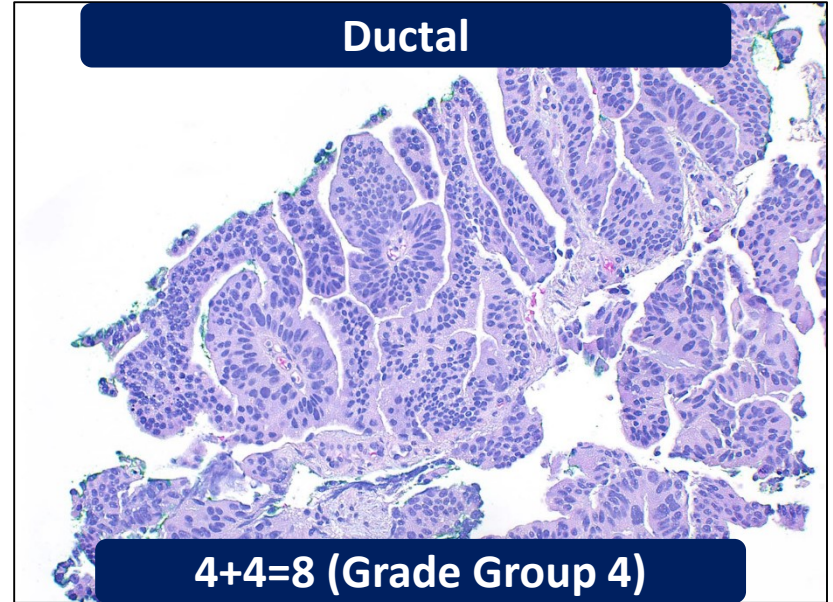
# Grading variants and variations

**Pseudohyperplastic**



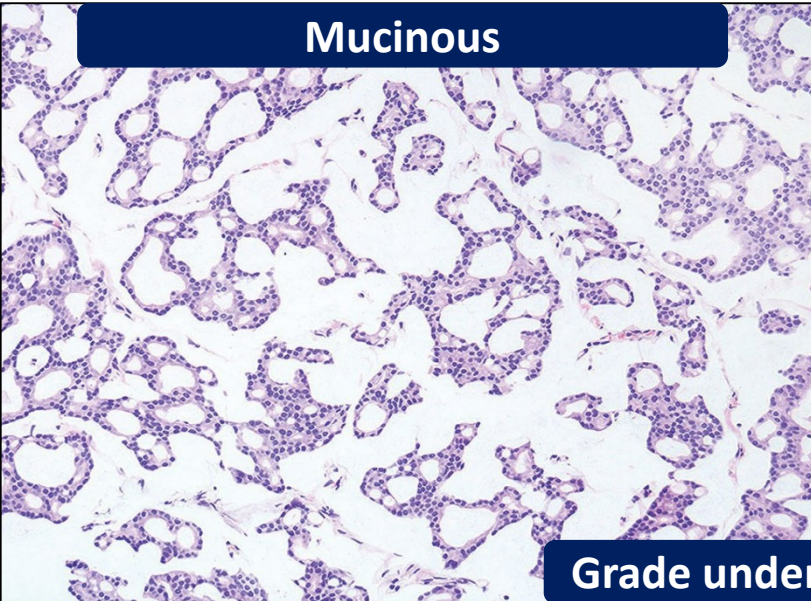
**3+3=6 (Grade Group 1)**

**Ductal**



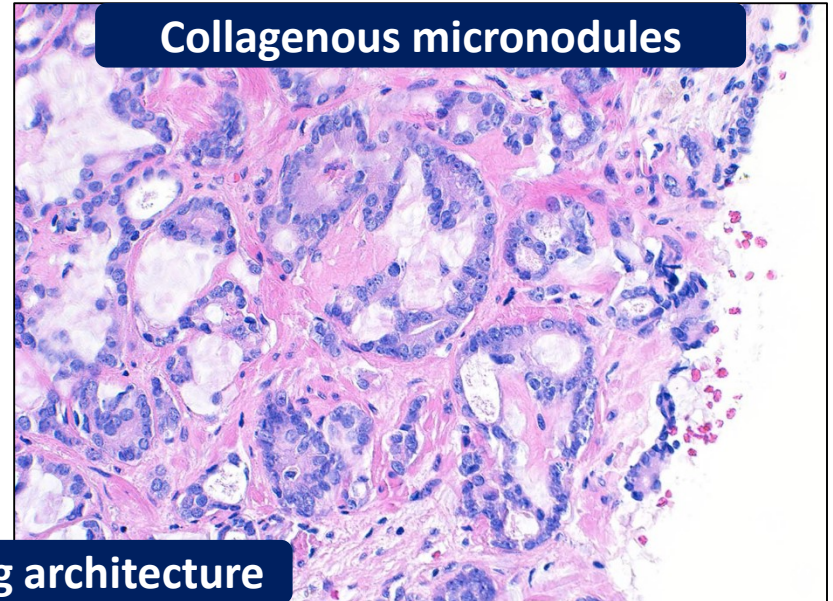
**4+4=8 (Grade Group 4)**

**Mucinous**



**Grade underlying architecture**

**Collagenous micronodules**



# Problematic areas: reproducibility of gleason patterns

90 prostate biopsies



Panel of 24 international experts

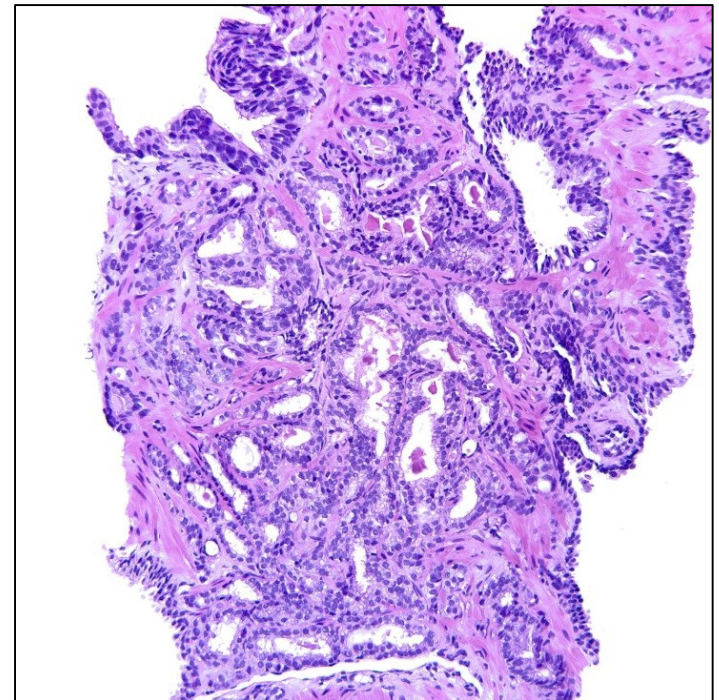
**Consensus ( $\geq 2/3$ ) reached in 50/90 cases**

kappa of 0.67 (95% CI= 0.62–0.72)

Table 3. Reproducibility by proposed ISUP grade among all cases

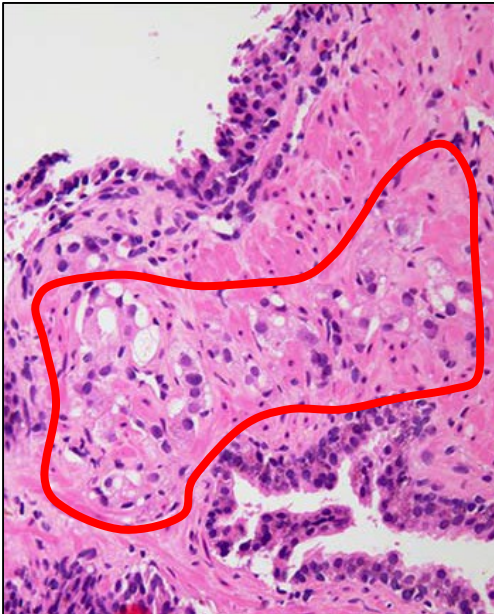
Proposed grade	Consensus, <i>n</i>	Total, <i>n</i>	% Consensus	
			Proposed grade	Any grade
1	16*	20	80.0	85.0
2	17	32	53.1	53.1
3	3†	14	21.4	35.7
4	5	11	45.5	45.5
5	6	13	46.2	46.2

**Poorly formed glands  $\approx$  40% GG2**

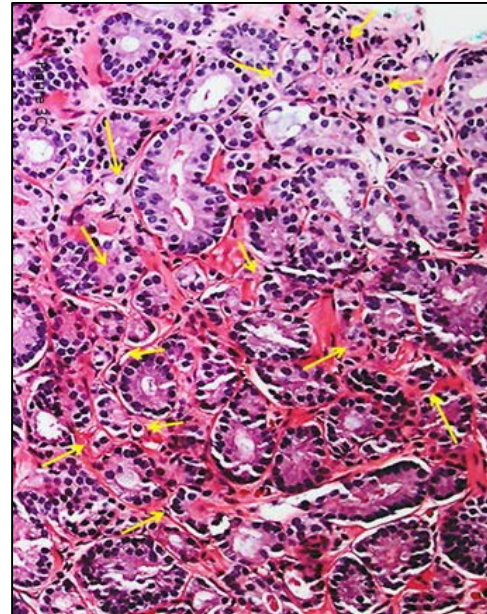


# Problematic areas: poorly formed glands

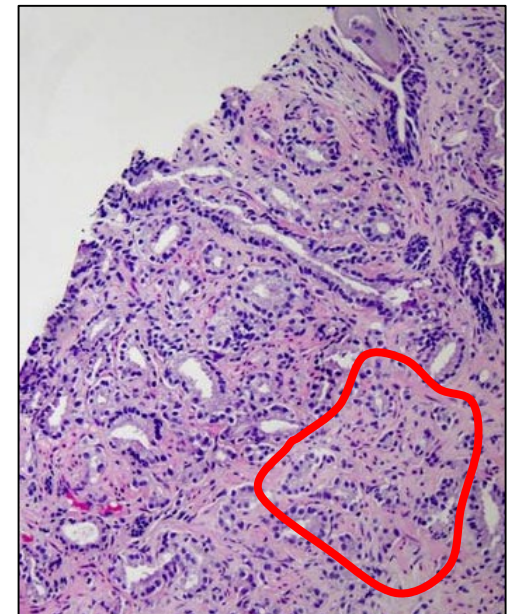
«Clustered»



«Adjacent»



«Intermixed»



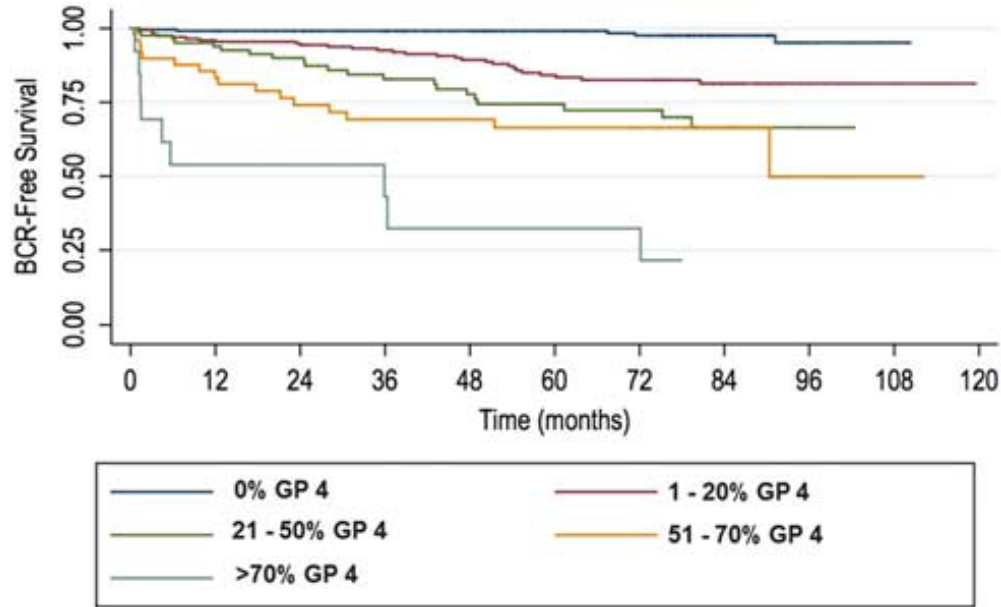
**TABLE 4. Histologic Features That Are Diagnostic of and Against GP4 Poorly Formed Glands by Urologic Pathologists**

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






# Problematic areas: quantification of GS 4



Neoplasia = 40%

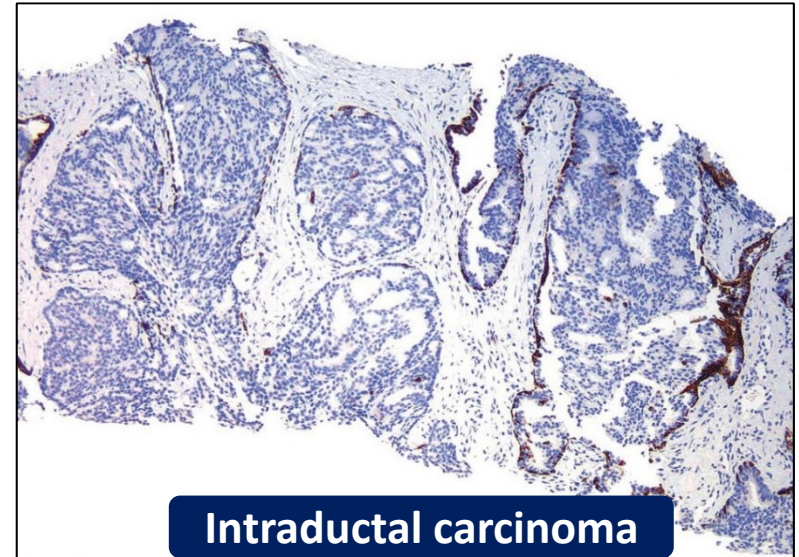
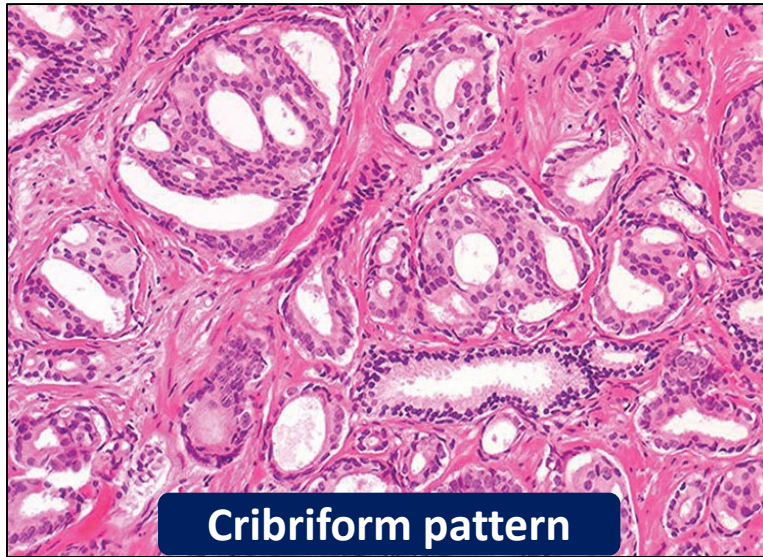
Pattern 4 = 30% of neoplasia



-  = pattern 3
-  = pattern 4
-  = benign glands



# The cribriform pattern: prognosis



***Not all Gleason 4 patterns are created equal!***

**TABLE 4. BCR-free Survival Among GS 7 Prostate Cancers Comparing Presence and Absence of 1 of GP 4 Architectures**

Architectures	5-y BCR-free Survival With Architecture (% [95% CI])	5-Year BCR-free Survival without Architecture (% [95% CI])	<i>P</i> value
Cribriform	68 (59-76)	85 (78-89)	< 0.01
Fused	82 (74-88)	75 (74-88)	0.4
Poorly formed	76 (67-83)	78 (71-84)	0.8
Glomeruloid	87 (76-93)	75 (68-80)	0.01

# The cribriform/IC pattern: better than GP4 % in GG2

**Table 1** Clinical and pathologic characteristics of Gleason score 3+4 = 7 biopsies

Parameter	Percentage Gleason grade 4			P-value
	0-10%	10-25%	25-50%	
Number	121	131	118	
Age (years)	65 (66; 61-70)	67 (68; 63-72)	68 (69; 65-72)	0.001
PSA (ng/ml)	7.8 (5.2; 3.7-7.1)	9.2 (5.9; 4.2-9.0)	11.7 (8.5; 5.4-13.4)	< 0.001
% Positive biopsies	51 (50; 33-67)	44 (43; 29-57)	48 (43; 29-67)	0.01
% Tumor volume	39 (37; 25-52)	44 (45; 27-59)	50 (51; 34-65)	0.001
<b>CR/IDC</b>	<b>7 (6%)</b>	<b>29 (22%)</b>	<b>52 (44%)</b>	<b>&lt; 0.001</b>
<i>Therapy</i>				
Radical prostatectomy	58 (48%)	50 (38%)	38 (32%)	0.04
Radiation therapy	52 (43%)	71 (54%)	72 (61%)	0.02
Endocrine therapy	1 (1%)	2 (2%)	0	0.41
Watchful waiting	9 (7%)	8 (6%)	8 (7%)	0.92
Unknown	1 (1%)	0	0	
Disease-specific death	4 (3%)	6 (5%)	13 (11%)	0.02

Abbreviations: CR/IDC, invasive cribriform and/or intraductal carcinoma; PSA, prostate-specific antigen. Mean (median; IQR) or absolute number (%) are given.

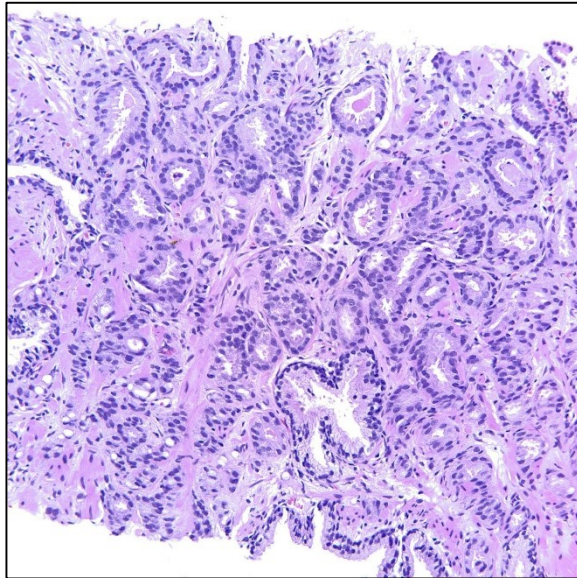
**Table 2** Crude and adjusted Cox regression analysis for time to biochemical recurrence after radical prostatectomy

	Univariate HR (95% CI)	P-value	Multivariate HR (95% CI)	P-value
Age (years)	1.03 (0.95-1.11)	0.49	1.03 (0.95-1.11)	0.54
PSA	1.03 (0.98-1.09)	0.31	1.01 (0.95-1.08)	0.69
Percentage positive biopsies	3.68 (0.85-15.95)	0.08	2.27 (0.51-10.09)	0.28
Tumor volume	2.20 (0.50-9.76)	0.30	1.71 (0.34-8.50)	0.51
Percentage GG4	1.01 (0.99-1.04)	0.29	1.00 (0.97-1.03)	0.80
<b>CR/IDC</b>	<b>2.72 (1.33-5.95)</b>	<b>0.006</b>	<b>2.40 (1.03-5.60)</b>	<b>0.04</b>

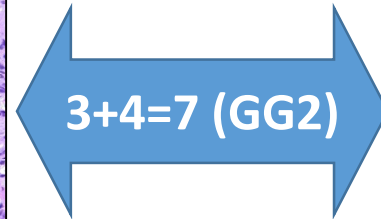
Abbreviations: CI, confidence interval; CR/IDC, invasive cribriform and/or intraductal carcinoma; HR, hazard ratio; PSA, prostate-specific antigen.

# The cribriform/IC pattern: a better grading?

**cGrade = GG if CR/IC is present; GG – 1 if CR/IC is absent**



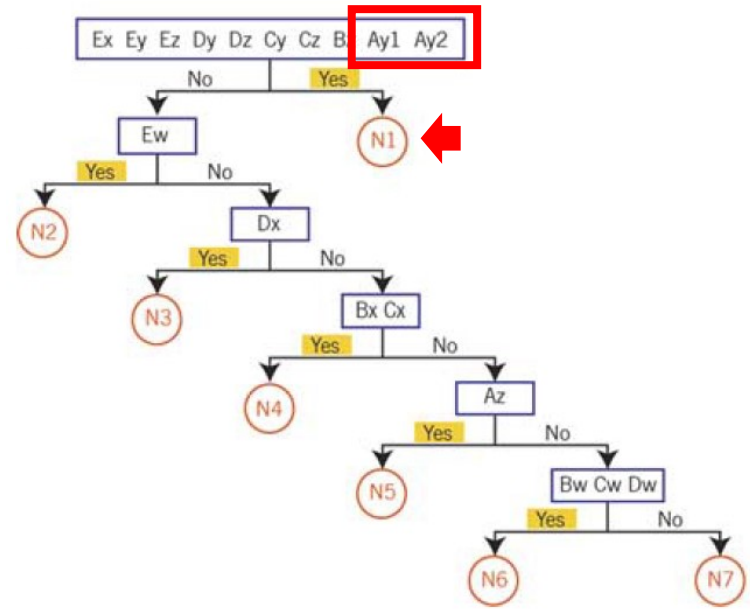
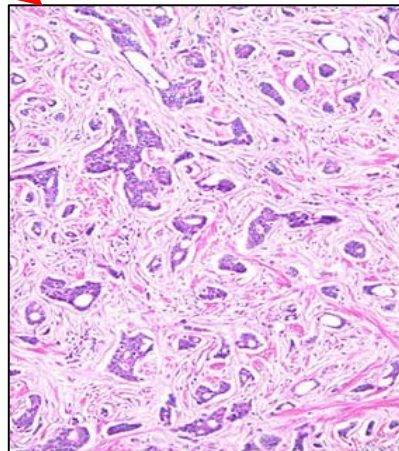
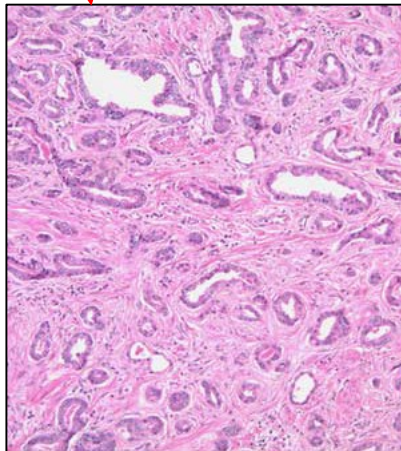
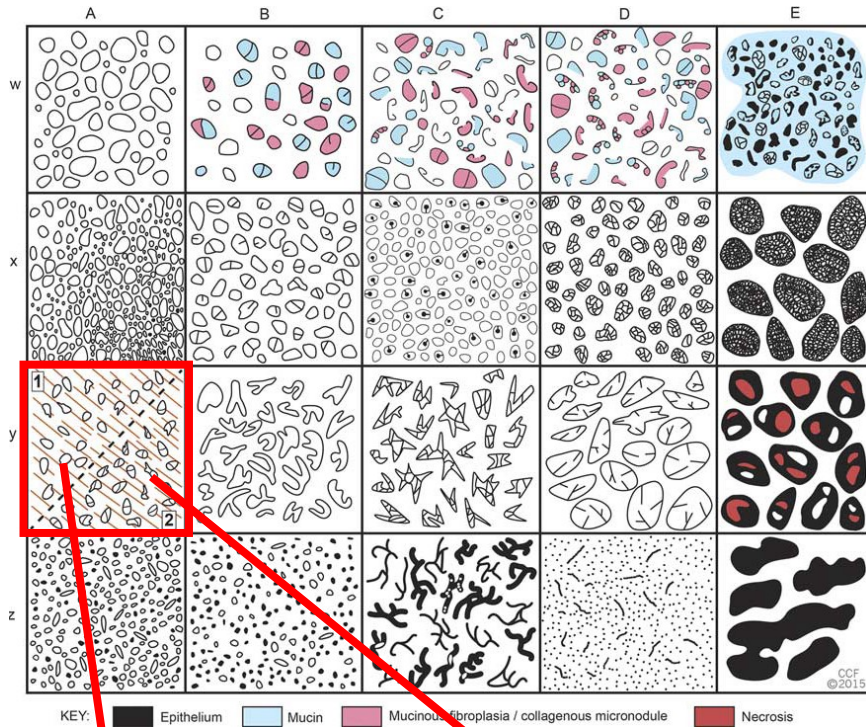
**cGrade 1**



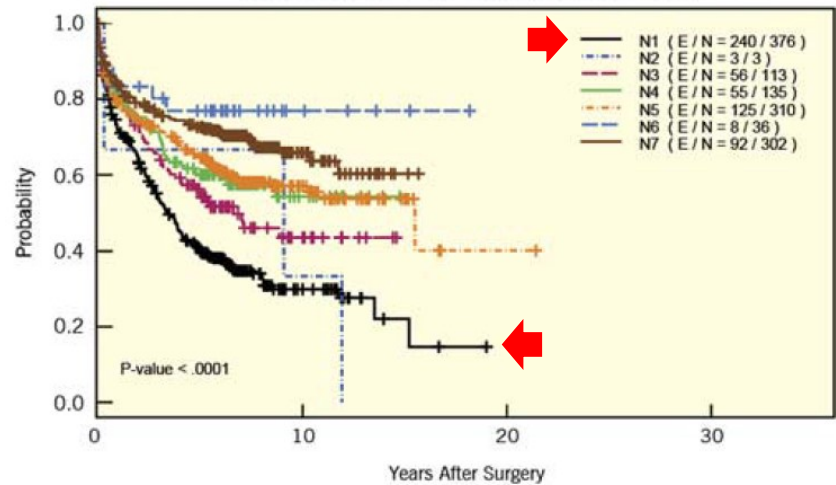
**cGrade 2**

***Men with biopsy GG2 Pca without CR/IC had comparable clinical outcome to those with GG1 disease (>1000 men).***

# Beyond the single gland evaluation



Recurrence Free Survival by Terminal Node



# Take home messages

- Prostate cancer grading... a work in progress
- Many controversies (reproducibility)
- Cribriform pattern incorporation may be beneficial
- Overall architecture (e.g. stroma) is also important

***Sharing is caring for the patient***

