

# Gleason Derecelendirme ve Skorlama

## Yeni Ne Var?

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Kocaeli Üniversitesi Tıp Fakóltesi



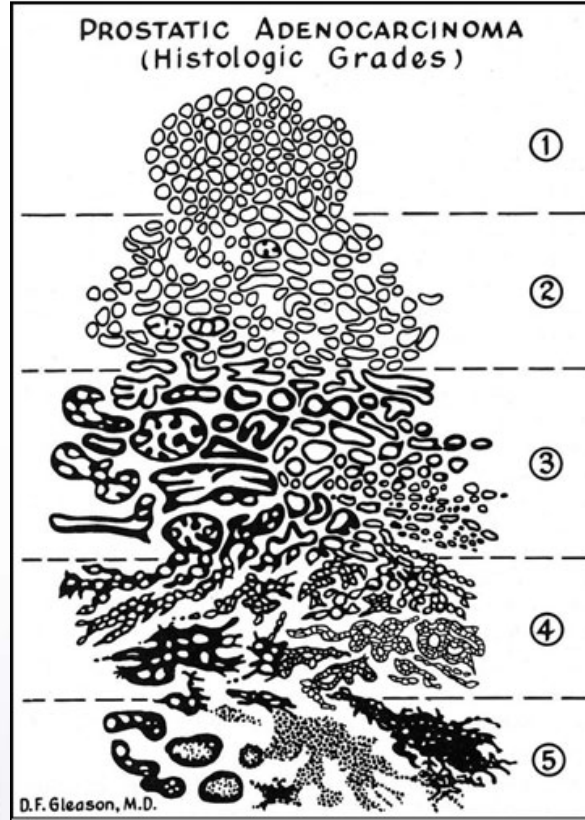
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# Gleason Derecelendirme Sistemi

1960 lar Dr Gleason



1920-2008



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# 40 yılda Prostat kanserinde neler deęiřti?

- serum PSA (tarama programları)
- Tümörler lokal ileri veya metastatik → organ sınırlı
- Radikal prostatektomi
- Biyopsi? Kalın 1-2 kor biyopsi → ≥6 kor biyopsi
- İmmünohistokimya
- Varyant, farklı patern



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

# 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<sup>||</sup>*

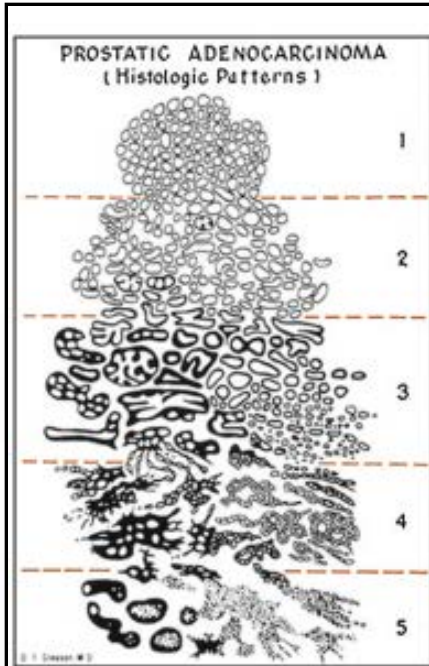


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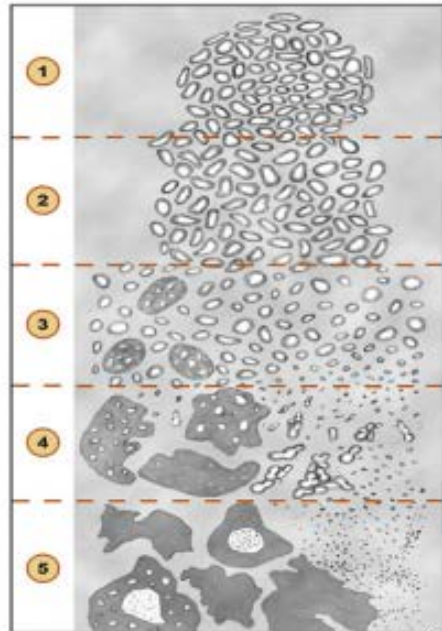


## Orijinal Gleason



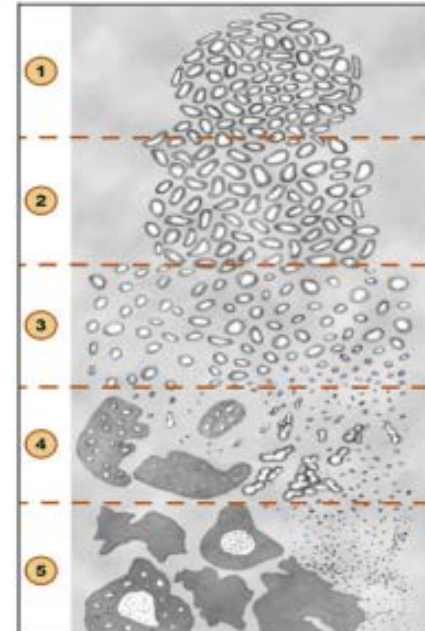
Hum Pathol 23;273-79, 1992

## ISUP 2005



Am J Surg Pathol 29;1228-42, 2005  
*Brunsting*

## Gleason 2010



J Urol 183;433-40, 2010  
*Brunsting*



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## 6. Sitopatoloji Kongresi

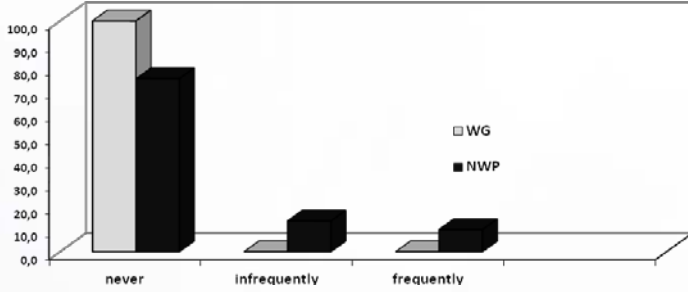
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# Gleason paternler

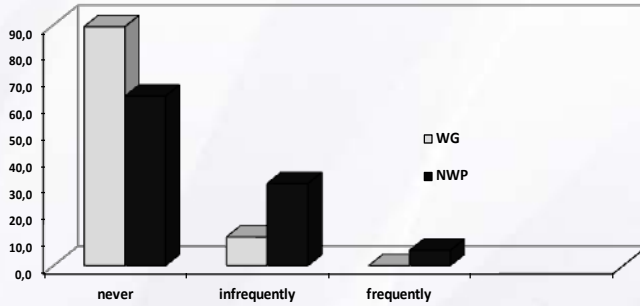
## GP 1,2

### GS 4 sıklığı



- GP 1 ve 2 pratik olarak ortadan kalktı
- adenozis (AAH) (immün öncesi dönem)
- tekrarlanabilirlik düşük,
- RP materyalinde GS daha yüksek, yanıltıcı iyi huylu gidiş mesajı veriliyor

### GS 5 sıklığı



Pathology - Research and Practice

Volume 211, Issue 5, May 2015, Pages 374–380



Original Article

Current practice in handling and reporting prostate needle biopsies: Results of a Turkish survey

Bahar Muezzinoglu<sup>a</sup>, Kutsal Yorukoglu<sup>b</sup>



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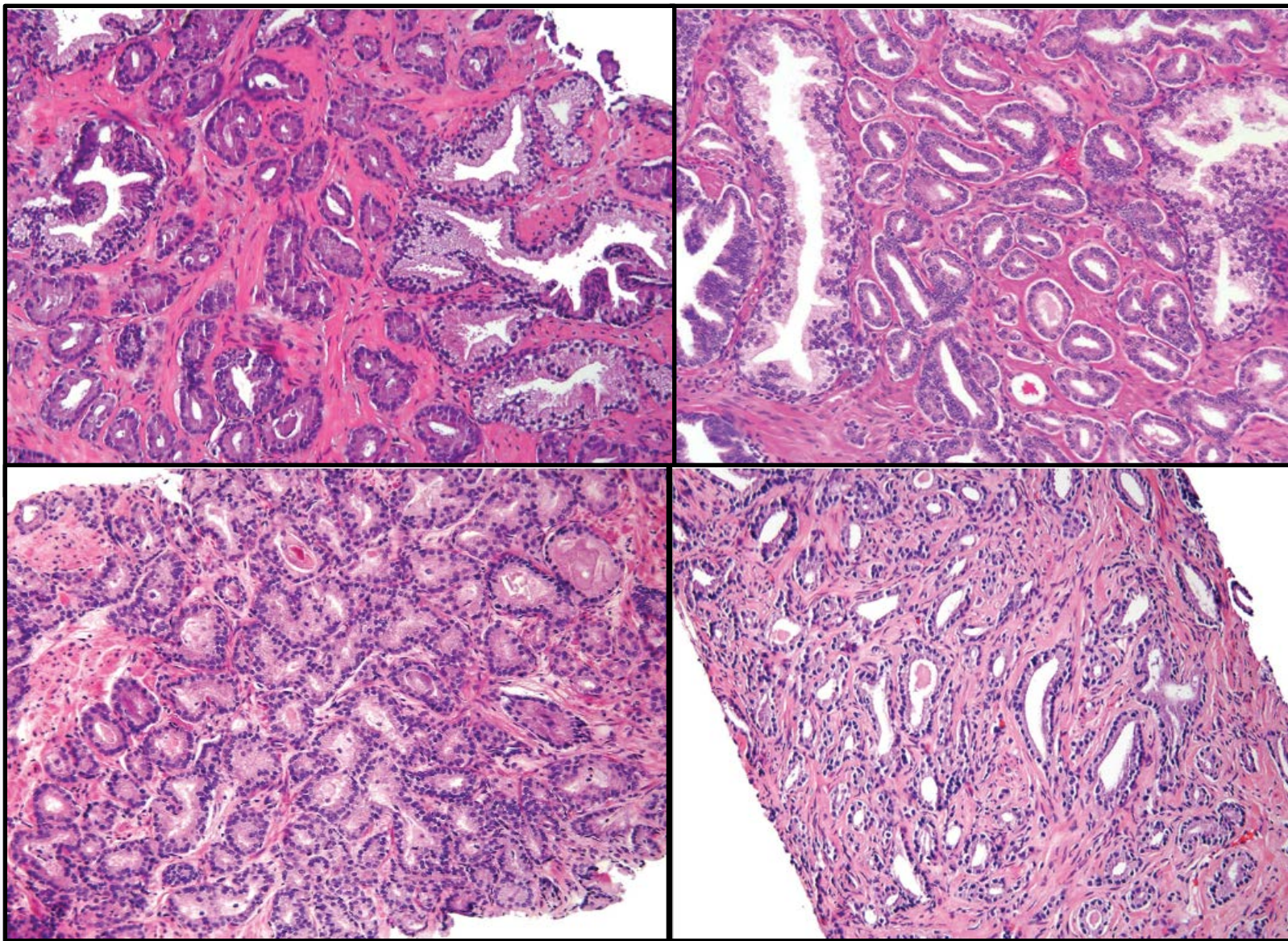


# Gleason paternler

## GP 3

- ~~tek tek hücreler, solid kordonlar~~
- ~~kribriform patern~~
- GP 3 de temel özellik boyutları ve şekilleri değişken olabilen ancak lümeni bulunan düzgün yapıda bezler
- Bazen GP 4 sanılan GP 3 görüntüleri olabilir
  - Kalabalık bezler, tanjansiyel kesit, sıkışma artefaktı , dallanma gösteren bezler, kollagenöz mikronodüller





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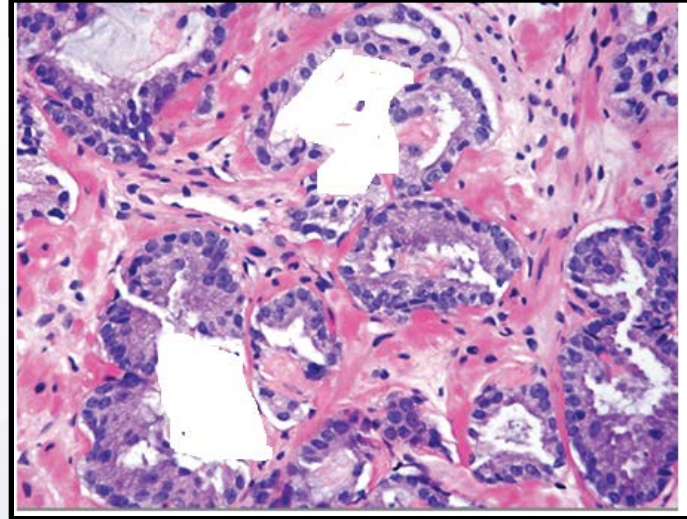
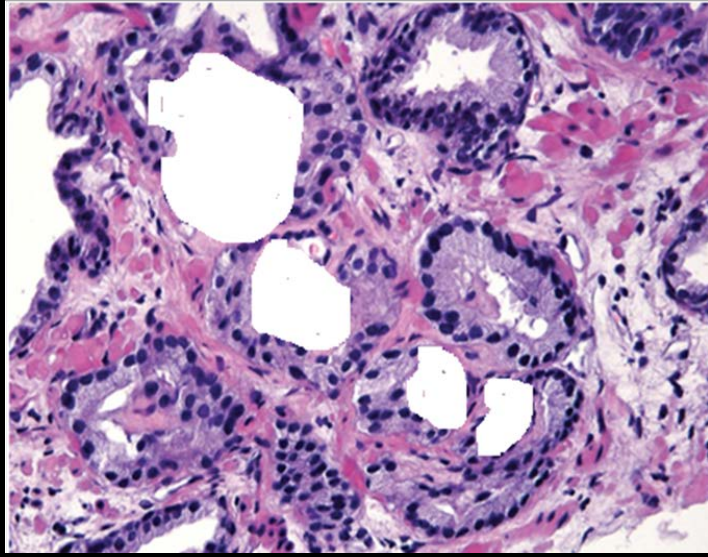
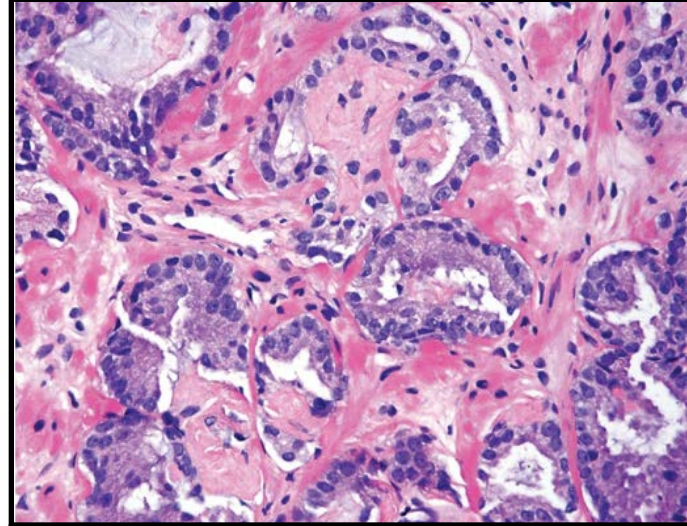
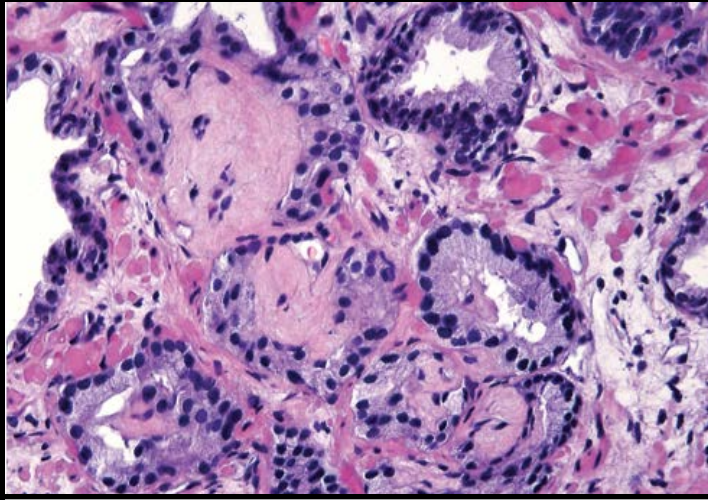
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# Kollajenöz mikronodüller



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# GP 3 (GS6) neden önemli

- **GS 6 en sık tanı konan prostat kanser derecesi**
- Do Adenocarcinomas Of The Prostate With Gleason Score (Gs)  $\leq 6$  Have The Potential To Metastasize To Lymph Nodes? Am J Surg Pathol 2012;36(9): 1346-52  
**14123 RP GS 3+3 19 LN (+), tekrar bakıldığında tümü GP 4 (+), Sonuç LN(+) =0**
- Nationwide prevalence of lymph node metastases in Gleason score 3 + 3 = 6 prostate cancer. Pathology 2014 46(4):306-10  
**SEER data, 21960 RP GS 6 LN(+) %0.48**
- Disease-specific death and metastasis do not occur in patients with Gleason score  $\leq 6$  at radical prostatectomy. BJU Int, 2015 Aug;116(2):230-5. Kweldam CF,  
**449 RP, GS $\leq 6$ , takip süresi 100 ay (48-150) hastalık spesifik ölüm ve metastaz yok.**



# Prostat kanseri

- En sık tanı konulan kanser
- Yeni tanı konulmuş hastaların %15-84 ü tedavi edilmezse yaşam üzerinde olumsuz etkisi olmayacak
- Gereksiz tedavi, yan etkiler
- Hasta anksiyetesi
- Ailesel risk?
- Hasta yönetiminde **AKTİF İZLEM**



# Neden GP 3 (GS6) önemli

## **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 Amaratunga, 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; Jan 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—Vol 138, October 2014



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# Aktif izlem için kriterler

Klinik evre < cT2,

PSA < 10 ng/ml,

**GS ≤ 6, LVI, EPY, ID CA yok, PNI olabilir, ASAP immun**

**Tümör : < %33 pozitif kor oranı,**

**< 3 pozitif kor sayısı,**

**< %50 bir pozitif korda tümör miktarı**

izlem nasıl? PSA ölçümü, RT, tekrar biyopsi



# Gleason Paternler

## GP 4

- Kribriform patern = GP 4
- Glomeruloid patern = GP 4
- Lumenleri belirsiz bezler =GP4
- Füzyon, zincir gösteren bezler = GP 4



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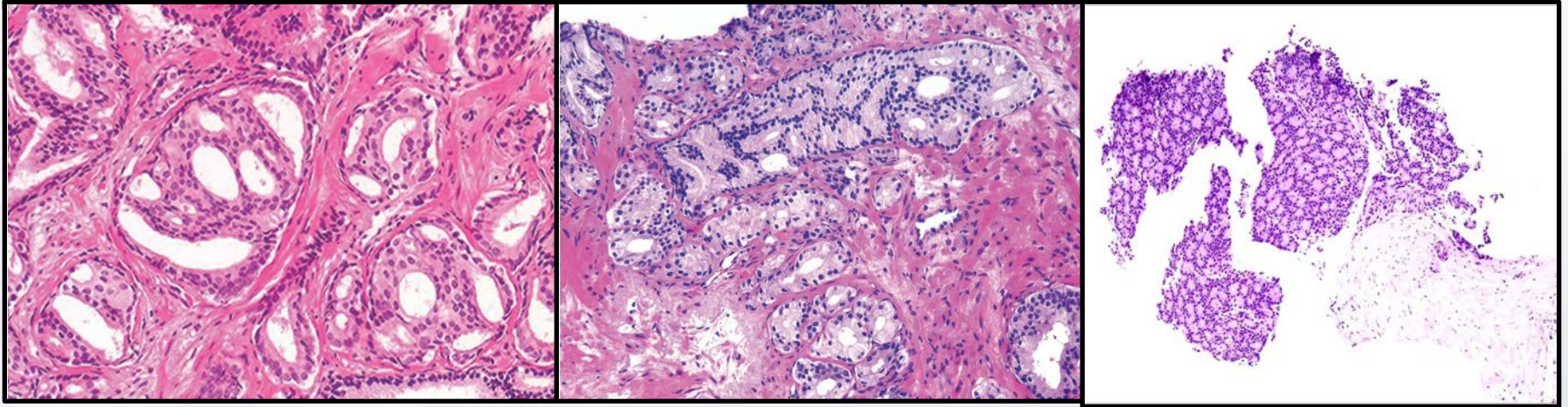
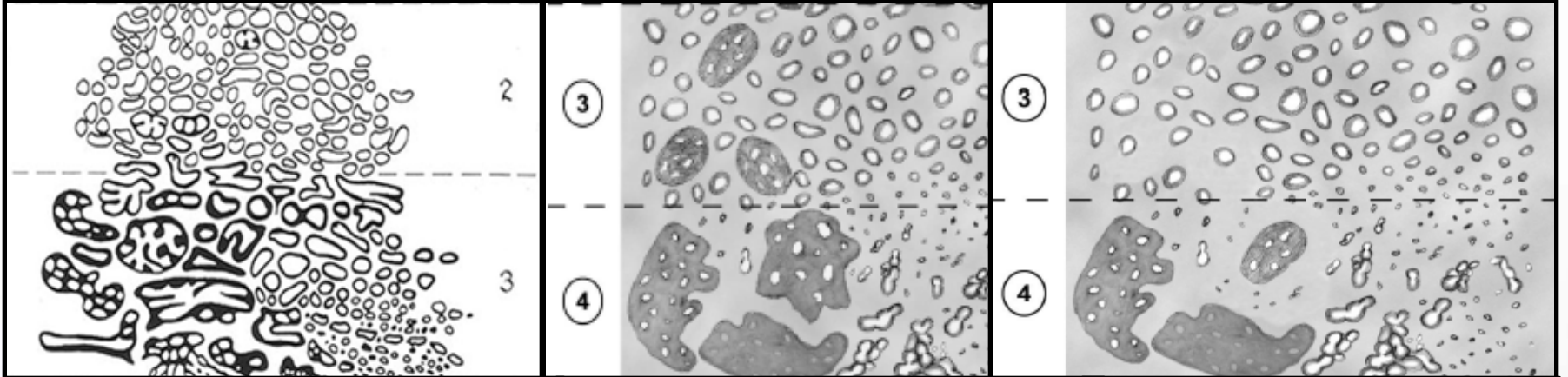


# Kribriform patern

Orijinal Gleason

ISUP 2005

Yeni deęişiklik (2010)

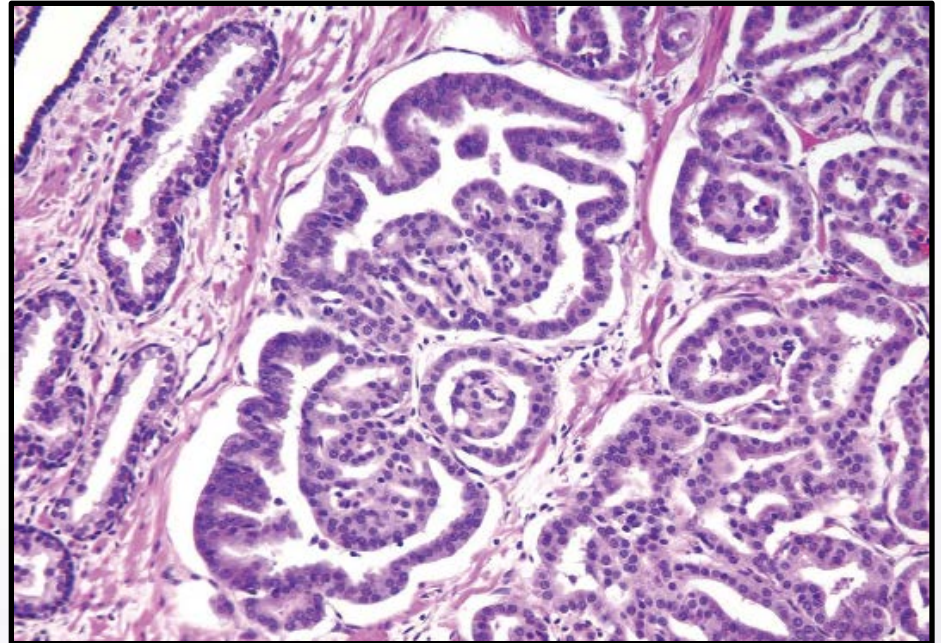
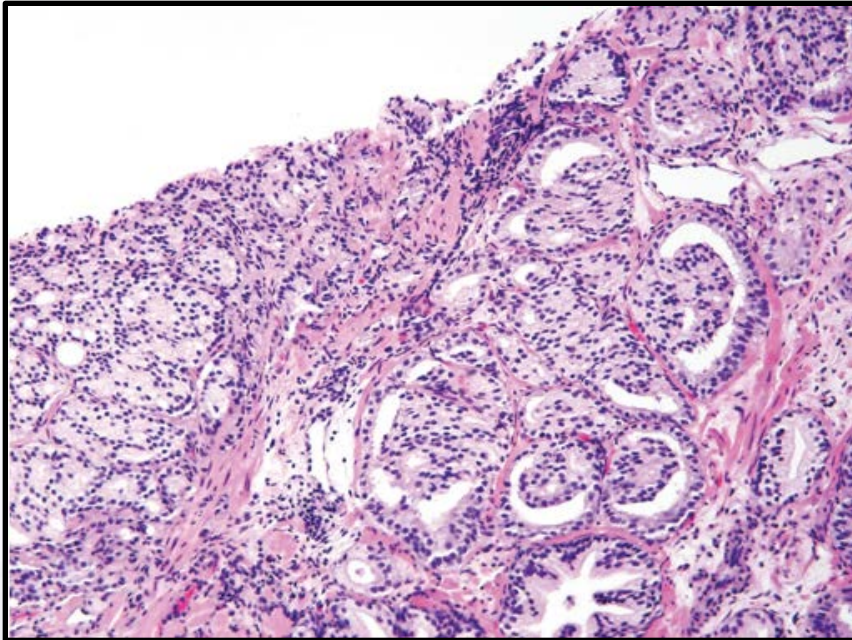


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# Glomeruloid pattern



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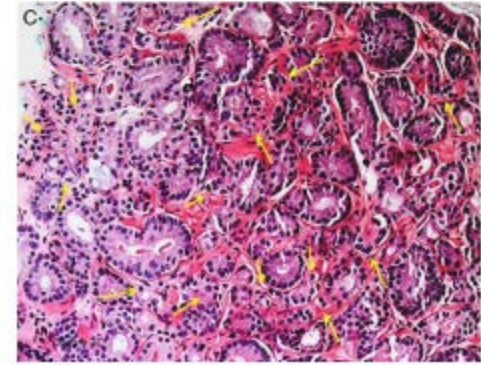
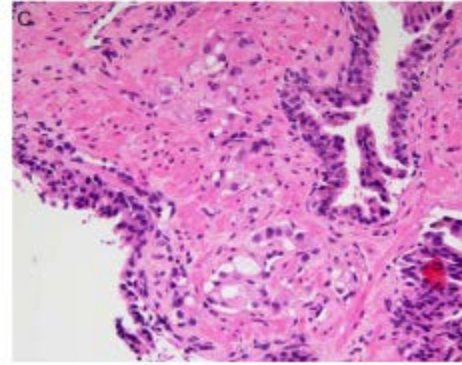
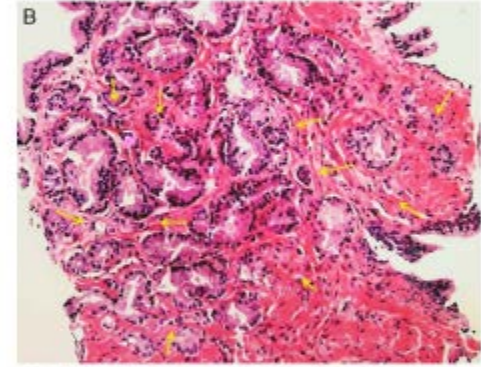
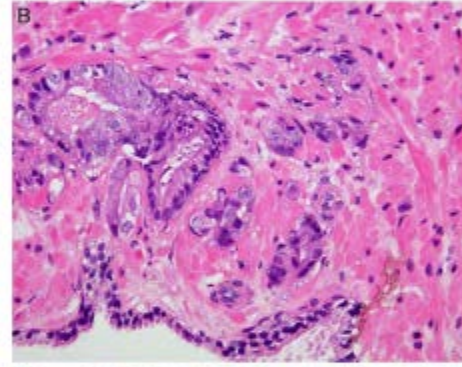
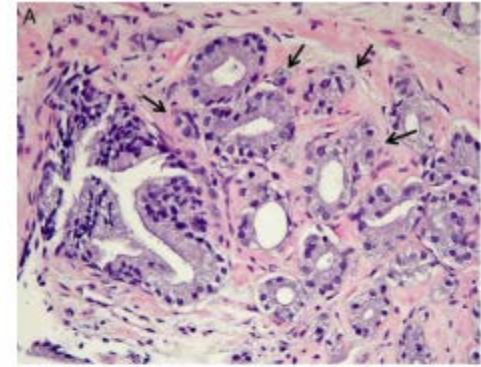
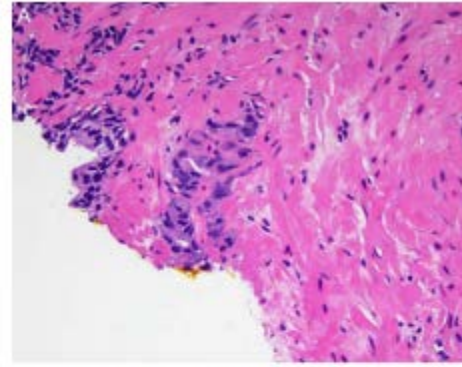




Diagnosis of “Poorly Formed Glands” Gleason Pattern 4  
Prostatic Adenocarcinoma on Needle Biopsy  
An Interobserver Reproducibility Study Among Urologic Pathologists  
With Recommendations

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 Mendrinou, 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



K=0.34 (orta)

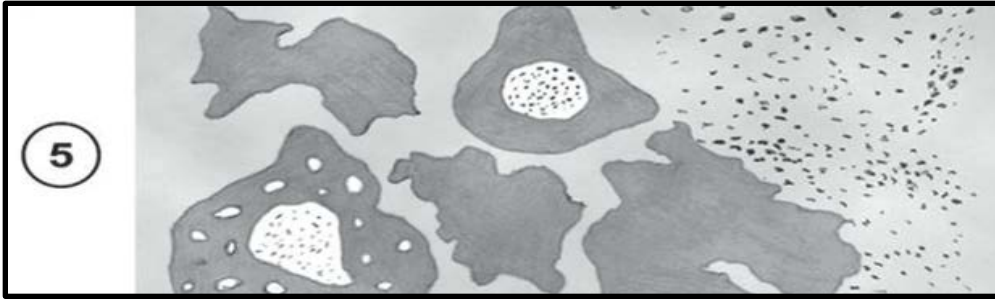
- Tanım: Lümeni belirsiz tümöral bezleri
- Düzenli görünümdeki tümöral bezlerle iç içe olanlar GP 4 değil
- <5 bez GP4 değil
- Düzenli bezlerle iç içe olmayan >10 bez GP4 kabul edilebilir
- >2 kesit tanı için
- Şüphe varsa GP3 kabul et



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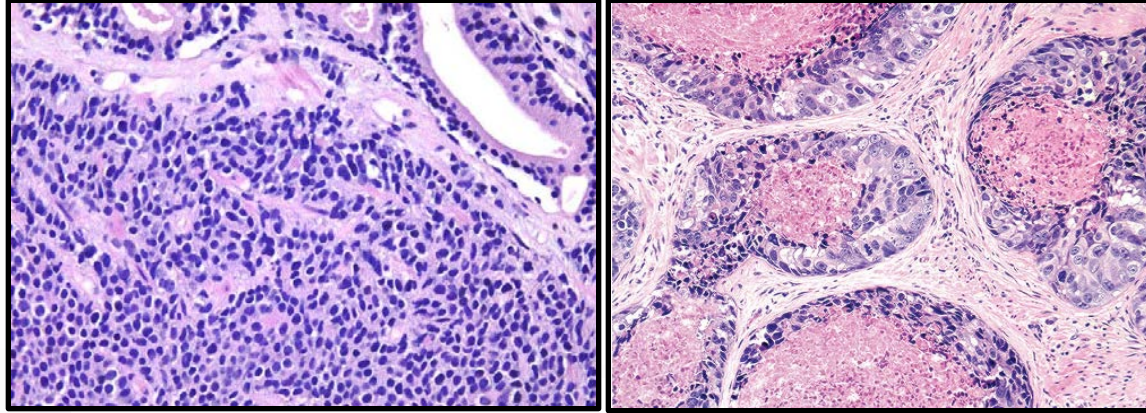
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✓ Bez yapısı yok, solid , kordon, tek tek hücreler

✓ kribriform veya solid yapıların ortasında komedonekroz



## Diagnosis of Gleason Pattern 5 Prostate Adenocarcinoma on Core Needle Biopsy

*An Interobserver Reproducibility Study Among Urologic Pathologists*

Rajal B. Shah, MD,\* Jianbo Li, PhD,† Liang Cheng, MD, PhD,‡ Lars Egevad, MD,§  
Fang-Ming Deng, MD,|| Samson W. Fine, MD,¶ Lakshmi P. Kunju, MD,# Jonathan Melamed, MD,||  
Rohit Mehra, MD,# Adeboye O. Osunkoya, MD,\*\* Gladell P. Paner, MD,†† Steve S. Shen, MD,‡‡  
Toyonori Tsuzuki, MD,§§ Kiril Trpkov, MD,||| Wei Tian, MD,\* Ximing J. Yang, MD, PhD,¶¶  
and Ming Zhou, MD, PhD||

$\kappa = 0.34$

Am J Surg Pathol • Volume 39, Number 9, September 2015

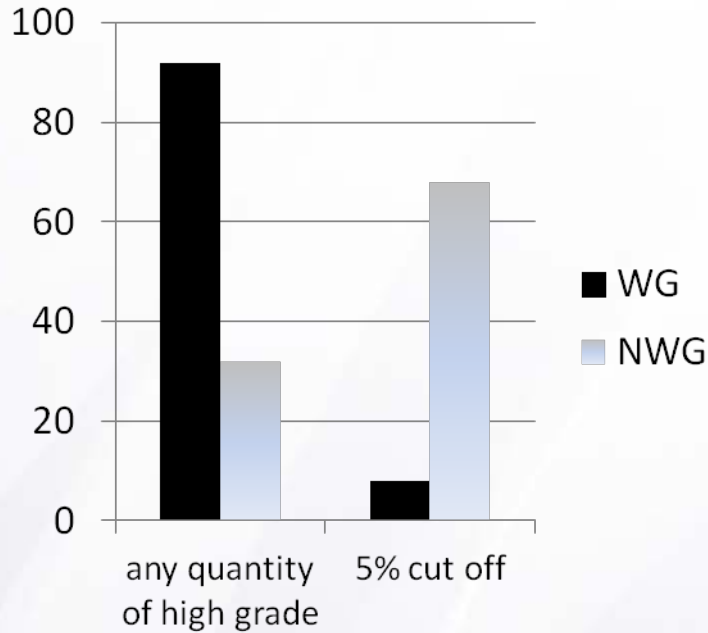


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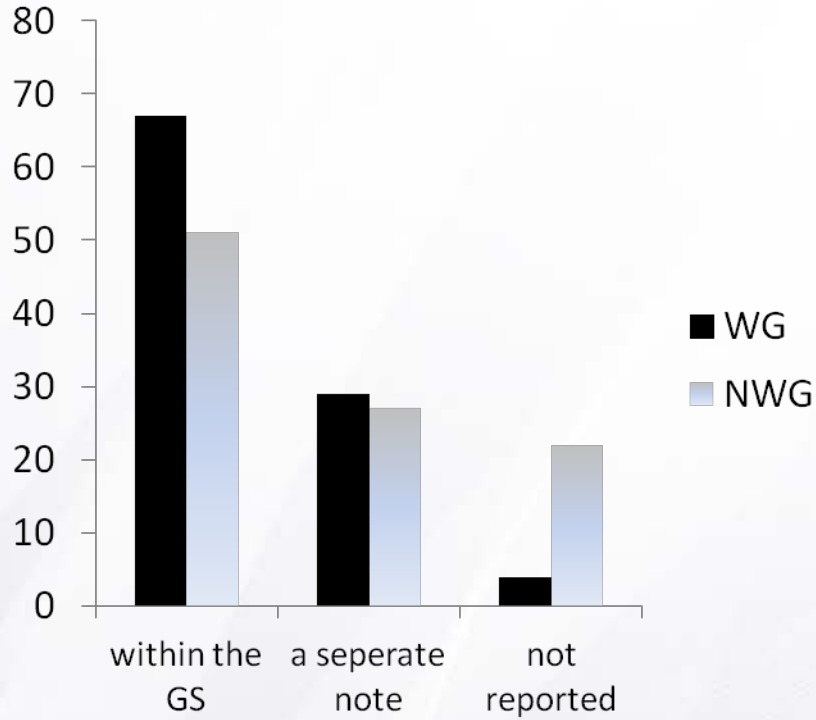
# yüksek dereceli Sekonder Patern



- İğne biyopsisinde yüksek dereceli sekonder paternin **görülmesi** Gleason Skor içinde yer alması için yeterli



# Tersiyer patern



- Aynı kor içinde 3 patern varlığında
- GS= primer patern + en yüksek patern

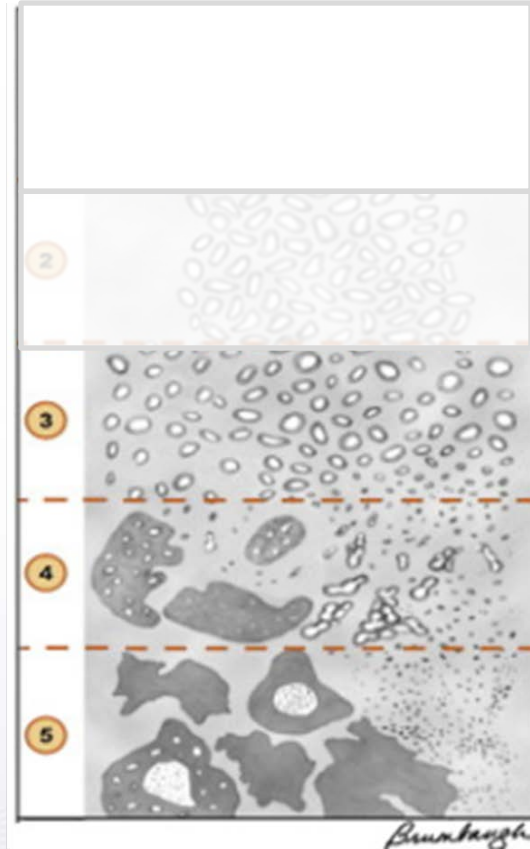
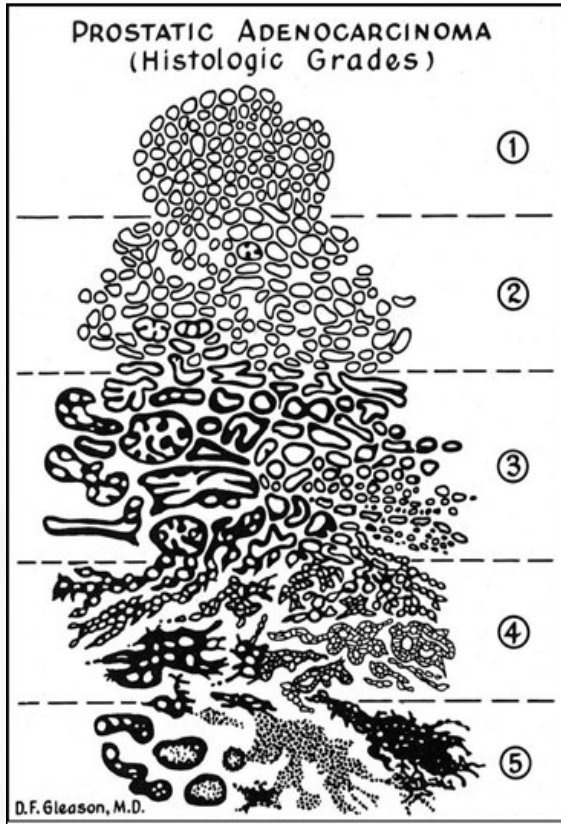


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# 2005 sonrası neler oldu?



GS	GS
GS2	
GS3	
GS4	GS4
GS5	GS5
GS6	GS6
GS7	GS7
GS8	GS8
GS9	GS9
GS10	GS10



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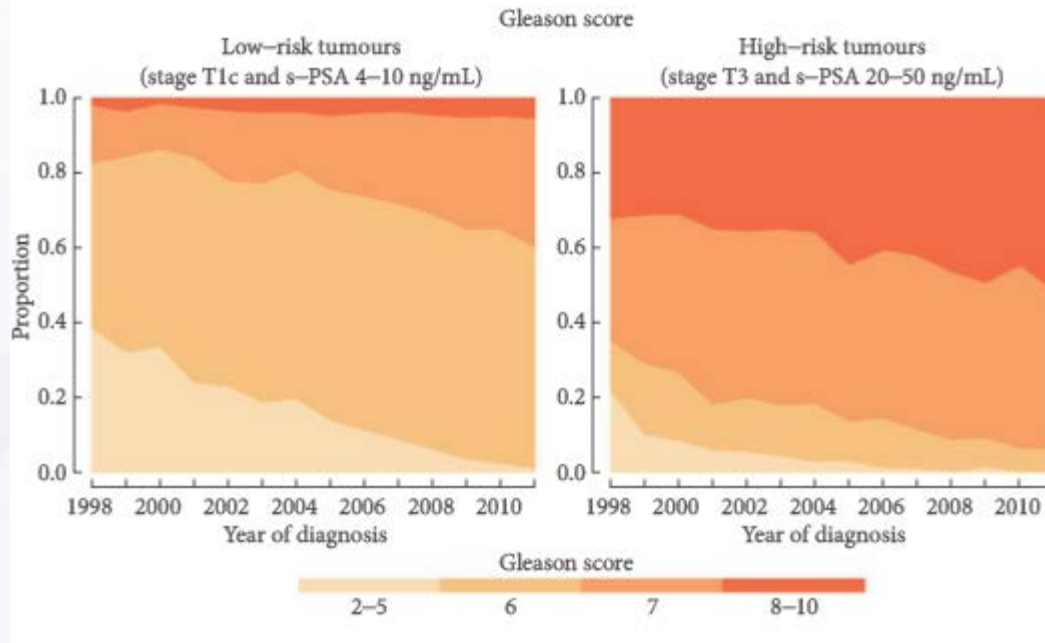
# 2005 sonrası neler oldu?

## Gleason inflation 1998–2011: a registry study of 97 168 men

Daniela Danneman, Linda Drevin\*, David Robinson†, Pär Stattin‡ and Lars Egevad

Department of Oncology-Pathology, Karolinska Institutet, Stockholm, \*Regional Cancer Centre, Uppsala University Hospital, Uppsala, †Department of Urology, Ryhov County Hospital, Jönköping, ‡Department of Surgery and Perioperative Sciences, Urology and Andrology, Umeå University, Umeå, Sweden

*BJU Int* 2015; **115**: 248–255



Derecelendirme sistemleri stabil olmalı zaman içindeki prognostik önemini belirlemek zorlaşıyor



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# 2005 sonrası ne oldu

- GS 2-5 oranı %27 → <%1
- 2005 öncesi GS 6 (%34) → GS7
- Biyopside GS  $\geq 7$  %32 → %45
- Biyopsi RP arası uyum ( %31 →44, % 58→72%, %64→70)



# GS 7 (3+4 ve 4+3)

- **Gleason score 7 prostate cancer on needle biopsy: relation of primary pattern 3 or 4 to pathological stage and progression after radical prostatectomy.**
- Amin A, J Urol 2011Oct;186(4):1286-90.
- **Prognostic significance of primary Gleason pattern in Japanese men with Gleason score 7 prostate cancer treated with radical prostatectomy.**
- Miyake H. Urol Oncol. 2013 Nov;31(8):1511-6.
- **Primary Gleason pattern in biopsy Gleason score 7 is predictive of adverse histopathological features and biochemical failure following radical prostatectomy.** Berg KD, Scand J Urol. 2014 Apr;48(2):168-76.
- .
- .





# GS 8, 9,10 (yüksek riskli grup)

- **Gleason score 3+5 or 5+3 versus 4+4 prostate cancer: The risk of death**

Huynh MA, Chen MH, Wu J, Braccioforte MH, Moran BJ, D'Amico AV. Eur Urol. 2015 Sep 17

- **Patients with Biopsy Gleason 9 and 10 Prostate Cancer Have Significantly Worse Outcomes Compared to Patients with Gleason 8 Disease.**

TsaoCK, Gray KP, Nakabayashi M, Evan CJ Urol 2015 Jul 194 (1) :91-7

- 



# Gelinen durum

- Gleason skor 2-5 artık yok, 10 lu skala gerçekte 6 dan başlıyor
- GS 6, 5 yıllık sağkalım %96, LN metastazı potansiyeli yok
- GS 7 (orta risk grubu) heterojen (3+4 ve 4+3)
- GS 8-10 (yüksek risk grubu) heterojen



# Prognostic Gleason grade grouping: data based on the modified Gleason scoring system

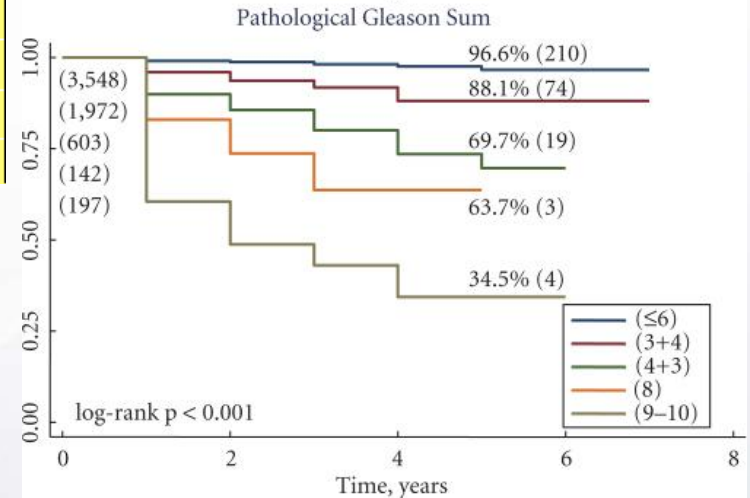
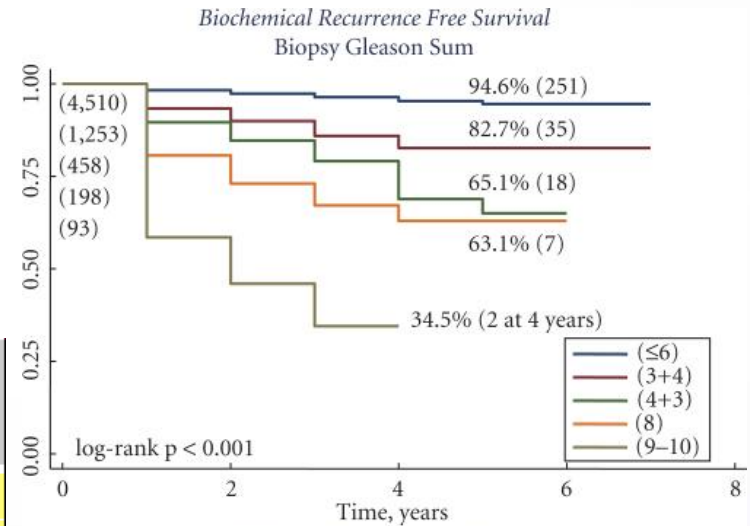
BJU Int 2013 May 11(5)

Pierorazio PM, Walsh PC, Partin AW, Epstein JI.

7869 RP

The overall Gleason score 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 $\leq 6$ :	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



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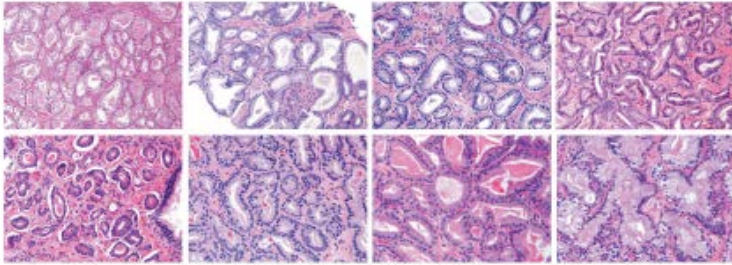
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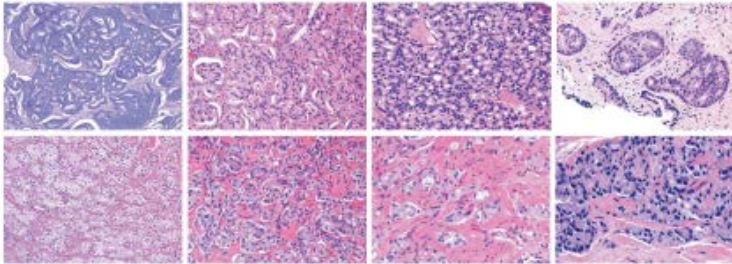
# ISUP 2014

## A NEW CONTEMPORARY PROSTATE CANCER GRADING SYSTEM

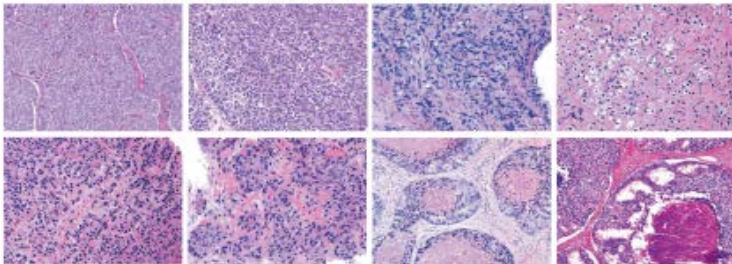
Discrete Well-formed Glands (Gleason Patterns 1-3)



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



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



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Jonathan Epstein, M.D.

**Table 4 – Histologic definition of new grading system**

Grade group 1 (Gleason score 3 + 3 = 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 8)

- Only poorly formed/fused/cribriform glands or
- Predominantly well-formed glands and lesser component lacking glands ††
- Predominantly lacking glands and lesser component of well-formed glands ††

Grade group 5 (Gleason scores 9–10): Lack of 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 radical prostatectomy, the component of <5% well-formed glands is not factored into the grade.

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

2016 WHO da yer alacak

Gleason sistemi ile birlikte raporda yer alması öneriliyor



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

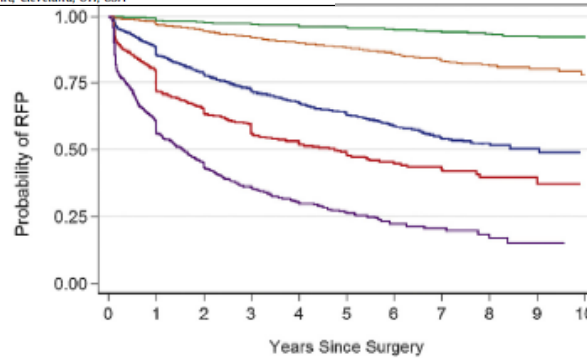
## A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score

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

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

5 akademik merkezden 20845 RP,  
2 merkezden 5501 RT

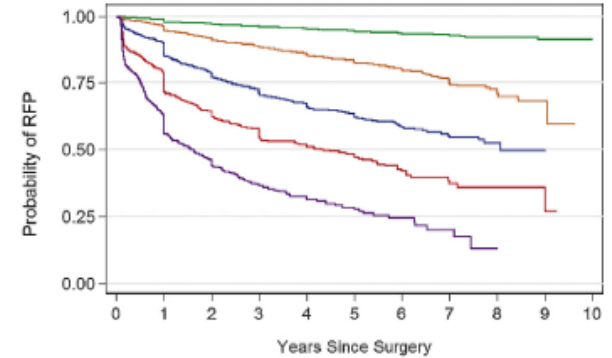
**5 yıllık BFS**  
**Group I %96**  
**Group II %88**  
**Group III %63**  
**Group IV %48**  
**Group V %26**



Number at risk

≤6	7397	6873	5104	4064	3226	2461	1798	1186	670	278	108
3 + 4	8263	7202	5208	3993	2956	2071	1293	778	393	135	45
4 + 3	3106	2452	1605	1162	839	589	350	199	90	39	13
8	917	678	412	280	191	129	86	59	35	14	7
≥9	1051	578	376	194	118	73	41	24	12	4	2

**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.



Number at risk

≤6	8039	7264	5154	3943	3018	2177	1383	618	371	80	1
3 + 4	4595	3875	2624	1845	1291	845	470	244	102	21	0
4 + 3	1972	1513	934	634	432	282	157	99	35	5	0
8	1005	719	413	270	185	120	68	33	13	4	0
≥9	861	385	199	118	75	41	25	11	2	0	0

**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.



**25. Ulusal Patoloji Kongresi**  
**6. Sitopatoloji Kongresi**

14 - 17 Ekim 2015 / Merinos AKKM - BURSA



## ANATOMICAL PATHOLOGY

### The prognostic significance of the 2014 International Society of Urological Pathology (ISUP) grading system for prostate cancer

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**Table 4** Cox proportional hazards regression: patient age, serum prostate specific antigen at presentation and needle biopsy 2014 ISUP grade versus biochemical recurrence-free interval

Term	Coef	Hazards ratio	SE (coef)	Z	p value
Age	-0.00217	0.998	0.0157	-0.139	0.9
PSA	0.03591	1.0	0.0140	2.564	0.01
1	-	1.0	-	-	-
2	0.54761	1.7	0.5338	1.026	0.3
3	1.39397	4	0.5432	2.566	0.01
4	1.92436	6.9	0.6318	3.046	0.002
5	2.40274	11.1	0.5335	4.503	0.000007

Coef, coefficient; PSA, prostate specific antigen; SE, standard error.



## ANATOMICAL PATHOLOGY

### Validation of International Society of Urological Pathology (ISUP) grading for prostatic adenocarcinoma in thin core biopsies using TROG 03.04 ‘RADAR’ trial clinical data

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**Table 5** Comparison of predictive ability of 2005 MGS and 2014 ISUP grading systems

Endpoint	C-index (95% CI)		<i>p</i>
	2005 MGS	2014 ISUP	
Distant progression-free survival	0.709 (0.650–0.767)	0.748 (0.696–0.799)	0.013
PSA progression-free survival	0.701 (0.661–0.741)	0.724 (0.686–0.761)	0.048
Prostate cancer-specific survival	0.750 (0.667–0.833)	0.782 (0.714–0.850)	0.001

c-index, Harrell's concordance index; CI, confidence interval; ISUP, International Society of Urological Pathology; MGS, modified Gleason score; PSA, prostate-specific antigen.



# Prostat kanseri ile ilgili olarak

- Yoğun PSA taramaları ile tanı konulmuş ve patolojik derecesine ve yaşam beklentisine bakılmaksızın tedavi edilmiş çok fazla hasta
- **Doğru risk grupları ile doğru hasta yönetimi**
- Gleason sistemi çok önemli prognostik faktör ancak bazı kısıtlamalar var
- GS 6 (Grup I en düşük risk grubu) minimal metastaz riski ile aktif izleme alınabilir
- Yüksek riskli gruplara yönelik, iyi görüntüleme ve biyobelirteçler ile desteklenen yüksek dereceli kanserlerin tanı ve uygun tedavisini hedefleyen bir yaklaşım
- Bu yaklaşımda da patologun rolü çok önemli
  - Eksiklerin saptanması
  - geniş tabana ulaşacak eğitim çalışmaları

