

# Changing Distribution, Size and Grade of Prostate Cancer: A 16-Year Whole-Mount Prostatectomy Analysis



M. Scott Lucia, MD  
Professor and Vice Chair of Anatomic Pathology  
Chief of Genitourinary and Renal Pathology  
Dept. of Pathology  
University of Colorado SOM

# Disclosures

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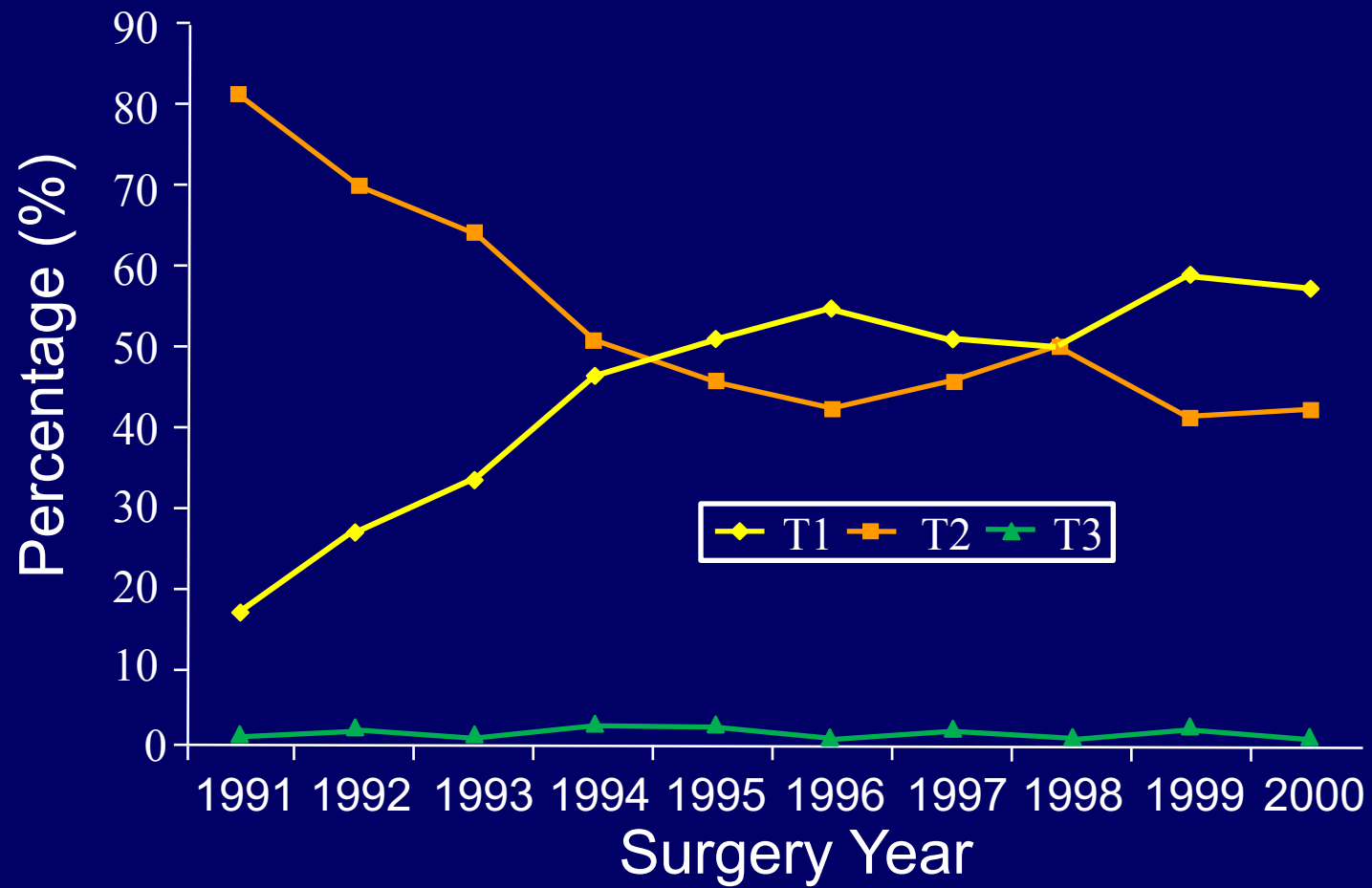
- MDxHealth– consultant
- 3DBiopsy - shareholder

# Prostate Cancer: The Landscape has Changed

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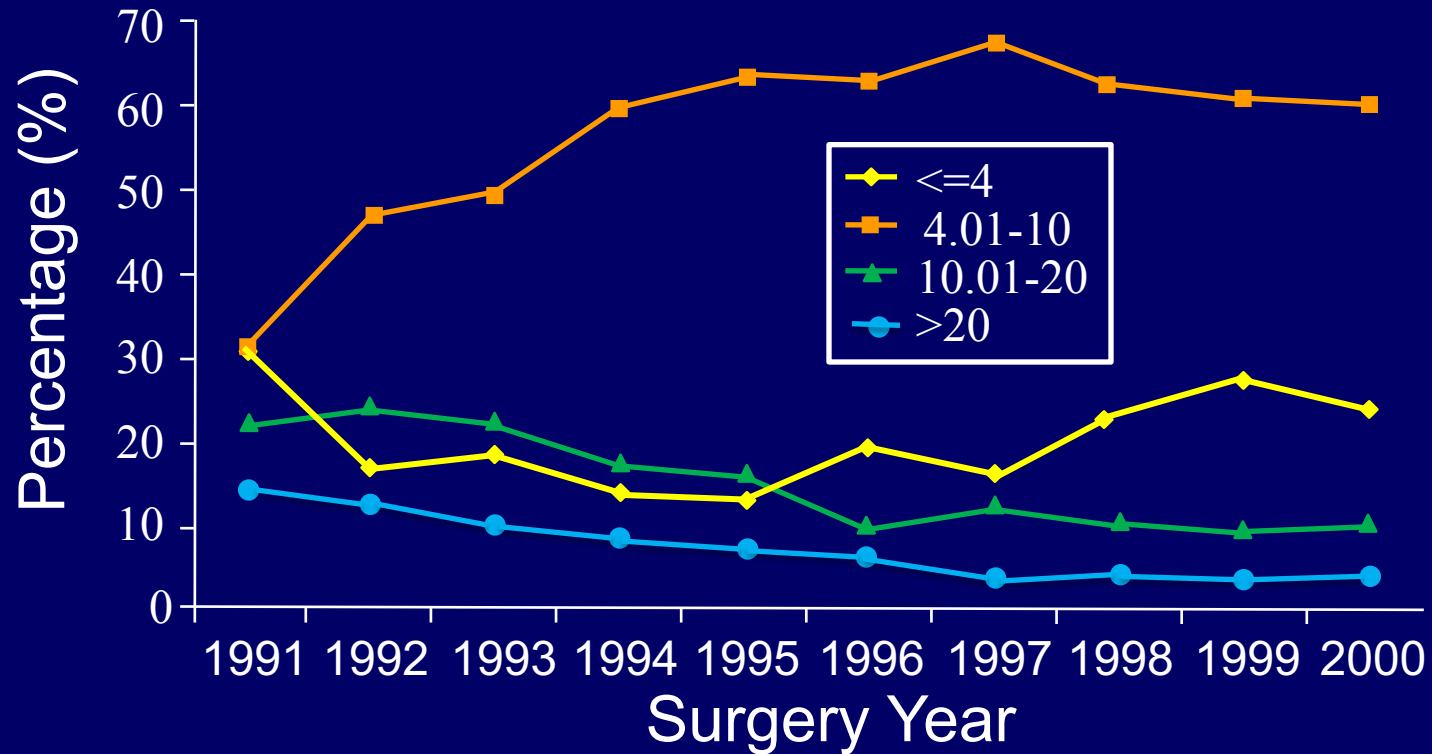
- Shift in clinical presentation – PSA era
  - 1990s – 2000s: Earlier stage; lower PSAs

# DoD CPDR National Database: Clinical T stage at diagnosis for patients who underwent prostatectomy





# DoD CPDR National Database: PSA level at diagnosis for patients who underwent prostatectomy

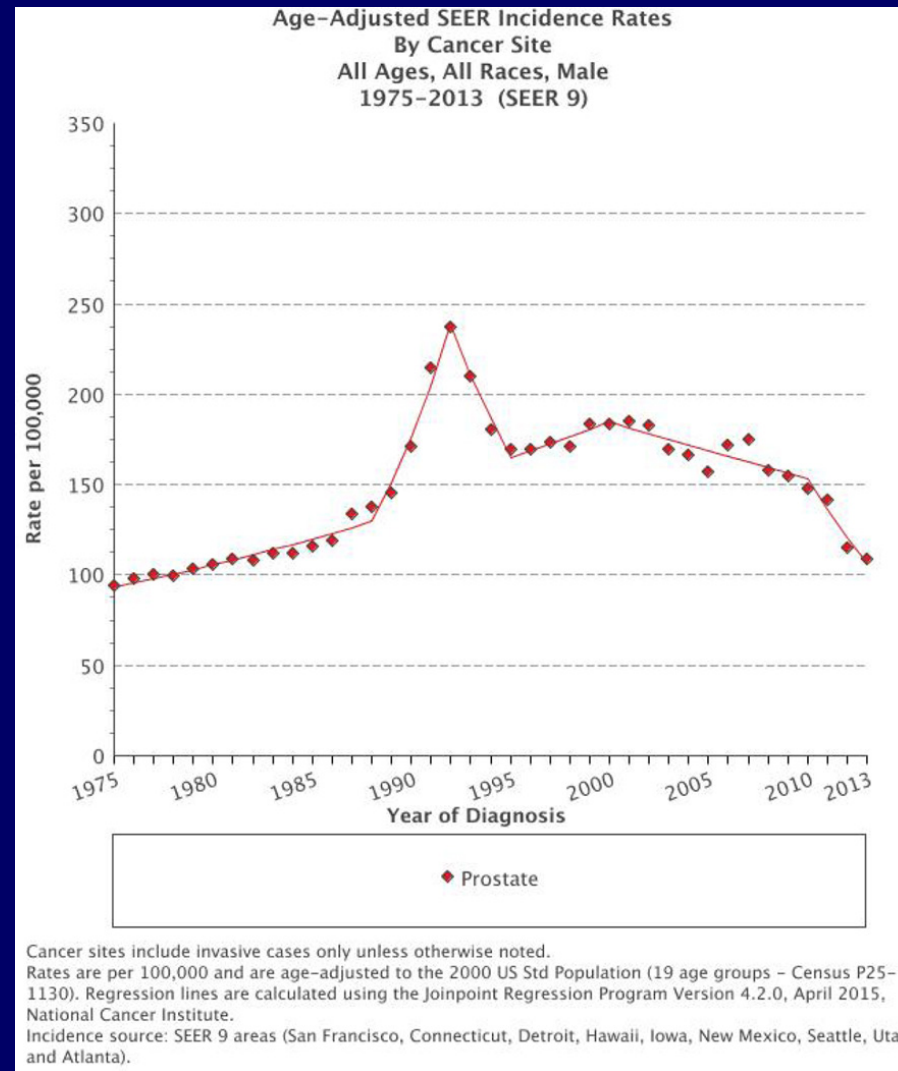


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- Shift in clinical presentation – PSA era
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- Shift in screening
  - Overtreatment of biologically indolent tumors
  - 2012: PSA receives “D” rating for screening
  - Recent decline in prostate cancer diagnoses

# Yearly Trends in Prostate Cancer Diagnosis: SEER Registry

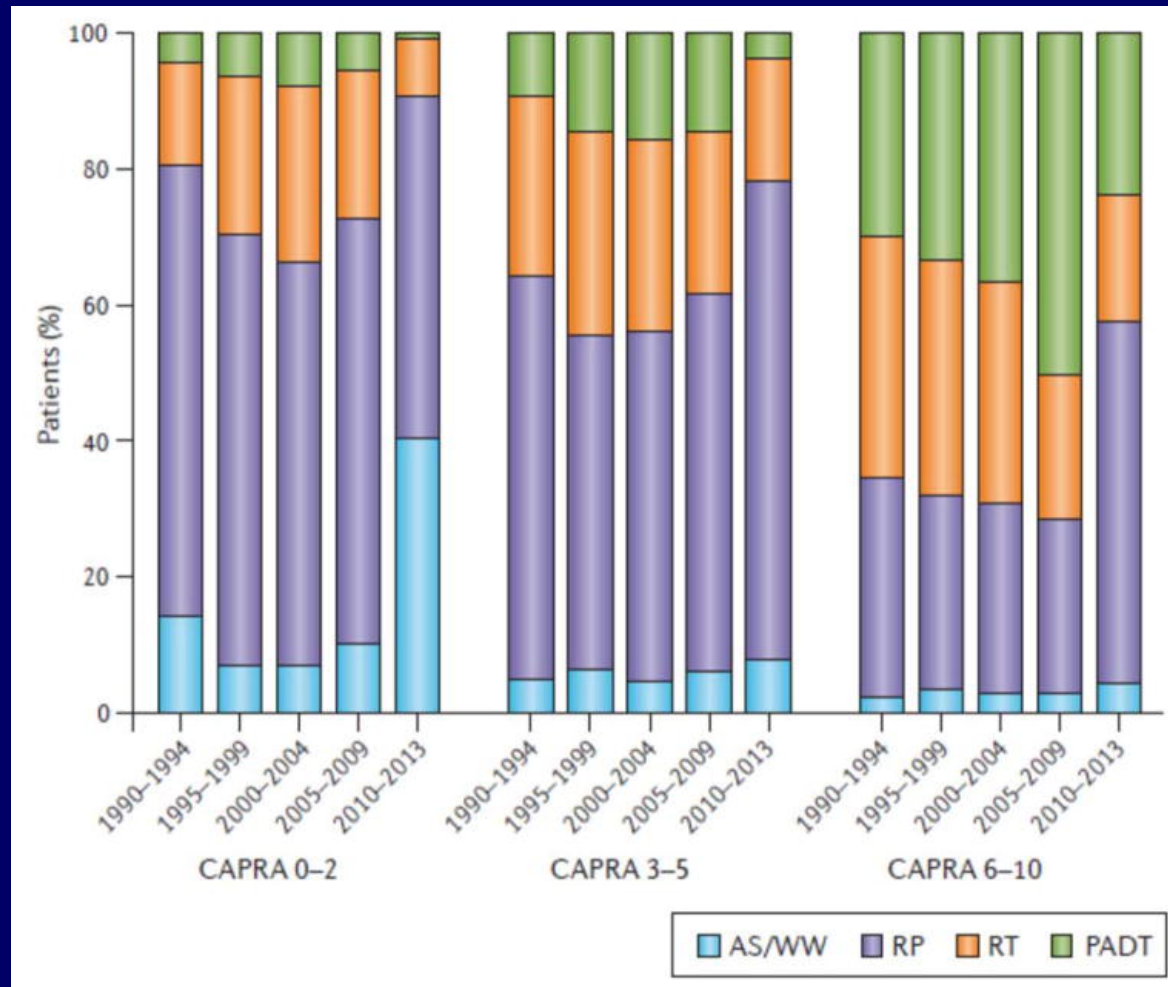


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- Shift in treatment paradigms
  - Recognition that not all cancers need treatment
  - Active surveillance and TFT for low-risk cancer

# Trends in prostate cancer treatment



Data from CapSURE Registry

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- Shift in pathologist’s grading practices
  - ISUP 2005 & 2014
  - Prognostic grade groups

# Prostatic Adenocarcinoma

## Gleason Grading<sup>1</sup>

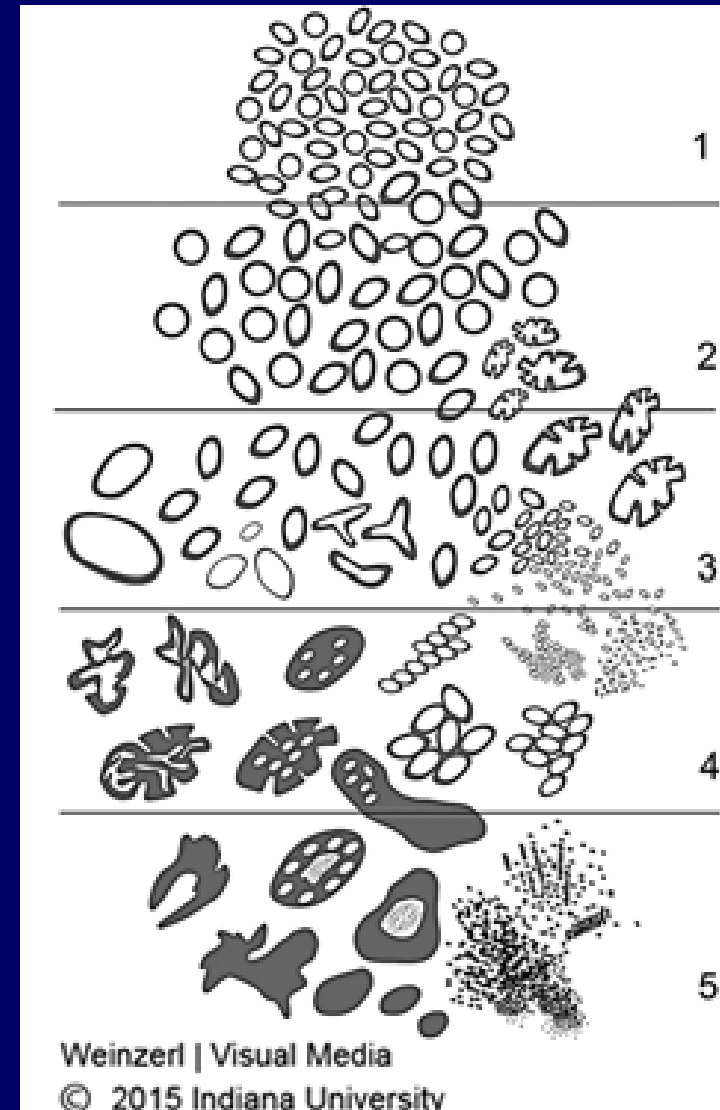
- Morphologic resemblance to normal prostate
- Degree of invasiveness
- Score = most + 2nd most
- Biopsies: most + highest remaining grade present<sup>2,3</sup>
- Amount of pattern 4/5 most important for prognosis
- ISUP: Refinements adopted in 2005<sup>3</sup> and 2014<sup>4</sup>

1. Gleason DF. *Urologic Pathology: The Prostate*, 1977.

2. CAP: *Arch Pathol Lab Med*, 2000.

3. ISUP: *Amer J Surg Pathol*, 2005.

4. ISUP: *Amer J Surg Pathol*, 2016.



# Impact of 2005 ISUP Gleason Grading Consensus on biopsy Gleason scores and grade patterns<sup>1</sup>

Distribution of biopsy Gleason scores (GS) before and after ISUP consensus.

	GS≤6	GS=7	GS≥8
2000-2004 (n=908)	617 (68%)	271 (30%)	20 (2%)
2005-2007 (n=423)	232 (55%)	180 (43%)	11 (3%)

Comparison of mean biopsy Gleason scores and primary (1°) and secondary (2°) Gleason patterns (GP) before and after ISUP consensus.

	2000-2004	2005-2007	P-value*
GS	6.34	6.49	<0.0001
1° GP	3.08	3.10	0.314
2° GP	3.26	3.39	<0.001

\* Student's *t*-test



# Prostate cancer mortality rates according to prostatectomy Gleason score<sup>1</sup>

N=693 patients from 1984-2004

Standardized Review*					Original Source			
GS	No. of PCa Deaths	Person-Years	No.	Mortality Rate (per 1000 person -years)	No. of PCa Deaths	Person-Years	No.	Mortality Rate (per 1000 person -years)
2-5	0	64.6	6	0	1	2,178.8	171	0.5
6	0	2,216.0	200	0	3	2,331.5	221	1.3
3+4	6	2,864.9	257	2.1	12	1,701.8	171	7.1
4+3	9	1,419.1	134	6.3	9	542.5	55	16.6
8	7	482.3	51	14.5	4	435.3	47	9.2
9-10	15	383.7	45	39.1	8	240.7	28	33.2
Total	37	7,430.6	693	5.0	37	7,430.6	693	5.0

\* Using contemporary Gleason grading.

# Classification of Prostate Cancer Using 5-tiered Prognostic Grade Groupings

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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).

<b>Gleason score <math>\leq 6</math>:</b>	<b>Prognostic Grade Group I</b>
<b>Gleason score <math>3 + 4 = 7</math>:</b>	<b>Prognostic Grade Group II</b>
<b>Gleason score <math>4 + 3 = 7</math>:</b>	<b>Prognostic Grade Group III</b>
<b>Gleason score 8:</b>	<b>Prognostic Grade Group IV</b>
<b>Gleason score 9-10:</b>	<b>Prognostic Grade Group V</b>

# Prostate Cancer: The Landscape has Changed

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- Shift in clinical presentation – PSA era
  - 1990s – 2000s: Earlier stage; lower PSA
- Shift in clinical presentation – PSA era
  - Overdiagnosis
  - 2012: 10% of prostatectomies
  - Recent trends
- Shift in clinical presentation – PSA era
  - Record incidence
  - Active surveillance
- Shift in pathologist's grading practices
  - ISUP 2005 & 2014
  - Prognostic grade groups

*??? Impact on  
Pathological Features  
of Tumors on  
Prostatectomy*

# Assessing the Impact of Practice Changes

	Possible impact on Prostatectomy
ISUP Grading	Shift towards higher grade
Increase in AS	↓ in low grade cancers Relative proportional ↑ in higher grades
Decrease in screening	? ↓ in low grade cancers ? Disproportional ↑ in higher grades ? ↑ in stage/ volume

- Univ. of Colo Prostate Cancer Database:
  - All prostates that were whole-mount processed
  - Tumors graded by 2 genitourinary pathologists
  - Grade, stage, and tumor volume



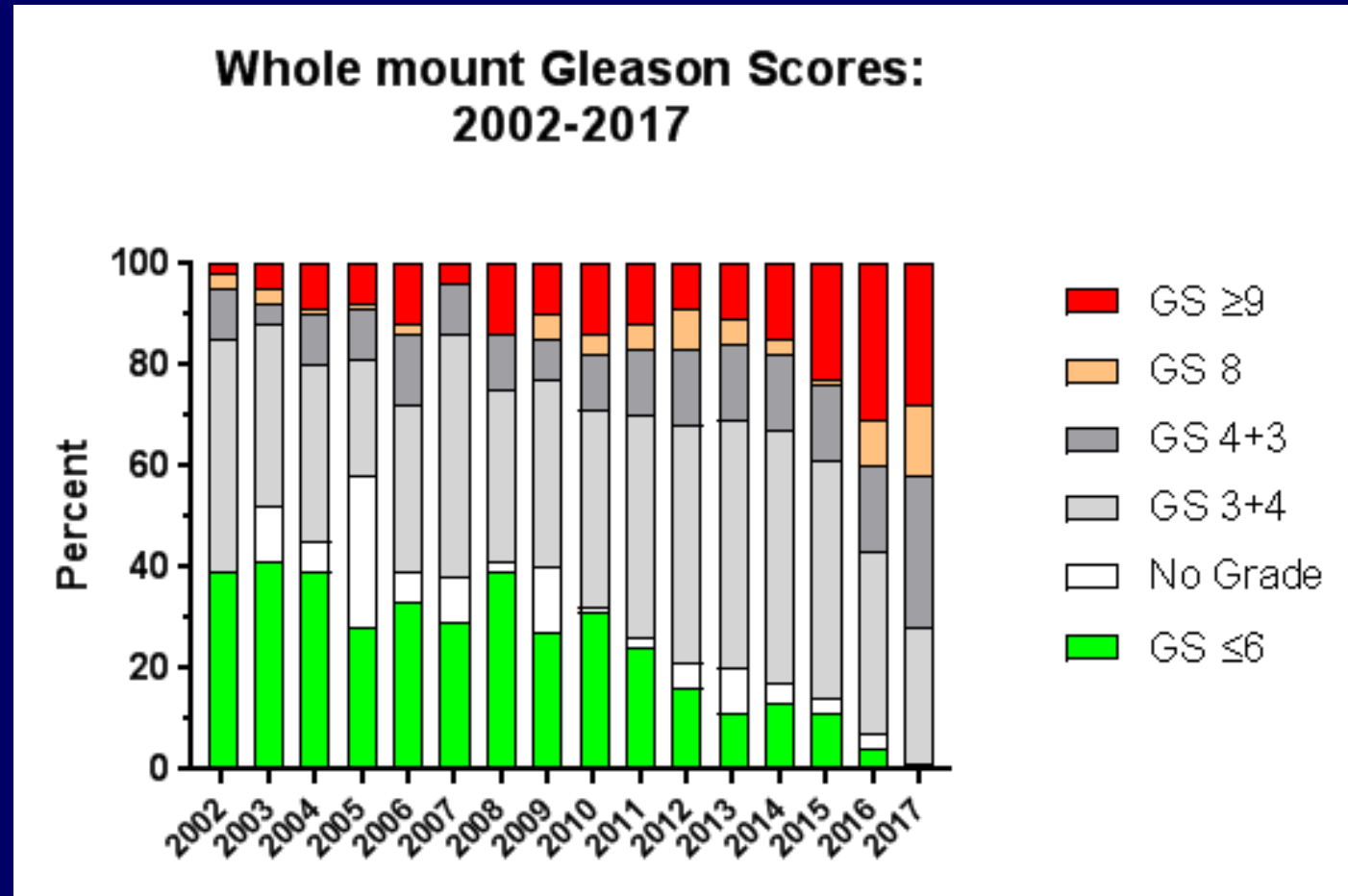
# Whole-mount prostatectomy





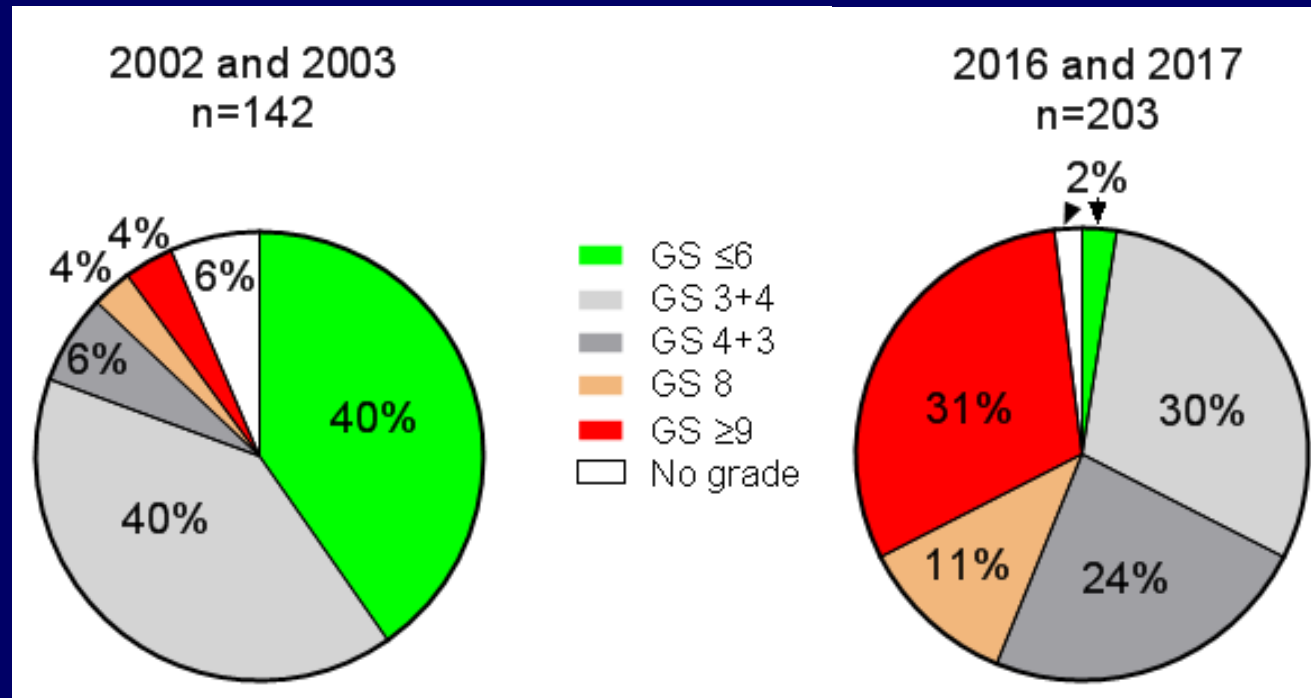


# Changes in Tumor Grade Over Last 16 Years



N=1182

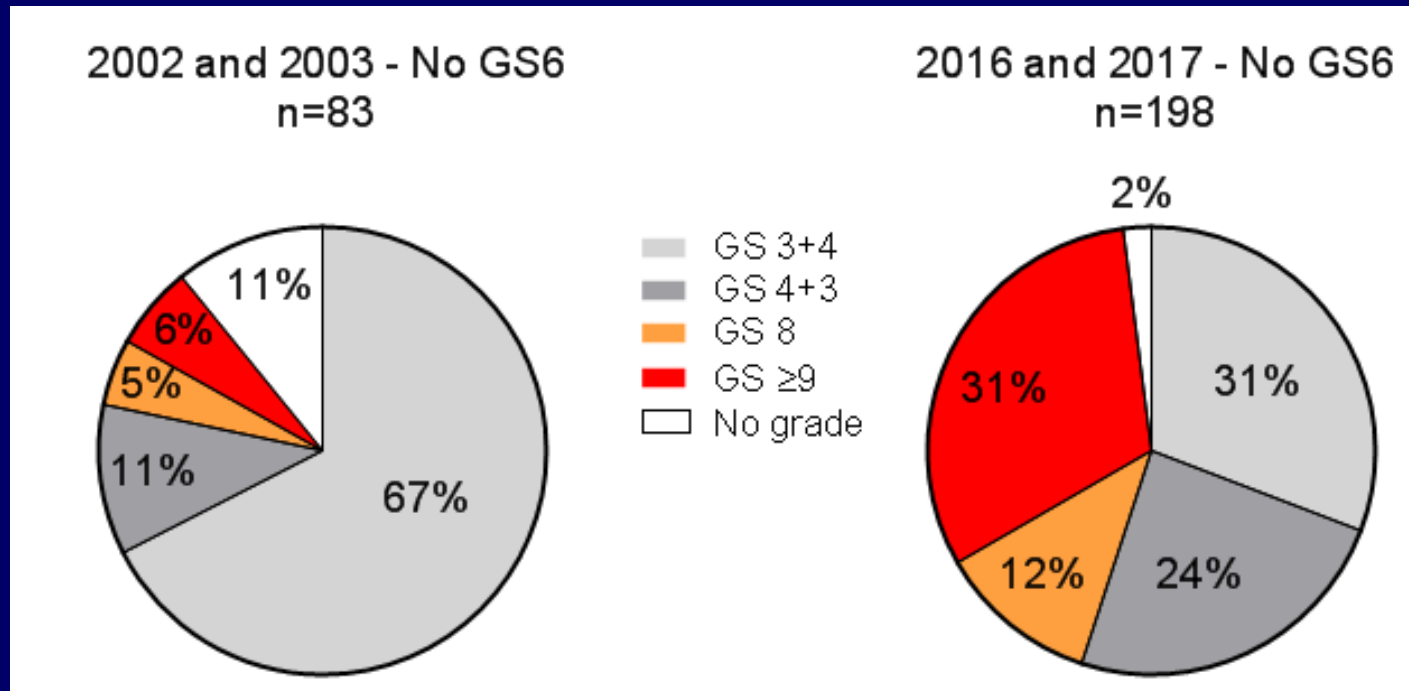
# Prostate Cancer Grade: Then and Now



Chi-square test for independence  
 $p < 0.0001$

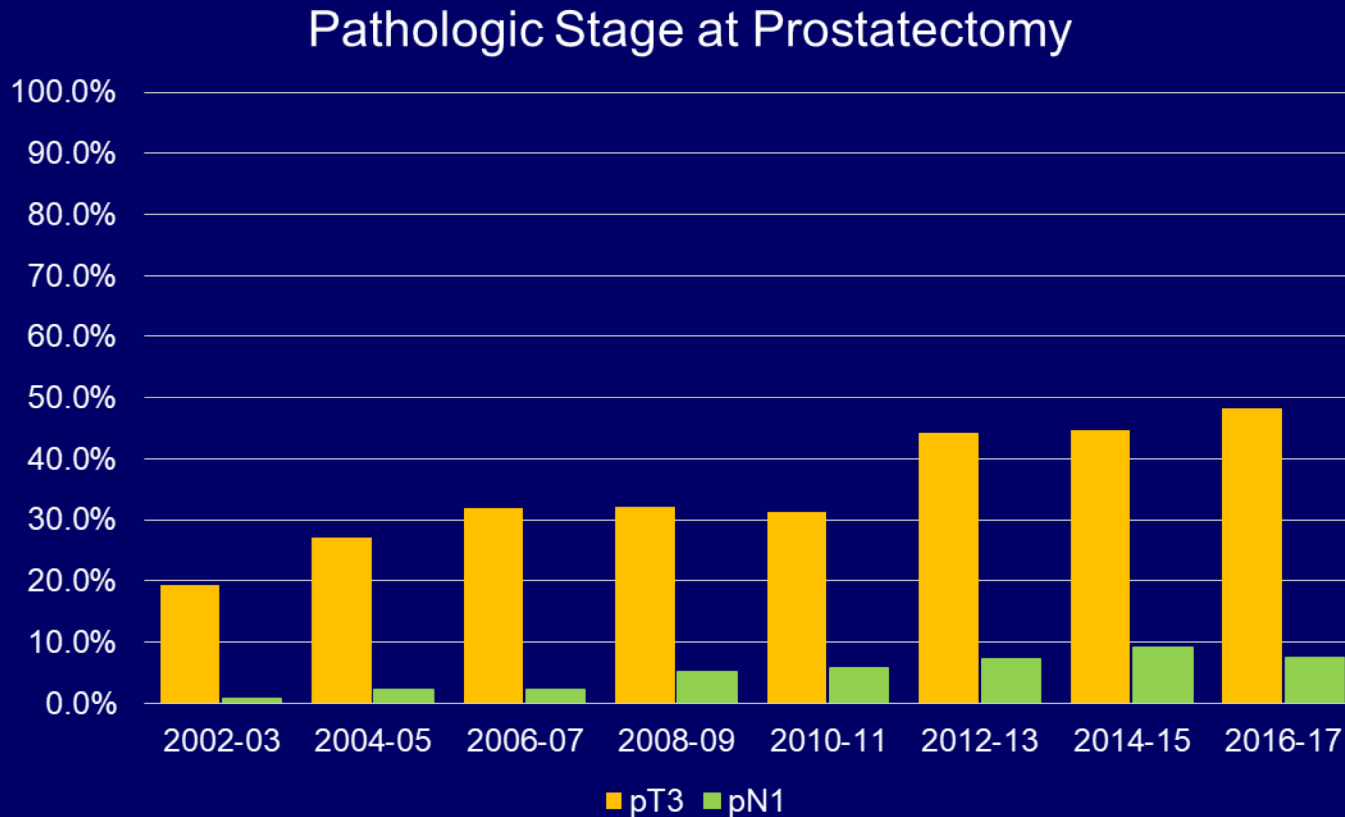


# Changes in Tumor Grades Not Proportional When GS≤6 Excluded



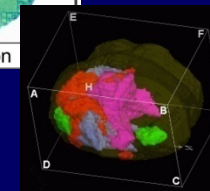
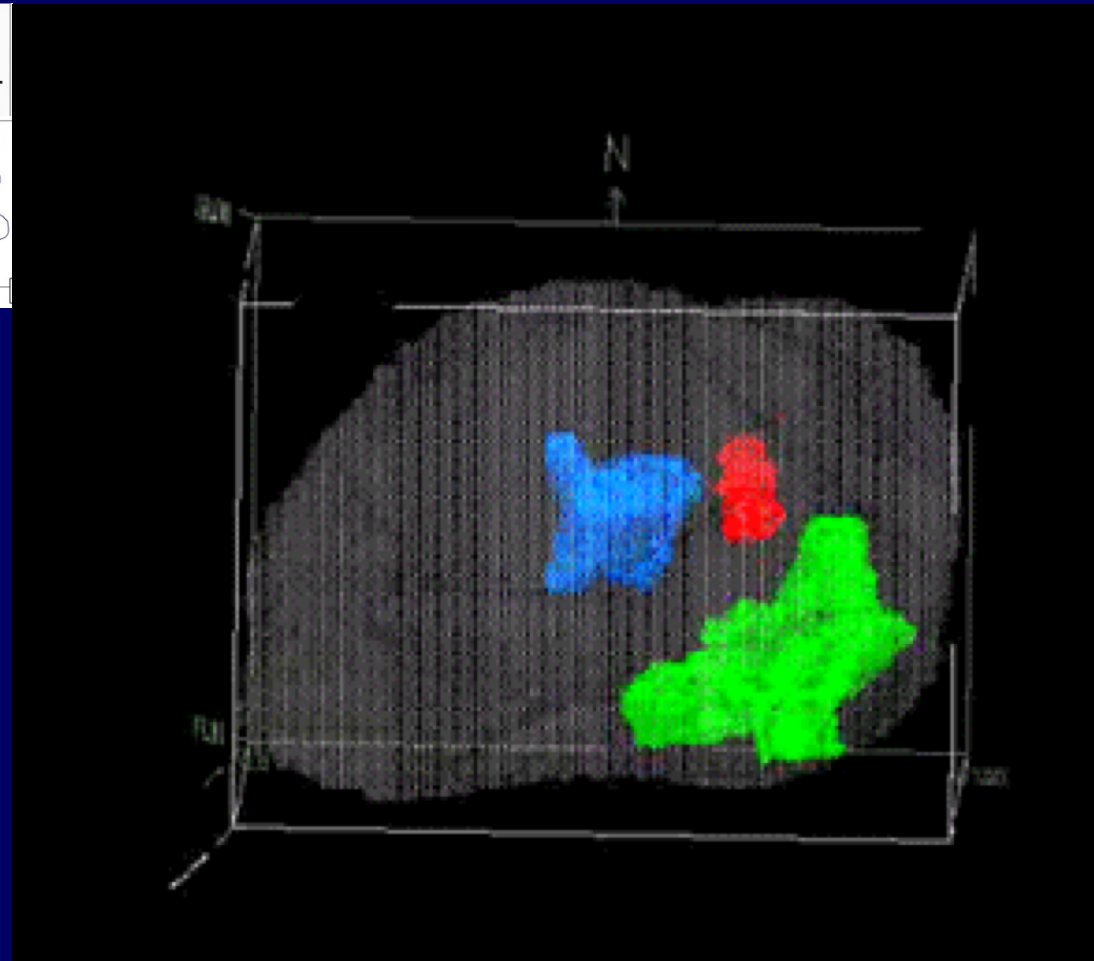
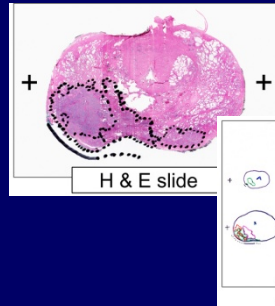
Chi-square test for independence  
 $p < 0.0001$

# Recent Rise in Advanced Stage Prostate Cancer at Prostatectomy



Chi square test for trend:  $p < 0.0001$   
 $p < 0.0001$

# 3-Dimensional Reconstruction of Whole-Mounted Prostatectomy Specimens



# Multifocality of 293 carcinomas from 151 prostates (< 1994)<sup>1</sup>

Tumors/Pt.	No. Pts. (%)	No. Tumors	Mean Tumor Vol. (cc)
1	66 (43.7)	66	6.52
2	47 (31.1)	94	1.48
3	25 (16.6)	75	1.01
4	8 (5.3)	32	0.59
5	4 (2.6)	20	0.40
6	1 (0.7)	6	0.22
Totals	151 (100)	293 (1.9/pt)	4.46

## Prostate Cancer Database, Univ. of Colorado AMC:

2002-12: 72% multifocal (21.8% ant), 2.7 tumors/pt, Mean tum vol = 2.08 cc

2016-17: 74% multifocal (26.7% ant), 2.4 tumors/pt, Mean tum vol = 3.62 cc

# Conclusions

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- Changes in the clinical management of prostate cancer over the last 16 years have led to changes in the pathological features of tumors undergoing prostatectomy at the Univ. of Colorado:
  - Shift towards higher grade tumors
  - Increased stage (↑ pT3, ↑ pN1)
  - Larger tumor volumes
- *Pending:*
  - Impact on mortality???

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