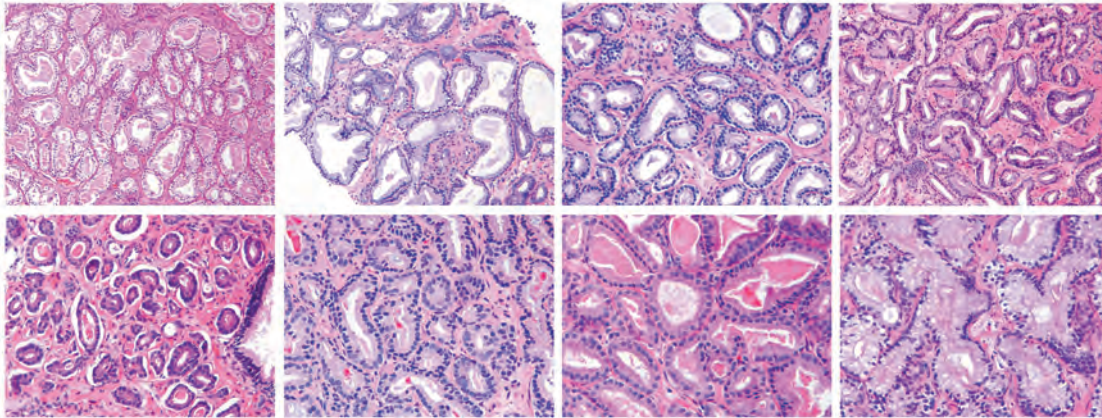
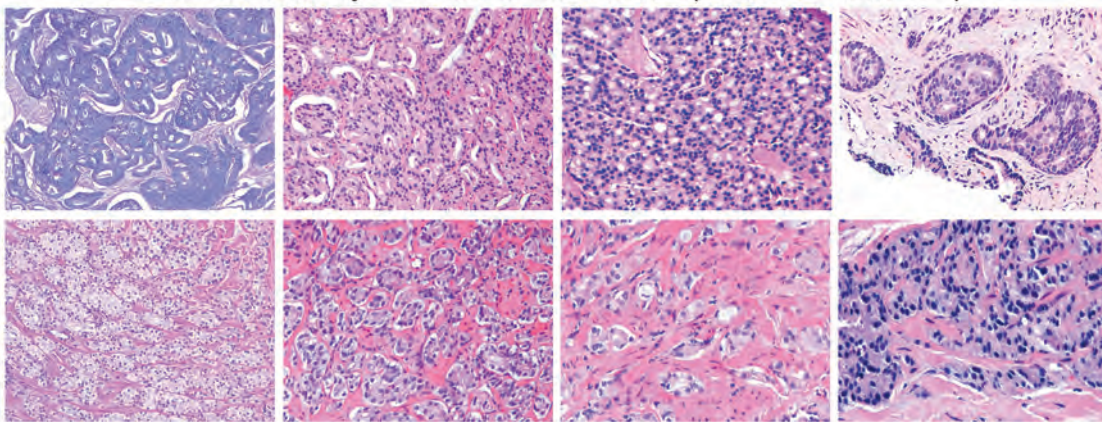


A NEW CONTEMPORARY PROSTATE CANCER GRADING SYSTEM

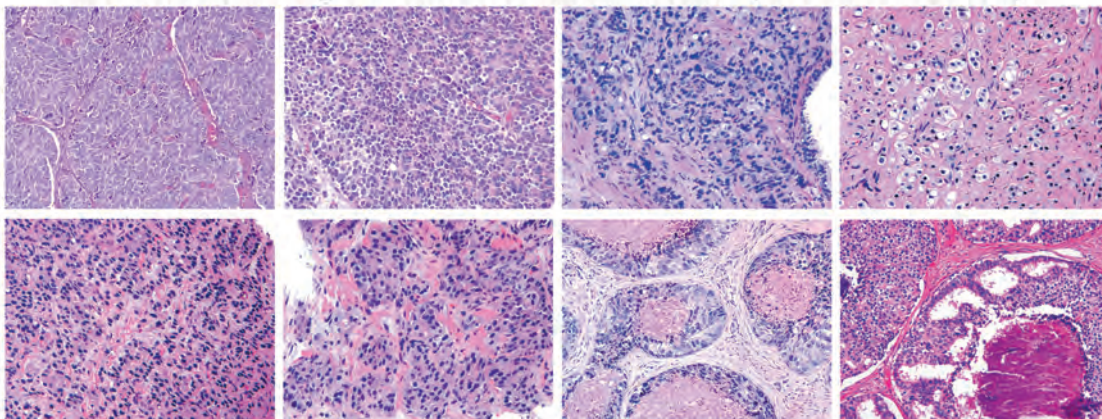
Discrete Well-formed Glands (Gleason Patterns 1-3)



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



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



Copyright 2013 The Johns Hopkins University. All rights reserved

Jonathan Epstein, M.D.

From Left to Right:

1st Row: Closely packed uniform sized and shaped large glands; Large variably sized and shaped glands, some with infolding; Uniform medium sized glands; Variably sized glands

2nd Row: Occasional tangentially sectioned glands amongst well-formed small glands; Occasional tangentially sectioned glands amongst well-formed glands with open lumina; Back-to-back discrete glands; Branching glands

3rd Row: Large irregular cribriform glands with well-formed lumina; Irregular cribriform glands with slit-like lumina, glomeruloid structures, and fused glands; Irregular cribriform glands with small round lumina; Small round cribriform glands

4th Row: Poorly-formed glands with peripherally arranged nuclei; Small poorly-formed glands; Small poorly-formed glands; Fused poorly-formed glands

5th Row: Sheets of cancer; Sheets of cancer with rosette formation; Small nests and cords of tumor with scattered clear vacuoles; Individual cells

6th Row: Nests and cords of cells with only vague attempt at lumina formation; Solid nests of cancer; Solid nests with comedonecrosis; Cribriform glands with central comedonecrosis

A NEW CONTEMPORARY PROSTATE CANCER GRADING SYSTEM

Problems with the Current Gleason System:

- 1) Scores 2-5 are currently no longer assigned and certain patterns that Gleason defined as a score of 6 are now graded as 7, thus leading to contemporary Gleason score 6 cancers having a better prognosis than historic score 6 cancers.
- 2) The combination of Gleason scores into a 3-tier grouping (6,7,8-10) is used most frequently for prognostic and therapeutic purposes, despite $3+4=7$ vs. $4+3=7$ and 8 vs. 9-10 having very different prognoses.
- 3) In practice the lowest score is now assigned a 6, although it is on a scale of 2-10. This leads to a logical yet incorrect assumption on the part of patients that their cancer is in the middle of the scale, compounding the fear of their cancer diagnosis with the belief that the cancer is serious, thus leading to an expectation that treatment is necessary.

Proposal for a new Grading System

To address the above deficiencies, a new 5 Grade Group system has been developed based on a study of >20,000 prostate cancer cases treated with radical prostatectomy and >5,000 cases treated by radiation therapy (see composite photograph for different patterns).

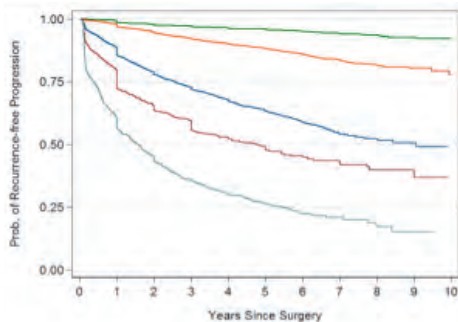
- Grade Group 1 (Gleason score ≤ 6) – Only individual discrete well-formed glands
- Grade Group 2 (Gleason score $3+4=7$) – Predominantly well-formed glands with a lesser component of poorly-formed/fused/cribriform glands
- Grade Group 3 (Gleason score $4+3=7$) – Predominantly poorly-formed/fused/cribriform glands with a lesser component of well-formed glands†
- Grade Group 4 (Gleason score 8)
 - Only poorly-formed/fused/cribriform glands or
 - Predominantly well-formed glands with a lesser component lacking glands†† or
 - Predominantly lacking glands with a lesser component of well-formed glands††
- Grade Group 5 (Gleason scores 9-10) – Lacks gland formation (or with necrosis) with or w/o 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 also be a more minor component

A NEW CONTEMPORARY PROSTATE CANCER GRADING SYSTEM

1. The five-year biochemical recurrence-free progression probabilities for radical prostatectomy Grade Groups 1-5 were 96%, 88%, 63%, 48%, and 26%.



2. The 5 Grade Groups were also predictive for biopsy grade followed by radical prostatectomy or radiation therapy.
3. The new system distills grades of prostate cancer down to the lowest number of grades, each with a unique prognosis. As a result of significant differences in criteria and reporting compared to the Gleason's original grading system, we have regarded the newly proposed grade groups as a new grading system.

SUMMARY

The new grading system for prostate cancer has obvious benefits:

- 1) More accurate grade stratification than the current Gleason system
- 2) Simplified grading system of 5 as opposed to multiple possible scores depending on various Gleason pattern combinations
- 3) Lowest grade is 1 as opposed to current practice of Gleason score 6, with the potential to reduce overtreatment of indolent prostate cancer

The new grading system, using the above terminology, has been accepted by the 2016 World Health Organization (WHO).

To avoid confusion, it will be prudent to report the new grading system, in conjunction with the Gleason system, until it becomes widely accepted and practiced [ie. *Gleason score 3+3=6 (Grade Group 1)*].

Epstein JI, Zelefsky MJ, Sjoberg DD, et al. A contemporary prostate cancer grading system: A validated alternative to the Gleason score. *Eur Urol* (2015).