Gleason Grading System

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WHY THE NEED FOR A CONSENSUS ON GLEASON GRADING?

Gleason’s Era

• More advanced clinical disease
• Fewer RPs which were not processed in entirety
  – Grading of multiple nodules
  – Tertiary patterns
• Needle biopsy only a few thick cores
  – Grading thin needle cores
  – Grading multiple cores from different sites
• Lesions diagnosed differently with more modern tests
• New entities
Reporting Grade

• “Gleason grade 4” - ? Gleason pattern 4 (ie 4+4=8) or 2+2=4

• “Gleason grade 3/5” - ? Gleason pattern 3 out of 5 patterns (ie. 3+3=6) or 3+5=8

• Gleason score 3+4=7 (preferred method even if limited cancer)
VARIANTS of ADENOCARCINOMA

Foamy Gland Cancer

- One should ignore the foamy cytoplasm and grade the tumor solely based on the underlying architecture.

- Most will be Gleason score 3+3=6

- Occasionally high grade foamy cancer
Foamy Gland:  Pattern 5

Ductal Adenocarcinoma

- Cribriform/papillary ductal adenocarcinomas should be graded as Gleason score 4+4=8, while retaining the diagnostic term of ductal adenocarcinoma to denote their unique clinical and pathological findings.

- This can be achieved by diagnosing such a tumor as “prostatic ductal adenocarcinoma (Gleason score 4+4=8).”

- PIN-Like ductal adenocarcinoma graded 3+3=6.

- Duct adenocarcinoma with necrosis grades as Gleason pattern 5.
Ductal Adenocarcinoma: Gleason Pattern 4

Ductal Adenocarcinoma: Gleason Pattern 4
Reporting Grade

PIN-like ductal adenocarcinomas co-exist with acinar Gleason score 3+3=6 prostate cancer and have favorable pathological findings at radical prostatectomy such that we consider them to be Gleason score 3+3=6.

Ductal adenocarcinomas of the prostate can be graded by their pattern:

- Cribriform & Papillary: pattern 4
- PIN-like ductal: pattern 3
- Duct with necrosis: pattern 5
Vacuoles

Graded, as if the vacuoles were not present, by only evaluating the underlying architectural pattern.

• Mostly Gleason patterns 4 & 5

• Occasionally Gleason pattern 3

Vacuoles: Pattern 3
Vacuoles: Pattern 4

Vacuoles: Pattern 5
Colloid (Mucinous) Carcinoma

There is no consensus whether all colloid carcinomas should be assigned a Gleason score of 8, or that one should ignore the extracellular mucin and grade the tumor based on the underlying architectural pattern.

Most Gleason pattern 4

? Some Gleason pattern 3
Small cell carcinoma of the prostate has unique histological, immunohistochemical, and clinical features, which differ from those associated with Gleason pattern 5 prostatic acinar carcinoma, such that small cell carcinoma should not be assigned a Gleason grade.
Mucinous Fibroplasia (Collagenous Micronodules)

- One should try to subtract away the mucinous fibroplasia and grade the tumor based on the underlying glandular architecture. The majority of these cases would accordingly be graded as Gleason score 3+3=6.

Mucinous Fibroplasia: Pattern 3
Mucinous Fibroplasia: Pattern 3

Mucinous Fibroplasia: Pattern 4
Glomeruloid Structures

• Larger glomeruloid - Most agree pattern 4

• Small glomeruloid- ? pattern 3 or pattern 4.

• Newer data demonstrates that even small glomeruloid typically associated with pattern 4 cancer, such that growing evidence that all glomeruloid is pattern 4.

Glomeruloid Glands: ? Pattern 3 or 4
Pseudohyperplastic Adenocarcinoma

Should be graded as Gleason score 3+3=6 with pseudohyperplastic features.
REPORTING SECONDARY PATTERNS OF LOWER GRADE WHEN PRESENT TO A LIMITED EXTENT

In the setting of high grade cancer one should ignore lower grade patterns if they occupy less than 5% of the area of the tumor.

Gleason pattern 4 (98%) and pattern 3 (2%) = Gleason score 4+4=8

Standard: 4 + 3 = 7
Consensus: 4 + 4 = 8
REPORTING SECONDARY PATTERNS OF HIGHER GRADE WHEN PRESENT TO A LIMITED EXTENT (NEEDLE)

High grade tumor of any quantity on needle biopsy, as long as it was identified at low to medium magnification should be included within the Gleason score. A needle biopsy which is entirely involved by cancer with 98% Gleason pattern 3 and 2% Gleason pattern 4 would be diagnosed as Gleason score 3+4=7.

Consensus: 3 + 4 = 7
REPORTING SECONDARY PATTERNS OF HIGHER GRADE WHEN PRESENT TO A LIMITED EXTENT (RP)

Tumor nodule having 98% Gleason pattern 3 and 2% pattern 4, there is no consensus as to whether diagnose these foci in an analogous fashion to that done on needle biopsy and interpret the case as Gleason score 3+4=7 regardless of the percentage of pattern 4 or grade these tumors as Gleason score 3+3=6 with a tertiary component of Gleason pattern 4.

TERTIARY GLEASON PATTERNS (N)

Patterns 3, 4, and 5 in various proportions, classify as high grade (Gleason score 8-10) given the presence of high grade tumor (patterns 4 and 5).

Both the primary pattern and the highest grade should be recorded.

Gleason score 3+4 and a tertiary pattern 5 = Gleason score 3+5=8.
TERTIARY GLEASON PATTERNS (RP)

In radical prostatectomy specimens, the situation is not analogous to that seen on needle biopsy, as one has the entire nodule available for examination.

For a radical prostatectomy specimen one assigns the Gleason score based on the primary and secondary patterns with a comment as to the tertiary pattern.

In general, the tertiary pattern increases the grade by $\frac{1}{2}$ (ie. Gleason score $3+3=6$ with tertiary 4 has a prognosis in between Gleason score $3+3=6$ and $3+4=7$.)
NEEDLE BIOPSIES WITH DIFFERENT CORES DIFFERENT GRADES

Greatest importance when \( \geq 1 \) cores pure high grade cancer (i.e. Gleason score 4+4=8) and other cores pattern 3 (3+3=6, 3+4=7, 4+3=7) cancer.

Highest or Average Gleason Score

• Gleason score 4+4=8 on \( \geq 1 \) cores with pattern 3 in other cores more likely higher stage and higher grade at RP, comparable to pure 4+4=8.

• Several studies show that the highest Gleason score correlates better with RP grade and stage as opposed to the most common (global) Gleason score.

NEEDLE BIOPSY WITH DIFFERENT CORES SHOWING DIFFERENT GRADES

One should assign individual Gleason scores to separate cores as long as the cores were submitted in separate containers or the cores were in the same container yet specified by the urologist as to their location (i.e. by different color inks).

Assigning a global (composite) score is optional.
Gleason Score 2-4 on Needle

- Diagnosis of Gleason 2-4 should not be made on needle.

- 1) Poor reproducibility among experts for lower grade tumors.

- 2) Correlation with the prostatectomy score for Gleason 2-4 tumors is poor and up to 50% of the corresponding prostatectomies may have extraprostatic extension.

- 3) Gleason 2-4 may misguide clinicians and patients into believing that there is an indolent tumor.

Low Grade Prostate Cancer Does Exist

- Transition zone

- Small foci

- Seen on TURP – often indicates “insignificant” cancer

- Rarely sampled on needle biopsy – not indicate “indolent” tumor
## Correlation Needle & RP Grade

<table>
<thead>
<tr>
<th>Needle</th>
<th>RP</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>3+4 (22%)</td>
</tr>
<tr>
<td>3+4=7</td>
<td>16% (3+3); 16% (4+3)</td>
</tr>
<tr>
<td>4+3=7</td>
<td>39% (3+4); 40% (4+3)</td>
</tr>
<tr>
<td>8</td>
<td>26% (4+3); 30% (8); 25% (9-10)</td>
</tr>
</tbody>
</table>

## Risk of Upgrading

- Increased clinical stage
- Increased PSA
- Increased cancer on biopsy
- Decreased biopsy sampling
- Decrease prostate volume
Gleason Score 2+2=4
Gleason Score 3+3=6
Gleason Score 3+4=7/4+3=7
Gleason Score 4+4=8
Gleason Score 9-10
**Biopsy Gleason Score \( \leq 6 \) vs. \( >7 \)**

- Watchful waiting vs. definitive treatment

- Surgery vs. radiation

- Decision whether to spare NVB

- Brachytherapy vs. XRT ± brachytherapy

**Biopsy Gleason Score 3+4 vs. 4+3**

Radiation therapy

vs.

Hormones + radiation therapy
Biopsy Gleason Score 8 vs. 9-10

Surgery vs. Radiation

<table>
<thead>
<tr>
<th>PSA Range (ng/mL)</th>
<th>Pathologic Stage</th>
<th>Gleason Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2-4</td>
</tr>
<tr>
<td>0-2.5</td>
<td>Organ confined</td>
<td>95 (89-99)</td>
</tr>
<tr>
<td></td>
<td>Extraprostatic extension</td>
<td>5 (1-11)</td>
</tr>
<tr>
<td></td>
<td>Seminal vesicle (+)</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Lymph node (+)</td>
<td>—</td>
</tr>
<tr>
<td>2.6-4.0</td>
<td>Organ confined</td>
<td>92 (82-98)</td>
</tr>
<tr>
<td></td>
<td>Extraprostatic extension</td>
<td>8 (2-18)</td>
</tr>
<tr>
<td></td>
<td>Seminal vesicle (+)</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Lymph node (+)</td>
<td>—</td>
</tr>
<tr>
<td>4.1-6.0</td>
<td>Organ confined</td>
<td>90 (78-98)</td>
</tr>
<tr>
<td></td>
<td>Extraprostatic extension</td>
<td>10 (2-22)</td>
</tr>
<tr>
<td></td>
<td>Seminal vesicle (+)</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Lymph node (+)</td>
<td>—</td>
</tr>
<tr>
<td>6.1-10.0</td>
<td>Organ confined</td>
<td>87 (73-97)</td>
</tr>
<tr>
<td></td>
<td>Extraprostatic extension</td>
<td>13 (3-27)</td>
</tr>
<tr>
<td></td>
<td>Seminal vesicle (+)</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Lymph node (+)</td>
<td>—</td>
</tr>
<tr>
<td>&gt; 10.0</td>
<td>Organ confined</td>
<td>80 (61-95)</td>
</tr>
<tr>
<td></td>
<td>Extraprostatic extension</td>
<td>20 (5-39)</td>
</tr>
<tr>
<td></td>
<td>Seminal vesicle (+)</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Lymph node (+)</td>
<td>—</td>
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</table>
Instructions: Locate the patient's pretreatment PSA on the PreTxPSA axis. Draw a line straight upward to
the points axis to determine how many points toward the probability of positive lymph nodes the patient
receives for his PSA. Repeat the process for each variable. Sum the points achieved for each of the
predictors. Locate the final sum on the total points axis. Draw a line straight down to find the patient's
probability of having positive lymph nodes.

Biochemical Recurrence Free Survival
Simplified Biopsy Gleason Sum

(4,510) 94.6% (251)
(1,253) 82.7% (35)
(458) 65.1% (18)
(198) 63.1% (7)
(93) 34.5% (2 at 4 years)

log-rank p<0.001
Prognostic Grade Grouping with Descriptive Terminology

- Gleason score 2-6 (well-differentiated), Prognostic Grade Group I/V

- Gleason score 3+4=7 (moderately differentiated), Prognostic Grade Group II/V

- Gleason score 4+3=7 (moderately-poorly differentiated), Prognostic Grade Group III/V

- Gleason score 8 (poorly differentiated), Prognostic Grade Group IV/V

- Gleason score 9-10 (undifferentiated), Prognostic Grade Group V/V