PROSTATE CANCER: CONTEMPORARY APPROACH AND ISSUES RELATED TO GLEASON GRADING AND SCORE REPORTING
ORIGINAL GLEASON DRAWINGS
September 8, 1968

1. Dark plaque
2. Pale cells + Rel. large + Pore old
3. Schematic 9.5 cm.6 CA prostate
4. Solid or minimal spaces
5. Diffuse undiff.
ORIGINAL GLEASON DRAWINGS 1968

- Old
- New

As before. As before. Well-diffused glands but too much per II. 2

Cancerous. papillary structure, some solid but dispersed glandular somatic

Large circumscribed buds - papillary structure, some solid but dispersed glandular somatic

Small cells - but much glandular formation


6. Fluid glands, difficulty grading, not necessarily pale.
GLEASON GRADING

- Based on architecture
- Perceived as a continuum
- Subjectivity in gray areas between grades
- Recognizes heterogeneity of prostate cancer
- “Score” is based on recognizing a “primary” and “secondary” grade and summing the two
HEALTH JOURNAL
By Tara Parker-Pope

Risk of Error May Justify Second Opinion On Pathology Reports

"Members of the jury, have you reached a verdict?"
APPLICATION IN 18 GUAGE NEEDLE BIOPSIES

Amin, Grignon, Humphrey & Srigley

GLEASON GRADING

Prostatic Adenocarcinoma
(Histologic Grades)
GLEASON GRADE 1

- Circumscribed nodule, almost exclusive to TZ
- Glands are uniform and round
GLEASON GRADE 1
GLEASON GRADE 2

- Glands more variable in shape than grade 1
- Increased stroma between glands
- Some infiltration at periphery
GLEASON GRADE 2
Small focus of Grade 3 - Not grade 1 or 2
Nodule of Gleason score 9
GLEASON SCORE 5

“Transition zone biopsies”
CONSENSUS STATEMENTS ON LOW GRADE PATTERNS

• Gleason score 1+2=3 and 2+1=3 can be seen in TUR and RP material but are not to be diagnosed in needle biopsy
• Gleason score 2+2=4 in needle biopsy very controversial
• *Consensus that this score should “rarely if ever” be made in needle biopsy material*
GLEASON GRADE 3

- Well formed glands with infiltrative growth
- May be small, angulated or compressed
- Cribriform architecture with round nests
GLEASON GRADE 3
GLEASON GRADING
CRIBRIFORM PATTERNS

Amin, Grignon, Humphrey & Srigley, 2004
GLEASON GRADING
CRIBRIFORM PATTERNS

• “rounded, well-circumscribed glands of the same size as normal glands”

• “… most of cribriform patterns be diagnosed as Gleason pattern 4 with only rare cribriform lesions satisfying diagnostic criteria for cribriform pattern 3”

Consensus opinion, 2005
Gleason score 7 - not score 6

Currently all cribriform glands are considered to be grade 4
Complex Gleason grade 3 - not fused grade 4
Closely packed Gleason grade 3 - not fused grade 4
“Columns” of Gleason grade 3 - not nodule of grade 2
Gleason score 6, not a nodule of score 4
GLEASON GRADE 4

- Raggedly infiltrating, poorly formed glands
- Fused glands - chains or solid masses
- Complex papillary-cribriform islands
- Hypernephroid and mucinous variants
Hypernephroid grade 4, not grade 5
Foamy grade 3 - not hypernephroid grade 4
GLEASON GRADE 5

- Solid masses with no gland formation
- Infiltrating cords and single cells (including signet-ring cells)
- Comedonecrosis
GLEASON GRADE 5
GLEASON GRADE 5
Granular debris - not comedo necrosis grade 5

Gleason score 7 (4 + 3)
GLEASON SCORE 8
GLEASON SCORE 8 (5 + 3)
GLEASON SCORING

Collagenous micronodules

Glomerulations
# GLEASON GRADING OF VARIANTS

<table>
<thead>
<tr>
<th>Ductal - endometrioid</th>
<th>Grade 4, 5 with necrosis, rarely 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucinous</td>
<td>Grade 4 (rarely 3)</td>
</tr>
<tr>
<td>Signet ring</td>
<td>Grade 5</td>
</tr>
<tr>
<td>Sarcomatoid</td>
<td>Grade 5</td>
</tr>
<tr>
<td>Pseudohyperplastic</td>
<td>Grade 2 or 3, rarely 4</td>
</tr>
<tr>
<td>Xanthomatous (foamy)</td>
<td>Grade 3 or 4</td>
</tr>
<tr>
<td>Atrophic</td>
<td>Grade 3 or 2</td>
</tr>
</tbody>
</table>

*From Amin, Grignon, Humphrey & Srigley, 2004*
MUCINOUS CARCINOMA
Grade 3 - not mucinous grade 4
SIGNET RING CARCINOMA
PROSTATE CARCINOMAS NOT TO BE GRADED

- Adenosquamous and squamous carcinoma
- Basaloid and adenoid cystic carcinoma
- Lymphoepithelioma-like carcinoma
- Small cell carcinoma
- Urothelial carcinoma

From Amin, Grignon, Humphrey & Srigley, 2004
GLEASON SCORING OF NBx
RECOGNIZED PROBLEMS

- Poor correlation between needle biopsy score and radical prostatectomy score
- Significant inter- and intra-observer variability
- Issues related to sampling errors
70% of pT2 tumors had ≥ 3 foci
In < 10% did all foci have the same GS

Figure 1. Whole-mount section of a radical prostatectomy specimen showing three outlined tumor foci with corresponding individual Gleason scores. The Gleason score of the index tumor differs from the overall Gleason score.

Arora et al. Cancer 100:2362-2366, 2004
### Concordance of Biopsy and Prostatectomy Gleason Score

Comparison by Biopsy Technique

<table>
<thead>
<tr>
<th>Biopsy score</th>
<th>Sextant</th>
<th>Extended</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS 6 or less</td>
<td>67% (12/18)</td>
<td>37% (7/19)</td>
<td>0.039</td>
</tr>
<tr>
<td>GS 7</td>
<td>32% (12/38)</td>
<td>24% (11/45)</td>
<td>0.068</td>
</tr>
</tbody>
</table>

*GS 6 = any 7 or higher; GS 7 = 3+4 to 4+3 or higher, 4+3 to 8 or higher

RECOMMENDATIONS FOR THE REPORTING OF GLEASON GRADE

• Report a Gleason score for all newly diagnosed prostate cancer
• Report the grades (patterns) with the score (sum) to make it clear what is present [eg Gleason score 7 (3 + 4)]
• Reporting the % grade 4/5 is optional

Note that the concept of simply reporting the % high grade carcinoma (4/5) continues to have advocates (Vis et al. Eur Urol 51:931-939, 2007)
FIG. 3. Kaplan–Meier curves correlating progression with Gleason score. Comparison of typical Gleason score 5 to 6 with tertiary pattern 4/5 with typical Gleason score 5 to 6 and typical Gleason score 7 without tertiary patterns. Numbers above curves denote censored patients.

FIG. 5. Kaplan–Meier curves correlating progression with Gleason score. Comparison of typical Gleason score 7 with tertiary pattern 5 with typical Gleason score 7 and typical Gleason score 8 without tertiary patterns. Numbers above curves denote censored patients.

SIGNIFICANCE OF TERTIARY HG GLEASON PATTERN (RP)


Fig. 1. Kaplan-Meier curves of the PSA progression free interval of patients with a tertiary pattern pattern (g13++; upper green line) and those without a tertiary pattern (g13--; lower blue line).

**FIGURE 2.** Progression-free survival of patients with Gleason score 7 prostate carcinoma who were treated with radical prostatectomy when tertiary Gleason pattern 5 foci were present and absent. The numbers above the curves denote those patients at risk at 5 years and at the end of follow-up. PSA: prostate-specific antigen.
SIGNIFICANCE OF TERTIARY (<5%) HG GLEASON PATTERN (NBx)

Figure. Estimates of Prostate-Specific Antigen (PSA) Recurrence Following Radical Prostatectomy or External Beam Radiation Therapy With or Without Androgen Suppression Therapy

“In needle biopsy specimens in which more than two patterns are present and the worst grade is neither the primary or secondary grade, the predominant and the highest grade should be chosen to arrive at a score (e.g. 60% grade 3, 30% grade 4 and 10% grade 5 is scored \(3 + 5 = 8\)).”

Srigley et al, Arch Pathol Lab Med 133:1568, 2009
TERTIARY GRADE

- Gleason grades $4 > 3 > 5$
- Report Gleason score as:
  \[4 + 5 = 9\]
“In needle biopsy specimens where two patterns are present and the worst grade is neither the primary or secondary grade (eg. < 5% of volume) the predominant and the highest grade should be chosen to arrive at a score (eg. 98% grade 3, 2% grade 4 is scored $3 + 4 = 7$)”

Srigley et al, Arch Pathol Lab Med 133:1568, 2009
“In needle biopsy specimens where two patterns are present and the lower grade is neither the primary or secondary grade (eg. < 5% of volume) the lower grade should be ignored in arriving at a score (eg. 96% grade 4, 4% grade 3 is scored 4 + 4 = 8)”

Srigley et al, Arch Pathol Lab Med 133:1568, 2009
RECOMMENDATIONS FOR THE REPORTING OF GLEASON SCORES

- Report a Gleason score for each positive biopsy when the biopsies are submitted as separate specimens.
- If needle biopsies from several sites are submitted in a single container, report the Gleason score for the specimen.
- In the situation where different cores are given different Gleason scores, it is optional to provide an overall Gleason score based on the total material received.
IMPACT OF GLEASON SCORING CHANGES

• Decreased % of cases in GS ≤ 6
  – Biopsy: 68% → 54%
  – RP: 47% → 32%

• Improved concordance between BX & RP
  • Uemura et al. BJU Int 103:1190, 2008

• Improved prognostic prediction
  • Uemura et al. BJU Int 103:1190, 2008
PCA NBX REPORT
CAP RECOMMENDATIONS

- Histologic type
- Gleason score (include 1º and 2º and 3º)
- Quantitation of tumor (as # of cores and % tissue or other method)
- Local invasion (document if identified)
  - peri-prostatic fat
  - seminal vesicle
- Perineural invasion*
- Blood/lymphatic vessel invasion*
- Other pathologic findings*

*Srigley et al, Arch Pathol Lab Med 133:936, 2009
REPORTING OF “NEGATIVE” NEEDLE BIOPSIES

#4 - Left base prostate needle biopsy: Prostatic tissue, no evidence of malignancy.
#5 - Left mid prostate needle biopsy: Prostatic tissue, no evidence of malignancy.
#6 - Left apex prostate needle biopsy: Prostatic tissue, no evidence of malignancy.
REPORTING OF “NEGATIVE” NEEDLE BIOPSIIES

Extent of Prostatic Atrophy in Needle Biopsies and Serum PSA Levels: Is There an Association?
Athanase Billis, Luciana R. Meirelles, Luis A. Magna, Jamal Baracat, Adilson Prando, and Ubirajara Ferreira

Association of Extent and Aggressiveness of Inflammation with Serum PSA Levels and PSA Density in Asymptomatic Patients
Engin Kandirali, Cetin Boran, Erdinc Serin, Atilla Semercioz, and Ahmet Metin

Inverse Association Between Histologic Inflammation in Needle Biopsy Specimens and Prostate Cancer in Men With Serum PSA of 10-50 ng/mL
Tomoaki Terakawa, Hideaki Miyake, Naoki Kanomata, Masafumi Kumano, Atsushi Takenaka, and Masato Fujisawao
FINAL DIAGNOSIS:
RIGHT AND LEFT RANDOM PROSTATE BIOPSIES:
STROMAL AND GLANDULAR HYPERPLASIA. THERE IS NO EVIDENCE OF MALIGNANCY.

DIAGNOSIS:
Benign prostatic hypertrophy, biopsy of.
FINAL DIAGNOSIS:
RIGHT AND LEFT RANDOM PROSTATE BIOPSIES:
STROMAL AND GLANDULAR HYPERPLASIA. THERE IS NO EVIDENCE OF MALIGNANCY.

DIAGNOSIS:
Benign prostatic hypertrophy, biopsy of.