Gleason Scoring System: Nuances in Interpretation

Jasreman Dhillon, MD
Assistant Member
Anatomic Pathology, GU
Moffitt Cancer Center
Gleason Grading System

- Created by Donald F. Gleason in 1966
- Based solely on the architectural pattern of the tumor
- Tumors are assigned a Gleason score based on sum of the two most common grade patterns
- Certain aspects of the original Gleason system are interpreted differently in today’s practice
- Remarkable that more than 40 years after it’s inception, it remains one of the most powerful prognostic predictors in prostate cancer
- Multiple molecular marker studies in serum and tissue have largely failed to improve upon the prognostic power of this system.
Gleason Score

Gleason Grade

1977

ISUP Modified Gleason Grade

2005
Consensus Conference on Gleason Grading of Prostatic Carcinoma

• International Society of Urological Pathology (ISUP) in 2005
  – Incorporate changes in the reporting of Gleason score in pathology reports that reflect the changing clinical practices
  – Obtain consensus on how to grade newly described variants of prostatic ca e.g. mucinous carcinoma, ductal carcinoma, foamy gland carcinoma
  – Pathologists:
    • Achieve consensus on Gleason grading
    • Help pathologists adapt the Gleason grading system to current day practice in a more uniform manner
Variations in Reporting

• Do all pathologists follow ISUP 2005 recommendations
• How different pathologists interpret ISUP 2005 recommendations
• ISUP 2005 Committee could not come to consensus in certain areas of reporting
Interpretation of 2005 ISUP Recommendations by Pathologists

- European study in 2013 by Berney et al
- Web-based survey to 266 European pathologists in 22 countries
- 89% claimed to follow ISUP 2005 recommendations
Gleason Pattern 4

**ISUP 2005**
- Cribiform glands with an irregular border

**Survey**
- Reported as GP4
  - 97.5%
- Reported as GP3
  - 2%
- 2% Reported as GP5
  - 0.5%
Gleason Pattern 3

**ISUP 2005**
- Smoothly circumscribed small cribriform nodules of tumor

**SURVEY**
- Reported as GP3
  - 51%
- Reported as GP4
  - 49%

Epstein *J Urol* proposed modifications 2010
Gleason pattern 4
Gleason Pattern 4

**ISUP 2005**
- Poorly formed glands

**Survey**
- Reported as GP4
  - 84%
- Reported as GP3
  - 6.5%
- Reported as GP5
  - 9.5%
Concordance/Disconcordance

• Most cribriform patterns and poorly formed glands there is 80% agreement that these should be assigned a GP 4

• No consensus for rounded cribriform glands
Glomeruloid Glands

ISUP 2005
• No consensus
  – 6 (3+3); 8 (4+4)

Survey
• Reported as GP3
  – 12.4%
• Reported as GP4
  – 86.1%
• Reported as GP5
  – 1.5%
Low Gleason Scores on Biopsy

**ISUP 2005 Recommendation**

- GS 2, 3 and 4 – should not be made on a biopsy
  - Poor reproducibility
  - Poor correlation with prostatectomy grade
  - Misguide the clinician and the patient into believing that the tumor is indolent
- GS 3-4 – can occasionally be made on TURP and radical prostatectomy specimens

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**GS of 2, 3-4 and 5**

<table>
<thead>
<tr>
<th>Score used in biopsy reporting</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score 2-3</td>
<td>2%</td>
<td>98%</td>
</tr>
<tr>
<td>Score 4</td>
<td>6.5%</td>
<td>93.5%</td>
</tr>
<tr>
<td>Score 5</td>
<td>29.7%</td>
<td>70%</td>
</tr>
</tbody>
</table>
Concordance of Opinion

• Vast majority of uropathologists will not report a GS of <6 on a prostatic biopsy
• Pathologists over 50 years of age tended to diagnose Gleason score 2-4 on needle biopsy to a statistically significantly higher frequency than younger pathologists who are trained to do so rarely if ever.
Gleason Pattern 5

**ISUP 2005**
- Cribriform glands with necrosis

**Survey**
- Reported as GP5
  - 85.5%
- Reported as GP3
  - 1.5%
- Reported as GP4
  - 13%
Diagnosis of GP5

**ISUP 2005**
- Essentially no glandular differentiation, composed of solid sheets, cords, or single cells
- Comedocarcinoma with central necrosis surrounded by papillary, cribriform, or solid masses

**Survey**
- Cluster of single cells or solid sheets of carcinoma
  - 72% GP5 only if these features are seen at hp (20X)

**Necrosis**
- 62% call it GP5
- 38% would not
Discordance Regarding GP 5

- Criteria for diagnosis of GP 5 are not clear
- No minimum criteria given
- Further consensus is necessary to define GP 5 by morphology and amount
Assignation of Secondary Pattern

ISUP 2005

- High grade pattern of any quantity should be included in the Gleason score as long as it is identified at low to medium magnification e.g.
  - Needle biopsy with 98% Gleason pattern 3 and 2% Gleason pattern 4 should be diagnosed as Gleason score 7 (3+4)
- Lower grade pattern should be ignored if it occupies <5% of the tumor area e.g.
  - Needle biopsy with 98% Gleason pattern 4 and 2% Gleason pattern 3 should be diagnosed as 8 (4+4) and not as 7 (4+3)

Survey

<table>
<thead>
<tr>
<th></th>
<th>Any amount, no matter how small</th>
<th>GP identified at medium to low power</th>
<th>GP comprises 5% or greater of tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary pattern of higher grade</td>
<td>58%</td>
<td>18%</td>
<td>20%</td>
</tr>
<tr>
<td>Secondary pattern of lower grade</td>
<td>17.5%</td>
<td>20%</td>
<td>59%</td>
</tr>
</tbody>
</table>
Concordance/Discordance

• Most concerning area of the survey
• Threshold of reporting of the secondary grade
• There are differences in the minimum threshold required to report a secondary pattern
• Only <20% of participants were aware of the criteria for inclusion of a higher secondary grade with many thinking no matter how small it is, is sufficient to upstage
  – Suggests that many cases with GS 6 are upstaged to GS 7 (3+4) that may lead to clinical consequences such as entry into active surveillance programmes and overtreatment
Gleason Score

• Borderline cases where the primary and the secondary patterns are more or less in same quantity, one can give percentage of the higher component when reporting the GS e.g.
  – GS 7 = 3 + 4 (45%)

• Interpretation of minimal degrees of glandular fusion grey zone
  – 6 (3+3) or 7 (3+4)
Use of Tertiary Gleason Score

**ISUP 2005**

- In prostate biopsies, both primary pattern and the highest grade should be recorded e.g.
  - Tumors with Gleason score 7 (3+4) and a tertiary pattern 5, should be reported as Gleason score 8 (3+5)

**Survey**

- Include tertiary score in the GS – 58%
- Note it separately – 31%
- Ignore it – 11%
Concordance/Discordance

• Up to 58% would include tertiary grade while reporting GS
• Requires continuing education
Overall Reporting of GS for Biopsy Series

ISUP 2005

• Recommended to assign individual GS to separate cores as long as the cores are submitted in separate containers or are specified by the urologists as to their location
• Assigning of an overall score to needle biopsy specimens with different grades on different cores is more of a phenomenon practiced in Europe as compared to the United States
• No consensus as how to grade different cores with different grades when present within the same specimen container – generally give an overall score for that container

Survey

<table>
<thead>
<tr>
<th></th>
<th>GS for each biopsy core</th>
<th>Overall GS for block</th>
<th>Overall GS for case</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2 biopsies per block</td>
<td>57%</td>
<td>12%</td>
<td>31%</td>
</tr>
<tr>
<td>Multiple biopsies</td>
<td>12%</td>
<td>42%</td>
<td>46%</td>
</tr>
</tbody>
</table>
Reporting of Variants

**ISUP 2005**

- Ductal carcinoma
  - GS 8(4+4)
- Small cell carcinoma
  - Not be assigned a GS

**Survey**

<table>
<thead>
<tr>
<th></th>
<th>Assign a GS</th>
<th>Not assign a GS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ductal Ca</td>
<td>73%</td>
<td>27%</td>
</tr>
<tr>
<td>Small cell ca</td>
<td>24%</td>
<td>76%</td>
</tr>
</tbody>
</table>
Reporting of Treated Cancer

**ISUP 2005**
- Does not address this issue

**Survey**
- Never give a GS to hormonally treated ca
  - 54%
- Only use GS in areas showing no treatment effect
  - 24%

![Shrunken carcinoma cells with few cytoplasm](image)
Concordance/Discordance

• Area of concern as Gleason scoring of a hormonally treated prostate cancer may lead to spurious over-grading of tumors changing the therapeutic options

• Opinion is split

• Further consensus is needed
RADICAL PROSTATECTOMY SPECIMENS WITH SEPARATE TUMOR NODULES

Prostatectomy specimen can have a dominant nodule with separate tumor nodules
One nodule Gleason score 8 (4+4) within the peripheral zone and a second nodule Gleason score 4 (2+2) within the transition zone.
If one assigns a GS of 6 (2+4) or 6 (4+2) that would be misleading and would not accurately reflect the nature of the lesion
Recommended that one should assign a separate GS to each tumor nodule and not lump the score of the two separate nodules
Interobserver Variation

• Styles of reporting
• Use of tertiary scores
• Application of Gleason scoring to different tumor patterns

Interobserver variation in assignment of GS

Variation in patient management
ISUP 2005

- Widely adopted
- Many areas of the guidelines are being misinterpreted
- There are areas where no consensus is reached
- These factors are responsible for the variations seen in the Gleason grading which lead to differences in treatment options for the patients
- Clarity in teaching ISUP 2005 recommendations is necessary
- Further consensus is required to minimize intra- and interobserver variability in reporting of GS.
References

• Berney DM, Algaba F, Camparo P et al. The reasons behind variation in Gleason grading of prostatic biopsies: areas of agreement and misconception among 266 European pathologists. *Histopathology* 2014; 64: 405-411

