Impact of pathology on diagnosis and prognosis of prostate cancer

No Conf Ict of Interest

F. Algaba
Unit of Pathology
How is the appearance of prostate cancer and how its biology is recognized?
Prostate cancer low proliferative rate

Secretory phenotype

- Androgen Receptors
- PSA
Prostate cancer high proliferative rate
Prostate cancer high proliferative rate

- Intermediate cells (AR+/-)
- Secretory cells (AR+)
- Stem and Neuroendocrine Cells (AR-)
- Intermediate cells (AR+/-)

Indifferentiated or Neuroendocrine phenotype

- No Androgen Receptors
- PSA negative
What is the Gleason grading system of prostate cancer?
GLEASON GRADING SYSTEM
• 1966 PSA had not yet discovered
• 1974 86% advanced disease
• Only 2 cores biopsy
• Radical prostectomies infrequents
• No immunohistocemistry
Original Gleason

Prostatic adenocarcinoma (Histologic Patterns)

1966  1974  1977
PROSTATIC ADENOCARCINOMA
(HISTOLOGICAL PATTERNS)
Gleason grade (pattern) 3:
• Discrete glandular units
• Infiltrates in and amongst non-neoplastic prostate acini.
• Marked variation in size and shape.
Gleason grade (pattern) 4

- **Fused glands** are composed of a group of glands that are no longer completely separated by stroma. The edge of a group of fused glands is scalloped and there are occasional thin strands of connective tissue within this group.

- **Cribriform glands** represent a glandular proliferation with multiple punched-out lumina. There are, opposed to fused glands, no strands of stroma within a cribriform gland.

- **ill-defined glands** have poorly formed or absent glandular lumina. Only a cluster of such glands is acceptable, to exclude the possibility of tangentially sectioned Gleason pattern 3 glands.

- **Glomeruloid glands** are dilated glands containing a cribriform proliferation that is attached to only one edge of the gland, resulting in the structure resembling a glomerulus.
Gleason grade (pattern) 5:
- Essentially no glandular differentiation, composed of solid sheets, cords, or single cells.
- Comedocarcinoma with central necrosis surrounded by papillary, cribriform, or solid.
Biopsy

\[
\begin{align*}
\text{Gs 6} & \quad \text{Low aggressive PCa but 6/10} \\
\text{Gs 7} & \quad \begin{cases} 
3 + 4 \\
4 + 3 
\end{cases} \quad \text{No differences} \\
4 + 4 & \quad \text{High aggressive PCa} \\
\text{Gs 9 to 10} &
\end{align*}
\]

WHO 2016
WHO 2016 Prognostic Grade Group

WHO 2016 recommendation

The Johns Hopkins University System (J. Epstein)

<table>
<thead>
<tr>
<th>Prognostic Grade Group</th>
<th>6</th>
<th>1</th>
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<tbody>
<tr>
<td>3 + 4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>4 + 3</td>
<td>3</td>
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<tr>
<td>4 + 4</td>
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<tr>
<td>sG 9 to 10</td>
<td>5</td>
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</tbody>
</table>
Recurrence-free progression following radical prostatectomy stratified by pre-prostatectomy biopsy grade (16176 patients)
Recurrence-free progression following radical prostatectomy stratified by prostatectomy grade. (20845 patients)
This new system provides several benefits:

(1) More accurate grade stratification
(2) A simplified categorization of 5 groups
(3) A more intuitive scale, starting at 1 as opposed to 6.

These grade groups should be reported in conjunction with the 2016 WHO modified Gleason scores
How prostate cancer spread?
PROSTATE CANCER PATHOLOGY

- **pT2**
- **pT3a,b**
- **pT4**
Pathological stage versus 10-years biochemical recurrence–free survival.

Grading in non-surgical treatment
Biopsy grading and radiotherapy response
Recurrence-free progression following radiation stratified by pre–radiation therapy biopsy grade (entire cohort).

Eur Urol (2015), http://dx.doi.org/10.1016/j.eururo.2015.06.046
Recurrence-free progression following radiation stratified by pre–radiation therapy biopsy grade (no hormone therapy cohort).
Grading after non-surgical treatment
Other grading systems after non-surgical treatment?
No treatment effect (0)  Nuclear treatment effect (3)

Cytoplasm treatment effect (3)

0... no effect
3... Maximum effect
Score
N. effect + C. effect
<table>
<thead>
<tr>
<th>Effect</th>
<th>Score</th>
<th>Local Failure</th>
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<tbody>
<tr>
<td>Minimal effect</td>
<td>(0-2)</td>
<td>55%</td>
</tr>
<tr>
<td>Moderate effect</td>
<td>(3-4)</td>
<td>30%</td>
</tr>
<tr>
<td>Severe effect</td>
<td>(5-6)</td>
<td>similar</td>
</tr>
<tr>
<td></td>
<td></td>
<td>negative</td>
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Cellular transformation after non-surgical treatment
Just like the rest of evolution in Mother Nature, the evolution of cancers may be driven by natural selection, and not by haphazard mutations.

Ju Zhang¹, Xiaomin Lou¹, Lucas Zellmer², Siqi Liu¹, Ningzhi Xu³, and D. Joshua Liao²
Staining of prostatic carcinoma was scored as
0 = no staining;
1 = staining cells <10%;
2 = staining cells 10–20%;
3 = staining cells >20%.

<table>
<thead>
<tr>
<th>Hormonal Treatment</th>
<th>Chromogranine A score (neuroendocrine)</th>
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<tbody>
<tr>
<td>No hormonal treatment</td>
<td>0.4 ± 0.07</td>
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<tr>
<td>3-6 m. hormonal treatment</td>
<td>0.7 ± 0.7</td>
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<tr>
<td>1 year hormonal treatment</td>
<td>1.4 ± 1.1</td>
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Overall survival according intermediate/neuroendocrine transformation after treatment

Presented By Eric J Small at 2015 ASCO Annual Meeting
How can we improve the prediction of the biology of prostate cancer?