PROSTATE CANCER

Diagnosis, pathology and prognosis including variant pathology

No Conflict of Interest
Diagnosis

How confident is the PCa diagnosis?
Macroscopic prostate cancer
What's a microscopic prostate cancer? Why?

Normal prostate acini

Malignant prostate acini
What's a microscopic prostate cancer?

Normal prostate acini
- Secretory cells
- Basal cells

Malignant prostate acini
- Malignant secretory cells
- No basal cells
What's a microscopic prostate cancer?
In difficult cases
No basal cells

Cancer markers

AMACR 85%

ERG 50%
In difficult cases
Without conclusive result with ancillary methods
Atypical Small Acinar Proliferation (ASAP)
Suspicious but not diagnostic of PCa
Completely different
High Grade Prostatic Intraepithelial Neoplasia (HGPIN)
Isolated High grade PIN

Risk of cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Cases</th>
<th>Total</th>
<th>Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brawer et al</td>
<td>1991</td>
<td>8/8</td>
<td>16</td>
<td>100%</td>
</tr>
<tr>
<td>Aboseif et al</td>
<td>1995</td>
<td>19/24</td>
<td>43</td>
<td>79.2%</td>
</tr>
<tr>
<td>Langer et al</td>
<td>1996</td>
<td>13/48</td>
<td>61</td>
<td>27.1%</td>
</tr>
<tr>
<td>Raviv et al</td>
<td>1996</td>
<td>23/48</td>
<td>71</td>
<td>47.9%</td>
</tr>
<tr>
<td>Shepherd et al</td>
<td>1996</td>
<td>26/45</td>
<td>71</td>
<td>58%</td>
</tr>
<tr>
<td>Goeman et al</td>
<td>2003</td>
<td>17/63</td>
<td>80</td>
<td>27%</td>
</tr>
</tbody>
</table>

Epstein et al J. Urol. 2006; 175: 820

With 6 to 8 cores

<table>
<thead>
<tr>
<th>Category</th>
<th>Cases</th>
<th>Total</th>
<th>Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HGPIN</td>
<td>217/716</td>
<td>217/716</td>
<td>30.3%</td>
</tr>
<tr>
<td>NONMALIGNANT</td>
<td>255/1254</td>
<td>255/1254</td>
<td>20.3%</td>
</tr>
</tbody>
</table>

p = 0.0001

Algaba. Fundació Puigvert 2008
Isolated High grade PIN

Risk of cancer

- No HGPIN.. 0
- in 1 core..... 1.02
- in 2 cores... 1.55
- in 3 cores... 1.99
- In 4 cores... 2.66


Unifocal HGPIN repeat biopsy between 1 and 3 years
Multifocal HGPIN repeat biopsy within the first year

Atypical glands (ASAP)

- HGPIN: 217/716 (30.3%)
- ASAP: 42/114 (36.8%)

Algaba. Fundació Puigvert 2008

Atypical glands + HGPIN (PINATYP)

- HGPIN: 217/716 (30.3%)
- PINATYP: 31/58 (53.4%)

$p = 0.01$

Algaba. Fundació Puigvert 2008

Early repeat biopsy

Pathology

Some considerations about
Topography
Multifocality
PROSTATE CANCER LOCATION (785 patients)

14%

58%

Both 28%

Tiguert et al. Prostate. 1998; 37: 230
Multifocality Prostate Cancer

56.3% to 87%

17.3% (2)
28.6% (3)
14.7% (4)
11.3% (5)
14.7% (>5)

Cancer 2004; 100: 2362
Index tumor is the biological marker of the malignant potential of PCa.

Biological behaviour of multifocal PCa is not different from the unifocal PCa.

To determine the index tumor features, 12 to 18 core biopsies can be enough.
PROSTATE CANCER

Pathology and Prognosis

How representative is the needle biopsy of the real status of the patient?
PROSTATE CANCER

GRADING

Prognosis
Prostate cancer classical evolution?

Gleason system
But... another prostate cancer evolution?

HGPIN to PCa (Cribriform)
Needle biopsy
Grade migration 43.2%
Higher grade 30.9%
Lower grade 12.3%

Urology 2009; 74:1090

Concordance Gleason biopsy/prostatectomy
58% (original)
72% (modified)

Virchows Arch. 2006; 449: 622

Biochemical recurrence
Post-prostatectomy
Gs 6 vs 7
(p=0.002)
Gs 7 vs 8-10
(p=0.014)

Virchows Arch. 2006; 449: 622

Urology 2009; 74:1090

In biopsy

Original Gleason

ISUP 2005
AJSP 2005;29:1228
<table>
<thead>
<tr>
<th></th>
<th>BIOPSY Classical Gleason score 6 2005+2010 Gleason score 6</th>
<th>BIOPSY Classical Gleason score 6 2005+2010 Gleason score 7-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV invasion</td>
<td>0.7%</td>
<td>5.2%</td>
</tr>
<tr>
<td>pT3</td>
<td>7%</td>
<td>26%</td>
</tr>
</tbody>
</table>

PROSTATE CANCER

Pathology and Prognosis

STAGING

pT2  pT3a,b  pT4
PROSTATE CANCER

STAGING IN NEEDLE BIOPSY

Prognosis
T3a in prostate needle biopsy

Extraprostatic tissue
T3b in prostate needle biopsy

Muscle of Seminal vesicle

Seminal vesicle mucosa

PCa
Volume principal (index) PCa nodule
PCa Volume evaluation in needle biopsy

- Number positive cores
- Fraction of positive cores
- Total millimeters of cancer among all cores
- Total percentage of cancer of entire specimen
- Millimeters of cancer per core
- Percentage of cancer per core
# PCa Volume evaluation in needle biopsy

<table>
<thead>
<tr>
<th></th>
<th>pT2</th>
<th>pT3</th>
<th>( P )</th>
<th>Crude OR</th>
<th>Adjusted OR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bilateral</strong></td>
<td>60 (24.8%)</td>
<td>29 (48.3%)</td>
<td>&lt; 0.0005</td>
<td>2.8 (1.6-5.1)</td>
<td>1.2 (0.6-2.5)</td>
</tr>
<tr>
<td><strong>Number</strong></td>
<td>2.2 ± 1.5</td>
<td>3.75 ± 2.2</td>
<td>&lt; 0.0005</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Positive</strong></td>
<td>2 (1 to 3)</td>
<td>3 (2 to 5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>cores</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>% positive</strong></td>
<td>32.1 ± 21.6</td>
<td>52.4 ± 26.9</td>
<td>&lt; 0.0005</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>cores</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>≥37.5%</strong></td>
<td>65 (26.9%)</td>
<td>43 (71.7%)</td>
<td>&lt; 0.0005</td>
<td>6.9 (3.7-12.9)</td>
<td>5.8 (2.9-11.8)</td>
</tr>
<tr>
<td><strong>Positive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>cores</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Eur Urol 2005;48:566-71
### PCa Volume evaluation in needle biopsy

**Low or very low risk PCa**

<table>
<thead>
<tr>
<th>Institution</th>
<th>Clinical stage</th>
<th>PSA</th>
<th>Gleason grade</th>
<th>Total positive cores</th>
<th>Single core positivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johns Hopkins [7,8]</td>
<td>≤T2a</td>
<td>-</td>
<td>≤3 + 3</td>
<td>≤2</td>
<td>≤50%</td>
</tr>
<tr>
<td>University of Toronto [9]</td>
<td>NS</td>
<td>≤10</td>
<td>≤3 + 3'</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>UCSF [10]</td>
<td>≤T2a</td>
<td>≤10</td>
<td>≤3 + 3</td>
<td>≤33%</td>
<td>≤50%</td>
</tr>
<tr>
<td>ERSPC (PRIAS criteria) [11]</td>
<td>≤T2a</td>
<td>≤10</td>
<td>≤3 + 3</td>
<td>≤2</td>
<td>NR</td>
</tr>
<tr>
<td>Royal Marsden Hospital [12]</td>
<td>≤T2a</td>
<td>≤15</td>
<td>≤3 + 4</td>
<td>≤50%</td>
<td>NR</td>
</tr>
<tr>
<td>MSKCC [13]</td>
<td>≤T2a</td>
<td>≤10</td>
<td>≤3 + 3</td>
<td>≤3</td>
<td>≤50%</td>
</tr>
<tr>
<td>University of Miami [14,15]</td>
<td>≤T2a</td>
<td>≤10</td>
<td>≤3 + 3</td>
<td>≤2</td>
<td>≤20%</td>
</tr>
</tbody>
</table>

**T2**  **PSA ≤ 10ng/mL**  **Gs 6**  **2 cores**  **≤50%**
High probability of cancer between them
<table>
<thead>
<tr>
<th>Prostatectomy specimen</th>
<th>pT2 (N (%))</th>
<th>pT3 (N (%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraprostatic Perineural invasion</td>
<td>13 (5.4%)</td>
<td>11 (18.3%)</td>
</tr>
</tbody>
</table>

\[ P = 0.002 \]

Eur Urol 2005;48:566-71

<table>
<thead>
<tr>
<th>5 years Recurrence-free survival in pT2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without vascular invasion</td>
</tr>
<tr>
<td>With vascular invasion</td>
</tr>
</tbody>
</table>

BJU Int. 2007; 99: 539
Pathology and Prognosis

How useful is the pathology of radical prostatectomy specimen?
<table>
<thead>
<tr>
<th></th>
<th>PSA recurrence</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 years</td>
<td>4 years</td>
</tr>
<tr>
<td>&lt; 0.75 mm</td>
<td>38%</td>
<td>65%</td>
</tr>
<tr>
<td>&gt; 0.75 mm</td>
<td>65%</td>
<td>82%</td>
</tr>
</tbody>
</table>

AJSP 2007; 31: 311
PROSTATE CANCER

Pathology and prognosis
Margin in prostatectomy
Margins in prostatectomy specimen

Tumor extending close to the “capsular” margin yet not to it should be reported as a negative margin.
Smooth positive margin
Irregular positive margin
Margins in prostatectomy specimen

<table>
<thead>
<tr>
<th>Smooth + margin</th>
<th>Irregular + margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA recurrence</td>
<td></td>
</tr>
<tr>
<td>30.6%</td>
<td>65.5%</td>
</tr>
</tbody>
</table>

Actas Urol Esp. 2005;29:641-56
Positive margin in pT3a

Fat tissue
Limits and pitfalls PCa margin
Limits and pitfalls PCa margin

POSITIVE MARGIN IN CRUSH ARTIFACT
Limits and pitfalls PCa margin

NEGATIVE MARGIN

+ ?
PROSTATE CANCER

Variant pathology

How different are the morphological subtypes of PCa?
Acinar prostate adenocarcinoma
Variant prostate carcinoma

• Morphological variations of acinar PCa without clinical implications
• Morphological variations of acinar PCa with clinical implications?
Mucinous

Signet-ring cells

Glomeruloid
• Non acinar PCa
Large duct carcinomas
Endometrioid
G 4
Neuroendocrine carcinoma

No Gleason