Thursday, May 26th

FOCAL THERAPY FOR PROSTATE CANCER: FOCUS ON PATIENT SELECTION

Dr. Andrea Losa
San Raffaele Turro Hospital, Milan
Group Consensus Reports from the Consensus Conference on Focal Treatment of Prostatic Carcinoma Celebration, Florida, February 24, 2006

Report of Consensus Group 1: Pathobiology of Prostate Cancer: Implications for Focal Therapy
David G. Bostwick, David J. Waters, Edward R. Farley and Isabelle Meiers

Report of Consensus Group 2: Definition and Rationale of Focal Therapy for Prostate Cancer
Daniel Rukstalis, William A. Cavanaugh, Haakon Ragde, and Martin K. Dineen

Report of Consensus Group 3: Patient Selection Factors for Focal Therapy for Prostate Cancer
Duke Bahn, Stephen Scionti, Richard Babian, David S. Ellis, and John C. Newcastle

Report of Consensus Group 4: 3-Dimensional Prostate Mapping Biopsies for Patients Being Considered for Focal Therapy
Harry B. Burke, Gerald L. Andriole, Gary Onik, Ali E. Barqawi, John Maksem, and Winston E. Barzell
FOCAL THERAPY FOR PCa

REPORT OF CONSENSUS GROUP 4:
3-DIMENSIONAL PROSTATE MAPPING
BIOPSIES FOR PATIENTS BEING
CONSIDERED FOR FOCAL THERAPY

- Current imaging is not sufficiently sensitive and specific to allow detection of the full extent of prostate cancer.
- Current biopsy methods provide incomplete and possibly inaccurate information regarding the presence of cancer and its location, extent and Gleason score.
- The accuracy of prostate biopsy sampling depends on the number of biopsies, in relation to the size and the shape of the prostate, a reproducible 3-D coordinate system, and an accurate imaging system.
INCLUSION CRITERIA

Focal Therapy for Localized Prostate Cancer:
A Critical Appraisal of Rationale and Modalities
Scott E. Eggener, Peter T. Scardino, Peter R. Carroll, Michael J. Zelefsky, Oliver Sartor, Hedvig Hricak, Thomas M. Wheeler, Samson W. Fine, John Trachtenberg, Mark A. Rubin, Mak Ohori, Kentaro Kuroiwa, Michel Rossignol and Lucien Abenhaim for the International Task Force on Prostate Cancer and the Focal Lesion Paradigm†

Proposed Clinical, Biopsy and Imaging Criteria for Focal Therapy Patient Selection

Clinical
- Clinical stage T1 or T2a
- PSA less than 10 ng/ml
- PSA density less than 0.15 ng/ml/cc
- PSA velocity less than 2 ng/ml yearly in the year prior to diagnosis

Biopsy
- Minimum of 12 cores
- No Gleason grade 4 or 5
- Maximum percentage of cancer in each core (e.g. 20%)
- Maximum length of cancer in each core (e.g. 7 mm)
- Maximum percentage of total cores with cancer (e.g. 33%)

Imaging
- Single lesion with a maximum size (e.g. 12 mm)
- Maximum length of capsular contact (e.g. 10 mm)
- No evidence of extraprostatic extension or seminal vesicle invasion

First International Workshop on
Focal Therapy and Imaging of Prostate Cancer

The first world summit exploring groundbreaking techniques in the treatment of prostate cancer

This two-day conference will feature live case studies and international experts who will provide insight into imaging of individual foci within the gland and minimally invasive focal, gland-preserving techniques for the prostate cancer patient.

Washington Duke Inn
February 21-22, 2008

Sponsored by the Duke University School of Medicine
# Predicting Unilateral Prostate Cancer: HSR Experience

<table>
<thead>
<tr>
<th>Points</th>
<th>0</th>
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<th>20</th>
<th>30</th>
<th>40</th>
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<th>70</th>
<th>80</th>
<th>90</th>
<th>100</th>
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<tbody>
<tr>
<td>PSA at diagnosis</td>
<td>10</td>
<td>7</td>
<td>4</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Age at diagnosis</td>
<td>40</td>
<td>80</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Number of biopsy cores</td>
<td>26</td>
<td>24</td>
<td>22</td>
<td>20</td>
<td>18</td>
<td>16</td>
<td>14</td>
<td>12</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of positive biopsy cores</td>
<td>11</td>
<td>10</td>
<td>9</td>
<td>8</td>
<td>7</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Prostate volume (cc)</td>
<td>0</td>
<td>20</td>
<td>40</td>
<td>60</td>
<td>80</td>
<td>100</td>
<td>120</td>
<td>140</td>
<td>160</td>
<td>180</td>
<td>200</td>
</tr>
<tr>
<td>Total Points</td>
<td>0</td>
<td>20</td>
<td>40</td>
<td>60</td>
<td>80</td>
<td>100</td>
<td>120</td>
<td>140</td>
<td>160</td>
<td>180</td>
<td>200</td>
</tr>
<tr>
<td>Prob. of Unilateral PCa</td>
<td>0.075</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
<td>0.4</td>
<td>0.5</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

AUC: (only) 59.0% !!

Briganti A et al, EAU Meeting, 2010
Focal Therapy in Prostate Cancer—Report from a Consensus Panel

**Table 3. Candidate Selection for Focal Therapy**

1. Candidates for focal therapy should ideally undergo transperineal template mapping biopsies, although a state-of-the-art multifunctional MRI with TRUS biopsy at expert centers may be acceptable.
2. Candidates for focal therapy should have a life expectancy of 10 or more years.
3. Patients with previous prostate surgery should be counseled with caution.
4. Patients with previous radiotherapy to the prostate or pelvis should not be treated until more data are available, although the panel accepted that focal salvage therapy may be a possibility in the future.
5. The effects of focal therapy on men with lower urinary tract symptoms are not well known. These men should be counseled with caution.
6. There will be specific attributes that are more related to the energy source than to focal therapy in general. Issues such as prostate size, presence of prostatic calcification, cysts, TUR cavity, access to rectum, and concurrent inflammation of rectal mucosa may need to be taken into consideration when selecting the optimal therapy.
7. Focal therapy should be limited to patients of low to moderate risk.
8. Focal therapy should be limited to men with clinical $T_{2a}$ or less $N_0M_0$ disease.
9. Focal therapy should be limited to men with radiologic $T_{2b}$, $N_0M_0$ disease.
10. Defining the topography of the cancer is important. Disease that is predominantly apical or anterior in disposition may be technically difficult to manage with existing treatment modalities.
11. The long-term effects of focal therapy on potency/erectile functions are not known. Men should be counseled in this regard before therapy.

MRI = magnetic resonance imaging; TRUS = transrectal ultrasonography; TUR = transurethral resection.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Modality</th>
<th>PSA levels</th>
<th>Clinical stage</th>
<th>Gleason score</th>
<th>Biopsy scheme</th>
<th>Biopsy rules</th>
<th>Additional imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lambert et al.</td>
<td>Cryotherapy: hemiablation</td>
<td>All</td>
<td>≤T1c</td>
<td>6 or 7 (3+4 only)</td>
<td>TRUS biopsy</td>
<td>Cancer confined to 1 lobe in 1 or 2 contiguous biopsies and a tumor volume of ≤10% in a 12-core biopsy</td>
<td>Not used</td>
</tr>
<tr>
<td>(2007)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bahn et al.</td>
<td>Cryotherapy: less than complete ablation</td>
<td>NA</td>
<td>NA</td>
<td>≤7</td>
<td>TRUS biopsy</td>
<td>Unilateral 6–8 cores and targeted biopsy if extracapsular extension was suspected</td>
<td>Color Doppler</td>
</tr>
<tr>
<td>(2006)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ellis et al.</td>
<td>Cryotherapy: focal ablation</td>
<td>All</td>
<td>Pathological stage ≤T2c</td>
<td>All (only 1.7% ≥Gleason 8)</td>
<td>TRUS biopsy</td>
<td>None applied: all ‘known cancer’ targeted</td>
<td>Not used</td>
</tr>
<tr>
<td>(2007)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onik et al.</td>
<td>Cryotherapy: focal ablation</td>
<td>Mean 7.8ng/dl</td>
<td>Pathological stage ≤T2c</td>
<td>All (exact proportions not reported) (≥Gleason 8 placed on hormones for 6 months)</td>
<td>TRUS biopsy</td>
<td>All cancer targeted provided one neurovascular bundle avoided (majority unilateral)</td>
<td>Not used</td>
</tr>
<tr>
<td>(2008)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lindner et al.</td>
<td>Photothermal ablation: focal ablation</td>
<td>&lt;10 ng/dl</td>
<td>≤T2a</td>
<td>≤6</td>
<td>TRUS biopsy</td>
<td>≤30% of cores positive and ≤50% of 1 core taken up by cancer positive cores relegated to only 1 of the 12 conventional prostate sectors (right or left, apex, mid or base, medial or lateral)</td>
<td>Tumor location confirmed by multiparametric MRI</td>
</tr>
<tr>
<td>(2009)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crawford et al.</td>
<td>Cryotherapy: focal ablation</td>
<td>&lt;10 ng/dl</td>
<td>T1c</td>
<td>≤7</td>
<td>Template transperineal mapping biopsies</td>
<td>Unilateral disease</td>
<td>Not used</td>
</tr>
<tr>
<td>(2007)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muto et al.</td>
<td>HIFU: focal ablation</td>
<td>NA</td>
<td>≤T2</td>
<td>All</td>
<td>TRUS biopsy</td>
<td>Unilateral but ablation extended to contralateral peripheral zone (extended ‘dog-leg’)</td>
<td>Pelvic T2-weighted MRI</td>
</tr>
<tr>
<td>(2008)</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Karavitakis M et al. Nat Rev Urol 2011
INCLUSION CRITERIA

FIVE ONGOING PROTOCOLS ON FOCAL THERAPY:

- Clinical stage: T1c-T2a (all studies)
- Gleason Score: <7 (not considered in 1 study)
- Number of biopsy cores: 12 cores (3 studies) Not specified (2 studies)
- Number of positive cores: 1 (1 study) <=2 (1 study) Not specified (2 studies)
- % of cancer in any core: <20% (1 study) 10-50% (1 study) <50% (1 study) Not specified (2 studies)
EXCLUSION CRITERIA

FIVE ONGOING PROTOCOLS ON FOCAL THERAPY:

- **Bioptic criteria:**
  - Apex involvement (1 study)
  - Transition zone involvement (1 study)
  - Not specified (2 studies)

- Previous surgery (2 studies)

- Previous treatment for PCa (4 studies)
Novel promising experiences with prostate cancer antigen 3, a urine-based mRNA test, and the TMPRSS2–ERG gene fusion product may one day provide meaningful prognostic information that would contribute to management decisions.

Shukla-Dave A, Clin Cancer Res. 2009 1;15:3842-9
The PCA3 Score in low volume / low grade PCa is significantly lower than in significant PCa.

Low volume: tumour volume < 0.5 mL; Low grade: Gleason Score ≤ 6

The PCA3 Score in intermediate to high volume tumor prostatectomies is significantly higher than in low volume tumors.

96 American men scheduled for radical prostatectomy: PCA3 Score is associated with Gleason score in prostatectomy specimens but not with Gleason score in biopsy specimens.

The PCA3 Score significantly predicts stage and significance of PCa in the biopsy.

Indolent: T1c, PSAD < 0.15, Gleason score < 7, % positive cores ≤ 33%

Hessels et al. (Prostate 2010): n=70 patients, PCA3 before RP

- No correlation of PCA3 with:
  - tumor volume
  - Gleason Score <7 vs. ≥7,
  - ECE
  - insignificant PCa

### TABLE IV. Relationship Between PCA3 Ratio and Pathological Variables

<table>
<thead>
<tr>
<th>PCA3 in</th>
<th>N</th>
<th>Median</th>
<th>Mean</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>70</td>
<td>42</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>Tumor volume</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.5 (ml)</td>
<td>10</td>
<td>47</td>
<td>105</td>
<td></td>
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<tr>
<td>0.5–2 (ml)</td>
<td>13</td>
<td>33</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>&gt;2 (ml)</td>
<td>33</td>
<td>52</td>
<td>116</td>
<td></td>
</tr>
<tr>
<td>Insignificant PCa</td>
<td>5</td>
<td>42</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Significant PCa</td>
<td>54</td>
<td>45</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td>Prostatectomy GS</td>
<td></td>
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<td></td>
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<tr>
<td>4</td>
<td>1</td>
<td>42</td>
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<tr>
<td>5</td>
<td>7</td>
<td>20</td>
<td>241</td>
<td>0.680&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>21</td>
<td>32</td>
<td>54</td>
<td>0.804&lt;sup&gt;bc&lt;/sup&gt; (&lt;0.5 ml vs. 0.5–2.0 ml)</td>
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<tr>
<td>7</td>
<td>30</td>
<td>54</td>
<td>100</td>
<td>0.428&lt;sup&gt;b&lt;/sup&gt; (&lt;0.5–2.0 ml vs. &gt;2.0 ml)</td>
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<tr>
<td>8</td>
<td>4</td>
<td>99</td>
<td>96</td>
<td>0.486&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>9</td>
<td>5</td>
<td>42</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>&lt;7</td>
<td>29</td>
<td>32</td>
<td>99</td>
<td>0.199&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>≥7</td>
<td>39</td>
<td>52</td>
<td>92</td>
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<tr>
<td>Pathological stage</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>pT2</td>
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<td>108</td>
<td>0.76&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>pT3</td>
<td>28</td>
<td>38</td>
<td>77</td>
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</tr>
</tbody>
</table>

GS, Gleason score; PCa, prostate cancer; PCA3, prostate cancer gene 3; PSA, prostate-specific antigen.
<sup>a</sup>Kruskal–Wallis test.
<sup>b</sup>Mann–Whitney U-test.
The PCA3 Score significantly predicts PCa multifocality

TEMPLATE BIOPSIES

Transverse view

Anterior urethral zone to be avoided!

Columns chosen for left-side biopsies

Longitudinal view

Needle poised for a posterior proximal biopsy

Needle poised for an anterior distal biopsy

Visualize needle with longitudinal array
Contrast-enhanced colour Doppler-targeted prostate biopsy: correlation of a subjective blood-flow rating scale with the histopathological outcome of the biopsy

Vascular abnormalities associated with prostate cancer might help in defining its biological aggressiveness

Table 1: The five CECD TRUS blood-flow score groups and the corresponding histopathological outcome

<table>
<thead>
<tr>
<th>Score</th>
<th>Benign</th>
<th>Malignant</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>90 (98%)</td>
<td>2 (2%)</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>267 (94%)</td>
<td>17 (6%)</td>
<td>284</td>
</tr>
<tr>
<td>3</td>
<td>97 (74%)</td>
<td>34 (26%)</td>
<td>131</td>
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<tr>
<td>4</td>
<td>23 (15%)</td>
<td>130 (85%)</td>
<td>153</td>
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<tr>
<td>5</td>
<td>0 (0%)</td>
<td>100 (100%)</td>
<td>100</td>
</tr>
<tr>
<td>All</td>
<td>477 (63%)</td>
<td>283 (37%)</td>
<td>760</td>
</tr>
</tbody>
</table>

Mitterberger M et al. BJU Int 2010

Editorial comment; Gomella LG et al. BJU Int 2010
CONTRAST-ENHANCED ULTRASONOGRAPHY

- Visualization and localization of PCa in 78% of cases
  - Clear association between contrast enhancement and diagnosis of clinically significant PCa
    
    Wink et al, Eur Urol 2008

- CEUS blood-flow rating score strongly correlated with the histopathological outcome
  
  Mitterberger et al, BJU Int 2010
However, MR is not without limitations. It is expensive, interpretation may be limited by biopsy induced hemorrhage or inflammation, it requires considerable reader training to realize its full capability and it has yet to be used prospectively to identify candidates for focal therapy.
Conclusions: Consensus was reached on a number of areas related to the conduct, interpretation, and reporting of mpMRI for the detection, localisation, and characterisation of prostate cancer. Before optimal dissemination of this technology, these outcomes will require formal validation in prospective trials.
Multiparametric MRI can provide metabolic information; characterise tissue and tumour vascularity, as well as tissue cellularity and integrity; and correlate with tumour aggressiveness.

Multiparametric MRI is helpful and clinically relevant for the following tasks:

- Detection of PCa in patients with previous negative prostate biopsies and persistently elevated serum markers, in whom it reduces the need for additional and more extensive biopsies and identifies suspicious areas for targeted sampling;
- Characterization of PCa to facilitate appropriate treatment selection; after primary therapy;
- MR-guided prostate biopsy and MR-guided focal therapy
...the general use of MPMRI and MPMRI-guided prostate biopsy cannot be recommended.
Anterior tumors have a higher positive surgical margin rate

Not easily diagnosed by transrectal biopsies

In patients with negative biopsies and discrepancy between PSA level and PSA dynamics, MRI can help to direct biopsy to the anterior prostate with a high degree of accuracy
Relationship between Apparent Diffusion Coefficients at 3.0-T MR Imaging and Gleason Grade in Peripheral Zone Prostate Cancer

**Advances in Knowledge**

- Apparent diffusion coefficients (ADCs) of prostate cancer in the peripheral zone demonstrated an inverse relationship to Gleason grades, with low-, intermediate-, and high-grade tumors showing significant differences in ADCs ($P < .001$).

- With use of the median ADCs of the most aggressive tumor regions, a high discriminatory accuracy is achieved for discerning low-grade from combined intermediate- and high-grade cancers (area under the receiver operating characteristic curve = 0.90).

**Implication for Patient Care**

- Noninvasive prediction of Gleason grades may improve patient treatment by enabling more accurate risk stratification and follow-up in patients undergoing active surveillance or by targeting biopsies toward the most aggressive components.

Hambrock T et al. Radiology 2011
ENHANCING THE STANDARDIZATION IN SELECTION CRITERIA:
> IMAGING, BIOPSY TECHNIQUES

IMPROVING PATIENTS SELECTION MEANS ASSIGNING PATIENTS TO THE “IDEAL,” TREATMENT…

IDENTIFYING/CREATING REFERENCE CENTERS
OPEN ISSUES

- Test new markers (PCA3, proPSA)

- Extend indications for focal therapy?
  - RT recurrences
  - Extracapsular disease
  - Secondary pattern 4
  - Anterior zone cancers

- Identify/create reference centers
Focal Therapy in Prostate Cancer—
Report from a Consensus Panel

Results

Definition of focal therapy

The following definition was agreed: Focal therapy is a type of treatment that aims to eradicate known cancer within the prostate and at the same time preserve uninvolved prostatic tissue with the aim of preserving genitourinary function.
# PATIENT SELECTION

<table>
<thead>
<tr>
<th>Variable</th>
<th>University of Toronto, Canada</th>
<th>Johns Hopkins, USA</th>
<th>Multicenter European study (PRIAS)</th>
<th>University of California, San Francisco, USA</th>
<th>University of Miami, USA</th>
<th>Multicenter Japanese study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical stage</td>
<td>T1c</td>
<td>T1c</td>
<td>T1c or T2</td>
<td>T1 or T2a</td>
<td>NI</td>
<td>T1c</td>
</tr>
<tr>
<td>PSA (ng/ml)</td>
<td>≤10–15</td>
<td>NI</td>
<td>≤10</td>
<td>≤10</td>
<td>NI</td>
<td>≤20</td>
</tr>
<tr>
<td>Gleason score on biopsy</td>
<td>≤3+3=6</td>
<td>≤3+3=6</td>
<td>≤3+3=6</td>
<td>≤3+3=6</td>
<td>NI</td>
<td>≤3+3=6</td>
</tr>
<tr>
<td>PSA density (ng/ml per ml)</td>
<td>NI</td>
<td>≤0.15</td>
<td>&lt;0.2</td>
<td>NI</td>
<td>NI</td>
<td>NI</td>
</tr>
<tr>
<td>Number of positive cores on biopsy</td>
<td>NI</td>
<td>2† (core total not specified)</td>
<td>2 (of 8–12 cores)</td>
<td>&lt;33% biopsy cores‡</td>
<td>≤2‡ (of 10 cores minimum)</td>
<td>2‡ (of 6–12 cores)</td>
</tr>
</tbody>
</table>

Lawrentschuk N, Nat Rev Urol 2011
EXTRAPROSTATIC EXTENSION (EPE)

- EPE usually occurs near the neurovascular bundle
- Unilateral EPE is a frequent event (only 15% bilateral)


- Index lesion → 80% cancer volume
- Index lesion → 92% EPE

Ohori M et al, J Urol 2006
EXTRAPROSTATIC EXTENSION (EPE)

- EPE is a critical pathological variable of the natural history and prognosis of PCa.
- Theoretically, patients with unifocal or unilateral PCa and localized EPE could be eligible for focal therapy.
- Several ablative techniques are capable of treating EPE, but such situation has to be carefully considered.
Gleason grade remains a main determinant to predict biochemical failure, local and systemic recurrence, and overall survival. While primary Gleason pattern $\leq 3$ represents a main indication for the selection of FT candidates, a limited percentage of those with secondary pattern 4 and with a locally defined lesion(s) within the prostate could also be considered, but this requires further study.
ACTIVE SURVEILLANCE VS. FOCAL THERAPY

could be construed as ‘Surveillance Plus’. A probable future scenario is that both approaches will have a role, with AS being the treatment of choice for patients with favorable biomarkers and no significant lesion on MRI, and focal therapy being preferred for those with a unifocal index lesion on MRI and favorable biopsy findings. Thus, radical treatment is reserved for those with adverse pathology.

Lawrentschuk N, Nat Rev Urol 2011
**CLINICALLY INSIGNIFICANT PROSTATE TUMORS**

- PCa volume $<0.5$ mL
- Gleason score $<7$

  Epstein et al., J Urol 1994; 151: 1587-92

- Single positive core
- $<3$mm cancer involvement
- Gleason score $<7$ (no grades 4-5)

  Harnden et al. Cancer 2008; 112: 971-81
PATIENTS SELECTION

- PSA ≤ 10 ng/ml (?)
- T1c-T2a
- GS 3+3 (3+4 ?)
- UNILATERAL DISEASE
- NUMBER OF POS. BIOPSIES ≤ 2
- % POS. BIOPSIES
- % CANCER INVOLVEMENT
- TO BE INTRODUCED
- MPMRI
- TEMPLATE BIOPSIES
- NEW MARKERS
- NEW IMAGING MODALITIES
FOCAL THERAPY: RATIONALE

- Ultimately, the treatment paradigm of managing early stage, localized Pca, is to distinguish patients who harbor low-risk cancer for active surveillance approach from those who might have a potentially dangerous index lesion that can be ablated and those who have life-threatening bilateral cancer requiring a whole gland radical treatment.
### DEFINITION OF LOW-RISK/INSIGNIFICANT PCa

<table>
<thead>
<tr>
<th>Reference</th>
<th>PSA density</th>
<th>Clinical stage cT</th>
<th>Gleason score</th>
<th>No. of positive cores</th>
<th>Maximum % of positive cores</th>
<th>Extent (mm)</th>
<th>Volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D’Amico et al. [26]</td>
<td>&lt;10</td>
<td>T1c-T2</td>
<td>≤6</td>
<td></td>
<td>≤3</td>
<td>&lt;50</td>
<td></td>
</tr>
<tr>
<td>Epstein et al. [27]</td>
<td>0.15</td>
<td></td>
<td>≤6</td>
<td>≤3</td>
<td></td>
<td>&lt;5</td>
<td></td>
</tr>
<tr>
<td>Gardner et al. [28]</td>
<td></td>
<td></td>
<td>≤6 (w/o any 4)</td>
<td>1</td>
<td></td>
<td>&lt;3</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Terris et al. [29]</td>
<td></td>
<td></td>
<td>≤6</td>
<td>1</td>
<td></td>
<td>&lt;3</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Boccon-Gibod et al. [30]</td>
<td></td>
<td>T2</td>
<td>≤6</td>
<td>1</td>
<td></td>
<td>&lt;3</td>
<td>&lt;0.5</td>
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<tr>
<td>Noguchi et al. [31]</td>
<td>&lt;0.15</td>
<td></td>
<td>≤6</td>
<td>1</td>
<td></td>
<td>&lt;3</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Harnden et al. [32]</td>
<td></td>
<td></td>
<td>≤6</td>
<td>1</td>
<td></td>
<td>&lt;3</td>
<td></td>
</tr>
</tbody>
</table>

### DEFINITION OF SIGNIFICANT PCa

<table>
<thead>
<tr>
<th>Reference</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conrad et al. [34]</td>
<td>Volume &gt; 0.5 cm³, Gleason score ≥7, Gleason pattern ≥4, Gleason pattern ≥4, pT3, positive surgical margins, multifocality &gt; 3, nondiploid DNA content, proliferative index &gt; 5%</td>
</tr>
<tr>
<td>Prange et al. [35]</td>
<td>Volume &gt; 0.5 cm³, Gleason pattern ≥4, pT3, lymph node metastasis</td>
</tr>
<tr>
<td>Ward et al. [36]</td>
<td>Volume &gt; 0.5 cm³, Gleason score ≥7, pT3</td>
</tr>
<tr>
<td>Revelo et al. [37]</td>
<td>Volume &gt; 0.5 cm³, Gleason grade ≥4, extracapsular extension, seminal vesicle invasion, lymph node metastasis, positive surgical margins</td>
</tr>
<tr>
<td>Delongchamps et al. [38]</td>
<td></td>
</tr>
<tr>
<td>Ruffion et al. [39]</td>
<td></td>
</tr>
<tr>
<td>Abdelhady et al. [40]</td>
<td></td>
</tr>
<tr>
<td>Weizer et al. [41]</td>
<td>Volume &gt; 0.5 cm³, Gleason score ≥7</td>
</tr>
</tbody>
</table>