Prostate MRI Fusion Biopsy
“Not your Father’s Prostate Biopsy”

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Prostate Biopsy History
Classic McNeal Zonal Anatomy

3 main compartments
1. Peripheral Zone
2. “Central gland”
3. AFMS

Peripheral Zone-Green, Central Zone-Orange, Transition Zone-Blue, Anterior Fibromuscular Stroma-Yellow
Classic Sextant Biopsy Scheme
(1989 Hodge)
12 core (Double Sextant Biopsy) 1997-2000

Importance of lateral Directed biopsies

Base

Importance of lateral Directed biopsies

Apex
Clinical suspicion of prostate cancer

Trans-rectal (TRUS) ultrasound guided biopsy

Negative Biopsy with rising PSA

Repeat TRUS biopsy

Prostate cancer

Active Surveillance

Intervention

Repeat TRUS Biopsy

Saturation Biopsy (>20 cores)

Extended cores (13-18 cores)

Sextant (10-14 cores)

Current practice

‘Circle of Doom’
Cancer Detection Rate—More not always better

- 6-core biopsy: ~26%
- 12-core biopsy: ~37%
- >12-core biopsy: ~40%

Table 1: Cancer detection rates by number of prostate biopsy cores

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Prostate Biopsy Cores</th>
<th>Cancer Detection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eskew et al, 1997</td>
<td>6</td>
<td>26.1%</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>40.3%</td>
</tr>
<tr>
<td>Naughton et al, 2000</td>
<td>6</td>
<td>26%</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>27%</td>
</tr>
<tr>
<td>Presti et al, 2000</td>
<td>6</td>
<td>33.5%</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>39.7%</td>
</tr>
<tr>
<td>Babaian et al, 2000</td>
<td>6</td>
<td>20%</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>30%</td>
</tr>
<tr>
<td>Elabbady &amp; Khedr, 2006</td>
<td>6</td>
<td>24.8%</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>36.4%</td>
</tr>
<tr>
<td>Gore et al, 2001</td>
<td>6</td>
<td>31%</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>43%</td>
</tr>
<tr>
<td>Philip et al, 2004</td>
<td>6</td>
<td>23%</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>32%</td>
</tr>
<tr>
<td>Shim et al, 2007</td>
<td>6</td>
<td>22%</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>28%</td>
</tr>
<tr>
<td>Scattoni et al, 2008</td>
<td>6</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>38.5%</td>
</tr>
<tr>
<td>de la Taille et al, 2003</td>
<td>6</td>
<td>22.7%</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>28.3%</td>
</tr>
<tr>
<td>Pepe &amp; Aragona, 2007</td>
<td>6</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>39.8%</td>
</tr>
<tr>
<td>Jones et al, 2006</td>
<td>6</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>52%</td>
</tr>
<tr>
<td>Guichard et al, 2007</td>
<td>6</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>38.7%</td>
</tr>
<tr>
<td>Ploussard et al, 2012</td>
<td>6</td>
<td>32.5%</td>
</tr>
<tr>
<td></td>
<td>10–12</td>
<td>40.4%</td>
</tr>
</tbody>
</table>

*Bjurlin et al., Urol Clin N Am 2014*
Correlation Number of Cores and Probability of Finding Clinically insignificant CaP

Insignificant CaP - Epstein Criteria

1. Gleason score $\leq 6$ without Gleason pattern 4 or 5
2. Organ confined disease
3. Tumor volume less than 0.5 cc
4. Less then 3 positive cores (6 core sample)
5. Less than 50% cancer per core

30% risk of under staging

Epstein JI, et al. JAMA 1994; 271: 368
Did we hit the target?

Only solid organ biopsied with the hope of hitting the tumor!
Limitations of Conventional “Biopsy/Sampling”

• Sampling error/Incorrect Risk Stratification
• False negative ~ 30%
• Undersampling ~ 30%
  – Missed clinically significant disease
• Oversampling
  – Detection of clinically insignificant disease
• Need for repetitive biopsy
• Often misses anterior lesions

Serefoglu EC, et al, 2014
Bjurlin MA et al, 2014
Hong YM et al, 2004
Gray Zone
Prostate MRI

Axial  sagittal  coronal

State of the art prostate imaging
Prostate MRI
Multiparametric MRI and Cancer

- **T2W**: Composite T2 weighted imaging (Anatomy)
  - Measures water content
  - Tumors are water poor (dark on T2W)
- **DWI**: Diffusion weighted imaging
  - Measures water diffusion in tissue
  - Tumors are dense (dark on DWI) (Functional/Physiological)
- **DCE**: Dynamic contrast enhanced
  - Measures contrast flow through tissue
  - Tumors are hypervascular (bright on DCE)
- +/- **MRS**: Magnetic resonance spectroscopy (Not used often)
  - Measures tissue choline, citrate concentrations
  - Tumors metabolize citrate, therefore choline/citrate ratio is high
  - Normal prostate is high in citrate
T2 Weighted Image

Tumors are water poor
DWI: Diffusion weighted imaging

Tumors are dense (dark on DWI)
Dynamic contrast Enhancement

Dynamic contrast-enhanced MRI

- Evaluates microvascular structure and function by tracking the pharmacokinetics of injected low-molecular-weight contrast agents as they pass through the vasculature

- Tumors show early enhancement and early washout of the contrast agent

- Dynamic contrast uptake and washout curves can be used to generate images - overlaid over high resolution T2

Tumors are hypervascular (bright on DCE)
Predictive reporting

- Assigning levels of suspicion
- Low, moderate, high
- PI-RADS
  - Prostate Imaging Reporting and Data System
- Grade 1-5
- Evaluate clinical data with respect to MRI scoring systems
- Important to speak the same language
PI-RADS 2.0 (2015)

• Uniform scoring system developed for mpMRI prostate exams
  – Assesses T2W,DWI,DCE sequences
  – Assessment of peripheral zone & transition zone separate
  – T2W & DWI weighted 1-5
  – DCE is yes/no
  – Integration of scores into an overall score for first time
## 5 level scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Meaning</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score 1</td>
<td>Not suspicious</td>
<td>Highly unlikely to contain a clinically significant lesion</td>
</tr>
<tr>
<td>Score 2</td>
<td>Not very suspicious</td>
<td>Unlikely to contain a clinically significant lesion</td>
</tr>
<tr>
<td>Score 3</td>
<td>Ambiguous</td>
<td>Impossible to offer an opinion as to whether or not it contains a clinically significant lesion</td>
</tr>
<tr>
<td>Score 4</td>
<td>Suspicious</td>
<td>Likely to contain a clinically significant lesion</td>
</tr>
<tr>
<td>Score 5</td>
<td>Very suspicious</td>
<td>Highly likely to contain a clinically significant lesion</td>
</tr>
</tbody>
</table>
Correlation of Gleason score and MRI findings

- Strong cellularity and density is easier to detect on MRI.
- Correlation of Gleason score and intensity of T2W images, diffusion weighted imaging (ADC), wash in rate in perfusion imaging

Predicting PCa aggressiveness

- Reflects the pathologic grade of prostate cancer
- Lower Apparent Diffusion Coefficient (ADC) values found in higher Gleason Grade cancers
- Better differentiation between low grade (G ≤ 6) and high grade G >7

Verma AJR Am J Roentgenol, Feb 2011
Turkbey, Radiology, Feb 2011
Yoshimitsu, J Magn Reson Imaging, Jan 2008
Detectability of lesion on MRI

- Tumor size and Gleason score on T2-W imaging
- Tumor size, Gleason score, and stroma on Diffusion weighted imaging
- High malignant epithelium to stroma ratio on Dynamic contrast enhancement T1-W imaging


Prostate cancer foci detected on multiparametric magnetic resonance imaging are histologically distinct from those not detected.

Rosenkrantz AB¹, Mendrinos S, Babb JS, Taneja SS.
Comparison of detected and undetected tumors on multiparametric MRI by Histopathologic Features

<table>
<thead>
<tr>
<th>Feature</th>
<th>% Detected (No./total No.)</th>
<th>% Undetected (No./total No.)</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor size 1 cm or greater</td>
<td>62.2 (28/45)</td>
<td>9.5 (4/42)</td>
<td>15.7</td>
</tr>
<tr>
<td>Gleason score 7 or greater</td>
<td>84.4 (38/45)</td>
<td>35.7 (15/42)</td>
<td>9.8</td>
</tr>
<tr>
<td>Loose stroma</td>
<td>22.2 (10/45)</td>
<td>78.6 (33/42)</td>
<td>0.078</td>
</tr>
<tr>
<td>Desmoplastic stroma</td>
<td>100 (45/45)</td>
<td>33.3 (14/42)</td>
<td>*</td>
</tr>
<tr>
<td>Solid tumor growth</td>
<td>91.1 (41/45)</td>
<td>21.4 (9/42)</td>
<td>37.6</td>
</tr>
<tr>
<td>Intermixed benign epithelium</td>
<td>22.2 (10/45)</td>
<td>66.7 (28/42)</td>
<td>0.14</td>
</tr>
<tr>
<td>High ratio of malignant epithelium/stroma</td>
<td>62.2 (28/45)</td>
<td>11.9 (5/42)</td>
<td>12.2</td>
</tr>
</tbody>
</table>

Prostate cancer foci detected on multiparametric magnetic resonance imaging are histologically distinct from those not detected.

Rosenkrantz AB, Mendrinos S, Babb JS, Taneja SS.
HOW do we hit the target?

Cognitive guidance (MRI suggested)

MRI guided biopsy (in gantry)

MRI-US Fusion systems
Fusion Biopsy

MRI

U/S
Fusion value?

• MRI provides:
  – Great spatial resolution
  – Sensitivity/specificity

• TRUS provides:
  – Temporal resolution
  – Cost effective
  – Familiarity with procedure, outpatient setting, local anesthesia
27 Sectors MRI/Fusion Biopsy Era

12 Posterior
12 Anterior
3 Antero/medial

Version 2.0- 39 sectors
36 prostate
2 seminal vesical
1 external sphincter
Anterior Horn of Peripheral Zone
Anterior Prostate Cancer
Steps for Fusion biopsy

• Scan (MRI)
• Plan (locate targets, MRI segmentation)
• Prostate ultrasound (sweep, US segmentation)
• Registration- Align/fuse ultrasound and MRI
• Re-identify targets
• Biopsy targets
• Review of biopsies
“Man-O-Gram”
Review segmentation and targets for MRI
Electromagnetic tracking
Sweep
Sweep and segmentation
Fiducials to improve alignment
Manual alignment of Ultrasound
Align US volume with MR (Registration)
Improved Registration
Target
Biopsy Target
Review of Targets and Biopsies
When should we Target?

- Previous negative biopsy
- Active surveillance
- Search for local recurrence after treatment
- Elevated PSA/clinical suspicion of prostate cancer – first biopsy
MRI targeted versus systematic

- 532 patients
- Gleason upgrading in 32%
- Able to detect 67% more Gleason 4 and 5 tumors than the standard systematic biopsy alone
- Negative predictive value of ~ 90%

Siddiqui MM et al. Eur Uolo 2013
Arumainayagam et al, Radiology 2013
Previous negative biopsy

- Serial biopsy results
  - 17% (1), 14% (2), 11% (3), 9% (4)

- MRI US fusion biopsy
  - 34%
  - Independent of number of prior biopsies
  - Clinically significant disease

Sonn et al. European Urology 2013
Prostate Ca Detection Rate
MRI-US Fusion Biopsy 171 men

Sonn et al. Journal of Urology 2012
Prostate Ca Diagnosis by Target (279)

% Cancer Diagnosis

Image Grade

<table>
<thead>
<tr>
<th>Image Grade</th>
<th>Gleason ≥7</th>
<th>CaP</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>6%</td>
<td>9%</td>
</tr>
<tr>
<td>3</td>
<td>6%</td>
<td>20%</td>
</tr>
<tr>
<td>4</td>
<td>11%</td>
<td>29%</td>
</tr>
<tr>
<td>5</td>
<td>21%</td>
<td>58%</td>
</tr>
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</table>

# Targets

<table>
<thead>
<tr>
<th># Targets</th>
<th>34</th>
<th>142</th>
<th>84</th>
<th>19</th>
</tr>
</thead>
</table>

# Any CaP

<table>
<thead>
<tr>
<th></th>
<th>3</th>
<th>29</th>
<th>24</th>
<th>11</th>
</tr>
</thead>
</table>

# Gleason ≥7 CaP

<table>
<thead>
<tr>
<th></th>
<th>2</th>
<th>9</th>
<th>9</th>
<th>4</th>
</tr>
</thead>
</table>

Sonn et al. Journal of Urology 2012
Prostate MRI & Fusion

Results Summary:

- PCa found in 53% (90 of 171) men
- 3 times better diagnostic PCa yield/core for fusion vs systematic
  - (21% vs 7%)
- Higher mean cancer length biopsied/positive core for fusion vs systematic
  - (5.1mm vs 3.3mm)
- Higher detection rate of clinically significant cancer for fusion vs systematic
  - (36% vs 24%)

Sonn et al., Journal of Urology, 2013 at UCLA used fusion + systematic biopsy on 106 active surveillance and 65 prior negative patients
MRI-US Fusion ..... 

• Improves diagnostic accuracy of TRUS prostate biopsy

• Role in
  – Rising PSA with previous negative biopsy
  – Active Surveillance
  – Clinical suspicion of prostate cancer
    • Need for cost effective analysis of repeat biopsies versus initial MRI and Fusion Targeted Biopsy

• Ability to detect high risk cancer

• Ability to sample “grey zone”
With thanks

• Dr. Krish Gaitonde at UC
• Dr. Jeffrey Nix at UAB