Biopsy Tracking and MRI Fusion to Enhance Imaging of Cancer Within the Prostate

D. J. Margolis¹, S. Natarajan², D. Kumar³, M. Macairan⁴, R. Narayanan³, and L. Marks⁴

¹Dept. of Radiology, UCLA David Geffen School of Medicine, Los Angeles, CA, United States,
²Center for Advanced Surgical and Interventional Technology, UCLA DG School of Medicine,
³Eigen, Grass Valley, CA,
⁴Dept. of Urology, UCLA David Geffen School of Medicine, Los Angeles, CA, United States
Speaker Name: Daniel J A Margolis

I have the following relevant financial interest or relationship to disclose with regard to the subject matter of this presentation:

- Company name: Eigen
- Type of relationship: Authors employed by this company
Purpose: Conventional Prostate Cancer Detection and Management

PSA & physical exam

Systematic transrectal ultrasound-guided 12-core biopsy

Abnormal

Surgery or radiation therapy (or active surveillance)
Purpose: Can This Paradigm Be Improved With MRI?

- 30% false negative systematic biopsy\(^1\)
- MRI can identify cancer in over half of men with prior negative biopsies\(^2, 3\)
- *But*, direct MRI-guided biopsy is not universally available
Ultrasound (US)-guided biopsy of MRI-delineated targets has been shown feasible\textsuperscript{4}.

→ Show yield of MR/US fusion biopsy
Purpose: Proposed Prostate Cancer Detection and Management

- PSA & physical exam

  - Abnormal

  - External-Array Prostate MRI

    - Systematic & targeted transrectal ultrasound-guided 12-core biopsy

      - Abnormal

        - Surgery or radiation therapy (or active surveillance)
Materials and Methods:

Demographics

- IRB Approval
- 57 consecutive men
- Limited external array MRI at 3.0 Tesla
  - T2-, diffusion-, and perfusion-weighted
- MRI targets scored by radiologist
- Prostate and target contours transferred to ultrasound fusion
- Targeted and systematic ultrasound-guided biopsies on Artemis (Eigen, Inc)
Materials and Methods: MRI Protocol

Overview

- 3.0 Tesla Siemens Magnetom Trio
- External Phased Array
- Intramuscular glucagon
- Multiparametric acquisition
  - T2-weighted imaging
  - Diffusion-weighted imaging
  - Dynamic contrast-enhanced perfusion imaging
- CADstream, Merge Healthcare
Materials and Methods: T2-Weighted Imaging

- 3D-Turbo Spin-Echo (Siemens SPACE)
- TR 3800-5040 TE 101 ms
- ETL 13
- 1.5 mm slice, no gap
- Matrix 256 x 205
- 14 x 14 cm FOV
Materials and Methods: Diffusion-Weighted Imaging

- Echo-planar
- \( b = 0, 100, 400, 800 \text{ mm/s}^2 \)
- TR 3900 TE 60 ms
- 3.6 mm
- 160 x 130 matrix
- FOV 26 x 26 cm
Materials and Methods: Dynamic Contrast-Enhanced Imaging

- TWIST k-space sharing gradient
- TR/TE/FA 3.9/1.4 ms/12°
- 3.6 mm reconstruction
- Matrix 160 x 160
- 26 x 26 cm FOV
- 70 acquisitions every 6 s
- 0.1 mg/kg gadopentetate dimeglumine (Magnevist, Bayer)
### Materials and Methods: Scoring

#### Targets

<table>
<thead>
<tr>
<th>Score</th>
<th>T2WI</th>
<th>DWI (ADC)</th>
<th>DCE (curve analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not visible</td>
<td>&gt;1400</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>Faint low signal</td>
<td>1200-1400</td>
<td>Early or intense enhancement</td>
</tr>
<tr>
<td>3</td>
<td>Distinct low SI</td>
<td>1000-1200</td>
<td>Both, or either plus washout</td>
</tr>
<tr>
<td>4</td>
<td>Very low SI</td>
<td>800-1000</td>
<td>All 3</td>
</tr>
<tr>
<td>5</td>
<td>Invasive low SI</td>
<td>&lt;800</td>
<td>Early=Intense, plus washout</td>
</tr>
</tbody>
</table>

- T2WI, DWI (ADC), and DCE scored 1-5
- CADstream generates screen captures
- T2WI contoured using Osirix
- VRML file imported into Artemis
Curve Examples
(based on breast MRI + intensity)

- The red arrow points to intense, early enhancement + washout = 5/5 suspicion
- The green arrow shows early and intense enhancement + washout = 4/5 suspicion
- The gold curve shows early and intense enhancement, 3/5 suspicion
- The red curve shows early enhancement + washout, also 3/5 suspicion
Findings: Overview

- 101 suspicious areas in 56 patients
- 28 positive targets in 22 men
  - 19 Gleason 3+3 (68%)
  - 8 Gleason 3+4 (29%)
  - 1 high-grade prostate intraepithelial neoplasia (HGPIN)
Findings: Systematic vs. Targeted

- Positive biopsies were found in...
- 12 patients in targets only
  - 6 Gleason 3+3
  - 6 Gleason 3+4
- 9 patients in both targets and systematic
  - Identical Gleason 3+4 in 2
  - Identical Gleason 3+3 in 6
  - One Gleason 3+3 systematic but 3+4 target
- 7 patients on systematic only
  - All Gleason 3+3, < 4 mm, < 25% core
- 28 patients, all biopsies were negative
In one patient
  - Systematic biopsy Gleason 4+4
  - Target negative

However, retrospective analysis of targeting showed that the systematic biopsy came from the target, and that the targeted biopsy actually missed the target
  - Negative based on intent-to-treat
  - Positive based on MRI analysis
Fisher exact test: target vs. systematic
- \( p = 0.06 \) for any cancer identified
- \( p = 0.03 \) for Gleason 3+4 disease only.

Fisher exact test: correlating ADC
- Biopsy positivity and ADC, \( p = 0.007 \)
- Gleason 3+4 vs (3+3 or negative) \( p = 0.08 \)

No correlation was found with overall suspicion or perfusion score or size or location (peripheral versus central) of the lesion
Example #1

- 62-year old man, PSA 2.5 → 4.0
- Systematic biopsies <1% of one core Gleason 3+3=6/10
- Repeat biopsy done with MR guidance
Example #1

- T2 with contour
- ADC map
- Early Enhancement
- Score:
  - T2-highly suspicious (4/5)
  - ADC 700 μm²/s (4/5)
  - Early+intense enhancement plus washout (4/5)
- T2 with contour
- Corresponding ultrasound image (flipped for targeting)
- Ultrasound image with biopsy tracking
Example #1

- 3D Parallax contour with targets identified
Example #1

- Composite image from targeting
Both targeted cores positive for Gleason 3+3=6/10
- 8 mm and 15 mm, for 80% of core
- Prostatectomy:
  - Large volume
  - Organ confined
  - Gleason 3+3=6/10
Example #2

- 65 y/o
- PSA 3→11 over 6 months
- Microfocus of Gleason 3+3
- Normal appearance
  - Image noise from patient factors
- Targeted bx consult prompted 2nd look
- Anterior suspicious focus
- Target bx negative
- Systematic cores Gleason 4+4
  - Retrospectively shown to correspond to target
- Bone scan: no metatatic disease
Example #2

- Ultrasound showing biopsy trajectory
- 3D contour with targets identified
Example #3: Active 63-Year Old on Active Surveillance

- MRI January 2010
  - Slight asymmetry on the right
  - Parameters only slightly abnormal
  - Biopsies negative

- MRI January 2011
  - Tumor on the right has declared itself
  - Multiple parameters are now highly abnormal

Targeted biopsy (only): Gleason 3+4 cancer
- MRI-US fusion for targeted biopsy finds additional cancers compared to systematic biopsies
- This may replace systematic biopsies
  - Fewer total biopsies
  - Improved yield
  - Improved confidence for active surveillance
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