MR-US Fusion

Image-guided prostate biopsy

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Who am I?

• An instructor in the Department of Urology
  • Quick plug for MED 275B – Intro to Biodesign for Undergraduates

• A research engineer working in Urologic Oncology
  • Focused on device research to improve the detection and focal treatment of prostate cancer
    • MR-US Fusion Biopsy
    • HIFU
    • Needle based therapies (laser, IRE)

• An engineer embedded within a clinical department
  • 1 day a week of clinical support
‘Translational Engineering’

• The modern practice of medicine is very busy
• The solution isn’t always a better tool, even if the tool is better
• Specialties are very silo-ed
  • Always moving, overworked
• Reaching ‘across the aisle’ is non-trivial
  • Each specialty has its own language and culture
• Engineers and Physicians can view each other as a monolith
Medical Imaging and Robotics

• How to make an impact on clinical efficacy without incurring great cost
  • Financial
  • Practical/Workflow

• Identification of a clear clinical “gap” or “need”
  • Biodesign/Design Thinking

• Clinical need that has been addressed via the novel application of imaging and robotics
  • Prostate Cancer Detection
Observation

Observation: Mr. Smith is a 55 year old man, who gets a PSA blood test as part of an annual check up. It is found that his PSA level is 7.9, which is elevated, and he is referred to a urologic oncologist.

Mr. Smith undergoes a prostate biopsy. The results comes back negative. Unfortunately the uro-oncologist is still suspicious that there is cancer present (repeat PSA has risen to 9 in the last year), and schedules a follow-up biopsy. During that follow-up biopsy, we find small amounts of cancer, that was missed on first biopsy.

Mr. Smith goes on to surgical treatment, where it is revealed that he has pockets of aggressive prostate cancer that were missed on both biopsies. Additionally, he is having a hard time recovering from surgery.
The Prostate

• The role of the prostate is to aid in male reproduction
• Due to its small size and anatomy, historically difficult to assess
Prostate Cancer

Prostate cancer is a serious public health concern:
- 2nd most common form of cancer in men
- In the US: 220,800 new diagnosis per year; 27,540 deaths (est. 2015)
- An estimated 2.8 M men living with prostate cancer in the US
Do you have questions about this graphic?
Prostate Cancer

Most men will not die from prostate cancer
• 5 year relative survival is 98.9%
  • Compared with 17.4% in Lung
• Localized vs Distant (100% vs 28.2%)
  • Treat local disease to reduce risk of progression
  • Early detection and accurate cancer staging is key
Prostate Cancer History

• In the 1980’s
  • Biochemical screening (PSA)

• In the 2000’s
  • Robotic Prostatectomy

• Recently
  • Recognition of ‘over-treatment’

• Motivation of more accurate diagnostics
  • More targeted treatment
  • How can we differentiate between low and high risk cancer?

• The history of cancer treatment is a swinging pendulum
Prostate Biopsy

• Only definitive way to confirm prostate cancer
• Estimated 1 million biopsies performed annually in the USA
• Approximately 750,000 out of these men with high PSA levels return (multiple) negative biopsies using the current clinical standard
Conventional TRUS Biopsy

• Introduced in 1989
• A needle attached to a spring loaded biopsy gun
• Transrectal ultrasound probe is inserted into the rectum to directly image the prostate
  • Acquire cylindrical cores under the guidance of 2D ultrasound
• Prior methods lacked any image guidance
• 12-cores ‘randomly and systematically’ acquired – about 70% tumors are in the peripheral zone
What are the issues with Conventional TRUS Biopsy?

Any clear clinical care ‘gaps’ or ‘needs’ that come to mind?
Problems with Conventional Prostate Biopsy

• 12-core systematic biopsies are rarely “systematic”
• ‘Game of chance’
  • 0.45% of gland is sampled
• 30% of cancer is missed by initial prostate biopsy
• 30% of cancer is understaged
Need Statement

• A way to improve prostate cancer detection, in men, to reduce mortality
• A way to better detect aggressive prostate cancer, in men with an elevated PSA, to reduce mortality
• A way to treat prostate cancer, in men, with fewer treatment related side effects
What are possible solutions?
Solutions?

• 12-core systematic biopsies are rarely “systematic”
  • Guidance system to ensure systematic spread of biopsy?

• ‘Game of chance’ & 30% of cancer is missed by initial prostate biopsy
  • Better imaging of the prostate to directly detect prostate cancer?

• 30% of cancer is understaged
  • Leverage imaging to direct biopsies?
Can we see prostate cancer?
Prostate Imaging

• Current imaging is insufficient to diagnose prostate cancers

• CT: Cannot delineate anatomy

• Ultrasound: Cannot distinguish benign from malignant tissue
  • Susceptible to image artifacts

• MRI: Multiparametric imaging allows exquisite detail
  • at great cost and time (10 x cost compared to US), requires 2x scans
  • no standard for interpretation
Other Solutions?
MR-US Fusion for Prostate Biopsy

• One approach described in 2008
  • Aaron Fenster’s group at Robarts Research Institute

• Combines strength of two modalities
  • Lesion identification on multi-parametric MR
    • Registration of MR with TRUS
  • Guided biopsy using TRUS
MR-US Fusion for Prostate Biopsy

- Commercial 3D TRUS biopsy tracking system
  - 510(k) approval imaging/tracking
- Utilizes standard TRUS probe and machine
  - Probe is rotated 180+20 degrees
  - Video frames captured by device
- Mechanical tracking via encoders
  - No direct line of sight needed (optical)
  - Unaffected by environment (magnetic)
- Biopsy sites are tracked and recorded for future recall
MR-US Fusion Workflow

A: mpMRI Exam

B: Suspicious lesions marked on mpMRI with ProFuse™

C: MR/TRUS Fusion-guided Bx with Artemis™
Artemis for MR – US Fusion

MRI

Ultrasound

Segmentation
3D TRUS Volume Acquisition
1. SEGMENTATION
2. RIGID ALIGNMENT
3. SURFACE REGISTRATION
4. ELASTIC INTERPOLATION

TRUS VOLUME

MRI T2

TRUS REGISTERED TO MRI

COMPUTED TRUS ON MRI FRAME OF REFERENCE
Map ROI from MRI to US
Artemis Robotic Arm

Shoulder

Wrist

Elbow
Navigating to Targets
MR-US Fusion at Stanford

• Multidisciplinary team of urologists, radiologists, pathologists, scientists and engineers
  • Urology
    • Dr. Geoff Sonn
    • Dr. Richard Fan
  • Radiology
    • Body MR Faculty (Bruce Daniel, Peji Ghanouni, Andy Loening, others)
    • 3DQ Lab
  • Pathology
    • Dr. Christian Kunder
Case Review – Prior Negative (Hidden cancer)

- 63 year old man, PSA 60, 4 prior negative biopsies
- Single high suspicion target
- All systematic biopsies reveal benign tissue,
- Targeted biopsies reveal very aggressive prostate cancer
  - Missed by conventional technique
Case Review – Active Surveillance

- Known low grade cancer
- 66 year old man, PSA 6.35, on Active Surveillance
- 2 targets, left and right side
- Cancer was understaged by conventional biopsy
Case Review – First Time Biopsy

• No known cancer
• 56 year old man, PSA 6.96, no prior biopsy
• 2 targets, moderate risk and low risk
• Low risk target was benign, but moderate risk target showed cancer
Results at Stanford

PCa Detection by Level of Suspicion

<table>
<thead>
<tr>
<th>Level</th>
<th>Gleason 7 or Higher</th>
<th>Any PCa</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIRADS 1-3</td>
<td>13%</td>
<td>23%</td>
</tr>
<tr>
<td>PIRADS 4</td>
<td>32%</td>
<td>47%</td>
</tr>
<tr>
<td>PIRADS 5</td>
<td>78%</td>
<td>92%</td>
</tr>
</tbody>
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(n = 195) (n = 198) (n = 93)
Results at Stanford

Detection of Significant Cancer in PIRADS 4 Lesions from 11 Radiologists

- Radiologist 1: 50%
- Radiologist 2: 33%
- Radiologist 3: 0%
- Radiologist 4: 40%
- Radiologist 5: 25%
- Radiologist 6: 50%
- Radiologist 7: 80%
- Radiologist 8: 67%
- Radiologist 9: 0%
- Radiologist 10: 100%
- Radiologist 11: 83%
Challenges

• MR-US Fusion can improve the detection of prostate cancer
  • Currently limited to large academic centers
  • Can this be translated to community practice?

• Technical challenges
  • Automatic segmentation of MRI and US
  • Misregistration during a procedure
  • Deformable, real time, US volume models
  • Needle steering, deflection, visualization during procedures
Next Frontier

• Can we leverage this technology on more than just cancer detection?
  • What about treatment?

• Focal therapy
  • Aims to achieve oncological control while reducing side effects commonly associated with radical treatment (whole gland)
    • HIFU
    • Laser
    • Irreversible Electroporation

• Improved Registration
  • Statistical Deformation Models