MR-US Fusion Guided Biopsy: Is it fulfilling expectations?

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Outline

• Brief Overview of Prostate Cancer
  ✓ The “Radiologist” Perspective
• Desire for Directed Biopsies
• Review MR-US Fusion Biopsy Experience
• Established? and Developing Applications
• Summary
Introduction

Prostate cancer (PCa) is a **heterogeneous** disease, with indolent and aggressive forms.

The traditional elements used for risk stratification and management of PCa patients include:

- Clinical H&P and digital rectal exam (DRE)
- Prostate-specific antigen (PSA) test
- Gleason results from 10-12 core extended sextant biopsy
TRUS: The Standard of Care

Transrectal ultrasound (TRUS) guided biopsy is standard of care for the diagnosis and surveillance of prostate cancer.

Benefits:
• Established procedure
• Can be performed in the office setting

Limitations:
• TRUS biopsies may (over)detect indolent PCa
• Significant Gleason understaging
• Undersampling of anterior gland, transition zone
Prostate multiparametric magnetic resonance imaging (mpMRI) is the most accurate imaging method for the detection and staging of PCa.

- Initial use was for staging PCa patients.
- Increasing role in evaluating patients with suspicion of PCa, planning biopsy, etc.

Why not combine mpMRI and TRUS?
MRI-TRUS Fusion Biopsy
Pre Biopsy

Lesion Identification

Prostate Segmentation

Lesion Volume of Interest

MRI-TRUS Fusion Biopsy
Biopsy Procedure

Prostate Segmentation

Lesion VOI Projection

Biopsy Mapping

MRI-TRUS Fusion Biopsy
Post Biopsy

Potential Role of MRI-US Biopsy

Incorporation in Current Risk Stratification
• Biopsy naïve patients?
• Standard biopsy negative patients?

Specific Patient Groups
• Role in active surveillance?
• Focal therapies?
• Role in previously treated disease?
MRI-US Fusion Biopsy Results

MRI-US fusion targeted biopsy data suggest potential improvements over standard biopsy:

• Targeted approach detects more higher grade PCa over standard biopsy alone (32%).
• Targeted approach detects more clinically significant (Gleason ≥ 4+3) disease (67%) and missed lower grade (Gleason ≤ 3+4), potentially indolent disease (36%).
• Standard biopsy also led to upgrading (26%) but detected less clinically significant disease (only 8% Gleason ≥ 4+3).

MRI-US Fusion Biopsy Results

Recent systematic review reveals similar findings

- 15 studies with >2000 patients
- Median detection rate for “clinically significant disease” in standard biopsy was 23.6% (range: 4.8-52%)
- Median detection rate in targeted biopsy was 33.3% (range: 13.2 - 50%).
- “Clinically significant” was variably defined.

Why Do Targeted Biopsies Fail?

13.5% (135/1003) of studied patients upgraded on systemic vs targeted biopsies

Identified predictors of upgrading on systemic vs targeted biopsies include:

• Lower PSA (p<0.001)
• Larger gland size on MRI (p<0.001)
• Lower number of targeted cores (p=0.001)

Why do Targeted Biopsies Fail?

Several main reasons identified for undergrading of disease:

• mpMRI reader oversight
• mpMRI “invisible” disease
• Tumor heterogeneity
• Biopsy technique error

Role in Active Surveillance

Targeted biopsies may be superior for detecting Gleason upgrading in AS cohorts

- 166 patients undergoing AS with 2 or more bx
  - Mean follow-up of 25.5 months
- Progression identified in 29.5% of patients
  - 44.9% identified on targeted biopsy alone
  - Fusion biopsy (targeted + systematic) found 26% more cases of progression than systematic alone
- Sole predictor of upgrading was mpMRI findings
  - 81% NPV; 35% PPV; 77.6% Sens; 40.5% Spec

*Frye TP, et. al., Magnetic Resonance Imaging-Transrectal Ultrasound Guided Fusion Biopsy to Detect Progression in Patients with Existing Lesions on Active Surveillance for Low and Intermediate Risk Prostate Cancer J Urol 2017 197(3 Pt 1) 640-646.
Role in Active Surveillance

Others have reported more positive results

- 259 patients undergoing AS
  - 196 Gleason 6(3+3); 63 Gleason 7(3+4)
- Surveilled up to 4 yrs with 33 patients progressing
  - 97% of Gleason upgrading occurred at targeted sites
- Predictors of upgrading included
  - PSAD ≥ 0.15 ng/mL/cc
  - mpMRI lesion score of 5
  - Gleason 3+4 disease; 4.65x more likely than 3+3

*Nassiri, et. al., Targeted Biopsy to Detect Gleason Score Upgrading during Active Surveillance for Men with Low versus Intermediate Risk Prostate Cancer *J Urol* 2017 197(3 Pt 1) 632-639.
Role in Focal Treatments

It has been argued that MRI-US fusion-guided biopsy the “modality of choice” for selecting patients for focal therapy*. BUT it is still imperfect#

- 454 pts with MR-US biopsy proven PCa
- 175 eligible for focal therapy (NCCN intermediate)
- 64 proceeded to prostatectomy
- 75% concordance for eligibility

Role in Post-treatment Prostates

Little available data for assessment.

Unclear even what mpMRI sequences are needed.

However, small studies have shown benefit in cases of recurrence after RP

Limitations of MRI-US Biopsy

Limitations of the Fusion Technology

• Expensive
• Learning curve

Limitations Specific to mpMRI

• The Radiologists
• Ongoing questions regarding acquisition protocols and scoring
Limitations Specific to mpMRI

Recent study compared initial and second opinion reads on outside mpMRIs for patients presenting to tertiary center for transperineal MR-US fusion biopsies

• Specialist tertiary reads had a higher NPV
  ✓NPV for Gleason 7(3+4) or higher: 97% vs 84% (p=0.039)

• Tertiary reads more often read as negative
  ✓41% vs 20% (p<0.001)

*Hansen NL, et. al. Comparison of initial and tertiary centre second opinion reads of multiparametric magnetic resonance imaging of the prostate prior to repeat biopsy. Eur Radiol 2017 27(6) 2259-63.
Limitations Specific to mpMRI

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• Specialist tertiary reads had a higher NPV
  ✓ NPV for Gleason 7(3+4) or higher: 97% vs 84% (p=0.039)

• Tertiary reads more often read as negative
  ✓ 41% vs 20% (p<0.001)

Limitations Specific to mpMRI

Recent switch from PI-RADS v1 to v2

Continued ongoing debate regarding need for contrast

Head to head comparison shows high agreement but differing AUC based on zone*

✓ PI-RADS v2 higher AUC in TZ
✓ PI-RADS v1 higher AUC in PZ

Summary

Increasing evidence of improved patient stratification with MR-US fusion biopsy.

Increasing supportive evidence for role in AS cohorts.

May be best method for selecting patients for focal treatments and evaluating post treatment recurrence.
Selected References


