PROSTATE CANCER SCREENING

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Prostate Cancer Screening and the Nurse's Role

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UNC UNC

Physiology

- Partly glandular and muscular organ within lower pelvis
- Accessory reproductive gland
- Aids in motility and nourishment of sperm
- 28-47cc

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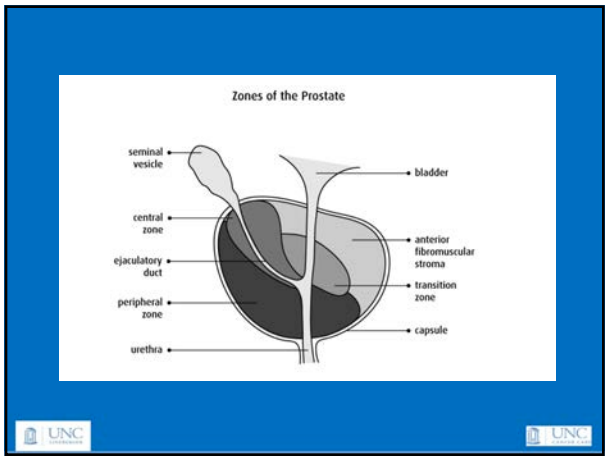

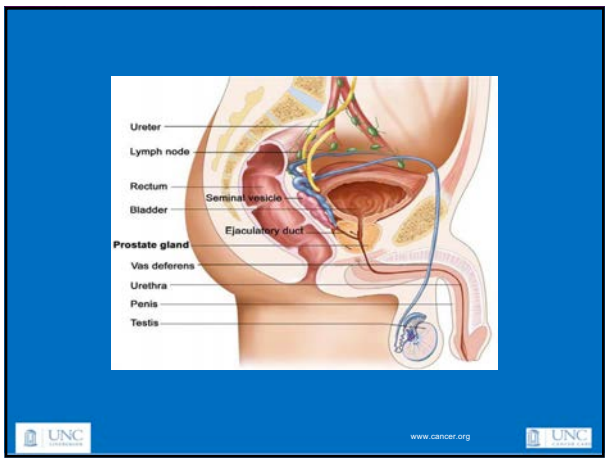

Epidemiology

- Most commonly diagnosed (non cutaneous) malignancy in men
- >2.9 million men living with prostate cancer in the US
- Lifetime risk: 1 in 9 men
- 2nd leading cause of cancer death in men in the US
- 1 in 41 men die of prostate cancer

Survival Rates

SEER Stage	5 Year Relative Survival Rate
Localized	Nearly 100%
Regional	Nearly 100%
Distant	30%

Clinical Presentation

- **Usually asymptomatic**
- Lower urinary tract symptoms (LUTS)
- Bone pain
- Bladder Outlet Obstruction /Renal failure

Risk Factors

- Age
  - 60% dx at ≥65 years old
- Race
  - AA men highest incidence & mortality
- Family History
  - History of metastatic or lethal adenocarcinomas

AUA Recommendations

- Recommends against screening <40yo
- Average risk men: Shared decision making to begin screening, beginning at age 55
- High risk men: Individualized decision based on risk factors

Screening

- Prostate exam called digital rectal exam (DRE)
- Blood test called prostate specific antigen (PSA) .
  - Protein produced exclusively by prostate cells
  - PSA density, PSA velocity, free PSA
- New Tools: biomarkers, MRI, targeted biopsy

Goal of screening

Identify a high-risk prostate cancer that will affect a patient's quality of life that can be successfully treated

Benefit of Early Detection

Prevent morbidity and mortality associated with metastatic disease

Harms of Early Detection

- Psychological distress
- Potential complications of biopsy
  - Bleeding, pain, infection
- Overtreatment

PSA: Screening Smarter

- Artificially high
  - Infection
  - Lab error
  - Inflammation
  - Retention
  - BPH
  - Intercourse
- Artificially low
  - BPH meds: 5- ARI
  - Lab error
  - Chemotherapy

The Role of the Nurse or APP: Pre-treatment

- Monitoring of elevated PSA
- Monitoring patients on active surveillance
- Managing urinary symptoms
- Counsel patients on risk factors, screening guidelines
- Patient Education:
  - " Nobody dies from prostate cancer"
  - "I don't believe in PSA"
- Reinforcing discussions on treatment options, side effect management, post-operative pathway

The Role of the Nurse or APP: Post-treatment

- Mental and emotional implications
- Managing side effects:
  - Urinary incontinence, ED
  - Make referrals when appropriate
- Surveillance for disease recurrence
- Survivorship Care Plan

References

- Does Age Really Matter? Recall of Information Presented to Newly Referred Patients with Cancer. (2008). *Journal of Clinical Oncology, 26*, 1-8. Retrieved May 7, 2019, from http://www.uhbs-international.net/fileadmin/unispitalbaselch/Bereiche/Medizin/Psychosomatik/Publikationen/Kiss_Alexander/7A75DD71d01.pdf
- Oh WK, Hurwitz M, D'Amico AV, et al. Biology of Prostate Cancer. In: Kufe DW, Pollock RE, Weichselbaum RR, et al., editors. Holland-Frei Cancer Medicine. 6th edition. Hamilton (ON): BC Decker; 2003. Available from: https://www.ncbi.nlm.nih.gov/books/NBK13217/
- Survival Rates for Prostate Cancer. (2019). *American Cancer Society.* https://www.cancer.org/cancer/prostate-cancer/detection-diagnosis-staging/survival-rates.html
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MRI ULTRASOUND FUSION TARGETED PROSTATE BIOPSY IN PROSTATE CANCER LOCALIZATION AND RISK ASSESSMENT

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PROBLEMS WITH CURRENT DETECTION PARADIGM

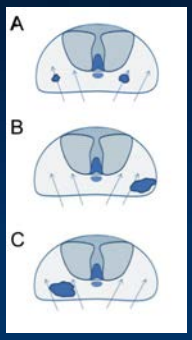
- PSA sensitivity is set by threshold, but specificity is poor at all threshold
- No ability of PSA to distinguish aggressive disease
- Huge number of biopsies
  - Repeat biopsies for men with cancer
  - Repeat biopsies for men without cancer
- Resulting over-detection leading to over-treatment leading to criticism of our field

WHAT IS THE PROBLEM?

- The biomarker
- The response to the biomarker
- The biopsy
- The response to the biopsy

We can probably do better with all of the above.

CURRENT LIMITATIONS OF PROSTATE BIOPSY



Clinically insignificant cancers are identified by chance

Important cancers are incorrectly risk stratified

Clinically significant tumours are missed

(Bjurlin, et al, J Urol, 2014; **adapted from H Ahmed, UCL)**

DEFINITION OF BIOPSY OPTIMIZATION

- Detection of potentially lethal prostate cancer
- Avoidance of "over-detection" of clinically insignificant cancer
- Generation of clinically useful data
  - accurate depiction of risk and cancer location
- Maintenance of cost effectiveness
  - Avoidance of repetitive biopsy
  - Cost effective specimen handling

Taneja, et al, AUA White Paper: Optimization of Prostate Biopsy and Specimen Handling, 2013
Bjurlin, et al, J Urol, 2013

OPTIONS FOR IMPROVING THE BIOPSY PARADIGM

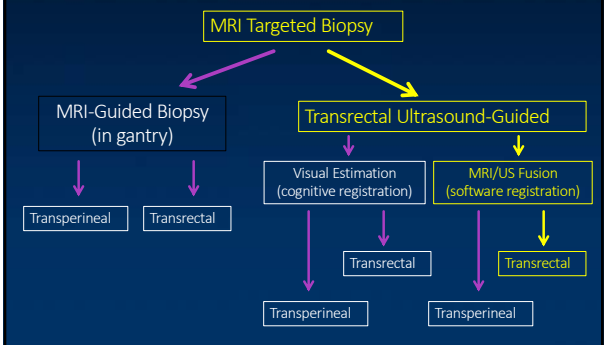
- Better candidate selection
  - Biomarkers: PCA3, PHI, 4k score
  - Nomograms: PCPT calculator, Vienna nomogram
- Saturation techniques
  - Overcome sampling error through excessive sampling
- Targeted biopsy/Imaging
  - Use of imaging to guide biopsy
  - Use of imaging to stratify risk

MRI COULD CORRECT ALL THE LIMITATIONS OF SYSTEMATIC BIOPSY

- Targeting of patients with MR detected abnormality
  - fewer false negatives
    - fewer repeat biopsies
  - more accurate cancer classification
    - greater cancer core length
    - better grade concordance
    - better patient selection for AS/therapy
- No biopsy for MRI normal patients
  - avoidance of over-detection of indolent tumors

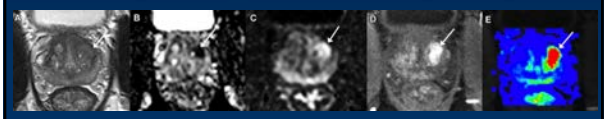
THE NYU EXPERIENCE TO DATE

NYU APPROACH SINCE MAY, 2012



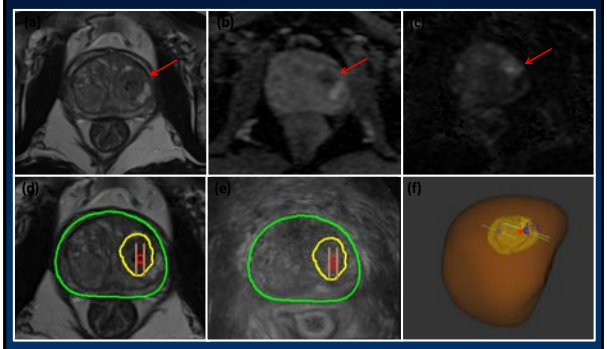
MULTIPARAMETRIC MRI OF THE PROSTATE

- Pre-biopsy 3T multi-parametric MRI
  - Identify areas of suspicion for sampling
  - Predicts likelihood of prostate cancer through MRI suspicion score (mSS)
  - Selection of patients for biopsy

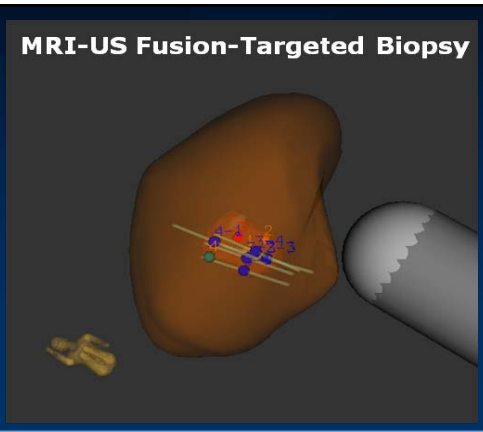


T2WI ADC DWI DCE Perfusion Map

Bjurlin, et al, J Urol, 2013



MRI-US Fusion-Targeted Biopsy



RATES OF ADHERENCE WITH PRE-BIOPSY MRI

- 1526 patients underwent prostate biopsy at our center by one of 5 urologists between June 1, 2012 and Jan 1, 2016
  - 1509/1526 (98.9%) underwent pre-biopsy MRI
  - 17 biopsied without MRI
    - 8 cardiac pacemaker
    - 3 insurance denial
    - 2 embedded shrapnel
    - 2 claustrophobia
    - 2 physician preference

Rosenkrantz, et al, Urologia Internat 2016

CLINICAL APPLICATIONS OF PRE-BIOPSY MRI PRIOR TO TARGETED BIOPSY

- Previous negative biopsy
  - Finding missed disease
- Active surveillance/ known cancer
  - Localizing dominant disease
  - Accurate classification of disease risk
- No previous biopsy
  - Goal of finding lethal disease while missing non-lethal disease
  - Reduction of over-detection

Enrollment

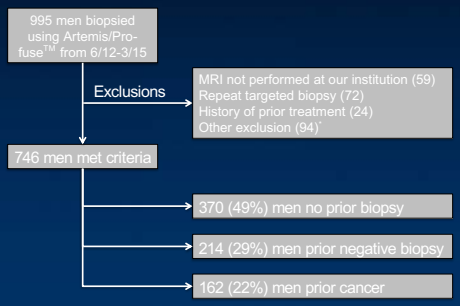


Figure 1 - Study flow diagram
MRI = magnetic resonance imaging
*Exclusion due to non-standard MRI protocol or missing data element

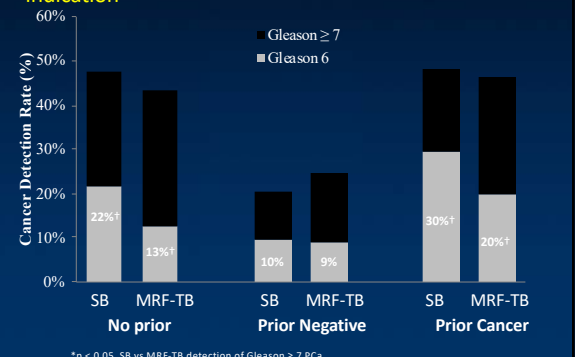
Meng, et al, European Urology, 2016

Systematic vs Targeted biopsy, whole cohort (n = 746)

*p < 0.05, SB vs MRF-TB detection of Gleason ≥ 7 PCa
†p < 0.05, SB vs MRF-TB detection of Gleason 6 PCa

Meng, et al, European Urology, 2016

Performance of MRF-TB vs SB varies by biopsy indication



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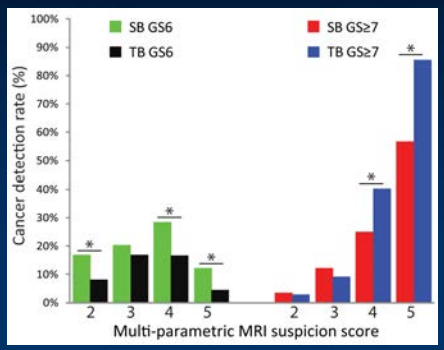
Meng, et al, European Urology, 2016

INCREASING MSS IS ASSOCIATED WITH INCREASING DETECTION OF GS≥7 BUT NOT GS6 DISEASE



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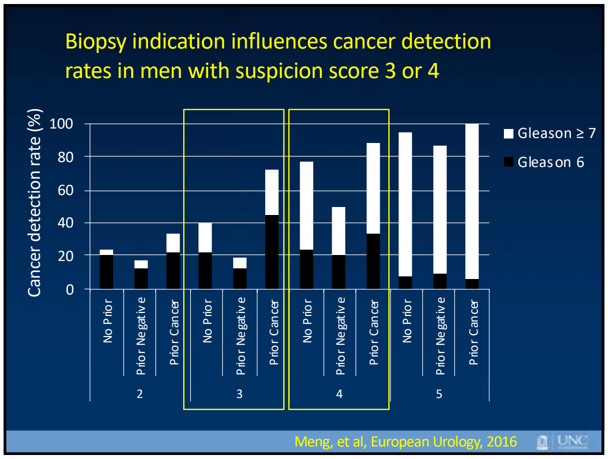
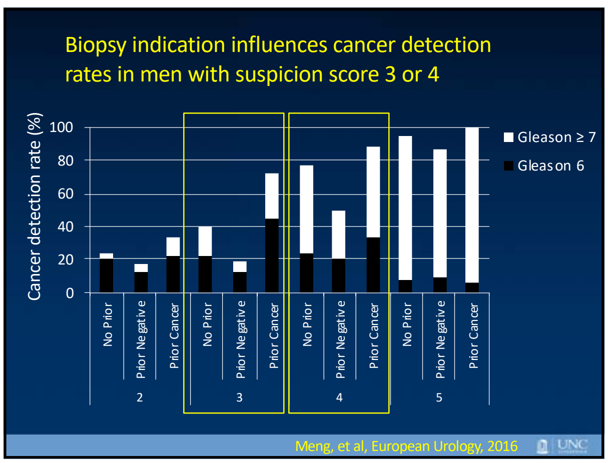

Biopsy indication influences cancer detection
rates in men with suspicion score 3 or 4
Cancer detection rate (%)
100
80
60
40
20
0
No Prior
Prior Negative
Prior Cancer
2
3
4
5
Gleason ≥ 7
Gleason 6
Meng, et al, European Urology, 2016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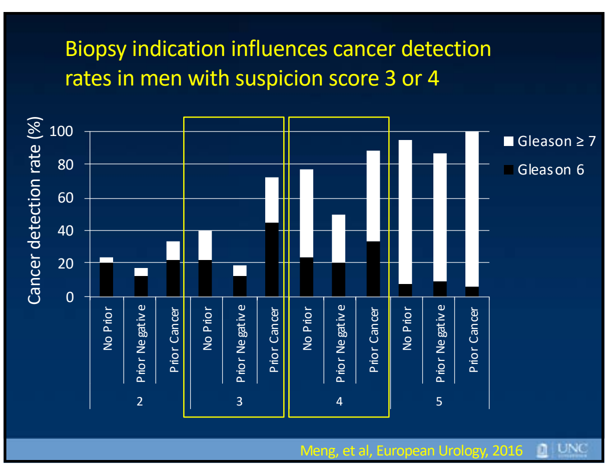
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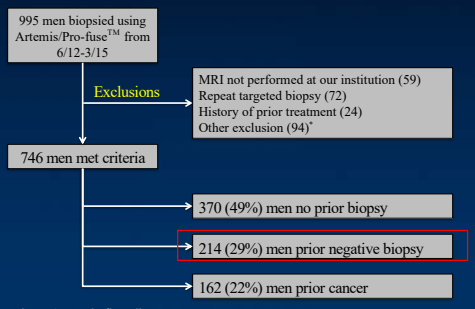
Meng, et al, European Urology, 2016

MEN WITH PREVIOUS NEGATIVE BIOPSY

Patient Cohort



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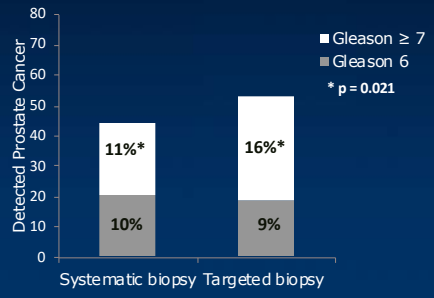
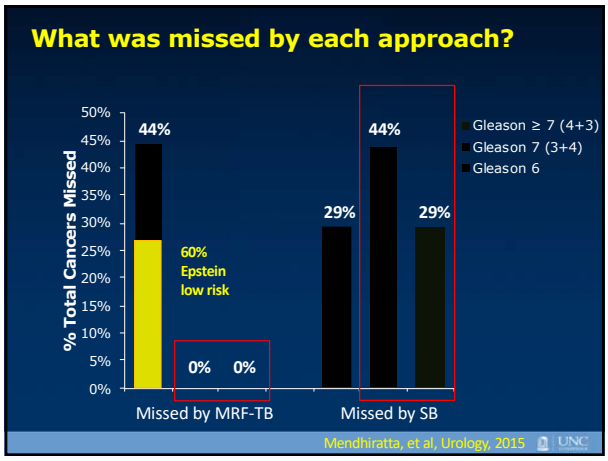
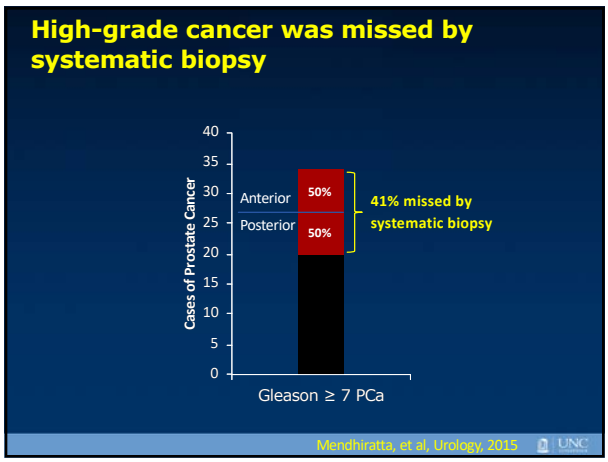
Mendhiratta, et al, Urology, 2015

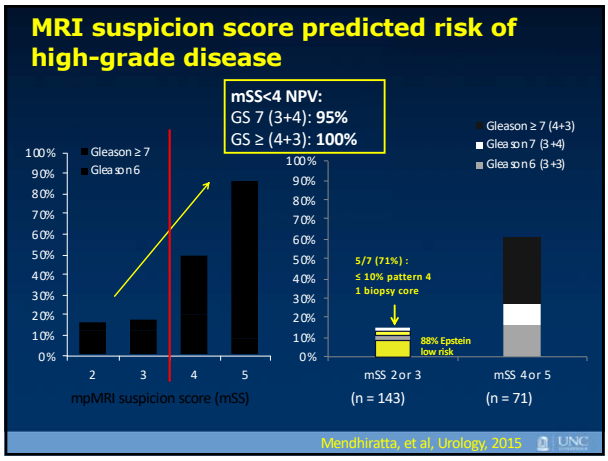
Outcomes: Targeted biopsy detected more high-grade cancer



Mendhiratta, et al, Urology, 2015


What was missed by each approach?
% Total Cancers Missed
50%
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
44%
60%
Epstein
low risk
0%
0%
29%
44%
29%
Gleason ≥ 7 (4+3)
Gleason 7 (3+4)
Gleason 6
Missed by MRF-TB
Missed by SB
Mendhiratta, et al, Urology, 2015


High-grade cancer was missed by systematic biopsy
Cases of Prostate Cancer
40
35
30
25
20
15
10
5
0
Anterior
Posterior
50%
50%
41% missed by systematic biopsy
Gleason ≥ 7 PCa
Mendhiratta, et al, Urology, 2015


MRI suspicion score predicted risk of high-grade disease
mSS<4 NPV:
GS 7 (3+4): 95%
GS ≥ (4+3): 100%
Gleason ≥ 7
Gleason 6
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2
3
4
5
mpMRI suspicion score (mSS)
Gleason ≥ 7 (4+3)
Gleason 7 (3+4)
Gleason 6 (3+3)
5/7 (71%) :
≤ 10% pattern 4
1 biopsy core
88% Epstein low risk
mSS 2 or 3
(n = 143)
mSS 4 or 5
(n = 71)
Mendhiratta, et al, Urology, 2015

WHITE PAPER: PROSTATE MRI AND MRI-TARGETED BIOPSY IN PATIENTS WITH PRIOR NEGATIVE BIOPSY
COLLABORATIVE INITIATIVE OF THE AMERICAN UROLOGICAL ASSOCIATION AND THE SOCIETY OF ABDOMINAL RADIOLOGY'S PROSTATE CANCER DISEASE-FOCUSED PANEL
(AUA WEBSITE, J UROLOGY)

SAR Members

- Andrew B Rosenkrantz MD
- Sadhna Verma MD
- Peter Choyke MD
- Masoom A Haider MD
- Daniel J Margolis MD
- Steven C Eberhardt MD

AUA Members

- Scott E Eggener MD
- Krishnanath Gaitonde MD
- Leonard S Marks MD
- Peter Pinto MD
- Geoffrey A Sonn MD
- Samir S Taneja MD

JOINT STATEMENT

- When high quality MRI is available it should be strongly considered in any patient undergoing repeat biopsy
- Other considerations:
  - Results of other biomarkers
  - Cost of the MRI
  - Availability of high quality MRI
    - Proper equipment, properly used
    - Properly interpreted using PI-RADS criteria

Rosenkrantz, et al, J Urology, 2016

PI-RADS V2

- MRI should be interpreted with PIRADS v2 guidelines
  - Experience by radiologist in interpretation
  - Experience by urologist in performing biopsies
  - Quality Assurance Programs are recommended to monitor targeted biopsy results
- Any MRI lesion interpreted as PI-RADS 3, 4 ,5 warrants biopsy with image guidance

Rosenkrantz, et al, J Urology, 2016

RECOMMENDED METHODS OF TARGETED MRI BIOPSIES

- Acceptable methods
  - TRUS-MRI fusion biopsy
  - In bore MRI targeted biopsy
    - Fusion and in-bore may be valuable for small lesions or lesions in difficult locations
  - Cognitive (visual) targeting
- At least two cores from each MRI target
  - Separately label cores, denoting targeted and non targeted biopsies
- Case specific decision regarding additional systematic sampling

Rosenkrantz, et al, J Urology, 2016

ARE MR GUIDED BIOPSIES ENOUGH?

- Targeted biopsy only:
  - Only if QA efforts have validated prostate MRI results are consistent with literature
  - Acknowledge 5-15% false negative rate with MR targeted MRI
  - Consider early re-biopsy of PI-RADS 5 lesion that is negative at biopsy

Rosenkrantz, et al, J Urology, 2016

WHAT IF MRI IS NORMAL OR LOW RISK?

- If lesions are PI-RADS 1 or 2, other markers/clinical factors may indicate a need to repeat systematic biopsy
- If a repeat biopsy is deferred on the basis of the MRI findings:
  - Continued clinical and laboratory followup
  - Consider repeat MRI

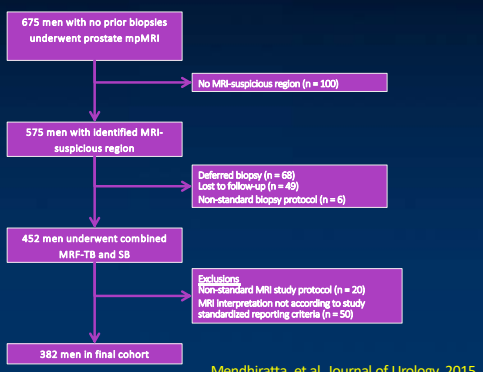
Rosenkrantz, et al, J Urology, 2016

JOINT STATEMENT (NOT A GUIDELINE!)

- If considering repeat biopsy after initial negative biopsy, MRI and targeted biopsy may help detect CS disease over standard repeat biopsy
- Strongly consider obtaining prostate MRI in any patient being considered for repeat biopsy when high quality MRI is available; also consider other markers and cost of exam
  - Distribute document to AUA website and short version in the Journal of Urology

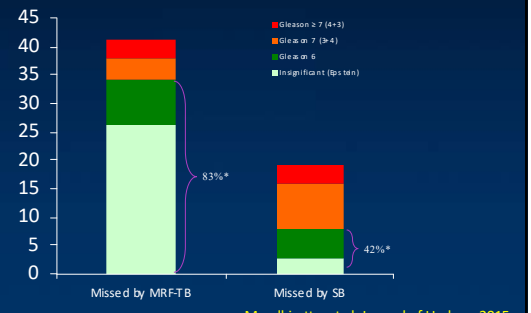
Rosenkrantz, et al, J Urology, 2016

MEN WITHOUT PREVIOUS BIOPSY



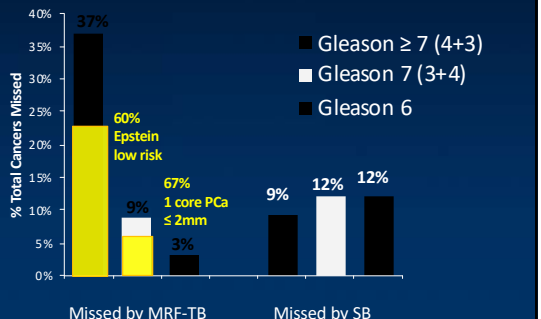
Mendhiratta, et al, Journal of Urology, 2015

WHAT ARE WE MISSING WITH EACH APPROACH? NO PRIOR BIOPSY (N = 382)



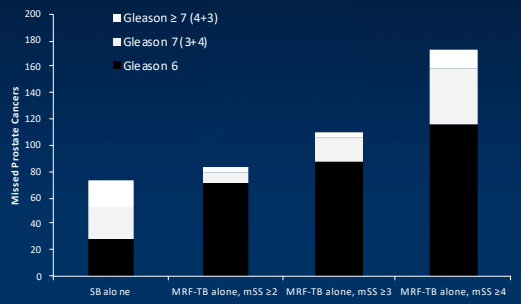
Mendhiratta, et al, Journal of Urology, 2015

What percentage of cancer are we missing with each approach? (no prior biopsy)

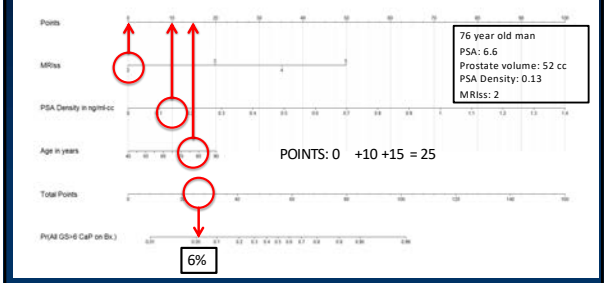


Mendhiratta, et al, Journal of Urology, 2015

What would we miss? Possible clinical strategies for pre-biopsy MRI and targeted biopsy

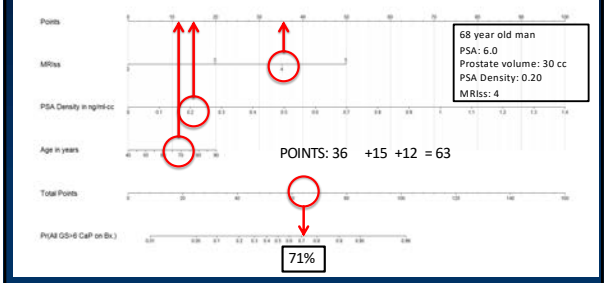


NO PRIOR CANCER- PREDICTIVE NOMOGRAM OF GS ≥7 PROSTATE CANCER ON A COMBINED TARGETED AND SYSTEMATIC BIOPSY



Bjurlin, et al. Urology

NO PRIOR CANCER- PREDICTIVE NOMOGRAM OF GS ≥7 PROSTATE CANCER ON A COMBINED TARGETED AND SYSTEMATIC BIOPSY



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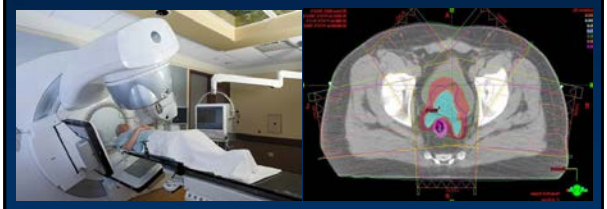
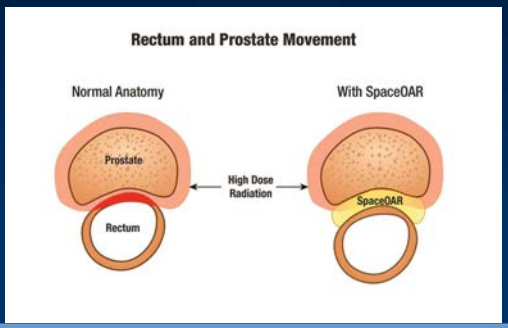
NEW TECHNOLOGY TO PREVENT SIDE EFFECTS OF RADIATION IN THE MANAGEMENT OF PROSTATE CANCER



NEW TECHNOLOGY TO PREVENT SIDE EFFECTS OF RADIATION IN THE MANAGEMENT OF PROSTATE CANCER

- Proximity of rectum to prostate: risk for GI toxicity
- Bleeding, frequency, urgency, pain, fistulas

DECREASE RECTAL TOXICITY BY INCREASING SPACE BETWEEN RECTUM AND PROSTATE



CONCLUSIONS

- MR targeted biopsy offers unique benefits in all biopsy indications:
  - Improved detection of cancer and high grade disease in men with previous negative biopsy
  - Optimized risk stratification of men with history of cancer, reducing need for repeat biopsy
  - Reduction of Gleason 6 cancer detection without reduction of high grade detection in men with no previous biopsy
- MR suspicion score, biopsy indication, and secondary biomarkers may aid in deciding who needs biopsy in each of these groups
- SpaceOAR is new technology to reduce radiation side effects