Clinical Prostate Cancer Imaging

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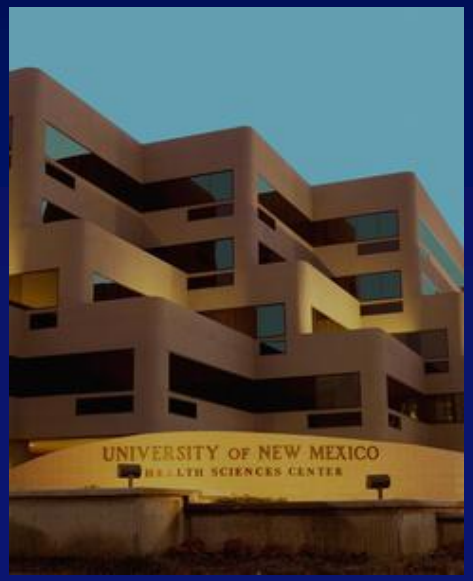
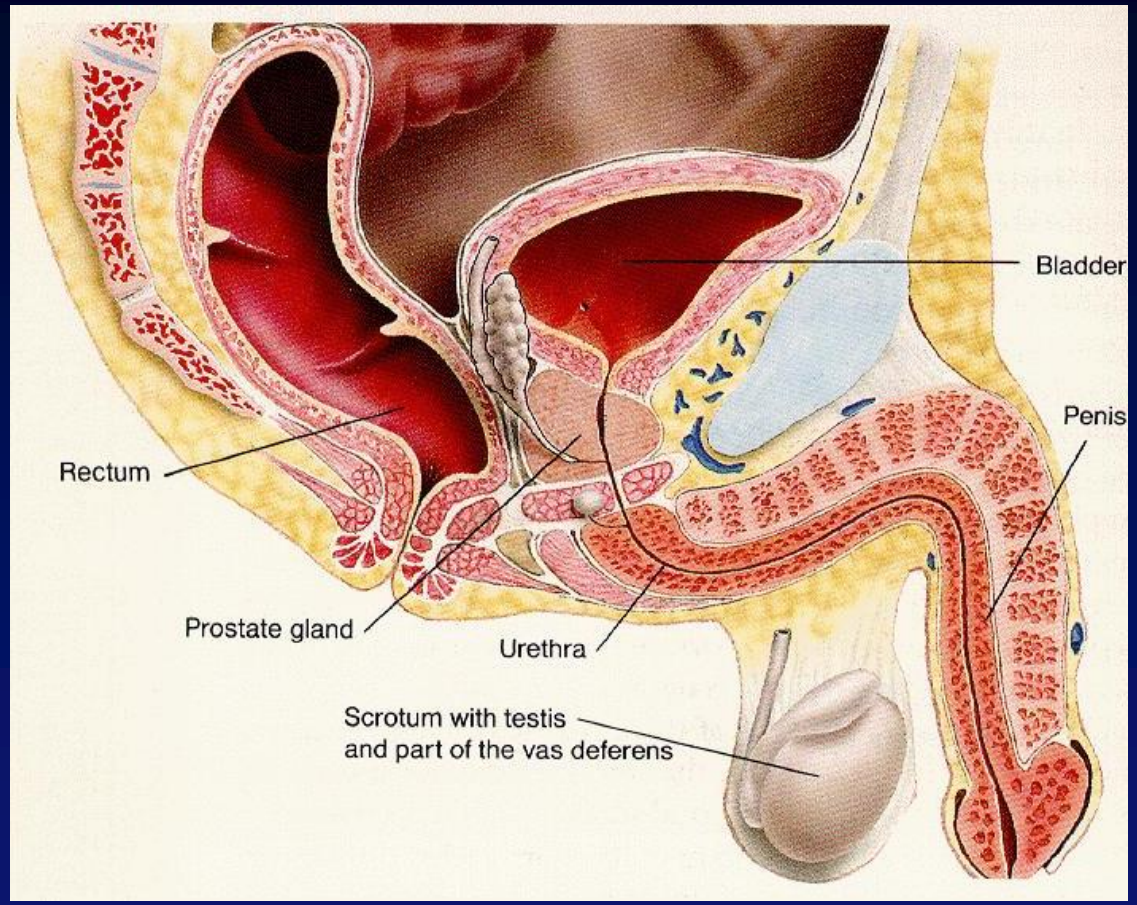


The Prostate Gland

- Part of male sexual organs
- Size of a walnut
- Between bladder and penis
- Anterior to the rectum
- Surrounds the urethra
- Provides fluid for ejaculate (30%)
- Seminal vesicles joined at the base



Common Prostate Diseases

- Benign
  - Prostatitis
    - Infectious (antibiotics)
    - Noninfectious (more common)
  - Benign prostatic hypertrophy (BPH)
    - 50% men > age 50
    - 95% men > age 90
    - Significant morbidity
- Malignant
  - Primary: adenocarcinoma (common acinar, 95%)
  - Secondary: direct (bladder, urethra)

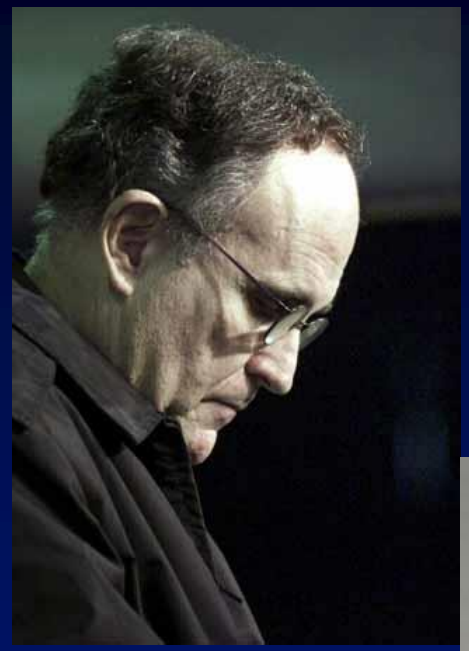
Uncommon Prostatic Malignancies ~5%

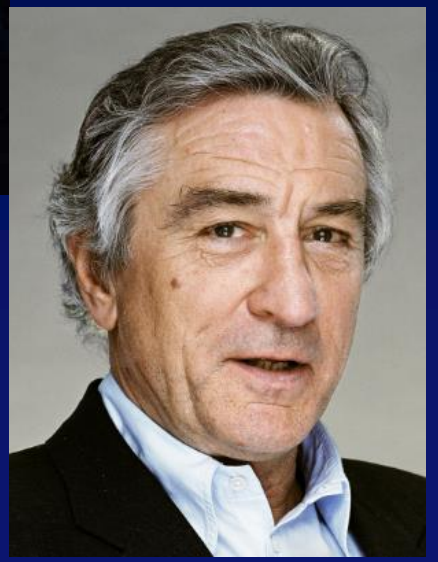
- Epithelial
  - Adenocarcinoma variants
    - Comedocarcinoma
    - Mucinous carcinoma
    - Adenoid cystic carcinoma
    - Signet ring cell carcinoma
    - Adenosquamous carcinoma
  - Squamous cell
  - Transitional cell
  - Neuroendocrine (carcinoid, small cell)
- Nonepithelial
  - Rhabdosarcoma
  - Leiomyosarcoma
  - Fibrosarcoma
  - MFH
  - Osteosarcoma
  - Angiosarcoma
  - Chondrosarcoma
  - Carcinosarcoma
  - Malignant phyllodes
  - Lymphoma
  - Leukemia
  - PSS and PSPUMP

    (Prostatic stromal sarcoma and prostatic stromal proliferation of uncertain malignant potential)

Prostate Cancer in 2017

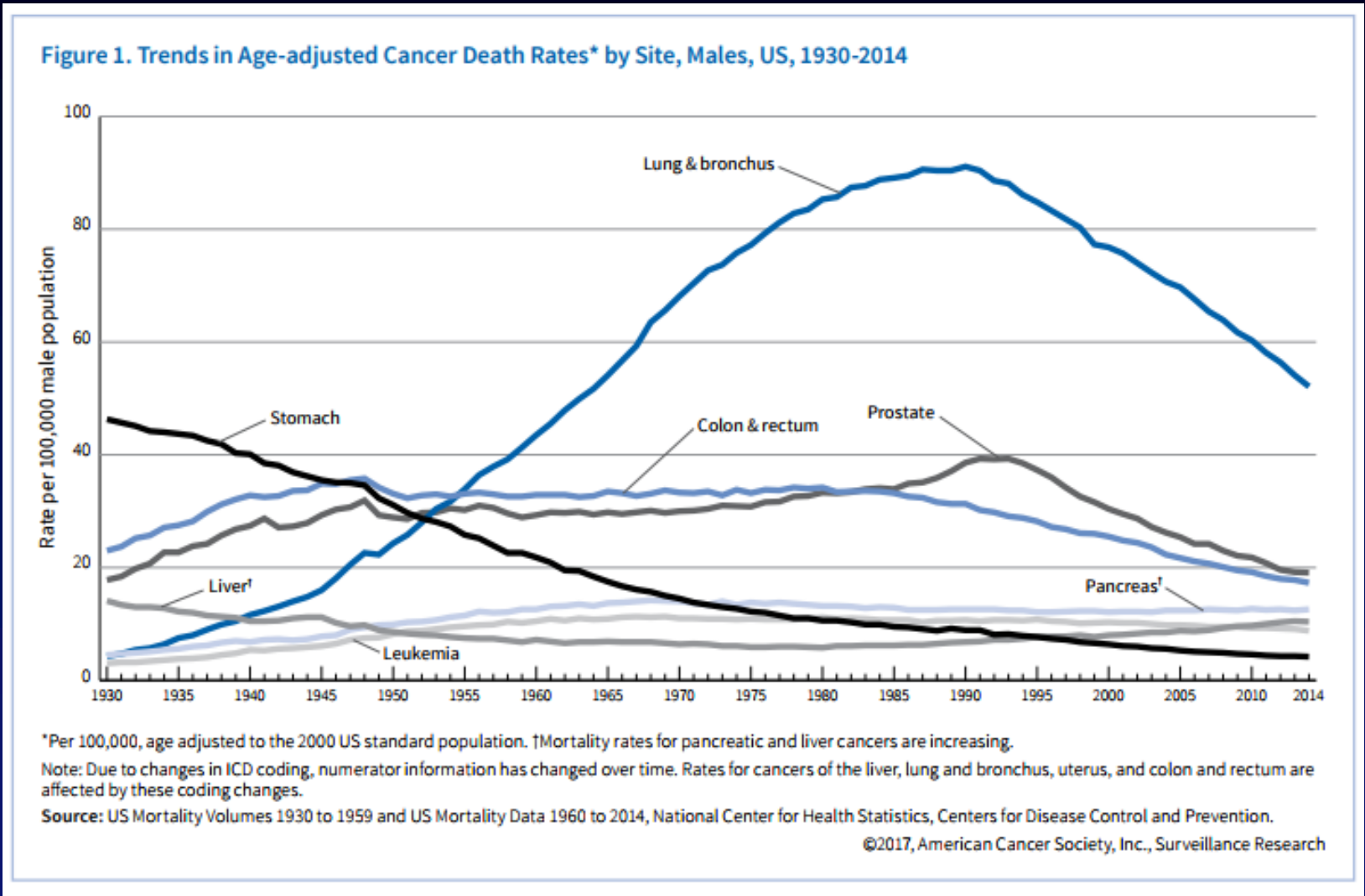
- Most common malignancy in American men
- About 160,000 new cases per year
- Second leading cause of cancer death (26,700/ year)





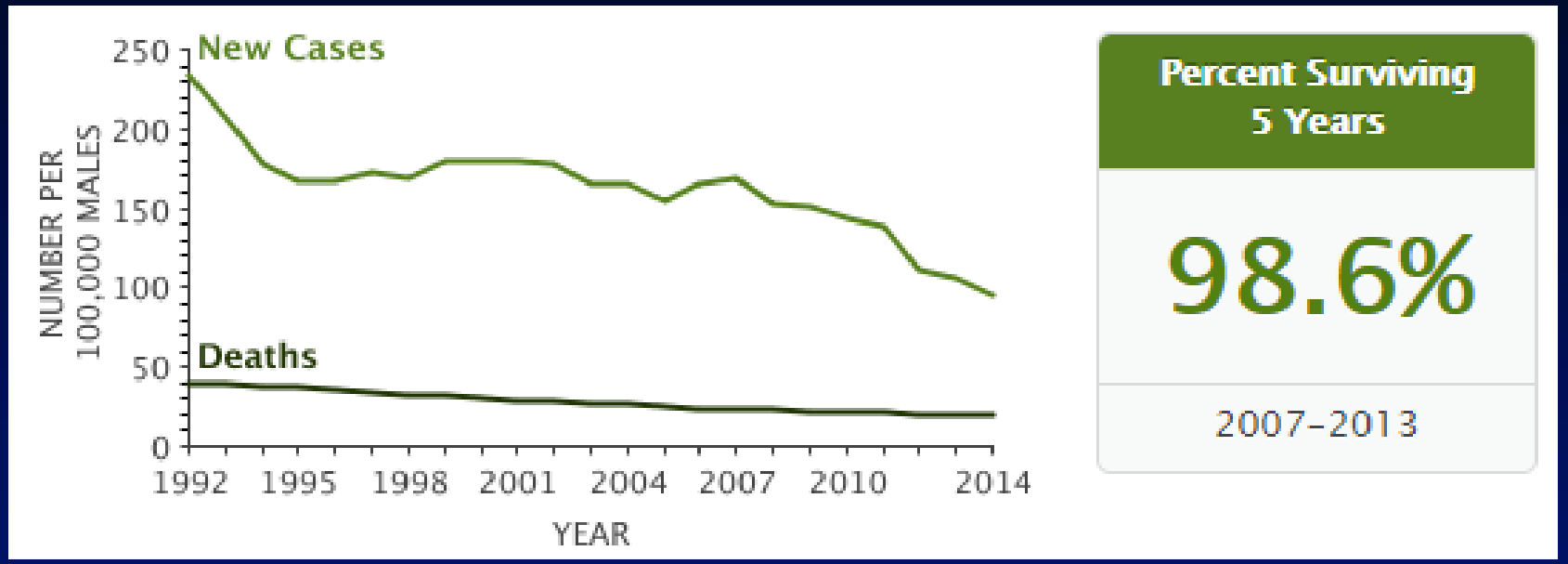
Source: American Cancer Society, http://www.cancer.org

Cancer Death Rates*, for Men, US, 1930-2014



https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2017/trends-in-age-adjusted-cancer-death-rates-by-site-males-us-1930-2014.pdf

Prostate Cancer



Percent Surviving 5 Years
98.6%
2007–2013

Established Screening Methods

- PSA blood test (serum PSA)
  - 0 to 4 ng/ml normal range
  - 4 to 10 ng/ml slightly elevated
  - 10 to 20 ng/ml moderately elevated
  - Greater than 20 highly elevated
  - Increases with age, BPH, prostatitis
- Digital rectal exam (DRE)
- Imaging NOT used for screening

PSA Controversy

- Goal of PSA Screening = reduce disease specific mortality
- PSA: low specificity, cannot discriminate between lethal and nonlethal cancers. Has led to over-diagnosis and over-treatment.
- Conflicting results from trials on mortality have not given a clear picture of PSAs utility as a screening test.

PSA Controversy – March 2009

- European (ERSPC): Showed PSA screening led to lower death rate from prostate cancer (but is also associated with a high risk of over-diagnosis).
  - Incidence 8.2% in the PSA screening group: 20% less likely to die from prostate cancer.
  - Incidence 4.8% in the control group.
  - The absolute risk difference between the two groups was 0.71 deaths per 1,000 men.
  - To prevent one death from prostate cancer, 1,410 men would need to be screened with PSA testing and 48 additional cases of prostate cancer would need to be treated.

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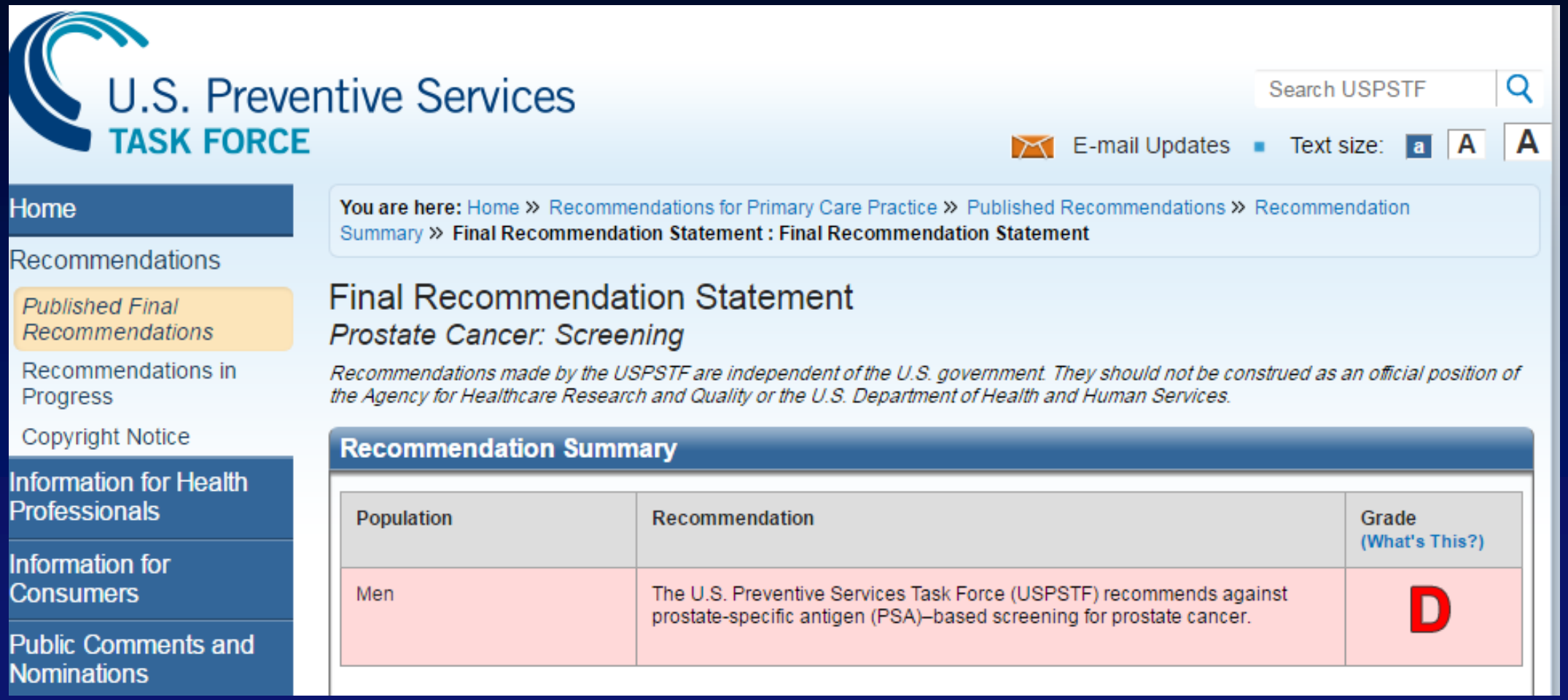
  - The absolute risk difference between the two groups was 0.71 deaths per 1,000 men.
  - To prevent one death from prostate cancer, 1,410 men would need to be screened with PSA testing and 48 additional cases of prostate cancer would need to be treated.
- USA (PLCO): Showed no evidence of reduced death rate from prostate cancer with annual PSA screening compared with usual medical care.
  - 13 yrs of f/u: mortality rates from prostate cancer for intervention and control groups: 3.7 and 3.4 deaths per 10,000 person-years, no significant difference.
  - Based on results: U.S. Preventive Service Task Force (USPSTF) advised against PSA screening in 2011.
  - Nevertheless, experts continue to believe that not using PSA screening would result in the deaths of many men with curable prostate cancer.
  - Many large, national urological associations (American Urological Association [AUA], Canadian Urological Association [CUA] and European Urological Association [EAU]) endorse benefit of PSA screening for men after age 45 to 50, recommend physician-patient discussions about screening on an individual basis.

USPSTF 2012



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Final Recommendation Statement

Prostate Cancer: Screening

Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Recommendation Summary

Population	Recommendation	Grade (What's This?)
Men	The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA)–based screening for prostate cancer.	D

USPSTF

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Govt. Panel Scuttles Prostate Cancer Testing Recommendations

May 21, 2012

By VERONICA SIKKA M.D., ABC News Medical Unit via **WORLD NEWS**

By **RYAN JASLOW** / **CBS NEWS** / *May 22, 2012, 9:37 AM*

U.S. panel recommends against PSA tests for screening prostate cancer in men of all ages

AUA Guidelines: 2013

1. Men < 40 yo: no screening
2. Men 40-54 yo: no routine screening at average risk
3. Men 55-69 yo: shared decision-making
4. An interval of two years or more may be preferred over annual screening.
5. Men ≥ 70 yo: no routine screening
6. Men with < 10-15 y life expectancy: no routine screening

USPSTF 2017

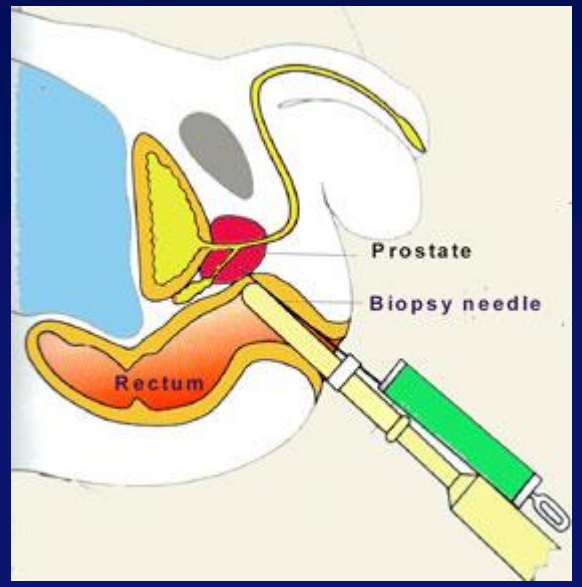
- Comment period ended May 8, 2017

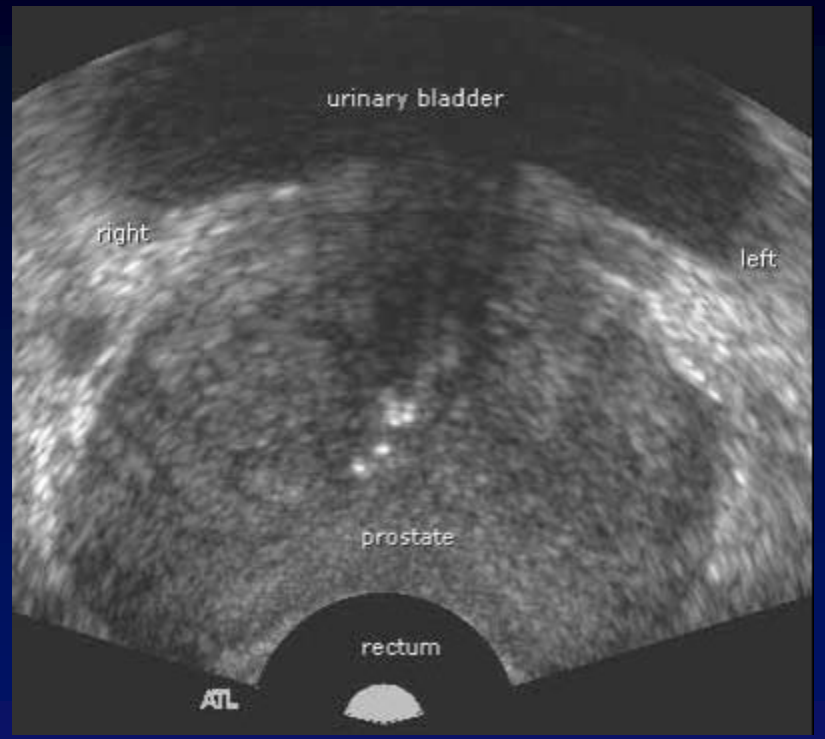
Draft: Recommendation Summary

Population	Recommendation	Grade (What's This?)
Men ages 55 to 69 years	The USPSTF recommends that clinicians inform men ages 55 to 69 years about the potential benefits and harms of prostate-specific antigen (PSA)–based screening for prostate cancer. The decision about whether to be screened for prostate cancer should be an individual one. Screening offers a small potential benefit of reducing the chance of dying of prostate cancer. However, many men will experience potential harms of screening, including false-positive results that require additional testing and possible prostate biopsy; overdiagnosis and overtreatment; and treatment complications, such as incontinence and impotence. The USPSTF recommends individualized decisionmaking about screening for prostate cancer after discussion with a clinician, so that each man has an opportunity to understand the potential benefits and harms of screening and to incorporate his values and preferences into his decision. Please refer to the Clinical Considerations sections on screening in African American men and men with a family history of prostate cancer for more information on these higher-risk populations.	C
Men age 70 years and older	The USPSTF recommends against PSA-based screening for prostate cancer in men age 70 years and older.	D

Diagnosis

- Needle biopsy
  - Standard approach - image guidance using transrectal ultrasound – usual for 1st attempt at diagnosis
  - Result: Normal or Cancer or Other (Inflammation or Prostatic intraepithelial neoplasia (PIN))



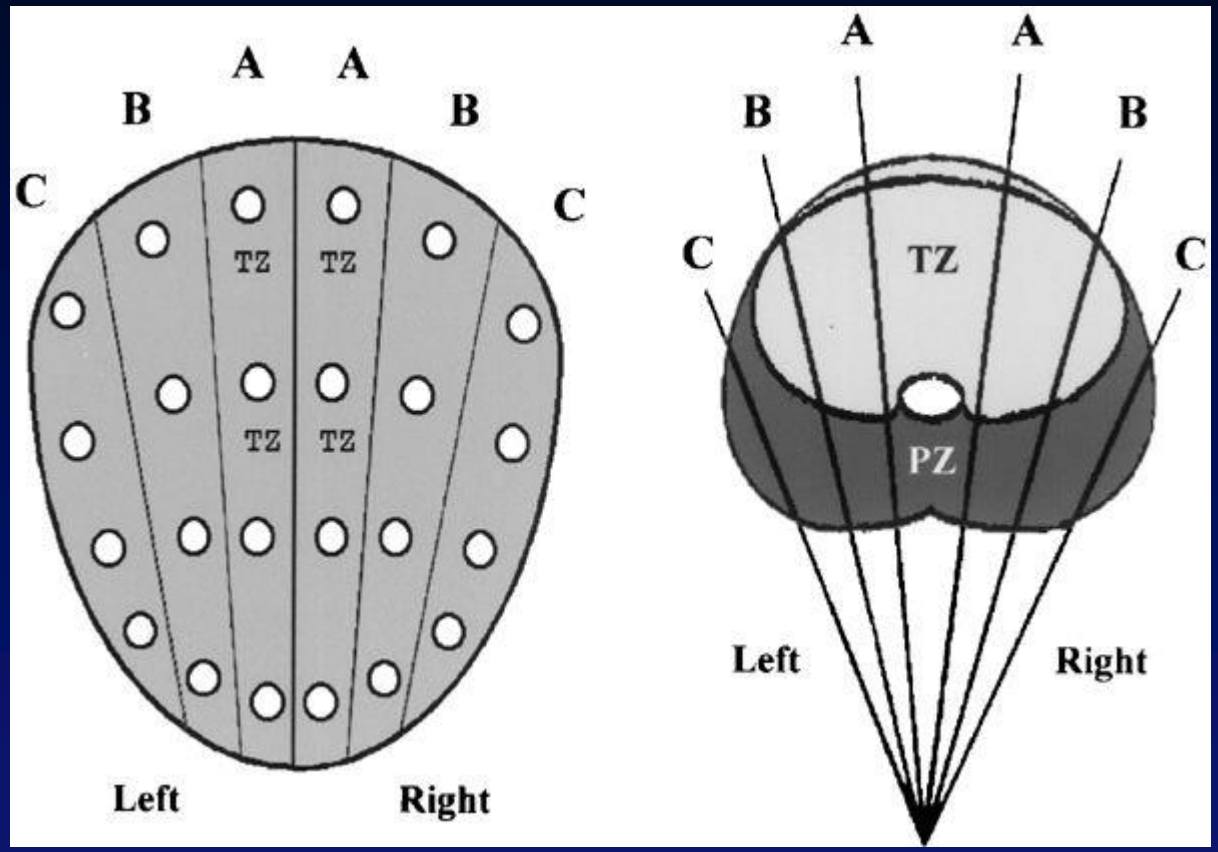


Ultrasound

- For imaging Dx: as accurate as the DRE
- Biopsy tool
  - Systematic biopsies – US guided
  - Directed to suspicious sites
  - Local size/extent in some cases (not very accurate staging)
  - Color Doppler – helpful in studies, not widely practiced.
  - Elastography – good for peripheral zone cancers in studies, but not widely practiced.
- Therapy guidance
  - Brachy, cryo-, high intensity focused US

Diagnosis

- US not very good at visualizing tumor sites.
- Systematic Biopsy
- 12-24 needle core samples



Other imaging prior to diagnosis?

- Limited studies of MRI use in biopsy naïve patients.
- Effective but more expensive.
- Studies have shown approach to be cost effective, but not widely adopted.

Prostate Cancer

- Data available at diagnosis
  - PSA
  - DRE / TRUS (T-stage)
  - Biopsy
    - Histologic grade (Gleason score, 2-10)
      - Sum of Major (listed first) and Minor (listed second) histology.
      - Cancer = pattern 3,4,5; Sum (i.e.): 3+3 = 6 (best), 3+4=7,4+3=7, 4+4=8, 4+5=9, 5+4=9, 5+5=10 (worst).
    - Map: # cores, locations (volume estimate)
  - Imaging results
    - MRI results (if used to guide bx and/or stage)
    - CT and bone scan results (appropriate in higher risk pts.)

Clinical Staging (AJCC 2017)

T Stage

TX Primary tumor cannot be assessed

T0 No evidence of primary tumor

T1 Clinically not palpable

T1a Incidental histologic finding in 5% or less of tissue resected (TURP)

T1b Incidental histologic finding >5% of tissue resected

T1c Tumor in needle biopsy but not palpable

T2 Tumor is palpable and confined within prostate

T2a Tumor involves one-half of one side or less

T2b Tumor involves more than one-half of one side but not both sides

T2c Tumor involves both sides

T3 Extraprostatic tumor that is not fixed or does not invade adjacent structures

T3a Extraprostatic extension (unilateral or bilateral)

T3b Tumor invades seminal vesicle(s)

T4 Tumor is fixed or invades adjacent structures other than seminal vesicles, such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall

Lymph nodes

- **NX:** Regional nodes cannot be assessed
- **N0:** No regional lymph node metastasis
- **N1:** Regional lymph node metastasis

Distant Metastases

- **MX:** distant metastasis cannot be evaluated
- **M0:** No distant metastases
- **M1:** Distant metastasis
  - **M1a:** nonregional lymph node
  - **M1b:** bone
  - **M1c:** Other sites

Use of Nomograms

- Individual parameters limited
  - PSA
  - Gleason score
  - Clinical T-stage
- Combined are good predictors of actual disease
  - Tumor extent (stage)
  - Likely outcomes

Nomograms: example

Partin Table for PSA 4.1 – 10.0 ng/ml

PSA 4.1-10.0 ng/ml

Gleason Grade	Pathologic Stage	Clinical Stage						
		T1a	T1b	T1c	T2a	T2b	T2c	T3a
2-4	Organ-Confined Disease	84(75-82)	70(60-79)	83(78-88)	71(64-78)	81(52-69)	66(57-74)	43(27-58)
	Established Capsular Penetration	14(7-3)	27(18-37)	15(11-20)	26(19-33)	35(26-43)	29(21-37)	44(30-59)
	Seminal Vesicle Involvement	1(0-4)	2(0-6)	1(0-3)	2(1-5)	4(1-9)	5(1-10)	10(3-23)
	Lymph Node Involvement	0(0-2)	1(0-3)	0(0-1)	0(0-1)	1(0-2)	1(0-2)	1(0-5)
5	Organ-Confined Disease	72(60-85)	53(44-63)	71(67-75)	55(51-60)	43(38-49)	49(42-55)	27(17-39)
	Established Capsular Penetration	25(14-36)	42(32-51)	27(23-30)	41(36-46)	50(45-55)	43(37-50)	57(46-68)
	Seminal Vesicle Involvement	2(0-5)	3(1-7)	2(1-3)	3(2-5)	5(3-8)	6(4-10)	12(6-20)
	Lymph Node Involvement	1(0-5)	2(1-5)	0(0-1)	1(0-1)	2(1-3)	2(1-3)	3(1-7)
6	Organ-Confined Disease	67(55-82)	47(38-57)	67(64-70)	51(47-54)	38(34-43)	43(38-49)	23(14-34)
	Established Capsular Penetration	27(15-39)	44(35-53)	30(27-33)	44(41-48)	52(48-56)	46(40-51)	57(47-67)
	Seminal Vesicle Involvement	2(0-6)	3(1-6)	2(2-3)	3(2-4)	5(4-7)	6(4-9)	11(6-18)
	Lymph Node Involvement	3(0-15)	5(2-11)	1(1-2)	2(1-3)	4(3-6)	4(3-6)	9(5-15)
7	Organ-Confined Disease	49(34-68)	29(21-38)	49(45-54)	33(29-38)	22(18-26)	25(20-30)	11(6-17)
	Established Capsular Penetration	36(20-51)	48(38-60)	40(35-44)	52(48-57)	54(49-59)	48(42-54)	48(37-58)
	Seminal Vesicle Involvement	6(0-19)	9(2-18)	8(5-11)	10(8-13)	15(11-19)	18(13-24)	26(17-36)
	Lymph Node Involvement	8(0-32)	12(5-23)	3(2-5)	4(3-6)	9(6-12)	9(6-13)	15(8-23)
8-10	Organ-Confined Disease	35(18-62)	18(11-28)	37(28-46)	23(16-31)	14(9-19)	15(10-22)	6(3-10)
	Established Capsular Penetration	34(17-58)	42(28-57)	40(33-49)	49(42-57)	46(39-53)	40(31-48)	34(24-46)
	Seminal Vesicle Involvement	10(0-34)	15(4-29)	15(10-22)	19(13-26)	24(17-31)	28(20-37)	35(23-48)
	Lymph Node Involvement	18(0-55)	23(10-43)	8(4-12)	9(5-13)	16(11-24)	17(10-26)	24(13-38)

Partin AW, et al., Combination of prostate-specific antigen, clinical stage, and Gleason score to predict pathological stage of localized prostate cancer. A multi-institutional update.JAMA, 277(18):1445-51 1997

Prostate Cancer

- Treatment goals - individualized
  - Risk adjusted
  - Patient specific
  - Maximize cancer control
  - Minimize risks of complications
  - Not over-treat

- Treatment selection
  - Surveillance – watchful waiting
  - Prostatectomy
  - Radiation therapy (RT) +/- hormones
  - Hormones/castration

Prostate Cancer Imaging

- Imaging Goals
  - Disease (tumor) detection, monitoring (active surveillance)
  - Accurate state of disease (Stage)
    - MRI is more accurate than nomograms
    - Determine specific patient risk (risk stratification)
- Evolution over last decade:
  - When and how to use imaging.
  - Newer methods for disease assessments in suspected recurrence

Prostate Cancer: *Computed Tomography*

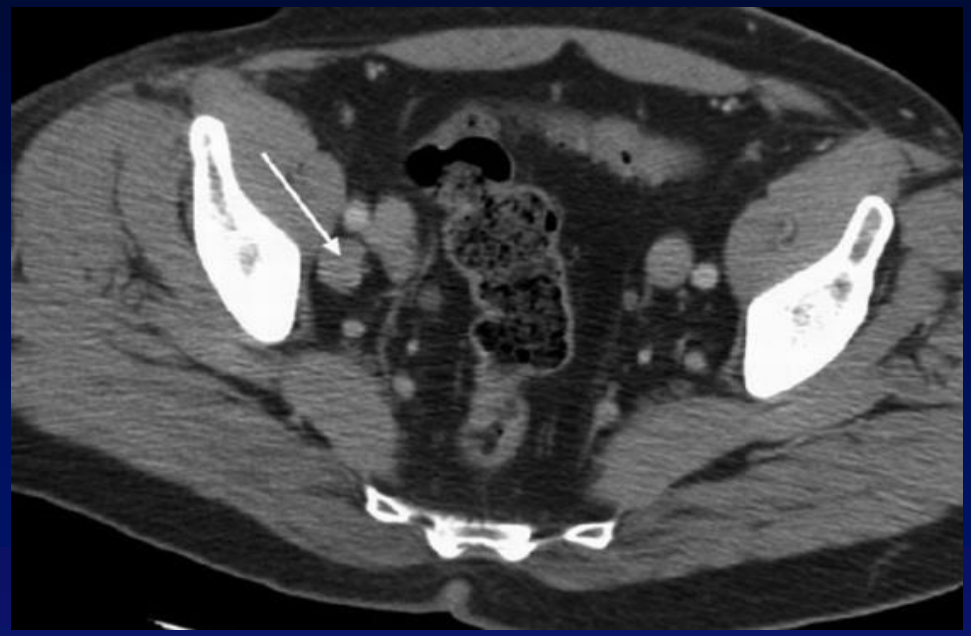
- Not effective local staging
- Routine screening for comorbid disease not cost effective*
- Nodes: routine imaging not justified**
- Selected criteria for use:
  - PSA > 20 ng/ml
  - Gleason score > 7
  - T3 lesion by DRE
- Nodes, Bone, Gross local dx

* Forman, AJR 1994
**Partin, J Urol 1993
Blaustein J Urol 1994
Wolf, J Urol 1995

Prostate Cancer

CT Lymph Nodes

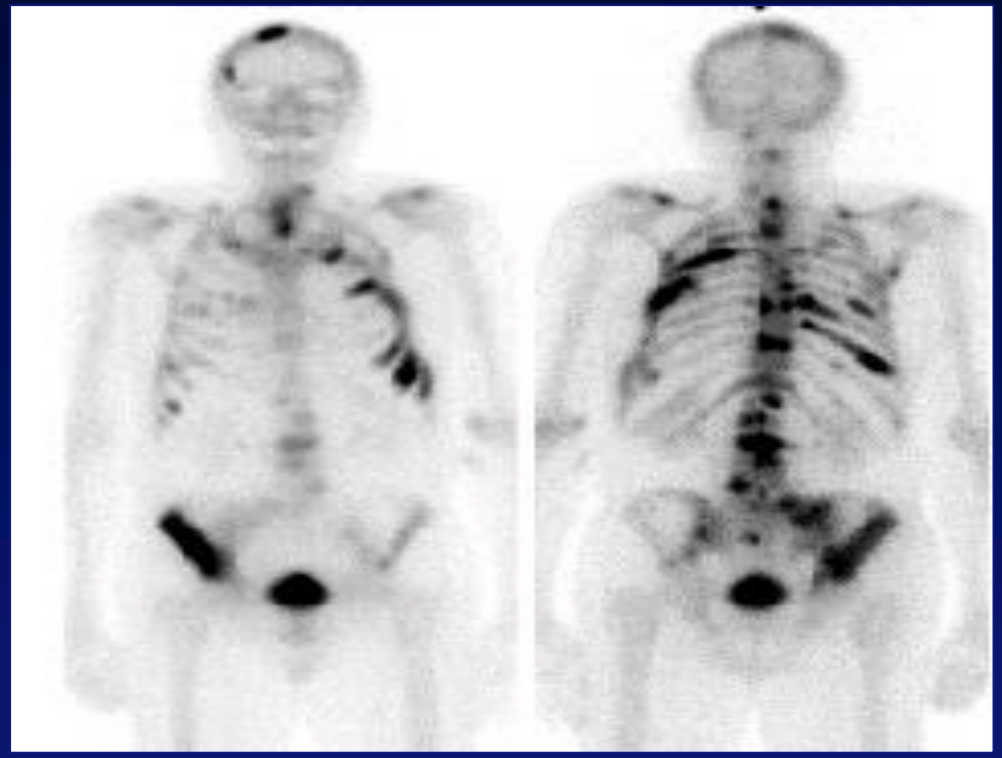
- Size criteria
  (usually 1.0 cm)
- Poor sensitivity ~35% (25-75)
  - Misses lots of small metastases
- CT and MRI equivalent
- Image abdomen if regional adenopathy present



PROSTATE CANCER

Radionuclide Bone Scan

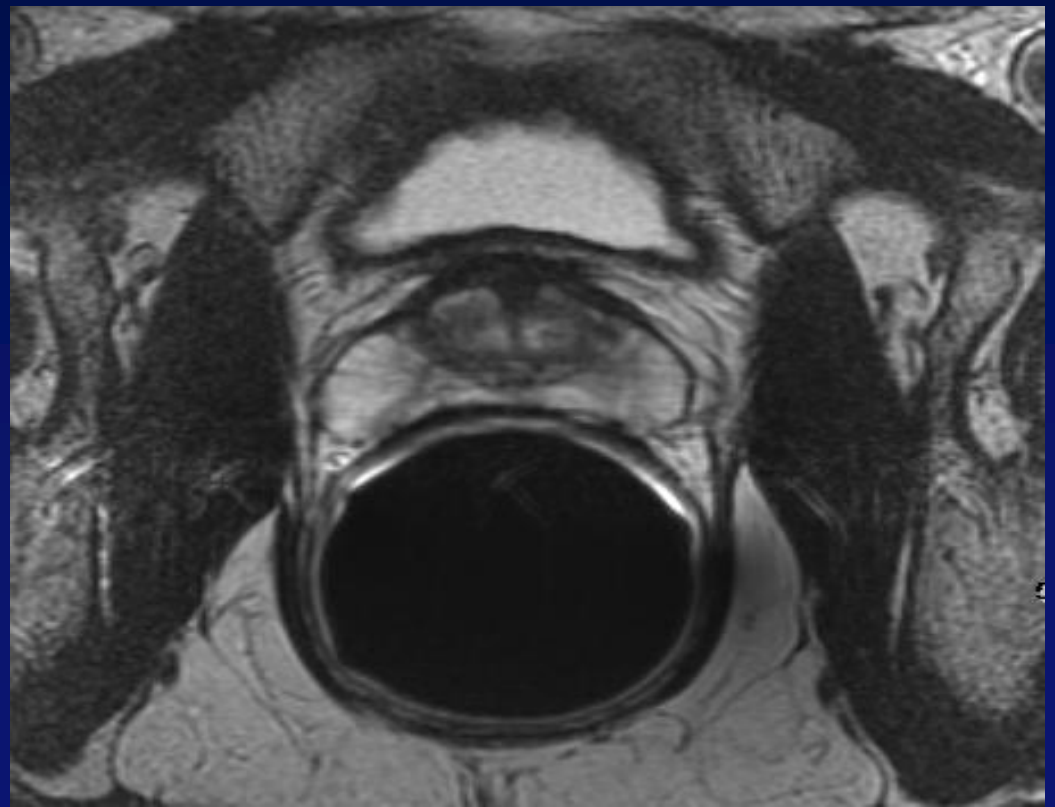
Pre-Treatment Evaluation:
Staging Radionuclide bone scan is NOT needed if PSA value is < 10ng/ml & there are no skeletal symptoms*



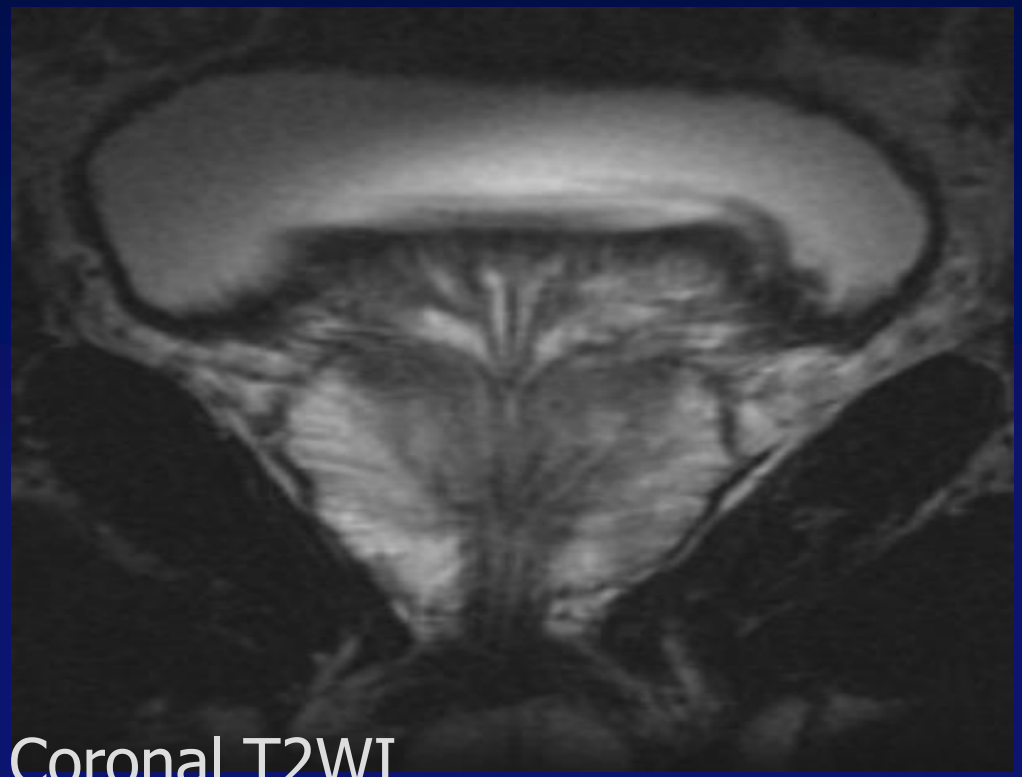
* JAMA 1993

MRI Prostate
T2-weighted Images

- Prostate zonal anatomy displayed
- Multi-planar assessment for anatomic cross-referencing
- Lesion detection/characterization: based on signal characteristics and morphology
- Periprostatic tissues well assessed



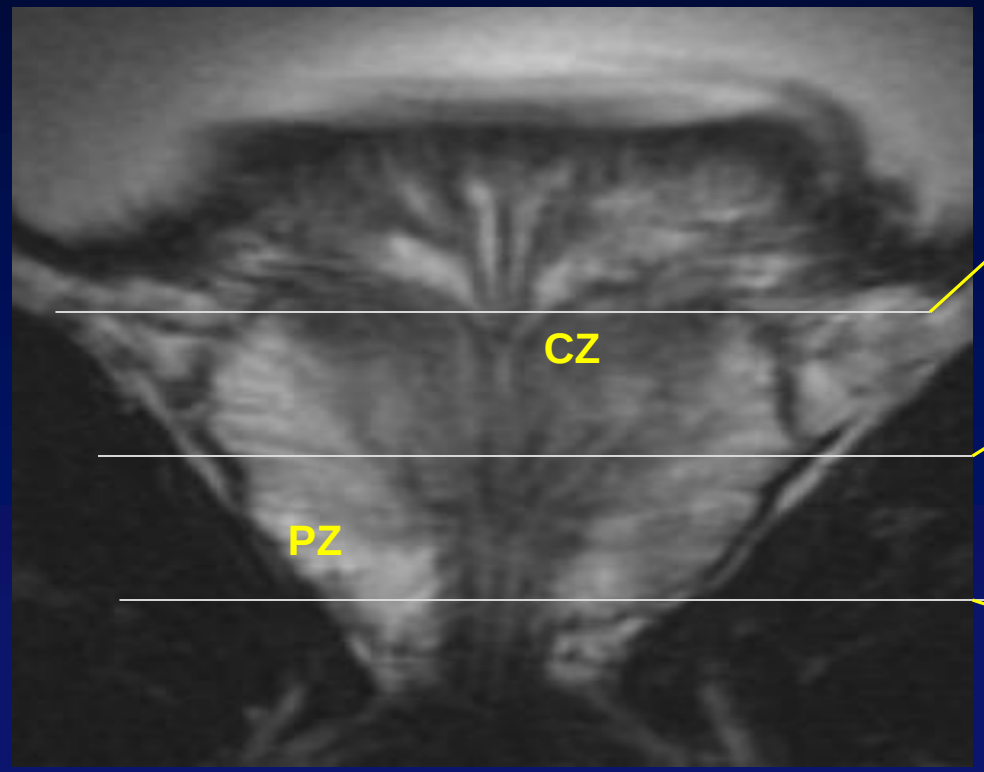
Axial T2WI



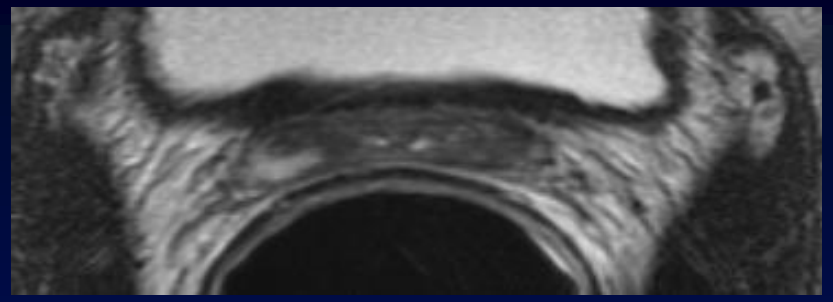
Coronal T2WI

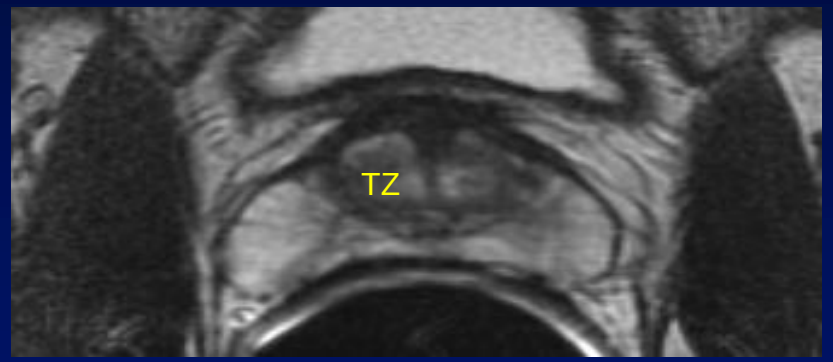
Zonal anatomy

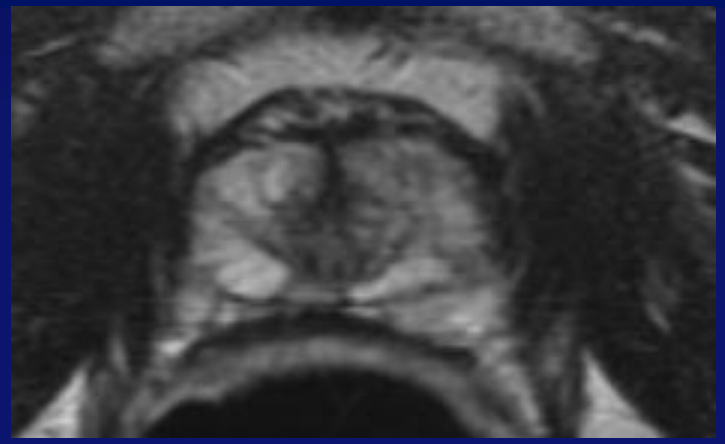
Coronal at urethra



COR T2WI





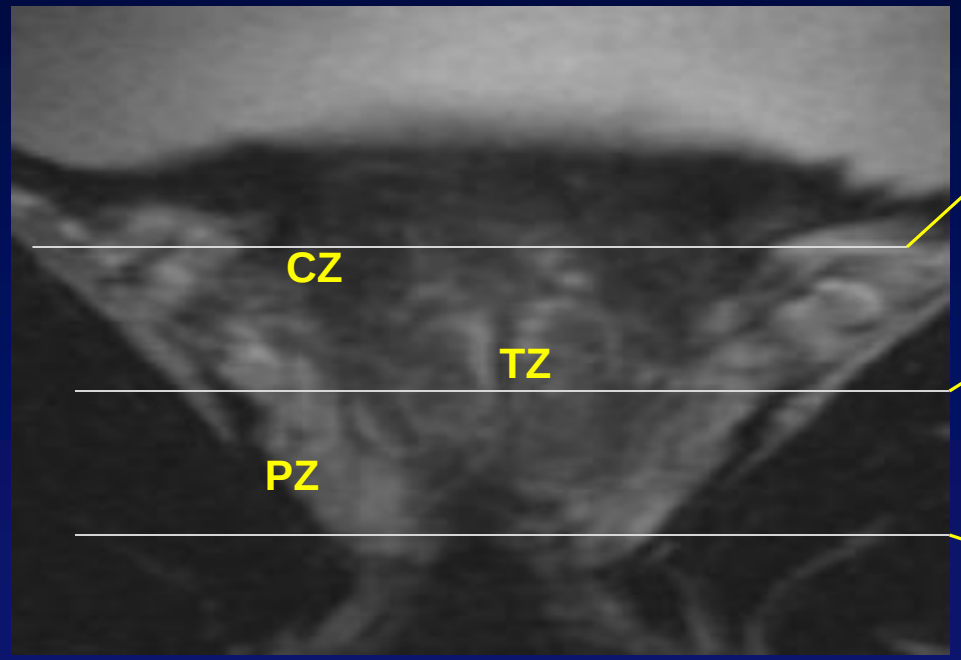


AX

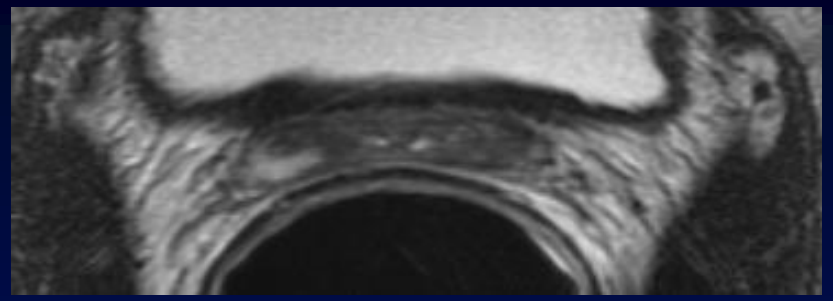
T2WI

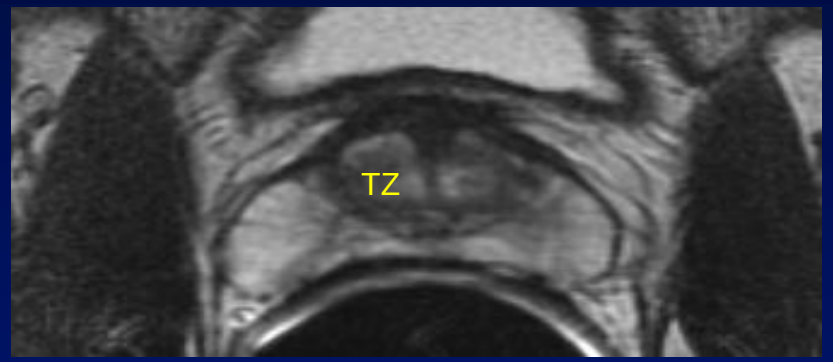
Zonal anatomy

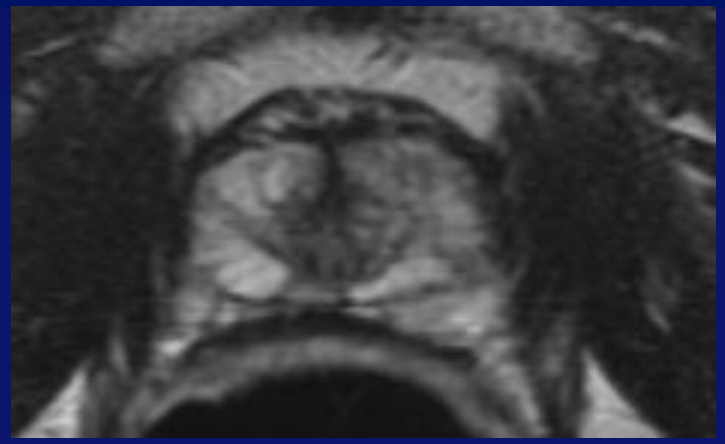
Coronal anterior to urethra



COR T2WI





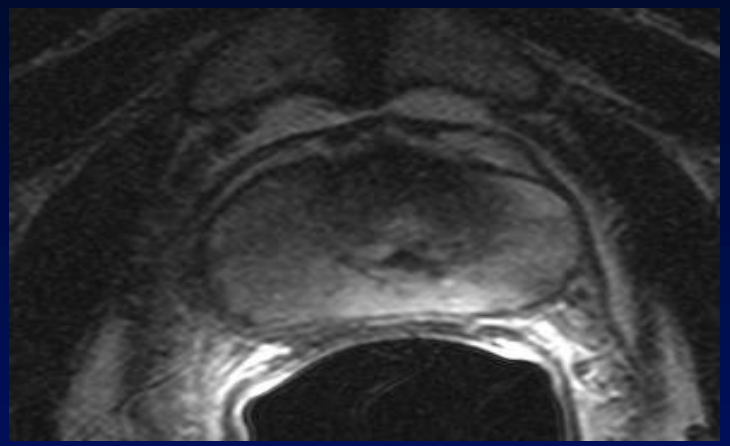


AX

T2WI

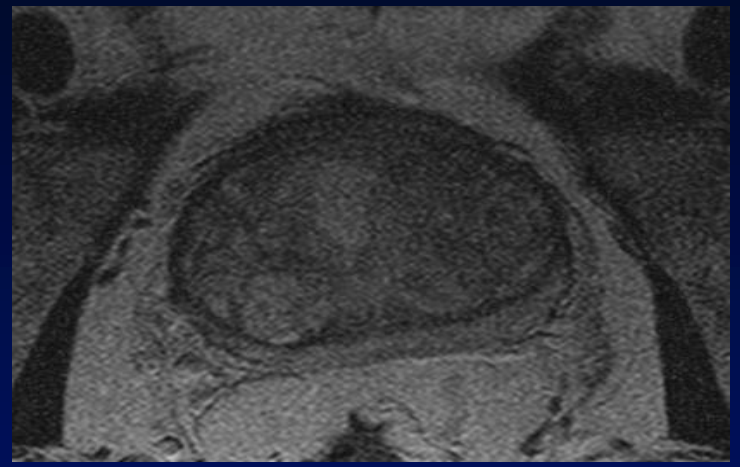
Prostate - MRI

Benign Prostatic Hyperplasia (BPH)



Small vol.

Moderate vol.



Large vol.

- Transition zone = 95%
- Rare BPH nodules in PZ, CZ, exophytic besides median lobe
- Trend but not direct causative relationship between volume of BPH and symptoms
- Secondary importance to cancer for almost all MRI exams
- Gland volumes: 22-25 g (or mL) young males to > 200 g (mL) older males from BPH

MRI Technique

- Prostate MRI, 1.5 T fairly standardized
  - Best image quality with use of an endorectal coil
- 3.0 T (More powerful MRI)
  - with or without ER coil

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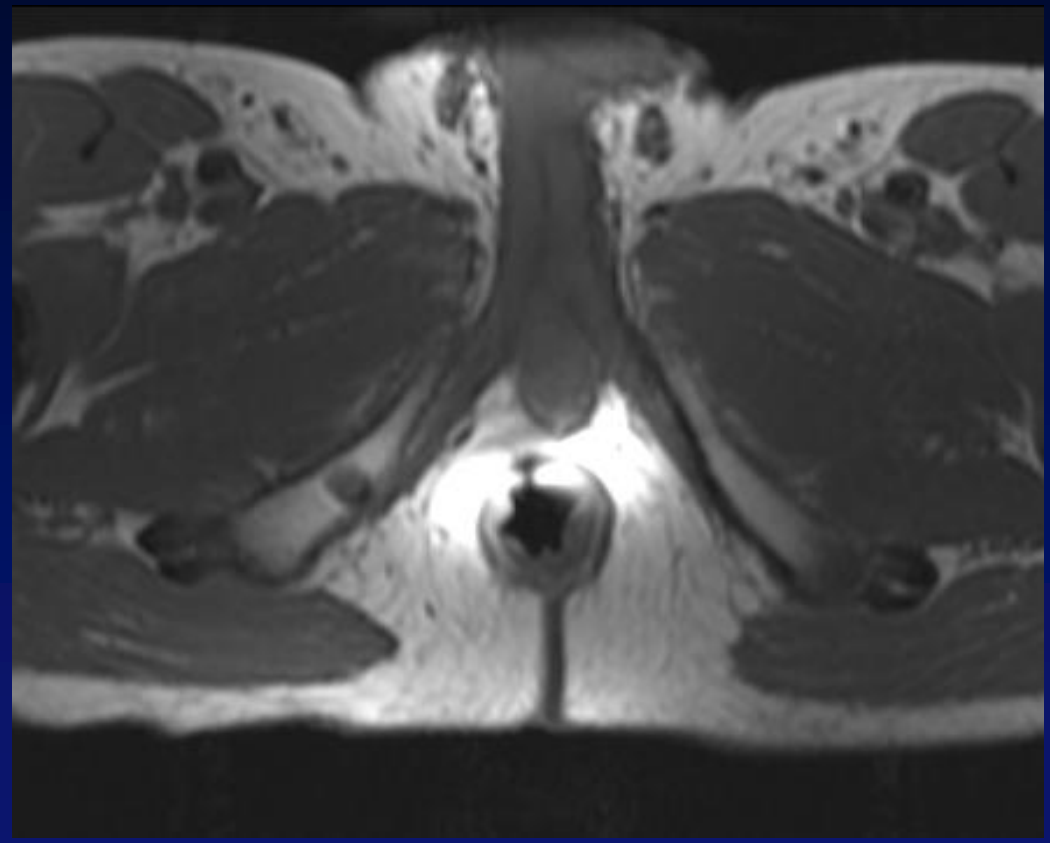
MRI Prostate
T1-weighted Pelvis

- Prostate homogeneous low intensity like CT
- Bone lesions
  - More sensitive than bone scan for small intramedulary mets*
- Enlarged nodes
- Post-biopsy hemorrhage



Axial T1WI

*Taoka T, et al., AJR Dec. 2001

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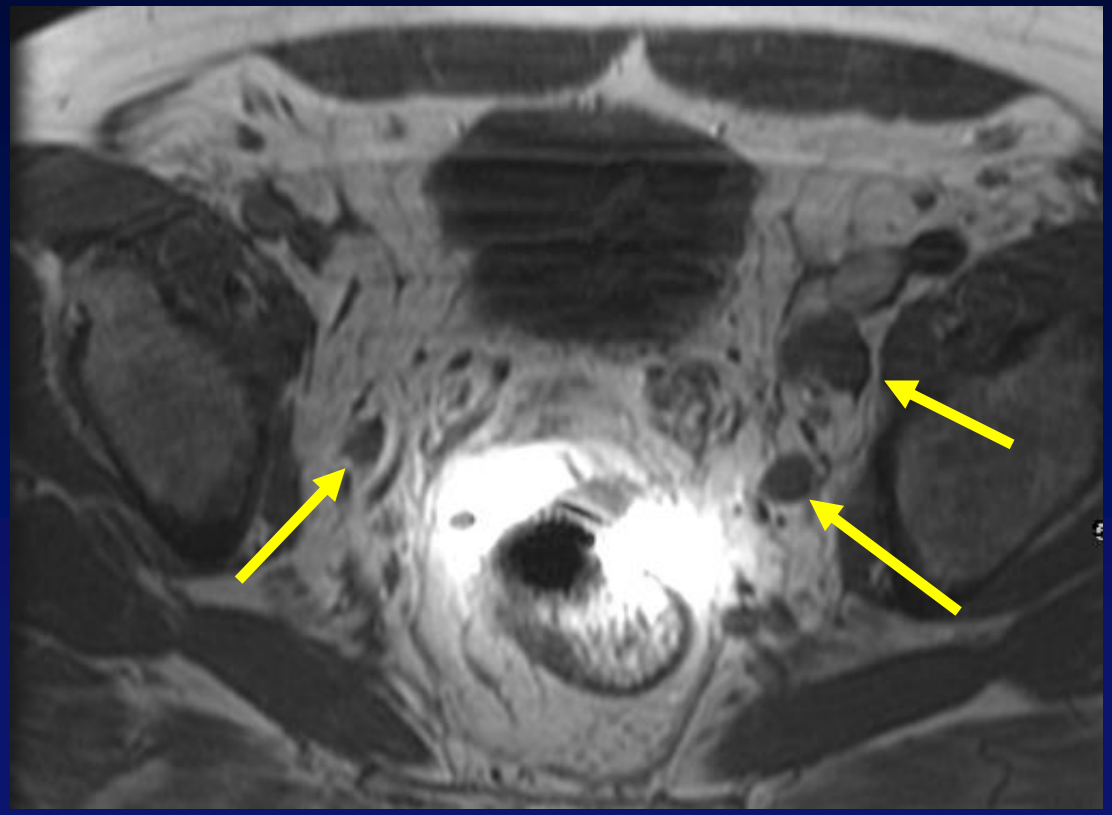
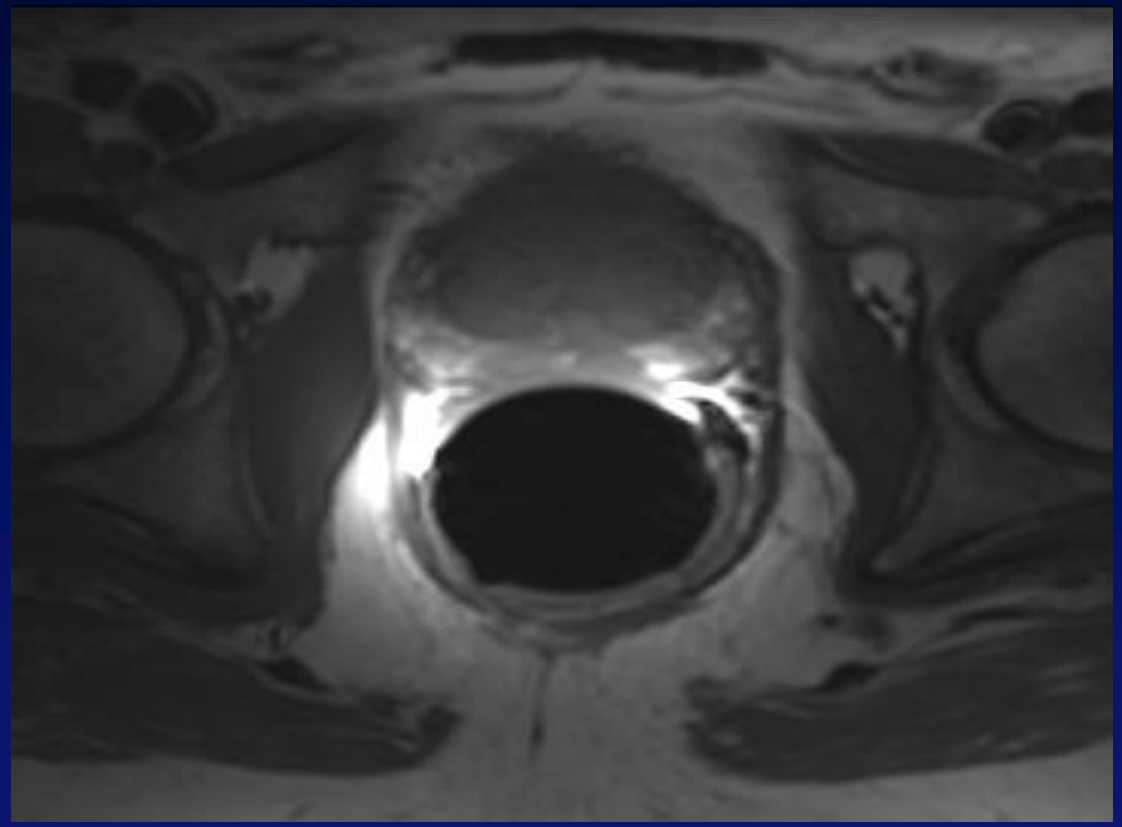


Axial T1WI

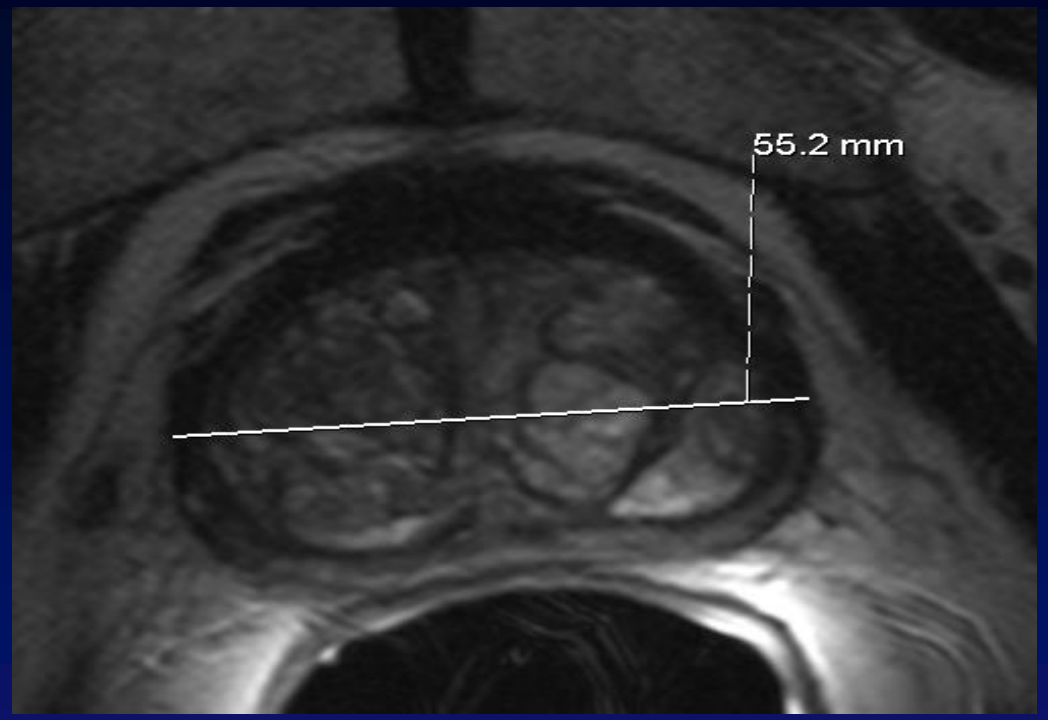
MRI Prostate
T1-weighted Pelvis

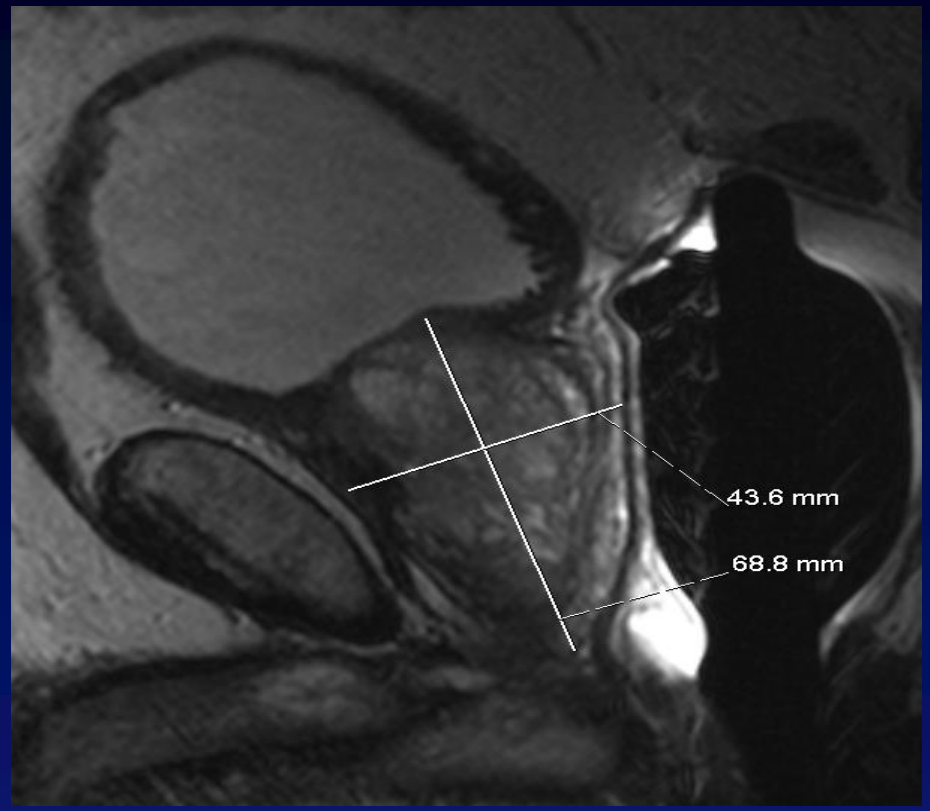
- Prostate homogeneous low intensity like CT
- Bone lesions
- Enlarged nodes
- Post-biopsy hemorrhage
  - image 3-4 weeks (minimum) after bx



Axial T1WI

Reporting gland volume

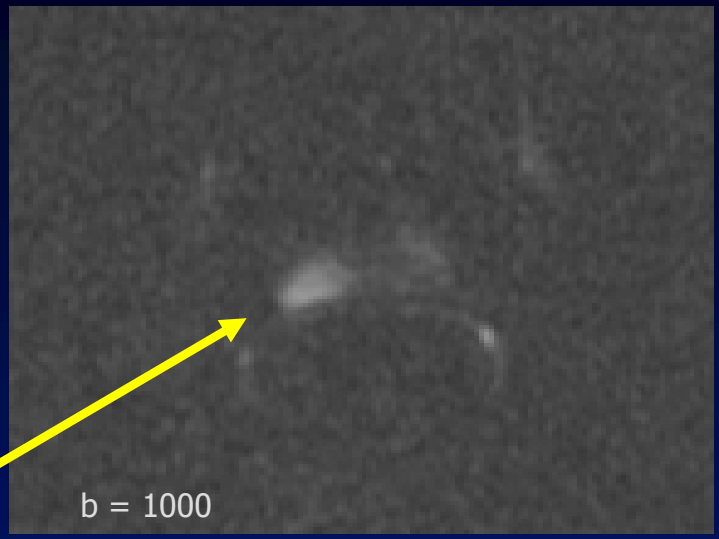




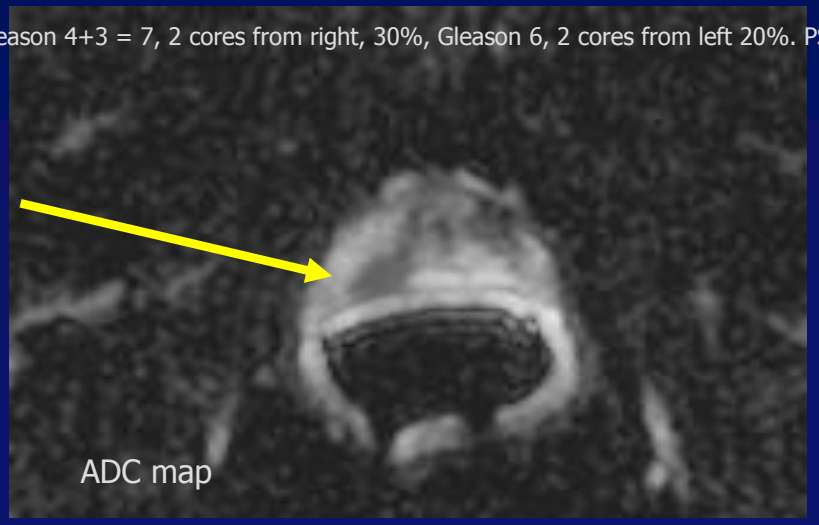
- Method of volume estimation
  - 3 dimensions
  - Use sagittal and transaxial – imitates sono technique
  - Be sure to extend AP back to anterior rectal margin
  - Calculate ellipsoid volume (4/3 PI * width axis radius * length axis radius * height axis radius.) appx. = W*H*L/2 or W*L*H*0.52

MRI: Diffusion – weighted imaging = DWI

- A method of prostate cancer detection in the peripheral zone (PZ)
- Measures free diffusion of water
- Restricted diffusion high SI on high b value image set = cancer suspicious lesion
- Dark lesions in PZ on ADC map = cancer suspect lesions



Gleason 4+3 = 7, 2 cores from right, 30%, Gleason 6, 2 cores from left 20%. PSA 8.4.

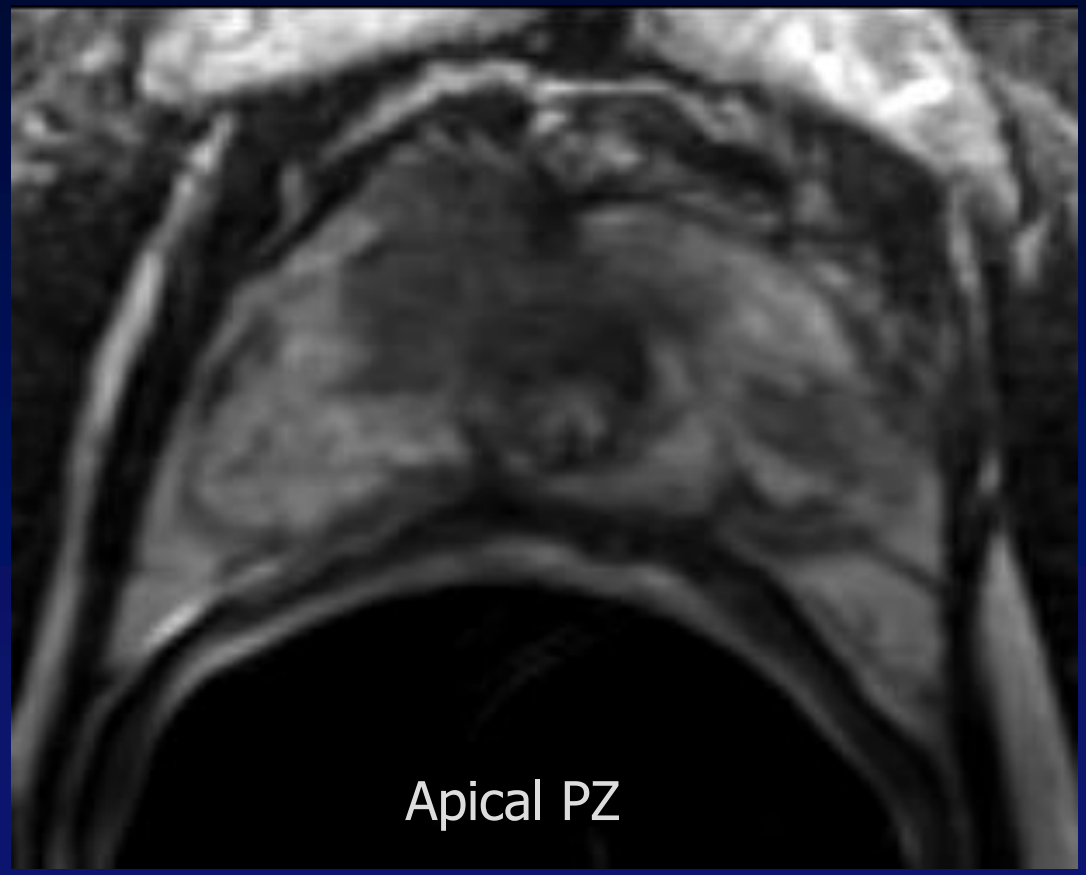


T2 Tumor localization: PZ

- Dominant mass
  - Confluent low signal centered in PZ
  - Tumor bulge
  - Loss of internal architecture

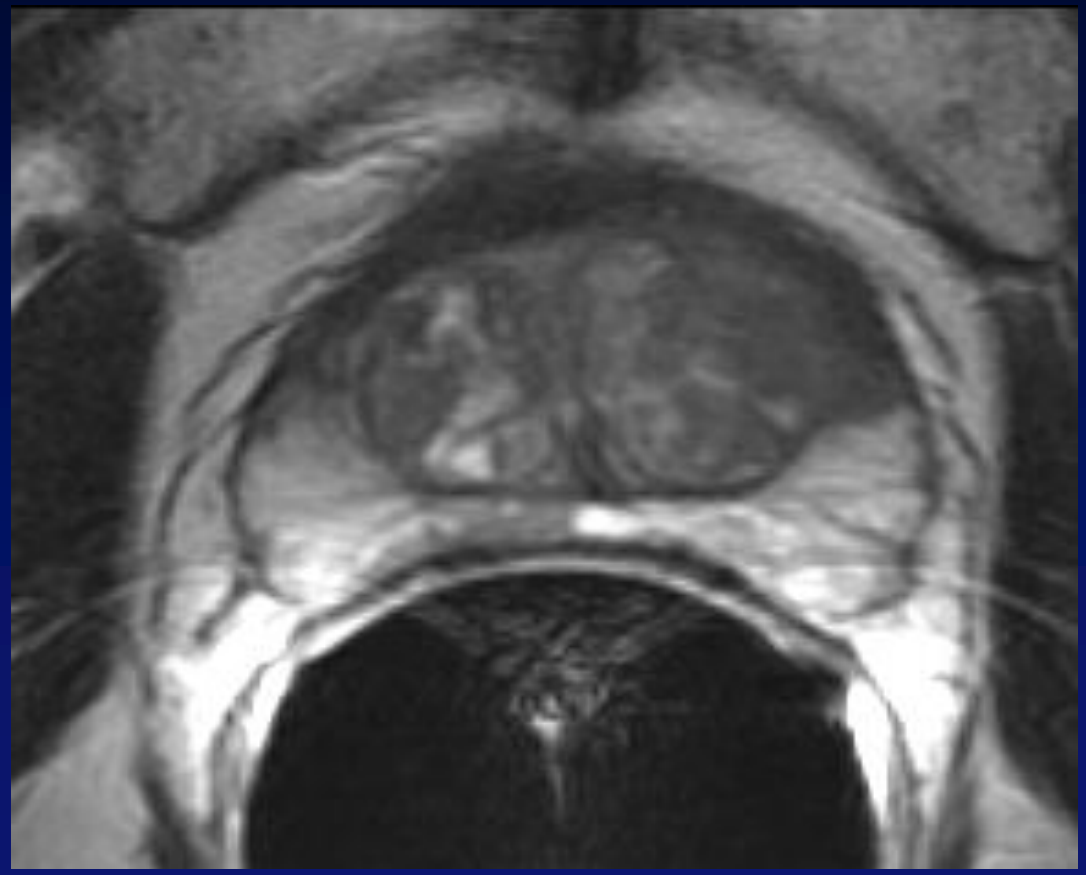
Tumor localization: PZ

- Dominant mass
  - Confluent low signal
  - Tumor bulge
  - Loss of internal architecture



Transition Zone Tumors

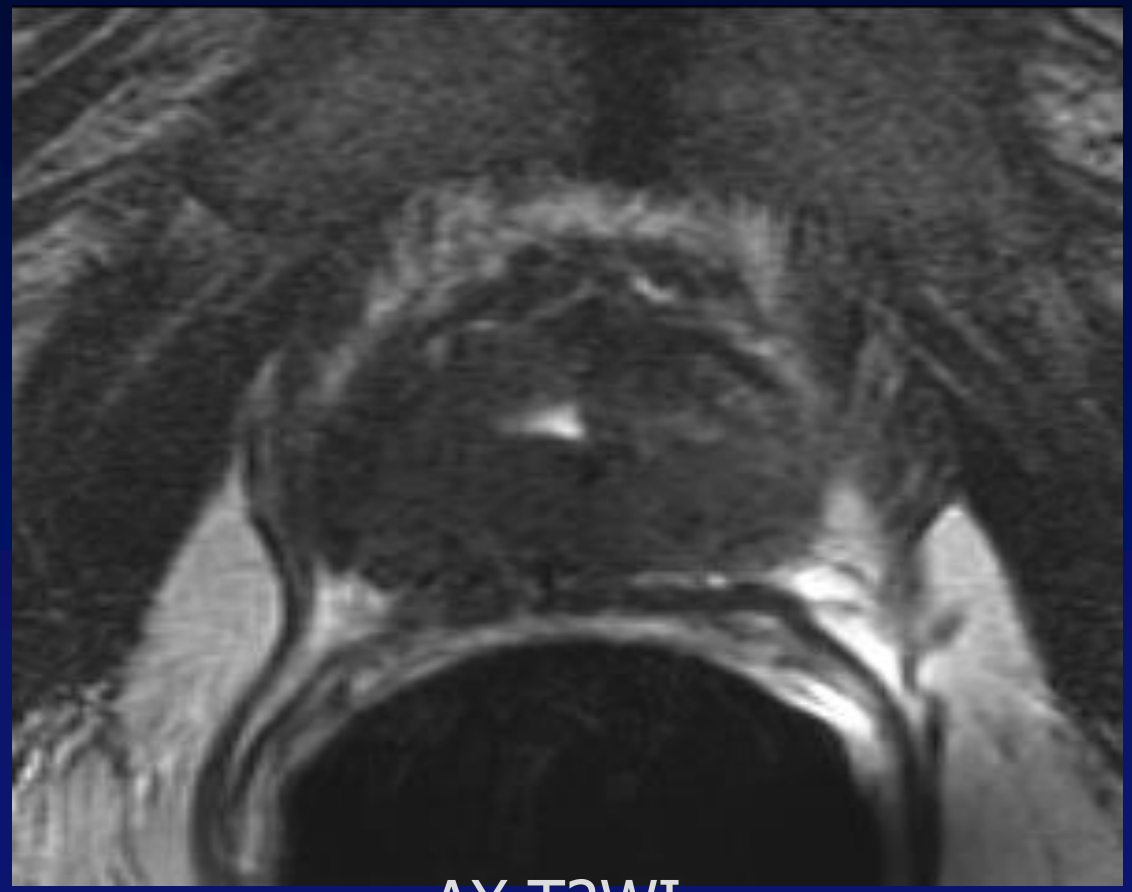
- Confluent low signal
- Lack of low signal capsule
- Loss of internal architecture
  - "smudged charcoal sign"
  - Crossing/invading nodules
  - Through TZ/PZ pseudocapsule
- Anterior fibromuscular stromal invasion



AX T2WI

Extraglandular Extension

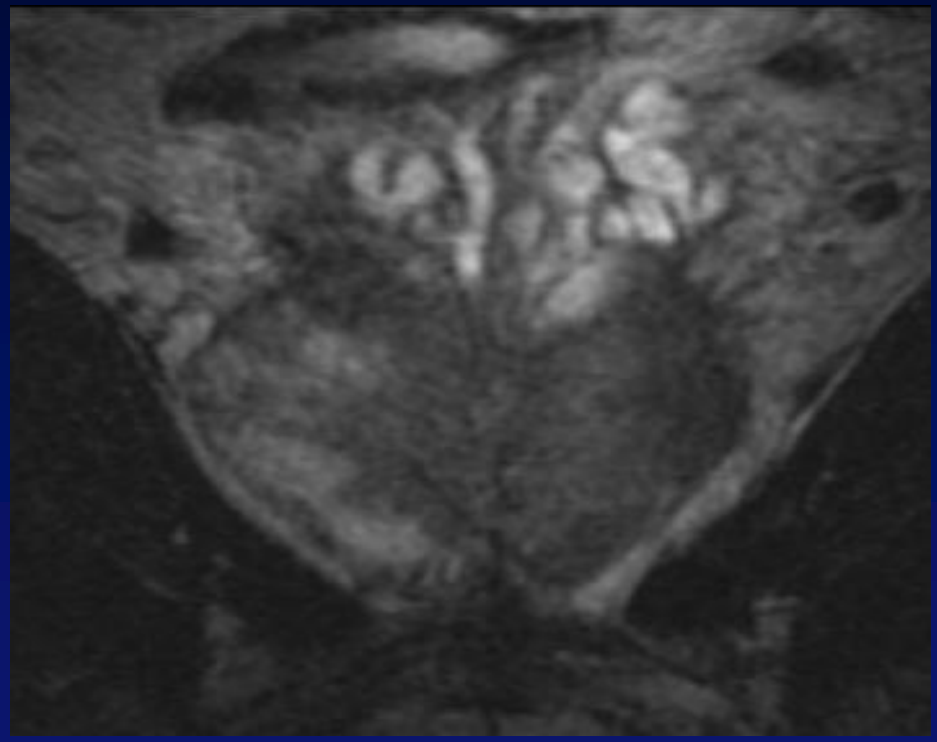
- Signs
  - Asymmetric NVB
    - Squared
    - Pointed
    - Spicules
    - Retraction
  - Extension to rectoprostatic angle
  - Extension through capsular margin
  - Bulging with irregularity



AX T2WI

Seminal Vesicle Invasion

- Types
  - Superiorly up the ducts (Type I, 26%)
  - From ECE to SVI (Type II, 33%)
  - "Metastatic" (Type III, 13%)
  - Type I+II, 28%

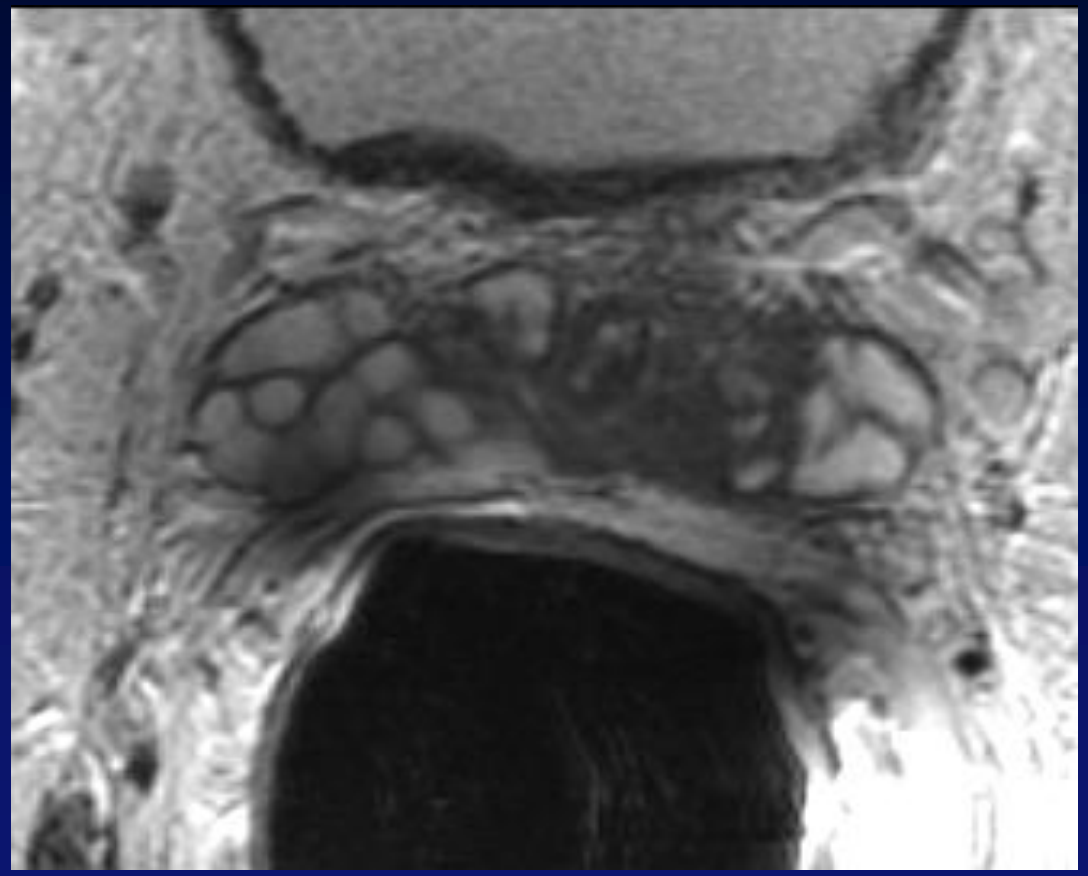


COR T2WI

Ohori et al, Am J Surg Pathol. 1993 Dec;17(12):1252-61
64/312 RRP with SVI (21%)

Seminal Vesicle Invasion

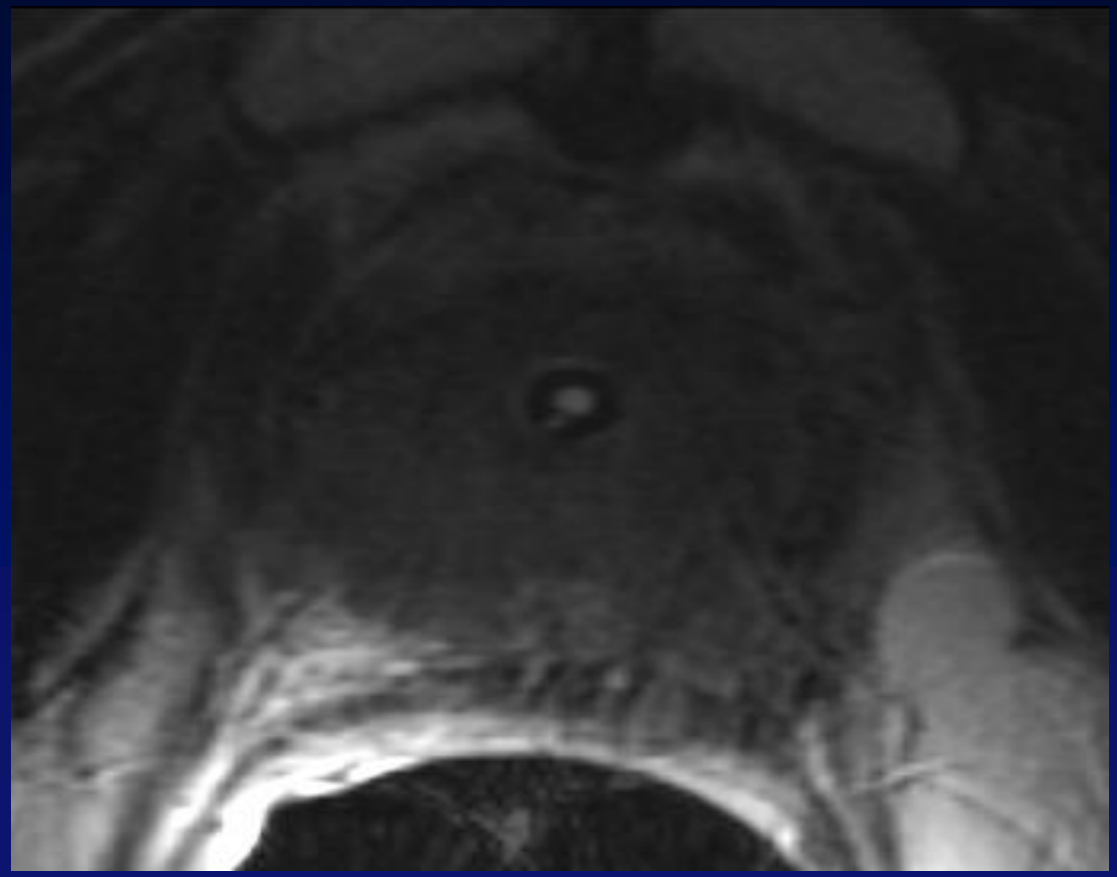
- Signs
  - Thickened walls
    - Asymmetric, side of tumor (Type II)
    - Up the ducts (Type I), transition
  - Filled in vesicles
  - Recognition based upon firm sense of normal



AX T2WI

T4 Disease

- Rectum
  - Gross invasion
  - Not with broad contact and bulge
- Bladder neck
  - Early difficult
  - Invasion of muscular wall



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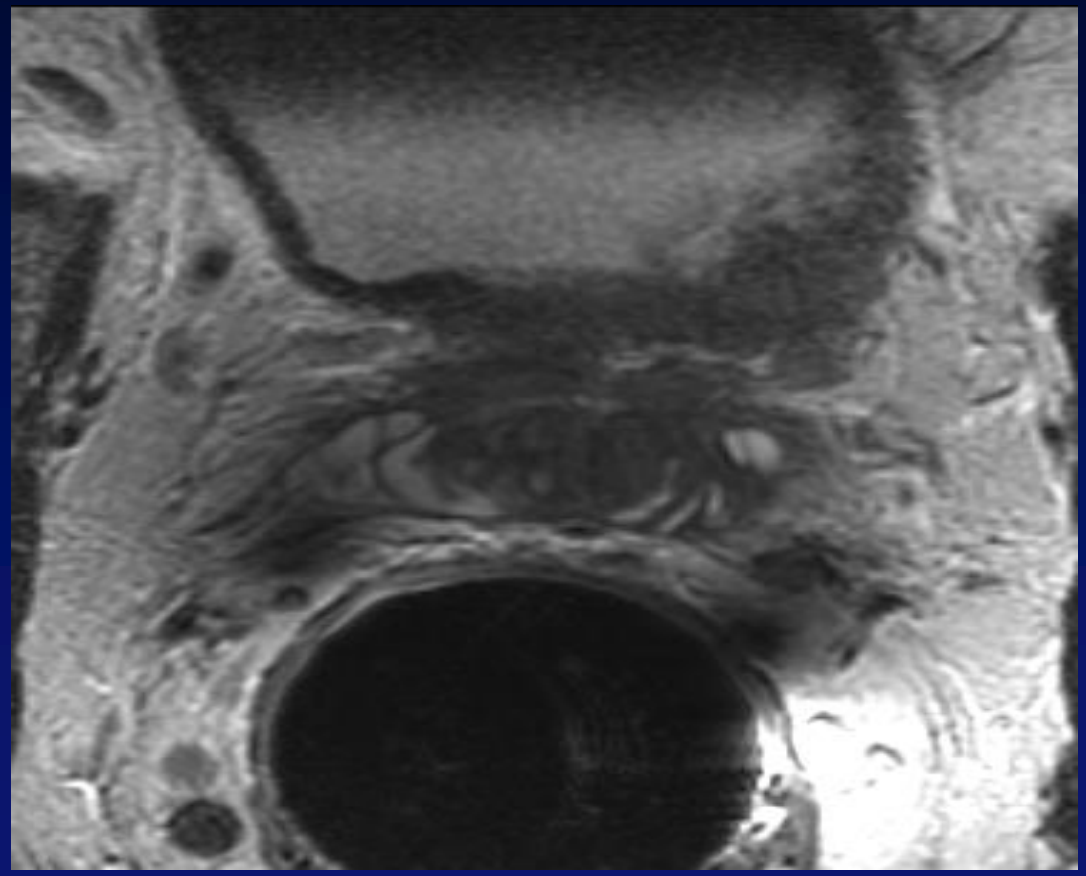
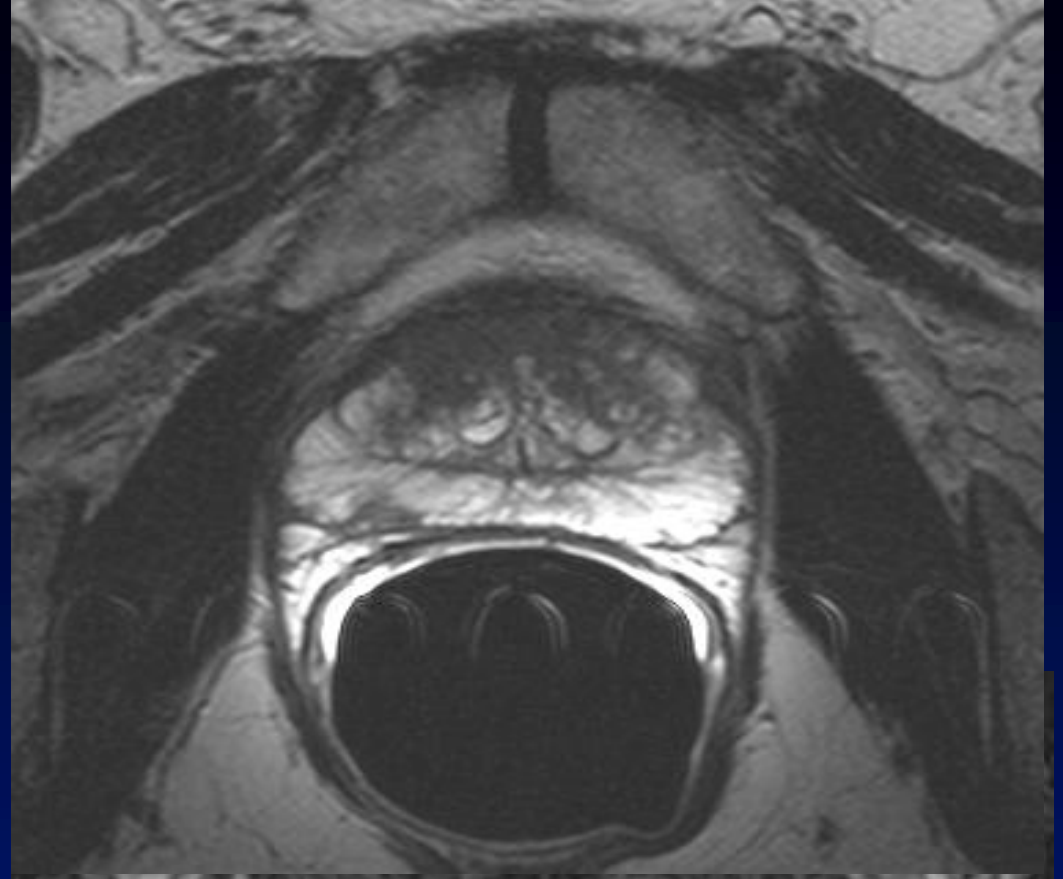
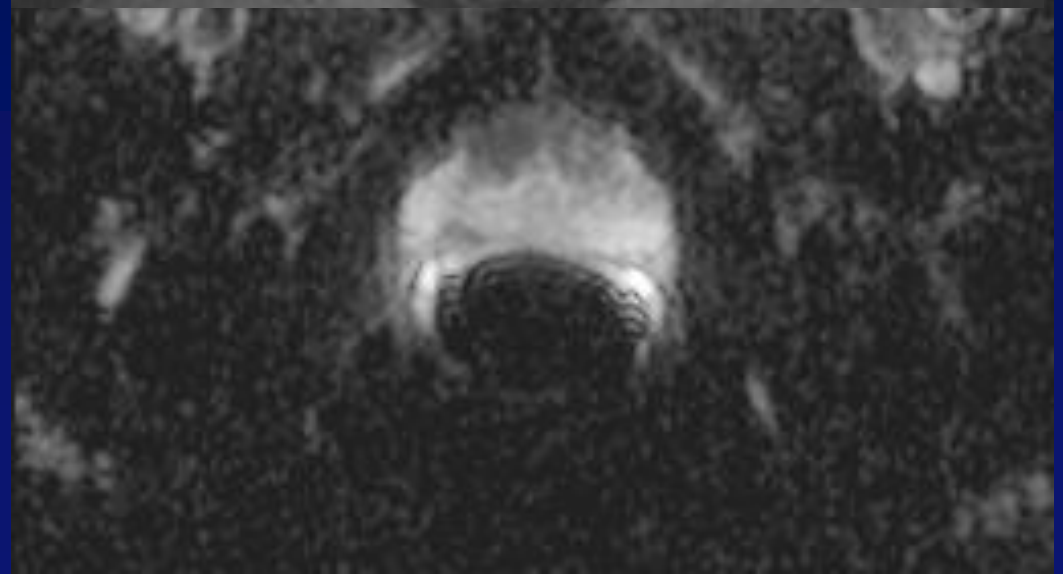


AX T2WI

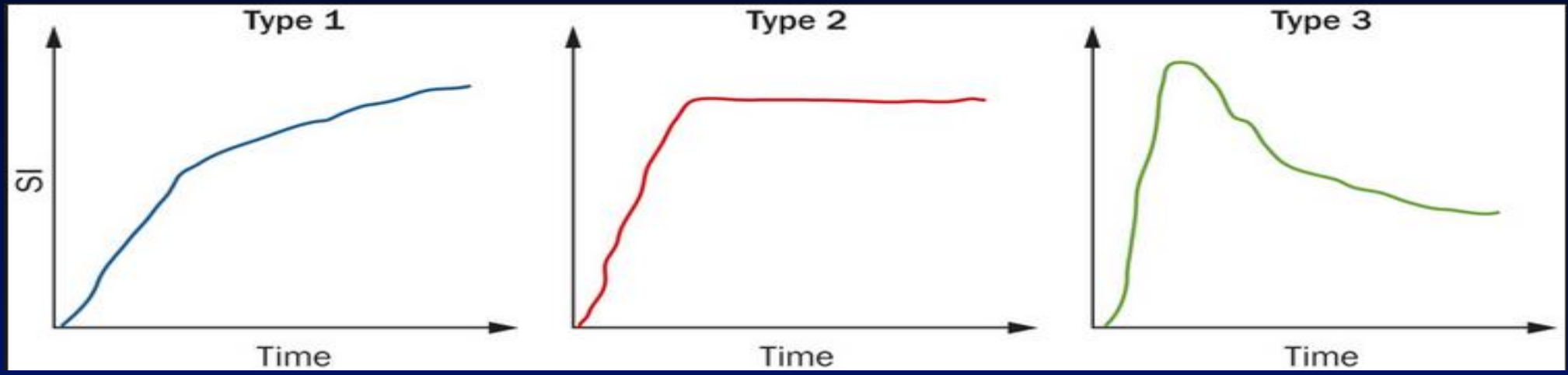
Multifocal DWI and T2WI: Suspected TZ and PZ tumors

- Possible FMS extension, questionable ECE
- Positive lesions on DWI (ADC map)
- Path showed no ECE, Gleason 3+4 = 7, tumor at both sites





Dynamic Contrast Enhanced (DCE)



Normal	Suspect	Ca
Rising	Plateau	Early peak
		Washout

Multiparametric MRI in prostate cancer management

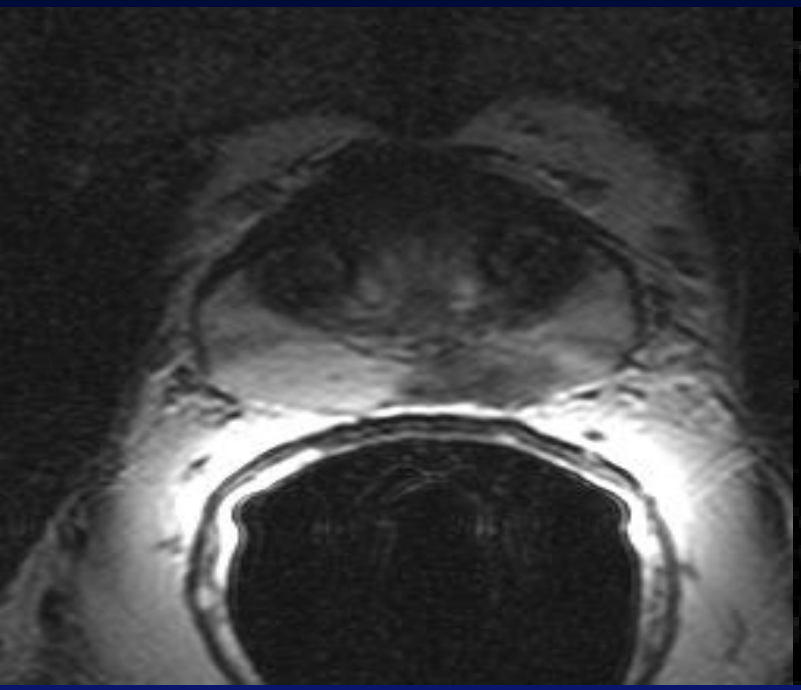
Linda M. Johnson, Baris Turkbey, William D. Figg & Peter L. Choyke

Affiliations | Contributions | Corresponding author

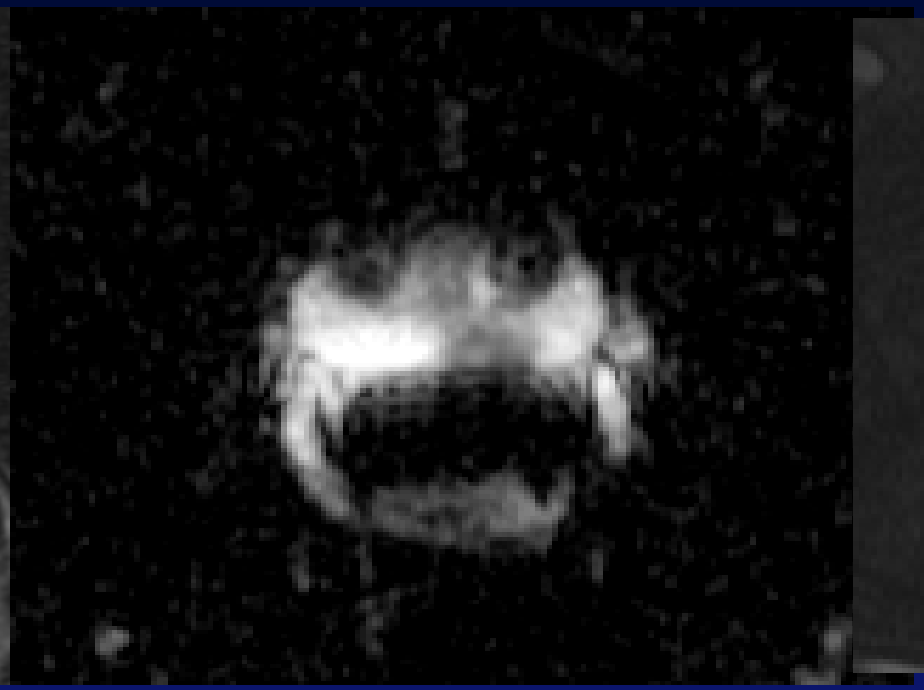
Nature Reviews Clinical Oncology **11**, 346–353 (2014) | doi:10.1038/nrclinonc.2014.69

Published online 20 May 2014

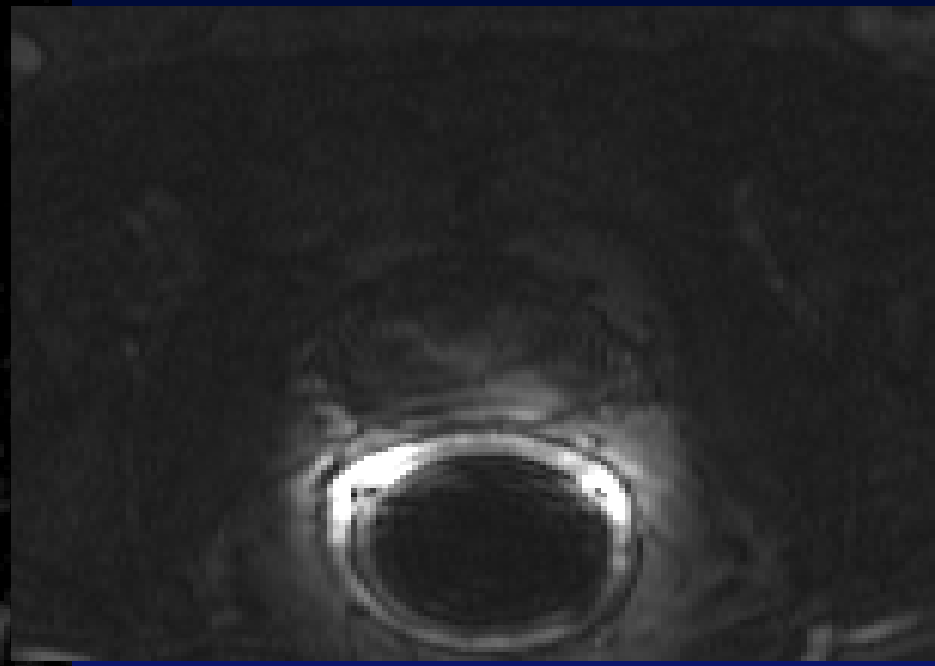
Small L PZ prostate cancer



T2WI



ADC



DCE early

Prostate Cancer Interpretation and Reporting System: PI-RADS v2 (2105)

- Based on *T2WI, DWI and DCE*
- PI-RADS v2 Assessment Categories
  - PIRADS 1 – Very low
    - (clinically significant cancer is highly unlikely to be present)
  - PIRADS 2 – Low
    - (clinically significant cancer is unlikely to be present)
  - PIRADS 3 – Intermediate
    - (the presence of clinically significant cancer is equivocal)
  - PIRADS 4 – High
    - (clinically significant cancer is likely to be present)
  - PIRADS 5 – Very high
    - (clinically significant cancer is highly likely to be present)

Active Surveillance

- “aim to maintain the opportunity of curing more aggressive disease via structured monitoring (e.g., with PSA testing and repeat prostate biopsies), which attempts to identify any change in disease risk (e.g., an increase in Gleason score) that would merit definitive treatment.”

Filson CP, Marks LS, Litwin MS.CA Cancer J Clin. 2015 Jul-Aug;65(4):265-82.

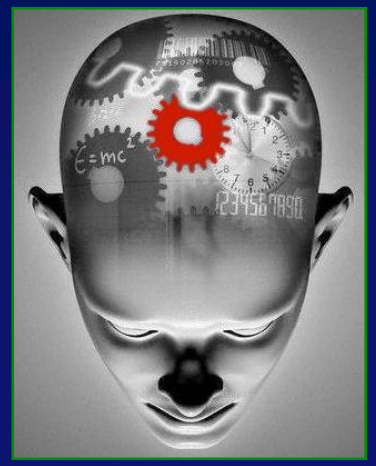
MRI in Active surveillance

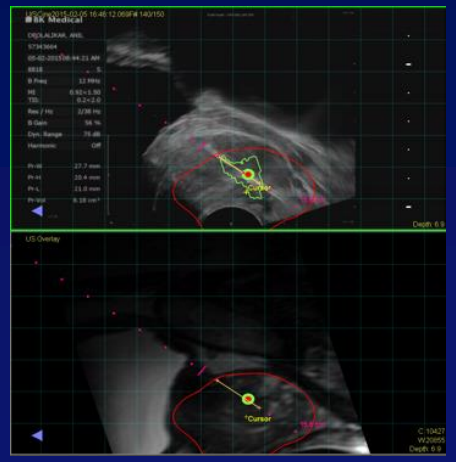
- MRI used to verify clinically insignificant disease
  - Small tumor or none
  - Safe to delay treatment
  - Continue PSA monitoring
  - Repeat biopsy, sometimes with another MRI to find target
  - Sometimes finds target for biopsy or repeat biopsy

MR guided biopsy

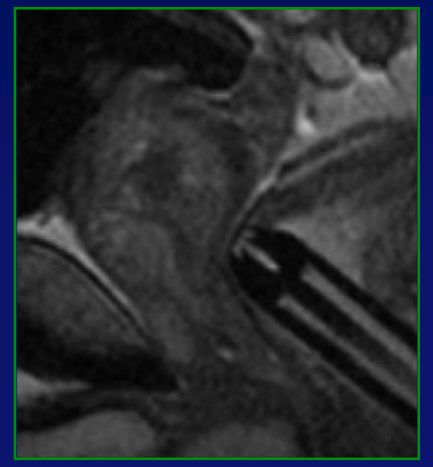
US-MRI fusion

Cognitive





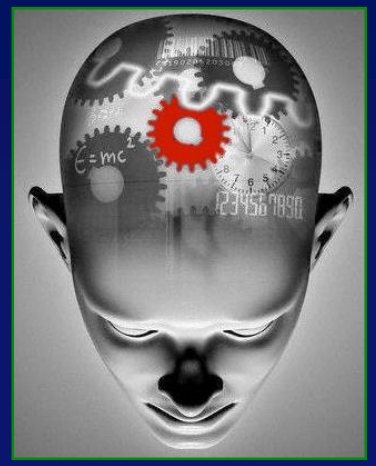
In-bore

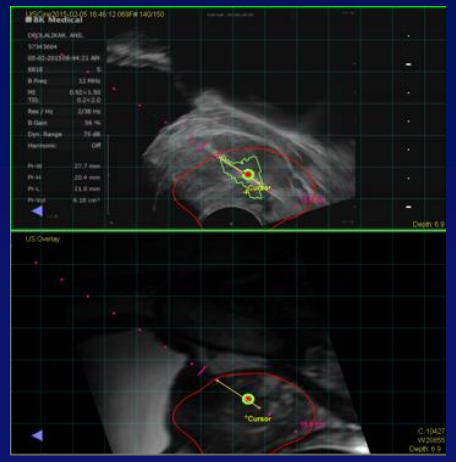


MR guided biopsy

US-MRI fusion

Cognitive





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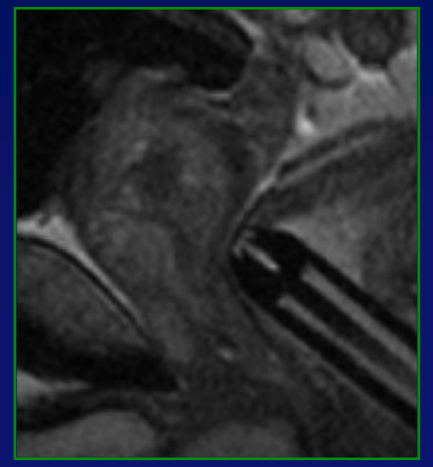
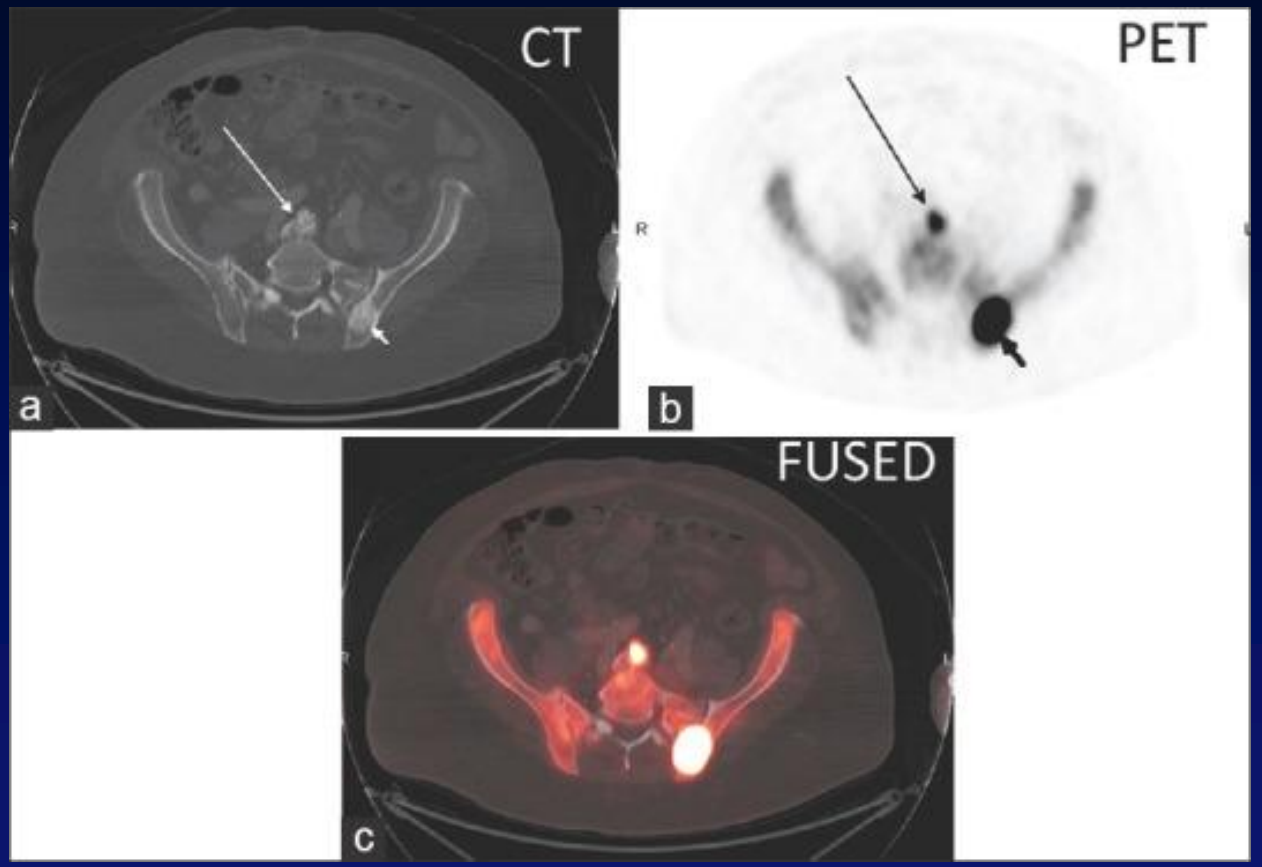


Imaging after treatment

- Indications (when appropriate)
  - Suspected local recurrence after prostatectomy or radiation therapy (PSA recurrence)
  - Suspected metastatic disease based on clinical features and absence of disease at the treated prostate site.
  - Re-imaging detected metastatic disease to judge treatment effect
  - May allow for localized recurrence or metastatic treatments.
- Options
  - CT, MRI, Bone scan
  - FDG PET (Only some utility for very aggressive advanced disease)
  - Newer nuclear medicine tests

^{18}F Sodium Fluoride PET/CT

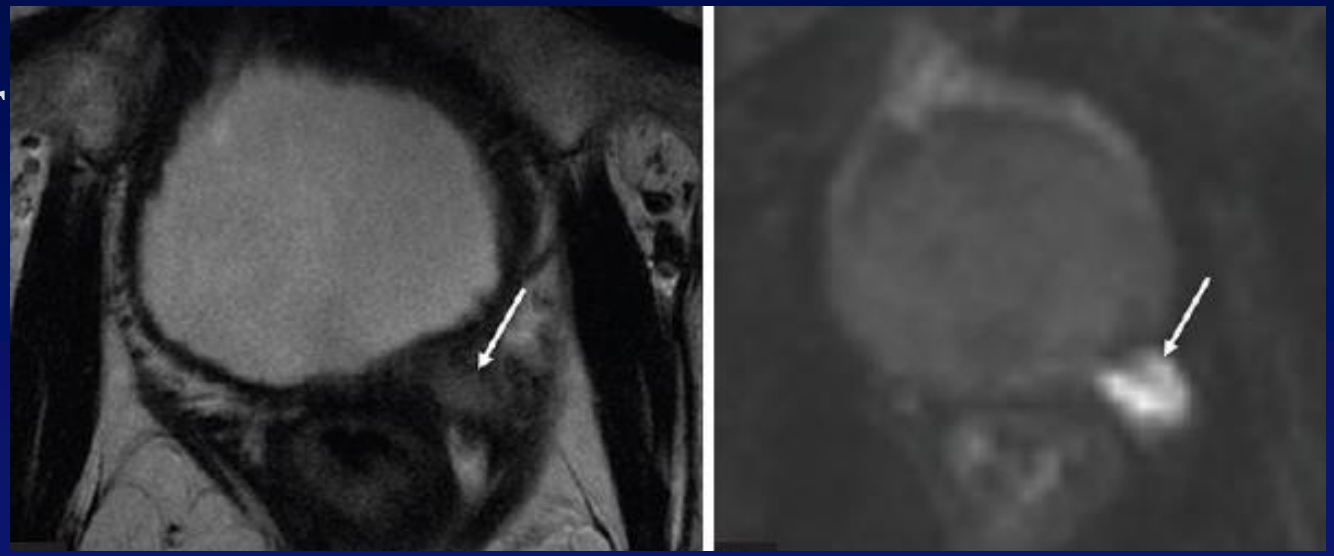
- More sensitive than traditional bone scan
- Risk of false positive sites detected
- Example: 2 “hot spots” – the larger one is a metastasis, the smaller one is degenerative bone changes
- Available at VAMC, many insurances not covering



Oldan JD, Hawkins AS, Chin BB. 18F Sodium Fluoride PET/CT in Patients with Prostate Cancer: Quantification of Normal Tissues, Benign Degenerative Lesions, and Malignant Lesions. World journal of nuclear medicine. 2016 May;15(2):102.

MRI for local recurrence

- Effective for detection of local disease recurrence after prostatectomy when PSA recurs
- More likely positive for higher PSA (1.5 or higher)
- Detection of recurrence after radiation therapy more challenging but possible

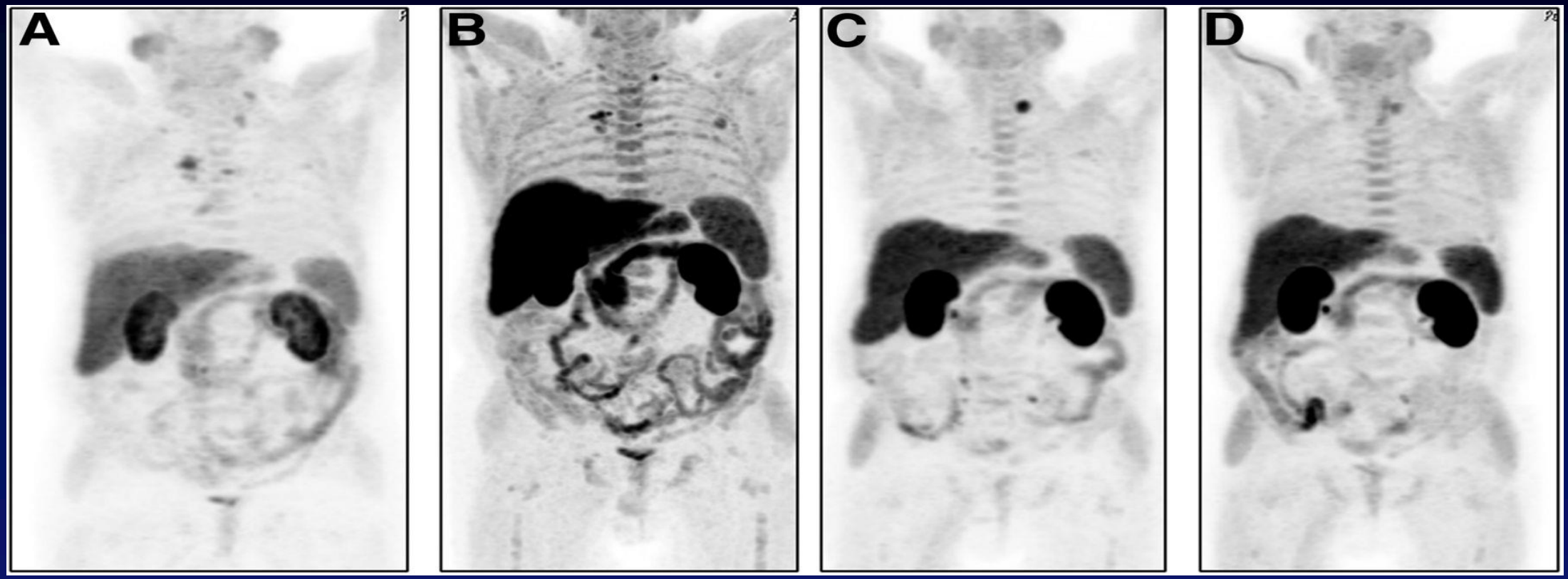


Oppenheimer DC, Weinberg EP, Hollenberg GM, Meyers SP. Multiparametric magnetic resonance imaging of recurrent prostate cancer. Journal of clinical imaging science. 2016;6.

Axumin (18F-fluciclovine or FACBC)

- FDA approved since May 2016 for detection of recurrence suspected from elevated PSA after treatment
- Axumin (fluciclovine)
- Has shown efficacy in detection of metastatic disease in normal sized nodes, bone mets without CT abnormality

C-11 Choline PET



Post RRP, PSA up, mets detected

Progressed on anti-androgen

Localized treatments – partial response

62-y-old patient with Gleason score of 4 + 4 and pT3b N1(8/24)Mx cancer. Francesco Ceci et al. J Nucl Med 2016;57:49S-54S

JNM The Journal of NUCLEAR MEDICINE

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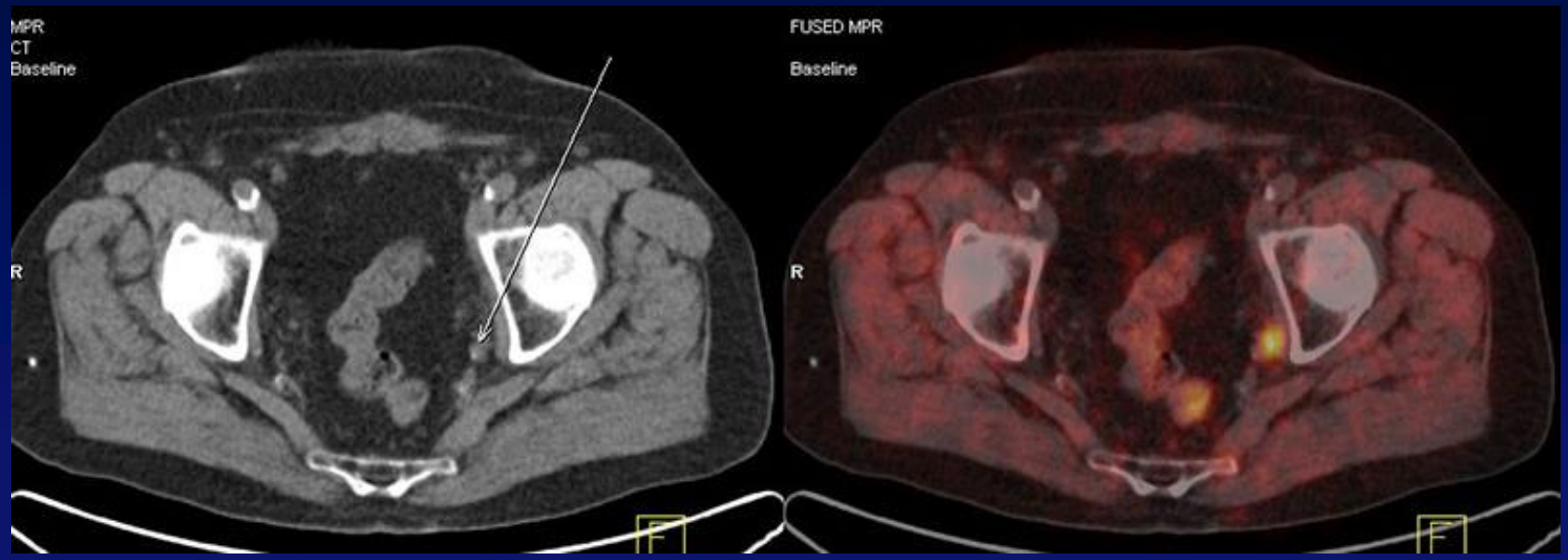
68Ga-PSMA PET/CT

- 68Ga-PSMA PET/CT
  - Multiple studies showing ability to detect bone and lymph node metastases where other modalities fail



http://www.praxis-nuklearmedizin.de/en/services/pet-ct/pet-ct-in-prostate-cancer-psma-petct/

Thank You – Q and A