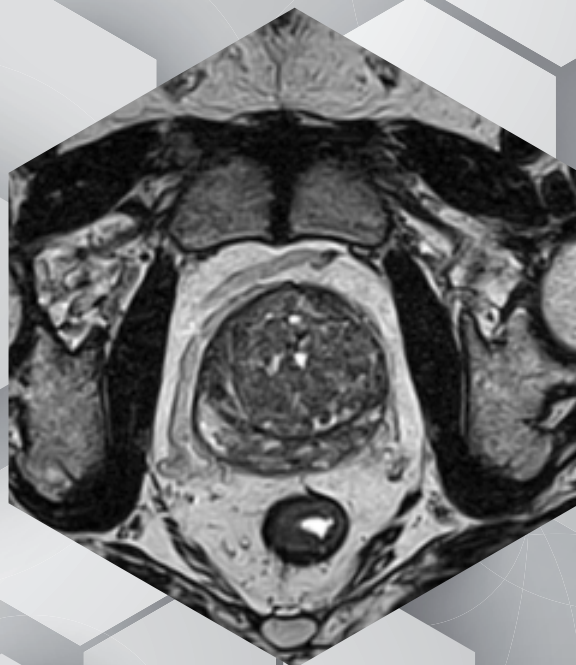


PROSCAN
MRI ONLINE

IMAGING GUIDE

Prostate



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INTRODUCTION

Background (Story)

It is universally and scientifically accepted that prostate cancer occurs in asymptomatic men or as an incidental finding later in life. Prostate cancer is the second leading cause of male cancer deaths. About 250,000 cases occur in the USA alone. Until now we have used the digital rectal screening exam and the serum PSA (prostate-specific antigen). Discrepancies as to how to use these tools have occurred domestically and internationally. This makes the decision regarding definitive treatments (e.g. nothing, surgery, radiation, hormone therapy, chemotherapy) all challenging.

Distinguishing which cancers are aggressive, and which are nonaggressive, has relied previously on sonographic guided biopsy using Trans Rectal Ultrasonography (TRUS). The Gleason score has been used pathologically after biopsy to determine which cancers have aggressive potential (Gleason 6 or greater, more aggressive).

Why MRI?

- **Advantages**

- A major advantage, and real value, of MRI is in visualizing tumors that involve the distal anteroapical prostate. This is difficult to see with other modalities, and more challenging to reach surgically.

- **Disadvantages**

- Bleeding after biopsy can obscure a tumor, but a tumor often pushes blood out of the way (i.e. "tumor exclusion sign") so blood circumscribes the tumor.
- Artifacts can be caused by air and stool in the rectum. Therefore, preparation for exam is key (see protocols at end of this section).
- Low signal-to-noise ratio (SNR) on diffusion-weighted imaging (DWI) with high b-value diffusion imaging (over 1,000). However, aggressive tumors "stand out" while benign or nonaggressive tissue "fades away" as b-value goes up.
- Anything above a 3mm slice of T2 weighted imaging for T staging is too thick.
- 3D MRI provides very thin slices (1mm or less), but tissue contrast is slightly lower than 2D.
- Lower grades of tumor (i.e. non-aggressive) are often not seen on MRI.
- Tumors 5mm or less may not be seen without doing dynamic contrast-enhanced (DCE) MRI (e.g. injecting contrast).

- Hormone therapy (e.g. dutasteride) decreases utility of DCE MRI.
- It is unclear what minoxidil therapy for baldness or hair loss does to the appearance of an MRI exam.
- **Indications**
 - Benign Prostatic Hypertrophy (BPH)
 - Prostate-Specific Antigen (PSA)

Pearls of MRI

- **Various signs have been proposed for the diagnosis of extracapsular extension (stage T3a)**
 - contact with the capsule >12 mm
 - protrusion with rounded margins of the glandular borders
 - deformation or interruption of the capsular profile
 - tissue layering in the periprostatic fat
 - obliteration of rectoprostatic angle and asymmetry of the neurovascular bundles
- **Therefore, invasion is certain when the neurovascular bundle is absent in its usually identifiable portion. In contrast, invasion cannot be excluded in the tracts where the neurovascular bundle is not normally visualized.**
- **DCE MRI plays a much more important role in breast MR than it does in the prostate MR, at this time.**
- **DWI is more important in the prostate than breast.**

Exam Preparation and Protocols

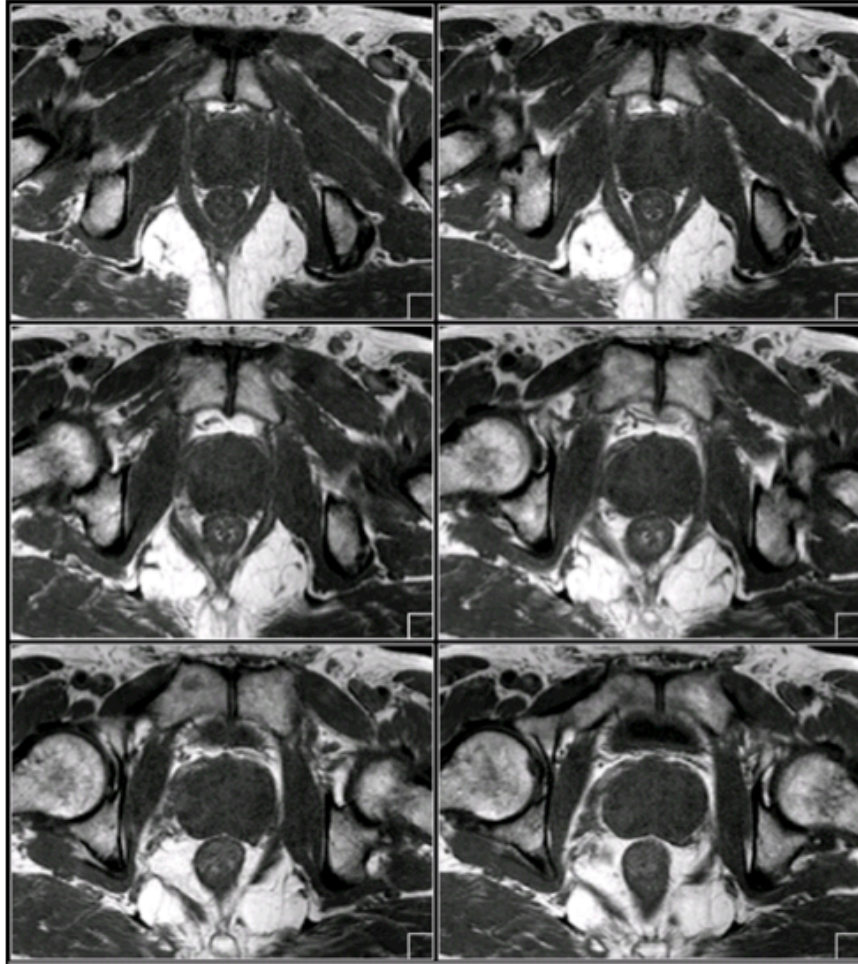
- **Preparation for the Exam**
 - Nothing by mouth (i.e. nil per os, NPO) 3 Hours; Soft Diet 24 hours
 - Screen for Claustrophobia
 - Feet First
 - Fleets 1-3 Hours Before Arrival Enema
 - Manual Cleansing in Restroom Right Before Exam
 - Bentyl 10 mg by mouth (i.e. per os, PO), optional
- **Protocol at 1.5 Tesla for Prostate (see below but add 3D if mapping with TRUS for biopsy is under consideration)**
 - T2WI 2D axial + sagittal + coronal (Sag and Ax only if no 3D T2 isotropic TSE FSE)
 - DWI axial
 - b-values 0 and 400, 800, 1200, 1600 s/mm², and apparent diffusion coefficient (ADC) maps
 - T1-weighted image (T1W1) axial 2D or 3D
 - 3D turbo-spin-echo (TSE) T2WI sagittal or axial (isotropic) only for mapping programs
 - Multiplanar reconstruction (MPR) of < 1.5 mm slice thickness with 50% overlap

- DCE-MRI axial
 - Only aggressive prostate cancer is fast wash-in in early phase (<2 min), and wash-out in delay phase (4-5 min); speed = slice every 15 sec or less ~ ideal 8 sec
- Gd-DTPA equilibrium enhanced 3D turbo-field-echo (TFE) axial

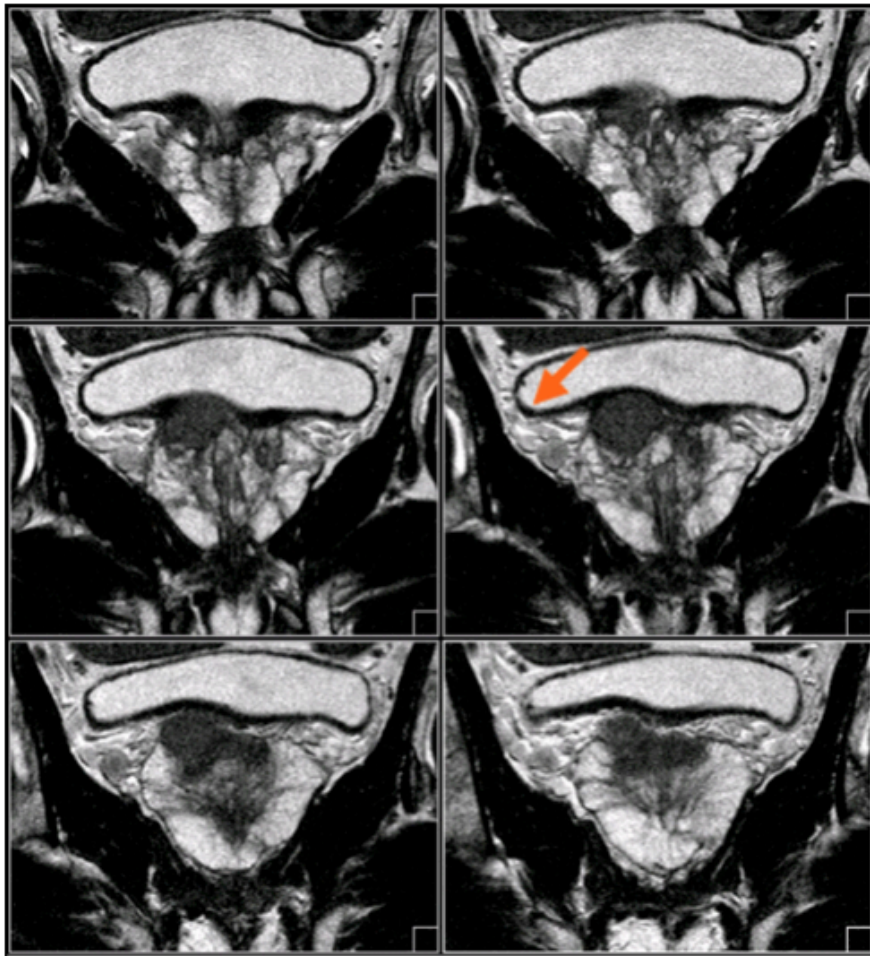
- **Imaging Introduction**
 - A five-point scoring system has been developed based on a combination of mpMRI (multi-parametric MRI) findings that consist of:
 - T2 hypointense mass-type lesion
 - Diffusion-weighted imaging (DWI) and the severity of restriction (greater restriction = higher signal)
 - The ADC parametric map which is simply a pixel by pixel display of micromolecular motion or lack thereof (more restriction = slower velocity = lower signal)
 - Dynamic contrast enhanced MRI (DCE-MRI) which demonstrates enhancement, enhancement peak or intensity; speed of enhancement, and enhancement washout
 - +/- Spectroscopy (little used routinely)

- **Pearls Regarding Technique**
 - Avoid reliance on contrast enhancement (e.g. DCE MRI) when a patient is on hormone therapy.
 - Patients on dutasteride should be off for at least two cycles before DCE MRI.
 - Diffusion imaging must include a series of b-values. The b-value reflects the intensity and sensitivity of diffusion restriction, and is like the torque of a car's engine. The higher the b-value, the more sensitive the sequence is to diffusion restriction. YOU MUST have a b-value of at least 1,400. A typical series of b-values would be 0, 50, 150, 800, and 1,600.

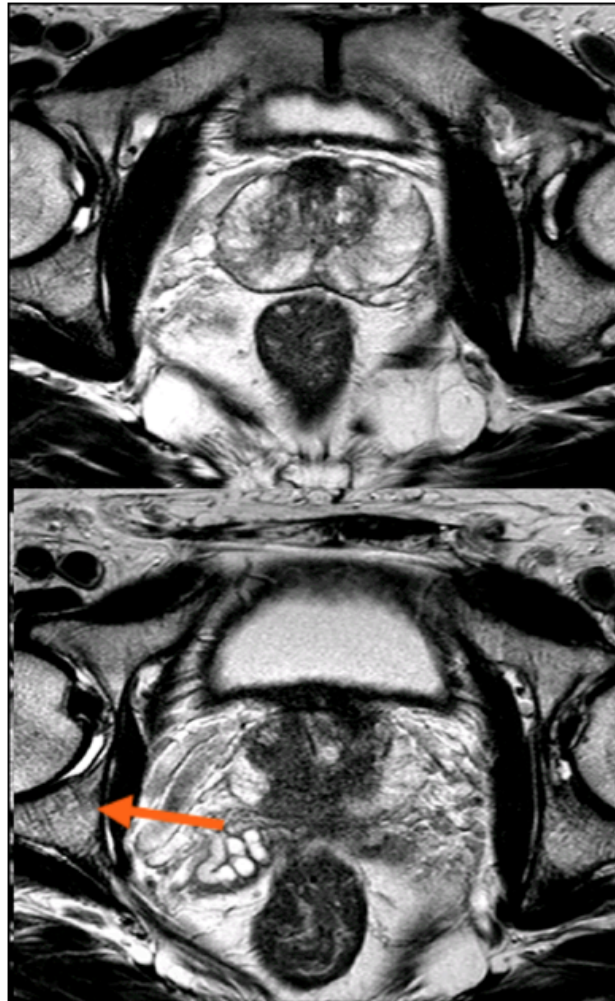
Sample Cardiac Coil Non-Endorectal Prostate Study



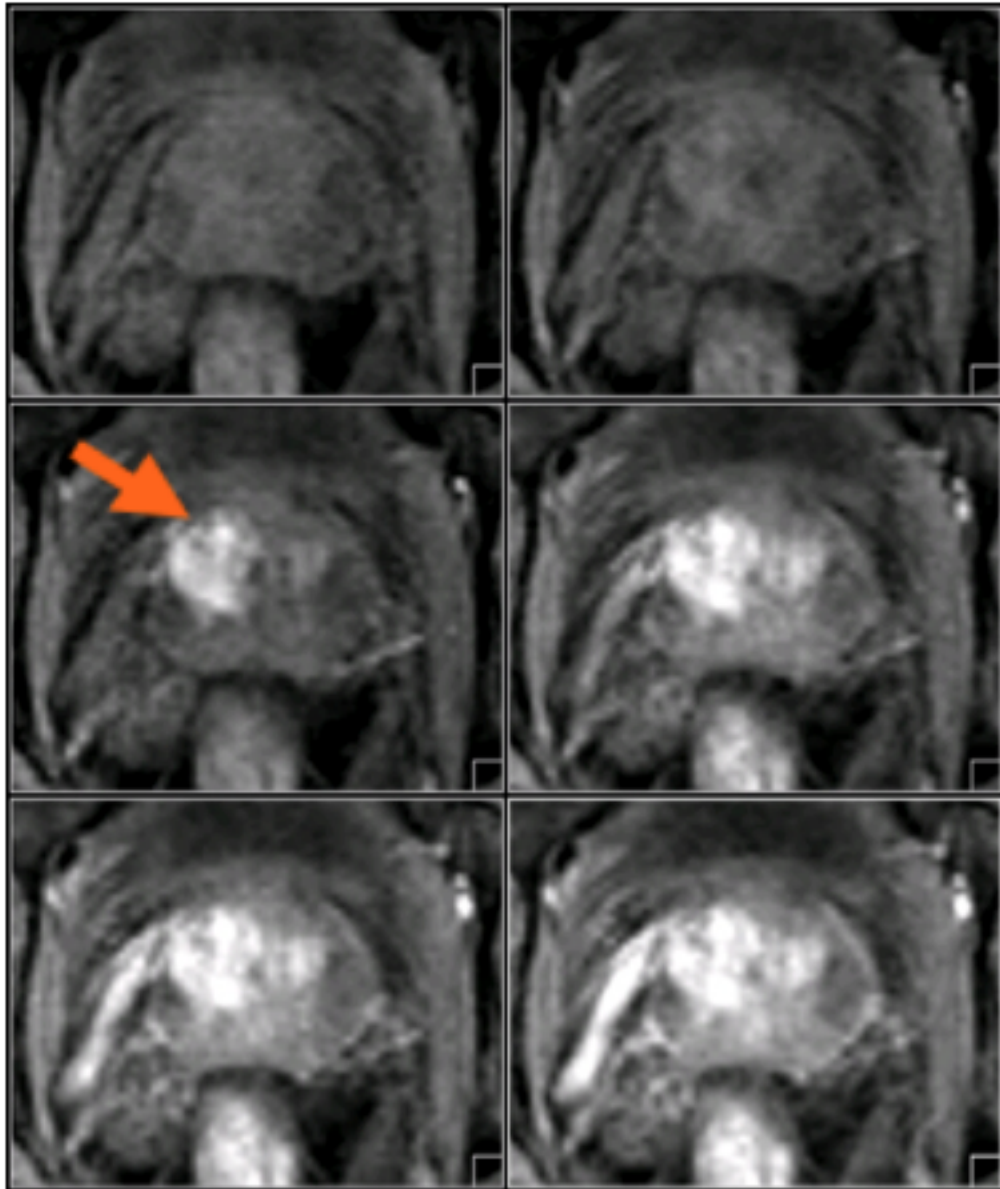
T1WI: TSE T1w TSE; FOV = 420mm; 512 matrix; 1.0 x 1.2 mm pixel size; 38 slices of 3.5 mm;
SENSE FACTOR 2; TR = 600; TE = 8; TF = 4; Scantime 1:21



Coronal T2WI TSE/FSE: TSE T2w TSE; FOV = 200 mm; 512 matrix; 0.5 x 0.7 mm pixel size; 24 slices of 3.5 mm; TR = 3200; TE = 130; TF = 24; Scantime 3:48



Axial T2WI FSE/TSE: 2 slices shown: FOV = 200 mm; 512 matrix; 0.6 x 0.7 mm pixel size; 24 slices of 3.5 mm; TR = 3200; TE = 130; TF = 24; Scantime 4:26

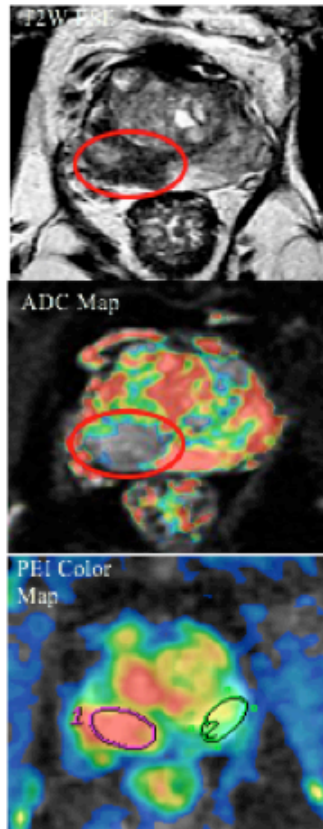


Dynamic Contrast-enhanced MRI DCE MRI: Images acquired from the first 6 dynamic 3D acquisitions; 3D T1 TFE with SPIR; FOV = 420 mm; 256 matrix; 1.6 x 1.6 mm pixel size; 30 slices of 3.5 mm; SENSE FACTOR 2;TR = 4.8;TE = 2.4; FA = 10; Scantime 13.5s/3D

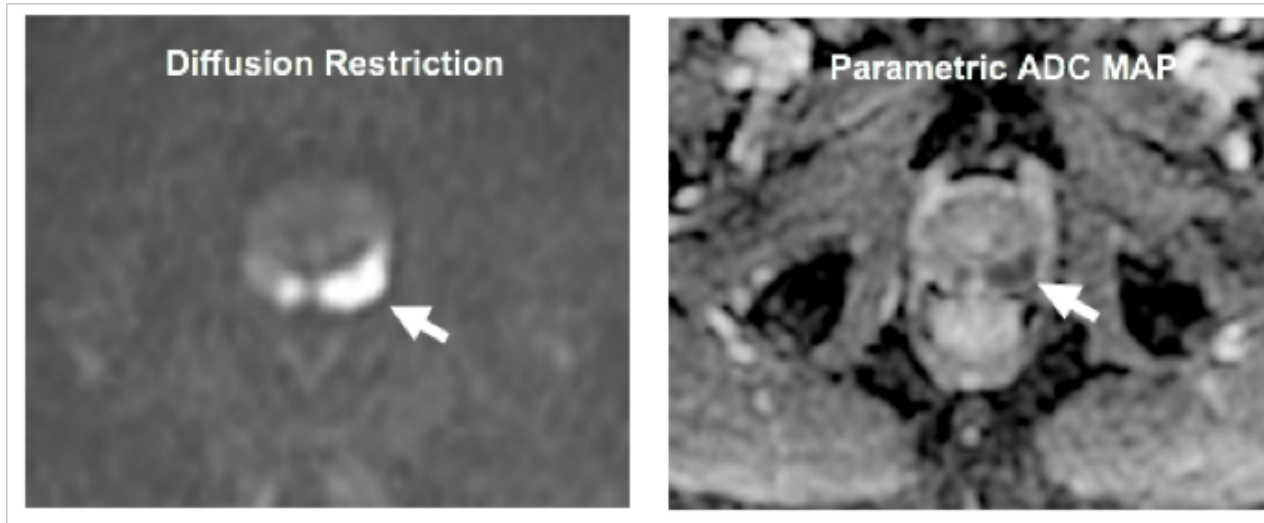
T2 TSE/FSE (top image)

ADC (middle image) parametric map of micromolecular diffusion velocities derived from diffusion images.. (low velocity = lower color or signal)

PEI Color map (bottom image)

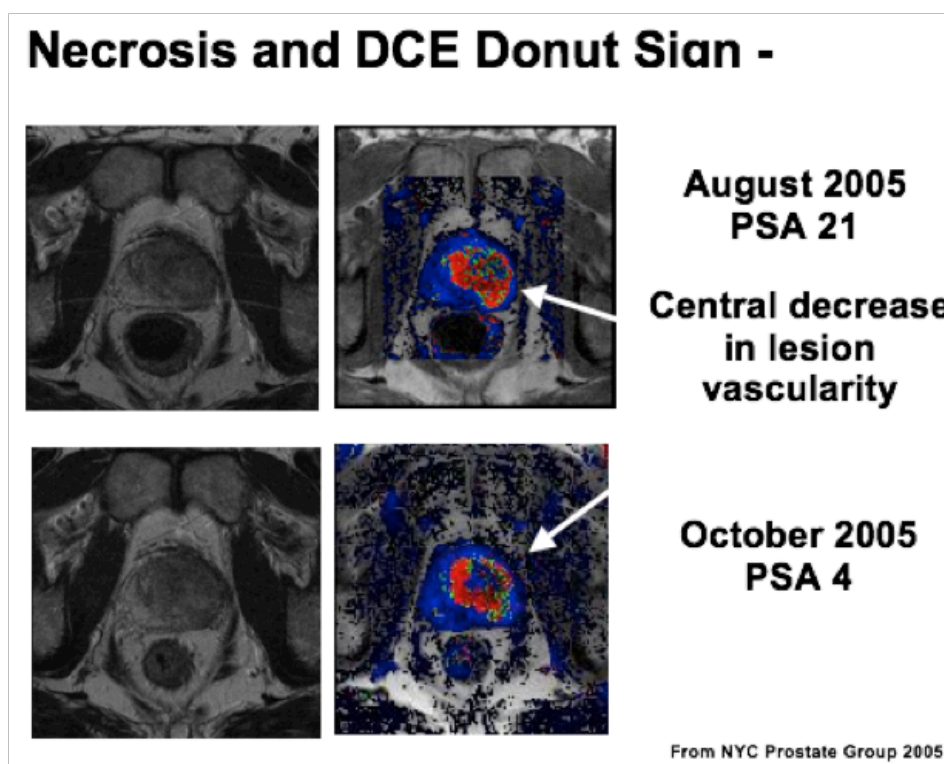


The area of low ADC (middle image) correlates with the hypointense peripheral zone PZ mass on the anatomical T2W FSE image (top image). The suspicious right peripheral zone demonstrated substantially higher enhancement relative to the opposite side (bottom image).



- **Diffusion Imaging should be performed on all prostate cancer patients undergoing MRI using multiple b-values. The highest b-value should exceed 1,200-1,400. Cancers diffusion restrict, therefore, they get brighter as the b-value is increased (and darker on the ADC map). Generalized causes of diffusion restriction include:**
 - Highly cellular objects with increased nuclear to cytoplasmic ratio
 - High viscosity
 - Stiffness in tight spaces
 - Cell death with trapped intracellular fluid
 - Tissue vacuolization

- Thus, the causes of false positive or negative diffusion MRI in prostate cancer include:
 - Spatial resolution often limited to 1 cm tumors
 - Mucinous tumors do NOT restrict
 - Benign nodules in Central Zone (CZ) and Peripheral Zone (PZ) can restrict since cells are tightly packed
 - Pitfall: Abscess “Vanilla donut” restricts inside; Tumor “Chocolate donut” restricts peripherally more than centrally; Any cytotoxic necrotic edema may be positive for diffusion restriction



- **Opinion Position Statement Regarding Field Strength and Endorectal Coil Imaging:**
 - “In the past, 3.0 Tesla MR system was recommended for examination of prostate cancer because of higher SNR, spectroscopy and it enables high quality imaging within a short time without the use of an endorectal coil.
 - This is no longer supported by data or practitioners who are active in the field with proper prep and newer technology. Spectroscopy has, for now, become a research tool, coil technology is superior at 1.5 T, artifacts are fewer, isotropic 3D mapping TSE/ FSE is excellent at 1.5 T. Finally, technology has evolved such that endorectal coil imaging is no longer needed for a quality exam and is not viewed favorably by patients.”

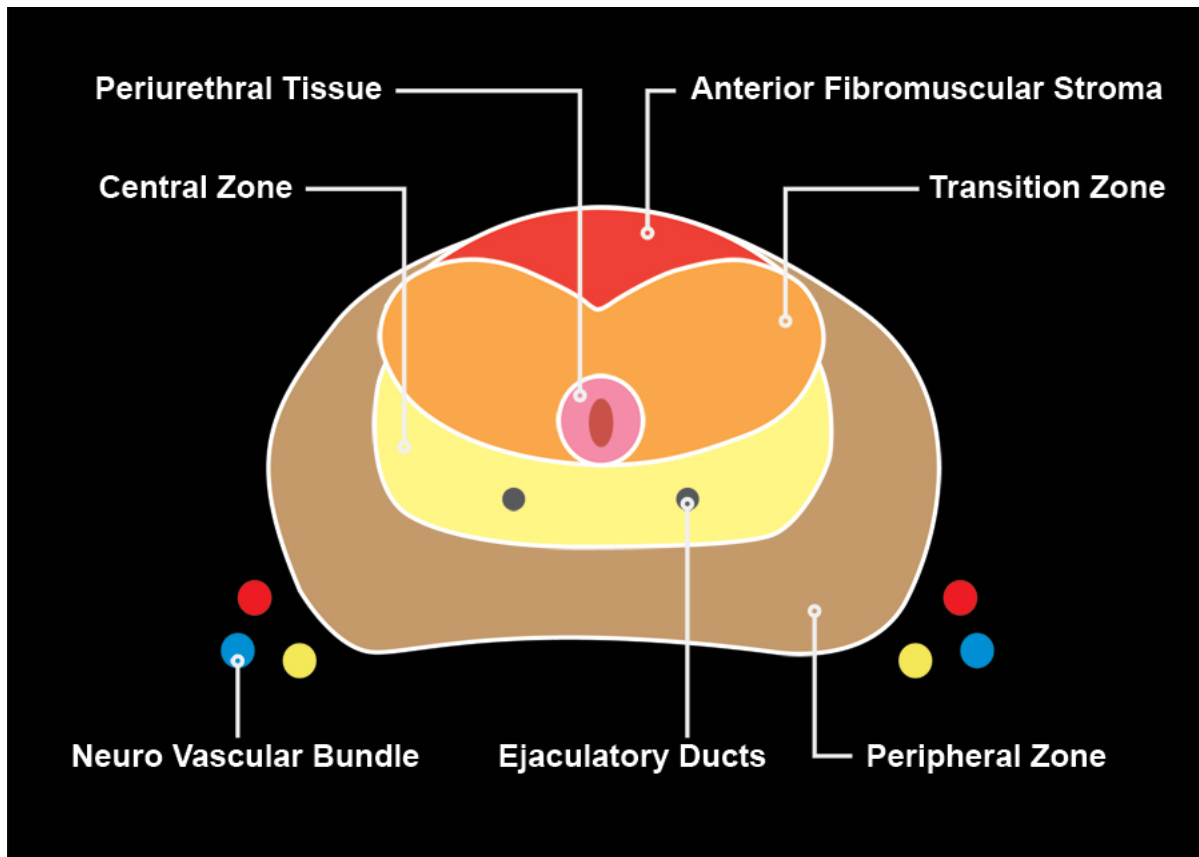
- **Screening Options for Prostate MRI: Position Statement for Consideration:**
 - Axial 2D T2 FSE + Diffusion + DCE MRI is a 20 minute screening exam and very economical for the patient.
- **Advantages:**
 - Detects aggressive cancer
 - Fast
 - Not expensive
 - No cavitory coils needed
- **This has been referred to as “Abbreviated Biparametric Prostate MR”**
- **Kuhl CK. Et al. Radiology 285(2) p. 483:**
 - In this long term study by a respected expert in Germany on DCE MRI the detection rate for “clinically significant” prostate lesions was equal to “full” parametric MRI.
 - In her study of over 500 patients, gadolinium enhanced DCE MRI is also eliminated. DCE MRI is only used as a major criterion to “characterize lesion” in PZ (peripheral zone lesions), and this eliminates the need for IV access and saves time. Total scan time is under 10 minutes. Additionally in this study, ALL PI-RAD 3s were biopsied (which would normally not be the case). 93.5% were benign.
- **Disadvantages:**
 - If an aggressive lesion is found, the patient must return for diagnostic 3 planar MRI with 2D or 3D technique for purposes of TRUS / MRI guided biopsy. T staging with the abbreviated study is less accurate. Localization in the gland requires more expertise. Still, detection of aggressive significant cancers is equal between the two techniques

ANATOMY

- **Functionality**
 - The main function of the prostate is to secrete prostatic fluid. Prostatic fluid is a key component of semen, and during ejaculation, prostate muscles contribute to propulsion of the semen through the urethra.
- **Geographic synopsis (Location)**
 - From the base of the bladder to the membranous urethra, the prostate envelops the prostatic urethra. Within the lesser pelvis, the prostate is located behind the inferior border of the symphysis pubis and pubic arch, and anterior to the rectal ampulla.
- **Zonal Anatomy – Prostate is divided into three major compartments:**
 - A. Peripheral zone:
 - 70% of volume in young males
 - Surrounds the entire central zone posterolaterally and extends anteriorly to the fibromuscular stroma
 - High in water content = T2 bright
 - 75% of prostate cancers arise in peripheral zone
 - B. Central zone:
 - In young males, the central zone makes up 25% of the prostate, respectively
 - Prostate is anterior to the rectal wall
 - Denonvilliers fascia separates from rectum
 - Bladder is anterosuperior to the prostate
 - Seminal vesicles are posterosuperior
 - Normally T2 bright
 - May not be filled in older men
 - Patients asked to abstain from ejaculation for 1 week prior to exam
 - Dried out inspissated concretions may be LOW signal on T2, especially with seminal vesicle obstruction of any etiology. Tumor is also low signal in the seminal vesicles on T2 but enhances, unlike simple non-tumoral obstruction.
 - Neurovascular bundles
 - Insert at 5 and 7 o'clock positions toward base (posterolateral)
 - Surgical capsule is the plane between the central and peripheral zone
 - Fibromuscular "capsule" of prostate
 - Pseudocapsule
 - Muscular Stroma forms an inverted "v" in the posterior prostate
 - Fibromuscular Stroma, anterior prostate
 - Site of involvement in a significant percentage of anterior cancers

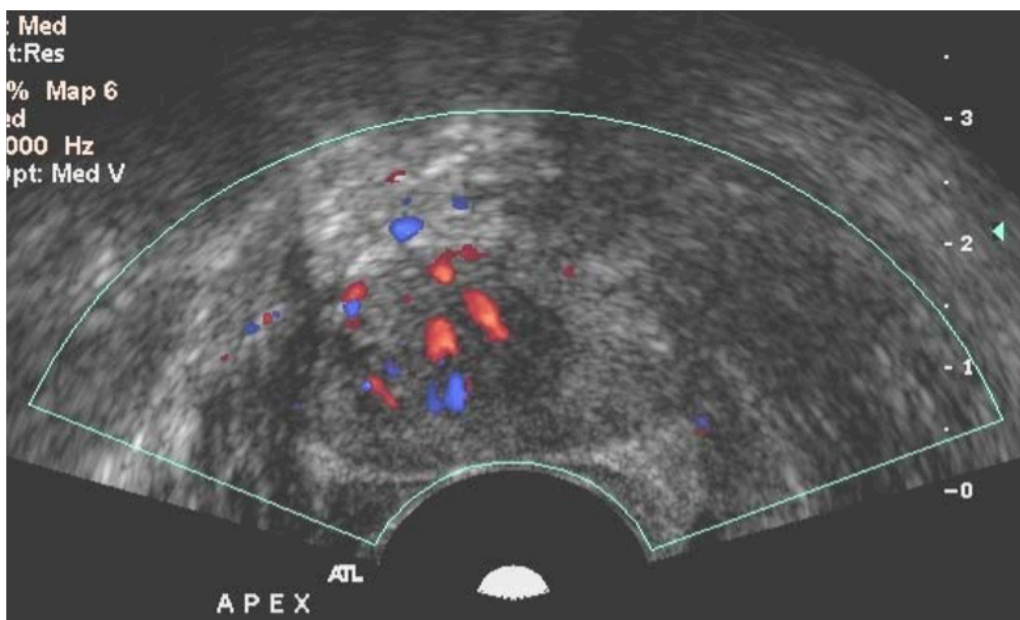
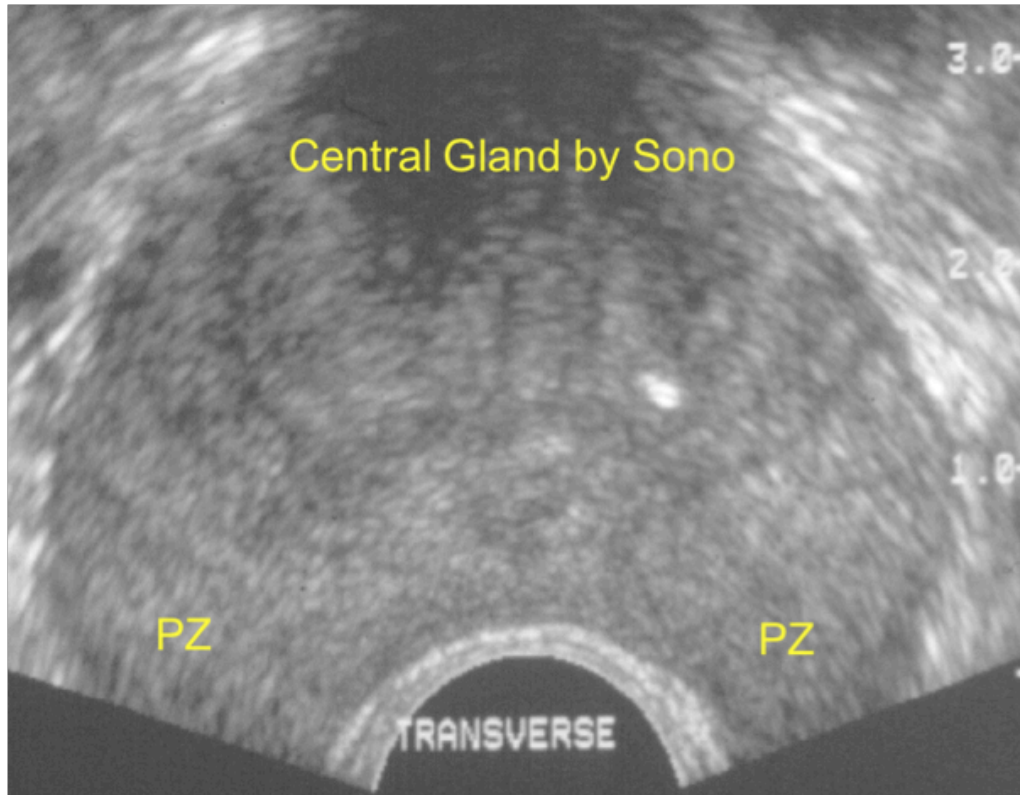
C. Transition zone:

- In young males, the transitional zone makes up 5% of the prostate, respectively
- As men get older, the transitional zone becomes more predominant (benign prostatic hypertrophy, BPH)



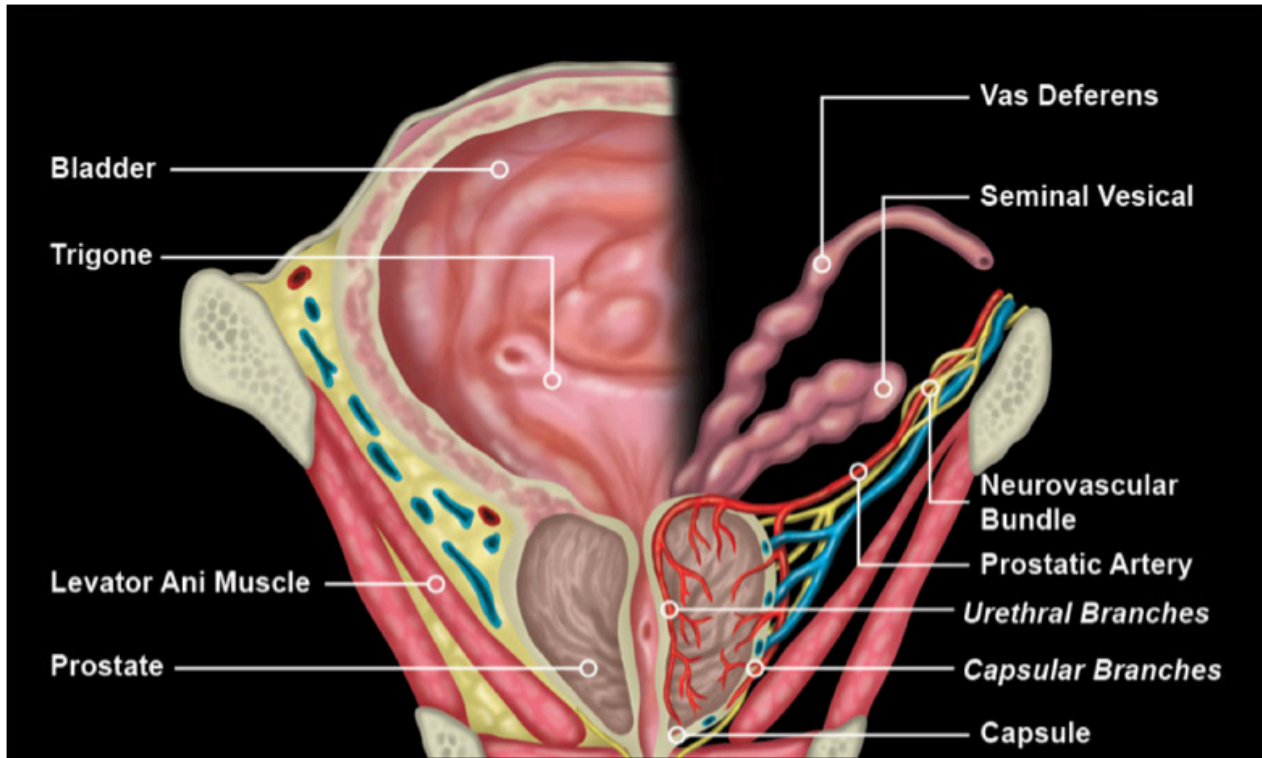
Coronal and axial, planar

Basic axial Sonography of Central and Peripheral Zone PZ

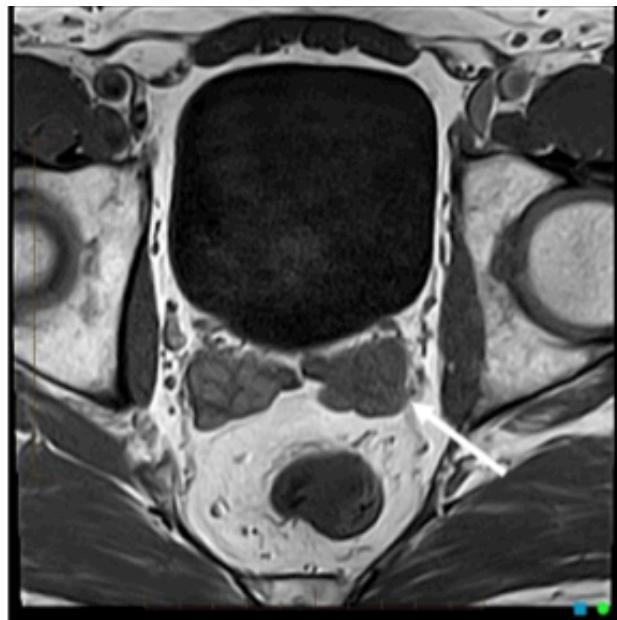
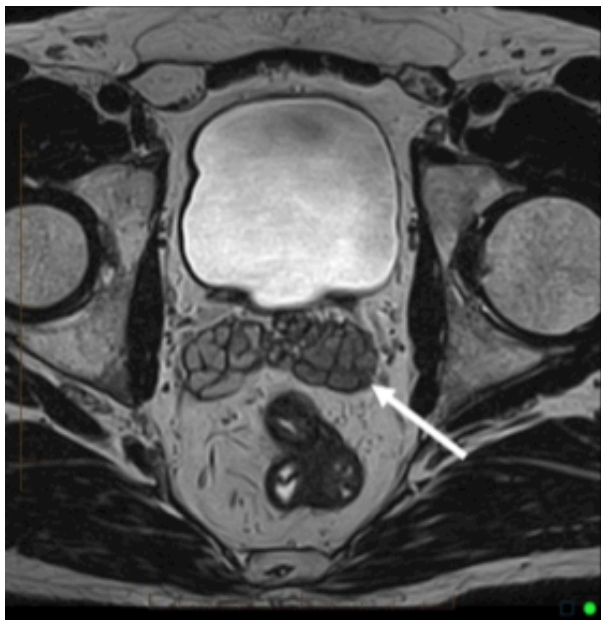
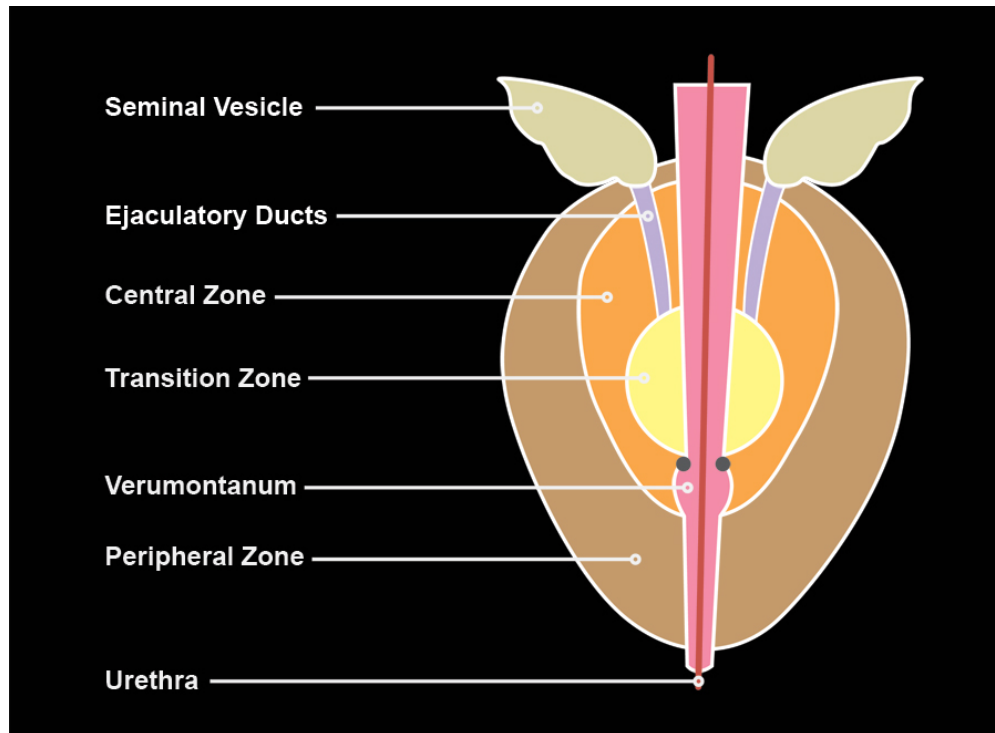


- Sono with Doppler, hypervascularity favors tumor- 85% of aggressive tumors (Gleason 8, 9, 10) have hypervascularity

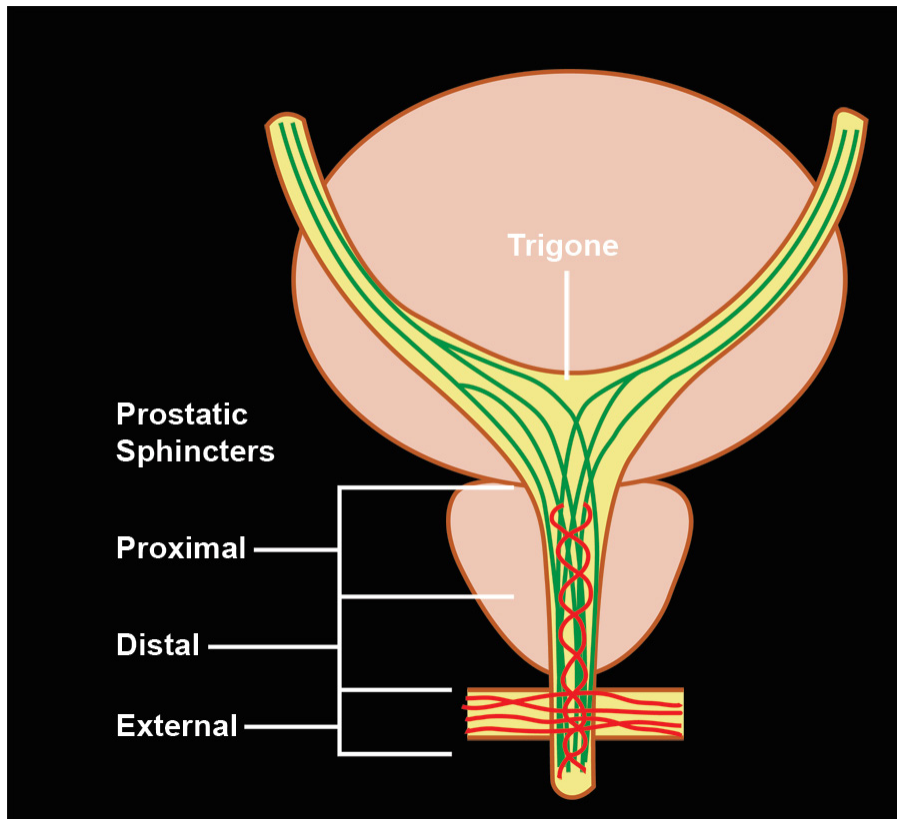
Coronal surface rendered front view



Coronal posterior or rear view – Highlights seminal vesicles

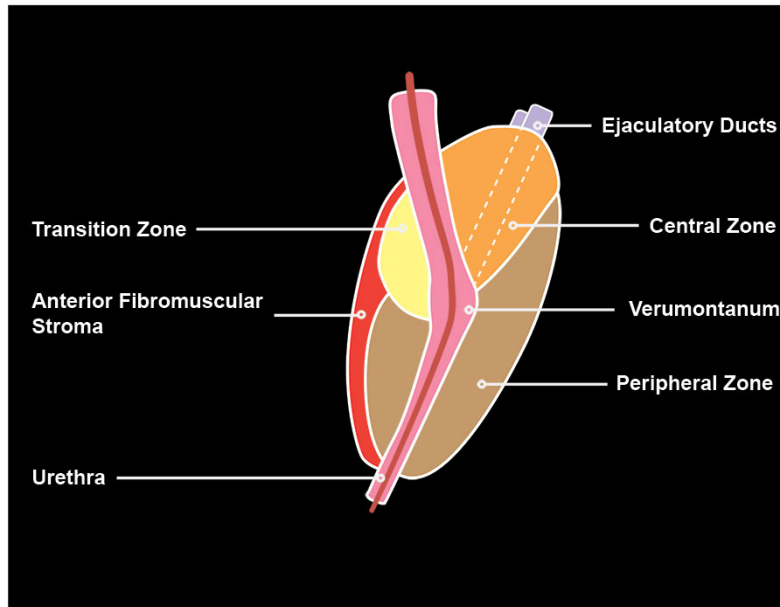


Blood in left SV (arrow)

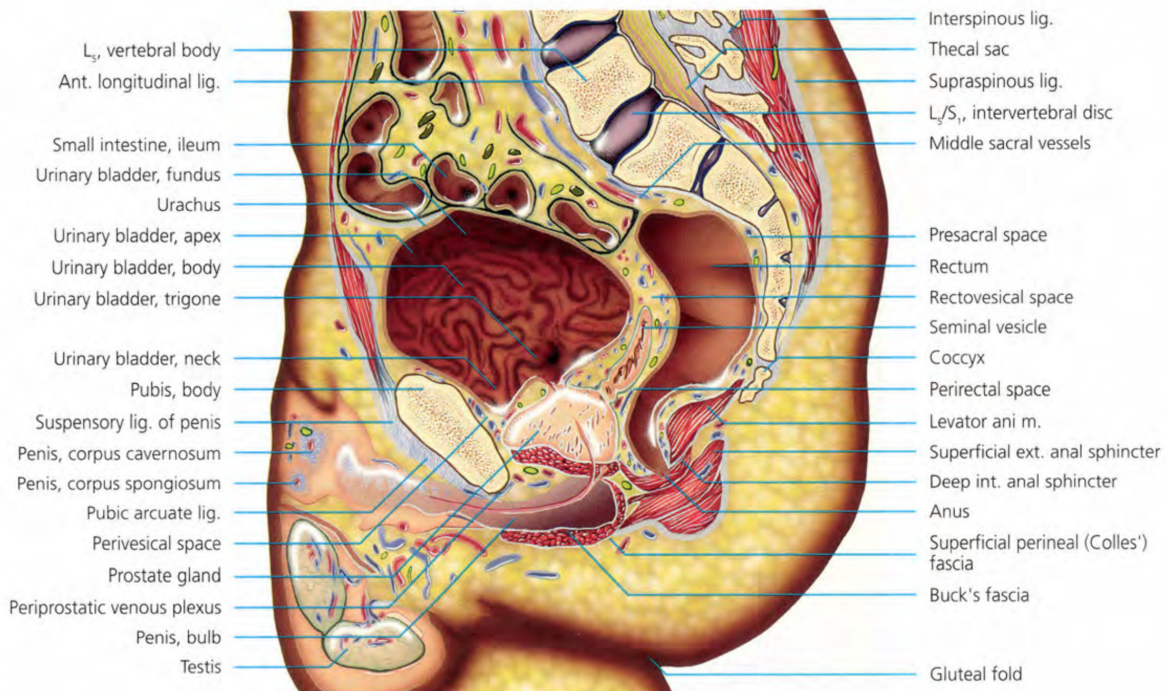


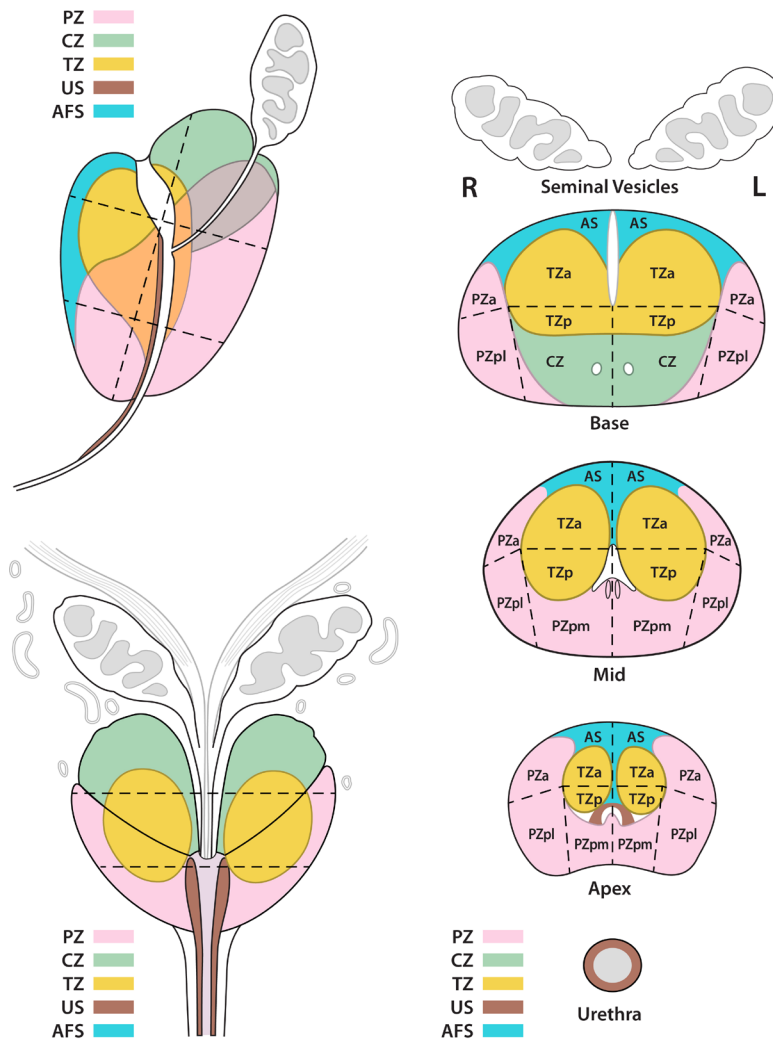
- **Coronal Anatomic Descriptors:**
 - Base = Proximal
 - Distal = Apical
 - Mid is divided into:
 - intermediate or int. (closer to the midline)
 - lat. or more lateral

Sagittal



Sagittal pathways of spread





Vasculature and Lymphatic Drainage

- Blood is supplied to the prostate by way of the inferior vesical, internal pudendal, and middle rectal arteries.
- The arteries interact with the gland from the junction of the prostate and bladder to the apex of the prostate.
- Veins form a plexus around the anterolateral region of the prostate where the primary tributary is the deep dorsal vein of the penis.
- With regard to lymphatic drainage, vessels from the prostate culminate in the internal iliac, sacral, and obturator nodes.
- The vesical vessel is adjoined by a posterior vessel leading toward external iliac nodes.
- In addition, an anterior vessel is connected to internal iliac nodes via vessels with the purpose of draining the membranous urethra.

Innervation

- The prostate consists of a dense web of nerve fibres and ganglia known as the periprostatic nerve plexus.
- This consists of:
 - preprostatic sphincter
 - anterior fibromuscular stroma
 - peripheral zone
- Given the density of the neurovascular bundles, damage from prostate surgery for cancer has been known to result in impotence.

Anatomy with Age

Note: All ages are approximate

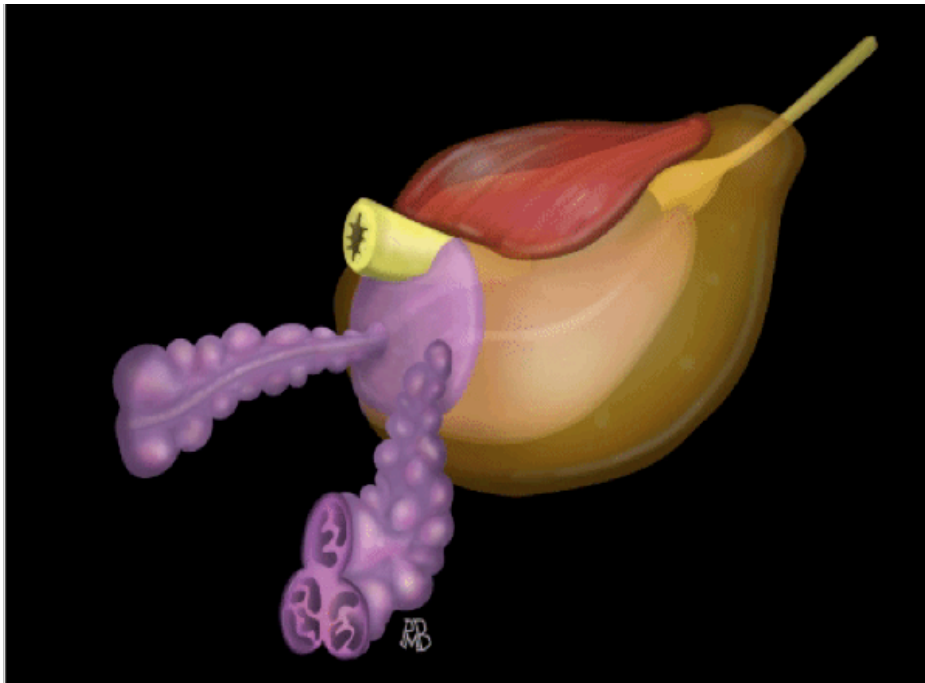
- **Birth**
 - System of ducts in stroma
 - End buds of ducts are follicles
- **Birth to 12-14 years**
 - Stable; no real change
- **12-14 to 17-18 years**
 - Puberty; maturation stage
 - Doubles in size (at least) due to follicular development, end-buds on ducts, and ductal branch modification
- **17-18 years to 30 years**
 - Multi-layered squamous or cuboidal epithelium transitions into pseudostratified epithelium (i.e. basal, exocrine secretory, and neuroendocrine)
 - Exocrine secretory cells generate acid phosphatase, prostate-specific antigen (PSA), and B-microseminoprotein
- **30 to 39 years**
 - Epithelial cells undergo irregular multiplication into the lumen of the follicles
- **40 to 44 years**
 - Stable; no real change
- **45 to 50 years**
 - Follicular outlines become more regular and amyloid bodies increase, resulting in involution of the prostate
- **After 50 years**
 - Benign Prostatic Hyperplasia (BPH) takes place
 - BPH is inevitable, but may not be symptomatic

Prostate Cancer Dysfunction

- **What can you determine with MRI?**
 - Extracapsular extension (stage T3A) (78% sensitive, 96% specific)
 - Involvement of the neurovascular bundle
 - Seminal vesicle invasion (stage T3B) (88% sensitive, 98% specific)
 - Invasion into adjacent structures (bladder to rectum)
 - Local lymph node involvement
 - T3 lesions have a worse prognosis and more likely to recur after treatment or surgery
 - MRI may correlate with Gleason grade
 - Apparent diffusion coefficient

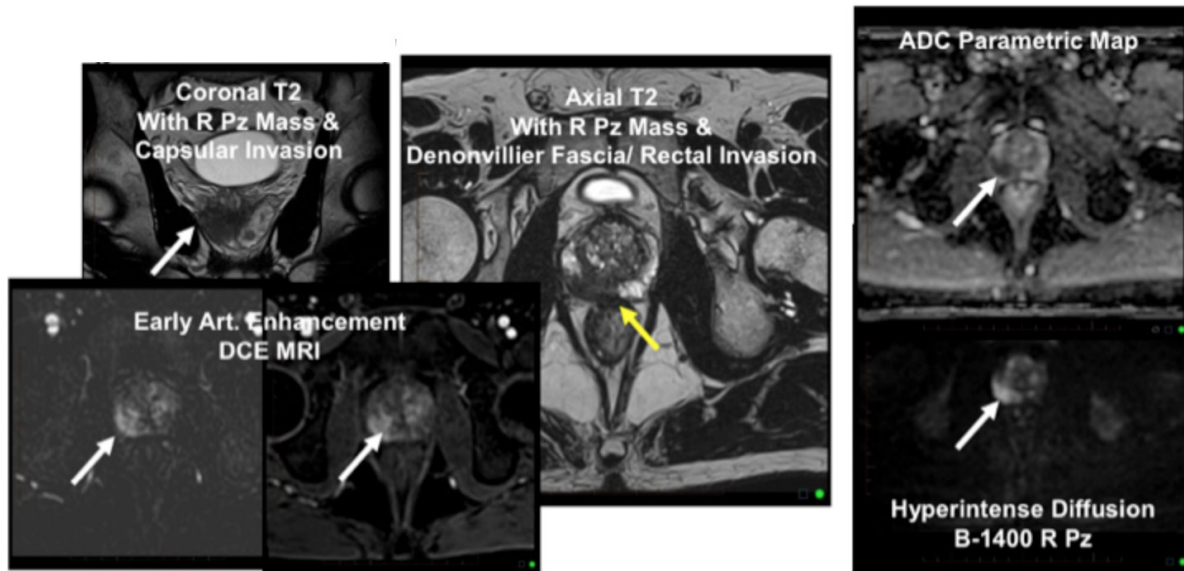
PI-RADS v.2 Scoring

- [Click here to see a case example of PI-RADS 1](#)
- [Click here to see a case example of PI-RADS 2](#)
- [Click here to see a case example of PI-RADS 3](#)
- [Click here to see a case example of PI-RADS 4](#)
- [Click here to see a case example of PI-RADS 5](#)
- PI-RADS utilizes a 5-point scale based on the probability that a combination of mpMRI findings on T2W, DWI, and Dynamic Contrast Enhanced (DCE) images correlate with clinically significant prostate cancer.

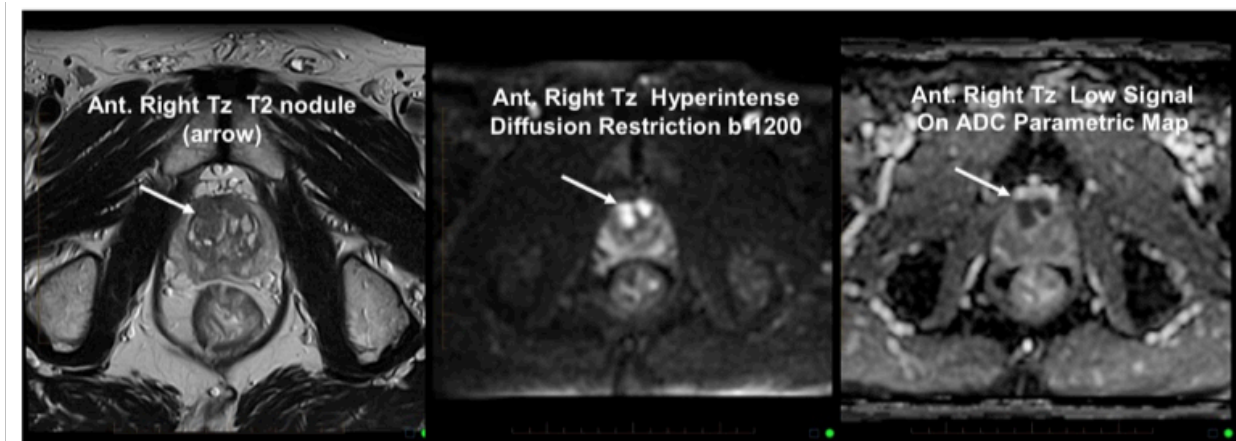


From: Pomeranz SJ, Bohart Case Review Series

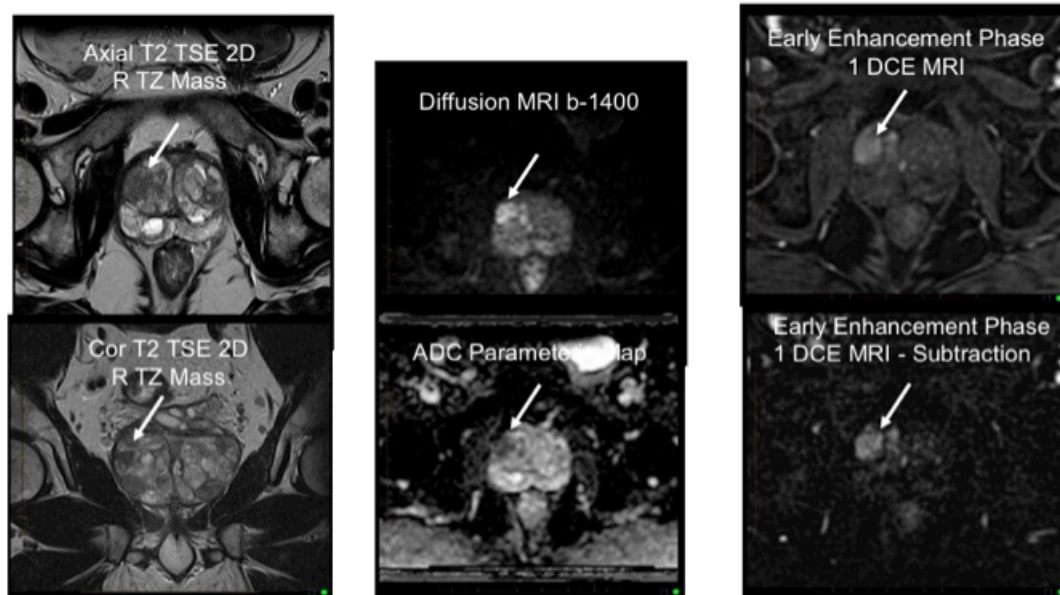
PI-RADS 5 – Example of early arterial enhancement of PZ (peripheral zone) rectum wall microinvasion (yellow arrow)



Example of far anterior TZ (transitional zone) PI-RADS 4 – difficult to approach with TRUS biopsy based on anterior location (arrow)



Example PI-RADS 5 – TZ Ca



- PI-RADS v2 has flaws (i.e. a TZ lesion can be moved from a 2 to 4 category with slight changes in T2 morphology.)
- The following are links to some publications about this:
 - <https://pubs.rsna.org/doi/pdf/10.1148/rg.313105139>
 - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4656245/pdf/13244_2015_Article_426.pdf
 - <https://link.springer.com/content/pdf/10.1007%2Fs13244-017-0578-x.pdf>
- PROMIS study:
 - For clinically significant cancer, MP-MRI was more sensitive (93%) than TRUS-biopsy (48%).
 - 37% negative TRUS still had clinically significant Ca.
 - MR can avoid biopsy in 27% of men with high PSA.
- Anatomy PEARL:
 - Central zone tumours are rare, hard to detect as CZ normally is hypo on T2 and restrict.
 - Symmetry is key (18% CZ is asymmetrical), Also CZ does not extend below verumontanum!
- How to do it:
 - Mention up to 4 most suspicious lesions in report, and include index lesion.
 - Index lesion is Highest PI-RADS >> EPE (Extraprostatic extension) >> Size.
 - Lesion size is largest axial dimension measurement.

PI-RADS Assessment Categories

- **PI-RADS 1 – Very low (clinically significant cancer is highly unlikely to be present)**
- **PI-RADS 2 – Low (clinically significant cancer is unlikely to be present)**
 - NOTE: PI-RADS 2 is good for beginners, but the Likert system is more flexible and useful for experienced readers. However, you need to have good working relationship with urologists to use this.
- **PI-RADS 3 – Intermediate (the presence of clinically significant cancer is equivocal)**
- **PI-RADS 4 – High (clinically significant cancer is likely to be present)**
- **PI-RADS 5 – Very high (clinically significant cancer is highly likely to be present)**

- **PI-RAD PERSONAL PEARL:**
 - PSA density of > 0.2 ng/ml² is suspicious, should consider biopsy irrespective of MR results, unless there has been prostatitis or instrumentation.
 - Conversely, PSA density < 0.1 ng/ml² is usually benign.
 - Therefore if you are contemplating PI-RADS 3 (2 or 4):
 - If PSA density is > 0.2 ng/ml² err on the side of PI-RADS 4.
 - If PSA density is < 0.1 ng/ml² err towards PI-RADS 2 and follow-up in one year.

- **PI-RADS 3 Pearl:**
 - A PI-RADS 3 upgraded to 4 using either DCE or ADC correlated with better clinical outcome than an initial PI-RADS 4, ie PI-RADS 3+1 is not equal to a 4

PI-RADS Assessment for T2W2

Score	Peripheral Zone (PZ)
1	Uniform hyperintense signal intensity (normal)
2	Linear or wedge-shaped hypointensity or diffuse mild hypointensity, usually indistinct margin
3	Heterogeneous signal intensity or non-circumscribed, rounded, moderate hypointensity. Includes others that do not qualify as 2,4, or 5
4	Circumscribed, homogeneous moderate hypointense focus/mass confined to prostate and <1.5cm in greatest dimension
5	Same as 4 but $\geq 1.5\text{cm}$ in greatest dimension or definite extraprostatic extension/invasive behavior
PEARL	Extruded BPH nodules can mimic PZ lesions, known pitfall.

Score	Transition Zone (TZ)
1	Homogeneous intermediate signal intensity (normal)
2	Circumscribed hypointense or heterogeneous encapsulated nodule(s) (BPH)
3	Heterogeneous signal intensity with obscured margins. Includes others that do not qualify as 2,4, or 5
4	Lenticular or non-circumscribed, homogeneous, moderately hypointense, and <1.5 cm in greatest dimension
5	Same as 4, but $\geq 1.5\text{cm}$ in greatest dimension or definite extraprostatic extension/invasive behavior

PI-RADS Assessment for DWI2

Score	Peripheral Zone (PZ) or Transition Zone (TZ)
1	No abnormality (i.e., normal) on ADC and high b-value DWI
2	Indistinct hypointense on ADC
3	Focal mildly/moderately hypointense on ADC and isointense/mildly hyperintense on high b-value DWI
4	Focal markedly hypointense on ADC and markedly hyperintense on high b-value DWI; <1.5cm in greatest dimension
5	Same as 4 but ≥1.5cm in greatest dimension or definite extraprostatic extension/invasive behavior.
PEARL	T2 Blackout effect: lesions with very short T2 or T2* values create blackout phenomenon on T2, ADC and DWI. Tumors are not black, they are gray. T2 blackout can be due to paramagnetic effect.
PEARL	PZ in younger pt normally shows mild symmetrical restricted diffusion due to higher glandular density.

- **Principle of Computed DWI – (Diffusion – weighted imaging)**
 - The computed DW imaging (cDWI) is a mathematical method in which b-value is calculated from two real DW images with different b-values.
 - The apparent diffusion coefficient (ADC) is calculated with the following equation:
 - $ADC = \ln[-S/S_0] / (b - b_0)$
 - Using two real DWI signals in a monoexponential model, signals on arbitrarily set b-value are calculated with the following equation:
 - $S_c = S_0 \exp[-(b_c - b_0)ADC]$

PI-RADS Assessment for DCE2

Score	Peripheral Zone (PZ) or Transition Zone (TZ)
(-)	No early enhancement, or diffuse enhancement not corresponding to a focal finding on T2 and / or DWI or focal enhancement corresponding to a lesion demonstrating features of BPH on T2WI
(+)	Focal, and; earlier than or contemporaneously with enhancement of adjacent normal prostatic tissues, and; corresponds to suspicious finding on T2W and / or DWI
PEARL	Prostatitis and BPH can show early enhancement and washout

PI-RADS Assessment - Peripheral Zone

DWI	T2W	DCE	PI-RADS
1	Any	Any	1
2	Any	Any	2
3	Any	(-)	3
		(+)	4
4	Any	Any	4
5	Any	Any	5

PI-RADS Assessment - Transition Zone

T2W	DWI	DCE	PI-RADS
1	Any	Any	1
2	Any	Any	2
3	≤4	Any	3
	5	Any	4
4	Any	Any	4
5	Any	Any	5

- **PEARL 1:** TZ cancers almost never develop posteriorly, usually anterior half and in the apical third. Caveat is the tumor in the anterior half is so big it extends into the posterior half.
- **PEARL 2:** A good sign of benign TZ nodules are microcysts (discrete foci of T2 hyperintensity), this is correlated by pathologic histology and are dilated hyperplastic acini.
- **PEARL 3:** Negative predictive value for MR prostate done well and read well is 90% for Gleason 3+4 and above, and more than 90% for 4+3 and above.
- **PEARL 4:** AS & CZ zone lesions are a gray “difficult” area. It is not clear which parameter to use but use ADC first and then early b value DCE to assess further.
- **PEARL 5:** TZ tumors tend to be lower grade, don’t overcall TZ lesions. Look for excuse not to call a tumor in the TZ.
- **PEARL 6:** DCE is useful in 10% of cases as a second line of defense in case of initially missed DWI or T2 lesion, Especially if DWI fails from metal or post-focal radiation or other pitfalls like air in the rectum.

PI-RADS 1 - Example

This 62-year-old male presents with prostate-specific antigen (PSA) of 6.44.



Image 1 - Axial T2 FSE / TSE 2D (3mm)

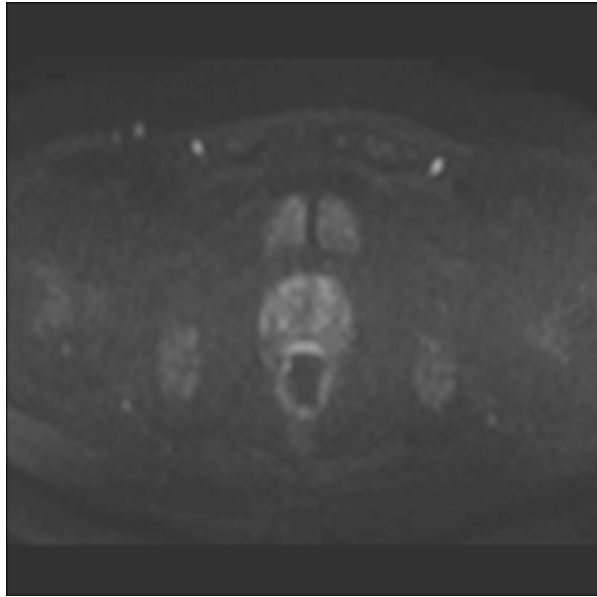


Image 2 - Diffusion MRI b1500

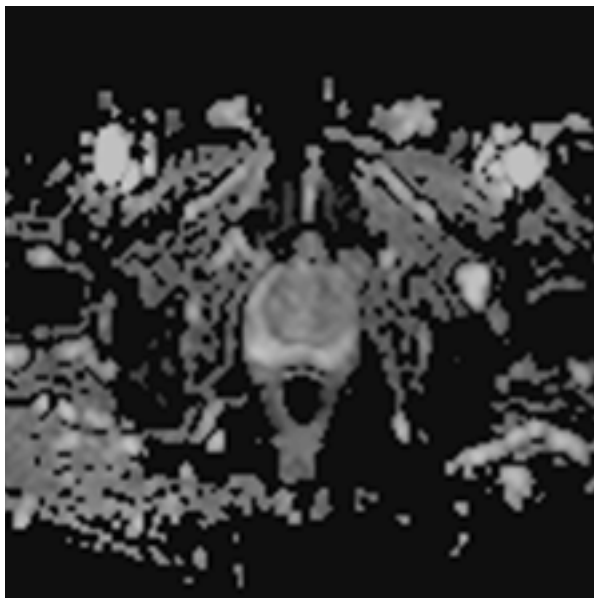


Image 3 - Parametric ADC Map

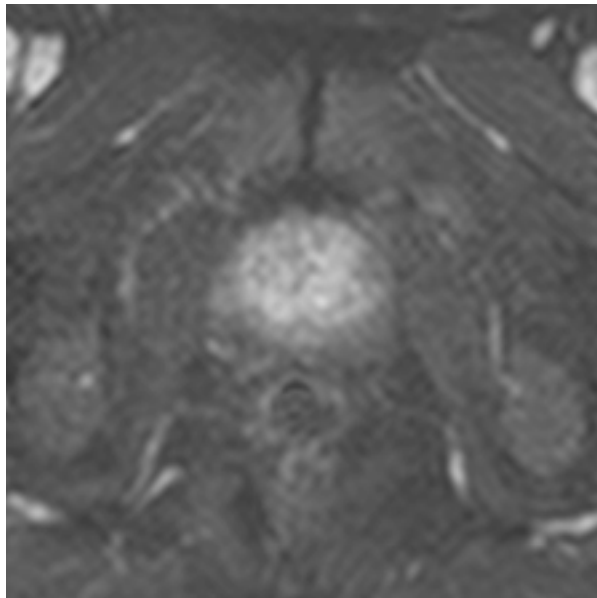


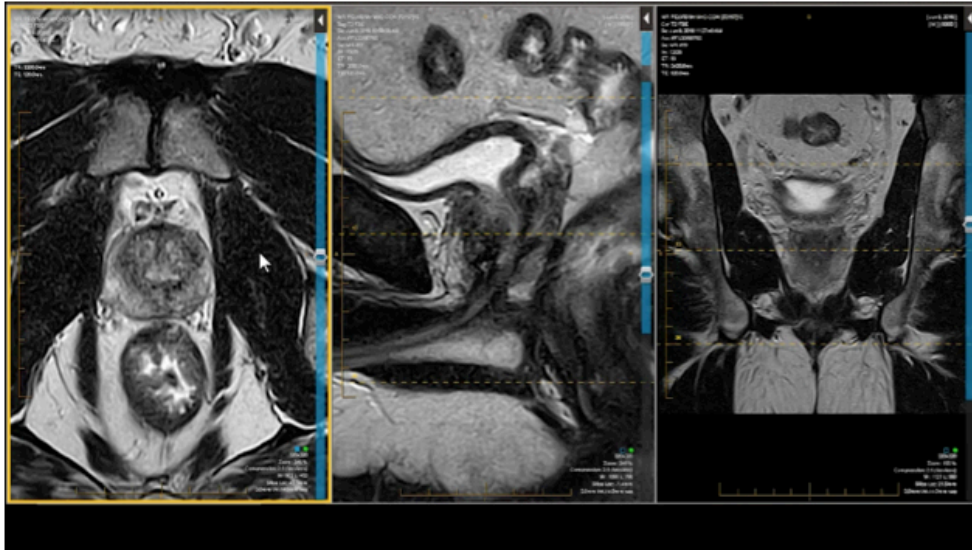
Image 4 - DCE MRI Phase 5
(60 seconds post-injection)

- **Findings:**
 - The prostate is 4.7cm in transverse dimension, 3.9cm in AP dimension, and 4.8cm in craniocaudal dimension. No areas of restricted diffusion or hypointensities in the peripheral zone. Generalized ill-defined non mass-like moderate hypointensity in the transitional zone. Small cystic nodule at the anterior right transitional zone. The capsule intact. Seminal vesicles and neurovascular bundles normal in appearance.
 - No lymphadenopathy in the pelvis. No focal abnormal signal intensity in the osseous structures. A 1.3 x 1.5 x 1 cm fluid intensity abutting the anterior inferior left acetabulum probably is a paralabral cyst. Arthrosis of the pubic symphysis.
- **CONCLUSION:**
 - No focal hypointense mass or areas of restricted diffusion, PI-RADS 1.

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PI-RADS 2 - Example

- This 62-year-old male presents with elevated prostate-specific antigen (PSA) level measuring 8.3ng/mL.

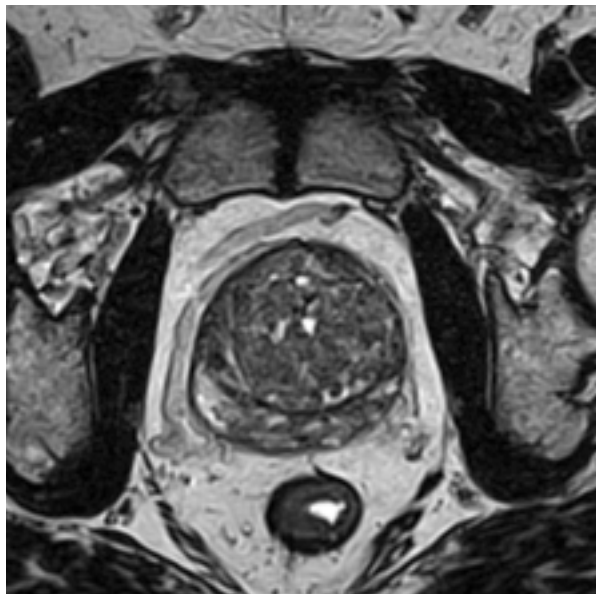


Image 1 - Axial T2 BPH, TZ hypertrophy (1mm) Contiguous, 3D TSE / FSE



Image 2 - Axial DWI Parametric ADC map, TZ hypertrophy, BPH, no low signal velocity restriction particularly in PZ

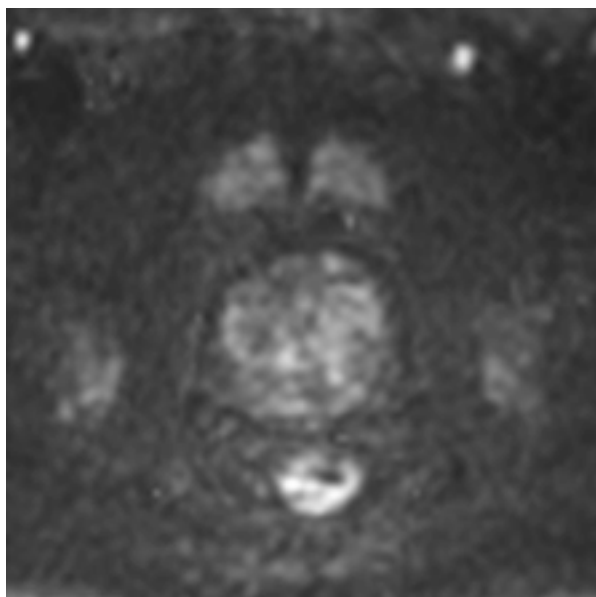


Image 3 - Axial DWI Diffusion, b1600, TZ hypertrophy BPH, No high signal diffusion

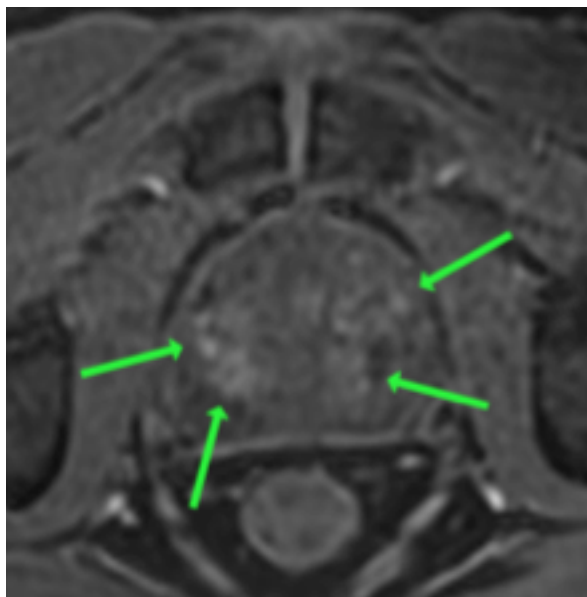


Image 4 - Axial DCE MRI with Gadolinium, 8 seconds after injection, scattered TZ enhancement of low amplitude (arrows)

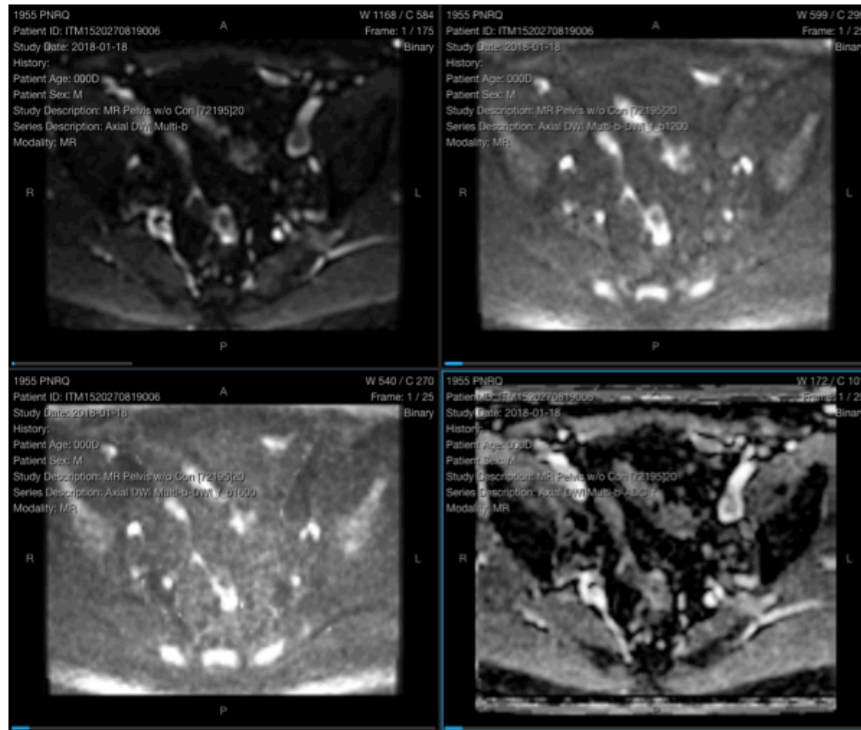
- **FINDINGS**

- The prostate gland measures 6cm in CC, 5cm in AP, and 6cm in RL dimensions. Calculated prostate volume is 94cc and PSA density is 0.09. Transitional zone hyperplasia is present. Stromal hyperplasia areas demonstrate mild to moderate diffusion restriction. No suspicious T2 hypointensity with substantive diffusion restriction to suggest malignant neoplastic process in the transitional zone. Peripheral zone demonstrates linear T2 hypointense scarring regions. Anatomical prostate capsule, bilateral neurovascular bundles, rectoprostatic angles and seminal vesicles are clear.
- No lymphadenopathy in the pelvis or inguinal regions. Subcentimeter in diameter right external iliac chain lymph node is noted. Mild diverticular disease of the sigmoid colon without evidence of acute diverticulitis. Rectal wall is unremarkable. Visualized musculoskeletal structures are within normal limits. Urinary bladder is partially full and demonstrates mild wall thickening. No pseudo diverticula formation.

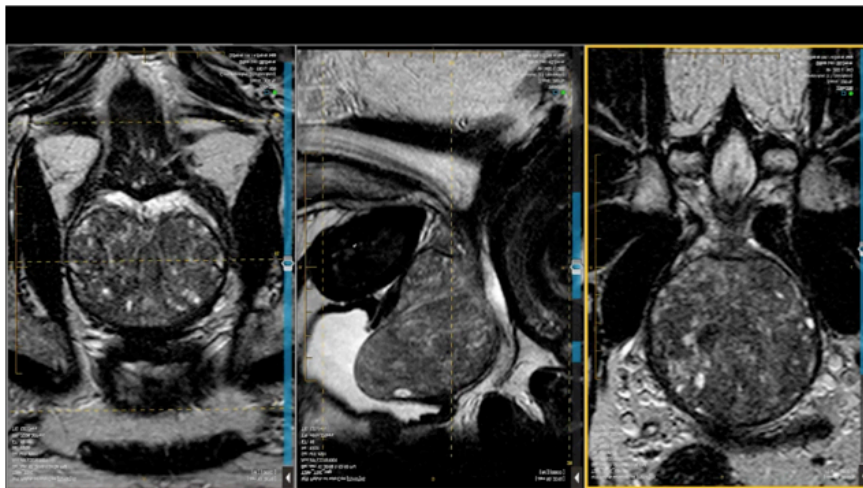
- **CONCLUSION:**

- PI-RADS 2; benign hyperplasia of the transitional zone.
 - Mild diverticular disease of the sigmoid colon without evidence of acute diverticulitis.
 - DWI images did not cover the whole prostate. Patient will be call back for complete DWI imaging.
- **Additional diffusion-weighted images through the prostate are obtained. No substantive diffusion-restricted, T2- hypointense region in the transitional or peripheral zone of the prostate gland to suggest malignant neoplastic process.**

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PI-RADS 3 - Example

- This 72-year-old male presents with elevated prostate-specific antigen (PSA).

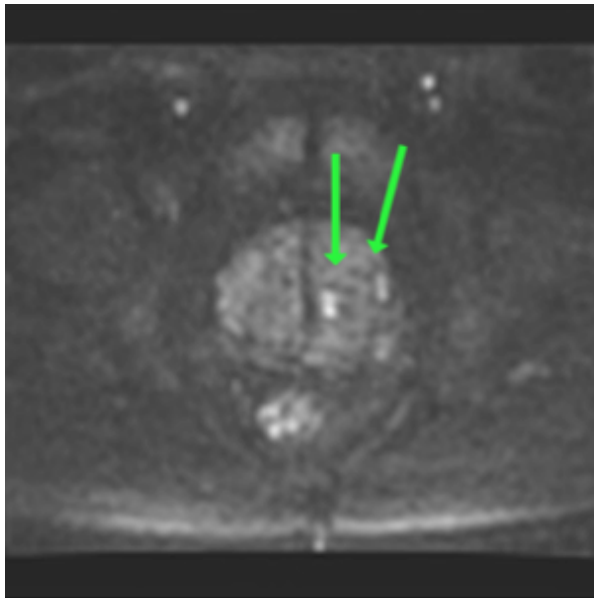


Image 1 - Axial DWI, b1600 (arrows)

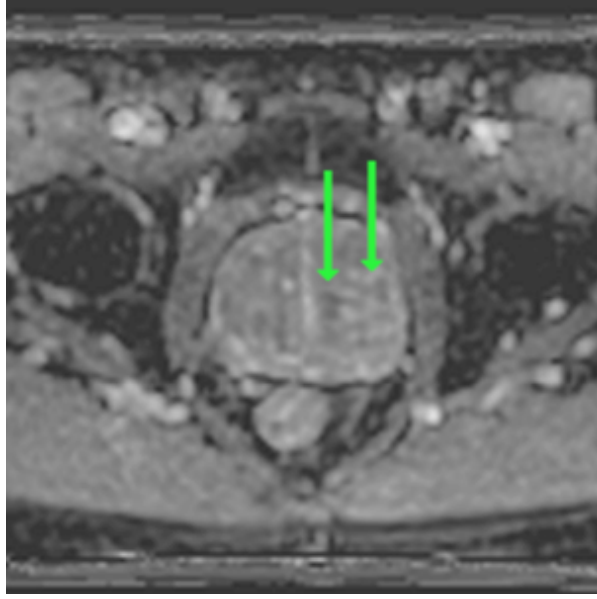


Image 2 - Axial DWI (arrows)

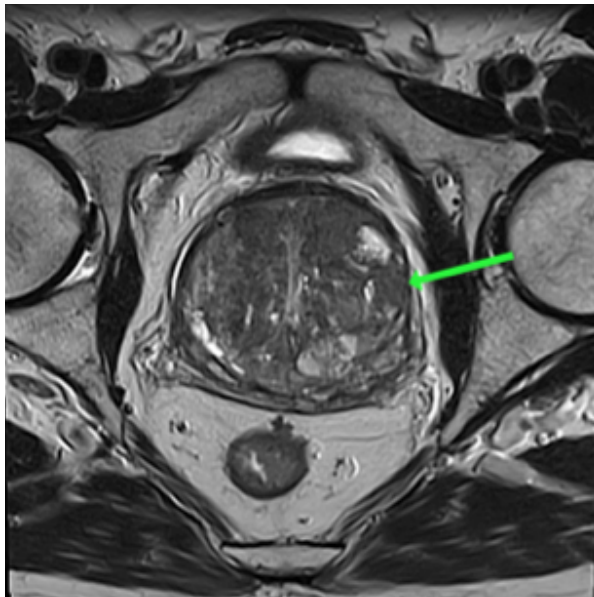


Image 3 - Axial T2 FSE / TSE (arrow)

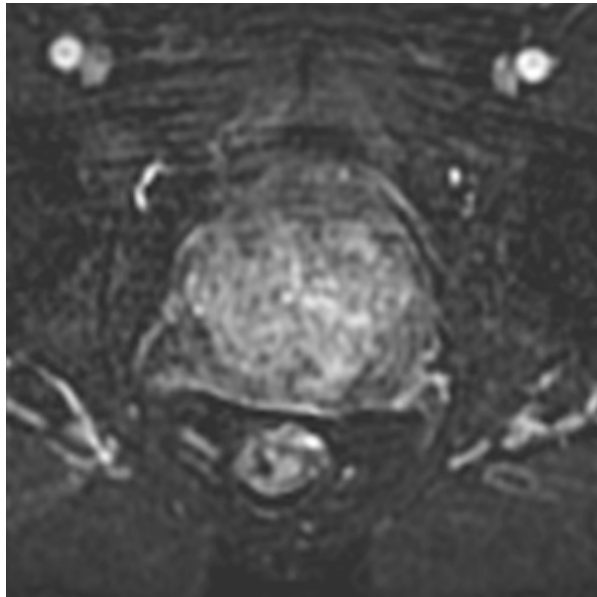


Image 4 - Axial TIGRE 2D (3mm) DCE MRI Phase 1 (10 seconds). No hypervascularity in area of diffusion restriction in left mid TZ

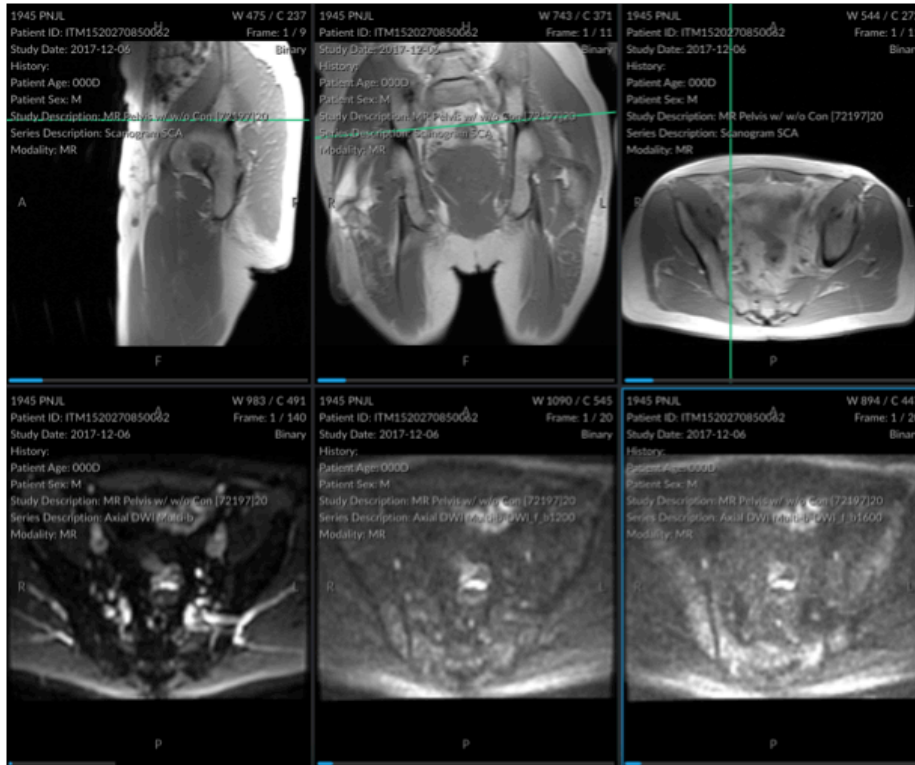
- **FINDINGS:**

- The prostate measures 7.6 x 6.0 x 7.1cm for an estimated volume, using the ellipsoid formula, of 169.4cc and tumor density of 0.062 ng/mL/cc which is at the lower end of the indeterminate risk range.
- Peripheral Zone: Bilobed diffusion restricting signal abnormality within the right mid gland PZpa measuring 1.7 x 1.0cm with greater than a centimeter of capsular contact but no extracapsular extension. There is vascularity in this region but no corresponding T2 signal abnormality. PI-RADS 3.
- Central Gland: Bilobed 10 x 7mm lesion in the central gland TZp mid prostate near the midline and a second area in the lateral aspect of the left midgland TZp on the same key image, this lateral lesion measuring 9 x 5mm. The vascularity is equivocal. No corresponding T2 lesion.
- Normal rectoprostatic angles and neurovascular bundles. The left seminal vesicle is desiccated. The right is normal. Normal space of Retzius. Prostatomegaly protruding into the bladder trigone. Bladder wall thickening compatible with outlet obstruction. No lymphadenopathy or bone lesion.

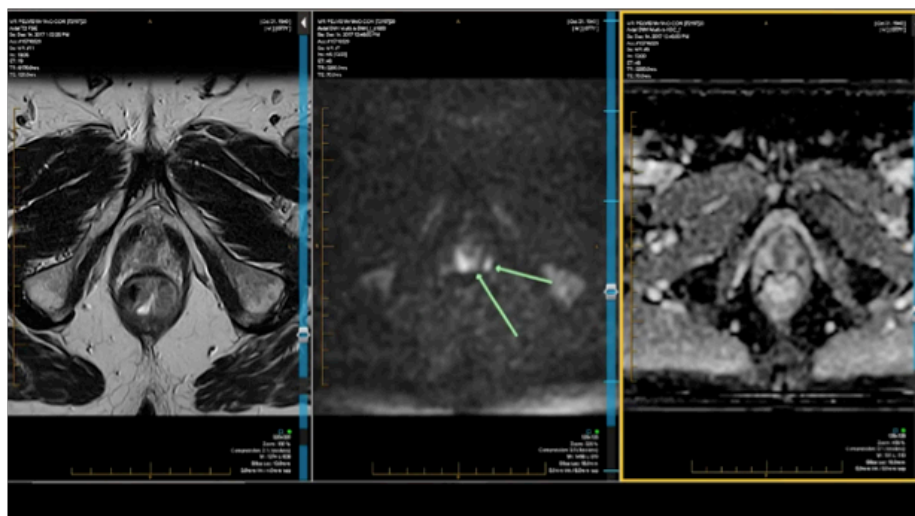
- **CONCLUSION:**

- PI-RADS 3:
 - Multiple areas of diffusion restriction within the prostate, as above, three lesions identified, though none of which have suspicious T2 correlates.
 - BPH and bladder outlet obstruction.
 - No lymphadenopathy or bone lesion.

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PI-RADS 4 - Example

- This 64-year-old male presents with increasing prostate-specific antigen (PSA) from 5.07 to 9.00 in seven months.

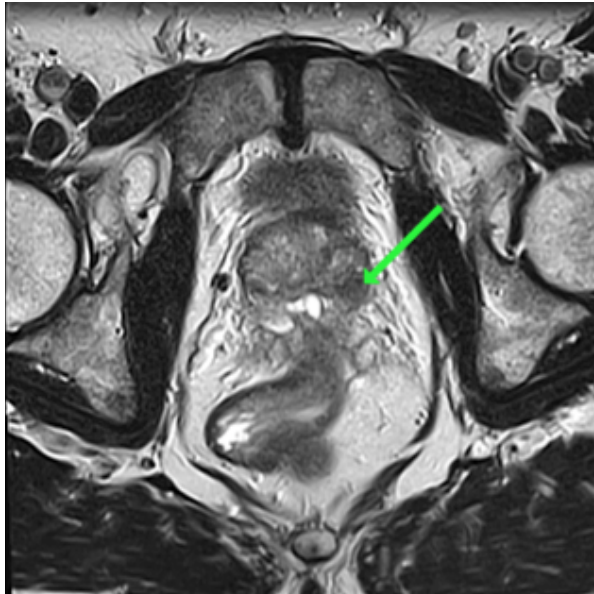


Image 1 - Axial T2 FSE / TSE (arrow); (3mm) 2D, nodule left PZ pl (base)



Image 2 - Coronal T2 FSE / TSE (arrow); (3mm) 2D, nodule left PZ pl (base)

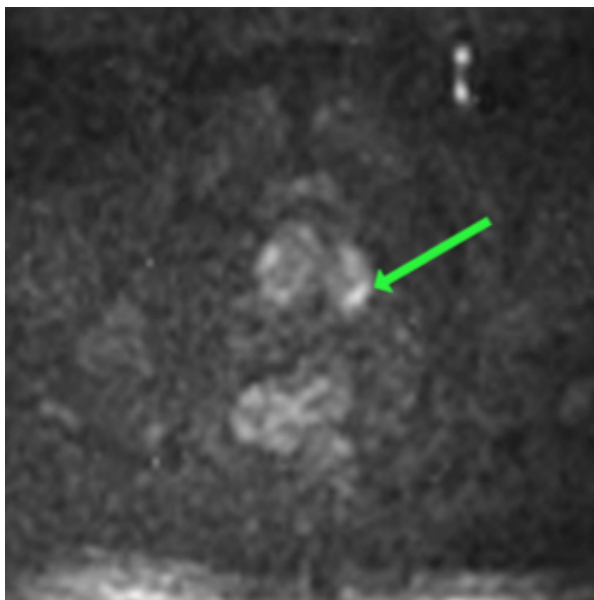


Image 3 - Axial DWI (arrow); Diffusion b-1600, hyperintense diffusion restriction left PZpl (base).

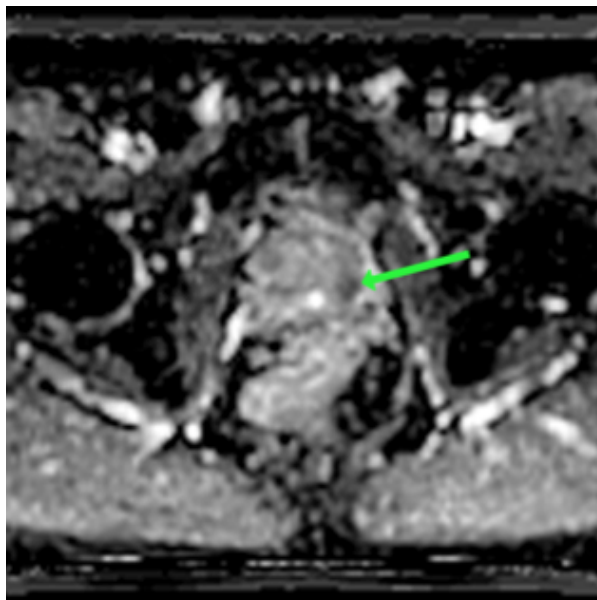


Image 4 - Axial DWI (arrow) ADC parametric map shows low signal velocity restriction left PZpl (base).

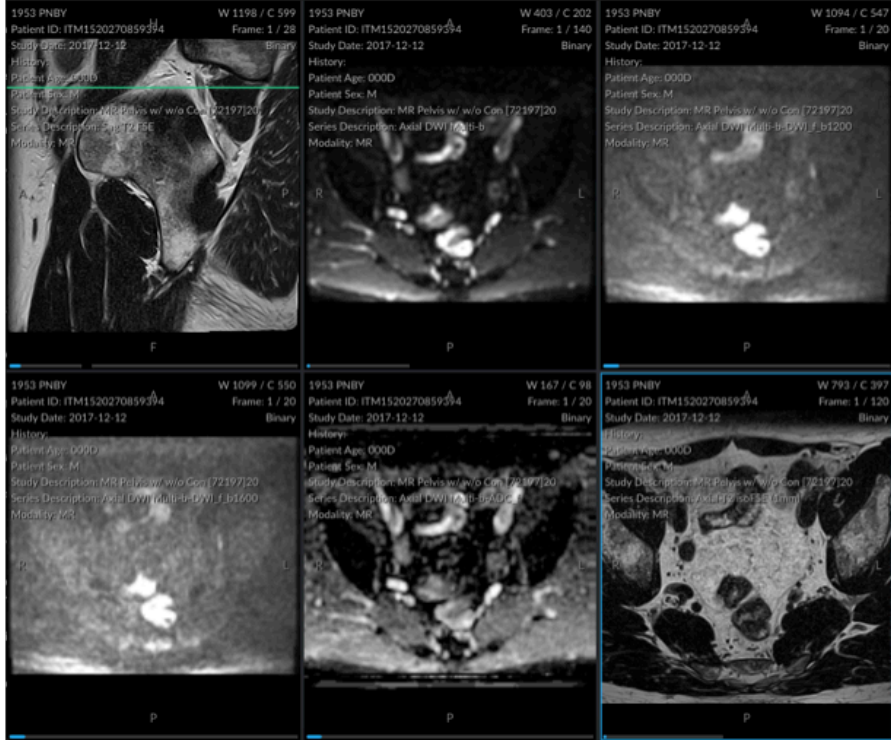
- **FINDINGS:**

- The prostate measures 3.5 x 3.5 x 4.6cm for an estimated volume, using the bullet formula, of 37cc and tumor density of 0.246ng/mL/cc which is in the high risk range.
- Peripheral Zone: Diffusion restricting crescent T2 hypointensity in the left base measuring 1.0 x 0.6cm involving the entrance of the left seminal vesicle. No right-sided lesion in the peripheral zone.
- Prostate utricle cyst.
- Central Gland: CZ/TZ hypertrophy with bladder wall thickening compatible with outlet obstruction. Innumerable T2 hypointensities and patchy areas of diffusion restriction, too numerous to count, favored to reflect hyperplastic nodules without suspicious lesion.
- Heterogeneous vascularity throughout the prostate. No lymphadenopathy or bone lesion. Colonic diverticulosis. Mild symphysis pubis arthrosis. Normal space of Retzius. Normal rectoprostatic angles.

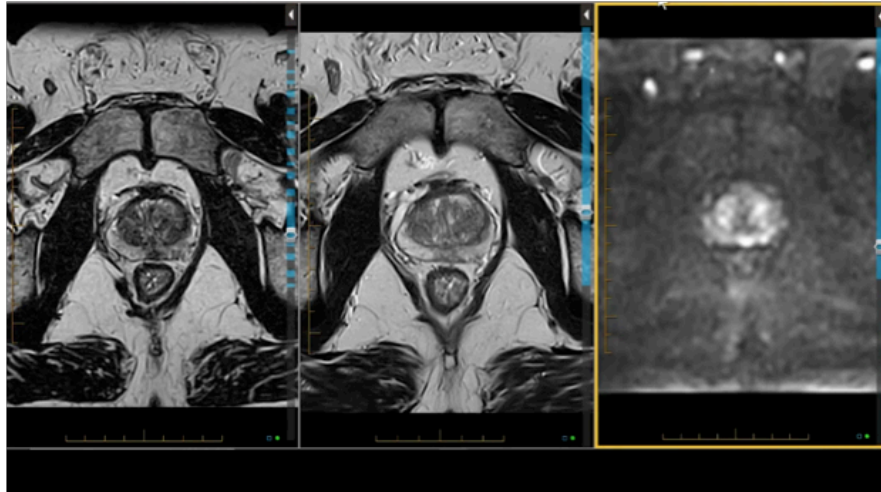
- **CONCLUSION:**

- PI-RADS 4:
 - Left base lesion in the PZpm with diffusion restriction, T2 hypointensity and possible seminal vesicle involvement, which would make this a T3b lesion. No visible extracapsular extension.
 - BPH and bladder outlet obstruction. Heterogeneous signal throughout the central gland without suspicious focus.
 - Incidental prostate utricle cyst.

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PI-RADS 5 - Example

- This 63-year-old male presents with elevated prostate-specific antigen (PSA).



Image 1 - Axial 2D T2 FSE / TSE (2.5mm) apex to base right isointense mass over 2cm with extensive capsular contact

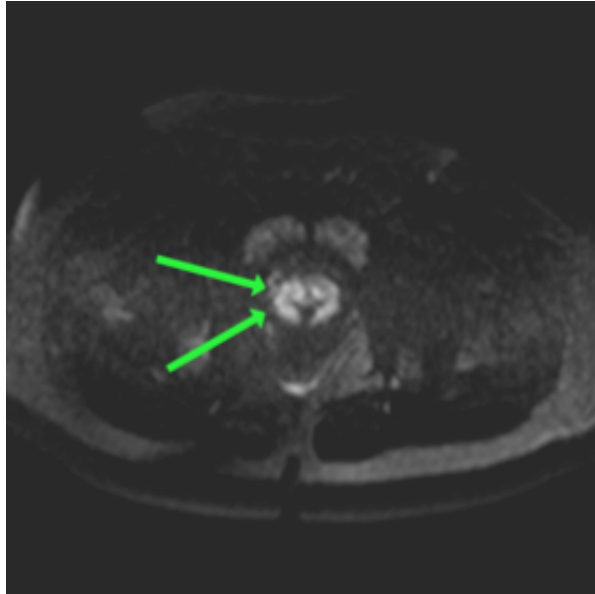


Image 2 - Diffusion b-1600 (arrows) hyperintensity right relative to left gland consistent with diffusion restriction more easily seen on ADC map.

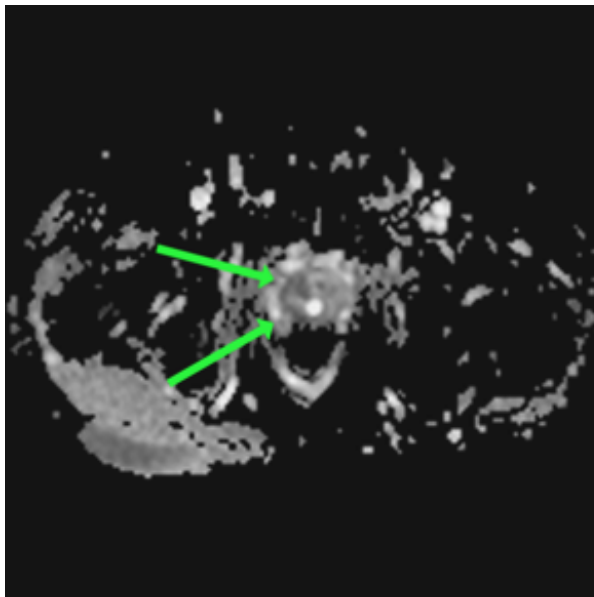


Image 3 - ADC b-1600 parametric map (arrows) shows low signal right gland velocity restriction.

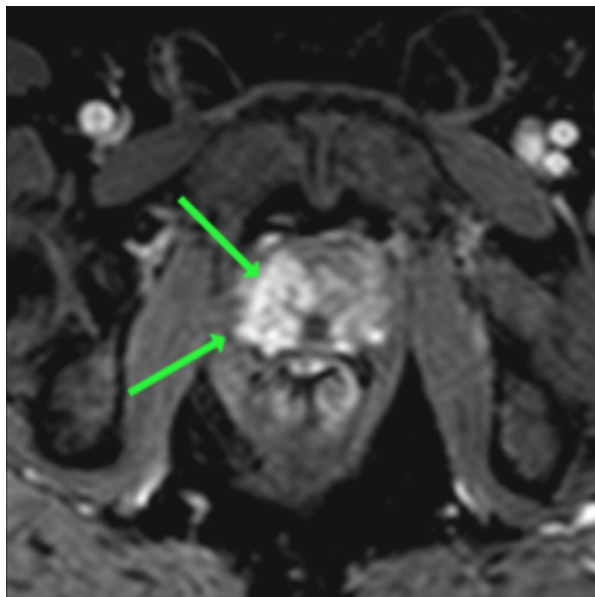


Image 4 - DYN THRIVE (arrows) DCE MRI post contrast Phase 1 (7 seconds) (4mm) with 50% overlap; pronounced enhancement right gland.

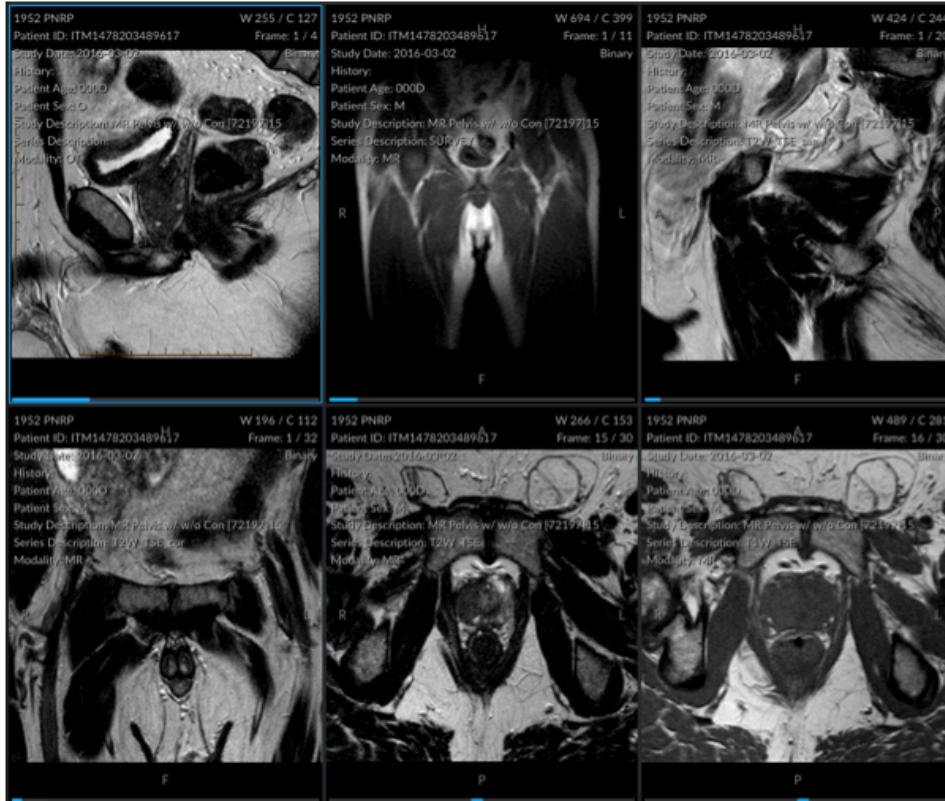
- **FINDINGS:**

- The prostate is 4.2cm in transverse dimension, 3.5cm in AP dimension and 3.5cm in craniocaudal dimension. A uniformly hypointense mass throughout the right hemisphere involving both the peripheral zone and central gland from apex through the base with probable areas of crossing midline. There is suggestion of extension to the base of the seminal vesicle. Subtle irregularity of the right side capsule probably represents transcapsular extension. The neurovascular bundle appears spared. Moderate restricted diffusion of the lesion with early and persistent enhancement. A fluid intensity posterior of midline probably is utricule cyst.
- No direct invasion through the urinary bladder. No lymphadenopathy in the visualized pelvis. Bilateral small inguinal hernia with fat. Visualized osseous structures normal in signal intensity.

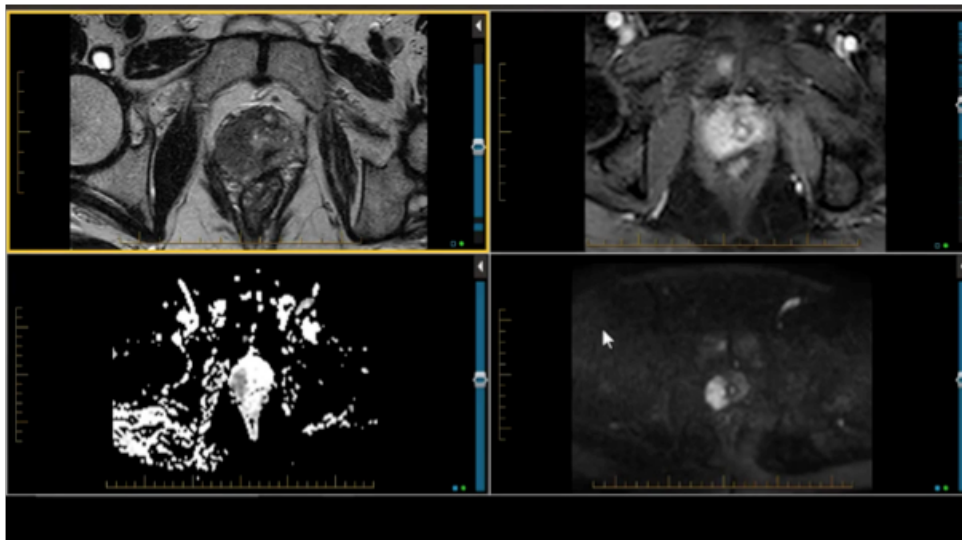
- **CONCLUSION:**

- Large mass replacing the right hemisphere of the prostate from apex to the base with suspicious invasion of the base of the right seminal vesicle and probable transcapsular extension, PI-RADS 5.
- No evidence of lymphadenopathy in the visualized pelvis. No evidence of direct involvement of the neurovascular bundle.

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SURVEILLANCE

- **Application of prostate MRI from a urologic perspective:**
 - Patient must qualify for surveillance by way of the Epstein Inclusion Criteria and Tiers of Assessment (i.e. Gleason, PSA, Tumor count).

Epstein Inclusion Criteria

- The Epstein Inclusion Criteria was developed in 1994 for the purpose of assessing prostate cancer significance.
- Insignificant prostate cancer was defined as having a tumor volume less than 0.2cm³, organ-confined, and no Gleason patterns 4 or 5. Being characterized as a 'minimal tumor' implied that the tumor volume was 0.2-0.5cm³.
- As originally defined by Epstein in the validation studies, the optimum preoperative criteria were:
 - PSA density must be less than 0.1ng/mL
 - Gleason score must be less than 7
 - Number of cores positive for tumor must be less than 3
 - Volume of core positive for tumor must be 50% or less
 - Must be clinically organ-confined

Tiers Of Assessment For Surveillance: Gleason

Correlating ADC and Gleason Score

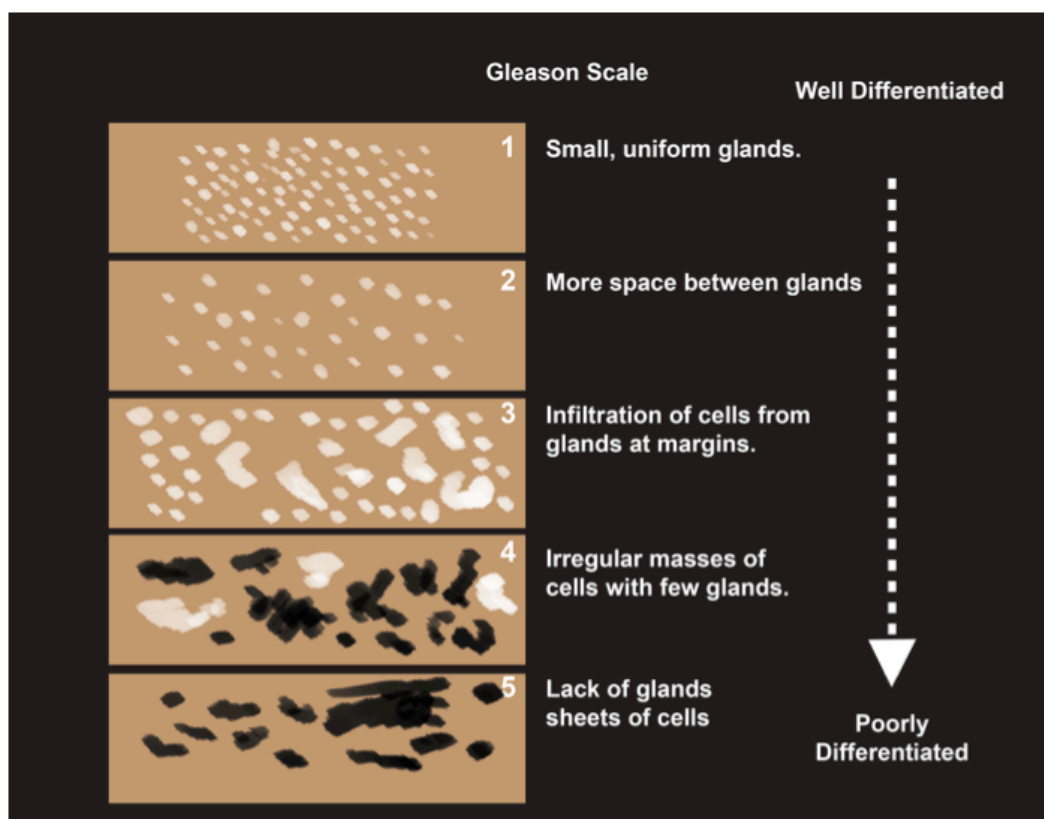
Example of a study showing Apparent Diffusion Coefficient (ADC) values and their Gleason Score Correlation (more studies are still needed to validate)

Gleason Score	Number of Tumors	Least-Squares Mean	Standard Error of Mean	Range - ADC (x10 ⁻³ mm ² /s)
6	25	0.860	0.036	0.659-1.263
7	37	0.702	0.030	0.108-0.963
8	10	0.672	0.057	0.417-0.875
9	9	0.686	0.067	0.534-0.848

Gleason Classification or Scale

Pathology - Malignant Neoplasms

Grade 1	Tumor composed of well-defined individual glandular nodules, closely arranged, uniform and separate from each other
Grade 2	Tumor still relatively well defined, but with possible minimal extension of the neoplastic acini to the periphery of the tumor nodule in the noncancerous prostatic tissue
Grade 3	Tumor infiltrates the noncancerous prostatic tissue; the gland shows marked variation in size and organization
Grade 4	Markedly atypical cells with extensive infiltration into surrounding tissues
Grade 5	Tumor presents no glandular differentiation; composed of sheets of undifferentiated cancer cells



- **The score is defined by the combination of the primary predominant grade, and the secondary grade.**
- **Its range is potentially from 2 (1+1) to 10 (5+5).**
- **A score of 2 to 4 in biopsies is rare:**
 - these are generally lesions present in the transition zone which are sampled during transurethral resection of the prostate (TURP).
- **The Gleason grade is reported for each individual biopsy sample, and the biopsy with the highest grade is considered representative of the Gleason score of the patient.**
- **Patients can have a well-differentiated tumor (Gleason score 2 to 4), moderately differentiated (5 to 7), or poorly differentiated (8 to 10).**
 - However, it should be borne in mind that a Gleason score of 4+3=7 is different from 3+4=7, because, although the sum is the same, in reality the first case has a higher primary grade.
 - In other words, the Gleason 4 is in more samples or “chips” than the Gleason 3 in the 4+3=7 scenario. Therefore, this is a more serious scenario than the 3+4=7.
- **In addition to the primary and the secondary grades, the tumor also shows a tertiary grade which is higher than the other two.**
 - Despite being less represented, this tertiary grade needs to be included (and added to the primary grade) in the Gleason score since a small focus of high-grade carcinoma present in the biopsy may correlate with a significant presence throughout the entire prostate, thus influencing prognosis.
 - Therefore, 3+4+5=8 and not 7, and 2+3+4=6 and not 5. You take the highest and lowest numbers and add them together.
- **The application of the Gleason score is unreliable in the evaluation of tumors which have been subject to neoadjuvant hormone therapy or radiotherapy. In these cases it is better to refer to the pretreatment Gleason biopsy.**

Tiers Of Assessment For Surveillance: PSA Assay

- As PCA3 testing has not become a part of routine clinical practice, PSA (glycoprotein produced mainly by the prostate) can currently be considered the only marker used on a routine basis in patients with prostate disease.
- PSA is however nonspecific, since it can be elevated in the presence not only of malignant lesions, but also of benign ones (e.g. hyperplasia, acute inflammation, infarction, urinary retention), as well as after several diagnostic procedures such as digital rectal examination (DRE), cystoscopy, and prostatic biopsy.
- In the latter case, increases of up to 50 times may be observed with a slow return to normal values in 30 to 60 days.
- Therefore, when we want to evaluate therapy-induced changes in PSA, the assay should be done prior to DRE, TRUS, and instrumental procedures in the rectum and colon (e.g. rectoscopy or colonoscopy).
- In addition, a period of four weeks should pass after prostatic biopsy if the measured serum PSA is to be considered reliable.
- On the other hand, PSA levels in the bloodstream can decrease following the use of several drugs utilized in the treatment of benign prostatic hyperplasia (BPH).
- The PSA drops in men who use minoxidil for hair growth.
- Considering the prevalence of prostate cancer in the population affected by BPH, a drug-induced reduction in PSA can compromise the diagnostic utility of the marker in the presence of malignant tumor.
- **Therefore, to exclude the concomitant presence of the latter, the following is advisable:**
 - Baseline measurement prior to the beginning of treatment
 - Successive six-monthly monitoring
 - Further diagnostic procedures if any decrease in PSA >50% is not observed or if PSA levels rise over time
- **PSA is generally evaluated with reference to a threshold value calculated on the basis of the distribution of the marker in normal subjects.**
 - The threshold value used is 4 ng/mL, although this value may be considered conventional since it is characterized by low positive and negative predictive values.
 - This is due to several reasons including patient age (PSA tends to increase in the elderly), and the overlap between patients with neoplasm confined to the prostate and patients with BPH who present values ranging from 4 to 10 ng/mL.

- **Positive biopsy for prostate cancer correlation**
 - The possibility of a positive biopsy for prostate cancer can be correlated with tPSA values.
 - The probability of carcinoma in patients with tPSA of 0.0-4.0 ng/mL is 10%, and in 90% of cases the tumor is confined to the prostate.
 - With a tPSA of 4.0-10.0 ng/mL the probability of carcinoma is 25% with the tumor confined to the prostate in 70% of cases.
 - With a tPSA >10.0 ng/mL the probability of carcinoma is 50%, with the tumor confined to the prostate in 50% of cases.
- **Age-adjusted PSA**
 - Adjusting the PSA value on the basis of patient age has been introduced to improve the sensitivity of the marker in young subjects and the specificity in the elderly.
 - The correlation of PSA values by age does not guarantee an acceptable increase in sensitivity and specificity.
- **PSA Ratio**
 - Serum PSA exists in various forms, even though most of it is in complex with protease inhibitors such as alpha 1-antichymotrypsin, and only a small amount is present in the free form.
 - The ratio between free PSA (fPSA) and total PSA (tPSA) is defined PSA ratio.
 - The percentage of fPSA is lower in subjects with prostate cancer.
 - Therefore, the percentage of fPSA can be useful in determining which patients should undergo prostatic biopsy.
 - It has been demonstrated that the percentage of fPSA can increase the specificity of tPSA in subjects with a tPSA between 2.5 and 10 ng/mL.
 - The sensitivity and specificity of the percentage of fPSA are independent of the age of the subject undergoing the examination.
- **PSA Velocity and PSA Doubling Time**
 - PSA velocity measures the changes in PSA over one year, thus making possible a longitudinal evaluation of serum PSA levels.
 - In the first half of the 1990s, the concept was introduced that an increase in tPSA greater than 0.75 ng/mL per year is suggestive of carcinoma.
 - PSA doubling time measures the rate of change in a different manner, using a logarithmic formula to calculate the time it takes for PSA to double in value. The formula is:
 - $\log(2x)$ divided by $\log(\text{final PSA}) - \log(\text{initial PSA})$.
 - PSA doubling time is expressed in months.

- **PSA Density**
 - PSA density refers to the tPSA divided by the prostate volume expressed in cubic centimeters (cc).
 - The calculation can be made in terms of the total prostate volume (PSA density), or in the terms of the volume of the transition zone, the site of BPH (PSA transition zone density).
 - Normally, in subjects with a tPSA between 4 and 10 ng/mL a normal PSA density value is 0.15.
- **cPSA**
 - Currently it is possible to assay PSA in complex with alpha 1-antichymotrypsin (cPSA).
- **Formulas for Calculating Prostate Volume**

$$\text{Ellipsoid volume} = L \times W \times H \times \frac{\pi}{5}$$

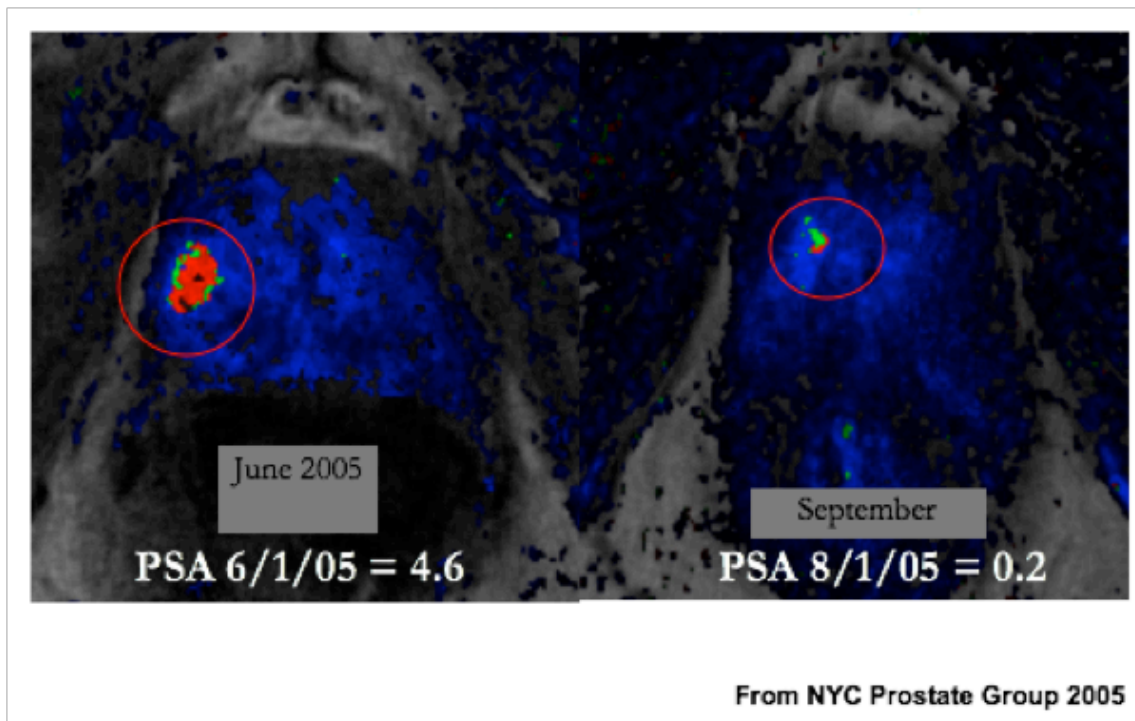
$$\text{"Bullet" (cylinder + half ellipsoid) volume} = L \times W \times H \times \frac{5\pi}{24}$$

The "bullet" volume may be a better representation of prostate volume for prostate glands smaller than 55cc

$$\text{PSA density (PSAD)} = \text{PSA level} / \text{Prostate Volume}$$

Active Surveillance

- **Leads to less frequent biopsies and unnecessary prostatectomies**
 - Can watch low grade tumors over time to observe if they grow or become more advanced based on size, shape, DCE MRI and ADC
- **Provides guidance for biopsy technique when matched with TRUS**
- **MRI usually ordered six months post-biopsy (if negative), then annually (if elevated PSA)**
- **Wait at least eight weeks after positive biopsy for MRI (due to hemorrhage)**
- **Greatest value of MRI is in excluding high grade Gleason 7, 8, 9, and 10 carcinomas**
- **Second greatest value is in evaluating high risk morphologies for capsular and extracapsular spread**

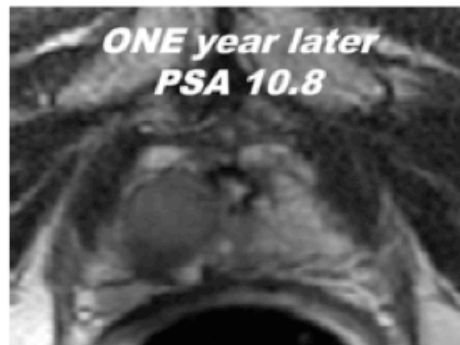
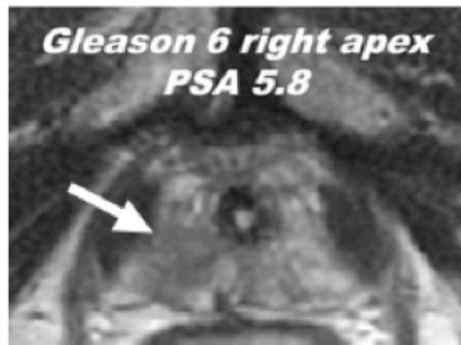
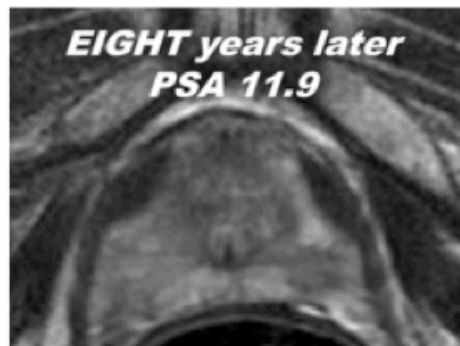
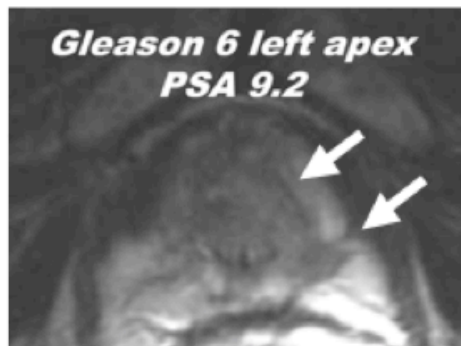




BASELINE – G6 PSA = 5.8



4 YEARS LATER



Surgical planning

- **MRI aids in decision making for nerve sparing:**
 - Prostatectomy, robotic
 - Radical prostatectomy
 - No surgery because tumor is too advanced
 - No surgery because tumor is lower grade (e.g. MR negative with positive biopsy Gleason 6 or less)
- **Capsular abutment (2cm or more) and / or direct infiltration seen on high resolution MRI consistent with capsular INVASION (82% likely)**
- **Lymph node dissection**

MRI aids in timing of surveillance biopsies

- **For patients with low risk disease**
- **MRI obtained at four to six months post initial biopsy**
- **Non-concerning MRI, can use PSA velocity, and exam: Repeat biopsies may be extended to 24 months or longer**
- **Concerning MRI, PSA, or exam: Biopsy indicated for restaging**

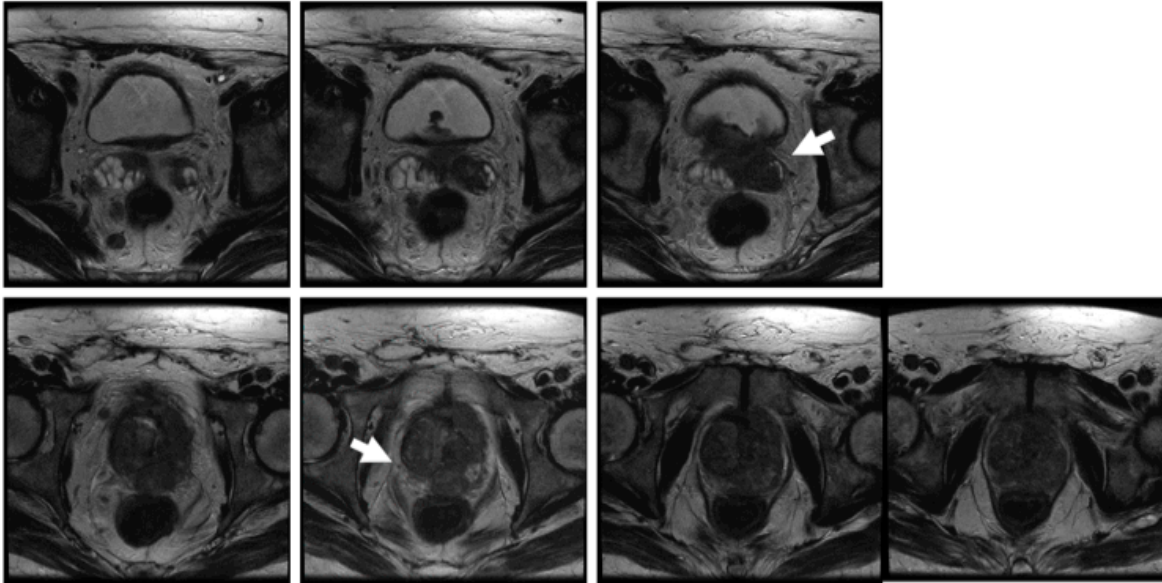
MRI aids in planning biopsy technique

- **If a concerning lesion on MRI is difficult to sample transrectally, then may get transperineal biopsy**
- **Can attempt to target area of lesion on biopsy (via “cognitive fusion” or MRI / ultrasound digital fusion)**

Diagnosis of extracapsular extension

- **Imaging findings suggesting extraprostatic extension:**
 - Soft tissue tumor growing over the capsule
 - Capsular bulging or irregularity
 - Broad capsular contact
 - >1cm and certainly as indicated above
 - 2cm of abutment = 82% likelihood
 - Filling in of the rectoprostatic angle, posterolaterally on T1WI (e.g. loss of fat planes)
 - Asymmetry or invasion of the neurovascular bundles

Capsule and Seminal Vesicle Invasion Axial T2 TSE

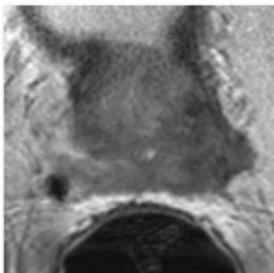


- Capsular contact for predicting extracapsular extension
- >2 cm: an accuracy of 82%
- <1 cm: the chance of extracapsular extension was 5%
-

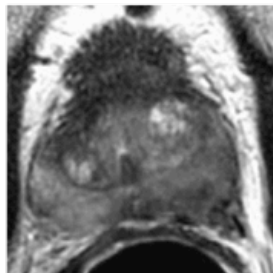
MRI Findings in T3 Disease with Capsular Signs of Involvement

- Source: *Radiology* 1997; 202: 697-702 and 2005; 237: 541-549
- Abbreviations: RP = Rectoprostatic angle; NVB = Neurovascular Bundle

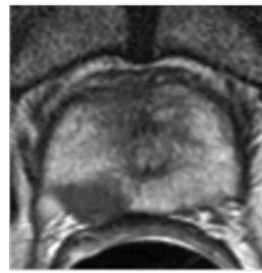
***Focal
irregular
bulge***



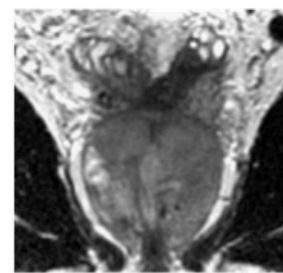
***NVB
asymmetry***



***Obliteration of
RP angle***



***Seminal
vesicle
invasion***



T-stage of TNM classification for prostate cancer

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Clinically inapparent tumor neither palpable nor visible by imaging
T1a	Tumor incidental histologic finding in 5% or less, or tissue resected
T1b	Tumor incidental histologic finding in more than 5% of tissue resected
T1c	Tumor identified by needle biopsy (e.g. because of elevated PSA)
T2	Tumor confined within prostate
T2a	Tumor involves one-half of one lobe or less
T2b	Tumor involves more than one-half of one lobe but not both lobes
T2c	Tumor involves both lobes
T3	Tumor extends through the prostate capsule
T3a	Extracapsular 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 pelvis wall

MODALITIES OTHER THAN MRI

MR Spectroscopy

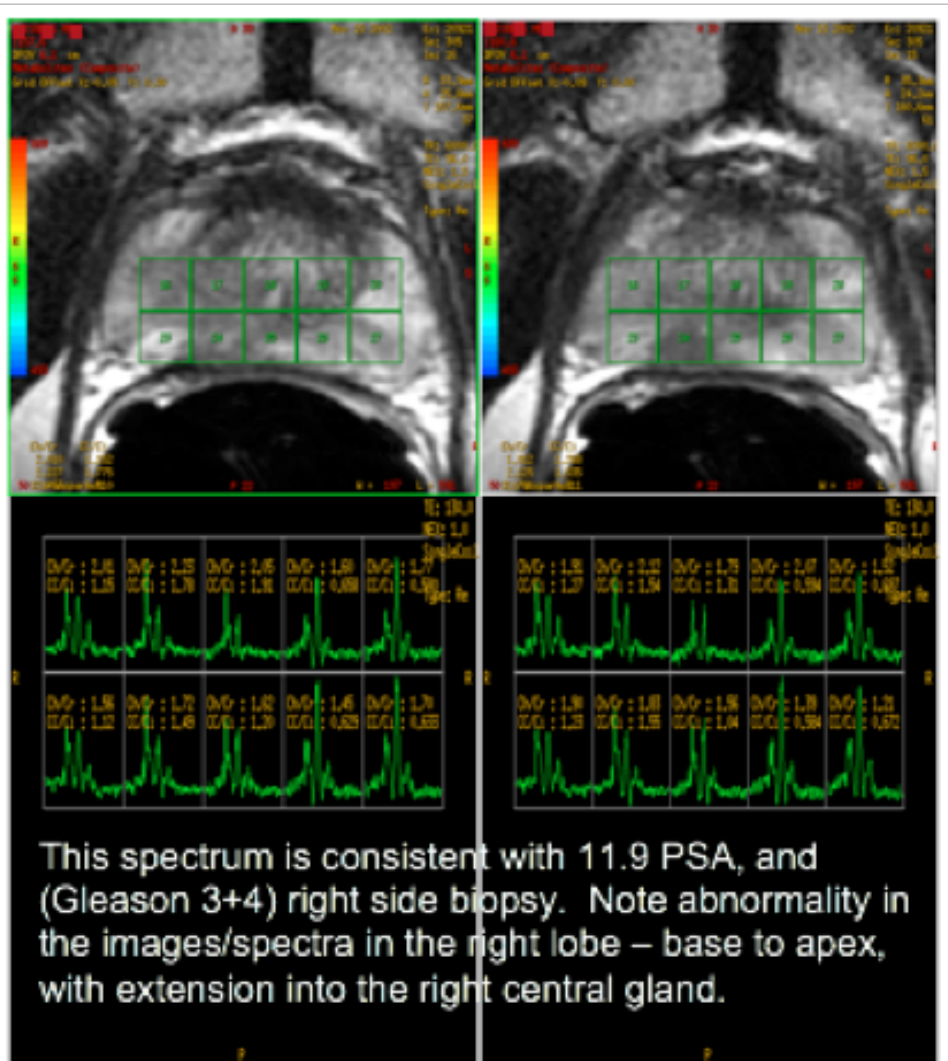
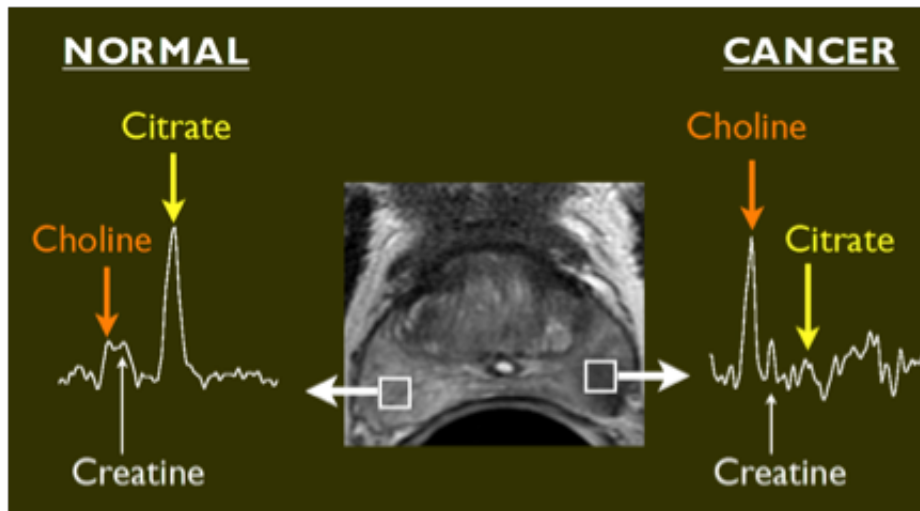
The rationale behind the use of magnetic resonance spectroscopy (MRS) is provided by the demonstration of elevated levels of choline and low levels of citrate in the carcinoma. This is the opposite of normal prostate tissue where the concentration of citrate is high and choline is low. The low concentrations of citrate in the tumor are the result of changes in cellular function and tissue architecture. In fact, the neoplastic cells are less able to synthesize citrate, and the normal glandular epithelium is substituted by the newly formed tissue. High concentrations of choline, which is a component of the cellular membranes, are found in carcinoma of the prostate due to the irregular multiplication of the tumor membranes.

The presence of cancer is hypothesized when the ratio (>0.75) of $(\text{Cho}+\text{Cr})/\text{Cit}$ in the suspicious zone deviates by more than 2 to 3 standard deviations (SD) with respect to the value obtained in the healthy reference zone. A ratio (>0.86) of $(\text{Cho}+\text{Cr})/\text{Cit}$ greater than 3 SD with respect to the value of the normal zone is defined as the definite presence of neoplasia. The voxels with a ratio less than 0.75 are defined as normal tissue of the peripheral zone.

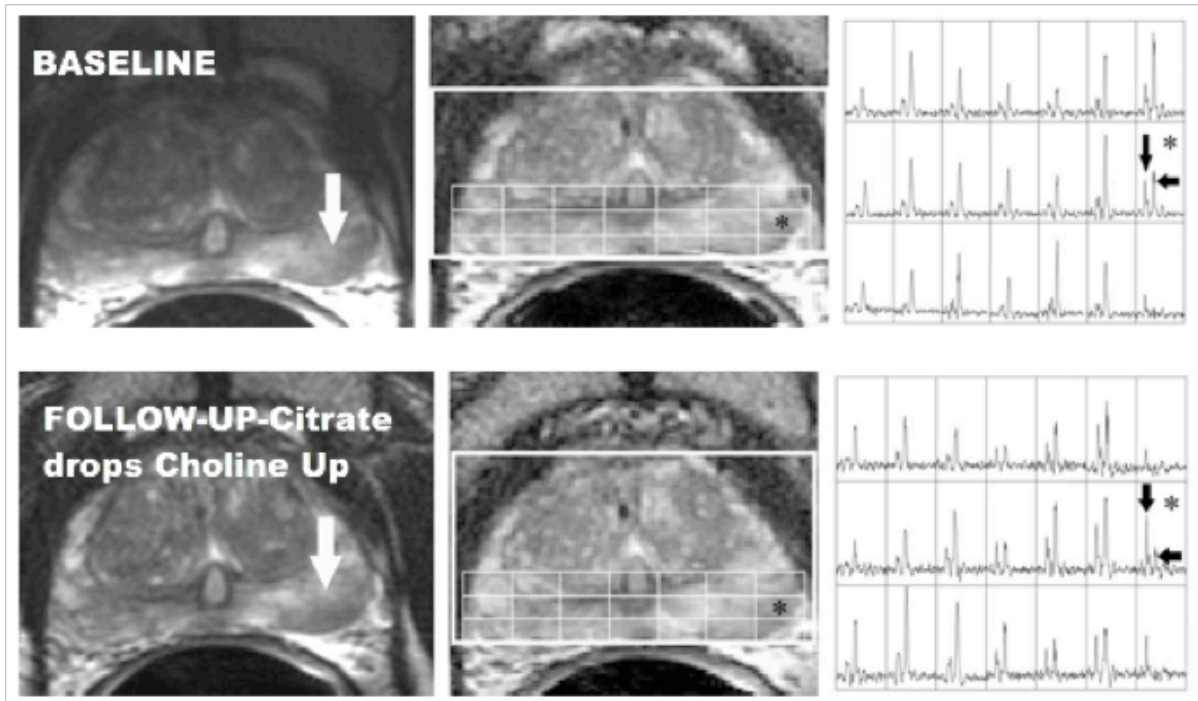
A marked reduction to the point of absence of the citrate peak has been observed in cases of high-grade Gleason tumors and a smaller reduction in the peak in low-grade Gleason tumors.

The Key Peaks: Citrate, Creatine, and Choline

- **Normal Peripheral Zone and Hyperplastic Central Zone of the Prostate Contain Citrate**
- **Low Citrate Occurs in Prostate Cancer due to Conversion from Citrate Producing to Citrate Oxidizing**
- **Elevated Choline due to High Phospholipid Cell Membrane Turnover in Proliferating Cells in Prostate Cancer**



Disease monitoring by MRI/MRSI (e.g. Spectroscopy)



Bone Scintigraphy

- **A positive scintigraphy is highly uncommon with PSA levels below 20 ng/mL. The examination is therefore indicated in patients with:**
 - PSA >20 ng/mL
 - Clinically staged disease \geq T3
 - A primary Gleason \geq 4
 - Gleason score \geq 8 and PSA >10 ng/mL

Whole body bone scan - example

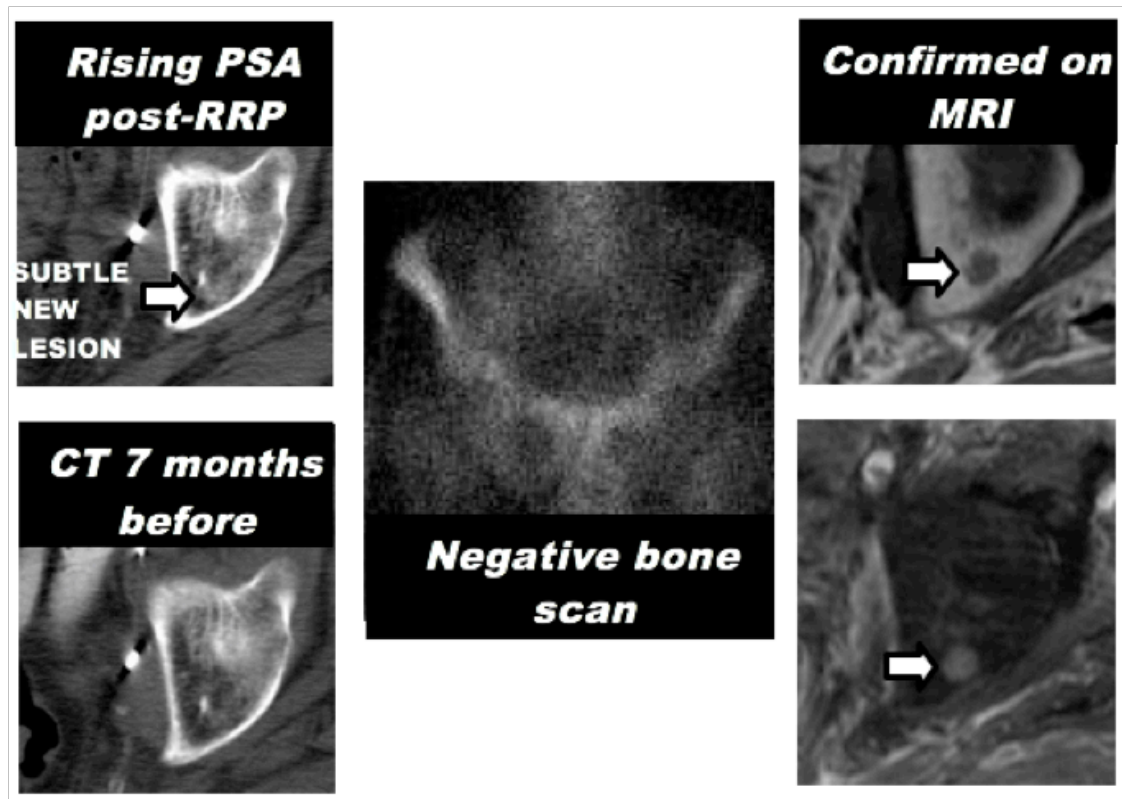


Scintigraphy and Bone Scan Positivity

PSA Level	Positive bone scan		
	0%	0%	0%
< 10	0% (0/290)	0% (0/71)	0% (0/161)
10-20	4.5% (4/88)	1.6% (1/61)	2.1% (2/95)
> 20	21% (24/112)	41% (34/82)	-

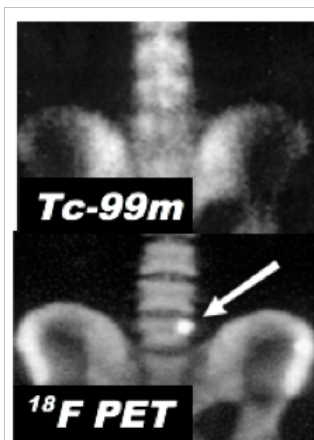
Gleave et al, Urology 1996; 47: 708-12 Rhoden et al, Int Braz J Urol 2003; 29: 121-125 Hirobe et al, Jpn J Clin Oncol 2007

Negative Bone Scintigraphy, Positive CT and MRI



Fluoride Positron Emission Tomography (fPET)

- Pearls
 - ¹⁸F PET "Fluoride PET" more sensitive than Tech 99m bone scintigraphy
 - Dawson, Semin Oncol 1999; 26: 174-84
 - Schirrmeyer et al, J Clin Oncol 1999; 17: 2381-9
- 80% of Stage IV Disease is Bone positive only

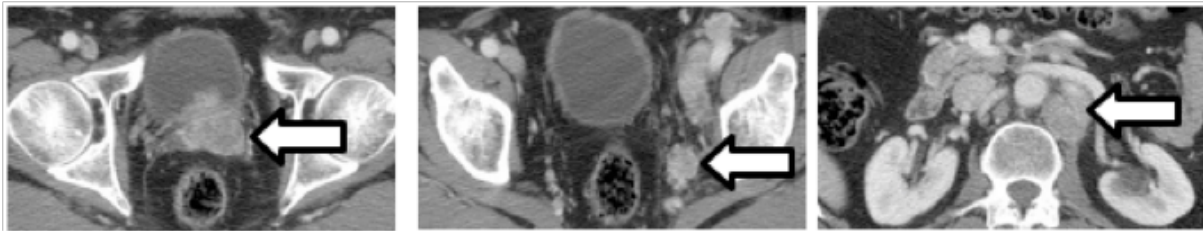


Computed Tomography (CT)

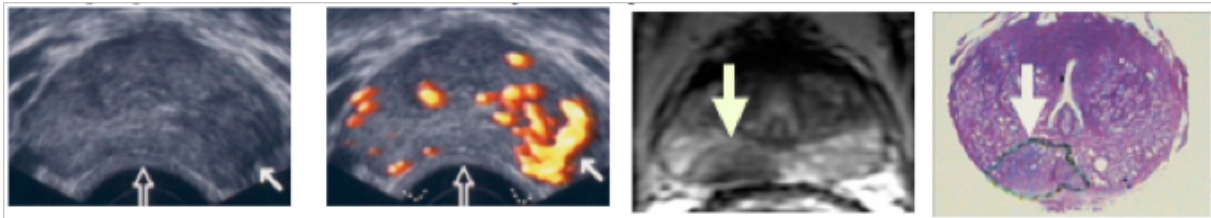
CT and Nodal/ Disease Positivity in New Untreated Patients

N	Positive CT	PSA cut-off
300	10 (3%)	> 20 in 8
588	41 (7%)	> 15 in 33
425	13 (3%)	> 30 in 11

Huncharek et al, Cancer Invest 1995;13: 31-5 Lee et al. Urology 1999; 54: 490-4
Huncharek et al. Abdom Imaging 1996; 21: 364-7

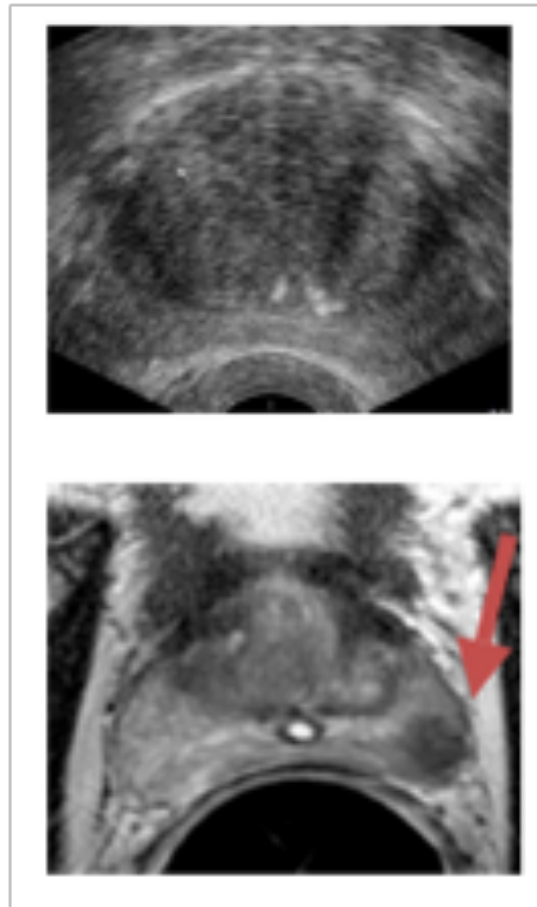


Comparison of Sonography, MRI and Pathology with Peripepheral Zone Tumor (arrow)



Transrectal Urethral Ultrasound (TRUS)

TRUS with Peripheral Zone tumor (arrow)



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