Prostate Cancer Imaging: What the Urologist Needs to Know

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Learning objectives

our objectives are to:

1. describe différents imaging modalities used in détection and staging of prostatic cancer including US (B mode, doppler and real time elastography), multiparametric MRI(dynamic contrast-enhanced imaging, diffusion-weighted Imaging) and CT.

2. review different aspect of prostatic cancer in each modalitie.

3. be familiar with essential radiologic findings helpful in staging cancer
Background

Prostate cancer is the most commonly diagnosed cancer in men in the USA and Europe, and the second most common cause of cancer death.

The incidence rates of prostate cancer vary worldwide, with the lowest rates in many parts of Asia and the highest rates in Europe, North America, and Oceania [1,2].

Risk factors that may increase a person's chance for developing prostate cancer include older age, family history, ethnicity, high consumption of fat and red meat, and geographic location[3].

The prognosis for men with localized prostate cancer is excellent. Nearly 100% of men with localized prostate cancer live at least 5 years after diagnosis. The same is true for men with regional prostate cancer, which means the cancer has spread from the prostate gland to nearby areas in the body [4].

So early detection and accurate staging of the disease is mandatory for optimal disease management.

Making a diagnosis of prostate cancer generally includes investigating presenting features from prostate-specific antigen (PSA) blood testing, PSA velocity (how much a patient's PSA levels increase from year to year), digital rectal examination (DRE), blood count and biochemical profile, transrectal ultrasound (TRUS), magnetic resonance imaging (MRI), and biopsy.

two clinical situations arise requiring a different exploration imaging:

• Patients who do not have a prostate cancer diagnosis: the role of imaging is to diagnose cancer.
• Patients who have clinically localized prostate cancer: imaging aims is to make an accurate staging to plan therapy.
Findings and procedure details

Anatomy (Fig 1):

The prostate is a compound tubuloalveolar exocrine gland that is part of the male reproductive system [5].

It is situated at the base of the bladder and surrounds the urethra. The rectum sits posteriorly, allowing for the prostate to be palpated via rectal examination.

Prostate cancer is usually described by zones according to McNeal's concept that includes glandular tissue (Peripheral, Central and Transition) and nonglandular tissue (Anterior fibromuscular stroma):

- **Peripheral zone (PZ):** comprises of the posterior part of the gland surrounding the distal urethra. Between 80-85% of cancers arise in the PZ [6].

- **Central zone (CZ):** surrounds the ejaculatory ducts. Only approximately 5-10% of cancers arise in the CZ [6].

- **Transition zone (TZ):** surrounds the proximal urethra. The TZ enlarges throughout life (BPH). Approximately 10-15% of cancers originate from the TZ [6].

- **Anterior fibromuscular stroma:** forms the entire anterior surface of the prostate as a thick, nonglandular apron, shielding from view the anterior surface of the three glandular regions [7].

The surgical or the pseudocapsule marks the junction between the transition and the peripheral zone.

The true capsule surrounds the peripheral zone.

Normal appearance of prostate:

Ultrasound:

Distinction between central and peripheral zones is not ordinarily visualized by ultrasound, with both zones normally demonstrating a homogeneous light- to medium-gray area occupying the posterior third of the prostate (Fig 2 A).

Transition zone, located anteriorly, on either side of the urethra can exhibit wide variability in size depending on the degree of benign prostatic hyperplasia (BPH). Relative to the peripheral zone, transition zone exhibits moderately heterogeneous hypoechogenicity (Fig 2 B).
With increased size of the transition zone, the peripheral and central zones become progressively more compressed (Fig 2 C).

Doppler:

We can distinguish the two arterial prostatic systems: urethral arteries whose path is parallel to the prostatic urethra and capsular arteries whose pedicle is visible to the posterolateral angle (Fig 2 D).

The peripheral zone appears most often hypovascular.

In BPH, vascularisation appears clearly in the periurethral region. In rest hyperplasia, vascularization is variable, the vessels usually circumscribing the hyperplastic nodules with rare spots within these nodules.

MRI:

• The zonal differentiation is not observed in T1 without contrast medium injection (Fig 3 A).

• In T2 WI:

  **The peripheral** zone typically has a high signal and sometimes crossed by homogeneous hypointense bays corresponding to the perforating vessels (Fig 3 B).

  **The central zone** is intermediate signal, triangular coronal, and crossed by the ejaculatory ducts which light can be seen as hyperintense fluid.

  **The transition zone** is rarely identifiable outside BPH where it has a heterogeneous structure, often nodular in significant hyperplasia, whose signal depends partly on the histological type (Fig 3 B).

The peripheral zone appears pent back, compressed by the adenoma, and this high signal, which becomes more heterogeneous. The adenoma is separated from the peripheral zone by a hypointense rim corresponding to the surgical capsule (Fig 3 B).

**Prostatic capsule**

The peripheral zone is surrounded by a hypointense edged whose presence is attributed to the prostatic capsule (Fig 3 B).

**Fibromuscular tissue**

The low signal intensity of the prostatic capsule thickens forward, forming anterior fibromuscular stroma.

**Seminal vesicles and deferential bulbs**
The seminal vesicles are visible as hyperintense structures with thin hypointense walls, giving it an aspect curled (Fig 3 C and D).

The role of the imaging is different depending on whether the cancer diagnosis is established or not.

- Patients who do not have a prostate cancer diagnosis but who have a high clinical suspicion due to a positive digital rectal examination or a high or rapidly rising PSA, where imaging must first diagnose the cancer:

**Ultrasound:**

TRUS is the most common form of prostate imaging, largely to its role in directing biopsies.

TRUS alone has poor test characteristics for the diagnosis of prostate cancer, with a positive predictive value of 52.7%, a negative predictive value of 72%, and an accuracy of 67% in modern series [8].

Historically hypoechoic lesions have been associated with a prostate cancer and should be noted on TRUS (Fig 4 A). However, lack of hypoechoic lesion does not mean cancer is not present.

Isoechoic areas demonstrated relatively equal per core cancer detection compared to hypoechoic areas (9.3 % vs. 10.4 % respectively) [9].

Hyperechoic lesions are less common than either hypoechoic or isoechoic lesion but display a similar propensity to cancer detection with a possible association with higher Gleason grade [10].

Based on unreliability of hypoechoic lesions to identify prostate cancer, most authors recommend including hypoechoic lesions in the systematic biopsy template.

**Doppler:**

Because higher blood flow is often associated with tumour, Colour Doppler US has been shown to be an important adjunct to conventional gray-scale transrectal US, improving the accuracy of cancer detection, especially for isoechoic cancers with higher Gleason grades [11].

In Colour Doppler US, either a focal area of increased vascularity or asymmetry in colour between the two sides of the prostate can be seen (Fig 4 B).

Microbubble contrast agents have been reported to improve detection of tumour vascularity, but not used for routine detection.
**US-elastography:** Prostate cancers have a higher elastic modulus (stiffness) than that of surrounding normal prostate tissue (Fig 4 C).

Endorectal real-time elastography enables the diagnosis of prostate cancer with a reported accuracy of 76% [12].

**Biopsy:**

TRUS-directed prostate needle biopsy is the gold standard for the diagnosis of prostate cancer.

Oral or intravenous antibiotics are state-of-the-art treatment using quinolones (ciprofloxacin superior to ofloxacin). Optimal dosing and treatment time vary. [13].

No consensus in the literature exists in regard to the impact of a bowel-cleansing enema before biopsy on transrectal guided prostate biopsy complication rates [14].

The procedure is performed after a periprostatic nerve block.

A core biopsy needle is deployed to obtain specimens from anatomically distinct areas of the prostate (from the left and right lobes and at the levels of the apex, middle, and base).

Extended biopsies in which 8, 10, or 12 specimens are obtained have resulted in improved detection of prostate cancers. However, no standardized guidelines exist regarding which biopsy technique should be used [14].

In our practice, at least 12 samples are obtained at all three levels in the peripheral zone (Fig 5).

**MRI**

The endorectal MRI, MRI spectroscopy and dynamics MRI can sometimes help to improve detection by looking for targets for biopsy.

T2-weighted sequences detect low-signal areas of tumour within the relatively high-signal and homogenous peripheral zone (Fig 6 A).

Detection of cancer foci is much worse in the transitional zone where their distinction from the heterogeneous signal of benign prostatic hyperplasia (BPH) in T2-weighted sequences has been almost impossible unless they are large or distorting, recent papers have suggested that homogenous low signal, lenticular shape, and invasion of the anterior fibromuscular stroma can all be used to identify transitional zone cancer.

**Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI)**

The purpose of the injection of gadolinium is to characterize intratumoral angiogenesis kinetics.
Contrast enhancement including slope (wash in), the maximum value of the peak, and the slope of washing (wash out). There is a difference between the cancer and the normal peripheral tissue (Fig 6 B). However, there is no correlation between the signal strength, the PSA and Gleason score.

**Diffusion-Weighted MRI:**

Diffusion-Weighted MRI (DW-MRI) sequences can detect and quantify the Brownian motion of water within tissue in vivo.

In the malignant setting, relative higher nuclear/cytoplasmic ratio and loss of extracellular spaces due to cellular proliferation results in decreased free water diffusion and thus relative decreased signal intensity on DW-MRI (Fig 6 C and D).

Furthermore, DW-MRI findings have been significantly correlated to underlying histopathologic grade and clinical risk scores [16].

Despite its relatively poor spatial resolution, addition of DW-MRI to standard anatomic T2-WI has been demonstrated to improved diagnostic accuracy [17].

**MRI spectroscopy** collects biochemical spectral information and not an image. We can then study the concentration of different metabolites located within the tissue, such as choline and citrate. Thus, the spectroscopic scores allow differentiating normal tissue from cancerous tissue.

In case of negative biopsies with increase of the PSA and a normal conventional MRI, MR-spectroscopy may allow diagnosis from 29 to 40% of cancers [18].

- Patients who have clinically localized prostate cancer: Imaging in this disease state can provide useful information. Differentiating between T3 disease (prostate cancer that has spread outside the prostatic capsule) and T2 disease (prostate cancer confined within the capsule) is critical because it often drives the decision to use radiation therapy as opposed to radical prostatectomy.

**Ultrasound:**

It is usually performed prior to cancer diagnosis, and staging before a biopsy is dependent on the operator experience. An experienced observer may easily assess a locally advanced tumour (T3) (Fig 7).

**MRI**

**Local extension**

MRI is the only morphological examination that can detect an extraprostatic invasion without the need for biopsy.
The highest reliability is obtained by the use of an endorectal antenna whose superiority was confirmed this gain in sensitivity is less important with a 3T magnet.

Three direct signs were selected whose sensitivity and specificity are different[19]:

• Irregular deformation of the capsule (Fig 8 A), including spike appearance of prostate contours (sensitivity 35%, specificity 80%).

• Obliteration of the recto-prostatic angle (Fig 8 B) (sensitivity 45%, specificity 90%).

• Asymmetry or invasion of the neurovascular pedicles (Fig 8 C)). (Sensitivity 30%, specificity 90%)

The key sign is the continuity of the lesion hypointense with peri-prostatic tissue responsible for the irregular distortion or spiculated prostate contour and / or direct visibility of low signal intensity of the tumour in the peri-prostatic tissue.

The invasion of the striated sphincter (rarely seen) at the apex is a direct sign of T3 MRI apical and sub apical (Fig 9 A and B).

**The seminal vesicle invasion**

Stage T3b is only detectable in the extraprostatic portion of vesicles.

When the invasion is massive with unilateral or bilateral hypointense visible in all or part of the bladder, the diagnosis does not pose a problem (Fig 9 C and D).

In other patients, with a stage T2 prostate cancer or less, but at intermediate risk pT3, invasion of one or both of the vesicles is an MRI discovery that led to rethinking the strategy of treatment.

If radical prostatectomy is in play, guided biopsy of the vesicles becomes desirable to have histological evidence of seminal invasion.

**Assessment of lymph node:**

Accurate detection of lymph-node metastases in prostate cancer is an essential component of the approach to treatment.

Conventional CT and MRI have limited reliability for detecting lymph node involvement as they use purely morphological criteria based on size of the node, to distinguish normal nodes of metastatic lymph nodes [20] (Fig 10 A and B).

It is not possible to state the character of a metastatic lymph node because its signal and its density is often the same as those of normal lymph nodes (poor specificity).
In addition, many of lymph node metastases of prostate cancer develop in lymph nodes of normal size (poor sensitivity).

**Place of lympho-MRI:** the signal of metastatic lymph nodes was not significantly modified by the injection of superparamagnetic particles and remains high, identical to that obtained in the same sequence performed before injection (type T2 gradient echo sequence).

A non-metastatic lymph node structure sees its signal fall on the injected sequence due to its uptake of iron particles.

**Place of diffusion imaging:** The restriction of diffusion results in a high signal intensity on diffusion image correlated with a fall in the value of apparent diffusion coefficient, while the benign tissues and fluids have low signal and a value of apparent diffusion coefficient more high ([Fig 10 C and D]).

The sensitivity was 86% and specificity of 85% with an overall efficiency of 86%[21].

**Detection of bone metastases:** can be realized by scintigraphy or MRI, The sensitivity and specificity of MRI is superior to that of bone scintigraphy in all territories, except for the ribs and skull

MRI uses a whole body survey covering the bone marrow of the skull to toe with a T1-weighted gadolinium-free. T2-weighted sequence is optional ([Fig 11 A and B]).

The whole body diffusion imaging is a promising sequence being validated with excellent specificity of 92-94%[22] ([Fig 11 C and D]).
Fig. 1: prostate anatomy and zonal anatomy.

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**Fig. 2:** Normal US anatomy of the prostate.

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**Fig. 3:** normal MRI appearance of the prostate. A. axial T1 WI. B. axial T2 WI. C. coronal T2WI. D. axial T2 WI.

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**Fig. 4:** Typical ultrasound appearance of prostate cancer. A. Axial gray scale image showing a relatively well-defined focal hypoechoic lesion within peripheral zone. B. Color Doppler image showing increased vascularity versus surrounding prostatic tissue. Pathologic targeted biopsy reports revealed the presence of Gleason 8(4+4) prostate cancer. C. Real Time Elastography in another case shows a blue focal area in the left peripheral zone of the prostate indicant its hard character (Gleason 7 in targeted biopsy).

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Fig. 5: Recommended systematic 12-core prostatic biopsy, at base, mid, and apical prostate gland.

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**Fig. 6:** typical MRI appearance of prostate cancer. Axial section T2 weighted MRI shows low signal along the left peripheral zone (apex). Axial post-contrast MR image demonstrates intense enhancement of a mass in the left peripheral zone (apex). Diffusion weighted image and Apparant diffusion coefficient-map shows a right apical cancer.

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**Fig. 7:** ultrasound of right peripheral tumours with locally advanced spread.

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Fig. 8: MRI of T3 prostate cancer. A. Irregular deformation of the capsule. B. Obliteration of the recto-prostatic angle. C. invasion of the right neurovascular pedicles.

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Fig. 9: post contrast T1 WI (A) and T2 WI(B): left apical cancer with invasion of the striated sphincter. post contrast T1 WI (D) and T2 WI(C): right basal cancer with massive invasion of seminal vesicle.

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Fig. 10: Lymph node metastases of prostate cancer. A. T2 WI. B. Enhanced T1 WI. C-D. Diffusion weighted image and Apparant diffusion coefficient-map.

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**Fig. 11:** Bone metastases of prostate cancer. A. enhanced T1 WI. B. T2 WI. C-D. Diffusion weighted image and Apparant diffusion coefficient-map.

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Conclusion

Appropriate imaging for prostate cancer patients depends on the clinical disease state of the patient and the question being asked.

For patients who do not have a cancer diagnosis, US is the standard approach, in combination with a sextant biopsy. Contrast-enhanced US and MR imaging-directed biopsy improves biopsy yield and decrease biopsy number.

For patients who have clinically localized disease, MR imaging and bone scintigraphy may play a role in patients who have risk factors for extracapsular extension, but more data are needed to define the role of MR spectroscopy and lymphotropic nanoparticle MR imaging.
References


