Diagnostic Imaging Pathways - Prostate Cancer (Suspected and Staging)

Population Covered By The Guidance

This pathway provides guidance on the diagnosis and staging of adult male patients with suspected prostate cancer.

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Quick User Guide

Move the mouse cursor over the PINK text boxes inside the flow chart to bring up a pop up box with salient points.
Clicking on the PINK text box will bring up the full text.
The relative radiation level (RRL) of each imaging investigation is displayed in the pop up box.

SYMBOL	RRL	EFFECTIVE DOSE RANGE
	None	0
	Minimal	< 1 millisieverts
	Low	1-5 mSv
	Medium	5-10 mSv
	High	> 10 mSv

Pathway Diagram

What do I need to know?

1. What are the patient's risk factors?
2. Is the patient symptomatic?
3. Are there any contraindications for MRI?
4. Is there ongoing clinical suspicion despite a negative biopsy?

PROSTATE CANCER (SUSPECTED AND STAGING)

Date reviewed November 2015
Please note that this pathway is subject to review and revision

Indications for investigation

- Clinical suspicion of prostate cancer → Refer to urology → Consider mpMRI (pre-biopsy)
- Low clinical suspicion → Observation

Consider mpMRI (pre-biopsy)

- mpMRI prostate performed
  - PI-RADS 1-3 or no focal lesion
    - Low concern → Observe
    - Clinical or biochemical concern → Systematic prostate biopsy (TRUS or TP)
  - PI-RADS 4-5 → Prostate biopsy (MRI assisted) ± systematic biopsy
- mpMRI prostate not performed → Systematic prostate biopsy (TRUS or TP)

Biopsy positve

- Low risk on biopsy and clinical → Consider enrolment in active surveillance program and mpMRI if not already performed
- Intermediate or high risk on biopsy and clinical → Definitive therapy. Consider mpMRI if not already performed and further staging → Other staging modalities
  - CT (if MRI not available or contraindicated)
  - Bone scintigraphy
  - PSMA PET / CT (re-staging)

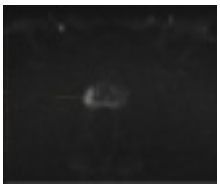
Biopsy negative → mpMRI prostate already performed?

- Yes → Ongoing clinical assessment and if clinical suspicion remains high or increases → Consider biopsy with in-bore MRI guidance or MRI-US fusion if cognitive fusion used and/or repeat mpMRI prostate at 1 year
- No → Consider mpMRI prostate

Image Gallery

Note: These images open in a new page

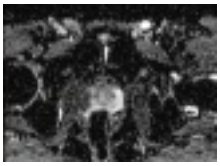
1



Prostate Carcinoma

Image 1 (Multi-parametric MRI, DWI) : peripheral zone lesion

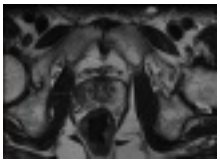
2



Prostate Carcinoma

Image 2 (Multi-parametric MRI, ADC) : peripheral zone lesion

3



Prostate Carcinoma

Image 3 (Multi-parametric MRI, T2WI) : peripheral zone lesion

Teaching Points

- With the rationale of performing pre-biopsy MRI in the initial assessment, subsequent MRI assisted biopsy may result in fewer men biopsied overall with far less cores needed or no further biopsies and prevents the diagnosis of clinically insignificant cancer
- In clinically low risk patients who have no focal lesion or a PI-RADS 1-3 lesion on mpMRI, no further imaging is indicated
- For initial staging of advanced prostate cancer, 99mTc bone scintigraphy and CT abdomen/pelvis/chest should be considered as the imaging modalities
- In patients with suspected biochemical recurrence, 68Ga-PSMA PET / CT can detect prostate cancer at low PSA levels and may be preferred over conventional imaging for re-staging.The role of 68Ga-PSMA PET / CT in primary staging is still under investigation

Prostate Cancer (Suspected and Staging)

- As prostate cancer is very age-dependent, more than two-thirds of all new prostate cancers are diagnosed in men aged 60-79 and >80% of prostate cancer deaths occur in men >70 years 1
- Around 9 in 10 Australian men with prostate cancer have a 93% 5-year survival rate. Nearly all patients who present with localised disease will live beyond five years, with the 10- and 15-year survival rates being 84% and 77% respectively. Prostate cancer relative survival (period 2006–2010) varies with age, with: 2-4
    - 1-year relative survival

- Age 0-79: 96% to nearly 100%
- Age ?80 years: 89%

- 5-year relative survival
  - Age 40-69: 95% and 97% (highest)
  - Age 70-79: 91%
  - Age

Prostate Imaging – Reporting and Data System (PI-RADS) Scoring

Guidance for assignment of overall PI-RADS v2 score [25, 26]

Peripheral zone lesion	DWI Score (dominant sequence)	DCE Score (secondary sequence)	T2WI Score	Overall PI-RADS v2 Score
	1	Any	Any	1
	2	Any	Any	2
	3	-	Any	3
	3	+	Any	4
	4	Any	Any	4
	5	Any	Any	5

Transition zone lesion	T2WI Score (dominant sequence)	DWI Score (secondary sequence)	DCE Score	Overall PI-RADS v2 Score
	1	Any	Any	1
	2	Any	Any	2
	3	?4	Any	3
	3	5	Any	4
	4	Any	Any	4
	5	Any	Any	5

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)

Multi-parametric Magnetic Resonance Imaging (mpMRI)

- mpMRI combines anatomic (T1- and T2-weighted imaging) with functional and physiologic assessment using diffusion-weighted imaging (DWI) and its derivative apparent diffusion coefficient (ADC) maps, dynamic contrast-enhanced (DCE) MRI and sometimes other techniques such as MR proton spectroscopy (though not routinely used). Although use has grown in recent years, one of the biggest challenges with mpMRI has been the substantial variation in diagnostic performance reported across different centres and lack of consistency in reporting and interpretation
- Clinical guidelines for the acquisition and reporting of mpMRI called the Prostate Imaging-Reporting and Data System (PI-RADS) were developed in 2012 by the European Society of Urogenital Radiology with a later revised version developed in conjunction with the American College of Radiology and the AdMeTechFoundation in 2014. The PI-RADS version 2 (v2) includes recommendations for risk stratification of patients with PCa, image acquisition, an overview of normal anatomy and benign findings, a lexicon of terminology as well as a proposed scoring system in order to promote global standardisation of interpretation and reporting of mpMRI
- PI-RADS v2 introduced the concept of dominant sequences based on the location of the prostate lesion. For peripheral zone lesions, the dominant sequence is DWI, which determines the PI-RADS score, with the secondary sequence DCE used for PI-RADS 3 lesions. For transitional zone lesions, the dominant sequence is T2WI and DWI is the secondary sequence used

to differentiate PI-RADS 3 lesions. The PI-RADS score reflects the probability that the findings correlate with the presence of clinically significant cancer. The assigned score is based solely on mpMRI findings alone and do not take into account PSA level, DRE findings or clinical history

- PI-RADS v1 has been validated in several studies 27-29. Since its publication, several retrospective validation studies looking at the diagnostic performance of PI-RADS v2 in PCa have shown promising results, with a reported lesion-based AUC of 0.83 and good inter-reader reliability (k=0.68) 30-32
- PI-RADS v2 is designed to be used in a pre-therapy patient and has not been tested for the detection of suspected recurrent PCa, progression during surveillance or for evaluation of other parts of the body that may be involved with PCa
- It is likely that a mpMRI showing no evidence of tumour has a negative predictive value for significant disease similar to or better than a standard 12 core prostate biopsy thus performing MRI as the first investigation in a man suspected of having prostate cancer might in some cases prevent the need for biopsy 17 in up to 51% of cases. 18 Furthermore, an MRGB pathway decreased the diagnosis of low-risk prostate cancer by 89.4%, and increased the detection of intermediate/high-risk prostate cancer by 17.7%. compared with a 12 core TRUS biopsy pathway 18
- MpMRI demonstrates high specificity (0.82-0.92), negative predictive value (NPV) (0.66-0.81) and sensitivity (0.66-0.81) for prostate cancer detection utilizing T2-weighted imaging combined with two functional techniques: diffusion-weighted imaging (DWI) and dynamic contrast-enhanced MRI (DCE-MRI) while the combination of T2WI and DWI or Magnetic Resonance Spectroscopic Imaging (MRSI) with DCE-MRI has the potential to guide biopsy to the most aggressive cancer foci in patients with previously negative biopsies, increasing the accuracy of the procedure 19
- In biopsy naive patients with elevated PSA and normal DRE, pre-biopsy mpMRI reports a sensitivity (61-71%), specificity (89-96%), accuracy (85-87%), and area under the curve (AUC) values (0.79-0.81) for the detection of significant prostate cancer 20
- Detection of clinically significant prostate cancer using mpMRI ranged from 44% to 87% and the negative predictive value for exclusion of significant disease ranged from 63% to 98% for both biopsy na?ve males and men with prior negative biopsies 21
- This may result in fewer (up to a third) of men biopsied overall with far less cores needed or no further biopsies. Additionally, the targeted approach prevented the diagnosis of clinically insignificant cancer in 10% of the population 17, 18, 22, 23 fewer or no systematic or targeted biopsies in patients with PSA suspicious for prostate cancer
- Pre-biopsy MRI also improves accuracy for smaller lesions. The indications for repeat biopsy are 6, 8
    a. Rising and / or persistently elevated PSA 24
    b. Suspicious DRE (5-30% cancer risk)
    c. Atypical small acinar proliferation (40% cancer risk)
    d. Extensive high grade prostatic intraepithelial neoplasia (HGPIN) from > 3 biopsy sites) (~30% cancer risk)
    e. A few atypical glands immediately adjacent to high grade prostatic

intraepithelial neoplasia (PINATYP) (~50% cancer risk)

- In patients with elevated PSA and previous negative TRUS-biopsy sessions, MRGB of mpMRI suspicious regions report good prostate cancer-detection rate of between 52%-65% [24, 33, 34] with high sensitivity (91%) [35]. The majority of detected cancers were clinically significant (80.8%-93%) [7, 24, 34, 36, 37] while the detection of insignificant prostate cancer was much lower (44%) [35, 38]
- Serum PSA levels is predictive for a positive biopsy result while the number of preceding negative biopsies was not associated with the likelihood of a positive biopsy result [24]. With this strategy, almost two-thirds (59%) of men with 2 or more previous negative TRUS biopsies have been diagnosed with cancer [39]
- There are significant histological differences between detected and missed prostate tumours using magnetic resonance imaging with independent predictors of detection being size, Gleason score and solid growth
    a. Identification with T2-weighted imaging is associated with size and Gleason score
    b. Identification with DWI is associated with size, Gleason score and loose stroma
    c. Identification with DCE was associated with intermixed benign epithelium, loose stroma and a high malignant epithelium-to-stroma

  Knowledge to this may aid in the use of mpMRI for treatment selection for patients with prostate cancer
- Cancers, in the anterior prostate, apex, and midline are either under-sampled or never sampled, resulting in clinically significant cancers going undetected [39]
- Furthermore, the majority of tumours missed by TRUS biopsy are anteriorly located [33, 40] Anterior prostate cancer can be missed in up to 46% of cases and of the detected cases, there was significant Gleason score upgrading in 44% of cases [41] prostate cancer or significant cancer missed by trans-rectal biopsy can be well identified by mpMRI [42-44]
- However, it should be noted that most tumours missed by MRI guided in-bore biopsy alone had a Gleason score of 3+3=6 [40] About 25% of patients with Gleason scores of 6 will be found to have more aggressive disease after radical prostatectomy [13] Men with low-risk disease (Gleason score 6, PSA

Prostate Ultrasound and Prostate Systematic Biopsy Under US

- Ultrasound (transrectal or transperineal) should not be used for local staging of prostate cancer. It has a tendency to under-stage. [8] It cannot accurately differentiate between T2 and T3 tumours [6, 8], nor can it reliably predict extra-capsular extension (accuracy 37-83%) [13] due to inadequate spatial resolution. This results in biopsies not specifically targeted to areas most likely to be malignant [3]
- Cancer detection rates (CDR) are comparable with both approaches TRUS and transperineal (TP) [6] with reasonable, self-limiting morbidity [50] and negligible sepsis rate [51] of the TP saturation approach. In grey-zone PSA cases, more TZ cores were positive

with the TP approach than with TRUS [52]
- Saturation biopsy appears to be necessary in the repeat setting [53, 54], the indications for which include: Rising and / or persistently elevated PSA [24]; Suspicious DRE (5-30% cancer risk); atypical small acinar proliferation (40% cancer risk); extensive high grade prostatic intraepithelial neoplasia (HGPIN) from > 3 biopsy sites) (~30% cancer risk); a few atypical glands immediately adjacent to high grade prostatic intraepithelial neoplasia (PINATYP) (~50% cancer risk). [6, 8] If performed transperineally, it may detect an additional 38% of prostate cancer [6] Apart from improving the cancer detection rate, it also is responsible for the increase of clinically insignificant disease [24] and high rate of urinary retention (10%). Therefore, saturation biopsy is often reserved for high risk patients with rising or persistently elevated PSA, previous abnormal biopsies or DRE [6]
- Sextant biopsy (6 cores) is no longer considered adequate. For prostate volume 30-40 mL, > 8 cores should be sampled. Ten to 12 core biopsies are recommended, with > 12 cores not being significantly more conclusive. [6] A cut-off of 0.5 mL is commonly used to distinguish insignificant from clinically relevant cancer [6, 17] There are studies that report that there is no clear advantage of targeted biopsies over the current standard of systematic biopsies (SB) when considering overall CDR as an outcome. However the combination of fusion of systematic and targeted biopsy schemes provides the highest detection rate [50, 55]

Positive Biopsy for Cancer

- Clinically ‘insignificant’ prostate cancer can be defined as a cancer, which will not affect the patient during the natural course of his lifetime. [5]
- To date, the most commonly used criteria for defining ‘insignificant’ prostate cancer are based on the pathologic assessment of the radical prostatectomy specimen and include the well-established prognostic factors of: [56]
  - Gleason score ?6 without Gleason pattern 4 or 5
  - Organ-confined disease (no extra-prostatic extension, no seminal vesicle or lymph node invasion) and
  - Tumour volume <0.5cm^3

Gleason’s Pattern Scale

- Prostate cancer is graded histologically using normal healthy prostate tissue as a comparison. The tissue architectural appearance indicates the aggressiveness of the tumour and ultimately provides information regarding the risk posed by the cancer to direct patient management. Scores from 1(most normal or differentiated) to 5 (most abnormal or poorly differentiated) are assigned. The Gleason score is given as two numbers added together to give a score out of 10 (for example, 3 + 4 = 7). The first

number is the tumour's dominant pattern (primary grade) while the second number is the tumour's next most frequent pattern (secondary grade). A high Gleason score indicates an aggressive cancer and predilection for rapid disease progression.
    - Low risk (Gleason score 2-6): Low grade, well differentiated tumour
    - Intermediate risk (Gleason score 7): Intermediate grade, moderately differentiated tumour
    - High risk (Gleason score 8-10): High grade, poorly differentiated tumour
- There are multiple organisational pre-treatment prostate cancer risk stratification systems [57] based on the initial PSA, biopsy Gleason score and clinical T stage. This includes the European Association of Urology (EAU) [8], American Urology Association (AUA) [58], National Institute For Health and Clinical Excellence (NICE) [59], National Cancer Control Network (NCCN) [11] and European Society for Medical Oncology (ESMO) [60] risk stratification systems as summarised in the table below. There is no consensus as to which system is superior and clinical practice varies across institutions.

Organisation	Low risk	Intermediate risk	High risk
AUA EAU	• T1-T2a and • PSA <10 ng/mL and • Gleason score ?6	• T2b and/or • PSA 10-20 ng/mL not low-risk or • Gleason score 7	• ?T2c or • PSA >20 ng/mL or • Gleason score 8-10
NICE	• T1-T2a and • PSA ?10 ng/mL and • Gleason score ?6	• T1-T2 and/or • PSA ?20 ng/mL not low-risk or • Gleason score ?7	• ?T3a or • PSA >20 ng/mL or • Gleason score 8-10

NCCN	T1-T2a and Gleason score 2-6 and PSA ?10 ng/mL not very low-risk AND very-low risk category: T1c and GS ?6 and PSA <10 ng/mL and fewer than 3 biopsy cores positive and ?50% cancer in each core	• T2b or T2c and/or • PSA >10–20 ng/mL not low-risk and/or • Gleason score 7	• T3a or • PSA >20 ng/mL or • Gleason score 8-10 not very high risk AND very high-risk: category T3b-4
ESMO	• T1-T2a and • PSA <10 ng/mL and • Gleason score ?6	Not high risk and not low risk (the remainder)	• T3-4 or • PSA >20 ng/mL or • Gleason score 8-10

Table: Organisational pre-treatment prostate cancer risk stratification systems that were used to support the literature and proposed imaging pathway (table adapted from Rodrigues G, et al. 57)

Active Surveillance (AS)

- It is recommended that patients and their treating physicians consider active surveillance based on careful consideration of the patient's prostate cancer risk profile, age, health and personal preferences 11
- Active surveillance is recommended for patients with low risk prostate cancer and those with intermediate risk prostate cancer who

do not wish to have immediate treatment. 59 Active surveillance is not recommended for patients with high risk cancer
- Most guidelines make a distinction between active surveillance and observation (or watchful waiting) in the management of prostate cancer 11, 61
- In active surveillance the intent is curative and involves regular follow-up of patients with the expectation to intervene if there is evidence of disease progression
- The intent of observation is to provide palliative treatment for the development of symptoms associated with disease progression in a patient with limited life expectancy

Year 1
- The recommended protocol for active surveillance is 59
- Every 3-4 months: measure PSA and monitor PSA kinetics
- Every 6-12 months: perform DRE

Years 2-4
- At 12 months: prostate re-biopsy *
- Every 3-6 months: measure PSA and monitor PSA kinetics
- Every 6-12 months: perform DRE

Year 5 and thereafter
- Every 6 months: measure PSA and monitor PSA kinetics
- Every 12 months: perform DRE

* Prostate re-biopsy at 12 months, then every 3 years and at any time if there is clinical or biochemical concern. If no evidence of disease progression, then continue active surveillance. If evidence of disease progression, then offer treatment.

- Although mpMRI is not routinely recommended for active surveillance, MRI has a high specificity for clinically significant carcinoma 62 and it may be useful when a patient's clinical findings are discordant with the pathological findings and to exclude the presence of an anterior cancer 63
- A positive MRI is more likely to be associated with upgrading (Gleason score >3+3) than a negative MRI (43% vs 27%) while a positive MRI is not significantly more likely to be associated with upstaging at radical prostatectomy (>T2) than a negative MRI (10% vs 8%). 64 Available clinical evidence demonstrates that Gleason 6 cancer (3 + 3) has little or no metastatic potential 65
- A small percentage of low-grade cancers (1% of patients per year) harbour molecular alterations that result in grade progression, which means that long term follow up is required 65
- Therefore MRI is appropriate to clarify a patient's risk status and to detect cases that have been under-staged and misclassified 13, 17
- Visible tumours can be monitored for progression and MRI has the capacity to contribute to follow-up cases in such instances 17

Prostate Cancer Staging

TNM Staging

- The most widely used staging system for prostate cancer is the American Joint Committee on Cancer (AJCC) TNM system. 66

Primary Tumour (T) (Clinical)	
TX	Primary tumour cannot be assessed
T0	No evidence of primary

	tumour
T1	Clinically inapparent tumour neither palpable nor visible by imaging
T1a	Tumour incidental histologic finding in 5% or less of tissue resected
T1b	Tumour incidental histologic finding in more than 5% of tissue resected
T1c	Tumour identified by needle biopsy (for example, because of elevated PSA)
T2	Tumour confined within prostate[1]
T2a	Tumour involves one-half of one lobe or less
T2b	Tumour involves more than one-half of one lobe but not both lobes
T2c	Tumour involves both lobes
T3	Tumour extends through the prostate capsule[2]
T3a	Extra-capsular extension (unilateral or bilateral)
T3b	Tumour invades seminal vesicle(s)
T4	Tumour is fixed or invades adjacent structures other than seminal vesicles, such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall
Note 1. Tumor found in one or both lobes by needle biopsy, but not palpable or reliably visible by imaging, is classified as T1c 2. Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is classified not as T3 but as T2	
Regional Lymph Nodes (N)	
Nx	Regional lymph nodes were not assessed
No	No regional lymph node metastasis

N1	Metastasis in regional lymph node(s)
Distant Metastasis (M)[3]	
M0	No distant metastasis
M1	Distant metastasis
M1a	Nonregional lymph node(s)
M1b	Bone(s)
M1c	Other site(s) with or without bone disease

Note

3. When more than one site of metastasis is present, the most advanced category is used. pM1c is most advanced

Anatomic Stage / Prognostic Groups

Group	T	N	M	PSA	Gleason
I	T1a-c	N0	M0	<10	?6
	T2a	N0	M0	<10	?6
	T1-2a	N0	M0	X	X
IIA	T1a-c	N0	M0	<20	7
	T1a-c	N0	M0	?10 <20	?6
	T2a	N0	M0	?10 <20	?6
	T2a	N0	M0	<20	7
	T2b	N0	M0	<20	?7
	T2b	N0	M0	X	X
IIB	T2c	N0	M0	Any	Any
	T1-2	N0	M0	?20	Any
	T1-2	N0	M0	Any	?8
III	T3a-b	N0	M0	Any	Any
IV	T4	N0	M0	Any	Any
	Any T	N1	M0	Any	Any
	Any T	Any N	M1	Any	Any

Computed Tomography (CT)

- CT may be used as an initial staging imaging modality in select patients [11]
    a. T3 or T4 disease
    b. Patients with T1 or T2 disease and nomogram indicated

probability of lymph node involvement >10% may be candidates for pelvic imaging, but the level of evidence is low
- CT may be considered in patients after RP when [3]
  a. PSA fails to fall to undetectable levels, or
  b. when an undetectable PSA becomes detectable and increases on 2 subsequent determinations, or
  c. after RT for rising PSA or positive DRE if the patient is a candidate for salvage therapy

CT and MRI should not be used for nodal staging in low-risk patients and consider mpMRI (or CT if MRI is unavailable / contraindicated), for men with histologically proven prostate cancer if knowledge of the T or N stage could affect management [6, 8, 11, 13, 16]

Bone Scintigraphy (BS)

- No single imaging modality is consistently best for the assessment of metastatic bone disease across all tumour types and clinical situations [15]
- However, metastatic bone disease occurs in approximately 90% of patients with metastatic prostate cancer, thus making bone scans (single photon, using Tc-99m labelled phosphonates) the mainstay of imaging in advanced prostate cancer [6, 8, 13, 67]
- In low risk patients, no imaging is indicated [8, 15, 16] as BS positivity rate in this group of patients are extremely low (6 Bone scans are rarely positive in asymptomatic men with PSA 20 ng/mL [6]
- PSA ?20 ng/mL or poorly differentiated primary tumours [15]
- Advanced disease (T1 disease and PSA 20, T2 disease and PSA 10, Gleason score 8, or T3/T4 disease) and / or symptomatic patients [11]

- Limitations of bone scanning include [67]
  a. lack of specificity
  b. unclear relationship between bone scan changes and disease progression or response to therapy
- Owing to bone scintigraphy's low specificity, and in equivocal cases, 18F-fluorodeoxyglucose PET or PET / CT could be of value to differentiate active metastases and healing bones [6, 8, 15]
- Combined whole-body MRI and mpMRI of the prostate plays a vital role (both sensitivity [68] and specificity of 100%) as a single-step, non-irradiating technique to perform TNM staging in high-risk PCa on 3T when compared to a combination of BS + TXR and CT (sensitivity 85% and specificity of 88%) [69]
- Considering the cost-effectiveness when implementing new strategies for bone and soft tissue imaging, it is recommended that 99mTc bone scintigraphy and CT abdomen / pelvis / chest as the imaging modalities for initial staging in intermediate and high risk [70]

Positron Emission Tomography/Computed Tomography (PET / CT) and PSMA

- The gold standard for nodal staging is open or laparoscopic lymphadenectomy. Pre-treatment imaging facilitates the visual detection of tumour bearing sentinel lymph nodes (SN) allowing for appropriate management planning with the aim to reduce morbidity associated with extended pelvic lymph node dissection. However, difficulty in accessing the SN and the lack of clinical evidence are limitations to its use 6
- In the last several years PET and PET / CT have been playing an increasing role in the staging workup of newly diagnosed and recurrent prostate cancer with the potential to play an important role in detecting early metastatic spread and monitoring post-therapy response 13
- The radiotracers available include 68Ga-PSMA-ligand, 11C or 18F choline and acetate, 11C methionine, 18F fluoride, fluorodihydrotestosterone and 18F-FDG
- PSMA or prostate-specific membrane antigen is a cell surface protein which is physiologically expressed at relatively low levels in the kidneys and salivary glands. Prostate cancer cells have a significantly increased expression of PSMA which enables excellent contrast between malignant and most healthy tissues 71
- Several isotopes and ligands have been developed for use in PSMA PET, and currently there is no consensus as to which is best. 72 The most commonly used ligand in Australia is 68Ga-HBED-PSMA
- Preliminary studies looking at the accuracy of 68Ga-PSMA PET in primary staging have been promising, but larger trials are needed for it to be recommended in this setting. 72 In patients with biopsy-proven PCa and at intermediate to high risk of metastases, 68Ga-PSMA PET / CT accurately detects lymph node metastases prior to primary lymph node dissection, with a reported sensitivity, specificity, NPV and PPV of 86%, 88%, 92% and 80% respectively in one series. 73 68Ga-PSMA PET / CT also has demonstrated superior performance when compared with morphological imaging alone (CT or MRI) for the correct identification of lymph node metastases in one small retrospective study 74
- In re-staging of prostate cancer, conventional bone scintigraphy and CT have limited detection rates for metastases at low serum PSA levels, hence most guidelines recommend such imaging for patients who have symptomatic recurrent prostate cancer or when PSA levels > 10ngml. 72, 75 Biochemical recurrence following radical prostatectomy is expected with PSA levels > 0.2ng/ml hence imaging techniques with improved sensitivity would be valuable
- 68Ga-PSMA PET is a promising new technique in re-staging of prostate cancer and it is increasingly being used in this setting. In one study of a cohort of patients with suspected prostate cancer recurrence and a median PSA level of 4.6 ng/ml, at least one lesion typical of prostate cancer was found in 83% of patients. The detection rates were found to be 50% for PSA values 2ng/ml. 76, 77 When compared directly to 18F-fluoroethylcholine, 68Ga-PSMA PET / CT has higher sensitivity (71% vs 86.9% respectively), specificity (86.9% vs 93.1%), PPV (67.3% vs 75.7%) and NPV (88.8% vs 96.6%) with an overall higher accuracy (82.%% vs 91.9%) for the detection of metastatic lesions prior to salvage lymphadenectomy
- The reported sensitivity of11C-choline and 18F-fluorocholine for primary tumour detection ranges from 10 %-67 %, too low to be of clinical interest for detecting nodal metastasis

- In restaging patients with biochemical failure after local treatment with curative intent choline PET / CT may be useful for guiding re-biopsy in highly selected patients suffering from clinically suspected PCa with repeatedly negative prostate biopsies. Sensitivity is crucially dependent on the level of serum PSA, with a linear relationship
- 18F-fluorodeoxyglucose (18F-FDG) FDG PET is not used in prostate cancer staging as prostate cancer has variable accumulation of FDG and FDG is excreted in the urine leading to poor visualisation of the lower urinary tract.

References

Date of literature search: November 2015

The search methodology is available on request. Email

References are graded from Level I to V according to the Oxford Centre for Evidence-Based Medicine, Levels of Evidence. Download the document

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