

Welcome to the EANM Focus 5 on molecular imaging and theranostics in prostate cancer**IMPORTANT:**

To assist our expert panel, we have systematically searched for and quality assessed the literature on molecular imaging and theranostics in prostate cancer.

You can access the literature review and a selection of the highest quality studies here:

<https://focusmeeting.eanm.org/delphi-survey-literature-review-download/>

Password: EANM_Focus5!

The project's aim is to define the role of advanced imaging techniques (i.e., hybrid functional and anatomic PET-CT/PET-MRI imaging and MRI) in prostate cancer diagnosis and therapy beyond the existing guidelines, as well as define knowledge gaps for future studies.

Explanatory notes:

We realise there will be instances where a particular patient should not be diagnosed/treated in the same way as most others and so, to reflect this, we have chosen to frame the statements as "the majority of patients" rather than "in all patients".

Furthermore, the following statements are not meant to test the panellist's knowledge of national or international guidelines. The statements are to investigate your own view on these matters in terms of best possible care for the patient.

Section I. Imaging in Intermediate and High Risk Prostate Cancer (histopathology proven)**Aims:**

- to define the role of multiparametric prostate MRI (mpMRI) in prostate cancer (detection, local staging).
- to define the role of whole-body MRI, in local and distant disease staging.
- to define the role of hybrid PET imaging (i.e., PET-CT/PET-MRI) in local and distant disease staging.

Not taken into consideration: the role of local expertise, availability, costs.

Explanatory note: the definition of different risk groups for biochemical recurrence of localised and locally advanced prostate cancer is in coformance with the EAU - EANM - ESTRO - ESUR - ISUP - SIOG Guidelines on Prostate Cancer 2022 (please see Table below):

Definitions

Low-risk	Intermediate-risk	High-risk	High-risk
PSA < 10 ng/mL and GS < 7 (ISUP grade 1) and cT1-2a	PSA 10-20 ng/mL or GS 7 (ISUP grade 2/3) or cT2b	PSA > 20 ng/mL or GS > 7 (ISUP grade 4/5) or cT2c	any PSA any GS (any ISUP grade) cT3-4 or cN+
Localised	Localised	Localised	Locally advanced

GS = Gleason score; ISUP = International Society for Urological Pathology; PSA = prostate-specific antigen.

Further sub-stratification of the intermediate-risk group is made according to the National Cancer Center Network (NCCN) Guidelines, subdividing intermediate-risk disease into favourable intermediate-risk and unfavourable intermediate-risk (unfavourable features including ISUP grade 3, and/or $\geq 50\%$ positive biopsy cores and/or at least two intermediate-risk factors).

Please state your agreement with the following statements from 1 (strongly disagree) to 9 (strongly agree). Please only choose '5' where you truly neither agree nor disagree with the statement. If you feel you do not have enough expertise to answer, please choose 'unable to score'.

1.1. mpMRI of the prostate is recommended for patients with a clinical suspicion of prostate cancer (i.e., mpMRI in first detection setting).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.2 mpMRI of the prostate is the most useful imaging method for local staging of intermediate- and high-risk prostate cancer.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.3 PSMA PET-CT/PET-MRI for staging should only be performed after mpMRI of prostate and targeted biopsy.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.4 PSMA PET-CT/PET-MRI should be used for staging of the majority of patients with favourable intermediate-risk prostate cancer.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.5 PSMA PET-CT/PET-MRI should be used for staging of the majority of patients with unfavourable intermediate-risk prostate cancer (i.e., primary Gleason pattern of 4, $\geq 50\%$ percentage of prostate biopsy cores, or ≥ 2 NCCN intermediate risk factors: clinical stage T2b or T2c, total Gleason score = 7 or PSA level = 10-20 ng/mL).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.6 Please rank the following methods to assess nodal metastases at initial diagnosis of high-risk prostate cancer, with 1 being your top preference, 2 your second, and so on:

(*¹⁸F-Fluciclovine is a radiolabelled amino acid analogue that functions based on amino acid transport upregulation in prostate cancer)

IF YOU CAN'T ANSWER THE QUESTION PLEASE JUST LEAVE IT BLANK

(One selection allowed per column)

	1	2	3	4	5
Abdominopelvic CT	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Whole-body MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Choline PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
PSMA PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
¹⁸F-Fluciclovine* PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

1.7 Modern nomograms, that incorporate PSMA PET-CT findings together with mpMRI findings and MRI-targeted biopsy, should be used to identify candidates for extended lymph node dissection (i.e., dissection of presacral, obturator, external, internal and common iliac nodes) at the time of radical prostatectomy, as opposed to classic nomograms using only clinical and biopsy findings (on random TRUS).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.8 PSMA PET-CT/PET-MRI (skull base to mid-thigh) is preferred over pelvic or whole-body MRI for detection of loco-regional (N1/N2) and distant (M1a) lymph node metastases in intermediate- and high-risk prostate cancer.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.9 PSMA PET-CT should replace both bone scan, and abdominopelvic CT in patients with high-risk prostate cancer, undergoing initial staging.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.10 Choline PET-CT/PET-MRI is preferred over bone scan for staging of primary prostate cancer, when staging is indicated.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.11 Please rank the following methods to assess distant metastases at initial diagnosis of prostate cancer, with 1 being your top preference, 2 your second, and so on:

(*18F-Fluciclovine is a radiolabelled amino acid analogue that functions based on amino acid transport upregulation in prostate cancer)

IF YOU CAN'T ANSWER THE QUESTION PLEASE JUST LEAVE IT BLANK

(One selection allowed per column)

	1	2	3	4	5	6
Bone scan	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Whole-body MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Choline PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Fluoride PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
PSMA PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
18F-Fluciclovine PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

1.12 mpMRI of prostate is useful for local treatment planning (e.g., targeted biopsy, tumor delineation) in patients with intermediate-high risk prostate cancer.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.13 The availability of 68Ga/18F-PSMA PET-CT is often limited to some nuclear medicine centers. Given that 99mTc-PSMA-SPECT-CT could be widely available, 99mTc-PSMA-SPECT/CT should be preferred over PSMA PET/CT.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.14 99mTc-MDP-SPECT bone scan and 99mTc-PSMA-SPECT scan share similar procedures and radiation exposures. 99mTc-PSMA-SPECT scan should replace 99mTc-MDP-SPECT bone scan.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

1.15 Patients with distant metastases at diagnosis, **detectable only with advanced imaging techniques** (e.g., PSMA PET-CT/PET-MRI or whole-body MRI), should be offered definitive local therapy along with metastasis-directed therapies, even though the impact of these techniques for prognosis and optimal patient management is unknown.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

Section 2. Imaging for Biochemical Recurrence of Prostate Cancer

Aims:

- to define the role of hybrid PET imaging (i.e., PET-CT/PET-MRI) and MRI (i.e., prostate mpMRI, Whole-body MRI) in patients with persistent PSA or biochemical relapse of prostate cancer.

- to define the role of prostate mpMRI for biopsy delineation/targeting, treatment planning and for salvage therapy.

Explanatory note: In the statements below, when using advanced imaging techniques, the definition of biochemical relapse may deviate from the classic definition of relapse after radical prostatectomy or radiotherapy.

2.1 mpMRI of the prostate should be performed in patients with suspicion of local recurrent disease (regardless of the PSA level).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.2 A PSMA PET-CT/PET-MRI scan should be performed if a mpMRI of the prostate is negative for recurrent prostate cancer.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.3 mpMRI should **NOT** be used for local recurrences in the prostatic bed in patients with low PSA level (< 0.5 ng/mL, after prostatectomy).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.4 A PSMA PET-CT/PET-MRI should be performed in the majority of patients with a suspicion of recurrent prostate cancer.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.5 A PSMA PET-CT/PET-MRI should always be performed in adjunct to mpMRI of the prostate in patients with (any level of risk or PSA) a suspicion of recurrent prostate cancer.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.6 Choline PET-CT/PET-MRI is useful in biochemical recurrence setting after curative local treatment (i.e., surgery or radiotherapy) of prostate cancer, with raising PSA above 4 ng/mL.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.7 18F-Fluciclovine PET-CT/PET-MRI is the preferred imaging method for detecting metastases in the setting of local relapse after radical prostatectomy.

(*18F-Fluciclovine is a radiolabelled amino acid analogue that functions based on amino acid transport upregulation in prostate cancer)

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.8 Please rank the following methods to assess recurrent prostate cancer, with '1' being your top preference, '2' your second, and so on:

IF YOU CAN'T ANSWER THE QUESTION PLEASE JUST LEAVE IT BLANK

(One selection allowed per column)	1	2	3	4	5	6	7
Conventional imaging (i.e., bone scan and CT)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
mpMRI of the prostate	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Whole body MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Fluoride PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Choline PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Fluciclovine PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
PSMA PET-CT/PET-MRI	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

2.9 PSMA PET-CT/PET-MRI is the preferred imaging method for the detection of recurrent disease after radical prostatectomy, at PSA levels < 0.5 ng/mL.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.10 mpMRI of the prostate should be used for the detection of local recurrences after radiotherapy, at low PSA levels <0.5 ng/mL.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.11 PSMA PET/CT should be used for the detection of local recurrences after radiation therapy, even at low PSA levels <0.5 ng/mL.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.12 PSMA PET-CT/PET-MRI should be used to guide metastasis-directed therapy in patients relapsing after a local treatment.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.13 Men with a persistent detectable PSA after radical prostatectomy (i.e., a PSA >0.1 ng/ml, > 6 weeks post radical prostatectomy; irrespectively of the surgical margin status) should be investigated with PSMA PET-CT or PET-MRI.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

2.14 Fluoride PET-CT/PET-MRI should be preferred over bone scan for detection of bone metastases at biochemical recurrence of prostate cancer.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

Section 3 . Imaging of Advanced Prostate Cancer

Aims:

- to emphasize that CHARTED criteria cannot be translated yet to the most performant imaging techniques available. These CHARTED criteria are based on conventional imaging techniques (i.e., bone scan and CT).
- to define when to implement advanced imaging techniques (in advanced prostate cancer).
- to establish newer definitions of oligo metastatic disease.
- to define potential clinical consequences (treatment of oligo-(recurrent) metastatic patients).

3.1 Advanced imaging modalities (i.e., PSMA PET-CT/PET-MRI , Whole-body MRI) can be used to define high- and low-volume metastases (CHAARTED criteria) in metastatic hormone sensitive prostate cancer (mHSPC).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

3.2 The management of patients with non-metastatic castrate-resistant prostate cancer (nmCRPC) (by conventional imaging) is likely to be modified by advanced imaging techniques (e.g., PSMA PET-CT/PET-MRI or whole-body MRI).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

3.3 Oligo-metastatic prostate cancer should be defined as ≤ 5 metastases (detected on advanced imaging modalities, e.g. PSMA PET-CT/PET-MRI or whole-body MRI).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

3.4 PSMA PET-MRI is equivalent (in terms of diagnostic accuracy) to PET-CT, in the majority of patients with metastatic advanced prostate cancer.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

Section 4. Therapy of Advanced Prostate Cancer

Aims:

- to define the role of theranostics in relation to the classical approach of conservative hormonal- or chemotherapies.
- to define what is necessary to implement theranostics into clinical practice.

4.1 ^{177}Lu -PSMA can be administered at the outpatient clinic (if allowed by local regulators).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.2 Please rank the following options in order of the maximum activity of ^{177}Lu -PSMA that you think can be administered safely in mCRPC, with '1' being your top preference, '2' your second, and so on:

IF YOU CAN'T ANSWER THE QUESTION PLEASE JUST LEAVE IT BLANK

(One selection allowed per column)

	1	2	3	4	5
9 GBq	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7.4 GBq	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6 GBq	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5 GBq	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4 GBq	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

4.3 Please rank the following options in order of the maximum number of cycles of ^{177}Lu -PSMA (7.4 GBq per cycle) that you think can be administered safely AND efficiently in mCRPC, with '1' being your top preference, '2' your second, and so on

IF YOU CAN'T ANSWER THE QUESTION PLEASE JUST LEAVE IT BLANK

(One selection allowed per column)

	1	2	3	4	5	6
1 cycle	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2 cycles	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3 cycles	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4 cycles	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5 cycles	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6 cycles	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

4.4 Retreatment with another 4-6 cycles of ^{177}Lu -PSMA should be considered in patients with disease recurrence who received 6 injections of ^{177}Lu -PSMA (and had an initial good response, e.g., progression-free survival of at least 6 months).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.5 In bone only mCRPC, ^{223}Ra remains a valid therapeutic option, despite the availability of ^{177}Lu -PSMA.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.6 In mCRPC, patients should receive ^{177}Lu -PSMA only after progression to cabazitaxel.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.7 ^{177}Lu -PSMA should be used before PARP inhibitors in patients with mCRPC.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.8 177Lu-PSMA should only be used in patients with concordant findings on both 18F-FDG PET and PSMA PET, assuming that metastases show adequate PSMA expression.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.9 Patients with extensive bone metastases and bone marrow involvement are eligible for 177Lu-PSMA therapy (assuming the bone marrow function is adequate).

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.10 Patients with brain metastases are eligible for 177Lu-PSMA therapy.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.11 Kidney dysfunction (GFR < 45) is a contraindication for 177Lu-PSMA therapy.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.12 WHO ECOG 3 patients can be considered for 177Lu-PSMA therapy.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.13 177Lu-PSMA-I&T and 177Lu-PSMA-617 have similar efficacy in the treatment of mCRPC.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.14 Therapy with 225Ac-PSMA (if available) should be considered as an alternative to 177Lu-PSMA, in patients with mCRPC, being 177Lu-PSMA naive or progressing after 177Lu-PSMA.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

4.15 In patients with metastatic advanced prostate cancer, the combinations of 177Lu-PSMA with novel hormonal agents do play a role.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

Section 5. Important factors to consider in prostate cancer consensus statement projects

Aim:

- to establish the important steps in building a consensus driven diagnostic process in prostate cancer.

5.1 Consensus statements agreed by clinical experts should be shared with patient advocates who should be invited to review and comment on the statements.

* must provide value

1 2 3 4 5 6 7 8 9 unable to score

5.2 Please rank the following factors that are likely to influence your willingness to refer a patient for imaging with advanced modalities (assuming that availability is unlimited), with '1' being your top preference, '2' your second, and so on:

IF YOU CAN'T ANSWER THE QUESTION PLEASE JUST LEAVE IT BLANK

(One selection allowed per column)	1	2	3	4	5
Incorporation into guidelines	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patient's preferences	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Evidence of benefit from scientific literature	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Personal experience	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Costs-related aspects	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please suggest any other important statements for consensus or ranking questions (with response options) that you feel we may have missed

Please leave any other feedback here