Review Article on Current and Future Topics on Prostate Cancer

MRI/PET Imaging in elevated PSA and localized prostate cancer: a narrative review

Subodh K. Regmi[1]^, Niranjan Sathianathen[2], Thomas E. Stout[1], Badrinath R. Konety[3]

[1]Department of Urology, University of Minnesota, Minneapolis, MN, USA; [2]Department of Urology, University of Melbourne, Melbourne, Australia; [3]Rush Medical College, Chicago, IL, USA

Contributions: (I) Conception and design: BR Konety, SK Regmi; (II) Administrative support: BR Konety, SK Regmi; (III) Provision of study materials or patients: SK Regmi, N Sathianathen, TE Stout; (IV) Collection and assembly of data: SK Regmi, N Sathianathen, TE Stout; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Subodh K. Regmi. Department of Urology, University of Minnesota, Minneapolis, MN, 55455, USA. Email: regmi014@umn.edu.

Objective: To review the recent milestones in MRI and PET based imaging and evaluate their evolving role in the setting of elevated PSA as well as localized prostate cancer.

Background: The importance of multiparametric MRI (mpMRI) and PET based imaging for the diagnosis and staging of prostate cancer cannot be understated. Accurate staging has become another significant milestone with the use of PET scans, particularly with prostate specific radiotracers like 68-Gallium Prostate Specific Membrane Antigen (68Ga-PSMA). Integrated PET/MRI systems are commercially available and can be modulated to evaluate the unique needs of localized as well as recurrent prostate cancer.

Methods: A literature search was performed using PubMed and Google Scholar using the MeSH compliant and other keywords that included prostate cancer, PSA, mpMRI, PET CT, PET/MRI.

Conclusions: mpMRI has now established itself as the gold-standard of local prostate imaging and has been incorporated into international guidelines as part of the diagnostic work-up of prostate cancer. PSMA PET/CT has shown superiority over conventional imaging even in staging of localized prostate cancer based on recent randomized control data. Imaging parameters from PET/MRI have been shown to be associated with malignancy, Gleason score and tumour volume. As mpMRI and PSMA PET/CT become more ubiquitous and established; we can anticipate more high-quality data, cost optimization and increasing availability of PET/MRI to be ready for primetime in localized prostate cancer.

Keywords: Prostate cancer; PSA; mpMRI; PET CT; PET/MRI

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Introduction

The role of newer imaging modalities for diagnosis and staging of prostate cancer cannot be understated. Their importance lies not only in the ability to accurately identify clinically significant cancer but also in the improved diagnostic predictability, which can help avoid unnecessary biopsies. Accurate staging has become another significant milestone with the use of PET scans, particularly with prostate specific radiotracers like PSMA. An enhanced ability to potentially identify oligo-metastatic disease has led to newer treatment paradigms and fueled further research into multimodality management of these patients (1).

Multiparametric MRI (mpMRI) improves the

^ ORCID: 0000-0001-5940-6302.

identification and detection of clinically significant prostate cancer in biopsy naïve patients as well as those with prior negative biopsies (2). Prostate Imaging Reporting and Data System version 2 (PI-RADS v2) (3), initially developed with a multinational consensus based process, has been updated to the recent PI-RADS v2.1 (4) to improve reproducibility between the readers. This has greatly improved the accuracy of MRI reporting and MRI targeted biopsies in academic as well as community settings (2). Additional roles have emerged in risk stratification for potential biopsies when combined with PSA density, substantially increasing the yield of clinically significant prostate cancer (2). The use of mpMRI as part of a predictive nomogram has also been proposed and is awaiting further external validation (1).

PET utilizes various radiotracers and has been on the forefront of cancer imaging in view of its combined functional and morphological value with cross sectional imaging with CT. 11C-choline and 18F-FACBC (fluciclovine) are two tracers that are currently FDA approved in the US for evaluation of biochemically recurrent disease whereas in other parts of the world, 68Ga-PSMA has been more routinely employed in clinical practice (5). Recent evidence has shown that the use of PSMA PET CT can significantly impact clinical decision making (6) or even result in treatment change (7).

PET/MRI was developed with the intent of improving on the weaknesses of existing PET /CT systems (8). Over the years this evolution itself, which was late to start, currently boasts of a variety of advantages that have been primarily attributed to the incorporation of the MRI platform (9). PET/MRI started with the concept of isochronous fusion of PET and MRI technologies postulating benefits in brain as well as oncological imaging (8). In localized prostate cancer, initial reports utilized parametric fusion of separately acquired PET and MRI images (10) which later paved way for the use of less cumbersome hybrid scanners.

The ongoing use and development of several prostate specific PET radiotracers has also fueled this progress. Recent strong recommendations for the use of multi parametric MRI (mpMRI) prior to prostate biopsy (2) and the promising results from PSMA PET trials (11) have paved way for further substantiative research. As standardized protocols and optimal radiotracers are being developed for prostate cancer diagnosis and staging, it is necessary to evaluate the current role and future prospects of these modalities. The following review is presented in accordance with the Narrative Review reporting checklist (available at https://dx.doi.org/10.21037/tau-21-374).

Methods

A literature search was performed using PubMed and Google Scholar using the MeSH compliant and other keywords that included prostate cancer, PSA, mpMRI, PET CT, PET/MRI. All authors reviewed relevant published literature until 2021 March for inclusion in this narrative review.

mpMRI for localized prostate cancer

mpMRI has now established itself as the gold-standard of local prostate imaging. The PROMIS study of 576 men undergoing mpMRI prior to biopsy reported that mpMRI was significantly more sensitive at detecting clinically significant prostate cancer than transrectal ultrasound guided biopsy (93% *vs.* 48%, P<0.01) (12). A recently published meta-analysis of 7,321 men found that the negative predictive value of mpMRI for the detection of clinically significant disease was 87–97% depending on the definitions set for "positive" MRI and "clinically significant cancer" (13). The high diagnostic performance of MRI has seen it being incorporated into international guidelines as part of the diagnostic work-up of prostate cancer. The European Association of Urology (EAU) guidelines make a level 1a, strong recommendation to perform an mpMRI prior to prostate biopsy (2). Furthermore, there is a level 2a, weak recommendation to omit biopsy when the mpMRI is negative and the clinical suspicion of disease is low. Although the data for mpMRI is impressive, it is not a perfect test (14) The accuracy of mpMRI is highly dependent on the experience of the radiologists interpreting it. In a study of 409 men with an elevated PSA who underwent an mpMRI, Sonn *et al.* reported that there was marked variation in PIRADS scores and cancer detection amongst nine radiologists in an academic centre (15). The challenge, in one study, was the individual cancer detection rates for radiologists in PIRADS 3 lesions (16). Even for PIRADS 4 and 5 lesions the cancer detection rate spanned

across a broad range of 23–65% and 40–80%, respectively. The area under the receiver operating characteristic curve ranged from 0.69 to 0.81 for the detection of significant prostate cancer amongst the radiologists involved int the study. Additional factors such as the magnetic field, the use of an endorectal coil and assessment system have all been shown to influence the performance of mpMRI (17). Moreover, there is a subgroup of prostate cancer that are 'invisible' on mpMRI and are missed when only targeted biopsies are taken. Radtke et. al showed that biopsy of targeted cores only missed up to 12.8% Gleason 7 or more cancers (18). Therefore, clinicians cannot be entirely reliant on mpMRI to make decisions on clinical prostate cancer and need to incorporate other tools into the process.

PET/CT: current status

Positron emission tomography (PET) has been extensively used for whole-body staging of cancers to evaluate metastatic spread. PET tracers such as 68-Gallium Prostate Specific Membrane Antigen (68Ga-PSMA) has superseded conventional staging modalities such as bone scintigraphy and computer tomography (CT) for prostate cancer in many centres globally (5,19). The success of using PET imaging in the secondary staging settings has encouraged their use earlier in the disease process to primary staging of prostate cancer. There are several retrospective studies that have demonstrated the potential of PET in staging of primary prostate cancer.

Tracers in prostate cancer

Many different PET radiotracers have been investigated for use in CaP, and some of those have been used for PET/MRI. The goal of diagnostic functional imaging with PET is to use tracers that selectively target components of CaP cells *in vivo*. There is also ongoing work regarding the use of PET-directed theranostics in CaP patients, however that is outside the scope of this review. The various PET tracers investigated for their use in CaP are outlined below.

Fluorodeoxyglucose (FDG)

FDG, a glucose analog, is taken up by glucose transporters and sequestered in cells as FDG-6-phosphatase (20). While most cancers have upregulated glucose metabolism making FDG a useful tracer, CaP has relatively lower glucose metabolism and instead uses alternative metabolic pathways such as fructose and fatty acids (21,22). Additionally, FDG has low utility in the detection of localized prostate cancer due to difficulties resulting from urinary excretion and uptake sometimes seen in BPH or prostatitis (23). For these reasons FDG PET is rarely used in prostate cancer.

^{11}C-Choline

This membrane phospholipid is internalized by the enzyme choline kinase, which is overexpressed in CaP and was the first PET radiotracer approved for CaP by the FDA (24). Choline PET has been shown to have superior detection rates for pelvic lymph nodes in patients undergoing radical prostatectomy, with a sensitivity and specificity upwards of 70% and 90%, respectively (25,26). As is the case with FDG, the role of choline PET in the localization of primary prostate cancer is limited due to multiple false positives. Other choline-based tracers including ^{18}F-fluoroethylcholine and ^{18}F-fluoromethylcholine have been studied. While ^{18}F isotopes have the benefits of longer half-lives thereby negating the need for an onsite cyclotron, their use has been limited significantly due to urinary excretion, which obfuscates the prostatic bed and periprostatic tissues. There have been relatively few studies of ^{11}C and ^{18}F choline PET/MRIs in CaP, which have shown promise in terms of improved accuracy per lesion as well as per patient in the PET/MRI model as compared to the mpMRI model only (27-30).

^{18}F-Fluciclovine (Axumin®)

As amino acid synthesis and transportation is upregulated in CaP cells, the amino acid analogue ^{18}F-fluciclovine has been shown to be a viable PET tracer. ^{18}F-fluciclovine PET, or Axumin, was FDA approved in 2016 for the use in recurrent CaP. Benefits of Axumin include minimal renal excretion or bladder uptake and a longer half-life compared to ^{11}C choline (31). Axumin has a limited role in evaluating primary prostate lesions. While it does not outperform MRI, the combination of Axumin PET and

MRI has a superior PPV for tumor localization (82%) than either modality alone (32,33). The value of Axumin in initial staging is also unclear, as one multicenter study demonstrated similar lymph node detection rates (85.5–87.3%) compared to CT but a higher detection rate of small bone metastases (91.6%) compared to traditional scintigraphy (61.1%) (34). The primary role of Axumin PET is detecting CaP recurrence either in the prostate bed or elsewhere. PET/MRI with ^{18}F-Fluciclovine has been investigated for CaP, both for primary nodal staging and to evaluate response to ADT (35-37). In one single center prospective study of 14 patients with high risk CaP and negative conventional imaging, Axumin PET/MRI detected lymph node metastases in seven patients. Of the 10 patients in this cohort treated with ADT and radiation, all demonstrated interval decrease in tracer activity within the primary lesion after ADT (37).

Prostate-specific membrane antigen (PSMA)

To date the most studied tracer for PET/MRI is PSMA. This membrane glycoprotein is expressed in the prostate and highly upregulated in prostate cancer (38,39). While the enzyme is found in other tissues including salivary glands, renal tubules, and non-genitourinary malignant blood vessels, PSMA expression in CaP is 100–1000× higher comparatively (40,41). Unlike PSA, PSMA also continues to be expressed in cancers that are androgen-deprived (42). The most common ligand used for PSMA PET is ^{68}Ga-PSMA-HBED-CC, primarily due to its ease of synthesis. Alternative ligands including PSMA-inhibitor and ^{18}F have been investigated, but data are limited (43).

While most studies of PSMA PET have focused in recurrent and advanced disease, there has been some work investigating primary tumor localization and staging. The sensitivity and specificity of PSMA PET in detecting clinically significant prostate lesions is similar to that of MRI, and simultaneous PSMA PET/MRI outperforms either modality alone (44,45). PET/MRI studies using PSMA significantly outnumber those using alternative PET tracers, and are described in the next section.

Greater tracer uptake has been seen in Grade Group 2 two or higher cancers and in those with PSA >10, indicating usefulness in identifying high risk disease (46). PSMA PET appears to outperform conventional imaging when staging patients with primary CaP. In one study of 130 patients with intermediate- or high-risk CaP the accuracy of nodal staging using a templated lymph node dissection as the reference was 89% for PSMA PET *vs.* 72% for CT (47). PSMA also outperforms bone scans in the detection of bone metastases with sensitivities and specificities of 99–100% and 88–100%, respectively (48).

However, only recently have randomized data been available to support the superiority of PSMA PET over conventional staging in this setting. The proPSMA study was a randomised, cross-over study where 302 men with high-risk localized prostate cancer underwent primary staging with conventional imaging and gallium-68 PSMA-11 PET-CT. The study found that the latter modality was 27% more accurate than CT and bone scanning (11). The reported sensitivity and specificity of PSMA PET/CT in this trial was 85% and 98%, respectively, which was significantly higher than conventional imaging. It was also found that PSMA PET/CT changed management more often than CT and bone scan. This study has entrenched the superiority of PSMA PET/CT.

The rationale for PET/MRI

The proposed benefit of PET/MRI in localized prostate cancer is based on our current limited ability to accurately diagnose and stage patients, and perhaps also on the necessity to perform multiple distinct imaging tests with inherent fallacies. Conventional staging modalities have limited ability to accurately stage lymph nodes and can even miss bony metastases (12,49,50) including in high risk disease with low osteoblastic activity (51). ^{18}F-NaF PET/CT can detect bony metastasis better but are less specific and therefore, not recommended for initial staging by either the AUA or EUA (2,50). The promise of PET/MRI lies in its ability to combine the soft tissue detail inherent to MRI with the functional imaging of PET using CaP-specific tracers. It also adds value due to the incorporation of diffusion weighted imaging (DWI), better motion correction and the increased available time to collect PET data (9). However, standardized study protocols of these

complex imaging modalities are still being optimized and higher cost and limited installations prohibit widespread usage (9).

PET/MRI basics and image acquisition

PET/MRI imaging systems can be either in tandem or integrated. Tandem systems have the MRI and PET machines located either in adjacent rooms or side-by-side in the same room with a moveable patient table between (52,53). Tandem PET/MRI units such as the Phillips Ingenuity (Phillips Healthcare, Cleveland, USA) were the initial systems developed because the magnetic field generated by the MRI machine did not interfere with the PET unit. Due to the large footprint and cumbersome nature of tandem PET/MRIs, these have largely been supplanted by their integrated counterparts. A major hurdle of integrated or simultaneous systems is the fact that the photomultiplier tubes used in traditional PET scanners cannot function within a strong magnetic field. The development of "avalanche" photodiodes, photon detectors insensitive to magnetic changes, was the breakthrough that allowed development of and commercialization of modern integrated PET/MRIs (54,55). While one drawback of avalanche photodiodes is the inability to measure time of flight, silicon photomultiplier detectors have been developed to circumvent this limitation (56).

Two integrated PET/MRI systems are commercially available: The Siemens Biograph MR (Siemens Healthcare, Germany) and the GE Signa (General Electric Healthcare, Chicago, IL) (55,57). Both models utilize a 60-cm bore 3-T MR gantry. The Biograph MR utilizes avalanche photodiodes and places the PET detector between the body radiofrequency coil and gradient set. The GE system uses silicon photomultipliers instead of avalanche photodiodes and the PET component is between the radiofrequency shield of the body coil and the gradient coils (58). There is no standardized imaging protocol for PET/MRI, and each study should be tailored to the clinical scenario. As is the case with PET/CT, absorption and scatter due to photon-tissue interaction leads to attenuation and decreased signal reduction (59,60). A variety of attenuation correction techniques may be employed and include bed and coil hardware attenuation correction, truncation correction, and patient attenuation correction (61). For the MR-portion of the exam, anatomic (T1, T2) and functional (DWI, DCE) sequences are obtained to assist in identifying lesions within the transition and peripheral zones, respectively. Protocols may also differ between patients with primary CaP or in those with concern for recurrence. In the former isotropic T2 sequences allow for assessment of neurovascular and seminal vesical invasion, while in the latter high-resolution axial T2 images allow to better evaluate the prostatic fossa (62). While endorectal coils are currently not used with integrated PET-MRIs due to imaging interference and limited space, novel endorectal coils are being investigated (63).

The excellent results of MRI to image the prostate and PET for primary staging has naturally led to investigations into the possibility of combining these two modalities for potentially even better results. There have been several reports of PET/MRI being superior to mpMRI in detecting intra-prostatic lesions. In a study of 66 men with biopsy proven prostate cancer undergoing PET, mpMRI, and combined 68Ga-PSMA HBED-CC PET/MRI, it was found that the latter was superior to mpMRI (0.88 *vs.* 0.73) (64). Similarly, Hicks *et al.* performed a retrospective analysis of 32 men who underwent 68Ga-PSMA-11 PET/MRI prior to radical prostatectomy and reported that the region-specific sensitivity of PET/MRI and mpMRI alone was 74% and 50% compared to whole-mount histology (65). These findings were also seen in 22 men who were imaged with mpMRI and integrated 68Ga-PSMA-11 PET/MRI prior to prostatectomy where PET/MRI had a significantly greater area under the curve (AUC; 0.95 *vs.* 0.68) (66). It should be noted that Al-Bayati and colleagues reported that the number of equivocal results were significantly lower in the PET/MRI group. This may have important clinical relevance in determining the need for biopsy in patients with equivocal MRI results. de Perrot and colleagues suggested that the benefit of PET/MRI compared to mpMRI is mainly in characterising peripheral zone lesions where the reported AUC was 0.89 (67). They hypothesised that the adenomatous hyperplasia in the transition zone interfered with the detection of hypermetabolic foci by PET/MR co-registration. Although PSMA has been the dominant tracer in PET imaging of prostate cancer (5), both 18 F-choline

PET/MRI and 18 F-FDG PET/MRI have exhibited high diagnostic performance in primary staging (68). In a study of 31 men who underwent both 18 F-choline PET/MRI and 18 F-FDG PET/MRI followed by radical prostatectomy, it was reported that integrated PET/MRI imaging with either tracer performed better than combined interpretation of mpMRI and 18 F-FDG PET/CT (68).

Imaging parameters from PET/MRI have been shown to be associated with malignancy, Gleason score and tumour volume. Several studies have demonstrated that malignant tissue displays a higher uptake ratio on PET compared to benign tissue aiding differentiation between the two (64). Metabolic volumetric PET uptake volume product which is a metabolic burden index that is calculated by the product of the mean standardized uptake volume (SUV) and tumour volume within an MRI-matched lesion, was shown to be significantly associated with Gleason score (69). Some of these volumetric indices were also shown to be associated with perineural invasion, lymphovascular invasion, extracapsular extension and seminal vesicle invasion (69). The additional information provided by PET/MRI may assist clinicians in risk stratification and to make important clinical decisions such as which patients to biopsy, who is suitable for active surveillance and who requires radical treatment. A retrospective cohort study of 71 men who underwent prostatectomy and received a pre-operative 68Ga-PSMA-11 PET/CT beforehand demonstrated that lesion intensity was able to predict Gleason score, upgrading from biopsy to RP histopathology, pathological stage, positive surgical margins and progression free survival (70).

Eiber *et al.* (64) have shown that MRI/PET improved the detection of PCa lesions based on sextant based analysis of the prostatectomy specimen compared to mpMRI alone (AUC: 0.88 *vs.* 0.73; P<0.001). Similarly, other studies by Taneja *et al.* (71), and Jena *et al.* (72) have shown that dual phase differential assessment of PSMA uptake in combination with mpMRI significantly increased the accuracy of the PET/MRI to identify malignant lesions on pathology. At this point, mpMRI guided biopsies are the preferred and recommended option (2) but nevertheless, there is data to fuel further research in using it as a prebiopsy modality.

Existing relevant experience on the multi-faceted use of PET/MRI in prostate cancer is summarized in *Table 1*.

Future directions

In the context of localized prostate cancer, there are three distinct directions in which further research is headed with regards to PET/MRI. These include evaluation of newer radiotracers, PET/MRI guided prostate biopsies and planning and response assessment in focal as well as radiation treatment of localized prostate cancer (83) (*Table 2*). The newer radiotracers being investigated are [18F] DCFPyL (84), and 68Ga DOTA Bombesin (85). [18F] DCFPyL has the distinction of superior kinetics and is rapidly cleared from tissues whereas 68Ga DOTA Bombesin targets Gastrin-releasing peptide receptor proteins which are highly expressed in prostate cancer cells (86). Several trials have also been initiated to evaluate the usefulness of this multiparametric metabolic hybrid imaging modality (*Table 2*) in the prebiopsy setting. Perhaps the most intriguing ongoing research is the use of PET /MRI in guiding surgical as well as non-surgical options like HIFU, cryotherapy, high dose brachytherapy and even external beam radiotherapy (*Table 2*).

Conclusions

Multi parametric MRI clearly stands out on the basis of strong evidence for pre biopsy evaluation and the role of PSMA PET/CT as a staging modality in localized prostate cancer is rising. The advantage of PET/MRI lies in the fact that it combines two of these excellent imaging modalities and MRI offers better soft tissue definition than CT. Areas where we could see its emerging role would be in oligometastatic disease and high-risk disease where the ability to identify more lesions would have a significant impact on the treatment approach (83). PET/MRI, therefore, has promising implications in the diagnosis and staging of prostate cancer but needs further validation in terms of research and logistics to be of primetime use.

Table 1 PET/MRI data based on prebiopsy diagnosis of clinically significant disease, local disease staging pre prostatectomy and detection of local or distant recurrence post primary therapy

Disease setting	Authors	Isotope used	No of patients	Study purpose	Study results
Pre biopsy	Eiber *et al.* (64)	68Ga-PSMA-11	53	PET/MRI *vs.* mpMRI	PET/MRI improves diagnostic accuracy for PCa localization both compared with mpMRI and with PET imaging alone
	Taneja *et al.* (71)	68Ga-PSMA-11	35	PET/MRI	Dual-phase PSMA uptake improves accuracy of classifying malignant versus benign prostate lesions
	Ferraro *et al.* (73)	68Ga-PSMA-11	42	PET/MRI	PSMA-PET/MRI has a high accuracy for detecting significant PCa when using section-based saturation template biopsy as the reference standard
	Davenport *et al.* (29)	18F -choline	52	PET/MRI *vs.* mpMRI	18F-choline PET/mpMRI improved the identification of significant prostate cancer compared with mpMRI with improved risk stratification of intermediate-risk mpMRI lesions
Disease staging	Lee *et al.* (68)	18F -choline	30	Detection of disease	Simultaneous PET/MRI is better for the detection of cancer and MRI-assisted metabolic volumetric parameters provide better characterization of primary prostate cancers than conventional PET and MRI parameters
	Freitag *et al.* (74)	68Ga-PSMA-11	26	PET/CT *vs.* PET/MRI	Lymph node and osseous metastases of PCa are accurately and reliably depicted by PET/MRI with very high concordance 98.5% compared with PET/CT including PET-positive LNs of normal size
	Thalgott *et al.* (75)	68Ga-PSMA-11	102	Detection of Disease	PET/MRI performs at least equally for tumor and lymph node stage prediction compared with nomograms in high-risk PCa patients
	Muehlematter *et al.* (76)	68Ga-PSMA-11	40	PET/MRI *vs.* mpMRI	PET/MRI and mpMRI perform similarly for local staging of intermediate-to-high-risk prostate cancer. 68Ga-PSMA-11 PET/MRI has higher sensitivity but lower specificity than mpMRI
	Garcia *et al.* (77)	18 F-choline	31	Impact of PET/MRI on Treatment	18F-choline PET/MRI had a complementary role for the T staging, with a high detection rate for nodal and distant metastasis. PET/MRI findings helped avoid radical treatment in 22.6% of patients
Detection of Recurrence	Selnæs *et al.* (36)	18F-Fluciclovine	84	PET/MRI *vs.* mpMRI	Combined PET/MRI with 18F-Fluciclovine limited use at low PSA values or in patients classified as EAU Low-Risk BCR
	Lütje *et al.* (78)	68Ga-PSMA 11	44	PET/CT *vs.* PET/MRI	68Ga-PSMA 11 PET/MRI is superior to PET/CT in detecting prostate bed recurrences
	Kranzbühler *et al.* (79)	68Ga-PSMA 11	56	PET/MRI *vs.* PET/CT	68Ga-PSMA 11PET/MRI has a high detection rate for recurrent prostate cancer even at very low PSA levels
	Joshi *et al.* (80)	68Ga-PSMA 11	30	PET/MRI *vs.* Conventional Imaging	PSMA PET/MRI detected local and pelvic lesions more accurately than conventional imaging
	García *et al.* (81)	(18) F-Choline	36	Detection of recurrence	18F-Choline PET/MRI had a high detection rate for recurrence with rising PSA levels <1 ng/ml after prostatectomy, and resulted in a better tailored approach to treatment
	Gordon *et al.* (82)	68Ga-PSMA 11	30	Cost effectiveness	68 Ga-PSMA PET/MRI appears to be cost-effective than usual care to detect prostate cancer recurrence

Table 2 Clinical Trials with PET/MRI for localized prostate cancer

Study group	NCT identifier	Study title	Study goals	Study phase	Completion date
Radio tracer	NCT03809078	A Pilot Study of 68Ga PSMA 11 PET/MRI and 68Ga RM2 PET/MRI for Biopsy Guidance in Patients with Suspected Prostate Cancer	to evaluate 68Ga PSMA 11 PET/MRI and 68Ga RM2 PET/MRI for biopsy guidance in patients with suspected prostate cancer	Phase II	January 2022
	NCT03181867	18F-DCFPyL PET/CT in High Risk and Recurrent Prostate Cancer	To see if the radiotracer 18F-DCFyL can help identify prostate cancer in the body before or after therapy	Phase II	October 2023
	NCT02420977	Evaluation of PSMA-based PET as an Imaging Biomarker in Prostate Cancer	To compare the detection, sextant localization and response of 18F-DCFPyL PET-MRI before and after 2-3 months of ADT in men with biopsy-positive high-risk localized or locally advanced CaP	Phase I	February 2023
Biopsy guidance	NCT03429244	PSMA-PET for Biopsy and Treatment Guidance in Primary Prostate Cancer	To define the accuracy of 68Ga-PSMA-11 for detecting the location and size of clinically significant prostate cancer lesions in low and intermediate risk disease	Phase II	October 2021
	NCT03809078	A Pilot Study of 68Ga PSMA 11 PET/MRI and 68Ga RM2 PET/MRI for Biopsy Guidance in Patients With Suspected Prostate Cancer	To evaluate 68Ga PSMA 11 PET/MRI and 68Ga RM2 PET/MRI for biopsy guidance in patients with suspected prostate cancer	Phase II	January 2022
Therapy guidance	NCT04167969	The Use of Nanoparticles to Guide the Surgical Treatment of Prostate Cancer	To see whether 64Cu-NOTA-PSMA-PEG-Cy5.5-C' dot tracer is safe to identify tumor deposits with PET/MRI before and during surgery for prostate cancer	Phase II	November 2022
	NCT04009083	Axumin PET/MRI Imaging Following Focal Cryo-ablation (FCA)	To study whether 18F-Fluciclovine PET/MRI imaging at two years following FCA will improve sensitivity for detection of in field recurrence of significant prostate cancer defined as any Gleason pattern 4 disease	N/A	April 2021
	NCT03949517	A Pilot Study of 68-Ga PSMA 11 PET/MRI and 68-Ga RM2 PET/MRI for Evaluation of Prostate Cancer Response to HIFU or HDR Therapy	To determine whether the combination of imaging agents 68-Ga RM2 and 68-Ga PMSA11 is better at assessing response to high intensity focused ultrasound (HIFU) or high dose rate (HDR) local therapy than standard imaging or biopsy in patients with known prostate cancer	Phase I/ Phase II	October 2022
	NCT04243941	PSMA-PET/MRI Low- and Intermediate-Risk Prostate Cancer	To determine the safety of using PSMA-PET/mpMRI to define radiotherapy and feasibility of stereotactic body radiation therapy	Phase II	October 2023

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