[^{68}Ga]Ga-PSMA-11 PET/CT for staging and patient management of high-risk prostate cancer: A single-center experience from Iran

Original Article

Sara Shakeri[1], Emran Askari[1], Soroush Zarehparvar[1], Fatemeh Farahmandfar[1], Nasim Norouzbeigi[2], Roham Salek[3], Kamran Aryana[1]

[1]Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
[2]Nuclear Medicine Department, Razavi Hospital, Imam Reza International University, Mashhad, Iran
[3]Department of Radiation Oncology, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

(Received 20 June 2021, Revised 28 August 2021, Accepted 31 August 2021)

ABSTRACT

Introduction: Accurate staging plays an important role in management of patients with prostate cancer especially in high-risk group. Today, [^{68}Ga]Ga-PSMA-11 PET/CT should be considered as the preferred imaging tool for treatment planning and initial staging of the disease.

Methods: A total number of 628 patients with prostate cancer referred to Razavi hospital nuclear medicine department between March 2016 and December 2019. Among 103 patients in initial staging category, 23 cases met our inclusion criteria and entered the study. All patients performed CT scan or MRI accompanied with bone scintigraphy before [^{68}Ga]Ga-PSMA-11 PET/CT**.** The scan results were compared with conventional imaging and their treatment plan determined before and after performing [^{68}Ga]Ga-PSMA-11 PET/CT.

Results: The detection rate of [^{68}Ga]Ga-PSMA-11 PET/CT was superior to CT/MRI in local lymph node involvements (56.5% to 21.7%), as well as for distant metastases (47.83% to 13%). The scan findings lead to upstaging in 9 patients and down staging in 4 patients. [^{68}Ga]Ga-PSMA-11 PET/CT results changes the therapeutic plan in 13 patients (56.5%).

Conclusion: [^{68}Ga]Ga-PSMA-11 PET/CT is a promising imaging tool for initial staging of high-risk prostate cancer patients with significant higher detection rate in comparison to the conventional imaging. The study showed 56.5% changes in treatment planning following [^{68}Ga]Ga-PSMA-11 PET/CT study.

Key words: [^{68}Ga]Ga-PSMA-11; PET/CT; Prostate cancer; High risk; Staging

Iran J Nucl Med 2022;30(1):33-39
Published: January, 2022
http://irjnm.tums.ac.ir

Corresponding author: Dr. Kamran Aryana, Nuclear Medicine Research Center, Ghaem Hospital, Mashhad, Iran.
E-mail: aryanak@mums.ac.ir

INTRODUCTION

Patients with high-risk prostate cancer (PCa) are at increased risk of invasive disease, therefore staging of the tumor and management of these patients play a very important role in overall burden of the disease and the treatment options for the tumor and its metastases. Traditionally, definitive treatment options for localized prostate cancer are described as surgery or radiotherapy with or without androgen deprivation therapy (ADT), while treatment of metastatic disease includes systemic therapy with or without palliative radiotherapy [1]. Accurate delineation of the tumor burden and disease extension is necessary for primary staging and treatment planning [2].

Because of high incidence of metastatic disease in patients with high-risk PCa [3], current guidelines from the European Association of Urology (EAU) and the National Comprehensive Cancer Network (NCCN) recommend in favor of performing computed tomography (CT) or magnetic resonance imaging (MRI) of the lower abdomen accompanied by bone scintigraphy (BS) for initial treatment planning [4]. However, some studies have found insufficient sensitivity and accuracy of conventional imaging for the detection of lymph node and bone metastases. Unlike conventional imaging, the new generation of molecular imaging modalities, in particular PET/CT, offer significant improvements in diagnosis and management of PCa.[3, 5, 6].

Among PET/CT imaging radioligands, [68Ga] attached to Prostate-Specific Membrane Antigen (PSMA) has offered significant improvement in diagnosis and management of PCa with superior sensitivity and specificity compared to conventional imaging (CI) [1, 3, 7].

[68Ga]Ga-PSMA PET/CT has been praised as a promising imaging tool for detection of metastatic PCa in some meta-analyses, especially in patients with biochemical recurrence (BCR) [8, 9].

The experience with [68Ga]Ga-PSMA PET/CT for primary staging of high- and very-high risk PCa is growing rapidly. Previous studies have shown high specificity and moderate sensitivity for nodal staging [5, 10, 11], as well as high sensitivity and specificity for detection of bone metastases [5, 11-13].

Recently, the phase III Australian multi-center proPSMA trial proved a promising role for [68Ga]Ga-PSMA PET/CT imaging for staging of high-risk PCa patients [14].

We started this procedure for the first time since the year 2016 in Iran, when [68Ga]Ga-PSMA became available at our PET/CT facility. The aim of our study was to retrospectively evaluate the added value of this modality for primary staging and management of patients with high- and/or very high-risk PCa.

METHODS

Patients

From March 2016 to December 2019, 628 PCa patients underwent [68Ga]Ga-PSMA-11 PET/CT in our center, of which, 103 were referred for initial staging. However, due to our strict inclusion criteria only 23 patients entered the study. The inclusion criteria were as following: newly diagnosed biopsy-proven PCa in high and very high-risk group (Gleason score >7, or PSA >20 ng/mL or clinical stage of at least T3a), with no history of previous radical prostatectomy, no hormonal therapy or any types of treatment, available follow-up data for at least 6 months, prior CI (CT/MRI) accompanied with BS, and no concurrent malignancy. The [68Ga]Ga-PSMA-11 PET/CT results of all PCa patients in our center until September 2018 have been described elsewhere [15].

This study was approved by Mashhad University of Medical Sciences and Imam Reza International University ethics committees (ethics code: IR.MUMS.fm.REC.1396.439). In addition, written and verbal consent was provided for all patients to use their individual clinical information for the research.

Conventional imaging

Results of abdominopelvic CT scan with/without contrast and pelvic MRI were classified as local lymphatic invasion and/or distant nodal or bone involvement. Results of BS were classified into three groups: (1) no evidence of bone metastasis, (2) bone metastasis, and (3) equivocal findings.

[68Ga]Ga-PSMA PET/CT protocol

The PET/CT scan was performed one hour after intravenous injection of 5 mCi (185 Mbq (2 Mbq/kg)) of [68Ga]Ga-PSMA-11. Hydration and diuretic injection was done according to the latest EANM/SNMMI guideline [16]. We also recommended 4 hours of fasting aiming to reduce the gastrointestinal activity. Images were acquired by a 2007 Biograph 6 Truepoint Siemens PET/CT scanner. Attenuation correction was done with CT scan (50 mA, 110 keV), using 4 mm slice thickness on a spiral 6-slice scanner. Then, 3D PET images were obtained with 6–8-bed positions (3 min/bed position) from the skull top to the mid-thigh. All PET images were reconstructed with the iterative method using ordered-subset expectation maximization with two iterations and 8 subsets, and 5mm Gaussian filter size [15].

Review of PET/CT results

Two experienced nuclear medicine specialists, independently reviewed PET/CT images. Relevant clinical information including age, PSA value at the time of PET/CT scan, biopsy information (Gleason

score (GS) and Gleason grade (GG)), and clinical staging, as well as available CI work-up (CT/pelvic MRI, and BS) within 1 month before the [^{68}Ga]Ga-PSMA-11 PET/CT were also reviewed.

Assessing the impact of PET/CT results on primary staging

Comparing the result of CI and [^{68}Ga]Ga-PSMA-11 PET/CT in primary staging, we divided our findings into three subgroups: (1) prostate involvement with/without local invasion (rectum, seminal vesicles, and bladder wall), (2) local lymph node involvement, and (3) distant metastases (abdominal or retroperitoneal lymph nodes, bone or visceral metastases). Nuclear medicine specialists were totally blind to the results of the CIs, so all the patients PET/CTs were reviewed and the primary staging were determined one time based on CI results alone, and again based on the PET/CT results.

Assessing the impact of PET/CT results on treatment planning

To assess the potential impact of [^{68}Ga]Ga-PSMA-11 PET/CT on treatment planning, a board-certified radiation oncologist was asked to hypothetically determine the management of each patient based on patient's clinical history, pathologic findings and the results of CIs according to the latest international guidelines. Then, PET/CT information was provided and changes in staging and management plan were recorded.

Change in treatment management was defined as an alteration in treatment options and/or therapy details (e.g. changes in the field of radiotherapy), as described previously by Ferraro et al. [7]. Following this classification, we divided the patient managements into 4 categories:

(A) Local treatment with either surgery or radiotherapy (RT) + prophylactic ADT (for high-risk PCa)

(B) Local treatment with only RT + ADT

(C) Systemic therapy for low-volume metastatic disease with ADT ± prostate bed RT

(D) Systemic therapy of high-volume metastases including ADT ± chemotherapy

We also followed-up the patients for 18 months to evaluate the temporal changes in the PSA levels.

Statistical analysis

All data were analyzed with SPSS software (Windows software version 11.5, SPSS Inc.). Wilcoxon rank and McNemar tests were used to compare continuous variables. Pearson correlation was applied to test the relationship between the maximum standard uptake value (SUV_{max}) of the primary tumor and GS, GG, and PSA.

RESULTS

Patient characteristics

The clinical and histopathological information of the patients are described in Table 1. There was no significant correlation between SUV_{max} of the primary tumor and PSA, GS and GG ($p > 0.05$).

Table 1: Patient characteristics (N = 23).

Variable	Mean ± SD	Range
Age	70.1 ± 6.7 years	56-83 years
PSA	25.3 ± 22.8 ng/mL	7-100 ng/mL
SUV_{max} of PT	21.2 ± 11.3	5.8-59.6
Variable	**Median**	**Frequency (%)**
GS [a]	7 (3+4)	4 (17.4%)
	8	9 (39.1%)
	8	
	9	9 (39.1%)
	10	1 (4.3%)
ISUP group[a]	2	4 (17.4%)
	4	9 (39.1%)
	4	
	5	10 (43.5%)

PT= the primary tumor, GS= Gleason Score, ISUP= The International Society of Urological Pathology, SUV_{max} = maximum standard uptake value.

[a] Based on the results of transrectal ultrasound biopsy.

Comparison of CI with [^{68}Ga]Ga-PSMA-11 PET/CT

A summary of radiologic findings is depicted in Table 2. All positive findings in CI were also detected by [^{68}Ga]Ga-PSMA-11 PET/CT imaging.

[^{68}Ga]Ga-PSMA-11 PET/CT detected 13 patients (56.5%) with nodal metastases, while CI detected nodal metastasis only in 5 patients (21.7%). [^{68}Ga]Ga-PSMA-11 PET/CT significantly outperformed CI for N staging ($p = 0.008$, Table 2).

Table 2: Comparison of [^{68}Ga]^{68}Ga-PSMA-11 PET/CT results with CT/MRI for N and M staging.

Modality	[^{68}Ga]^{68}Ga-PSMA-11 PET/CT		
	N Staging	N_0	N_1
CT/MRI	N_0	10	8
	N_1	0	5

In addition, [^{68}Ga]Ga-PSMA-11 PET/CT was significantly more successful than CI for M staging (p-value = 0.014). As shown in Table 3, both modalities did not found visceral metastasis in any patients, but [^{68}Ga]Ga-PSMA-11 PET/CT detected 4 patients (13%) with distant nodal (M_{1a} group) and 7 patients

(30.4%) with bone metastases (M_{1b}). Detection rate for metastasis with [68Ga]Ga-PSMA-11 PET/CT was 47.8% in comparison with 13% for CI. The overall detection rate of [68Ga]Ga-PSMA-11 PET/CT was ~65% in our study.

Table 3: Comparison of [68Ga]Ga-PSMA-11 PET/CT results with CT/MRI for M staging.

Modality	[68Ga]68Ga-PSMA-11 PET/CT			
CT/MRI	M Staging	M_0	M_{1a}	M_{1b}
	M_0	12	3	5
	M_{1a}	0	1	0
	M_{1b}	0	0	2

BS findings were in favor of bone metastases in 5 patients (21.7%), while in 7 patients (30.4%) the results were equivalent, and in 11 patients (47.9%) negative BS was reported (Table 4). The results of BS were concordant with [68Ga]Ga-PSMA-11 PET/CT in 8 cases (34.8%). All equivocal cases reported in BS (7 patients) were considered negative by [68Ga]Ga-PSMA-11 PET/CT imaging. [68Ga]Ga-PSMA-11 PET/CT was significantly superior to BS for detection of bone metastasis and revealed bone metastases in 7 BS-negative patients (30.4%, p = 0.028).

Table 4: Comparison of [68Ga]Ga-PSMA-11 PET/CT results with bone scan for M metastasis.

Modality	[68Ga]68Ga-PSMA-11 PET/CT		
Bone Scan	M Staging	M_0	M_{1b}
	M_0	6	5
	M_{1b}	3	2
	Equivocal	7	0

Figure 1 shows an example of discordant results between BS and [68Ga]Ga-PSMA-11 PET/CT.

Change in staging

[68Ga]Ga-PSMA-11 PET/CT results lead to a change the staging in 13 cases (56.5%). Nine (39.1%) and 4 (17.4%) patients were up-staged and down-staged, respectively.

Figure 2a is a schematic appearance of changes in staging of the patients.

Change in treatment planning

All cases with a change in staging (13 of 23) also had altered treatment plan. Before including the results of PET/CT scan into decision-making, local therapy for 16 (69.6%) patients and systemic therapy for 7 (30.4%) patients was considered.

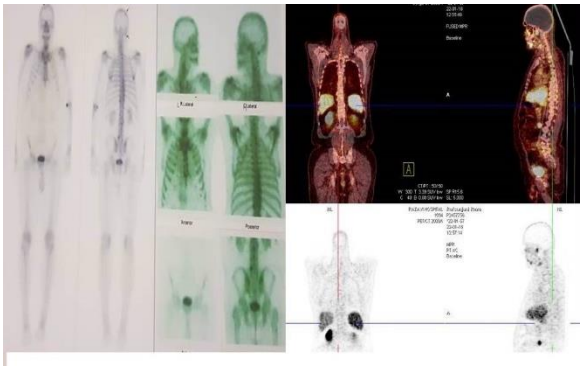

Fig 1. A 61y/o patient with PSA=21.4 and GS=9. Bone scan on the left side of the image was reported as widespread bone metastases, while [68Ga]Ga-PSMA PET/CT on the right side of the image proved no abnormal uptake.

After PET/CT results were also taken into account, treatment changed the final decision to local treatment for 12 (52.2%) patients and systemic treatment for 11 (47.8%) cases. [68Ga]Ga-PSMA-11 PET/CT results changed the treatment from local to systemic therapy in 8 (34.8%), systemic to local therapy in 4 (17.4%) and omitted the option of surgery for one patient, also changing the field considered for his RT (Figure 2b).

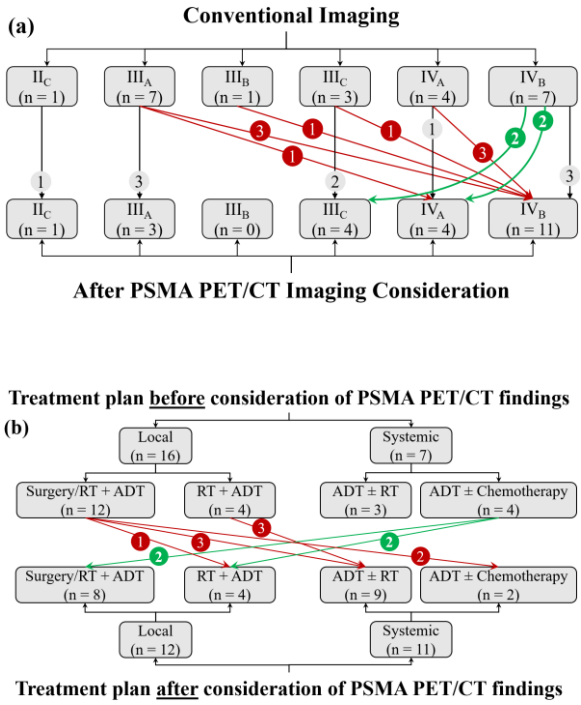

Fig 2. (a) Primary staging and (b) treatment planning of advanced prostate cancer patients enrolled in this study (n = 23), before and after considering the results of [68Ga]Ga-PSMA PET/CT imaging.

Based on CI findings, 4 (17.4%) and 3 (9.4%) of the patients were considered as high- and low-volume disease, respectively. When [^{68}Ga]Ga-PSMA-11 PET/CT findings were taken into account, these numbers changed to 2 (8.7%) and 9 (39.1%), respectively. The mean follow-up duration was 18.6 months (range: 6-32 months).

All patients showed a decline in PSA during follow-up. The mean PSA values after starting the treatment was decreased to 2.0 ± 5.5 ng/mL. Of 8 patients with the final decision of surgery or prostate bed radiotherapy, only 3 underwent surgery plus lymph node dissection. During this period, four patients (17.4%) underwent reassessment with [^{68}Ga]Ga-PSMA-11 PET/CT. The follow-up scan after treatment was negative for PSMA-avid lesion in two patients. Of two patients receiving ADT, one showed decreased PSMA uptake while in the other one, the disease was progressive which ultimately led to his death.

DISCUSSION

In recent years, various studies have shown that [^{68}Ga]Ga-PSMA-11 PET/CT could change the management for both primary staging and following biochemical recurrence [17, 18]. Improved diagnostic accuracy has been translated into a change in treatment planning in about 20-50% of the PCa patients, which is compatible with the findings of the present study [7, 17]. These encouraging results have been addressed by the recent EAU and ASCO guidelines considering a role for the next generation imaging (including PSMA PET/CT) for primary staging of advanced prostate cancer as well as BCR [14]. However, it is still debatable whether improved diagnostic efficacy is cost-effective or translates into improved patient survival [19]. We have comprehensively reviewed the literature for studies addressing the role of PSMA PET/CT vs. CI for primary staging of PCa, which is shown in Table 3. PSMA PET/CT led to a change in management of PCa patients in 27-52% of the cases [4, 7, 14].

Recently, the phase III proPSMA trial has shown superior accuracy, greater treatment impact, fewer uncertain results, less radiation exposure, and higher reporting agreement of PSMA PET/CT as compared to that of CI [14]. The result of our study is consistent with previously published data and showed that [^{68}Ga]Ga-PSMA PET/CT is approximately 34% more informative for detection of local/distant metastases in comparison with CI.

Using PSMA PET/CT for initial staging usually leads to the upstaging of PCa patients warranting a shift from local therapies to systemic or metastasis-directed therapies. Interestingly, our results show that down staging is also not uncommon. 17.4% of our patients were down-staged mainly with the help of PSMA PET/CT to exclude equivocal/suspicious bone metastases found in BS. The superior accuracy of PSMA PET/CT as compared to BS has been addressed previously [12].

We found that the most common change in the therapeutic regimen made by [^{68}Ga]Ga-PSMA PET/CT was from local to systemic treatment. We also observed an increase in the rate of patients eligible for RT after considering the results of [^{68}Ga]Ga-PSMA PET/CT (83% before vs. 91% after PET/CT). Similarly, previous studies have suggested a trend toward radiation therapy approaches after considering the results of PSMA PET/CT [20-24]. Although there is more focus on the RT management changes with PSMA PET/CT in BCR groups [25, 26], less is known about its impact on definitive RT for intact PCa patients [25]. It was reported about 26-33% changes in definitive RT in prior studies [26-28].

Study limitations

The main limitations of our study were its retrospective design, small sample size, and short follow-up duration. Also, the absence of lesion verification by biopsy of all suspicious lesions to prove the [^{68}Ga]Ga-PSMA-11 PET/CT findings and lack of complete and same conventional imaging work-up for all the patients are important limitations of our investigation. Therefore, the possibility of bias toward considering false-positive PSMA PET/CT findings as true metastases require special consideration.

CONCLUSION

[^{68}Ga]Ga-PSMA-11 PET/CT is more accurate and superior to CI for the detection of nodal or distant metastases in high- and /or very high-risk PCa patients. It can have a substantial impact on the management of at least half of these patients, making it a valuable tool for the initial staging of PCa patients.

REFERENCES

1. Ergül N, Günes BY, Yücetas U, Toktas MG, Çermik TF. 68Ga-PSMA-11 PET/CT in newly diagnosed prostate adenocarcinoma. Clin Nucl Med. 2018;43(12):e422-e7.
2. Lengana T, Lawal IO, Boshomane TG, Popoola GO, Mokoala KMG, Moshokoa E, Maes A, Mokgoro NP, Van de Wiele C, Vorster M, Sathekge MM. 68Ga-PSMA PET/CT replacing bone scan in the initial staging of skeletal metastasis in prostate cancer: a fait accompli? Clin Genitourin Cancer. 2018;16(5):392-401.
3. Thalgott M, Düwel C, Rauscher I, Heck MM, Haller B, Gafita A, Gschwend JE, Schwaiger M, Maurer T, Eiber M. One-stop-shop whole-body 68Ga-PSMA-11 PET/MRI compared with clinical nomograms for preoperative T and N staging of high-risk prostate cancer. J Nucl Med. 2018;59(12):1850-6.

4. Hirmas N, Al-Ibraheem A, Herrmann K, Alsharif A, Muhsin H, Khader J, Al-Daghmin A, Salah S. [68 Ga] PSMA PET/CT improves initial staging and management plan of patients with high-risk prostate cancer. Mol Imaging Biol. 2019;21(3):574-81.

5. Wu SY, Boreta L, Shinohara K, Nguyen H, Gottschalk AR, Hsu IC, Roach M 3rd, Westphalen AC, Feng FY, Carroll PR, Chang AJ, Hope TA. Impact of staging 68Ga-PSMA-11 PET scans on radiation treatment plansin patients with prostate cancer. Urology. 2019;125:154-62.

6. Koerber SA, Stach G, Kratochwil C, Haefner MF, Rathke H, Herfarth K, Kopka K, Holland-Letz T, Choyke PL, Haberkorn U, Debus J, Giesel FL. Lymph node involvement in treatment-naïve prostate cancer patients: correlation of PSMA PET/CT imaging and roach formula in 280 men in radiotherapeutic management. J Nucl Med. 2020;61(1):46-50.

7. Ferraro DA, Garcia Schüler HI, Muehlematter UJ, Eberli D, Müller J, Müller A, Gablinger R, Kranzbühler H, Omlin A, Kaufmann PA, Hermanns T, Burger IA. Impact of 68 Ga-PSMA-11 PET staging on clinical decision-making in patients with intermediate or high-risk prostate cancer. Eur J Nucl Med Mol Imaging. 2020;47(3):652-64.

8. Kimura S, Abufaraj M, Janisch F, Iwata T, Parizi MK, Foerster B, Fossati N, Briganti A, Egawa S, Hartenbach M, Shariat SF. Performance of [68 Ga] Ga-PSMA 11 PET for detecting prostate cancer in the lymph nodes before salvage lymph node dissection: a systematic review and meta-analysis. Prostate Cancer Prostatic Dis. 2020 Mar;23(1):1-10.

9. Perera M, Papa N, Christidis D, Wetherell D, Hofman MS, Murphy DG, Bolton D, Lawrentschuk N. Sensitivity, specificity, and predictors of positive 68Ga–prostate-specific membrane antigen positron emission tomography in advanced prostate cancer: a systematic review and meta-analysis. Eur Urol. 2016;70(6):926-37.

10. Maurer T, Gschwend JE, Rauscher I, Souvatzoglou M, Haller B, Weirich G, Wester HJ, Heck M, Kübler H, Beer AJ, Schwaiger M, Eiber M. Diagnostic efficacy of 68gallium-PSMA positron emission tomography compared to conventional imaging for lymph node staging of 130 consecutive patients with intermediate to high risk prostate cancer. J Urol 2016;195(5):1436-43.

11. Esen T, Kılıç M, Seymen H, Acar Ö, Demirkol MO. Can Ga-68 PSMA PET/CT replace conventional imaging modalities for primary lymph node and bone staging of prostate cancer? Eur Urol focus. 2020;6(2):218-20.

12. Pyka T, Okamoto S, Dahlbender M, Tauber R, Retz M, Heck M, Tamaki N, Schwaiger M, Maurer T, Eiber M. Comparison of bone scintigraphy and 68 Ga-PSMA PET for skeletal staging in prostate cancer. Eur J Nucl Med Mol Imaging. 2016;43(12):2114-21.

13. Pomykala KL, Czernin J, Grogan TR, Armstrong WR, Williams J, Calais J. Total-body 68Ga-PSMA-11 PET/CT for bone metastasis detection in prostate cancer patients: Potential impact on bone scan guidelines. J Nucl Med. 2020;61(3):405-11.

14. Hofman MS, Lawrentschuk N, Francis RJ, Tang C, Vela I, Thomas P, Rutherford N, Martin JM, Frydenberg M, Shakher R, Wong LM, Taubman K, Ting Lee S, Hsiao E, Roach P, Nottage M, Kirkwood I, Hayne D, Link E, Marusic P, Matera A, Herschtal A, Iravani A, Hicks RJ, Williams S, Murphy DG. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. Lancet. 2020;395(10231):1208-16.

15. Dadgar H, Emami F, Norouzbeigi N, Vafaee MS, Jafari E, Gholamrezanezhad A, Assadi M, Ahmadzadehfar H. Application of [(68)Ga]PSMA PET/CT in diagnosis and management of prostate cancer patients. Mol Imaging Biol. 2020 Aug;22(4):1062-1069.

16. Fendler WP, Eiber M, Beheshti M, Bomanji J, Ceci F, Cho S, Giesel F, Haberkorn U, Hope TA, Kopka K, Krause BJ, Mottaghy FM, Schöder H, Sunderland J, Wan S, Wester HJ, Fanti S, Herrmann K. 68Ga-PSMA PET/CT: Joint EANM and SNMMI procedure guideline for prostate cancer imaging: version 1.0. Eur J Nucl Med Mol Imaging. 2017;44(6):1014-24.

17. Roach PJ, Francis R, Emmett L, Hsiao E, Kneebone A, Hruby G, Eade T, Nguyen QA, Thompson BD, Cusick T, McCarthy M, Tang C, Ho B, Stricker PD, Scott AM. The impact of 68Ga-PSMA PET/CT on management intent in prostate cancer: results of an Australian prospective multicenter study. J Nucl Med. 2018;59(1):82-8.

18. Han S, Woo S, Kim YJ, Suh CH. Impact of (68)Ga-PSMA PET on the management of patients with prostate cancer: A systematic review and meta-analysis. Eur Urol. 2018;74(2):179-90.

19. Trabulsi EJ, Rumble RB, Jadvar H, Hope T, Pomper M, Turkbey B, Rosenkrantz AB, Verma S, Margolis DJ, Froemming A, Oto A, Purysko A, Milowsky MI, Schlemmer HP, Eiber M, Morris MJ, Choyke PL, Padhani A, Oldan J, Fanti S, Jain S, Pinto PA, Keegan KA, Porter CR, Coleman JA, Bauman GS, Jani AB, Kamradt JM, Sholes W, Vargas HA. Optimum imaging strategies for advanced prostate cancer: ASCO guideline. J Clin Oncol. 2020:JCO. 19.02757.

20. Grubmüller B, Baltzer P, D'Andrea D, Korn S, Haug AR, Hacker M, Grubmüller KH, Goldner GM, Wadsak W, Pfaff S, Babich J, Seitz C, Fajkovic H, Susani M, Mazal P, Kramer G, Shariat SF, Hartenbach M. (68)Ga-PSMA 11 ligand PET imaging in patients with biochemical recurrence after radical prostatectomy - diagnostic performance and impact on therapeutic decision-making. Eur J Nucl Med Mol Imaging. 2018;45(2):235-42.

21. Müller J, Ferraro DA, Muehlematter UJ, Garcia Schüler HI, Kedzia S, Eberli D, Guckenberger M, Kroeze SGC, Sulser T, Schmid DM, Omlin A, Müller A, Zilli T, John H, Kranzbuehler H, Kaufmann PA, von Schulthess GK, Burger IA. Clinical impact of (68)Ga-PSMA-11 PET on patient management and outcome, including all patients referred for an increase in PSA level during the first year after its clinical introduction. Eur J Nucl Med Mol Imaging. 2019;46(4):889-900.

22. Henkenberens C, VON Klot CA, Ross TL, Bengel FM, Wester HJ, Katja H, Christiansen H, Derlin T. 68Ga-PSMA ligand PET/CT-based radiotherapy for lymph node relapse of prostate cancer after primary therapy delays initiation of systemic therapy. Anticancer Res. 2017;37(3):1273-9.

23. Albisinni S, Artigas C, Aoun F, Biaou I, Grosman J, Gil T, Hawaux E, Limani K, Otte FX, Peltier A, Sideris S, Sirtaine N, Flamen P, van Velthoven R. Clinical impact of (68) Ga-prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) in patients with prostate cancer with rising prostate-specific antigen after treatment with curative intent: preliminary analysis of a multidisciplinary approach. BJU Int. 2017;120(2):197-203.

24. Calais J, Fendler WP, Eiber M, Gartmann J, Chu FI, Nickols NG, Reiter RE, Rettig MB, Marks LS, Ahlering

TE, Huynh LM, Slavik R, Gupta P, Quon A, Allen-Auerbach MS, Czernin J, Herrmann K. Impact of 68Ga-PSMA-11 PET/CT on the management of prostate cancer patients with biochemical recurrence. J Nucl Med. 2018;59(3):434-41.

25. Calais J, Kishan AU, Cao M, Fendler WP, Eiber M, Herrmann K, Ceci F, Reiter RE, Rettig MB, Hegde JV, Shaverdian N, King CR, Steinberg ML, Czernin J, Nickols NG. Potential impact of (68)Ga-PSMA-11 PET/CT on the planning of definitive radiation therapy for prostate cancer. J Nucl Med. 2018;59(11):1714-21.

26. Calais J, Cao M, Nickols NG. The Utility of PET/CT in the planning of external radiation therapy for prostate cancer. J Nucl Med. 2018;59(4):557-67.

27. Sterzing F, Kratochwil C, Fiedler H, Katayama S, Habl G, Kopka K, Afshar-Oromieh A, Debus J, Haberkorn U, Giesel FL. 68 Ga-PSMA-11 PET/CT: a new technique with high potential for the radiotherapeutic management of prostate cancer patients. Eur J Nucl Med Mol Imaging. 2016;43(1):34-41.

28. Dewes S, Schiller K, Sauter K, Eiber M, Maurer T, Schwaiger M, Gschwend JE, Combs SE, Habl G. Integration of (68)Ga-PSMA-PET imaging in planning of primary definitive radiotherapy in prostate cancer: a retrospective study. Radiat Oncol. 2016;11:73.