International Journal of Biomedicine 14(1) (2024) 72-76
http://dx.doi.org/10.21103/Article14(1)_OA10

ORIGINAL ARTICLE

Radiology

INTERNATIONAL JOURNAL OF BIOMEDICINE

^{68}Ga-PSMA PET/CT in Initial Diagnosis and Bone Metastasis Evaluation in Saudi Patients with High-Grade Prostate Cancer

Sahar Mansour[1*], Meshael Al-Khalaf[1], Sarah Al-Hantoshi[1], Mead Al-Mutairi[1], Fatima Al-Asqah[1], Nouf Al-Subaie[1], Sadeem Al-Qarni[1], Futun Suwaylim[1], Rawan F. Alkhodiri[2], Ola Faden[2], Abdulrahman Albatly[3]

[1]*Radiological Sciences Department, College of Health and Rehabilitation Sciences, Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia*
[2]*Nuclear Medicine Department, King Abdulaziz Medical City, Riyadh, Saudi Arabia*
[3]*Nuclear Medicine Department, Prince Sultan Military Medical City, Riyadh, Saudi Arabia*

Abstract

We present the first study performed in Saudi Arabia to evaluate ^{68}Ga-PSMA PET/CT in prostate cancer (PCa) initial diagnosis and its added value in bone metastases (BM) diagnosis in such patients. Twenty-six male patients underwent prostate histopathological examination and all imaging studies (^{68}Ga-PSMA PET/CT and CT); all of them were confirmed with high-grade PCa. Patients' mean PSA levels and Gleason score were 5.12±1.12 and 7.0±0.9, respectively. ^{68}Ga-PSMA PET/CT (20/26; sensitivity of 76.9%) was superior to traditional CT (18/26; sensitivity of 69.2%) in PCa detection. There was a non-significant association (*P*=0.332) between patients' age and BM. Based on bone scintigraphy (BS), in patients without BM (n=16), ^{68}Ga-PSMA PET/CT detected metastasis-suspicious lesions in six patients (37.5%) and negative results in ten patients (62.5%). ^{68}Ga-PSMA PET/CT showed no false-negative cases among patients with confirmed BM using BS.

In conclusion, ^{68}Ga-PSMA PET/CT performed well in PCa initial diagnosis in Saudi male patients with high-grade tumors. ^{68}Ga-PSMA PET/CT also accurately detected BM in all PCa patients with confirmed BM by BS. Larger prospective studies are urgently required to compare ^{68}Ga-PSMA PET/CT diagnostic performance with other standard modalities in PCa and BM diagnosis. **(International Journal of Biomedicine. 2024;14(1):72-76.)**

Keywords: prostate cancer • ^{68}Ga-PSMA PET/CT • diagnosis • bone metastasis • sensitivity

For citation: Mansour S, Al-Khalaf M, Al-Hantoshi S, Al-Mutairi M, Al-Asqah F, Al-Subaie N, Al-Qarni S, Suwaylim F, Alkhodiri RF, Faden O, Albatly A. ^{68}Ga-PSMA PET/CT in Initial Diagnosis and Bone Metastasis Evaluation in Saudi Patients with High-Grade Prostate Cancer. International Journal of Biomedicine. 2024;14(1):72-76. doi:10.21103/Article14(1)_OA10

Abbreviations

BM, bone metastases; **BS**, bone scintigraphy; **PCa**, prostate cancer; **PSA**, prostate-specific antigen; **PET/CT**, positron emission tomography/computed tomography

Introduction

Prostate cancer (PCa) is the second most frequently diagnosed tumor Among men worldwide, with about 1414000 new cases in 2020, and the fifth leading cause of cancer-related death, with about 375304 related deaths in 2020.[1] Owing to the economic growth and population aging, it is worth noting that the PCa burden is assumed to increase.[2] PCa incidence varies from nation to nation. In the Kingdom of Saudi Arabia (KSA), PCa poses a burden to public health, and its estimated age-standardized incidence rate was 7.7/100,000 men, and its age-standardized mortality rate was 5.1/100,000 men.[3]

Early PCa diagnosis plays a vital role in its overall management.[4] Traditionally, PCa diagnosis depends on serum prostate-specific antigen (PSA) testing and digital rectal examination (DRE) with confirmation on transrectal

ultrasound (TRUS)-guided biopsy.[5] However, the PSA test is far from specificity due to the reported false-positive results in many benign inflammations, including benign prostatic hyperplasia (BPH) and prostatitis.[6] The gold standard PCa diagnostic method, TRUS-guided biopsy, has inherent disadvantages, including the risk of potentially life-threatening infections. It is an invasive procedure, and it can miss lesions in the apical and anterior prostate and can yield false-negative findings.[7] In light of these disadvantages, there is an urgent need for alternative, accurate, and noninvasive methods for PCa lesion detection.[4]

Another noninvasive method, multiparametric MRI (mpMRI), has shown considerable promise in PCa staging and diagnosis.[8] Although reports have found that mpMRI has a high sensitivity for PCa detection,[9] its use is limited by the extreme range of negative predictive values, moderate interreader reproducibility, and moderate specificity.[10,9] Thus, there is still a need to use and/or develop alternative noninvasive methods.

In virtually all PCas, prostate-specific membrane antigen (PSMA), a transmembrane glycoprotein (type II), is overexpressed.[11] It is a glutamate carboxypeptidase II metalloproteinase mainly presenting in PCa tissues.[11] In patients with intermediate-high risk PCa, gallium-68–labeled PSMA (^{68}Ga-PSMA) positron emission tomography/computed tomography (PET/CT) has been reported to have a potential role in recurrent PCa detection as well as PCa staging with a high degree of accuracy.[11] In advanced disease stages, bone metastases (BM) are present. BM imaging is important not only for characterization and localization but also to assess their number and size and to follow up on the disease after and during treatment.[12]

Therefore, this study was designated to evaluate the diagnostic accuracy of ^{68}Ga-PSMA PET/CT in PCa initial diagnosis in Saudi patients with histopathologically proven high-grade PCa and to assess the ^{68}Ga-PSMA PET/CT ability to detect BM in those patients.

Materials and Methods

Study protocol and ethical considerations

This retrospective study was conducted in the Medical Imaging - Nuclear Medicine Department of King Abdulaziz Medical City (KAMC) at the Prince Sultan Military Medical City (PSMMC), Riyadh, Saudi Arabia, from December 2019 to December 2020, and included 26 patients. The ethical approval of the study protocol was obtained from the Institutional Review Board (IRB) at the Princess Norah bint Abdulrahman University. All data was confidently obtained from the patient's medical records, and thus, the need to obtain informed consent was waived.

Patients

The study included male patients aged ≥40 with proven high stages PCa by histopathological findings as the gold standard. Patients with other benign diseases like BPH who have the same PCa pathological symptoms and patients who underwent post-prostatectomy were excluded. All patients were screened using traditional CT scans and ^{68}Ga-PSMA PET/CT. Age, indication, Gleason score, and lab tests were also involved.

^{68}Ga-PSMA PET/CT

Images were obtained using ^{68}Ga-PSMA. 68Ga-PSMA ligand complex solution was applied to all patients through an intravenous bolus (mean 6.1, SD 154.5, 6.1-27.4 MBq; range, 87–241 MBq). After tracer injection (range, 50-70 minutes), PET acquisition began at a mean time of 58.5±9.5 minutes. All patients underwent ^{68}Ga-PSMA PET/CT on a Biograph mCT scanner (Siemens, Germany). For attenuation correction, low-dose CT covered by PET (from skull to mid-thigh) was taken place. After CT scan completion, PET data were gained for three minutes/bed position. After CT scan completion, PET data were gained for three minutes/bed position. After CT scan completion, PET data were gained for three minutes/bed position. Emission data were corrected for attenuation, scatter, dead time, and randoms. They were reconstructed iteratively by an ordered-subsets expectation maximization algorithm (8 subsets, 4 iterations) followed by a post-reconstruction smoothing Gaussian filter (5 mm in full width at one-half maximum).

The dedicated software (Syngo; Siemens) was used to review PET/CT images. Two different nuclear medicine physicians quantitatively and visually analyzed images.

Briefly, the assay involved obtaining a circular semi-automated volume of interest (VOI) from the prostate bed. Concerning the assessment of distant bone and lymph node metastases, any focal uptake > surrounding background activity that did not correspond to physiological tracer uptake was suggestive of tumor pathology.

^{99m}Tc bone scintigraphy

In agreement with the guidelines of the European Association of Nuclear Medicine/Society of Nuclear Medicine (EANM),[13] bone scintigraphy (BS) was conducted. Two-three hours after 9.4 MBq/kg body weight ^{99m}Tc-labelled methylene disphosphonate intravenous injection, a planar whole body BS scan was performed using a 2-headed gamma camera (Symbia T16, Siemens, Germany). At the discretion of the treating physician, supplemental single-photon emission CT (SPECT)/CT, covering 1- or 2-bed positions was conducted. SPECT/CT parameters were 16 views with 10 seconds/view, as previously described.[14] Images were reconstructed using iterative reconstruction with scatter correction. Low-dose CT was performed for anatomical co-registration and attenuation correction. In clinical guideline recommendations, BS and any supplementary SPECT/low-dose CT are represented as the standard bone evaluation. Another contrast-enhanced CT could be conducted after BS to assess soft tissue and lymph node metastasis.

Statistical analysis

The diagnostic values for CT and ^{68}Ga-PSMA PET/CT were evaluated and compared. Diagnostic sensitivity for each modality was calculated. Statistical analysis was performed using the statistical software package SPSS version 20.0 (SPSS Inc, Armonk, NY: IBM Corp) and GraphPad prism (ver. 8.0, San Diego, USA). Baseline characteristics were summarized as frequencies and percentages for categorical variables and as mean ± standard deviation (SD) for continuous variables.

Inter-group comparisons were performed using Student's t-test. Group comparisons with respect to categorical variables are performed using chi-square tests or, alternatively, Fisher's exact test when expected cell counts were less than 5. A probability value of $P<0.05$ was considered statistically significant.

Results

Twenty-six male patients underwent prostate histopathological examination and all imaging studies; all of them were with histopathologically confirmed high-grade PCa. Patient characteristics are described in Table 1. The mean PSA levels and Gleason score were 5.12±1.12 ng/mL and 7.0±0.9, respectively.

Table 1.

Characteristics of the study patients.

Variable	Mean	SD
Age (years)	70.08	12.17
<50 (number; percentage)	2 (7.7)	—
51 to 60 (number; percentage)	2 (7.7)	—
61 to 70 (number; percentage)	10 (38.5)	—
71 to 80 (number; percentage)	6 (23.1)	—
>80 (number; percentage)	6 (23.1)	—
PSA (ng/mL)	5.12	1.12
Gleason score	7.0	0.9

^{68}Ga-PSMA PET/CT was superior to traditional CT in PCa detection

^{68}Ga-PSMA PET/CT and CT examinations were performed for each patient, and the histologic findings were recorded. As shown in Table 2, the diagnostic ability of ^{68}Ga-PSMA PET/CT (20/26; sensitivity of 76.9%) was superior to CT (18/26; sensitivity of 69.2%) in identifying PCa.

Table 2.

Diagnostic values for different imaging modalities.

Imaging method	PCa patients	TP	FN	Sensitivity
Computed tomography	26	18	8	69.2%
^{68}Ga-PSMA PET/CT	26	20	6	76.9%

TP: true positive; FN: false negative.

^{68}Ga-PSMA PET/CT for evaluating bone metastasis

A cross-tabulation for patients' age and the values of non-metastatic and metastatic cancer after a diagnosis of patients with PCa revealed that there was a non-significant association ($P=0.332$) between age categories and bone metastasis (Table 3).

Based on BS, in patients without BM (n=16), ^{68}Ga-PSMA PET/CT detected metastasis-suspicious lesions in six patients (37.5%) and negative results in ten patients (62.5%) (Table 4). ^{68}Ga-PSMA PET/CT showed no false-negative cases among patients with confirmed BM using BS (Table 4).

Table 3.

Age categories and BS metastasis cross-tabulation.

			BS metastasis		*P*-value
			Positive	Negative	
			n=10	n=16	
Age (years)	>50	n=2	2 (100%)	0	0.332
	51-60	n=2	0	2 (100%)	
	61-70	n=10	4 (40%)	6 (60%)	
	71-80	n=6	2 (33.3%)	4 (66.7%)	
	>81	n=6	2 (33.3%)	4 (66.7%)	

Table 4.

^{68}Ga-PSMA PET/CT assessment.

			^{68}Ga-PSMA PET/CT		*P*-value
			Positive	Negative	
			n=20	n=6	
BS metastasis	Positive	n=10	10	0	0.0025
	Negative	n=16	6	10	

Discussion

PET/CT using PSMA ligands has gained increasing attention for diagnosing PCa and evaluating the extent of the disease.[15] It is recommended for high-risk cases with various advantages, including the ability to perform multimodal hybrid imaging, great specificity, and improved target-to-background ratio.[16] Reports demonstrating ^{68}Ga-PSMA PET/CT for initial detection of suspected PCa are scarce.[4] This study is the first conducted in Saudi Arabia to investigate ^{68}Ga-PSMA PET/CT diagnostic accuracy for PCa initial diagnosis in Saudi patients with histopathologically proven high-grade PCa. Also, this study evaluated the added value of ^{68}Ga-PSMA PET/CT in BM diagnosis in PCa patients who recently underwent BS.

In the present research, as a gold standard, the biopsy showed hormonal and functional results for positive PCa in all patients (n=26). Also, CT showed an anatomical result to locate PCa in 18/26 patients (sensitivity - 69.2%). The 68Ga-PSMA PET/CT was superior to CT and showed functional and

anatomical results to detect PCa in 20/26 (sensitivity - 76.9%).

Similar to our results, Lopci et al.[17] found that ^{68}Ga-PSMA PET/CT was capable of detecting malignancy and accurately identifying clinically relevant PCa in patients with high suspicion of cancer.

In a prospective Australian multicenter study, ^{68}Ga-PSMA PET/CT impact on PCa management was greater in cases with biochemical recurrence after radiation treatment or definitive surgery than in cases undergoing primary staging.[18] Interestingly, ^{68}Ga-PSMA PET/CT detected distant metastatic disease in 16% of patients, locoregional lymph nodes in 39%, and unsuspected disease in the prostate bed in 27%.[18]

A recent meta-analysis and systematic review including 7 studies that comprised 389 patients revealed that PCa initial diagnosis using ^{68}Ga-PSMA PET/CT had pooled specificity, sensitivity, negative likelihood ratio, and positive likelihood ratio of 66%, 97%, 0.05, and 2.86, respectively.[4] This finding indicates a 20-fold decrease in PCa odds being found in cases with negative PET results, thus making ^{68}Ga-PSMA PET/CT a potential rule-out test in patients with PCa suspicious biochemical or clinical findings and allowing unnecessary biopsies to be avoided.[4]

A PCa's typical characteristic is its tendency to metastasize to the bones.[19] Accurate and timely detection of bone involvement is critical in PCa management.[19] The highly sensitive, widely available, and cost-effective BS technique remains the standard for bone metastase diagnosis and is recommended by international guidelines.[20] However, given its poor performance compared with modern imaging techniques using tumor-specific tracers, its lack of specificity, and its poor performance in diagnosing small metastases in the bone marrow that have not resulted in enough osteoblastic response, it is debatable if classical BS is the suitable method for bone metastases diagnosis.[21]

In this study, ^{68}Ga-PSMA PET/CT diagnosed BM in 100% of patients with positive BS findings. However, ^{68}Ga-PSMA PET/CT also identified a notable proportion of cases in whom PSMA-avid lesions in the ribs were false positive. In line with this finding, research comparing planar BS and ^{68}Ga-PSMA PET in PCa cases demonstrated that ^{68}Ga-PSMA PET demonstrated a significantly lower equivocal lesions number, showed higher diagnostic accuracy for evaluating involved bone regions and had higher performance in diagnosing BM status of the patients.[22] Furthermore compared to BS, a similar study in 30 PCa cases reported that ^{68}Ga-PSMA PET/CT detected a significantly higher number of BM.[23] Sachpekidis et al.[19] reported that ^{68}Ga-PSMA PET/CT is a useful diagnostic method in BM detection in PCa. Compared to low-dose CT, ^{68}Ga-PSMA PET/CT visualizes more BM.[19] Authors also found that many parameters of ^{68}Ga-PSMA PET significantly correlate with plasma PSA levels.[19]

Conclusion

Using histology examination as the reference standard, compared to CT, ^{68}Ga-PSMA PET/CT performed well in PCa initial diagnosis in Saudi male patients with high-grade tumors. Also, ^{68}Ga-PSMA PET/CT accurately detected BM in all PCa patients with confirmed BM by BS. Furthermore, whereas ^{68}Ga-PSMA PET/CT commonly detected BM in patients with negative BS results, BS rarely detected BM in patients with negative ^{68}Ga-PSMA PET/CT results. Given these findings, ^{68}Ga-PSMA PET/CT is a promising technique in PCa detection and may be a potential additive in identifying BM in PCa patients. In this setting, larger prospective studies are urgently required to compare mpMRI diagnostic performance with ^{68}Ga-PSMA PET/CT.

Competing Interests

The authors declare that they have no competing interests.

References

1. Wang L, Lu B, He M, Wang Y, Wang Z, Du L. Prostate Cancer Incidence and Mortality: Global Status and Temporal Trends in 89 Countries From 2000 to 2019. Front Public Health. 2022 Feb 16;10:811044. doi: 10.3389/fpubh.2022.811044. PMID: 35252092; PMCID: PMC8888523.
2. Patasius A, Smailyte G. Re: MaryBeth B. Culp, Isabelle Soerjomataram, Jason A. Efstathiou, Freddie Bray, Ahmedin Jemal. Recent Global Patterns in Prostate Cancer Incidence and Mortality Rates. Eur Urol 2020;77:38-52. Eur Urol. 2020 May;77(5):e132. doi: 10.1016/j.eururo.2019.11.030. Epub 2019 Dec 13. PMID: 31843337.
3. Alasker A, Alghafees M, Chaudhri EN, Al Qurashi AA, Abdul Rab S, Sabbah BN, Musalli Z, Alyami A. An unusually high prevalence of isolated prostatic ductal adenocarcinoma among Saudi patients: A registry-based study. Urol Ann. 2023 Jul-Sep;15(3):320-324. doi: 10.4103/ua.ua_46_23. Epub 2023 Jul 17. PMID: 37664104; PMCID: PMC10471815.
4. Satapathy S, Singh H, Kumar R, Mittal BR. Diagnostic Accuracy of ^{68}Ga-PSMA PET/CT for Initial Detection in Patients With Suspected Prostate Cancer: A Systematic Review and Meta-Analysis. AJR Am J Roentgenol. 2021 Mar;216(3):599-607. doi: 10.2214/AJR.20.23912. Epub 2021 Jan 21. PMID: 32755196.
5. Descotes JL. Diagnosis of prostate cancer. Asian J Urol. 2019 Apr;6(2):129-136. doi: 10.1016/j.ajur.2018.11.007. Epub 2019 Feb 14. PMID: 31061798; PMCID: PMC6488713.
6. Prcic A, Begic E, Hiros M. Usefulness of Total PSA Value in Prostate Diseases Diagnosis. Acta Inform Med. 2016 Jun;24(3):156-61. doi: 10.5455/aim.2016.24.156-161. Epub 2016 Jun 4. PMID: 27482127; PMCID: PMC4949038.
7. Lomas DJ, Ahmed HU. All change in the prostate cancer diagnostic pathway. Nat Rev Clin Oncol. 2020 Jun;17(6):372-381. doi: 10.1038/s41571-020-0332-z. Epub 2020 Feb 28. PMID: 32112055.
8. Stabile A, Giganti F, Rosenkrantz AB, Taneja SS, Villeirs G, Gill IS, Allen C, Emberton M, Moore CM, Kasivisvanathan V. Multiparametric MRI for prostate cancer diagnosis: current status and future directions. Nat Rev Urol. 2020 Jan;17(1):41-61. doi: 10.1038/s41585-019-0212-4. Epub 2019 Jul 17. PMID: 31316185.
9. Zhen L, Liu X, Yegang C, Yongjiao Y, Yawei X, Jiaqi K, Xianhao W, Yuxuan S, Rui H, Wei Z, Ningjing O. Accuracy of multiparametric magnetic resonance imaging for diagnosing

prostate Cancer: a systematic review and meta-analysis. BMC Cancer. 2019 Dec 23;19(1):1244. doi: 10.1186/s12885-019-6434-2. PMID: 31870327; PMCID: PMC6929472.
10. Richenberg J, Løgager V, Panebianco V, Rouviere O, Villeirs G, Schoots IG. The primacy of multiparametric MRI in men with suspected prostate cancer. Eur Radiol. 2019 Dec;29(12):6940-6952. doi: 10.1007/s00330-019-06166-z. Epub 2019 Jun 6. PMID: 31172275; PMCID: PMC6828624.
11. Palot Manzil FF, Kaur H, Szabados L. Gallium-68 Prostate-Specific Membrane Antigen Positron Emission Tomography: A Practical Guide for Radiologists and Clinicians. Cureus. 2022 Mar 7;14(3):e22917. doi: 10.7759/cureus.22917. PMID: 35399427; PMCID: PMC8986511.
12. Pianou NK, Stavrou PZ, Vlontzou E, Rondogianni P, Exarhos DN, Datseris IE. More advantages in detecting bone and soft tissue metastases from prostate cancer using ^{18}F-PSMA PET/CT. Hell J Nucl Med. 2019 Jan-Apr;22(1):6-9. doi: 10.1967/s002449910952. Epub 2019 Mar 7. PMID: 30843003.
13. Van den Wyngaert T, Strobel K, Kampen WU, Kuwert T, van der Bruggen W, Mohan HK, Gnanasegaran G, Delgado-Bolton R, Weber WA, Beheshti M, Langsteger W, Giammarile F, Mottaghy FM, Paycha F; EANM Bone & Joint Committee and the Oncology Committee. The EANM practice guidelines for bone scintigraphy. Eur J Nucl Med Mol Imaging. 2016 Aug;43(9):1723-38. doi: 10.1007/s00259-016-3415-4. Epub 2016 Jun 4. PMID: 27262701; PMCID: PMC4932135.
14. Zacho HD, Manresa JAB, Aleksyniene R, Ejlersen JA, Fledelius J, Bertelsen H, Petersen LJ. Three-minute SPECT/CT is sufficient for the assessment of bone metastasis as add-on to planar bone scintigraphy: prospective head-to-head comparison to 11-min SPECT/CT. EJNMMI Res. 2017 Dec;7(1):1. doi: 10.1186/s13550-016-0252-1. Epub 2017 Jan 5. PMID: 28058659; PMCID: PMC5215994.
15. Zhao G, Ji B. Head-To-Head Comparison of ^{68}Ga-PSMA-11 PET/CT and ^{99m}Tc-MDP Bone Scintigraphy for the Detection of Bone Metastases in Patients With Prostate Cancer: A Meta-Analysis. AJR Am J Roentgenol. 2022 Sep;219(3):386-395. doi: 10.2214/AJR.21.27323. Epub 2022 Apr 20. Erratum in: AJR Am J Roentgenol. 2022 Sep;219(3):529. PMID: 35441529.
16. Haran C, McBean R, Parsons R, Wong D. Five-year trends of bone scan and prostate-specific membrane antigen positron emission tomography utilization in prostate cancer: A retrospective review in a private centre. J Med Imaging Radiat Oncol. 2019 Aug;63(4):495-499. doi: 10.1111/1754-9485.12885. Epub 2019 Apr 11. PMID: 30972933.
17. Lopci E, Lughezzani G, Castello A, Saita A, Colombo P, Hurle R, Peschechera R, Benetti A, Zandegiacomo S, Pasini L, Casale P, Pietro D, Bevilacqua G, Balzarini L, Buffi NM, Guazzoni G, Lazzeri M. Prospective Evaluation of ^{68}Ga-labeled Prostate-specific Membrane Antigen Ligand Positron Emission Tomography/Computed Tomography in Primary Prostate Cancer Diagnosis. Eur Urol Focus. 2021 Jul;7(4):764-771. doi: 10.1016/j.euf.2020.03.004. Epub 2020 Apr 17. PMID: 32312701.
18. 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 ^{68}Ga-PSMA PET/CT on Management Intent in Prostate Cancer: Results of an Australian Prospective Multicenter Study. J Nucl Med. 2018 Jan;59(1):82-88. doi: 10.2967/jnumed.117.197160. Epub 2017 Jun 23. PMID: 28646014.
19. Sachpekidis C, Bäumer P, Kopka K, Hadaschik BA, Hohenfellner M, Kopp-Schneider A, Haberkorn U, Dimitrakopoulou-Strauss A. ^{68}Ga-PSMA PET/CT in the evaluation of bone metastases in prostate cancer. Eur J Nucl Med Mol Imaging. 2018 Jun;45(6):904-912. doi: 10.1007/s00259-018-3936-0. Epub 2018 Jan 23. PMID: 29362859.
20. Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, et al, EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol. 2017 Apr;71(4):618-629. doi: 10.1016/j.eururo.2016.08.003. Epub 2016 Aug 25. PMID: 27568654.
21. Fonager RF, Zacho HD, Langkilde NC, Petersen LJ. (18)F-fluoride positron emission tomography/computed tomography and bone scintigraphy for diagnosis of bone metastases in newly diagnosed, high-risk prostate cancer patients: study protocol for a multicentre, diagnostic test accuracy study. BMC Cancer. 2016 Jan 11;16:10. doi: 10.1186/s12885-016-2047-1. PMID: 26753880; PMCID: PMC4709935.
22. 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 Nov;43(12):2114-2121. doi: 10.1007/s00259-016-3435-0. Epub 2016 Jun 12. PMID: 27290607.
23. Thomas L, Balmus C, Ahmadzadehfar H, Essler M, Strunk H, Bundschuh RAJP. Assessment of bone metastases in patients with prostate cancer—a comparison between 99mTc-bone-scintigraphy and [68Ga] Ga-PSMA PET/CT. Pharmaceuticals (Basel). 2017;31:68.