Original article

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Head-to-head comparison between 68Ga-PSMA and 18F-FDG-PET/CT in lymphomas: a preliminary analysis

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Purpose Isolated case reports mention the uptake of radiolabeled PSMA in lymphoma. However, it is not clear if the intensity of 68Ga-PSMA expression varies among different histological subtypes or if it correlates with 18F-FDG uptake. This study compared both tracers in patients with diverse lymphoma subtypes.

Methods Ten patients with biopsy-proven-lymphoma underwent 18F-FDG and 68Ga-PSMA-PET/CT (maximum time interval: 6 days). Lymphoma subtypes included Hodgkin's lymphoma (HL, three patients) and aggressive and indolent non-Hodgkin's lymphoma (NHL, seven patients). The intensity of PSMA uptake was classified visually as low, intermediate, or high, using blood pool, liver and parotid gland uptake as references. Maximum standardized-uptake value (SUVmax) of each affected site was measured in both sets of images.

Results FDG detected 59/59 involved sites in 10 patients and PSMA 47/59 sites in nine patients. PSMA uptake was generally low, regardless of the intensity of FDG uptake, but it was classified as intermediate in two patients. The median SUVmax varied from 2.0 (2.0–8.2) to 30.9 for FDG and from 1.7 (1.7–1.7) to 4.4 for PSMA, $P < 0.0001$. The primary lesion of one patient had a marked intralesional mismatch uptake pattern of the tracers, with areas of higher PSMA expression than FDG uptake, and vice-versa. A brain lesion was more easily identified with PSMA than with FDG images.

Conclusion HL and several NHL subtypes may present PSMA uptake. The intensity of PSMA expression is generally lower than that of FDG uptake and seems to present less variation among the different histological subtypes of lymphomas. *Nucl Med Commun* 42: 1355–1360 Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

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Keywords: 18F-FDG, 68Ga-PSMA, Hodgkin's lymphoma, non-Hodgkin's lymphoma, PET/CT

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Introduction

Gallium-68 prostate-specific membrane antigen (68Ga-PSMA) PET/computed tomography (CT) is a new diagnostic tool for prostate cancer imaging, with high sensitivity, especially in the setting of biochemical recurrence [1,2]. Its specificity was also initially supposed to be high, however, PSMA has been reported to be expressed in several non-prostate malignancies [3–5]. The proposed mechanism for nonspecific PSMA uptake in neoplasms is its expression in tumor angiogenesis, demonstrated by immunohistochemical studies [2,6].

Understanding the avidity of PSMA due to different pathological processes is important for the correct evaluation of PSMA-PET/CT images of patients with prostate cancer. This is also relevant for exploring the potential use of PSMA for diagnosis and theranostics of different neoplasms. In fact, an increasing number of manuscripts have discussed the possible use of radiolabeled PSMA imaging or treatment of colorectal cancer [3,7,8], brain tumors [4,9,10], women's and men's breast cancer [11,12], head and neck cancer [5] and other solid tumors. Few isolated reports have also documented the uptake of radiolabeled PSMA in lymphomas [13,14,15].

2-deoxy-2-[18F]fluoro-d-glucose (18F-FDG) is the radiopharmaceutical of choice for studying Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL), but some subtypes of indolent NHL are FDG-non-avid [16]. FDG uptake tends to be more intense in aggressive lymphomas [16,17]. PSMA uptake has been shown to correlate with the aggressiveness of prostate cancer [1,18]. However, it is not known how radiolabeled PSMA uptake varies among the various histological subtypes of lymphomas.

The aim of this study was to perform a head-to-head comparison of 68Ga-PSMA and 18F-FDG in different lymphoma subtypes.

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Patients and methods

The local Institutional Review Board approved the study (CAAE number: 13520619.0.0000.5404) and all patients signed the Informed Consent Form. Four male and six female patients, median age 41.5 (32–70) years old, with biopsy-proven lymphoma and referred for 18F-FDG-PET/CT examination were additionally submitted to 68Ga-PSMA-PET/CT. Patients with previous neoplasia were excluded. Eight patients were imaged as part of their initial staging, one with disease relapse after stem cell transplantation and one patient with disease relapse after first-line chemotherapy. Three patients had HL, all nodular sclerosis type. Seven patients presented with NHL: two marginal zone lymphoma, one MALT lymphoma, one follicular lymphoma (FL), one diffuse large B-cell lymphoma, one lymphoplasmacytic lymphoma and one low-grade B-cell lymphoma of unspecified immunophenotype (Table 1).

Image acquisition

Patients fasted for 6 hours before 18F-FDG-PET/CT imaging. Whole-body images were acquired 60 minutes after intravenous (IV) administration of 0.12 mCi/kg (4.4 MBq/kg) of 18F-FDG in patients with glucose level less than 180 mg/dl using a Siemens Biograph True-Point mCT 40 (Siemens Medical Solutions Inc., Knoxville, Tennessee, USA). IV contrast media was not used. CT was acquired with 120–140 kV, 120 mA, rotation time 0.8 seconds, and slice thickness 2.1 mm. PET images were acquired in 3-dimensional mode using 1.5 minutes/bed position. PET images were reconstructed using a standard iterative algorithm (3D-OSEM + PSF + TOF with two iterations and 21 subsets), with the CT data utilized for attenuation correction and image fusion.

No specific patient preparation was used for PSMA-PET/CT. Whole-body images were acquired 45 minutes after IV administration of 0.05 mCi/kg (1.85 MBq/kg) of 68Ga-PSMA using the same acquisition (except for the use of 3.0 minutes/bed position) and imaging reconstruction protocols described above for FDG-PET/CT.

The time interval between the procedures varied from 0 to 6 days. FDG images were performed first for two patients and PSMA for eight patients.

Image analysis

PSMA and FDG-PET/CT images were interpreted separately and in consensus by two nuclear medicine physicians and one radiologist by visual analysis. While analyzing the scans, they were aware of clinical data, but blind to the results of the other imaging study.

Criteria for defining the positivity of PET/CT images included presence of focal areas of tracer uptake above blood pool. Diffuse involvement in the bone marrow was defined as above liver uptake for FDG and above blood pool for PSMA.

The intensity of PSMA uptake was classified using the visual score proposed by the PROMISE Classification [18], which was defined for patients with prostate cancer: low (uptake ≥ blood pool but < liver); intermediate (uptake ≥ liver but < parotid gland); and high (uptake ≥ parotid gland).

The involved sites were counted and the maximum standardized uptake value (SUVmax) of each affected site was measured in both sets of images.

Statistical analysis

Data related to numerical variables were described as median, minimum and maximum values. To compare FDG-PET/CT and PSMA-PET/CT findings, the Wilcoxon test was used for paired data and the Mann–Whitney for the unpaired data. The significance level adopted for the study was 5%. Data were statistically tested using the Prism software (GraphPad Software, version 5.0.0.0).

Results

Analysis by patient

PSMA and FDG-PET/CT were positive in nine and 10 patients, respectively (Table 1). The median SUVmax

Table 1 **Lesions detected by prostate-specific membrane antigen and FDG-PET/CT in different lymphoma subtypes**

Pat. No.	Sex	Age (years)	Lymphoma subtype	FDG sites (N)	PSMA sites (N)	PSMA visual score[a]	PSMA > FDG sites (N)	FDG Median SUVmax	PSMA median SUVmax
1	F	32	HL (IS)	10	10	low	-	9.3 (5.6–12.3)	2.4 (1.7–3.7)
2	M	35	HL (DR-C)	5	2	low	-	4.0 (2.5–5.9)	3.2 (3.0–3.5)
3	F	33	HL (DR-T)	1	1	interm.	-	30.9 (30.9–30.9)	4.4 (4.4–4.4)
4	M	40	DLBCL	3	3	low	-	25.0 (12.9–28.9)	2.6 (1.3–2.9)
5	F	54	MZ	6	6	low	3	2.0 (2.0–8.2)	2.8 (2.1–3.3)
6	F	70	MZ	8	2	low	-	17.0 (5.0–31.1)	2.8 (2.8–2.8)
7	F	39	ML	1	0	-	-	4.8 (4.8–4.8)	-
8	F	43	LP	6	4	low	-	5.4 (3.6–5.9)	1.7 (1.7–1.7)
9	M	62	BCNHL-U	10	10	low	4	4.0 (2.0–5.4)	3.0 (2.0–3.9)
10	M	50	FL	9	9	interm.	1	3.3 (2.1–22.8)	2.5 (1.7–5.4)

BCNHL-U, low-grade B-cell non-Hodgkin's lymphoma, unspecified; DLBCL, diffuse large B-cell lymphoma; DR-C, disease relapse after initial chemotherapy; DR-T, disease relapse after stem cell transplantation; FL, follicular lymphoma; HL, nodular-sclerosis Hodgkin's lymphoma; interm., intermediate; IS, initial staging; LP, lymphoplasmacytic lymphoma; ML, MALT lymphoma; MZ, marginal zone lymphoma; PSMA > FDG, PSMA higher than FDG uptake; SUVmax, maximum standardized uptake value.
[a]According to PROMISE classification [18].

varied from 2.0 (2.0–8.2) to 30.9 for FDG and from 1.7 (1.7–1.7) to 4.4 for PSMA (Table 1), $P < 0.0001$. According to PROMISE criteria (40), the intensity of PSMA uptake was classified as high in 0/9 patients, intermediate in 2/9 patients and low in 7/9 patients.

Comparing the SUV quantifications, PSMA uptake in the involved sites was generally low, regardless the intensity of FDG uptake. Four patients (number 1, 3, 4 and 6, Table 1) presented high FDG uptake (maximum SUVmax from 12.3 to 31.1) and low PSMA uptake (maximum SUVmax from 2.8 to 4.4). Three patients (number 2, 5 and 9, Table 1) had low FDG uptake (median SUVmax from 2.0 to 4.0) and also a similar low-intensity PSMA uptake (median SUVmax from 2.5 to 3.0) (Fig. 1). One patient (number 8, Table 1) with intermediate-intensity FDG uptake also presented low PSMA uptake (maximum SUVmax of 5.9 and 1.7, respectively). A single lesion with mild FDG uptake of one patient (number 7, Table 1) was not detected by PSMA-PET/CT. The remaining patient (number 10, Table 1) presented a large spectrum of uptake intensities, with different lesions presenting high, intermediate or low FDG uptake, most of them with low-intensity PSMA uptake.

Analysis by involved sites

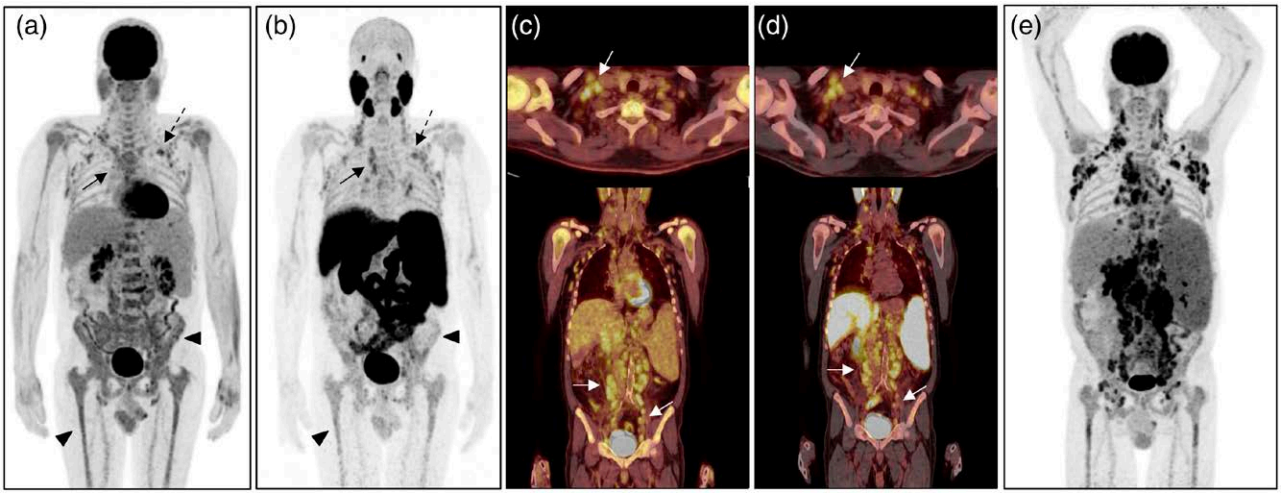
A total of 59 involved sites were detected in all patients. FDG detected all 59 and PSMA 47 sites. The 59 FDG and the 47 PSMA avid sites had a median SUV of 5.4 (2.0–31.1) and 2.8 (1.3–5.4), respectively ($P < 0.0001$). Three patients presented lesions with greater uptake of PSMA than FDG, 3/6, 4/10 and 1/10 involved sites, respectively (Table 1). One patient (number 10, Table 1) had intralesional mismatch of FDG/PSMA uptake with different parts of an extensive abdominal lesion presenting predominant PSMA or FDG uptake. A cervical lesion of this patient also had more intense PSMA than FDG uptake, although the opposite occurred in most of the lesions of this patient (Fig. 2). Brain infiltration in one patient (number 4, Table 1) was more easily identified on PSMA than on FDG images (Fig. 3).

Discussion

The present study demonstrates that several types of lymphomas, including HL, high-grade NHL and indolent lymphomas, can present PSMA uptake. These findings are consistent with three reports that described PSMA uptake in FL [13–15]. In those reports, the degree of PSMA uptake was similar to that found in this preliminary study. In fact, our results suggest that, regardless of histological grade, most lymphomas tend to present PSMA expression, generally with low-intensity uptake.

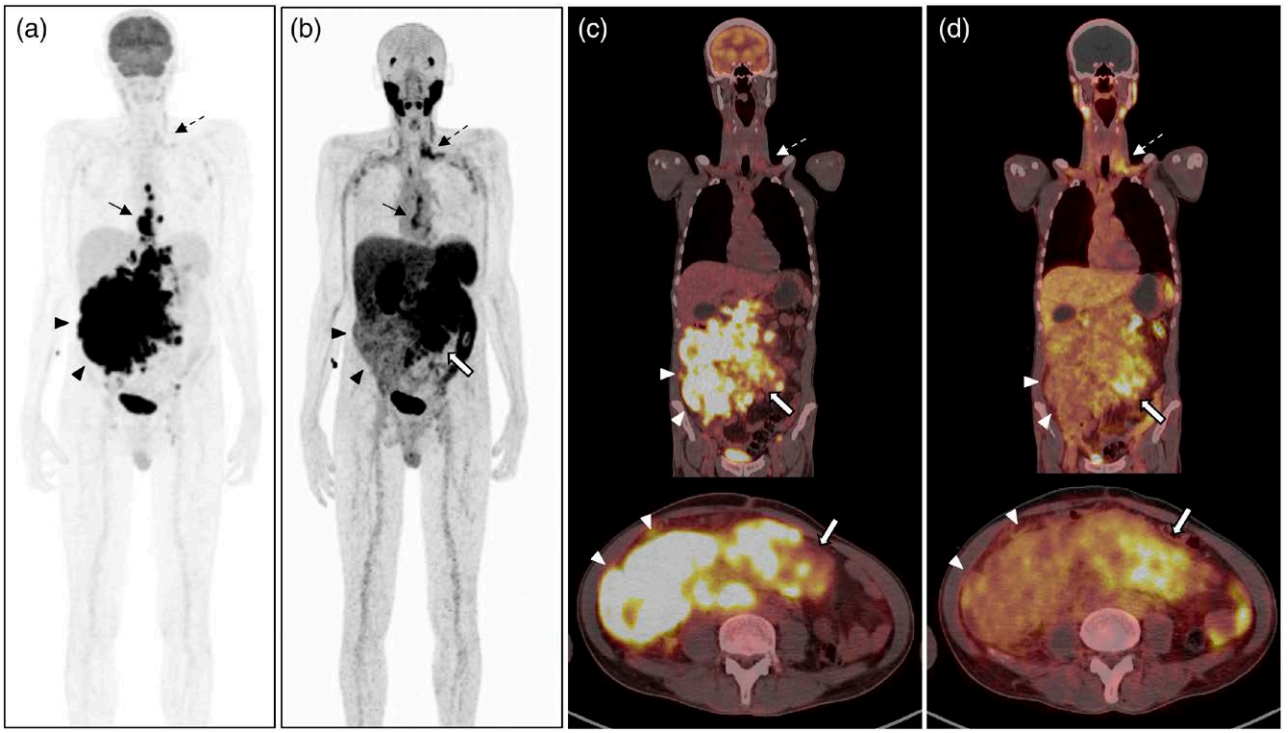
There is age overlap between some lymphoma subtypes and prostate cancer [19,20]. They can also involve the same anatomic structures, especially pelvic and abdominal lymph nodes. This preliminary study found PSMA uptake in nine of 10 patients with lymphoma, reinforcing the importance of considering this disease as a potential cause of false-positive results of PSMA-PET/CT

Fig. 1



A 62-year-old man with low-grade B-cell lymphoma of unspecified immunophenotype, at disease staging (patient 9, Table 1). Maximum projection image of 18F-FDG (a) and 68Ga-PSMA-PET/CT (b) show low-intensity uptake of both tracers in the lymphoma lesions. Some involved sites present higher PSMA uptake than FDG uptake, such as in the right superior paratracheal chain (arrows). The opposite (FDG more intense than PSMA) is seen in other sites, such as in a level III left axillary lymph node (dashed arrows) and in diffuse bone marrow involvement, which was biopsy confirmed (arrowheads). Axial and coronal slices of FDG (c) and PSMA (d) images show that most sites present similar low-intensity uptake of both tracers, as in right supraclavicular (arrows on upper images) and retroperitoneal and pelvic lymph node chains (arrows on bottom images). The patient evolved with disease relapse after initial treatment and a new FDG-PET/CT was requested, which confirmed disease progression in all sites detected at disease staging (e). PSMA, prostate-specific membrane antigen.

Fig. 2



A 50-year-old male patient with follicular lymphoma, at disease staging (patient 10, Table 1). Maximum projection image of 18F-FDG (a) and 68Ga-PSMA-PET/CT (b) and coronal and axial slices of FDG (c) and PSMA (d) show an extensive abdominal lesion presenting predominant high-intensity FDG uptake and low PSMA expression (arrow heads). However, a left portion of this lesion shows intermediate-intensity PSMA uptake (uptake ≥ liver but < parotid gland), which is greater than FDG uptake in this area (thick arrows). This characterizes intralesional mismatch uptake of the tracers and suggests different biological behaviors inside the same lesion. This uptake pattern of FDG > PSMA or PSMA > FDG is followed respectively by lesions in lower mediastinum (arrows) and lower cervical region (dashed arrows). PSMA, prostate-specific membrane antigen.

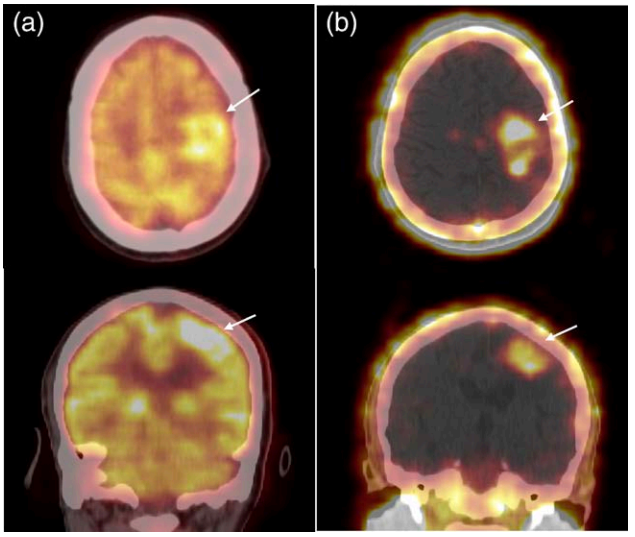
performed for prostate cancer evaluation, as previously suggested [13,14]. Although high PSMA expression was not identified in any of the patients, two of them had intermediate tracer uptake, which is equally considered typical for prostate cancer lesions [18]. In addition, low-intensity uptake, found in seven patients, can also occur in prostate cancer, especially in less aggressive disease [1,18,21].

The study also showed that the intensity of PSMA expression did not correlate with FDG uptake, and it was relatively constant among the various lymphoma subtypes. It was observed that even lymphomas with high FDG uptake tend to present low or intermediate PSMA expression. Of note, some lesions with low FDG uptake may present a greater expression of PSMA. This is probably related to the different mechanisms for FDG and PSMA uptake in this disease: glycolytic activity [17] and tumor angiogenesis [2,6], respectively. Aggressive NHL and, especially, HL have a high inflammatory component [22], with high energy requirements [17], characteristics that are directly related to the uptake of FDG, but not to PSMA expression [2,6], at least not in the same proportion. On the other hand, the importance of angiogenesis in human lymphoma is well recognized [23,24], although PSMA uptake in activated macrophages has also been proposed [25]. The present results suggest that intensity of the neoplastic angiogenesis is possibly similar in high and low-grade lymphomas.

Interestingly, one patient with FL presented a clear intralesional mismatch of FDG/PSMA uptake. Most of this lesion presented high FDG uptake and low PSMA expression. But a significant part of it had a much higher uptake of PSMA than FDG. Although it was not possible to biopsy the lesion, this finding strongly suggests different biological behaviors inside the same lesion, with possible different phenotypes. The potential relationship between this finding and lymphoma transformation should be explored in future studies.

Cerebral infiltration in one patient with DLBCL was more clearly detected in PSMA images than in FDG images. This was due to the high PSMA target-to-background ratio in this location, since there is no significant uptake of this tracer in the normal brain. This suggests

Fig. 3



A 40-year-old man with diffuse large B-cell lymphoma at disease staging (patient 4, Table 1). Axial and coronal slices of 18F-FDG (a) and 68Ga-PSMA-PET/CT (b) show brain infiltration of the left hemisphere (arrows). Although the lesion presents a much lower maximum SUV in PSMA than in FDG images (1.3 and 12.9, respectively), it is more clearly identified by PSMA, which is favored by its high target-to-background ratio in this location. PSMA, prostate-specific membrane antigen.

a potential use of radiolabeled PSMA therapy with α or β-emitters as well as for prediction of treatment with antiangiogenic drugs, as previously proposed for glioblastoma multiforme [4]. On the other hand, although this malignance is responsive to radiation therapy [26], the low-intensity PSMA uptake in the lesion may implicate high toxicity to liver and kidneys. Intrarterial radiopharmaceutical administration, as already used for the treatment of liver lesions of neuroendocrine tumors [27], might be an object of study.

The small number of patients is an intrinsic limitation of this preliminary study. However, the consistency of the results reported here provide relevant information. Biopsies of all affected sites would also have been very informative, but they were not possible for ethical reasons. Studies with a greater number of patients and other histological types of lymphoma are necessary to confirm these results.

Conclusion

HL and distinct subtypes of NHL may present PSMA uptake. The intensity of PSMA expression is usually lower than that of FDG uptake in lymphoma, but this disease might cause false-positive results in PSMA-PET/CT performed to assess prostate cancer. The intensity of PSMA uptake seems to present less variation than that of FDG when comparing aggressive and indolent subtypes of lymphomas.

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Conflicts of interest

There are no conflicts of interest.

References

1 Keidar Z, Gill R, Goshen E, Israel O, Davidson T, Morgulis M, *et al.* 68Ga-PSMA PET/CT in prostate cancer patients - patterns of disease, benign findings and pitfalls. *Cancer Imaging* 2018; **18**:39.
2 Silver DA, Pellicer I, Fair WR, Heston WD, Cordon-Cardo C. Prostate-specific membrane antigen expression in normal and malignant human tissues. *Clin Cancer Res* 1997; **3**:81–85.
3 Stoykow C, Huber-Schumacher S, Almanasreh N, Jilg C, Ruf J. Strong PSMA radioligand uptake by rectal carcinoma: who put the “S” in PSMA? *Clin Nucl Med* 2017; **42**:225–226.
4 Sasikumar A, Joy A, Pillai MR, Nanabala R, Anees KM, Jayaprakash PG, *et al.* Diagnostic value of 68Ga PSMA-11 PET/CT imaging of brain tumors-preliminary analysis. *Clin Nucl Med* 2017; **42**:e41–e48.
5 Lawhn-Heath C, Flavell RR, Glastonbury C, Hope TA, Behr SC. Incidental detection of head and neck squamous cell carcinoma on 68Ga-PSMA-11 PET/CT. *Clin Nucl Med* 2017; **42**:e218–e220.
6 Chang SS, Reuter VE, Heston WD, Bander NH, Grauer LS, Gaudin PB. Five different anti-prostate-specific membrane antigen (PSMA) antibodies confirm PSMA expression in tumor-associated neovasculature. *Cancer Res* 1999; **59**:3192–3198.
7 Hangaard L, Jochumsen MR, Vendelbo MH, Bouchelouche K. Metastases from colorectal cancer avid on 68Ga-PSMA PET/CT. *Clin Nucl Med* 2017; **42**:532–533.
8 Arçay A, Eiber M, Langbein T. Incidental finding of colon carcinoma related to high uptake in 18F-PSMA-1007 PET. *Clin Nucl Med* 2020; **45**:561–562.
9 Kunikowska J, Kuliński R, Muylle K, Koziara H, Królicki L. 68Ga-prostate-specific membrane antigen-11 PET/CT: a new imaging option for recurrent glioblastoma multiforme? *Clin Nucl Med* 2020; **45**:11–18.
10 Pernthaler B, Nazerani Hooshmand T, Igrec J, Kvaternik H, Aigner RM. Oligodendroglioma in 68Ga-PSMA-11 and 18F-Fluciclovine PET/CT. *Clin Nucl Med* 2021; **46**:e231–e232.
11 Medina-Ornelas S, García-Perez F, Estrada-Lobato E, Ochoa-Carrillo F. 68Ga-PSMA PET/CT in the evaluation of locally advanced and metastatic breast cancer, a single center experience. *Am J Nucl Med Mol Imaging* 2020; **10**:135–142.
12 Marafi F, Sasikumar A, Alfeeli M, Thuruthel S. 18F-PSMA 1007 uptake in a man with metastatic breast cancer. *Clin Nucl Med* 2020; **45**:e276–e278.
13 Kanthan GL, Coyle L, Kneebone A, Schembri GP, Hsiao E. Follicular lymphoma showing avid uptake on 68Ga PSMA-HBED-CC PET/CT. *Clin Nucl Med* 2016; **41**:500–501.
14 Vamadevan S, Le K, Bui C, Mansberg R. Prostate-specific membrane antigen uptake in small cleaved B-cell follicular non-Hodgkin lymphoma. *Clin Nucl Med* 2016; **41**:980–981.
15 Dhiantravan N, Hovey E, Bosco A, Wegner EA. Concomitant prostate carcinoma and follicular lymphoma: “flip-flop” appearances on PSMA and FDG PET/CT scans. *Clin Nucl Med* 2019; **44**:797–798.
16 Weiler-Sagie M, Bushelev O, Epelbaum R, Dann EJ, Haim N, Avivi I, *et al.* (18)F-FDG avidity in lymphoma readdressed: a study of 766 patients. *J Nucl Med* 2010; **51**:25–30.
17 Calvo-Vidal MN, Cerchietti L. The metabolism of lymphomas. *Curr Opin Hematol* 2013; **20**:345–354.
18 Eiber M, Herrmann K, Calais J, Hadaschik B, Giesel FL, Hartenbach M, *et al.* Prostate cancer molecular imaging standardized evaluation (PROMISE): proposed miTNM classification for the interpretation of PSMA-ligand PET/CT. *J Nucl Med* 2018; **59**:469–478.

19 Daniyal M, Siddiqui ZA, Akram M, Asif HM, Sultana S, Khan A. Epidemiology, etiology, diagnosis and treatment of prostate cancer. *Asian Pac J Cancer Prev* 2014; **15**:9575–9578.
20 Smedby KE, Hjalgrim H. Epidemiology and etiology of mantle cell lymphoma and other non-Hodgkin lymphoma subtypes. *Semin Cancer Biol* 2011; **21**:293–298.
21 Thang SP, Violet J, Sandhu S, Iravani A, Akhurst T, Kong G, *et al*. Poor outcomes for patients with metastatic castration-resistant prostate cancer with low prostate-specific membrane antigen (PSMA) expression deemed ineligible for 177Lu-labelled PSMA radioligand therapy. *Eur Urol Oncol* 2019; **2**:670–676.
22 Amini RM, Enblad G. Relationship between Hodgkin's and non-Hodgkin's lymphomas. *Med Oncol* 2003; **20**:211–220.
23 Ruan J, Hajjar K, Rafii S, Leonard JP. Angiogenesis and antiangiogenic therapy in non-Hodgkin's lymphoma. *Ann Oncol* 2009; **20**:413–424.
24 Ribatti D, Nico B, Ranieri G, Specchia G, Vacca A. The role of angiogenesis in human non-Hodgkin lymphomas. *Neoplasia* 2013; **15**:231–238.
25 Hermann RM, Djannatian M, Czech N, Nitsche M. Prostate-specific membrane antigen PET/CT: false-positive results due to sarcoidosis? *Case Rep Oncol* 2016; **9**:457–463.
26 Han CH, Batchelor TT. Diagnosis and management of primary central nervous system lymphoma. *Cancer* 2017; **123**:4314–4324.
27 Limouris GS, Poulantzas V, Trompoukis N, Karfis I, Chondrogiannis S, Triantafyllou N, *et al*. Comparison of 111In-[DTPA0]octreotide versus non carrier added 177Lu- [DOTA0,Tyr3]-octreotate efficacy in patients with GEP-NET treated intra-arterially for liver metastases. *Clin Nucl Med* 2016; **41**:194–200.