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FULL PAPER

Testicular fluorine-18 fludeoxyglucose uptake on positron emission tomography CT in patients with lymphoma: clinical significance and management impact

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Objective: This is the first case series examining the role of fluorine-18 fludeoxyglucose (¹⁸F-FDG) positron emission tomography-CT (PET-CT) in the diagnosis of lymphoma, and its impact on the clinical management of patients with secondary testicular involvement. This study explores the clinical significance of abnormal testicular uptake, maximum standardized uptake values and the diagnostic value of the CT component in PET-CT scans of these patients.

Methods: The case notes and PET scans of 12 patients with diagnosis of lymphoma that were reported to have abnormal ¹⁸F-FDG uptake in the testes were examined. Case notes were reviewed for the underlying diagnosis, indication for the scan and its effect on the management decision.

Results: 12 patients demonstrated abnormal ¹⁸F-FDG uptake on the PET-CT scans (mean age, 63 years; range, 37–82 years). Seven patients were diagnosed with

testicular lymphoma. Six out of the seven (86%) patients received additional intrathecal chemotherapy in addition to their systemic chemotherapy, and one patient had testicular radiotherapy.

Conclusion: This study establishes the importance of identifying and reporting abnormal ¹⁸F-FDG uptake in the testes on PET-CT in patients with lymphoma. ¹⁸F-FDG PET-CT is superior to conventional imaging in identifying testicular lymphoma and has significant management impact. It also emphasizes the importance of incorporating the testes as part of the scan coverage.

Advances in knowledge: The appearances of testicular lymphoma on ¹⁸F-FDG PET-CT can be variable and abnormal testicular uptake warrants further investigations and confirmation. FDG PET-CT is an important tool and can be used in addition to conventional imaging in the identification of testicular lymphoma.

Testicular lymphoma is a rare but lethal disease with a poor prognosis if not detected and treated early. Testicular lymphomas account for 1–2% of all non-Hodgkin's lymphoma (NHL) with an incidence of 0.26 per 100,000 people per year.¹ Testicular lymphoma, whether primary or secondary, is the most common testicular malignancy in males older than 60 years.² Primary testicular lymphoma (PTL) is diagnosed if the testicular mass is the main or primary site of disease. Secondary involvement of the testes as an extranodal site occurs in 1% of all NHL and is more common than PTL.²

Identification of secondary testicular involvement in lymphoma is crucial as these patients have a poorer prognosis (median survival, 12–24 months) without additional treatment.³ There is a high relapse rate (50–80%) in the central nervous system (CNS) or contralateral testes after locoregional therapy alone (orchidectomy and radiation

therapy). The addition of prophylactic intrathecal therapy to systemic chemotherapy and adjuvant radiotherapy improves survival.^{4–7}

Fluorine-18 fludeoxyglucose (¹⁸F-FDG) positron emission tomography (PET)-CT has become a well-established method for initial staging, monitoring response to therapy and restaging after treatment of patients with Hodgkin's lymphoma (HL) and NHL.^{8,9} On PET scanning, multiple organs demonstrate physiological ¹⁸F-FDG uptake, notably the brain, heart and liver. The testes have also been shown to demonstrate normal physiological ¹⁸F-FDG uptake, which is moderate in intensity and symmetrical in pattern, and the level of uptake declines with advancing age.¹⁰ A recent study in 20 consecutive patients with cancer also found a positive correlation between testicular ¹⁸F-FDG uptake and sperm quality indicated by total sperm count, sperm concentration and sperm motility.¹¹

There are currently no standard interpretative criteria to evaluate ^{18}F -FDG testicular uptake. The interpretation generally relies on visual analysis, and the presence of focal or asymmetrical uptake on PET would be regarded as pathological. A retrospective study that examined normal testicular ^{18}F -FDG uptake in 203 patients who did not have a history of lymphoma showed that the level of ^{18}F -FDG uptake in terms of mean maximum standardized uptake value (SUV_{max}) was 2.44 (range, 1.23–3.85) with significant age-dependent variability.¹² However, there is a paucity of literature, limited to several case reports, evaluating the pattern, prevalence and clinical significance of abnormal testicular ^{18}F -FDG uptake on PET in patients with lymphoma.^{13,14}

To our knowledge, this is the first study of its kind examining the clinical and management impact of abnormal testicular ^{18}F -FDG uptake on PET in patients with lymphoma. The role of ^{18}F -FDG PET-CT in the diagnosis of testicular lymphoma and its management will also be discussed.

METHODS AND MATERIALS

Subjects

This retrospective study was performed in a single institution. The study was approved by the Sydney South West Area Health Service Human Research Ethics Committee (Western Zone). A search of our institutional departmental database from July 2002 to December 2010 revealed 3781 male patients with lymphoma who were referred for PET or PET-CT scans for staging, therapy response assessment or restaging. Patients with more than one PET examination during this period were counted once. 12 out of 3781 patients had abnormal ^{18}F -FDG uptake in the testes or scrotum above that of background activity noted in the PET reports.

The exclusion criteria included patients with a known diagnosis of PTL who were referred for a staging PET-CT. In addition to this, patients who had recent surgery involving the testes prior to PET-CT were excluded on the basis that abnormal uptake was likely to be confounded by post-operative inflammation.

Fluorine-18 fludeoxyglucose positron emission tomography or positron emission tomography-CT

A standard protocol for ^{18}F -FDG PET or PET-CT included a fasting period of at least 4 h. Capillary blood glucose levels were measured, and patients with blood glucose levels $>10 \text{ mmol l}^{-1}$ were usually rescheduled. Patients were administered an injected activity of 5.14 MBq kg^{-1} (minimum, 185 MBq; maximum, 444 MBq) of FDG intravenously. Imaging was conducted from the level of mid-brain to proximal femora. PET-alone studies were performed with a dedicated full-ring PET scanner (PhilipsTM ADACTM Allegro[®]; Philips Medical Systems, Philadelphia, PA). Transmission data for attenuation correction were acquired with a caesium-137 line source and reconstructed using ordered subset expectation maximization and row action maximum-likelihood algorithm. PET-CT studies were conducted on a PET-CT scanner (Gemini GXL-6; Philips Medical Systems, Milpitas, CA). A low-dose non-contrast-enhanced CT scan (20–40 mAs, 120–140 kV) was acquired followed by PET.

PET and PET-CT scans were reviewed on a computer workstation (Extended Brilliance Workstation; Philips Medical Systems) visually and semi-quantitatively by two PET-accredited nuclear medicine physicians (ML, PL) by consensus blinded to all other clinical and imaging data.

Abnormal testicular uptake of increased ^{18}F -FDG accumulation was described qualitatively as one of three distinct patterns:

1. Focal or multifocal uptake: single or multiple foci of uptake within but not involving the entire testicle.
2. Diffuse asymmetric uptake: relatively uniform tracer uptake involving one testicle at a level significantly above that of the contralateral testicle.
3. Diffuse symmetrical increased uptake: relatively uniformly increased tracer uptake involving both testicles.

Lesions were assessed semi-quantitatively using the region of interest (ROI) analysis and were calculated as the maximum activity concentration detected in the lesion divided by the injected activity and corrected for body weight (SUV_{max}). In patients with focal uptake, a ROI of a fixed diameter of 15 mm was drawn around the testicular lesion and the SUV_{max} was recorded. In patients with multifocal uptake, SUV_{max} of the most intense lesion was measured. The ROI of the entire abnormal testicle was evaluated in patients with diffuse asymmetric uptake, and in patients with symmetric increased uptake, the mean SUV_{max} of both testes was used in the analyses. A radiologist (HS) interpreted all concurrent low-dose non-contrast-enhanced CT scans of the testicles on PET-CT independently.

Follow-up information was correlated to ascertain the aetiology of testicular uptake. The diagnostic reference standards were based on histopathology (core biopsy, scrotal exploration or orchidectomy) or follow-up imaging (progress PET-CT and ultrasound). Patients with abnormal testicular uptake that resolved following treatment (e.g. chemotherapy) in addition to resolution of disease at other sites on progress PET-CT were interpreted as secondary testicular lymphoma. If the testicular uptake resolved without treatment, it was considered benign, and if unchanged with therapy, the aetiology was unable to be determined. The management impact of PET in these patients was also evaluated.

RESULTS

12 out of 3781 (0.3%) patients with lymphoma demonstrated abnormal ^{18}F -FDG testicular uptake on PET or PET-CT. Eight patients presented for initial-staging PET scan. Patient characteristics including the histological type of lymphoma and International Prognostic Index (IPI) are described in Table 1. The mean age of all patients was 63 years (range, 37–82 years). The mean age of patients who presented for initial staging was 62 years (range, 37–82 years). 11 out of 12 patients had further investigations for abnormal testicular uptake with the exception of Patient 5 who passed away 12 days after PET-CT.

Histopathological confirmation was obtained in six patients (50%). Five out of the six (83%) patients underwent orchidectomy that confirmed testicular lymphoma [diffuse large B-cell

Table 1. Patient characteristics

Identity	Age (years)	Original histopathology	Indication	International Prognostic Index
1	82	DLBCL	Staging	High
2	37	Burkitt's	Staging	High-intermediate
3	54	Burkitt's	Staging	High-intermediate
4	73	DLBCL	Staging	High-intermediate
5	69	DLBCL	Staging	High
6	72	Follicular	Staging	High
7 ^a	48	Burkitt's	Staging	High-intermediate
8	70	DLBCL	Staging	High
9	47	Nodular sclerosing Hodgkin's disease	Restaging	N/A
10	68	Follicular	Restaging	N/A
11	74	DLBCL	Restaging	N/A
12	62	DLBCL	Mid-treatment	N/A

DLBCL, diffuse large B-cell lymphoma; N/A, not applicable.

^aPatient underwent staging positron emission tomography scan after one cycle of chemotherapy.

lymphoma (DLBCL), $n = 3$; Burkitt's lymphoma, $n = 2$] (Figure 1), and one patient had bilateral core biopsies that showed idiopathic granulomatous orchitis (Figure 2). Three patients underwent scrotal ultrasound, out of which one patient (Patient 7) had multiple solid vascular lesions on ultrasound consistent with lymphoma. One patient (Patient 6) was assumed to have secondary testicular involvement, as serial PET-CT after the completion of six cycles of chemotherapy showed resolution of testicular uptake. The different patterns of ^{18}F -FDG testicular uptake, which were reported as abnormal, are listed in Table 2.

All the confirmed patients with secondary testicular lymphoma ($n = 7$) had staging PET-CT scans. In this case series, the prevalence of testicular lymphoma is 58% (7 out of 12 patients) with a mean age of 62 years.

The pattern of ^{18}F -FDG uptake comprised focal or multifocal ($n = 6$) and asymmetric diffuse ($n = 1$). There was bilateral involvement in three cases. The mean SUV_{max} was 8.1 and varied significantly between 3.2 and 17.5. Concurrent CT scans were interpreted as normal in five patients. In two patients, there was evidence of a thickened spermatic cord (Patient 4) (Figure 3), asymmetrical testicular enlargement (Patient 8) and hydroceles in both.

In four patients, the aetiology of the testicular uptake was benign. The mean SUV_{max} was 8.1 (range, 2.8–16.4). Patient 10 who presented for a restaging PET-CT scan, as he was in remission, had resolution of the focal testicular uptake on a follow-up PET-CT scan performed 6 months later. He did not have any treatment between the scans and the initial increased testicular uptake was thought to likely represent asymmetric benign physiological testicular uptake. In Patient 11, the relatively increased ^{18}F -FDG uptake resided in the normal testicle owing to contralateral testicular atrophy, which was reported on the testicular ultrasound study. Patient 12 who had focal ^{18}F -FDG

uptake in a single testis had a completely normal testicular ultrasound study, and no suspicious or mass lesion was identified.

In terms of management impact (Table 2), in patients with testicular lymphoma, five had orchidectomy (71%) and six out of seven patients (86%) received intrathecal chemotherapy in

Figure 1. A 70-year-old patient with newly diagnosed diffuse large B-cell lymphoma presented for a staging positron emission tomography-CT, which showed asymmetric diffuse uptake in the right testes. He underwent right orchidectomy, which confirmed lymphomatous involvement and received intrathecal methotrexate in addition to six cycles of rituximab-cyclophosphamide, doxorubicin, vincristine, prednisolone (R-CHOP) chemotherapy.

Figure 2. A 47-year-old male with nodular sclerosing Hodgkin's lymphoma presented for restaging positron emission tomography-CT (PET-CT), which shows bilateral testicular uptake that is considerably more in the left than in the right testicle. He underwent fine-needle aspiration biopsy of the left testes, which showed evidence of idiopathic granulomatous orchitis. Serial PET-CT performed 3 months later showed resolution of fluorine-18 fludeoxyglucose uptake in the testes.

addition to their systemic chemotherapy. Patient 2 underwent prophylactic contralateral testicular radiotherapy following orchidectomy for secondary testicular lymphoma, which was diagnosed during PET-CT.

DISCUSSION

^{18}F -FDG PET has been an important advancement in oncological imaging. It has been shown to have a major impact on the staging and management of patients with lymphoma by altering the clinical stage in 44% and the clinical management in up to 62% of cases.⁸

This is the first case series that is focused on the use of PET-CT to detect the presence of testicular involvement in patients with lymphoma. The prompt diagnosis of testicular lymphoma is vital because the testis is considered a sanctuary site where lymphoma cells and chemotherapy may have reduced efficacy owing to the blood–testes barrier.^{15,16} Patients with secondary testicular involvement have a poorer prognosis and increased risk of widespread metastases to unusual sites, including the CNS, Waldeyer's ring, skin and lung.

The testis has been shown to be an organ with higher ^{18}F -FDG activity than background or physiological mediastinal blood pool.¹⁷ Based on the retrospective study on normal testicular uptake in 203 patients who did not have a history of lymphoma, the SUV_{max} was 2.44, with significant variability in values depending on age. SUV_{max} ranged from 2.81 (19–30 years) to 2.18 (80–89 years) with a statistically significant negative correlation between testicular volume and age.¹² On literature review, no study on normal levels of testicular SUV_{max} in patients with lymphoma was found. In our series, the SUV_{max} of

testicular lesions varied significantly (3.2–17.5). The mean SUV_{max} was 8.1 for both benign and malignant lesions. There was also significant variation in the pattern of testicular uptake comprising focal, multifocal and diffuse asymmetric/symmetric patterns, as reported previously.^{13,14,18} Abnormal diffuse symmetrical uptake may be less indicative of malignant infiltration and more likely to be owing to a diffuse inflammatory process, such as bilateral idiopathic granulomatous orchitis (Patient 9).

This study confirms that the presence of abnormal testicular uptake pattern on PET warrants further assessment. Ultrasound is generally used as the initial imaging modality of choice.¹⁹ Ultrasound features of testicular lymphoma include focal or diffuse hypoechoic enlarged testes with hypervascularity.¹⁹

Although CT has been shown to be of benefit in the staging of testicular cancer allowing the examination of the retroperitoneum for evidence of metastatic disease,²⁰ in patients with lymphoma, the CT component of PET-CT was less helpful. In most patients in our case series, CT did not demonstrate significant abnormalities. Asymmetry of size of the testes on CT can also be interpreted as a normal variant. Only one patient demonstrated prominent and thickened spermatic cord, which was suspicious for local infiltration. This study demonstrated the superior diagnostic value of PET in detection of testicular lymphoma over that of conventional imaging.

This study has significant implications for standard scanning protocols for PET-CT in patients with lymphoma. It illustrates the importance of incorporating the testes as part of the scan coverage. This will prevent inadvertently omitting the testes

Table 2. Pattern of fluorine-18 fludeoxyglucose (^{18}F -FDG) uptake, maximum standardized uptake values (SUV_{max}), mode of diagnostic confirmation and management changes in patients with testicular uptake on positron emission tomography (PET)/CT

Identity	Pattern of increased FDG uptake		SUV_{max}		Diagnostic confirmation	Final diagnosis	Additional therapy
	Right	Left	Right	Left			
1	Focal	Multifocal ^a	6.2	14.9	Bilateral orchidectomy	DLBCL	Orchidectomy, IT-MTX
2	Multifocal	Normal	8.1	2.4	R orchidectomy	Burkitt's	Orchidectomy, IT-MTX RT
3	Multifocal	Multifocal	7.0		Bilateral orchidectomy	Burkitt's	Orchidectomy, IT-MTX
4	Normal	Focal	2.7	17.5	Left orchidectomy	DLBCL	Orchidectomy, IT-MTX
5	Focal	Normal	5.7	1.0	None	Not confirmed	None ^b
6	Multifocal	Normal	3.2	1.9	Serial PET-CT	Follicular	None
7	Multifocal	Multifocal	3.3		Serial PET-CT and scrotal ultrasound	Burkitt's	IT-MTX and cytarabine
8	Asymmetric diffuse	Normal	10.5	3.8	R orchidectomy	DLBCL	Orchidectomy, IT-MTX
9	Diffuse symmetrical	Diffuse symmetrical	16.4		Fine-needle aspiration biopsy	Idiopathic granulomatous orchitis	None
10	Focal	Diffuse	2.4	4.0	Serial PET-CT	Benign	None
11	Asymmetric diffuse	Normal	2.8	0.9	Serial PET-CT and scrotal ultrasound	Atrophic left testis	None
12	Focal	Normal	5.0	2.7	Serial PET-CT and scrotal ultrasound	Benign	None

DLBCL, diffuse large B-cell lymphoma; IT, intrathecal; MTX, methotrexate; R, right; RT, scrotal radiotherapy.

^aMultiple foci of ^{18}F -FDG uptake within the testes.

^bPatient passed away 12 days after PET.

during PET scanning where testicular involvement and relapses may potentially be missed (Figure 2), especially in high-grade DLBCL and Burkitt's disease.

Our study also demonstrated that detection of testicular involvement necessitated a change in treatment approach with additional therapy, such as orchidectomy, CNS prophylaxis with intrathecal methotrexate or cytarabine, and scrotal radiotherapy. Multiple studies have shown that locoregional treatment such as orchidectomy/radiotherapy is not sufficient to prevent relapse in the CNS or at other sites. Retrospective studies have shown superior outcomes in patients with known testicular lymphoma who are treated with prophylactic intrathecal therapy $\pm$ locoregional radiotherapy in addition to six to eight cycles of rituximab–cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP).^{5,6,21}

Patients with high-grade lymphoma (DLBCL/Burkitt's disease) and with known immunodeficiency (e.g. human immunodeficiency virus) are at an increased risk of developing testicular involvement.²² The rate of testicular involvement in advanced stage DLBCL is 10–18%.²³ Most patients found to have testicular

involvement were diagnosed with DLBCL or Burkitt's lymphoma except one patient who had disseminated follicular lymphoma. All these patients had high and high-intermediate IPI. Testicular involvement in Hodgkin's disease is rare. In our series, one patient with HL and abnormal testicular uptake was found to have idiopathic granulomatous orchitis.

There were some limitations of this study. Firstly, owing to the retrospective nature of the study, there was some selection bias. Patients were selected based on the inclusion of any abnormal testicular or scrotal uptake in the conclusion of their report. The false-negative rate of PET for detecting testicular lymphoma is therefore unknown. The small number of patients included in this study precludes firm conclusions regarding the benefits of different management strategies. However, it was established that further investigation of abnormal testicular uptake on PET-CT is important especially at the initial staging where the positive-predictive value is high.

Secondly, histological confirmation of testicular lymphoma was obtained in only five out of seven (71%) patients in this study. Histological confirmation of lymphomatous involvement of the

Figure 3. A 74-year-old male with diffuse large B-cell lymphoma underwent restaging positron emission tomography-CT that shows asymmetrical increased testicular uptake. Follow-up scrotal ultrasound showed unilateral testicular atrophy that explained the pattern of uptake.

testes through orchidectomy and core biopsies is invasive, poses risks and is not possible in all patients. Hence, it is reasonable to utilize alternative imaging such as scrotal ultrasound in the first instance.

Resolution of abnormal testicular uptake on progress PET-CT following treatment (*e.g.* systemic chemotherapy) was used as a surrogate marker for lymphomatous involvement. While this is not ideal, it has been used in previous studies in the evaluation of an imaging modality.²⁴

There is a paucity of data on the testicular appearances on ¹⁸F-FDG PET in patients with lymphoma. This case series illustrates the importance of PET in the detection of testicular lymphoma. Further studies to establish a normal range of testicular SUV_{max} for patients with lymphoma and whether chemotherapy affects the level of ¹⁸F-FDG uptake in the testicles are areas for potential research.

CONCLUSION

Testicular lymphoma is rare, but it is aggressive with a high rate of relapse in the contralateral testes, CNS (mesenchymal and parenchymal) and other organs. The appearances of testicular lymphoma on FDG PET-CT can be variable and abnormal testicular uptake warrants further investigations and confirmation. FDG PET-CT is superior to conventional imaging in identifying testicular lymphoma and has significant management impact. Although consensus standards for treatment are lacking, current evidence suggests a regimen including systemic chemotherapy, intrathecal chemotherapy and locoregional treatment such as orchidectomy and radiotherapy.

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REFERENCES

1. Moller MB, d'Amore F, Christensen BE. Testicular lymphoma: a population-based study of incidence, clinicopathological correlations and prognosis. The Danish Lymphoma Study Group, LYFO. *Eur J Cancer* 1994; **30A**: 1760–4.
2. Verma N, Lazarchick J, Gudena V, Turner J, Chaudhary UB. Testicular lymphoma: an update for clinicians. *Am J Med Sci* 2008; **336**:

- 336–41. doi: [10.1097/MAJ.0b013e31817242bc](https://doi.org/10.1097/MAJ.0b013e31817242bc)
3. Gospodarowicz MK, Sutcliffe SB, Brown TC, Chua T, Bush RS. Patterns of disease in localized extranodal lymphomas. *J Clin Oncol* 1987; **5**: 875–80.
4. Duncan PR, Checa F, Gowing NF, McElwain TJ, Peckham MJ. Extranodal non-Hodgkin's lymphoma presenting in the testicle: a clinical and pathologic study of 24 cases. *Cancer* 1980; **45**: 1578–84.
5. Vitolo U, Chiappella A, Ferreri AJ, Martelli M, Baldi I, Balzarotti M, et al. First-line treatment for primary testicular diffuse large B-cell lymphoma with rituximab-CHOP, CNS prophylaxis, and contralateral testis irradiation: final results of an international Phase II trial. *J Clin Oncol* 2011; **29**: 2766–72. doi: [10.1200/JCO.2010.31.4187](https://doi.org/10.1200/JCO.2010.31.4187)
6. Visco C, Medeiros LJ, Mesina OM, Rodriguez MA, Hagemeister FB, McLaughlin P, et al. Non-Hodgkin's lymphoma affecting the testis: is it curable with doxorubicin-based therapy? *Clin Lymphoma* 2001; **2**: 40–6.
7. Zicherman JM, Weissman D, Gribbin C, Epstein R. Best cases from the AFIP: primary diffuse large B-cell lymphoma of the epididymis and testis. *Radiographics* 2005; **25**: 243–8.
8. Kwee TC, Kwee RM, Nievelstein RA. Imaging in staging of malignant lymphoma: a systematic review. *Blood* 2008; **111**: 504–16.
9. Isasi CR, Lu P, Blafox MD. A metaanalysis of 18F-2-deoxy-2-fluoro-D-glucose positron emission tomography in the staging and restaging of patients with lymphoma. *Cancer* 2005; **104**: 1066–74.
10. Kosuda S, Fisher S, Kison PV, Wahl RL, Grossman HB. Uptake of 2-deoxy-2-[18F]fluoro-D-glucose in the normal testis: retrospective PET study and animal experiment. *Ann Nucl Med* 1997; **11**: 195–9.
11. Dierickx L, Huyghe E, Nogueira D, Zerdoud S, Filleron T, Brillouet S, et al. Functional testicular evaluation using PET/CT with 18F-fluorodeoxyglucose. *Eur J Nucl Med Mol Imaging* 2012; **39**: 129–37. doi: [10.1007/s00259-011-1929-3](https://doi.org/10.1007/s00259-011-1929-3)
12. Kitajima K, Nakamoto Y, Senda M, Onishi Y, Okizuka H, Sugimura K. Normal uptake of 18F-FDG in the testis: an assessment by PET/CT. *Ann Nucl Med* 2007; **21**: 405–10.
13. Kuo PH, Cooper DL, Cheng DW. Recurrence of lymphoma presenting as asymmetrically increased testicular activity on FDG-PET/CT. *Semin Nucl Med* 2006; **36**: 105–7.
14. Scalcione LR, Katz DS, Santoro MS, Mahboob S, Badler RL, Yung EY. Primary testicular lymphoma involving the spermatic cord and gonadal vein. *Clin Nucl Med* 2009; **34**: 222–3. doi: [10.1097/RLU.0b013e31819a20b5](https://doi.org/10.1097/RLU.0b013e31819a20b5)
15. Zucca E, Conconi A, Mughal TI, Sarris AH, Seymour JF, Vitolo U, et al. Patterns of outcome and prognostic factors in primary large-cell lymphoma of the testis in a survey by the International Extranodal Lymphoma Study Group. *J Clin Oncol* 2003; **21**: 20–7.
16. Arkenau HT, Chong G, Cunningham D, Watkins D, Agarwal R, Sirohi B, et al. The role of intrathecal chemotherapy prophylaxis in patients with diffuse large B-cell lymphoma. *Ann Oncol* 2007; **18**: 541–5.
17. Shreve PD, Anzai Y, Wahl RL. Pitfalls in oncologic diagnosis with FDG PET imaging: physiologic and benign variants. *Radiographics* 1999; **19**: 61–77; quiz 150–1.
18. Paes FM, Kalkanis DG, Sideras PA, Serafini AN. FDG PET/CT of extranodal involvement in non-Hodgkin lymphoma and Hodgkin disease. *Radiographics* 2010; **30**: 269–91. doi: [10.1148/rg.301095088](https://doi.org/10.1148/rg.301095088)
19. Lau MW, Taylor PM, Payne SR. The indications for scrotal ultrasound. *Br J Radiol* 1999; **72**: 833–7.
20. Gatti JM, Stephenson RA. Staging of testis cancer. Combining serum markers, histologic parameters, and radiographic imaging. *Urol Clin North Am* 1998; **25**: 397–403.
21. Coiffier B, Thieblemont C, Van Den Neste E, Lepage G, Plantier I, Castaigne S, et al. Long-term outcome of patients in the LNH-98.5 trial, the first randomized study comparing rituximab-CHOP to standard CHOP chemotherapy in DLBCL patients: a study by the Groupe d'Etudes des Lymphomes de l'Adulte. *Blood* 2010; **116**: 2040–5. doi: [10.1182/blood-2010-03-276246](https://doi.org/10.1182/blood-2010-03-276246)
22. Lagrange JL, Ramaoli A, Theodore CH, Terrier-Lacombe MJ, Beckendorf V, Biron P, et al. Non-Hodgkin's lymphoma of the testis: a retrospective study of 84 patients treated in the French anticancer centres. *Ann Oncol* 2001; **12**: 1313–19.
23. Doll DC, Weiss RB. Malignant lymphoma of the testis. *Am J Med* 1986; **81**: 515–24.
24. Wahl R, Jacene H, Kasamon Y, Lodge M. From RECIST to PERCIST: evolving considerations for PET response criteria in solid tumours. *J Nucl Med* 2009; **50**(Suppl. 1): 122S–50. doi: [10.2967/jnumed.108.057307](https://doi.org/10.2967/jnumed.108.057307)