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^{18}F-FDG PET–CT dual-time imaging in detection and characterization of recurrent lesions in patients with testicular cancer

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Abstract

Background: Testicular cancer is the second most frequent form of male genital tumors. Globally, testicular malignancy has risen over the last forty years. Among malignant testicular tumors, germ cell tumors represent approximately 95% of all tumors. They are classified into seminomatous and non-seminomatous tumors as they differ in clinical features, therapy, and prognosis. Despite the increasing value of whole-body fluorodeoxyglucose positron emotion tomography/computerized tomography (^{18}FDG-PET/CT) for all malignancies, the practical function of this imaging method in testicular germ cell tumors is still unknown. We aim to assess the diagnostic performance of ^{18}FDG-PET/CT dual-time-point imaging (DTPI) in the detection and characterization of recurrent testicular cancer lesions.

Results: ^{18}FDG-PET/CT DTPI showed higher specificity (SP) in lesions' delectability and characterization for local, nodal, and distant lesions than the single-time-point imaging (STPI) (97.6%, 93.8%, and 97% versus 95.2%, 68.8%, and 84.8%, respectively) and higher sensitivity (SN) for nodal and distant lesions (97% and 93.8% versus 87.8% and 87.5%, respectively). The mean SUVmaxD and the RI values—not the SUVmaxE—of the malignant lesions were significantly greater than the benign lesions (p 0.001*).

Conclusions: ^{18}FDG-PET/CT DTPI and its related indices (SUVmaxD and the RI) are more accurate, sensitive, and specific than the STPI in the characterization of recurrent lesions in testicular cancer patients.

Keywords: ^{18}F FDG-PET/CT, Testicular cancer, Recurrence

Background

Testicular cancer is the second most frequent form of male genital tumors. Globally, testicular malignancy has doubled over the last forty years, but it is still uncommon in most countries, with an age-standardized incidence rate of 1–9.2/100,000 [1]. Among malignant testicular tumors, germ cell tumors (GCTs) represent approximately 95% of all tumors [2]. They are classified into seminomatous and non-seminomatous tumors as they differ in clinical features, therapy, and prognosis [3]. The pathology of the resected testis, tumor markers (AFP, HCG, and LDH) pre- and post-orchiectomy, chest X-ray, and/or pelvi-abdominal CT scan are typically used to stage testicular tumors[4]. Imaging is crucial in defining the N and M components of testicular tumor staging. However, the T category depends on the surgical pathology. The extent of retroperitoneal lymphadenopathy governs the N category; affection of distant organs (distant metastases) is described by the M category [5]. Recently, ^{18}F-FDG PET/CT has been used to check patients for recurrence. Although CT is the usual method for the detection of lymphadenopathy or retroperitoneal tumors, up to 30–59% of its results have been reported as false-negative [6, 7]. Despite the widespread increase in the use

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of PET/CT for all malignancies, the practical function of this imaging method in testicular GCTs is still unknown due to the conflicting outcomes of previous studies and the paucity of data [8]. Although FDG uptake in malignant lesions is generally greater than in benign lesions, it is occasionally challenging to distinguish between them, leading to false-positive or ambiguous FDG-PET results. ^{18}FDG-PET/CT DTPI is used to clarify the changes in the FDG uptake between benign and malignant lesions [9–17]. The study's objective is to assess the diagnostic performance of ^{18}FDG-PET/CT DTPI in the detection and characterization of recurrent testicular cancer lesions.

Methods

This prospective study comprised 49 patients between January 2015 and December 2019 who had a suspected recurrence of testicular cancer, either local or distant. Suspicion of recurrence, relied on the clinical data, laboratory investigations, and imaging results (ultrasound (US) and/or CT). Patients with a second primary cancer, an expected life expectancy of fewer than six months, a fulminant abdominal infection, or uncontrolled diabetes mellitus were excluded. Patients who met the eligibility requirements (treated testicular cancer patients with at least 6 months disease-free duration) underwent whole-body ^{18}FDG-PET/CT DTPI at the nuclear medicine unit of the National Cancer Institute, Cairo University. Before the study began, the Institutional Review Board at the NCI gave its ethical approval.

Whole-body ^{18}FDG-PET/CT DTPI scan

The study was obtained using an integrated PET/CT system (GE Medical Systems with 16 slice CT) in two phases: the early phase after 45–60 min following intravenous (IV) injection of 5.2 Mbq/Kg of ^{18}FDG and the delayed phase after 120–140 min post-injection. All patients were instructed to fast for at least 6 h before the I.V tracer injection and till the end of imaging, with serum glucose levels under 200 mg/dL, in addition to other instructions required for the imaging process to run ideally and smoothly. The patient underwent a standard ^{18}FDG-PET/CT imaging procedure from the head to the knees. A 2.0-min acquisition period was used for each of the six different bed positions used for the PET scans. Low-dose CT without IV contrast was acquired for anatomical localization and attenuation correction. Three reconstruction and reformatting planes were used for both PET and CT images (axial, sagittal, and coronal images). Fusion images were also formed by the combination of PET and CT images. Attenuation correction of the PET images was performed using CT data. Images were interpreted by at least one radiologist and one nuclear medicine doctor with more than 15 years experience who were blinded to the patients history. In case of discrepancy between them, the case was reviewed by another nuclear medicine physician and /or radiologist and the final consensus result is the one that was considered. The SUVmax for both stages and the retention index RI were calculated. RI = [late standardized uptake value (SUVmaxD)-early standardized uptake value (SUVmaxE)] / SUVmaxE. These indices were correlated with the reference slandered (histopathology and clinical–radiological follow-up). All patients received a comprehensive clarification of the procedure before imaging, and they all subsequently gave their informed consent to participate in the study.

Malignant lesions include those that have been pathologically confirmed, rapidly progressed over short time or metastasized.

Benign lesions include those that have been pathologically proven, spontaneously regressed, and remained stationary or slowly increased in size over long time.

Statistical analysis

SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL) version 22 was used to code and enter the data. For categorical variables, frequencies (the number of occurrences) and relative frequencies (percentages) were applied, whereas for quantitative variables, the mean, standard deviation, median, minimum, and maximum were utilized. The ideal cutoff values for predicting malignant lesions were determined using receiver operator characteristic (ROC) curves and area-under-the-curve (AUC) analysis. For early and late PET/CT scans, accuracy measures [sensitivity (SN), specificity (SP), positive predictive value (PPV), and negative predictive value (NPV), as well as their 95% confidence intervals (95% CI)] and RI were identified. A probability value (*P* value) less than 0.05 was used to indicate statistical significance.

Results

The current study included forty-nine patients with mean age of 32.6 ± 11.9 years [range 17–66 years]. Except for two patients, who had radiotherapy, all patients underwent orchiectomy followed by chemotherapy. Seminomas were the most frequent primary tumors (67.3%), followed by non-seminomatous tumors (24.5%), while stromal tumors and lymphomas were the least common [2 (4.1%) patients each] (Table 1).

According to the reference criteria (pathological and/or clinical–radiological follow-up data), the total number of lesions was 108, of which 92 (85.2%) were malignant and 16 (14.8%) were benign. Nine of them (8.3%) were local lesions (7 malignant and 2 benign), 70 (64.8%) were lymph nodes (LNs) lesions (63 malignant and 7 benign), and 29 (26.9%) were remote lesions affecting distant organs (22 malignant and 7 benign) (Table 2).

Table 1 Clinical data of the studied patients

		Total No. = 49	%
Age/years	32.6 ± 11.9		
Primary size (cm)	5.1 ± 2.3		
Primary site	Right testis	26	53.1
	Left testis	23	46.9
Pathology type	Seminomatous tumors	33	67.3
	Non-seminomatous tumors	12	24.5
	Stromal	2	4.1
	Lymphoma	2	4.1
Therapy received			
Chemotherapy	+ ve	47	95.9
	− ve	2	4.1
Radiotherapy	+ ve	2	4.1
	− ve	47	95.9

Table 2 Pathological data of the studied patients

Lesion type	Lesion nature	No.	%
Primary site lesions (no. = 9.0)	Malignant	7	77.8
	Benign	2	22.2
LNs lesions (no. = 70.0)	Malignant	63	90
	Benign	7	10
Distant lesions (no. = 29.0)	Malignant	22	75.9
	Benign	7	24.1

Recurrence was confirmed in 38 patients (77.55%), with 17 having LNs metastases, 9 having LNs and distant metastases (DM), 5 having local recurrence (LR) and DM, 5 having DM, and 2 having only LR. The lung was the organ most frequently affected (12 lesions), whereas other organs like the liver, bone, suprarenal gland, peritoneum, and brain were less commonly affected.

Dual-time point imaging suggested that 39 patients had recurrence. Of these, 37 patients had true recurrences along with two false positives; the high uptake in the lesions of these 2 patients was related to their informatory nature. Ten patients were thought to be free of the disease, but one of them had a true recurrence (false negative because of the small size of the lesion). Although the delayed PET–CT phase demonstrated better SN for detecting LNs and DM lesions than the early phase (97.4% and 93.8% vs. 87.8% and 87.5%, respectively), both the early and delayed phases of PET–CT had 100% SN for primary lesion detection. Additionally, when compared to the early phase, the late phase exhibited considerably higher SP regarding the primary site, LNs and distant organs lesions (97.6%, 93.8%, and 97% vs. 95.2%, 68.8%, and 84.8%). Also, the accuracy of the delayed phase is significantly higher than the early phase (Table 3).

Semi-quantitative ^{18}FDG-PET/CT data from the early scan showed that the mean SUVmaxE of malignant lesions was greater than that of benign lesions with no statistically significant difference between them ($P = 0.29$). But on the delayed scan, the mean SUVmaxD and RI values of the malignant lesions were significantly higher than those of the benign lesions, (P 0.001). Similar findings were seen at each specific site, i.e., the primary site, the LNs, and the DM. The majority (94.6%) of malignant lesions had higher SUVmaxD compared to the early SUVmaxE (+ ve RI), but 5.4% (5/92 lesions) showed a slight decline in the SUVmaxD compared to the early SUVmaxE (− ve RI). However, all benign lesions except one displayed -ve RI (Table 4).

Receiver operator characteristic (ROC) curve analysis identified 4.05, 3.85, and 22% as optimal cutoff points for SUVmaxE, SUVmaxD, and RI, respectively, for prediction of malignancy at all sites. At SUVmaxD 3.85, malignancy could be predicted with 94.4% SN and 87.5% SP while at RI 22% the sensitivity slightly decreased to 93.5%, but the SP notably raised to 93.8% [SUVmaxD and RI area under the curve (AUC) were 0.9 with 95% CI = 0.9–1.000 and 0.8–1.1, respectively] (Fig. 1a).

For the prediction of recurrence at the primary site, the optimal SUVmaxE, SUVmaxD, and RI cutoff thresholds were 6.85, 7.35, and 35.3%, respectively; at these

Table 3 Validity of early & late SUV in the detection of studied lesions

	Local rec		LNs met's		Distant met's	
	Early	Late	Early	Late	Early	Late
SN	100%	100%	87.8%	97.4%	87.5%	93.8%
SP	95.2%	97.6%	68.8%	93.8%	84.8%	97%
PPV	78%	87.5%	85.3%	97%	73.7%	93.8%
NPV	100%	100%	73.3%	93.8%	93.3%	97%
ACC	95.9%	98%	81.6%	95.9%	85.7%	95.9%

SN sensitivity, *SP* specificity, *PPV* positive predictive value, *NPV* negative predictive value, *Acc* accuracy

Table 4 Comparison between the benign and malignant lesions regarding early, late SUVmax, and RI

	Item	Benign lesions	Malignant lesions	*P* value
Primary site	Early SUV	6.95 ± 2.1	7.7 ± 3.7	1.0
	Late SUV	2.9 ± 0.9	12.2 ± 5.2	0.04*
	RI	− 0.6 ± 0.01	0.7 ± 0.32	0.04*
LN mets	Early SUV	4.5 ± 1.0	4.7 ± 3.2	0.30
	Late SUV	2.7 ± 1.01	8.2 ± 5.7	< 0.001*
	RI	− 0.45 ± 0.12	0.8 ± 0.3	< 0.001*
Distant mets	Early SUV	4.5 ± 1.6	5.7 ± 4.8	0.86
	Late SUV	2.9 ± 1.4	9.5 ± 7.7	< 0.001*
	RI	− 0.23 ± 0.7	0.7 ± 0.5	0.006*
Total lesions	Early SUV	4.8 ± 1.6	5.2 ± 3.8	0.29
	Late SUV	2.8 ± 1.1	8.8 ± 6.2	< 0.001*
	RI	− 0.4 ± 0.5	0.8 ± 0.4	< 0.001*
No. of RI	− ve	15 (93.8%)	5 (5.4%)	0.001*
	+ ve	1 (6.2%)	87 (94.6%)	

* means staistically highly significant

cutoff values primary site recurrence can be predicted with 57.1%, 85.7%, and 85.7% SN and 50%, 100%, and 100% SP, respectively. At the SUVmaxD cutoff value of 4.8. [SUVmaxD and RI's AUC were 1.0 and 1.0, (95.0% CI = 1.0–1.0%, [Fig. 1b]. The details of the LNs and DM lesions are shown in Fig. 1c, d. Comparing the AUC of the SUVmaxE, SUVmazD, and RI, it is found that there was a statistically significant difference between the early phase and the late phase as well as the early phase and the RI ($P < 0.05$), but there was no significant difference between the late phase and the RI ($P > 0.05$). In summary, ROC curve analysis of the SUVmax revealed that the delayed phase and the RI had the potential to differentiate malignant from benign lesions with higher SN and SP than the early phase at all sites (Figs. 2, 3).

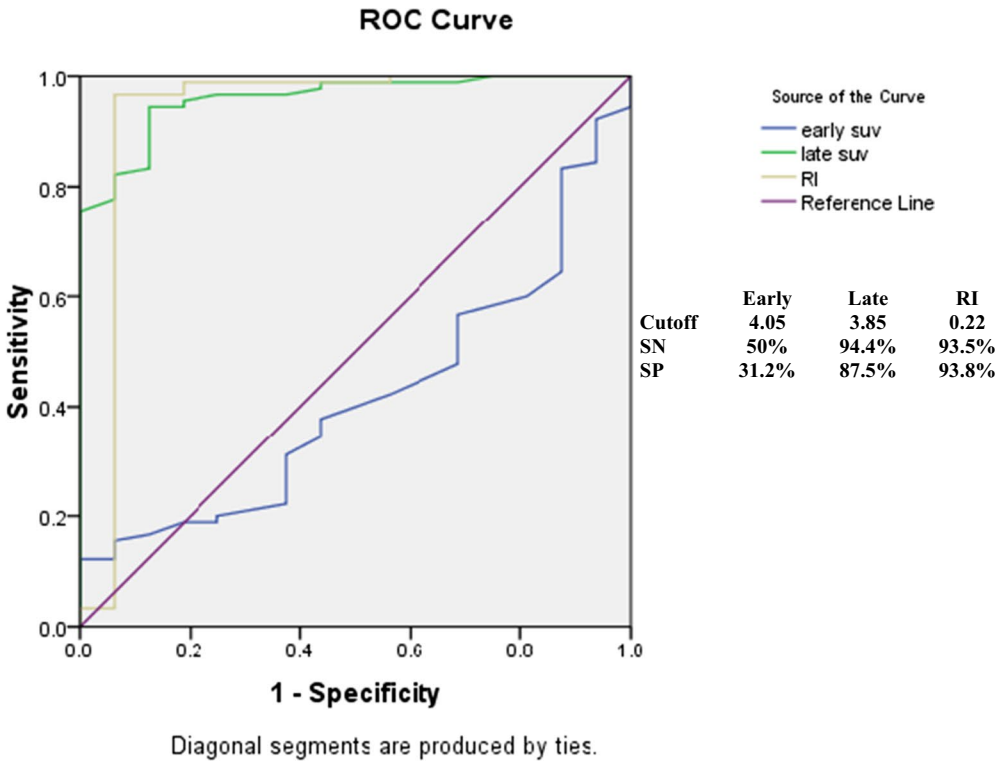
Discussion

Malignant lesions frequently attain their peak FDG pickup between 2 and 4 h after injection, but the majority of inflammatory lesions typically do so within an hour after injection. It is believed that ^{18}FDG-PET scans performed at two different time periods can help discriminate between benign and malignant tumors [9–17]. Inflammations or infectious diseases show decreased ^{18}FDG uptake at the second scan compared to the first scan. Conversely, malignant cells have been demonstrated to exhibit increased ^{18}FDG uptake at the second scan compared to the first scan [18]. To the best of our knowledge, no study has looked into the use of ^{18}FDG-PET/CT DTPI in the discrimination of benign from malignant lesions in testicular cancer patients.

The current study demonstrated that ^{18}FDG-PET/CT DTPI had 97.4% SN, 81.8% SP, 94.9% PPV, and 90% NPV value to detect recurrence, which agrees with Conduit et al. [19] in the subset of 71 patients who underwent PET/CT performed for suspicion of recurrence of cancer testicular seminoma with stage 1 disease, of whom 16 (23%) were positive, with all correctly detected recurrence (PPV 100%), and 44 (77%) were negative at 24 months; 3 of them showed recurrences on PET/CT (NPV is 93%). Our findings somewhat matched the findings of the Rashid et al. [20] who found that STPI ^{18}FDG-PET/CT was positive in 26/45 (57.8%) of the patients, all of whom had a genuine recurrence, and unremarkable in 19/45 (42.2%) of the patients, with no false negatives (100% NPV). It is noteworthy that none of the PET/CT scans were labeled as being inconclusive.

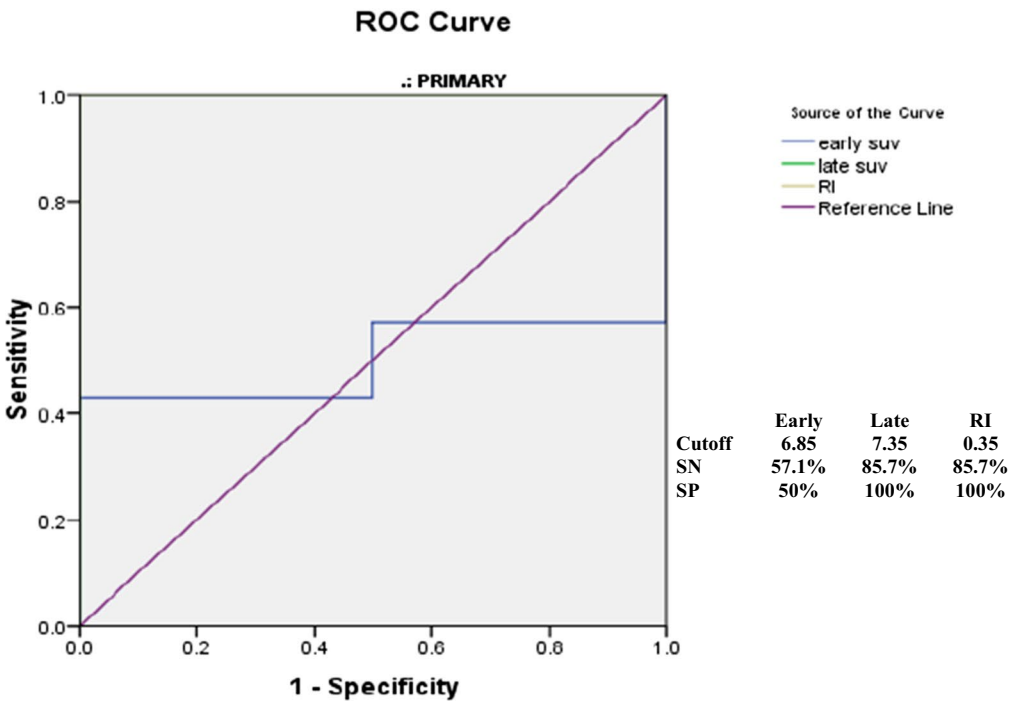
According to Ambrosini et al. [21], ^{18}F-FDG PET/CT had a lower SN (77%) but a greater SP (95%) for detection of NSGCT compared to seminoma lesions, which had 92% SN and 84% SP (retrospective study of 56 patients with seminoma and NSGCT). Sharma et al. [22] showed that ^{18}F-FDG-PET/CT had good diagnostic accuracy for restaging both seminomatous and NSGCT in 96 patients. Overall, the SN, SP, PPV, NPV, and accuracy were 94.2%, 75.0%, 83.0%, 90.9%, and 85.8%, respectively. Notably, there was no significant difference in accuracy between seminomatous and NSGCT. On the other hand, according to Lassen et al. [23], ^{18}FDG-PET/CT had a low SN (70%) to recognize recurrence in patients with normal-sized LNs who later had relapse of NSGST, which might be owing to the small volume of the disease in normal-sized LNs.

As anticipated, we generally found that DTPI is typically more sensitive than STPI, which provides time for slowly accumulating lesions on the early scan to accumulate more FDG and the background to fade, resulting in a higher target to background ratio (TBR) and better lesion identification. Moreover, DTPI improved SP and accuracy for detecting lymph node metastases (LNM), which can be explained by the fact that non-cancerous lesions tend to lose their FDG pick-up with time; consequently, in the delayed scan, the false-positive lesions from the early scan are less noticeable or have disappeared. SUVmax (RI) elevation greater than 5.2% was the ideal cutoff value for identifying LNM. On the other hand, Nogami et al. [24] found that the SN decreased with DTPI compared to STPI, but the SP and accuracy rose in the identification of LNM in gynecological malignancies with a RI of more than 9.0% as the ideal cutoff value. In earlier studies on different cancers, higher cutoff values of 10% were identified. ^{18}FDG-PET/



	Early	Late	RI
Cutoff	4.05	3.85	0.22
SN	50%	94.4%	93.5%
SP	31.2%	87.5%	93.8%

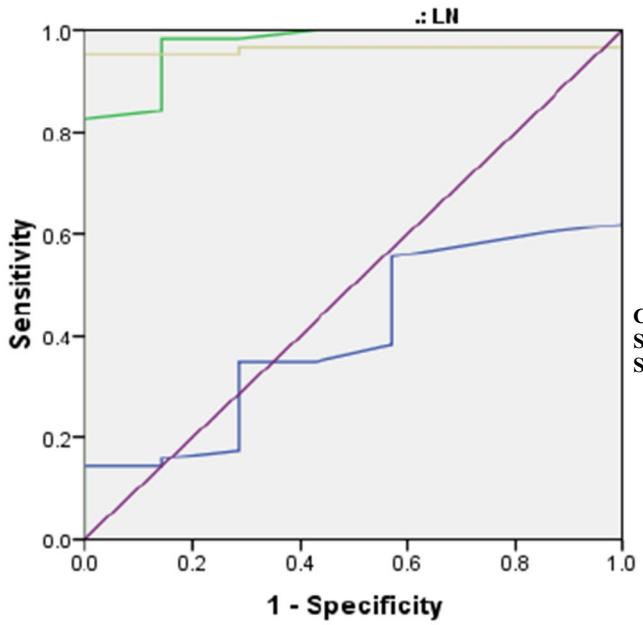
a: ROC curve of all lesions



	Early	Late	RI
Cutoff	6.85	7.35	0.35
SN	57.1%	85.7%	85.7%
SP	50%	100%	100%

b: ROC of primary site lesions.

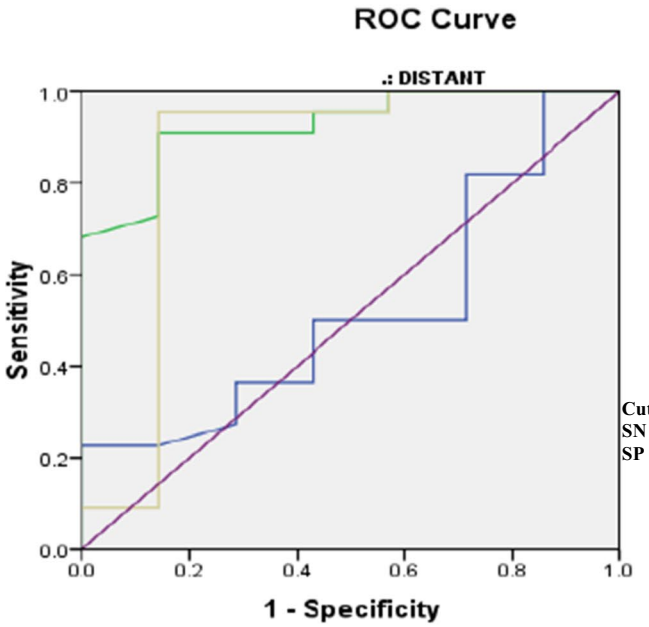
Fig. 1 **a**–**d** ROC curves of the SUVmaxE. SUVmaxD and RI



	Early	Late	RI
Cutoff	3.85	4.65	0.052
SN	54%	83.6%	98.4%
SP	42.9%	85.7%	85.7%

Diagonal segments are produced by ties.

c: ROC curve of LNs lesions



	Early	Late	RI
Cutoff	4.36	3.55	0.37
SN	50%	90.9%	86.4%
SP	57.1%	71.4%	85.7%

Diagonal segments are produced by ties.

d: ROC curve of DM lesions

Fig. 1 continued

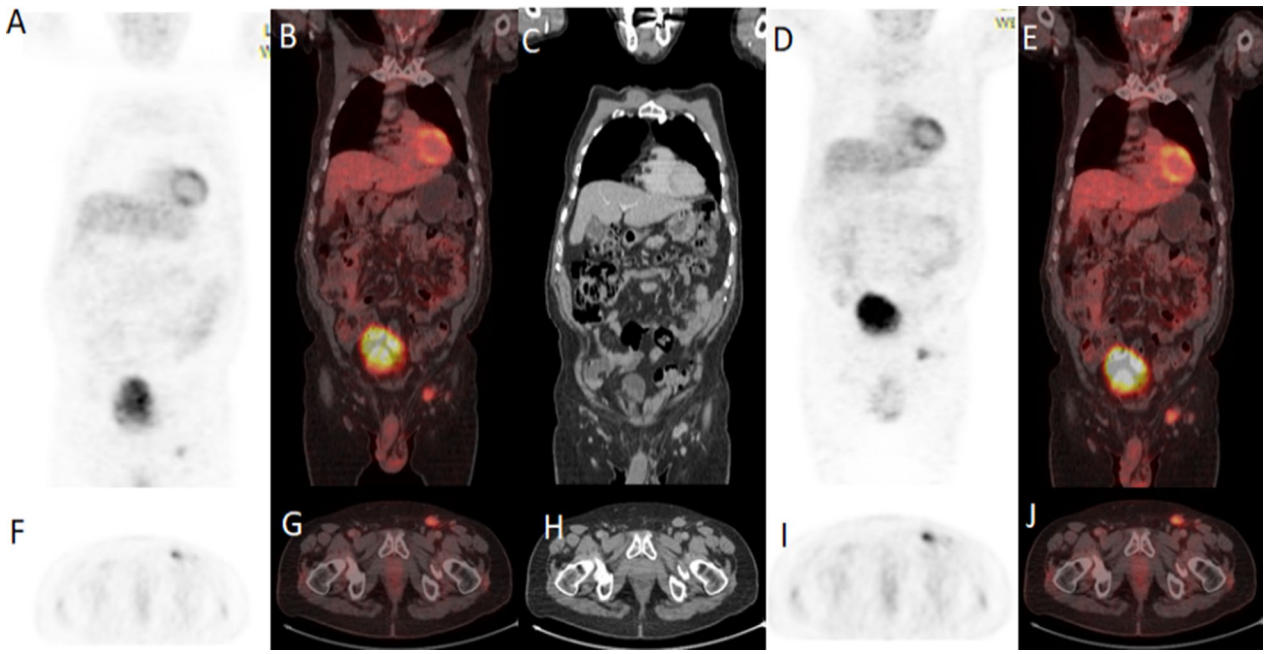


Fig. 2 A 35-year-old male with treated right testicle germ cell tumor. Post-therapy follow-up PET/CT scan (**A**, **B**, **C**, **F**, **G**, **H** Images) revealed FDG avid inguinal lymph node measuring 3.8 cm on the early scan with an early SUV max of 3.6. The delayed PET/CT scan (**D**, **E**, **I**, **J** images) revealed FDG retention in the inguinal lymph node, with a late SUV max of 6.3. The recurrence was confirmed by histopathology

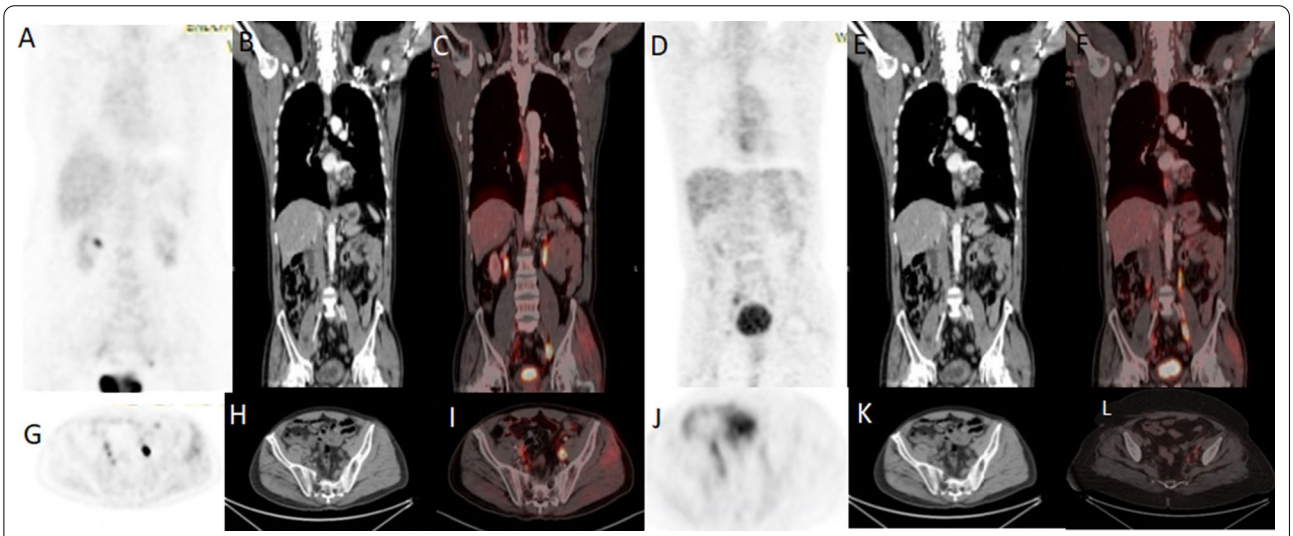


Fig. 3 A 56-year-old male with a treated left testicular germ cell tumor. Early post-therapy follow-up PET/CT scan (**A**, **B**, **C**, **G**, **H**, **I** images) revealed an active left iliac lymph node measuring 2.2 cm with an early SUV max of 8.6. The delayed PET/CT scan (**D**, **E**, **F**, **J**, **K**, **L** images) revealed FDG washout from the left iliac lymph node. Clinico-radiological follow-up confirmed its benign innocent (inflammatory) nature

CT dual-time-point imaging performed marginally better than STPI in Shen et al.[25] meta-analysis for the evaluation of the diagnostic performance of DTPI and STPI in the detection of mediastinal nodal metastases in non-small cell lung cancer. However, because of the limited number of patients and the heterogeneity of the included patients, they advised further researches to be carried out to know what function DTPI might serve for this purpose.

The tracer kinetics between the early and late scans were strongly related to lesion nature rather than the absolute value of the SUVmax, as on the early scan both benign and malignant lesions had high SUVmax, although with higher malignant lesion values yet without significant difference ($P=0.28$). However, on the delayed scan, malignant lesions had significantly higher mean SUVmax values compared to benign lesions ($P=0.001$). Tracer washout (negative RI) and tracer retention (positive RI) between the early and late scans were strongly corrected to benign and malignant lesions nature, respectively, as all benign lesions except one had negative RI and all malignant lesions except five had positive RI. Benign lesion that displayed positive RI can be explained on the bases of some inflammatory lesions may slowly accumulate the tracer over time. The retention index of 22% was highly specific (93.8%) and sensitive (93.5%) in distinguishing malignant lesions from benign ones. SUVmaxE demonstrated significantly lower SN (50%) and SP (31%) than both RI and SUVmaxD. However, Shao et al. [26] noted that the STPI can discern between benign and malignant testicular lesions as there were statistically significant differences in SUVmax values and SUVmax lesion/background ratios between benign and malignant lesions (SUVmax: $p=0.000$; SUVmax lesion/background ratio: $p=0.000$); both of them were higher in malignant than in benign lesions. The best SUVmax cutoff value for identifying benign and malignant testicular lesions was 3.8, with SN, SP, accuracy, PPV, and NPV values of 90.6%, 80.9%, 86.8%, 87.9%, and 85.0%, respectively. El-kholi and Khaled [27] found that malignant recurrent pancreatic lesions had higher mean SUVmax values than benign lesions on early and late scans. The late scan but not the early exhibited a statistically significant difference. They observed that malignancy can be predicted with 95.8% and 87.50% SN, 90% and 100% SP and a 92% accuracy rate when aSUVmaxD cutoff value of 4.9 (the same as in the present study) and RI cutoff value of 16% are used, respectively. Mavi et al. [28] found an increase in ^{18}FDG uptake over time (+ve RI)when comparing malignant lesions to healthy breast tissue in a sizable number (152) of breast cancer patients who underwent two scans, with a mean gap of 52 min between both scans. They also stated that variations in ^{18}FDG uptake over time may reflect tumor biology and the level of aggressiveness of the malignant lesion.

Caprio et al. [29] examined the diagnostic performance of DTPI in suspected breast cancer lesions for 59 patients at 1 and 3 h after receiving ^{18}FDG injections, measuring changes in ^{18}FDG using qualitative and semiquantitative uptake parameters and contrasting their findings with those from histological examinations of the resected lesions; DTPI evidenced an accuracy of 85% for lesions with SUVmax greater than or equal to 2.5 which is below the cutoff value of the current study (4.8) and/or a positive percentage in SUVmax. This difference in the cutoff point can be explained by the fact that the primary lesions in the current study are few, have different tumor types and/or grades, and have higher SUVmax values. The SN and SP of DTPI were 81% and 100% versus 63% and 100% for STPI. They stated that DTPI increases the accuracy of breast cancer recognition in patients with suspicious lesions when compared to STPI alone. In patients with lung cancer, Matthies et al. [15] observed SN and SP values of 80% and 94%, respectively, at the SUV cutoff of 2.5 on the STPI ^{18}FDG-PET scan. Their study states that DTPI raised the SN to 100% but did not appreciably alter the SP (89%). According to the Cheng et al. [30] study on patients with proven or suspected lung cancer, DTPI moderately improves the diagnostic accuracies of ^{18}FDG PET in the evaluation of lung lesions. They evaluated the dynamic changes in ^{18}FDG uptake prospectively at three consecutive hours post-injection. The optimum diagnostic performance was found to be the SUVmax of 4.2 at the third hour (88%). The TBR increased over time, and the overall quality of the images in the delayed phase appeared to be superior to that of the early scans.

To compare the potential efficacy of DTPI with STPI ^{18}FDG-PET imaging of lung cancer, Lin et al. [31] thoroughly reviewed 11 studies including 788 patients. The AUC for dual-time-point imaging and single-time-point imaging was 0.84 (0.079) and 0.76 (0.074), respectively, but it was 0.4 and 0.9 in the present study. According to their analysis, DTPI may not be indicated for routine clinical use; however, in some non-diagnostic contexts, where STPI is limited in its utility for finding lesions, it might offer extra information. However, Alkhawaldeh et al. [9] showed an improvement in the diagnostic specificity of ^{18}FDG-PET in various trials utilizing DTPI to evaluate solitary pulmonary nodules. In their meta-analysis of eight studies that included 430 pulmonary nodules in 415 patients, Zhang et al. [32] discovered that DTPI had relatively better SN and SP than STPI (79% and 73%, versus 77% and 59%, respectively). They came to the conclusion that while DTPI was more specific, both dual-time-point imaging and single-time-point imaging with 18FDG PET were equally accurate at differentiating pulmonary nodules.

Differentiating benign from malignant lesions helps to avoid needless surgical procedures and improves life quality. Therefore, it is suggested that lesions with high activity that display increasing SUVmaxD on the delayed scan (positive percentage in SUVmax) could be predicted and considered malignant, while lesions that show decreased SUVmaxD (negative percentage in SUVmax) could be predicted as benign lesions. However, there are

still a few malignant lesions with decreasing SUVmaxD between the early and the delayed images and vice versa, so a correlation with clinical data, serum tumor markers, and other radiologic imaging findings is useful in lesion differentiation. It is better to avoid additional invasive diagnostic procedures like biopsy, and the patients should be kept under follow-up.

Limitations

The current study has some limitations, including a wide age range of the patient population (17–66 years), limited number of study population, particularly for those with local recurrence, heterogeneity in tumor pathology and in the time of recurrence discovery, and finally, histopathology was not performed for all metastatic lesions, and verification of the nature of many lesions depended on clinico-radiological follow-up. Further prospective studies with suitable sample sizes are needed to assess the definitive advantage of ^{18}FDG-PET/CT DTPI in clinical practice.

Conclusions

In patients with suspected testicular cancer recurrence, ^{18}FDG-PET/CT DTPI is a valuable technique and significantly more effective than the STPI at differentiation between malignant and benign lesions. The SUVmaxD and RI are both more sensitive and specific than the SUVmaxE.

Abbreviations

^{18}FDG: Florodeoxyglucose; PET–CT: Positron emotion tomography/computerized tomography; SUV: Standardized uptake value; DTPI: Dual-time point imaging; STPI: Single-time point imaging; SUVmaxE: Early standardized uptake value; SUVmaxD: Delayed standardized uptake value; RI: Retention index; GCTs: Germ cell tumors; SN: Sensitivity; SP: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; SPSS: Statistical Package for the Social Sciences; LNs: Lymph nodes; Mets: Metastases; LR: Local recurrence; DM: Distant metastases; LNM: Lymph node metastases; ROC: Receiver operator characteristic; TBR: Target to background ratio.

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Author contributions

IN suggested and discussed the idea of the work, MR and OT planned and designed the work, acquired, and saved the data, IA interpreted the data, reviewed literature drafted, revised, and edited the manuscript, and IN and IA reviewed the manuscript. All authors have read and approved the manuscript.

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Availability of data and materials

All data and material included in our study are available. The data sets used and analyzed during the current study are available on reasonable request from the author.

Declarations

Ethics approval and consent to participate

Informed consent obtained from study participants was written and assigned by participants or their first-degree relatives. The study was approved by the research committee of national cancer institute, Cairo University 2018. No reference number provided as the committee just say yes or no according to the system in our institute at 2019 (date of starting of this research).

Consent for publication

Written informed consent for the publication of these data was obtained from the patients.

Competing interests

The authors declare that they have no competing interests.

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References

1. Garner MJ, Turner MC, Ghadirian P, Krewski D (2005) Epidemiology of testicular cancer: an overview. Int J Cancer 116:331–339
2. Epstein JI. The lower urinary tract and male genital system, testis and epididymis. In: Robbins pathologic basis of disease. 8th ed. Philadelphia: WB; 2010. Ch.21, p. 984–986.
3. SurhonneSP SAP, Gosavi AV, Agashe SR, Phansopkar MA (2018) Clinicopathological study of testicular tumors. Int J Med Sci 4(3):63–70
4. Kundra V (2004) Testicular cancer. Semin Roentgenol 39:437–450
5. Howlader N, Noone AM, Krapcho M, et al. SEER cancer statistics review, (vintage 2009 populations). National Cancer Institute Updated August 20, 2012 (1975–2009). http://seer.cancer.gov/csr/1975_2009_pops09/index.html. Accessed 1 Feb 2013.
6. Fernandez EB, Moul JW, Foley JP, Colon E, McLeod DG (1994) Retroperitoneal imaging with third and fourth generation computedaxial tomography in clinical stage I non seminomatousgerm cell tumors. Urology 44:548–552
7. McLeod DG, Weiss RB, Stablein DM et al (1991) Staging relationships and outcome in early stage testicular cancer: a report from the Testicular Cancer Intergroup Study. J Urol 145:1178–1183
8. Albano D, Caobelli F, Quartuccio N et al (2018) PET/CT for the diagnostic assessment of patients with testicular cancer. ClinTransl Imaging 6:217–221
9. Alkhawaldeh K, Bural G, Kumar R, Alavi A (2008) Impact of dual-time-point ^{18}F-FDG PET imaging and partial volume correction in the assessment of solitary pulmonary nodules. Eur J Nucl Med Mol Imaging 35:246–252
10. Buck A, Schirrmeister H, Kühn T, Shen C, Kalker T, Kotzerke J et al (2002) FDG uptake in breast cancer: Correlation with biological and clinical prognostic parameters. Eur J Nucl Med Mol Imaging 29:1317–1323
11. Hamberg LM, Hunter GJ, Alpert NM, Choi NC, Babich JW, Fischman AJ (1994) The dose uptake ratio as an index of glucose metabolism: Useful parameter or oversimplification? J Nucl Med 35:1308–1312
12. Toriihara A, Nakamura S, Kubota K, Makino T, Okochi K, Shibuya H (2013) Can dual-time-point ^{18}F-FDG PET/CT differentiate malignant salivary gland tumors from benign tumors? AJR Am J Roentgenol 201:639–644
13. Kumar R, Loving VA, Chauhan A, Zhuang H, Mitchell S, Alavi A (2005) Potential of dual-time-point imaging to improve breast cancer diagnosis with ^{18}F-FDG PET. J Nucl Med 46:1819–1824
14. Lodge MA, Lucas JD, Marsden PK, Cronin BF, O'Doherty MJ, Smith MA (1999) A PET study of ^{18}FDG uptake in soft tissue masses. Eur J Nucl Med 26:22–30

15. Matthies A, Hickeson M, Cuchiara A, Alavi A (2002) Dual time point ^{18}F-FDG PET for the evaluation of pulmonary nodules. J Nucl Med 43:871–875
16. Zhuang H, Pourdehnad M, Lambright ES, Yamamoto AJ, Lanuti M, Li P et al (2001) Dual time point ^{18}F-FDG PET imaging for differentiating malignant from inflammatory processes. J Nucl Med 42:1412–1417
17. Tian R, Su M, Tian Y, Li F, Li L, Kuang A et al (2009) Dual-time point PET/CT with ^{18}F- FDG for the differentiation of malignant and benign bone lesions. Skeletal Radiol 38:451–458
18. Cheng G, Torigian DA, Zhuang H, Alavi A (2013) When shouldwe recommend use of dual time-point and delayed time-pointimaging techniques in FDG PET? Eur J Nucl Med Mol Imaging 40:779–787
19. Conduit C, Hofman MS, Lewin JH, Toner GC, Tran B (2021) Clinical utility of FDG PET–CT in stage 1 and advanced testicular seminoma. J Clin Oncol 39(15_suppl):5027–5027
20. Rasheed R, Al-Kandari F, Ghanem M, Marafi F, Usmani S (2020) Significance of ^{18}F-FDG PET/CT in characterization of equivocal lesions in high-risk testicular carcinoma in restaging setting. Asian Pac J Cancer Prev 21(2):511–515
21. Ambrosini V, Zucchini G, Nicolini S, Berselli A, Nanni C, Allegri V, et al (2014) ^{18}F-FDG PET/CT impact on testicular tumours clinical management. Eur J Nucl Med Mol Imaging 41:668–673
22. Sharma P, Jain TK, Parida GK, Karunanithi S, Patel C, Sharma A et al (2014) Diagnostic accuracy of integrated ^{18}F-FDG PET/CT for restaging patients with malignant germ cell tumours. Br J Radiol 87:20140263
23. Lassen U, Daugaard G, Eigtved A, Hjgaard L, DamgaardK RM (2003) Whole-body FDG-PET in patients with stage I non-seminomatous germ cell tumours. Eur J Nucl Med Mol Imaging 30:396–402
24. Nogami Y, Banno K, Irie H, Iida M, Masugi Y, Murakami K, Aoki D (2015) Efficacy of ^{18}F-FDG PET–CT dual-phase scanning for detection of lymph node metastasis in gynecological cancer. Anticancer Res 35(4):2247–2253
25. Shen G, Hu S, Deng H, Jia Z (2015) Diagnostic value of dual time-point ^{18}F-FDG PET/CT versus single time-point imaging for detection of mediastinal nodal metastasis in non-small cell lung cancer patients: a meta-analysis. Acta Radiol 56:681–687
26. Shao D, Gao Q, Tian XW, Wang SY, Liang CH, Wang SX (2017) Differentiation and diagnosis of benign and malignant testicular lesions using ^{18}F-FDG PET/CT. Eur J Radiol 93:114–120
27. El-Kholy E, Khaled L (2019) Diagnostic accuracy of dual-time-point fluorodeoxyglucose-positron emission tomography/ computed tomography in verification local recurrence in pancreatic cancer patients. Indian J Nucl Med 34:271–277
28. Mavi A, Urhan M, Yu JQ et al (2006) Dual time point 18F-FDG PET imaging detects breast cancer with high sensitivity and correlates well with histologic subtypes. J Nucl Med 47(9):1440–1446
29. Caprio MG, Cangiano A, Imbriaco M et al (2010) Dual-time-point [18F]-FDG PET/CT in the diagnostic evaluation of suspicious breast lesions. Radiol Med 115:215–224
30. Cheng G, Alavi A, Werner TJ, Del Bello CV, Akers SR (2014) Serial changes of FDG uptake and diagnosis of suspected lung malignancy: a lesion-based analysis. Clin Nucl Med 39:147–155
31. Lin YY, Chen JH, Ding HJ, Liang JA, Yeh JJ, Kao CH (2012) Potential value of dual-time-point ^{18}F-FDG PET compared with initial single-time-point imaging in differentiating malignant from benign pulmonary nodules: a systematic review and metaanalysis. Nucl Med Commun 33:1011–1018
32. Zhang L, Wang Y, Lei J, Tian J, Zhai Y (2013) Dual time point^{18}FDG-PET/CT versus single time point ^{18}FDG-PET/CT for the differential diagnosis of pulmonary nodules: a meta-analysis. Acta Radiol 54:770–777

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