Chemotherapy: Open Access
ISSN: 2167-7700

Kara et al., Chemotherapy 2018, 7:2
DOI: 10.4172/2167-7700.1000258

Research Article Open Access

Is Dual-Time-Point Imaging Necessary for Discrimination of Adrenal Benign Lesions Versus Malignant Masses: A Study Comparing Standard Methods with Dual-Time-Point FDG PET-CT Imaging

Pelin Ozcan Kara[1]*, Zehra Pinar KOC[1] , Taylan Kara[2], Bugra Kaya[3] and Tamer Aksoy[4]

[1]Department of Nuclear Medicine, Faculty of Medicine, Mersin University, Mersin, Turkey
[2]Department of Radiology, Faculty of Medicine, Mersin University, Mersin, Turkey
[3]Department of Nuclear Medicine, Faculty of Medicine, Necmeddin Erbakan University, Turkey
[4]Department of Nuclear Medicine, Okmeydani Education and Research Hospital, İstanbul, Turkey

Abstract

Objectives: This retrospective study was designed to investigate the clinical role of FDG PET-CT, for the evaluation of adrenal lesions and to compare the standart methods with dual-time-point imaging (DTPI) method to distinguish benign from malignant lesions in various cancer patients.

Materials and methods: A total of 60 patients with confirmed primary malignancies underwent PET-CT examinations. Of the 60 patients, 79 adrenal lesions (36 benign and 43 malignant adrenal lesions) were shown by CT. Patients were grouped as benign adrenal group (I), malignant adrenal group (II) and dual-phase-group (III).

Results: A total of 20 (33%) patients were included in benign adrenal group (Group I) with 28 adrenal lesions. Mean SUVmax value 2.95 were evaluated. All adrenal lesions in Group I had SUVmax value below cut-off 4.2 except 2.

A total of 19 (32%) patients were included in malignant adrenal group (Group II) with 22 adrenal lesions. Mean SUVmax value 8.16 were evaluated. All adrenal lesions in Group II had SUVmax value over cut-off 4.2 except 2.

A total of 21 (35%) patients were included in dual phase adrenal group (Group III) with 29 adrenal lesions. For malignant adrenal lesions in group III, all of the 21 malign lesions showed increased FDG uptake and SUVmax value in late imaging.

Conclusion: Dual time point imaging of PET-CT seems to be very effective especially in adrenal lesions, addition of dual phase study routinely is not necessary and recommented in only indeterminated lesions.

Keywords: Adrenal lesions; Malignant; Metastases; Lungs

Introduction

The adrenal gland is one of the most common sites of metastases after the lungs, liver and bone. Discrimination of adrenal benign lesions versus malignant masses is essential, especially in patients with cancer, for choosing the appropriate treatment approach and assessing prognosis. Maximum standardized uptake value (SUVmax) or tumor/liver (T/L) SUV ratios per se are semiquantitative parameters that reflect metabolic activity, but are not specific markers of malignancies. As the uptake of 2-(18F) fluoro-2-deoxy-D-glucose (FDG) in malignancies is expected to increase over time, dual time point acquisition (DTPI) could be potentially useful in partially overcoming the relatively low specificity of the SUVmax value. Benign and inflamatory lesions tend to maintain stable or reduce SUV over time whereas malignant lesions show higher SUV values. The impact of DTPI has been assessed in various benign and malignant conditions however the clinical usefulness is not assessed in adrenal lesions [1-3]. This retrospective study was designed to investigate the clinical role of PET-CT DTPI method to distinguish benign from malignant adrenal lesions in various cancer patients and to compare the standart methods proposed in the literature such as SUVmax value, T/L SUV ratio, visual analysis.

Materials and Methods

Patients

A total of 60 patients (34 male and 26 female, age range: 25-89, mean: 60.7) were included. Primary malignancies of the patients were demonstrated in Table 1. Patients with adrenal lesions on contrast enhanced (CE) CT imaging were selected. Informed consent was taken from all patients. Patients were grouped as benign adrenal group (I), malignant adrenal group (II) and dual-phase-group (III).

Primary lesion	No. of patients
Lung cancer	36
Gastrointestinal malignancies	4
Malignant melanoma	1
Geitourinary malignancies	4
Brain	1
Breast carcinoma	6
Gynecological Malignancies	3
Head and Neck Primary	1
Primary Surrenal	2
Lymphoma	1
Leiomyosarcoma	1

Table 1: 18F-FDG PET/CT Indications.

***Corresponding author:** Pelin Ozcan Kara, Department of Nuclear Medicine, Faculty of Medicine, Mersin University, Mersin, Turkey, Tel: 903242410000; Fax: 903242410098; E-mail: ppelinozcan@gmail.com

Received: May 28, 2018; **Accepted:** June 19, 2018; **Published:** June 25, 2018

Citation: Kara PO, Zehra Pinar KOC, Kara T, Kaya B, Aksoy T (2018) Is Dual-Time-Point Imaging Necessary for Discrimination of Adrenal Benign Lesions Versus Malignant Masses: A Study Comparing Standard Methods with Dual-Time-Point FDG PET-CT Imaging. Chemotherapy 7: 258. doi:10.4172/2167-7700.1000258

Imaging protocol

All patients fasted for at least 6 h before an FDG injection of 370MBq (10 mCi). PET-CT scans were obtained 60 min after injection using an integrated scanner (Siemens, Biograph True Point 6 PET-CT, Germany or GE Discovery PET-CT 610, US). A whole-body CT scan was performed without intravenous contrast administration with 130 kV, 50 mAs, a pitch of 1.5, a section thickness of 5 mm, and a field of view of 70 cm. A PET scan was performed immediately after an unenhanced CT scan, and acquired from the skull base to the upper thigh with a 3-min acquisition per bed position using a three-dimensional acquisition mode. Group III patients were re-imaged 60 min later from the first image at 2nd hour.

Diagnostic criteria for benign and malignant adrenal lesions

Histopathology and follow-up information after PET-CT scanning served as the standard of reference. For final assessment, the standards of references for adrenal malignant lesions were based on biopsy, interval growth, or reduction after chemotherapy. A mass was considered malignant if follow-up CECT scans showed a 30% decrease in the longest diameter (partially response) or disappearance (complete response) after chemotherapy or a 20% increase in the longest diameter (progressive disease) on follow-up CECT imaging. These criteria were based on Response Evaluation Criteria In Solid Tumors criteria [4,5]. An adrenal lesion remained unchanged on clinical and imaging follow-up was decided as a benign lesion.

Image analysis

CECT scans were reviewed by a radiologist with more than 10 years' experience on abdominal imaging who had no knowledge of either the other imaging results or the clinical information. The PET-CT images were qualitatively evaluated and prospectively assessed in consensus by three nuclear medicine physicians (readers A, B, and C with more than 10 years of experience) on PET-CT. PET-CT images were viewed in the coronal, axial, and sagittal sections. SUVmax of adrenal lesions were calculated on PET-CT by using Region of interest (ROI) included at least two-thirds of the adrenal lesions. Partial volume effect was minimized by this way. The regions were drawn by generating sphere circles. The quantitative uptake values of FDG (SUVmax) in the adrenal ROIs were semiautomatically calculated using workstations (Siemens and GE). SUVmean from the liver were also obtained from the ROI placed over the homogenous distribution of radioactivity in the right lobe of the liver that was free of metastasis and tumor SUVmax/liver SUVmean ratios were calculated. An SUVmax cut-off value of 4.2 and 1.68 as the threshold for T/L SUV ratio was used for the differentiation of adrenal benign and malignant lesions according to earlier report [6]. in Group I and II patients. Decrease in SUVmax value in benign lesions and increase in SUVmax value in malignant lesions on late imaging criteria was used in group III. For final assessment standards of references for adrenal malignant lesions was based on biopsy, interval growth, or reduction after chemotherapy. An adrenal lesion, which remained unchanged on clinical and imaging follow-up was decided as a benign lesion.

Statistical analysis

The statistical analysis was performed by package program (IBM SPSS 21.0) and students T test was performed for determination of mean values.

Results

A total of 60 patients (34 male and 26 female, age range: 25-89, mean: 60.7) who had confirmed primary malignancies (lung cancer in 36 patients, gastrointestinal malignancies in 4 patients, genitourinary malignancies in 4 patient, malignant melanoma in 1 patient, breast carcinoma in 6 patients, gynecological malignancies in 3 patients, brain cancer in 1 patient, primary surrenal malignancies in 2 patients, leiomyosarcoma in 1 patient, head and neck primer in 1 patient and lymphoma in 1 patient) underwent PET-CT examinations for cancer screening, staging, restaging, and detection of suspected recurrence. All 60 patients had histopathologically proven malignancies. FDG PET-CT indications and primary malignancies of 60 patients are summarized in Table 1. The most common malignancy was lung cancer. Of the 60 patients 79 adrenal lesions (36 benign and 43 malignant adrenal lesions) were shown by CT. Seventeeth of 60 (28%) patients had bilateral adrenal lesions whereas 43 of the 60 patients (72%) had unilateral lesions. Figures 1 and 2 illustrate two patients with adrenal lesions and Table 2 summarize the demographic characteristics of patients in three groups.

A total of 20 (33%) patients (12 M, 8 FM) with mean age 62.1 (Range: 42-89) were included in benign adrenal group (Group I). Bilateral adrenal lesions was detected in 8 patients and a total of 28 adrenal lesions in 20 patients (18 left, 10 right) with mean SUVmax value 2.95 were evaluated. All adrenal lesions in Group I had SUVmax value below cut-off 4.2 except 2. An SUVmax cut-off value of 4.2 and 1.68 as the threshold for T/L SUV ratio corresponded to a sensitivity of 92.8%, spesificity of 100%, and accuracy of 96.4% for the differentiation of adrenal benign and malignant lesions.

A total of 19 (32%) patients (9 M, 10 FM) with mean age 59.5 (Range: 35-85) were included in malignant adrenal group (Group II). Bilateral adrenal lesions was detected in 3 patients and a total of 22 adrenal lesions in 19 patients (13 left, 9 right) with mean SUVmax value 8.16 were evaluated. All adrenal lesions in Group II had SUVmax value over cut-off 4.2 except 2. An SUVmax cut-off value of 4.2 and 1.68 as the threshold for T/L SUV ratio corresponded to a sensitivity of 90.9%, specificity of 100%, and accuracy of 95.4% for the differentiation of adrenal benign and malignant lesions. In adrenal malignant lesions maximum standardized uptake value (SUVmax: 8.16) was higher than that of adrenal benign lesions (SUVmax: 2.95, P< 0.0001) in Group I and II. SUVmax values for benign and malignant adrenal lesions and sensitivty, specificity and accuracy in Group I and II are shown in Table 3.

A total of 21 (35%) patients (13 M, 8 FM) with mean age 60.7 (Range: 25-75) were included in dual phase adrenal group (Group III). Bilateral adrenal lesions was detected in 6 patients and a total of 29 adrenal lesions in 21 patients (17 left, 12 right) were evaluated. A total of 7 patients with 8 adrenal lesions (27.5%) were benign subgroup I and 14 patients with 21 adrenal lesions (72.5%) were malign subgroup II. Decrease in SUVmax value in benign lesions and increase in SUVmax

	Patient (%)	Gender	Age mean (Range)
Group I (Benign)	20/60 (33%)	(12 M*, 8 FM**)	62.1 (42-89)
Group II (Malignant)	19/60 (32%)	(9 M, 10 FM)	59.5 (35-85)
Group III (Dual Phase)	21/60 (35%)	(13 M, 8 FM)	60.7 (25-75)

Table 2: Demographic characteristics of the patients in three groups;*Male; **Female.

Group	SUVmax.	Sens. %	Spec. %	Acc
Group I	2.95	92.8	100	96.4
Group II	8.16	90.9	100	95.4
Total		92	100	96

Table 3: SUVmax. values and sensitivity, specificity and accuracy in Group I and II; SUVmax: Maximum standardized uptake value.

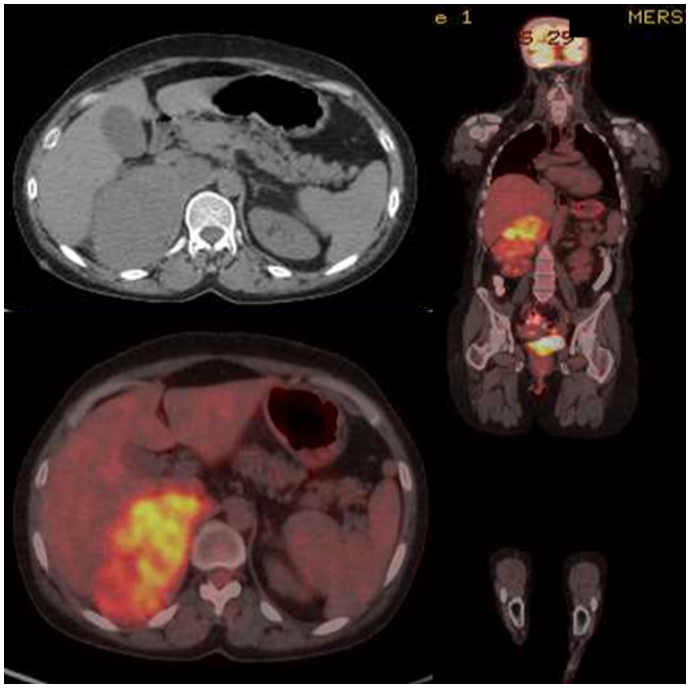

Figure 1: FDG PET-CT axial CT, axial PET-CT and coronal PET-CT images illustrate right adrenal malignant mass in a 35-year-old woman.

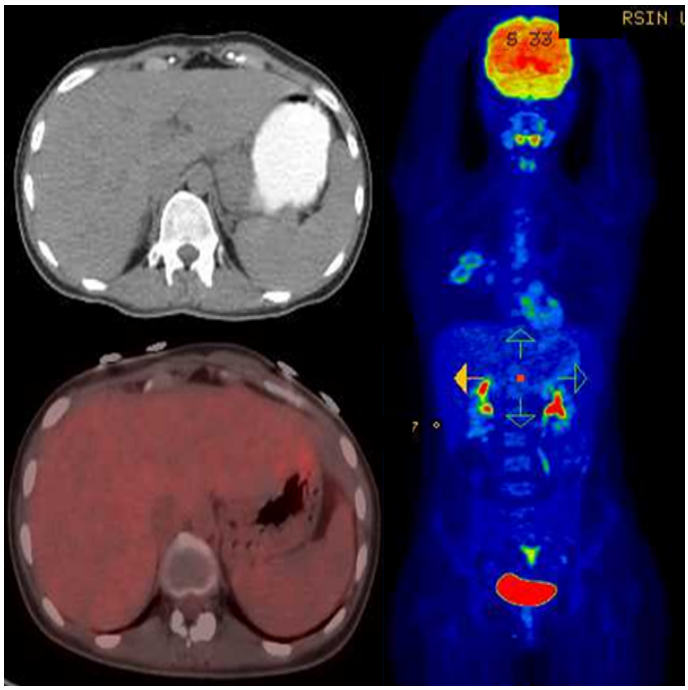

Figure 2: FDG PET-CT axial CT, axial PET-CT and MIP (Maximum intensity projection) images illustrate bilateral adrenal benign FDG non-avid adrenal lesions in a 25-years-old woman.

value in malignant lesions on late imaging criteria was used in group III. For malignant adrenal lesions in group III, all of the 21 malign lesions showed increased FDG uptake and SUVmax value with a sensitivity, specificity and accuracy % 100, 100 and 100, respectively. There was no adrenal malignant lesion showing decrease or stable SUVmax value in late imaging. Two adrenal malign lesions in this group had SUVmax values 4.11 and 3.52 below 4.2 cut-off on early images showed increased FDG uptake over time (Table 4). Especially, these two suspected lesions for malignancy with borderline SUVmax values had increase in uptake over time was found useful and proved malignancy in this group. Mean

Patient	Age	Gender	Primary diagnosis	Early SUVmax left	Late SUVmax left	Early SUVmax right	Late SUVmax right
1	63	M	Lung ca	8.74	9.6	7.09	7.8
2	62	M	Lung ca	7.77	12.56		
3	75	FM	Genitourinary malignancy			4.83	5.38
4	59	FM	Leiomyosarkom			4.22	6.21
5	62	FM	Breast ca	10.73 and 8.21	11.41 and 8.81	7.18	7.23
6	68	M	Lung ca	8.81 and 4.11*	11.60 and 4.60		
7	72	M	Lung ca	4.9	5.75		
8	77	M	Genitourinary malignancy			7.22	7.63
9	66	M	Lung ca	6.19	8.56	3.52*	6.14
10	61	M	Genitourinary malignancy	10.17	16.09		
11	74	M	Malign melanoma	9.43	12.35	10.09	11.81
12	60	M	Lung ca			15.16	16.35
13	54	FM	Breast ca			7.84	9.19
14	57	M	Lung ca	8.98	11.66	9.23	9.26

Table 4: Demographic characteristics, early and late SUVmax values of the patients in Group III patients.

Patient	Age	Gender	Primary diagnosis	Early SUVmax left	Late SUVmax left	Early SUVmax right	Late SUVmax right
1	75	M	Lung ca	4.07	4.87*		
2	64	FM	Gastrointestinal	2.5	2.2		
3	65	M	Lung ca			2.73	2.45
4	60	M	Gastrointestinal	1.34	1.12	1.34	1.12
5	25	FM	Lung ca	2.76	2.52		
6	75	FM	Gynecological	4.05	5.21*		
7	51	FM	Lung ca	2.94	2.59		

Table 5: Two benign lesions showing falsely increased uptake on late images had 4.07 and 4.05 SUVmax values in early images both of which were below 4.2 SUVmax cut-off. SUVmax values on late images for these lesions were 4.87 and 5.21.

SUVmax value on early and late images in malignant lesions were 7.82 and 9.52, respectively. For adrenal benign lesions in group III, 6 of the 8 lesions (75%) showed decrease in late images. Although, 2 benign lesions (25%) showed increase in SUVmax value against long odds. Two benign lesions showing falsely increased uptake on late images had 4.07 and 4.05 SUVmax values in early images both of which were below 4.2 SUVmax cut-off. SUVmax values on late images for these lesions were 4.87 and 5.21, respectively for these benign lesions (Table 5). In DTPI two benign lesions showed increased SUVmax value in late images. Although, if we had cut-off value 4.2 as a reference, these lesions would be reported as benign instead of malignant. Mean SUVmax value on early and late images in benign lesions were 2.71 and 2.74, respectively. When decrease in SUVmax and FDG uptake over time was taken as a criteria for benign lesions sensitivity, spesificity and accuracy were 75%, 100% and 87.5%, respectively.

Discussion

Malignant lesions appear as 'hot spot' and have elevated SUVmax on FDG PET-CT imaging 1 hour after the intravenous injection of FDG tracer because of glucose usage preferentially. However, infective processes also induce increased FDG uptake. SUV or T/L SUV ratios per se are semiquantitative parameters that reflect metabolic activity, but are not specific markers of malignancies. Dual-time-point imaging (DTPI), which employs both early (first hour) and delayed scans (second hour or later) have been introduced to overcome the nonspesificity of PET. DTPI is acquisition of 2 PET scan one of which after 60 min and second after 120-180 min following FDG injection. Malignant cells have upregulated GLUT transporter and hexokinase activity, trapping FDG [7,8]. If a malignant cell is present, the continued FDG uptake between early and late scans results in higher intensity of retained FDG. Inflammatory cells, which retain normal glucose-6-phosphatase activity, will have decreased signal. The different pattern of FDG uptake in malignant versus nonmalignant cells is lower glucose-6-phosphatase levels in cancerous tissue. Inflamatuar and infectious processes have different FDG uptake pattern because of higher level of glucose-6-phosphatase. As the uptake of 18F-FDG in malignancies is expected to increase over time DTPI could be potentially useful in partially overcoming the relatively low specificity of the SUVmax value. Recently, many studies have found interesting and sometimes confusing results using DTPI of 18F-FDG PET and PET-CT scanning for the differentiation of benign from malignant conditions [9-13]. The impact of DTPI has been assessed in various benign and malignant conditions including breast, lung, lymphoma, brain, head and neck, pancreatic lesions. However the clinical usefulness is not assessed in adrenal lesions. There are few case reports on this topic. In a case report, the authors present a 59-year-old male with an unknown primary malignancy who was referred for a 18F-FDG PET/CT imaging. Images revealed primary lung malignancy with co existing bilateral renal tuberculosis imitate metastases which otherwise would have gone amiss or would have been considered as metastases without dual phase [14]. In a case report the authors found useful delayed images in a case of benign retroperitoneal pheochromocytoma showing multiple hypermetabolic regions corresponding with common locations of Brown adipose tissue [15].

A study by Okada et al. [16] reported 89% sensitivity and 94% specificity with an standardized uptake value SUVmax cutoff value of 2.5 in 35 adrenal lesions in 30 patients. However, in our cancer patient population, who had 18F-FDG PET-CT examination, we observed that malignant adrenal lesions often have higher SUVmax values. On the basis of receiver operating curves, a SUVmax cutoff value of 4.2 (88.6% sensitivity; 88.2% specificity) and T/L SUV ratio of 1.68 (90% sensitivity; 91.1% specificity) have been identified [6]. confirming the usefulness

of these parameters in differentiating benign from malignant adrenal lesions. An SUVmax cut-off value of 4.2 and 1.68 as the threshold for T/L SUV ratio corresponded to a sensitivity of 92%, specificity of 100%, and accuracy of 96% for the differentiation of adrenal benign and malignant lesions in the current study. In adrenal malignant lesions maximum standardized uptake value (SUVmax: 8.16) was higher than that of adrenal benign lesions (SUVmax: 2.95, P<0.0001) in Group I and II.

All of the 21 malign lesions showed increased FDG uptake and SUVmax value with a sensitivity, specificity and accuracy % 100, 100 and 100, respectively in DTPI patients. There was no adrenal malignant lesion showing decrease or stable SUVmax value in late imaging. Mean SUVmax value on early and late images in malignant lesions were found 7.82 and 9.52, respectively. Two adrenal malign lesions in this group had SUVmax values 4.11 and 3.52 below 4.2 cut-off on early images showed increased FDG uptake over time. Especially, these two suspected lesions for malignancy with borderline SUVmax values had increase in uptake over time was found useful and proved malignancy in this group. For adrenal benign lesions in group III, 6 of the 8 lesions (75%) showed decrease in late images. Although, 2 benign lesions (25%) showed increase in SUVmax value against long odds. Two benign lesions showing falsely increased uptake on late images had 4.07 and 4.05 SUVmax values in early images both of which were below 4.2 SUVmax cut-off. SUVmax values on late images for these lesions were 4.87 and 5.21, respectively for these benign lesions. In DTPI two benign lesions showed increased SUVmax value in late images. Although, if we had cut-off value 4.2 as a reference, these lesions would be reported as benign instead of malignant. Mean SUVmax value on early and late images in benign lesions were 2.71 and 2.74, respectively. When decrease in SUVmax and FDG uptake over time was taken as a criteria for benign lesions sensitivity, spesificity and accuracy were 75%, 100% and 87.5%, respectively.

In a study by Kumar et al. including fifty-four breast cancer patients with 57 breast lesions, the authors concluded that a percent change of +3.75 or more in SUVs over time is highly sensitive and specific in differentiating inflammatory lesions from malignant lesions [17]. Preliminary data showed that dual time imaging appears to be useful in distinguishing malignant from benign lesions [18]. In a study by Lyshchik and co-authors, the authors reported that retention index calculated with dual-phase FDG-PET can be used not only as a tool for initial diagnosis and staging of pancreatic cancer but also as a strong independent prognostic parameter that can allow accurate identification of those patients who will benefit from intensive anticancer treatment at different stages of the disease [19]. Delayed (18) F-FDG PET/CT imaging at 180 minutes was reported improving quantitation of atherosclerotic plaque inflammation over imaging at 90 minutes [20]. The dual-time-point (18) F-FDG PET/CT was not found useful method for differentiating malignant and benign thyroid nodules [21]. The techniques of dual-time-point imaging (DTPI) and delayed-time-point imaging, which are mostly being used for distinction between inflammatory and malignant diseases, has increased the specificity of fluorodeoxyglucose (FDG)-PET for diagnosis and prognosis of certain diseases [22]. Many studies have shown improvement in the diagnostic performance of using DTPI. In the current study, DTPI was found useful in majority of adrenal lesions. Despite additional cost, and radiation dose from abdominal late images, a washout study can alter the management strategy of patients.

Conclusion

Combined information obtained from PET-CT (SUVmax, T/L SUV ratio, visual analysis is recommended for better differentiation. Although, dual time point imaging of 18F-FDG PET/CT seems to be very effective especially in surrenal lesions, addition of dual phase study is not necessary routinely and recommented in only indeterminated lesions.

References

1. Hustinx R, Smith RJ, Benard F, Rosenthal DI, Machtay M, et al. (1999) Dual time point fluorine-18 fluorodeoxyglucose positron emission tomography: a potential method to differentiate malignancy from inflammation and normal tissue in the head and neck. Eur J Nucl Med 26: 1345-1348.
2. Matthies A, Hickeson M, Cuchiara A, Alavi A (2002) Dual time point 18F-FDG PET for the evaluation of pulmonary nodules. J Nucl Med 43: 871-875.
3. Barger RL Jr, Nandalur KR (2012) Diagnostic performance of dual-time 18F-FDG PET in the diagnosis of pulmonary nodules: a meta-analysis. Acad Radiol 19: 153-158.
4. Therasse P, Arbuck SG, Eisenhauer EA, Wanders J, Kaplan RS, et al. (2000) New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. J Natl Cancer Inst 92: 205-216.
5. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, et al. (2009) New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 45: 228-247.
6. Ozcan Kara P, KaraT, Kara Gedik G, Kara F, Sahin O, et. al. (2011) The role of fluorodeoxyglucose-positron emission tomography/computed tomography in differentiating between benign and malignant adrenal lesions. Nucl Med Commun 32: 106-112.
7. Jones C, Badger SA, Lynch T, Diamond T (2010) Role of PET-CT in the management of colorectal metastatic disease. Oncol News 5: 17-19.
8. He YX, Guo QY (2008) Clinical applications and advances of positron emission tomography with fluorine-18-flurordeoxyglucose (18F-FDG) in the diagnosis of liver neoplasms. Postgrad Med J 84: 246-251.
9. 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.
10. Kaneko K, Sadashima E, Irie K, Hayashi A, Masunari S, et al. (2013) Assessment of FDG retention differences between the FDG avid benign pulmonary lesion and primary lung cancer using dual-time-point FDG-PET imaging. Ann Nucl Med 27: 392-399.
11. Khan AN, Al-Jahdali H (2013) Value of delayed 18F-FDG PET in the diagnosis of solitary pulmonary nodule. J Thorac Dis 5: 373-374.
12. Caprio MG, Cangiano A, Imbriaco M, Soscia F, Di Martino G, et al. (2010) Dualtime- point [18F]-FDG PET/CT in the diagnostic evaluation of suspicious breast lesions. Radiol Med 115: 215-224.
13. Garcia Vicente AM, Soriano Castrejo´n A, Cruz Mora MA, Ortega Ruiperez C, Espinosa Aunión R, et al. (2014) Dual time point 2-deoxy-2-[18F]fluoro-D-glucose PET/CT: nodal staging in locally advanced breast cancer. Rev Esp Med Nucl Imagen Mol 33: 1-5.
14. Subramanyam P, Palaniswamy SS (2015) Dual Time Point 18F-FDG PET/CT Imaging Identifies Bilateral Renal Tuberculosis in an Immunocompromised Patient with an Unknown Primary Malignancy. Infect Chemother 47: 117-119.
15. Dong A, Wang Y, Lu J, Zuo C (2014) Hypermetabolic Mesenteric Brown Adipose Tissue on Dual-Time Point FDG PET/CT in a Patient With Benign Retroperitoneal Pheochromocytoma. Clin Nucl Med 39: e229-e232.
16. Okada M, Shimono T, Komeya Y, Ando R, Kagawa Y, et al. (2009) Adrenal masses: the value of additional fluorodeoxyglucose-positron emission tomography/computed tomography (FDG PET/CT) in differentiating between benign and malignant lesions. Ann Nucl Med 23: 349-354.
17. Kumar R, Loving VA, Chauhan A, Zhuang H, Mitchell S, et al. (2005) Potential of dual-time-point imaging to improve breast cancer diagnosis with (18)F-FDG PET. J Nucl Med 46: 1819-1824.
18. Zhuang H, Pourdehnad M, Lambright ES, Yamamoto AJ, Lanuti M, et al. (2001) Dual time point 18F-FDG PET imaging for differentiating malignant from inflammatory processes. J Nucl Med 42: 1412-1417.

19. Lyshchik A, Higashi T, Nakamoto Y, Fujimoto K, Doi R, et al. (2005) Dualphase 18F-fluoro-2-deoxy-D-glucose positron emission tomography as a prognostic parameter in patients with pancreatic cancer. Eur J Nucl Med Mol Imaging 32: 389-397.

20. Blomberg BA, Akers SR, Saboury B, Mehta NN, Cheng G, et al. (2013) Delayed time-point 18F-FDG PET CT imaging enhances assessment of atherosclerotic plaque inflammation. Nucl Med Commun 34: 860-867.

21. Kim SJ, Kim BH, Jeon YK, Kim SS, Kim IJ (2011) Limited diagnostic and predictive values of dual-time-point (18)F FDG PET/CT for differentiation of incidentally detected thyroid nodules. Ann Nucl Med 25: 347-353.

22. Houshmand S, Salavati A, Segtnan EA, Grupe P, Høilund-Carlsen PF, et al. (2016) Dual-time-point Imaging and Delayed-time-point Fluorodeoxyglucose-PET/Computed Tomography Imaging in Various Clinical Settings. PET Clin 11: 65-84.