Int J Clin Exp Med 2015;8(7):11146-11152
www.ijcem.com /ISSN:1940-5901/IJCEM0009494

Original Article

The role of FDG PET/CT in evaluation of mediastinal masses and neurogenic tumors of chest wall

Ebru Tatci[1], Ozlem Ozmen[1], Yeliz Dadali[2], Inci Uslu Biner[1], Atila Gokcek[3], Funda Demirag[4], Funda Incekara[5], Nuri Arslan[6]

[1]Department of Nuclear Medicine, Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey; [2]Department of Radiology, Faculty of Medicine, Ahi Evran University, Kirşehir, Turkey; [3]Department of Radiology, Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey; [4]Department of Pathology, Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey; [5]Department of Thoracic Surgery, Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey; [6]Department of Nuclear Medicine, Gulhane Military Medical Academy and Medical Faculty, Ankara, Turkey

Received April 22, 2015; Accepted June 21, 2015; Epub July 15, 2015; Published July 30, 2015

Abstract: We evaluated the efficiency of FDG PET/CT for the differentiation of malignant from benign mediastinal masses and neurogenic tumors of chest-wall. Methods: The 88 patients with chest wall-mediastinal masses who underwent examination before operation were retrospectively reviewed. Size, CT density (HU mean) and SUV_{max} of mediastinal and chest wall lesions were determined. Statistical differences of these parameters were compared between groups by Mann-Whitney U test. Receiver-operating characteristic curve (ROC) analysis with respect to SUV_{max} was performed to determine the best cutoff value for differentiating benign from malignant masses. Results: The overall sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of PET/CT in detection of malignancy were 90%, 55.17%, 67%, 50.94% and 91.43%, respectively. The SUV_{max}, HU mean and size were higher in malignant cases ($P < 0.05$). To distinguish benign and malignant lesions, the cut off value of SUV_{max} was 4.67. The lesion SUV_{max} was significantly associated with the lesion size and lesion HU mean values ($P < 0.05$). The value of SUV_{max} and HU mean were higher in solid benign lesions than those of cystic benign lesions ($P < 0.05$). The lesion size was higher in cystic lesions ($P = 0.000$). The mean SUV_{max} was significantly higher in invasive thymomas than those of non-invasive forms ($P = 0.029$). Conclusion: FDG PET/CT may be complementary to conventional imaging methods for the evaluation of mediastinal and chest wall masses. PET/CT may reduce unnecessary invasive investigations for diagnosis in patients with nonavid or low avid FDG lesions. However confirmatory tissue sampling is required to confirm PET positive findings for the definite diagnosis.

Keywords: FDG PET/CT, castleman disease, schwannoma

Introduction

Mediastinal and chest-wall masses are caused by benign or malign, solid or cystic conditions. The differential diagnosis of these lesions is a common problem. Although, conventinal radiological methods can provide detailed information about their morphology such as size, location, tissue characteristics and extent of mediastinal tumors [1], none of these morphological imaging techniques can reliably differentiate benign tumours from malignant ones [2] The glucose analogue 2-Deoxy-2-[18F] Fluoro-D-Glucose (FDG) preferentially accumulates in most malignant tumors, reflecting increased glycolytic rate in these tumors [3]. Use of 18F-FDG Positron emission tomography (PET)/Compurized Tomograpy (CT) is recommended in a variety of tumor types by NCCN guidelines [4], and may be helpful for further evaluation of patients with mediastinal tumours. The objective of this study is: 1) to evaluate visual FDG PET/CT charecteristics of mediastinal tumours; 2) to determine whether quantitative evaluation of FDG PET/CT images can differentiate benign mediastinal tumours from malignant ones; 3) to document the usefulness of FDG PET/CT in differentiation non-invasive thymic epithelial tumors from invasive forms.

Material and methods

Patients

We retrospectively reviewed medical database of 88 patients with mediastinal and chest wall

Table 1. Baseline characteristics of the 88 patients with mediastinal masses

Characteristics	No.of patients
Sex	
Male	40
Female	48
Age, y (mean ± SD)	49.17 ± 15.5
Location	
Anterior med	60
Middle med	4
Posterior med	19
Chest-wall	5
Benign masses	58
Solid	43
Cystic	15
Malignant masses	30
Intervention	
Resection	74
Biopsy	14

Med = mediastinum.

Table 2. PET/CT findings of the 88 patients

Lesions	PET/CT (-)	PET/CT (+)	n
Benign cystic masses	15	0	15
Benign solid masses			
Retrosternal goiter	1	0	1
Parathyroid adenoma	1	0	1
Esophageal leiomyoma	1	0	1
Castleman disease	1	4	5
Thymic hyperplasia	6	3	9
Thymolipoma	1	0	1
Noninvasive thymoma	3	8	11
Schwannoma	3	10	13
Benign PRG	0	1	1
Malignant masses			
Invasive thymoma	2	16	18
Thymic carcinoma	1	5	6
Thymic carcinoid	0	2	2
Malignant PRG	0	1	1
MSRCT	0	1	1
Yolc sac	0	1	1
Esophageal leiomyosarcoma	0	1	1
Total (n)	35	53	88

PRG = paraganglioma, MSRCT = malignant small round cell tumor.

lesions between January 2009 and August 2014. Lung tumors, adenocarcinomas of and squamous cell carcinomas of the esophagus, lymphomas and granulomatous diseases were excluded from this study. Neurogenic tumors originating from the intercostal nerve were included the study as chest-wall lesions. All patients had preoperative FDG PET/CT. Besides PET/CT findings; age, sex and pathological findings were also recorded. Lesions were divided two main groups: benign and malignant. Benign lesions were categorized as solid and cystic. Thymomas were divided into 2 subgroups according to presence of capsule invasion or distant metastases: invasive and noninvasive. Noninvasive thymomas were included in the benign mediastinal mass group. Capsule and adjacent tissue invasion of thymomas investigated by pathologically in patients with complete resection. Ethics Review Board approved this retrospective study. For this type of study formal content is not required.

PET/CT imaging

PET/CT imaging was performed with a dedicated PET/CT scanner (Biograph LSO HI-REZ PET/CT; Siemens, Medical Solutions, Knoxville, TN, USA) by the same method that was described in a previous study [5].

FDG PET/CT analysis

All PET/CT images were evaluated qualitatively by two experienced nuclear medicine physician and one radiologist who were uninformed about the pathological diagnosis of masses. PET/CT findings were interpreted as positive for malignancy if the FDG uptake of lesion was greater than the uptake of mediastinal blood pool [6]. Lesion with FDG uptake equal to or less than the mediastinum was defined as negative.

Statistical analysis

The sensitivity, specificity, accuracy, positive predictive value, and negative predictive values of FDG PET/CT for detecting mediastinal and chest wall malignancy were calculated with using the pathological results as a reference standard. Statistical differences of SUV_{max}, attenuation value (HU mean) and lesion diameter were analysed on the groups by Mann-Whitney U test. Receiver-operating characteristic curve (ROC) analysis with respect to SUV_{max} was performed to determine the best cutoff value for differentiating benign lesions from

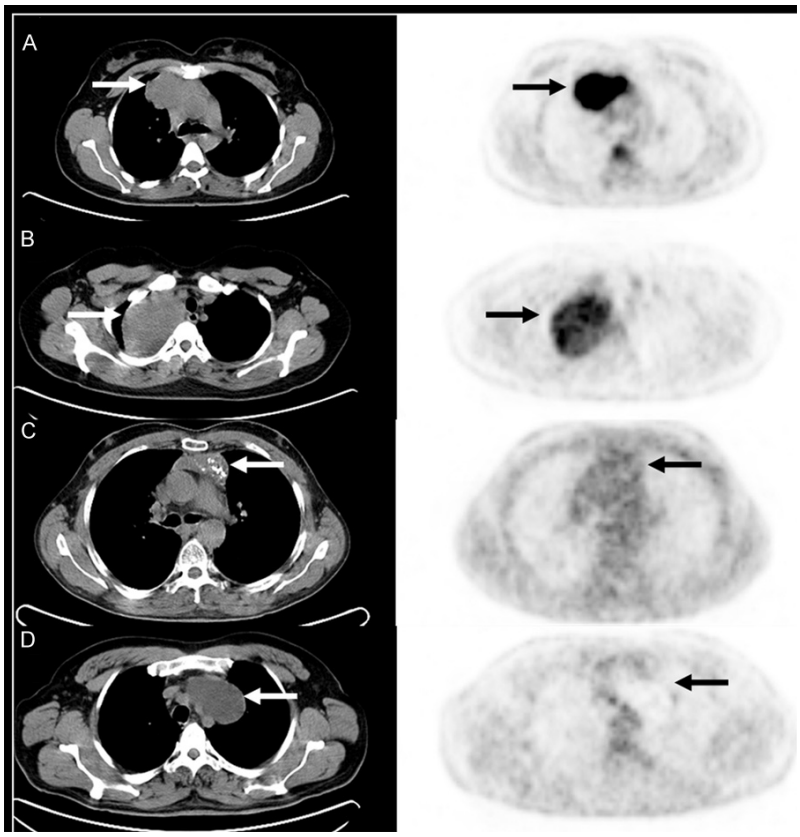

Figure 1. A. True-positive. A 44-year-old-woman with thymic carcinoma. FDG PET/CT images showed a mass in the anterior mediastinum with high FDG uptake (SUV_{max} = 12.57) (arrows). B. False positive. A 34-year-old-woman with schwannoma. FDG PET/CT images showed a mass in the posterior mediastinum with moderate FDG uptake (SUV_{max} = 5.46). C. False-negative. A 55-year-old man with type B3 thymoma (well-differentiated thymic carcinoma). FDG PET/CT images showed a mass with FDG uptake equal to mediastinum. D. True-negative. A 49-year-old man with parathyroid cyst. FDG PET/CT images showed a photopenic huge mass in the anterior mediastinum.

malignant ones. A *P*-value less than 0.05 was considered statistically significant.

Results

Patient characteristics

Detailed characteristics of the study population was presented in **Table 1**. Among the 88 patients, 83 patients had mediastinal lesion and 5 patients had chest wall lesion. Seventy-four of the 88 patients underwent surgical resection and the remaining 14 patients underwent biopsy. Of 88 cases, 58 (66%) were benign and 30 (34%) were malignant. Fifteen of 58 benign lesions were in cystic (4 bronchogenic cyst, 4 pericardial cyst, 4 thymic cyst, 1 parathyroid cyst, 1 gastroenteric cyst and 1 benign mature cystic teratoma). The remaining 43 of 58 benign lesions were solid. The majority of mediastinal lesions were thymic disorders (51/88, 57.95%), followed by neurogenic tumors (15/88, 17.04%) (**Table 2**).

Qualitative analyses

Three of 30 (10%) malignant cases (2 invasive thymomas and 1 thymic carcinomas) were false-negative on FDG PET (**Table 2**). There were 26 benign mediastinal and chest-wall lesions showing positive FDG uptake. Also, false-positive rate was high in non-invasive thymomas (8/11, 72.7%), Castleman diseases (4/5, 80%), Schwannomas (10/13, 76.9%), and thymic hyperplasia (3/9, 33.3%). There was one case of benign paraganglioma with false-positive FDG uptake. The images of false-positive, false-negative, true-positive, and true negative-cases were shown in **Figure 1**. The overall sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of PET/CT in detection of malignancy were 90%, 55.17%, 67%, 50.94% and 91.43%, respectively.

Quantitative analysis

Comparison of quantitative PET/CT indices in mediastinal and chest-wall lesions was shown in **Table 3**. The SUV_{max}, HU mean and size were higher in malignant cases (P = 0,002, P = 0.000, and P = 0.014 respectively). We found a cut-off value of 4.67 for SUV_{max} to discriminate benign lesions from malignant ones with a sensitivity and specificity of 73.7% and 75.9%, respectively (AUC 0.876, 95 % CI 0.805-0.948, P < 0.0001) (**Figure 2**). A positive correlation between lesion diameter and SUV_{max} value in all lesions was found in this study. This correlation

Table 3. Comparison of quantitative PET/CT indices in mediastinal lesions

	Malignant vs. benign lesions (n = 88)			Benign solid vs. cystic lesions (n = 58)			Invasive vs. noninvasive thymoma (n = 28)		
	Malignant (n = 30)	Benign (n = 58)	*P* value	Solid (n = 43)	Cystic (n = 15)	*P* value	Invasive (n = 17)	Non-invasive (n = 11)	*P* value
Size in mm (mean ± SD)	69.8 ± 32.1	56.3 ± 27.5	0.014*	46.2 ± 21.3	59.1 ± 21.8	0.000*	58.9 ± 29	49.5 ± 23.8	0,300
SUV_{max} (mean ± SD)	8.7 ± 4.8	3.3 ± 2.2	0.002*	4.0 ± 2	1.35 ± 1	0.000*	7.1 ± 3.5	4.1 ± 2.0	0.029*
HU mean (mean ± SD)	51.6 ± 19.9	34.4 ± 32.1	0.000*	37.0 ± 32.4	30.7 ± 30.2	0.032*			

HU = Hounsfield unit, *P < 0.05.

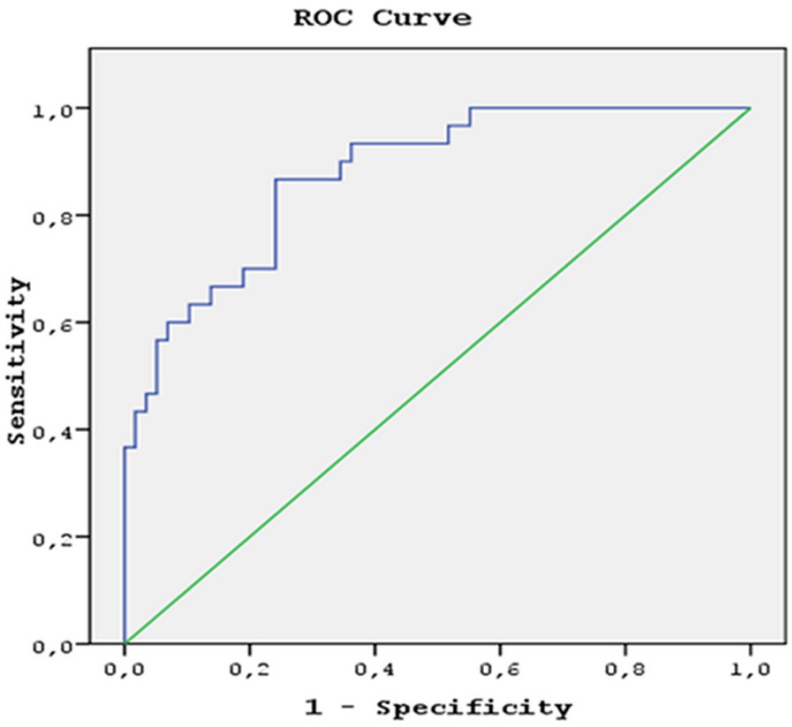

Figure 2. The receiver operating characteristics (ROC) curve used for differentiation between benign and malignant mediastinal lesions based on SUV_{max}. ROC analysis showed that the optimal cut-off value in these patients was 4.67 for SUV_{max} (AUC. 0.876, 95 % CI 0.805-0.948, P = 0.0001).

was statistically significant (R = 0.300, P < 0.05)

There was no significant difference in the lesion size between noninvasive and invasive thymomas (P = 0,300). The mean SUV_{max} was significantly higher in invasive thymomas (P = 0.029).

The values of SUV_{max} and HU mean were higher in solid benign lesions than those of cystic benign lesions (P = 0.000 and P = 0.032, respectively). The lesion size was higher in cystic lesions (P = 0.000).

Discussion

PET/CT had a limited specificity (55.17%) due to high false-positive PET results caused from Castleman diseases, benign neurogenic tumors, thymic hyperplasia and noninvasive thymomas in our study. Castleman disease (CD) is a rare lymphoproliferative disorder. There are recognized mainly two histologic types; hyaline-vascular and plasma cell types [7]. We found that mild to moderate FDG uptake on patients with CD concordance with literature [7, 8]. SUV_{max} was higher in a patient with plasma cell variant (6.75) than in hyaline vascular variants (range 2.94-4.06, mean 3.75 ± 0.9) in our limited study. The plasma cell variant of the disease is usually multicentric and more aggressive than the hyaline vascular forms [7]. The value of FDG PET/CT in prediction of histologic types may be evaluated with large sample size studies.

Schwannoma, which is a benign peripheral nerve sheath tumor. Differential diagnosis cannot be made between schwannomas and malignant peripheral nerve sheath tumors based on value SUV_{max} because of high FDG uptake can be seen in schwannomas [9]. Authors showed that uptake of FDG in patients with schwannoma was correlated with vascular endothelial growth factor/vascular permeability factor (VEGF/VPF) [10]. We found that intense FGD uptake in malignant paraganglioma (SUV_{max} = 24.13) and moderate uptake (SUV_{max} = 5.92) in benign paraganglioma. Increased FDG uptake of paraganglioma might be associated with specific mutations on the genes of B, C, and D subunits of the mitochondrial complex II enzyme succinate dehydrogenase [11, 12]. We suggest that PET/CT may be helpful in detection of schwannoma and paraganglioma.

We found high PET/CT sensitivity rates for identification of the malignancy (90%). All of 15 mediastinal cystic masses had true-negative PET findings. There were cases of a retrosternal goiter, thymolipoma, parathyroid adenoma and esophageal leiomyoma with true-negative PET results in our study. For evaluation of these lesions, PET/CT may have be complementary role to the CT for planning a management strategy. PET/CT may reduce unnecessary invasive investigations for diagnosis in patients with nonavid or low avid FDG lesions.

Among 30 malignant cases, there were 3 false-negative cases (2 invasive thymomas and 1 thymic carcinoma). Different results was obtained about effectiveness of PET/CT in predicting tumor invasiveness of thymomas in several studies. Some investigators reported that inability of FDG SUV_{max} to predict thymoma invasiveness [13-15]. However Kubota et al. and Sung et al. showed that higher FDG uptake in invasive thymoma than in noninvasive form [16, 17]. Similarly, we found that the mean SUV_{max} was significantly higher in invasive thymomas. Shibata et al. reported that the cutoff value of SUV_{max} was 6.3 for predicting type C thymoma (thymic carcinoma) with a sensitivity of 1.0 and a specificity of 0.92 [14]. All type C thymomas (n = 3) had an FDG-SUV ≥ 6.3. But we found 4 of totally 9 thymic carcinomas/carcinoid tumors (44.4%) had an FDG-SUV < 6.3. Also, 8 of all 18 invasive thymomas (44.4%) had an FDG-SUV > 6.3. We assumed that thymic carcinomas tends to have high FDG uptake but in the presence of low FDG uptake thymic carcinomas and invasive thymomas cannot be excluded.

Kubato et al. reported that mean FDG uptake of malignant mediastinal tumors was significantly higher than that of benign tumors, with cutoff line was about 3.5 by DUR (differential uptake ratio; synonym SUV) [16]. Similarly, our study showed significant difference between SUV_{max} of malignant and benign lesions, with optimal cut off was 4.67. We suggest that SUV_{max} can be a useful marker for discriminating malignant tumors from benign ones.

In conclusion, FDG PET/CT may be complementary to conventional imaging methods for the evaluation of mediastinal and chest wall masses. PET/CT may reduce unnecessary invasive investigations for diagnosis in patients with nonavid or low avid FDG lesions. However confirmatory tissue sampling is required to confirm PET positive findings for the definite diagnosis. Thymomas with high SUV_{max} have high potential to be invasive.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Ebru Tatcı, Department of Nuclear Medicine, Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital, Sanatoryum Cad Kecioren, Ankara 06280, Turkey. Tel: +90 312 567 73 42; +90 505 9145361; Fax: +90 312 3552135; E-mail: ebrualkandr@yahoo.com

References

[1] Juanpere S, Cañete N, Ortuño P, Martínez S, Sanchez G, Bernado L. A diagnostic approach to the mediastinal masses. Insights Imaging 2013; 4: 29-52.

[2] Jeung MY, Gasser B, Gangi A, Bogorin A, Charneau D, Wihlm JM, Dietemann JL, Roy C. Imaging of cystic tumours of the mediastinum. Radio Graphics 2002; 22: 79-93.

[3] Paulus P, Kaschten BJ, Hustinx R, Bury T, Jerusalem G, Benoit T, Foidart-Willems J. Oncological applications of positron emission tomography with fluorine-18 fluorodeoxyglucose. Eur J Nucl Med 1996; 12: 1641-1674.

[4] Podoloff DA, Ball DW, Ben-Josef E, Benson AB 3rd, Cohen SJ, Coleman RE, Delbeke D, Ho M, Ilson DH, Kalemkerian GP, Lee RJ, Loeffler JS, Macapinlac HA, Morgan RJ Jr, Siegel BA, Singhal S, Tyler DS, Wong RJ. NCCN task force: clinical utility of PET in a variety of tumor types. J Natl Compr Canc Netw 2009; 7 Supp 2: S1-26.

[5] Tatci E, Ozmen O, Gokcek A, Biner IU, Ozaydin E, Kaya S, Arslan N. 18F-FDG PET/CT rarely provides additional information other than primary tumor detection in patients with pulmonary carcinoid tumors. Ann Thorac Med 2014; 9: 227-31.

[6] Arslan N, Tuncel M, Kuzhan O, Alagoz E, Budakoglu B, Ozet A, Ozguven MA. Evaluation of outcome prediction and disease extension by quantitative 2-deoxy-2-[18F] fluoro-D-glucose with positron emission tomography in patients with small cell lung cancer. Ann Nucl Med 2011; 25: 406-413.

[7] Akosman C, Selcuk NA, Ordu C, Ercan S, Ekici ID, Oyan B. Unicentric mixed variant Castleman disease associated with Hashimoto disease: the role of PET/CT in staging and evaluating response to the treatment. Cancer Imaging 2011; 11: 52-55.

[8] Lee ES, Paeng JC, Park CM, Chang W, Lee WW, Kang KW, Chung JK, Lee DS. Metabolic characteristics of Castleman disease on 18F-FDG PET in relation to clinical implication. Clin Nucl Med 2013; 38: 339-342.

[9] Beaulieu S, Rubin B, Djang D, Conrad E, Turcotte E, Eary JF. Positron emission tomography of schwannomas: emphasizing its potential in preoperative planning. AJR Am J Roentgenol 2004; 182: 971-974.

[10] Hamada K, Tomita Y, Qiu Y, Tomoeda M, Ueda T, Tamai N, Hashimoto N, Yoshikawa H, Aozasa K, Hatazawa J. (18) F-FDG PET analysis of

schwannoma: increase of SUVmax in the delayed scan is correlated with elevated VEGF/VPF expression in the tumors. Skeletal Radiol 2009; 38: 261-266.

[11] Kim C, Oh SW, Bae JM, Jung KC, Kim SH, Kang KW, Lee DS. Nonfunctioning Periurethral Paraganglioma Incidentally Detected by FDG PET/CT. Nucl Med Mol Imaging 2011; 45: 145-148.

[12] Taïeb D, Tessonnier L, Sebag F, Niccoli-Sire P, Morange I, Colavolpe C, De Micco C, Barlier A, Palazzo FF, Henry JF, Mundler O. 18F-FDG avidity of pheochromocytomas and paragangliomas: a new molecular imaging signature? J Nucl Med 2009; 50: 711-777.

[13] Sasaki M, Kuwabara Y, Ichiya Y, Akashi Y, Yoshida T, Nakagawa M, Murayama S, Masuda K. Differential diagnosis of thymic tumors using a combination of 11C-methionine PET and FDG PET. J Nucl Med 1999; 40: 1595-1601.

[14] Shibata H, Nomori H, Uno K, Sakaguchi K, Nakashima R, Iyama K, Tomiyoshi K, Kaji M, Goya T, Suzuki T, Horio H. 18F-fluorodeoxyglucose and 11C-acetate positron emission tomography are useful modalities for diagnosing the histologic type of thymoma. Cancer 2009; 115: 2531-2538.

[15] Benveniste MF, Moran CA, Mawlawi O, Fox PS, Swisher SG, Munden RF, Marom EM. FDG PET-CT aids in the preoperative assessment of patients with newly diagnosed thymic epithelial malignancies. J Thorac Oncol 2013; 8: 502-510.

[16] Kubota K, Yamada S, Kondo T, Yamada K, Fukuda H, Fujiwara T, Ito M, Ido T. PET imaging of primary mediastinal tumours. Br J Cancer 1996; 73: 882-886.

[17] Sung YM, Lee KS, Kim BT, Choi JY, Shim YM, Yi CA. 18F-FDG PET/CT of thymic epithelial tumors: usefulness for distinguishing and staging tumor subgroups. J Nucl Med 2006; 47: 1628-1634.