The role of Tc-99m-2-Methoxy-Isobutyl-Isonitrile Single Photon Emission Computed Tomography in visualizing anterior mediastinal tumor and differentiating histologic type of thymoma

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1. Introduction

Anterior mediastinal tumors comprise a diverse group of neoplasms and account for 50% of all mediastinal masses. The representative tumors in the anterior mediastinum are thymoma, thymic carcinoma (TC), thymic cyst, mature teratoma, malignant germ cell tumor, and malignant lymphoma [1]. Morphological examinations, such as computed tomography (CT) and magnetic resonance imaging (MRI), are excellent in defining anatomic details, the relationship with surrounding tissue, and the location of the tumor. Despite the fact that, in some cases, the CT demonstration of fat, calcium or water attenuation suggests a specific diagnosis, it is usually difficult to distinguish thymoma, TC, and lymphoma, which are quite similar in radiographic appearance but different in treatment strategy [2, 3].

In the recent years, positron emission tomography with 18F-2-fluoro-2-deoxyglucose (18FDG-PET) has emerged as a powerful diagnostic tool for diagnosis, staging, and restaging of several neoplasms. However, the results of 18FDG-PET imaging in thymic pathology are frequently conflicting [4–7], and it remains an expensive and complicated procedure, performed with tracers and imaging equipment available at a limited number of sites in Italy.

Abstract

Objective: To evaluate the usefulness of 99mTc-2-Methoxy-Isobutyl-Isonitrile Single Photon Emission Computed Tomography (MIBI-SPECT) for assessing anterior mediastinal mass, and distinguishing the grade of malignancy of thymic epithelial tumors to offer guidance for decision making.

Methods: From January 2006 to November 2009, 31 consecutive patients with an anterior mediastinal mass at CT were enrolled. All patients underwent 99mTc-MIBI-SPECT before invasive diagnostic procedures and/or surgical resection. The uptake of the mediastinal tumor (T) was compared with the normal tissue (N) and the T/N ratio was calculated to define the metabolic activity of the lesions. Patients were divided into six groups according histologic patterns, which were then correlated to the T/N value: benign tumor (BT), lymphoma (LYM), other malignant tumor (OMT), and low-risk thymoma (LRT) including types A, AB, and B1, high-risk thymoma (HRT) including types B2 and B3, and thymic carcinoma (TC).

Results: There were five BT, eight LRT (four = A, two = AB, and two = B1), four HRT (three = B2 and one = B3), four thymic carcinoma, six LYM and four OMT. The T/N value of BT, LRT, HRT, CT, LYM, and OMT was 1.3 ± 0.3, 1.3 ± 0.2, 1.8 ± 0.3, 2.7 ± 0.5, 2.8 ± 0.1, and 2.9 ± 0.2, respectively. The T/N ratio of BT and of LRT was significantly lower than that of HRT, of CT, of LYM, and of OMT (p < 0.05), while there is no significant difference of MIBI uptake between BT and LRT. MIBI uptake in HRT was significantly lower than that in TC, LYM, and OMT (p < 0.05), whereas no significant difference was found between the different types of malignant lesions (TC, LYM, and OMT). Regarding thymoma, the degree of MIBI accumulation significantly increased as the World Health Organization (WHO) classification shifted from type A to type B and to TC. Yet, the T/N value of stages I and II was significantly lower than that of stages III and IV. The size of the lesion and the presence of myasthenia were not correlated with MIBI uptake.

Conclusion: 99mTc-MIBI-SPECT seems to be useful in the evaluation of malignancy in anterior mediastinal mass, and is significantly correlated with the WHO classification and the Masaoka stage. Thus, this technique may add further information to morphological studies for decision making.

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These reasons have generated interest in applying different radiopharmaceuticals such as $^{67}$Gallium ($^{67}$Ga), $^{201}$Thallium ($^{201}$Tl), and Tc-$^{99m}$-2-Methoxy-Isobutyl-Isonitrile ($^{99m}$Tc-MIBI) in using single photon emission computed tomography (SPECT) cameras as tumor tracers in various organs, for diagnosis, staging, follow-up, and monitoring the response to therapy. However, the results of $^{67}$Ga in diagnosing mediastinal mass are controversial, and $^{99m}$Tc-MIBI has some advantages as shortened half life and cost if compared with $^{201}$Tl [8,9]. In a previous article, we have showed that $^{99m}$Tc-MIBI-SPECT is a powerful diagnostic tool in diagnosing indeterminate pulmonary lesions [10].

The goals of the present study are to assess the usefulness of $^{99m}$Tc-MIBI-SPECT (1) for differentiating between benign and malignant lesions in patients affected by anterior mediastinal mass, and (2) for distinguishing the grade of malignancy of thymic epithelial tumors to offer guidance for decision making.

2. Materials and methods

2.1. Study design

A prospective single-center study was performed at the Thoracic Surgery Unit of Second University of Naples, Italy, with the aim of valuating the diagnostic role of $^{99m}$Tc-MIBI-SPECT in the differential diagnosis of anterior mediastinal mass and particularly of thymic pathology.

The clinical assessment included history, clinical examination, laboratory tests, chest X-ray, and contrast-enhanced total body CT scan. In selected cases, MRI of the chest was performed to assess the extent of mediastinal involvement. In patients with suspected thymoma, even if asymptomatic, anti-acetylcholine receptor antibodies test was performed to determine whether a sub-clinical myasthenic state was present. Yet, in any young patient, serum levels of beta-human chorionic gonadotropin ($\beta$-HCG) and alpha-fetoprotein (AFP) were assayed. Each patient underwent a $^{99m}$Tc-MIBI-SPECT before invasive diagnostic procedures and/or surgical resection, and the scintigraphic results were then correlated with pathologic studies.

The protocol of this study was approved by the Hospital Ethics Committee of the Second University of Naples, and written informed consent was obtained in all the cases before entering the study.

2.2. Study population

From January 2006 to January 2009, 33 consecutive patients with an isolated anterior mediastinal mass were referred to our unit for diagnosis and/or treatment. Of these, one patient refused to integrate radiological evaluation with a $^{99m}$Tc-MIBI-SPECT study, while the other patient rejected any invasive procedures proposed. Both patients were excluded from the present study that therefore included 31 patients. There were 13 females and 18 males, with a mean age $\pm$ standard deviation (SD) of 46.5 $\pm$ 16.1 years (range from 18 to 75 years).

2.3. $^{99m}$Tc-MIBI-SPECT

A commercial $^{99m}$Tc-MIBI preparation (Cardiolite; Squib International) was used. The labeling and quality control procedures were performed according to the manufacturer’s instructions. SPECT data were acquired 5 min after injection of the tracer while using a large-field-of-view, double-head rectangular gamma camera (ECAM; Siemens, Erlangen, Germany) equipped with low-energy, high-resolution, parallel-hole collimators; a 20% symmetric window at 140 keV; a 128 x 128 word matrix, zoom 1.45; an elliptic orbit with step-and-shoot acquisition at $3^\circ$ intervals over 360° (180° per head), and a 20-s dwell time per stop. After pre-filtering with a count-optimized Metz filter, images were reconstructed with a ramp filter to produce 4-pixel-thick transaxial slices. Coronal and sagittal views were also obtained.

2.4. Imaging interpretation

The study results were independently assessed by two nuclear medicine specialists (PR and LM) blinded from each other and from the results of the final true lesion status. Disagreements were resolved by consensus, with a third observer as referee (AR).

The $^{99m}$Tc-MIBI-SPECT examinations were reconstructed in three orthogonal planes (transaxial, sagittal and coronal). The analysis of $^{99m}$Tc-MIBI uptake was based on the lesion count number on the SPECT slices. The images were visually compared with the chest CT scan at the same time to aid in locating focal lesions, which were not tracers avid. Circular Regions of Interest (ROIs) were manually defined on the tumor (T) in several transaxial sections and tumor highest activity was selected. The same ROI in the contralateral normal tissue (N) was considered as background activity. Then, the uptake of the mediastinal tumor (T) was compared with N and the T/N ratio was calculated to define the metabolic activity of the lesions (Fig. 1).

2.5. Pathological diagnosis

For patients who had undergone surgery, the definitive pathological diagnosis was determined by surgically excised specimens. For those without surgery, the histology was made by specimens obtained through biopsy. According to histologic patterns, patients were divided into six groups, which were then correlated to the T/N value: benign tumor (BT), lymphoma (LYM), other malignant tumor (OMT) and low-risk thymoma (LRT) including types A, AB and B1, high-risk thymoma (HRT) including types B2 and B3, and TC, according to a simplified WHO histological classification described by Jeong et al. [11]. Histological typing was established for the first time in 1994 by WHO and reviewed in 2004. Thymomas are classified as type A or B according to their epithelial cell morphology. Type B thymomas are further subdivided into B1–B3, according to the atypia of epithelial cells and the extent of lymphocyte infiltration. The coexistence of both types A and B was designated type AB. The revision in 2004 eliminated the term ‘type C thymoma’ and defined TC as an independent entity [12]. In the present series, neuroendocrine tumors are not included among TC.
2.6. Clinical stage

The stage of thymic disease was classified according to the clinical and pathological classification by Masaoka et al. as follows: (stage I) encapsulated thymoma with no findings of microscopic or gross capsular invasion; (stage II) microscopic transcapsular invasion or gross tumor growth into the mediastinal fat or pleura; (stage III) invasion of pericardium, great vessels, or lung; (stage IVa) pleural or pericardial dissemination through direct extension or drop metastasis; and (stage IVb) lymphatic or hematogenous metastases [6]. For patients with surgical excision, the stage was determined by operative and pathological findings. By contrast, for patients with biopsy only, the stage was determined by diagnostic imaging including CT and/or MRI.

2.7. Statistical analysis

The mean and SD of the T/N ratio were calculated. Multiple comparison among the six groups was performed by a one-way factorial analysis of variance (ANOVA) with the Bonferroni post hoc test. Regarding thymic pathology, the differences of MIBI uptake among the histologic types of WHO classification and Masaoka stages were analyzed using a Student’s t-test. Spearman’s rank correlation test was performed for the correlation study of MIBI uptake and size of the lesion. A value of $p < 0.05$ was considered statistically significant. MedCalc® statistical software was used for analysis.

3. Results

This study included five BT (extramedullary hematopoiesis, amyloidosis, thymolipoma, bronchogenic cyst, and lipoma), eight LRT (four = type A, two = type AB, and two = type B1), four HRT (three = type B2, one = type B3), four TC, six LYM (four = type non Hodgkin and two = type Hodgkin) and four OMT (two angiosarcomas, seminoma, and adenocarcinoma arising from a bronchogenic cyst) (Table 1). Major clinical symptoms were: six (19.3%) myasthenia gravis (MG) (five thymomas and a TC), fever in five (16.1%) patients, chest pain in two (6%) and cough in six (19.3%) patients. A biopsy confirming the diagnosis was performed in each patient, except for two cases of BT in whom surgical resection was directly performed because the diagnosis was obtained by radiological patterns (lipoma and bronchogenic cyst, respectively).

The preoperative diagnosis was obtained in seven patients by fine-needle aspiration biopsy (FNAB) (one OMT, one LYM, one OMT, two LRT, one HRT, and one TC), in three patients by thoracoscopic biopsy (one BT and two OMT), and in the remaining 19 patients by anterior mediastinotomy. Surgical resection was performed in 17 patients as following: three BT (lipoma, thymolipoma, and bronchogenic cyst), eight LRT, two HRT (one following induction therapy), three TC (two following induction therapy), and one OMT (adenocarcinoma arising from bronchogenic cyst).

In three cases (TC, HRT, and angiosarcoma), radical resection was excluded because no response to induction treatment was obtained. Finally, two patients (angiosarcoma and HRT) refused the surgical treatment.

3.1. Comparison of MIBI uptake among six groups

The results of MIBI uptake for each group of patients are showed in Fig. 2. A high MIBI uptake was observed in TC (Fig. 1), in LYM and in OMT, whereas a moderate MIBI uptake was seen in HRT. Only a slight and/or no MIBI uptake were seen in BT and LRT.

<table>
<thead>
<tr>
<th>Masaoka stage</th>
<th>N</th>
<th>Diagnosis</th>
<th>T/N value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>4</td>
<td>LRT</td>
<td>1.2 ± 0.1</td>
</tr>
<tr>
<td>II</td>
<td>3</td>
<td>LRT</td>
<td>1.6 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>HRT</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>1</td>
<td>LRT</td>
<td>2.2 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>HRT</td>
<td></td>
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<tr>
<td></td>
<td>2</td>
<td>TC</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>1</td>
<td>HRT</td>
<td>2.3 ± 0.7</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>TC</td>
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</tbody>
</table>

Data are presented as number or mean ± SD.

1 Stage I versus II ($p = 0.07$), versus III ($p = 0.02$), versus IV ($p = 0.02$).
2 Stage II versus III ($p = 0.04$), versus IV ($p = 0.04$).
3 Stage III versus IV ($p = 0.9$).

Fig. 1. A 57 year-old man with thymic carcinoma in Masaoka stage III. CT scan detects a round tumor with regular border that projected in the anterior mediastinum (white arrow). It is suggested that tumor is perhaps a low-risk thymoma. However, 99mTc-MIBI-SPECT examination shows accentuated MIBI uptake in the tumor. To calculate the uptake of MIBI, Circular Region of Interest is manually defined on the tumor (T) (black arrow) and in the mediastinum normal tissue (T/N). The T/N value calculated is of 2.3.
The T/N value was 1.3 ± 0.3 in BT, 1.3 ± 0.2 in LRT, 1.8 ± 0.3 in HRT, 2.7 ± 0.5 in TC, 2.8 ± 0.1 in LYM, and 2.9 ± 0.2 in OMT. The T/N value of BT and of LRT was significantly lower than that of HRT, of CT, of LYM, and of OMT (p < 0.05) while there is no significant difference of MIBI uptake between BT and LRT. MIBI uptake in HRT was significantly lower than that in TC, LYM, and OMT (p < 0.05), whereas no significant difference was found between the different types of malignant lesions (TC, LYM, and OMT).

### 3.2. MIBI uptake correlated with size of the lesion

Among the six subgroups, there is no statistical correlation between the size of the lesion and MIBI uptake (Spearman’s correlation test: 0.3; 95% confidence interval (CI): 0.0—0.6; p = 0.07) (Fig. 4). No statistical correlation was also found if considering only the four subgroups of thymic epithelial A. Fiorelli et al. / European Journal of Cardio-thoracic Surgery 40 (2011) 136—142
3.3. MIBI uptake correlated with WHO classification

Fig. 6 illustrates the T/N value in each histological type of the WHO classification. Of thymic epithelial tumors, four were type A, two type AB, two type B1, three type B2, one type B3, and four type C. The mean T/N values ± SD in types A, AB, B1, B2/B3, and C were 1.2 ± 0.1, 1.4 ± 0.07, 1.6 ± 0.07, 2.0 ± 0.08, and 2.7 ± 0.5, respectively. The T/N value in type A was significantly lower than that in type AB (p < 0.04), B1 (p = 0.005), B2/B3 (p < 0.0001), and C (p < 0.0001). The T/N value in type AB was significantly lower than that in type B2/B3 (p = 0.007), and in C (p = 0.001) while no significant difference was found when we compared type AB with type B1 (p = 0.1). The T/N value in type B1 was significantly lower than that in type B2/B3 (p = 0.006) and in C (p = 0.001). Finally, the T/N value in type B2/B3 was significantly lower than that in type C (p = 0.03).

3.4. MIBI uptake correlated with Masaoka stage

The results are reported in Table 1. According to the Masaoka classification, four patients with LRTs were in stage I, three LRTs and one HRT in stage II, one LRT, two HRTs, and two TCs in stage III, and one HRT and two TCs in stage IV. The mean T/N values in stages I, II, III, and IV were: 1.2 ± 0.1, 1.6 ± 0.3, 2.2 ± 0.6, and 2.3 ± 0.7, respectively. There is no statistical difference in MIBI uptake between stages I and II (p = 0.07) and between stages III and IV (p = 0.9). Conversely, the T/N value of stage I and of stage II was significantly lower than that obtained in stage III (p = 0.02 and p = 0.04, respectively) and than that observed in stage IV (p = 0.02 and p = 0.04, respectively).

3.5. MIBI uptake correlated with MG

A total of 6/16 (37.5%) patients presented MG: two in stage I, two in II, one in III, and one in IV. The T/N value of myasthenic patients (1.6 ± 0.7) was lower than in non-myasthenic groups (1.9 ± 0.6), but no statistical difference was observed between the two groups (95% CI of difference: 0.48–1.01; p = 0.4).

4. Discussion

MIBI is a radiopharmaceutical originally developed for myocardial perfusion studies as an alternative to 201Tl. It is a monovalent cation complex with a central Tc (I) core octahedrally surrounded by six identical alkyl isonitrile groups that are coordinated through the isonitrile carbon. The surrounding terminal alkyl groups give the complex a moderate lipophilic property. Its uptake mechanism involves passive diffusion across plasma and mitochondrial membranes. At equilibrium, strong negative transmembrane potentials propagate a concentration of the agent within the inner matrix of mitochondria [13]. Recently, 99mTc-MIBI has been used as a tumor-imaging agent to detect various kind of tumors. The augmented uptake in malignant tumors is believed to be caused by stronger negative mitochondrial and plasma membrane potentials secondary to the increased metabolism of tumor cells. Indirect mechanisms, such as an increase of blood flow and capillary permeability, have also been suggested [14]. Many reports describe the accumulation of 99mTc-MIBI in breast, thyroid, bone, brain, and lung cancer [10], while only sporadic cases described 99mTc-MIBI uptake in patients with anterior mediastinal mass. Shih et al. [13] valued the role of 99mTc-MIBI uptake as an indicator of malignancy in 31 patients with intrathoracic masses; 2/31 patients were affected by anterior mediastinal lymphoma and both showed an increased uptake of tracer on SPECT images. The role of 99mTc-MIBI-SPECT in identifying lymphoma has been also confirmed by Maura et al. [15], who reported a diagnostic accuracy of 85% for the detection of this lesion in 31 patients, of whom five patients was affected by lymphoma localized within the anterior mediastinum. Yet, Perez-Monte et al. [14] reported a case of thymic carcinoid detected by 99mTc-MIBI-SPECT performed in an attempt to locate additional parathyroid tissue in a patient with recurrent biochemical hyperparathyroïdism. To our knowledge, no article investigates the role of 99mTc-MIBI-SPECT in patients with anterior mediastinal lesions; therefore, questions still exist regarding its potential role for the detection of these lesions and how it may help decision making.

Our results show, first, that 99mTc-MIBI is able to distinguish BT and LRT from other malignant lesions of the anterior mediastinum including TC and LYM. In fact, the T/N value of patients with benign lesion and LRT are significantly lower than that of other groups. Only one patient with benign lesion as extramedullary hematopoiesis (EMH), presents an high 99mTc-MIBI uptake (T/N value of 1.9). Theoretically, the intense uptake of 99mTc-MIBI may be secondary to the high vascularity of EMH, considering that EMH is the formation of apparently normal blood cells outside the confines of the
bone marrow [16]. For that reason, $^{99m}$Tc-MIBI has been used successfully for the investigation of parathyroid adenomas for more than 10 years. Similar to most malignancies, parathyroid tissue has a high level of mitochondrial activity and of vascularity; hence, there is an increased MIBI uptake in this pathology [14]. On the other hand, tumors with massive necrosis or those with a necrotic core did not demonstrate MIBI uptake or showed a ring-like mass to SPECT images just as MIBI does not accumulate in necrotic or irreversibly infarcted myocardial tissue [13].

In an evaluation of patients with anterior mediastinal mass, the key to the problem is to determine whether the mass is, in fact, benign or not so as to select the optimal treatment. The common first-line diagnostic approach is represented by noninvasive diagnostic studies including medical history, laboratory test, CT scan and/or MRI [3]. The CT demonstration of fat, calcium or water attenuation often suggests a specific diagnosis [5], as occurred in two of our cases (a lipoma and a bronchogenic cyst). In this instance, the absence or a low value of MIBI uptake (T/N value up to 1.7) may be a further confirmation of the benign nature of the lesion, which thus may be treated directly by surgical resection without further investigations. Conversely, the ability of CT to differentiate soft-tissue mediastinal masses is limited and, sometimes, there is little that can be done radiographically to distinguish a thymoma from a lymphoma, particularly when typical symptoms for either are absent [1]. Our experience shows that MIBI uptake in a thymoma (LRT and HRT) is significantly lower than that in a lymphoma. Thus, in the light of our results, $^{99m}$Tc-MIBI-SPECT may be useful in separating a thymoma that, in general, necessitates complete surgical resection without the need for a preoperative diagnosis from a lymphoma that requires tumor biopsy before therapeutic management. A well-encapsulated solid mass without any signs of invasiveness or malignancy, with a negative laboratory test, and with a moderate MIBI uptake (T/N value up to 2.1), has a high probability of being a thymoma rather than a lymphoma. Thus, complete resection is advisable, being diagnostic and therapeutic, simultaneously. This approach may be justified considering that biopsy of a presumed thymoma should be avoided because of tumor seedling in either the needle tract or the pleural space [17]. By contrast, if the mass is not well circumscribed on radiological evaluation, and presents a high $^{99m}$Tc-MIBI uptake (T/N value > 2.1), there is a high likelihood that it may be a lymphoma or other malignant tumor. Because our data show that this technique is not able to perform a differential diagnosis between the various kinds of neoplastic lesion, in this instance, a pre-operative diagnosis is mandatory to avoid unnecessary thoracotomy or sternotomy in case of diagnosis of lymphoma or other malignant tumors, for which surgery is not the initial treatment [18].

Second, our results suggest that $^{99m}$Tc-MIBI-SPECT assesses the biological, metabolic, and functional aspects of thymic pathologies, and may add further information to morphological images for better identifying the malignant nature of the tumors. Clinically, thymic epithelial tumors are diagnosed primarily by using morphological examinations, such as CT and MRI, both of which are excellent for identifying and defining the extent of these tumors. However, preoperative prediction of WHO histologic subtypes, based on imaging findings alone, is occasionally difficult [19]. Tomiyama et al. [20] compared the CT findings and histological features according to the WHO criteria and concluded that CT has a limited value in differentiating types AB, B1, B2, and B3. Our results confirm that $^{99m}$Tc-MIBI uptake is useful in differentiating LRT from HRT, and in distinguishing HRT from TC using the T/N ratio approach. The degree of MIBI accumulation becomes increasingly more accentuated as the WHO classification shifts from type A to type B, and eventually to TC. Meanwhile, the amount of lymphocyte infiltration in the tumor gradually decreased from type B1 to type B3. From a pathological point of view, $^{99m}$Tc-MIBI uptake accumulation in the tumor may not be affected by the amount of lymphocytes but, rather, is mainly affected by the atypia of cells. Yet, $^{99m}$Tc-MIBI accumulation is significantly correlated with Masaoka stage as a consequence of lower MIBI accumulation in stages I and II compared with stages III and IV. In our study, only two patients (one with HRT and the other with TC) appear as photon deficient on $^{99m}$Tc-MIBI-SPECT. Both patients are in stage IV, and it may explain why no statistical difference has been found between the T/N values of stage IV and of stage III; yet, the same patients have had no response to neo-adjuvant therapy. Theoretically, no response to chemotherapy may be correlated to low $^{99m}$Tc-MIBI uptake in tumor cells. Recently, $^{99m}$Tc-MIBI has been considered a suitable transport substrate for p-glycoprotein (PGP), which is encoded by the multidrug-resistance gene [21]. It has been reported that, in patients with breast or lung cancer, there may be an inverse correlation between the T/N ratios of $^{99m}$Tc-MIBI and the intensity of PGP expression [13]. Consequently, $^{99m}$Tc-MIBI has been also proposed as an effective tracer in monitoring neo-adjuvant chemotherapy in breast cancer. Yet, it also been proposed that, in patients with lung cancer, a higher $^{99m}$Tc-MIBI uptake may indicate a tumor that is more responsive to chemotherapy [13]. Thus, in our patients, the alteration of PGP expression may be taken into account as the cause of the low uptake of $^{99m}$Tc-MIBI and of the no response to neo-adjuvant chemotherapy.

Our results are of considerable significance because the preoperative identification of histologic subtype and stage of thymic pathology permit to plan the most appropriate management strategy for each patient [6,20,22]. By contrast, the size of thymoma is not correlated with MIBI uptake. Our results show that small size is not per se a guarantee of low invasiveness or favorable WHO subtype, according to previous data reported by Luzzi et al. [23]. Yet, there is no correlation between the presence of MG and $^{99m}$Tc-MIBI uptake. In most of the studies, MG patients are predominantly in stages I and II [7]. Conversely, in our population, MG was present not only in patients in stages I and II but also in stages III and IV. Thus, it may explain why no correlation was found between MG and MIBI uptake.

Finally, considering the small number of patients, the present study suggests only an indication but not conclusive results, which remain to be determined by studies dealing with a large number of patients. Yet, it has some limitations as the following.
First, a combined SPECT-CT unit are not available in this trial. It is certainly possible that an SPECT-CT unit may better define the consistency of the lesion, its relationship to adjacent structures, and the detection of lymph node or pleural metastases.

Second, in all of the patients, the disease location had already been identified by a previous CT scan, thereby excluding the study of extrathoracic sites.

Third, 99mTc-MIBI may also provide a sensitive means of detecting residual, recurrent, and metastatic disease. However, the observation period is short and a prognostic evaluation is not done.

5. Conclusion

The data of our study show that 99mTc-MIBI-SPECT seems to be useful in the evaluation of malignancy in patients with anterior mediastinal mass. Malignant lesions as TC and LYM showed high 99mTc-MIBI uptake, while LRT and BT showed low/ no uptake. Regarding thymic epithelial tumor, 99mTc-MIBI accumulation is significantly correlated with the different histologic subtypes of the WHO classification and with the Masaoka stage. Despite this, our data are not sufficient to change the standard criteria of the diagnostic approach of anterior mediastinal mass; however, 99mTc-MIBI-SPECT may add further information to clinical and morphological studies to offer guidance for decision making. As a consequence, in a mediastinal mass considered resectable on CT scan with low (T/N value up to 1.7) or moderate MIBI uptake (T/N value up to 2.1), surgical resection would be a preferred option rather than opting for an FNAB or surgical biopsy. Conversely, for mediastinal masses with high 99mTc-MIBI uptake (T/N value > 2.1) for whom other diagnoses such as lymphoma may be considered, a surgical biopsy is appropriate to obtain a tissue diagnosis because 99mTc-MIBI-SPECT is not able to distinguish between the various kinds of tumors. Finally, because of the small number of patients, further studies are warranted to corroborate our preliminary results.

References