POSITRON EMISSION TOMOGRAPHY - COMPUTER TOMOGRAPHY FUSION IMAGE, WITH 18-FLUORO-2-DEOXY-D-GLUCOSE IN THE FOLLOW-UP OF PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA

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Abstract

Aim. The aim of this study is to present the personal experience of the authors regarding the use of positron emission tomography-computer tomography fusion image (PET/CT), with 18F-fluoro-2-deoxy-D-glucose (FDG), in the follow-up of differentiated thyroid carcinoma (DTC).

Patients and Methods. Twenty seven cases of DTC admitted and treated in the “Prof. Ion Chiricuta” Institute of Oncology Cluj-Napoca (IOCN), performed PET/CT investigation between 2007 and 2009, in DOTE Centre Debrecen (Hungary) and Pozitron Center Oradea (Romania). The patients underwent the surgical intervention and had histology of differentiated carcinoma; they received radiiodine therapy with I-131, had suppression therapy with thyroid hormones and had in the follow-up whole body scans (WBS) with I-131, neck ultrasound and serological determination of thyroglobulin (Tg) and anti-thyroglobulin antibodies (anti-Tg). All patients were referred to PET/CT after radical treatment, after a negative WBS I-131 and a dynamic increase of the serological level of Tg or anti-Tg, without any clinical signs of recurrence and no neck ultrasound pathological findings.

Results. All patients included in this study presented abnormal levels of Tg: between 2.76 ng/ml and 4173 ng/ml, with a median value of 43.15 ng/ml. In 23 cases (85.1%) the PET/CT results revealed the neoplasm recurrence, in 3 cases we obtained true negative results and in 1 case a false negative image; in 2 cases (7.4%) we found a second malignancy. All patients needed to change the treatment strategies.

Conclusion. The significant increase of the number of DTC and the more aggressive behaviour of the disease in some situations, determines the existence of a clear strategy of treatment and monitoring, where the role of PET/CT is well defined.

Keywords: differentiated thyroid carcinoma, PET/CT 18F-FDG, follow-up.
INTRODUCTION

Among all the endocrine malignancies thyroid carcinoma is the most frequent, accounting for about 5% of thyroid nodules (1) and is responsible for the mortality by cancer for 0.12-1.2 % (2, 3). The differentiated thyroid cancer represents about 80-90% of all thyroid cancers (4), with a good prognosis and with a very specific treatment strategy based on surgery and radioiodine therapy (5,6). In the last decade a more aggressive natural history of this cancer was reported (7) and new investigation methods were developed.

The metabolic 18F-fluoro-2-deoxy-D-glucose has already been accepted as an essential tool in staging, re-staging and therapy response assessment of many tumours. The use of PET/CT fusion scanners has been demonstrated to significantly increase accuracy of lesion detection, combining the high anatomical definition of CT with the high sensitivity of PET (8). The PET radiotracer FDG has obtained a large acceptance in clinical oncology due to its excellent diagnostic performance in many cancers as: lung, colorectal, lymphoma, melanoma, oesophagus, pancreas, breast, ovary, and testicle. However, FDG has reduced performance in some other cancers, less aggressive and most differentiated ones such as prostate cancer or endocrine tumours. In these cancers it is mandatory to perform PET with tracers “beyond FDG” (9). In case of DTC, despite of the limited indication of FDG, there is a very well defined place of PET/CT: no clinical signs, but biochemical evolution of disease (serological Tg or anti-Tg increasing), with negative WBS I-131.

This study is the first one in Romania referring to the use of PET/CT in DTC.

PATIENTS AND METHODS

“Prof. Dr. Ion Chiricuță” Institute of Oncology Cluj-Napoca (IOCN) is one of the most important national tumour centres with a considerable high number of new cancer cases growing yearly. In 2008 thyroid carcinoma was the third prevalent cancer in IOCN, representing 6.67 % of all new registered malignancies.

Between 2004 and 2009, in IOCN 1938 patients with thyroid carcinoma were treated, 1767 (91.2%) being patients with DTC. All patients underwent radical treatment and the monitoring protocol of these patients consisted in: clinical examination at 6 months after treatment, determination of serum Tg and anti-Tg levels in conditions of elevated TSH, cervical ultrasound. WBS I-131 was performed to all patients at 6 months after the initial treatment, even if the levels of Tg were normal; after the first negative radioiodine scan, WBS I-131 was indicated only if the Tg levels were above 2 ng/mL, with normal values of anti-Tg. Also WBS I-131 was indicated if the serum levels of anti-Tg were higher than 115 UI/ml, with no previous context of Hashimoto thyroiditis associated to DTC.

After the first oncology negative control, a clinical evaluation at 3 months in
PET/CT in differentiated thyroid carcinoma

the endocrinology service was indicated and a yearly complete oncology check-up was recommended in the next 5 years. In case of recurrence (evidence by clinical exam, ultrasound or radioiodine scan) the treatment sequences were reconsidered: surgery, radioiodine or both.

The study protocol was targeted to those patients with DTC with biochemical recurrence of the disease and no objective signs of localisation of this relapse. Because of the financial difficulties (no reimbursement of examination by health insurances) and also because of lack of investigation centres in Romania till 2008, the selection of patients was strictly based on the next inclusion criteria:

- radical treatment of DTC: surgery, radioiodine therapy and suppressive hormonal treatment;
- no clinical signs of disease;
- dynamic rising of serum level of Tg or anti-Tg (at least in 2 determinations);
- neck ultrasound negative or doubtful;
- negative WBS I-131;
- negative conventional imaging (thorax radiographies, cervical and mediastinum computed tomographies);
- no other acute or chronic severe diseases that may lower the life expectancy under 1 year;
- financial support available.

The FDG PET/CT was indicated with respect to a minimum level of serum Tg above 2 ng/mL, if all previously mentioned criteria were fulfilled and it was demonstrated that in the same conditions of sample analysis, in 2 consecutive determinations at 6 months interval, there was a significant (at least 50% higher) rise of the Tg value.

The patient’s database of this study consists in 27 patients with DTC: 9 with pure papillary thyroid carcinoma, 6 with follicular thyroid carcinoma, 9 with folliculo-papillary carcinoma, and 3 with Hurthle cell carcinoma. The gender distribution shows an evident prevalence of females (22 females and 5 males). The mean age was 51.2 years. The staging of patients was as follows: 1 case in stage I, 8 cases in stage II, 12 cases in stage III and 7 patients in stage IV. All patients were treated in IOCN between 2004 and 2009 and evaluated on PET/CT between 2007 and 2009. The treatment strategies consisted in total or near total thyroidectomy, with or without lymphadenectomy according to lymph nodes status; radioiodine therapy with I-131 capsules at 4-6 weeks after surgery without any hormonal replacement with the range of total administered doses between 3.7 GBq and 23.05 GBq; suppression treatment with Levothyroxine, with regular evaluation of thyroid stimulating hormone (TSH) maintained at serum level under 0.1 mUI/L.

The follow-up after treatment at 6 months consisted in clinical examination, neck ultrasound, and determination of serum levels of Tg and anti-Tg and WBS I131. Tg and anti-Tg were determined on unsuppressed TSH with hormone withdrawal for 2-4 weeks in 26 cases and in 1 case with recombinant TSH, i.m. injection of 2 x 0.9 mg thyrotropin alpha - Thyrogen (rhTSH). The analyses were
performed on Roche kits and Cobas instruments.

Normal values for differentiated thyroid carcinoma patients with radical treatment according to the producers are: Tg < 0.1 ng/mL and anti-Tg < 115 UI/mL, with a serum value of TSH > 40 mUI/L or values elevated at least 100 times as compared with the suppression values. In 1 case with demonstrated extensive distant metastases the TSH value was normal, after the withdrawal of hormones.

The thyroid ultrasound on Toshiba echo-Doppler, model SSA-270A (Sonolayer). The I-131 WBS were made at all patients on Siemens gamma camera Ecam Signature, high energy collimator, at 48 h after the oral administration of 111 MBq of I-131, with 1 million counts acquisition on each image. Conventional computer tomographies (CT) were performed in IOCN on GE spiral CT and the magnetic resonance imaging (MRI) in Scandia SRL Cluj-Napoca on GE 1, 5 Tesla instrument. PET/CT was performed on Siemens Biograph 16 in Pozitron Centre Oradea (Romania) in 4 cases or on Siemens Biograph 6 in DOTE Centre Debrecen (Hungary) in 23 cases, after the i.v. administration of 555-740 MBq 18F-fluoro-2-deoxy-D-glucose.

Statistical methods used were based on EpiMax Table Calculator, sensitivity, specificity, predictive value positive, predictive value negative, false negative and positive rates and overall accuracy (10). All patients of this study were treated and followed-up in IOCN and there is an informed consent obtained both for the diagnosis and therapy procedures and for the scientific use of these data in this paper.

**RESULTS**

The clinical examination was negative in all 27 patients: no cervical abnormalities, no latero-cervical or supraclavicular lymph nodes detectable, no tumour clinically evident in whole body, no objective signs of disease evolution.

The evolution of the disease or of the recurrence was considered as being at biochemical level, until we performed PET/CT. In 25 cases the serum Tg levels were increased, with dynamic evolution and rising tendency in the follow-up period, at least in 2 different determinations at minimum 6 months interval (Fig.1); in these patients anti-Tg values were normal (anti-Tg < 115 UI/mL). The Tg range values in patient submitted to PET/CT were between 2.76 ng/mL and 4173 ng/mL, with a median at 43.15 ng/mL, a mean value of 344.3, a confidence interval of 95% and a standard deviation of Tg value of 912.3. The examination was indicated in 2 cases with anti-Tg elevated in serial analysis and undetectable serum Tg levels. The values were: anti-Tg-824 UI/mL and in the other case anti-Tg > 4000 UI/mL.

The conventional CT of the head, cervical and mediastinum regions, thorax and abdominal CT were negative in all patients. The abdominal CT was indicated only in 1 case, MRI was performed in 2 cases at cervical and thorax regions with negative results. Neck ultrasound was the standard investigation after clinical exam and tumour marker determination. The cervical ultrasound showed in 2 cases the
presence of neck lesions: 1 patient with neck lymph node features non-malignant, but at PET/CT was positive with high uptake and SUV 6.1%. The second patient referred to PET/CT with a very high Tg value (Tg - 429.3 ng/mL) had a negative result; at 4 months follow-up at ultrasound some latero-cervical lymph nodes were evident, under the sternocleidomastoidian muscle. Reevaluation of the initial PET results demonstrated that the lesions were present at the moment of examination, but were skipped out by the investigators.

The features of the group of patients took in study are presented in Table 1. The PET/CT exam was positive in 23/27 cases and negative in 4 cases. Among the 23 positive patients 13 of them (56.5%) underwent surgical procedure with a positive histopathology of the metastasis from DTC or confirming the second malignancy in breast and colon sigma. Cervical metastases (Fig. 2) were present in 5 cases, with selective lymph nodes dissection in 3 situations and radical neck dissection in 2 patients. For thoracic surgery 2 cases were referred with mediastinal tumour (Fig. 3) and 1 with lung tumour and costal invasion. In 1 case with dermal metastasis of the right knee and 1 case with dermal invasion of the skull, resections were performed in healthy tissues. In the situation of 1 patient orthopaedic surgery was performed for large metastasis of the femur. In 1 case there were made radical mastectomy and lymph node resection of axilar area (Fig. 4) and in 1 case hemicolectomy (Fig. 5); in these cases polychemotherapy was also performed. In these 2 cases the cancers were synchronous with DTC and were confirmed by histopathology specimens in IOCN.

All these patients were true positive (100%). A number of 8 patients with positive PET/CT and high SUV (> 3.5 %) were submitted to another radioiodine therapy. These patients were in the following situations: lesions under 1 cm, difficult surgical approach (mediastinum or loco-regional invasion with high surgical risks). Two cases with low value of SUV(<3.5%) and with impossibility of surgery due to local condition were referred to external radiotherapy.
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Regarding the negative results, 1 patient among 4 was false negative, with a further demonstration of the neck metastasis and with selective lymph node dissection. The other 3 negative patients were followed-up till the moment of the study without any signs of evolution.

According to the results obtained after the PET/CT examination, a number of 15 patients were referred to surgery for a surgical procedure: 7 patients for latero-cervical selective lymph nodes dissection, 3 patients for thoracic surgery, 2 patients for dermal excisions; 1 case for orthopaedic surgery; 8 patients continued the radioiodine therapy; 2 patients began the chemotherapy (both with the second malignancy of the breast and colon); 2 patients performed external radiotherapy; 3 patients were only followed-up.

Table 1. Features of 27 patients with 18F-fluoro-2-deoxy-D-glucose PET/CT examination

<table>
<thead>
<tr>
<th>No.</th>
<th>Histo.</th>
<th>TSH (mUI/L)</th>
<th>Tg (ng/mL)</th>
<th>anti-Tg (UI/mL)</th>
<th>Neck US</th>
<th>PET/CT</th>
<th>Treatment</th>
</tr>
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<tbody>
<tr>
<td>Case 1</td>
<td>PTC</td>
<td>47.2</td>
<td>271.3</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>DE</td>
</tr>
<tr>
<td>Case 2</td>
<td>PTC</td>
<td>&gt;100</td>
<td>104.6</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>RTE</td>
</tr>
<tr>
<td>Case 3</td>
<td>PTC</td>
<td>87.1</td>
<td>23.1</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>LND</td>
</tr>
<tr>
<td>Case 4</td>
<td>PTC</td>
<td>61.8</td>
<td>17.4</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>RIT</td>
</tr>
<tr>
<td>Case 5</td>
<td>PTC</td>
<td>55.6</td>
<td>429.3</td>
<td>&lt; 115</td>
<td>+</td>
<td>-</td>
<td>LND</td>
</tr>
<tr>
<td>Case 6</td>
<td>PTC</td>
<td>&gt;100</td>
<td>32.8</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>RIT</td>
</tr>
<tr>
<td>Case 7</td>
<td>PTC</td>
<td>8.8</td>
<td>2323</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>OS</td>
</tr>
<tr>
<td>Case 8</td>
<td>PTC</td>
<td>48.4</td>
<td>87.7</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>LND</td>
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<tr>
<td>Case 9</td>
<td>PTC</td>
<td>59.3</td>
<td>2.76</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>LND</td>
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<tr>
<td>Case 10</td>
<td>FTC</td>
<td>88.3</td>
<td>47.9</td>
<td>&lt; 115</td>
<td>+</td>
<td>+</td>
<td>RIT</td>
</tr>
<tr>
<td>Case 11</td>
<td>FTC</td>
<td>61.6</td>
<td>63.7</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>TC</td>
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<tr>
<td>Case 12</td>
<td>FTC</td>
<td>39.4</td>
<td>187</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>TC</td>
</tr>
<tr>
<td>Case 13</td>
<td>FTC</td>
<td>91.3</td>
<td>16.3</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>RIT</td>
</tr>
<tr>
<td>Case 14</td>
<td>FTC</td>
<td>56.8</td>
<td>45.8</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>RIT</td>
</tr>
<tr>
<td>Case 15</td>
<td>FPTC</td>
<td>40.1</td>
<td>7.3</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>RIT, PCT</td>
</tr>
<tr>
<td>Case 16</td>
<td>FPTC</td>
<td>1.2</td>
<td>4173</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>TC</td>
</tr>
<tr>
<td>Case 17</td>
<td>FPTC</td>
<td>17.8</td>
<td>163.6</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>RTE</td>
</tr>
<tr>
<td>Case 18</td>
<td>FPTC</td>
<td>57.1</td>
<td>201.5</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>DE</td>
</tr>
<tr>
<td>Case 19</td>
<td>FPTC</td>
<td>16.9</td>
<td>12.7</td>
<td>&lt; 115</td>
<td>-</td>
<td>-</td>
<td>F</td>
</tr>
<tr>
<td>Case 20</td>
<td>FPTC</td>
<td>44.2</td>
<td>21.4</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>LND</td>
</tr>
<tr>
<td>Case 21</td>
<td>FPTC</td>
<td>61.1</td>
<td>16.1</td>
<td>&lt; 115</td>
<td>-</td>
<td>-</td>
<td>F</td>
</tr>
<tr>
<td>Case 22</td>
<td>FPTC</td>
<td>48.9</td>
<td>28.5</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>RIT</td>
</tr>
<tr>
<td>Case 23</td>
<td>FPTC</td>
<td>22.8</td>
<td>&lt; 0.1</td>
<td>824</td>
<td>-</td>
<td>+</td>
<td>LND</td>
</tr>
<tr>
<td>Case 24</td>
<td>FPTC</td>
<td>73.8</td>
<td>91.5</td>
<td>&lt; 115</td>
<td>-</td>
<td>-</td>
<td>F</td>
</tr>
<tr>
<td>Case 25</td>
<td>HTC</td>
<td>&gt;100</td>
<td>54.9</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>RIT</td>
</tr>
<tr>
<td>Case 26</td>
<td>HTC</td>
<td>27.9</td>
<td>&lt; 0.1</td>
<td>&gt; 4000</td>
<td>-</td>
<td>+</td>
<td>PCT</td>
</tr>
<tr>
<td>Case 27</td>
<td>HTC</td>
<td>72.7</td>
<td>6.8</td>
<td>&lt; 115</td>
<td>-</td>
<td>+</td>
<td>LND</td>
</tr>
</tbody>
</table>

Legend: Histo-Histology; TSH- thyroid stimulating hormone; Tg- maximum serum value of thyroglobulin; Anti-Tg - maximum serum value of anti-thyroglobulin; PTC - papillary thyroid carcinoma; FTC- Follicular thyroid carcinoma, FPTC- Folliculo-papillary thyroid carcinoma; HTC - Hurthle thyroid carcinoma; US-ultrasonography; LND- latero-cervical selective lymph nodes dissection; TC- thoracic surgery, OS- orthopaedic surgery; DE- dermal excisions; RIT - radioiodine therapy; PCT-polychemotherapy ; RTE - radiotherapy; F- follow-up.
PET/CT in differentiated thyroid carcinoma

Figure 2. Positive 18FDG PET/CT - neck lymph node metastasis.

Figure 3. Positive 18FDG PET/CT - mediastinum lymph node metastasis.

Figure 4. Positive 18FDG PET/CT - breast carcinoma and axilar lymph node metastasis; second malignancy in DTC patient.
The PET/CT investigation in the thyroid pathology is related to 3 major subjects: the evaluation of thyroid nodules; the role of PET/CT in different forms of thyroid carcinoma; the diagnosis of other malignancies associated with thyroid carcinomas.

1. PET/CT in the differential diagnosis of benign and malignant thyroid nodules

Normally there is no $^{18}$F-fluoro-2-deoxy-D-glucose uptake in the thyroid bed. The presence in the area of the thyroid of this radiotracer in a PET/CT examination indicated for another type of pathology is described in literature as “metaboloma” (11). If focal FDG uptake is described on a PET/CT image it is important to refer the patient to the endocrinologist in order to make a clinical examination, thyroid functions tests and thyroid ultrasound.

A recent study, published in September 2009 (12), regarding the incidental thyroid lesions detected by FDG-PET/CT, demonstrated that prevalence and risk of thyroid cancer in these lesions are very low. FDG-PET/CT was performed on 3379 patients for evaluation of suspected or known cancer or cancer screening without any history of thyroid cancer. Among them 285 patients (8.4 %) were identified to have FDG uptake on thyroid area; 99 patients with focal or diffuse FDG uptake underwent further evaluation and 22 patients were diagnosed with thyroid cancer. The cancer risk of incidentally found thyroid lesions on FDG-PET/CT was 0.65 % (22 /3379), fact that underlines that this examination is not recommended as screening of thyroid carcinoma.

Regarding the differential diagnosis between the benign and malignant nodules, there is a factor that may play a role in the decision of further thyroid evaluation, after the discovery of a “metaboloma”: there is a significant difference in the standard uptake value (SUV maximum) between the benign and malignant nodules (3.35 ±1.69 vs. 6.64±4.12) (12). If SUV maximum is suspicious there was indicated the endocrinologist examination. In our study there were no cases of preoperative evaluation of thyroid nodules with this procedure.

![Figure 5. Positive 18FDG PET/CT - colon carcinoma and liver metastasis, second malignancy in DTC patient.](image-url)
2. PET/CT in the follow-up of thyroid carcinoma

2.1. PET/CT in the follow-up of differentiated thyroid carcinoma (DTC). DTC is not one of the types of cancers where PET/CT is a standard indication or is included in the guidelines of diagnosis and treatment. Despite that, there is a very well defined situation where PET/CT plays a major role: confirmed DTC with radical treatment, serum Tg rising, with WBS I-131 negative (13). The American Thyroid Association in the guidelines of thyroid cancer in 2009 (14) affirm: “if after an empiric dose of 100-200 mCi, I-131 WBS fails to localize the tumor, especially in patients with unstimulated serum Tg level of 10-20 ng/mL, FDG PET should be considered”.

The same recommendation was given by the National Cancer Comprehensive Network (NCCN) on thyroid cancer guideline in 2008 (15). Since 2003 the insurance system (Medicare) from the USA have paid for this condition of thyroid cancer patients who have the indication for this examination (16). In our study, the FDG PET/CT changed the therapeutic behavior in 23 cases of 27 patients (85.2 %): 13 cases were referred to surgery with positive metastasis results and in 2 patients second malignancies were discovered; 8 patients continued the radioiodine therapy and 2 patients started the external radiotherapy. Only in 1 case there was a false negative result.

The sensitivity of the PET/CT FDG method in DTC was 95.8 % with a specificity of 100%. False positive rate was zero and false negative rate was 4.1 %. The p (test positive) was 0.85 and p (test negative) 0.148. Predictive positive value was 1 and predictive negative value was 0.75. The overall accuracy was 96%. It is important to underline that even in the situation of a low value of Tg (ex. in case no. 9 a value of 2.67 ng/mL) in the condition of elevated TSH (75.6 mUI/L), the PET/CT was positive; the lymph nodes ablated at the anatomo-pathological report showed the neoplastic invasion. The presence of thoracic lymph nodes with no radioiodine uptake, but positive high FDG uptake, imposed the continuation of radioiodine therapy. The good response was considered in relation to Tg decreasing and of the SUV max in the following PET/CT examinations. In the situation of low FDG uptake the management of patient’s disease changed and the option of chemotherapy or external radiotherapy was taken. Regarding the FDG PET/CT in DTC there is a special attention that is important to be stressed: the role of TSH in the FDG uptake. Petrich et al. published in 2002 that the sensitivity of FGD-PET was 53% during TSH suppression and 87% following rhTSH stimulation (17). Another author, Bertagna, showed that there is no influence of TSH in FDG uptake, but the higher sensitivity is seen on Tg value > 20 ng/mL. (18). According to this data, in our study all patients were in TSH stimulated situation, so we cannot affirm personal experience; more multiple centers studies are necessary to clarify this topic.

2.2. PET/CT in the follow-up of medullary thyroid carcinoma (MTC). As in DTC situation in MTC there is a strict place of FDG PET/CT: radical treatment, serum calcitonin level rising, negative conventional imagery.

The overall sensitivity of FDG PET/CT is less than 75 % (19), but the new
Radiotracers such as $^{18}$F-dihydroxyphenylalanine, $^{18}$F-DOPA, $^{18}$F-fluorodopamine, $^{68}$Ga-labeled somatostatin analogs give optimistic horizons. As is known in the literature (20), in MTC there is lack of sensitivity of many investigations: $^{18}$F-fluoro-2-deoxy-D-glucose PET/CT-78%, Pentavalent $^{99m}$Tc dimercaptosuccinic (DMSA)-33%, $^{99m}$Tc sestamibi (MIBI)-25%, $^{111}$Indium pentetreotide (SMS) -25%, CT-50%, MRI-82%. Even if the specificity may rise to 100% (MIBI) these low rates of sensitivity, justify the efforts to develop new radiotracers for PET.

### 2.3. PET/CT in the follow-up of anaplastic thyroid carcinoma (ATC)

Unfortunately, there is no role of this examination, because of the very aggressive natural history of the disease, of rapid local evolution and often limited medical intervention.

### 3. The role of PET/CT in other malignancies associated with thyroid carcinoma

In the situation of second malignancies PET/CT give the chance of a better prognosis to patients, so synchronous or metachronic cancers benefit of early detection. A significantly elevated risk of thyroid cancer following breast cancer (standardized incidence ratios - SIR = 1.68) and breast cancer following thyroid cancer (SIR = 1.89) was demonstrated in data from the Connecticut Tumor Registry (21). The relations between disorders in the thyroid and breast leading to carcinomas were published by the oncologist and endocrinologist community (22, 23), so in both cancers there is special attention to screening. The PET/CT has an important role in these situations.

In the present study, the patient with breast carcinoma had no clinical signs and the possibility to discover the tumor was practically very low; PET/CT examination succeeded to reveal the tumor at least 6 months earlier, starting the treatment and increasing the chances of curability. Regarding the second case, the presence of liver tumor in a patient with history of DTC imposes an immediate liver biopsy. The alternative of a noninvasive procedure was preferable. In the same examination the primary digestive tumor was also found.

**In conclusion,** DTC is a malignant endocrine tumour with a rapid increase of the frequency in the latest decade. The aggressive behaviour of some cases, with modified response to standard treatment strategies, demands the introduction of other diagnostic procedures, such as FDG PET/CT, which are able to improve significantly the possibility of detection of the recurrence or evolution of the disease. According to the results of the present study, a correct indication of the examination in DTC may change the therapeutic strategy in more than 80% of the cases.

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