

## PET-CT IMAGING FUSION IN THE ASSESSMENT OF HEAD AND NECK CARCINOMA\*

Denise Takehana dos Santos<sup>1</sup>, Rubens Chojniak<sup>2</sup>, Eduardo Nóbrega Pereira Lima<sup>3</sup>, Marcelo Gusmão Paraíso Cavalcanti<sup>4</sup>

**Abstract** **OBJECTIVE:** The authors have established a methodological approach to evaluate head and neck squamous cell carcinoma aiming at identifying and distinguishing high metabolic activity inside the lesion, combining in a single examination, functional, metabolic and morphological data simultaneously acquired by means of different non-dedicated positron emission tomography (PET)-computed tomography (CT) device. **MATERIALS AND METHODS:** The study population included 17 patients with head and neck squamous cell carcinoma submitted to a non-dedicated <sup>18</sup>F-FDG-PET imaging at Department of Diagnostic Imaging of Hospital do Câncer, São Paulo, SP, Brazil. CT and <sup>18</sup>F-FDG-PET images were simultaneously acquired in a non-dedicated device. The original data were transferred to an independent workstation by means of the Entegra 2 NT software to generate PET-CT imaging fusion. **RESULTS:** The findings were defined as positive in the presence of a well defined focal area of increased radiopharmaceutical uptake in regions not related with the normal biodistribution of the tracer. **CONCLUSION:** The fusion of simultaneously acquired images in a single examination (<sup>18</sup>F-FDG-PET and CT) has allowed the topographic-metabolic mapping of the lesion as well as the localization of high metabolic activity areas inside the tumor, indicating recidivation or metastasis and widening the array of alternatives for radiotherapy or surgical planning.

*Keywords:* Squamous cell carcinoma; Computed tomography; Positron emission tomography; Face.

**Resumo** *Fusão de imagens PET-TC na avaliação do carcinoma espinocelular de cabeça e pescoço.*

**OBJETIVO:** Os autores estabeleceram uma metodologia para avaliar carcinoma espinocelular de cabeça e pescoço, identificando e distinguindo áreas de grande atividade metabólica dentro da neoplasia, associando dados simultaneamente adquiridos, obtidos por diferentes modalidades de aquisição de imagens, combinando informações metabólicas e anatômicas num único exame. **MATERIAIS E MÉTODOS:** A população estudada consistiu de 17 pacientes com carcinoma espinocelular pertencentes aos arquivos do Departamento de Imagem do Hospital do Câncer, São Paulo. As imagens de tomografia computadorizada (TC) e da tomografia por emissão de pósitrons (PET) com 2-[F-18]-fluoro-2-deoxi-d-glucose (<sup>18</sup>F-FDG-PET) foram simultaneamente adquiridas utilizando aparelho não dedicado. Os dados originais foram transferidos para uma estação de trabalho independente com o programa Entegra 2NT para gerar a fusão de imagens da PET e TC. **RESULTADOS:** Os achados foram definidos como positivos na presença de focos com aumento da concentração do radiofármaco em áreas não relacionadas à sua distribuição normal. **CONCLUSÃO:** A fusão de imagens simultaneamente adquiridas num único exame (<sup>18</sup>F-FDG-PET e TC) possibilitou o mapeamento topográfico metabólico das lesões estudadas e foi possível localizar áreas de maior atividade metabólica dentro do próprio tumor, verificando recidivas ou metástases, possibilitando aumentar as opções quanto ao planejamento radioterápico ou cirúrgico.

*Unitermos:* Carcinoma espinocelular; Tomografia computadorizada; Tomografia por emissão de pósitrons; Face.

### INTRODUCTION

The functional study of the tumor metabolism also should be considered, and for this purpose the Nuclear Medicine is the method of choice<sup>(1-3)</sup>. Computed tomography (CT) plays a significant role in the assessment of the tumor volume, this data being frequently utilized in the clinical practice as one of the patterns of therapy response. Another significant factor to be taken into consideration is the fact that the metabolic behavior of the tumor may not

be homogeneous. With the Nuclear Medicine development, the PET (positron emission tomography)/CT imaging fusion has become feasible by means of a mechanism of simultaneous images acquisition in a same device, so a metabolic/topographic mapping of the lesion can be performed<sup>(2)</sup>. Also, another advantage of this imaging modality to be highlighted is the possibility of determining an area of increased metabolic activity inside a lesion, that is to say, an area associated with a higher cellular mitotic activity. The detection of such

\* Study developed at Hospital do Câncer A.C. Camargo – Department of Diagnostic Imaging, and at Faculdade de Odontologia da Universidade de São Paulo – Department of Stomatology, São Paulo, SP, Brazil.

1. Doctor in Oral Diagnosis by Faculdade de Odontologia da Universidade de São Paulo.

2. Chief for Department of Diagnostic Imaging at Hospital do Câncer A.C. Camargo.

3. Director of Nuclear Medicine at Hospital do Câncer A.C. Camargo.

4. Private Docent, Professor of Radiology at Department of Stomatology – Faculdade de Odontologia da Universidade de São Paulo.

Mailing address: Prof. Dr. Marcelo Gusmão Paraíso Cavalcanti. Disciplina de Radiologia – FOU SP, Avenida Professor Lineu Prestes, 2227, Cidade Universitária. São Paulo, SP, Brazil 05508-900. E-mail: mgpcaval@usp.br.

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regions inside anatomical lesions could allow an accurate mapping for radiotherapy purposes, especially in cases of non-resectable tumors which must be treated exclusively with radiotherapy or combined radiotherapy/chemotherapy. The definition of this region could be of help for focusing the radiation beams onto a previously determined area, destructing the cells in mitotic activity, with a possible improvement in the therapeutic efficacy<sup>(1-4)</sup>.

The present study is aimed at developing a protocol utilizing CT and PET with 2-[F-18]-fluoro-2-deoxy-d-glucose (<sup>18</sup>F-FDG-PET) images fusion to detect areas with higher cellular activity in head and neck squamous cell carcinomas, obtaining a correct anatomical localization, and defining the largest area of increased radiopharmaceutical uptake, classifying it into centric or eccentric.

## MATERIALS AND METHODS

The research sample included imaging studies of 17 patients of Hospital do Câncer – A.C. Camargo, São Paulo, SP, Brazil (retrospective study), who had been histopathologically diagnosed with squamous cell carcinoma of oral cavity, rinopharynx and oropharynx, and classified, according to the American Joint Committee on Cancer (1997) criterion, into T2 and T3, with and without lymph nodes involvement (N0 and N1) and without metastasis (M0), therefore in stages II and III of the prognosis grouping (with 66% and 44% five-year survival rate). Histopathological results have shown differentiation grades I, II and III in the studied lesions.

The patients were submitted to PET-CT scans according to the protocol including the following steps:

### Dose

A 8–10 mCi (296–370 Bq) injection of <sup>18</sup>F-FDG was administered. Initially, CT images acquisition (80 10 mm thick transaxial slices) was performed in a 256 × 256 matrix for anatomical coregistration. For this purpose, we have utilized a non-dedicated Millennium VG Hawkeye equipment (GE Medical Systems; Milwaukee, Wis) with a low radiation dose (140 kV and 2.5 mA) system and 384 detectors, where

each acquisition takes approximately 14 seconds to be performed. After CT images acquisition, the PET images obtained 60 minutes following radiotracer injection underwent a registration process. Data were provided similarly to the sectional images and acquired in ten gantry rotations/360° over 30 minutes.

Interactive reconstruction of images was performed following data transference to an Entegra 2 NT (GE Medical System) workstation, running a specific software for individual groups processing and fusion into a single group, including physiological and metabolic data resulting from <sup>18</sup>F-FDG-PET and anatomical data originated from the co-registered CT. The images attenuation was corrected employing the CT correction algorithm<sup>(5)</sup>, which is dependent on the mean x-ray tube energy (40–130 keV). Pixels values in Hounsfield units were converted into linear attenuation coefficients in cm<sup>-1</sup> units at 511 keV with a bilinear function defined by 3 coordinates: –1,000 HU = 0 cm<sup>-1</sup>; 0 HU = 0,093 cm<sup>-1</sup>; and 1,326 HU = 0,172 cm<sup>-1</sup>.

### Qualitative analysis of the sample

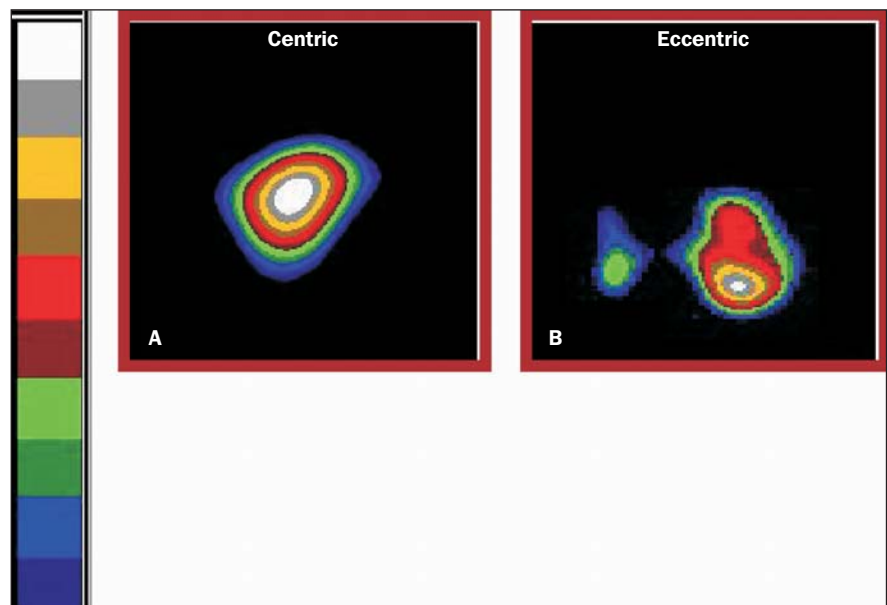
The findings were defined as positive in cases with an anomalous <sup>18</sup>F-FDG concentration in areas not related with a normal radiotracer biodistribution. Specific protocols and tools such as energy window set-

ting were employed to establish minimum and maximum uptake values inside the lesion itself. By means of a guidance device it was possible to identify the larger diameter of the lesion simultaneously in axial, coronal and sagittal planes.

The images analysis followed a pre-established order: firstly, the co-registered CT image, followed by the lesion metabolism image, and, finally, the combined images, allowing the topographic-metabolic mapping of the lesion. A nuclear physician and a radiologist performed, individually, the interpretation on the computer screen, identifying the site with higher tumor metabolic activity and classifying it into centric or eccentric (Figure 1). Conclusion was reached through analysis of the three planes, observing the existent predominance, i.e., if the site of higher radiotracer concentration was eccentrically found on the axial and coronal planes (for example), so it was considered as eccentric. In cases of interpretation disagreement, a consensus was reached. Data were consolidated into a digital data basis and the qualitative analysis of results was performed.

## RESULTS

According to the TNM classification, of the 17 patients, 11 were classified as T3 — 4 positive lymph nodes; and six patients



**Figure 1.** Areas with higher metabolic activity inside the tumor (A: centric; B: eccentric), on a progressive uptake scale (from blue to white).

were T2 — 3 positive lymph nodes. The anatomopathological study demonstrated grades I, II and III differentiation of the lesions studied. Analyzing the metabolic images visualized on axial, coronal and sagittal planes, in association or individually, we could observe the presence of an anomalous <sup>18</sup>F-FDG concentration in sites not related with a normal radiotracer bio-distribution in all of the patients. Affected regions were: nasal fossa, orbital region, tongue basis, mouth floor, and larynx.

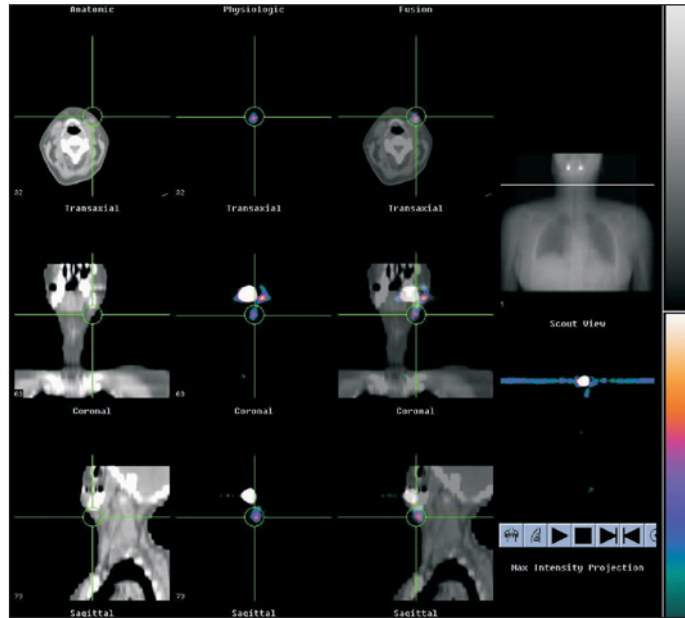
In 77% of cases (n = 13) the site with higher radiotracer uptake has demonstrated to be centrally located (Figure 2). In 23% of cases (n = 4) the tumor behavior was different, with eccentric hyper uptake (Figure 3). For a didactic analysis, these results were separated out into two charts including data of each lesion staging and grade of invasion. In group I included in Graphic 1 (eccentric hyper uptake), all the lesions were staged in T3N1M0, and classified into grade II (one lesion) and grade III (three lesions) of histopathological differentiation. Group II presented higher variation, both in staging and histopathological differentiation as follows: T2N0M0 (three lesions), T2N1M0 (three lesions), T3N0M0 (six lesions) and T3N1M0 (one lesion), and

grades I (four lesions), II (seven lesions) and III (two lesions) (Graphic 2).

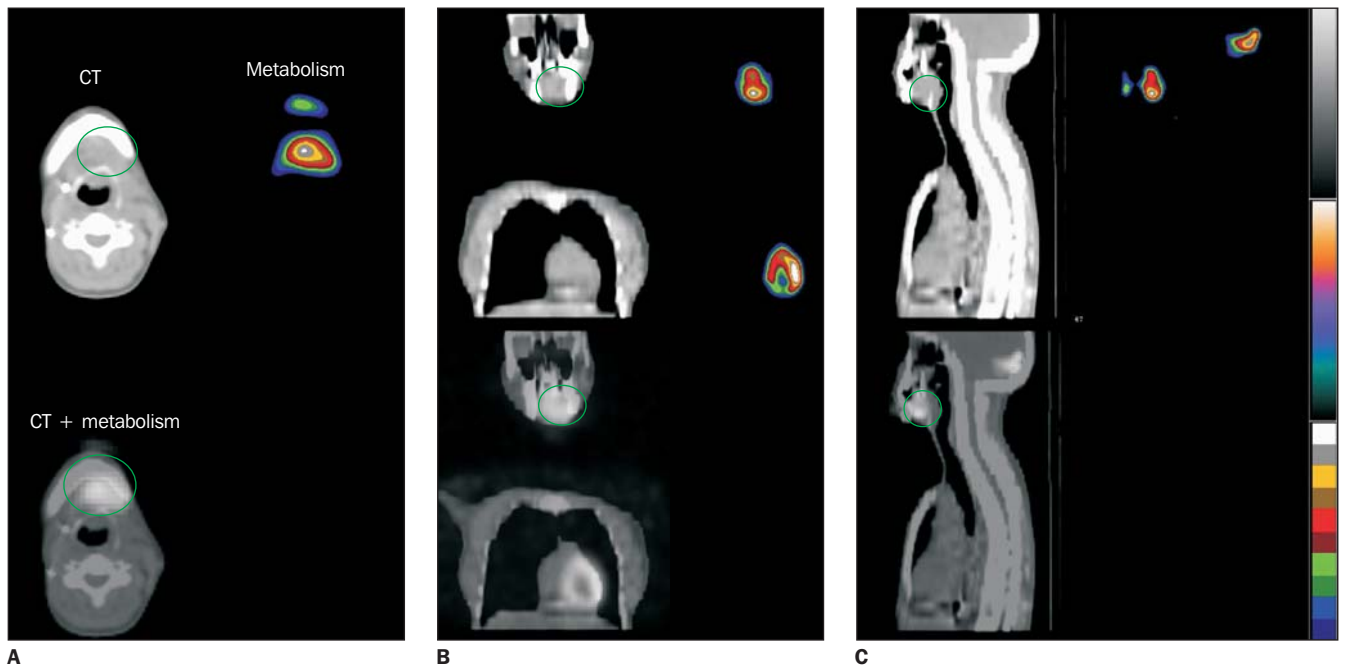
**DISCUSSION**

According to the literature<sup>(2,6)</sup>, FDG-PET has a great ability to metabolically

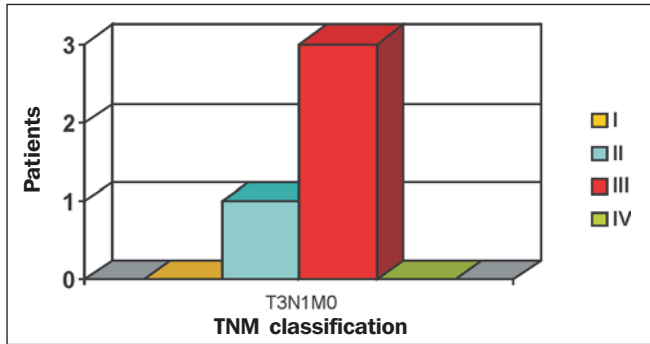
demonstrate small active lesions, and also those superficial and submucosal, which are potentially invisible to clinical and conventional imaging studies. This happens because, in head and neck studies, high metabolic structures are confined into a relatively small space, and the presence of



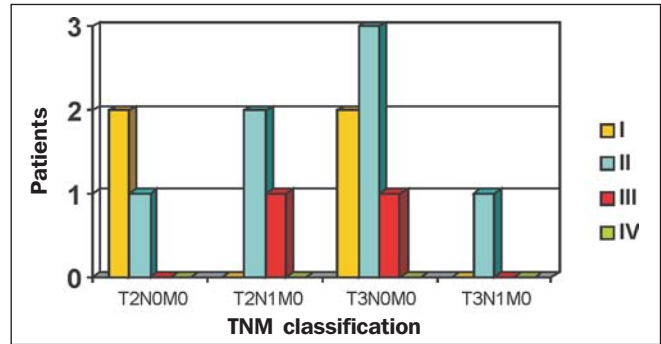
**Figure 2.** Patient with squamous cell carcinoma in the region of left submandibular gland. In this case, the radiotracer hyper uptake (demonstrated on CT, metabolic image and combined images) is centrally evidenced as per images observed in axial, coronal and sagittal planes.



**Figure 3.** Imaging sequence of a patient with squamous cell carcinoma in the tongue basis. Note that the radiotracer hyper uptake (demonstrated on CT, metabolic image and combined images) is centrally evidenced in the axial plane (A); however, in coronal (B) and sagittal planes (C) the hyper uptake is eccentric, so this lesion metabolism is classified as eccentric.



**Graphic 1.** Patients of group I (eccentric metabolism), according to the TNM classification by American Joint Committee on Cancer.



**Graphic 2.** Patients of group II (centric metabolism), according to the TNM classification by American Joint Committee on Cancer.

artifacts and/or previous therapies may generate distortions or even mask a situation in studies like CT or MRI.

In review studies, some authors<sup>(7,8)</sup> have reported a comparative study of dedicated and non-dedicated PET in malignant neoplasms of head and neck, showing quite similar results in terms of sensitivity and specificity for both systems. As regards other pulmonary lesions, in lymphomas and brain tumors, the data found in the literature could not lead to definite conclusions<sup>(7)</sup>. Despite the small number of studies<sup>(9-11)</sup> utilizing images acquired with dual-head coincidence gamma cameras (non-dedicated PET), the sensitivity has ranged between 64% and 100%, and specificity, between 70% and 100%. The highest values being found in studies on tumors recurrence, and the lowest, in those for detection of primary sites. With basis on the literature, and for logistics reasons, we have justified the use of dual-head coincidence gamma camera in the present study.

Another study deserving to be highlighted<sup>(12)</sup> has been performed comparing combined PET-CT and PET images independently obtained and analyzed by CT. The PET-CT advantages of (lower) cost, reduced dose, higher reliability in images interpretation have been emphasized, therefore we can say that, with this method, it is easy to differentiate a physiological uptake from possible malignant lesions. In our study, with a non-dedicated equipment, functional images were obtained and superposed to anatomical images by means of 3D volumetric reconstruction, which, according to the literature, may result in a significant increase in the accuracy of surgical and/or radiotherapy planning<sup>(22)</sup>.

In the present study, a qualitative analysis of the lesions was performed and the <sup>18</sup>F-FDG uptake grades were transcribed into a progressive color scale, facilitating the analysis, and answering two important questions: a) active lesion; and b) metabolic activity corresponding to an inflammatory process or malignization of cells. By choosing the FDG in the present study, these questions are immediately answered, since non-tumor, fibrotic and necrotic tissues present a reduced or absent uptake, while cells with mitotic activity and hypoxic cells which are radiation-resistant, and currently considered as one of the greatest challenges for oncologists, demonstrate a high substrate avidity<sup>(13)</sup>.

Additionally, we could identify areas with higher metabolic activity inside the tumor, classifying them into centric or eccentric. According to such classification, four patients (23%) presented lesion with eccentric substrate uptake, i.e., the uptake was not concentrated in the center of the lesion. These four patients had been staged as T3, with positive lymph node, and differentiation grades II and III (most of them). This suggests that the lesions could be in a phase of growth and tissues infiltration.

In the other 13 patients (77%), the area with higher metabolic activity was in the center of the lesion. In this group of lesions, the variation, both in staging and differentiation, was higher, with lesions in T2N0M0, T2N1M0, T3N0M0 and T3N1M0, and grades I (four lesions), II (seven lesions) and III (two lesions). This might indicate a mature lesion (well differentiated), in a slower growth phase. If the patients were in a post-therapy phase, one could suggest that this concentration in the

center of the lesion occurred because of hypoxic cells. Finally, this centric hyper uptake also could be attributed to the cellular metabolism due to the production of keratin, i.e. differentiated cells, although not being mitosis-prone cells. This analysis allows us to agree with studies in the literature asserting that radiotherapy planning could be more effective if the functional planning were also taken into consideration<sup>(13-15)</sup>. Even in a study with a small sample like this, more than 20% of cases have demonstrated a behavior different from the expected one, that is to say, in four patients, the site with highest cellular activity did not correspond to the center of the lesion. In the absence of these data, the target of the highest isodose to be applied would be, as usually, the center of the lesion (even utilizing latest generation softwares), which would result in a slower therapeutic response, or yet, would increase the probability of those active cells in eccentric regions being quickly infiltrated by the surrounding tissues. In our opinion, studies must be developed in the future for a better understanding and confirmation of the theories on high centric metabolism *versus* high eccentric metabolism. Also, it is very important that latest generation technologies are searched to combine PET and multislice CT, adding new contributions in this field.

Therefore, it is our understanding that, despite its preliminary character, this study suggests that the <sup>18</sup>F-FDG-PET-TC imaging fusion may serve as a guidance for topographic metabolic mapping of malignant lesions, widening the array of treatment options and, undoubtedly, improving patients' survival.

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