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CLINICAL INVESTIGATION **Head and Neck**

COMBINED ^{18}F-FDG-PET/CT IMAGING IN RADIOTHERAPY TARGET DELINEATION FOR HEAD-AND-NECK CANCER

Alessandra Guido, M.D.,* Lorenzo Fuccio, M.D.,† Barbara Rombi, M.D.,* Paolo Castellucci, M.D.,‡ Agnese Cecconi, M.D.,* Feisal Bunkheila, M.D.,* Chiara Fuccio, M.D.,‡ Emiliano Spezi, Ph.D.,* Anna Lisa Angelini, Ph.D.,* and Enza Barbieri, M.D.*

*Division of Radiation Oncology, †Department of Internal Medicine and Gastroenterology, and ‡Division of Nuclear Medicine, Policlinico S. Orsola, Bologna, Italy

Purpose: To evaluate the effect of the use of ^{18}F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)/computed tomography (CT) in radiotherapy target delineation for head-and-neck cancer compared with CT alone.
Methods and Materials: A total of 38 consecutive patients with head-and-neck cancer were included in this study. The primary tumor sites were as follow: 20 oropharyngeal tumors, 4 laryngeal tumors, 2 hypopharyngeal tumors, 2 paranasal sinuses tumors, 9 nasopharyngeal tumors, and 1 parotid gland tumor. The FDG-PET and CT scans were performed with a dedicated PET/CT scanner in one session and then fused. Subsequently, patients underwent treatment planning CT with intravenous contrast enhancement. The radiation oncologist defined all gross tumor volumes (GTVs) using both the PET/CT and CT scans.
Results: In 35 (92%) of 38 cases, the CT-based GTVs were larger than the PET/CT-based GTVs. The average total GTV from the CT and PET/CT scans was 34.54 cm^3 (range, 3.56–109) and 29.38 cm^3 (range, 2.87–95.02), respectively ($p < 0.05$). Separate analyses of the difference between the CT- and PET/CT-based GTVs of the primary tumor compared with the GTVs of nodal disease were not statistically significant. The comparison between the PET/CT-based and CT-based boost planning target volumes did not show a statistically significant difference. All patients were alive at the end of the follow-up period (range, 3–38 months).
Conclusion: GTVs, but not planning target volumes, were significantly changed by the implementation of combined PET/CT. Large multicenter studies are needed to ascertain whether combined PET/CT in target delineation can influence the main clinical outcomes. © 2009 Elsevier Inc.

^{18}F-fluorodeoxyglucose-positron emission tomography, ^{18}F-FDG-PET, Computed tomography, PET-CT, Image fusion, Head-and-neck cancer, Gross tumor volume, GTV, Planning target volume, PTV.

INTRODUCTION

Modern radiotherapy (RT) relies on three-dimensional imaging, such as computed tomography (CT) and magnetic resonance imaging (MRI), allowing for more precise target volume and organs at risk identification and delineation. Although CT and MRI allow for a dosimetric evaluation of the regions of interest, this information is only anatomic; thus, it is far from being devoid of potential errors. For instance, metastatic lymph nodes harboring tumor cells, but nevertheless within normal size, can be excluded from the target volume, hampering the potential for cure. In contrast, enlarged lymph nodes could be the result of an inflammatory process, rather than tumor dissemination, and extending the target volume to lymph nodes with false-positive findings could translate into an obstacle to dose escalation.

Positron emission tomography (PET) provides metabolic information through the use of radiotracers such as ^{18}F-fluoro-deoxyglucose (FDG), ^{11}C-methionine, ^{11}C-choline, and many others. Several investigators (1–3) have reported an increase in staging accuracy with metabolic (PET) information compared with the use of CT or MRI alone. Hence, this increased diagnostic accuracy could also play a role in RT planning, reducing interobserver variability in target delineation, and modifying the extension of gross tumor volume (GTV), clinical tumor volume (CTV) and planning target volume (PTV) for both primary tumor and regional lymph nodes, potentially, allowing additional dose escalation. In some cases, the intent of treatment could also change from curative to palliative when distant metastases have been detected by PET (4). Recently, integrated PET-CT scanning

Reprint requests to: Enza Barbieri, M.D., Division of Radiation Oncology, Policlinico S. Orsola, Via Massarenti 9, Bologna 40138 Italy. Tel: (+39) 051-636-3154; Fax: (+39) 051-636-4930; E-mail: ebarbieri@aosp.bo.it

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has been implemented, which has further improved both the accuracy and the interpretation of PET images (5).

The aim of this study was to evaluate the effect of the use of combined ^{18}F-FDG-PET/CT for RT target delineation of head-and-neck cancer compared with CT alone.

METHODS AND MATERIALS

Patient characteristics

Between April 2004 and December 2006, 38 consecutive patients (29 men and 9 women; mean age 59 years; range, 35–82) with head-and-neck cancer were included in this study.

The clinical stage of all patients according to the International Union Against Cancer staging criteria was determined by physical examination and contrast-enhanced CT and MRI. Of the 38 patients, 7 had Stage I, 11 had Stage II, 10 had Stage III, 8 had Stage IVA, and 2 had Stage IVB. The primary tumor sites were as follow: 20 oropharyngeal tumors, 4 laryngeal tumors, 2 hypopharyngeal tumors, 2 paranasal sinuses tumors, 9 nasopharyngeal tumors, and 1 parotid gland. The clinical characteristics and anatomic localizations of the primary tumor are summarized in Table 1.

^{18}F-FDG-PET/CT and CT image acquisition

All the patients were immobilized with a customized thermoplastic mask fixed to a flat tabletop. PET/CT was performed using a standard procedure. In brief, each patient, who had fasted for ≥6 h, and in absence of antidiabetic therapy, was injected with 5.3 MBq/kg of ^{18}F-FDG. After the injection, patients were hydrated, and the uptake phase was 60–80 min. The scan was performed with a dedicated PET-CT scanner (GE, Discovery). The acquisition time was 4 min/step, and the attenuation correction was performed with the CT-based method (120 KV, 80 mA). The field of view of PET/CT was from the skull to the upper abdomen. PET/CT acquisition was performed with the aid of three markers on the plastic immobilization mask, and data sets were sent, by way of Digital Imaging and Communications in Medicine, to a workstation treatment planning system.

The patient, immediately after PET/CT scanning, underwent RT planning CT in the same position in the combined PET/CT scanner as that used for PET/CT (i.e., the same flat tabletop and immobilization). All treatment planning CT scans were performed with intravenous contrast enhancement from the skull to the upper abdomen.

Table 1. Patient characteristics

Characteristic	*n* (%)
Gender	
Males	29 (76)
Females	9 (24)
Primary tumor site	
Oropharyngeal tumor	20 (53)
Laryngeal tumor	4 (11)
Hypopharyngeal tumor	2 (5)
Paranasal sinuses tumor	2 (5)
Nasopharyngeal tumor	9 (24)
Parotid gland	1 (2)
Stage	
I	7 (18)
II	11 (29)
III	10 (26)
IVA	8 (21)
IVB	2 (5)

Delineation of GTV

The ^{18}F-FDG-PET/CT scan was compared with all available clinical information from palpation and endoscopic evaluation. The radiation oncologist (A.G.), with experience in head-and-neck cancer, defined all the GTVs from both ^{18}F-FDG-PET/CT (GTV PET) and CT (GTV CT). The CT-based GTV was drawn without the information from the FDG-PET scans. A nuclear medicine physician (P.C.), with expertise in PET imaging, visually interpreted the ^{18}F-FDG PET studies and defined the ^{18}F-FDG-PET–positive regions interpreted as malignant on the emission images. A 50% intensity level relative to the tumor maximum was used to delineate the margins of the GTV PET. The CTVs, as well as the PTVs, were determined from the GTV ^{18}F-FDG-PET/CT. The absolute CT, ^{18}F-FDG-PET, and image fusion ^{18}F-FDG-PET/CT volumes were measured and are expressed in cubic centimeters.

Follow-up

During treatment, the patients were seen weekly by the treating radiation oncologist (A.G.) for assessment and management of toxicities. Toxicities were graded according to the Radiation Therapy Oncology Group toxicity criteria (6). All patients entered a follow-up program that began 1 month after RT completion. Scheduled visits then occurred every 3 months during the first 2 years and every 6 months thereafter. CT-PET was performed in the third month of follow-up, and MRI or CT with contrast enhancement was used in the case of suspicious lesions. CT-PET was repeated every 6 months thereafter.

Routine follow-up care was performed by the radiation oncologist together with an otolaryngologist and included complete head-and-neck examinations with appropriate endoscopic examination, performance status determination, and toxicity notations.

Statistical analysis

The GTV and PTV obtained from the ^{18}F-FDG-PET/CT scans were compared with the CT-based GTV and PTV, respectively, using Student' *t* test. A significance level of 5% was used throughout ($p < 0.05$).

RESULTS

Combined ^{18}F-FDG PET/CT determined a change in the tumor stage in 6 of 38 cases. All changes were related to additional nodal information. In 5 cases (3 with nasopharyngeal cancer and 2 with oropharyngeal cancer), the CT-based nodal information was upstaged by the PET/CT data. In contrast, in 1 oropharyngeal cancer case, it resulted in downstaging. Furthermore, additional nodal information was added to 9 more cases, but it did not result in a change in tumor stage.

We analyzed the differences in GTV obtained by the two modalities of measurement, CT and combined ^{18}F-FDG-PET/CT. All patients had positive, abnormal uptake on ^{18}F-FDG-PET. In 35 (92%) of 38 cases, the CT-based GTVs were larger than the ^{18}F-FDG-PET/CT-based GTVs. In the 3 remaining cases, the CT-based GTVs were smaller than the ^{18}F-FDG-PET/CT-based GTVs. The average total CT-based GTV and ^{18}F-FDG-PET/CT-based GTV was 34.54 cm^3 (range, 3.56–109) and 29.38 cm^3 (range, 2.87–95.02), respectively. The comparison between the mean ^{18}F-FDG-PET/CT-based GTVs and the mean CT-based GTVs showed a slight, but statistically significant, difference ($p = 0.0467$).