

## INFLUENCE OF [<sup>18</sup>F] FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY ON SALVAGE TREATMENT DECISION MAKING FOR LOCALLY PERSISTENT NASOPHARYNGEAL CARCINOMA

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**Purpose:** The purpose of this study was to evaluate the role of [<sup>18</sup>F] fluorodeoxyglucose positron emission tomography (FDG-PET) in influencing salvage treatment decision making for locally persistent nasopharyngeal carcinoma (NPC).

**Methods and Materials:** A total of 33 NPC patients with histologic persistence at nasopharynx 1 to 6 weeks after a full course of radiotherapy underwent both computed tomography (CT) and FDG-PET/CT simulation at the same treatment position. The salvage treatment decisions, with regard to the decision to offer salvage treatment and the definition of gross tumor volume (GTV), were made before knowledge of the FDG-PET findings. Subsequently the salvage treatment decisions were made again based on the FDG-PET findings and compared with the pre-FDG-PET decisions.

**Results:** All 33 patients were referred for salvage treatment in the pre-FDG-PET decision. After knowledge of the FDG-PET results, the decision to offer salvage treatment was withdrawn in 4 of 33 patients (12.1%), as no abnormal uptake of FDG was found at nasopharynx. Spontaneous remission was observed in repeat biopsies and no local recurrence was found in these 4 cases. For the remaining 29 patients, GTV based on FDG-PET was smaller than GTV based on CT in 24 (82.8%) cases and was greater in 5 (17.2%) cases, respectively. The target volume had to be significantly modified in 9 of 29 patients (31%), as GTV based on FDG-PET images failed to be enclosed by the treated volume in the salvage treatment plan performed based on GTV based on CT simulation images.

**Conclusion:** Use of FDG-PET was found to influence the salvage treatment decision making for locally persistent NPC by identifying patients who were not likely to benefit from additional treatment and by improving accuracy of GTV definition in salvage treatment planning. © 2006 Elsevier Inc.

Nasopharyngeal carcinoma, Radiotherapy, Persistent disease, [<sup>18</sup>F] Fluorodeoxyglucose positron emission tomography, Treatment decision making.

### INTRODUCTION

Local persistence occurs in 6.7% to 13% of patients with nasopharyngeal carcinoma (NPC) after a full course of radiotherapy (RT) (1–4) and has been found to be associated with an increased risk of local recurrence if no additional treatment is given (5–7). Treatment outcomes of locally recurrent NPC after repeated course of RT, which carries a high risk of late complications, are poor (8–10). Therefore, aggressive and effective salvage treatment for local persistence is very important.

However, the salvage treatment decision making for locally persistent NPC remains challenging and controversial. Kwong *et al.* (2) reported 16.3% of patients with NPC had delayed-histologic-remission (DHR) disease at nasopharynx, identified by repeat biopsies with negative histologic

findings within 12 weeks after a full course of RT. Nevertheless, identifying the patients with DHR disease by repeat biopsy will postpone the salvage treatment for the patients with truly persistent disease. Considering tumor cell repopulation during the prolonged gap period between the completion of the initial RT and salvage treatment, the requisite dose to treat the persistent disease would be increased greatly, and it might result in severe late complications. So, we used to give the patients with positive histologic findings at nasopharynx after a full course of radiotherapy an early intervention with salvage RT (11). However, this salvage RT should be unnecessary in patients who would experience DHR. Therefore, it is critical to find a way to identify the patients with DHR disease earlier than repeat biopsy, to improve the validity of patient selection to receive salvage treatment. Whether [<sup>18</sup>F] fluoro-

deoxyglucose positron emission tomography (FDG-PET) is such a way is of great importance to us.

On the other hand, definition of the target volume for locally persistent NPC also remains challenging for the vague border of the persistent disease on computed tomography (CT), which is the most commonly used RT simulation image. FDG-PET has a high sensitivity and specificity for detecting locally persistent NPC (12–14). It is logically believed that this advanced functional imaging will improve the accuracy of GTV definition for this disease.

The objective of this study was to evaluate the role of FDG-PET in influencing salvage treatment decision making, including the decision to offer salvage treatment and the definition of GTV to be treated, for locally persistent NPC.

## METHODS AND MATERIALS

Approval was granted from the Southern Medical University Institutional Review Board to proceed with this retrospective study. From August 2002 to September 2005, a total of 33 NPC patients with histologic persistence at nasopharynx after a full course of RT were enrolled in this study. Of these 33 patients, 24 were male and 9 were female. The median age at diagnosis of NPC was 45 years (range, 27–66 years). The distribution of histologic types, according to the World Health Organization (WHO) classification (15), was as follows: WHO II, 5 (15.2%); and WHO III, 28 (84.8%). The T-stage distribution according to AJCC/UICC 1997 staging system (16) was as follows: T<sub>2</sub>, 5 (15.2%); T<sub>3</sub>, 18 (54.5%); T<sub>4</sub>, 10 (30.3%). All patients had undergone a full course of 6-MV photons radiotherapy using conventional technique with a median total dose of 70 Gy (range, 68–72 Gy) at nasopharynx. All patients had histologic proof of local persistence. The interval between completion of RT and biopsy for diagnosis of local persistence ranged from 7 to 36 days (median, 15 days). Patient characteristics are shown in Table 1.

All patients underwent a CT simulation scan with contrast injection on the spiral CT scanner (PQS, Marconi Medical Systems, Highland Heights, OH) in the treatment position and immobilization in the radiotherapy department after histologic diagnosis of local persistence. The scope from the top of the head to the clavicle was scanned at 3-mm increments. The PET/CT scan was performed within 3 days of the CT simulation scan in the same position and immobilization. The interval between completion of RT and PET/CT scanning ranged from 14 to 40 days (median, 21 days). PET/CT integrates a four-slice helical CT scanner (Light Speed Plus, GE Medical System, Milwaukee, WI) and PET scanner (Advance Nxi, GE); and the imaging and data acquisition were performed on an integrated PET/CT system (Discovery LS, GE). The PET/CT images were then sent to the treatment planning system (XiO, CMS) and fused to the CT simulation images.

The GTV based on CT simulation images (GTV<sub>CT</sub>) was delineated without the FDG-PET images being viewed in advance or at the same time. The GTV based on FDG-PET images (GTV<sub>PET</sub>) was then delineated by another radiation oncologist with the assistance of an experienced nuclear medicine physician. A focus was considered positive if the activity was significantly above the expected background and could not be explained by a normal structure, and the 50% intensity level relative to the tumor maximum was used to delineate the borders of the GTV<sub>PET</sub>. On the basis of GTV<sub>CT</sub>, the corresponding planning target volume was

Table 1. Characteristics of 33 patients studied

Characteristic	Value (%)
Age (y)	
Range	27–66
Median	45
Gender	
Male	24 (72.7)
Female	9 (27.3)
Histologic type	
WHO II	5 (15.2)
WHO III	28 (84.8)
T stage	
T <sub>2</sub>	5 (15.2)
T <sub>3</sub>	18 (54.5)
T <sub>4</sub>	10 (30.3)
N stage	
N <sub>0</sub>	7 (21.2)
N <sub>1</sub>	14 (42.4)
N <sub>2</sub>	11 (33.3)
N <sub>3</sub>	1 (3.0)
Total dose at nasopharynx (Gy)	
Range	68–72
Median	70
Time of biopsy after RT (days)	
Range	7–36
Median	15
Time of CT scan after RT (days)	
Range	12–40
Median	20
Time of PET scan after RT (days)	
Range	14–40
Median	21

*Abbreviations:* CT = computed tomography; PET = positron emission tomography; RT = radiation therapy; WHO = World Health Organization.

derived to achieve a three-dimensional conformal radiotherapy (3D CRT) plan.

The salvage treatment decisions, with regard to both the decision to offer salvage treatment and the GTV to be treated, were made before knowledge of the FDG-PET findings. The salvage treatment decisions were then made again based on the FDG-PET findings and compared with the pre-PET salvage treatment decisions; and the 3D CRT plans performed based on the GTV<sub>CT</sub> were evaluated with the GTV<sub>PET</sub>.

In the patients who finally decided to receive salvage treatment, if there was a discrepancy between the GTV<sub>CT</sub> and GTV<sub>PET</sub>, the GTV<sub>PET</sub> was used instead of the GTV<sub>CT</sub> in the salvage treatment with 3D CRT in this study, and the PTV was defined as GTV<sub>PET</sub> plus a 5 mm margin. The detail about the salvage treatment protocol with 3D CRT for locally persistent NPC was reported in our previous study (11).

## RESULTS

All of the 33 patients were referred for salvage treatment in the pre-PET decision. After knowledge of the FDG-PET results, the decision to offer salvage treatment was withdrawn in 4 of the 33 patients (12.1%), as no abnormal uptake of FDG was found at nasopharynx. In these 4 cases, spontaneous remission was observed in repeat biopsies after

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