CONTRAST MEDIA & MOLECULAR IMAGING

Received: 7 June 2010, Revised: 12 September 2010, Accepted: 27 September 2010, Published online in Wiley Online Library: 2011

(wileyonlinelibrary.com) DOI:10.1002/cmmi.425

^{18}F-FDG PET/CT and MRI in the follow-up of head and neck squamous cell carcinoma

Rose Ghanooni[a]*, Isabelle Delpierre[b], Michèle Magremanne[c†], Catherine Vervaet[c], Nicolas Dumarey[d], Myriam Remmelink[e], Simon Lacroix[d], Nicola Trotta[d], Sergio Hassid[a] and Serge Goldman[d]

We evaluated the diagnostic performance of ^{18}F-FDG PET/CT and MRI for the assessment of head and neck squamous cell carcinoma (HNSCC) relapse. Since early treatment might prevent inoperable relapse, we also evaluated THE performance of early unenhanced ^{18}F-FDG PET/CT in residual tumor detection. The study was prospectively performed on 32 patients who underwent ^{18}F-FDG PET/CT and MRI before treatment and at 4 and 12 months after treatment. ^{18}F-FDG PET/CT was also performed 2 weeks after the end of radiotherapy. Histopathology or a minimum of 18 months follow-up were used as gold standard. Before treatment ^{18}F-FDG PET/CT and MRI detected all primary tumors except for two limited vocal fold lesions (sensitivity 94%). MRI was more sensitive than ^{18}F-FDG PET/CT for the detection of local extension sites (sensitivity 75 vs 58%), but at the cost of a higher rate of false positive results (positive predictive value 74 vs 86%). For relapse detection at 4 months, sensitivity was significantly higher for ^{18}F-FDG PET/CT (92%) than for MRI (70%), but the diagnostic performances were not significantly different at 12 months. For the detection of residual malignant tissue 2 weeks post-radiotherapy, sensitivity and specificity of ^{18}F-FDG PET/CT were respectively 86 and 85% (SUV cut-off value 5.8). ^{18}F-FDG PET/CT is effective in the differentiation between residual tumor and radiation-induced changes, as early as 2 weeks after treatment of a primary HNSCC. For follow-up, performance of ^{18}F-FDG PET/CT and MRI are similar except for a higher sensitivity of ^{18}F-FDG PET/CT at 4 months.

Keywords: squamous cell carcinoma; head and neck cancer; ^{18}F-FDG PET; fluorodeoxyglucose; MRI

1. INTRODUCTION

Loco-regional control of the disease is a key prognostic factor in head and neck squamous cell carcinoma (HNSCC). The impact of this factor is such that salvage therapies are beneficial when local recurrence of the cancer occurs (1). Salvage therapy is complicated by the post-therapeutic changes induced by the primary treatment applied. Efficacy and morbidity associated with the secondary therapy depend on the recurrence extent. It appears therefore pertinent to promote early detection of primary therapy failure in order to prevent large tumor recurrences and this approach is supported by a study on re-staging performed at 1–2 months post-therapy (1). Re-staging within the first month post-therapy is blurred by the major morphological changes induced by the therapeutical procedure itself. ^{18}F-FDG PET associated with CT imaging (^{18}F-FDG PET/CT) is efficient in primary staging and recurrence detection of HNSCC (2–6). Since ^{18}F-FDG PET/CT is less impacted by early structural post-therapeutical changes than CT or MRI, its use in early post-therapy re-staging appears appealing. Still, ^{18}F-FDG PET/CT that essentially relies on the metabolic detection of malignant tissue, might suffer from a lack of accuracy due to radiation-induced metabolic 'knockdown' and non-malignant tracer uptake by inflammatory cells. Several recent studies, however, have demonstrated a very high diagnostic accuracy of ^{18}F-FDG PET/CT performed 4–6 weeks after treatment (7–9). The optimal timing of such an early metabolic imaging is still unknown. We therefore performed ^{18}F-FDG PET/CT 2 weeks after radiation therapy in a prospective study comparing ^{18}F-FDG PET/CT and MRI in the follow-up at 4 and 12 months for patients treated for HNSCC. Analysis of ^{18}F-FDG PET/CT and MRI diagnostic accuracy at these two time points was motivated by the fact that direct comparisons of the two modalities, with recent acquisition systems and protocols, are rare and that optimal timing of

* *Correspondence to: R. Ghanooni, Department of Otorhinolaryngology, Hôpital Erasme, Université Libre de Bruxelles, 808 route de Lennik, 1070 Bruxelles, Belgium.*
E-mail: rosemaryam_ghanooni@yahoo.fr

a *R. Ghanooni, S. Hassid*
Department of Otorhinolaryngology, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium

b *I. Delpierre*
Department of Medical Imaging, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium

c *M. Magremanne, C. Vervaet*
Department of Stomatology, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium

d *N. Dumarey, S. Lacroix, N. Trotta, S. Goldman*
Department of Nuclear Medicine, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium

e *M. Remmelink*
Department of Histopathology, Erasme Hospital, Université Libre de Bruxelles, Brussels, Belgium

† *Present address: Department of Stomatology, Saint-Luc Hospital, Université Catholique de Louvain, Brussels, Belgium*

imaging surveillance after primary therapy of HNSCC is not established and might vary between modalities (5,10).

2. MATERIALS AND METHODS

2.1. Patient population

Patients were prospectively included in the study from July 2005 to December 2006. The main inclusion criterion was a primary diagnosis of a squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx and larynx. Patients at all stages were included, provided that a decision of curative therapy was taken. Therapeutic decision was taken by a multidisciplinary clinical panel of experts in head and neck oncology, using EORTC recommendations as guidelines. Diagnosis was performed by physical examination and pathologic analysis of tumor biopsies. Loco-regional staging and search for metastasis or secondary tumor was done by neck and liver echography, chest CT, bronchoscopy and gastroscopy. All patients had multiple biopsies made during panendoscopic exploration, to determine the local extension of the primary tumor to adjacent regions. ^{18}F-FDG PET/CT and MRI were performed at diagnosis, 4 months and one year after the end of the treatment. ^{18}F-FDG PET/CT was also performed 2 weeks after completion of radiotherapy or chemoradiotherapy in those patients who received these treatments. Follow-up lasted at least 18 months after the end of treatment, in order to allow for a data analysis after a clinical follow-up of 6 months after the last imaging procedure.

2.2. Whole-body ^{18}F-FDG PET/CT

All the patients were injected intravenously with a bolus of 10 mCi (370 MBq) after a fasting period of at least 6 h. Glucose blood level had to be less 7.5 mmol/l. ^{18}F-FDG PET/CT were performed on a Gemini-16 PET/CT camera (Philips Medical Systems, Cleveland, OH, USA) in full-3D acquisition mode. Static images from skull base to mid-thigh were acquired starting 80 ± 10 min after FDG injection (3 min per bed position). The images were iteratively reconstructed by means of the Philips-supplied 3D Raw Action Maximum-Likelihood Algorithm (3D-RAMLA) with scatter correction through single scatter simulation. Attenuation correction and anatomical correlation were carried out by the means of a low dose CT (4.4 mGy/slice, 40 mAs/slice) obtained without injection of contrast media.

2.3. MRI

MR images were obtained on a 1.5 T MRI (Philips Medical System). All studies included axial T_1 and axial T_2 fat suppression images of 3.5 mm. Contrast-enhanced images were obtained in axial and coronal planes with fat-suppression T_1-weighted images after intravenous injection of gadolinium.

2.4. Imaging analysis

^{18}F-FDG PET/CT were interpreted by two nuclear medicine practitioners blinded to tumor location, morphological imaging results and follow-up status. One of the practitioners was N.D. for the analysis of all patients' images. For follow-up examinations, the practitioners only knew the treatment that was applied. For visual interpretation, a five-point scoring system was applied that differed for pre-treatment (0 = no lesion, 1 = benign, 2 = equivocal, 3 = malignant, 4 = not interpretable) and follow-up scans, the latter being evaluated in comparison to the pre-treatment ^{18}F-FDG PET/CT (0 = no lesion, 1 = benign, 2 = lesion in regression, 3 = lesion stable or in progression, 4 = not interpretable). One of the practitioners (N.D.) reviewed all scoring and discordant interpretations were resolved by consensus between N.D. and the other nuclear medicine practitioner.

In addition, a semi-quantitative evaluation of all lesions detected was based on a standardized uptake value (SUV) calculation as follows:

SUV = [maximum lesion activity (kBq/ml tissue)/injected ^{18}F-FDG activity (kBq)/body mass in g]

MRI images were interpreted by a practitioner (I.D.) blinded to functional imaging results, tumor location and follow-up status. For follow-up examinations practitioners only knew the treatment that was applied. The five-point scoring system described above for ^{18}F-FDG PET/CT was also applied to MRI interpretation. For both ^{18}F-FDG PET/CT and MRI interpretation of local tumor extension to adjacent sites, 34 anatomical sites were defined from the lips to the subglottic region and lymph nodes were classified following the eight-region system proposed by the Sloan–Kettering Memorial (11).

2.5. Histopathology

Usual pathological techniques were used. The specimens were fixed in formalin, embedded in paraffin and hematoxylin–eosin sections were realized for checking the presence of squamous cell carcinoma in the tissues. No molecular markers or markers of proliferation were systematically used.

2.6. Data analysis

Pre-treatment and follow-up ^{18}F-FDG PET/CT and MRI findings were correlated with histopathological findings. Any suspicion of additional, residual or relapsing malignant mass (score of 2 or 3 on ^{18}F-FDG PET/CT or MRI) led to a biopsy for histological confirmation, except at 2 weeks post-radiotherapy if targeted physical examination only indicated local inflammation; in this case, biopsies were performed at 4 months if imaging at this later stage confirmed the suspicion. For data analysis, we considered separately each anatomical site (primary tumor location, adjacent extensions, lymph node regions). Imaging findings were considered true or false-positive as a function of the local histopathological findings obtained on biopsies or surgery, and as a function of the clinical follow-up (minimum 18 months). Diagnostic performances of ^{18}F-FDG PET/CT and MRI were compared by the McNemar test. SUV in malignant and benign sites were compared by unpaired *t*-test. *p*-Values less than 0.05 were considered significant. Receiver operator characteristics (ROC) curve analysis was performed to determine whether a SUV threshold could differentiate benign from malignant sites.

3. RESULTS

3.1. Clinical findings

Thirty-two patients, 23 men and nine women (mean age 59 years; age range: 40–76 years) were included in the study (Table 1). A total of 36 primary tumors were located as follows: 13 in the

Table 1. Patients characteristics

Patient (no., sex, age)	Tumor site	cTNM	Initial treatment
(1, F, 67)	Oropharynx	T3N0M0	RT
(2, F, 66)	Oropharynx	T2N0M0	RT
(3, M, 56)	Oropharynx	T2N0M0	RT
(4, F, 63)	Larynx	T2N0M0	RT
(5, M, 76)	Larynx	T1aN0M0	Surgery
(6, M, 60)	Hypopharynx	T4N0M0	Surgery
(7, M, 73)	Hypopharynx	T4N0M0	Surgery
(8, M, 42)	Hypopharynx	T4N0M0	Surgery + RT
(9, M, 58)	Oral cavity, oropharynx	T4N0M0, T2N0M0	RT + CT, RT + CT
(10, M, 55)	Oral cavity	T4N2cM0	RT + CT
(11, M, 56)	Oral cavity	T2N2bM0	Surgery + RT + CT
(12, M, 59)	Oral cavity	T2N0M0	Surgery
(13, M, 64)	Oral cavity	T4N0M1	RT + CT
(14, M, 67)	Oral cavity	T4N2bM0	RT + CT
(15, M, 54)	Oral cavity	T4N2bM0	RT + CT
(16, M, 75)	Larynx	T3N0M0	Surgery + RT
(17, F, 64)	Oropharynx	T2N1M0	RT
(18, M, 52)	Hypopharynx	T1N2bM0	Surgery + RT + CT
(19, M, 54)	Larynx	T3N0M0	Surgery + RT
(20, F, 56)	Oropharynx	T3N0M0	RT + CT
(21, M, 53)	Oropharynx	T3N2bM0	RT + CT
(22, M, 65)	Oropharynx	T2N2bM0	Surgery + RT + CT
(23, F, 63)	Larynx	T1N0M0	Surgery + RT
(24, M, 40)	Larynx	T4N1M0	Surgery + RT + CT
(25, M, 65)	Larynx	T1N0M0	Surgery + RT
(26, F, 48)	Oral cavity	T1N0M0	Surgery
(27, M, 56)	Oral cavity, oral cavity	T2N1M0, T2N1M0	Surgery + RT, surgery + RT + CT
(28, M, 51)	Oral cavity, oral cavity	T1N0M0, T1N0M0	RT, surgery + RT
(29, F, 58)	Oropharynx	T3N0M0	RT
(30, M, 48)	Oral cavity	T1N0M0	Surgery
(31, F, 63)	Larynx, oral cavity	T1N0M0, T2N0M0	RT + CT, RT + CT
(32, M, 60)	Larynx	T1N0M0	RT

RT, radiotherapy; CT, chemotherapy.

oral cavity, 10 in the oropharynx, four in the hypopharynx, and nine in the larynx. Initial therapeutic regimens were surgery ($n = 6$), radiotherapy ($n = 8$), surgery plus (chemo)radiotherapy ($n = 12$) and chemoradiotherapy ($n = 10$). After the follow-up period of 18 months, all patients were alive, 22 patients were considered free of disease and 10 patients were still in treatment for loco-regional recurrence or metastasis.

3.2. SUV thresholding

SUV values were statistically higher ($p < 0.01$) in malignant lesions (11.7 ± 5.0) than in benign post-treatment sites (4.1 ± 1.2), over 36 lesions evaluated in 32 patients on a total of 122 ^{18}F-FDG PET/CT. Based on these data a cut-off value of SUV set at 5.8 separated malignant and benign lesions with sensitivity and specificity of respectively 85 and 100%.

3.3. Pretreatment images

Primary malignant lesions were all detected by ^{18}F-FDG PET/CT and MRI, except for two limited vocal fold squamous cell carcinomas (T_1 in situ) undetected by both imaging modalities (sensitivity 94%). For the evaluation of the precise tumor local extension and the nodal staging (120 suspected sites histologically evaluated over 32 patients), sensitivity was significantly higher for MRI than for ^{18}F-FDG PET/CT, but at the cost of a higher rate of false-positive results, leading to a significantly lower positive predictive value of MRI (Fig. 1, Table 2). The lower sensitivity of ^{18}F-FDG PET/CT compared with MRI was essentially due to missed local extensions of tumors located either in the tongue (extending in the floor of the mouth) or in the floor of the mouth (extending in the tongue). Specificity and negative predictive value could not be calculated because all patients did not undergo neck dissection.

3.4. Post-treatment imaging evaluation

Few lesions were considered not interpretable (visual score = 4) on ^{18}F-FDG PET/CT ($n = 1$) and MRI ($n = 2$). The diagnostic performance of ^{18}F-FDG PET/CT for the detection of residual malignant tissue 2 weeks after radiation therapy is presented in Table 3 for the 26 patients who received this treatment (Figs. 2 and 3). Use of the SUV cut-off value of 5.8 led to a lower number of false-positive results than with the visual assessment that considered lesions with a score of 2 or 3 as malignant. For relapse detection at 4 and 12 months post-treatment, diagnostic

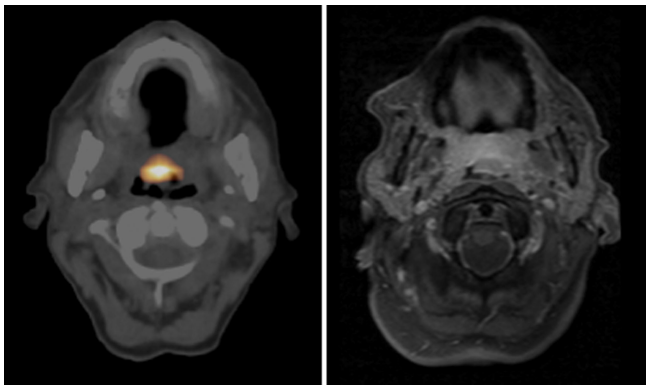

Figure 1. At initial staging of patient N°1, transaxial ^{18}F-FDG PET/CT images demonstrate a tumor limited to the soft palate (left). MRI images suggest bilateral extension to the palatine tonsils, not confirmed at pathology (right).

performance of ^{18}F-FDG PET/CT and MRI are presented in Tables 4 and 5 and illustrated in Fig. 4, showing that sensitivity was significantly higher for ^{18}F-FDG PET/CT than for MRI at 4 months ($p < 0.05$). No morbidity was encountered from the biopsy performed on the basis of the imaging results at 2 weeks, 4 months and 12 months.

4. DISCUSSION

While confirming the high accuracy of ^{18}F-FDG PET/CT for recurrence detection at 4 and 12 months after primary therapy of HNSCC, the present study indicates that this method is efficient to rule out the persistence of viable tumor residue as early as 2 weeks post-treatment. Detection of loco-regional recurrence is of paramount importance in HNSCC. Overall survival is indeed greatly influenced by neoplastic relapse in the treated region since distant metastases occur in only one-fifth of the patients (12). Great efforts are therefore made to control the disease in its primary location and the draining lymphatic system. Treatment of detected recurrence, when successful, improves the outcome and the clinical benefit of salvage therapy is largely recognized (1,13–24). Recurrent diseases amenable to surgical therapy have a better prognosis, indicating that early detection of the relapse is crucial in order to avoid distant extension of the infiltrative disease (1,23). Two questions then arise: how and when should we search for relapse? How to conduct follow-up is an issue because simple physical examination is obscured by the tissue changes and the anatomical modifications induced by the initial surgical and radiation therapies. Also, small residual lesions are often undetectable because they arise under the mucosa and some patients develop new positive lymph node or distant metastasis that require more extensive investigations to be detected. Imaging is therefore the obvious option for this follow-up but cost-effectiveness considerations impose recognition of the respective contributions of the most advanced imaging methods available. Continuous improvements in MRI equipments and acquisition protocols require periodic re-evaluation of its accuracy and, similarly, the emergence of hybrid ^{18}F-FDG PET/CT imaging outdates results obtained with 'PET alone' systems. A recent meta-analysis summarizes comparative evaluation of ^{18}F-FDG PET/CT, CT, MRI and physical examination, in the detection of nasopharyngeal carcinoma local recurrence (10). Based on a stringent selection of 21 articles published between 1990 and mid-2007, it shows that pooled sensitivity (95%) and specificity (90%) were higher than for CT and MRI. Slightly lower pooled sensitivity (89%) and specificity (74%) were found in a meta-analysis on ^{18}F-FDG PET performance for the detection of laryngeal carcinoma relapse (25). A recent study evaluated the value of ^{18}F-FDG PET/CT in patients with negative findings on conventional follow-up obtained at 12 months (no distant metastasis and no local recurrence). In this study on 91 consecutive patients, sensitivity and specificity of ^{18}F-FDG PET/CT for the diagnosis of HNSCC recurrence were 100 and 85%, respectively, with an overall accuracy of 90% (5). Our results at 12 months are very similar with a sensitivity of 100% and a specificity of 86%, despite the fact that our study design differed in the sense that comprehensive physical examination completed by biopsies was performed after imaging, precluding the exclusion of patients with clinical recurrence. Loss of sensitivity and specificity was minimal when ^{18}F-FDG PET/CT was advanced at 4 months, and at this time point sensitivity of MRI was significantly lower (70%).

Concerning the 'when' question about the imaging post-therapeutic follow-up of HNSCC, a balance should be found between two opposite tendencies: early follow-up will increase the odds of an efficient secondary therapy but it bears the risk of missing a minute residue overwhelmed by post-treatment tissue changes at their highest time point. Several recent studies have already indicated that the sensitivity of ^{18}F-FDG PET is such that ^{18}F-FDG PET imaging might be obtained as early as 1–2 months after therapy in order to program salvage surgery on restricted residue. Our study extends these results and indicates that an early ^{18}F-FDG PET/CT might be obtained 2 weeks post-radiotherapy without losing much of its value. High negative predictive value (97%) is the most important parameter since it defines the risk of deferring a potentially efficient early salvage surgery. The relatively poor positive predictive value (50% with SUV assessment) was predictable since the inflammatory reactions are abundant at this time point. The false positive rate might be reduced with a higher SUV cut-off value, but such a specific early time threshold could not be determined with the number of scans obtained at the 2-week time point. In any case, considering that the ^{18}F-FDG PET/CT results allows a precise, targeted, histological sampling of the suspected sites of recurrence, the risk brought by false positive ^{18}F-FDG PET/CT results related to inflammatory reactions is limited to the discomfort and morbidity of confirmatory biopsy procedures. What still needs to be determined is which patients might get the most significant benefit from such an early ^{18}F-FDG PET/CT imaging. Large and infiltrating tumors (T3–T4) in which complete resection represents a real challenge might require earlier detection of residue than smaller tumors. Also, tumors with high

Table 2. Anatomical precision of ^{18}F-FDG PET/CT and MRI for pretreatment assessment of tumor extension

	Sensitivity	Positive predictive value
^{18}F-FDG PET/CT	58% (54/93)	86% (54/63)
MRI	75% (69/92)	74% (69/93)
p-Value	<0.05	<0.05

Table 3. Diagnostic performance of ^{18}F-FDG PET/CT at 2 weeks post radiotherapy

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Visual assessment SUV assessment	86% (6/7) 86% (6/7)	71% (30/42) 85% (36/42)	33% (6/18) 50% (6/12)	97% (30/31) 97% (36/37)

proliferative activity are more likely to early produce macroscopic and symptomatic relapsing lesions and several studies have shown that early relapse is a factor of bad prognosis (13,21,23). Therefore, patients with very high FDG uptake at the presurgical staging PET examination and with high index of proliferation at histological examination should be considered for early ^{18}F-FDG PET/CT control and the differential benefit of early post-treatment ^{18}F-FDG PET/CT assessment should be tested in further studies (26,27). It remains to determine how earlier salvage therapy impacts on survival and disease-free interval in this type of patients, without significant increase in post-treatment side effects.

Our study also compared the value of ^{18}F-FDG PET/CT and MRI for primary staging of local tumor extension. This evaluation is of importance to estimate tumor operability and to plan the surgical procedure. Our comparison has some limitations because the image analysis procedure was not identical for the two modalities; the supervised image reading of the PET/CT was not applied for the MRI images, which were evaluated by a single experienced radiologist. Still, the comparison showed that ^{18}F-FDG PET/CT was less sensitive than MRI for the detection of this local anatomical extension (58 vs 75%) but its positive predictive value was higher because MRI suffered from a high number of false positive sites of extension (86 vs 74%). This result parallels those of a previous study that compared CT, MRI and ^{18}F-FDG PET for the evaluation of the tumor volume, and that showed an overestimation by MRI that might reach 30% (28). Of notice, we chose a low-dose-unenhanced CT imaging protocol that limits patient risk and discomfort. Sensitivity of PET/CT for the local anatomical extension might be higher with other CT protocols. Indeed, a recent study reports higher sensitivity for T and N status, which was similar for contrast-enhanced and unenhanced PET/CT (29). The benefit of contrast injection remains controversial since another recent study showed that contrast enhancement did not change T status but improved node detection by PET/CT in the initial staging of head and neck tumors (30). Improvement in PET/CT performance for HNSCC recurrence detection might come from the use of new tracers. The main problem with early ^{18}F-FDG PET/CT evaluations in this context is the deficient specificity of the method due to tracer uptake in inflammatory cells. Use of amino-acid tracers has been proposed to circumvent this problem but the intense uptake of these tracers in the salivary glands might be a new source of false-positive findings (31,32).

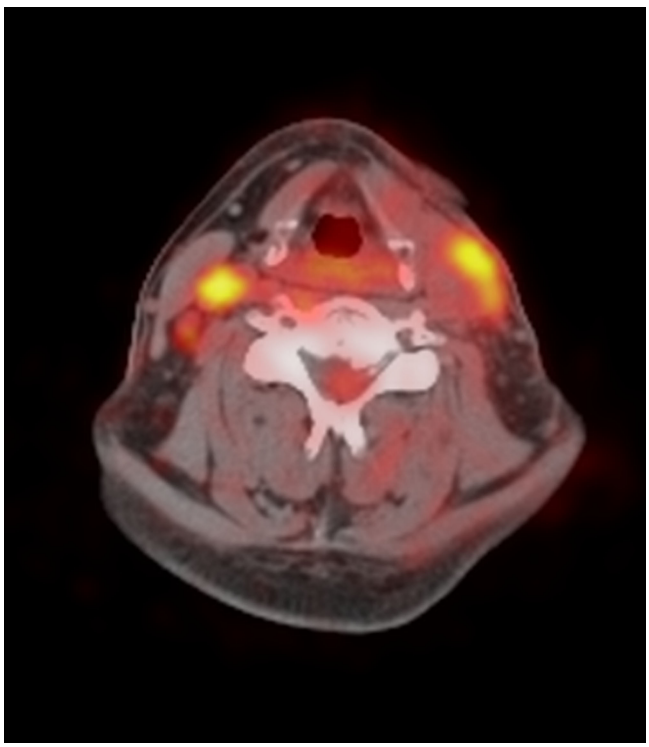

Figure 2. Two weeks post-radiotherapy in patient 11, transaxial ^{18}F-FDG PET/CT images demonstrate the apparition of a right jugular adenopathy; on the left side, a muscular FDG uptake is well characterized thanks to the PET/CT fusion.

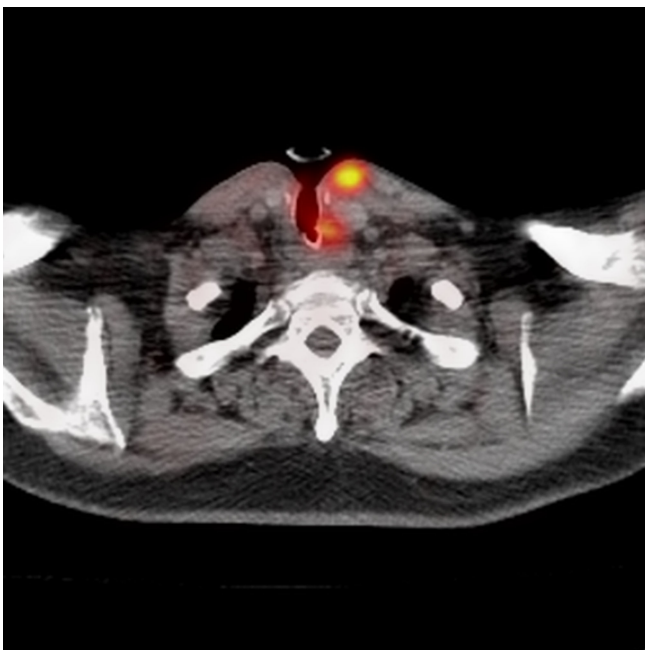

Figure 3. Two weeks post-radiotherapy in patient 24, transaxial ^{18}F-FDG PET/CT images demonstrate viable tumor tissue left to the tracheostomy, in a patient with tissue changes induced by initial laryngectomy followed by chemo-radiotherapy.

Table 4. Diagnostic performance of ^{18}F-FDG PET/CT and MRI at 4 months

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
^{18}F-FDG PET/CT Visual assessment	92%* (11/12)	81% (38/47)	55% (11/20)	98% (38/39)
^{18}F-FDG PET/CT SUV assessment	92%* (11/12)	87% (41/47)	64% (11/17)	98% (41/42)
MRI	70%* (12/17)	74% (46/62)	43% (12/28)	90% (46/51)

*$p < 0.05$.

Table 5. Diagnostic performance of ^{18}F-FDG PET/CT and MRI at 12 months

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
^{18}F-FDG PET/CT Visual assessment	100% (3/3)	86% (49/57)	27% (3/11)	100% (49/49)
^{18}F-FDG PET/CT SUV assessment	100% (3/3)	86% (49/57)	27% (3/11)	100% (49/49)
MRI	75% (3/4)	85% (50/59)	25% (3/12)	98% (50/51)

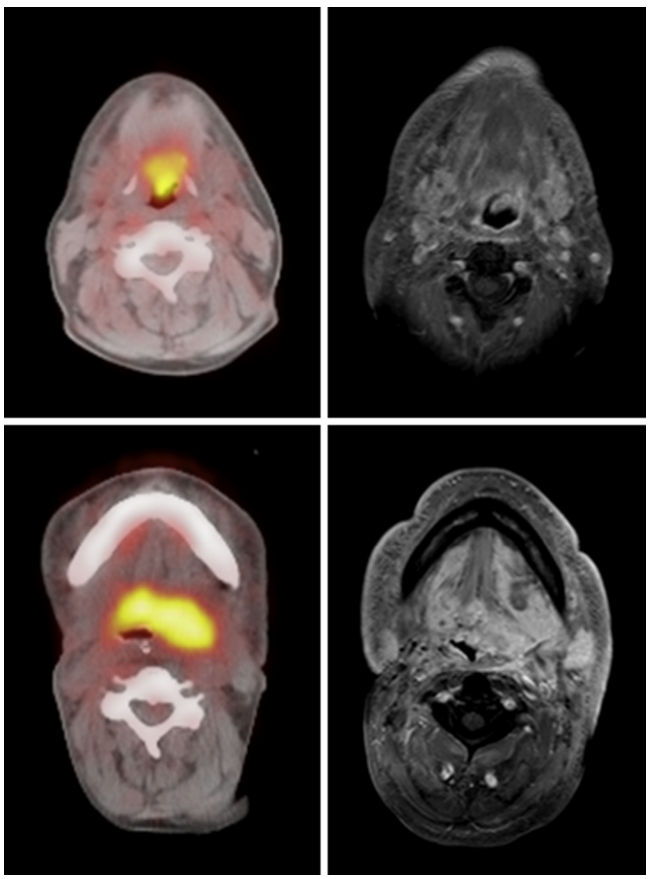

Figure 4. Four months post-radio-chemotherapy in patient 20, transaxial ^{18}F-FDG PET/CT images demonstrate tumor recurrence in the vallecula and epiglottis (left upper) while MRI remains inconclusive (right upper). Recurrence is treated by laryngectomy and, 12 months later, transaxial ^{18}F-FDG PET/CT images demonstrate a large submucosal tumor recurrence undetected at clinical examination (lower left), also detected on the MRI images (lower right).

The PET tracer 3′-deoxy-3′-(18)F-fluorothymidine (FLT) is a tracer proposed for treatment evaluation after radio- and chemotherapy, but it does not seem to solve the problem of specificity raised with FDG, in particular for the differentiation of metastatic and inflammatory lymph nodes in HSCC patients (33,34).

5. CONCLUSION

This study, based on a small number of patients, suggests that ^{18}F-FDG PET/CT might be effective to rule out the presence of residual tumor as early as 2 weeks after treatment of a primary HNSCC. For follow-up, accuracy of ^{18}F-FDG PET/CT and MRI are similar except for a higher sensitivity of ^{18}F-FDG PET/CT at 4 months. We consider that these promising results deserve confirmation in a larger clinical trial.

Acknowledgements

This work was funded by the FRS-FNRS and National Lottery – Belgium.

References

1. Yom SS, Machtay M, Biel MA, Sinard RJ, El-Naggar AK, Weber RS, Rosenthal DI. Survival impact of planned restaging and early surgical salvage following definitive chemoradiation for locally advanced squamous cell carcinomas of the oropharynx and hypopharynx. Am J Clin Oncol 2005; 28: 385–392.
2. Gordin A, Golz A, Keidar Z, Daitzchman M, Bar-Shalom R, Israel O. The role of FDG-PET/CT imaging in head and neck malignant conditions: impact on diagnostic accuracy and patient care. Otolaryngol Head Neck Surg 2007; 137: 130–137.
3. Jeong HS, Baek CH, Son YI, Ki Chung M, Kyung Lee D, Young Choi J, Kim BT, Kim HJ. Use of integrated 18F-FDG PET/CT to improve the accuracy of initial cervical nodal evaluation in patients with head and neck squamous cell carcinoma. Head Neck 2007; 29: 203–210.

4. Wong RJ. Current status of FDG-PET for head and neck cancer. J Surg Oncol 2008; 97: 649–652.
5. Abgral R, Querellou S, Potard G, Le Roux PY, Le Duc-Pennec A, Marianovski R, Pradier O, Bizais Y, Kraeber-Bodéré F, Salaun PY. Does 18F-FDG PET/CT improve the detection of posttreatment recurrence of head and neck squamous cell carcinoma in patients negative for disease on clinical follow-up? J Nucl Med 2009; 50: 24–29.
6. Kao J, Vu HL, Genden EM, Mocherla B, Park EE, Packer S, Som PM, Kostakoglu L. The diagnostic and prognostic utility of positron emission tomography/computed tomography-based follow-up after radiotherapy for head and neck cancer. Cancer 2009; 115: 4586–4594.
7. Goerres GW, Schmid DT, Bandhauer F, Huguenin PU, von Schulthess GK, Schmid S, Stoeckli SJ. Positron emission tomography in the early follow-up of advanced head and neck cancer. Arch Otolaryngol Head Neck Surg 2004; 130: 105–109; discussion 120–101.
8. Kim SY, Lee SW, Nam SY, Im KC, Kim JS, Oh SJ, Ahn SD, Shin SS, Choi EK, Kim JH. The Feasibility of 18F-FDG PET scans 1 month after completing radiotherapy of squamous cell carcinoma of the head and neck. J Nucl Med 2007; 48: 373–378.
9. Nam SY, Lee SW, Im KC, Kim JS, Kim SY, Choi SH, Ryu JS, Moon DH, Oh SJ, Yi BY, Kim JH, Ahn SD, SHin SS, Kim SB, Choi EK, Lee BJ. Early evaluation of the response to radiotherapy of patients with squamous cell carcinoma of the head and neck using 18FDG-PET. Oral Oncol 2005; 41: 390–395.
10. Liu T, Xu W, Yan WL, Ye M, Bai YR, Huang G. FDG-PET, CT, MRI for diagnosis of local residual or recurrent nasopharyngeal carcinoma, which one is the best? A systematic review. Radiother Oncol 2007; 85: 327–335.
11. Shah JP, Strong E, Spiro RH, Vikram B. Surgical grand rounds. Neck dissection: current status and future possibilities. Clin Bull 1981; 11: 25–33.
12. Leung TW, Tung SY, Sze WK, Wong FC, Yuen KK, Lui CM, Lo SH, Ng TY, O SK. Treatment results of 1070 patients with nasopharyngeal carcinoma: an analysis of survival and failure patterns. Head Neck 2005; 27: 555–565.
13. Agra IM, Carvalho AL, Ulbrich FS, de Campos OD, Martins EP, Magrin J, Kowalski LP. Prognostic factors in salvage surgery for recurrent oral and oropharyngeal cancer. Head Neck 2006; 28: 107–113.
14. Chopra S, Gupta T, Agarwal JP, Budrukkar A, Ghosh-Laskar S, Dinshaw K. Re-irradiation in the management of isolated neck recurrences: current status and recommendations. Radiother Oncol 2006; 81: 1–8.
15. Ganly I, Patel SG, Matsuo J, Singh B, Kraus DH, Boyle JO, Wong RJ, Shaha AR, Lee N, Shah JP. Results of surgical salvage after failure of definitive radiation therapy for early-stage squamous cell carcinoma of the glottic larynx. Arch Otolaryngol Head Neck Surg 2006; 132: 59–66.
16. Jeong WJ, Jung YH, Kwon SK, Hah JH, Kwon TK, Sung MW, Kim KH. Role of surgical salvage for regional recurrence in laryngeal cancer. Laryngoscope 2007; 117: 74–77.
17. Koo BS, Lim YC, Lee JS, Choi EC. Recurrence and salvage treatment of squamous cell carcinoma of the oral cavity. Oral Oncol 2006; 42: 789–794.
18. Kupferman ME, Morrison WH, Santillan AA, Roberts D, Diaz EM Jr, Garden AS, Weber R. The role of interstitial brachytherapy with salvage surgery for the management of recurrent head and neck cancers. Cancer 2007; 109: 2052–2057.
19. Langendijk JA, Bourhis J. Reirradiation in squamous cell head and neck cancer: recent developments and future directions. Curr Opin Oncol 2007; 19: 202–209.
20. Li P, Zhuang H, Mozley PD, Denittis A, Yeh D, Machtay M, Smith R, Alavi A. Evaluation of recurrent squamous cell carcinoma of the head and neck with FDG positron emission tomography. Clin Nucl Med 2001; 26: 131–135.
21. Liao CT, Chang JT, Wang HM, Ng SH, Hsueh C, Lee LY, Lin CH, Chen IH, Huang SF, Cheng AJ, Yen TC. Salvage therapy in relapsed squamous cell carcinoma of the oral cavity: how and when? Cancer 2008; 112: 94–103.
22. Ord RA, Kolokythas A, Reynolds MA. Surgical salvage for local and regional recurrence in oral cancer. J Oral Maxillofac Surg 2006; 64: 1409–1414.
23. Schwartz GJ, Mehta RH, Wenig BL, Shaligram C, Portugal LG. Salvage treatment for recurrent squamous cell carcinoma of the oral cavity. Head Neck 2000; 22: 34–41.
24. Studer G, Graetz KW, Glanzmann C. Outcome in recurrent head neck cancer treated with salvage-IMRT. Radiat Oncol 2008; 3: 43.
25. Brouwer J, Hooft L, Hoekstra OS, Riphagen II, Castelijns JA, de Bree R, Leemans CR. Systematic review: accuracy of imaging tests in the diagnosis of recurrent laryngeal carcinoma after radiotherapy. Head Neck 2008; 30: 889–897.
26. Haberkorn U, Strauss LG, Reisser C, Haag D, Dimitrakopoulou A, Ziegler S, Reisser C, Doll J, Helus F, van Kaick G. Glucose uptake, perfusion, and cell proliferation in head and neck tumors: relation of positron emission tomography to flow cytometry. J Nucl Med 1991; 32: 1548–1555.
27. Jacob R, Welkoborsky HJ, Mann WJ, Jauch M, Amedee R. [Fluorine-18]fluorodeoxyglucose positron emission tomography, DNA ploidy and growth fraction in squamous-cell carcinomas of the head and neck. J Otorhinolaryngol Relat Spec 2001; 63: 307–313.
28. Daisne JF, Duprez T, Weynand B, Lonneux M, Hamoir M, Reychler H, Grégoire V. Tumor volume in pharyngolaryngeal squamous cell carcinoma: comparison at CT, MR imaging, and FDG PET and validation with surgical specimen. Radiology 2004; 233: 93–100.
29. Yoshida K, Suzuki A, Nagashima T, Lee J, Horiuchi C, Tsukuda M, Inoue T. Staging primary head and neck cancers with 18F-FDG PET/CT: is intravenous contrast administration really necessary ? Eur J Nucl Med Mol Imag 2009; 36: 1417–1424.
30. Rodrigues RS, Bozza FA, Christian PE, Hoffman JM, Butterfield RI, Christensen CR, Heilbrun M, Wiggins RH 3rd, Hunt JP, Bentz BG, Hitchcock YJ, Morton KA. Comparison of whole-body PET/CT dedicated high-resolution head and neck PET/CT, and contrast-enhanced CT in preoperative staging of clinically M0 squamous cell carcinoma of the head and neck. J Nucl Med 2009; 50: 1205–1213.
31. Krabbe CA, van der Werff-Regelink G, Pruim J, van der Wal JE, and Roodenburg JL. Detection of cervical metastases with (11)C-tyrosine PET in patients with squamous carcinoma of the oral cavity or oropharynx: a comparison with (18)F-FDG PET. Head Neck 2010; 32: 368–374.
32. Sutinen E, Jyrkkio S, Alanen K, Nagren K, Minn H. Uptake of [N-methyl- 11C]alpha-methylaminoisobutyric acid in untreated head and neck cancer studied by PET. Eur J Nucl Med Mol Imag 2003; 30: 72–77.
33. Troost EG, Bussink J, Hoffmann AL, Boerman OC, Oyen WJ, Kaanders JH. 18F-FLT PET/CT for early response monitoring and dose escalation in oropharyngeal tumors. J Nucl Med 2010; 51: 866–874.
34. Troost EG, Vogel WV, Merkx MA, Slootweg PJ, Marres HA, Peeters WJ, Bussink J, van der Kogel AJ, Oyen WJ, Kaanders JH. 18F-FLT PET does not discriminate between reactive and metastatic lymph nodes in primary head and neck cancer patients. J Nucl Med 2007; 48: 726–735.