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Effectiveness of PET/CT with ^{18}F-fluorothymidine in the staging of patients with squamous cell head and neck carcinomas before radiotherapy

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ABSTRACT

Aim: The aim of our study was to compare the staging of the disease declared before anticancer treatment was begun with the staging that was found after the planning PET/CT scanning with ^{18}F-FLT was performed.

Background: PET/CT in radiotherapy planning of head and neck cancers can facilitate the contouring of the primary tumour and the definition of metastatic lymph nodes.

Materials and methods: Between November 2010 and November 2013, 26 patients suffering from head and neck carcinomas underwent planning PET/CT examination with ^{18}F-FLT. We compared the staging of the disease and the treatment strategy declared before and after ^{18}F-FLT-PET/CT was performed.

Results: The findings from ^{18}FLT-PET/CT led in 22 patients to a change of staging: in 19 patients it led to upstaging of the disease and in 3 patients it led to downstaging of the disease. In one patient, a secondary malignancy was found.

Conclusions: We have confirmed in this study that the use of ^{18}F-FLT-PET/CT scanning in radiotherapy planning of squamous cell head and neck carcinomas has a great potential in the precise evaluation of disease staging and consequently in the precise determination of target volumes.

1. Background

Radiotherapy has an important role to play in the treatment of locally and locoregionally advanced head and neck carcinomas, with or without concomitant chemotherapy. Using intensity modulated radiotherapy (IMRT), which is used more and more in routine practice, it is possible to achieve much better conformity in dose distribution than using standard 3D conformal radiotherapy (3D CRT). In the treatment of head and neck carcinomas, this technique allows the delivery of high doses to target volumes with better sparing of

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proximal organs at risk (spinal cord, parotid glands and swallowing structures).[1,2] Considering the high conformity of dose distribution and a steep dose gradient, both resulting from the use of the IMRT technique, it is very important to know the precise location and the exact boundaries of the primary tumour and metastatic lymph nodes. Positron emission tomography (PET) provides the biological information about the tumour that is complementary to the anatomical information obtained through computed tomography (CT) scanning. Thus, the combination of PET and CT scanning can significantly facilitate the contouring of the primary tumour as well as the definition of metastatic lymph nodes during radiotherapy planning of head and neck carcinomas.[3] Initial studies with the most commonly used radiopharmaceutical, ^{18}F-flurodeoxyglucose (^{18}F-FDG), showed that volumes irradiated at high doses can be reduced with consequent sparing of neighbouring organs at risk and that higher doses may thus be delivered to the target volume.[4–6]

The major limitations of PET/CT examination with ^{18}F-FDG are false-positive findings due to the accumulation of this radiopharmaceutical in inflammatory changed tissues or in reactively changed lymph nodes.[3] Unlike F-FDG, 3′-deoxy-3′-^{18}F-fluorothymidine (^{18}F-FLT), is a radiopharmaceutical that reflects DNA synthesis and is not as influenced by peritumourous inflammatory changes.[7] Inasmuch as squamous cell carcinomas of the head and neck show relatively intense accumulation of ^{18}F-FLT,[8] we decided to exploit PET/CT scanning with ^{18}F-FLT for radiotherapy planning of these tumours.

2. Aim

The aim of our representative study was to compare the staging of the disease declared before anticancer treatment was begun with the staging that was found after the planning PET/CT scanning with ^{18}F-FLT was performed. Furthermore, we investigated the impact of possible changes in the staging on the treatment strategy. To the best of our knowledge, no study has been published investigating radiotherapy planning of head and neck carcinomas using ^{18}F-FLT-PET/CT scanning.

3. Materials and methods

3.1. *Patients*

Between November 2010 and November 2013, 26 patients (24 men and 2 women, with a median age of 61, see details in Table 1) suffering from histologically proven squamous cell carcinoma of the head and neck referred for radical or adjuvant radiotherapy – either as a single method or in combination with concomitant chemotherapy – took part in our study. At the time of planning investigation, all patients were without proven distant metastatic spread (TNM category – M0). They were conventionally radiologically staged with the use of neck ultrasound and chest X-ray examination. All patients signed an informed consent.

Table 1 – Patients and disease characteristics.

All patients ($n = 26$)	
Sex	
Male	24 (92.3%)
Female	2 (7.7%)
Age at the time of diagnosis (median, range)	61 (46–82)
Histology	
Squamous cell carcinoma	26 (100%)
Grading	
G1	6 (23.1%)
G2	18 (69.3%)
G3	1 (3.8%)
G4	1 (3.8%)
Locality	
Oropharynx	11 (42.4%)
Hypopharynx	2 (7.7%)
Larynx	5 (19.2%)
Base of mouth	5 (19.2%)
Tongue	2 (7.7%)
Paranasal sinuses	1 (3.8%)
Radiotherapy purpose without the informations from ^{18}FLT-PET/CT	
Radical	20 (76.9%)
Adjuvant	6 (23.1%)
Radiotherapy purpose with the informations from ^{18}FLT-PET/CT	
Radical	18 (69.3%)
Adjuvant	1 (3.8%)
Palliative	6 (23.1%)
No radiotherapy indicated	1 (3.8%)

3.2. *Radiotherapy simulation and image acquisition*

All patients underwent initial preparation at the Department of Oncology and Radiotherapy, University Hospital in Pilsen according to our institutional standards, i.e. the choice of proper positioning (supine position with arms along the body) and immobilization using a customized thermoplastic mask by Efficast® (Orfit, Wijnegem, Belgium) for the head, neck and shoulders, determination of the reference plane on an X-ray simulator and drawing the projection points of the simulated isocentre on the mask. Planning PET/CT examination with ^{18}F-FLT was carried out at the Department of Imaging Methods at the same hospital and in the same manner as routine diagnostic examinations, the only difference being that patients were positioned in radiotherapy positions with dedicated immobilization devices ensuring the same position as during their initial examination on an X-ray simulator. The concavity of the examination table was compensated for with a radiolucent hand-made board. Patients were placed into the required position with the help of a laser positioning system, the projection points on the skin were marked with radiopaque marks.

PET scans were performed 70–80 min after intravenous administration of ^{18}F-FLT with a radioactivity level of about 80 MBq. CT scans were performed focusing on the head, neck and lungs on a Biograph HiRez/16 slice (Siemens, Forcheim, Germany) after intravenous administration of 80 ml of a non-ionic iodine contrast agent. CT scans were performed during inhalation; during PET acquisition the patient was instructed to breathe slowly and shallowly. CT and PET scans were then exported to our PlanW treatment planning system.