

## Head and neck

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### Management of cervical lymph node metastases from unknown primary tumours – Results from a Danish national survey

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The management of patients with cervical lymph node metastases from unknown primary tumours is a major challenge in oncology. This study presents data collected from all five oncology centres in Denmark. Of the 352 consecutive patients with squamous cell or undifferentiated tumours seen from 1975 to 1995, a total of 277 (79%) were treated with radical intent. The general treatment policy at all centres during the entire study period has been to treat all suitable candidates with radiotherapy to both sides of the neck and include elective irradiation of the mucosal sites in nasopharynx, oropharynx, hypopharynx and larynx (81%). Irradiation of the ipsilateral neck only was done in 26 patients (10%). Radical surgery alone, either lymph node excision or modified radical neck dissection was done in 23 N1–N2 patients (9%). The 5-year estimates of neck control, disease-free survival and overall survival for radically treated patients were 51%, 48% and 36%, respectively. The emergence of the occult primary was observed in 66 patients (19%). About half of the emerging primaries were within the head and neck region with oropharynx, hypopharynx and oral cavity being the most common sites. Emerging primaries outside the head and neck region were primarily located in the lung (19 patients) and oesophagus (5 patients). The frequency of emerging primary in the head and neck was significantly higher in patients not treated with radiotherapy compared to surgery alone, the actuarial risks at 5-year being 54±11% (no RT) vs. 15±3% (with RT),  $p < 0.0001$ . The most important factor for neck control was nodal stage (5-year estimates 69% (N1) 58% (N2) and 30% (N3)). Other important parameters for neck control and disease-specific survival included haemoglobin, gender and overall treatment time. Patients treated with ipsilateral radiotherapy had a relative risk of recurrence in the head and neck region of 1.9 compared to patients treated to both neck and mucosa. At five years, the estimated control rates were 27% (ipsilateral) and 51% (bilateral;  $p = 0.05$ ). The 5-year disease-free survival estimates were 28% and 45%, respectively ( $p = 0.10$ ). In conclusion, this study has confirmed that patients with neck node metastases from occult head and neck cancer have clinical features and prognosis similar to other head and neck malignancies. Extensive irradiation to both sides of the neck and the mucosa in the entire pharyngeal axis and larynx resulted in significantly less loco-regional failures compared to patients treated with ipsilateral techniques, but only a trend towards better survival. A prospective randomised trial is required to determine the optimal strategy in terms of loco-regional control, survival and morbidity.

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### 18f-FDG PET is a sensitive tool for the detection of the occult primary cancer (CUP-syndrome) with head and neck lymph node manifestation

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**Background:** The neck lymph nodes are a common site of metastases from carcinomas of unknown primary (CUP syndrome). 2[18F]-fluoro-2-deoxy-D-glucose – Positron Emission Tomography (18-FDG-PET) has been shown to be a sensitive tool for detecting primary malignant lesions as well as metastatic spread. We have prospectively investigated the sensitivity of 18-FDG-PET in detecting occult primary carcinomas with manifestation in the head and neck lymph nodes.

**Methods:** From 5/94 until 7/98, in 723 patients a cancer of the head and neck was diagnosed at the Department of Otorhinolaryngology, Head and Neck Surgery of the University of Cologne. The routinely performed staging procedures were chest radiography, full blood count, cervical and liver ultrasound, endoscopy of the naso-, oro-, and hypopharynx, the larynx

and the esophagus, and laboratory analyses. After the staging work-up, in 27/723 patients (3.7%) a CUP syndrome had to be presumed the primary cancer not being detected.

In these patients 18-FDG-PET was performed on a Siemens Ecat Exact 921 PET Scan with 370 MBq 18-FDG; images were reconstructed using a transmission – emission fusion technique.

**Results:** In 7/27 patients (26%) 18-FDG-PET revealed an unknown primary: in 2 patients a bronchial carcinoma, in 2 patients a nasopharyngeal carcinoma, in 1 patient a squamous cell carcinoma (SCC) of the parotid gland, in 1 patient a SCC of the hypopharynx and in one patient a carcinoma of the tonsil. In 4/7 patients the occult primary tumor was removed surgically. In a total of 8/27 patients therapeutic strategy was changed due to the 18-FDG-PET findings.

**Conclusion:** 18-FDG-PET should be performed in all patients suffering from a CUP syndrome after conventional diagnostic work-up fails to identify the primary.

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### FDG-positron-emission-tomography as a diagnostic tool in radiation treatment planning of head and neck tumors

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**Purpose:** An individualized radiation treatment planning requires an exact definition of local tumor spread. Despite of high reliability of methods like CT, sono-graphy and MRI the correct diagnosis of lymphonodal tumor infiltration is often difficult. In a prospective trial, we examined whether an additional FDG-PET gives a relevant gain of information for radiation treatment planning.

**Patients and Methods:** We studied data of 34 patients with histologically confirmed squamous cell carcinoma of the head and neck who received a FDG-PET additionally to conventional staging procedures. The extent of changes of treatment strategy or target volume due to FDG-PET findings were analysed.

**Results:** In 41% of patients with primary tumors and in 58% of patients with recurrent disease FDG-PET detected additional tumor manifestations. In all cases changes of treatment strategy or target volume were necessary. Regarding patients with primary tumors the percentage of treatment modifications was highest in patients with large tumors (T3 and T4) (58%) and patients with advanced lymph node involvement (N2 and N3) (46%).

**Conclusions:** FDG-PET is able to give clinically relevant information compared to conventional staging procedures especially in patients with high risk of lymphonodal tumor spread. Therefore in patients with recurrent disease and patients with advanced tumor stages FDG-PET study prior to radiotherapy planning should be considered.

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### Is repopulation of the tumour cells during radiotherapy doubled during treatment gaps?

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The aim of this work is to analyse the proliferation of tumour cells in treatment gap during the radiotherapy for head and neck cancer.

**Materials and Methods:** Clinical material is based on the records of 1350 patients treated by radiotherapy alone in Maria Skłodowska-Curie Memorial Institute in Gliwice during the period 1980–89. All patients had histologically confirmed SCC of larynx or pharynx. The mean gap duration was 9 days, only 10% of patients were treated without gaps. The dose per fraction was in range of 1.5 to 2.5 Gy.

Patient data were fitted directly to the mixed linear quadratic model using maximum-likelihood estimation. Tumour proliferation was assumed to be  $\exp(\lambda \cdot \text{gap\_duration})$  and additionally  $\exp(\lambda \cdot \text{gap\_duration})$  for days with treatment gap. Tumour stage or tumour localisation were introduced to equation as categorical variables.

**Results:** TCP was significantly correlated with dose of radiation, tumour progression (according to TNM), overall treatment time, and gap duration. Laryngeal cancers had better prognosis than cancers of oro- and nasopharynx.

Our model was significantly improved when the duration of the gap was introduced even in the presence of overall treatment time already in the