

PhD thesis defence of F. J. P. Hoebbers

"Prognostic factors and predictive tests in the treatment of head and neck squamous cell carcinoma"

November 8th 2007, 12:00 h
University of Amsterdam

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The treatment of head and neck cancer has changed during the last decades from single modality treatment into combined modality treatment for a large number of patients, including surgery with radiotherapy and/or chemotherapy. This has improved outcome, but also toxicity. Therefore, proper selection of patients for treatment options available is warranted.

In this thesis, a number of studies are presented that aimed at applying or developing prognostic and predictive tests in order to be able to improve the (future) selection of patients for the appropriate treatment.

In the first series of investigations, the predictive value of the formation of cisplatin-DNA adducts was studied in tumor biopsies and normal tissue in patients treated with concurrent chemoradiation. It was shown that higher intra-tumoral cisplatin-DNA adducts appeared to be associated with improved disease free survival.

Unfortunately, no correlation was observed between adducts in normal tissue and tumor, suggesting that easy obtainable normal tissue samples (like white blood cells) can not be used as surrogate markers for tumor. Therefore, at present, the data concerning the use of cisplatin-DNA adducts as predictive assay can not be regarded as conclusive.

In patients treated with concurrent chemoradiation with daily low dose cisplatin, we demonstrated that primary tumor-volume derived from pre-treatment MRI-scan was an independent prognostic factor for locoregional control and disease-free survival. Therefore, tumor volume may guide treatment-selection in addition to the standard staging-criteria like TNM-system.

Hypoxia is an important factor in head and neck cancer with a negative impact on treatment outcome. We demonstrated that in-vivo detection of intra-tumoral hypoxia by a radioactive-labeled hypoxia-marker BRU 59-21 showed an association with another established hypoxia-marker, pimonidazole, on tumor tissue sections suggesting that this in-vivo marker could be used for non-invasive detection of hypoxia.

Apoptosis is a process of programmed cell death in response to cytotoxic therapies, which can be visualized by non-invasive, in-vivo imaging using Annexin-scintigraphy. In previous studies in lymphoma, Annexin-uptake correlated with response. However, in head and neck cancer, no association could be established between Annexin-uptake and treatment outcome, probably due to the presence of necrosis in these advanced head and neck cancers.