Quantitative Tissue Perfusion Measurements in Head and Neck Carcinoma Patients before and during Radiation Therapy with a non-invasive MR Imaging Spin-Labeling Technique

P. Schmitt1, M. Kotas1, M. Flentje1, A. Haase1
1University of Würzburg, Würzburg, Germany

Synopsis
A non-invasive MR spin-labeling technique was evaluated at 2T for measuring perfusion in head and neck carcinoma patients. Eleven patients were investigated, five were examined twice during radiotherapy. For perfusion quantification, T1 was measured with IR-Snapshot-FLASH imaging after both slice-selective and non-selective inversion. Perfusion maps were obtained employing a two-compartment-model. In-plane resolution was (1.9x2.8)mm², scan time was 8:30min. Tumor perfusion and perfusion changes during therapy were heterogenous. In 4/5 patients, perfusion decreased, in one patient it increased. Without the need for exogeneous contrast agent, repetitive characterization of perfusion is possible. This may be very useful for stratification of vasomodulating treatments.

Introduction
Tumor tissue perfusion and oxygen supply substantially influence the responsiveness of tumors to therapy. Tumor hypoxia has been the target of several approaches which aim to modify tumor perfusion and oxygenation. Thus, non-invasive methods for repetitive evaluation of tumor perfusion as a predictive factor for treatment response may be of high clinical value.

Methods
A total of 11 patients with histologically proven head and neck carcinoma and/or lymphatic node metastases were investigated. Five patients were examined twice: once at the beginning of primary radiation therapy and once again after at least 54Gy. Explicit care was taken in the second examination to reproduce the slice position of the first examination. All experiments were performed on a 2T whole body scanner. For measuring perfusion, two series of 16 IR-Snapshot-FLASH images were acquired after slice-selective and after non-selective spin inversion, respectively. Imaging parameters were TE=13.3 ms, TR=25.9ms, flip angle=6°, slice thickness=10mm, in-plane resolution=(1.9x2.8)mm², NA=6, total scan time=8:30min. The two longitudinal relaxation time maps for T1sel and T1glob were calculated by a pixelwise 3 parameter exponential fit and subsequent correction for the influence of the continuously applied RF pulses [1]. For determination of tissue perfusion a a two-compartment tissue model was employed [2]. Thresholds were used to eliminate artifacts arising from bulk motion. Pixels in which the difference between T1glob and T1sel exceeded 150ms and/or pixels showing negative or unphysiologically high perfusion values of P>150ml/100g/min were not considered during further postprocessing. For data evaluation the distribution of perfusion values within the tumor region was visualized in cumulative histograms.

Results
In Fig1 representative data is provided showing a squamous cell carcinoma located at the paranasal sinus. The extent of the lesion can be seen from the reference image (a). The corresponding perfusion map shows a large asymmetrically located hyperperfused region (b). The percentage of pixels with low perfusion P<5ml/100g/min is less than 20%, as can be seen from the cumulative histogram (c). In our study, considerable intratumoral heterogeneity in perfusion and also marked differences between the studied patients were observed. In 4/10 patients a visual difference between a better perfused periphery and a central core was found. This characteristic was not seen in the remaining patients. In 4/5 patients studied twice, a decrease of tumor perfusion after total radiation doses >54 Gy was seen, while one patient showed increased perfusion in the tumor center.

Discussion
In four patients a decreased tumor perfusion was measured in the second examination, in one patient a perfusion increase was seen, what may be explained with local reperfusion due to the considerable size reduction of the initially large, but moderately responding tumor. Similar observations are reported from a dynamic CE-MRI study on cervical carcinoma, where parameters indicating lowered perfusion were measured as a general trend after therapy [3]. In our study, tumors with high initial perfusion tended to be smaller in size and to show better response to radiotherapy than those with weak pretreatment perfusion. This trend was also reported from a dynamic CT perfusion study on head and neck tumor patients [4]. However, to date, the number of investigated cases is too small to allow for clinical correlations. The potential of vasomodulating agents to improve tumor blood flow and oxygenation and, thus, radiosensitivity, were validated in animal models. Yet clinical trials have not been able to prove significant improvement in clinical outcome for unselected groups of patients [5]. In that context, a non-invasive technique for repetitive perfusion measurements may be useful to select patients that show response to vasodilators and may benefit from an according individualized therapy.

Acknowledgements
IZKF Würzburg, Project F5

References