Regional salivary gland function after radiotherapy of head and neck cancer measured by dynamic ^{11}C-methionine PET

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ABSTRACT

Loss of salivary gland function is a common and disturbing side-effect of radiotherapy of head and neck cancer patients. New radiotherapy techniques enable improved tumour irradiation and provide means for sparing salivary gland function. Optimised strategies for sparing salivary gland function during radiotherapy require insight of the dose-response relationship of salivary glands. ^{11}C-methionine positron emission tomography (PET) has potential for measuring regional loss of salivary gland function after radiotherapy, relevant for studying the dose-response relationship. The aim of the project was to establish a PET method for measuring regional salivary gland function and use this method for evaluating the individual radiation dose-response of salivary glands in head and neck cancer patients.

The project was based on animal studies of rat and clinical studies of head and neck cancer patients. In the animal studies, samples of parotid gland tissue and liver tissue were obtained in 29 rats at various time points following intravenous injection of ^{11}C-methionine. In rat parotid gland, ^{11}C-protein constituted half of the total ^{11}C-radioactivity after 12 min and reached a level of 80%. In rat liver, ^{11}C-protein constituted half of the total ^{11}C-radioactivity after 4 min and approached 100% with time. Non-protein ^{11}C-metabolites reached a level of 2-18% in parotid gland. In liver, non-protein ^{11}C-metabolites reached a peak of 25%.

In the clinical studies, 17 patients were examined by dynamic ^{11}C-methionine PET of the major salivary glands. PET data was analysed using a kinetic model of salivary gland ^{11}C-methionine metabolism, as suggested from the animal studies. Voxel-wise images of the kinetic parameter κ (net metabolic clearance of ^{11}C-methionine) were generated, co-registered and compared with the radiation dose plan in the major salivary glands. κ of parotid and submandibular glands was reduced dependent on the radiation dose. In a subgroup of 12 patients that received a heterogeneous radiation dose in the parotid glands, regional dose and κ was compared voxel-by-voxel for examining the individual dose-response relationship of parotid glands. Population-based analysis showed a sigmoid dose-response relationship of parotid gland, from which we estimated a threshold radiation dose of 16 Gy and a mean TD50 (dose reducing function by 50%) of 30 Gy. TD50 ranged from 7 to 50 Gy in the group of patients.

In conclusion, dynamic ^{11}C-methionine PET can measure regional loss of salivary gland function following irradiation for head and neck cancer, relevant for studying the individual dose-response relationship of major salivary glands. Results support the use of a threshold radiation dose of parotid glands in radiotherapy planning of head and neck cancer.