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Mechanism Underlying Individual Radiosensitivity of Breast and Head and Neck Cancer Patients

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It is known from clinical observation that an individual heterogeneity in response to radiation can be seen in radiotherapy patients. Part of these individual responses is related to treatment (dose, volume and localization). Other part is probably due to genetically controlled cellular response to DNA damage, DNA repair and life style factors. Studies on hypersensitivity syndromes with a clear-cut genetic component e.g. ATM, identified DNA damage recognition and repair as a central theme of radiosensitivity. However, these classical cases of radiosensitivity are rare and account for about 1 in 10 000 observed cases. As most gene products are part of multi-protein complexes and mutation of a particular gene may affect the expression of downstream genes involved in these cellular pathways and related pathways trying to compensate for the defect. Therefore, it is most likely that individuals in the relatively large group of radiosensitive individuals will carry more subtle defects in these pathways due to presence of SNP:s which are not limited to the two abovementioned groups of genes.

Several in vitro test systems measuring e.g. apoptosis, induction and repair of DNA breaks did not successfully distinguish the sensitive from non-sensitive at the individual level. There is strong support in the literature that elevated oxidative stress and related pathways can be correlated to the risk of radiation-induced healthy tissue damage. In our previous studies we have shown that radiation-induced oxidative stress could be a good indicator of individual radiosensitivity.

In this presentation the biomarkers of sensitivity in combination with mechanistic studies will be discussed based on side effects observed in breast cancer (acute side effect) and head and neck cancer (osteoradionecrosis as late side effect) patients. In ongoing project, blood samples were collected from breast and head and neck cancer patients that had been previously treated by radiotherapy (RT) and whose reactions to RT have been classified. The blood samples were exposed to radiation and incubated at 37 C allowing cells to respond to radiation. The oxidative stress response, proteomic changes and SNP analysis in particular genes as well as results on miRNA will be presented and discussed. This work is in part supported by DoReMi.