Reduced side effects by proton microchannel radiotherapy: study in a human skin model.

Abstract:
The application of a microchannel proton irradiation was compared to homogeneous irradiation in a three-dimensional human skin model. The goal is to minimize the risk of normal tissue damage by microchannel irradiation, while preserving local tumor control through a homogeneous irradiation of the tumor that is achieved because of beam widening with increasing track length. 20 MeV protons were administered to the skin models in 10- or 50-μm-wide irradiation channels on a quadratic raster with distances of 500 μm between each channel (center to center) applying an average dose of 2 Gy. For comparison, other samples were irradiated homogeneously at the same average dose. Normal tissue viability was significantly enhanced after microchannel irradiation compared to homogeneous irradiation. Levels of inflammatory parameters, such as Interleukin-6, TGF-Beta, and Pro-MMP1, were significantly lower in the supernatant of the human skin tissue after microchannel irradiation than after homogeneous irradiation. The genetic damage as determined by the measurement of micronuclei in keratinocytes also differed significantly. This difference was quantified via dose modification factors (DMF) describing the effect of each irradiation mode relative to homogeneous X-ray irradiation, so
that the DMF of 1.21 ± 0.20 after homogeneous proton irradiation was reduced to 0.23 ± 0.11 and 0.40 ± 0.12 after microchannel irradiation using 10- and 50-μm-wide channels, respectively. Our data indicate that proton microchannel irradiation maintains cell viability while significantly reducing inflammatory responses and genetic damage compared to homogeneous irradiation, and thus might improve protection of normal tissue after irradiation.