REDUCING SIDE EFFECTS BY USING PROTON MICROCHANNEL IRRADIATION IN A HUMAN SKIN MODEL

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We propose a novel strategy to reduce side effects of radiotherapy in normal tissue. The goal was to minimize the risk of damaging normal tissue, while preserving local tumor control. This is achieved by using microchannel irradiation that has been shown to protect normal tissue in close proximity to the beam source and enables a homogeneous dose distribution within the tumor by widening the beam with increasing track length. The principle of a microbeam irradiation is that only a small fraction of the skin within the beam channel obtains a very high dose which causes immediate cell death, whereas the rest of the skin receives only a very little dose. Due to the lethal damage in the DNA of cells which were hit by the high dose, mutations cannot be transferred into later cell generations and thus the risk to develop secondary tumors might be significantly reduced.

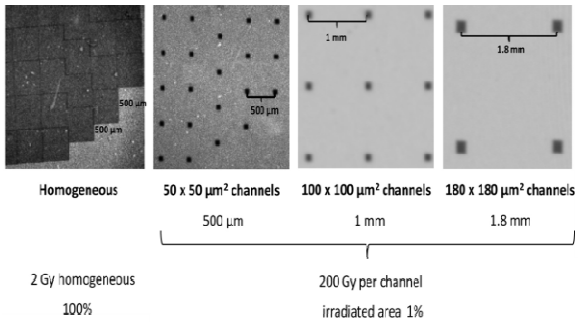

Figure 1 Irradiation fields of 20 MeV protons with a mean dose of 2 Gy visualized by Gafchromic films

To prove our hypothesis, 20 MeV protons were administered at the SNAKE microbeam to a human skin model (EpidermFTTM). Irradiation (average dose of 2 Gy) was applied in 10 to 180 µm wide channels on a quadratic raster with a distance of 500 to 1800 µm between each channel (centre-to-centre) (Figure 1). As a comparison, the human skin was also irradiated homogeneously by protons at the same average dose (HF).

Normal tissue viability was significantly higher after proton microchannel irradiation compared to homogenous irradiation. Furthermore, inflammatory markers, such as cytokines and chemokines, were significantly lower in the supernatant of the human skin tissue after microchannel irradiation than after homogeneous irradiation. As expected, genetic damage as determined by the measurement of micronuclei in keratinocytes was also significantly reduced after microchannel irradiation compared to homogeneous irradiation (Figure 2).

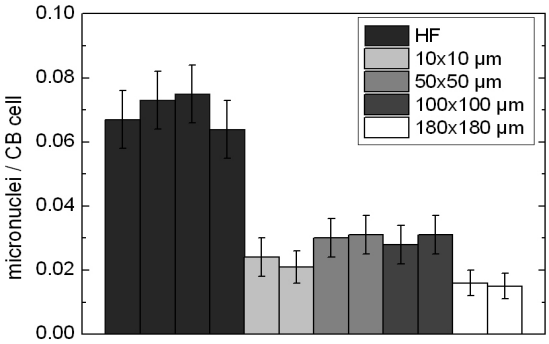

Figure 2 Micronuclei induction after 20 MeV protons with a mean dose of 2 Gy

In summary our data show that proton microchannel irradiation better maintains cell viability in normal tissue, reduces inflammatory responses, and greatly avoids genetic damage compared to homogeneous irradiation. These data indicate that microchannel beam irradiation might improve normal tissue protection. Normal tissue protection especially of the skin could be achieved in the future by developing a novel technique that provides proton beams within channels with a beam width of < 0.3 mm. By using this method side effects in the skin could be reduced, while tumor control would be maintained by widening the beam within the tumor which results in a homogeneous dose distribution.

REFERENCES

[1] Zlobinskaya et al, (2012) Radiat Environ Biophys. 52(1):123-33