Proton minibeam radiation therapy:  
a novel approach to minimize normal tissue damage

Thomas E. Schmid1,2, Stefanie Girst3, Christoph Greubel3, Judith Reindl3, Christian Siebenwirth1,3, Katarina Illicic1, Dietrich W.M. Walsh1,3, Günther Dollinger3, Jan J. Wilkens1,2, Gabriele Multhoff1,2, Stephanie E. Combs1,2

Background and Aim
Proton minibeam radiotherapy aims to minimize normal tissue damage in the entrance channel while keeping tumor control through a homogeneous tumor dose due to channel widening with increasing track length. Side effects of proton minibeam irradiation were examined in an in-vivo mouse model to account for immune system, vasculature and higher complexity. Here, we report on our comparative study of minibeam and broad beam irradiation in the ear of Balb/c mice, to prove this hypothesis of reduced adverse effects in normal tissue.

Methods
At the ion microprobe SNAKE, 20 MeV protons were administered to the right ear of 2-3 months old, female Balb/c mice, using an average dose of 60 Gy in a field of 7.2 × 7.2 mm² in the central part of the ear, in two irradiation modes, homogeneous and minibeams. The 4 × 4 minibeams of 180 × 180 µm² size were set in a distance of 1.8 mm, resulting in a dose of 6000 Gy in the channels, but with negligible dose in between. Inflammatory response, i.e. ear swelling and skin reactions were monitored for 90 days.

Results
No ear swelling or other skin reaction was detected after the minibeam irradiations, while significant ear swelling (up to 4-fold; Figure 4), erythema and desquamation (crust formation) developed in homogeneously irradiated ears 3-4 weeks after irradiation. Loss of hair follicles was only detected in the homogeneously irradiated fields after 4-5 weeks.

Figure 3: Ear thickness in µm

Figure 4: Skin reactions: The skin score is the sum of the erythema and desquamation score

Conclusion
Our results prove that proton minibeam radiotherapy leads to reduced side effects compared to conventional broad beam irradiation and could become an option in clinical proton and/or heavy ion therapy.

Acknowledgement
Supported by the DFG Cluster of Excellence: Munich-Centre for Advanced Photonics.