could involve schedules employing fewer fractions than CFRT, but more than in a typical SBRT treatment while partly escalating the fractional dose. It was the purpose of this study to investigate heterogeneous fractionation patterns with respect to the dose per fraction, taking into account the spatial and dynamic aspects of the tumour oxygenation and the effect of accelerated repopulation of tumour cells in treatments extending over several weeks.

**Materials and Methods:** Three-dimensional in silico tumours with heterogeneous oxygenation were simulated based on previous calculations from intervesSEL distance distributions. Homogeneous dose delivery was simulated employing 2 Gy per fraction as baseline and partly escalating the dose to 3 and 4 Gy per fraction corresponding to fractions delivered prior to or directly following a short interruption of the treatment as represented by the weekends. Survival was assessed on voxel level with the linear-quadratic (LQ) model taking into account the dose-modifying effect of the oxygenation. The effect of accelerated repopulation was incorporated assuming a kick-off time of 14 days and a potential doubling time of 5 days for NSCLC. Local control was evaluated as tumour control probability (TCP) through a Poisson-based model and dose-response curves were generated by systematically varying the total dose.

**Results:** For tumours with a negligible level of spread-out hypoxia (left panel of Figure 1) and assuming that accelerated repopulation starts after two weeks, partly increasing the fractional dose could substantially improve local control even if no reoxygenation takes place. If however the effects of repopulation are neglected and the hypoxia is geometrically concentrated instead of being spread out throughout the tumour, the impact of reoxygenation is far more important than partly escalating the fractional dose, even for small hypoxic fractions (right panel of Figure 1).

**Conclusions:** Heterogeneous fractionation might ensure high levels of control in well-oxygenated tumours even when inter-fraction reoxygenation cannot be assumed. For tumours with more concentrated hypoxia, moderately heterogeneous fractionation patterns cannot counteract the increased radioresistance of tumour hypoxia.
Conclusions: Results confirm previous studies showing large variation in duodenum volume between fractions in a given patient. For patients where the duodenum and PTV overlap, evaluation of volume receiving dose around 30-55Gy presents the largest error due to interfraction differences. This study suggests that a reduction in dose volume metrics of the duodenum is likely to be due to an increase in the percentage of the duodenum located outside the PTV. However, this parameter still suffers from interfraction effects. These findings suggest that toxicity predictions based on either duodenum volume, percentage of duodenum outside PTV or the DSH from the planning CT alone may be inaccurate. Further work needs to be undertaken in order to better estimate toxicity.

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Computational modelling of the microvasculature: effects of microbeams versus broad beam irradiation
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Purpose/Objective: Microbeam Radiation Therapy (MRT) is a still preclinical radiotherapy approach that uses synchrotron radiation to shape arrays of 25-100 µm wide planar beams separated by a few 100 µm. It places particular high hopes on the treatment of infantile, inoperable brain tumours. Several preclinical studies revealed an extremely high tolerance of normal tissue to these irradiation patterns while tumours were effectively controlled. Whereas several preclinical studies were able to impressively confirm the differential effect and the normal tissue sparing, a satisfying explanation does not yet exist. Apart from bystander effects the vessel system was identified to play an important role. Regeneration and repair originating in the tissue in the low dose regions could be responsible for a rapid recovery after treatment. By simulating irradiations of a computer modelled vascular system we investigate the possibility of a geometric explanation.

Materials and Methods: We simulated a cerebral cortical vascular and capillary network fitting important observed physiological parameters such as the vessel radii. Based on observed cell survival curves a radiation response model was developed for vessels and capillaries. After a simulated irradiation with either microbeams or a seamless beam at the same mean dose the vascular length and the average cell-vessel distance was assessed as a biological endpoint.

Results: Although our model does not incorporate repair mechanisms or bystander effects spatially fractionated beam geometries show a clear tissue sparing effect compared to seamless irradiations (s. figure). This effect increases with an increasing peak to valley dose ratio (PVDR). We were able to attribute this effect to a convex dose-response relationship. Furthermore we were able to show that the vascular network morphology has a strong influence on the tissue damage after MRT exposure. Especially the distribution of vessel radii appears to be crucial. This may explain the differential effect on tumours and normal tissue.

Conclusions: Even without taking into account repair mechanisms and bystander effects, a tissue sparing effect of MRT may be explained by a convex dose-response relationship. Assuming realistic treatment parameters an increase in the blood vessel surviving fraction by a factor of 3 is supported in our simulations. More accurate experimental data on dose dependent cell survival and on tumour vasculature will help to enable a more quantitative and predictive analysis.