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P59 - Enhanced RBE of submicron focused low LET protons

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Due to their physical and radiobiological properties, in particular their increased relative biological effectiveness (RBE), high linear energy transfer (LET) radiation qualities are of special interest for tumour therapy. To study the influence of spatial dose distribution on the biological effectiveness we use the ion microprobe SNAKE to concentrate the deposited dose in cells by focusing a certain number of low LET protons or ions to a submicron spot which approximate a high LET dose distribution. By changing the spot size and the number of focused ions one has opened a wide field to study RBE effects in dependence of dose distributions on submicron scale.
For our experiments we compare homogeneous proton irradiation with spots of focused 20 MeV protons (LET in water: 2.65 keV/µm) or 45 MeV Lithium ions (LET in water: 60 keV/µm) in a matrix pattern with certain numbers of ions per matrix point resulting in a constant dose of 1.7 Gy. For induction of chromosome aberrations we observed an increased effectiveness for higher number of ions per point and thus for a higher ionisation load per spot. 1.7 Gy irradiation with 541 protons per spot increases induction of dicentrics by a factor of 2.7 with respect to homogeneous proton application. However, the ionisation load per spot, the product of LET times the applied ions per spot, is not enough to understand RBE. At constant ionisation load at a single point of the matrix the effectiveness for the yield for dicentrics increases with LET. At the same mean dose of 1.7 Gy and the same matrix pattern 5 Li ions increase the yield for dicentrics by 45%, one Carbon (LET in water: 310 keV/µm) ion by 130%, with respect to 117 protons per spot.
The results indicate that at least two effects cause the increased RBE of high LET particles. On the one hand the focused dose application leads to an locally enhanced DNA double strand break (DSB) density, which increases the probability for misrepair, e.g. joining wrong ends of DSB. On the other hand the very high doses in the core of a heavy ion lead to an higher amount or more complex DNA damage, e.g. due to nonlinear effect in induction of DSB.

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