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Response of an experimental prostate tumor to single and fractionated doses of photons and carbon ions

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Introduction: Carbon ion radiotherapy enables the highly conformal treatment of deep-seated tumors due to the finite range and the inverted depth dose profile of charged particles. This physical advantage goes along with a higher linear energy transfer (LET) in the Bragg-peak as compared to the beam entrance region and results in an increase of the relative biological effectiveness (RBE) towards the distal edge of the depth dose curve. RBE is a complex quantity, which depends on physical parameters such as dose, LET and particle type as well as on biological properties (e.g. tissue type and biological endpoint). Although RBE-values have been published for a variety of tumor cell lines, only few in-vivo data are currently available. Here we describe the response of a highly radio-resistant prostate tumor with special focus on RBE, dose-dependence and fractionation behavior.
Material & Methods: Fresh pieces from the R3327-AT1 subline of the Dunning prostate tumor were transplanted s.c. into the distal thigh of anesthetized male young adult Copenhagen rats. Tumors were treated with 1, 2 and 6 fractions of either 12C-ions or photons. The target volume was positioned in a 2 cm SOBP of carbon ions. Local tumor control (LCT), which was the preferred biological endpoint to characterize treatment response was defined as no indication of tumor recurrence within an observation time of 300 days.
Results: Dose escalation studies revealed that LCT can be achieved with both, 12C and photons in the Dunning prostate tumor system. Based on complete dose-response curves, the D50-values (dose at 50% complication probability) were 32.9 ± 0.9 Gy and 75.7 ± 1.6 Gy, for 12C and photons, respectively. The respective values for split doses were 38.0 ± 2.3 Gy and 90.6 ± 2.3 Gy. The corresponding RBE-values were 2.30 ± 0.08 for single and 2.38 ± 0.16 for split doses. For the 6 fraction study a clear dose-dependence was seen, while the maximum RBE remained below 3. Transient dry and moist desquamation of the skin occurred as most prominent side effect, independently of radiation quality.
Conclusion: The increased effectiveness of carbon ions relative to photons is confirmed in an experimental tumor system. Exact positioning, a clear target verification and a well defined dosimetry enable a tumor conform treatment, which lead to only marginal side effects. Additional experiments are in progress to decipher possible mechanisms underlying the described differential radiation response.

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