Increased RBE of carbon ions in tumor growth inhibition using an in vivo lung adenocarcinoma model

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Carbon ion irradiation is an emerging therapy option for various tumor entities, including lung cancer [1]. This irradiation quality with a high linear energy transfer (LET) induces more complex and irreparable clustered DNA damage. Compared with low-LET photons and protons, carbon ions have a higher relative biological effectiveness (RBE) with less oxygen-dependent radiosensitivity [2]. Based on the colony formation assay we previously revealed a RBE of 3 for 10% cell survival in A549 cells [3].

Here we compared the effect of different irradiation qualities (carbon ions (^{12}C) and photon irradiations) on the tumor growth using a mouse tumor model of the human non small lung adenocarcinoma cell line (A549).

Adult BALBc nu/nu mice were maintained under pathogen-free conditions and handled in accordance with the recommendations for animal experimentation of European Community. After subcutaneous tumor initiation and a starting tumor volume of 200 mm³, local tumor irradiation with biologically equivalent doses of ^{12}C (LET 50-70 keV/µm, energy 122.36-183.74 MeV/u on target, 40 mm spread out bragg peak [SOBP]) and photons (6 MV-X) were performed. The tumor volumes were measured 3 times per week until reaching a target tumor volume of 400 mm³ or after an observation time of 40 days. The tumor volume (TV) was calculated by the formula: TV [mm ³] = (L x W²)/2; where L is the longest dimension of the tumor [mm], and W is the shortest dimension of the tumor [mm].

We found a tumor volume doubling time of 37.8 ± 1.6 days in the carbon ion irradiated group compared to 18.3 ± 1.2 days in the photon irradiated group and 11.9 ± 1.0 days in the unirradiated control group (Figure 1). Thus, the RBE of in vivo tumor growth is above 3 and clearly greater than for cell survival measurements, providing further support for a clinical application. However, it should be mentioned that 3 of 6 carbon ion irradiated tumors did not reach the target tumor volume of 400 mm³ within the observation time of 40 days.

In further experiments, we will focus on the analysis of the effects of carbon ion irradiation on the tumor microenvironment. These experiments will consider effects on tumor cells, tumor vasculature as well as distribution of immune cells.

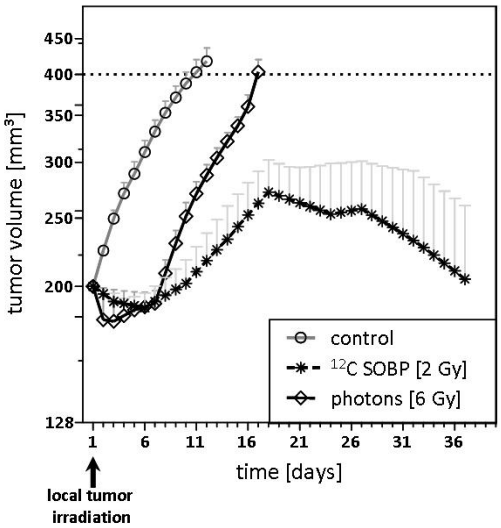

Figure 1: Growth curves of A549 tumors after irradiation with carbon ions (^{12}C SOBP) or photons. All data represent the means ± S.E.M.

References

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