RBE of carbon ions as determined in radiosensitive and radioresistant human tumour cells

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The reasons for the highly variable sensitivity of different cell types and tissues against ionising radiation are not well understood [1], [2], [3]. We studied cell killing and structural chromosome aberrations in tumour cells irradiated with carbon ions of different energies (400 MeV/u, 200 MeV/u, 100 MeV/u and extended Bragg peak) in comparison with X-rays [4]. Two tumour cell lines, a radioresistant WiDr-line and a radiosensitive MCF-7-line (modal chromosome number = 72 in both) were studied. The radiation-induced cell death of both cell lines was predominantly due to clonogenic cell death because of a small fraction of apoptotic cell death (<12 %, data not shown). The relative biological effectiveness was determined from the corresponding survival curves. Table 1 shows the RBE values determined for 10%-survival. RBE reached a maximum with RBE ≈ 3 after irradiation in extended Bragg peak in both cell lines.

Table 1. RBE-values determined for 10%-survival in WiDr and MCF-7 cells.

	LET [kev/µm]	WiDr	MCF-7
200 kV X-rays		1	1
400 MeV/u carbon ions	11.0	1.3	1.8
200 MeV/u carbon ions	16.5	1.5	1.9
100 MeV/u carbon ions	28.0	2.2	2.0
extended Bragg peak	89.0	2.9	2.9

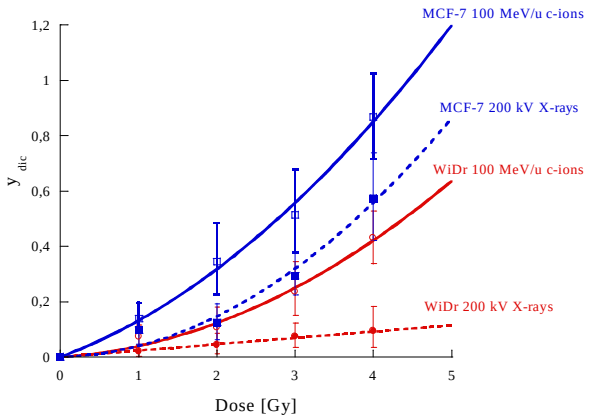

Figure 1. Genomic frequencies of radiation-induced total dicentric chromosomes per cell in WiDr and MCF-7 cells irradiated with 200 kV X-rays and 100 MeV/u carbon ions. Synchronised G_0/G_1-cells were irradiated with graded doses up to 4 Gy. Curves are fitted by linear or linear-quadratic equation. Error bars indicate 95% Poisson confidence limits.

Yields of total dicentrics, i.e. simple dicentrics plus dicentrics involved in complex exchanges, were determined in Giemsa-stained metaphases. The corresponding dose-effect relationships are plotted in fig.1. The RBE for the induction of 1 dicentric per cell amounted about 4 for WiDr cells and about 1 for MCF-7 cells irradiated with 100 MeV/u ions.

Taking into account that apoptosis-caused cell death was quite low, and that dicentrics are lethal in normal cells, these results indicate that: 1) WiDr cells might tolerate in some way these lethal aberrations and 2) in MCF-7 cells, the clonogenic death is also caused by another damage type. An increased biological effectiveness of carbon ions could be confirmed in radioresistant and radiosensitive tumour cells also with respect to the induction of simple reciprocal translocations (data not shown).

After irradiation with carbon ions, a higher proportion of complex exchanges including simple and multiple insertions, was observed in both cell lines. Complex exchanges visible with single-colour FISH resulted mostly from exchanges among three different chromosomes. A steep increase in the complex aberration yield was observed in the sensitive MCF-7 cells at a much lower dose than in the resistant WiDr cells, as shown in fig.2.

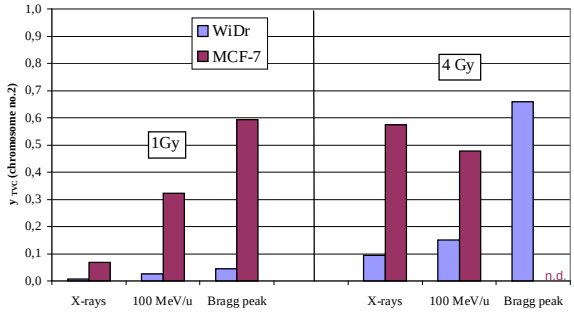

Figure 2. Yields of total visible complex exchanges per cell, involving the painted chromosome 2. Three intact copies of this chromosome were present in both cell lines.

References

[1] Olive, PL et al. : Lack of correlation between radiosensitivity and DNA double-strand break induction or rejoining in six human tumor cell lines. Cancer Res. 54, 3939-46, 1994

[2] Sirzen F. et al.: DNA-dependent protein kinase content and activity in lung carcinoma cell lines : correlation with intrinsic radiosensitivity. Eur. J. Cancer 35, 111-116, 1999

[3] Sheridan MT, West CM.: Ability to undergo apoptosis does not correlate with the intrinsic radio-sensitivity (SF2) of human cervix tumor cell lines. Int. J. Radiat. Oncol. Biol. Phys. 50, 503-509, 2001

[4] Hofman-Hüther, H.: Wirkung schwerer Ionen auf strahlenresistente und strahlensensitive Tumorzellen. Dissertation, Biologische Fakultät, Universität Göttingen, November 2002.