17. Biological Effectiveness of ^{12}C and ^{20}Ne Ions with Very High LET

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Knowledge of radiobiological effects of heavy ions at the cellular and molecular level is of fundamental importance in the field of radiation therapy (for example C ions) and space radiation biology (for example Ne ions). One of the issues that require deeper investigations is a determination of RBE values for a wide range of LET, for all relevant doses, for many cell types and various kinds of radiations [1].

During recent years, the biological effectiveness of heavy ions has been widely investigated with the aim to identify physical characteristics relevant to biological actions. These investigations are pertinent to the use of heavy ions in radiosurgery and radiotherapy. What has not been investigated so thoroughly is the biological effectiveness of heavy ions at low energies and very high LET values. The LET, which is equal to the stopping power of heavy particles, increases sharply at the end of the particle's path, forming a so-called Bragg peak. The shape of the Bragg peak depends on the particle type. Because overlying beams with different energies and components of primary and secondary particles are used in radiotherapy, the knowledge of RBE values of very high LET radiation need to be well characterized.

An experimental set-up designed for such investigations was constructed at the isochronic cyclotron in Heavy Ion Laboratory. A more detailed description of the set-up can be found in Ref. [2]. In the present work the partially stripped $^{12}C^{2+}$ and $^{20}Ne^{4+}$ ions were accelerated to 48.5 MeV and 105 MeV. The measured beam uniformity was better than ±2.5%.

CHO-K1 cells have been used as a suitable biological system for our studies. The cell line is characterized by genetic stability, the ability to form colonies, a relatively rapid growth rate with a cell cycle of 12-14 hours. For exposure to ions the cells were seeded in specially designed Petri dishes, which were filled with medium, sealed by a parafilm cover and placed in a vertical sample holder mounted in an x-y-z table that was connected to a special stepping motor. The irradiated sample moved under the beam according to a planned route. Movement was initiated when the number of counts detected by the 20^{o} particle detector reached the preset value. When all fields have been exposed the sample holder returned to the start position. Stored information enabled to evaluate the beam stability and intensity. The whole set-up was surveyed by a digital camera. The total time of exposure per dish was between 1-5 min. depending on the dose and beam intensity. The dose rates were changed from 0.05 Gy/min. to 1 Gy/min depending on the dose. Cell survival was estimated according to standard procedures [3]. To obtain RBE estimation cell survival data were fitted by the linear quadratic model $SF(D)=\exp(-\alpha D-\beta D^2)$ where SF is the survival at dose D. Fitting was performed by the non-linear

least squares method using a Trust-Region algorithm implemented in the commercial Matlab 7.1 software.

Survival data for the CHO-K1 cell line at various energies of ^{12}C and ^{20}Ne ions as a function of the absorbed dose are shown in Fig. 1. The dose response curves are presented for the inactivation of CHO-K1 cells irradiated with ^{12}C ions with LET (evaluated at cell entrance) of 438, 576 and 832 keV/µm, and for ^{20}Ne ions irradiated with LET of 933, 1245 and 1616 keV/µm.

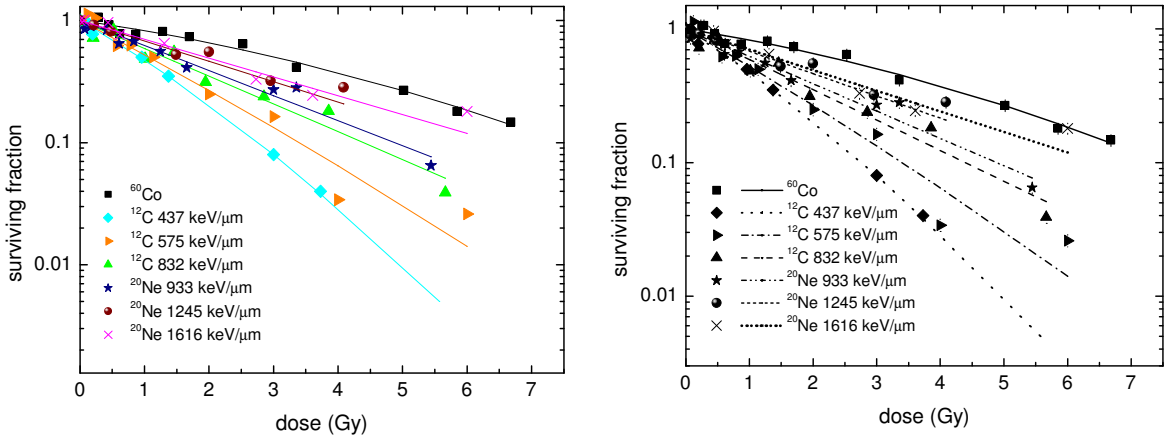

Figure 1. Survival curves of CHO-K1 cells as a function of dose for γ-rays, ^{12}C and ^{20}Ne ions.

The estimated values of α and β parameters of the linear quadratic model allow to determine the RBE_M values, obtained as the ratio of α terms for particle and ^{60}Co irradiation. The RBE_M were deduced from the initial slopes of the survival-dose curves. RBE_M corresponds to the maximum RBE assuming a monotonous decrease of the effectiveness with increasing dose [4] as shown in Fig. 3.

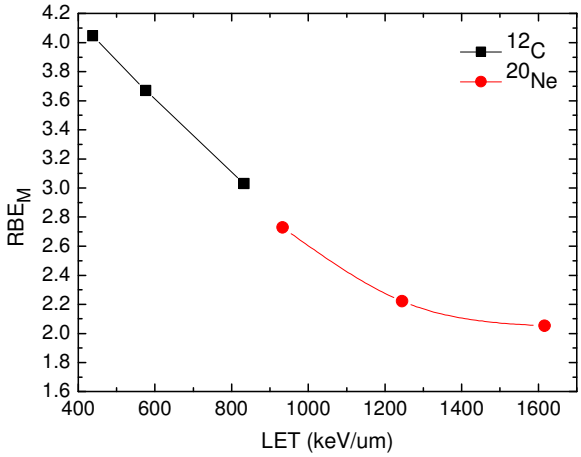

Figure 2. RBE_M of CHO-K1 cell line versus LET for ^{12}C and ^{20}Ne.

It is assumed that the increase of RBE with LET up to 100-200 keV/µm is caused by an increased spatial accumulation of DNA double-strand breaks that lead to cell death (Han *et al.*, 1998). The fall of RBE at LET above 250 keV/µm is caused by the deposition of more

energy than necessary for cell deactivation. The excess energy results in an 'overkill' effect and, per unit of Gy, the number of hit cells is reduced, leading to an increased survival.

Interestingly, the surviving fraction was ~30%, indicating that more than a half (60-65%) of the survivors have not been hit. The presence of non-hit cells among hit ones is one of the features characteristic for the exposure to very high LET heavy ions. A wider discussion on the decrease of RBE in the high LET region, along with the evaluation of the fraction of non-hit cells, will be presented in our forthcoming paper (Czub *et al.*, in preparation).

In conclusion, our results show that the RBE of ions depends solely on the LET and not on any physical characteristics of the ions. The inactivation cross sections describing the killing efficiency of a single particle at the end of particle track come close to the size of the cell nucleus.

Acknowledgments

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