



The effect of combined proton and carbon ion irradiation on chinese hamster B14-150 cells

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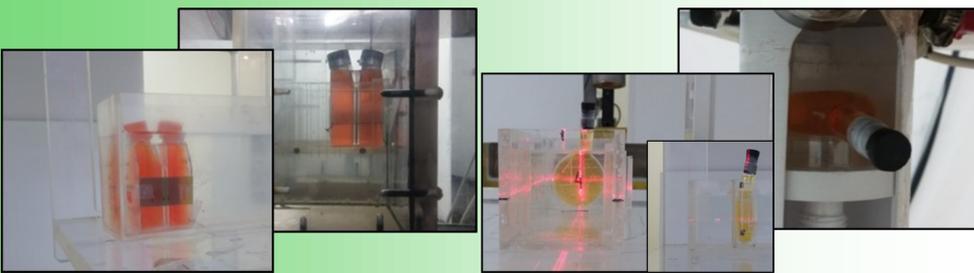
Introduction

Carbon ions are effective in the treatment of radioresistant tumors. However, concomitant irradiation of healthy tissues with high LET radiation can lead to significant radiation damage in cells adjacent to the tumor. In some research centers, carbon ions are used as boost to photon or proton therapy to reduce the risk of possible complications. In terms of radiobiology, it is of interest to study interactions of cell damage induced by sequential exposure to protons and carbon ions. In the case of carbon ions, contribution of high LET particles to the total effect is not completely clear. The LET spectrum of these particles is close to that of heavy recoils C, N, O (HR) induced by 14.5 MeV neutrons [1].

The irradiation schemes

Protons + ¹²C ions

Protons + HR



Time interval between two fractions was 2 hours

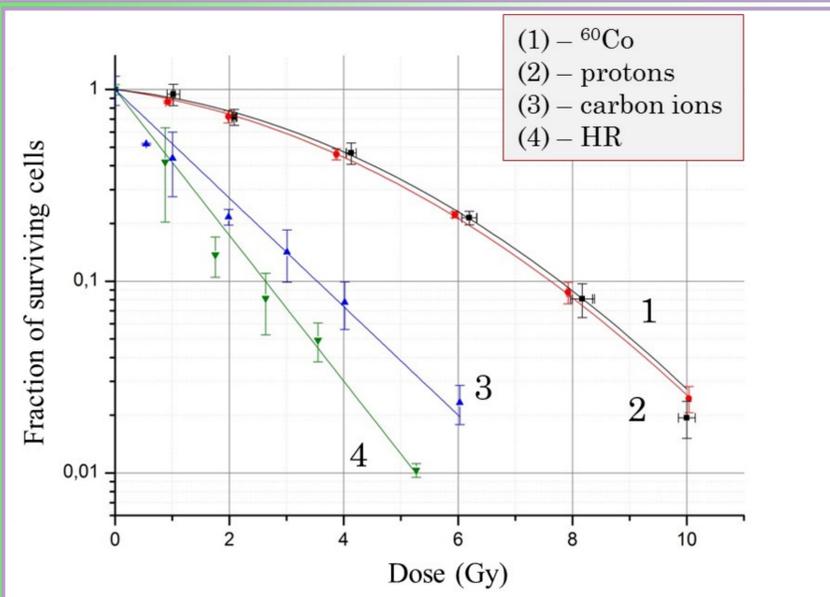
1. 6 Gy (p) + 1 Gy (¹²C)
2. 1 Gy (¹²C) + 6 Gy (p)
3. 4.5 Gy (p) + 1.7 Gy (¹²C)
4. 1.7 Gy (¹²C) + 4.5 Gy (p)
5. 1.7 Gy (¹²C) + 1.7 Gy (¹²C)

1. 6 Gy (p) + 0,48 Gy (HR)
2. 0.48 Gy (HR) + 6 Gy (p)
3. 4.5 Gy (p) + 0.96 Gy (HR)
4. 0.96 Gy (HR) + 4.5 Gy (p)
5. 1.2 Gy (HR) + 1.2 Gy (HR)

Results

The results obtained showed that the cell survival was higher when protons were given as the first dose fraction. On the contrary, the first dose fraction of carbon ions or HR followed by proton dose fraction resulted in lower cell survival. It suggests that cell lesions induced by low-LET protons were repaired between the fractions while those induced by high-LET carbon ions and HR were mainly unreparable.

Survival curves of B14-150 cells irradiated with photons of ⁶⁰Co, protons, ¹²C ion beam (center SOBP) and HR



Type of radiation	LET, keV/μm	RBE (S _{10%})
Protons	~ 5	1.2
¹² C (center SOBP)	~ 50	2.2
HR	~ 290	2.9

Conclusion

Thus, the order of sequential combined cells exposure to low- and high-LET radiations is important. The proton irradiation followed by carbon ions or HR is less effective than the opposite order of sequential irradiation.

Objective

The aim of the study was to assess the importance of irradiation order when Chinese hamster cells are exposed to protons and carbon ions or protons and heavy recoils.



Prometeus accelerator, MRRC, Obninsk

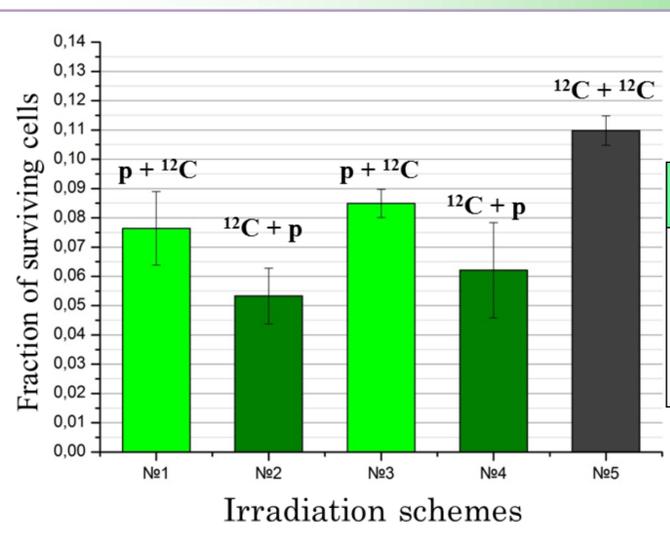


U-70 synchrotron, IHEP, Protvino

Materials and Methods

The survival of Chinese hamster cells B14-150 (fibrosarcoma) in the stationary growth phase was studied using clonogenic assay. Cell monolayers were irradiated sequentially with protons and carbon ions or with protons and HR. Protons with energies 65–85 MeV were produced using the Prometeus accelerator (MRRC, Obninsk). The irradiations with a ¹²C ion beam (initial energy 454 MeV/u) were carried out at the U-70 synchrotron (IHEP, Protvino) in a water phantom at the center of spread out Bragg peak [2]. The portable neutron generator NG-14 (MRRC, Obninsk) was the 14.5 MeV neutrons source. For studying the effects of HR cell monolayers were irradiated with 14.5 MeV neutrons through a glass Carrel flask bottom (1 mm) under the conditions of the proton equilibrium absence.

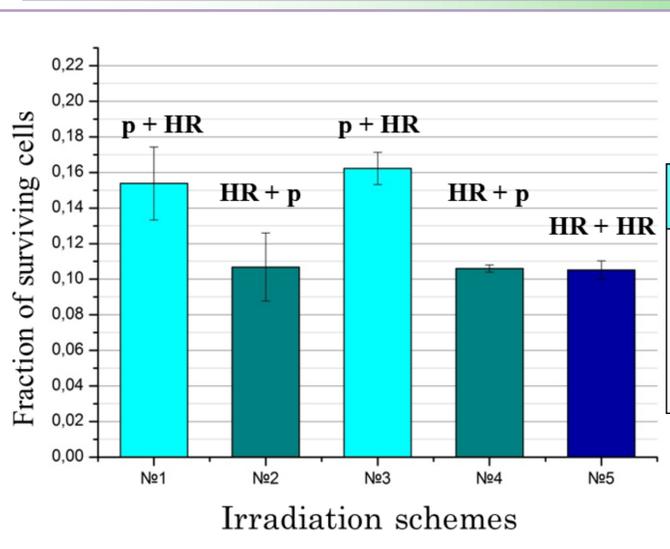
Survival of B14-150 cells after protons and ¹²C ion beam irradiation



Irradiation schemes	Total dose*	Dose fraction ¹² C*
1	8.2 Gy	27 %
2	8.2 Gy	27 %
3	8.24 Gy	45 %
4	8.24 Gy	45 %
5	7.48 Gy	50 + 50 %

* the RBE value is taken into account

Survival of B14-150 cells after protons and HR irradiation



Irradiation schemes	Total dose*	Dose fraction ¹² C*
1	7.4 Gy	19 %
2	7.4 Gy	19 %
3	7.3 Gy	38 %
4	7.3 Gy	38 %
5	6.96 Gy	50 + 50 %

* the RBE value is taken into account

References

1. Koryakina E.V., Potetnya V.I., Troshina M.V. et al. Comparison of biological efficiency of accelerated carbon ions and heavy recoils in Chinese hamster cells. *Radiation and Risk*, 2019; v. 28, no. 3, pp. 96-106.
2. Antipov Y.M., Britvich G.I., Ivanov S.V. et al. Transversally-flat dose field formation and primary radiobiological exercises with the carbon beam extracted from the U-70 synchrotron. *Instruments and Experimental Techniques*, 2015; v. 58, no. 4. pp. 552-561.