RBE of accelerated carbon ions and of neutron produced heavy charged particles in Chinese Hamster cells

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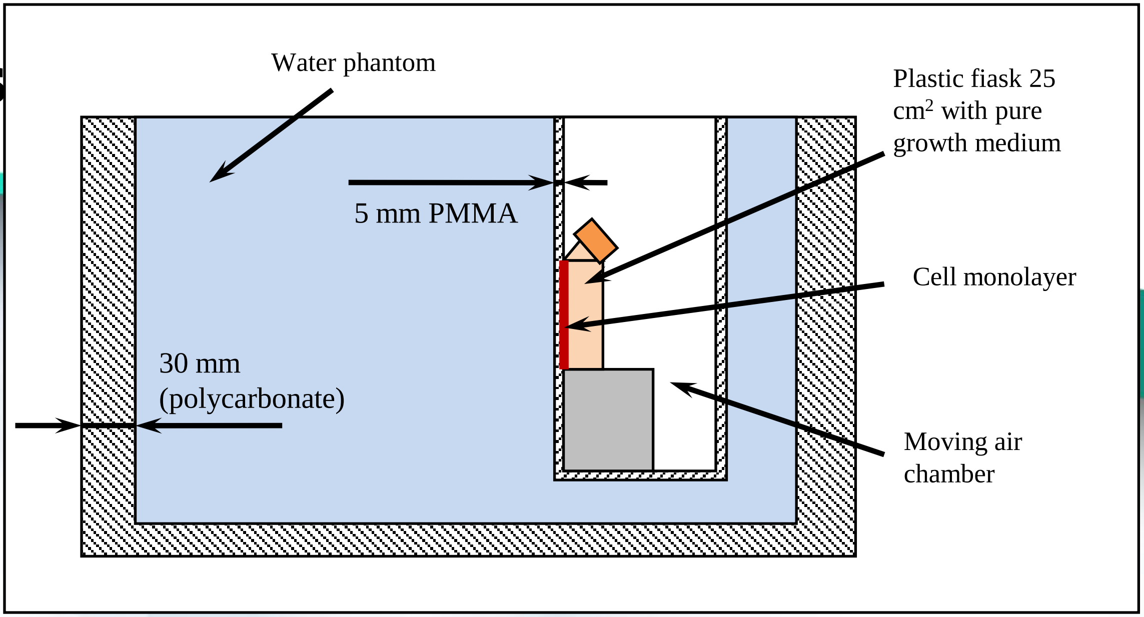
Introduction

The accurate evaluation of heavy charged particles RBE is important for estimating cancer risks and the “biological” doses in the ion therapy. In the latter case it’s necessary to study the mechanisms of ions RBE variations in the spread Bragg peak, and, in particular, in its distal edge, where the maximal RBEs (because of particles with maximum LETs and short ranges, 2–5 μm) are observed.

Materials and methods

Cell lines

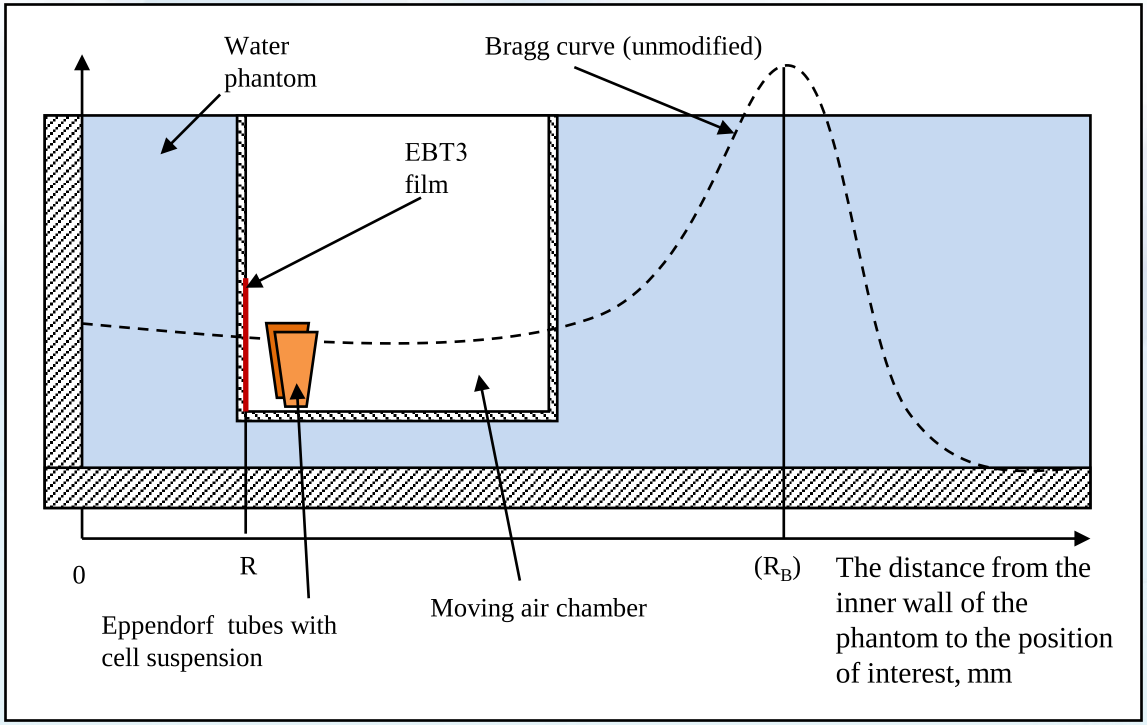
Two Chinese hamster cell lines in the late stationary growth phase (CHO-K1, V79) and cell surviving test were used in this investigations.
For inhibiting the repair processes cells were kept on ice between irradiation and replating.



Irradiations

^{12}C ion beam
(U-70 synchrotron, IHEP, Protvino):
initial energy 454 MeV/u

in the plateau region of the Bragg curve:
LET_d = 11 keV/μm,
D =1.0–8.5 Gy
in the unmodified Bragg peak:
LET_d = 120–140 keV/μm,
D = 0.5–4.5 Gy



Materials and methods

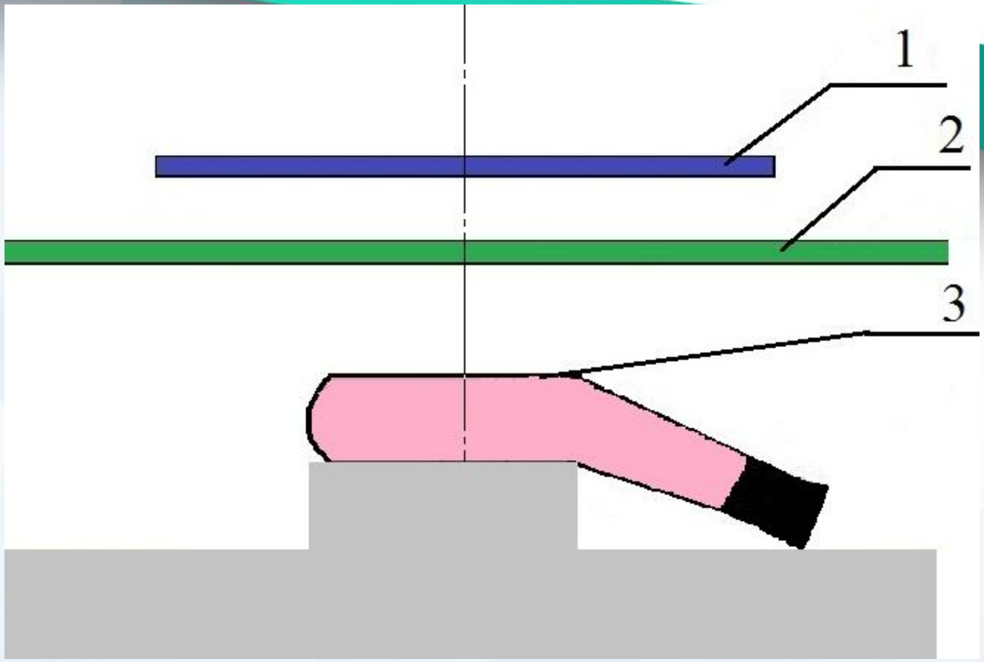
Irradiations

The effects of slow heavy charged particles (SHCP) C, N, O, p, α was studied by irradiating with 14.5 MeV neutrons *(portable neutron generator, N.L. Dukhov VNIIA, Moscow, Russia, A. Tsyb MRRC, Obninsk, Russia)*

Cell monolayers were exposured through a glass Carrel flask bottom (1 mm) under the conditions of the secondary charged-particle equilibrium (CPE) absence:

LET_d ~ 290 keV/μm
LET_d (SHCP) ~ 460 keV/μm

D = 1–5 Gy
$(D = 0.55 \cdot D_{SHCP} + 0.15 \cdot D_p + 0.3 \cdot D_\alpha)$



1 – generator target
2 – generator tube end
3 – cell monolayer at a Carrel flask bottom

Materials and methods

Data analysis

The surviving fraction data were obtained from the mean of at least three independent experiments and fitted by a least squares Linear Quadratic (LQ) Model equation:

$$S = \exp(-\alpha D - \beta D^2),$$

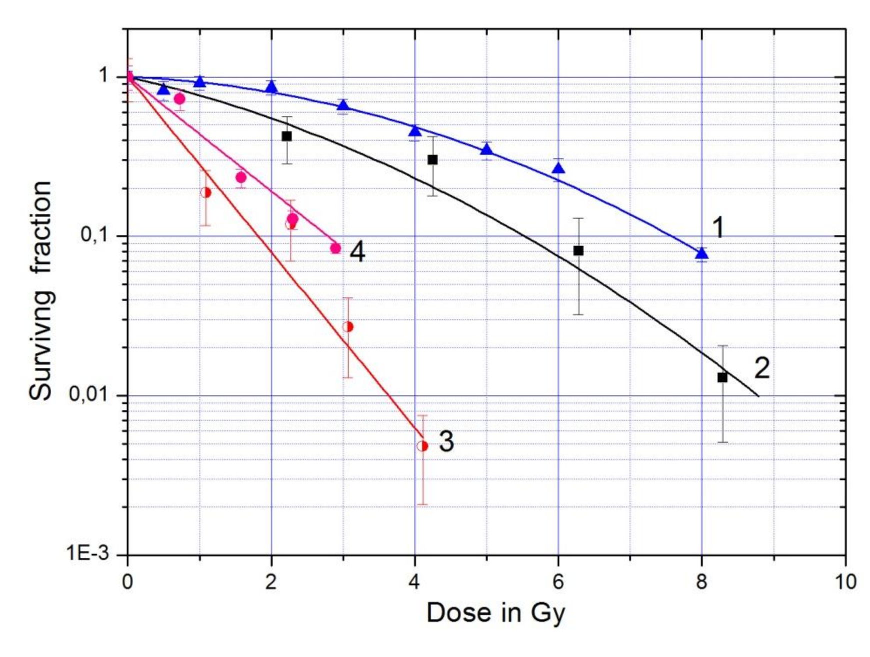
where S is the surviving fraction and D is the absorbed dose in gray. The α parameter describes the linear component of the curve, and the β component describes the quadratic portion of the curve. The α/β ratio is the point at which linear cell death is equivalent to quadratic cell death.

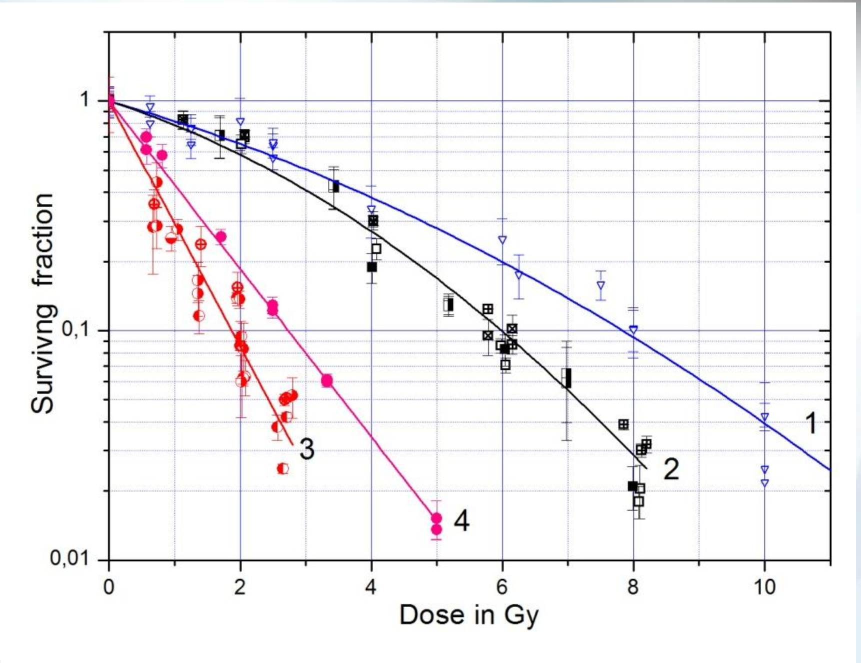
RBE is defined as the ratio of a photon dose (D_γ) to a corresponding ion dose (D_I) resulting in the same biological effect (0.1 surviving fraction):

$$RBE = D_\gamma / D_I$$

Results

The survival curves for carbon beam were linear-quadratic in the plateau region of the Bragg curve and linear in the unmodified Bragg peak. There are no differences between monolayer and suspension results. Dose curves of neutrons under the absence of CPE conditions were linear for both cell lines.





Cell survival curves of CHO-K1 (right) and V79 (left) cells when irradiated with photons of ^{60}Co (1); ^{12}C ion beam in the plateau region of the Bragg curve (2) and in the unmodified Bragg peak (3); SHCP C, N, O, p, α (4). Error bars indicate SD

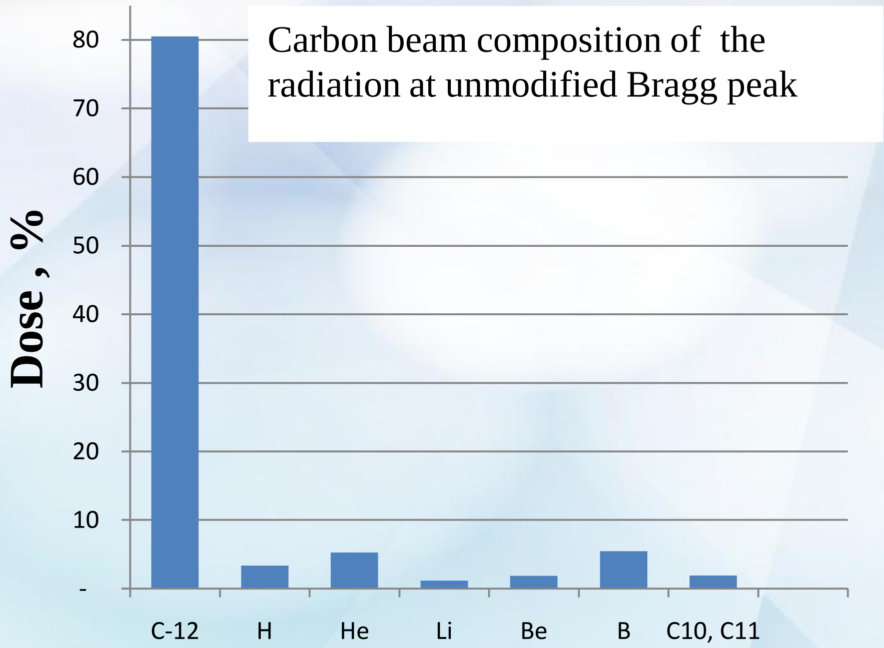
Results

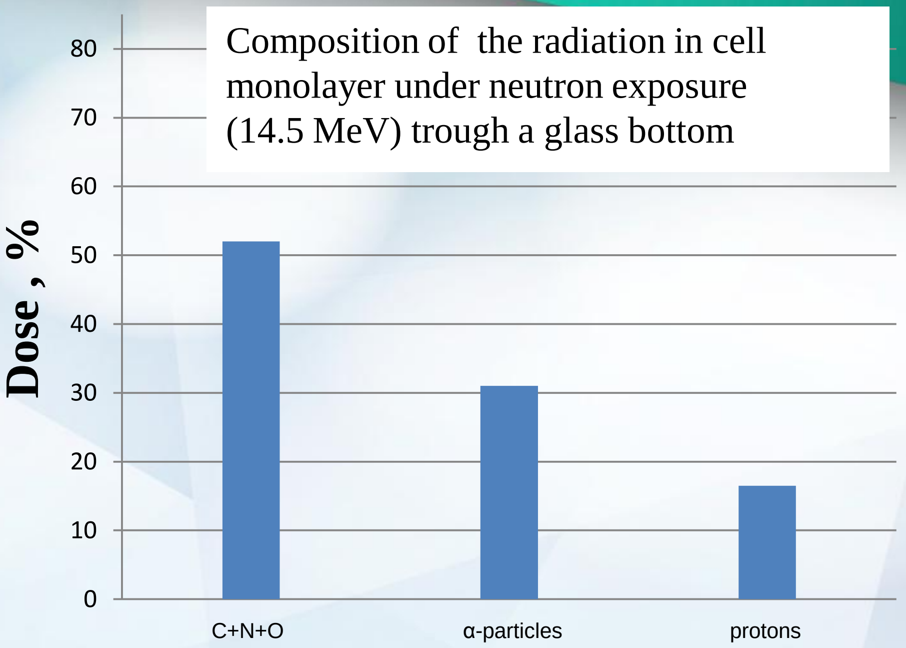
RBE values of carbon beam in the plateau of Bragg curve, in the Bragg peak and of neutrons under the absence of CPE conditions

	carbon beam		neutrons under the absence of CPE conditions
	in the plateau of Bragg curve	in the unmodified Bragg peak	
CHO-K1	1.37	4.17	2.76
V79	1.30	4.16	2.80

Discussion

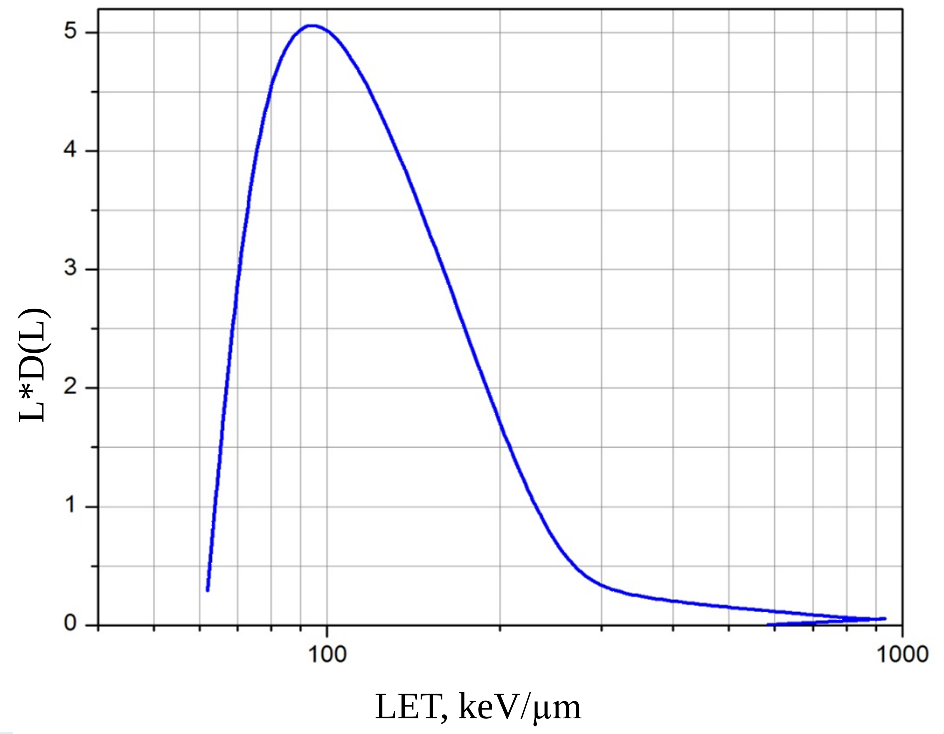
To interpret the obtained efficiencies the complex spectra of all types of radiations need to be taken into account.



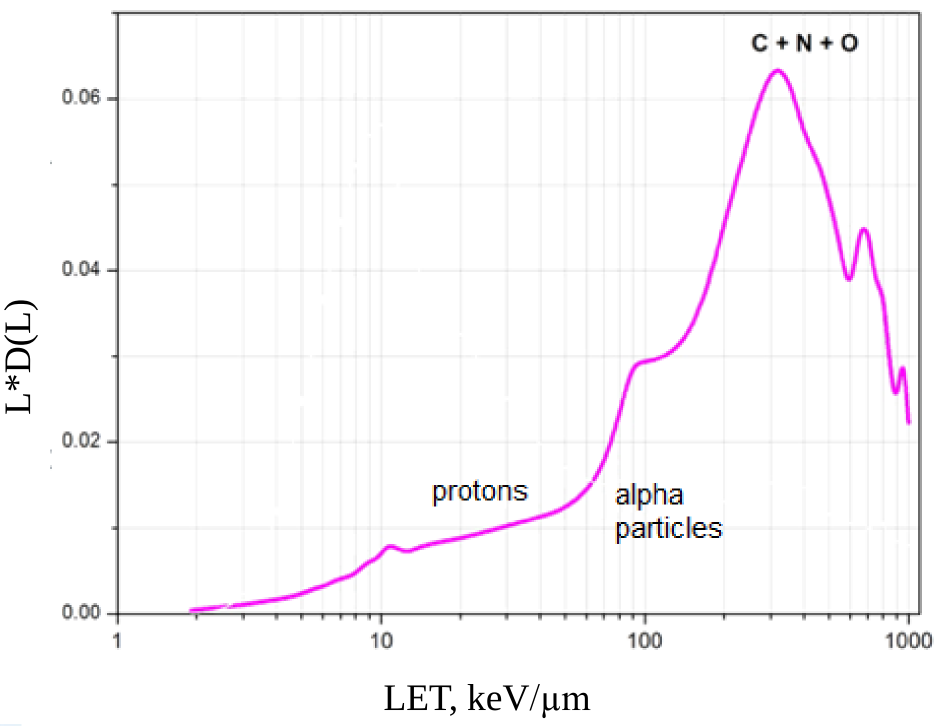


80 % of the dose in the Bragg peak is deposited by the primary ions ^{12}C (LET of more than half of the ions was 60–200 keV/μm), the others 20 % – by high energy (2–4 GeV) secondaries H, He, Li, Be, B with low LETs. So, the particles with LETs corresponding to the RBE maximum delivered quite half of the dose in the Bragg peak. As for SHCP experiments, approximately half of the dose is also formed by SHCP with LET_d ~460 keV/μm.

Discussion



Carbon ions dose-LET distribution at Bragg peak



SHCP dose-LET distribution when cell monolayer was irradiated with 14.5 MeV neutrons under the CPE absence

Discussion

Based on the dose composition of the radiation and on the assumption of the independent biological action of particles in the absence of CPE, the RBE value of the C, N, O heavy recoils was estimated to be 3.0–3.1.

$$RBE_{C,N,O} = (RBE_{n(OP)} - 0.30 \cdot RBE_{\alpha} - 0.15 \cdot RBE_{p})/0.55 = 3.0 \div 3.1$$

The higher RBE of ^{12}C ions compared to RBE of the heavy recoils in the same LET range (50–1000 keV/μm) may be explained by different LET_d: 120–140 keV/μm (maximal RBE) versus 460 keV/μm (RBE diminishing).

It should be noted that the problem of possible synergism of the carbon beam radiation components in the Bragg peak remains unexplored and could also lead to differences in RBEs.

THANK YOU FOR YOUR ATTENTION!