DOI 10.1007/s10517-022-05432-3

Bulletin of Experimental Biology and Medicine, Vol. 172, No. 5, March, 2022

BIOPHYSICS AND BIOCHEMISTRY

Dose Field Shaping and Biological Effectiveness of the Effect of Pulsed Electron Accelerator Novac-11 on Mammalian Cells

E. V. Koryakina[1], A. A. Lychagin[1], V. I. Potetnya[1], M. V. Troshina[1], V. O. Saburov[1], A. S. Moiseev[1], S. N. Koryakin[1], S. A. Ivanov[1], P. V. Shegai[2], and A. D. Kaprin[2]

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 172, No. 11, pp. 593-596, November, 2021
Original article submitted June 10, 2021

The development of technologies for using the Novac-11 pulsed electron accelerator in radiation therapy of animals with spontaneous neoplasms requires dosimetric and radiobiological studies. The studies were performed on cultured Chinese hamster V-79 fibroblasts after irradiation with 10 MeV electrons in a dose range up to 12 Gy and ^{60}Co γ-radiation. Chemical dosimeters FBX and Fricke were used as additional test-systems. The depth dose curves were measured and the maximum dose depth of the electron beam was determined in tissue-equivalent phantoms. Cell survival and the data of chemical dosimetric systems showed that the effects of electron irradiation did not differ from that of ^{60}Co γ-radiation. It was concluded that the use of Novac-11 in the therapy of animals with spontaneous neoplasms is advisable.

Key Words: *electrons; Novac-11; chemical FBX and Fricke dosimeters; V-79 cells; cell survival*

Nuclear technologies take a special place among promising methods of therapy for cancer patients providing efficiency, integration into combined treatment protocols, and personalized approach [2]. The most widespread and available method is photon therapy due to high penetration of γ-rays, accuracy of determination of the absorbed dose, and well-known dependencies of the action of radiation for live objects. The disadvantages of this method include the risk of damage to healthy organs adjacent to the tumor. The use of the electron beam in radiation therapy could be a certain alternative because limited range of electrons in a material and irradiation precision reduce the risk of damage to the adjacent tissues. Nevertheless, there are some differences between the two modalities. Electrons are directly ionizing particles, while γ-radiation acts through secondary electrons produced. So, energy spectra and dose distribution in the irradiated volume differ for electron and γ-ray beams. Unlike ^{60}Co radiation electron accelerators provide pulsed beams what can affect the development of biological reactions. However, the results of [1,4] showed that the effect dependence on pulse frequency was absent at 1-100 Hz. Though relative biological efficiency (RBE) of electrons does not practically change in the energy range from 0.2 to 10 MeV and is usually assumed to be 1, a lower efficiency of Novac-7 accelerator electron irradiation in comparison with γ-radiation was reported (in the study of MCF-7 cell survival) [7]. Thus, the use of various equipment and test-systems and shortcomings in the verification of dosimetric control can lead to ambiguous results, which necessitates further stu-

[1]A. F. Tsyb Medical Radiological Research Center — Affiliated Branch of the National Medical Research Radiological Center, Ministry of Health of the Russian Federation, Obninsk, Russia; [2]National Medical Research Radiological Center, Ministry of the Health of the Russian Federation, Obninsk, Russia. ***Address for correspondence:*** ek-koryakina@mrrc.obninsk.ru. E. V. Koryakina

dies, especially in terms of control of absorbed doses and the formation of a radiobiological response to a particular radiation source.

Our aim was to study the dose field formation and the radiobiological response of mammalian cells to pulsed electrons irradiation from Novac-11 accelerator in comparison with standard ^{60}Co γ-rays at similar radiation characteristics (linear energy transfer LET ~0.2 keV/μm).

MATERIALS AND METHODS

Irradiations with electrons were performed at a Novac-11 therapeutic accelerator (NRTS.p.A; E=10 MeV, pulse frequency 1 Hz), with γ-rays at a gamma unit with ^{60}Co source (E=1.25 MeV). Absorbed doses were measured using a Unidos dosimetry system (PTW) with a compact cylindrical ionization chamber TM30010. In field dosimetry at the accelerator, we additionally used a plane-parallel Markus-type camera (ROOS, 3194). The dosimetry error did not exceed 5% (p=0.95). Studies with tissue-equivalent materials (solid water RW3, polymethylmetacrylate (PMMA)) of different thickness were carried out to determine depth dose curves, the maximum dose depth of the electron beam.

Chinese hamster V-79 cells were used in radiobiological studies. The cells were cultured according to standard protocols [6]. The cell suspension was irradiated in 5 ml Eppendorf tubes. The electrons and γ-rays dose ranges during cell irradiation were 0.47-11.70 Gy. Cell survival was used to assess the biological effectiveness of electrons and γ-radiation. The post-irradiation cell culturing and the clonogenic assay were described somewhere else [3].

The FBX and Fricke chemical water dosimeters that are widely used in dosimetry at radiotherapy irradiation units were also used as test-systems. Preparation of the FBX dosimeter, its calibration, and sensitivity determination has been described in detail elsewhere [5]. Fricke chemical dosimeter was prepared by a standard way: 550 mg ferrous ammonium sulphate (Mohr's salt), 55 mg NaCl, and 22 ml H_2SO_4 were dissolved in 1 liter of tri-distilled water. The dose ranges for electrons and γ-radiation were 0.5-4.5 Gy for FBX and 10-60 Gy for Fricke. The optical densities of the irradiated solutions relative to the unirradiated control were measured at 304 nm (Fricke) and 540 nm (FBX) on a SF-56 spectrophotometer (Spektr). The calibration curves for the Fricke and FBX dosimeters were fitted using a linear model.

Statistical analysis, regression analysis, and the curve fitting were conducted using Microsoft Excel and OriginLab. The data are presented as *M±SEM*. The differences were assessed using the Student's *t* test and were considered statistically significant at p<0.05.

RESULTS

Uniformity within ±2% of the irradiation dose field for an electron beam with a collimator tube 100 mm in diameter is observed when using a solid water phantom RW3 with a thickness of 2 to 17 mm (a "plateau" spread is 15 mm) at an electron energy of 10 MeV, of 1 to 14 mm (13 mm) at 8 MeV, of 2 to 14 mm (12 mm) at 6 MeV, and of 0 to 9 mm (9 mm) at 4 MeV. Therefore, a 5 mm thick PMMA plate was placed above the Eppendorf tubes with cells and chemical dosimeters to provide uniform dose distribution.

The survival curves of V-79 cells after exposure to electrons and γ-radiation (Fig. 1) are fitted by linear-quadratic models with similar α and β coefficients values: $S_\gamma=\exp(-0.117\times D-0.023\times D^2)$; $S_e=\exp(-0.114\times D-0.023\times D^2)$. No significant differences were found between the survival curves after exposure to pulsed electron and γ-radiation. This also indicates the absence of differences in the cell damage induction.

Comparison of the dose dependences of the optical densities of irradiated dosimeters FBX and Fricke (Fig. 2) confirms the obtained results. There are no significant differences between electrons and γ-radiation. The parameters of linear regressions for the FBX dosimeter were (89.07±0.66)×10^{-3} for γ-radiation and (89.62±0.38)×10^{-3} for electrons, and in the case of Fricke they were (3.45±0.02)×10^{-3} and (3.59±0.32)×10^{-3}, respectively.

These findings suggest that the pulsed electrons with energy of 10 MeV do not differ from the standard γ-radiation of ^{60}Co by formation of dose loads detected by dosimetric systems, including chemical dosimeters, and the induced biological responses. The use of an electron beam with a collimator tube 100 mm in diameter makes it possible to apply the Novac-11 linear

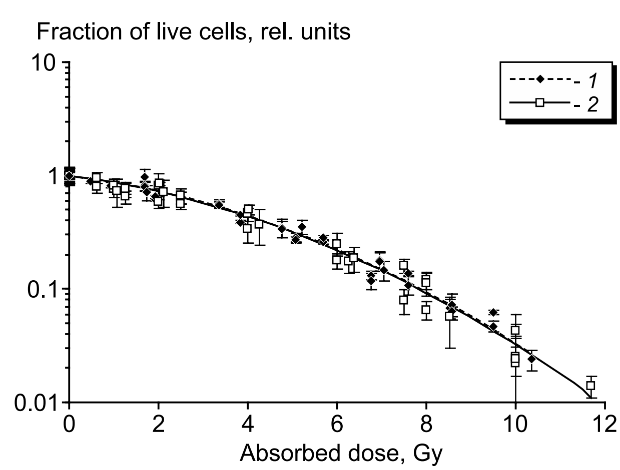

Fig. 1. Survival of Chinese hamster V-79 cells. *1*) Pulsed electron radiation, *2*) γ-radiation.

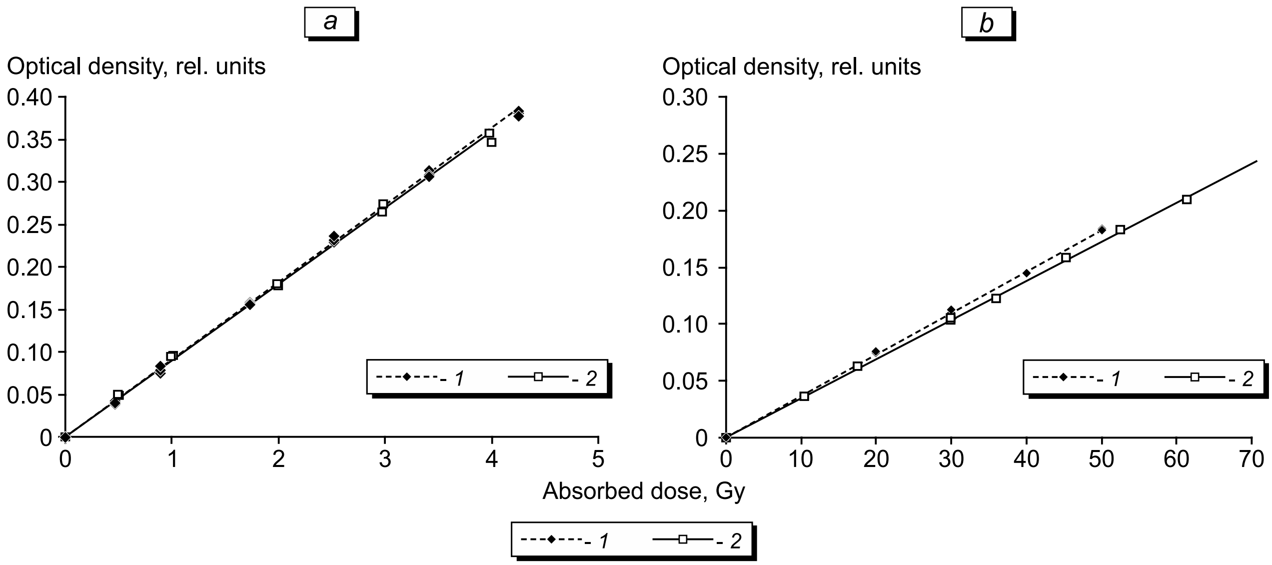

Fig. 2. Optical density of chemical dosimeters FBX (*a*) and Fricke (*b*) as a function of absorbed dose. *1*) Pulsed electron radiation, *2*) γ-radiation.

electron accelerator for the treatment of spontaneous animal tumors located at a depth up to 17 mm.

In general, it should be noted that accelerators with an electron energy closed to the energy of standard γ-ray sources (cobalt and cesium) are compact and quite simply to operate. At the same time, they allow achieving a higher dose rate than therapeutic gamma units, and a narrow electron beam obtained by a properly selected collimator can expand the field of electrons application in radiation therapy of animals with spontaneous neoplasms.

REFERENCES

1. Isaeva EV, Beketov EE, Koryakin SN, Lychagin AA, Ulianenko SE. Comparison of biological effectiveness of pulse and continuous radiation of 14 MeV neutrons on murine melanoma B-16 cell culture. Radiatsiya Risk. 2012;21(2):83-90. Russian.
2. Kaprin AD, Ul'yanenko SE. Hadron therapy — development points. Medicina: Tselevye Proekty. 2016;(23):56-59. Russian.
3. Koryakina EV, Potetnya VI, Troshina MV, Efimova MN, Baykuzina RM, Koryakin SN, Lychagin AA, Pikalov VA, Ulyanenko SE. Comparison of biological efficiency of accelerated carbon ions and heavy recoils in Chinese hamster cells. Radiatsiya Risk. 2019;28(3):96-106. doi: 10.21870/0131-3878-2019-28-3-96-106. Russian.
4. Koryakina EV, Potetnya VI, Ulianenko SE. The influence of impulse 14.5 MeV neutron irradiation on mammalian cells reactions. Med. Fizika. 2015;(4):69-74. Russian.
5. Koryakina EV, Troshina MV, Golovanova OYu, Potetnya VI, Baykuzina RM, Ulyanenko LN, Koryakin SN, Ulyanenko SE. Determination of absorbed dose at different methods of target irradiation with scanning proton beam by means of chemical dosimeter FBX. Radiatsiya Risk. 2020;29(2):78-88. doi: 10.21870/0131-3878-2020-29-2-78-88. Russian.
6. Freshney RI. Culture of Animal Cells: A Manual of Basic Technique and Specialized Applications. Moscow, 2010. Russian.
7. Scampoli P, Carpentieri C, Giannelli M, Magaddino V, Manti L, Moriello C, Piliero MA, Righi S, Di Martino F. Radiobiological characterization of the very high dose rate and dose per pulse electron beams produced by an IORT (intra operative radiation therapy) dedicated linac. Transl. Cancer Res. 2017;6(Suppl. 5):S761-S768. doi: 10.21037/tcr.2017.05.21