

RESEARCH OF THE FLASH EFFECT AT THE PROTON ACCELERATOR OF INR RAS

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The flash effect, which consists in better sparing of normal cells at mean dose rates $\dot{D}_m > 100$ Gy/s, has been experimentally established quite confidently. However, its practical application requires further study of the regularities and biological nature of this effect. To this end, we studied the change in various manifestations of the flash effect with an extreme increase in the mean proton dose rate $\dot{D}_m > 104$ Gy/s. This possibility is provided by the INR high-current linear proton accelerator, which in single-pulse flash (splash) mode allows increasing \dot{D}_m up to 106 Gy/s when biological targets are irradiated with a single pulse up to 100 μ s long with an instantaneous proton current up to 10 mA. We studied [1] the dependence of the response of cells and living organisms on \dot{D}_m in the widest range: in the conventional mode with $\dot{D}_m < 1$ Gy/s, in the flash mode with $\dot{D}_m \sim 102$ Gy/s and in the splash mode with $\dot{D}_m > 104$ Gy/s. Dosimetry in high dose-rate modes was provided with EBT-XD films [2,3] and with an original detector using Cherenkov radiation [4]. In continuation of previous work [1], we irradiated tumor cells HT29 and HCT116 and normal cells - fibroblasts (ADSC) in all three irradiation modes both at the SOBP and on the plateau. As living organisms for study, we used live fertilized quail eggs. Cell response was studied using the following methods: flow cytometry, fluorescence microscopy, PCR analysis of gene expression, clonogenic analysis of cell survival etc. To study the response of live embryos to irradiation in different modes, their development and properties were studied before and after hatching from eggs. The analysis of new data is still ongoing, but the following results can be stated with sufficient statistical significance ($p < 0.01$). In the single-pulse mode with extreme dose rates (splash), compared to the usual flash mode, the following effects are observed at the same values of the absorbed dose: further reduced apoptosis of normal cells compared to tumor cells; increased expression of some important genes; reduced embryonic mortality. These results allow us to make a cautious conclusion that the flash effect does not yet reach saturation upon irradiation by protons with \dot{D}_m in the region of 102 Gy/s. Confirmation and biological substantiation of these results may initiate a further development of new accelerator techniques for application in oncology.

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[2] S.V. Akulinichev, Yu.K. Gavrilov, R.M. Djilkibaev, D.A. Kokontsev, V.V. Martynova, G.V. Merzlikin, I.A. Yakovlev, «The Dosimetry of Proton Beams in Flash-Therapy», Bull. Russ. Acad. Sci. Phys. 87 (8), 1233 (2023), doi: 10.3103/S1062873823702878.

[3] G. V. Merzlikin, S. V. Akulinichev, I.A. Yakovlev. «Simulation of a proton beam facility in the TOPAS MC software package». Moscow Univ. Phys. Bull. 11 (2023), doi.org/ 10.55959/MSU0579-9392.78.2310201.

[4] S.V. Akulinichev, Yu.K. Gavrilov, R.M. Djilkibaev, «Calibration of the Proton Beam Cherenkov Monitor», Instrum. Exp. Tech. 66 (4), 365 (2023), doi: 10.1134/S0020441223020124.

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[3] G. V. Merzlikin, S. V. Akulinichev, I.A. Yakovlev. «Simulation of a proton beam facility in the TOPAS MC software package». Moscow Univ. Phys. Bull. 11 (2023), doi.org/ 10.55959/MSU0579-9392.78.2310201.

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Section

Applications of nuclear methods in science, technology, medicine and radioecology

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