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Direct and inverse dose and dose rate effects of low dose pulsed X-rays on DNA double-strand breaks repair in human cells

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Effects of ionizing radiation registered in cells after low dose irradiation are still poorly understood. In several studies both direct and reverse effects of dose and dose rates observed in this dose range. Pulsed mode of irradiation is a useful way to understand not only the effects of dose and dose rate but also to distinguish between effects of dose rate within pulse and average dose rate during the time of irradiation. Thus, the aim of this study was to analyse effects of dose and frequency of pulsed X-rays on level of radiation-induced DNA double-strand breaks and their repair kinetics in human peripheral blood lymphocytes and MOLT-4 cells in vitro. Analysis of radiation-induced γH2AX and 53BP1 repair foci was used for assessment of DNA double-strand breaks (DSB) in these cells. Cells were irradiated by pulsed X-rays using custom high-power electric pulse generator Sinus-150 (current intensity 4 kA, peak energy 90-100 keV, pulse length 4 ns) with various total doses formed by change of rate within pulse and fixed number of pulses - 4000. Dose-response curve of radiation-induced foci of both proteins had shown deviations from linearity to higher effect in 12-32 mGy dose range and lower effect at 72 mGy. Number of residual radiation-induced γH2AX and 53BP1 foci at 18 h after irradiation depended on frequency of X-ray pulses: highest effect was registered at 13 pulses per second for peripheral blood lymphocytes and at 8 pulses per second for MOLT-4 cells. It suggests that frequency effect is influenced by individual cell features.

For better understanding the role of average dose rate and dose rate within pulse in observed effects we exposed human peripheral blood lymphocytes to 32 and 72 mGy with various average dose rates (1.9-43.2 mGy/min) and dose rates within pulse (0.03-2.25 mGy/ns). It was shown that both effectiveness of DNA DSB repair and fraction of cells with γH2AX pan-staining used as a marker of apoptosis at 18 h after irradiation were depended on dose rate within pulse. Inverse effect of dose rate within pulse was observed in the range 0.5-1.0 mGy/ns with the total dose of 32 mGy. At lower dose rate within pulse direct effect was shown for both effectiveness of DNA DSB repair and fraction of cells with γH2AX pan-staining.

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Primary author: Dr VASILYEV, Stanislav (Institute of Medical Genetics, Tomsk, Russia)

Co-authors: Mr BELENKO, Andrey (Tomsk State University, Tomsk, Russia); Dr LEBEDEV, Igor (Institute of Medical Genetics, Tomsk, Russia); Prof. BOLSHAKOV, Mikhail (Tomsk State University, Tomsk, Russia); Mr KUTENKOV, Oleg (Institute of High Current Electronics, Tomsk, Russia); Prof. ROSTOV, Vladislav (Institute of High Current Electronics, Tom)

Presenter: Dr VASILYEV, Stanislav (Institute of Medical Genetics, Tomsk, Russia)

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