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## Comparison of the effects of various types of beta-irradiation on the cells of human epidermoid carcinoma A431

Sergey Soroko\*, Lydia Shestakova, Anna Brilkina, Andrey Yudintsev, Natalia Shilyagina

National Research Lobachevsky State University of Nizhny Novgorod; 603022, Nizhny Novgorod, Gagarin Ave., 23

\* Corresponding author: [kastarashan@gmail.com](mailto:kastarashan@gmail.com)

**Abstract:**

Targeted radiopharmaceuticals, which mainly include beta-emitting radionuclides, allow for selective action and reduction of the total radiation load. The aim of the study was to assess the viability of human epidermoid carcinoma cells A431 at various intervals after exposure to high-energy electrons in the regime of acute and chronic irradiation.

To simulate chronic or acute irradiation, cells were irradiated with closed Sr-Y-90 sources (STC, Amplituda) and a Novalis Tx linear accelerator (Varian Medical Systems, UK), respectively. At 24 and 72 hours after the start of irradiation, an MTT test was performed for the subsequent determination of LD50.

We registered a difference in the viability of A431 cells 24 and 72 hours after irradiation at the same dose: LD50, estimated 72 hours after irradiation, was 2 times lower than after 24 hours. The observed effect is apparently caused by a pronounced radiation block of mitosis 24 hours after exposure. In addition, 72 hours after irradiation, large numbers of "giant" cells are found, formed from several cells as a result of division attempts. In the case of acute irradiation, the radiosensitivity of A431 cells increases approximately fourfold. Apparently, different types of exposure, at the same dose, cause different levels of oxidative stress, which is suppressed to varying degrees by enzymes and the antioxidant system, which affect the repair systems in the cell, which must be taken into account when forming the dose load for patients undergoing radiotherapy.

**Keywords:** A431, beta-irradiation, radiosensitivity, radiotherapy



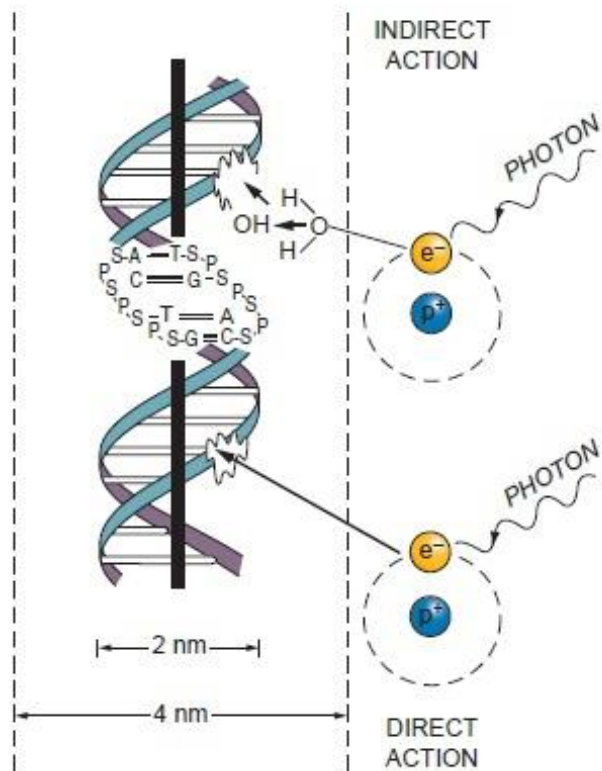
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# Introduction

Acute radiation therapy using gamma sources is one of the main methods of cancer treatment used in modern medicine. Along with the classical approach of wave irradiation, radionuclide therapy with the use of beta and alpha emitters, as well as brachytherapy, is gaining popularity.

However, despite the expanding range of possibilities of using beta emitters in the field of diagnostics and treatment of oncological diseases, the overwhelming majority of studies on radiosensitivity at the cellular level were performed using external acute gamma irradiation with a high dose rate. In turn, the mechanism of action of corpuscular, in particular chronic and acute beta-radiation, on animal and human cells has not been sufficiently studied, which does not allow using these types of therapy as efficiently as possible.



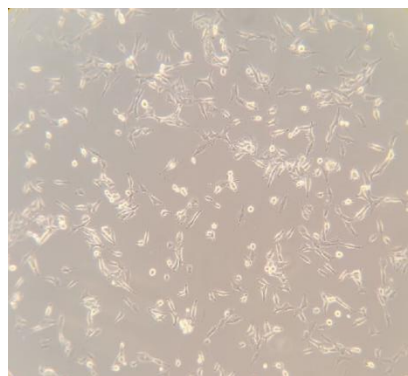
In this regard, the aim of the work was a comparative analysis of the mechanism of action of acute and chronic beta radiation on the cells of human epidermoid carcinoma A431.



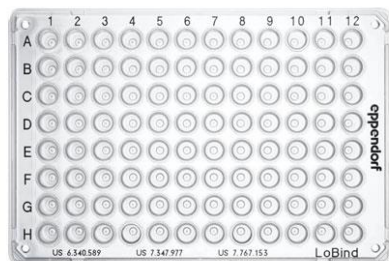
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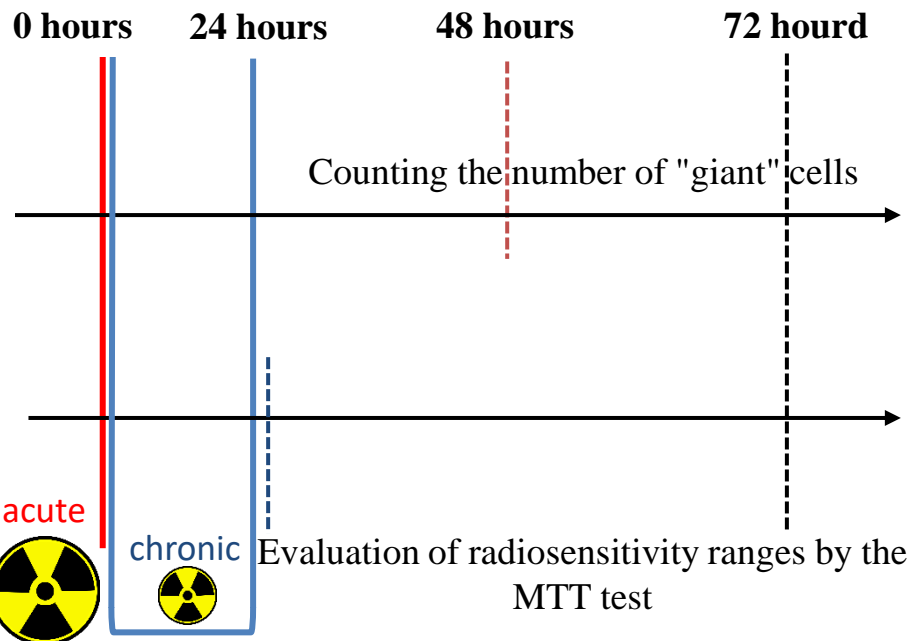
# Methods



Micrograph of human epidermoid carcinoma cells A431



$5 \times 10^3$  cell per well



A Novalis Tx linear accelerator with an electron energy of 6 MeV, a source-to-surface distance of 100 cm, an applicator of 25x25 cm<sup>2</sup>, and a dose rate of 10 Gy/min was used as a source for acute irradiation. Irradiation was performed in doses of 4-64 Gy. The dose was controlled by the exposure time, which did not exceed 8 minutes. For chronic irradiation, a closed beta emitter <sup>90</sup>Sr + <sup>90</sup>Y with a dose rate of 0.5-1.5 Gy/h was used. Irradiation lasted 24 hours, simulating doses of 6-72 Gy. The dose was controlled by the radiation dose rate in various combinations of sources and shielding films. Sources were placed above/below the plate wells.

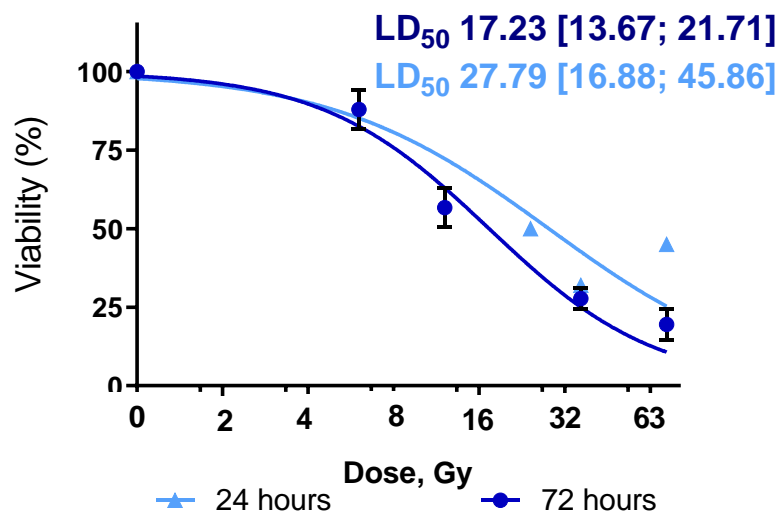


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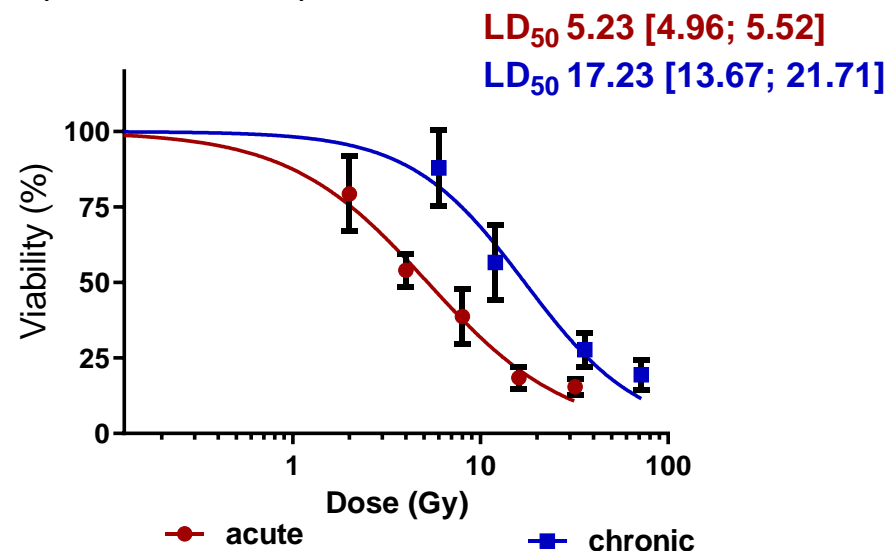
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# Results and discussion

At the first stage of the study, the curves of the A431 radiosensitivity were obtained under the action of acute and chronic beta radiation (24 and 72 hours after the start of irradiation). Viability was assessed by the MTT test.



Dose-effect curve of A431 cells 24 and 72 hours after the onset of chronic beta-irradiation.



Dose-effect curve of A431 cells 72 hours after the onset of acute and chronic beta-irradiation.

We have shown that at the same dose of irradiation, the percentage of viable cells after 24 and 72 hours for A431 cell culture is different. The observed effect may be due to the fact that radiation damage to cells can manifest itself both in the form of a cytotoxic action - a violation of the structure of the main macromolecules and membrane organelles of the cell - and in the form of a cytostatic action caused by blocking the cell cycle or mitosis.

Differences in the dose dependence of cell viability upon exposure to acute and chronic beta radiation indicate that the processes triggered by exposure to high-intensity and low-intensity sources of ionizing radiation are different. The fundamentally two different types of exposure to radiation in an equal dose investigated in this work, most likely, cause different levels of oxidative stress in the cell, suppressed by the work of enzymes to different degrees.



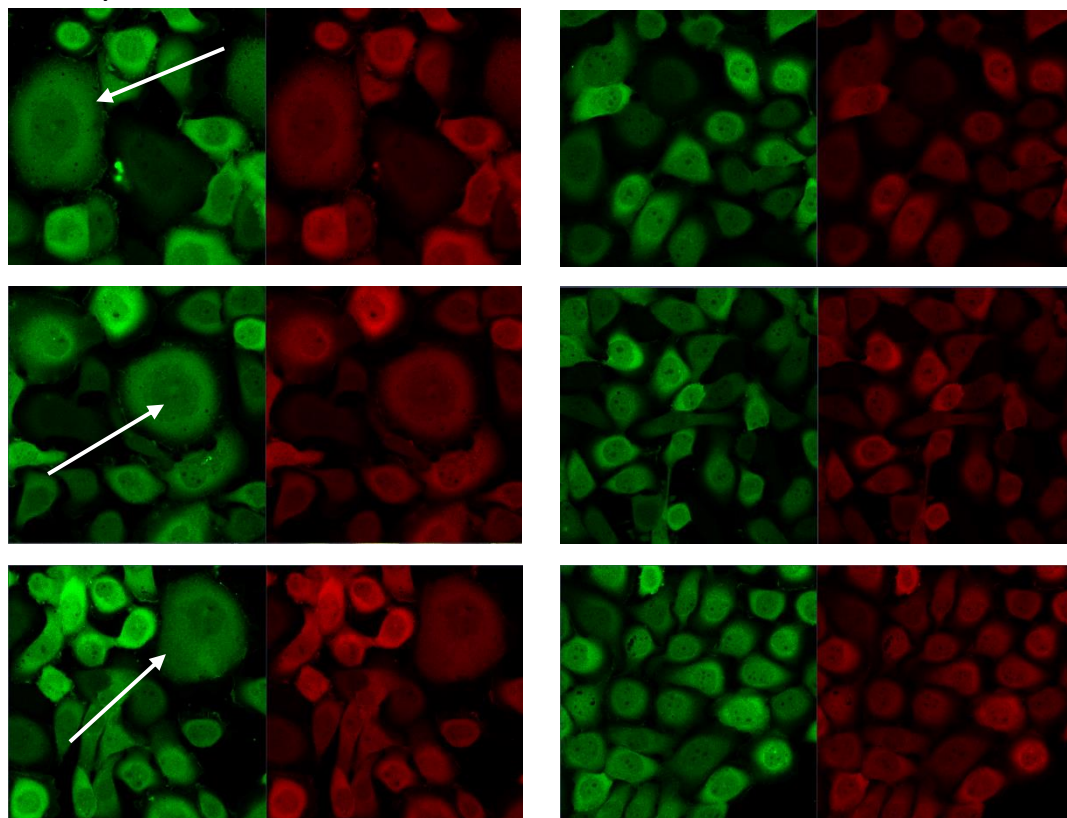
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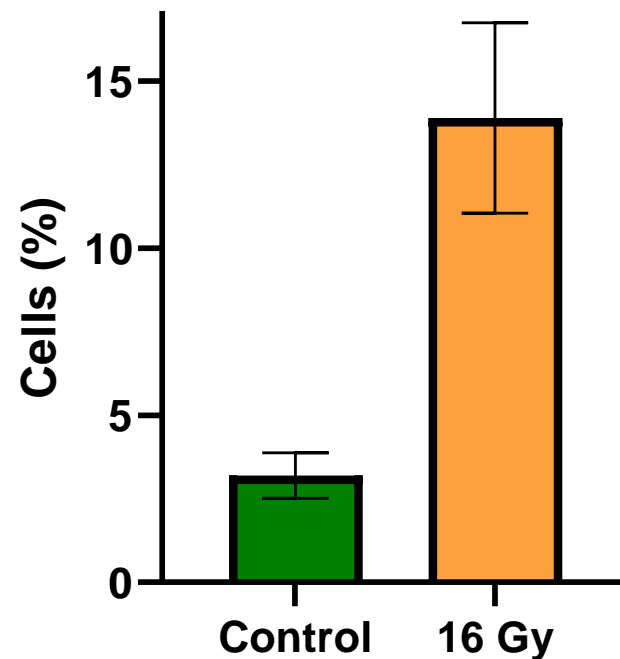
# Results and discussion

At the second stage of the study, the number of "giant" cells was estimated using laser scanning confocal fluorescence microscopy.

16 Gy, 72 hours after irradiation



Fluorescent images A431. The arrow indicates the "giant" cells.



The percentage of "giant" cells of the total number of A431 cells 72 hours after acute beta-irradiation.

The appearance of "giant" cells after irradiation can be taught by the presence of a radiation block of mitosis. The cell increases the amount of material required for division, grows in size, but the very act of division does not occur. As a rule, such cells die after 4-6 doubling cycles.



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# Conclusions

As a result, the following results were obtained:

1. Differences in  $LD_{50}$  were revealed when assessing the viability of A431 cells 24 and 72 hours after beta irradiation,  $LD_{50}$  was 27.79 and 17.23, respectively.
2. Differences in  $LD_{50}$  for acute and chronic beta irradiation were obtained by more than 3 times.  $LD_{50}$  for acute and chronic irradiation were 5.23 and 17.23 Gy, respectively.
3. The appearance of "giant" cells was shown 72 hours after exposure to beta radiation at a dose of 16 Gy, which is a consequence of the presence of a radiation block of mitosis.



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