Abstract

According to data from the World Health Organization's 2022 report, prostate cancer is one of the most commonly diagnosed malignancies among men worldwide, particularly in Europe and North America. Although several treatment options are available - including surgery, chemotherapy, radiotherapy, and immunotherapy - there is still a need for new and more effective therapies. In recent years, this has led to growing interest in the role of exosomes in cancer research.

The main objective of this doctoral project was to investigate the influence of exosomes on the radiosensitivity of prostate cancer cells and to determine whether the radiation-induced bystander effect (RIBE) can be activated in recipient cells via exosomes isolated from irradiated cells. To this end, apoptosis induction, a form of programmed cell death, was analyzed. Additionally, γH2AX foci formation was assessed to determine whether the exosomes induce DNA damage. The molecular content of the exosomes (so-called cargo) was performed using Western blot, which enabled their identification. Cellular responses to radiation were further evaluated using the clonogenic survival assay as well as cytotoxicity assays (LDH and IL-6). The effects of radiation-induced stress on the concentration and size of exosomes isolated from PC3 and DU145 prostate cancer cells were analyzed using NTA. Two radiation sources: a ^{241}Am α particle source and an X-ray tube, available at the Department of Biomedical Physics and the Heavy Ion Laboratory, were used. α radiation dose rate was estimated using Monte Carlo simulations in the Geant4-DNA framework, while X-ray dose measurements were validated using radiochromic film dosimetry.

The experimental results demonstrated that PC3 cells exhibit greater radiosensitivity compared to DU145 cells. NTA measurements revealed no significant differences in the size distribution of exosomes isolated from the two cell lines. The findings support the hypothesis that the bystander effect can be initiated in prostate cancer cells exposed to X-rays and co-cultured with exosomes derived from irradiated cells. These results contribute to a better understanding of radiosensitivity modulation and highlight the potential application of exosomes in the optimization of radiotherapy.

Keywords

ionizing radiation, exosomes, prostate cancer cells, Radiation-Induced Bystander Effects, radiosensitivity