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Functional changes in brain microvascular endothelial cells upon low-energy accelerated proton-irradiation

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Background

The ionizing radiation exposure can induce endothelial activation, dysfunction, ROS formation, BBB permeability elevation and tight junction morphology changes [1, 2]. Thus, in order to increase the distribution and efficacy of chemotherapeutics, a complex characterization of the brain microvasculature after irradiation is imposed.

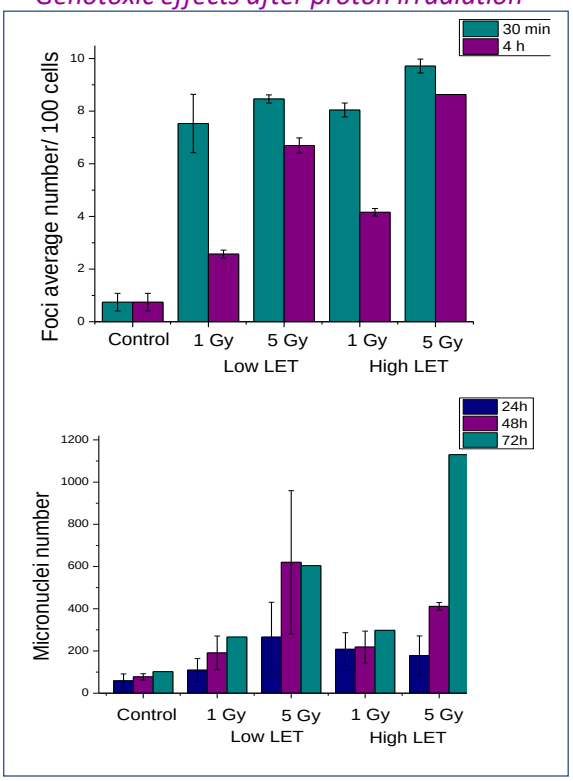
Aim

Our study is focused on understanding how accelerated proton beams affects the brain microvascular endothelial cells functionality.

Materials and methods

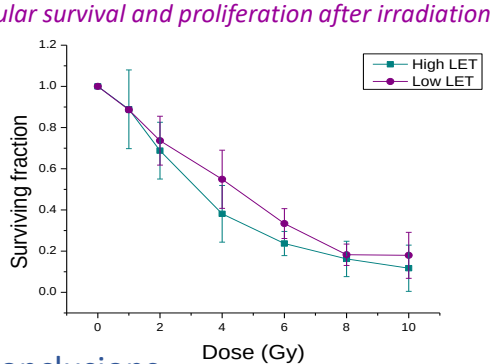
The *in vitro* model of murine cerebral microvasculature (bEnd.3 cell line) was exposed to various doses in the range 0-10 Gy (dose rate 1 Gy/min) using a TR19 cyclotron. For testing cellular capacity of proliferation and surviving after irradiation, the clonogenic assay method was used. Also, to assess the ionizing radiation-induced DNA damage, the expression of micronuclei (24,48,72 h after irradiation) and γ-H2AX foci (30 minutes and 4 h after irradiation) were measured. After 24 h from irradiation, the calcium ions dynamics was observed by activating the purinergic receptors signal pathway.

Genotoxic effects after proton irradiation

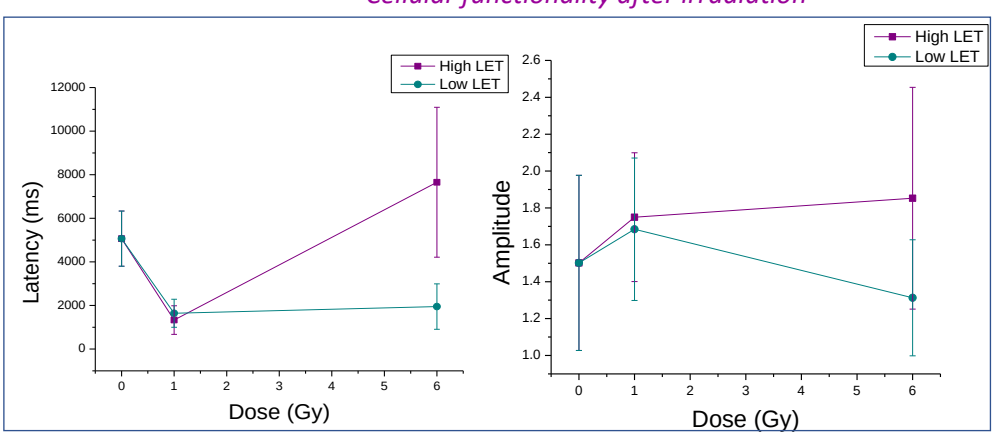


Results

Cellular survival and proliferation after irradiation



Cellular functionality after irradiation



Conclusions

✓ By comparison low (~5 keV/μm) and high (~10 keV/μm) LET radiation, it can be observed that the surviving fraction has higher values in the range 2-6 Gy. Also, the micronuclei formation seems to increase in time after irradiation, but the appearance of γ-H2AX foci decreases after 4 hours. We also observed a nonlinear modification of the calcium transient parameters (latency, amplitude) with the dose.

References

[1] Baselet Bjorn et al., *Pathological effects of ionizing radiation: endothelial activation and dysfunction*, (2019).
[2] Appelboom Geoff et al., *Stereotactic modulation of blood-brain barrier permeability to enhance drug delivery*, (2016).