Effects of X-rays and titanium ions on cardiomyocyte cultures*

J. Frieß[1], *A. Heselich*[2], *S. Ritter*[3], *P. G. Layer*[2], *and C. Thielemann*[1]

[1]University of Applied Sciences Aschaffenburg, Germany; [2]Technische Universität Darmstadt, Germany; [3]GSI, Darmstadt, Germany

Motivation

For the pursuit of the planning of manned space missions to Mars [1; 2] as well as for the application of heavy ion irradiation in radio-therapy [3] an assessment of possible effects of high LET radiation on the cardiovascular system, especially heart muscle cells is needed. In order to approach this important field, we used for the first time microelectrode arrays (MEA). This method allows the recording and monitoring of electrophysiologic cardiac signals of primary cardiac cultures, seeded onto MEA-chips. Additionally, DNA damage and cell cycle progression were examined.

Material and Methods

Cardiac cells were isolated from chicken at developmental embryonic stage E8 and cultivated. Cells were seeded onto 60 electrode MEAs and 15 mm coverslips. The cultures were exposed to carbon (25 mm Bragg Peak, mean LET 75 keV/μm at sample position) or titanium ions (1 GeV/u) at the SIS-facility (GSI, Germany). X-ray exposure was conducted at the Technische Universität Darmstadt (135 kV; 19 mA / 90 kV; 33.7 mA). Electrophysiological properties of the cell cultures were measured before and after exposure. Signals of cardiac cells could be recorded for approximately one week and were analysed in terms of beat rate, conduction velocity, field action potential duration and general spike shape using the MATLAB software tool DrCell [4]. Cardiomyocytes cultured on coverslips were fixed at different time points after exposure and double strand break (DSB) accumulation and repair, proliferation and apoptosis were examined by immunohistochemistry.

Results

Experiments up to now indicate that heavy ion irradiation reduces the conduction velocity of cardiac signals [5]. Furthermore, cultures irradiated with titanium ions show a slight increase in the field action potential durations four hours after exposure compared to the sham irradiated controls (see figure 1). In contrast, cultures exposed to the same doses of X-rays exhibit a reduction in their field action potential duration in comparison to the non-irradiated controls. These results indicate different radiation qualities may have opposing effects on the electrophysiology of the exposed cells. This is also supported by other physiologic parameters such as the beat rate.

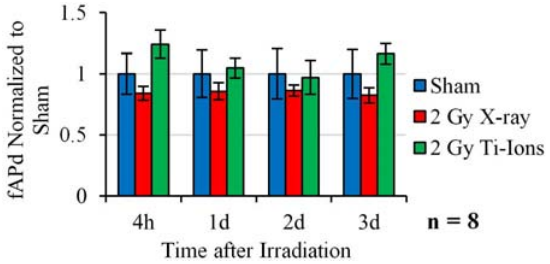

Figure 1: Field action potential durations (fAPd) are exemplarily plotted for cultures exposed to 2 Gy X-ray and titanium ions, respectively.

For both, X-ray and heavy ion radiation, we observed a late, but dose-dependent G1/S-checkpoint response analyzed by S-phase labeling. Irradiation with higher doses of heavy ions resulted in a stronger decrease of proliferation compared to similar doses of X-rays. We detected only small differences in G2/M-activation. We also observed a dose-dependent decrease in the number of mitotic figures 24 h after X-irradiation, whereas irradiation with heavy ions showed only slight decreases

Conclusion

X-ray and titanium ion exposure show opposing effects on some electrophysiologic characteristics at the same doses.

References

[1] Space Studies Board, National Research Council, "Radiation Hazards to Crews of Interplanetary Missions" National Academy Press, Washington DC, 1996

[2] R. J. White et al., "Humans in space", Nature, 2001, 409(6823), p. 1115

[3] M. P.Little et al., "Review and meta-analysis of epidemiological associations between low/moderate doses of ionising radiation and circulatory disease risks, and their possible mechanisms.", Radiat Environ Bio-phys, 2010 49(2), p. 139–53

[4] C Nick et al., "DrCell – A Software Tool for the Analysis of Cell Signals recorded with extracellular Microelectrodes", Signal Processing: An International Journal (SPIJ), 2013-2;7(2), p. 96-109

[5] J. Frieß et al, "Electrophysiological Effects of Heavy Ion Irradiation on Cardiomyocytes", GSI Report 2012 (2013) 480

* This work is supported by the DLR and ESA in the frame of the ESA IBER-10 program.