Electrophysiological Effects of Heavy Ion Irradiation on Cardiomyocytes*

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Motivation

Several effects of ionising radiation at low or moderate doses on the cardiovascular system are known [1, 2], but there is essentially no information available on the effects of high-LET radiation on the heart. Therefore, an assessment of possible late effects on the cardiovascular system after irradiation with high-LET radiation is needed, for instance with respect to particle therapy or the planning of long-term space missions [3]. In both cases the emergence of adverse effects following radiation exposure must be taken into consideration.

To address the question if and to what extent the cells in the heart muscle are affected by an exposure to high doses of heavy ions, primary avian cardiomyocytes were used. In parallel experiments cells were grown on microelectrode array chips (MEAs) or culture dishes and changes in the electrophysiological behaviour as well as in cell cycle propagation were investigated.

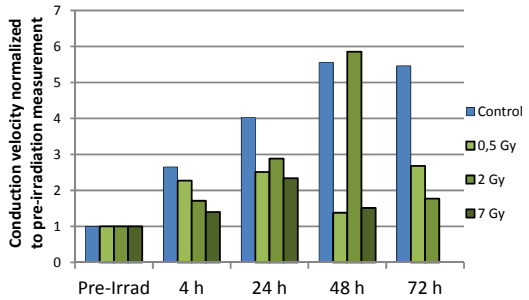

Figure 1: Conduction velocity of cardiomyocyte networks after titanium ion irradiation.

Material and Methods

Cardiac cells were isolated from chicken at developmental embryonic stage E8 and cultivated [4]. As a means to investigate electrophysiological signals, cells were seeded onto 60 electrode MEAs.

To analyse intracellular damage accumulation, cell cycle arrests and cell proliferation, cells were also seeded onto fibronectin coated glass coverslips cultured in multiwall plates.

In order to study the effects of high-LET radiation on the cells, the cultures were exposed to carbon (25 mm Bragg Peak, mean energy 75 keV/µm at sample position) and titanium (1 GeV/u) ions at the SIS-facility (GSI, Germany).

Electrophysiological properties of the cell cultures were measured before and after exposure. Cardiac signals 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. Cardiomyocytes cultured on coverslips were fixed at different time points after exposure and by immunohistochemistry double strand break (DSB) accumulation and repair, oxidative stress and apoptosis, were measured.

Results

As previously shown, the cardiac cultures exhibit a high resistance towards ionising radiation [5], since all cell networks maintained their contractive activity. In cultures irradiated with titanium ions, a reduction of the conduction velocity compared to the untreated controls was observed (see Figure 1). This effect might result from an alteration in gap junction activity due to irradiation. Further assays addressing the expression of connexion 43 could give insights into this phenomenon in future experiments.

Immunohistological stainings for γH2AX-phosphorylated DSBs in the nuclear DNA showed ion tracks through the cell nucleus in cultures fixed shortly after exposure to titanium ions (see Figure 2). Furthermore, our data show that independent of applied dose the cells were able to repair the induced genetic damage within 24 hours (data not shown).

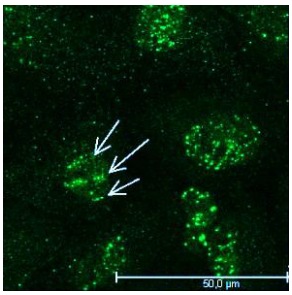

Figure 2: γH2AX-stained cardiac cell culture, fixed 15 min after exposure to titanium. Arrows indicate ion tracks through one nucleus.

References

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