Electrophysiological response of mouse embryonic stem cell-derived cardiomyocytes after X-ray and C-ion exposure*

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An increased risk for late-occurring ischemic heart diseases is a known consequence of a high dose radiation exposure to the heart [1]. Yet, there is growing evidence coming from epidemiological data for an increased risk at low doses [2]. To address the question whether the electrophysiology of the heart is affected by ionizing radiation, we used mouse embryonic stem cell (mESC)-derived cardiomyocytes as a model system. Cells were cultured on a microelectrode arrays (MEA) enabling electrophysiological measurements [3] and the effects of X-rays and C-ions were examined.

Briefly, commercially available purified mESC-derived cardiomyocytes (Cor.At, Axiogenesis) that build up spontaneously beating networks were used for experiments. Cor.At cells were seeded on the fibronectin-coated MEAs according to the manufacturer's protocol. Radiation exposure was performed two days after seeding applying either C-ions (SOBP, twelve energies ranging from 107-147 MeV/u, mean LET = 75 keV/µm at target position) accelerated at the SIS18 (GSI) or 250 kV X-rays. The doses used for both radiation qualities were 0.5 and 2 Gy. Measurements were conducted up to six days following exposure. Data were subsequently analyzed with the MATLAB-based software *DrCell* developed at University of Applied Sciences Aschaffenburg [4]. Electrophysiological endpoints such as number of active electrodes, beat rate, the QT-interval-like section or the conduction velocity were determined.
Generally, inter-experimental variations were large. Therefore the data sets were not pooled. In figures 1 and 2 data on the number of active electrodes and the beat rate measured two days after exposure to 2 Gy X-rays or C-ions are exemplarily shown. As depicted in figure 1, in each experiment the number of active electrodes was not significantly changed in the irradiated samples compared to the control. The inter-experimental difference in the number of active electrodes between both data sets was pronounced (mean values of 46 and 19 active electrodes for the X-ray and the C-ion experiment, respectively). As shown in figure 2, also the beat rate was not affected by exposure to X-rays or C-ions when compared to the respective controls. Notably, inter-experimental variations of the beat-rate were lower than those observed for the number of active electrodes (about 40 vs. 60 beats/min). Similarly, the QT-interval-like section of the cardiomyocytes' signal and their conduction velocities were not altered after exposure (data not shown).

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Altogether our data show that electrophysiological parameters of cardiomyoctes were not affected at two days after exposure to X-rays or C-ions. Currently, measurements performed at later time-points are analyzed to screen for putative effects occurring at later stages.

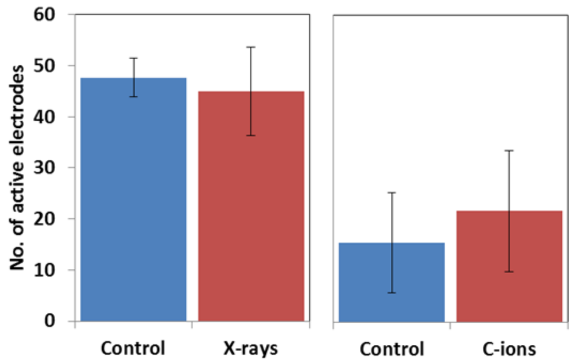

Fig. 1: Number of active electrodes. Measurements were performed two days after exposure to 2 Gy of X-rays or C-ions, respectively (mean values ± SD of a total n ≥ 8).

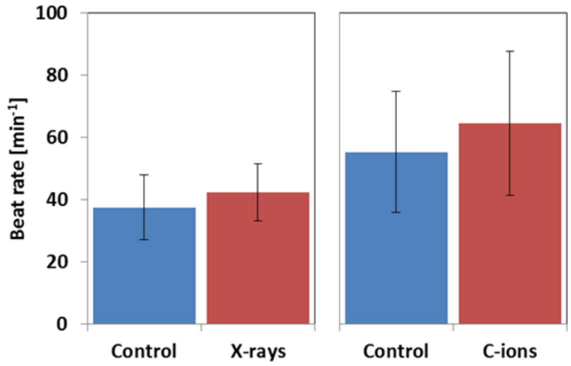

Fig. 2: Beat rate. Measurements were performed two days after exposure to 2 Gy of X-rays or C-ions, respectively (mean values ± SD of a total n ≥ 8).

References

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