Irradiation of thyorax triggers signaling with potential acute cardioprotective benefits in rats
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Objectives: Myocardial synchronisation and proper heart function depends on the expression and subcellular distribution of intercellular connexin-43 (Cx43) channels that are essential for electrical coupling and direct cell-to-cell communication. Radiotherapy is applied to treat cancer but chest irradiation can induce heart disease. We hypothesized that irradiation on thorax triggers endogenous compensatory mechanisms including the increased expression of Cx43, protein kinase C (PKC)-delta, PKC-epsilon, and microRNAs that may potentially modulate cardiac function.

Methods: Healthy adult, male Wistar rats were irradiated with a single 25 Gray (Gy) dose on thorax. Six weeks later, the animals were anaesthetized and hearts were excised. Left ventricular tissue was isolated for determination of Cx43 distribution and expression of Cx43, PKC-delta, PKC-epsilon, miRNA-1 and miR-21 using immunohisto-chemistry, western blotting and real-time PCR respectively.

Results: Body and heart mass were decreased in irradiated rats when compared to the controls. There were no changes in cardiomyocyte Cx43 localization between groups. Total Cx-43 protein and its functional phosphorylated forms were significantly increased in left ventricle of rats exposed to irradiation. In parallel, the level of miR-1 that down-regulates Cx43, was suppressed and expression of PKC-epsilon that phosphorylates Cx-43, was increased in those animals. Irradiation also induced increase in PKC-delta and miR-21 expression suggesting activation of pro-hypertrophic and pro-fibrotic pathways.

Conclusions: Irradiation of thorax triggers up-regulation of myocardial Cx43, PKC signaling and decrease miR-1 but increase miR-21 levels in the heart. Some of these endogenous compensatory mechanisms may be potentially important in acute preservation heart function following irradiation.