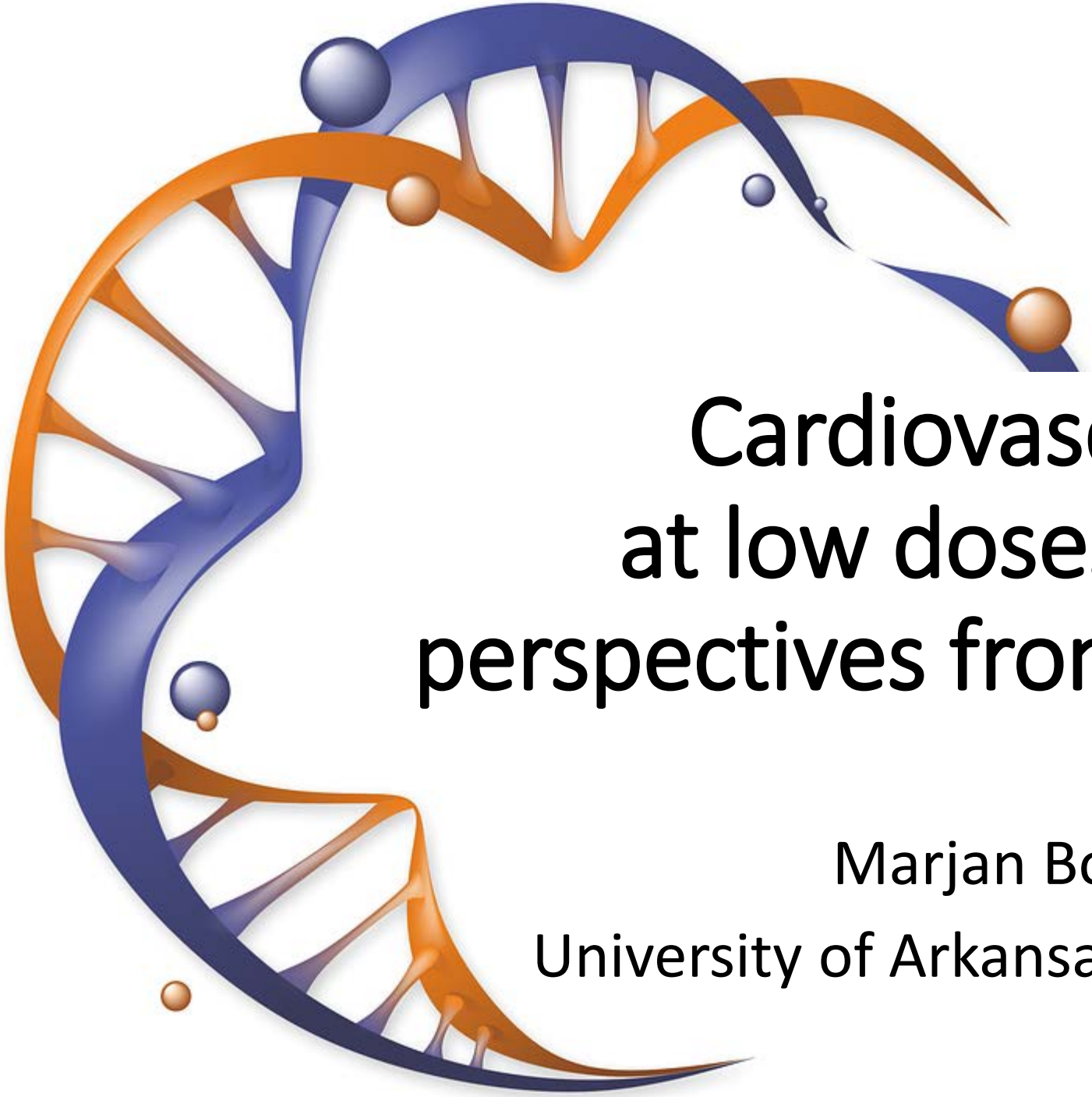

Cardiovascular effects at low doses of radiation: perspectives from radiation biology

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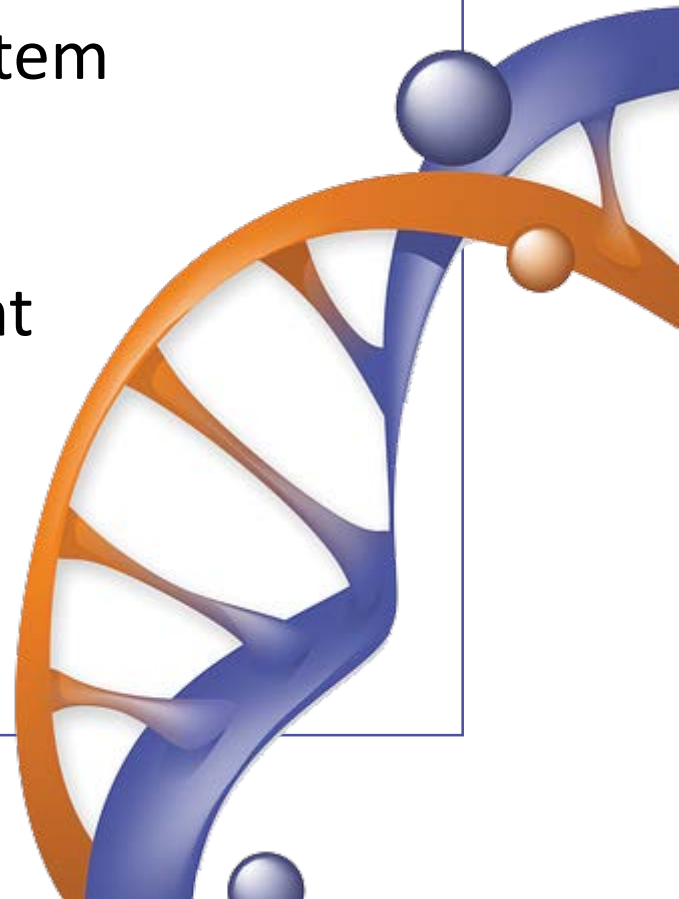
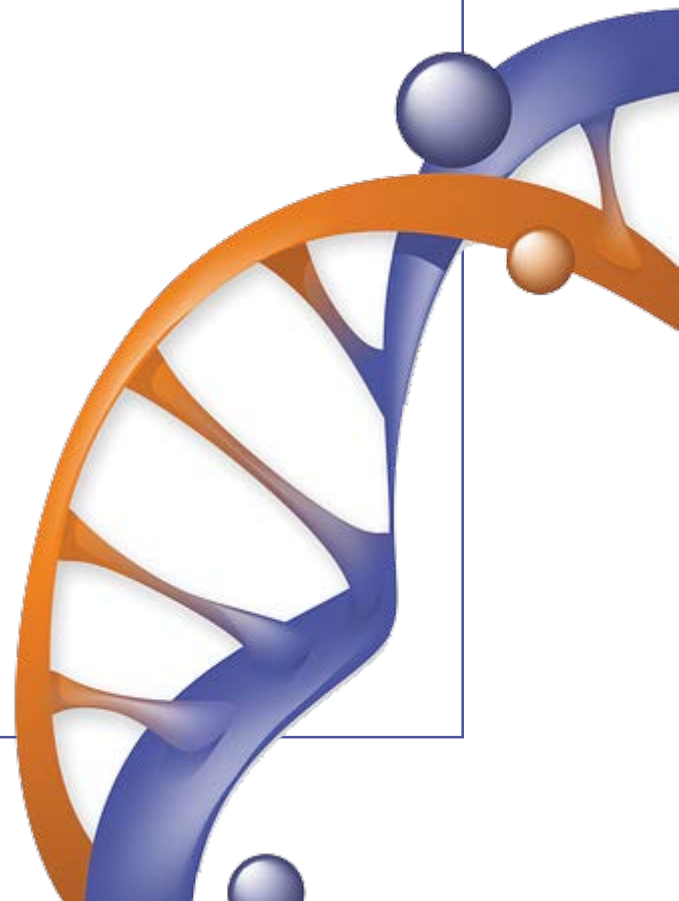
Experimental radiation models

- Epidemiological and clinical evidence indicates that low doses of ionizing radiation can alter the cardiovascular system
- Radiation biology:
  - Confirm these results in a controlled environment
  - Identify biological mechanisms



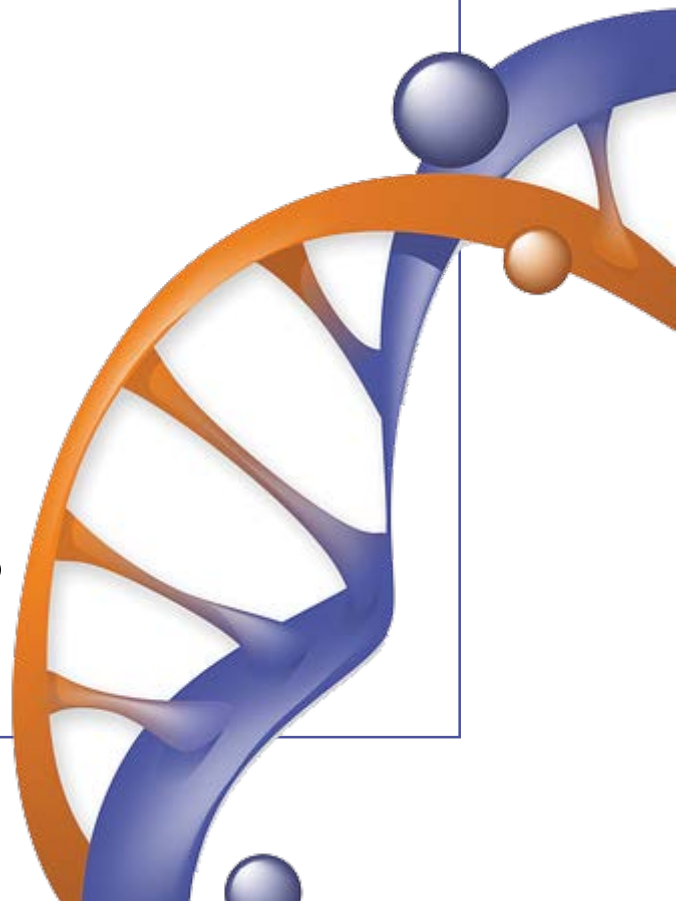
Radiation conditions

- Low or high linear energy transfer (LET)
- This presentation: low-LET radiation at doses ≤ 2 Gy
- Dose rate
- Energy

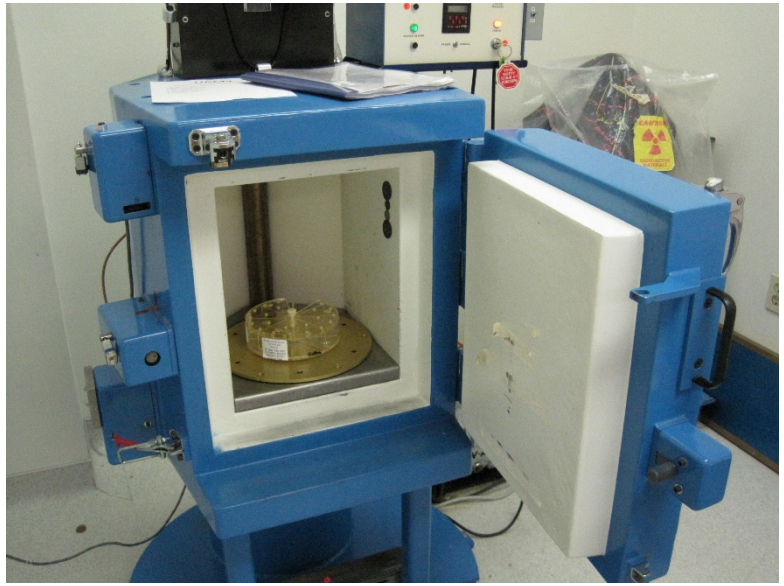


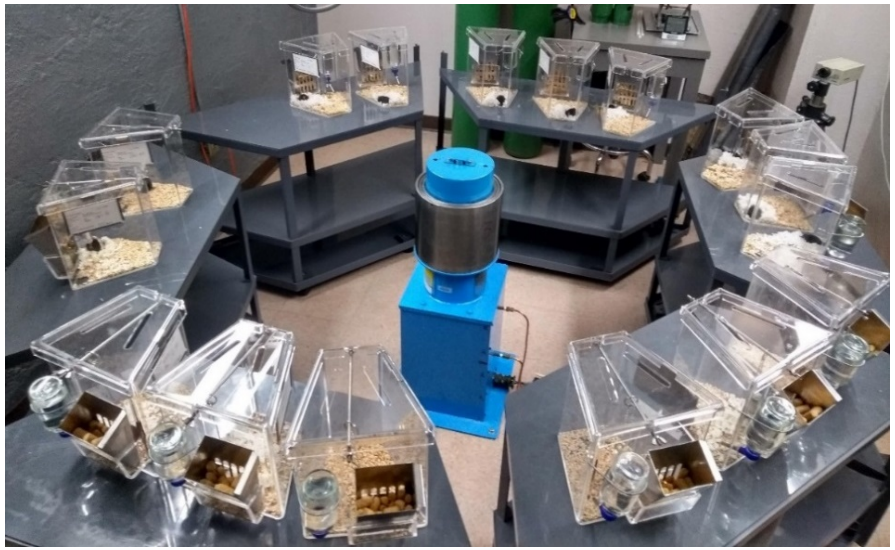
Animal models

- Species
- Wild-type or genetically modified
- Whole body or localized irradiation
- Recent review articles:
  - Puukila et al. Radiation Research 2017; 188: 539-546
  - Tapio et al. Environment International 2021; 146: 106235

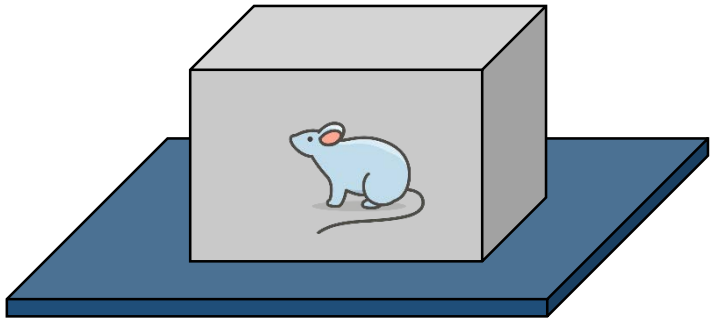


Low-LET experimental radiation facilities





Healthy animals



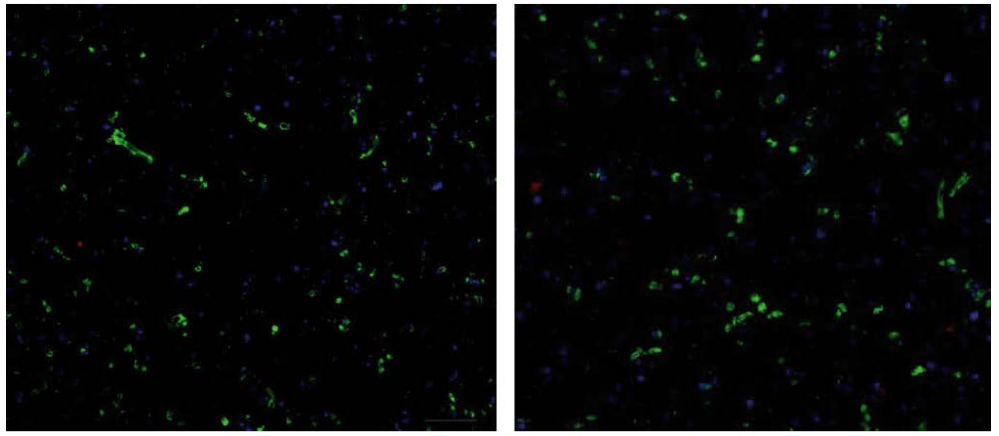
Female C57BL/6J mice

Cobalt-57, 0.04 Gy in 21 days

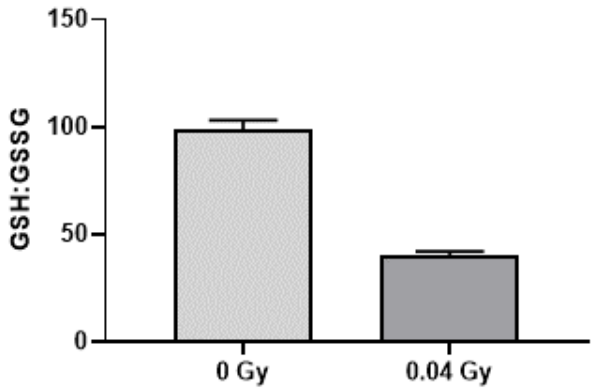
Brain cortex

Green: endothelium

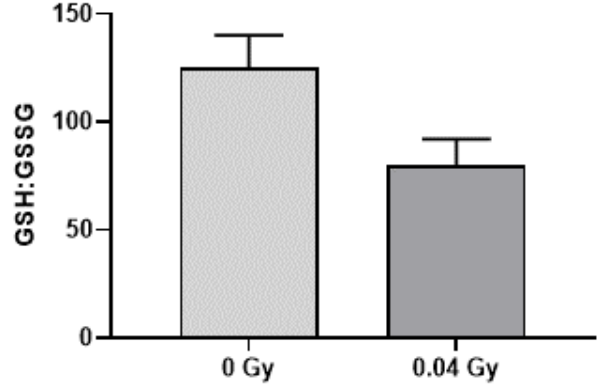
Red: 4-hydroxynonenal



Heart: glutathione



7 days



1 months

Mao et al. Radiation Research 2016; 185: 647-657
Seawright et al. PLoS One 2017; 12: e0180594

Metabolomics and proteomics

Wild-type mouse strains, inbred and outbred, neonatal and adult

γ-rays, 0.01 – 1 Gy whole body

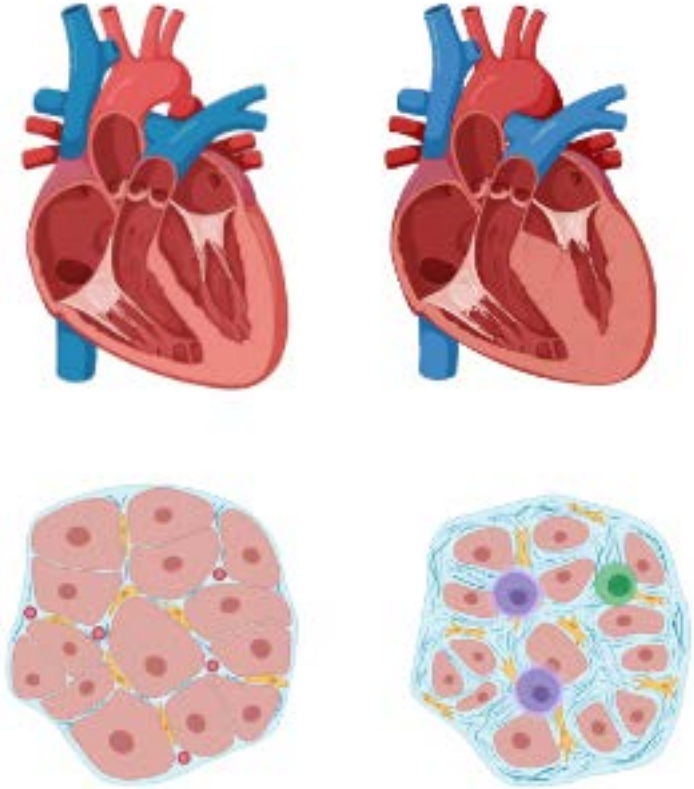
200 kV or 6 MV photons, 0.2 or 2 Gy local heart

- Mitochondrial metabolism and respiration
- Inflammatory response
- Cytoskeletal structure

Bakshi et al. Radiation and Environmental Biophysics 2013; 52: 451–461
Barjaktarovic et al. PLoS ONE 2011; 6: e27811
Gramatyka et al. Journal of Radiation Research 2020; 61: 14-26

Disease models

Male C57BL/6J mice, streptozotocin induced diabetes



Zhang et al. Radiation Research 2011; 175: 307-321
Zhang et al. J Cell Mol Med 2016; 20: 1352-1366

Disease models

Male C57BL/6J mice, streptozotocin induced diabetes

200 kV photons 0.013 – 0.05 Gy every other day for 7 – 56 fractions (total: 0.175 – 2.1 Gy)

- Reduced oxidative stress
- Reduced inflammatory cytokines
- Reduced apoptotic cell death
- Reduced cardiac fibrosis
- Improved cardiac function

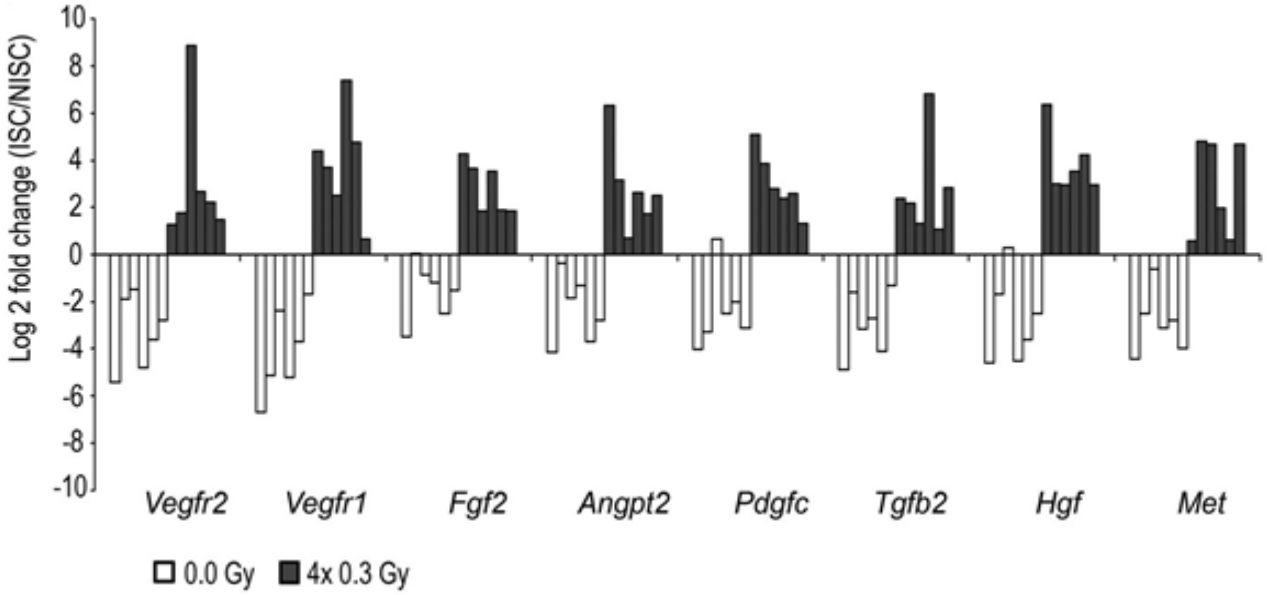
Zhang et al. Radiation Research 2011; 175: 307-321
Zhang et al. J Cell Mol Med 2016; 20: 1352-1366

Disease models

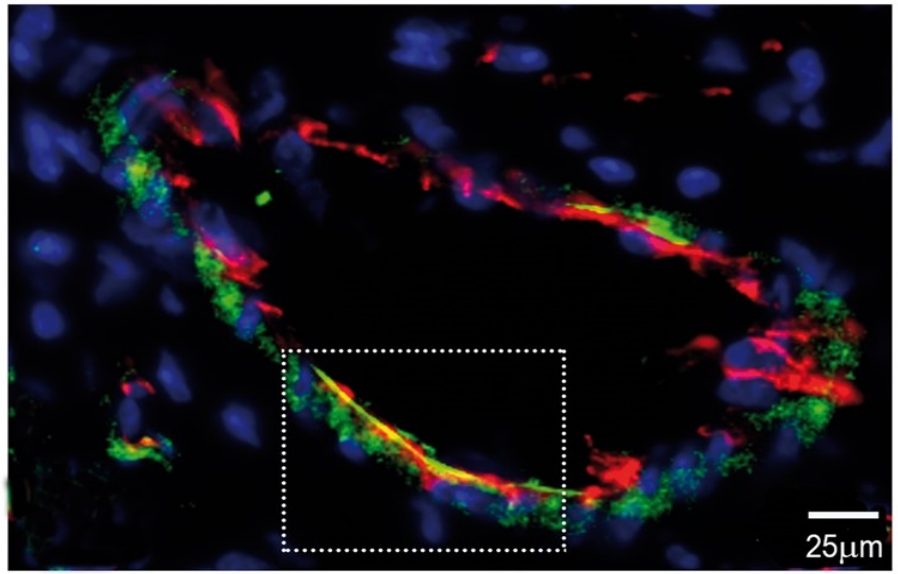
Female C57BL/6J mice subjected to hindlimb ischemia

6 MV photons 0.3 Gy per day for 4 days

Ischemia-induced neovascularization enhanced

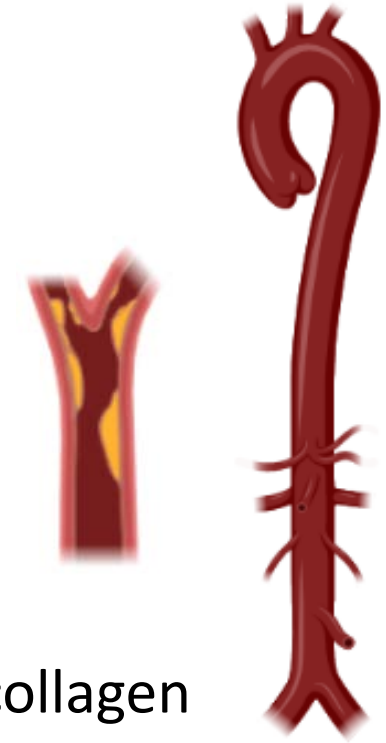


Endothelial progenitor cells



Ministro et al. Cardiovascular Research 2017; 113: 783-794

Disease models: ApoE$^{-/-}$ mice



- Female, γ-rays 0.025 – 0.5 Gy in 10 min – 8.5 hours

  Decreased lesion area

  Mitchel et al. Radiation Research 2011; 175: 665-676

- Male, γ-rays 0.067 or 0.157 Gy in 8 months

  Decreased lesion area, decreased macrophage numbers, increased collagen

  Ebrahimian et al. Radiation Research 2018; 189: 187-196

- Female, γ-rays 0.3 Gy in 10 months

  Increased lesion area, no change in macrophage numbers, increased matrix metallopeptidase 9

  Mancuso et al. Oncotarget 2015; 6: 31263-31271

Conclusions

- In common wild-type rodent strains, low-dose low-LET radiation can cause oxidative changes, metabolic responses
- In experimental disease models, low-dose low-LET radiation can have beneficial effects
- More research is required to identify biological mechanisms, radiation dose and dose rate effects, and influence of sex on outcome