Background: Radiation is a commonly used modality of treatment in cancer associated with development of cardiomyopathy, which is often subtle and delayed for years. Due to the cardioprotective effects of the cGMP-specific phosphodiesterase-5 inhibitors, we tested the ability of sildenafil to protect against radiation induced cardiomyopathy.

Methods: Twenty C57/B6 mice received thoracic irradiation with a single dose of ionizing radiation (20 Gy). Sham irradiations were performed in 12 mice as a control group. Half of the mice from each group were treated with sildenafil (0.7 mg/kg) twice a day for 7 days starting 24 hours before irradiation. Echocardiography was used to evaluate left ventricular (LV) size and systolic function at 1, 4 and 6 months after irradiation. Isoproterenol ([beta-adrenergic receptor agonist] 10 ng/mouse) was used to evaluate the contractile reserve (change in LV fractional shortening) at 4 and 6 months after radiation.

Results: Between the 1st and the 4th months the left ventricular function and contractile reserve remained unchanged in all group. Between the 4th and 6th month, 50% of all the saline treated irradiated mice died (vs 0% of non-irradiated, P=0.020) while the LV systolic function had significantly dropped by 22% (LV fractional shortening [28±1%] P<0.01 vs baseline [36±1%] and vs sham [34±1%]) as well as the LV contractile reserve (+9±3% increase in irradiated mice vs +37±4% in sham mice, P<0.05). Eight of the 10 irradiated mice treated with sildenafil (80%) were alive and showed preserved LV systolic function (35±1%, P=NS vs baseline, P<0.05 vs saline-treated mice) and preserved contractile reserved (+31±4%, P=NS vs sham, P<0.05 vs saline-treated mice)

Conclusions: Treatment with sildenafil reduced ventricular dysfunction and preserved contractile reserve after radiation injury in mice. If validated in clinical trials, sildenafil, with its established safety profile, may be considered as an adjuvant to prevent radiotherapy induced cardiac disease in patients with cancer.