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Improving cardiac sparing in lung cancer with FLASH proton radiotherapy

Radiation-induced heart disease (RIHD) remains a major limitation of thoracic radiotherapy (RT), contributing to late morbidity in survivors of breast, lung, and esophageal cancers. In this study, we evaluated the potential of FLASH proton RT (F-PRT), an emerging modality that delivers ultrahigh dose rates, to mitigate cardiac toxicity compared to conventional proton RT (S-PRT). Using a clinically relevant, image-guided murine model of focal heart irradiation, we demonstrate that F-PRT induces a distinct reparative gene expression program, attenuates pro-inflammatory and fibrotic signaling, and significantly reduces long-term myocardial fibrosis. Echocardiographic evaluation confirmed preserved cardiac function in F-PRT-treated animals at 30 weeks post-irradiation. These findings represent the first comprehensive preclinical evidence that F-PRT spares the cardiac tissue from radiation-induced damage, highlighting its strong translational potential to reduce cardiovascular toxicity in patients receiving thoracic RT. Ongoing work includes dose-escalation studies in lung tumor models, single-cell transcriptomic analyses, and support for early-phase clinical trials, positioning F-PRT as a promising strategy to enhance the therapeutic ratio in thoracic oncology.