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FLASH Irradiation of A549 Lung Cancer Cells and IMR90 Healthy Fibroblasts in the Synchocyclotron Room of a Clinical PT System

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Background and Aims

The discovery of the FLASH effect has spurred the development of clinical proton therapy (PT) facilities to include Ultra-High Dose Rate (UHDR) capabilities for in-vitro, pre-clinical, and clinical studies. Here, we present a cost-effective passive irradiation system for small samples that can be installed and commissioned within minutes in a clinical PT facility.

Methods

An irradiation system, comprising a lead scatterer and a 3D-printed positioning system, was placed in the synchrocyclotron room of a clinical PT facility. Dosimetry was performed with radiochromic films. Healthy lung fibroblasts (IMR90) and lung adenocarcinoma cells (A549), cultured under standard conditions, were pelleted in Eppendorf vials and irradiated under normoxic conditions at FLASH (>800 Gy/s) and conventional (<0.2 Gy/s) dose rates. Biological assays were conducted on the irradiated samples, including clonogenic and viability studies, irradiation-induced cell cycle arrest via flow cytometry, and dose-dependent expression of the p21 protein via immunofluorescence.

Results

The irradiation system produced a usable irradiation field of 3x12 mm^2 with a positioning accuracy of 0.5 mm and a dose homogeneity better than 10%. Clonogenic (A549) and viability (IMR90) assays showed no differential dose-rate effect on the biological response. Cell cycle analysis revealed a decreased rate of cells in arrest at the G2/M phase at FLASH rate for both cell lines, while A549 cells exhibited a lower rate of p21-positive cells when irradiated at FLASH rates.

Conclusions

The in-house designed and fabricated irradiation system enabled FLASH irradiation of biological samples in a clinical proton therapy center without any hardware or software system modifications. While no significant dose-rate effects were measured in cell survival for either healthy or cancerous cells, observed differences in cell cycle arrest rates might point to differential (FLASH vs. conventional) cell cycle arrest and cell death mechanisms, which should be further investigated in future experiments.

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