# A Comprehensive Validation of an In-House Preclinical Alpha Irradiation Platform

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## ABSTRACT

The objective of this study is to develop and validate a fully integrated, vacuum-based alpha irradiation platform to support preclinical radiobiological studies.

A vacuum-based irradiation system incorporating a radioactive alpha source was designed, fabricated, and validated. The platform provides independent modulation of key irradiation parameters: (i) temporal exposure patterns via a programmable gate valve; (ii) fluence rate across two orders of magnitude by varying the source-to-aperture distance (57 to 381 mm); (iii) peak incident alpha-particle energy (0 to 4.6 MeV) using adjustable aperture-to-sample absorption layers; and (iv) spatial exposure distributions using a programmable 3D motion stage. Temporal precision was assessed via synchronized audio-electronic recordings of valve actuation. Fluence rates and average energies were validated using CR-39 detectors compared with Monte Carlo (MC) simulations. Spatial precision was verified using programmed continuous and discrete trajectories. The system's radiobiological performance was validated via Mylar film based cellular irradiation studies.

Validation experiments demonstrated high system fidelity. Measured irradiation durations deviated from programmed values by less than 0.3 s. Measured and computed fluence rates showed excellent agreement, with differences within 3%. For energy validation, experimentally determined CR-39 track diameters matched MC model predictions within one standard deviation. Additionally, recorded spatial irradiation patterns and dimensions aligned well with programmed motion trajectories. Radiation induced cellular death is positively correlated with irradiation time (dose).

By providing precise, multi-parametric control over alpha-particle delivery, this system is poised to optimize targeted alpha therapies and refine radiation protection frameworks for low-dose alpha exposure.

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## INTRODUCTION

- Alpha particles have high linear energy transfer (LET), making them an attractive format for cancer therapy.
- However, beyond direct nuclear damage, non-targeted (bystander) effects can induce biological responses in neighboring, non-irradiated cells and may contribute substantially to therapeutic efficacy.
- These responses depend on radiation parameters (e.g., LET, dose distribution, fluence rate) and the cellular microenvironment, highlighting the need for precise experimental control.
- Existing radioactive source-based alpha irradiation systems typically use gas-filled particle transport, which introduces energy loss and limits control over irradiation conditions.
- This work is to develop and validate a vacuum-based alpha irradiation platform that enables precise control of alpha-particle entry energy, fluence rate, and spatial/temporal irradiation patterns to support mechanistic radiobiology studies and optimization of targeted alpha therapy.

## METHODS AND MATERIALS

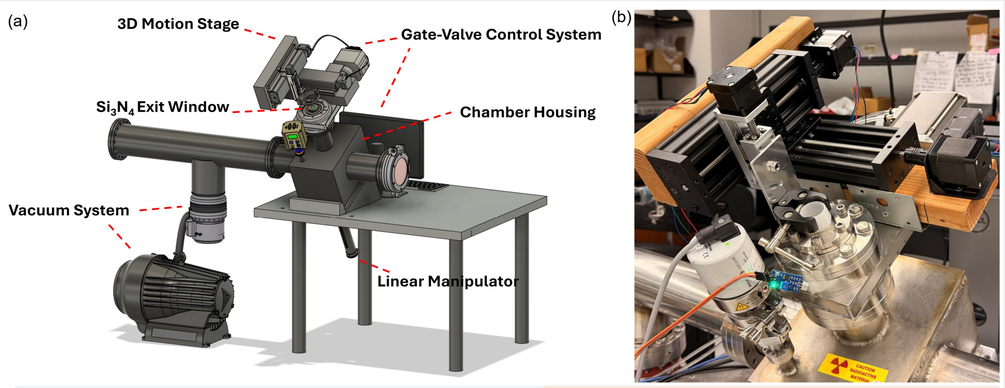



Figure 1. Schematic illustration and physical implementation of the alpha delivery system. (a) 3D design model showing major components. (b) Photograph of the fabricated system. (c) The overall design principle of the alpha irradiation platform.

### Validation

*Temporal Control*

- Raspberry Pi based control & GM counter based close/open detection
- Tests under 5 s, 10 s, 15 s programmed exposures

*Fluence Rate*

- Monte Carlo integration based fluence rate estimation as a function of source-to-aperture distance (d) and aperture-to-sample distance (g)

$$\dot{\Phi}(d) = \frac{A}{4\pi L W L_a W_a} \int_{-L/2}^{L/2} dx \int_{-W/2}^{W/2} dy \times \int_{-L_a/2}^{L_a/2} dx_m \int_{-W_a/2}^{W_a/2} dy_m \frac{d}{[(x-x_a)^2 + (y-y_a)^2 + d^2]^{3/2}}$$

$$S_{\text{eff}} = \left(L_a + \frac{g}{d}(L_a + L)\right)\left(W_a + \frac{g}{d}(W_a + W)\right) \quad \dot{\Phi}_{\text{eff}}(g,d) = \frac{L_a W_a}{S_{\text{eff}}}\dot{\Phi}(d)$$

- CR-39 detector-based fluence rate measurement at two source-to-aperture distances (279 and 381 mm) for 15 s irradiation time

*Energy Control*

- CR-39 detector based measurement
  - track diameter analysis
  - diameter to energy transfer
- Geant4 and SRIM MC simulation

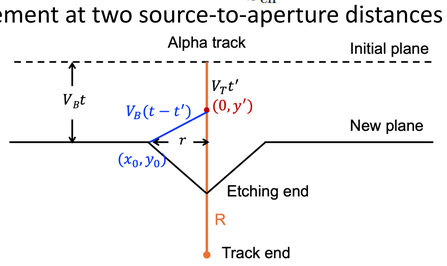



Figure 2. CR39 based track diameter analysis

*Spatial Control*

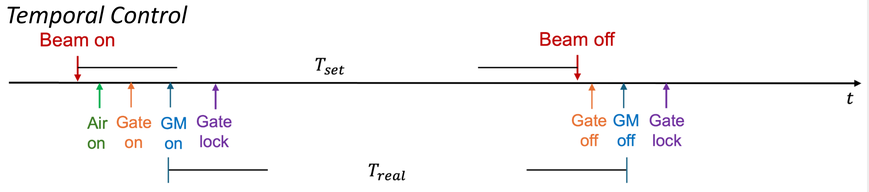
- CR-39 based scan pattern measurement under both continuous and discretized scan modes

*Radiobiological Studies*

- Mylar film bottomed ESCC cell dish, irradiated for 90 mins under two energy levels
- Post irradiation: fixation for cell viability and DNA damage analysis

## RESULTS

*Temporal Control*




| Tset | 5s | 10s | 15s |
|---|---|---|---|
| Treal | 4.73 ± 0.02 s | 9.71 ± 0.05 s | 14.72 ± 0.02 *s* |

*Fluence Rate*

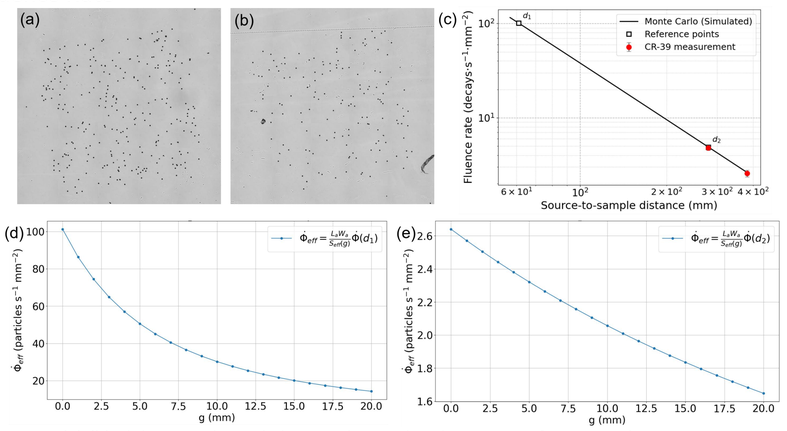



Figure 3. (a)-(b) Alpha-particle track density observed under 5x magnification at the two source-to-detector distances (279 and 381 mm). (b) Consistence between MC simulation and CR-39 based measurement. (d)-(e) Corresponding average fluence rate as a function of aperture-to-sample distance.

*Energy Control*

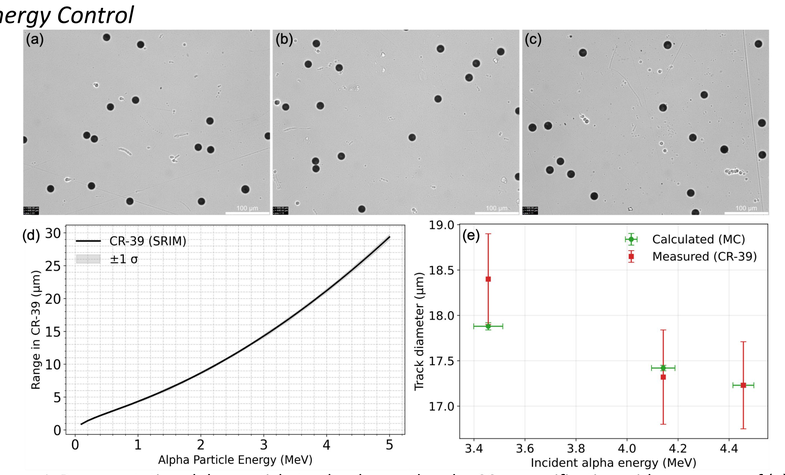



Figure 4. Representative alpha-particle tracks observed under 20x magnification with exposures of (a) 0 um Mylar film + 1mm air gap, (b) 2.5 um Mylar film + 1mm air gap, and (c) 7.5um Mylar film + 1 mm air gap. (d) SRIM-simulated relationship between alpha-particle energy and range in CR-39. (e) Calculated and measured alpha track diameters as a function of alpha incident energies for the three conditions.

*Spatial Control*

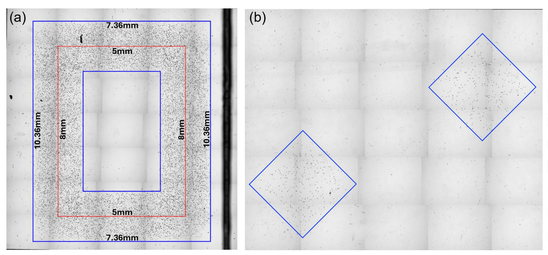



Figure 5. (a) Rectangular irradiation pattern showing continuous motion control. Blue line represents theoretical irradiation boundary and red represents central irradiation line. (b) Two discrete exposure sites generated by synchronizing the motion stage position with temporal gate valve actuation.

*Radiobiological Studies*

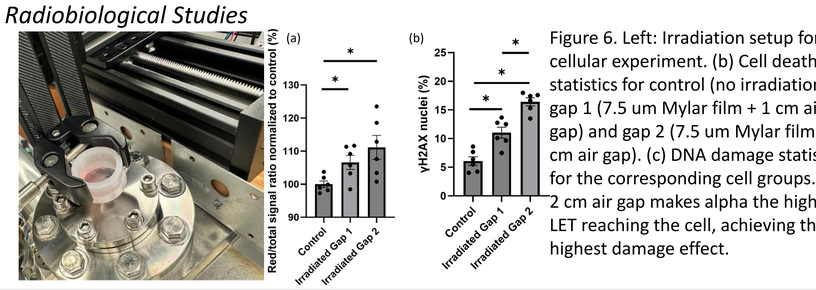



Figure 6. Left: Irradiation setup for the cellular experiment. (b) Cell death statistics for control (no irradiation), gap 1 (7.5 um Mylar film + 1 cm air gap) and gap 2 (7.5 um Mylar film + 2 cm air gap). (c) DNA damage statistics for the corresponding cell groups. The 2 cm air gap makes alpha the highest LET reaching the cell, achieving the highest damage effect.

## CONCLUSIONS

We successfully developed and validated a vacuum-based programmable alpha-irradiation platform, which can provide diverse irradiation control to support precise alpha radiobiological studies.