Biological effects of particles with very high energy deposition on mammalian cells utilizing the Brookhaven Tandem Van de Graaff accelerator

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Introduction

High LET radiation from GCR (Galactic Cosmic Rays) consisting mainly of high charge and energy (HZE) nuclei and secondary protons and neutrons, and secondaries from protons in SPE (Solar Particle Event) pose a major health risk to astronauts due to induction of DNA damage and oxidative stress. Experiments with high energy particles mimicking the space environment for estimation of radiation risk are being performed at NASA Space Radiation Laboratory at BNL. Experiments with low energy particles comparing to high energy particles of similar LET are of interest for investigation of the role of track structure on biological effects. For this purpose, we report results utilizing the Tandem Van de Graaff accelerator at BNL. The primary objective of our studies is to elucidate the influence of high vs low energy deposition on track structure, delta ray contribution and resulting biological responses. These low energy ions are of special relevance as these energies may occur following absorption through the spacecraft and shielding materials in human tissues and nuclear fragments produced in tissues by high energy protons and neutrons. This study will help to verify the efficiency of these low energy particles and better understand how various cell types respond to them.

Materials & Methods

hTERT-immortalized human fibroblast cell (82-6) and human esophageal epithelial cells (EPC2) were radiated with varying doses of 5.6MeV/n Boron (LET=200keV/µm) and 4.3MeV/n Silicon ions (LET=1241keV/µm) Tandem beam and 600MeV/n Fe particles (LET=180keV/µm from NSRL.

Techniques: Immunofluorescence, live cell imaging and PI staining for cell cycle determination were primarily employed for deriving data. Due to very low energy of ions involved, experimental setup was custom designed and employed.

Results

Fig. 1.

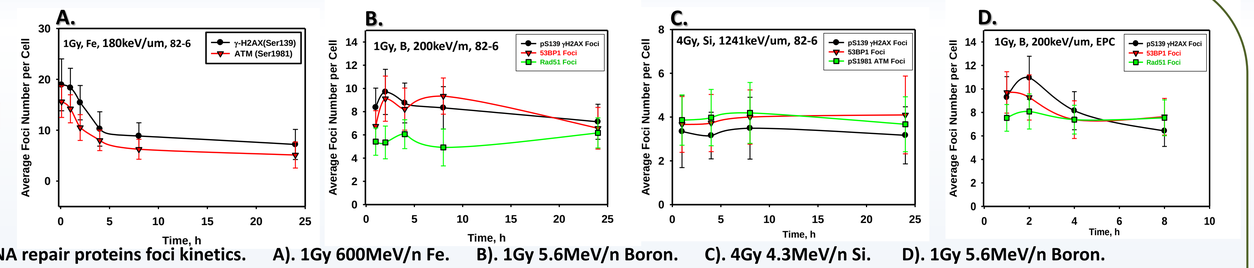

Fig1. DNA repair proteins foci kinetics. A). 1Gy 600MeV/n Fe. B). 1Gy 5.6MeV/n Boron. C). 4Gy 4.3MeV/n Si. D). 1Gy 5.6MeV/n Boron.

Fig. 2.

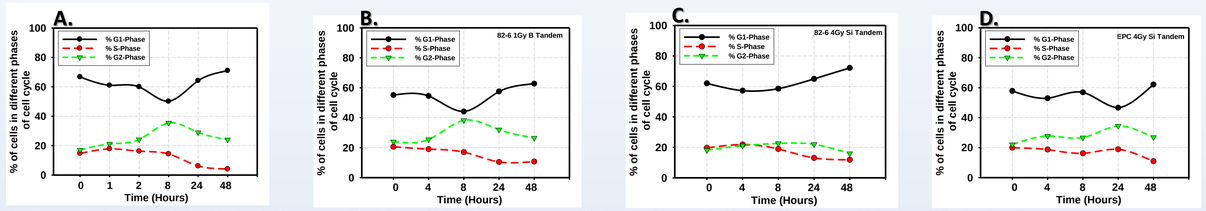

Fig2. Cell Cycle analysis. A). 1Gy 600MeV/n Fe. B). 1Gy 5.6MeV/n Boron. C). 4Gy 4.3MeV/n Si. D). 4Gy 4.3MeV/n Si in EPC cells.

Fig. 3.

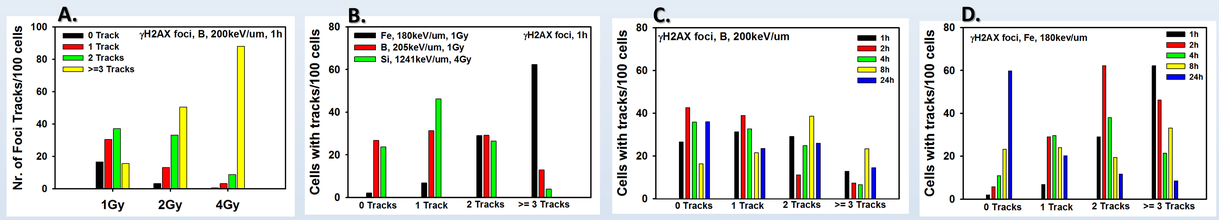

Fig3. Track number calculations for: A). 1Gy 5.6MeV/n Boron 1h. B). 1h B and Si (Tandem), Fe (NSRL) C). 1Gy 5.6MeV/n Boron. D). 1Gy 600MeV/n Fe.

Fig. 4.

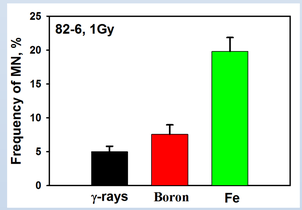

Fig4. Micronucleus assay in 82-6 human fibroblasts after 1Gy of γ-rays, B and Fe particles.

Fig. 5.

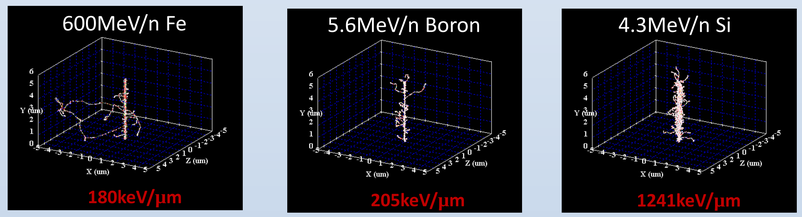

Fig5. Simulated high LET particle track projections of the indicated species in the XY plane calculated with RITRACKS software. Conditions are liquid water at 25°C with origination at the Y axis.

Fig. 6.

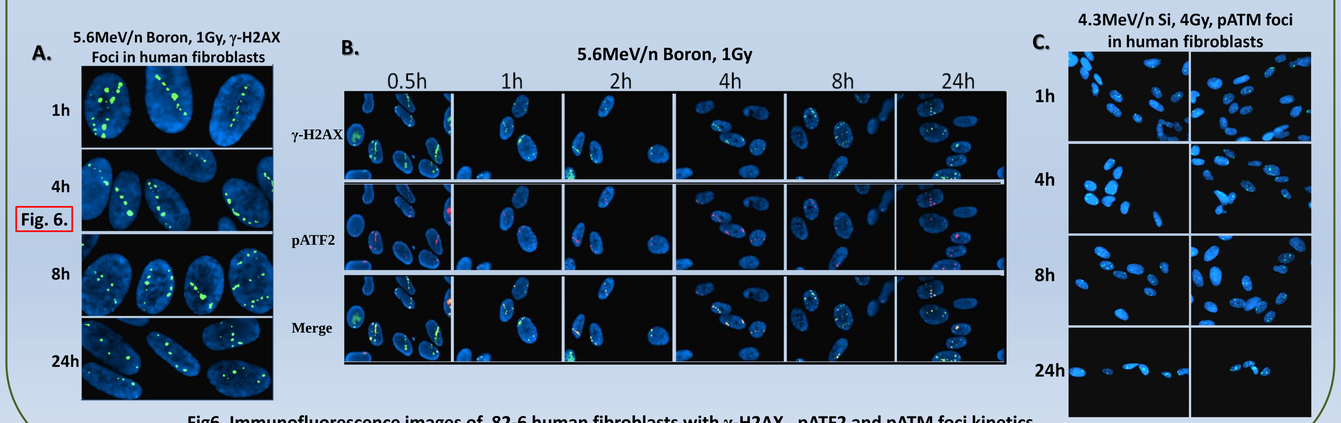

Fig6. Immunofluorescence images of 82-6 human fibroblasts with γ-H2AX , pATF2 and pATM foci kinetics obtained after varying doses of Boron and Silicon ions from Tandem accelerator.

Experimental setup

Conclusions

1. Immunofluorescence data show induction of larger-sized DNA repair protein foci (γ-H2AX, pATM, pATF2, 53BP1).

2. The induced foci were stable and persistent across all time points measured as compared to results with high energy ions, indicating that damage of higher complexity is induced by these ions.

2. Cell cycle data show a stronger G1 and G2 phase blocks with Boron ions with matched LET to Fe particles.

3. Reduced induction of micronuclei was observed with Boron ions as compared to LET matched Fe particles, probably owing to the stronger G2 block observed.

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Track structure simulations were created with RITRACKS software developed by Ianik Plante (USRA).