Can you simulate the space radiation environment for more accurate ground-based radiobiology outcomes?

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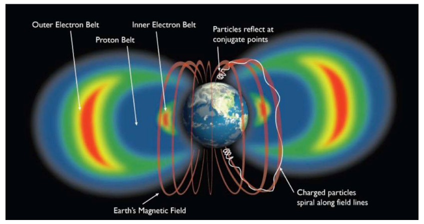
Me, some disclaimers

- These are my conclusions that are based on a diverse background in science, space vehicle design and spaceflight operations

- 15+ years of nuclear and space physics research
- Space vehicle design and shielding analysis
- Flight Controller in Mission Control
- Radiation Mission Manager and operational radiation risk assessment STS-118, STS-120, STS-122, and STS-125 (Hubble).



Take Home Message

- Clever application of well-validated nuclear physics principles can be applied to current accelerator and material technologies to generate the complex space radiation environment
  - Continuous generation of ionizing radiation that matches the LET spectrum, ion species, and dose rate Significantly more accurate approach for ground-based experiments
  - Accelerate our understanding of how space radiation affects mechanical, biological, and human systems.
  - Replicable results at any heavy-ion accelerator.

- Our approach represents the first true instance of a ground-based analog for characterizing the effects of space radiation.

Before We Start This Party…

Emulating the Space Radiation Environment for Materials and Radiobiological Experiments

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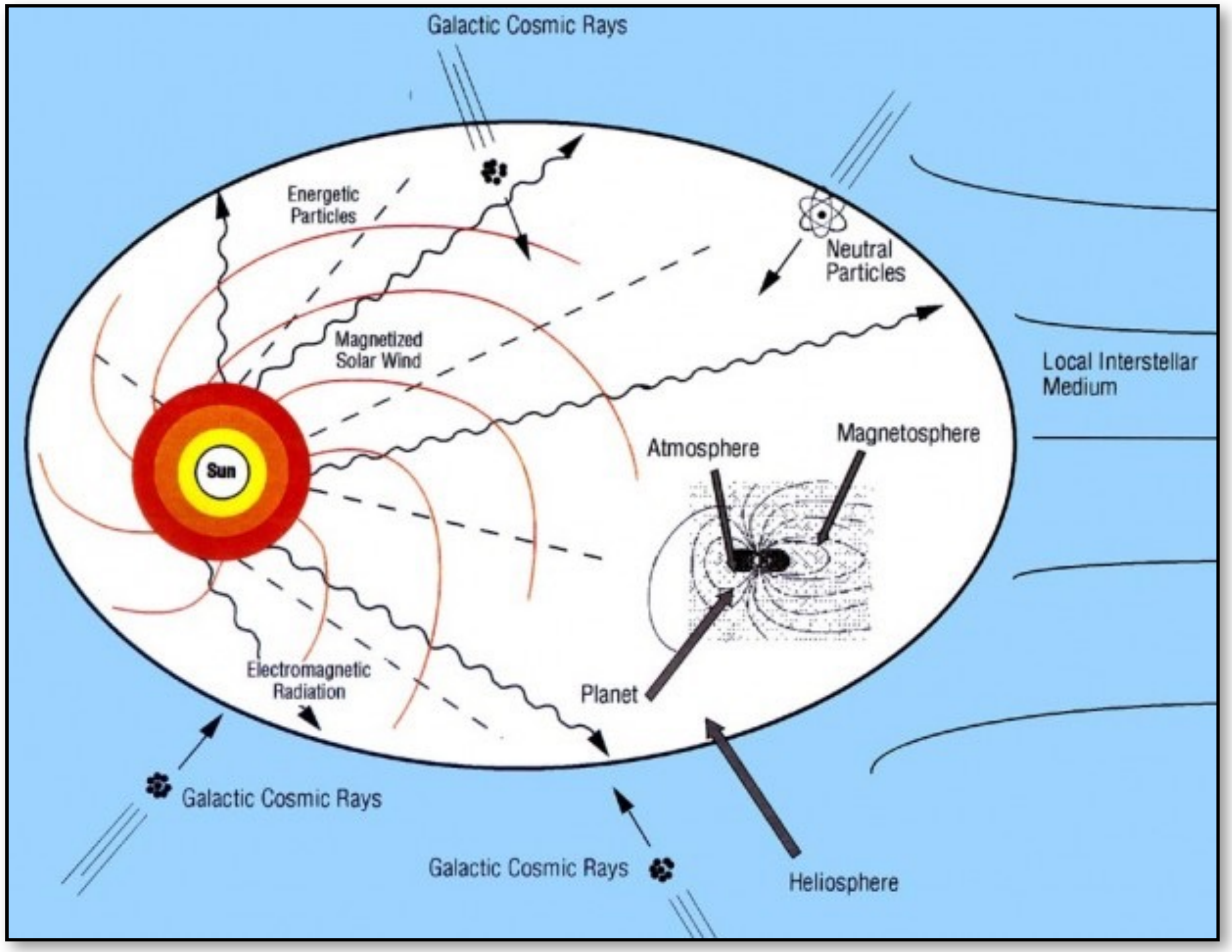
(Dated: February 6, 2017)

- Multi-discipline effort:
  - nuclear, space, health and computational physicist
  - radiation oncologist
  - radiobiologist
- Submitted manuscript to *Physical Review Applied*
- Available on *arXiv.org* June 13, 2017
  - physics: applied, condensed matter, materials science, space

Space Radiation - Short Course

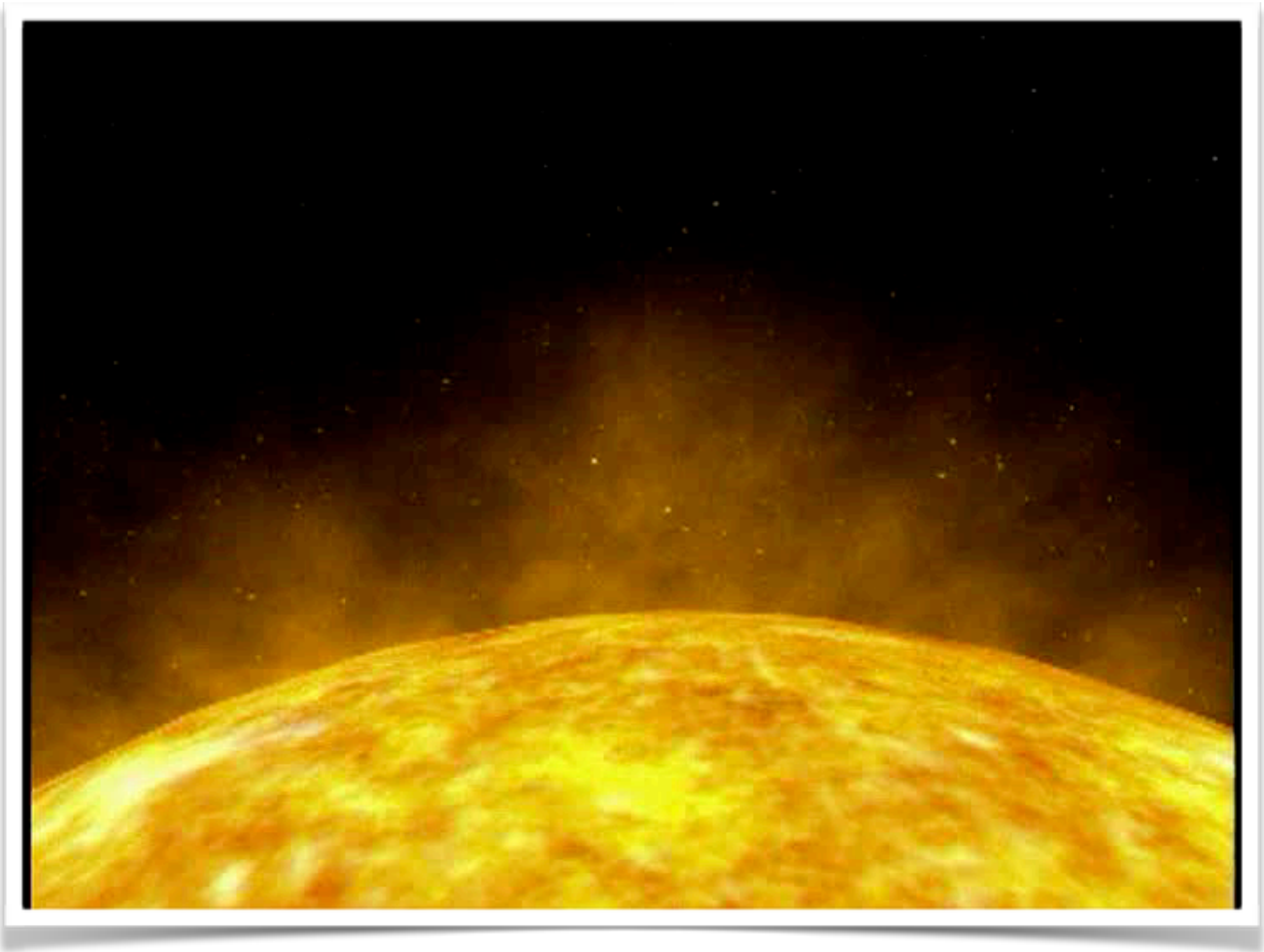
- Four types of *direct* radiation, all are direct ionizing radiation

  - Galactic Cosmic Rays (GCR)
  - ~~Solar Protons~~
  - Solar Particle Events (SPE)
  - ~~Trapped Radiation~~



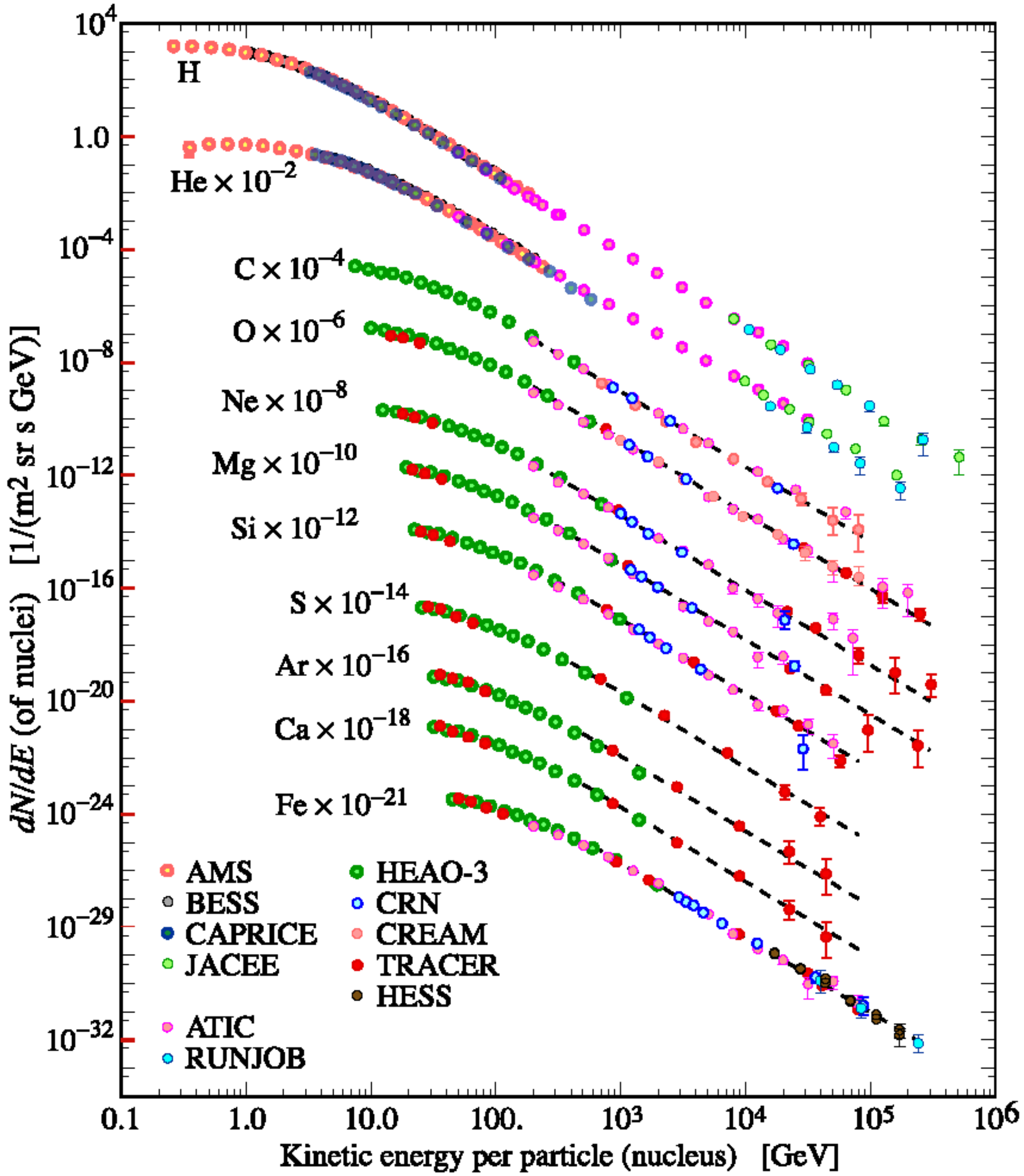
Solar Particle Events (SPEs)

- "Sexy" rock-star of space radiation
- Immediate risk to astronaut crews
- Difficult to predict:
  - Occurrence
  - Magnitude
  - Length of event
- Proton energies keV to GeV
- Arrival time can be minutes



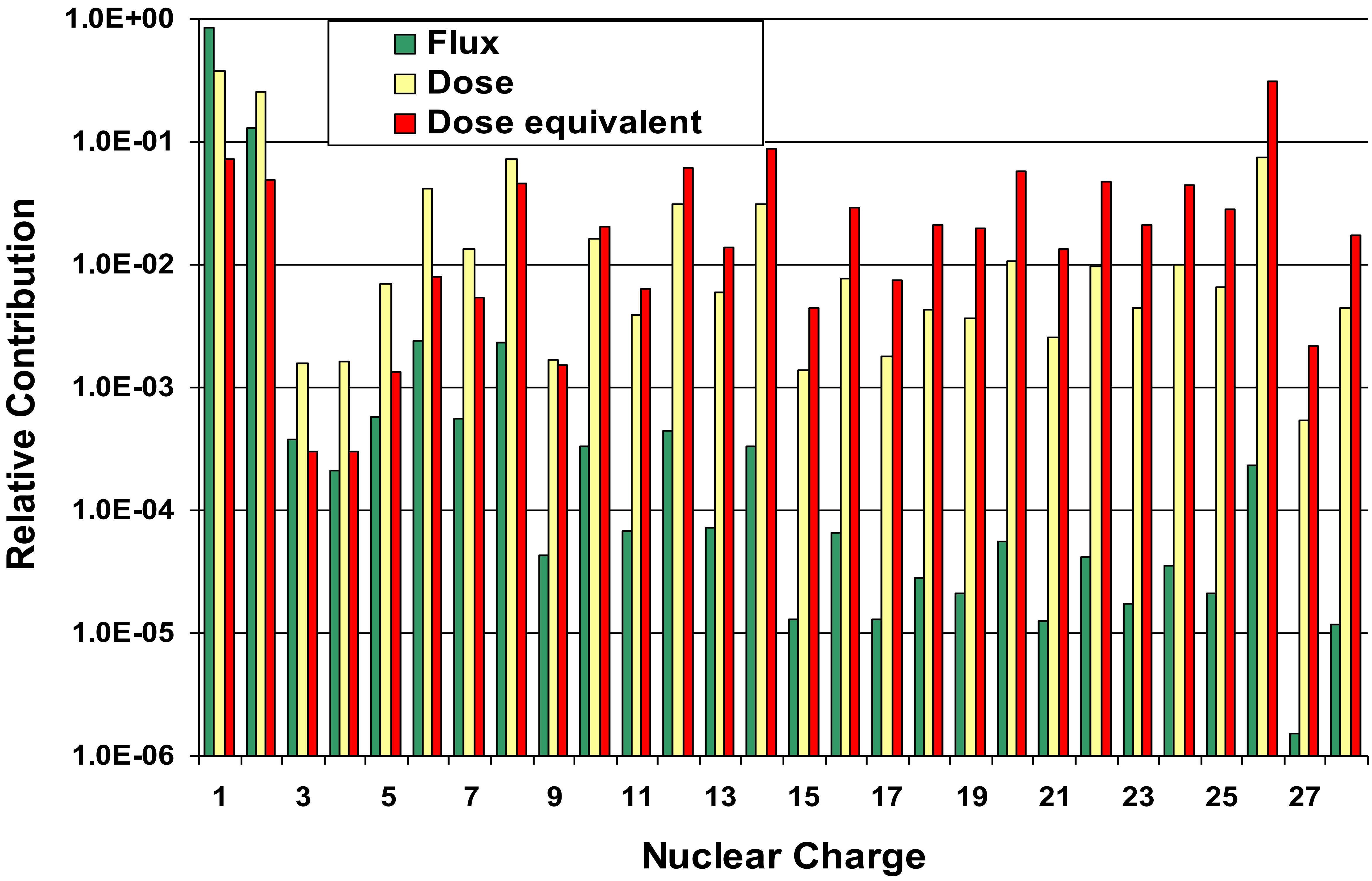
Galactic Cosmic Rays (GCR)

- Arch-nemesis of space radiation research
- Energetic, relativistic heavy ions that are very difficult to shield
- Includes all species in the periodic table
- Shielding can make *intravehicular* (IVA) dose much worse



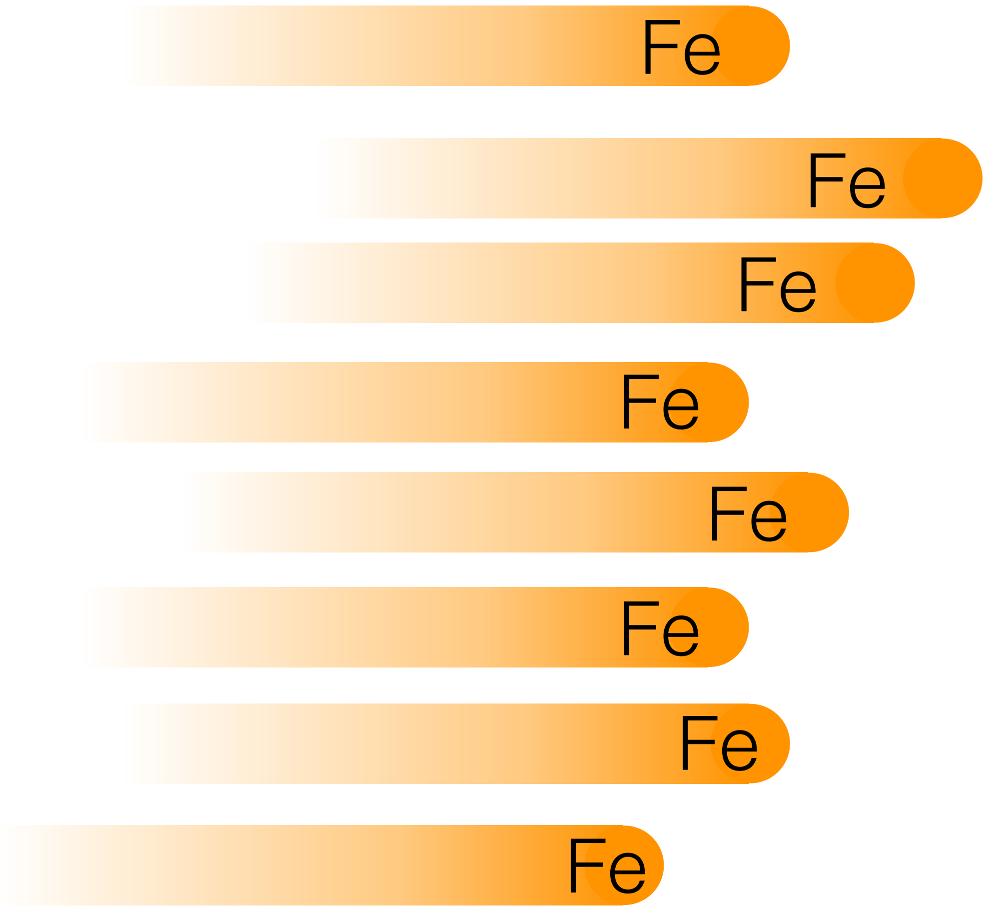
adapted from Simpson (1983)

Galactic Cosmic Rays (GCR)



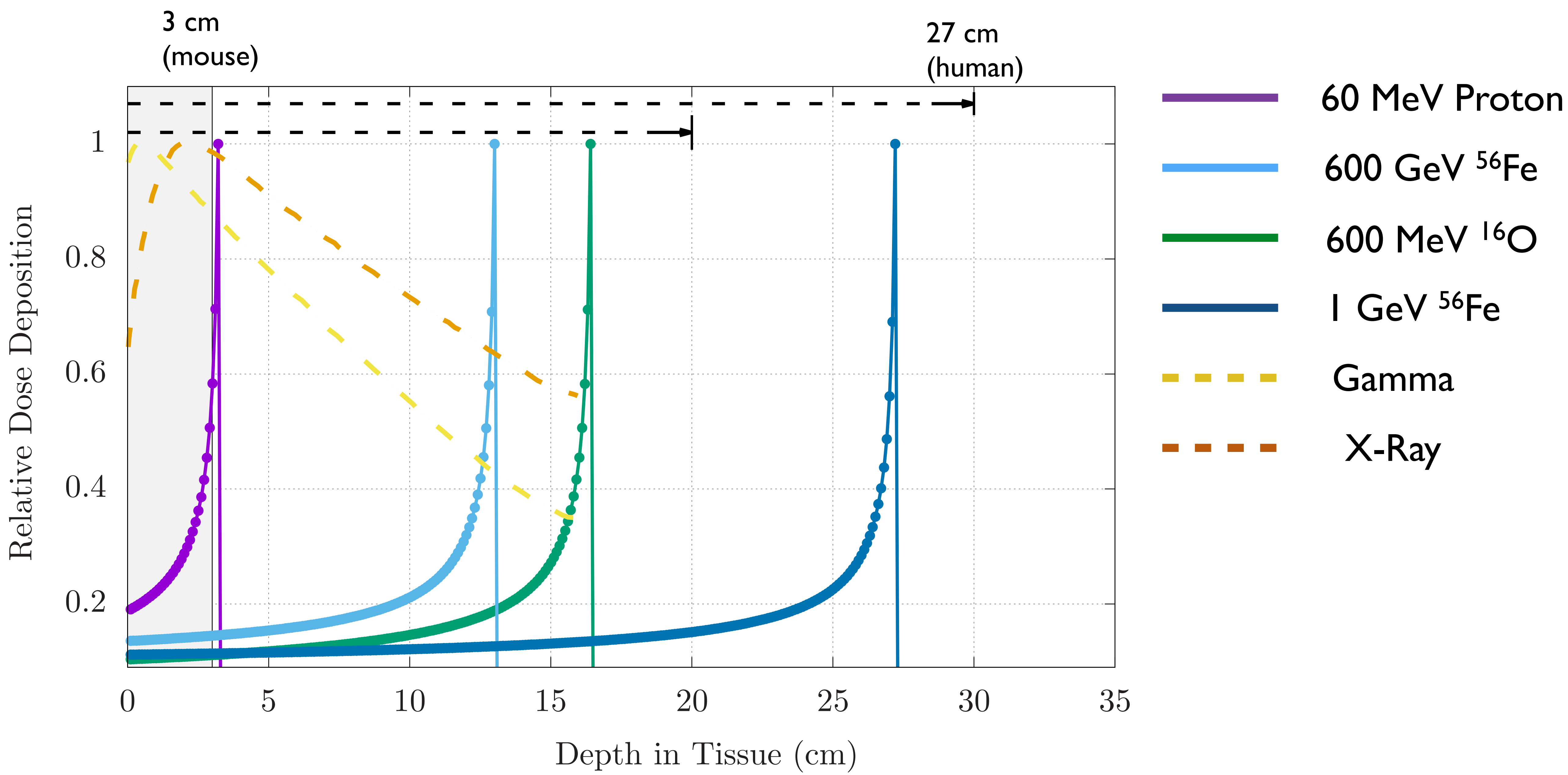
Current Space Radiation Studies

Mono-energetic, single ion beam

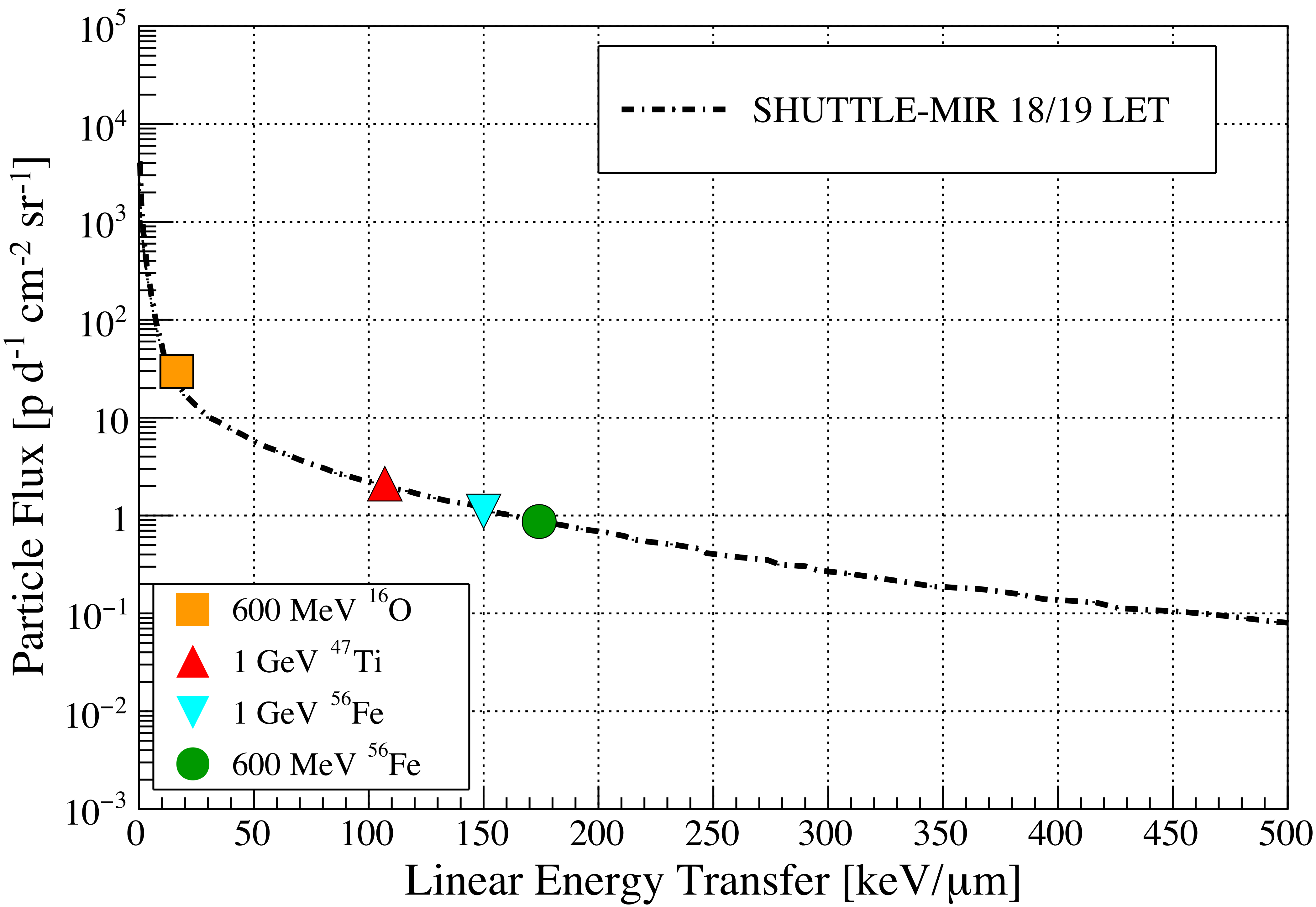


- biological analog does NOT resemble the physiology of humans
- environmental analog does NOT mimic the multi-ion, multi-energy space radiation spectrum.

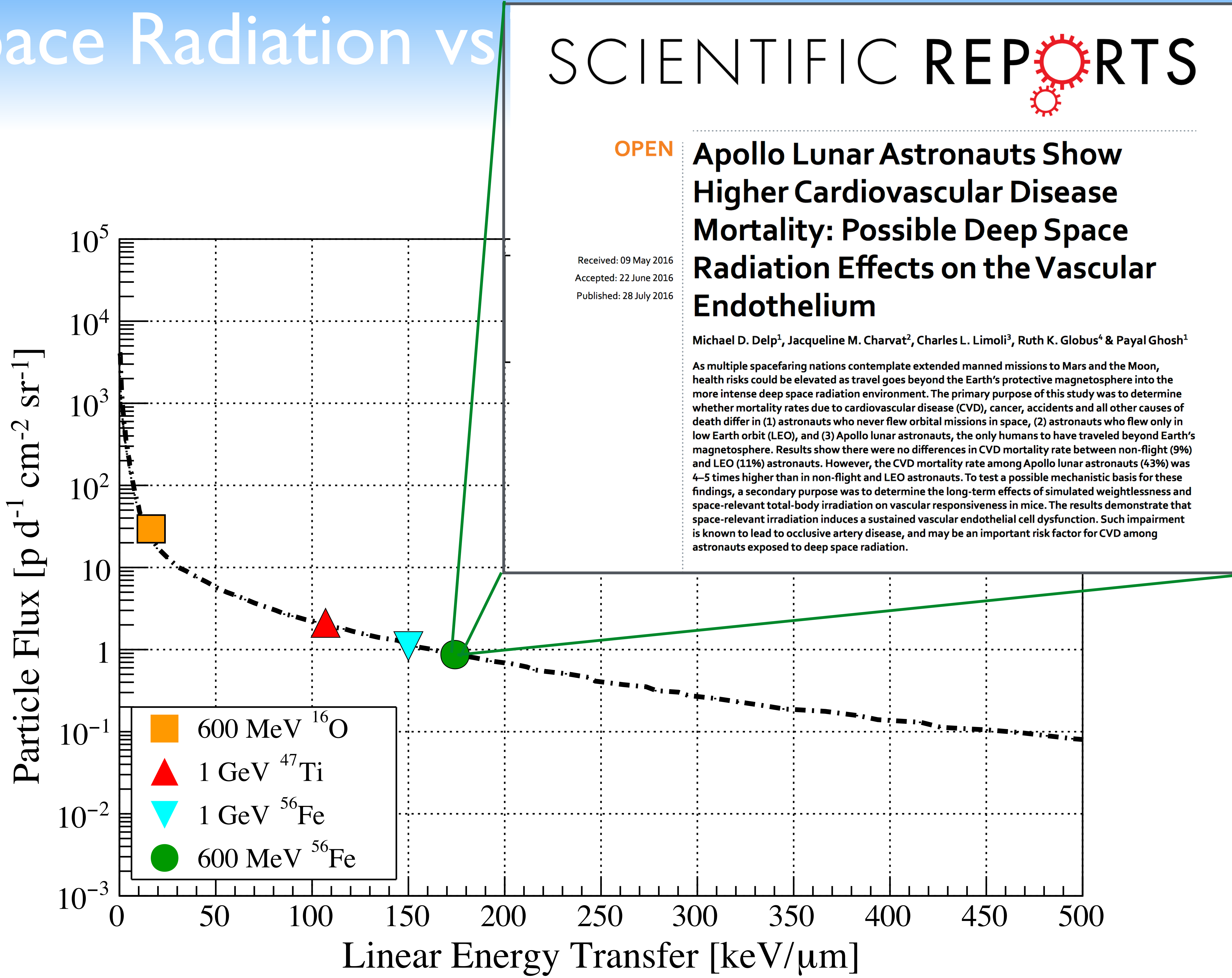
Space Radiation vs Terrestrial Radiation



Space Radiation vs Terrestrial Radiation



Space Radiation vs



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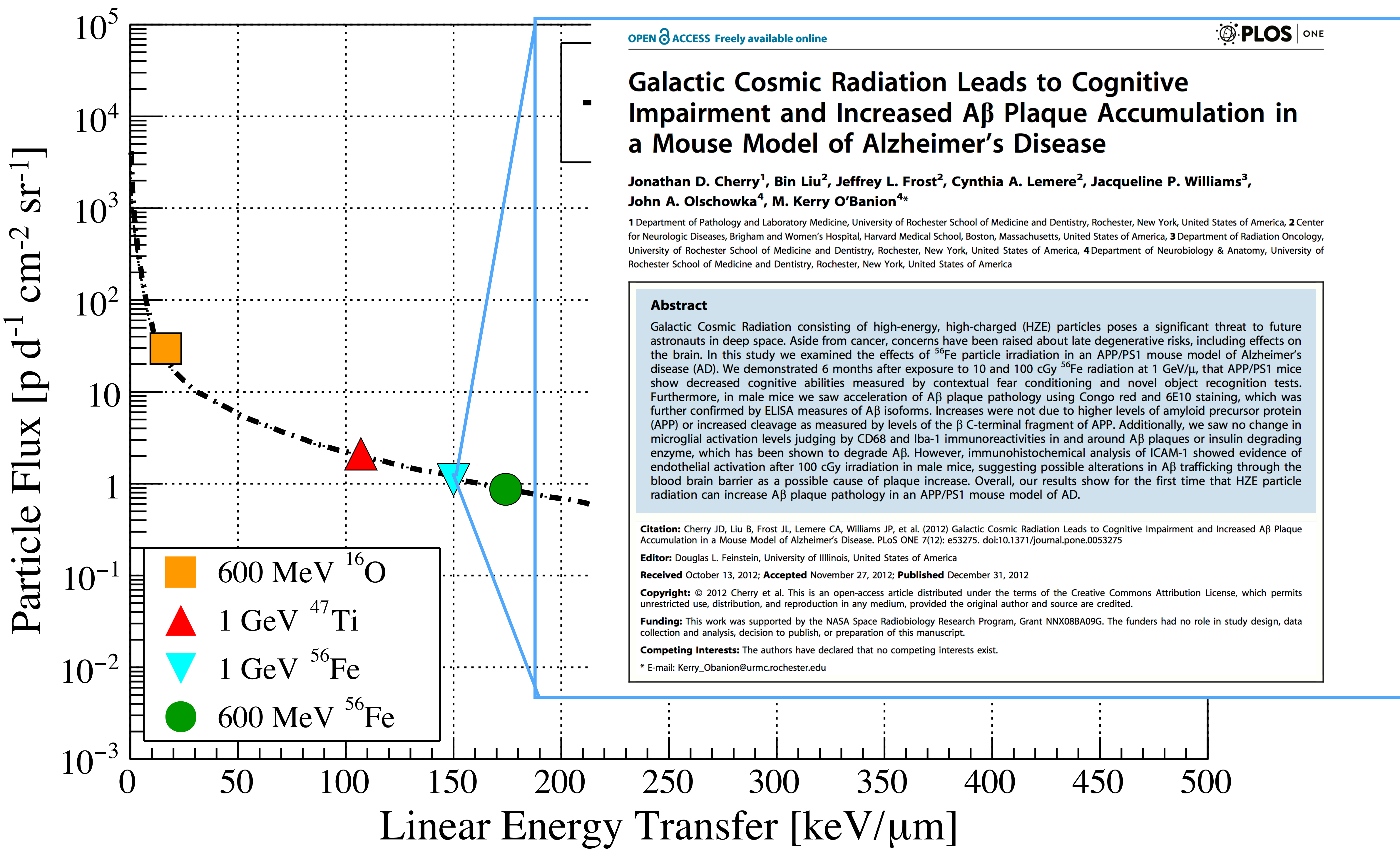
Apollo Lunar Astronauts Show Higher Cardiovascular Disease Mortality: Possible Deep Space Radiation Effects on the Vascular Endothelium

Michael D. Delp[1], Jacqueline M. Charvat[2], Charles L. Limoli[3], Ruth K. Globus[4] & Payal Ghosh[1]

As multiple spacefaring nations contemplate extended manned missions to Mars and the Moon, health risks could be elevated as travel goes beyond the Earth's protective magnetosphere into the more intense deep space radiation environment. The primary purpose of this study was to determine whether mortality rates due to cardiovascular disease (CVD), cancer, accidents and all other causes of death differ in (1) astronauts who never flew orbital missions in space, (2) astronauts who flew only in low Earth orbit (LEO), and (3) Apollo lunar astronauts, the only humans to have traveled beyond Earth's magnetosphere. Results show there were no differences in CVD mortality rate between non-flight (9%) and LEO (11%) astronauts. However, the CVD mortality rate among Apollo lunar astronauts (43%) was 4–5 times higher than in non-flight and LEO astronauts. To test a possible mechanistic basis for these findings, a secondary purpose was to determine the long-term effects of simulated weightlessness and space-relevant total-body irradiation on vascular responsiveness in mice. The results demonstrate that space-relevant irradiation induces a sustained vascular endothelial cell dysfunction. Such impairment is known to lead to occlusive artery disease, and may be an important risk factor for CVD among astronauts exposed to deep space radiation.

Space Radiation vs Terrestrial Radiation



OPEN ACCESS Freely available online PLOS ONE

Galactic Cosmic Radiation Leads to Cognitive Impairment and Increased Aβ Plaque Accumulation in a Mouse Model of Alzheimer's Disease

Jonathan D. Cherry[1], Bin Liu[2], Jeffrey L. Frost[2], Cynthia A. Lemere[2], Jacqueline P. Williams[3], John A. Olschowka[4], M. Kerry O'Banion[4]*

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Abstract

Galactic Cosmic Radiation consisting of high-energy, high-charged (HZE) particles poses a significant threat to future astronauts in deep space. Aside from cancer, concerns have been raised about late degenerative risks, including effects on the brain. In this study we examined the effects of ^{56}Fe particle irradiation in an APP/PS1 mouse model of Alzheimer's disease (AD). We demonstrated 6 months after exposure to 10 and 100 cGy ^{56}Fe radiation at 1 GeV/μ, that APP/PS1 mice show decreased cognitive abilities measured by contextual fear conditioning and novel object recognition tests. Furthermore, in male mice we saw acceleration of Aβ plaque pathology using Congo red and 6E10 staining, which was further confirmed by ELISA measures of Aβ isoforms. Increases were not due to higher levels of amyloid precursor protein (APP) or increased cleavage as measured by levels of the β C-terminal fragment of APP. Additionally, we saw no change in microglial activation levels judging by CD68 and Iba-1 immunoreactivities in and around Aβ plaques or insulin degrading enzyme, which has been shown to degrade Aβ. However, immunohistochemical analysis of ICAM-1 showed evidence of endothelial activation after 100 cGy irradiation in male mice, suggesting possible alterations in Aβ trafficking through the blood brain barrier as a possible cause of plaque increase. Overall, our results show for the first time that HZE particle radiation can increase Aβ plaque pathology in an APP/PS1 mouse model of AD.

Citation: Cherry JD, Liu B, Frost JL, Lemere CA, Williams JP, et al. (2012) Galactic Cosmic Radiation Leads to Cognitive Impairment and Increased Aβ Plaque Accumulation in a Mouse Model of Alzheimer's Disease. PLoS ONE 7(12): e53275. doi:10.1371/journal.pone.0053275

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Competing Interests: The authors have declared that no competing interests exist.

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Space Radiation vs Terrestrial Radiation

RESEARCH ARTICLE

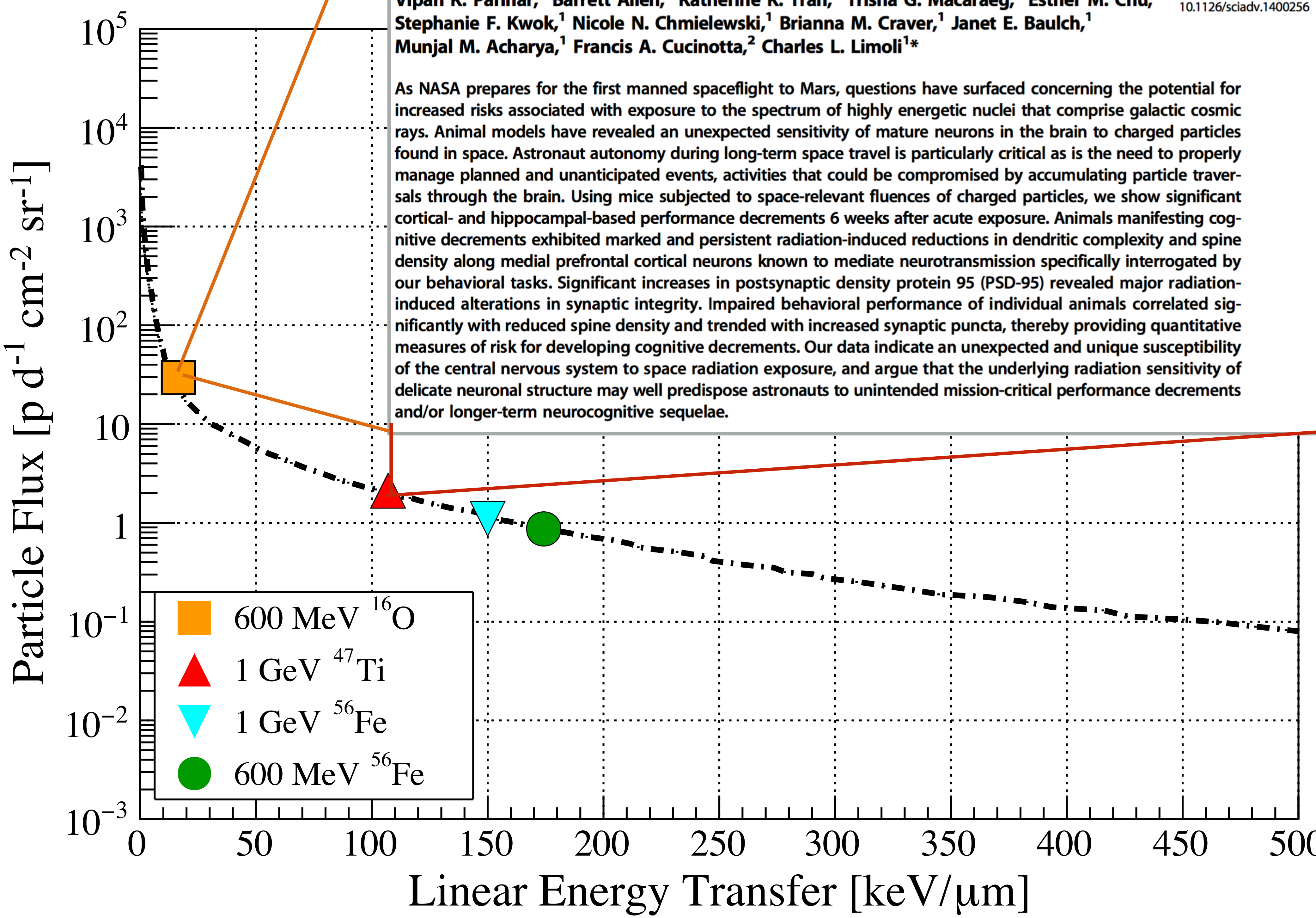
COGNITIVE NEUROSCIENCE

What happens to your brain on the way to Mars

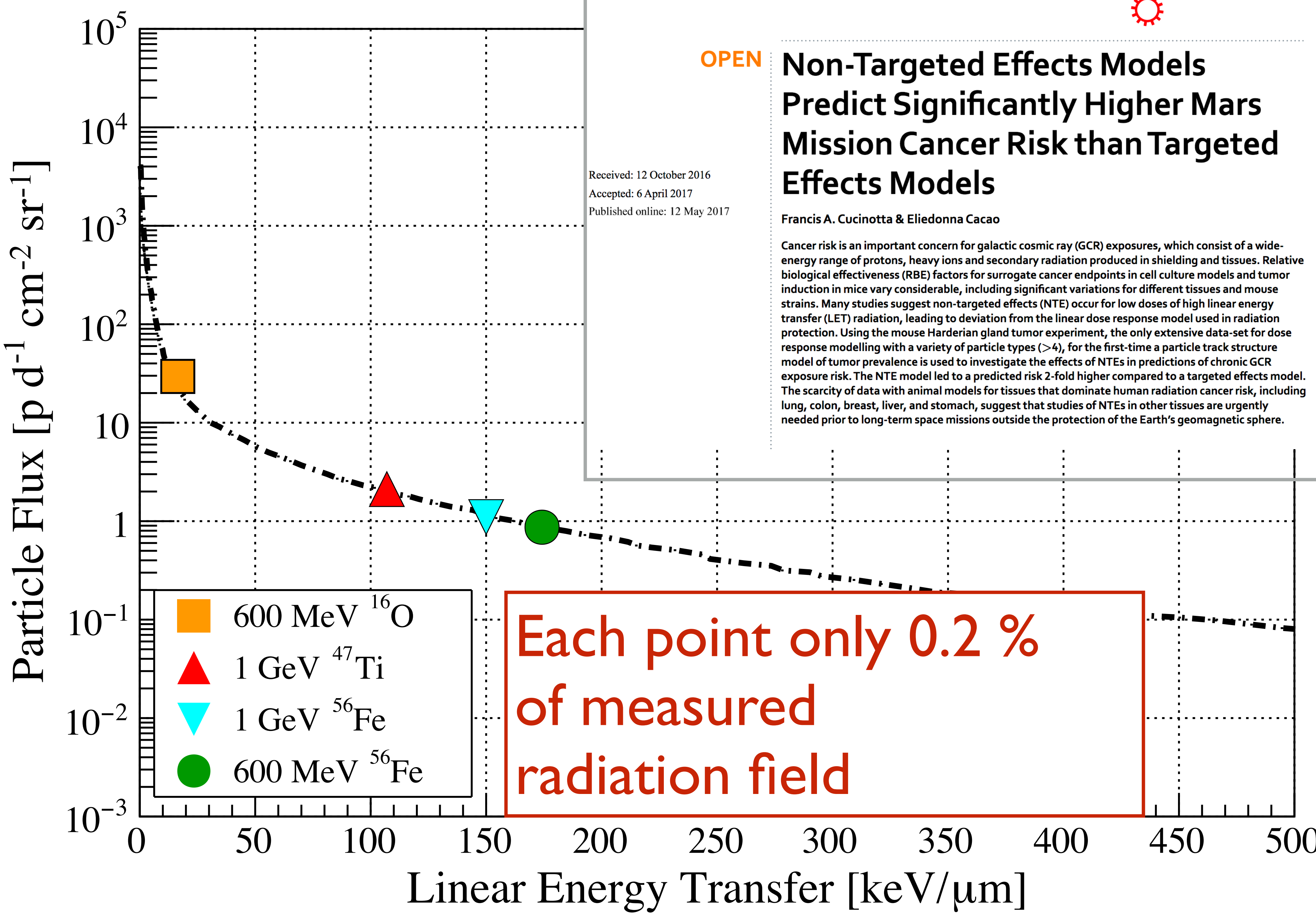
Vipan K. Parihar,[1] Barrett Allen,[1] Katherine K. Tran,[1] Trisha G. Macaraeg,[1] Esther M. Chu,[1] Stephanie F. Kwok,[1] Nicole N. Chmielewski,[1] Brianna M. Craver,[1] Janet E. Baulch,[1] Munjal M. Acharya,[1] Francis A. Cucinotta,[2] Charles L. Limoli[1]*

10.1126/sciadv.1400256

As NASA prepares for the first manned spaceflight to Mars, questions have surfaced concerning the potential for increased risks associated with exposure to the spectrum of highly energetic nuclei that comprise galactic cosmic rays. Animal models have revealed an unexpected sensitivity of mature neurons in the brain to charged particles found in space. Astronaut autonomy during long-term space travel is particularly critical as is the need to properly manage planned and unanticipated events, activities that could be compromised by accumulating particle traversals through the brain. Using mice subjected to space-relevant fluences of charged particles, we show significant cortical- and hippocampal-based performance decrements 6 weeks after acute exposure. Animals manifesting cognitive decrements exhibited marked and persistent radiation-induced reductions in dendritic complexity and spine density along medial prefrontal cortical neurons known to mediate neurotransmission specifically interrogated by our behavioral tasks. Significant increases in postsynaptic density protein 95 (PSD-95) revealed major radiation-induced alterations in synaptic integrity. Impaired behavioral performance of individual animals correlated significantly with reduced spine density and trended with increased synaptic puncta, thereby providing quantitative measures of risk for developing cognitive decrements. Our data indicate an unexpected and unique susceptibility of the central nervous system to space radiation exposure, and argue that the underlying radiation sensitivity of delicate neuronal structure may well predispose astronauts to unintended mission-critical performance decrements and/or longer-term neurocognitive sequelae.



Space Radiation vs Terrestrial Radiation



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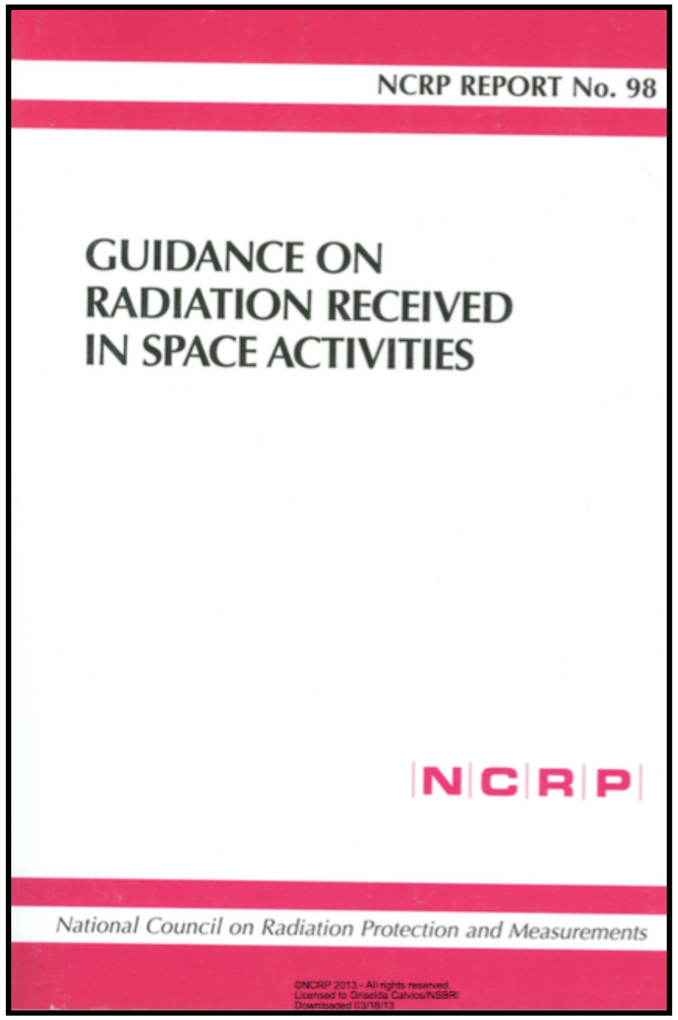
Non-Targeted Effects Models Predict Significantly Higher Mars Mission Cancer Risk than Targeted Effects Models

Francis A. Cucinotta & Eliedonna Cacao

Cancer risk is an important concern for galactic cosmic ray (GCR) exposures, which consist of a wide-energy range of protons, heavy ions and secondary radiation produced in shielding and tissues. Relative biological effectiveness (RBE) factors for surrogate cancer endpoints in cell culture models and tumor induction in mice vary considerable, including significant variations for different tissues and mouse strains. Many studies suggest non-targeted effects (NTE) occur for low doses of high linear energy transfer (LET) radiation, leading to deviation from the linear dose response model used in radiation protection. Using the mouse Harderian gland tumor experiment, the only extensive data-set for dose response modelling with a variety of particle types (>4), for the first-time a particle track structure model of tumor prevalence is used to investigate the effects of NTEs in predictions of chronic GCR exposure risk. The NTE model led to a predicted risk 2-fold higher compared to a targeted effects model. The scarcity of data with animal models for tissues that dominate human radiation cancer risk, including lung, colon, breast, liver, and stomach, suggest that studies of NTEs in other tissues are urgently needed prior to long-term space missions outside the protection of the Earth's geomagnetic sphere.

Each point only 0.2 % of measured radiation field

Motivation


NCRP REPORT No. 98

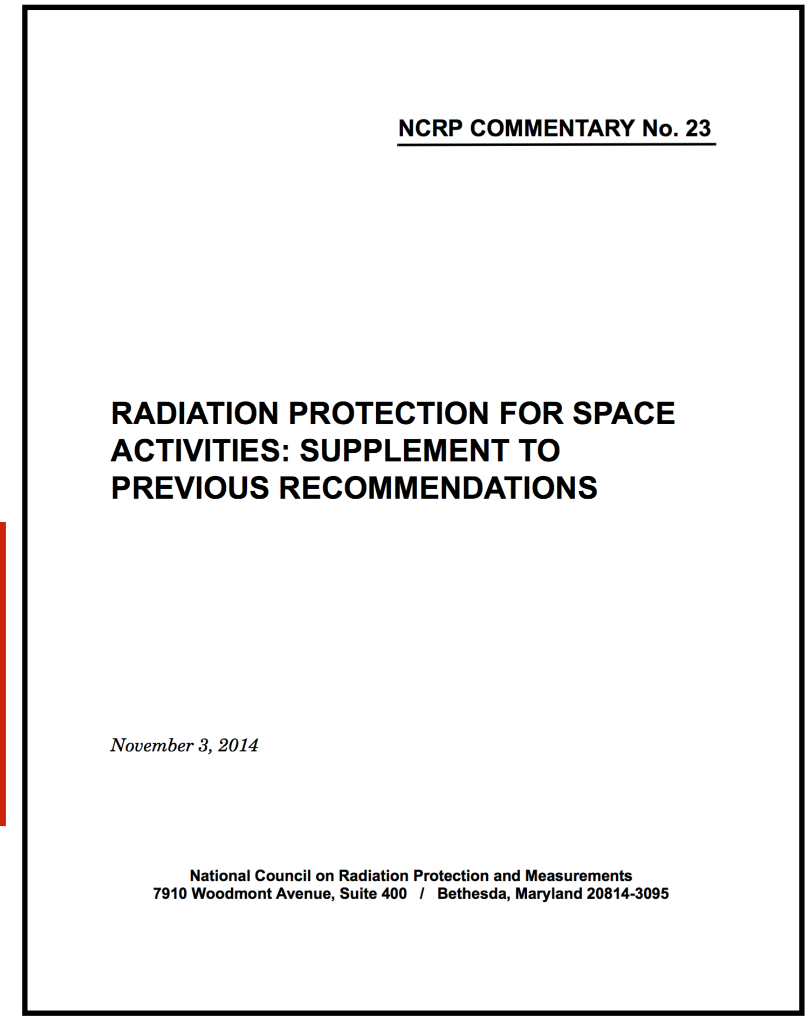
GUIDANCE ON
RADIATION RECEIVED
IN SPACE ACTIVITIES

NCRP

National Council on Radiation Protection and Measurements

~30 years

No change in risk posture!


NCRP COMMENTARY No. 23

RADIATION PROTECTION FOR SPACE
ACTIVITIES: SUPPLEMENT TO
PREVIOUS RECOMMENDATIONS

November 3, 2014

National Council on Radiation Protection and Measurements
7910 Woodmont Avenue, Suite 400 / Bethesda, Maryland 20814-3095

- Report No. 98 - Released in 1998
  - 3% Radiation Exposure Induced Death (REID)

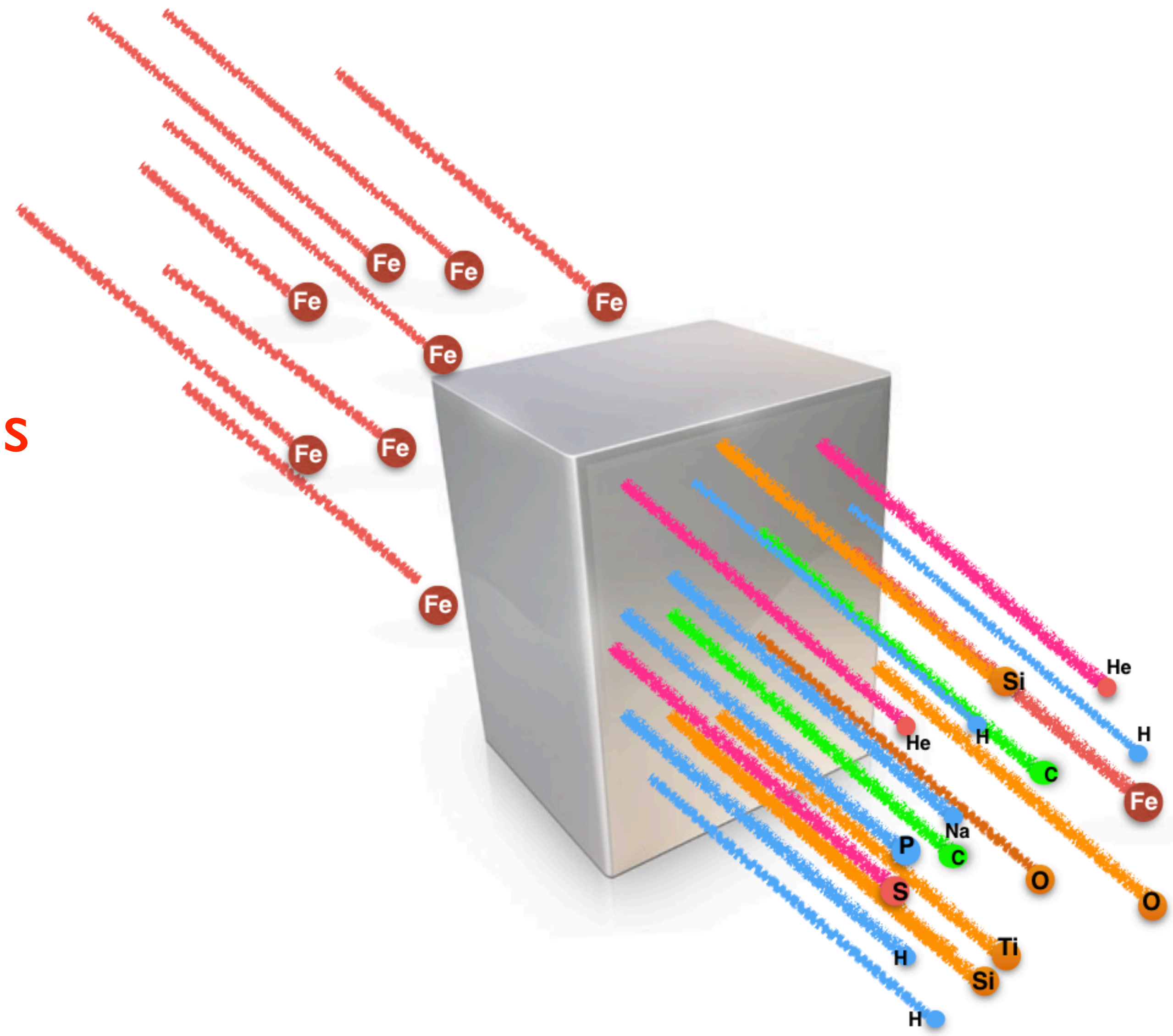
- Commentary No. 23 - Released in 2016
  - 3% REID for cancer… should be used for longer-term missions

Hypothesis:

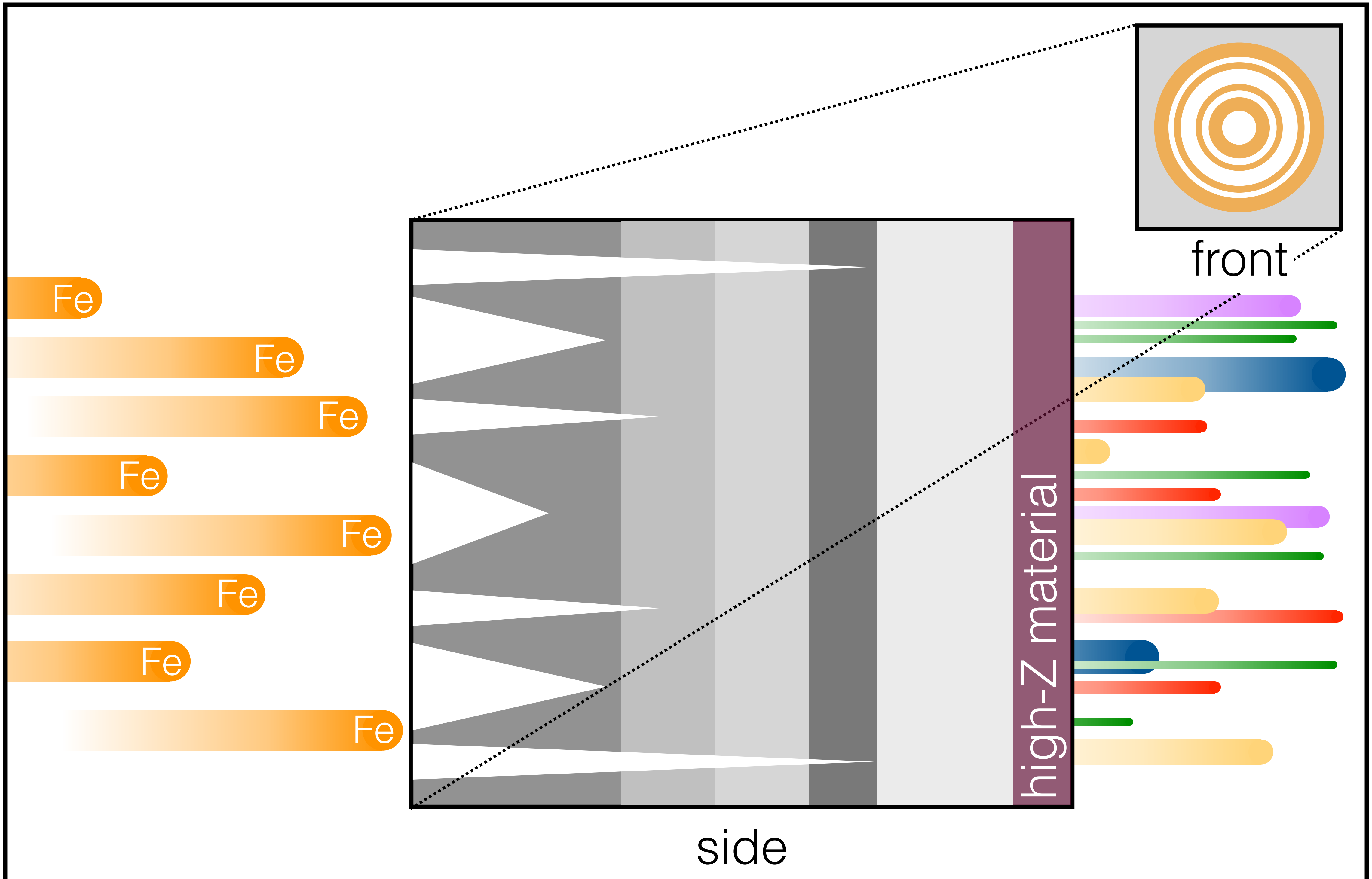
- 1GeV ^{56}Fe particle beam can be selectively degraded to closely resemble the IVA LET spectrum measured on previous spaceflights.

- Moderator block can be designed to preferentially select desired energy loss and spallation processes

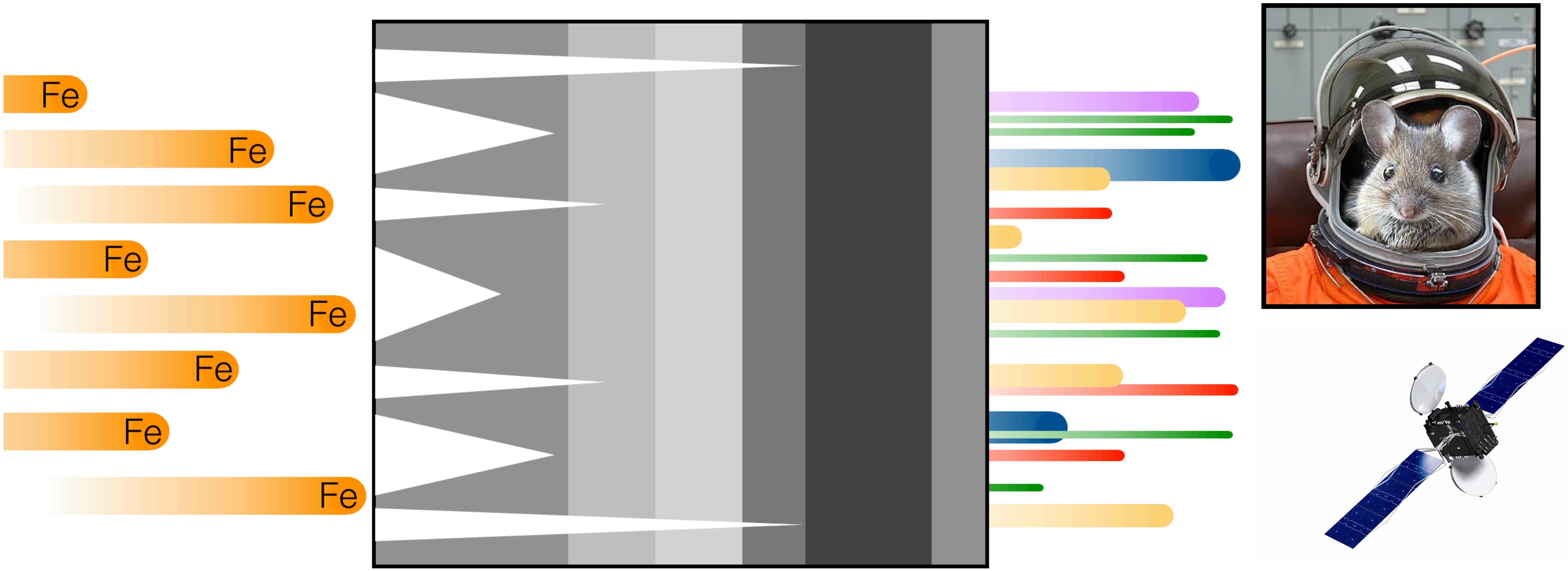
- Resulting in a complex mixed field of particle nuclei with different atomic number Z<Z≤26 and LETs≤500keV/µm.



Moderator Block Concept



Moderator Block Concept



Assumptions Made

- The interaction of the highly-charged heavy ion with the atomic structure of a material results in one of two outcomes:
  - Energy loss to the medium - described by *stopping power equation:*

$$\frac{dE}{dx} = \frac{4\pi e^4 Z_1 Z_2}{m_e \beta^2}\left[ln\left(\frac{2m_e v^2}{I}\right) - ln(1-\beta^2) - \beta^2 - \frac{C}{Z_2} - \frac{\delta}{2}\right]$$

Ahlen (1980) - Bohr (1913), Bethe (1930), Fermi (1940), Fano(1963)

  - Generation of smaller progeny nuclei through nuclear spallation.

$$\sigma_{cc} \approx \pi r_o^2 \left[(A_p)^{1/3} + (A_t)^{1/3} + \gamma(A_p^{-1}, A_t^{-1}, E)\right]^2$$

Bradt (1945), Wilson (1986)

Assumptions Made

- All radiation is unique, qualifying biological impact is heavily dependent on the ion species and energy.

  - The *Linear Energy Transfer* (LET) of a charged particle provides scaling for determination of the *effective dose*.

  - The LET provides a pseudo-normalization that strips the identification of radiation to a quantifiable number.

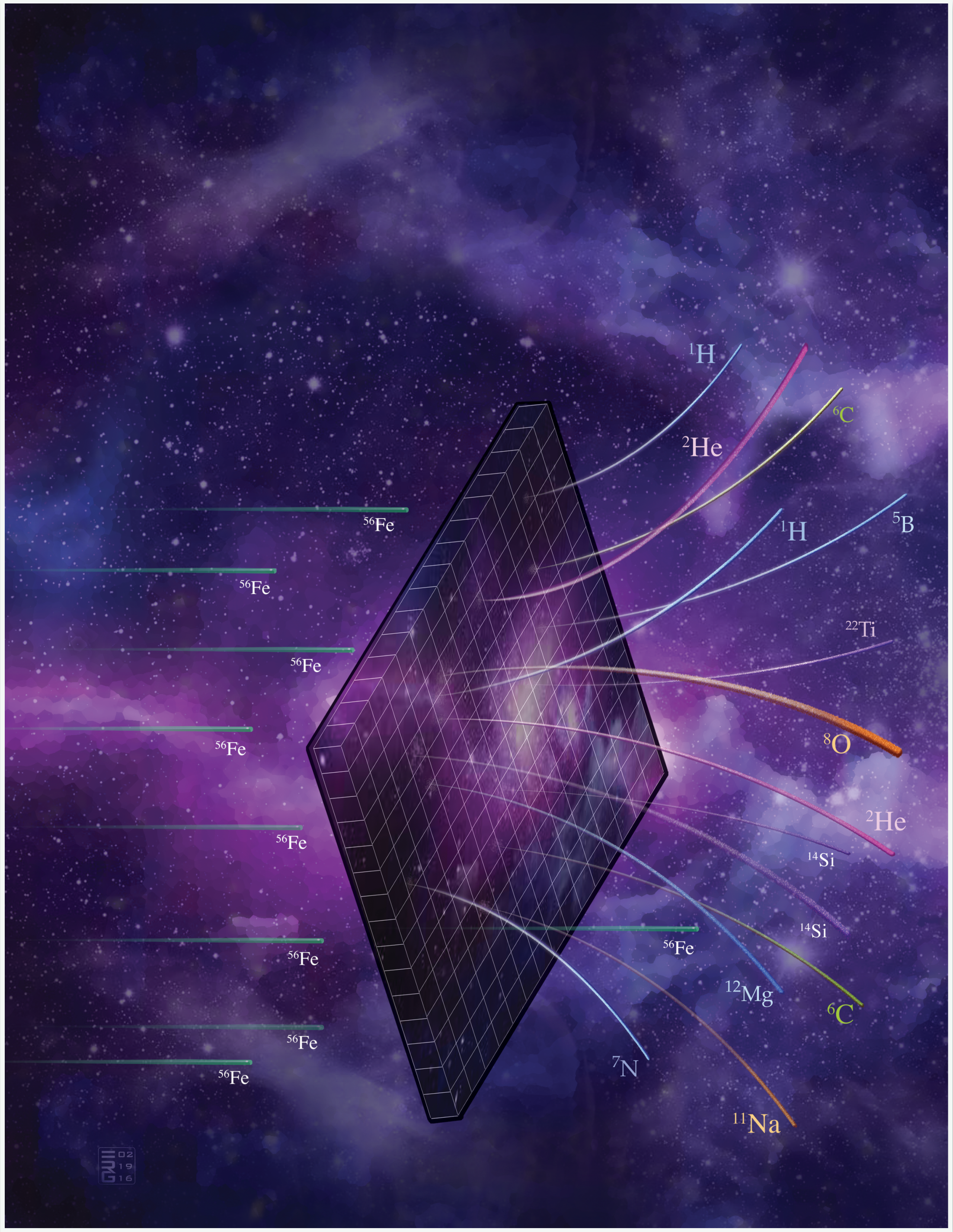
  - The stopping power is equivalent to the energy loss per unit path length of the primary ion, i.e., the LET,

$$LET = dE/dx$$

Methods

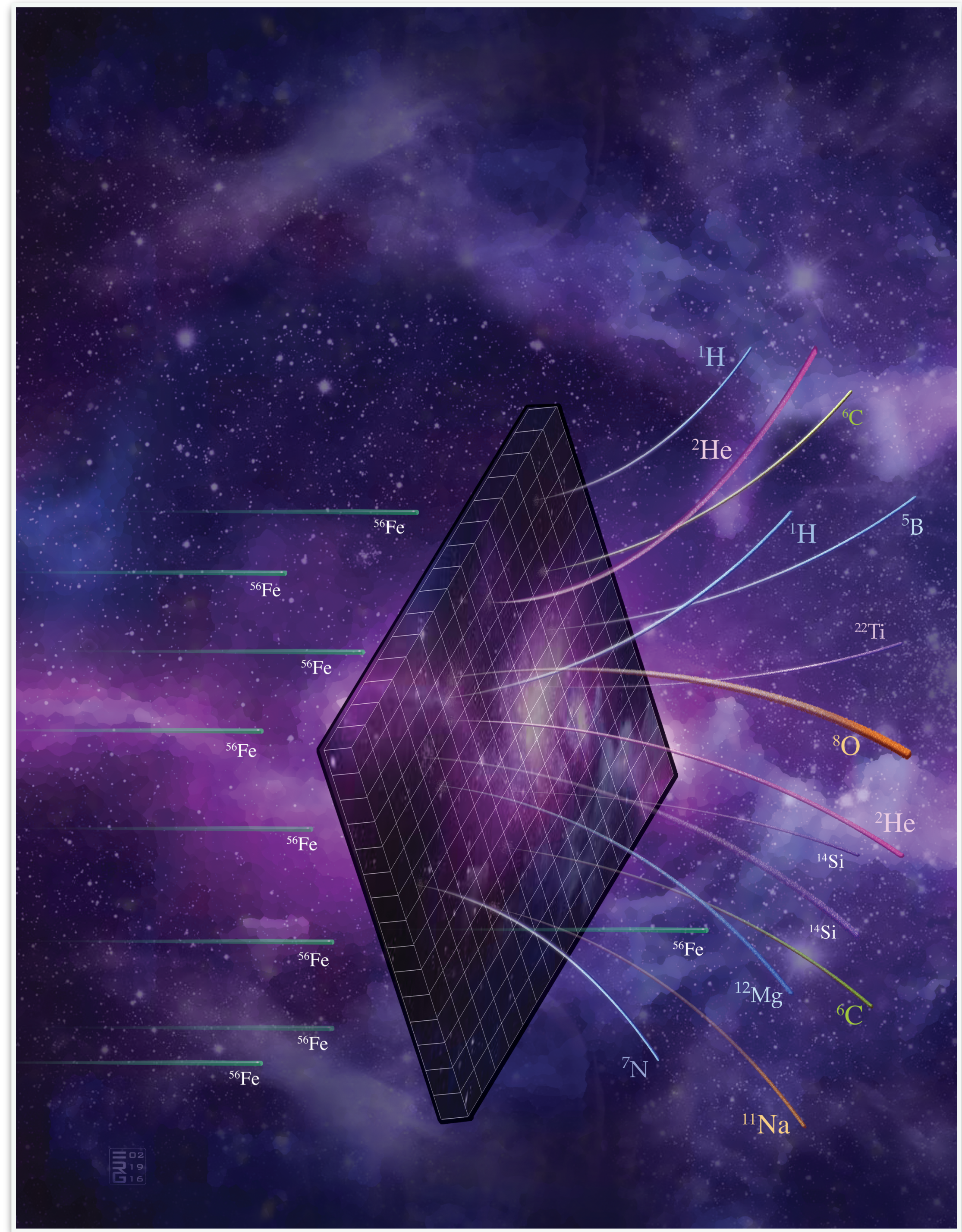
- Three initial test cases:
  - Shuttle-MIR
  - International Space Station
  - Orion EFT-1 test flight

- 3D Monte Carlo
- 1 GeV ^{56}Fe primary beam
- Hydrogen-rich polymers for target block
- Validation with experimental measurements

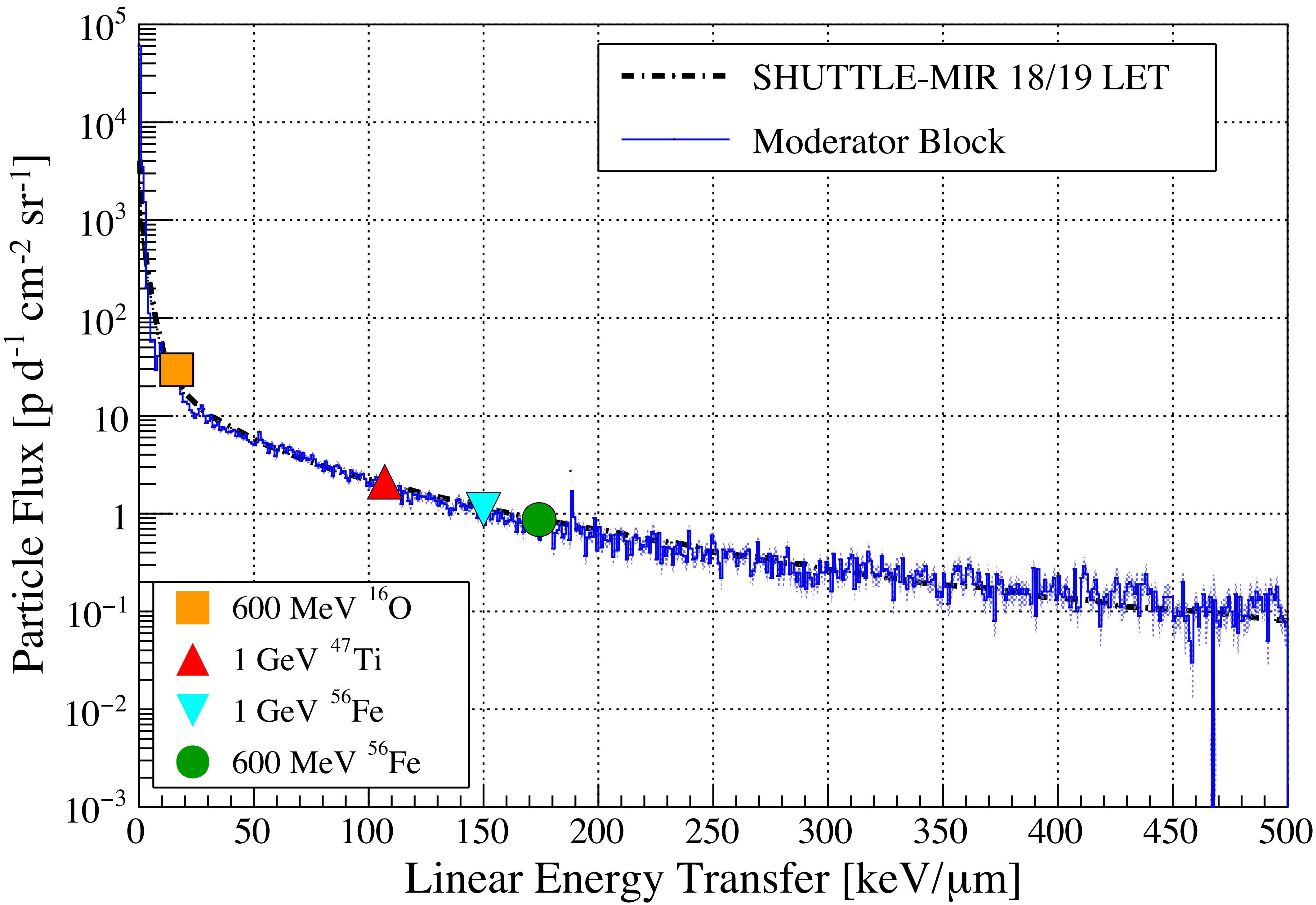


Methods

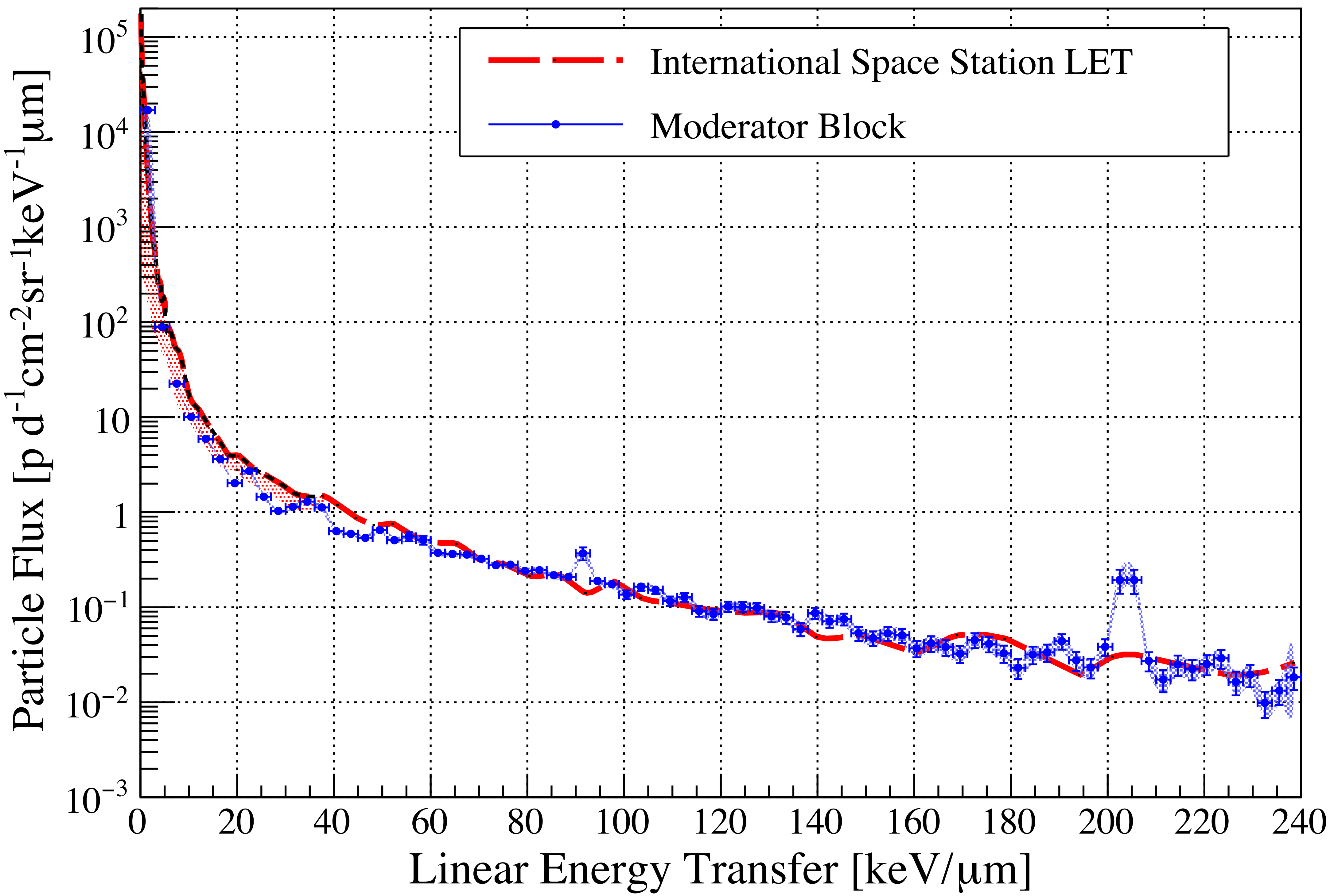
- Highly parallelized computational model
- For each test case:
  - 1e^6 samples
  - 5000 cores typically used
  - total computation time ~135,000 cpu hours
  - 2.5 TB of data generated
- Our approach would not be possible without multi cpu, high performance computers.



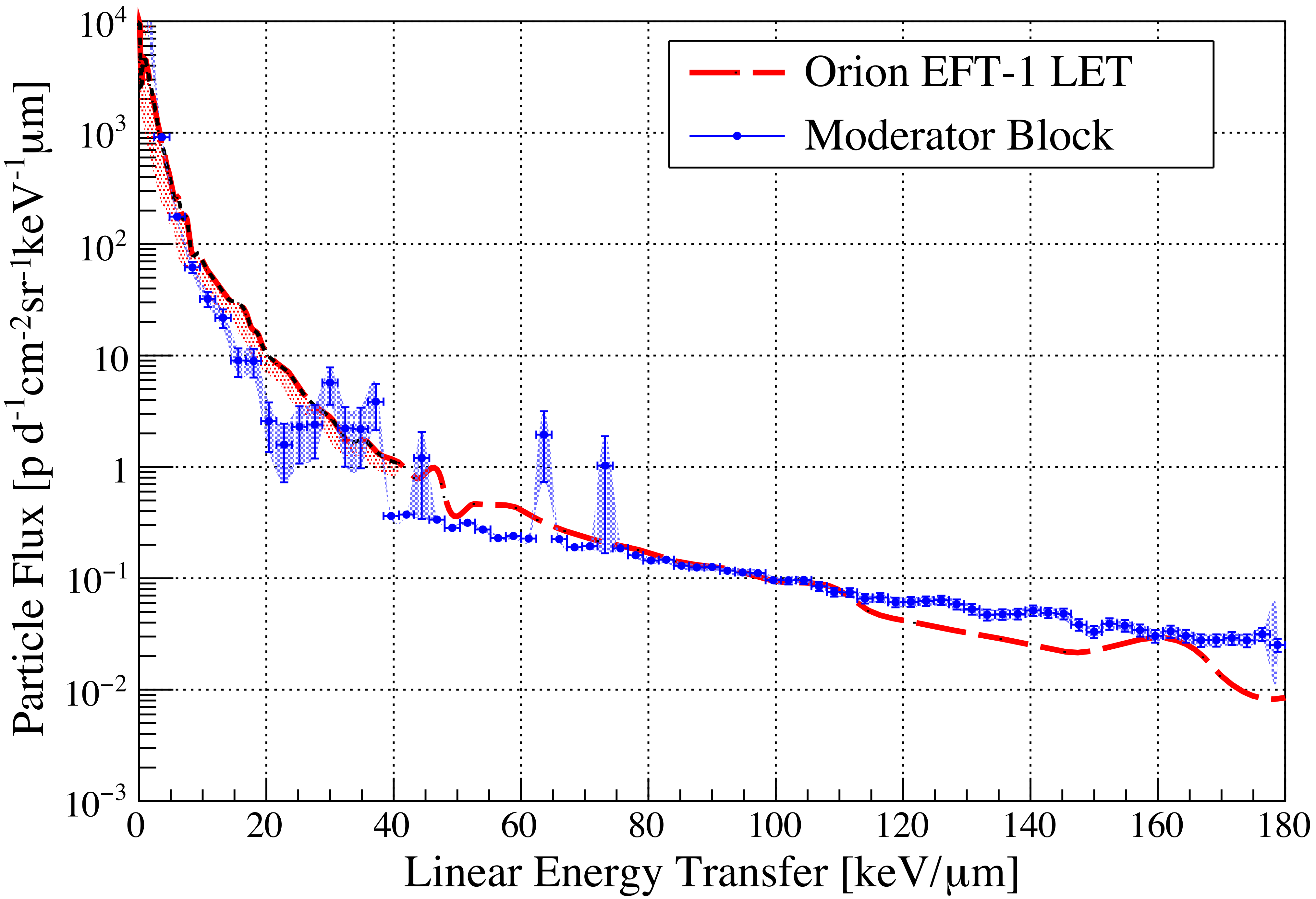
Test Case 1: Shuttle- Mir



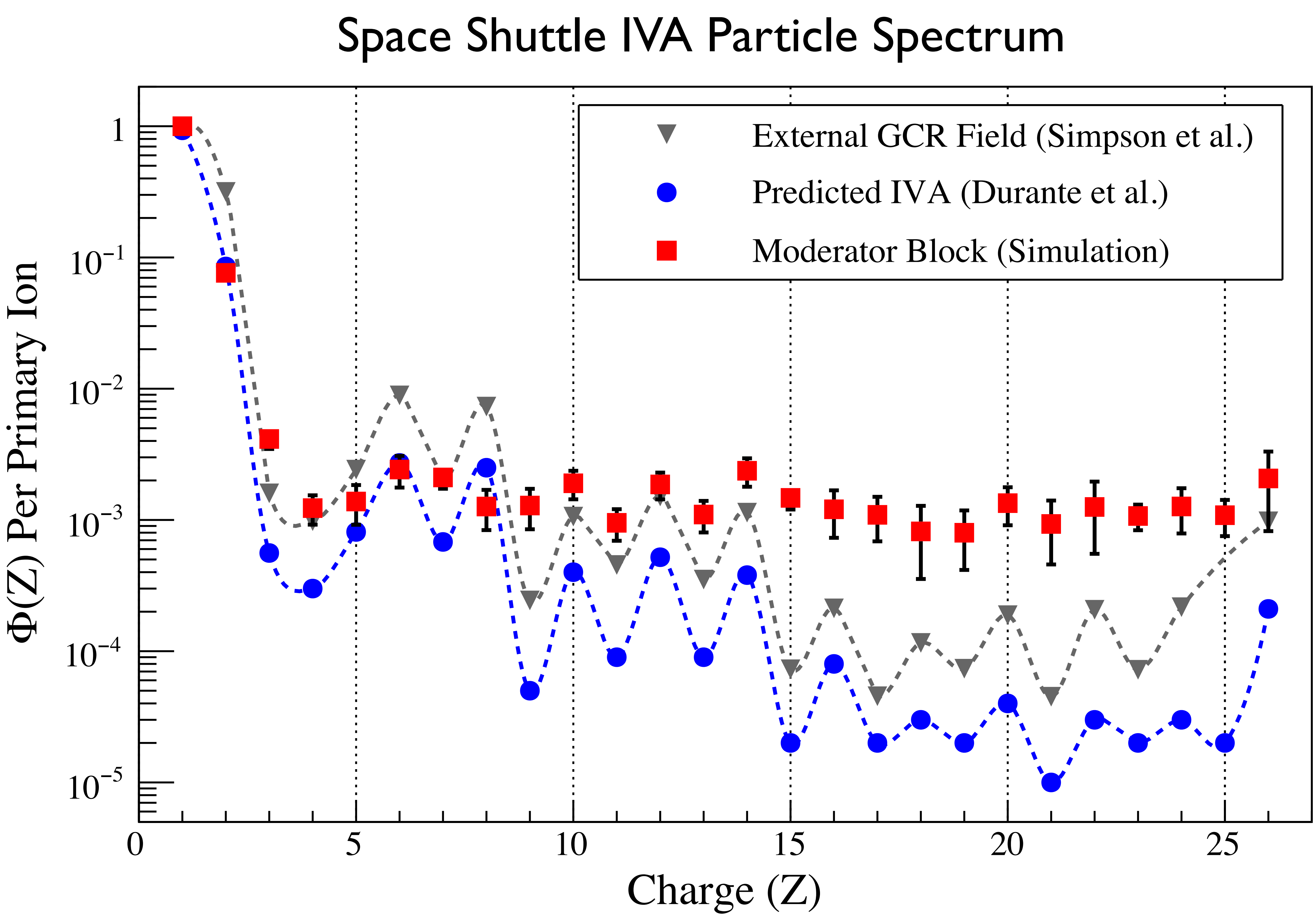
Test Case 2: International Space Station (ISS)



Test Case 3: EFT-1 (NASA Test Flight)



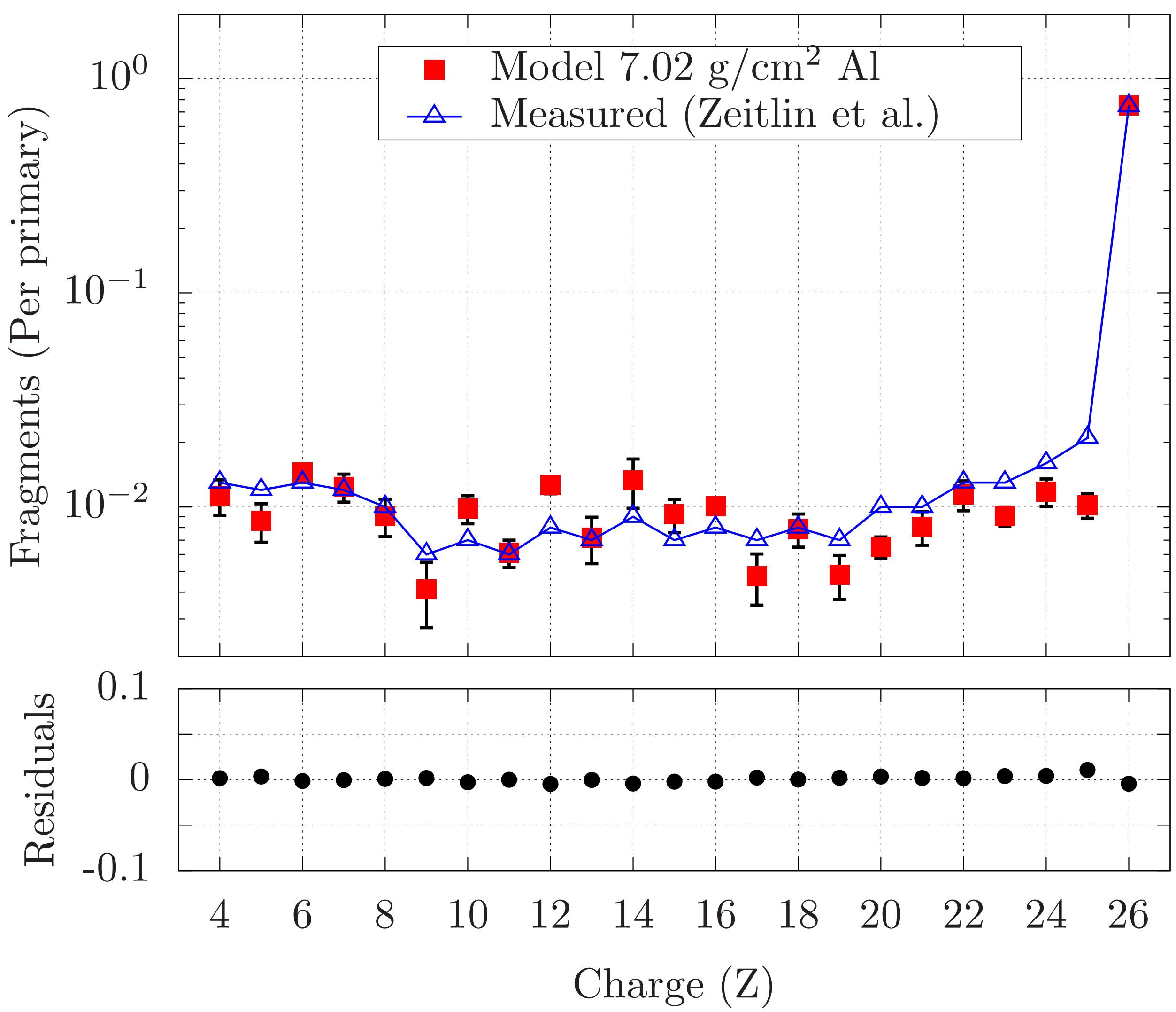
Proof is in the Pudding: Validation



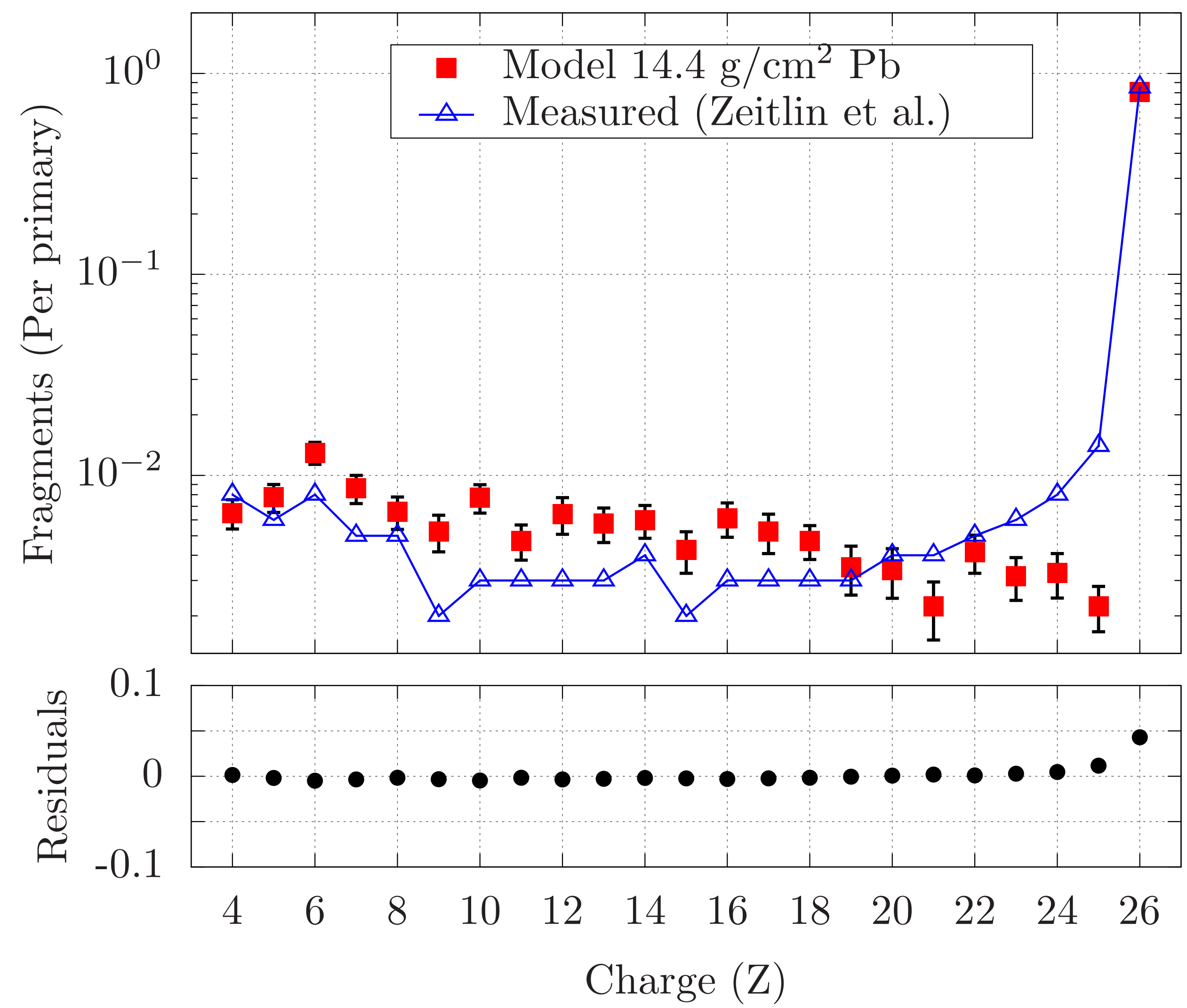
Proof is in the Pudding: Validation

Single Ion Target Blocks

Aluminum



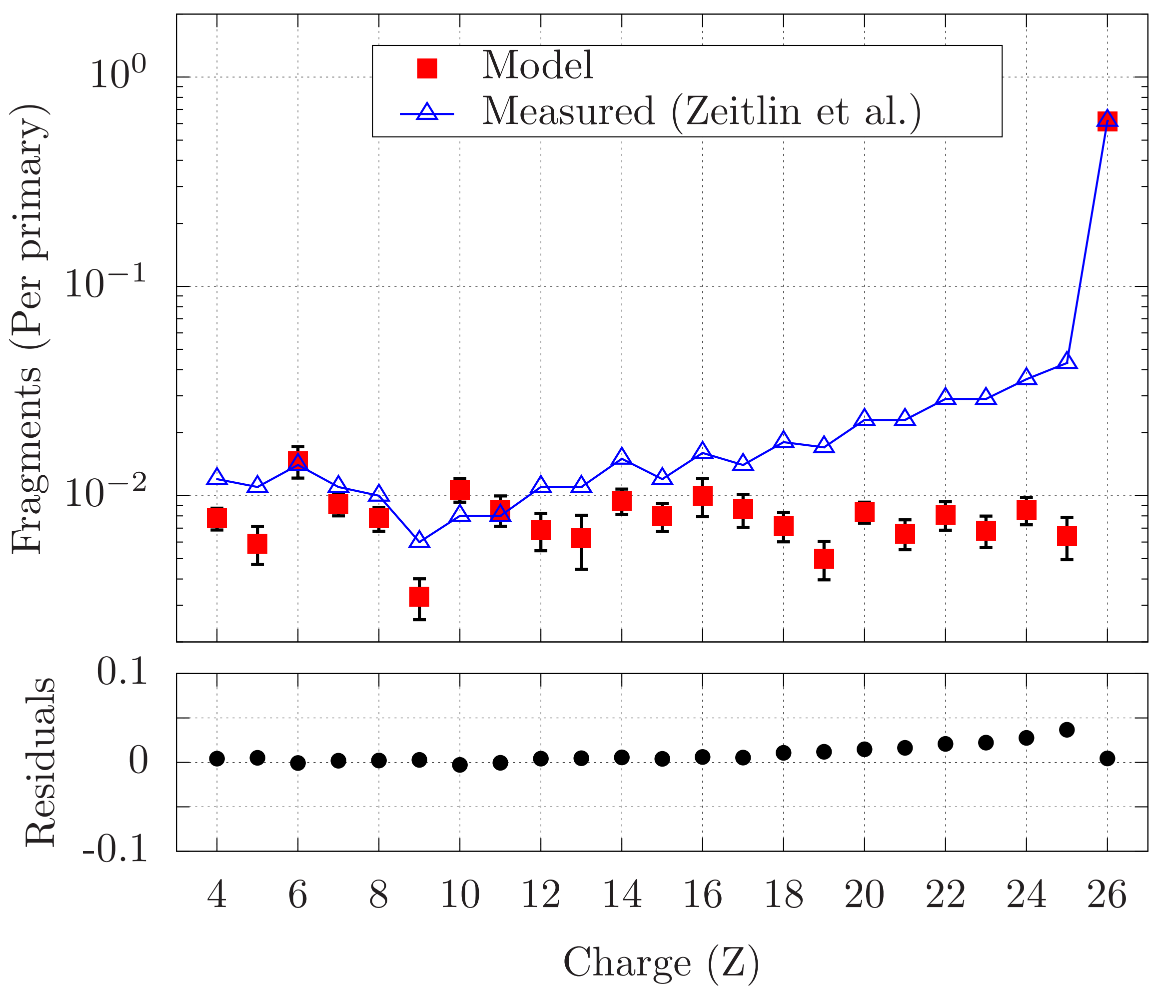
Lead



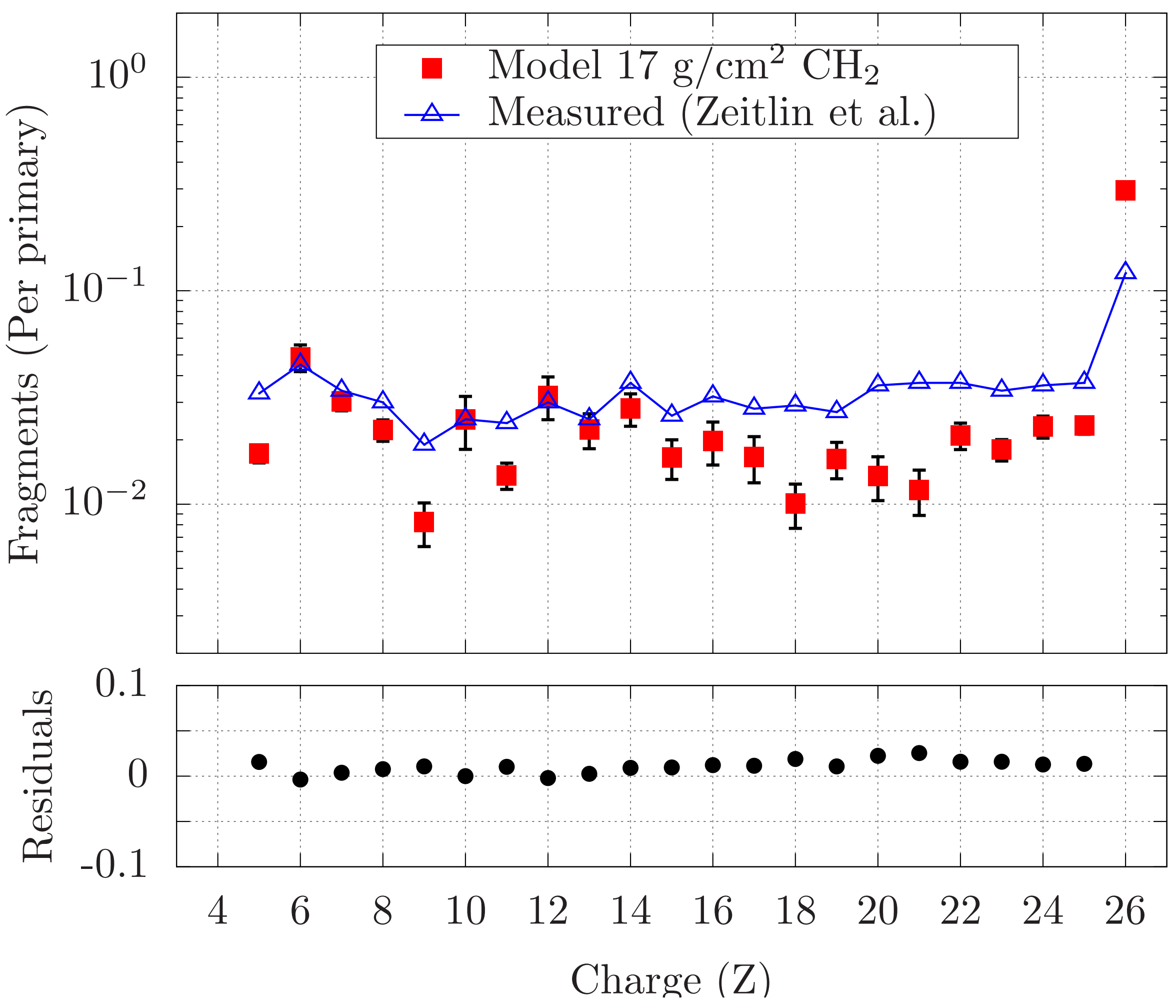
Proof is in the Pudding: Validation

Compound Target Blocks

4.2 g/cm² Polyethylene



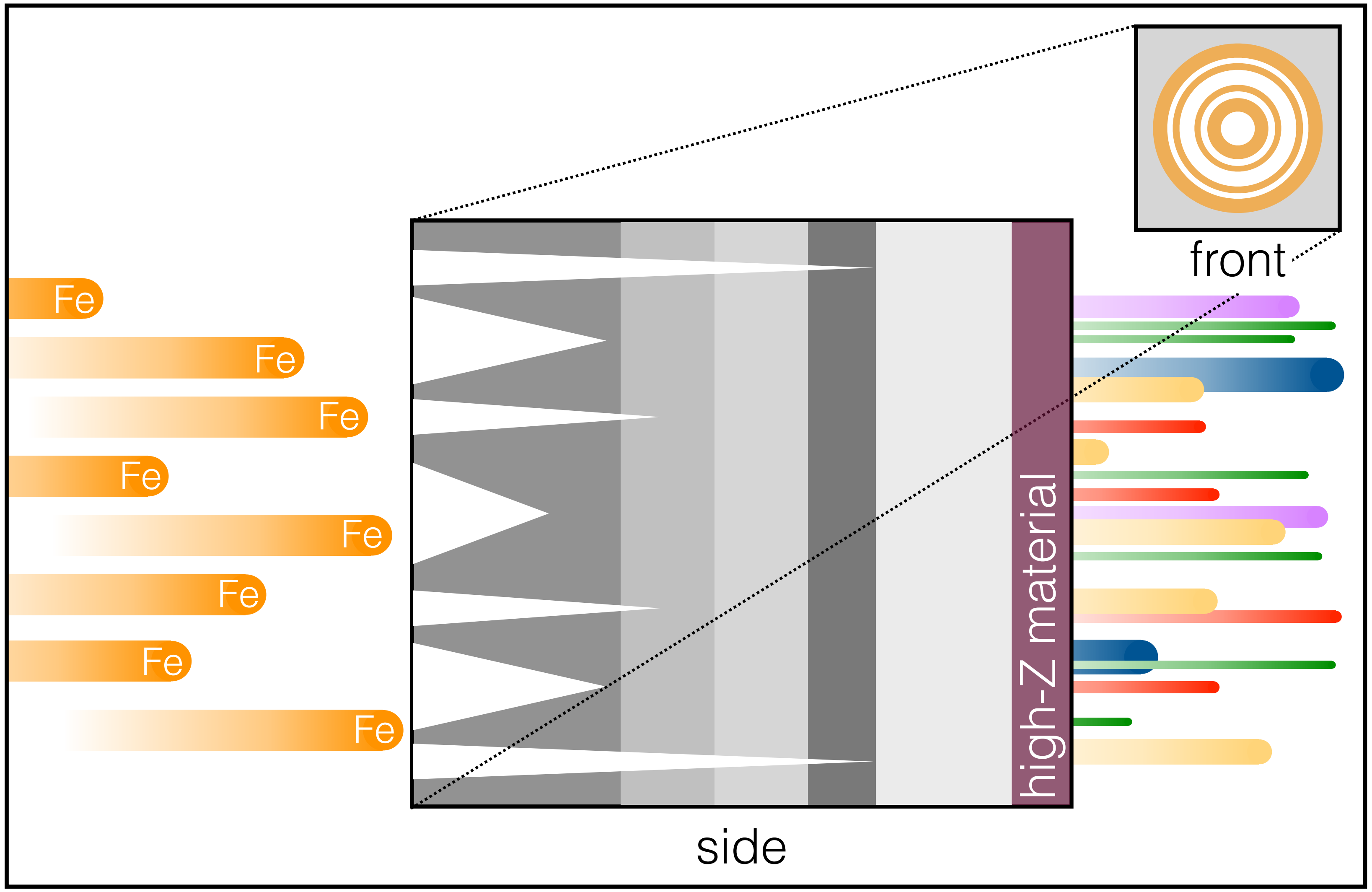
17 g/cm² Polyethylene



Take Home Message

- Can you simulate the space radiation environment for more accurate ground-based radiobiology outcomes?

☑ Yes



Questions?

Thank You

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or

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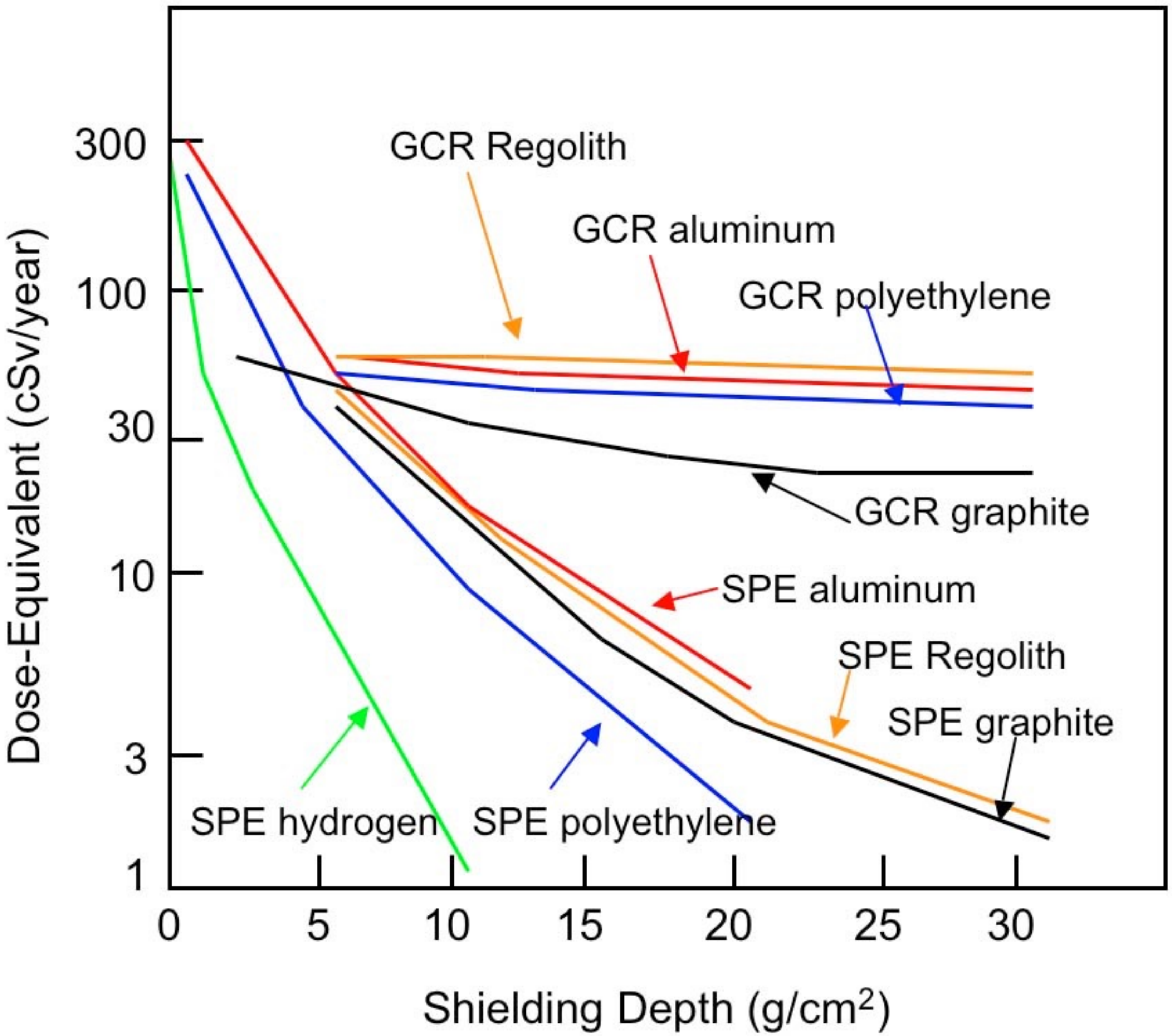
Questions?

BACKUP SLIDES

Shielding Strategies



Terrestrial Versus Space Radiation

- Total body exposure vs. single organ instigates different pathogenesis
- Multi-energy, multi-ion spectrum
- Healthy vs non-healthy tissue and organ exposures

Clinical Radiation Sources	**Clinical Radiation Sources**
• Electrons	• Electrons
• Protons	• Protons
• Carbon Ions	• Carbon Ions
Energies	**Energies**
• Electrons up to 20 keV	• Electrons up to 500 keV
• Protons: 150 - 200 MeV	• Protons: 1 - 250 MeV (mostly)
• Carbon Ions - 400 - 500 MeV	• Periodic table - 300-600 MeV (mostly)
Dose-rate	**Dose-rate**
• 0.25 Gy/min	• up to 0.025 Gy/min (SPE)
• 1-3 Gy/min	• up to 2×10^7 (5×10^7) solar min (solar max)