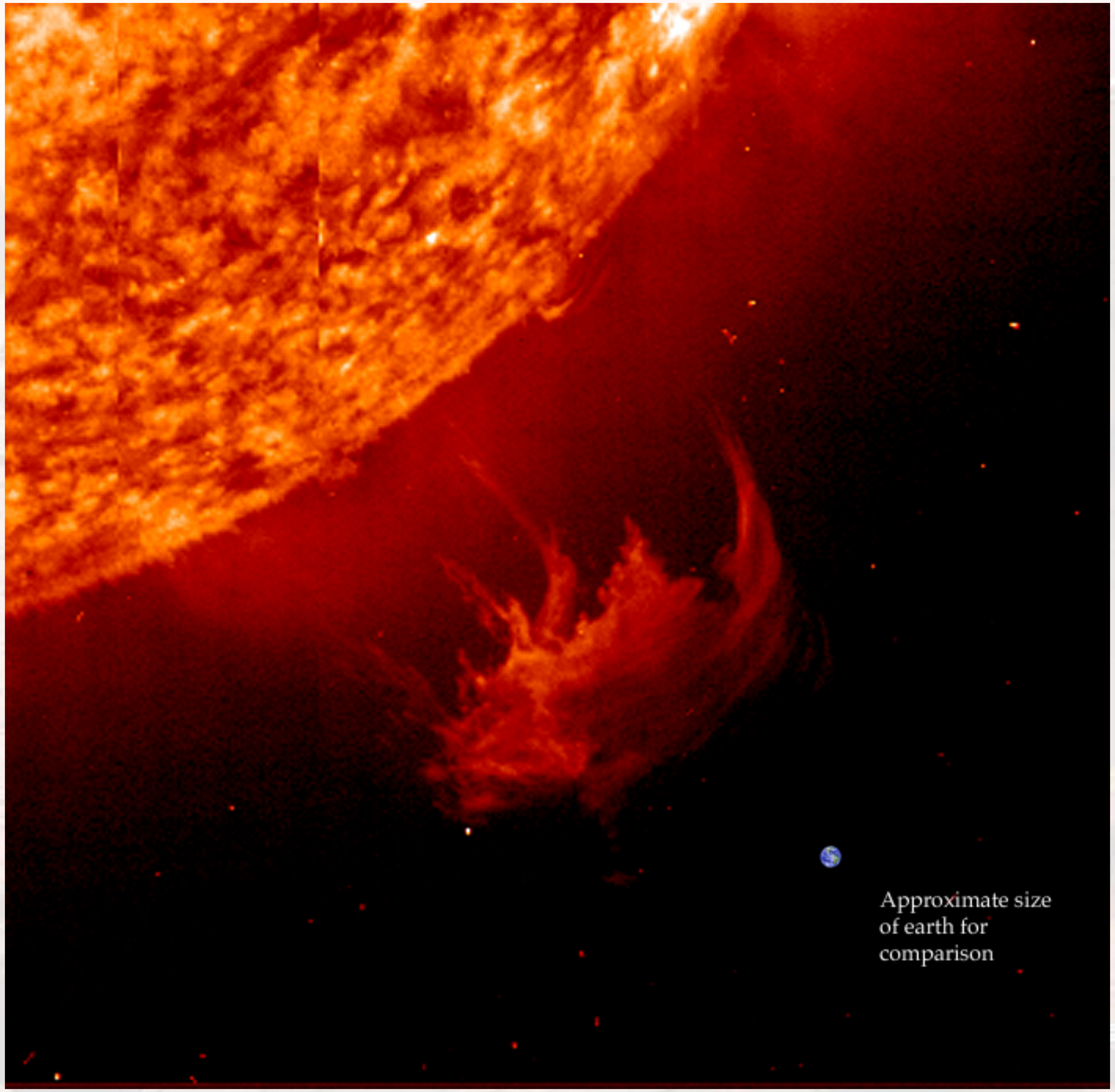
Space Radiation Effects

- Sources of radiation
- Biological effects
- Approaches to shielding
- Probabilistic estimation
- Spacecraft shielding design
- Recent revisions to understanding radiation effects

Issues of Human Radiation Exposure

- Acute dosage effects
- Carcinogenesis
- Central nervous system effects
- Chronic and degenerative tissue risks

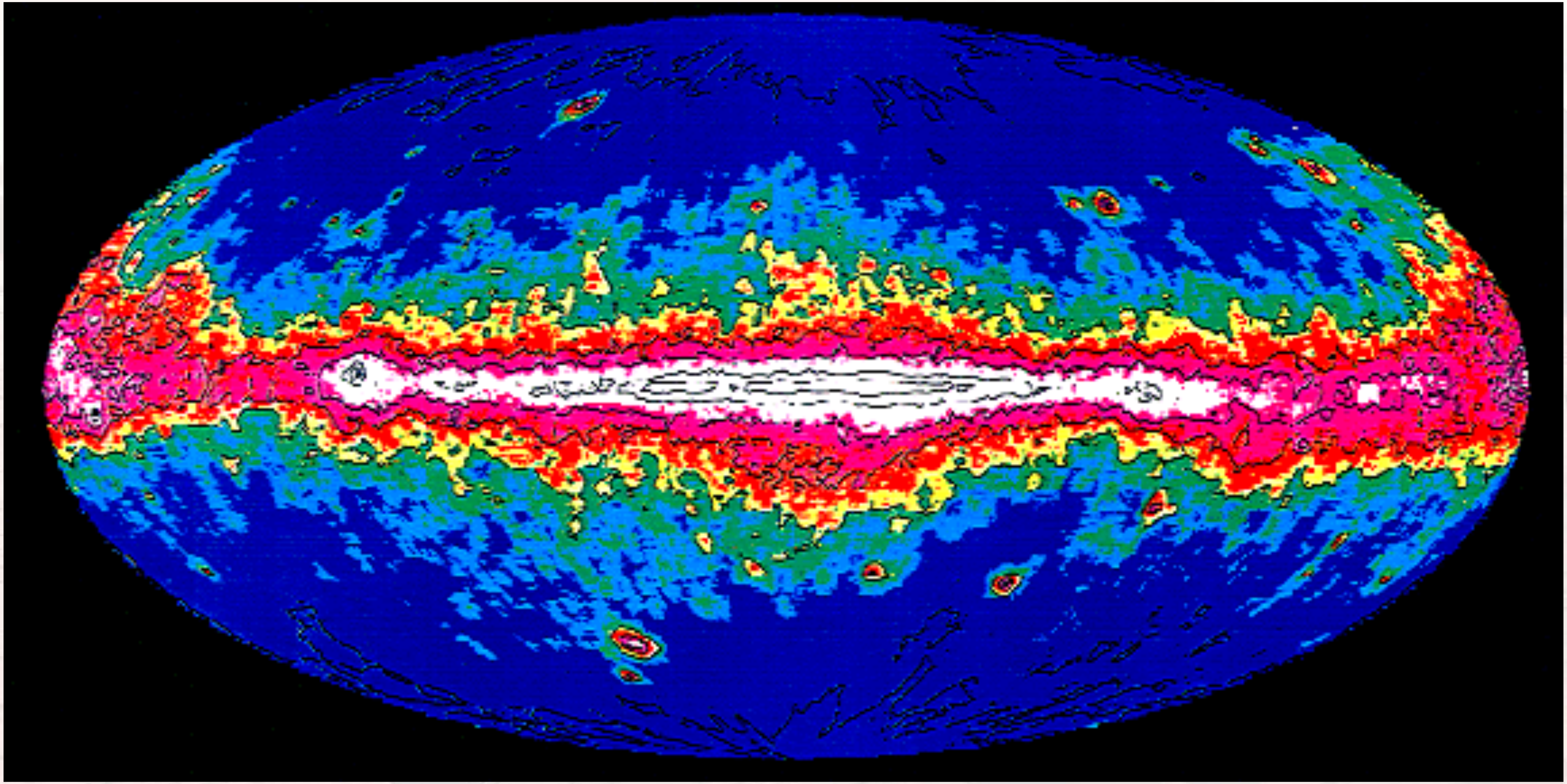
The Origin of a Class X1 Solar Flare



Solar Radiation

- Produced continuously (solar wind)
- Increases dramatically during solar particle events (SPEs)
  - Coronal ejections
  - Solar flares
- Primarily high-energy electrons and protons (10-500 MeV)

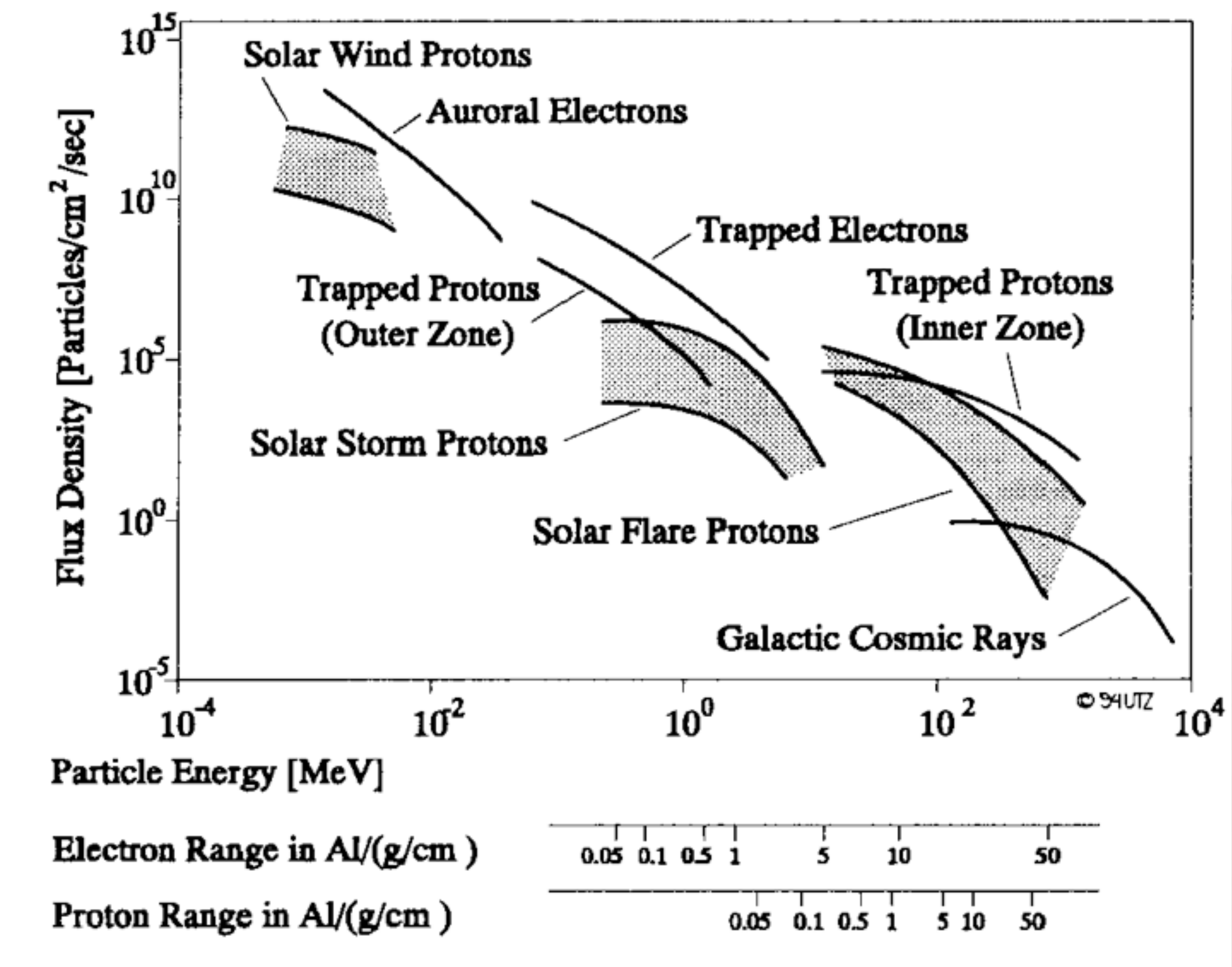
Image of Galaxy in Gamma Rays



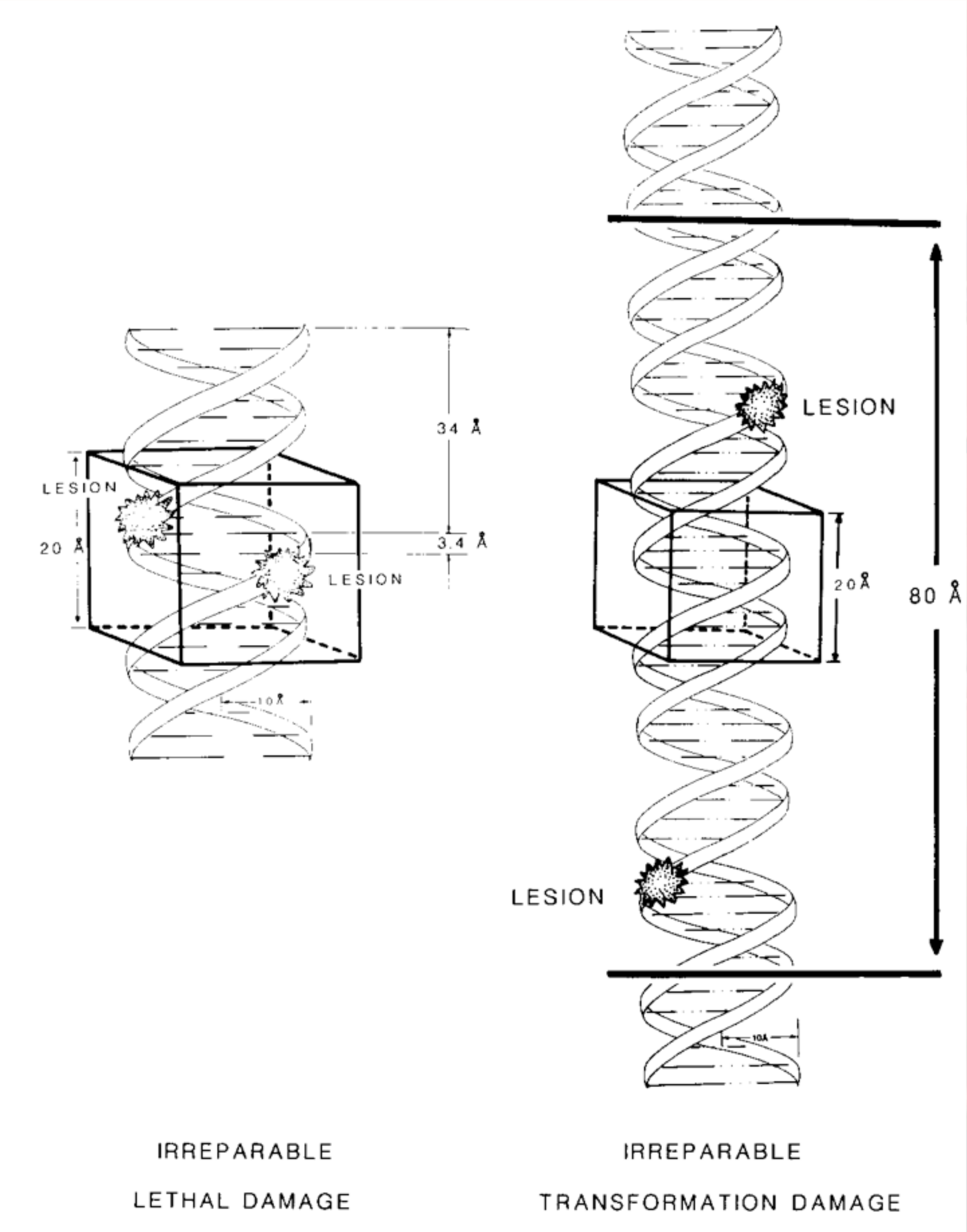
Galactic Cosmic Rays

- Atomic nuclei, stripped of electrons and accelerated by supernova explosions to nearly the speed of light
- Constituents:
  - 90% protons
  - 9% alpha particles
  - 1% heavier elements
- Ionization potential proportional to square of charge (Fe^{26+}=676 x p^+)

Radiation in Free Space



Radiation Damage to DNA



Radiation Units

- Dose D= absorbed radiation

$$1\ Gray = 1\ \frac{Joule}{kg} = 100\ rad = 10,000\ \frac{ergs}{gm}$$

- Dose equivalent H= effective absorbed radiation

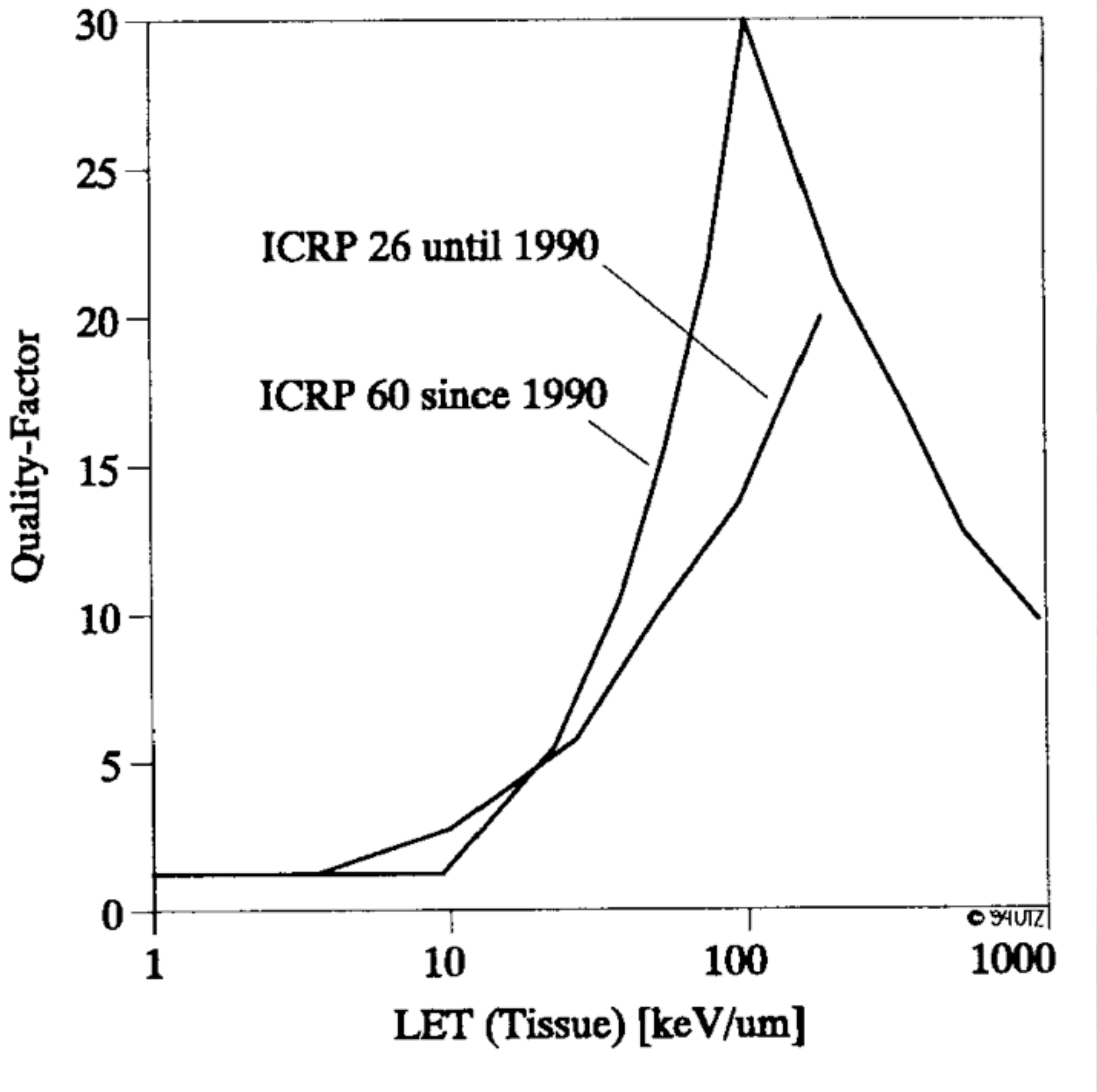
$$1\ Sievert = 1\ \frac{Joule}{kg} = 100\ rem = 10,000\ \frac{ergs}{gm}$$

$$H = DQ \qquad\qquad rem = RBE \times rad$$

- LET = Linear Energy Transfer <KeV/μ m>

Radiation Quality Factor

Radiation	Q
X-rays	1
5 MeV γ-rays	0.5
1 MeV γ-rays	0.7
200 KeV γ-rays	1
Electrons	1
Protons	2-10
Neutrons	2-10
α-particles	10-20
GCR	20+



Symptoms of Acute Radiation Exposure

- "Radiation sickness": headache, dizziness, malaise, nausea, vomiting, diarrhea, lowered RBC and WBC counts, irritability, insomnia
- 50 rem (0.5 Sv)
  - Mild symptoms, mostly on first day
  - ~100% survival
- 100-200 rem (1-2 Sv)
  - Increase in severity and duration
  - 70% incidence of vomiting at 200 rem
  - 25%-35% drop in blood cell production
  - Mild bleeding, fever, and infection in 4-5 weeks

Symptoms of Acute Radiation Exposure

- 200-350 rem (2-3.5 Sv)
  - Earlier and more severe symptoms
  - Moderate bleeding, fever, infection, and diarrhea at 4-5 weeks
- 350-550 rem (3.5-5.5 Sv)
  - Severe symptoms
  - Severe and prolonged vomiting - electrolyte imbalances
  - 50-90% mortality from damage to hematopoietic system if untreated

Symptoms of Acute Radiation Exposure

- 550-750 rem (5.5-7.5 Sv)
  - Severe vomiting and nausea on first day
  - Total destruction of blood-forming organs
  - Untreated survival time 2-3 weeks
- 750-1000 rem (7.5-10 Sv)
  - Survival time ~2 weeks
  - Severe nausea and vomiting over first three days
  - 75% prostrate by end of first week
- 1000-2000 rem (10-20 Sv)
  - Severe nausea and vomiting in 30 minutes
- 4500 rem (45 Sv)
  - Survival time as short as 32 hrs - 100% in one week

Long-Term Effects of Radiation Exposure

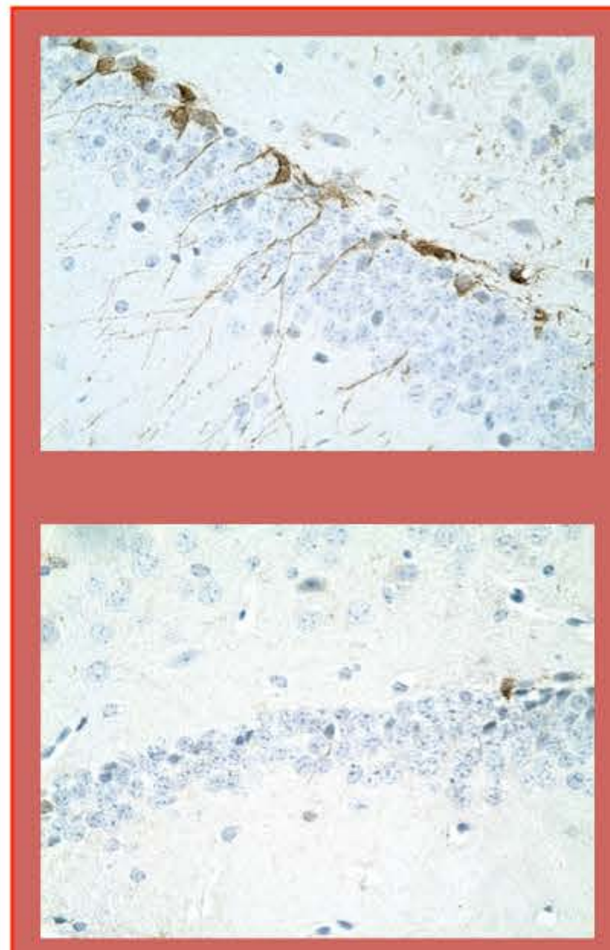
- Radiation carcinogenesis
  - Function of exposure, dosage, LET of radiation
- Radiation mutagenesis
  - Mutations in offspring
  - Mouse experiments show doubling in mutation rate at 15-30 rad (acute), 100 rad (chronic) exposures
- Radiation-induced cataracts
  - Observed correlation at 200 rad (acute), 550 rad (chronic)
  - Evidence of low onset (25 rad) at high LET

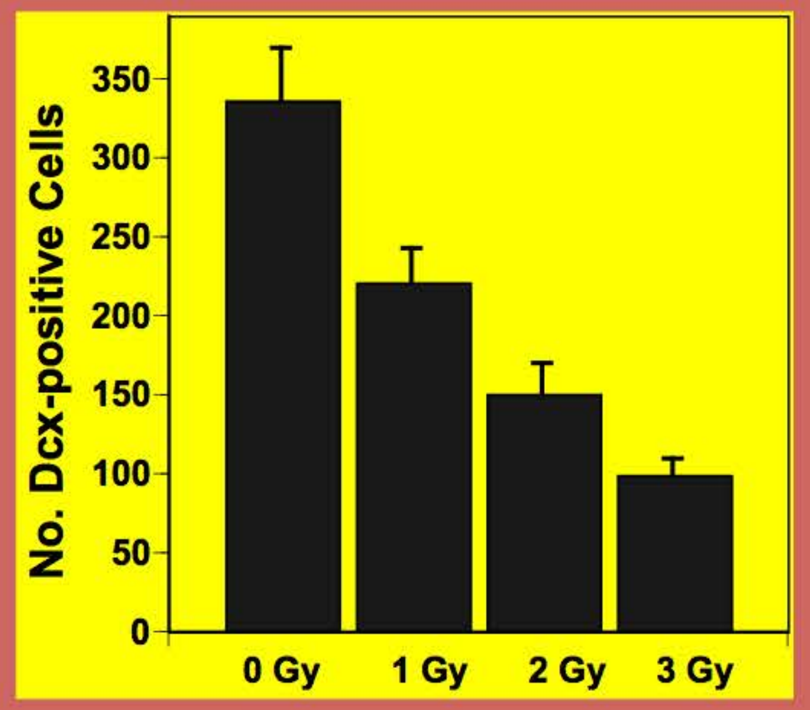
Radiation Carcinogenesis

- Manifestations
  - Myelocytic leukemia
  - Cancer of breast, lung, thyroid, and bowel
- Latency in atomic bomb survivors
  - Leukemia: mean 14 yrs, range 5-20 years
  - All other cancers: mean 25 years
- Overall marginal cancer risk
  - 70-165 deaths/million people/rem/year
  - 100,000 people exposed to 10 rem (acute) -> 800 additional deaths (20,000 natural cancer deaths) - 4%

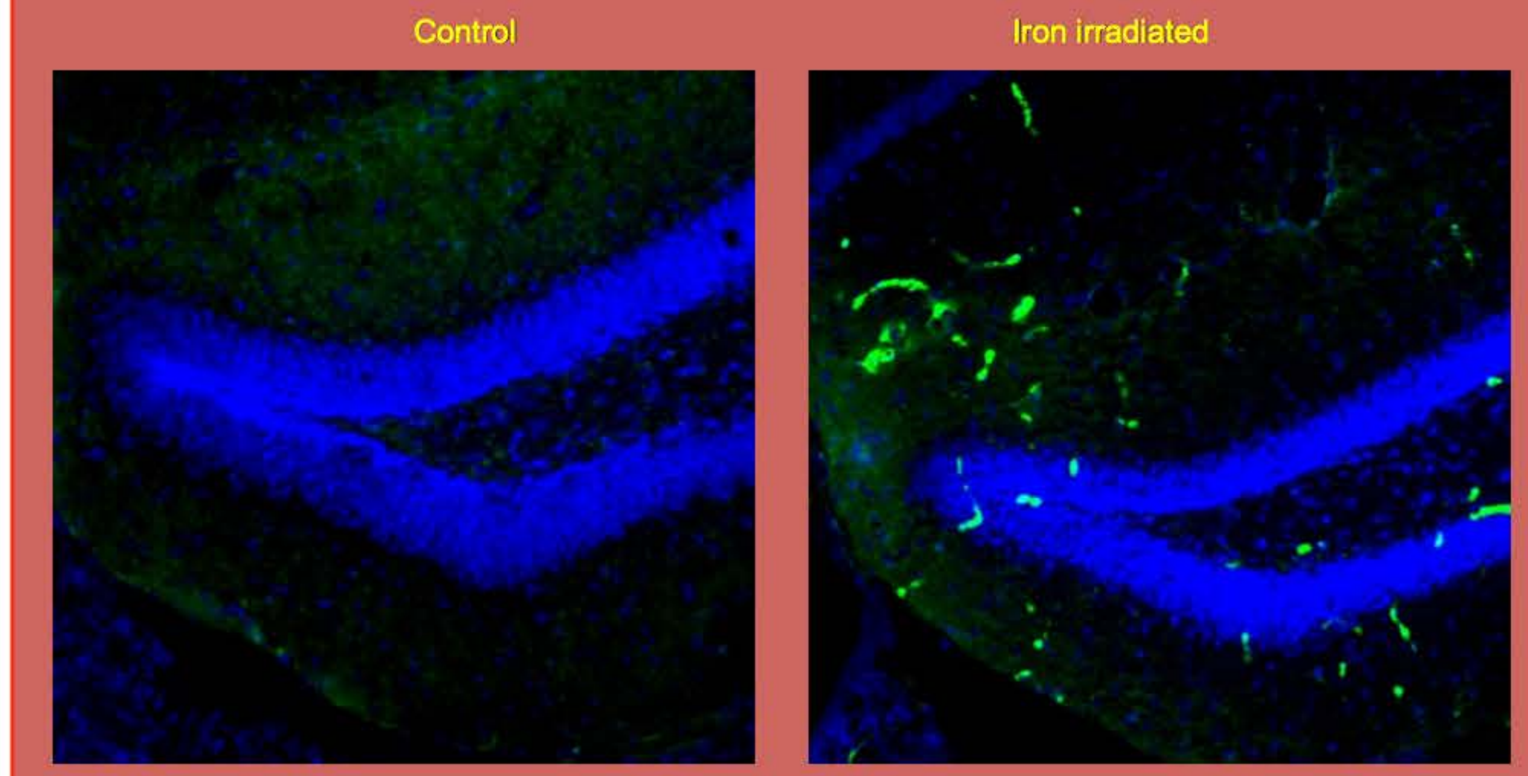
CNS Risks from Galactic Cosmic Rays (GCR)

- Retinal flashes observed by astronauts suggests single heavy nuclei can disrupt brain function.
  - **Central nervous system (CNS) damage by x-rays is not observed except at very high doses**
- In-flight cognitive changes and late effects similar to Alzheimer's disease are a concern for GCR.
- NASA research in cells and mouse/rat models has increased concern for CNS Risks
  - **Over 90 CNS journal publications supported by NASA since 2000**
  - **Studies have quantified rate of neuronal degeneration, oxidative stress, apoptosis, inflammation, and changes in dopamine function related to late CNS risks**
  - **Cognitive tests in rats/mice show detriments at doses as low as 10 mGy (1 rad)**
- Large hurdle remains to establish significance in humans





Reduction in number of neurons (neurodegeneration) for increasing Iron doses in mouse hippocampus



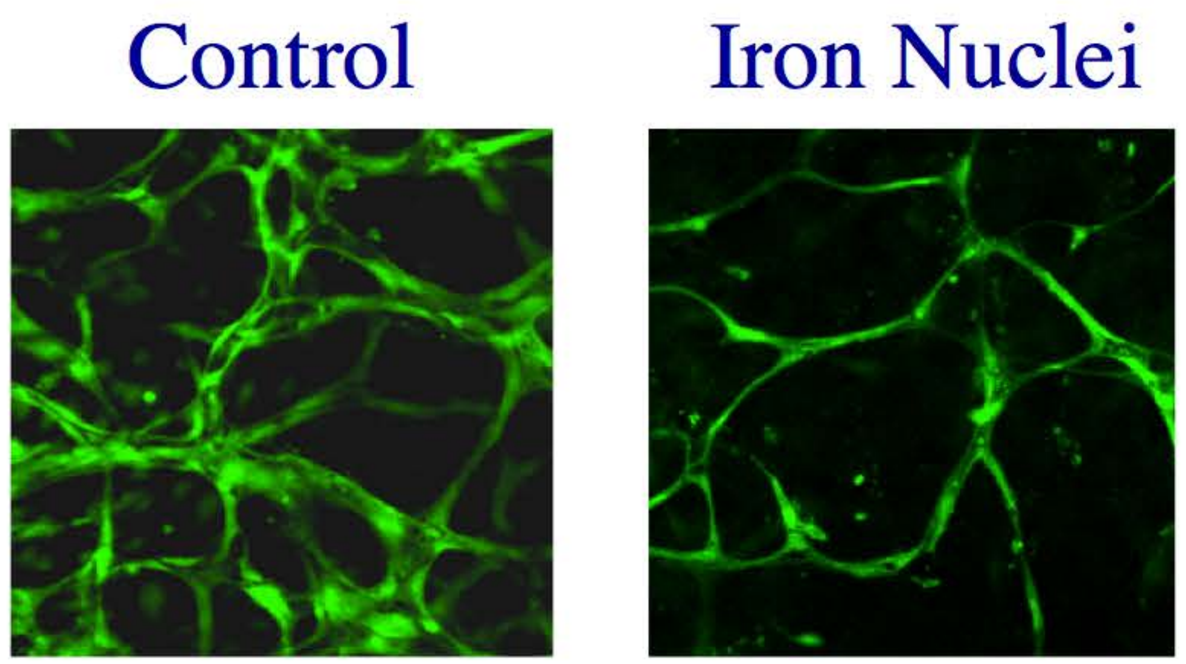
Oxidative Stress (Lipid peroxidation:4-Hydroxynonenal) is Increased in Mouse Hippocampus 9 Months After 2 Gy of ^{56}Fe Irradiation

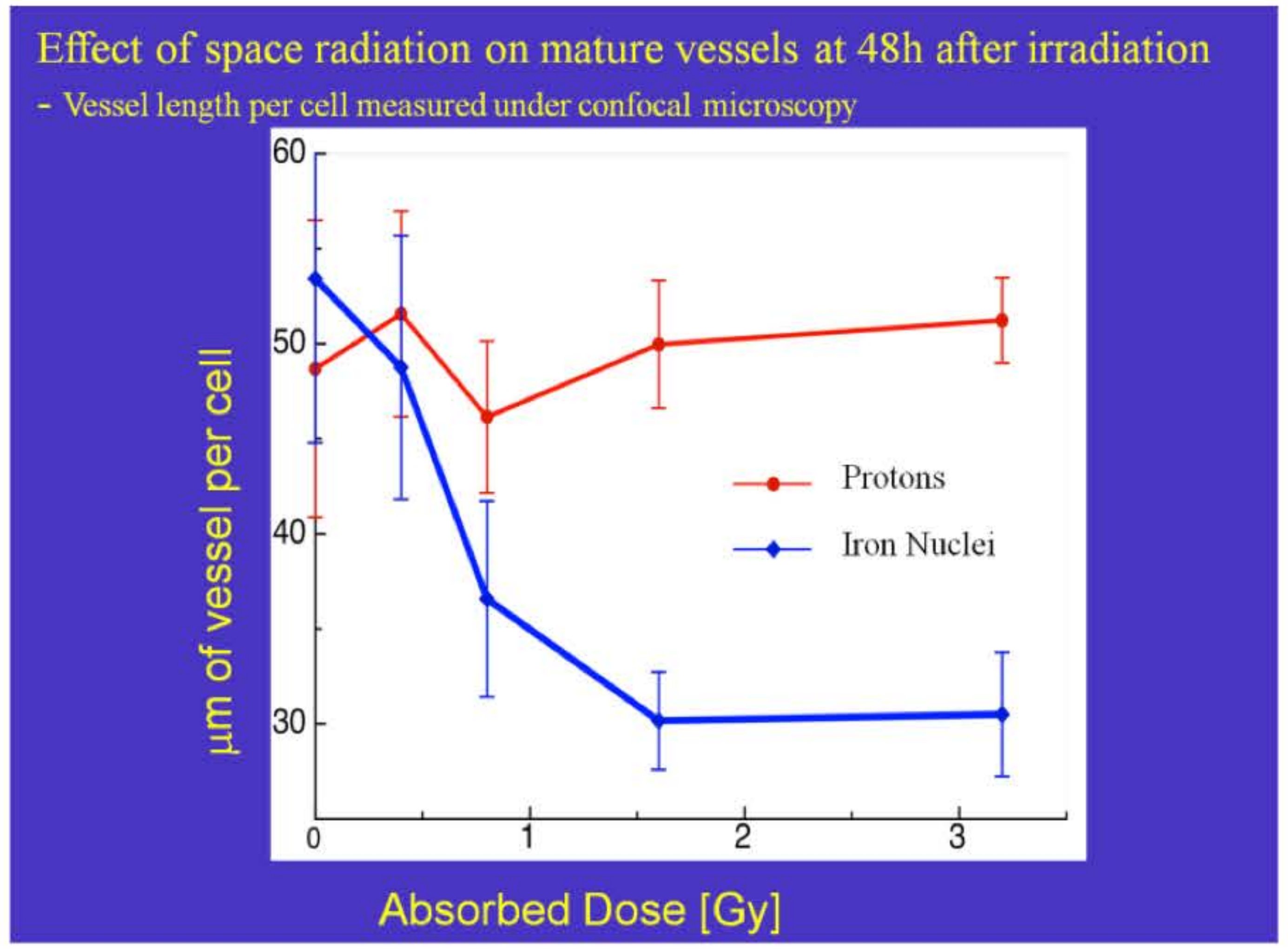
Francis Cucinotta, "What's New in Space Radiation Research for Exploration?" NASA FISO, May 18, 2011

Radiation and Non-Cancer Effects

- Early Acute risks are very unlikely:
  - Low or modest dose-rates for SPE's insufficient for risk of early death
  - SPE doses are greatly reduced by tissue or vehicle shielding
- Radiation induced Late Non-Cancer risks are well known at high doses and recently a concern at doses below 1 Sv (100 rem)
  - Significant Heart disease in Japanese Survivors and several patient and Reactor Worker Studies
  - Dose threshold is possible making risk unlikely for ISS Missions(<0.2 Sv) ; however a concern for Mars or lunar missions due to higher GCR and SPE dose
  - Qualitative differences between GCR and gamma-rays are a major concern

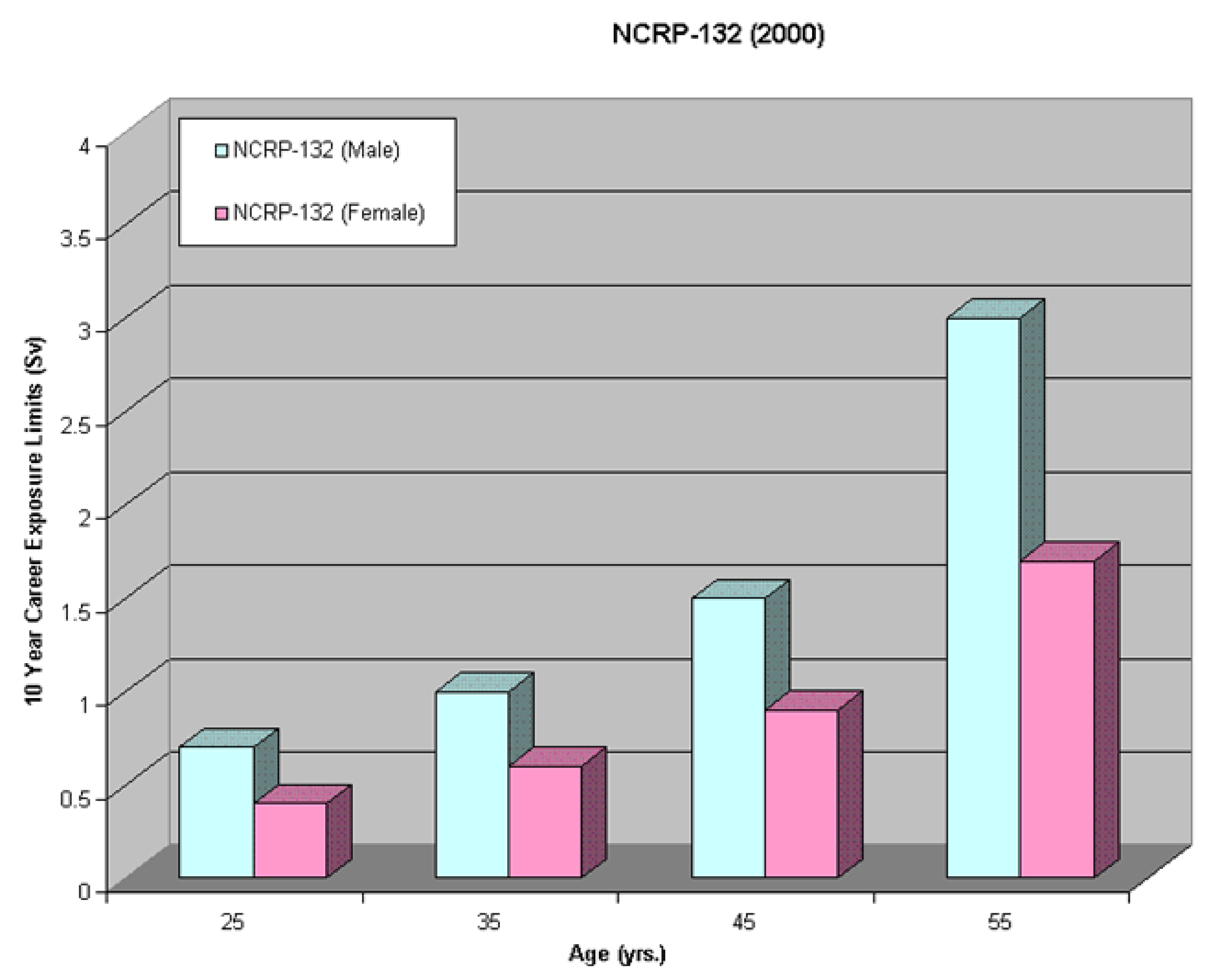
Vasculature Damage by GCR



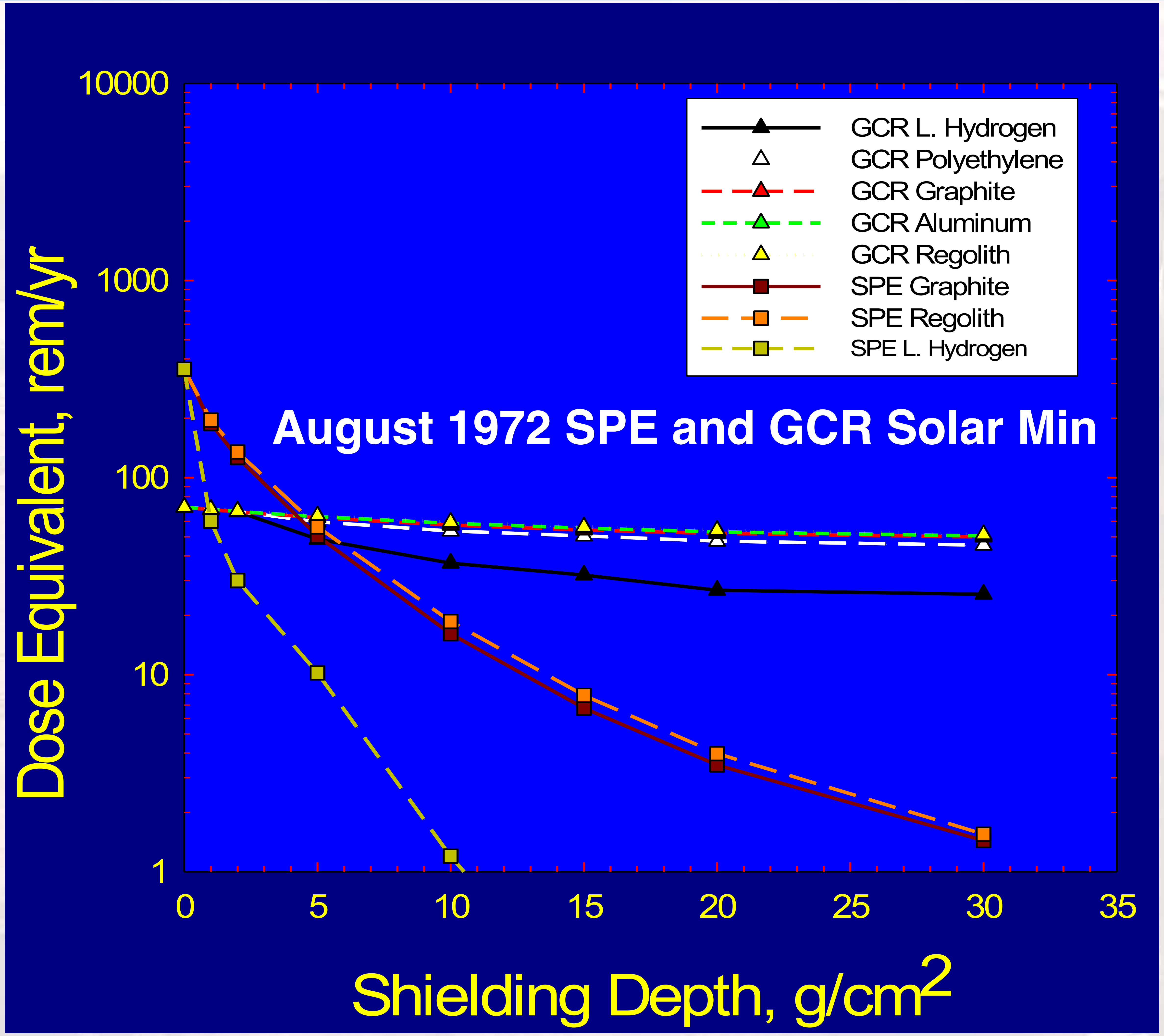


Francis Cucinotta, "What's New in Space Radiation Research for Exploration?" NASA FISO, May 18, 2011

NASA Radiation Dose Limits

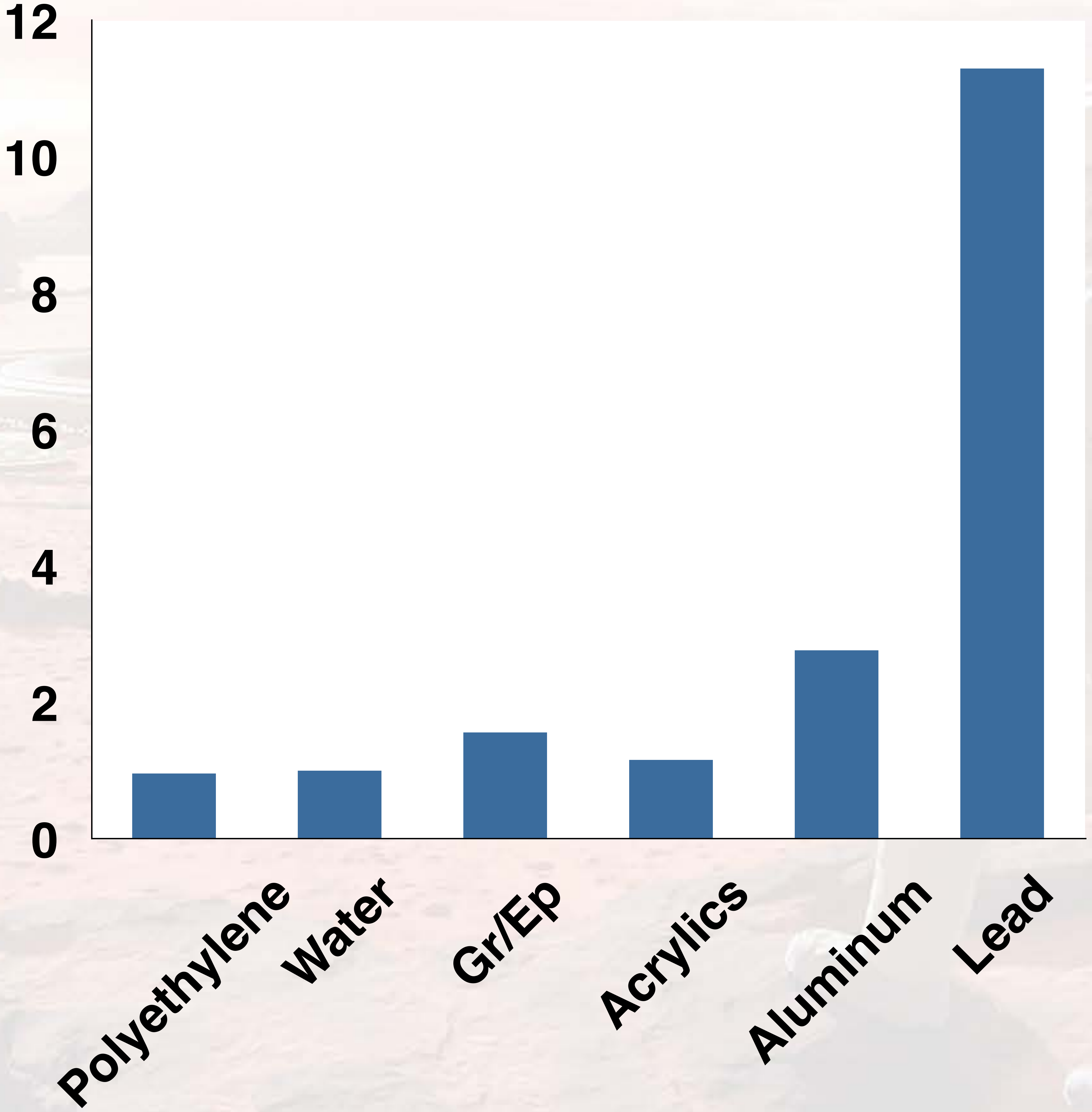


SPE and GCR Shielding Effectiveness

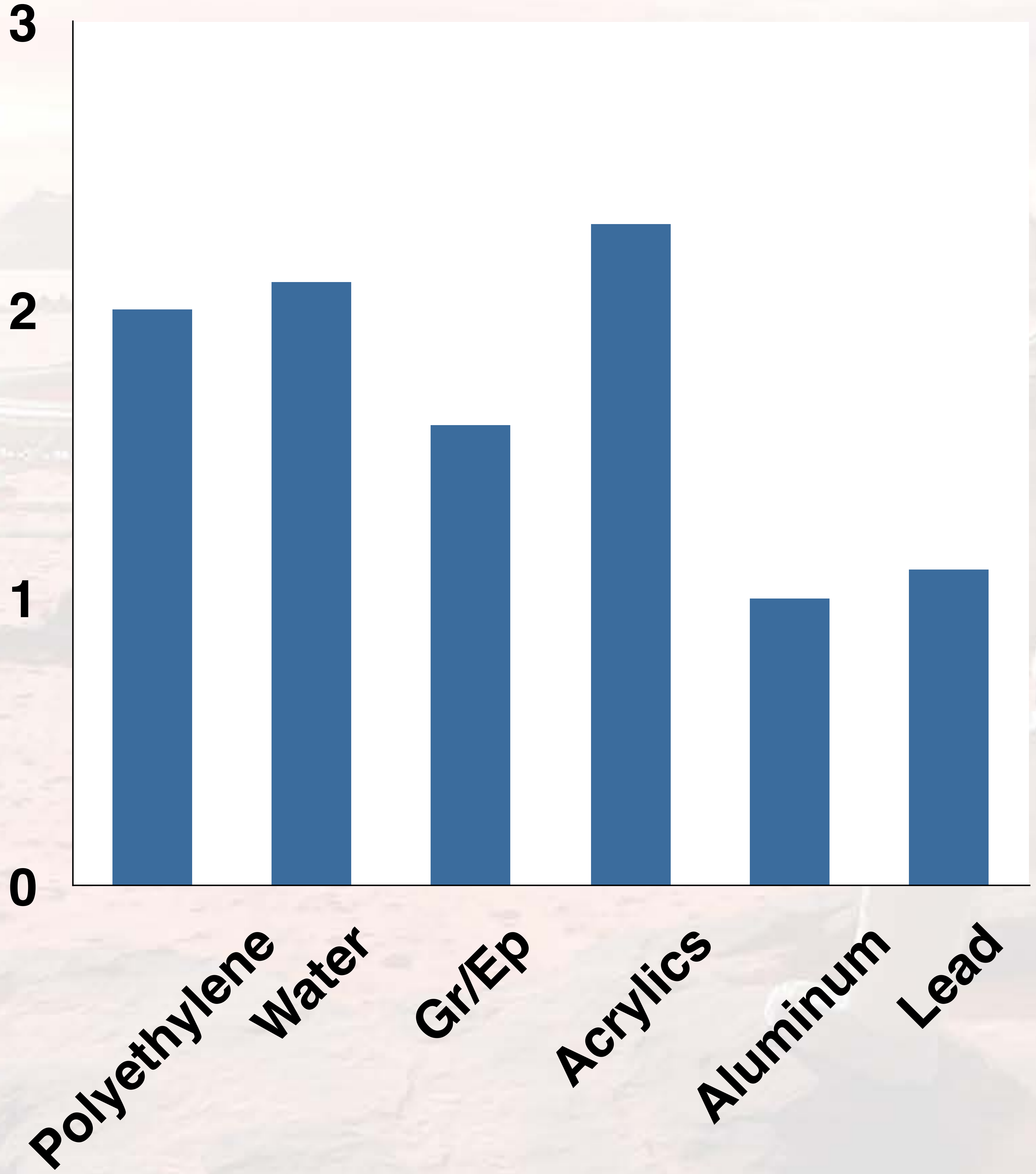


Francis Cucinotta, "What's New in Space Radiation Risk Assessments for Exploration" NASA Future In-Space Operations Telecon, May 18, 2011

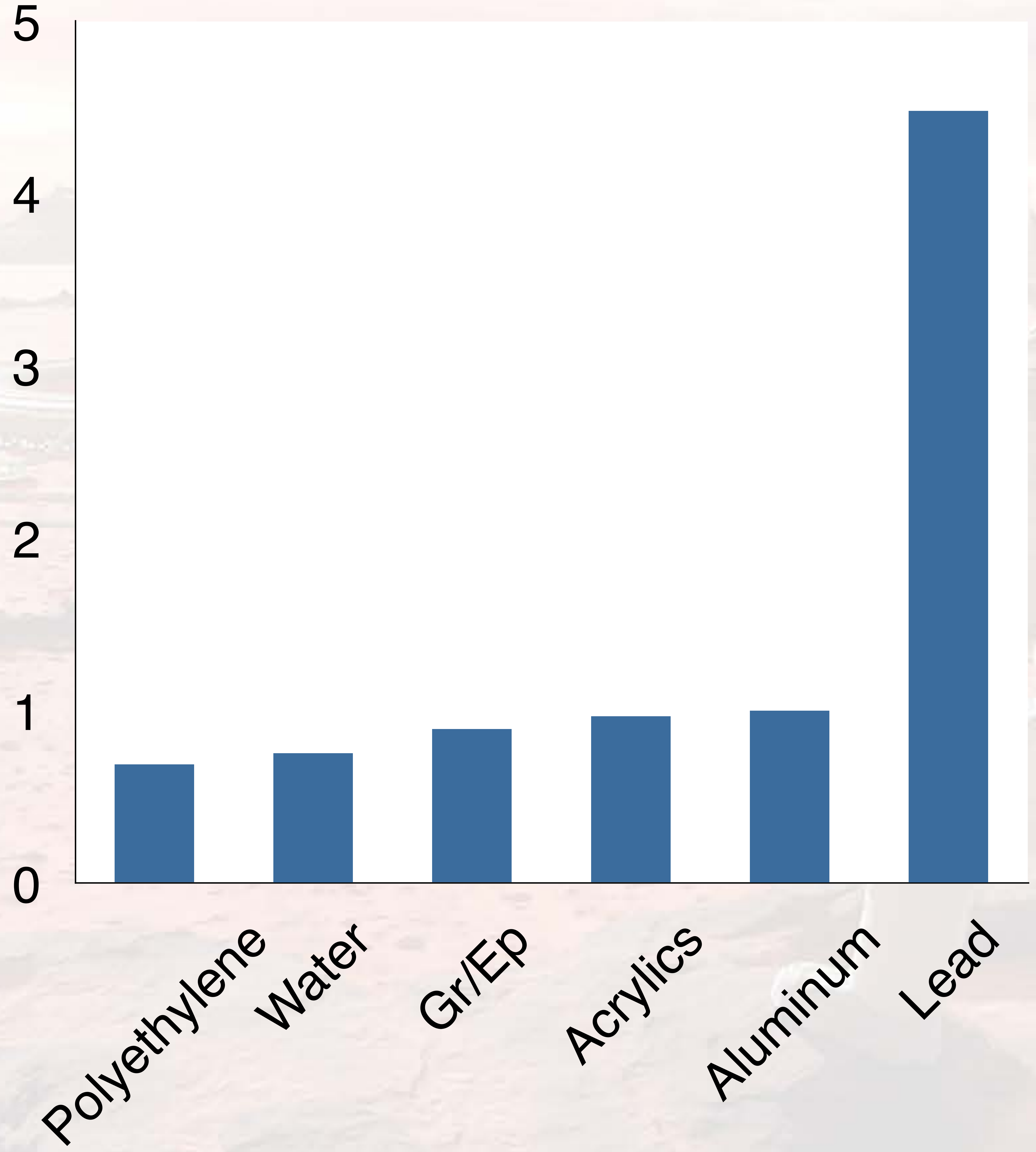
Density of Common Shielding Materials



Comparative Thickness of Shields (Al=1)



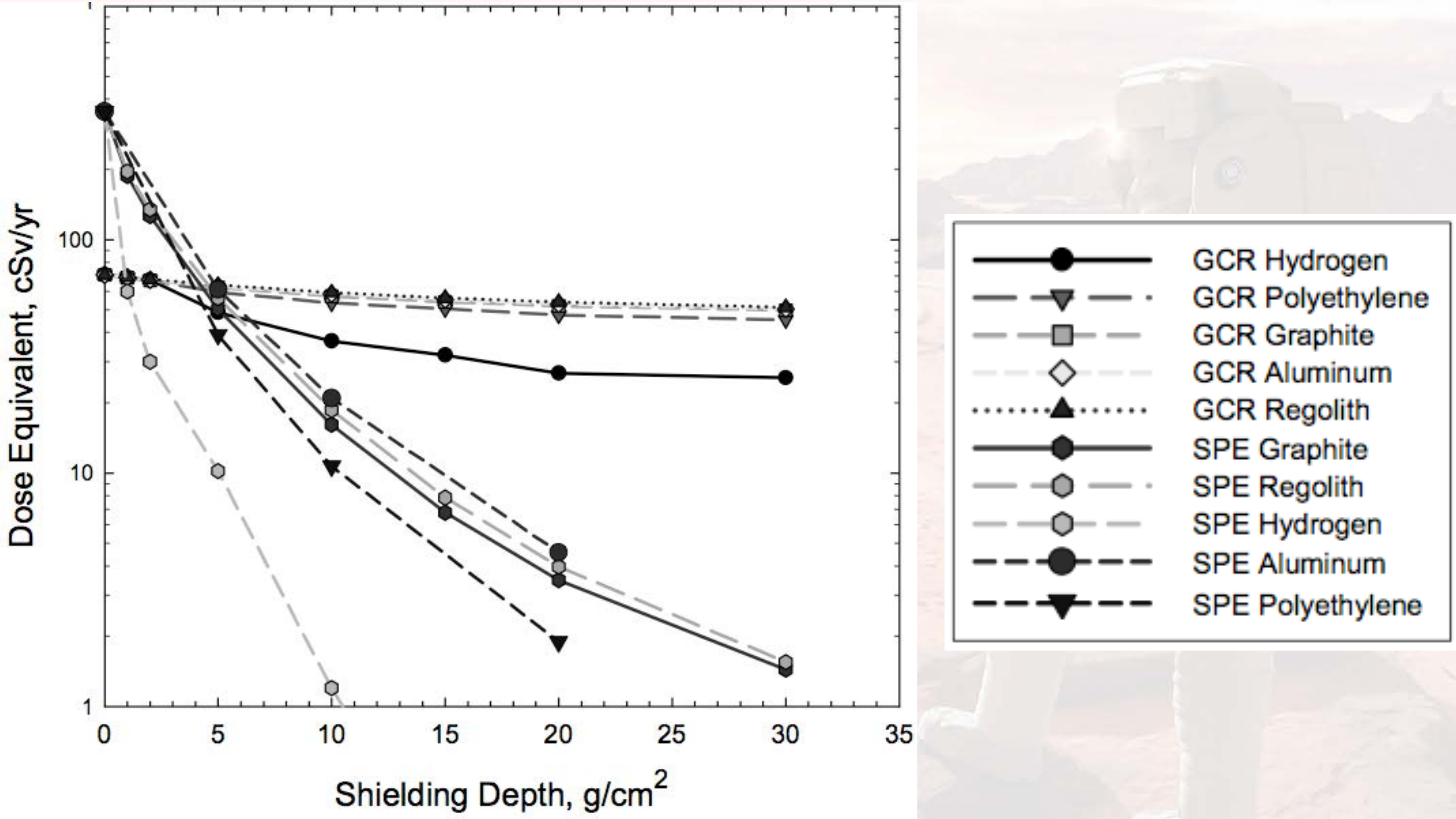
Comparative Mass for Shielding (Al=1)



Shielding Materials and GCR

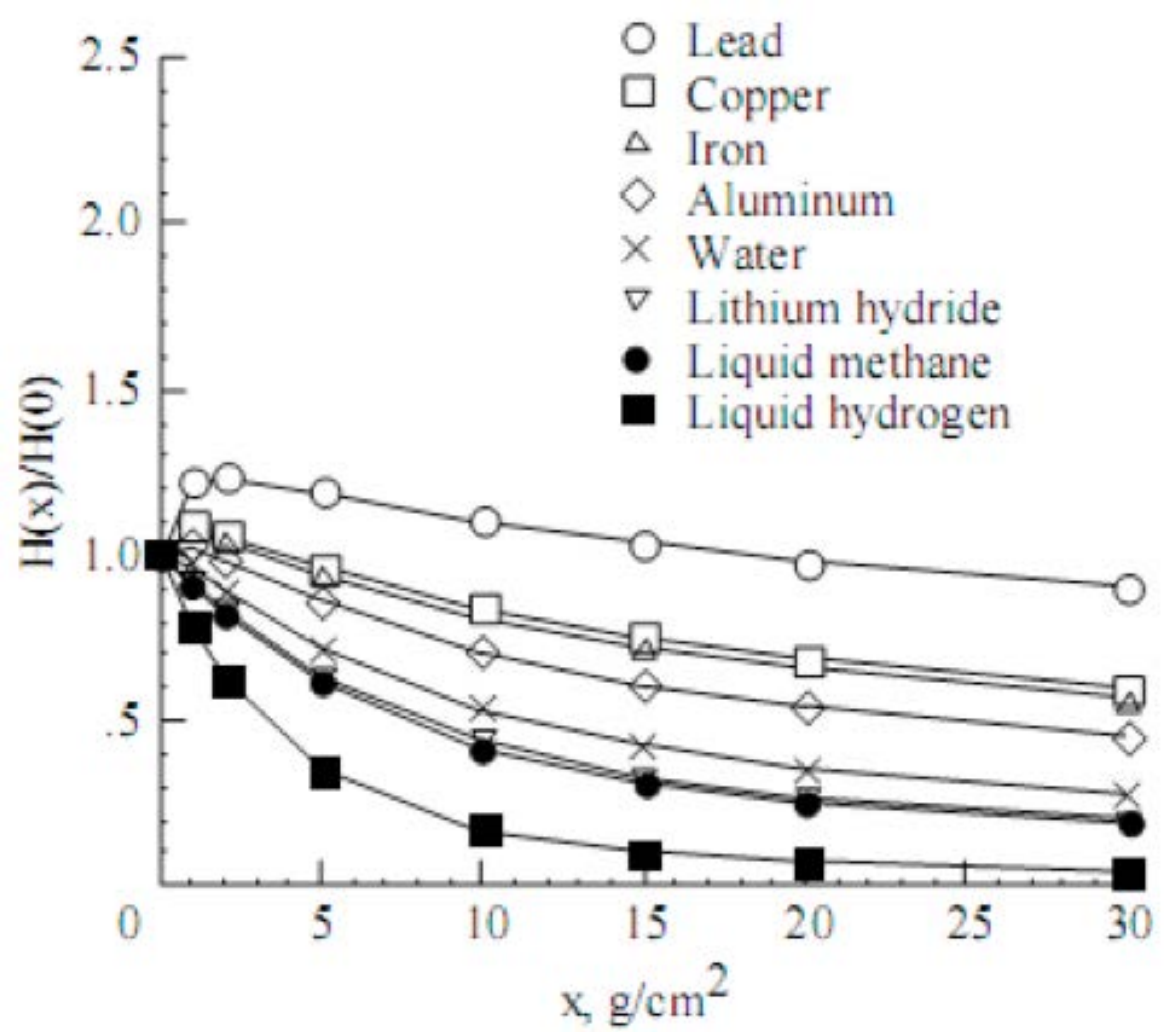
Material		E (Sv)	
		Solar Minimum	SPE + Solar Maximum
10 g/cm^2	Liquid H_2	0.40	0.19
	Liquid CH_4	0.50	0.30
	Polyethylene	0.52	0.33
	Water	0.53	0.35
	Epoxy	0.53	0.36
	Aluminum	0.57	0.43
20 g/cm^2	Liquid H_2	0.36	0.16
	Liquid CH_4	0.45	0.22
	Polyethylene	0.47	0.24
	Water	0.48	0.25
	Epoxy	0.49	0.26
	Aluminum	0.53	0.30
40 g/cm^2	Liquid H_2	0.31	0.15
	Liquid CH_4	0.43	0.21
	Polyethylene	0.46	0.23
	Water	0.46	0.23
	Epoxy	0.48	0.24
	Aluminum	0.51	0.26

Effective Dose Based on Shielding



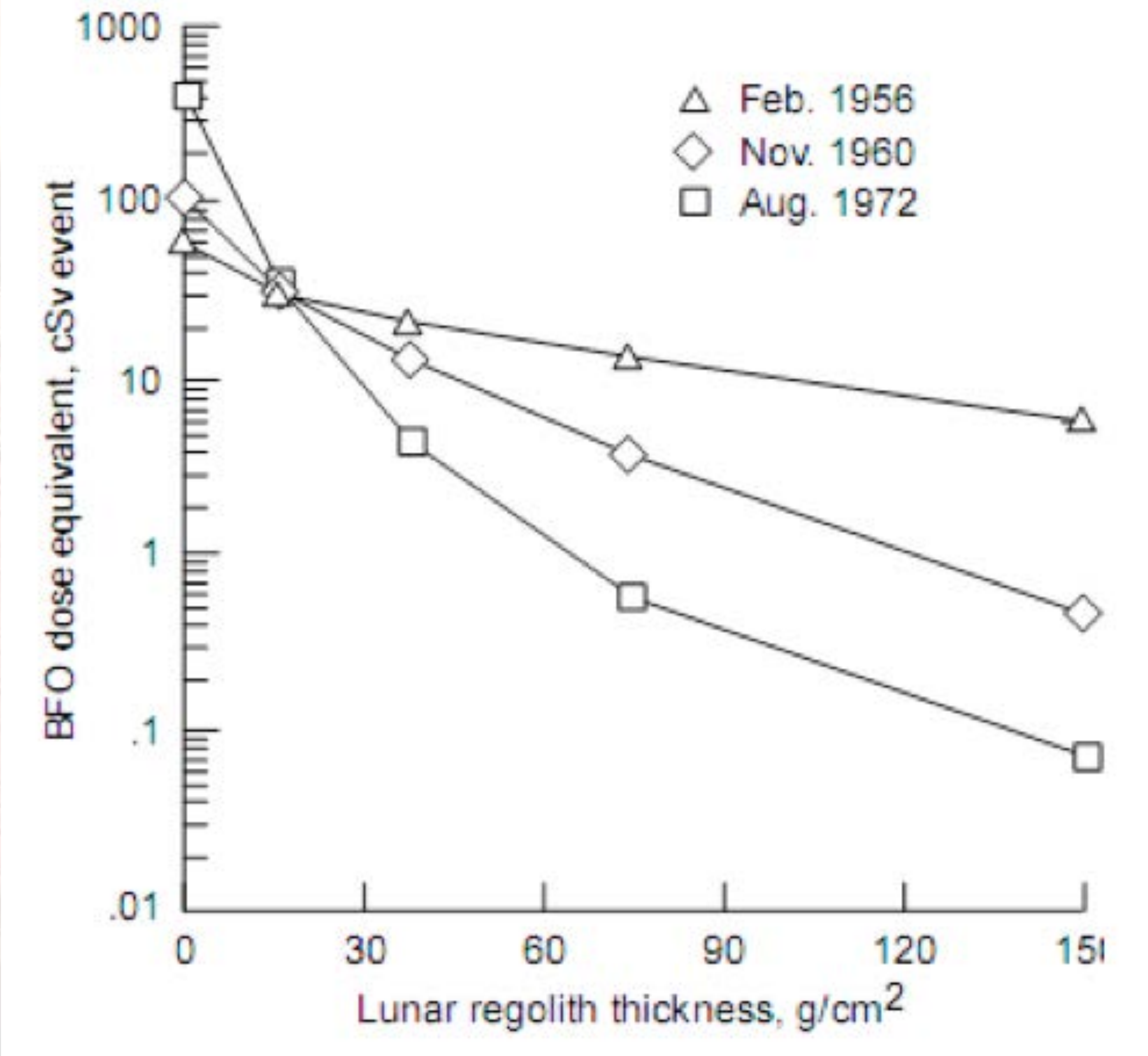
Francis A. Cucinotta, Myung-Hee Y. Kim, and Lei Ren, *Managing Lunar and Mars Mission Radiation Risks Part I: Cancer Risks, Uncertainties, and Shielding Effectiveness* NASA/TP-2005-213164, July, 2005

Shielding Materials Effect on GCR



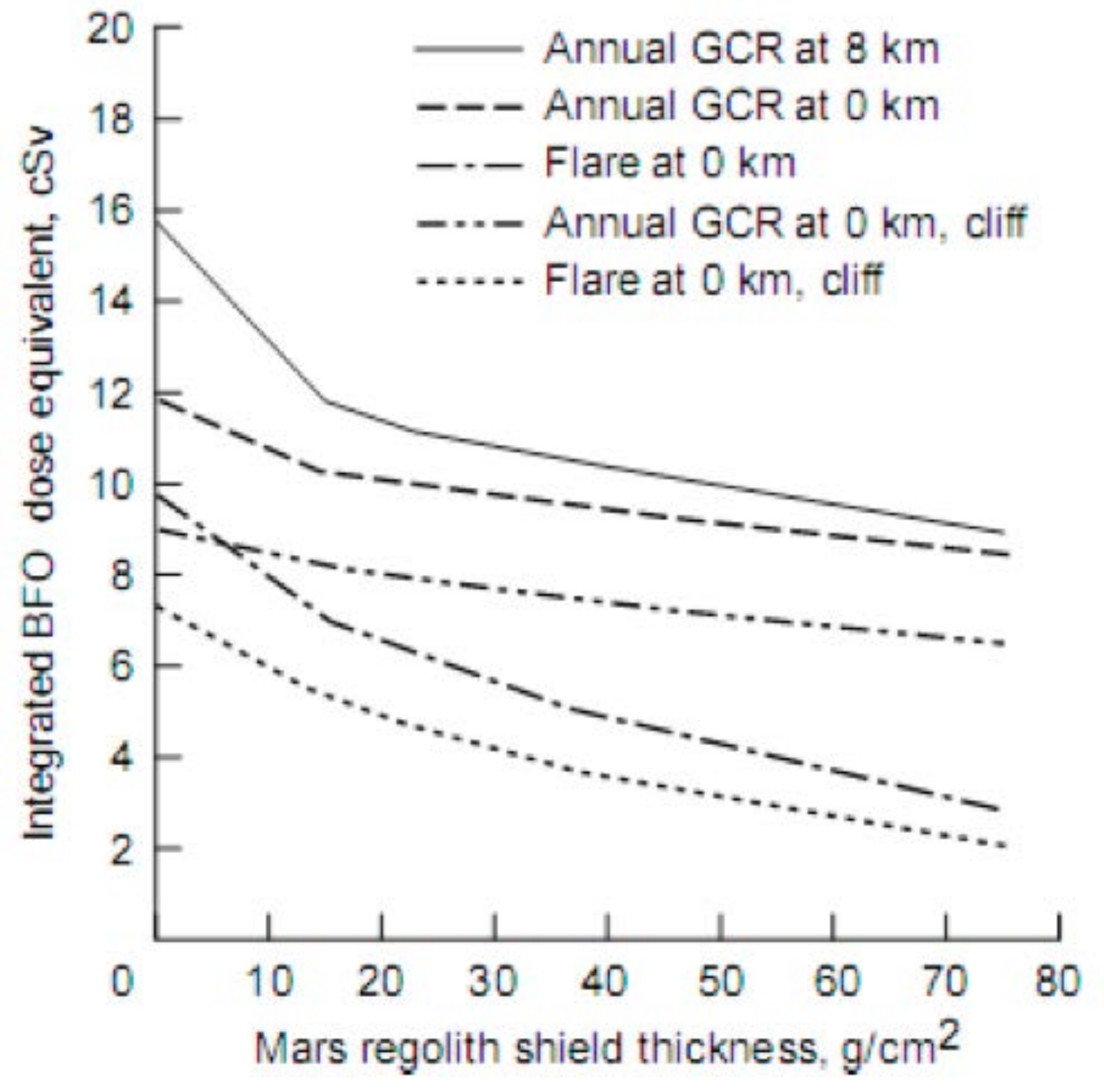
–, *Human Integration Design Handbook*, NASA SP-2010-3407, Jan. 2010

Lunar Regolith Shielding for SPE



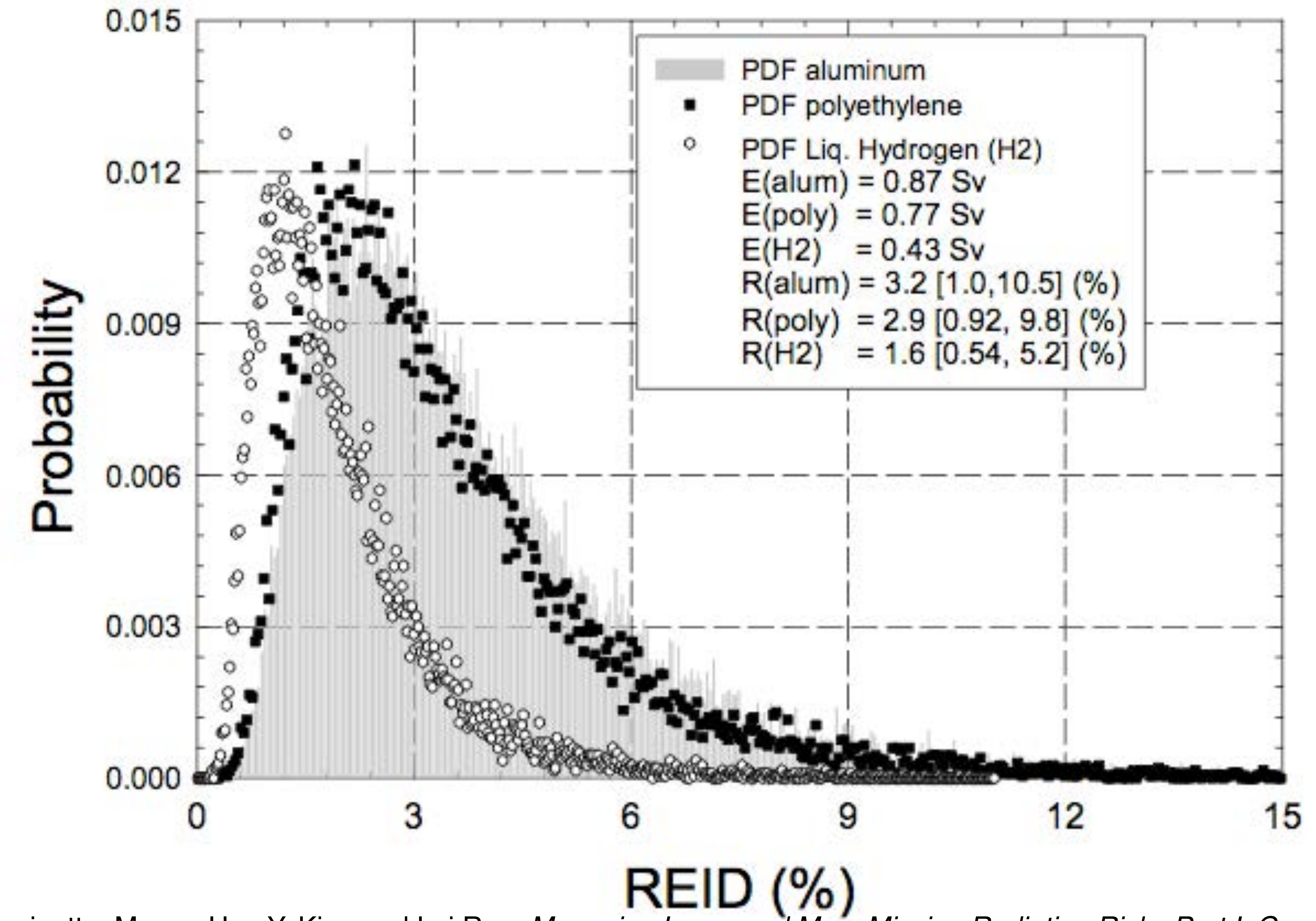
–, *Human Integration Design Handbook*, NASA SP-2010-3407, Jan. 2010

Mars Regolith Shielding Effectiveness



–, *Human Integration Design Handbook*, NASA SP-2010-3407, Jan. 2010

Radiation Exposure Induced Deaths



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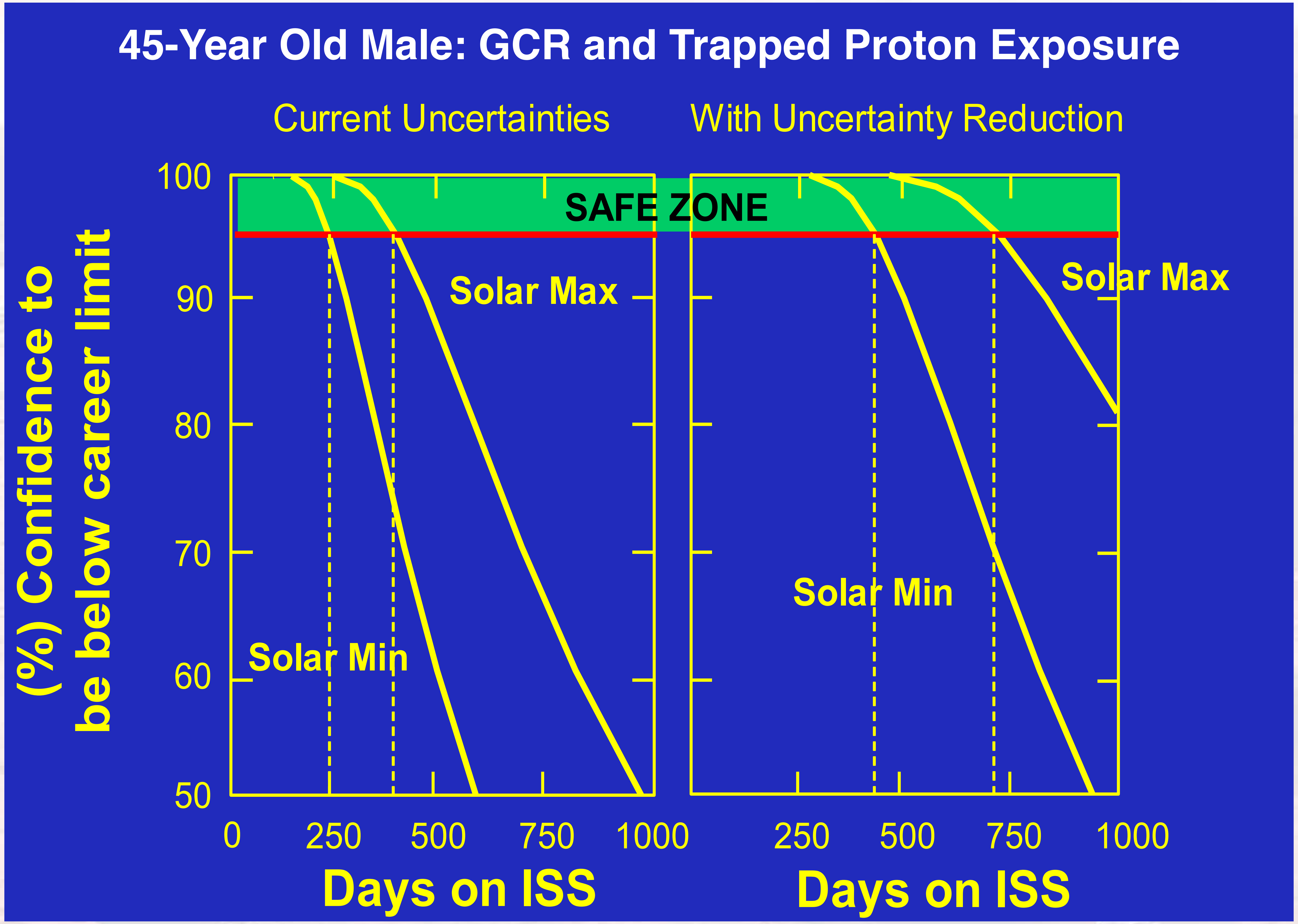
Deep Space Mortality Risks from GCRs

Number of Days in Deep Space At Solar Minimum at 20 gm/cm^2 shielding with a 95% or 90% confidence level to be below 3% or 6% REID (Avg US pop)

	3% Risk (REID)		6% Risk (REID)	
	95% CL	90% CL	95% CL	90% CL
Age, y	**Males**			
35	**140**	**184**	**290**	**361**
45	**150**	**196**	**311**	**392**
55	**169**	**219**	**349**	**439**
Age, y	**Females**			
35	**88**	**116**	**187**	**232**
45	**97**	**128**	**206**	**255**
55	**113**	**146**	**234**	**293**

SPE and GCR Shielding Effectiveness



Francis Cucinotta, "What's New in Space Radiation Risk Assessments for Exploration" NASA Future In-Space Operations Telecon, May 18, 2011

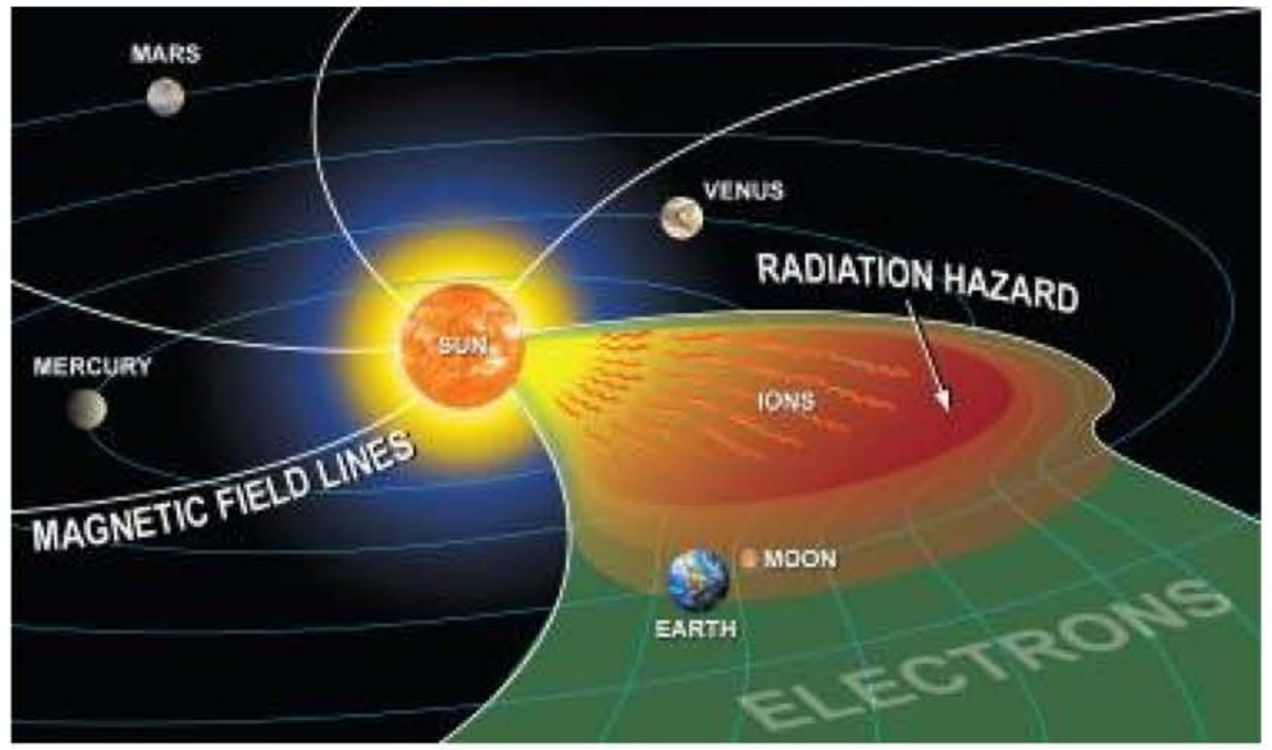
What's New in Space Radiation Research?

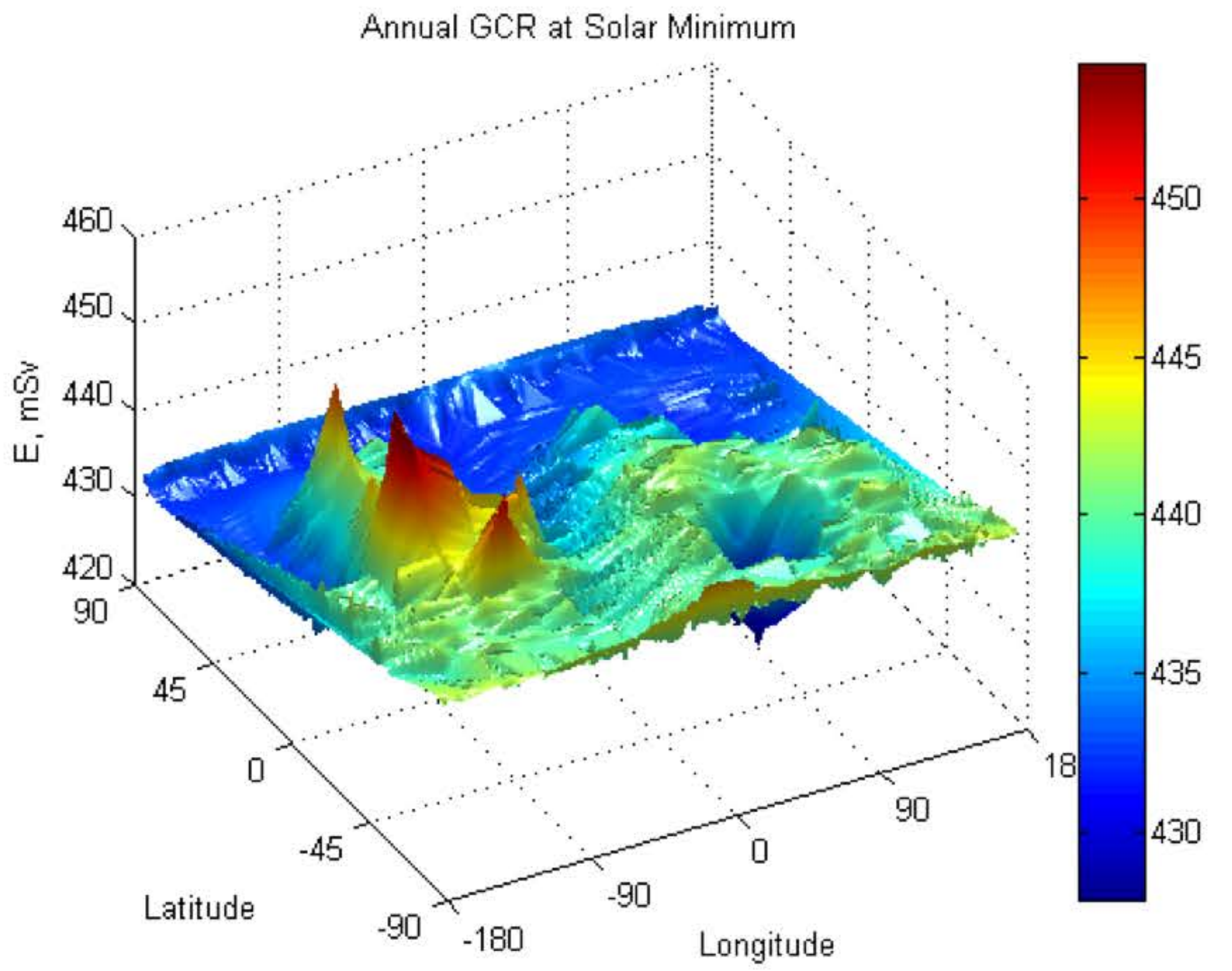
- New Epidemiology data suggests much weaker age dependence on radiation cancer risks
  - Number 1 Trade variable (Astronaut age) is negated
- Probabilistic risk assessments replace "rads and rem"
  - New Quality factors and uncertainty assessments
- Galactic cosmic rays (GCR) are much higher concern than Solar particle events
  - Shielding plays only a small role for GCR
- New health risks of concern from radiation
  - Heart disease, and Central nervous system (CNS) risks
- Risks estimated to be much smaller for "Never-smokers"

Francis Cucinotta, "What's New in Space Radiation Research for Exploration?" NASA FISO, May 18, 2011

NASA 2010 Cancer Projection Model

- NASA is developing new approaches to radiation risk assessment:
  - Probabilistic risk assessment framework
  - Tissue specific estimates
- Research focus is on uncertainty reduction
  - Smaller tolerances are needed as risk increases, with <50% uncertainty required for Mars mission
- NASA 2010 Model
  - Updates to Low LET Risk coefficients
  - Risks for Never-Smokers
  - Track Structure and Fluence based approach to radiation quality factors
    - Leukemia Q lower than Solid cancer Q





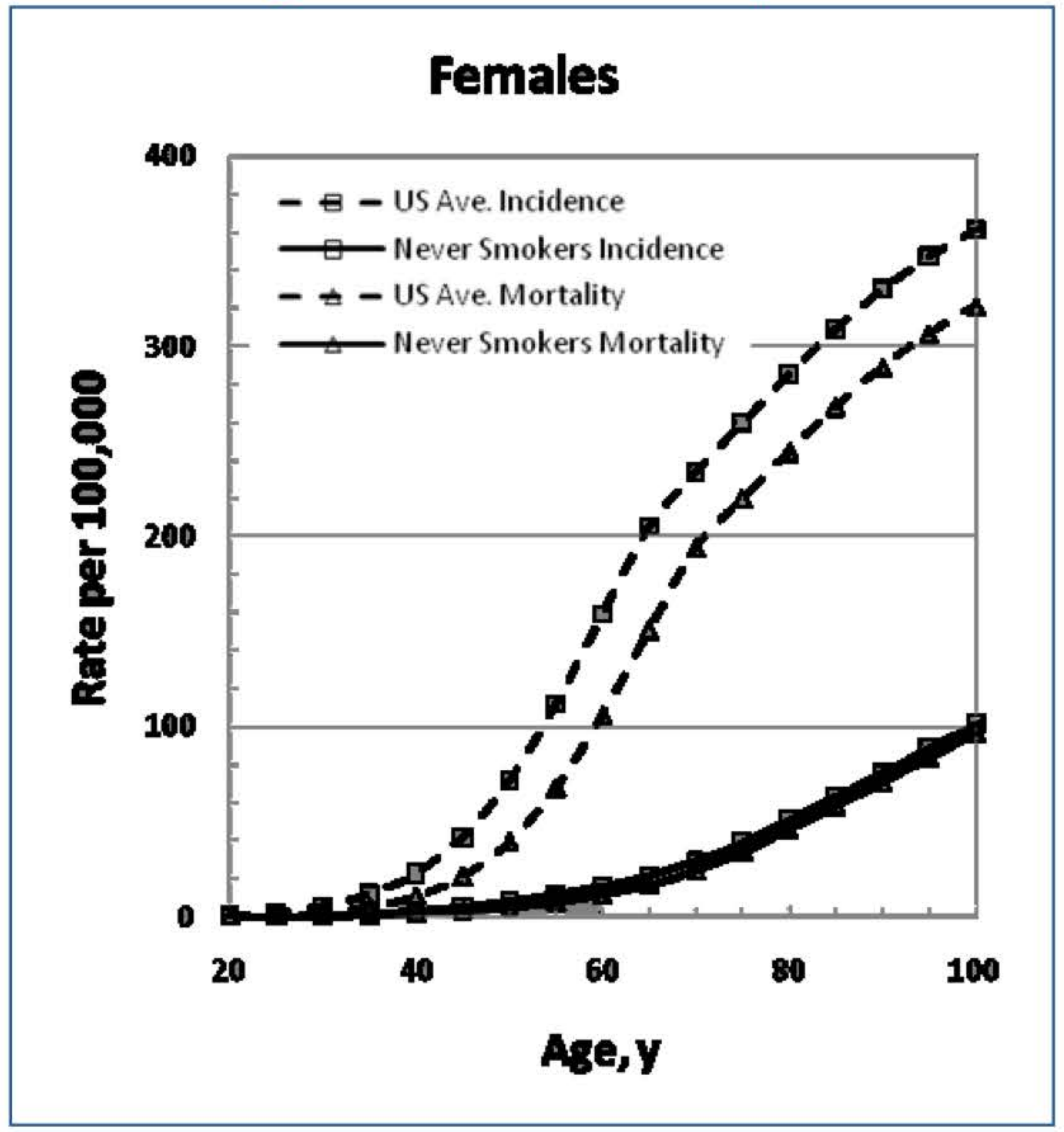
GCR doses on Mars

Francis Cucinotta, "What's New in Space Radiation Research for Exploration?" NASA FISO, May 18, 2011

Radiation Risks for Never-Smokers

- More than 90% of Astronauts are never-smokers and remainder are former smokers
- Smoking effects on Risk projections:
  - Epidemiology data confounded by possible radiation-smoking interactions, and errors documenting tobacco use
  - Average U.S. Population used by NCRP Reports 98 and 132
- NASA Model projects a 20 to 40-% risk reduction for never-smokers compared to U.S. Ave.
  - Larger decreases are possible if more were known on Risk Transfer models
  - Balance between Small Cell and Non-Small Cell Lung Cancer a critical question including high LET effects

Lung cancer in Unexposed



Thun et al., PLoS Med (2008)

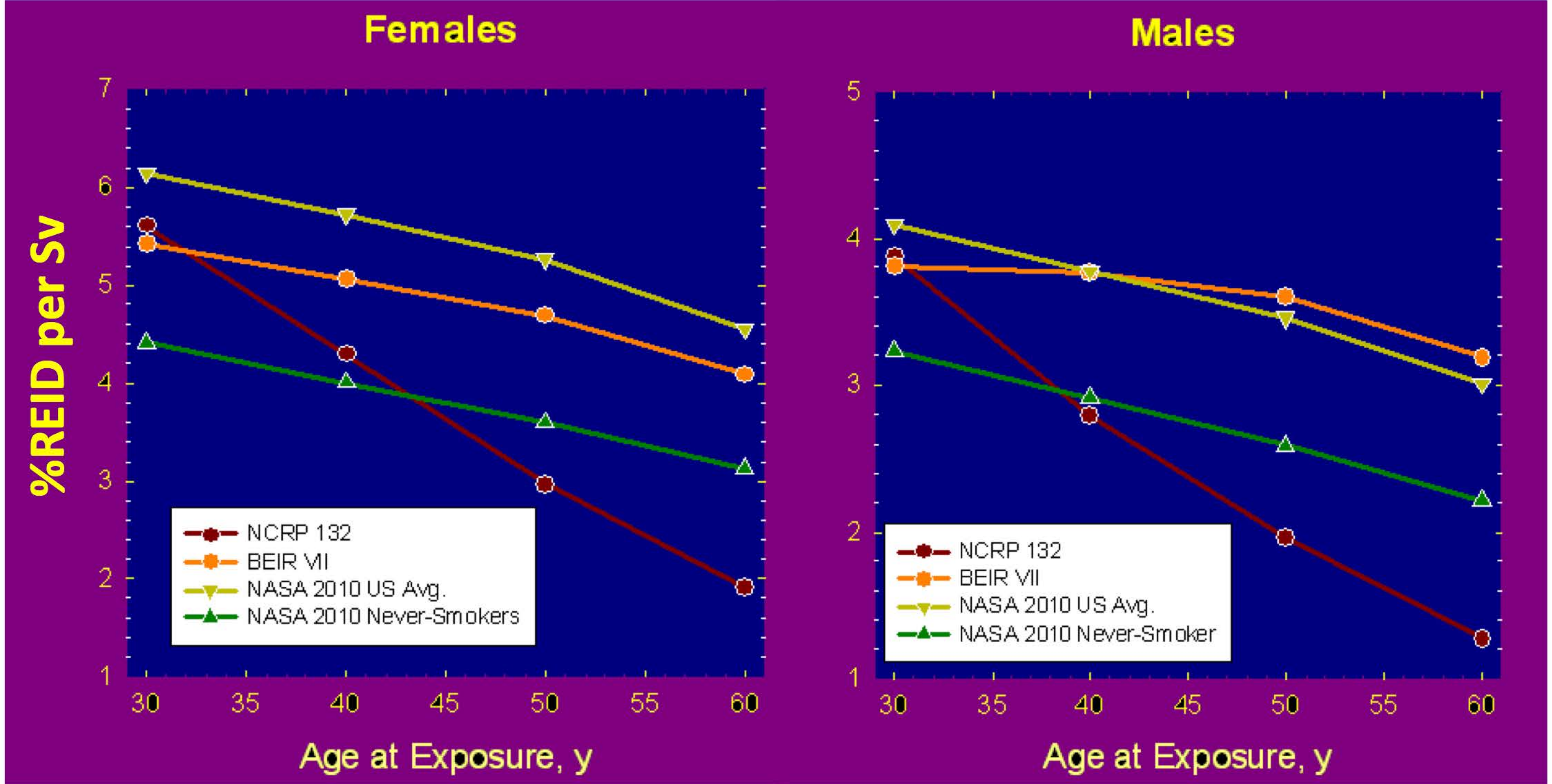
CDC Estimates of Smoking Attributable Cancers

	Relative Risk to Never-smokers (NS)			RR for NS to U.S. Avg
Males	**Current smokers**	**Former smokers**	**Never-smokers**	**RR(NS/U.S.)**
Esophagus	6.76	4.46	1	0.27
Stomach	1.96	1.47	1	0.71
Bladder	3.27	2.09	1	0.50
Oral Cavity	10.89	3.4	1	0.23
Lung*	23.26	8.7	1	0.11
Females	**Current smokers**	**Former smokers**	**Never-smokers**	**RR(NS/U.S.)**
Esophagus	7.75	2.79	1	0.35
Stomach	1.36	1.32	1	0.85
Bladder	2.22	1.89	1	0.65
Oral Cavity	5.08	2.29	1	0.46
Lung*	12.69	4.53	1	0.23

*Other cancers being considered Colon, leukemia, and liver

National Aeronautics and Space Administration

Point Estimates: Risk of Exposure Induced Death (REID)



Francis Cucinotta, "What's New in Space Radiation Research for Exploration?" NASA FISO, May 18, 2011

"Safe" days in Space: Uncertainties estimated using subjective PDFs propagated using Monte-Carlo techniques

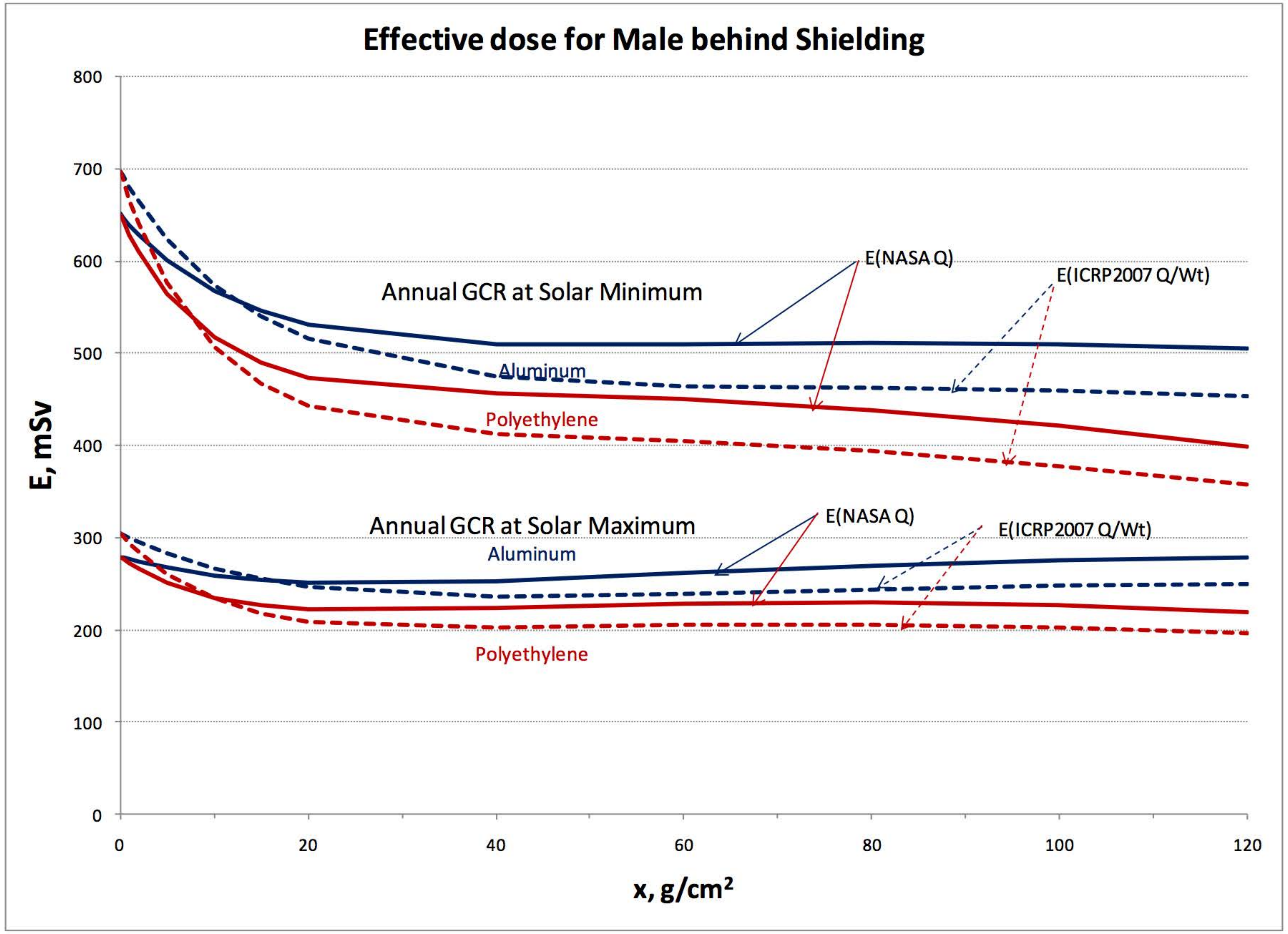
%REID predictions and 95% CI for never-smokers and average U.S. population for 1-year in deep space at solar minimum with 20 g/cm² aluminum shielding:

	%REID for Males and 95% CI			%REID for Females and 95% CI		
a_E, y	Avg. U.S.	Never-Smokers	Decrease (%)	Avg. U.S.	Never-Smokers	Decrease (%)
30	2.26 [0.76, 8.11]	1.79 [0.60, 6.42]	21	3.58 [1.15, 12.9]	2.52 [0.81, 9.06]	30
40	2.10 [0.71, 7.33]	1.63 [0.55, 5.69]	22	3.23 [1.03, 11.5]	2.18 [0.70, 7.66]	33
50	1.93 [0.65, 6.75]	1.46 [0.49, 5.11]	24	2.89 [0.88, 10.2]	1.89 [0.60, 6.70]	34

Maximum Days in Deep Space with 95% Confidence to be below Limits (alternative quality factor errors in parenthesis):

a_E, y	NASA 2005	NASA 2010 Avg. U.S.	NASA 2010 Never-Smokers
		Males	
35	**158**	**140 (186)**	**180 (239)**
45	**207**	**150 (200)**	**198 (263)**
55	**302**	**169 (218)**	**229 (297)**
		Females	
35	**129**	**88 (120)**	**130 (172)**
45	**173**	**97 (129)**	**150 (196)**
55	**259**	**113 (149)**	**177 (231)**

Solar Min and Max Comparison with Proposed NASA Quality Factor (Q) and Tissue Weights (Wt) vs ICRP Quality Factor Definition



Francis Cucinotta, "What's New in Space Radiation Research for Exploration?" NASA FISO, May 18, 2011

Solar Particle Event (SPE) Risks

Research studies show that risks of acute death from large SPEs has been over-estimated in the past:

- Proper evaluation of dose-rates, tissue shielding, and proton biological effectiveness show risk is very small

SPE risk remain important for lunar EVA

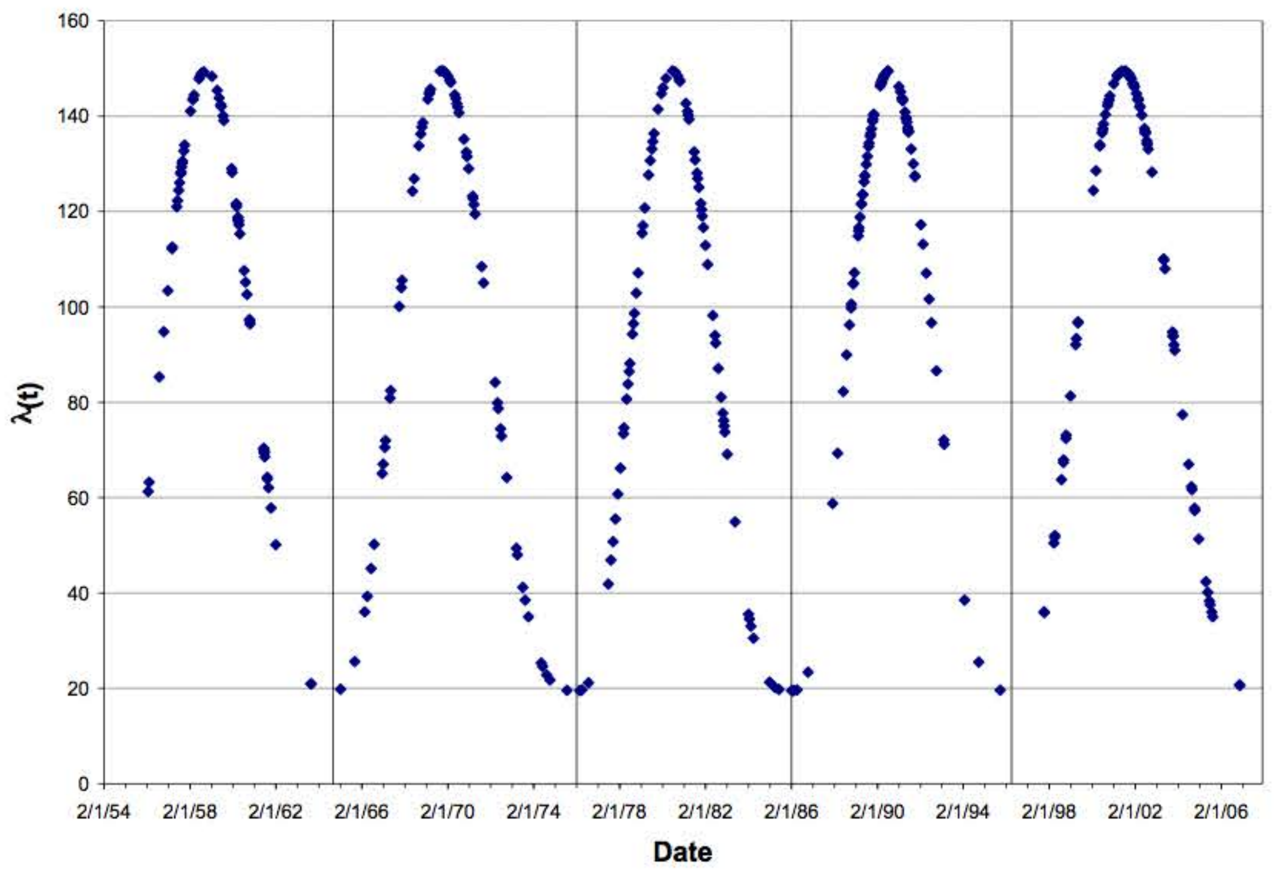
- Radiation sickness if unprotected > 2 hour EVA
- Cancer risk is priority for both EVA and IVA

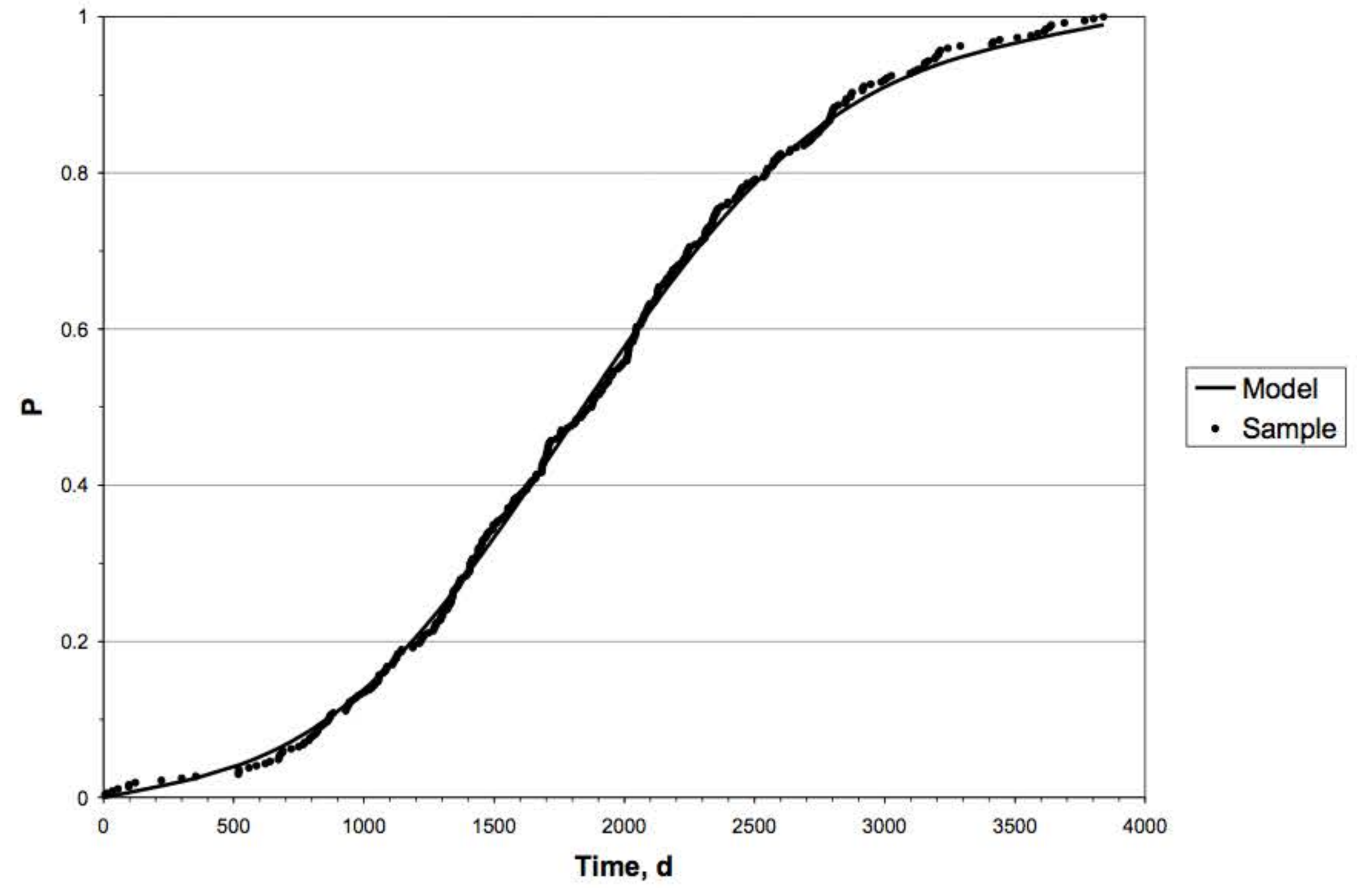
Proper resource management through research:

- Probabilistic risk assessment tools for Lunar and Mars Architecture studies
- Optimize shielding requirements by improved understanding of proton radiobiology & shielding design tools
- ESMD and SMD collaborations on research to improve SPE alert, monitoring and forecasting
- Biological countermeasure development for proton cancer, and Acute radiation syndromes (if needed)

SPE Probabilistic Risk Assessment

- Using detailed data base of all SPE's in space age (1955-current) and historical data on Ice-core nitrate samples (15th-century to current), SRP has developed a probabilistic model of SPE occurrence, size, and frequency
  - Hazard rate model using Survival analysis
  - Non-uniform Poisson process provides high quality fit of all SPE data
- Probabilistic model supports shielding design and resource management goals for Exploration missions
- Department of Defense model estimates various acute risks





Francis Cucinotta, "What's New in Space Radiation Research for Exploration?" NASA FISO, May 18, 2011

Acceptable Risk Levels for Exploration Missions

- The NASA Standard of 3% Risk of Exposure Induced Death was set in 1989 by NASA Administrator with OSHA Concurrence under Code of Federal Regulation (CFR 1960)
- NASA has set an identical acceptable risk level for Exploration missions under the OCHMO's 2006 Permissible Exposure Limits (PEL)
  - OSHA concurrences on NASA Health policy in Spaceflight dropped in 2004 after discussion with OCHMO
- The NCRP recommendation of 3% Limit based on 3 rationales:
  - Comparison of fatality rates in less-safe Industries made in 1989
  - Comparison to risk limits for ground-based workers
  - Recognition of other spaceflight risks
- Fatality rates in less-safe industries have improved more than 2-fold since 1989 and therefore no longer valid basis; however other 2 rationale from NCRP in 1989 are still valid

Acceptable Levels of Risk - continued

- A discussion of higher or lower Acceptable Risk Levels would consider
  - Over arching Ethical and Safety standards at NASA and in the U.S.
  - Benefits to Human-kind from Exploration missions
  - Emerging information on possible radiation mortality risks from non-cancer diseases, notably Heart (Stroke and Coronary Heart Disease) and Central Nervous System risks
  - The resulting burden for morbidity risks including cancer, cataracts, aging, and other diseases that entail pain, suffering, and economic impacts
    - Radiation cancer incidence probability approximately Two times higher than cancer death probability
  - Improvements in other areas of safety at NASA, other government agencies and work places since 1989
  - Balance between other space flight risks and space radiation risks
    - NCRP Recommendation is the high risk nature of space missions precludes allowing an overly large radiation risk to Astronauts
  - Impacts on finding solutions through research programs and mission design architectures that result from Acceptable Risk Standards

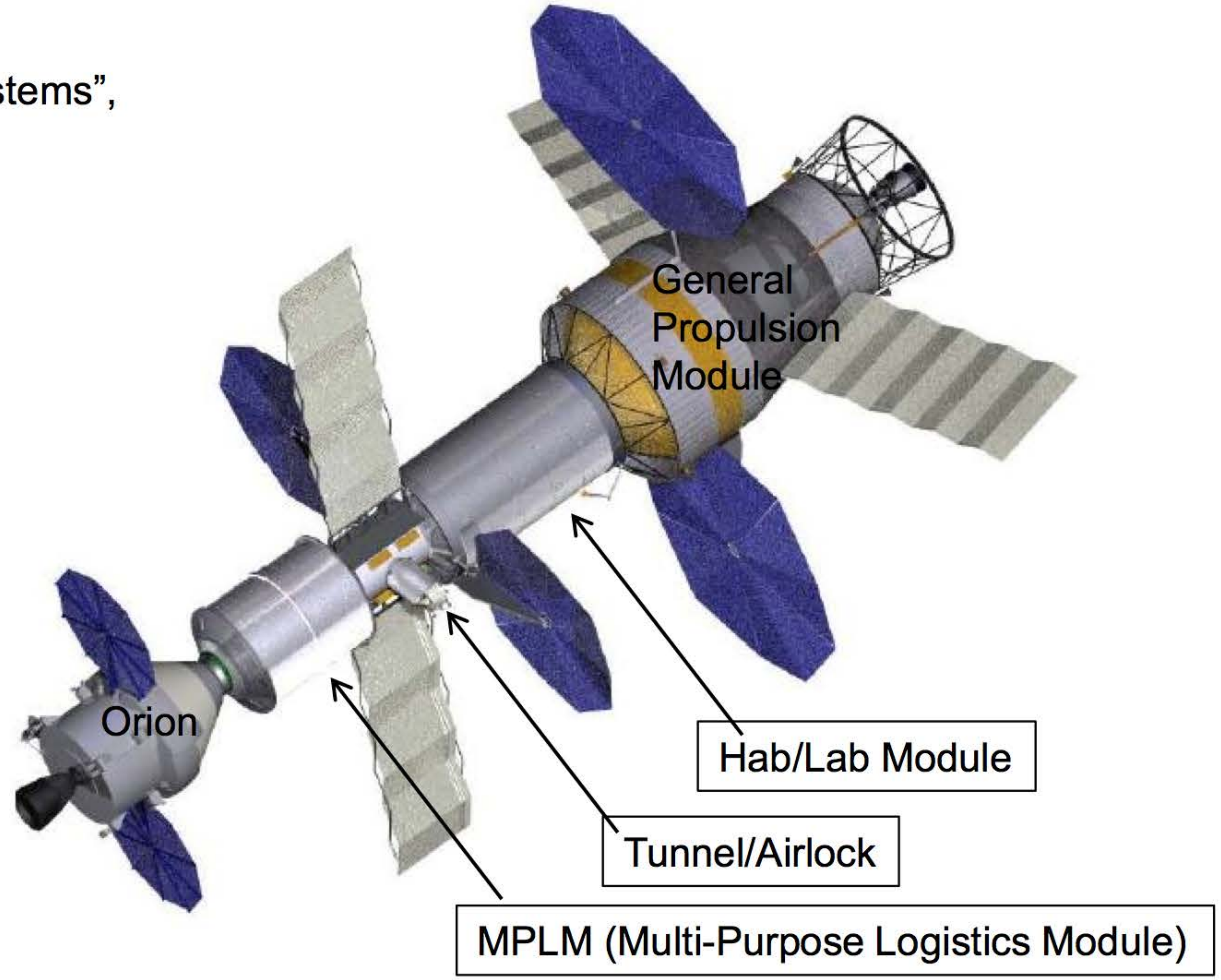
*MSFC study/ ISS-Derived Deep Space Facility

500-Day

*Reference chart from "DSH Configurations based on ISS Systems", D. Smitherman, et al, 12/2011.

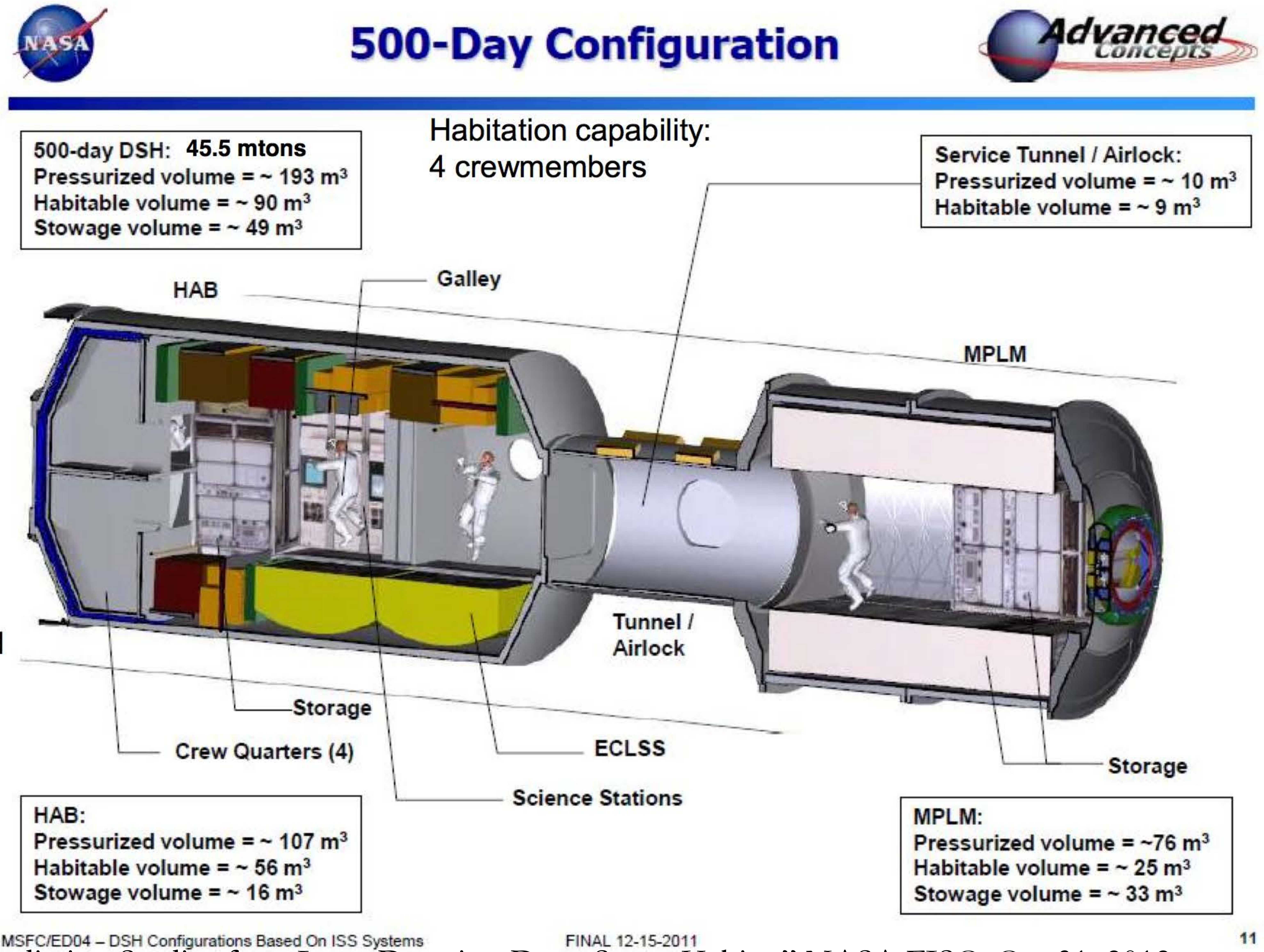
This transit habitat consists of three basic elements:

1. an ISS Hab/Lab Module
2. a Tunnel/Airlock
3. an ISS MPLM



Lora Bailey, "Radiation Studies for a Long Duration Deep Space Habitat" NASA FISO, Oct 31, 2012

*MSFC study/ ISS-Derived Deep Space Facility

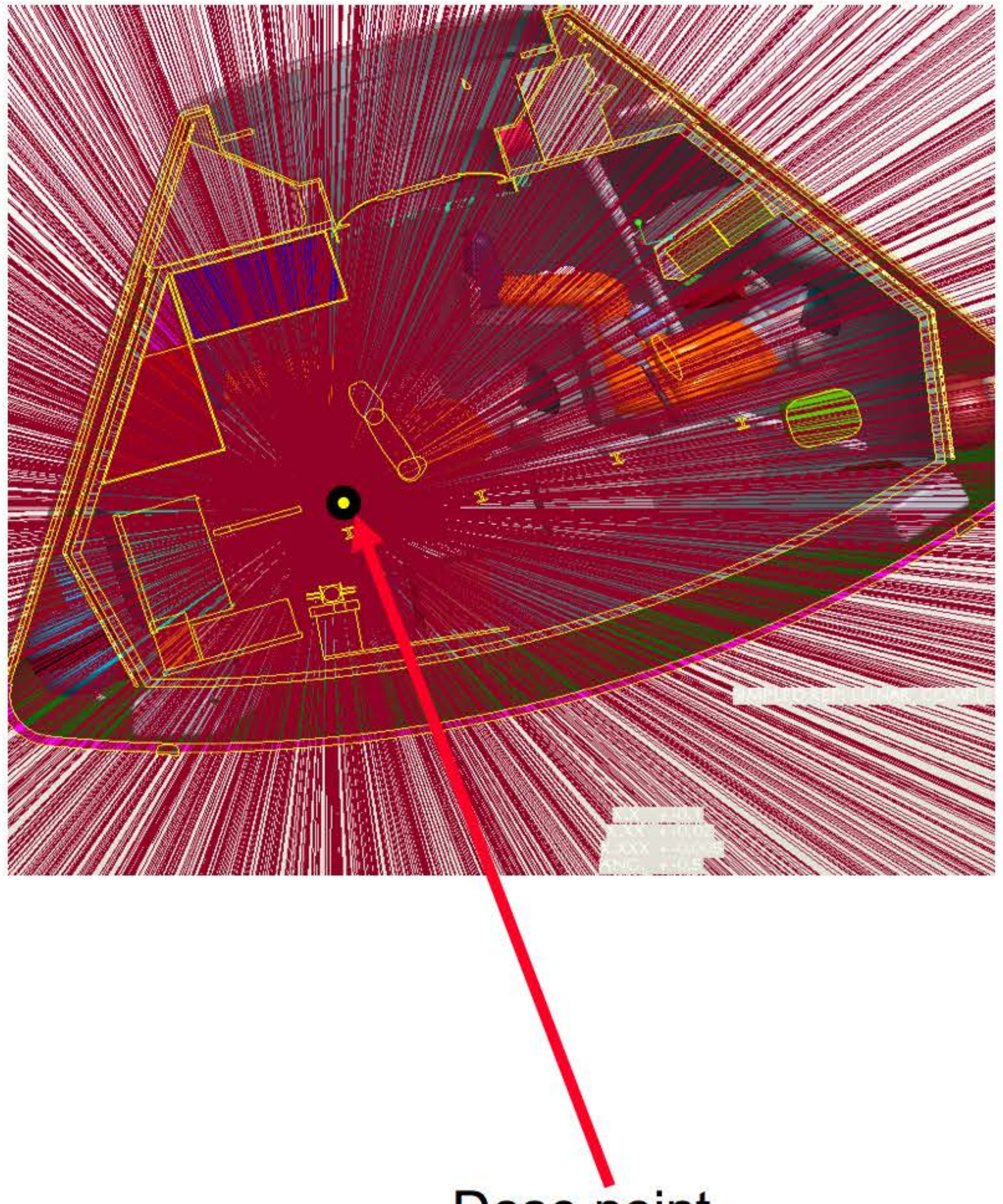


*Reference chart from "DSH Configurations based on ISS Systems", D. Smitherman, et al, 12/2011.

Shielding Assessment Technology
Software tool (*Pro/Engineer + Fishbowl tool kit*)

❑ Ray Tracing technology

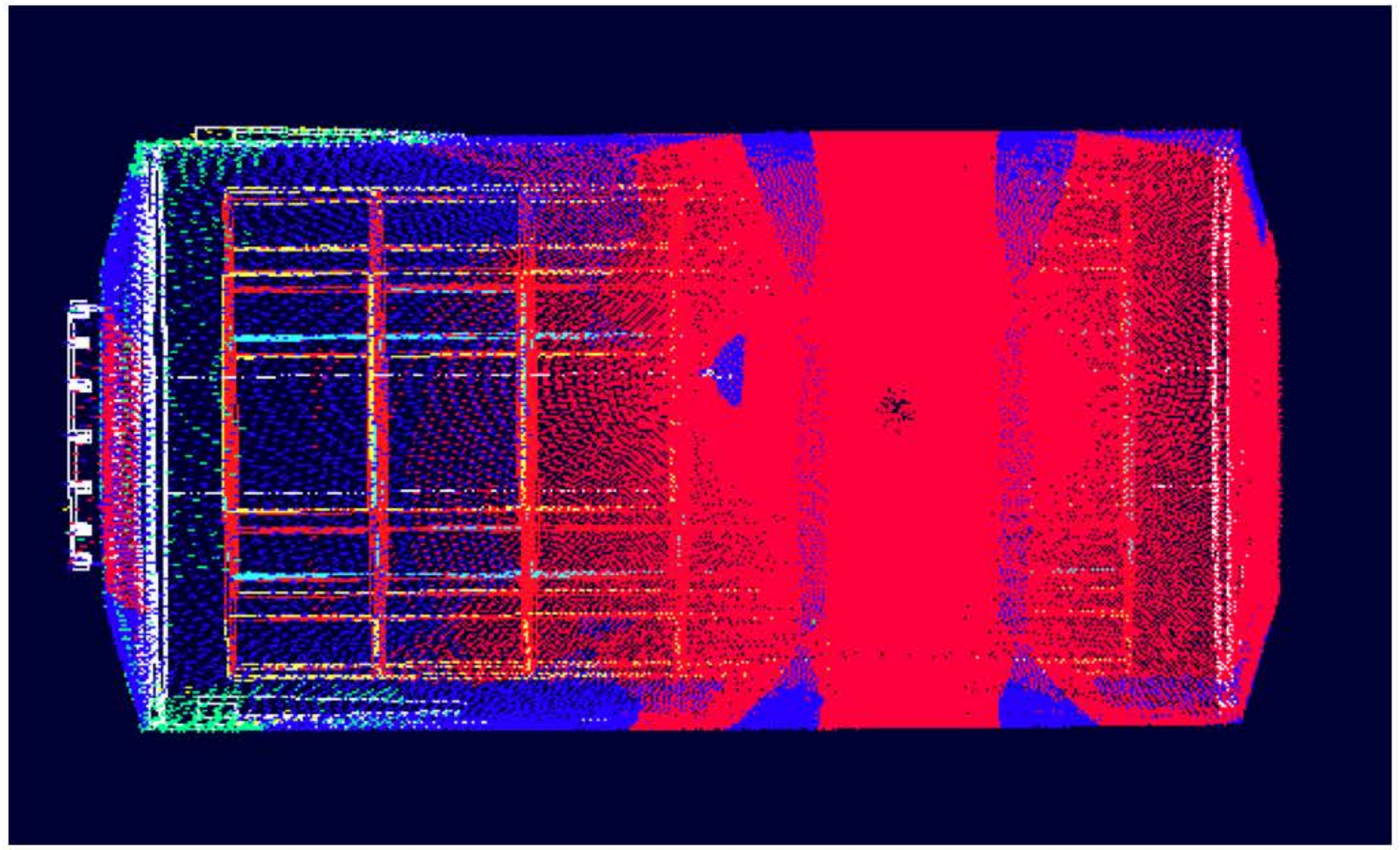
- Evenly distributed rays (up to 1 million rays) are created to start from dose point and end outside the vehicle.
- Each Ray records distance and respective density of the parts it passes
- Areal mass density is calculated.
- Areal mass density is used in transport code that evaluates particle flux at dose point.

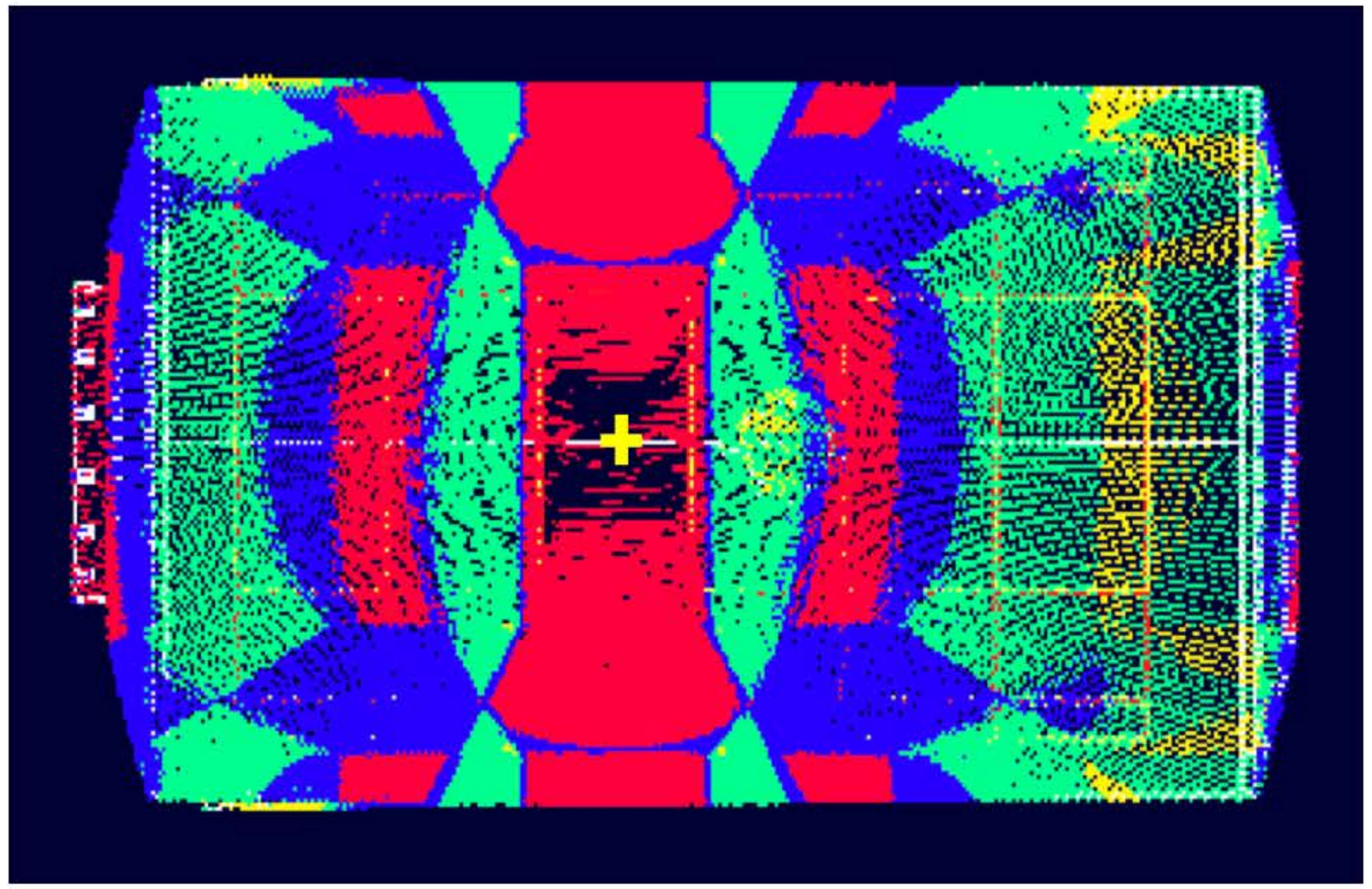


Lora Bailey, "Radiation Studies for a Long Duration Deep Space Habitat" NASA FISO, Oct 31, 2012

Hot Spots Detection Capabilities

Single dose point Color Coding



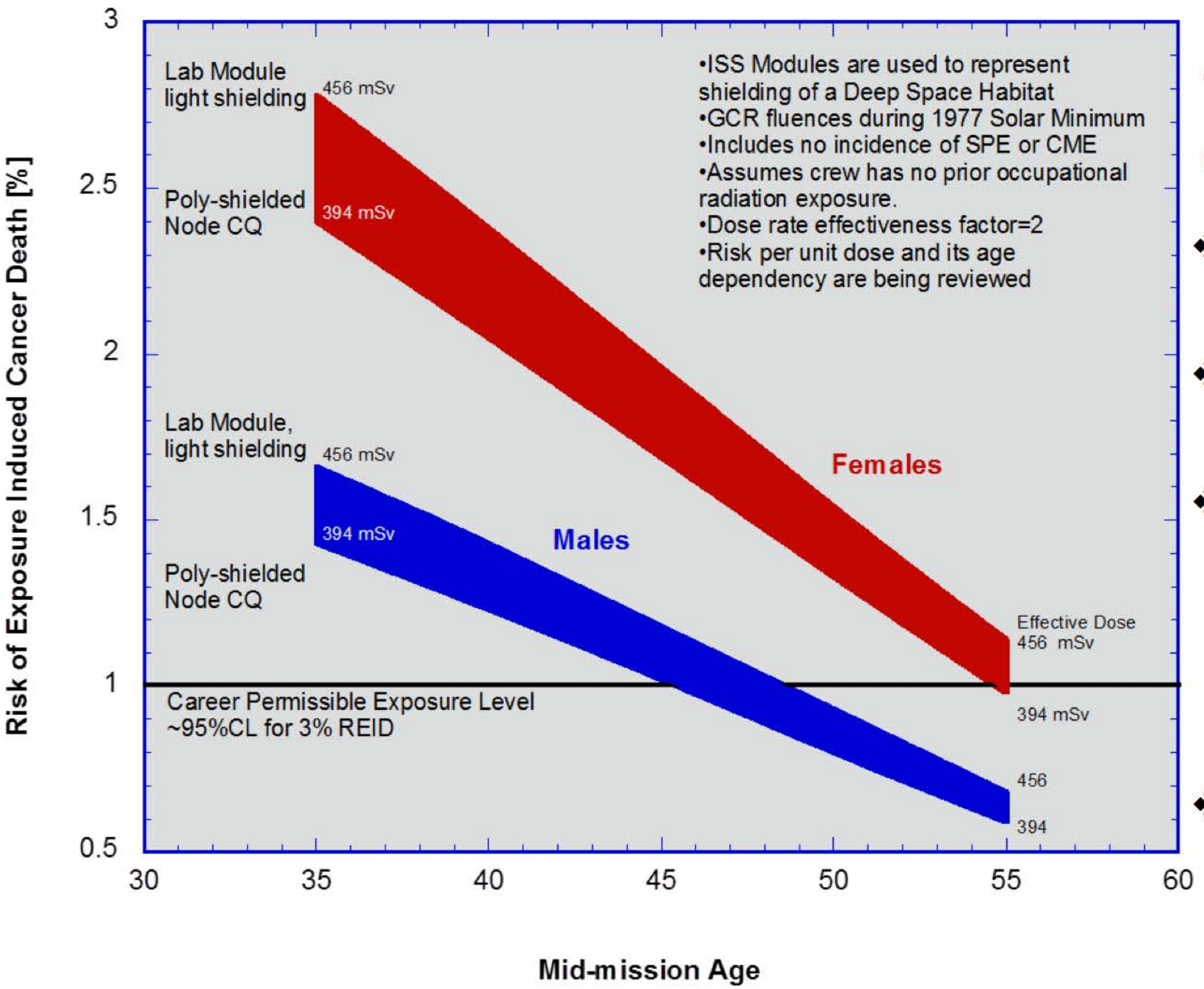


Every ray is color coded according to the areal density value-Shielding- it provides.

Only one dose point at a time-multiple colors

Risk of Exposure-Induced Death

*Risk of Exposure Induced Death (REID)
from Galactic Cosmic Radiation
for 365 day Mission at Earth L1 during Solar Minimum Activity



*Analysis Reference: Janet Barzilla charts, 04/30/2012, Pre-Decisional

For illustration purposes only, not representative of formal exploration limits

Notionally, this suggests that for a typical ISS structure exposure to 1 year at EML1:

- **Males about 47 years old or older are in range**
- **Females about 57 years old or older are in range**
- **Recall: design target GCR exposure of 150 mSv Effective Dose --- these dose values are 2 – 3 times higher**
  - Far away from arriving at 150 mSv
- **Multiply these doses by 500+ days divided by 365 days for a short trip to Mars → these radiation values are a "broke" for Mars/NEA space travel meeting the 3%REID at 95%CL at solar minimum levels**

Lora Bailey/10/31/2012

Lora Bailey, "Radiation Studies for a Long Duration Deep Space Habitat" NASA FISO, Oct 31, 2012

* Physical thickness corresponding to areal densities

Areal density g/cm^2	Aluminum Density = 2.7 g/cm^3	Polyethylene or Water Density = 1.0 g/cm^3	Liquid Hydrogen Density = 0.07 g/cm^3 Boiling point = 20.28^o K
1000	370 cm (146 in)	1,000 cm (394 in)	14, 285 cm (5624 in)
500	185 cm (72.8 in)	500 cm (197 in)	7,142 cm (2812 in)
100	37 cm (14.5 in)	100 cm (39.4 in)	1, 428 cm (562 in)
50	19 cm (7.5 in)	50 cm (20 in)	714 cm (281 in)
10	3.7 cm (1.5 in)	10 cm (4 in)	142 cm (56 in)

Thickness in cm = (areal density in g/cm^2)/(density in g/cm^3)

*Reference: Dr. S. Koontz charts, 01/31/2012

New Estimates of Radiations Risks are Favorable for Mars Exploration: However Major Scientific Questions Remain Unanswered

Francis A. Cucinotta
University of Nevada, Las Vegas NV, USA

UNLV UNIVERSITY OF NEVADA LAS VEGAS

Future In-Space Operations (FISO) colloquium (July 13, 2016)

Acknowledgements

- Funding: University of Nevada, Las Vegas
- UNLV: Murat Alp, Elliedonna Cacao

Outline

- Introduction
- Radiation Limits for Astronauts
- Cancer Risk Estimates for Deep Space
- Unanswered Science Questions in Cancer Risks
- Conclusions
- Backup Material on Space Environments and Shielding

Introduction to Space Radiation and Exploration

Space radiation is a major challenge to exploration:

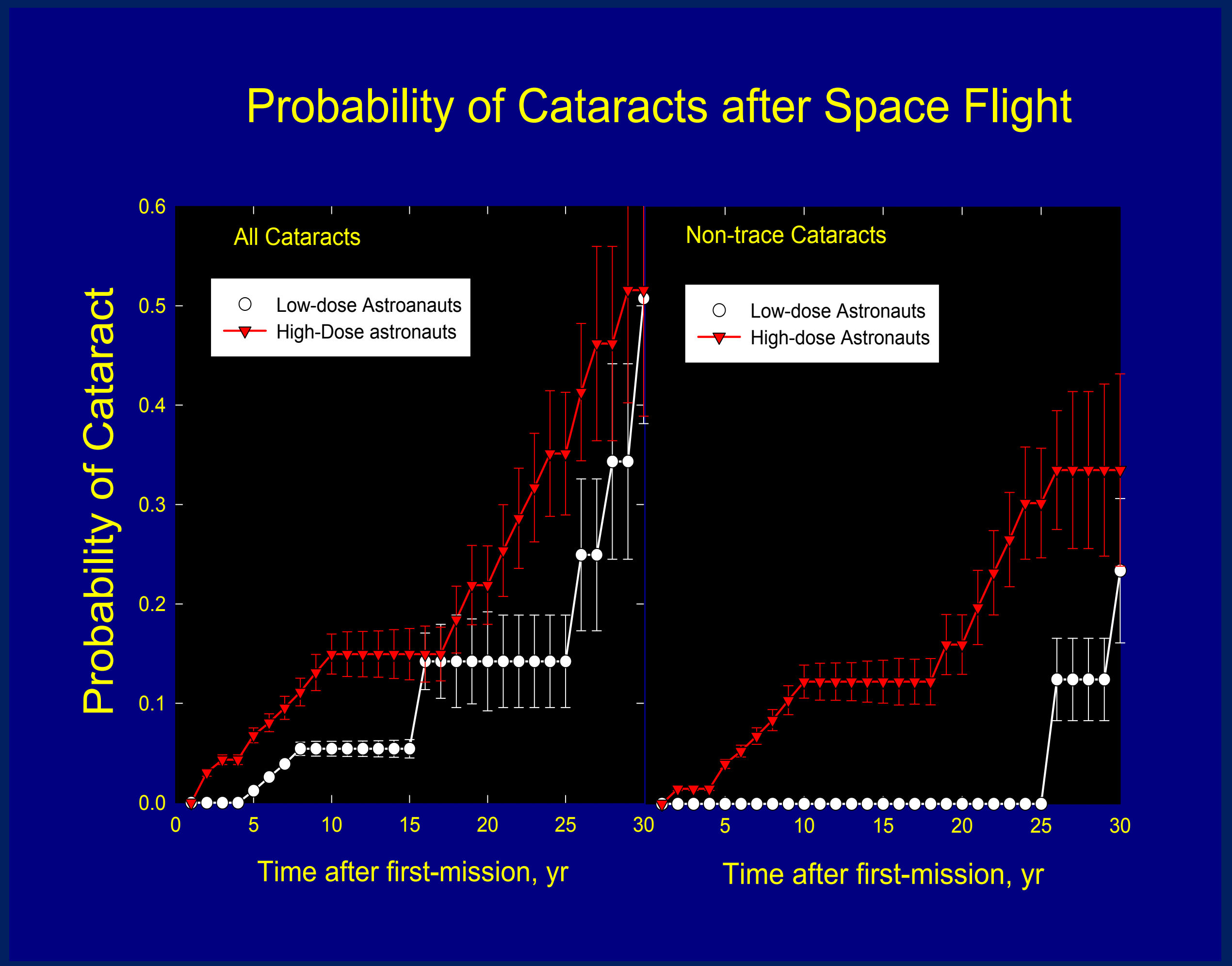
- Risks are high limiting mission length or crew selection with high cost to protect against risks and uncertainties
- Past missions have not led to attributable rad-effects except for cataracts, however for a Mars mission most cancers observed would be attributable to space radiation

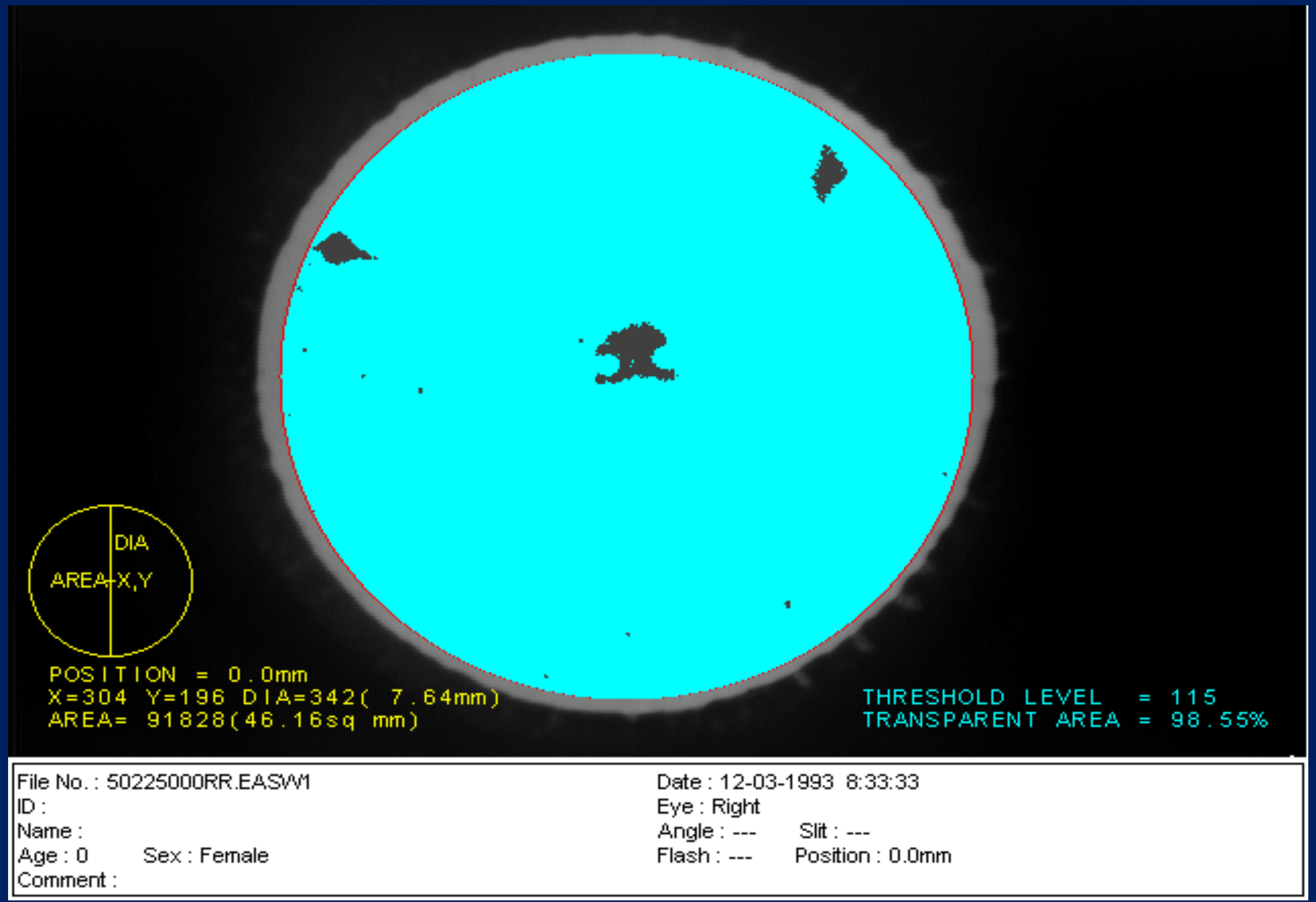
Approach to solve these problems:

- Probabilistic risk assessment framework for Space Mission Design
- Hypothesis & Ground-based research
- Medical Policy Foundations for Safety

Cosmic Ray Health Risks

- Risks:
  - Acute Radiation Syndromes (ARS)
  - Cancer
  - Cataracts
  - Central Nervous System Effects
  - Circulatory Diseases
  - Other normal tissue effects
- Focus: High Charge and Energy (HZE) particles have unique track structures leading to quantitative and qualitative differences in biological effects compared to γ-rays.

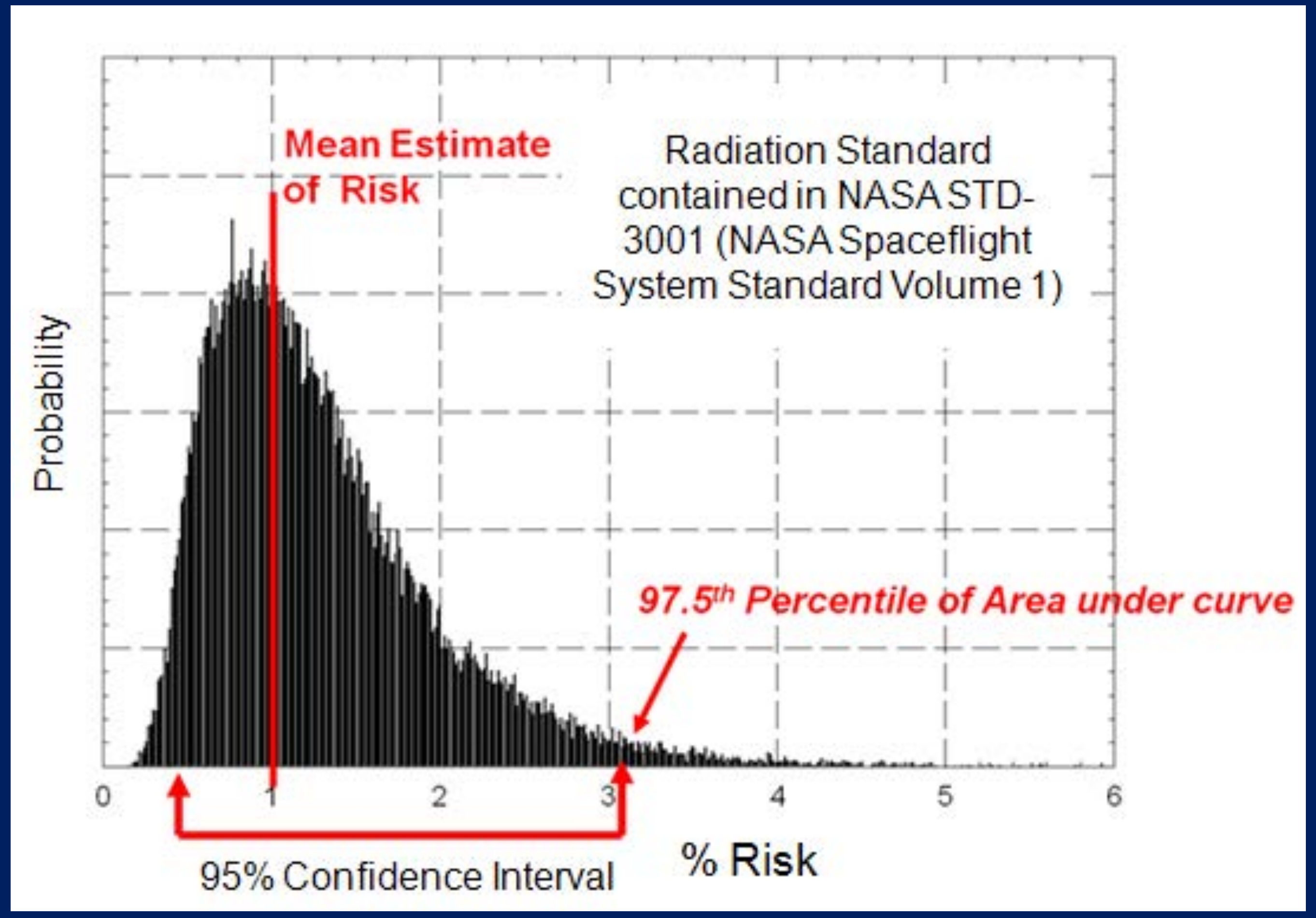


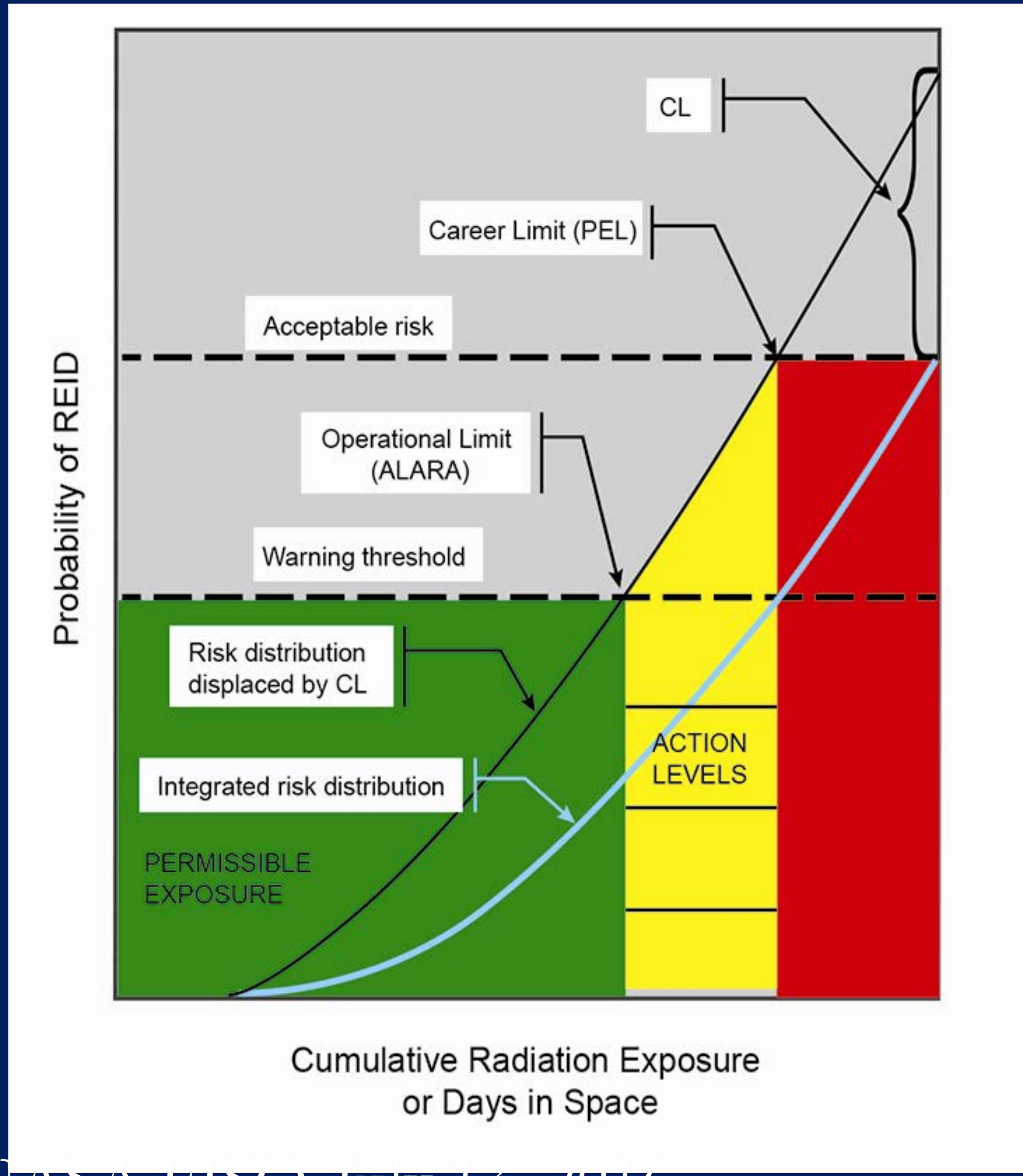


Cataracts in Astronauts

Space Radiation Safety Requirements

- Congress has chartered the National Council on Radiation Protection and Measurements (NCRP) to guide Federal agencies on radiation limits and procedures
  - Safety Principles of Risk Justification, Risk Limitation and ALARA (as low as reasonably achievable)
- Crew safety
  - limit of 3% fatal cancer risk based on 1989 comparison of risks in "unsafe" industries
  - NASA limits the 3% lifetime fatality risk at a 95% confidence level to protect against uncertainties in risk projections
  - Placeholder requirements in PEL limit Central Nervous System (CNS) and circulatory disease risks from space radiation
- Limits set Mission and Vehicle Requirements
  - shielding, dosimetry, countermeasures, & crew





Requirements to Limit Radiation Mortality

- The National Council on Radiation Protection and Measurements (NCRP) is Chartered by the U.S. Congress to guide Govt. Agencies on Radiation Safety.
- In 1989, NCRP recommended age at exposure and gender based dose limits using a 3% fatal cancer risk as basis for dose limits (<1 in 33 probability of occupational death).
- The NCRP Considered comparisons to accidental deaths in the so-called “Safe”, “Less-Safe” and “Unsafe” Industries and concluded Dose Limits should limit risk similar to “Less-safe” Industries.
- The NCRP noted that since Astronauts face other risks similar to “unsafe” industries it would be inappropriate for NASA’s radiation limits to be similar to risks in “unsafe” industries.
- However Safe, Less Safe and Unsafe Industry risks continue to decline.

Risk in Less-Safe Industries have decreased to <1%

Annual Fatality Rates from Accidents in Different Occupations noted by NCRP Report 98 (1989)[a], NCRP Report 132 (2000)[b], and recent values from National Safety Council[c]. Percent probabilities for occupational fatality for careers of 45 years are listed in parenthesis.

Occupation	Annual Fatal Accident Rate per 100,000 workers (%Lifetime Fatality for 45-y career)		
	1987[a]	1998[b]	2009[c]
Safe			
Manufacturing	6 (0.27%)	3 (0.14)	2 (0.1)
Trade	5 (0.23)	2 (0.1)	4.3 (0.2)
Services	5 (0.23)	1.5 (<0.1)	2 (0.1)
Government	8 (0.36)	2 (0.1)	1.8 (<0.1)
Less Safe			
Agriculture	49 (2.2)	22 (1.0)	25.4 (1.1)
Mining	38 (1.7)	24 (1.1)	12.8 (0.58)
Construction	35 (1.6)	14 (0.63)	9.3 (0.42)
Transportation	28 (1.3)	12 (0.54)	11 (0.5)
ALL	10 (0.45)	4 (0.18)	2.8 (0.13)

Alternative Comparative Risk Basis?

- Current Loss of Crew (LOC) risk for Spaceflight is 1 in 270 according to NASA.
- Aerospace Safety Advisory Panel (ASAP) recommends NASA can make investments to reduce LOC to less than 1 in 750.
- The Life-Loss for Radiation Death from Gamma-ray induced cancers is estimated at 15-years for Never-smokers compared to 40 years for LOC.
- Life-Loss for GCR is higher than gamma-rays.
- Is the 1 in 33 radiation limit comparable to LOC (1 in 270) probability when adjusted for life-loss? (ethics, euthanasia?)
- Risk to Fireman or soldiers in Iraqi war zone soldiers ~0.5 %
- **Note: Leadership is finding solutions to space radiation problem, while waiving radiation limits is not leadership.**

Mean Life-loss for Equivalent γ-ray exposure if Radiation Death Occurs for 18-months on ISS (Female and Male Never-smokers)

Tissue	H_T, Sv or Gy-Eq	LLE, y
Leukemia, Sv	0.151	23.1
Stomach	0.235	16.3
Colon	0.261	16.7
Liver	0.229	13.5
Bladder	0.231	11.2
Lung	0.264	13.2
Esophagus	0.249	15.1
Oral Cavity	0.308	15.3
Brain-CNS	0.286	18
Thyroid	0.308	22
Skin	0.282	11.8
Remainder	0.264	12
Breast	0.289	15.7
Ovarian	0.241	17.9
Uterine	0.241	17.1
Total Cancer	0.244	15
CVD, Gy-Eq	0.182	9.1
IHD	0.182	9.5

Tissue	H_T, Sv or Gy-Eq	LLE, y
Leukemia, Sv	0.145	22.1
Stomach	0.227	15.6
Colon	0.251	16.4
Liver	0.235	14
Bladder	0.224	10.9
Lung	0.245	13.6
Esophagus	0.242	14.9
Oral Cavity	0.261	15.8
Brain-CNS	0.279	17
Thyroid	0.261	20.8
Skin	0.308	12
Remainder	0.253	11.7
Prostate	0.260	11.5
Total Cancer	0.228	15
CVD, Gy-Eq	0.174	9.8
IHD	0.174	10.6

CVD=Cardiovascular disease, IHD=Ischemic Heart disease

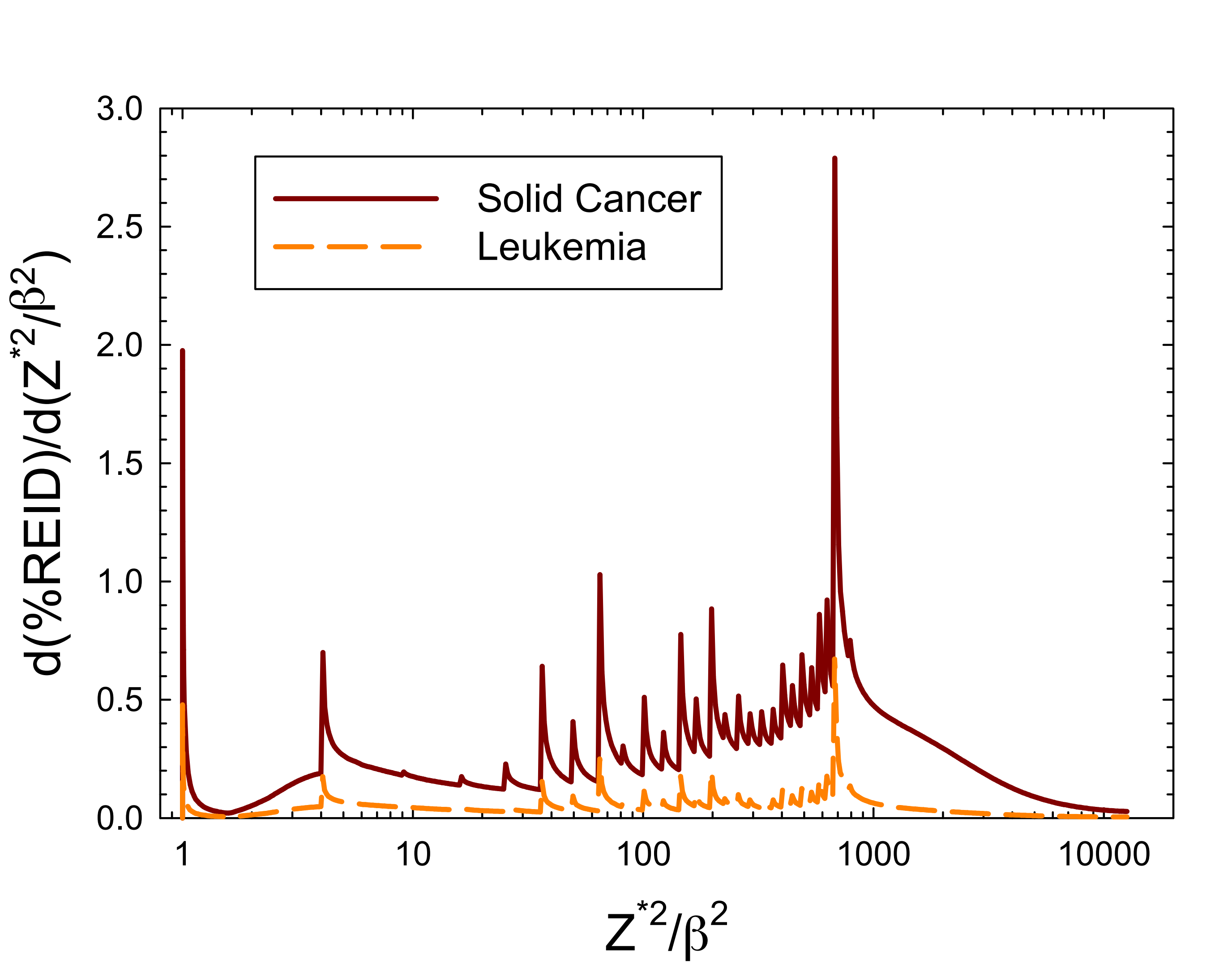
Uncertainties in Space Radiobiology Require New Knowledge and Approaches

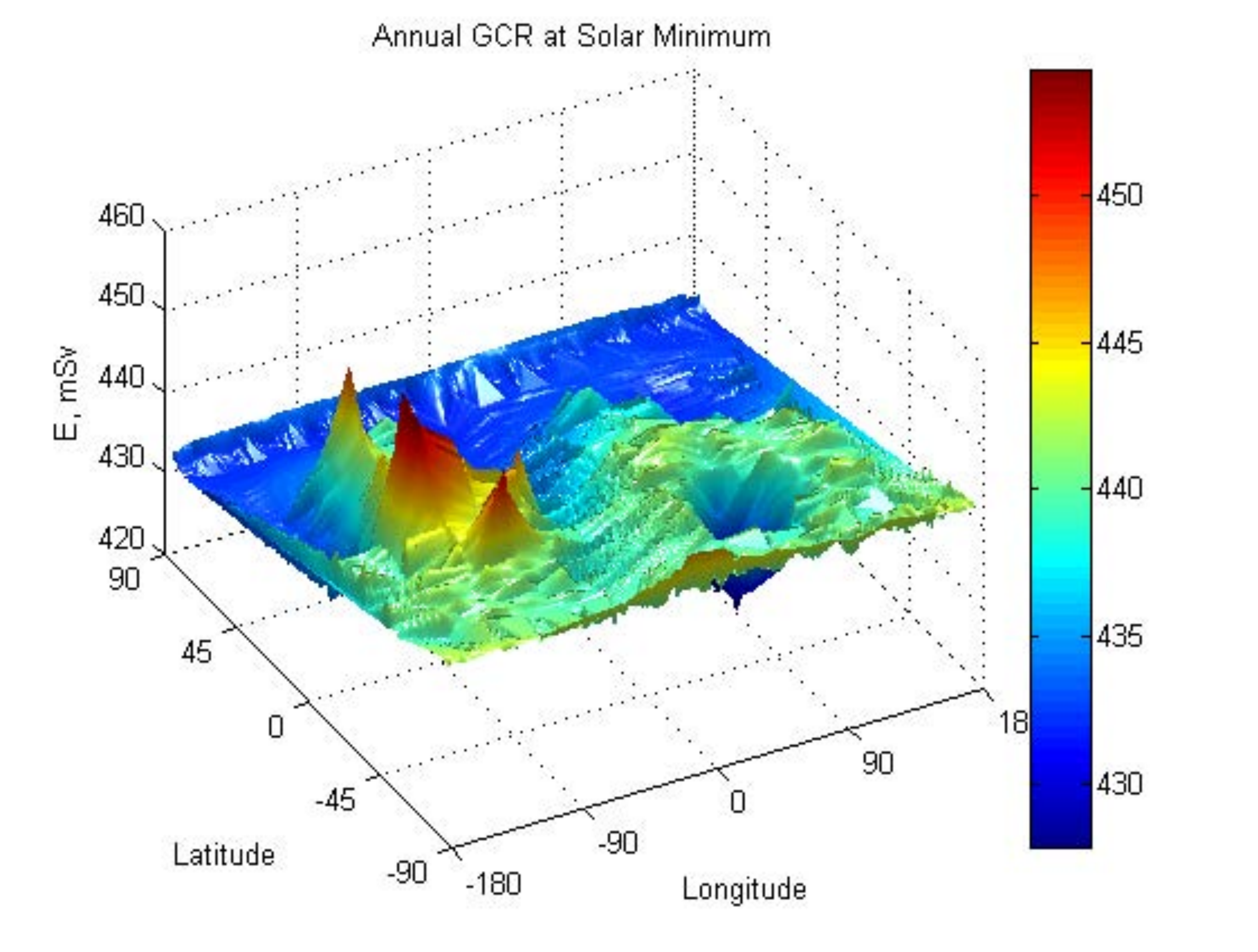
- NCRP Reports 98, 132, 152 noted risk estimates were highly uncertain for Galactic Cosmic Rays (GCR).
  - **Uncertainties too large for Earth based methods to be applied to GCR**
  - **NRC Reports in 1996, 1999 and 2008 echo these concerns**
- All experts agree that knowledge is limited:
  - Unlike other disciplines where the fundamental physiological basis of spaceflight biomedical problems is largely known, the scientific basis of HZE particle radiobiology is largely unknown
  - **Differences between biological damage of HZE particles in space vs. x-rays, limits Earth-based data on health effects for space applications**

NASA Space Cancer Risk (NSCR) Model- 2012

- Reviewed by U.S. National Academy of Sciences (NAS)
  - 95% Confidence level for Limit of 3% Radiation Exposure Induced Death (REID)
    - Not conservative due to non-cancer risks yet to be evaluated
  - Radiation quality described using track structure theory
    - PDF's for uncertainty evaluation
    - Leukemia lower Q than Solid cancer
  - Redefined age dependence of risk using BEIR VII approach
    - UNSCEAR Low LET Risk coefficients
  - Risks for Never-Smokers to represent healthy workers

GCR dominate ISS organ risk

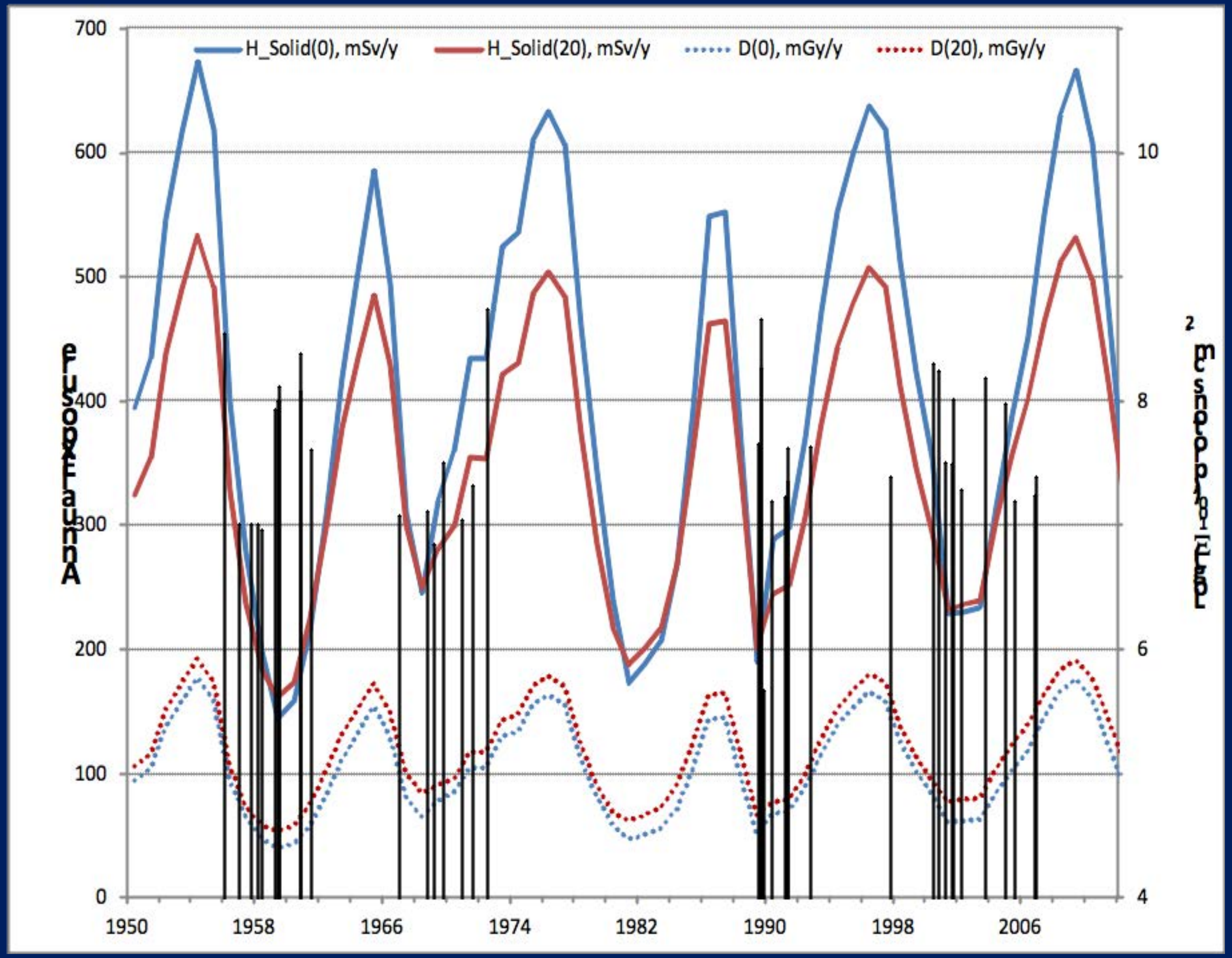




GCR doses on Mars

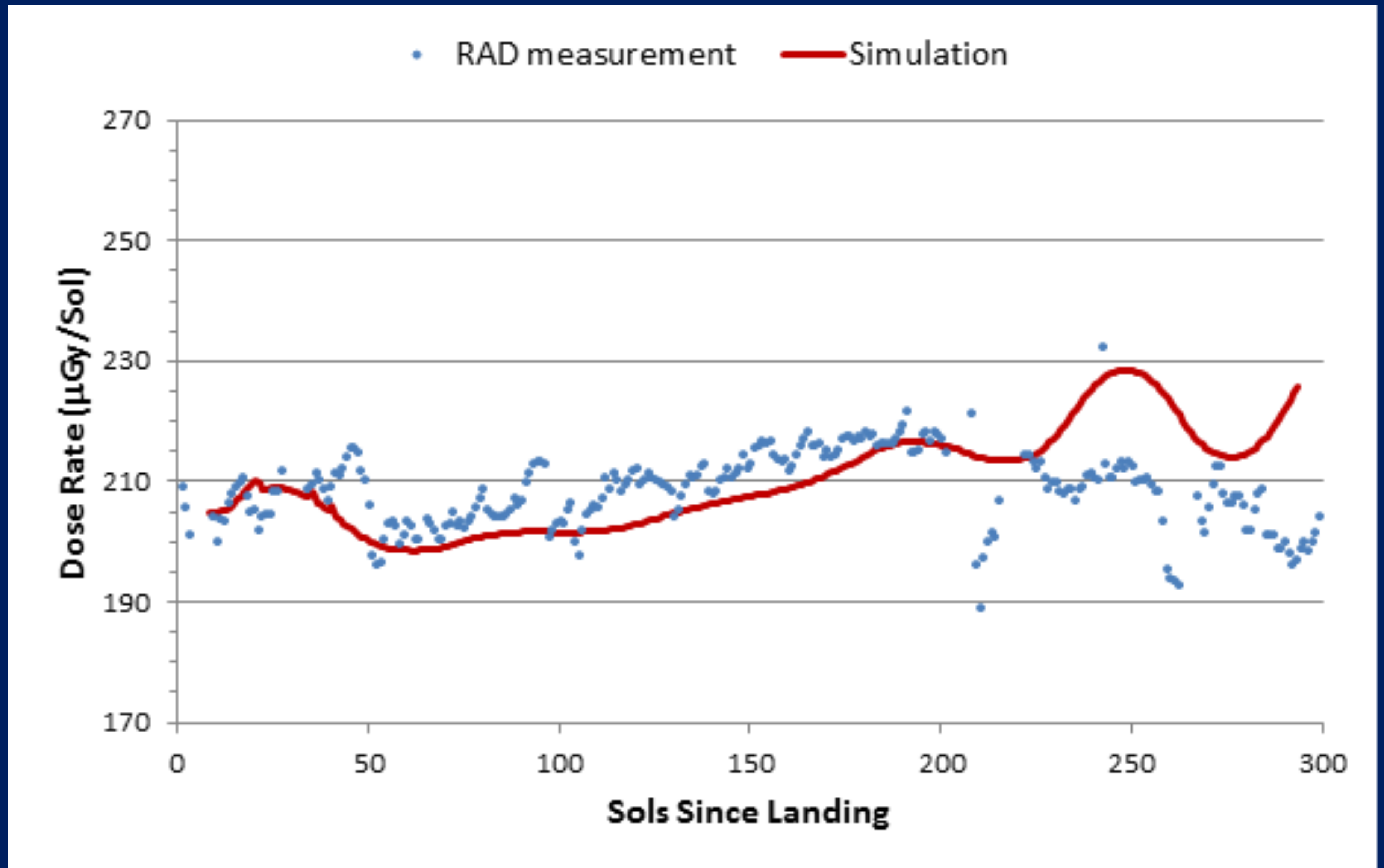
Space Radiation Environments

- Galactic cosmic rays (GCR) penetrating protons and heavy nuclei; a biological science challenge
  - shielding is not effective due to secondaries in shielding and tissue
  - large biological uncertainties limits ability to evaluate risks accurately
  - Uncertainties cloud understanding of effectiveness of possible mitigations
- Solar Particle Events (SPE): low to medium energy protons
  - shielding is effective; optimization needed to reduce weight
  - accurate event alert, dosimetry and responses are essential for crew safety
  - improved understanding of radiobiology needed to perform optimization



- GCR dose and SPE probability are anti-correlated over 11-year solar cycle.
- H_{solid} is Organ Dose Equivalent for Solid cancer risks
- Lines show times for 43 largest of ~400 SPE’s since 1950 (organ doses >10 mGy)

Comparison of MSL RAD Measurements to NASA Space Cancer Risk Model (NSCR-2012):

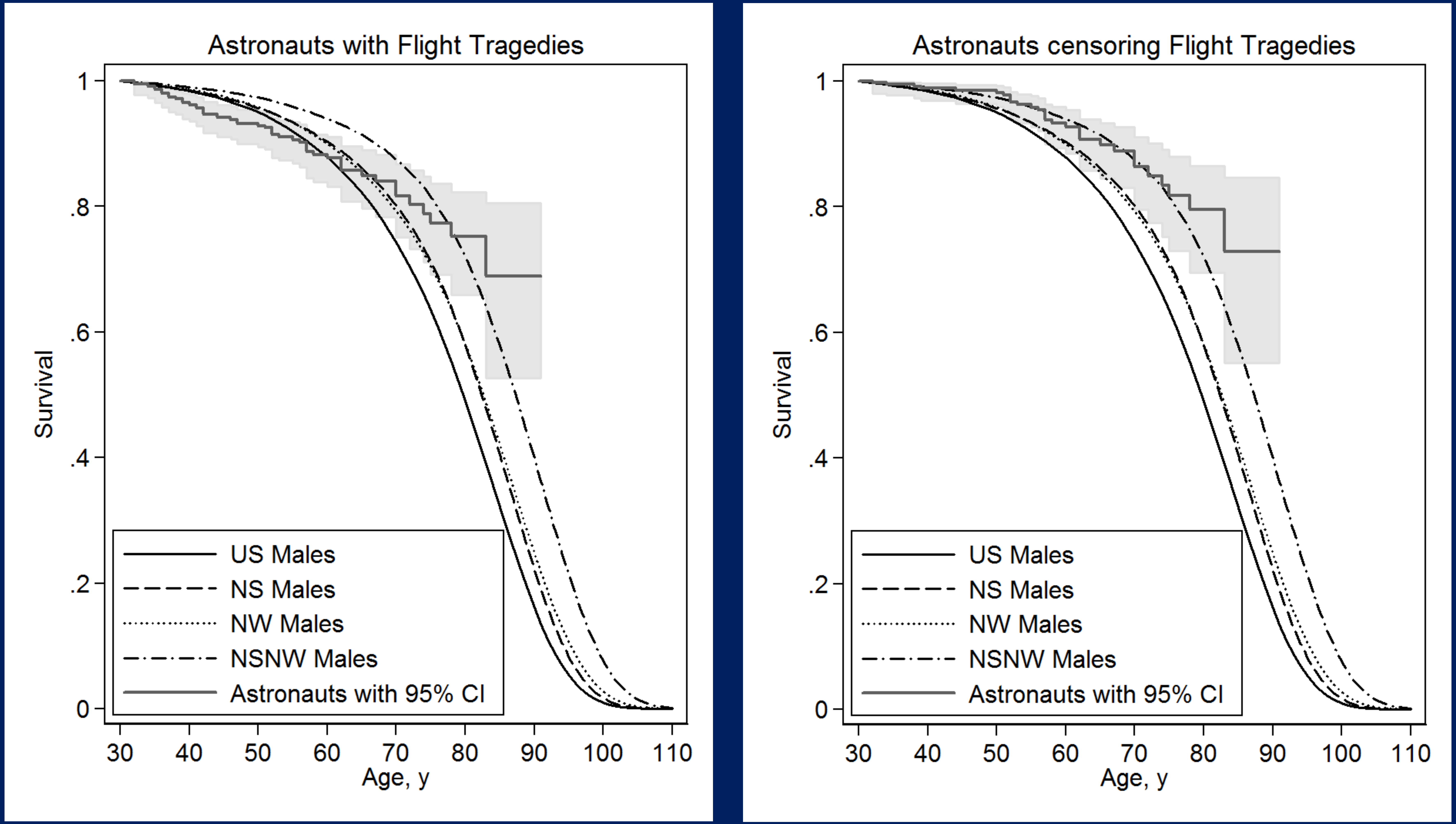


Comparison	GCR Dose Rate (mGy/day)	GCR Dose Equiv. Rate (mSv/day)
Model Cruise to Mars	**0.445**	**1.80**
RAD Cruise to Mars (Zeitlin et al. 2013)	0.481±0.08	1.84±0.33
Model Mars surface (Kim et al. 2014)	**0.20**	**0.72**
RAD Mars Surface (Hassler et al. 2014)	0.205±0.05	0.70±0.17

Reference Population for Astronauts?

- All prior analysis used the Average U.S. Population as the reference population for astronauts.
- Our Cancer risk model introduced some aspects of health worker effect for risk projections.
  - adapted by NASA after NAS review in 2012
- Astronauts should be considered as "healthy workers", which could modify risk estimates.
  - Lower cancer risks may occur due to improved BMI, exercise, diet, or early detection from improved health care compared to U.S. Average
  - More than 90% of astronauts are never-smokers and others former smokers
- Healthy worker effects are difficult to quantify with the exception of cancer rates for never-smokers.
  - Revised NASA projection models to consider estimates of radiation risks for never-smokers

Healthy Worker Effects in Astronauts (N=339)
(Cucinotta et al. 2013)



NS = Never-Smoker; NW = Normal Weight

Astronauts live very long due to low Circulatory Disease --even with low space doses (ave. 40 mSv)

Standard Cancer Mortality Ratio (SMR) for astronauts relative to other populations for **Cancer**

Comparison	***SMR***
Astronauts vs. U.S. avg.	0.60 [0.34, 1.06]
Astronauts vs. NS avg.	1.12 [0.64, 1.99]
Astronauts vs NW avg.	0.60 [0.34, 1.05]
Astronauts vs NS-NW Avg.	1.24 [0.70, 2.18]

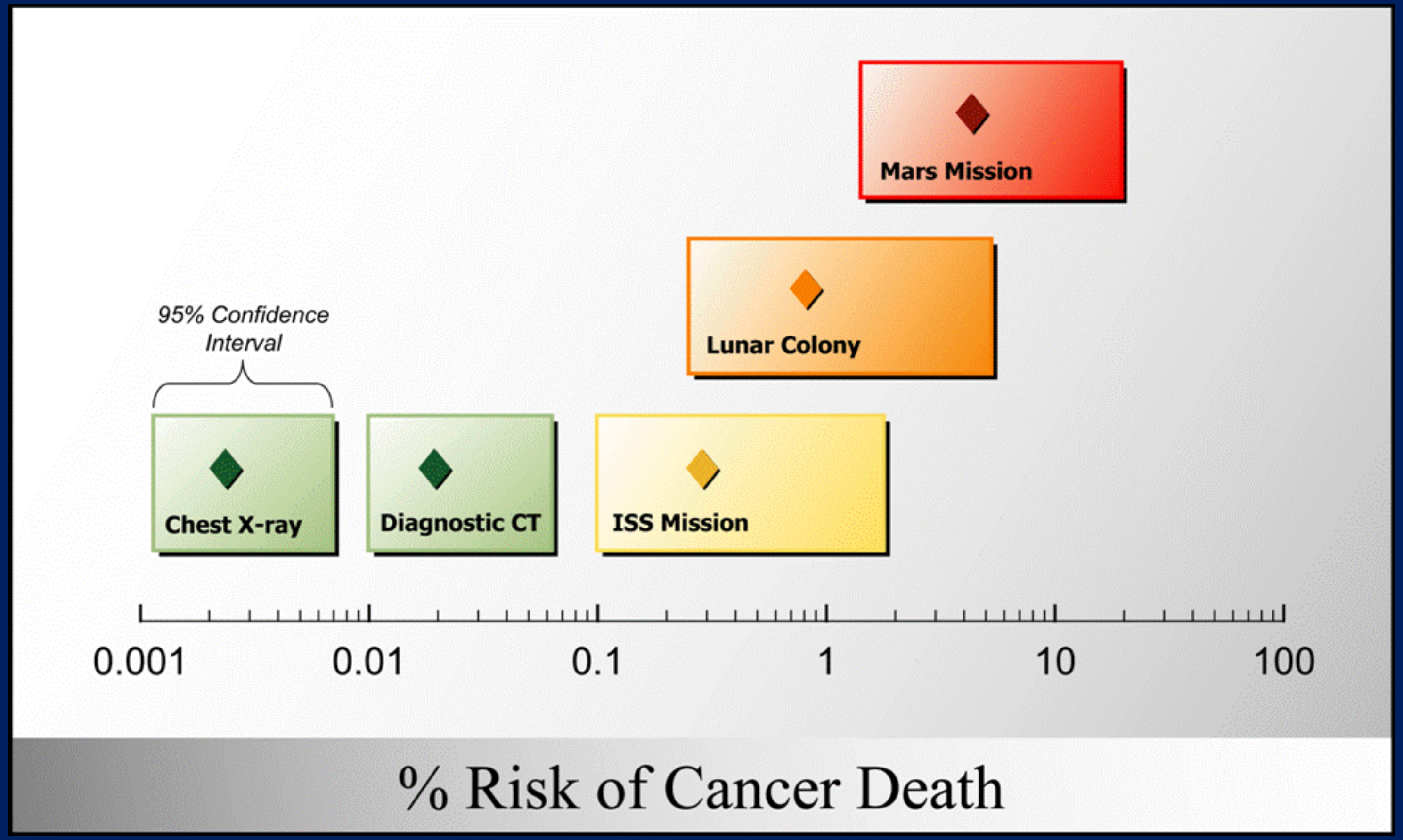
SMR for astronauts for **Circulatory diseases**

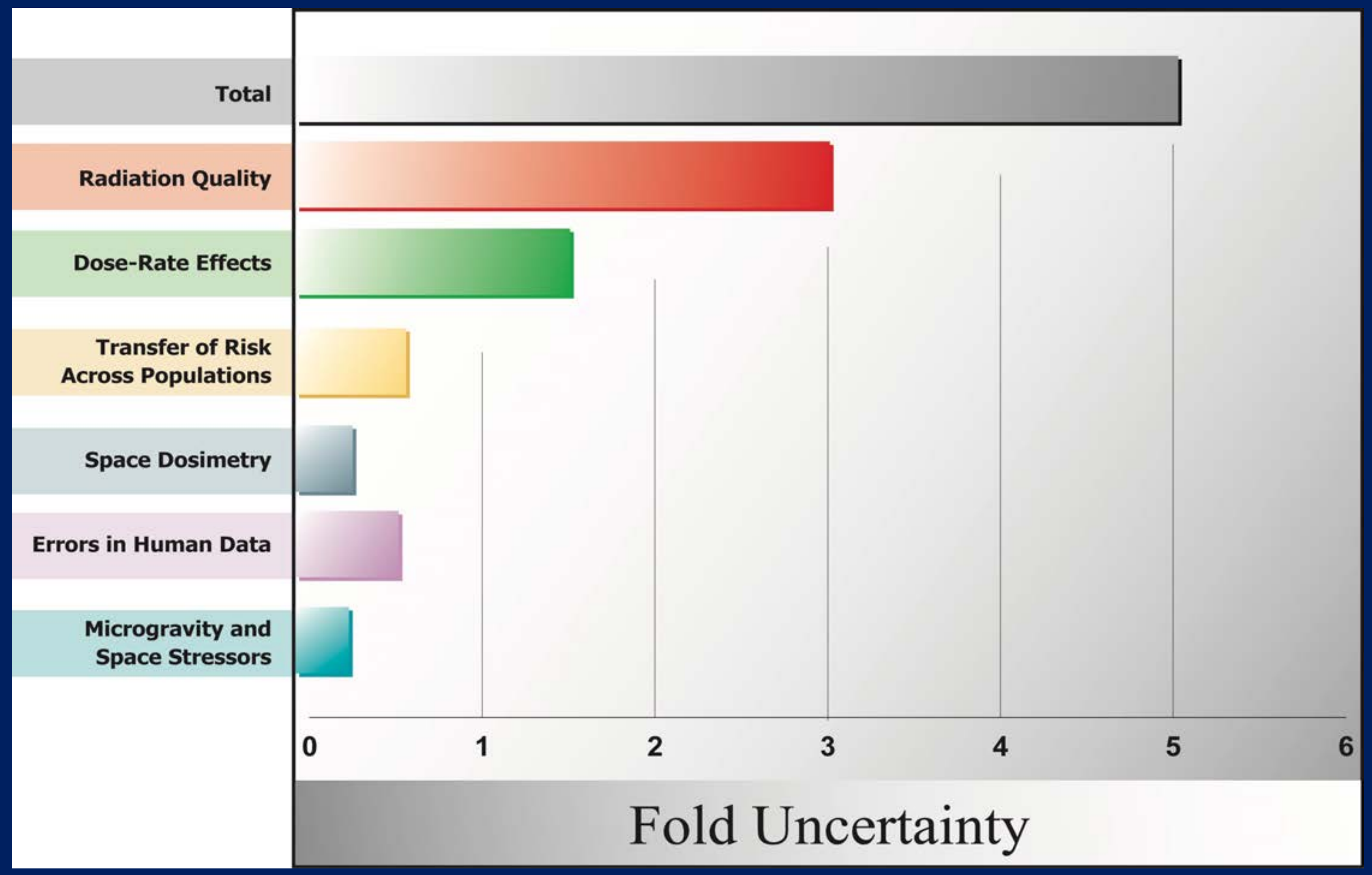
Comparison	***SMR***
Astronauts vs. U.S. avg.	0.33 [0.14, 0.80]
Astronauts vs. NS avg.	0.43 [0.18, 1.04]
Astronauts vs NW avg.	0.47 [0.19, 1.12]
Astronauts vs NS-NW Avg.	0.67 [0.28, 1.62]

NS = never-smoker, NW = Normal Weight

Major Sources of Uncertainty

- Radiation quality effects on biological damage (RBE – QF)
  - Qualitative and quantitative differences of Space Radiation compared to x-rays
- Dependence of risk on dose-rates in space (DDREF)
  - Biology of DNA repair, cell regulation
- Predicting solar events
  - Onset, temporal, and size predictions
- Extrapolation from experimental data to humans
- Individual radiation-sensitivity
  - Genetic, dietary and "healthy worker" effects





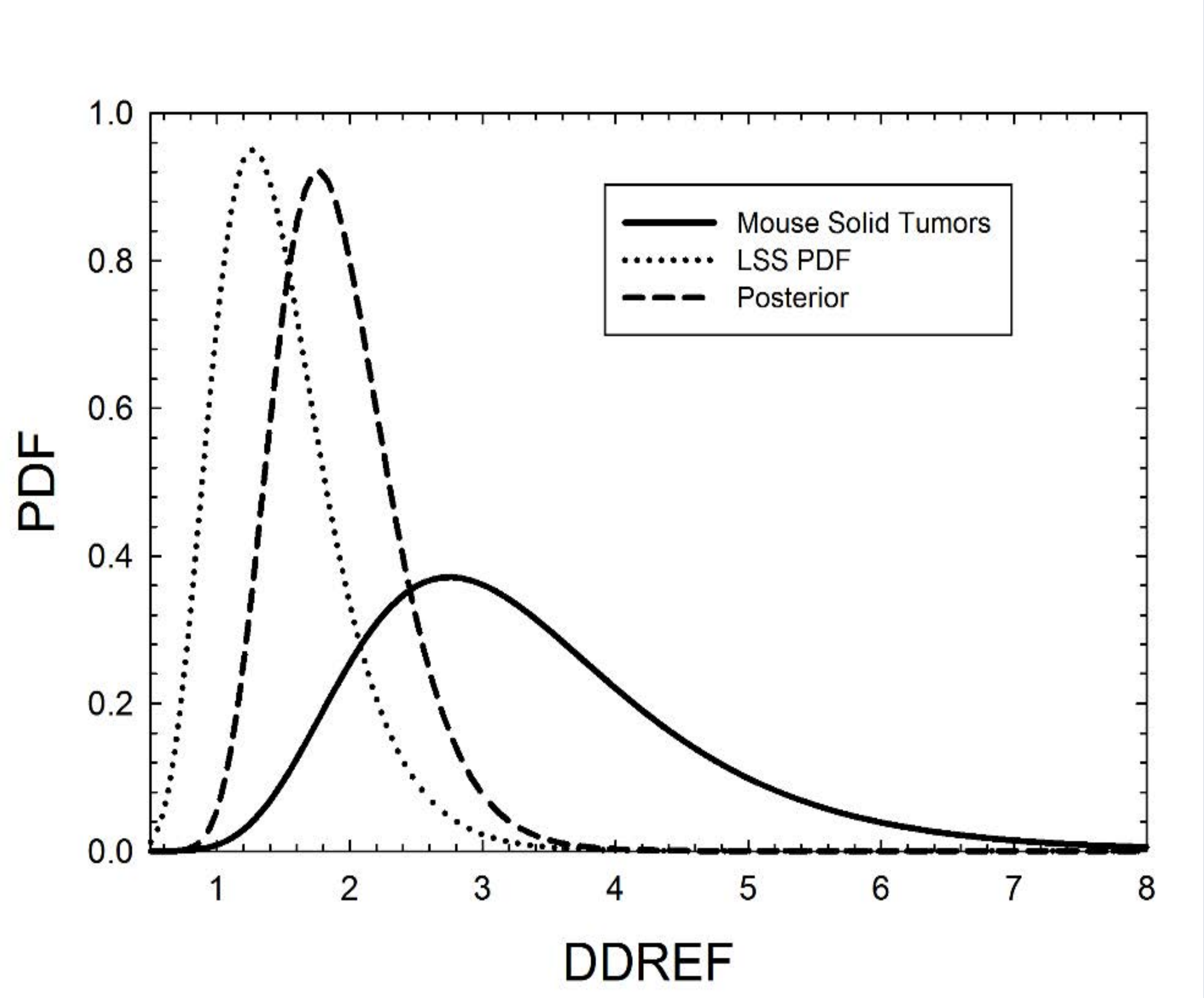
Nature Rev. Cancer (2008)

Fundamental Issue of Types of Radiation

- The ionizations and excitations in cells and tissue that occur **are not distributed at random**.
- They are stochastically produced but **localized along the track** of the incoming radiation.
- The pattern of this localization **depends on the type of radiation** involved.
- This means that different types of radiation will **deposit different amounts of energy in the same space**.
- The description of energy deposition at microscopic level is called **Microdosimetry** or **Track Structure**

The Dose and Dose-Rate Reduction Effectiveness Factor (DDREF)

- DDREF reduces cancer risk estimates.
- DDREF estimate from A-bomb survivors is 1.3 in National Academy of Science BEIR VII Report.
- DDREF estimate from animal experiments 2 to 3.



Bayesian Analysis using BEIR VII Prior Distribution and mouse data

NASA Radiation Quality Function (NQF)-2012

- International bodies use QF dependent on LET alone.
- Track structure concepts and existing radiobiology data used to guide choice on functional forms for QF:
  - Maximum effectiveness per particle can be estimated by experiments for RBE_{max} and occurs at "saturation point" of cross section for any Z
  - Delta-ray effects for relativistic particles accounted for in QF model; higher Z less effective at fixed LET compared to lower Z

$$Q_{NASA} = (1 - P(Z,E)) + \frac{6.24(\Sigma_0/\alpha_\gamma)}{LET} P(Z,E)$$

$$P(Z,E) = (1 - \exp(-Z^{*2}/\kappa\beta^2))^m P_{TD}$$

- PDFs account for variation of three parameters values:

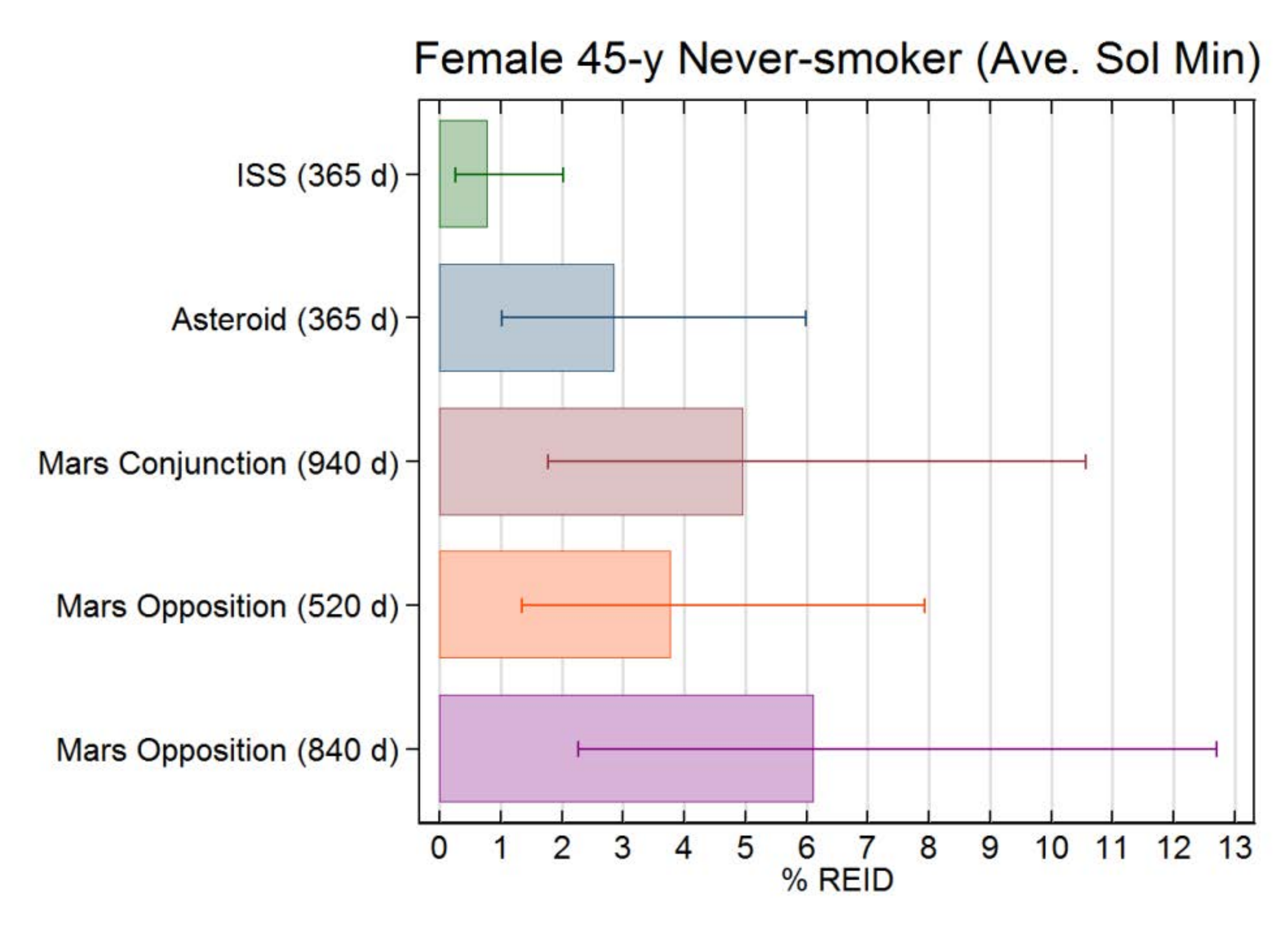
(Σ_0/α_γ, m, and κ) based on existing but limited radiobiology data. PTD low energy correction. Qmax~ Σ_0/α_γ

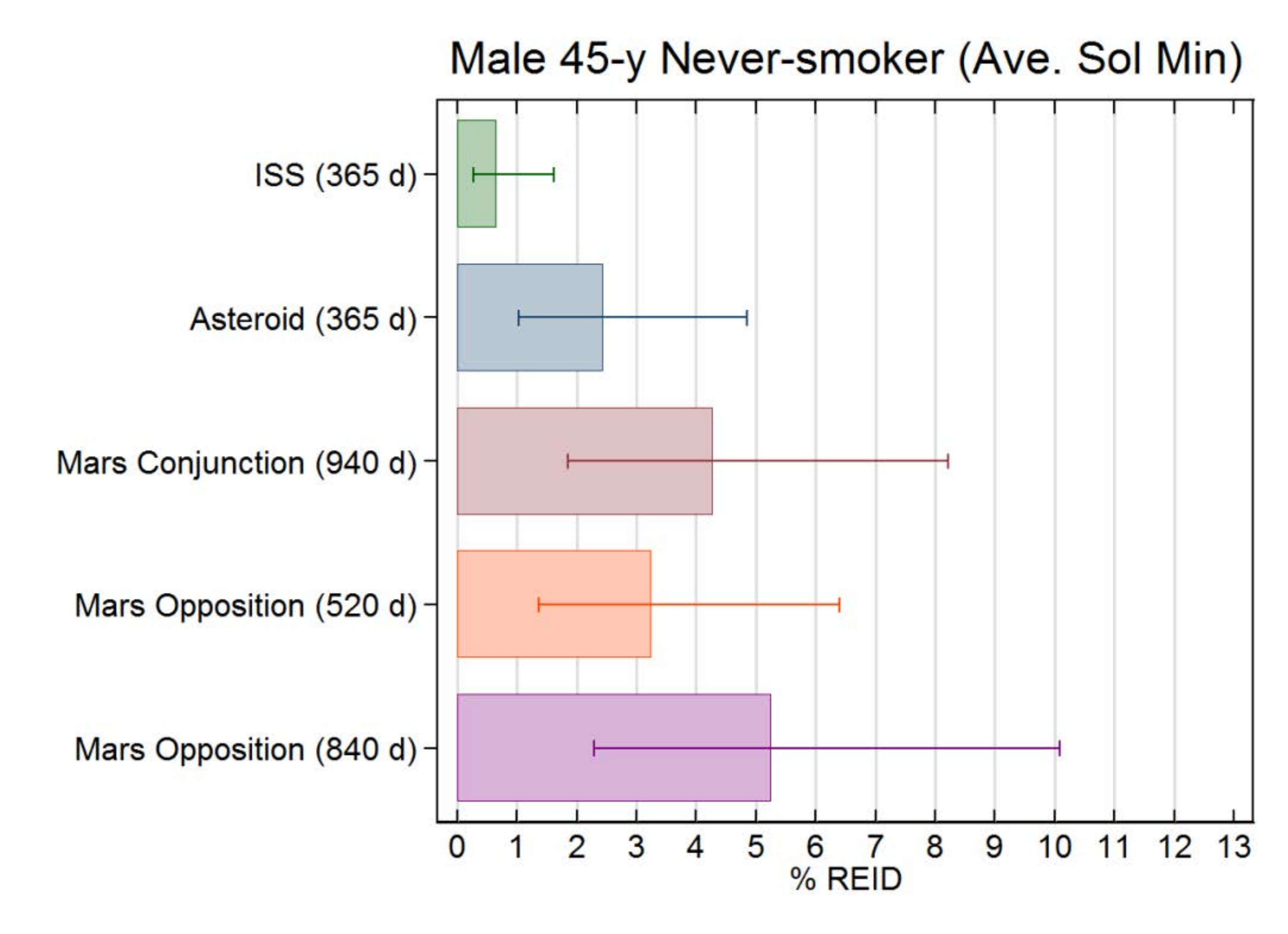
Uncertainty Analysis

- Monte-Carlo uncertainty analysis uses risk equation modified by normal deviates that represent possible values for key factors that enter represented by probability distribution functions (PDF):
  - define $X \in R(x)$ as a random variate that takes on quantiles $x_1, x_2, \ldots, x_n$ such that $p(x_i) = P(X=x_i)$ with the normalization condition $\Sigma\, p(x_i)=1$.
  - $C(x_i)$ is defined as the cumulative distribution function, $C(x)$, which maps X into the uniform distribution $U(0,1)$,
  - Define the inverse cumulative distribution function $C(x)^{-1}$ to perform inverse mapping of $U(0,1)$ into x: $x=C(x)^{-1}$
- PDF for QF, DDREF, Low-LET cancer rate, Organ dose, etc.
- For a Monte-Carlo trial, ξ, Risk Rate is like

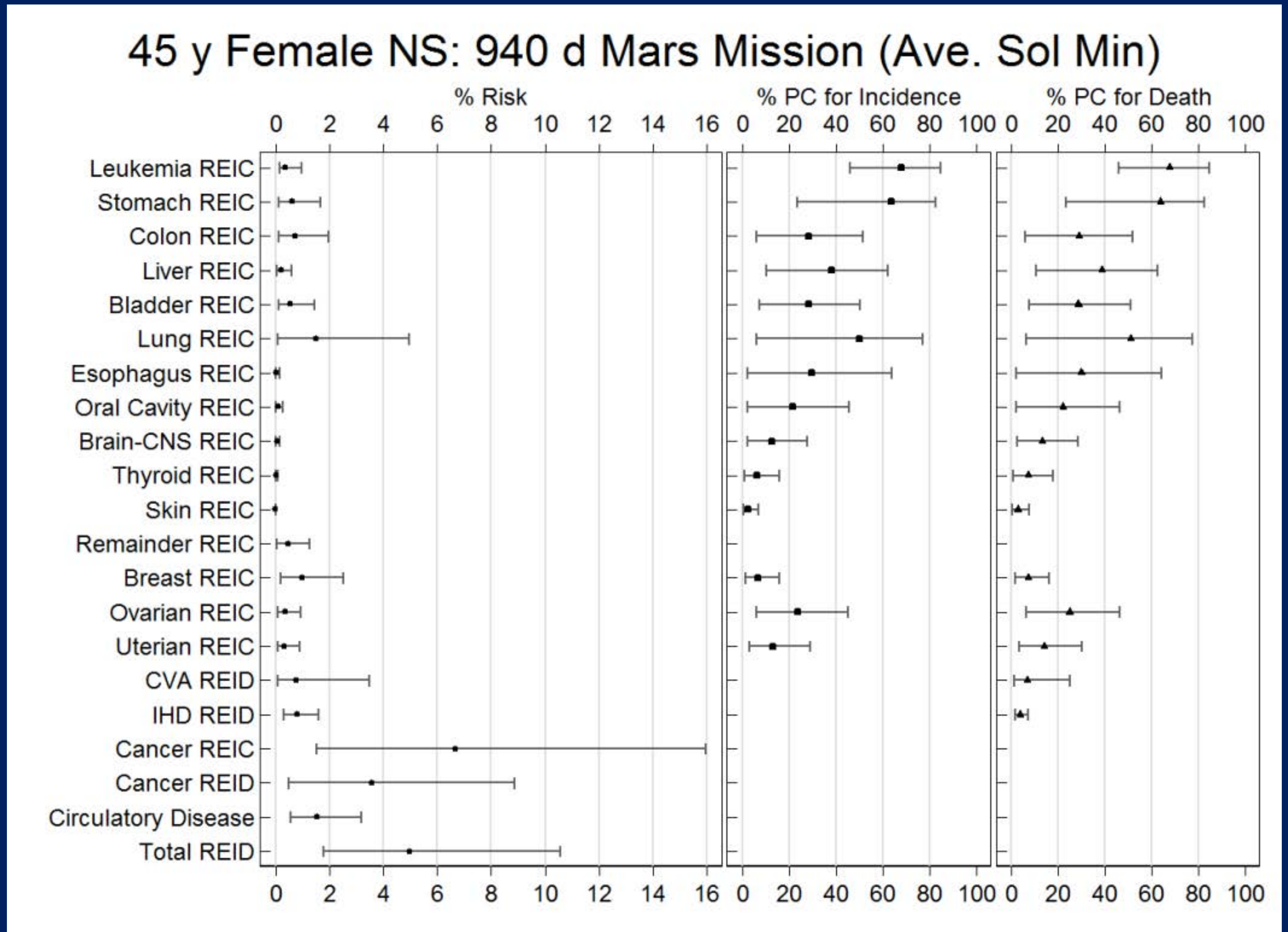
$$Risk_{\xi} = R_0(age, gender)\frac{FLQ}{DDREF}\left\{\frac{x_{R_0} x_{phys} x_Q}{x_{D_R}}\right\}_{\xi}$$

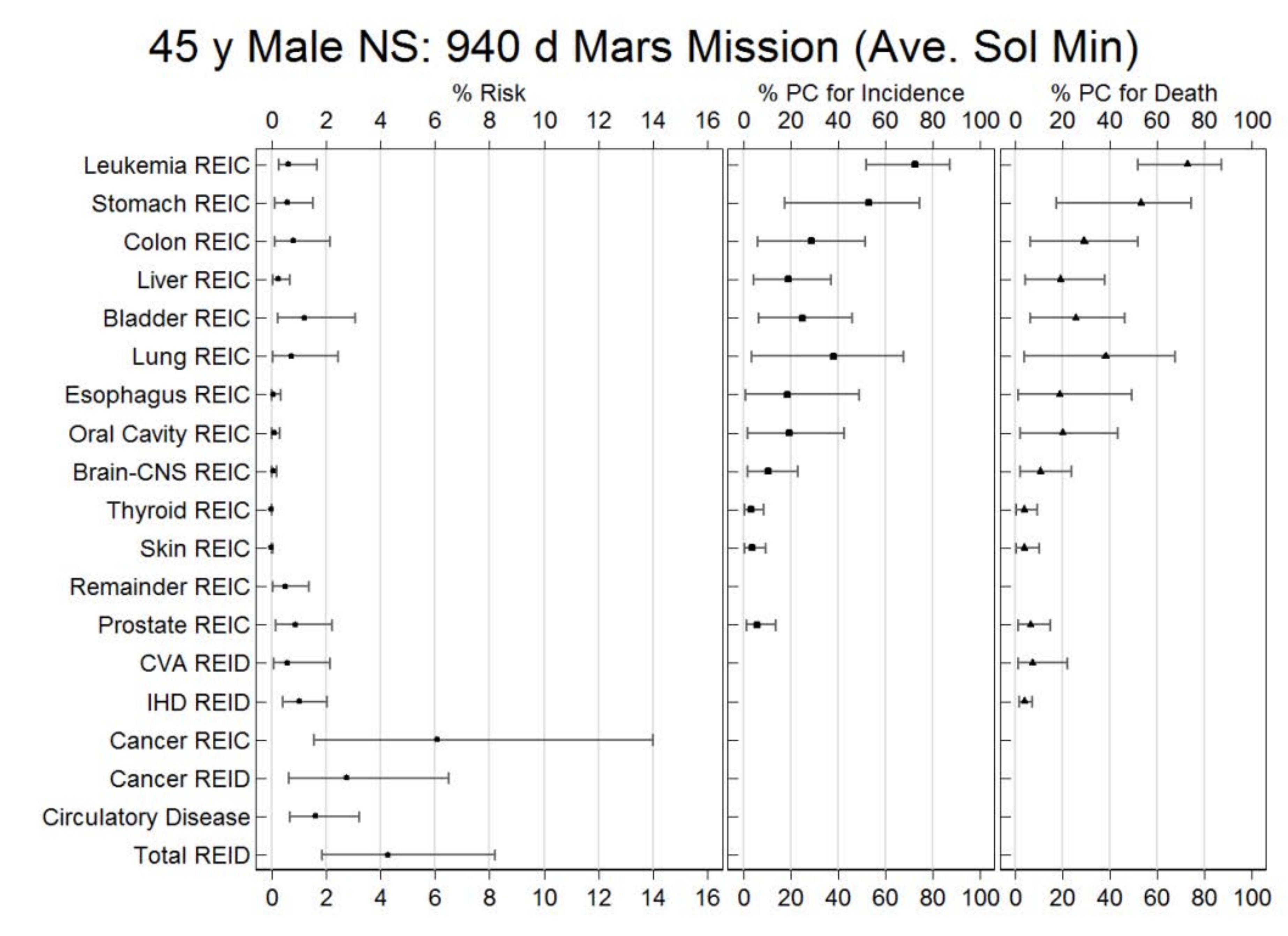
Risk for Exploration (Cucinotta et al. 2013) Cancer and Circulatory Disease





ISS = International Space Station; lower risk because GCR partially shielded
By Earth Shadow and Magnetic Field
Circulatory disease estimate from human data on Stroke and Ischemic Heart disease





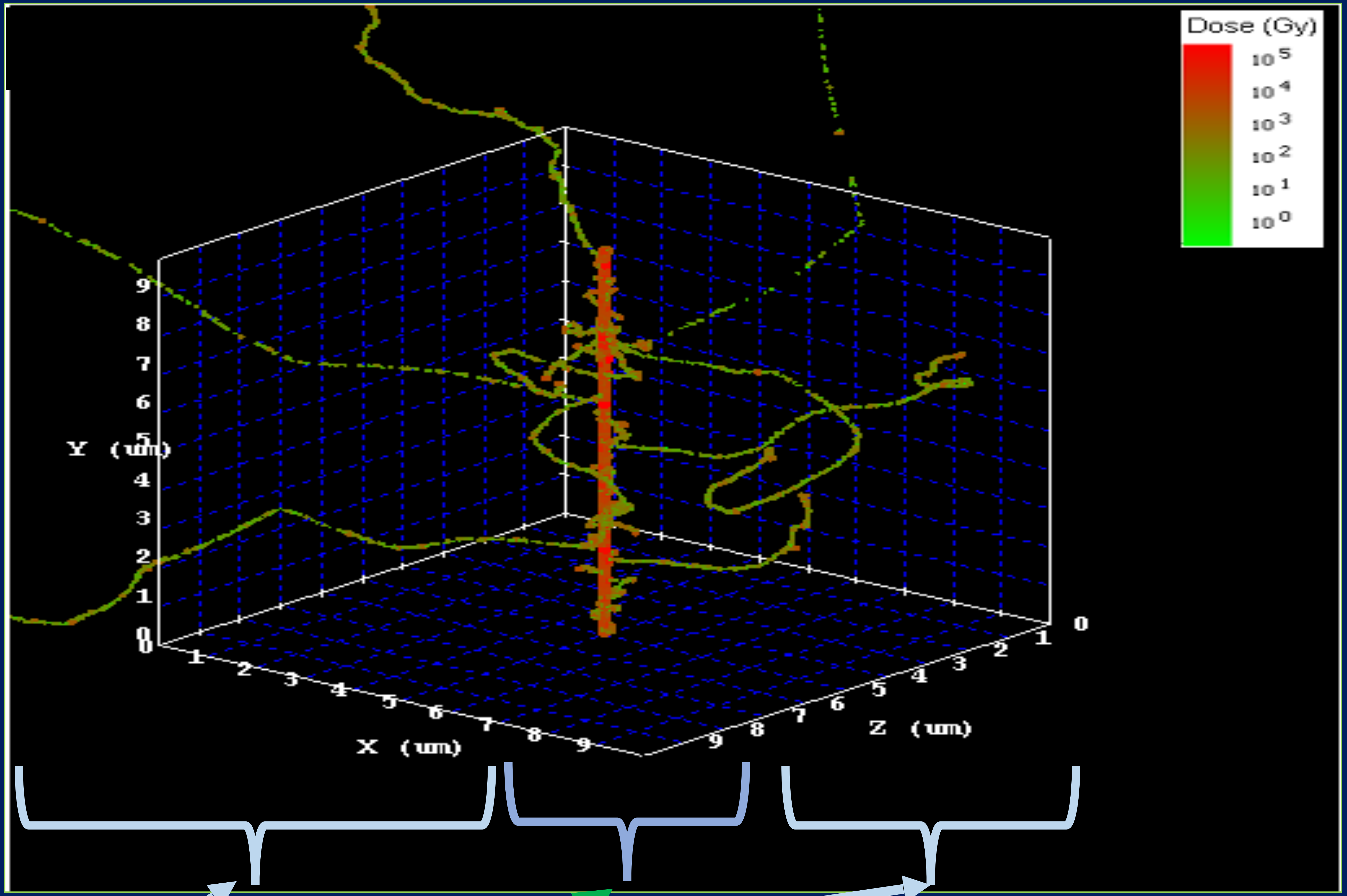
PC = Probability of Causation at 10 years Post-exposure in these Calculations.
If cancer is discovered In astronaut probability Radiation was the cause

Francis Cucinotta, "New Estimates of Radiation Risks…" NASA FISO, July 13, 2016

Redefining QFs to Reduce Uncertainty

- QF's are based on RBE_{max} that introduces uncertainty of low dose-rate gamma-rays.
- NSCR-2015 redefines QF's against RBE for acute gamma-rays at higher doses for solid tumors in mice.
- Numerous experiments show no dose-rate effect at high LET for exposure times < 2 weeks
- Bayesian analysis used to correlate DDREF for matched solid tumor data.
- Lowers risk and uncertainty estimates by 25% and 35%, respectively.

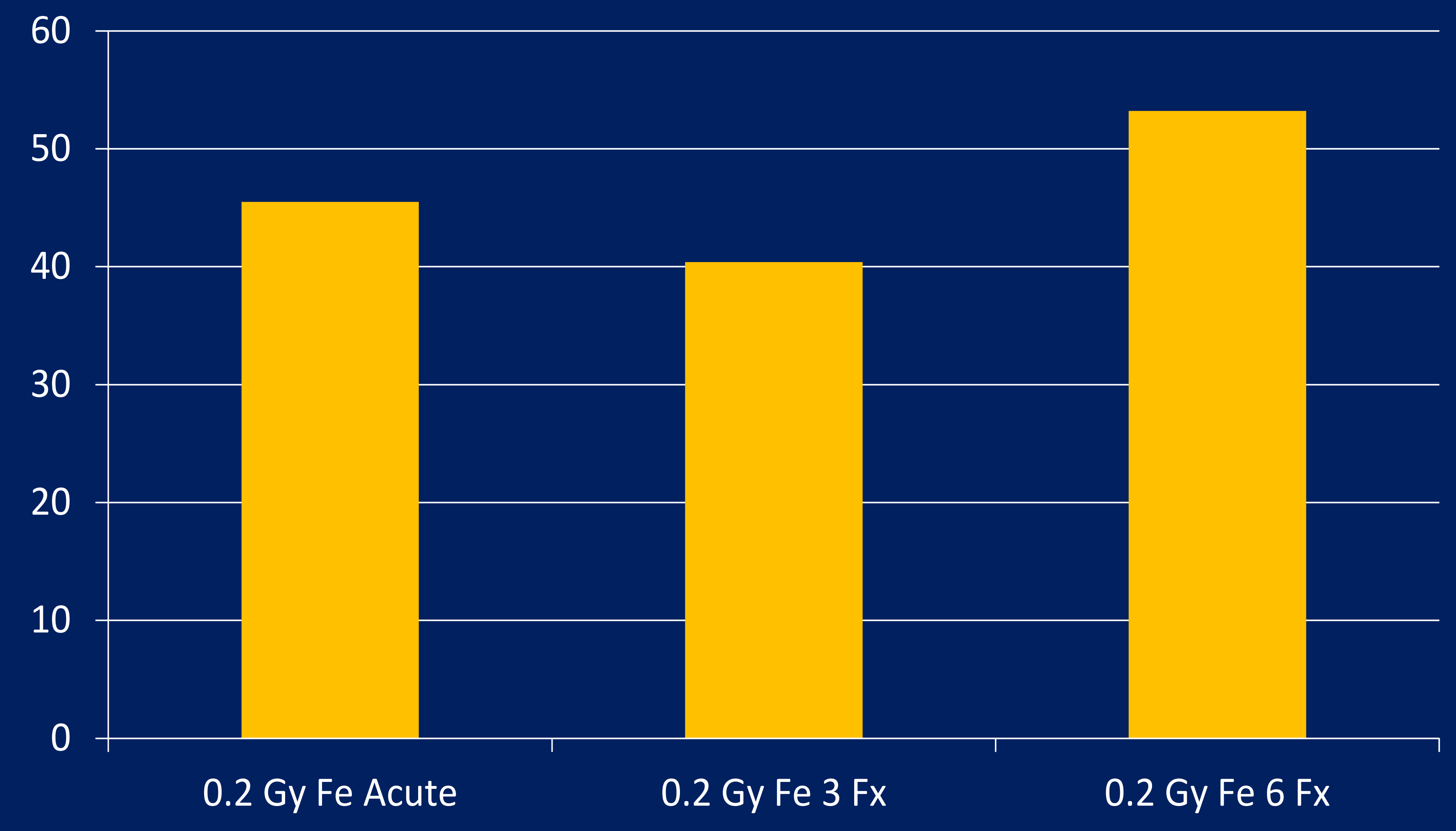
NSCR Revision : Track Structure Approach: "core" and "penumbra" in Biological Effects



$$Q_{NASA} = (1 - P(Z,E)) + \frac{6.24(\Sigma_0 / \alpha_\gamma)}{LET} P(Z,E) \qquad \frac{QF_{\gamma Acute}(Z,E)}{DDREF} = \frac{Q_{low}(Z,E)}{DDREF} + \overline{Q}_{high}(Z,E)$$

Lack of dose-rate effect for heavy ions

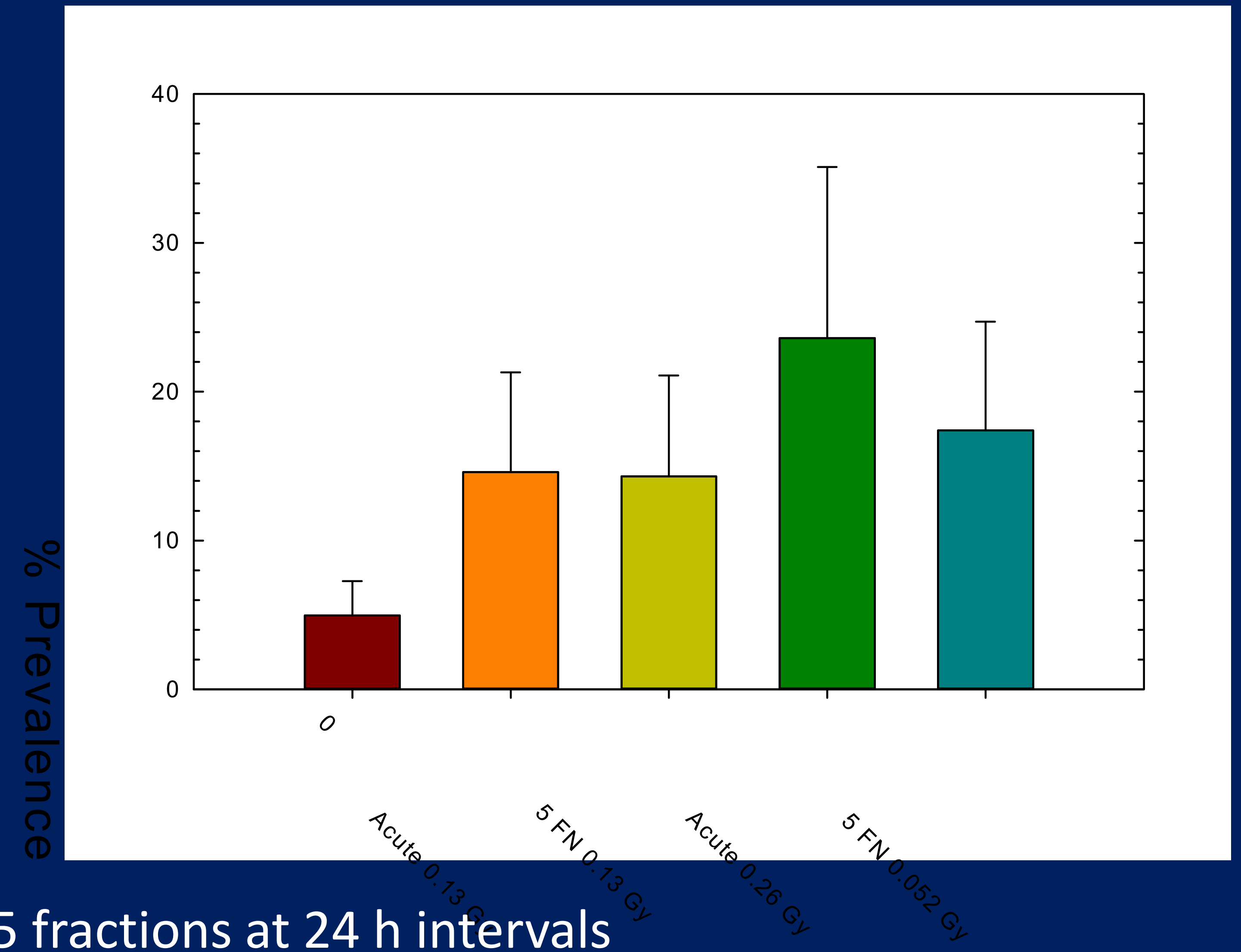
Incidence of HCC (%) following Acute or Fractionated Exposures of 600 MeV/nucleon ^{56}Fe Ions (Ullrich, Weil et al.)



48 hours between fractions about 300 mice per group.

33

Harderian Gland Tumors following acute or fractionated Titanium Exposures in B6CF1 mice (Blakeley, Chang et al. 2015)



5 fractions at 24 h intervals

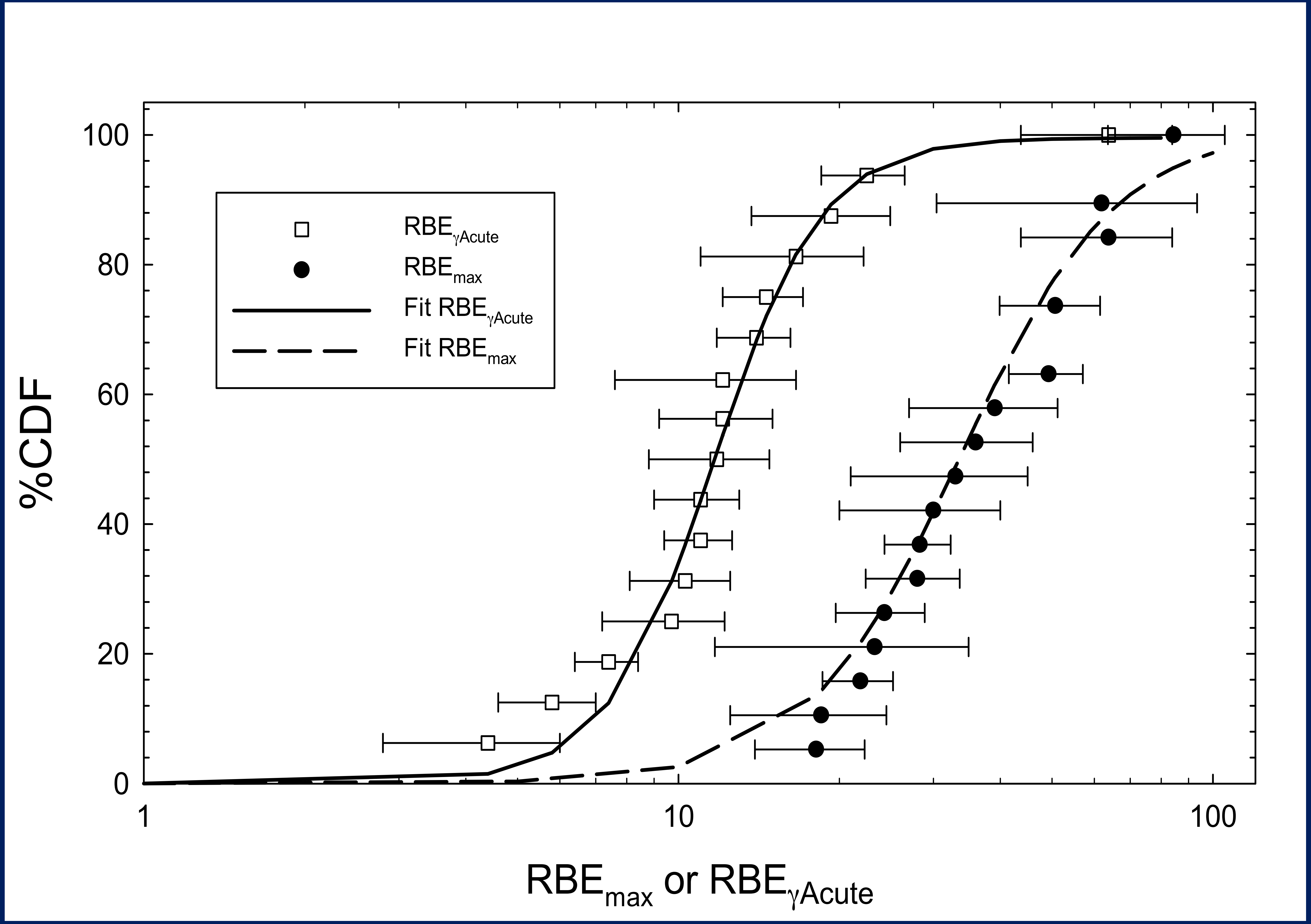
33

Estimates of, RBE_{max}, the tumor specific DDREF, and $RBE_{\gamma Acute}$ for low dose HZE particles or neutrons relative to acute $\gamma_{\text{-rays}}$.

Tumor	Model	Sex	Radiation,	RBE_{max}	DDREF	$RBE_{\gamma Acute}$
Harderian Gland*	B6CF1 mice	F	Fe, 180 (600 MeV/u)	39.6±11.5 27 28	- - 2.17 ± 1.1	- - 14
Harderian Gland	B6CF1 mice	F	Ar SOBP**, ~200	27	-	-
Heptocellular carcinoma	CBA mice	M	Fe, 155 (1 GeV/u)	Not Estimated	-	50.9±9.9
Heptocellular	C3H/HeNCrl mice	M	Fe (600 MeV/u), 175	Not Estimated	-	66.9±41.1
Heptocellular	C3H/HeNCrl mice	M	Si, (300 MeV/u), 70	Not Estimated	-	73.5±46.6
Lung	BALB/c mice	F	Fission neutrons	33±12	2.8	11.8
Mammary	Balbc mice	F	Fission neutrons	18.5±6	1.9	9.7
Pituitary	RFM mice	F	Fission neutrons	59±52	2.6	22.5
Harderian Gland	RFM mice	F	Fission neutrons	36±10	2.5	14.6
All Epithelial	B6CF1 mice	M	Fission neutrons	28.3±4.0	2.3±0.3	12.1±4.5
Lung	B6CF1 mice	M	Fission neutrons	24.3±4.6	2.2±0.3	11.0±2
Liver	B6CF1 mice	M	Fission neutrons	39.1±12.1	2.0±0.3	19.3±5.6
Glandular and Reproductive Organs	B6CF1 mice	M	Fission neutrons	49.3±7.8	4.3±0.3	16.6±5.6
Harderian Gland	B6CF1 mice	M	Fission neutrons	50.7±10.8	4.7±0.3	12.1±2.9
All Epithelial	B6CF1 mice	F	Fission neutrons	21.9±3.3	1.7±0.3	11.0±1.6
Lung	B6CF1 mice	F	Fission neutrons	18.1±4.2	1.8±0.3	10.3±2.2
Liver	B6CF1 mice	F	Fission neutrons	23.3±11.6	5.9±0.3	4.4±1.6
Glandular Reproduct	B6CF1 mice	F	Fission neutrons	84.4±20.8	12.2±0.3	7.4±1
Harderian Gland	B6CF1 mice	F	Fission neutrons	61.9+31.5	8.7±0.3	5.8±1.2

Data of Fry et al., Alpen et al.. Weil et al., Grahn et al. (24 week) and Ullrich et al.

Reducing Uncertainty in QF_{max} parameter



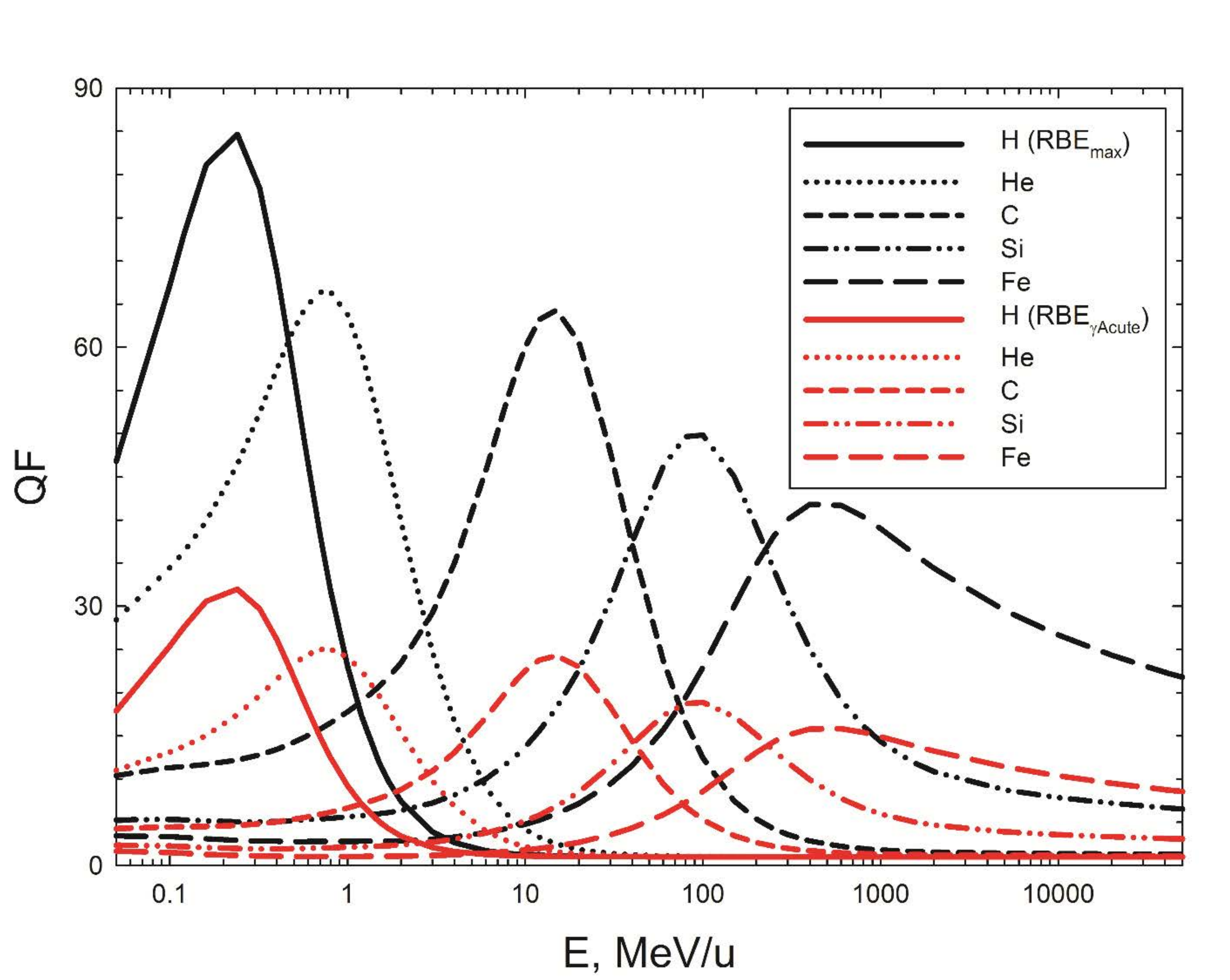
Cucinotta PLoS One (2015)

Revised NASA Quality Factor- 2015

based on mouse solid tumor RBE data for neutrons and HZE particles against low dose-rate or acute gamma-rays

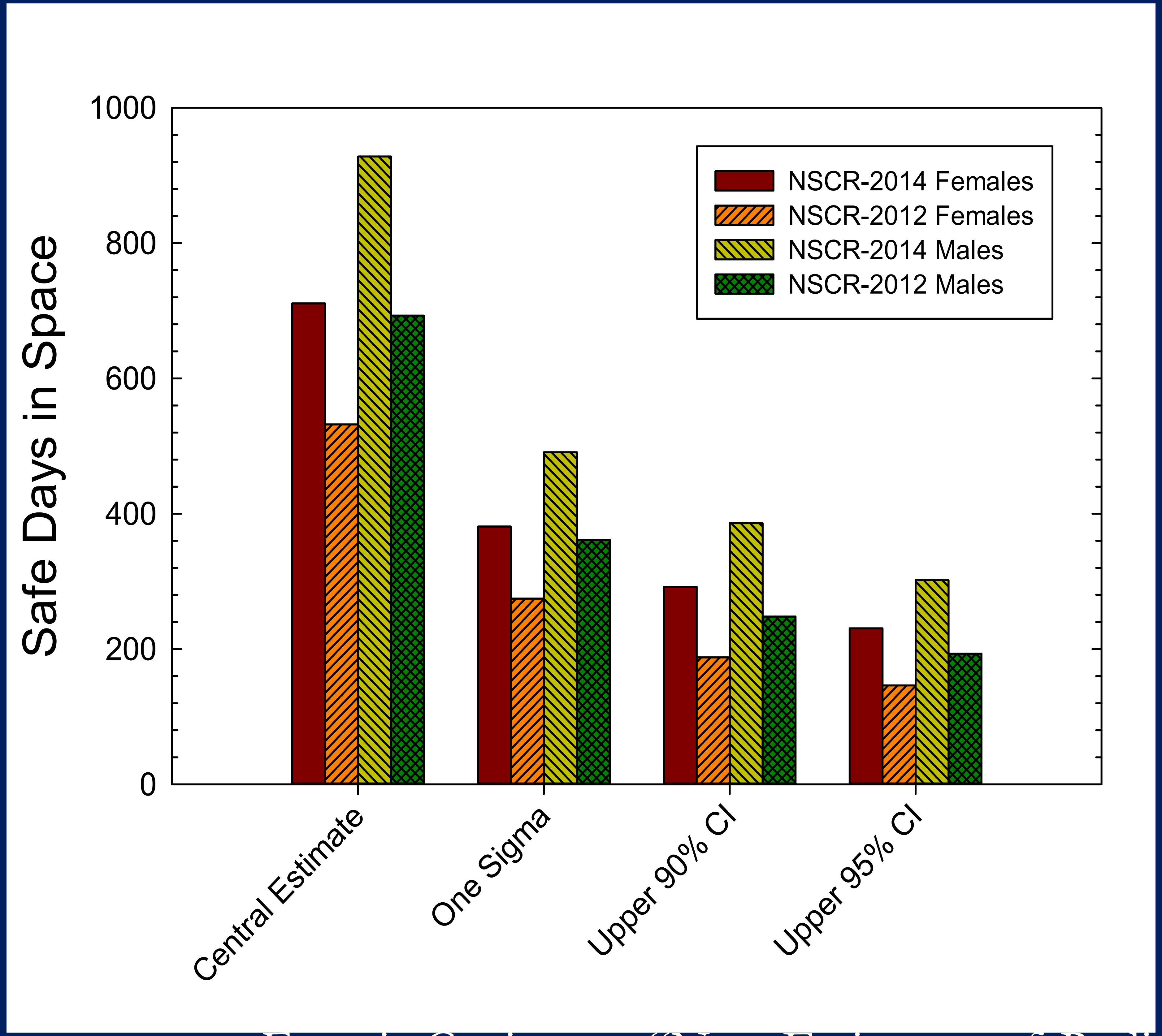
RBE or QF for Fission neutrons are averaged over low energy proton, HI recoils etc. Spectra

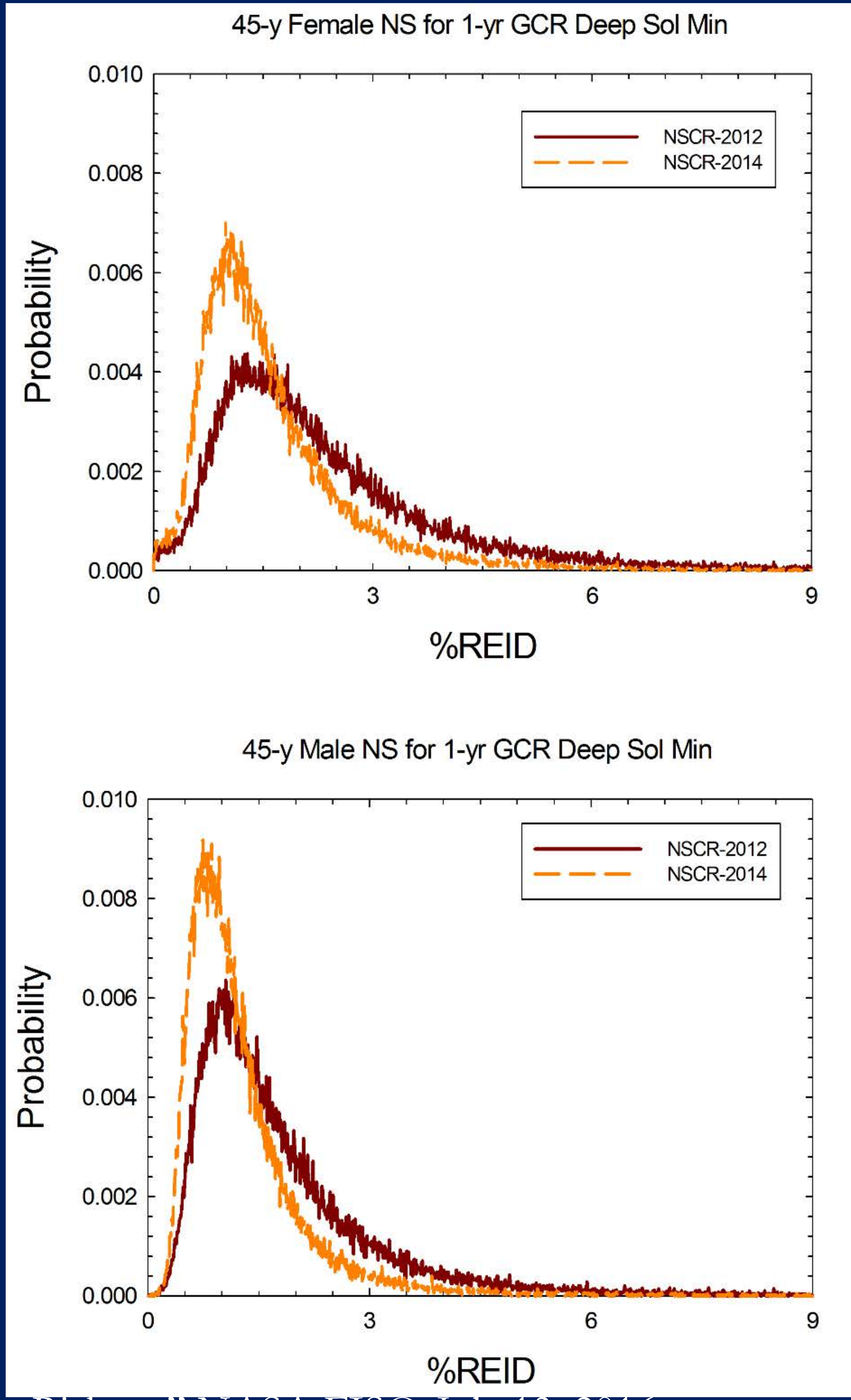
Results suggest Fission neutrons and HZE Iron have similar RBEs and not max effective radiations

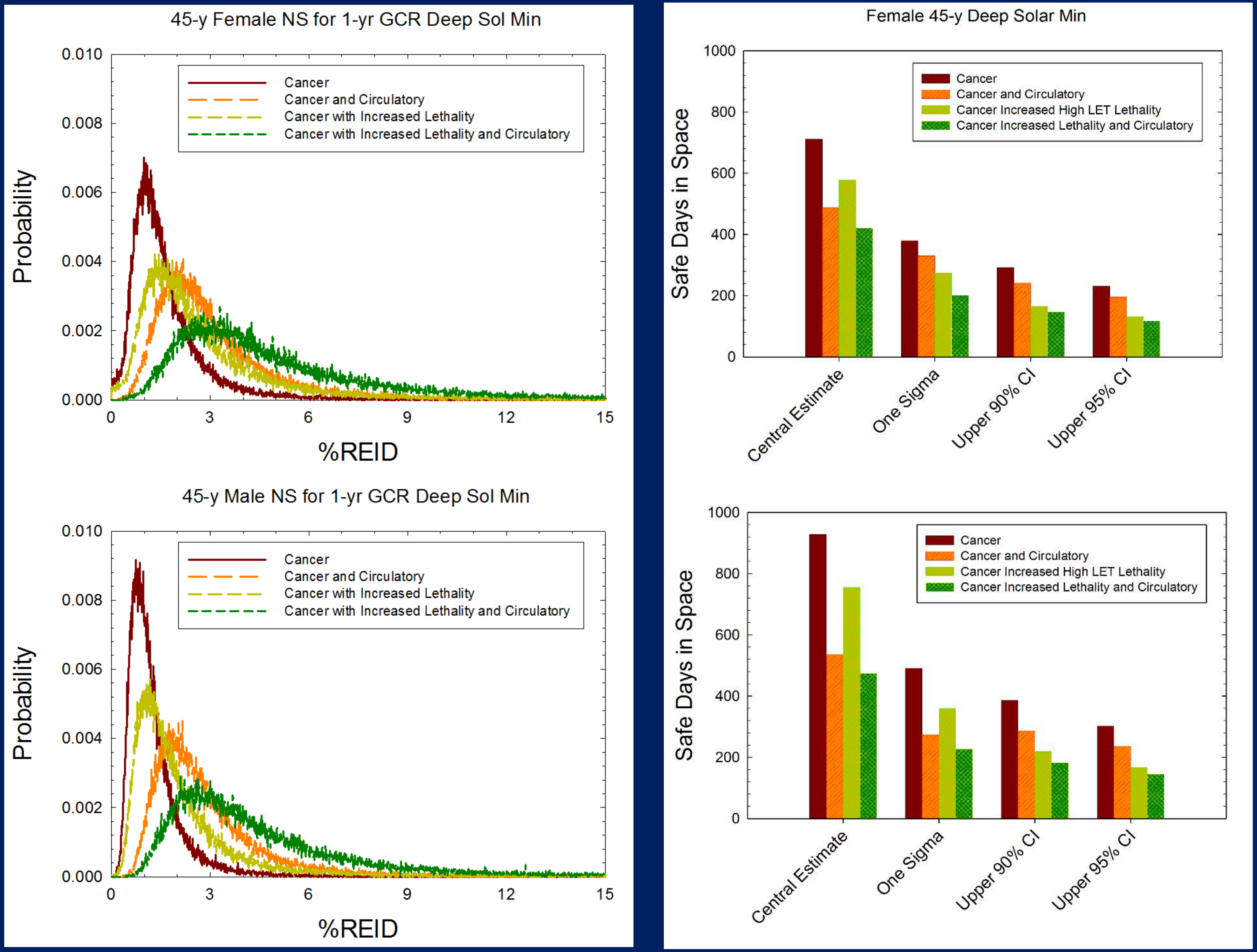


Cucinotta PloS One (2015)

Revised NSCR adds ~120 Safe Days in Space
Risk and Uncertainties reduced ~30% in this new approach







Cucinotta et al., Life Sci Space Res (2015)

Francis Cucinotta, "New Estimates of Radiation Risks…" NASA FISO, July 13, 2016

Predictions of percentage risk of exposure induced death (%REID) for 1-year space missions at deep solar minimum.

Table 2. Predictions under different assumptions of the %REID (mean values), and 90% or 95% confidence intervals for annual GCR exposure in deep space with 20 g/cm^2 aluminum shielding. Predictions shown are for 45-y Feale or Male never-smokers for the 2009 GCR environment and the average annual GCR exposure over many solar cycles.

	%REID	90% CI	95% CI	REID	90% CI	95% CI
	Females Average GCR environment			Females 2009 GCR environment		
Cancer	1.16	[0.37, 2.83]	[0.27, 3.7]	1.54	[0.5, 3.74]	[0.37, 4.76]
Cancer + Circulatory	1.69	[0.81, 3.41]	[0.69, 4.23]	2.25	[1.07, 4.53]	[0.93, 5.58]
Cancer with increased high LET lethality	1.42	[0.53, 5.25]	[0.39, 6.63]	1.89	[0.72, 6.67]	[0.53, 8.45]
Cancer with increased high LET lethality + Circulatory	1.95	[0.99, 5.77]	[0.81, 7.34]	2.6	[1.33, 7.54]	[1.1, 9.51]
	Males Average GCR environment			Males 2009 GCR environment		
Cancer	0.88	[0.34, 2.09]	[0.28, 2.69]	1.18	[0.45, 2.83]	[0.38, 3.61]
Cancer + Circulatory	1.53	[0.85, 2.85]	[0.77, 3.41]	2.04	[1.13, 3.81]	[1.0, 4.59]
Cancer with increased high LET lethality	1.09	[0.46, 3.81]	[0.39, 5.04]	1.45	[0.62, 5.0]	[0.52, 6.47]
Cancer with increased high LET lethality + Circulatory	1.73	[1.01, 4.51]	[0.9, 5.81]	2.31	[1.34, 5.94]	[1.19, 7.46]

Francis Cucinotta, "New Estimates of Radiation Risks…" NASA FISO, July 13, 2016

Major Unanswered Questions in Cancer Risk Estimates

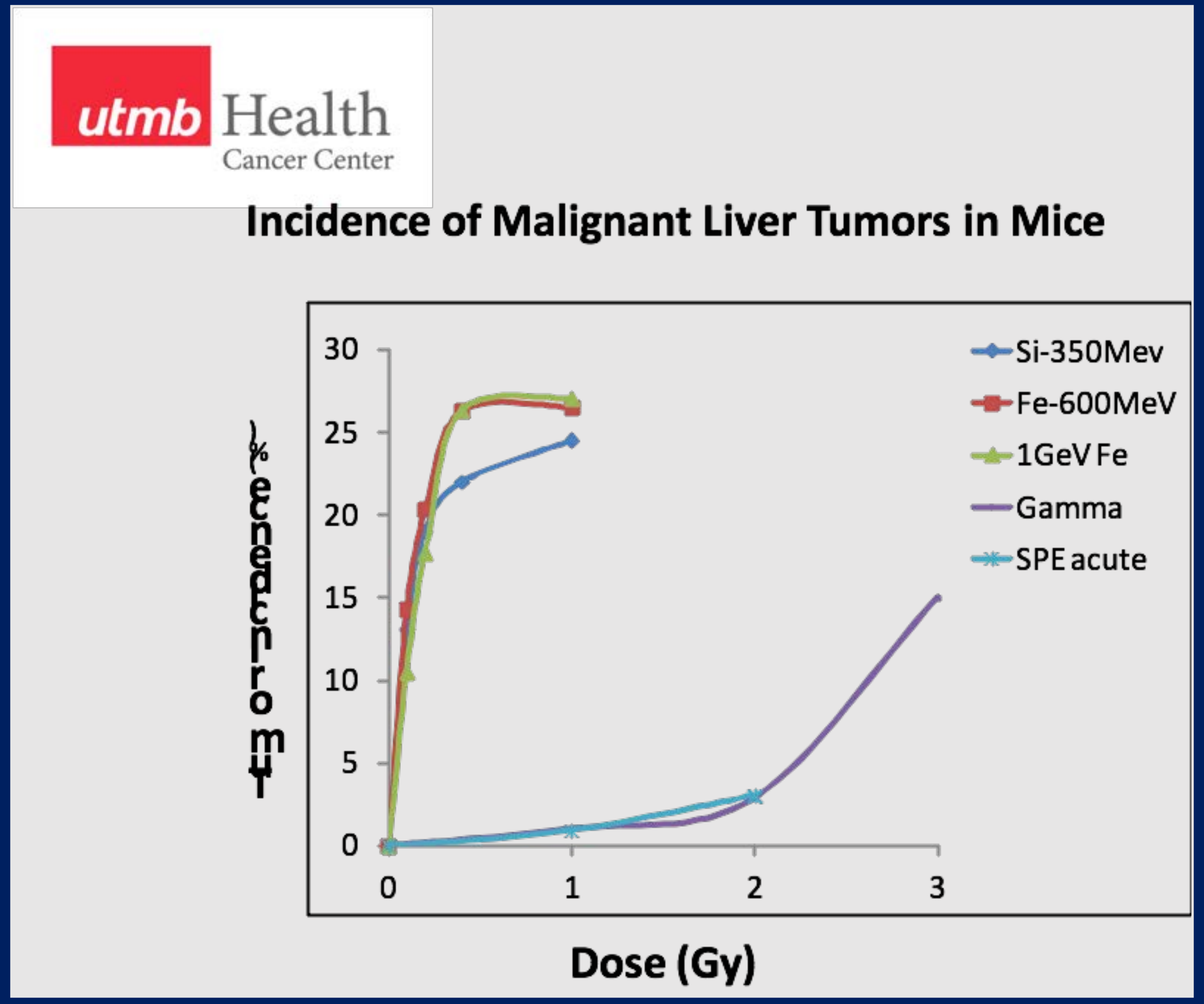
1) There is a lack of Animal Data for Heavy ion quality factors for major tissues in humans (lung, breast, stomach, etc.). Will NASA ever fund such studies?
2) Are the tumors produced by Heavy ions and Neutrons more malignant than that of Gamma-rays?
3) Do Inverse Dose-Rate Effects Occur for High LET radiation?
4) Do Non-Targeted Effects (NTE) dominate dose-responses at space relevant doses?

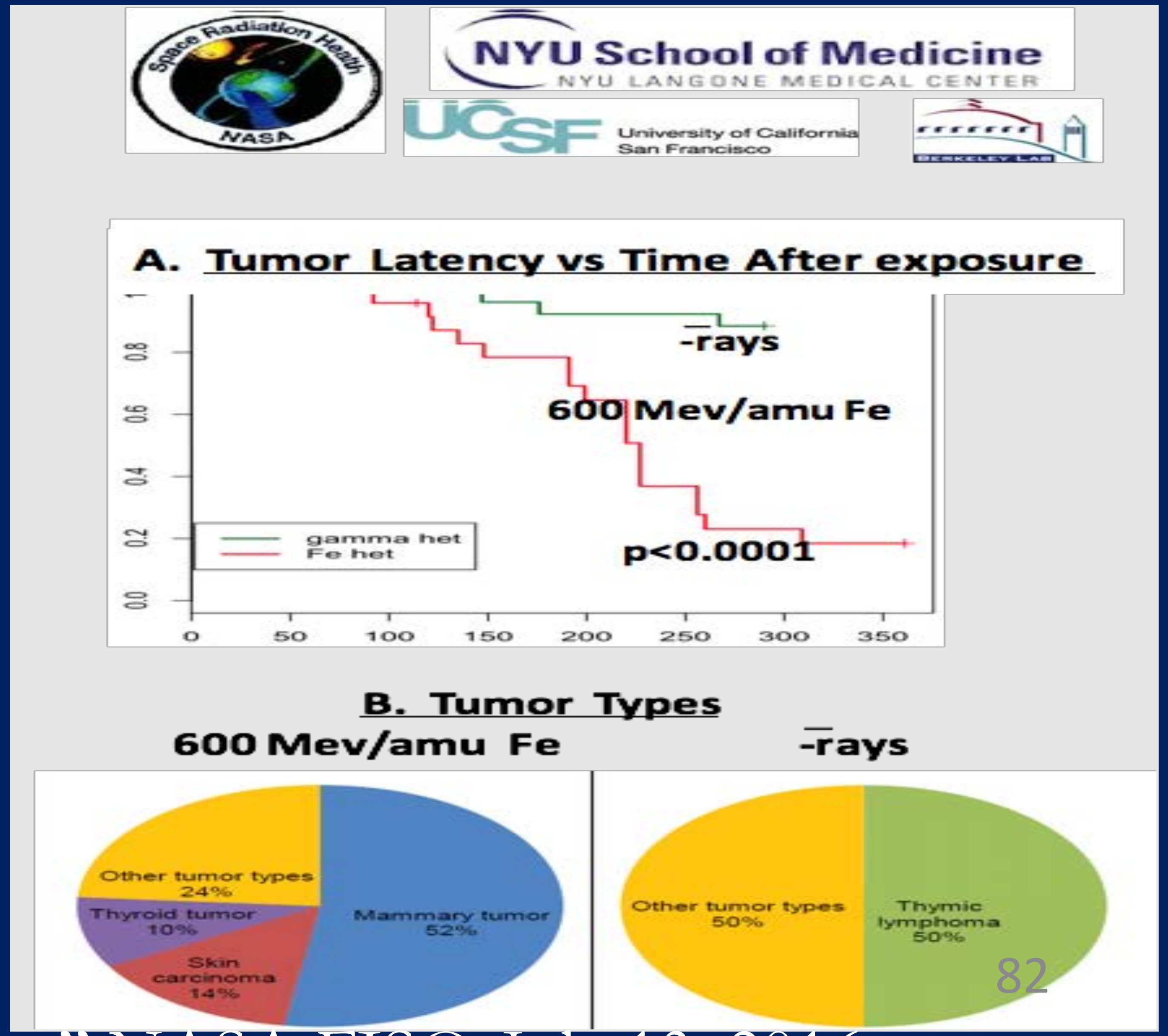
1) Lack of Data for Human Tissues

- Experts agree that Mice are reasonable model to estimate Quality Factors and Dose-Rate modifiers.
- However, human data suggests Lung, Stomach, Breast, Colon, Bladder etc. dominate human radiation risk.
- Mouse experiments show wide variation in radiation quality effects for different tumors for gamma-rays and neutrons.
- NASA has only funded a 1970's model of Harderian Gland tumors with 3 or more particle beams.
  - H. Gland does not occur in Humans.
  - Only limited data available for relevant tumor types!
- 21st Century Mouse models have not been funded for risk estimates, only limited mechanistic studies.
- <u>Major implications leading to large uncertainties which reflects variability in Available data rather than Best Data.</u>

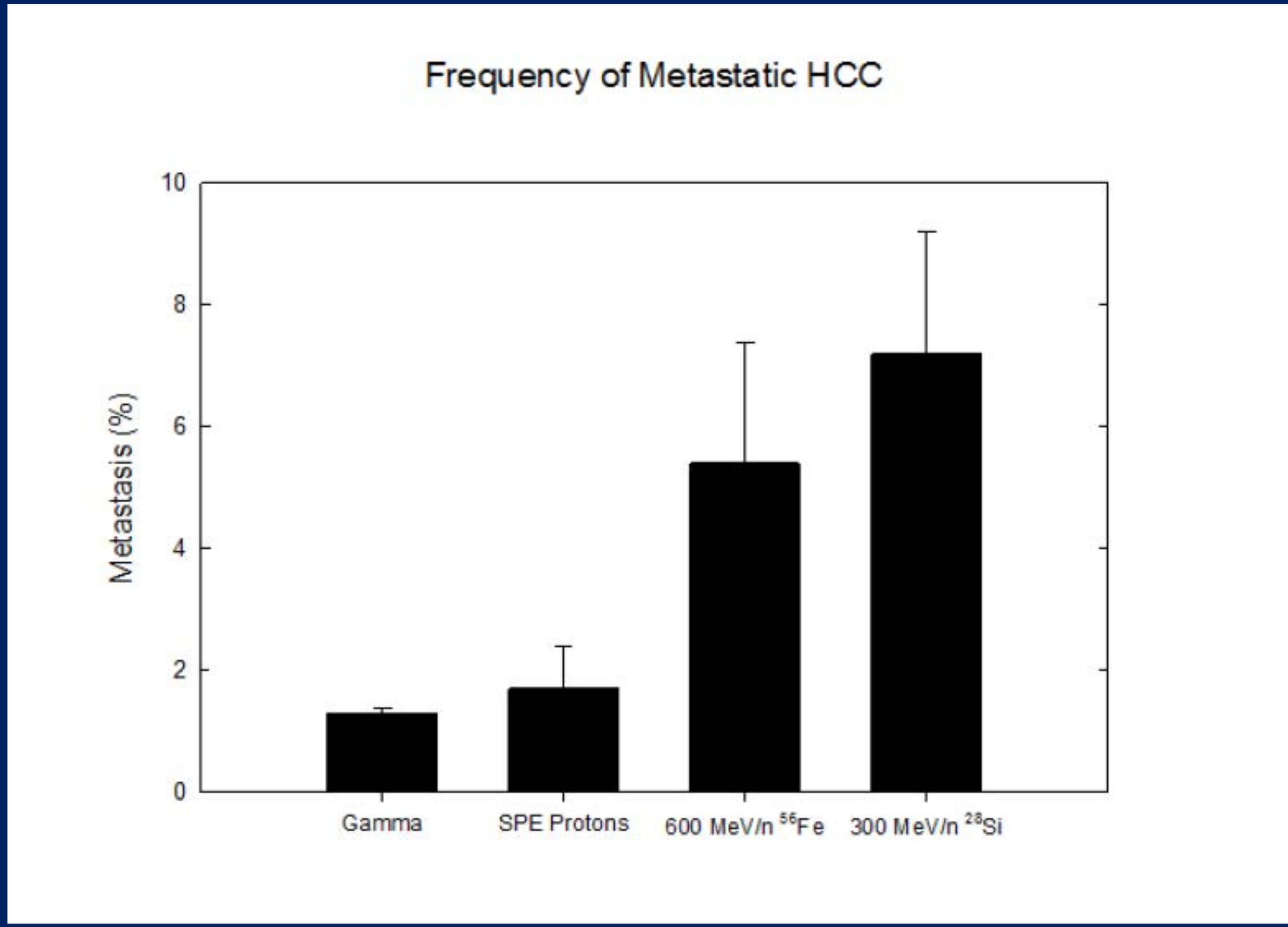
2) Qualitative Differences in Cancer Risks from GCR

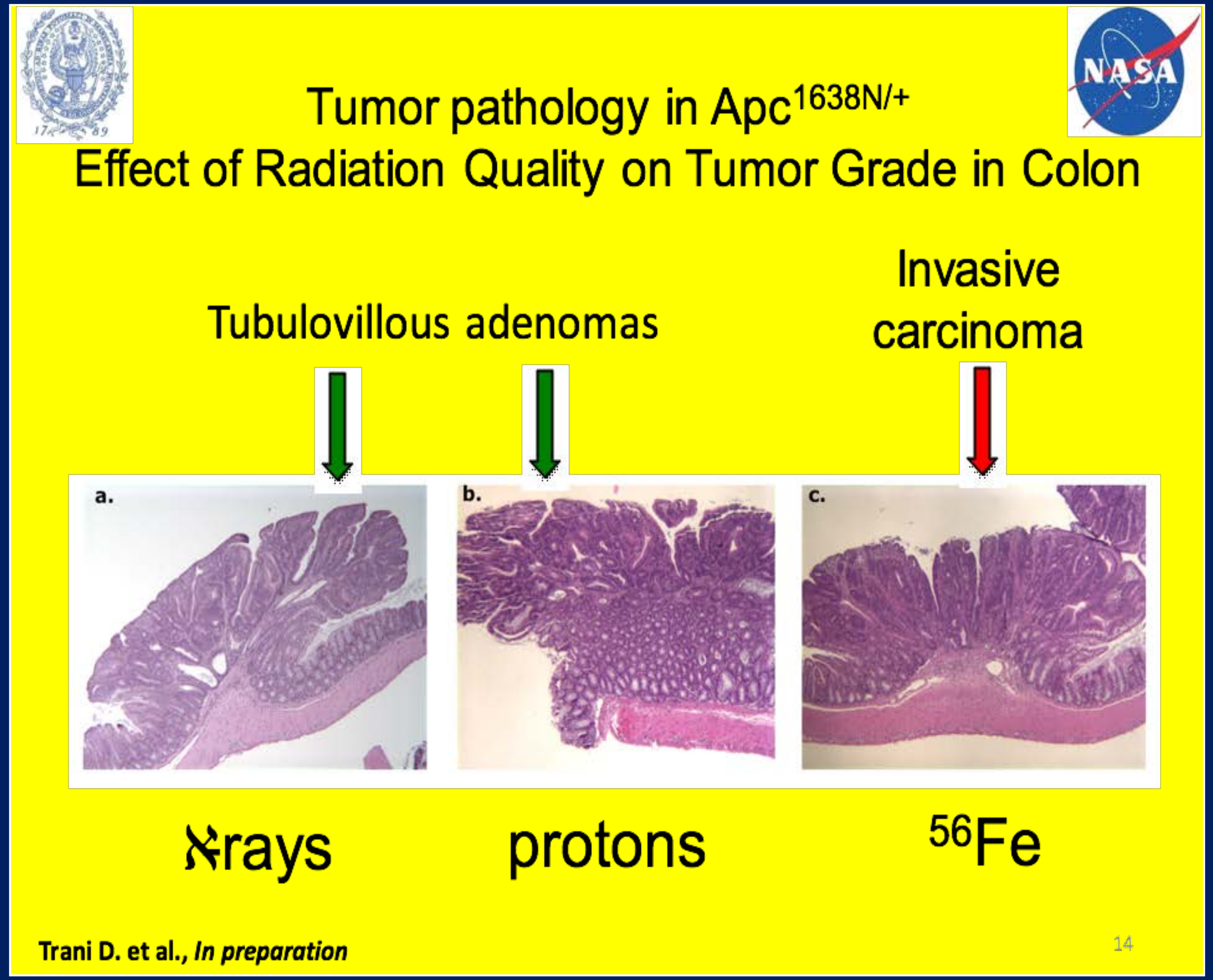
- Risk Models only account for quantitative differences using Quality Factors (QFs) or PDFs
- Issues emerging from research studies of GCR Solid cancer risks
  - Earlier appearance and aggressive tumors not seen with controls, gamma-rays or proton induced tumors
  - Non-linear response at low dose due to Non-Targeted Effects confounds conventional paradigms and RBE estimates
  - SPE (proton) tumors are similar to background tumors





GCR Heavy ions produce more aggressive tumors compared to background or X-ray tumors





UTMB NSCOR- PI Robert Ullrich
Shows much higher occurrence of metastatic Liver (HCC) tumors from GCR Fe or Si nuclei compared to gamma-rays or protons

Georgetown NSCOR- PI Al Fornace
Shows much higher occurrence of invasive carcinomas tumors from GCR Fe nuclei compared to gamma-rays or protons

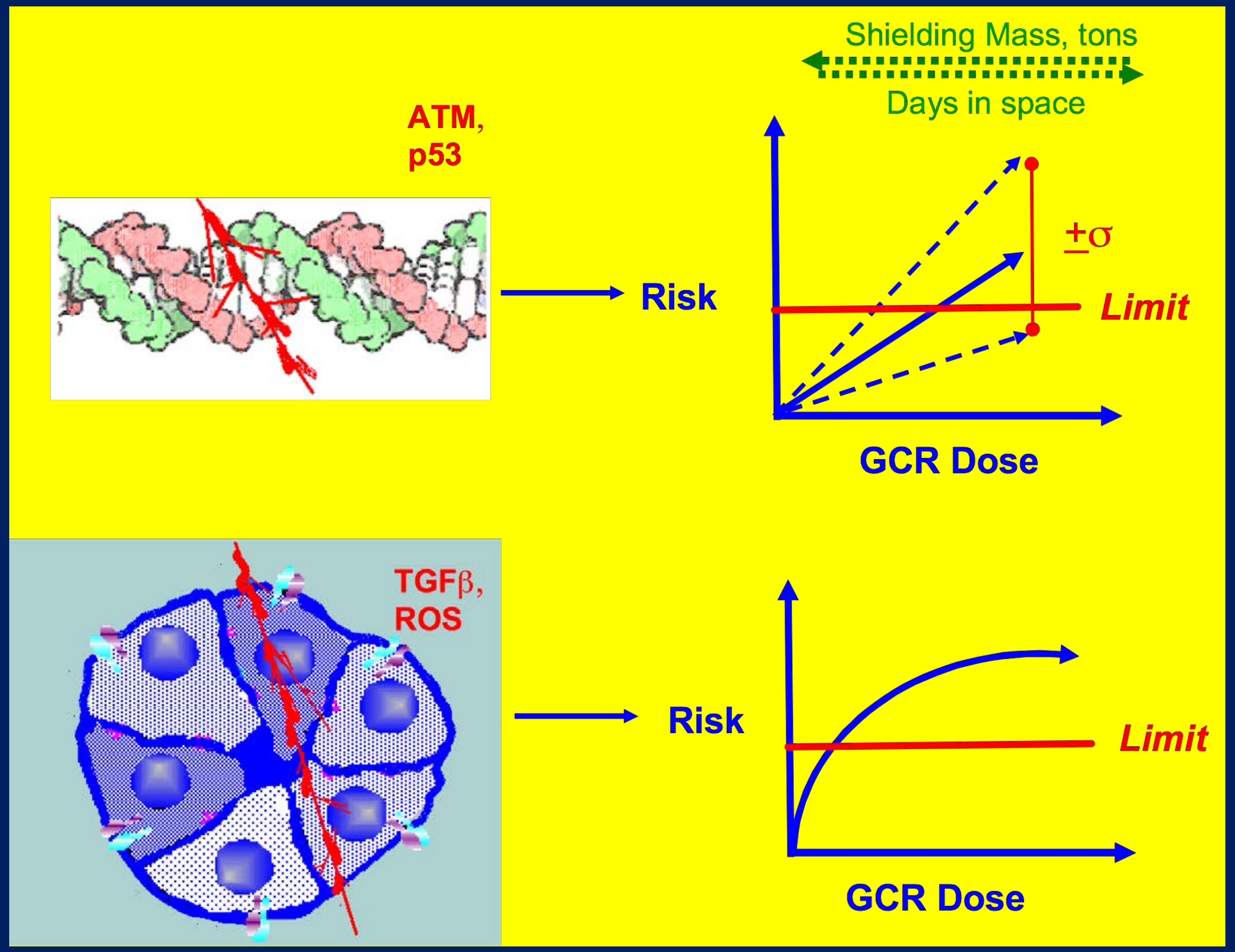
3) Inverse Dose-Rate Effects?

- Studies with fission neutrons demonstrated an Inverse dose-rate effect for solid tumors in mice where chronic exposures were more effective than acute exposures.
  - Reports of inverse dose-rate effects varied with tissue type, dose, sex, etc.
  - Cell sterilization effects are confounder.
  - Not observed with gamma-rays or X rays.
- Short-term studies with HZE particles have only considered dose fractionation and do not suggest an inverse-dose rate effect occurs.
- Long-term chronic HZE particle irradiation similar to old fission neutron studies have not been conducted
- NSCR-2015 utilizes Grahn et al. 24 week Fission neutron data. Therefore inverse dose-rate effects should be reflected in RBE values considered, however lacking underlying understanding of the effect.

4) Non-Targeted Effects and GCR

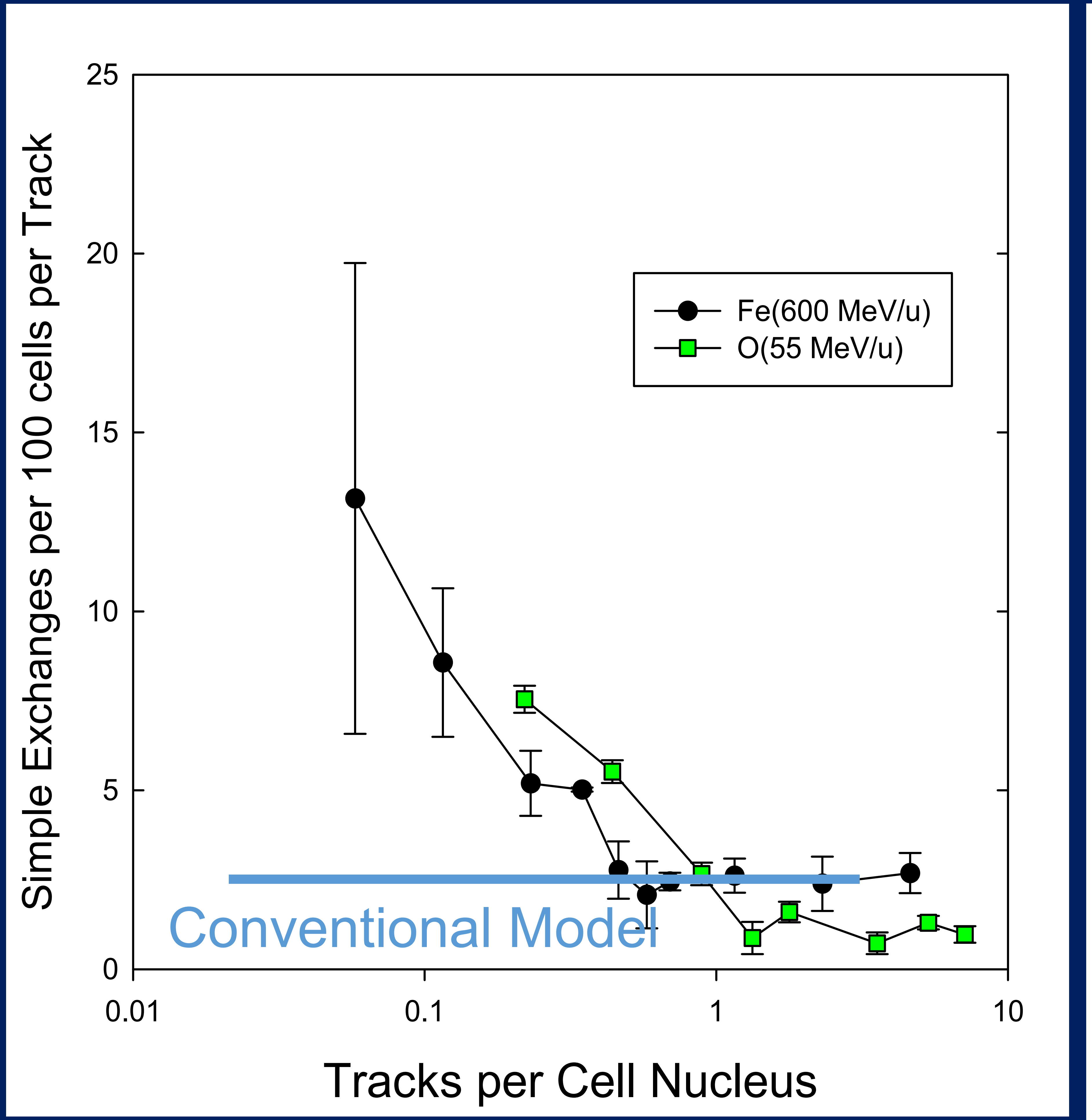
- Non-targeted effects (NTE) include genomic instability in the progeny of irradiated cells and various bystander effects
- NTE challenges linear model used at NASA is a potential game-changer on role of Mission length, shielding and biological countermeasures
- Non-linear or "flat" dose responses is suggested for many non-targeted effects at low dose
  - Epithelial-mesenchymal transition (EMT)
  - Chromosomal aberrations and micro-nuclei
  - Mouse solid tumors
  - Gene expression and signaling
- Understanding NTE's is critical research area to reduce cancer risk uncertainty

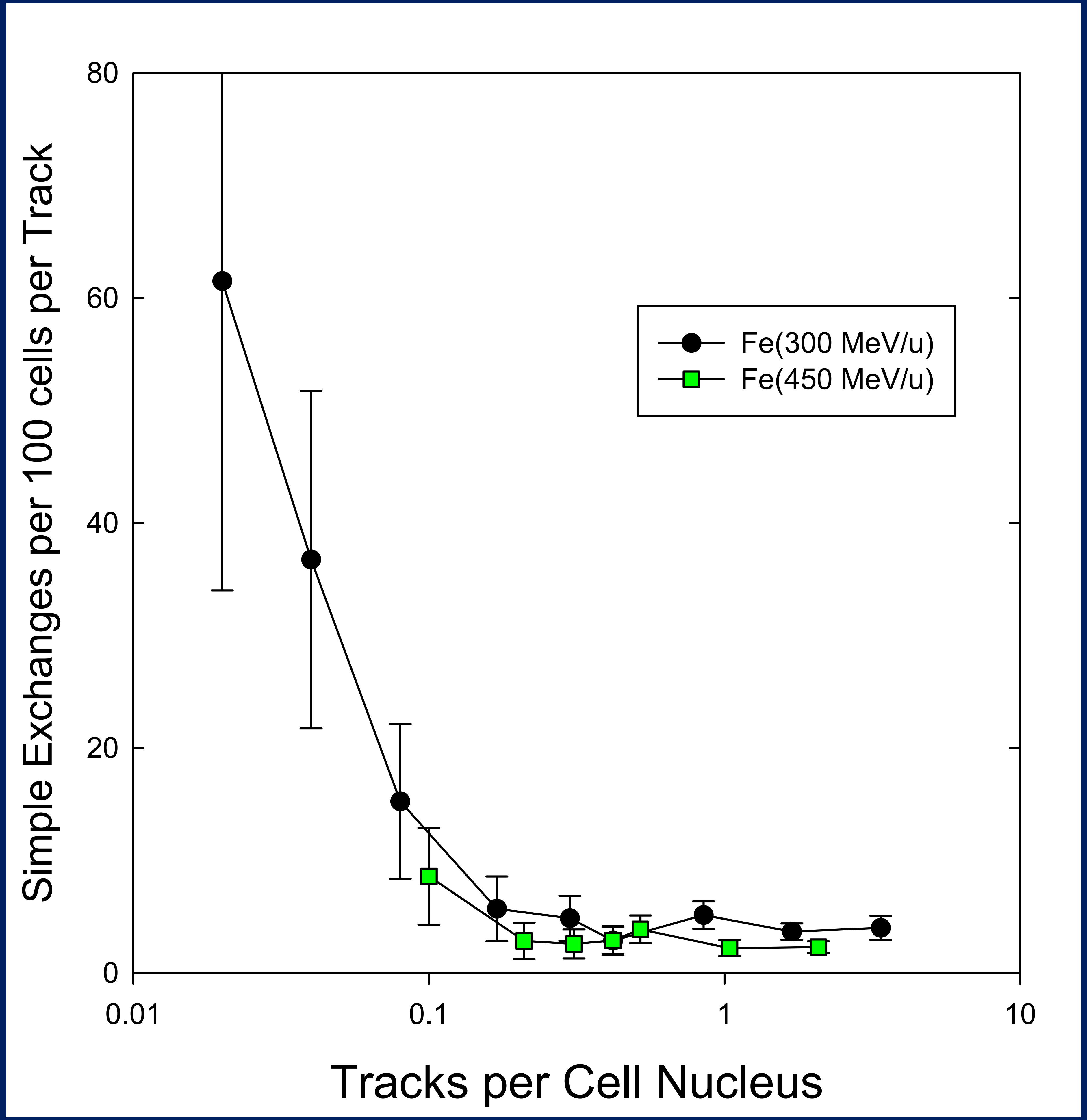
Conventional vs NTE Dose Response



The Lancet Oncology (2006)

Broad Beam Heavy Ion Irradiation Leads to Non-Linear Response at low doses for Chromosome Aberrations in Human Fibroblasts but not Lymphocytes





Hada, George, Wang and Cucinotta, Radiat Res (2014)

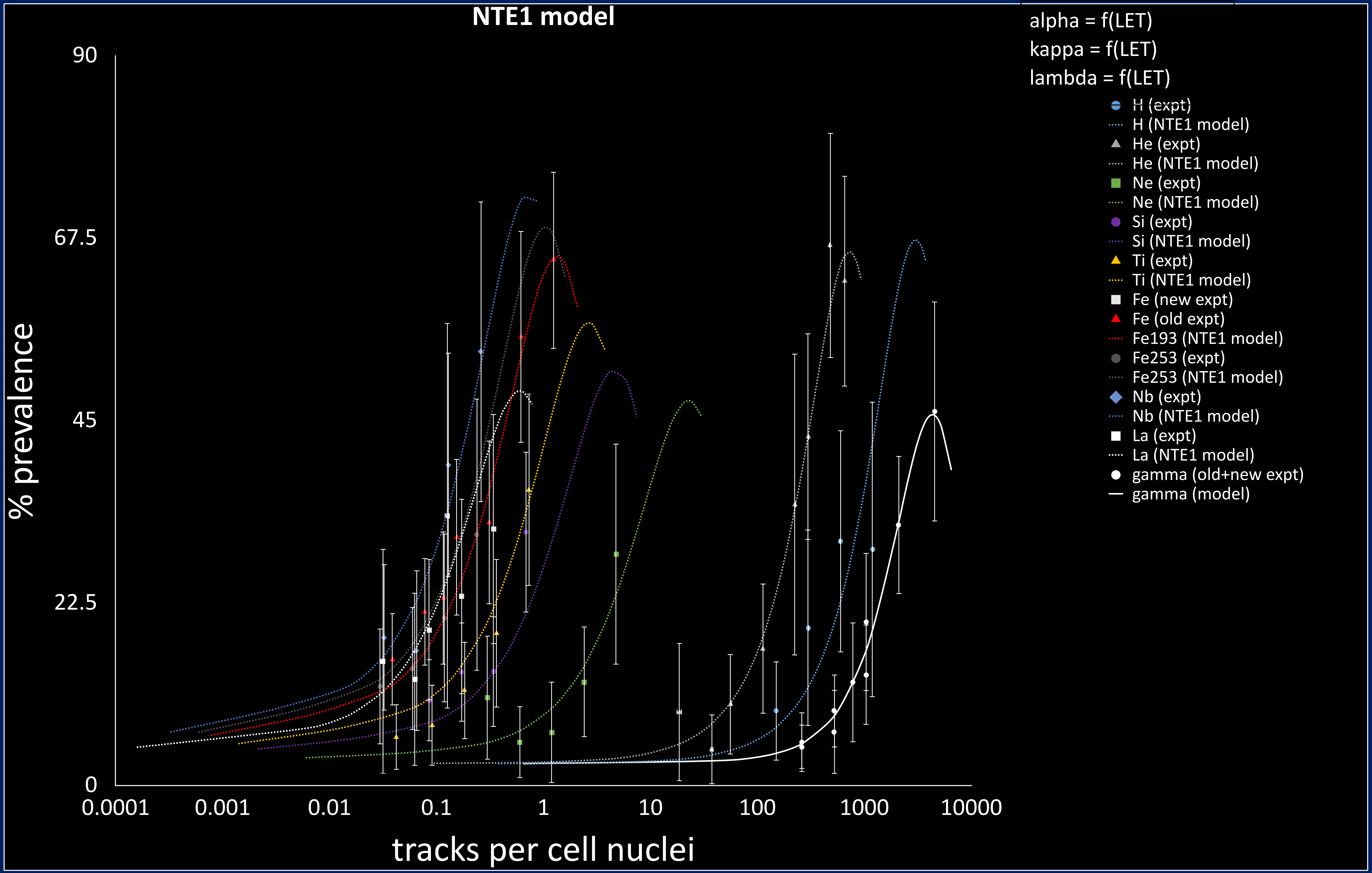
H. Gland Experiment Update

- E. Blakely has collected data on low dose irradiation of B6CF1 mice with Si, Ti, and Fe particles. This is partly a continuation of experiment funded largely by DoE in 1980s and early 1990s (Fry and Alpen).
  - Most complete set of Heavy ion tumor data (p, He, Ne, Fe, Nb, La)
- UNLV (E. Cacao and F. Cucinotta) have performed data analysis of TE and NTE dose response models and RBE_{max} and $RBE_{\gamma Acute}$ estimates.
- New and old Gamma-ray data and Fe particle data are not significantly different; One-way repeated Nova: 0.57 and 0.24, respectively.
  - Old expt. used partial body with pituitary isografts
  - New expt. whole body with data on other tumors collected

Table 6. Parameter estimates for combined data sets for TE and NTE models for the dose response for percentage tumor prevalence. For each statistical test considered, which adjust for the differences in the number of model parameters, the model providing the optimal fit is shown in bold-face.

Parameter	TE	NTE1	NTE2
P_0	3.07±0.36 (<10^{-4})	2.75±0.34 (<10^{-4})	2.77+0.36 (<10^{-4})
α_0, Gy^{-1}	7.65±3.94 (<0.058)	10.05±3.56 (<0.007)	1.21±4.5 (<0.789)
α_1, Gy^{-1} $(keV/\mu m)^{-1}$	1.25±0.14 (<10^{-4})	0.90±0.21 (<10^{-4})	1.07 ±0.14 (<10^{-4})
α_2, $(keV/\mu m)^{-1}$	0.0038±0.0004(<10^{-4})	0.0039±0.0009(<10^{-4})	0.0036 ±0.0003 (<10^{-4})
β, Gy^{-2}	6.02±3.51 (<0.093)	4.61±3.33 (<0.173)	9.24±3.46 (<0.01)
λ_0, Gy^{-1}	0.243±0.07 (<0.001)	0.219±0.078 (<0.007)	0.286±0.0533 (<10^{-4})
λ_1, Gy^{-1} $(keV/\mu m)^{-1}$	0.006±0.0036 (<0.097)	0.0047±0.0059(<0.424)	0.0042±0.0037 (<0.258)
λ_2, $(keV/\mu m)^{-1}$	0.0043±0.0027 (<0.124)	0.0051±0.0059 (<0.391)	0.0045±0.0041 (<0.277)
κ_1, $(keV/\mu m)^{-1}$	-	0.048±0.023 (<0.038)	3.14±1.13 (<0.008)
κ_2, $(keV/\mu m)^{-1}$	-	0.0028±0.0019 (<0.141)	-
Statistical Tests			
Adjusted R^2	0.9248	**0.9373**	0.9337
AIC	269.6	**260.8**	263.3
BIC	285.9	**281.3**	281.7

H. Tumor Fluence Response



H. Gland RBE Estimates in UNLV Combined Old and New Data Models (Chang et al. (2015))

Z	LET, keV/μm	RBE_{max}	$RBE_{\gamma Acute}$	RBE(NTE1) at 0.1 Gy	RBE(NTE1) at 0.01 Gy
1	0.4	1.78±0.92	0.90±0.44	0.92	1.11
2	1.6	2.10+0.98	1.06±0.46	1.14	1.90
10	25	7.86±2.07	3.96±0.81	5.19	16.26
14	70	16.28±3.81	8.21±1.34	11.25	38.56
22	107	21.07±4.86	10.63±1.69	14.81	52.46
26	175	26.18±6.13	13.20+2.16	18.86	69.75
26	193	26.91±6.36	13.57±2.26	19.50	72.87
26	253	28.01±6.87	14.13±2.53	20.70	79.84
41	464	23.34±6.89	11.77±2.86	18.45	78.53
57	953	8.61±3.92	4.34±1.84	7.83	39.21

Conclusions

- Revised Model estimates significantly reduce REID predictions and uncertainty bands.
- However large questions remain:
  - Too many experiments at non-relevant doses (>0.2 Gy)
  - Scarcity of HZE particle tumor data?
  - Inverse-dose rate effects for chronic irradiation?
  - Higher lethality of HZE particle tumors?
  - Non-targeted effects altering shape of dose response and increasing RBE estimates?
  - Non-cancer risks contributions to REID?
  - Does chronic inflammation occur at low dose?
  - Under-developed approaches to use transgenic animals and other new experimental models to estimate human space radiation risks?

Other material

Dose Response Models: Linear vs NTE?

- Non-Targeted Effect (NTE) paradigm's have emerged for describing low dose effects, including thresholds and non-linear dose responses
- For Heavy Charged Particles most experiments performed at less than one track/cell show that the best representative model is a step-function (Θ) plus a linear dose response:

$$\mathbf{R} = \mathbf{R_0} + \kappa\Theta(D_{th}) + \alpha \text{ Dose}$$

- Low Dose expts. show that expts. at moderate or high dose finding a linear dose response should be challenged and likely not useful for NASA
- RBEs in the NTE model will exceed linear extrapolation by a large amount:

$$RBE_{NTE} = RBE_{TE} (1 + D_{cross}/\text{Dose});$$ D_{cross} is dose where TE=NTE

Components to Solution of Space Radiation Problem

- The current risk for a Mars mission is nearly 3-fold above acceptable risk levels
- Baseline DRM for a 1000 day mission has >3-fold uncertainties, assumes aluminum shielding, and radiation sensitivity of the U.S. average population

Solution Component	Reduction Required	Need
Uncertainty reduction *Radiation quality effects, chronic exposure, etc.*	<1-fold (±100%)	Science understanding, radiobiology data-base for cancer, CNS, and other risks
Radiation Shielding *Materials, Optimization, and neutron minimization*	15 ±σ %	Testing and validation
Crew Selection *Never-smokers, Screening for sensitivity to GCR*	50 ±σ %	Biomarker developments, science discovery and verification, largely based on uncertainty reduction research
Biological Mitigator's *New approaches to chronic, high LET exposure protection*	30 ±σ %	Drug testing and discovery, and validation based on uncertainty reduction research
Dosimetry and Forecasting *Ensure minimal SPE threat*	**Solar max. safety**	Testing and validation

CNS Injury After High and Low Doses

- Higher Doses:
  - Generally restricted to white matter;
  - A late effect, appearing after a latent period;
  - Imaging and clinical changes;
  - Histology: demyelination, vascular damage, necrosis.
- Low Doses: Neurocognitive effects occur after radiation doses that do not result in overt tissue destruction:
  - Progressive, currently untreatable and poorly understood;
  - Hippocampal functions of learning, memory and spatial information processing;
  - Other poorly understood - Unknown pathogenesis.

Low priorities - Space Physics and Acute Radiation Syndrome Research

2013 National Academy of Sciences Review of NSCR-2010 Model

"The Committee considers that the radiation environment and shielding transport models used in the NASA's proposed model are a major step forward compared to previous models used. This is especially the case for the statistical solar particle event model. The current models have been developed by making extensive use of the available data and rigorous mathematical analysis. The uncertainties conservatively allocated to the space physics parameters are deemed to be adequate at this time, considering that the space physics uncertainties are only a minor contributor to the overall cancer risk assessment. <u>Although further research in this area could reduce the uncertainty, the law of diminishing returns may prevail</u>."

Human Research Program – External Review (2010)

Cancer 11: What are the most effective shielding approaches to mitigate cancer risks?

The 2012 HRP External Standing Review Panel (SRP) concluded:

"This is not properly a gap in the HRP IRP but an engineering problem. The HRP IRP provides the scientific basis on which shielding evaluations can be based, but additional experiments to develop shielding are not needed. In the future, a carefully defined measurement of a restricted set of critical parameters may be useful to validate such calculations. The SRP identified this task as being of lower priority and using resources that would be better applied to the biological investigations."

Cancer 12: What level of accuracy do NASA's space environment, transport code and cross sections describe radiation environments in space (ISS, Lunar, or Mars)?

"The Panel believes that, at this time, the accuracy of predicting particle fluxes in space (of the order of ±15%) is sufficient for risk prediction and could not be significantly improved without a major investment in resources better utilized in addressing other gaps."

HRP External Review (2010)

Cancer 13: What are the most effective approaches to integrate radiation shielding analysis codes with collaborative engineering design environments used by spacecraft and planetary habitat design efforts?

SRP: *"This is a technology transfer problem and not a research problem. It should be addressed by the appropriate engineering programs and the resources devoted to it would be better utilized by expanding support of the higher priority gaps."*

Acute – 5: What are the optimal SPE alert and dosimetry technologies for EVAs?

SRP: *"This is a technology issue/engineering problem. If this gap remains, the SRP recommends assigning it a lower priority.*

Acute – 6: What are the most effective shielding approaches to mitigate acute radiation risks, how do we know, and implement?

SRP: "This is a technology transfer problem and not a research problem. It should be addressed by the appropriate engineering programs and the resources devoted to it would be better utilized by expanding support of the higher priority gaps."

GCR Environment Model

- Local Inter-stellar Spectra (LIS) (Leaky Box Model)

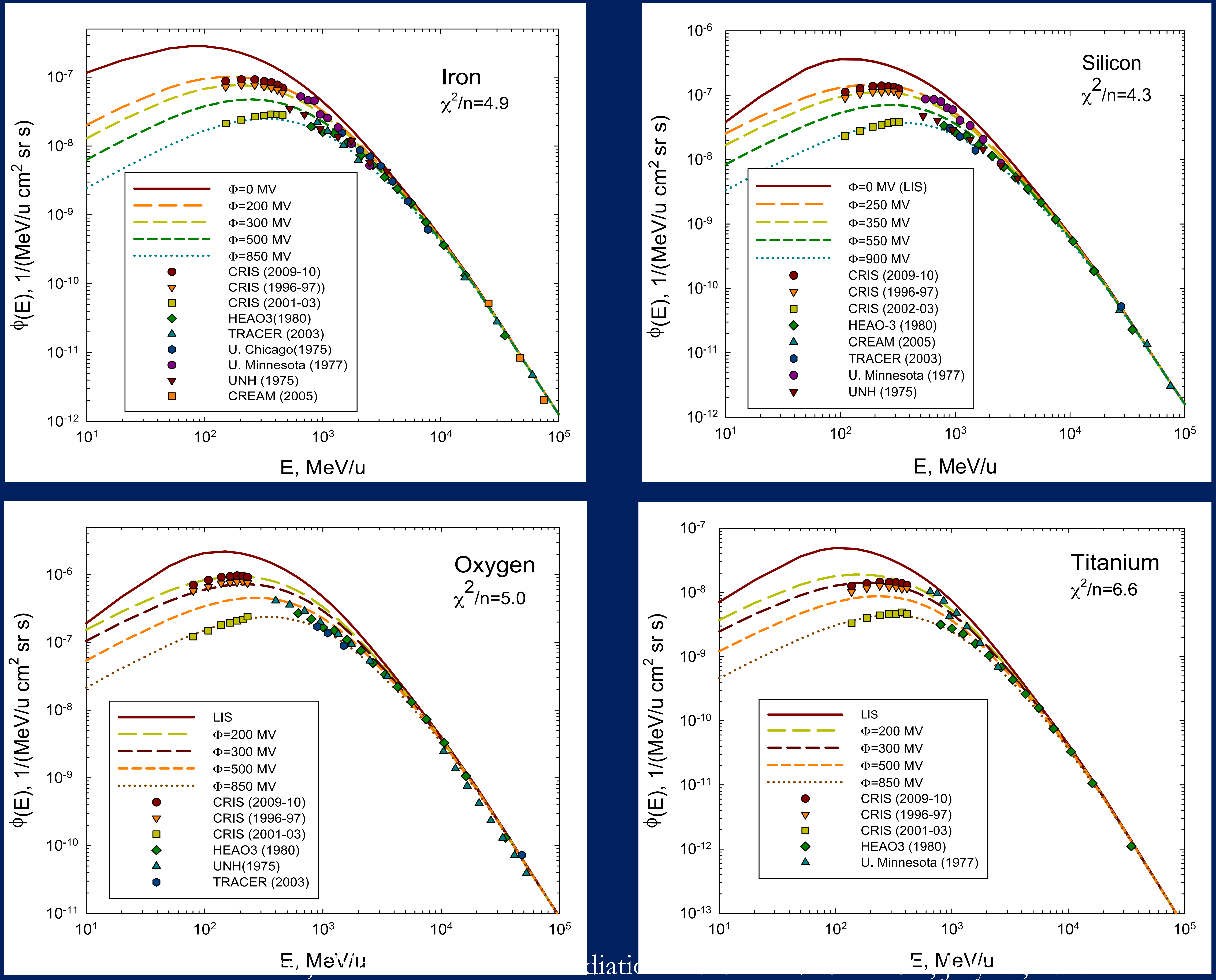
$$q_i + \sum_j \varphi_j \left(\frac{1}{\Lambda_{ji}^{\text{spall}}} + \frac{1}{\Lambda_{ji}^{\text{decay}}} + \frac{1}{\Lambda_{ji}^{\delta Q}} \right) = \varphi_i \left(\frac{1}{\Lambda_i^{\text{spall}}} + \frac{1}{\Lambda_i^{\text{decay}}} + \frac{1}{\Lambda_i^{\delta Q}} + \frac{1}{\Lambda_i^{\text{esc}}} \right) - \frac{d(w_i \varphi_i)}{d\varepsilon}.$$

- Modification of CRIS Leaky Box model (George et al. 2009; Lave et al., 2013)

$$F_{LIS}(Z,E) = \frac{F_0 E^{-\gamma}}{[1 + (E_1/E)^{\alpha_1} + (E_2/E)^{\alpha_2}]}$$

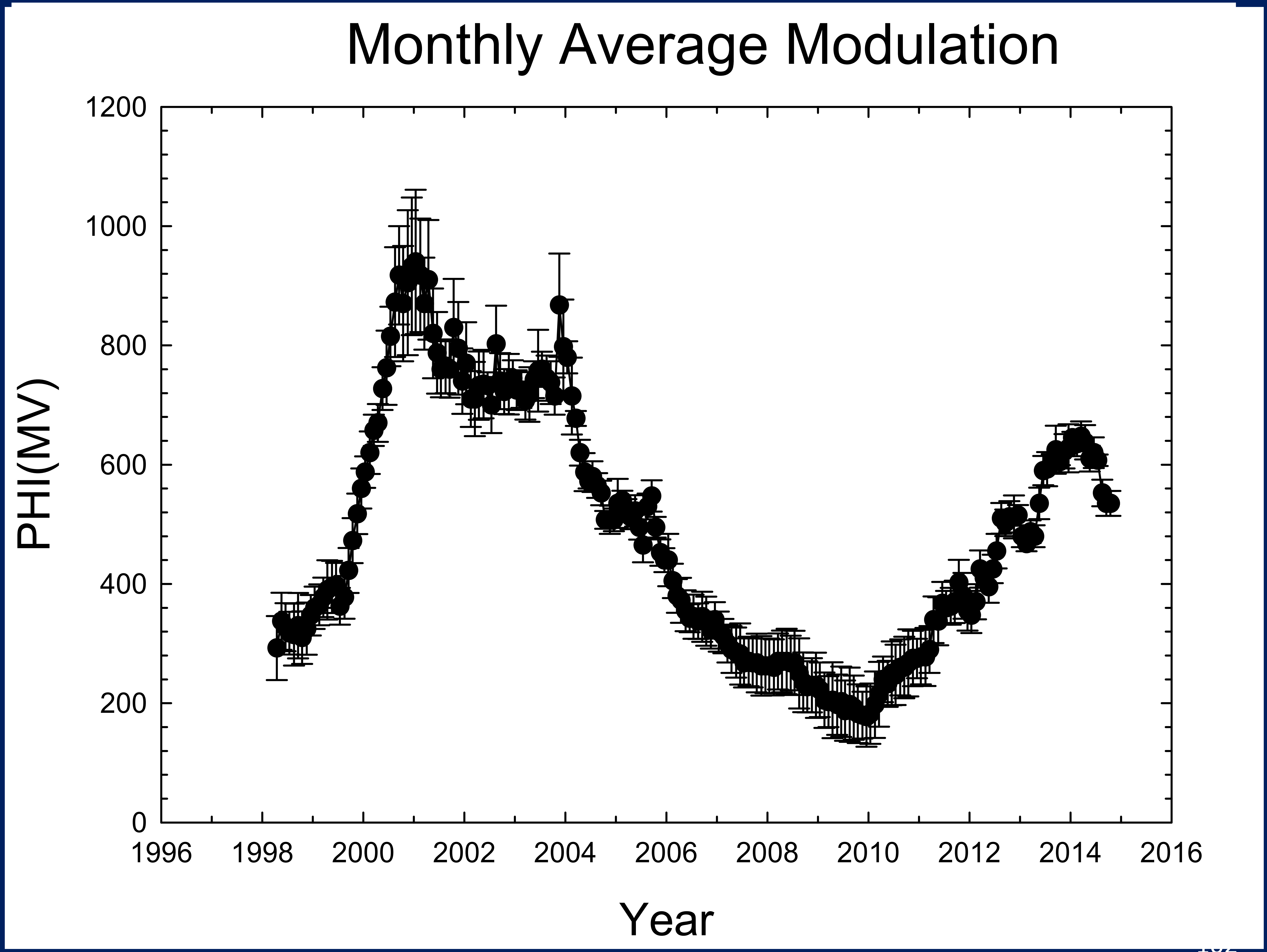
$$\gamma(E) = \gamma_0 + \gamma_1 [1 - e^{-(E/15000)}]^2$$

- Parker Theory of Solar Modulation

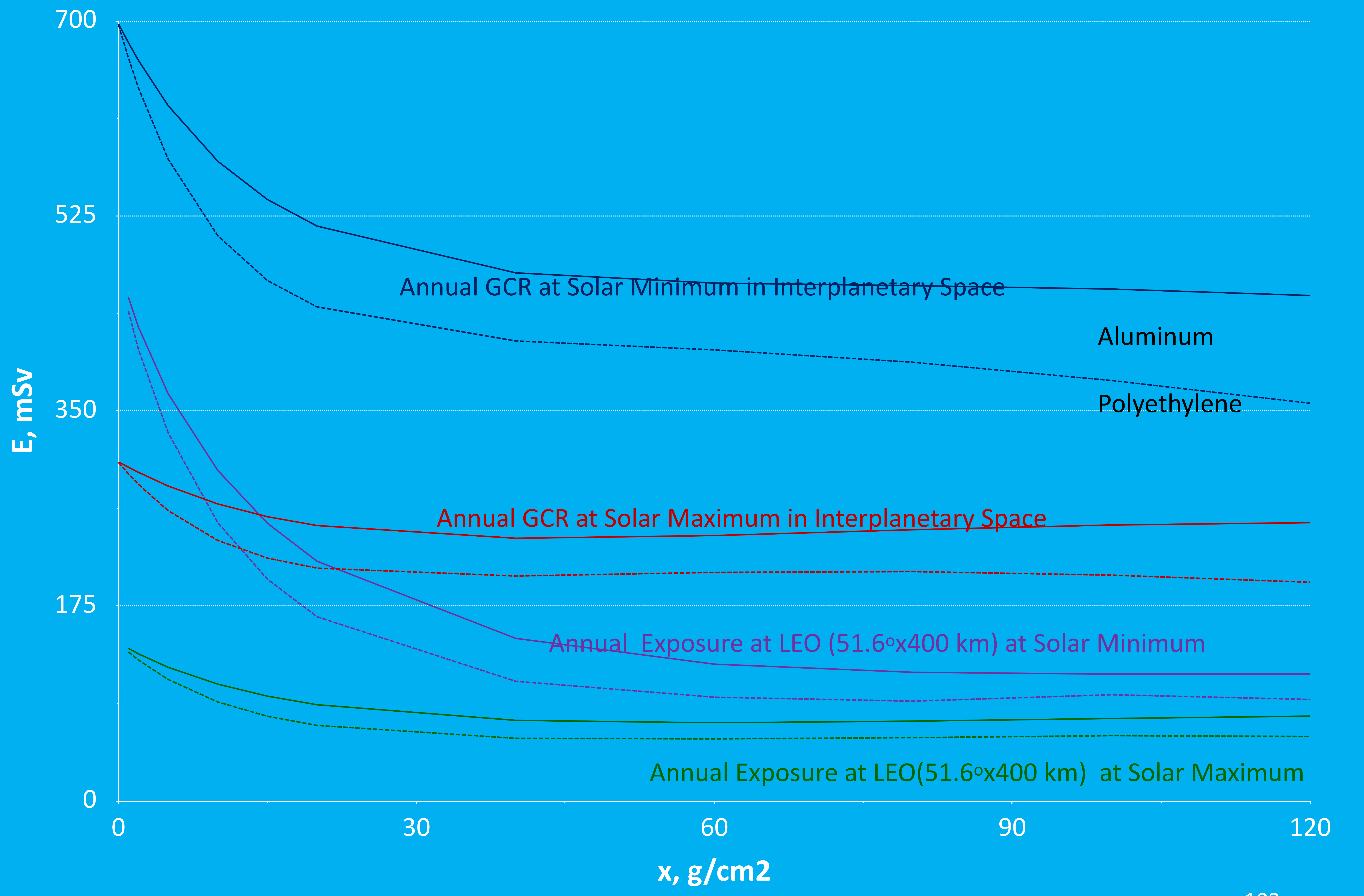


Iron
χ²/n=4.9
Φ=0 MV
Φ=200 MV
Φ=300 MV
Φ=500 MV
Φ=850 MV
CRIS (2009-10)
CRIS (1996-97))
CRIS (2001-03)
HEAO3(1980)
TRACER (2003)
U. Chicago(1975)
U. Minnesota (1977)
UNH (1975)
CREAM (2005)
Silicon
χ²/n=4.3
Φ=0 MV (LIS)
Φ=250 MV
Φ=350 MV
Φ=550 MV
Φ=900 MV
CRIS (2009-10)
CRIS (1996-97)
CRIS (2002-03)
HEAO-3 (1980)
CREAM (2005)
TRACER (2003)
U. Minnesota (1977)
UNH (1975)
Oxygen
χ²/n=5.0
LIS
Φ=200 MV
Φ=300 MV
Φ=500 MV
Φ=850 MV
CRIS (2009-10)
CRIS (1996-97)
CRIS (2001-03)
HEAO3 (1980)
UNH(1975)
TRACER (2003)
Titanium
χ²/n=6.6
LIS
Φ=200 MV
Φ=300 MV
Φ=500 MV
Φ=850 MV
CRIS (2009-10)
CRIS (1996-97)
CRIS (2001-03)
HEAO3 (1980)
U. Minnesota (1977)
φ(E), 1/(MeV/u cm² sr s)
E, MeV/u

Modulation Parameter Uncertainty -Fits to CRIS Data



Annual Effective Dose for Males



Francis Cucinotta, "New Estimates of Radiation Risks…" NASA FISO, July 13, 2016

Space Physics Over-Statements

Original claim

RECORD-SETTING COSMIC-RAY INTENSITIES IN 2009 AND 2010

R. A. Mewaldt[1], A. J. Davis[1], K. A. Lave[2], R. A. Leske[1], E. C. Stone[1], M. E. Wiedenbeck[3], W. R. Binns[2], E. R. Christian[4], A. C. Cummings[1], G. A. de Nolfo[4], M. H. Israel[2], A. W. Labrador[1], and T. T. von Rosenvinge[4]
[1] California Institute of Technology, Pasadena, CA 91125, USA
[2] Washington University, St. Louis, MO 63130, USA
[3] Jet Propulsion Laboratory, California Institute of Technology, Pasadena, CA 91109, USA
[4] NASA/Goddard Space Flight Center, Greenbelt, MD 20771, USA
Received 2010 June 5; accepted 2010 September 13; published 2010 October 7

Correction:

Mewaldt paper analyzed different solar min spectra with different methods leading to over-statement of 2009 spectra; error corrected in Lave et al.; APJ 2013

GALACTIC COSMIC-RAY ENERGY SPECTRA AND COMPOSITION DURING THE 2009–2010 SOLAR MINIMUM PERIOD

K. A. Lave[1], M. E. Wiedenbeck[2], W. R. Binns[1], E. R. Christian[3], A. C. Cummings[4], A. J. Davis[4], G. A. de Nolfo[3], M. H. Israel[1], R. A. Leske[4], R. A. Mewaldt[4], E. C. Stone[4], and T. T. von Rosenvinge[3]
[1] Department of Physics & the McDonnell Center for the Space Sciences, Washington University, St. Louis, MO 63130, USA
[2] Jet Propulsion Laboratory, California Institute of Technology, Pasadena, CA 91109, USA
[3] NASA Goddard Space Flight Center, Greenbelt, MD 20771, USA
[4] California Institute of Technology, Pasadena, CA 91125, USA
Received 2013 February 14; accepted 2013 May 11; published 2013 June 3

ABSTRACT

We report new measurements of the elemental energy spectra and composition of galactic cosmic rays during the 2009–2010 solar minimum period using observations from the Cosmic Ray Isotope Spectrometer (CRIS) onboard the *Advanced Composition Explorer*. This period of time exhibited record-setting cosmic-ray intensities and very low levels of solar activity. Results are given for particles with nuclear charge $5 \leqslant Z \leqslant 28$ in the energy range ~50–550 MeV nucleon^{-1}. Several recent improvements have been made to the earlier CRIS data analysis, and therefore updates of our previous observations for the 1997–1998 solar minimum and 2001–2003 solar maximum are also given here. For most species, the reported intensities changed by less than ~7%, and the relative abundances changed by less than ~4%. Compared with the 1997–1998 solar minimum relative abundances, the 2009–2010 abundances differ by less than 2σ, with a trend of fewer secondary species observed in the more recent time period. The new 2009–2010 data are also compared with results of a simple "leaky-box" galactic transport model combined with a spherically symmetric solar modulation model. We demonstrate that this model is able to give reasonable fits to the energy spectra and the secondary-to-primary ratios B/C and (Sc+Ti+V)/Fe. These results are also shown to be comparable to a GALPROP numerical model that includes the effects of diffusive reacceleration in the interstellar medium.

The Carrington event not observed in most ice core nitrate records
E. Wolff, J. Geophy Lett (2012)

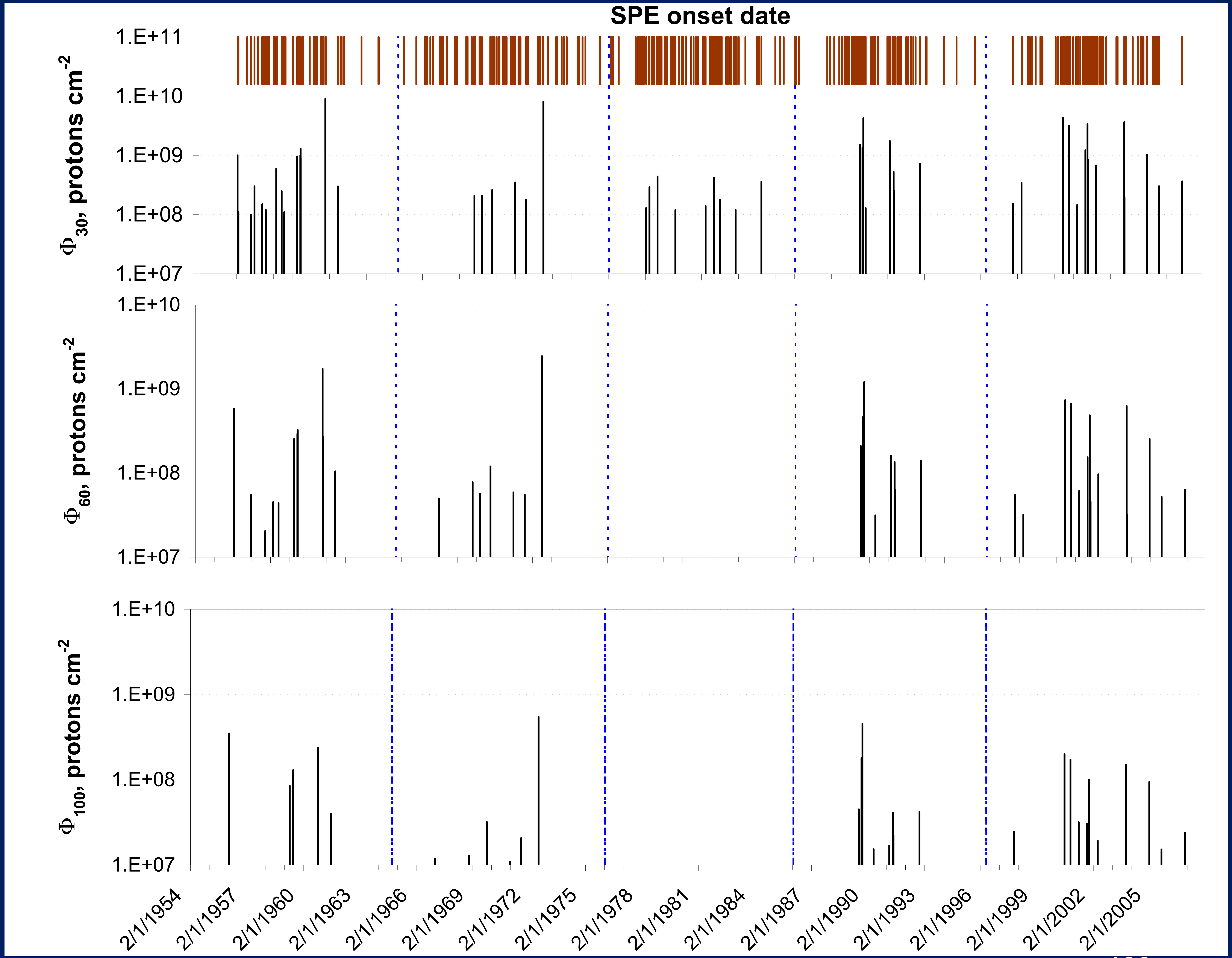
- The Carrington Event of 1859 is considered to be among the largest space weather events of the last 150 years. We show that only one out of 14 well-resolved ice core records from Greenland and Antarctica has a nitrate spike dated to 1859. No sharp spikes are observed in the Antarctic cores studied here. In Greenland numerous spikes are observed in the 40 years surrounding 1859, but where other chemistry was measured, all large spikes have the unequivocal signal, including co-located spikes in ammonium, formate, black carbon and vanillic acid, of biomass burning plumes. It seems certain that most spikes in an earlier core, including that claimed for 1859, are also due to biomass burning plumes, and not to solar energetic particle (SEP) events. We conclude that an event as large as the Carrington Event did not leave an observable, widespread imprint in nitrate in polar ice. <u>Nitrate spikes cannot be used to derive the statistics of SEPs.</u>

Solar protons a manageable issue with no significant acute risks

Flux>30 MeV

Flux>60 MeV

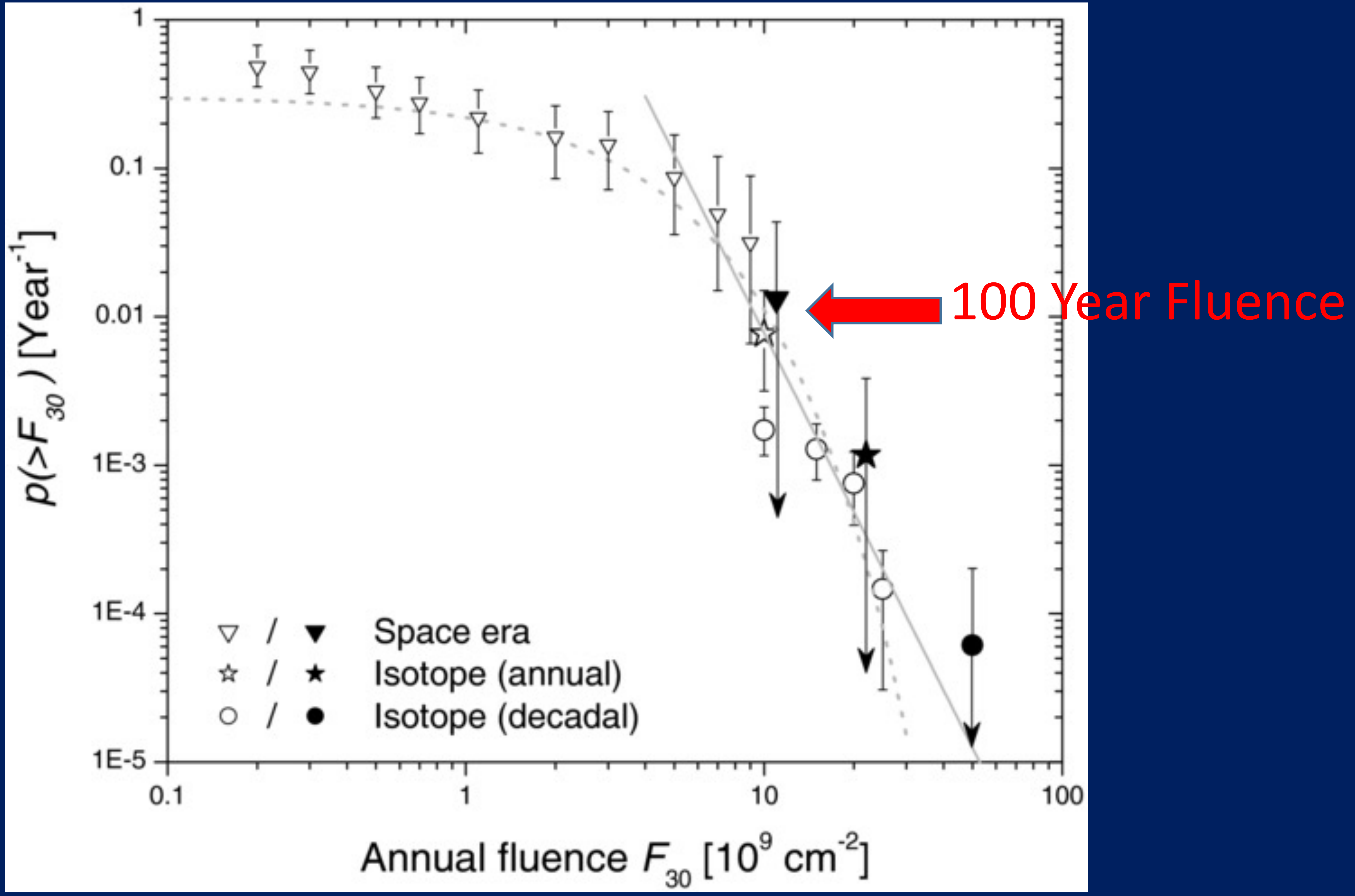
Flux>100 MeV



Kim, Feivesen, Cucinotta, 2009

Occurrence Of Extreme Solar Particle Events: Assessment From Historical Proxy Data

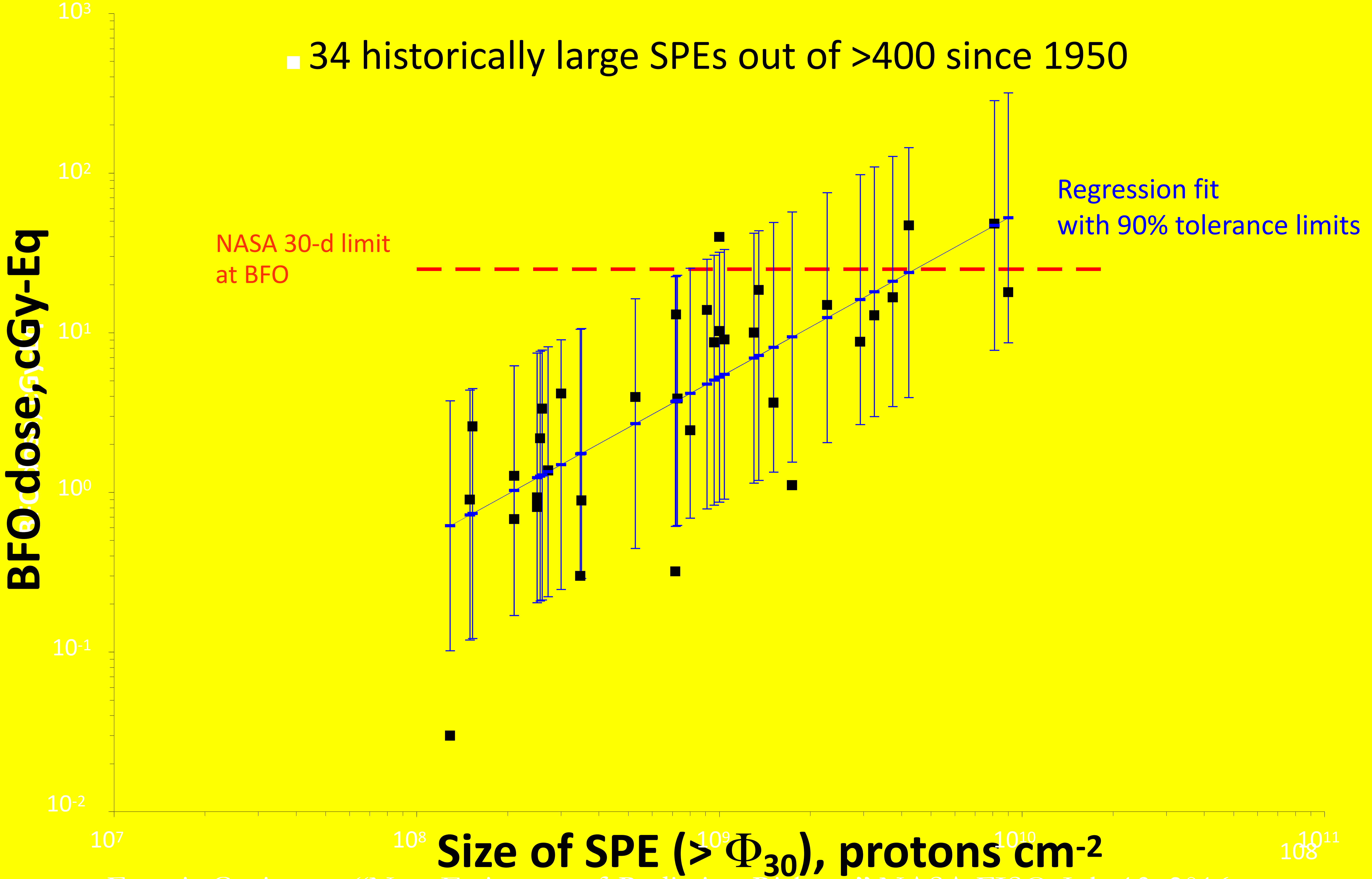
Usoskin and Kovalstov, Astrophy J (2012)



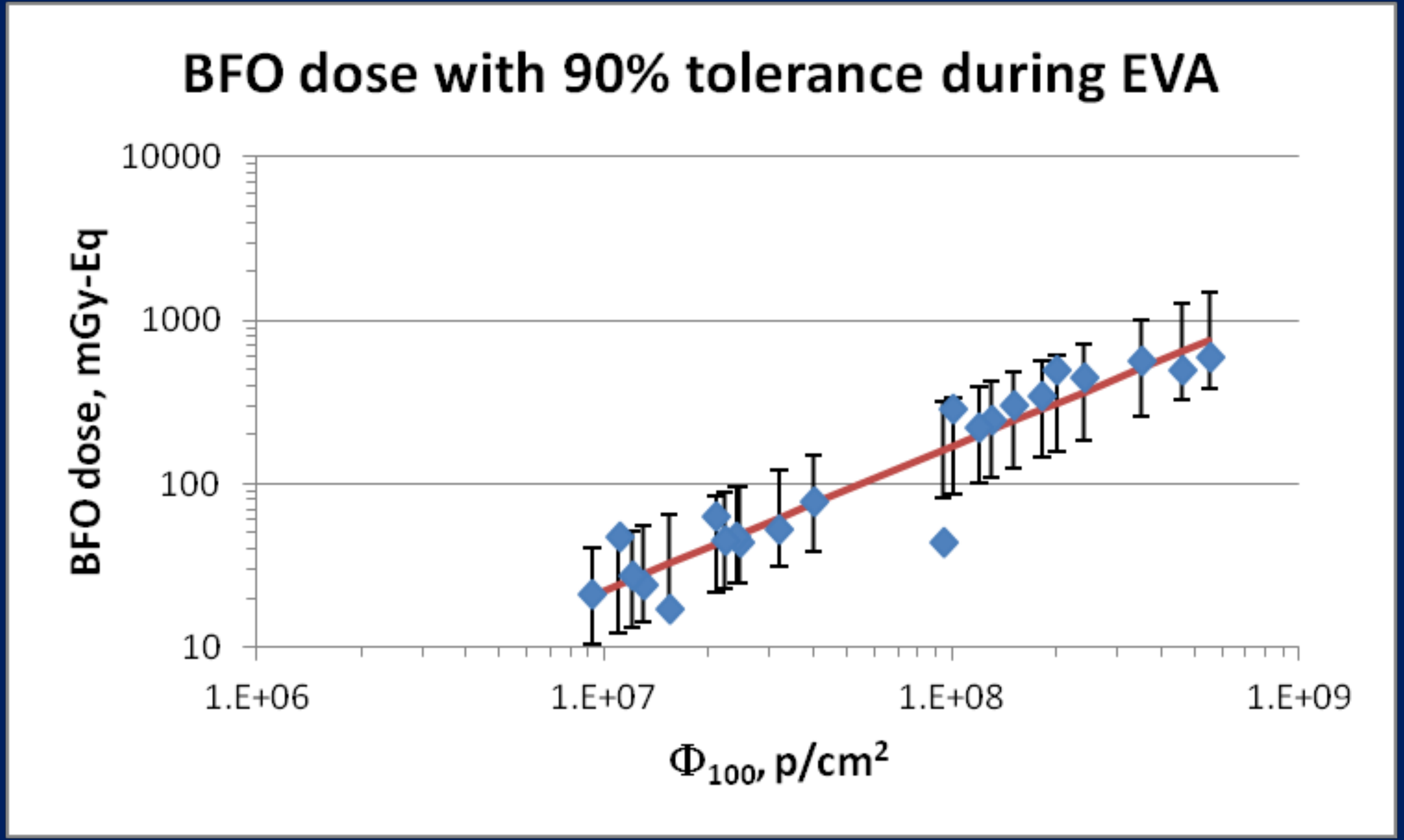
Predicting BFO Dose from $\Phi_{30\ MeV}$ (M.Y. Kim et al.)

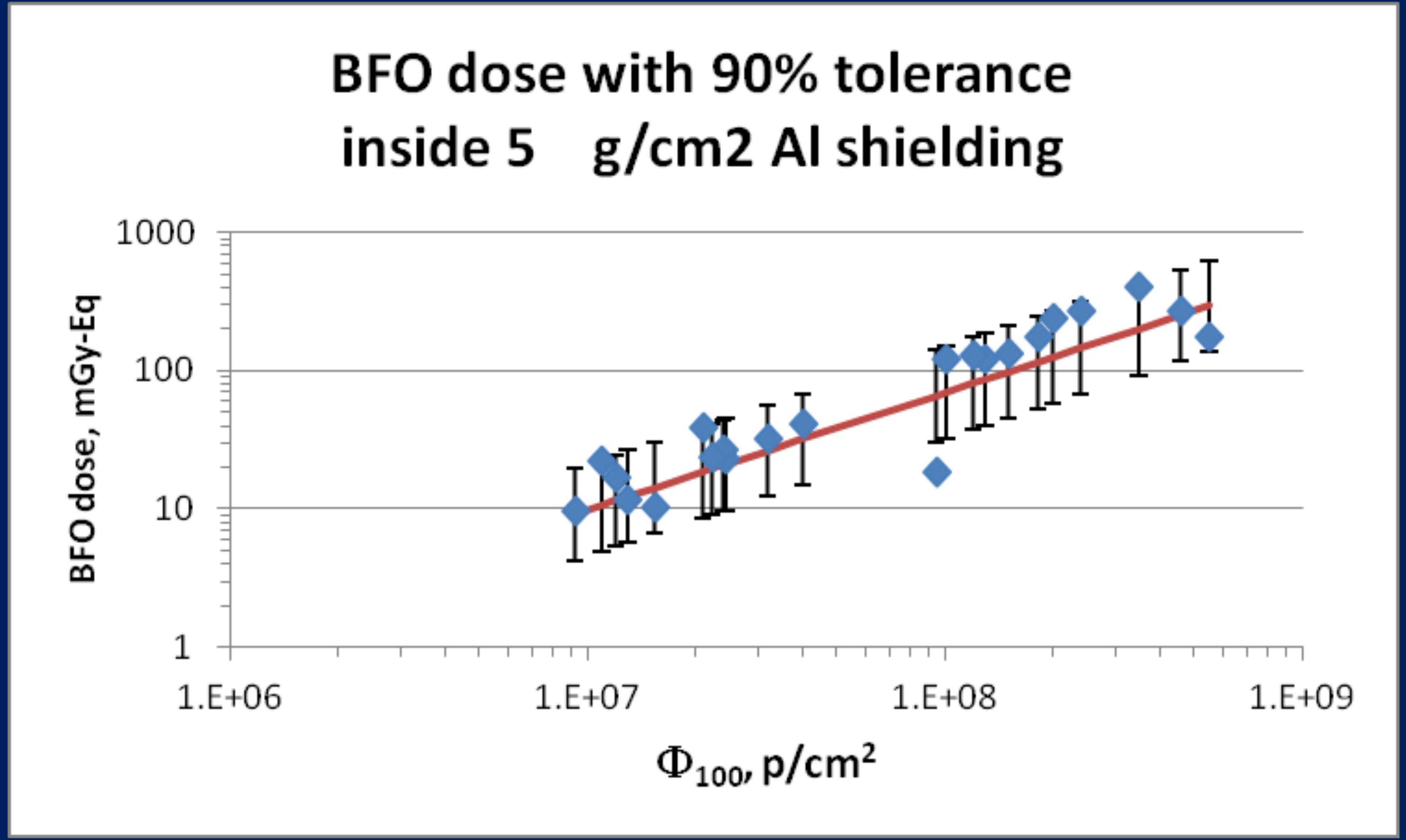
Equipment Room (5 g/cm² Alum) in Interplanetary Space

Tolerance Limits based on Variability of Detailed Energy Spectra



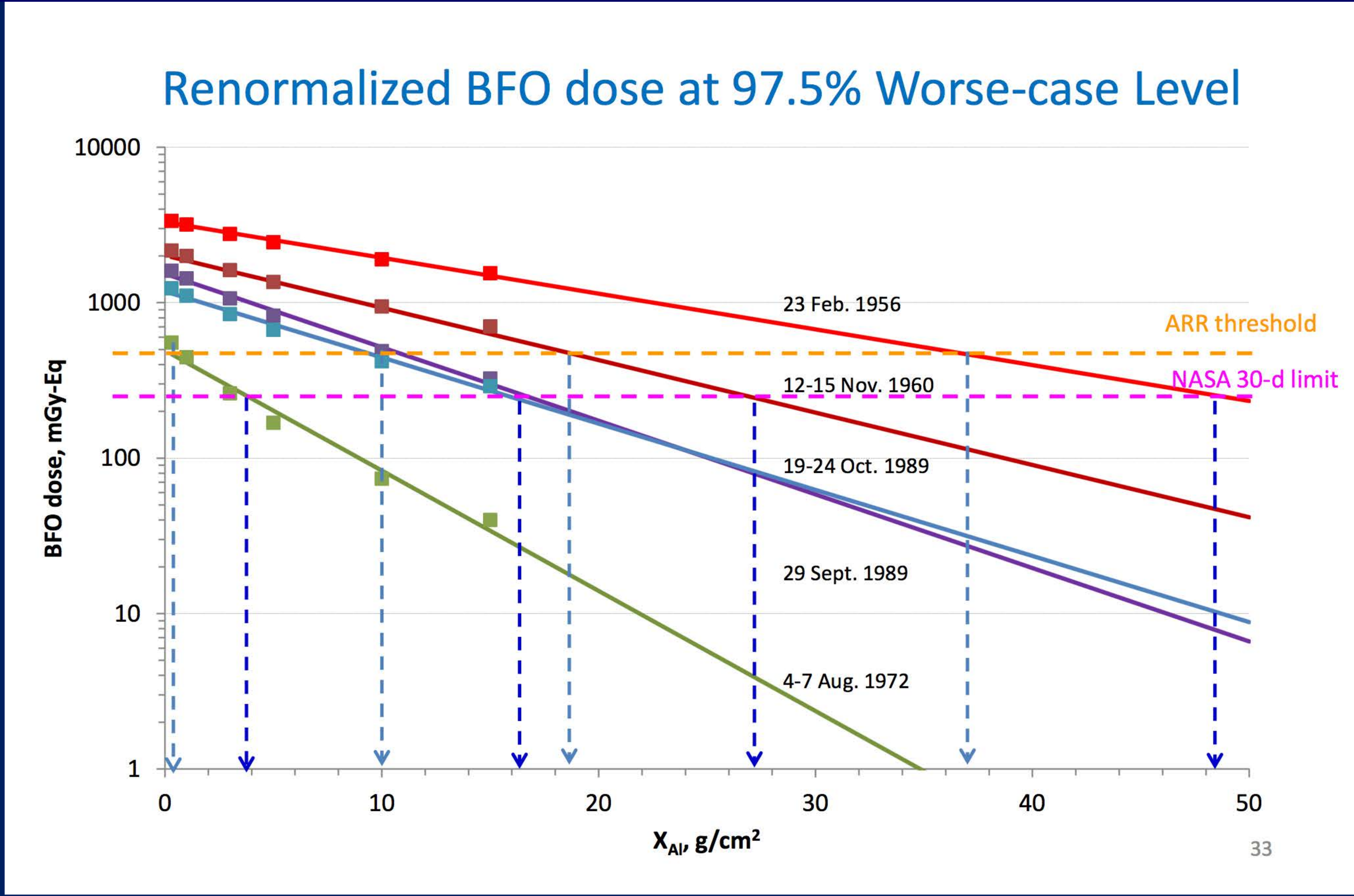
SPE Blood forming organ doses with No shelter
(Probability- D_{BFO}> 100 mGy per EVA) <1 x 10 $^{-6}$





1) Dose-rates are modest (events last >10 h)
2) EVA termination time < 2 h
3) ARS easily mitigated with real-time dosimetry and shielding because >100 MeV flux is too small
4) Spacecraft have areas with at least 20 g/cm^2 shielding
5) Probability to be on an EVA during an SPE <1 x 10^{-6}

Storm shelters with ~40 g/cm^2 shielding are practical

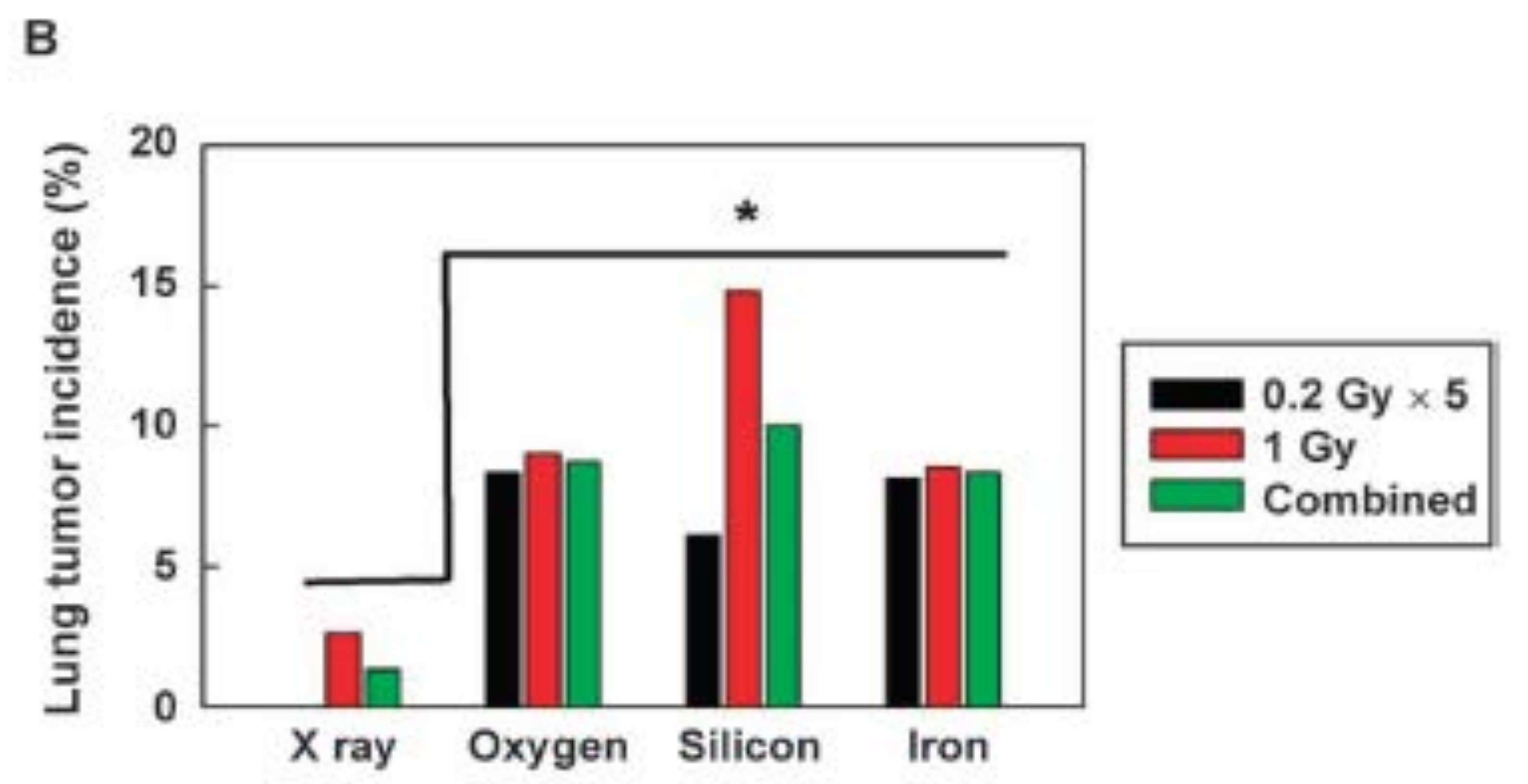


M.Y. Kim

Francis Cucinotta, "New Estimates of Radiation Risks…" NASA FISO, July 13, 2016

Lung Cancer Risk

- Lung cancer comprises the largest fraction of human radiation fatal risk (>30%).
- Ya Wang et al. have used a resistant mouse model (C57BL/6) to report on first Heavy ion lung tumor data.
- Results show little effect of dose fractionation for O, Si, and Fe particles at 1 Gy.
- Si particles produce more aggressive lung tumors compared to gamma-rays.
- Follow-up studies planned at lower doses.



C

Relative effectiveness at 1 Gy on lung tumorigenesis

Iron (175 keV/μm)	6.3
Silicon (70 keV/μm)	7.6
Oxygen (17 keV/μm)	6.7

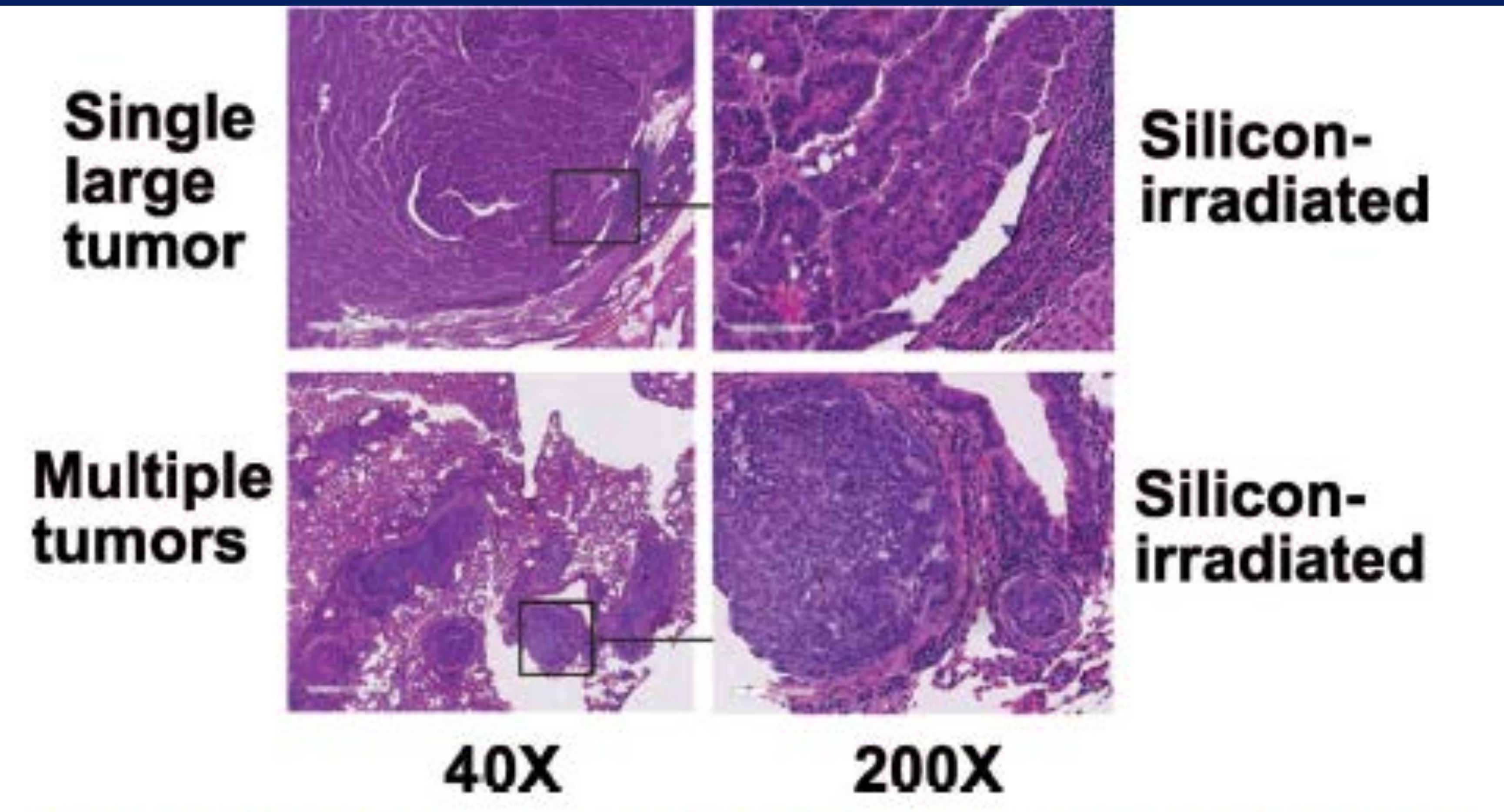


FIG. 4. Silicon exposure induced more aggressive lung tumors. Histological image of mouse lung tissue/tumor (left image, 40×) and local enlarged area (right image, 40×) from the mice at 1.5 year after sham irradiation (nonirradiated) or exposure to iron (0.2 Gy × 5) or silicon irradiation (1 Gy or 0.2 Gy × 5).

Wang et al. Radiat Res (2014)

Argonne National Lab Inverse Dose-Rate Effect- D. Grahn et al, 1993 (24 or 60 week x 5 d/wk gamma or fission neutron)

TABLE VI
Dose–Response Equations for the Occurrence of Lethal and Nonlethal Epithelial Tissue Tumors (Except Ovarian)

Sex	Radiation quality	Exposure pattern	n^a	$\alpha \times 10^{-4}$	±SE	P^b	$\beta \times 10^{-6}$	±SE	P^b	RBE ± SE
				Interval: 600–799 days						
♂	n	S	8	35.70	5.79	<0.01	−8.01	2.95	0.03	6 ± 1
		24	7	57.10	2.99	<0.01	−13.30	1.51	<0.01	13 ± 1
		60	8	71.40	7.23	<0.01	−21.80	4.90	<0.01	26 ± 4
	γ	S	8	6.48	0.41	<0.01				
		24	6	4.26	0.22	<0.01				
		60	7	2.73	0.26	<0.01				
		23	4	3.16	0.29	<0.01				
		59	3	1.55	0.24	0.02				
♀	n	S	11	53.20	8.64	<0.01	−12.90	4.15	0.01	7 ± 1
		24	4	74.70	4.13	<0.01	−17.40	1.95	0.01	15 ± 1
		60	6	82.20	9.40	<0.01				25 ± 4
	γ	S	9	7.16	0.85	<0.01				
		24	3	4.87	0.26	<0.01				
		60	5	3.32	0.46	<0.01				

Lung tumors: Inverse Dose-Rate Effect Found?

30 GRAHN, LOMBARD, AND CARNES

TABLE VII
Dose–Response Equations for the Occurrence of Lethal and Nonlethal Lung Tumors

Sex	Radiation quality	Exposure pattern	n^a	$\alpha \times 10^{-4}$	±SE	P^b	$\beta \times 10^{-6}$	±SE	P^b	RBE ± SE
		Interval: 600–799 days								
♂	n	S	8	29.10	4.41	<0.01	−9.38	2.24	0.01	5 ± 1
		24	7	45.50	2.93	<0.01	−9.84	1.48	<0.01	11 ± 1
		60	8	56.80	6.62	<0.01	−16.70	4.49	0.01	25 ± 4
	γ	S	8	5.33	0.38	<0.01				
		24	6	4.03	0.26	<0.01				
		60	7	2.31	0.29	<0.01				
		23	4	2.93	0.28	<0.01				
		59	3	1.55	0.27	0.03				
♀	n	S	11	36.60	5.24	<0.01	−11.10	2.51	<0.01	8 ± 2
		24	4	52.40	4.20	0.01	−9.04	1.98	0.04	12 ± 1
		60	6	57.50	6.25	<0.01				20 ± 4
	γ	S	9	4.49	0.84	<0.01				
		24	3	4.52	0.38	0.01				
		60	5	2.92	0.58	0.01				

References

- Francis Cucinotta, “New Estimates of Radiation Risks” NASA Future In-Space Operations Working Group, May 18, 2011
- –, Human Integration Design Handbook, NASA SP-2010-3407, Jan. 2010
- Lora Bailey, “Radiation Studies for a Long Duration Deep Space Habitat” NASA Future In-Space Operations Working Group, Oct 31, 2012
- Francis A. Cucinotta, Myung-Hee Y. Kim, and Lei Ren, Managing Lunar and Mars Mission Radiation Risks Part I: Cancer Risks, Uncertainties, and Shielding Effectiveness NASA/TP-2005-213164, July, 2005