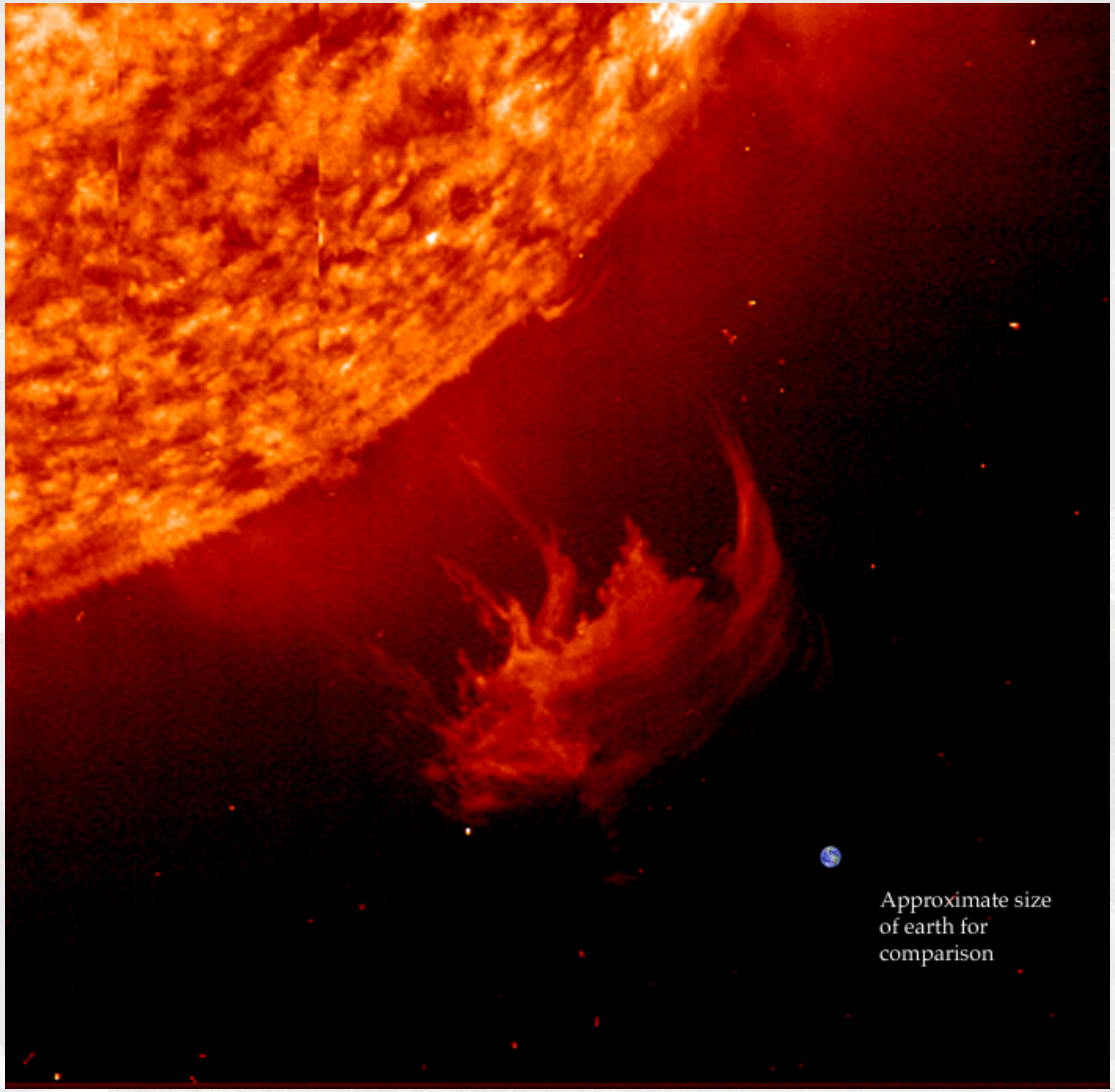
Space Radiation

- Lecture #16 – October 22, 2020
- Sources of radiation
- Biological effects
- Approaches to shielding
- Probabilistic estimation
- Spacecraft shielding design
- Recent revisions to understanding radiation effects
- Split into groups for Team Project 1 work

NASA Radiation Risk Concerns

- Carcinogenesis – increased risk of early death due to radiation exposure
- Central nervous system (CNS) – Acute (immediate) or late-life damage to CNS
- Chronic and degenerative tissue risks – e.g., cataracts, heart disease
- Acute radiation risks – high dosage effects

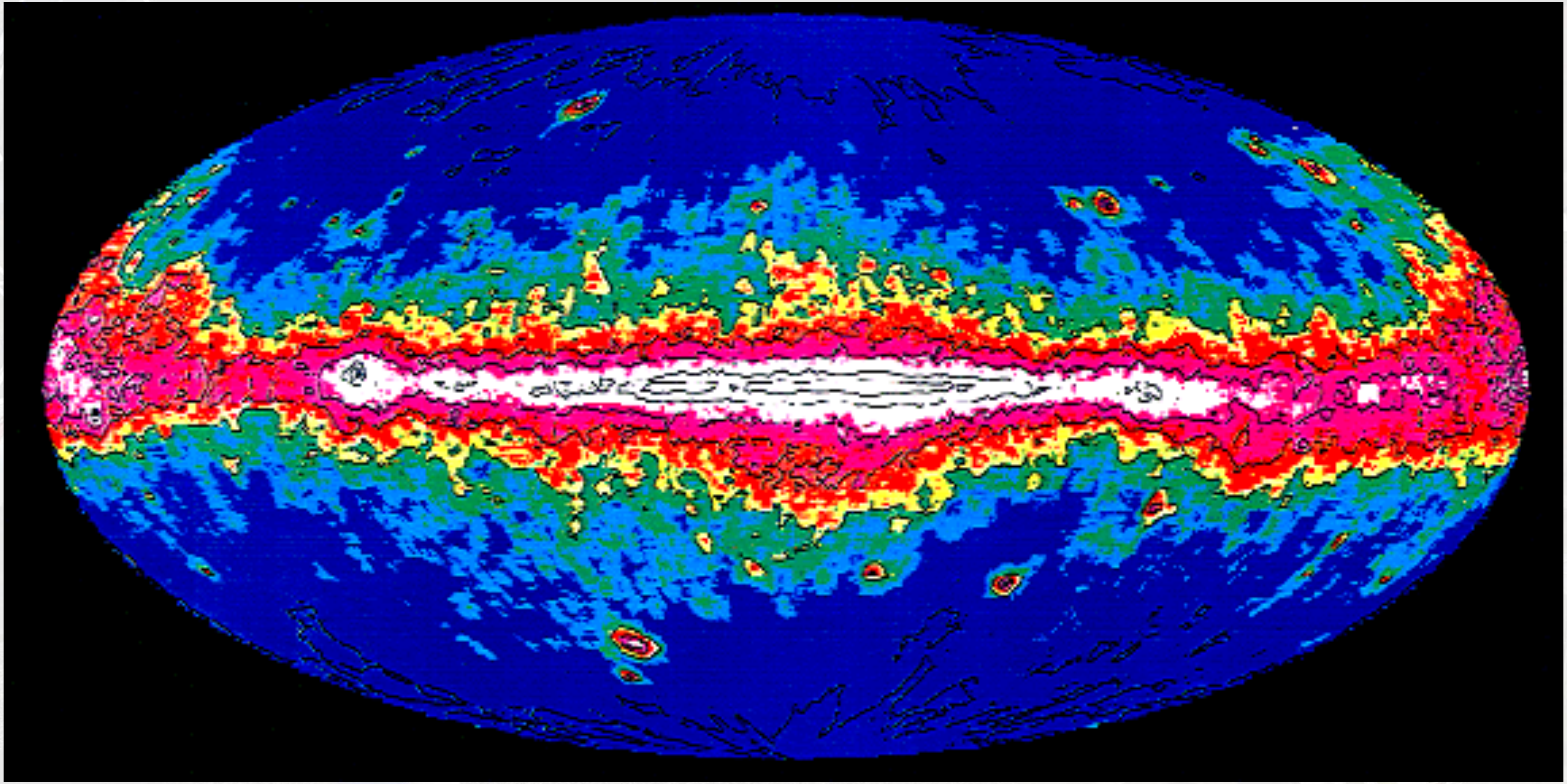
The Origin of a Class X1 Solar Flare



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)

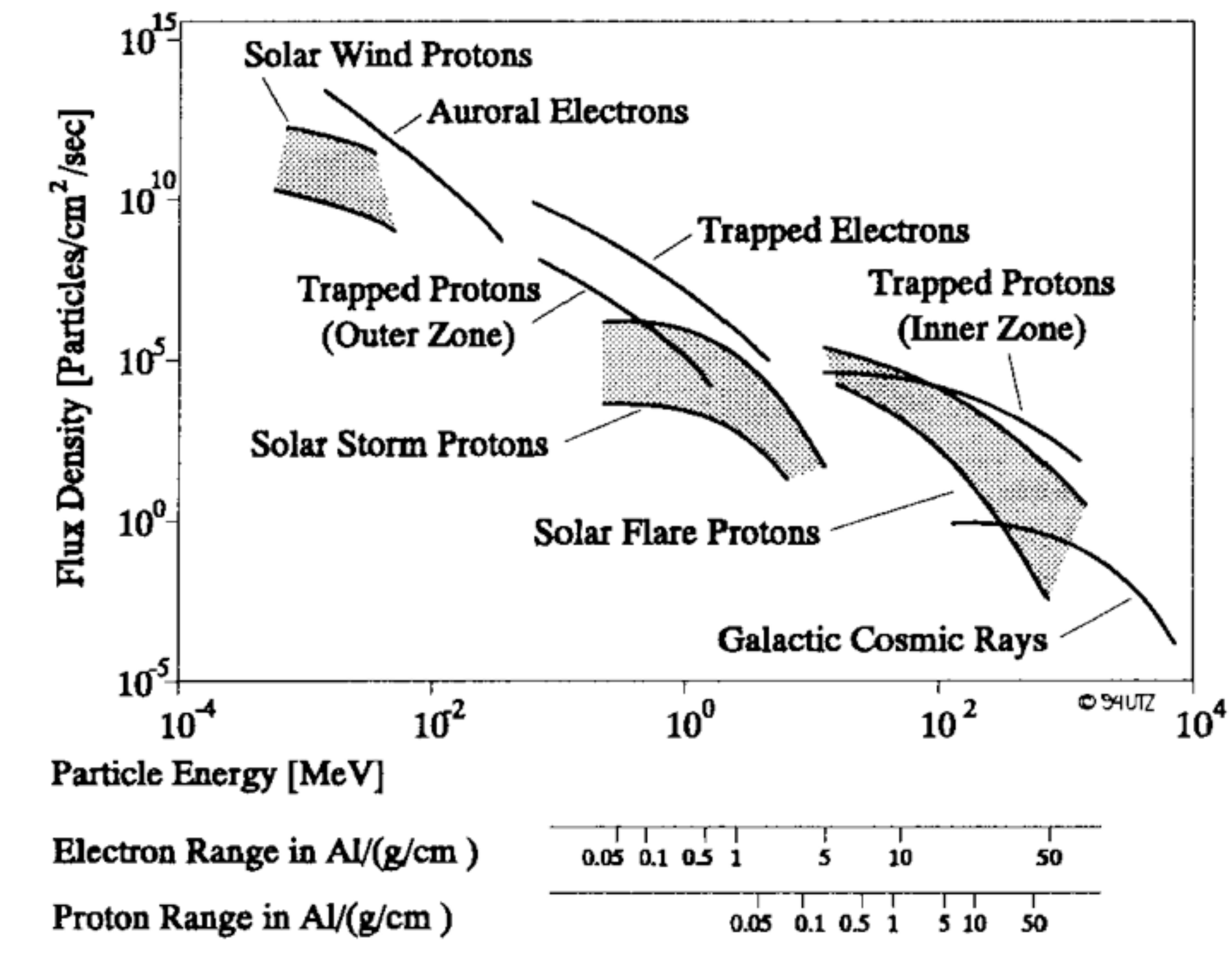
Image of Galaxy in Gamma Rays



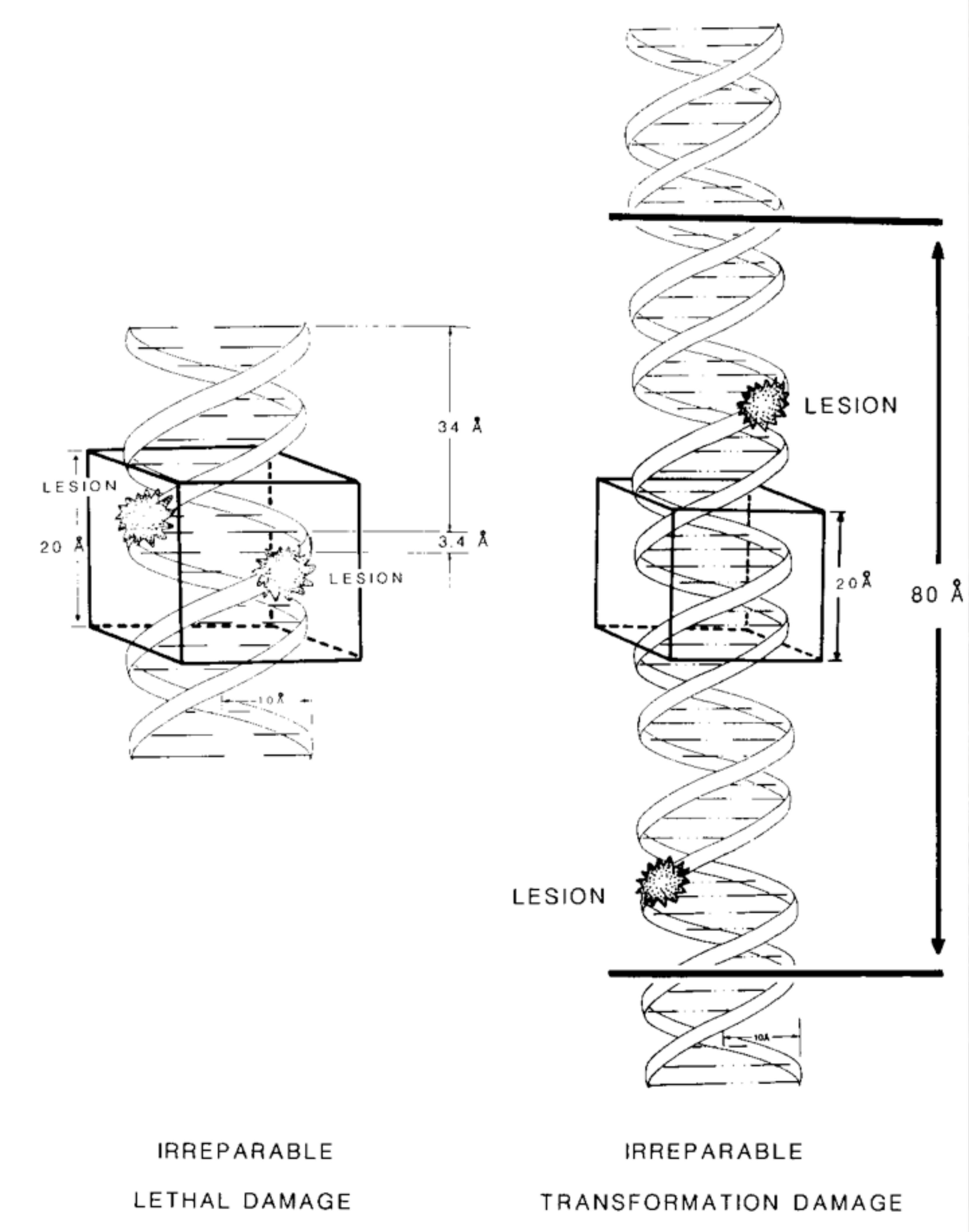
Galactic Cosmic Rays

- 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

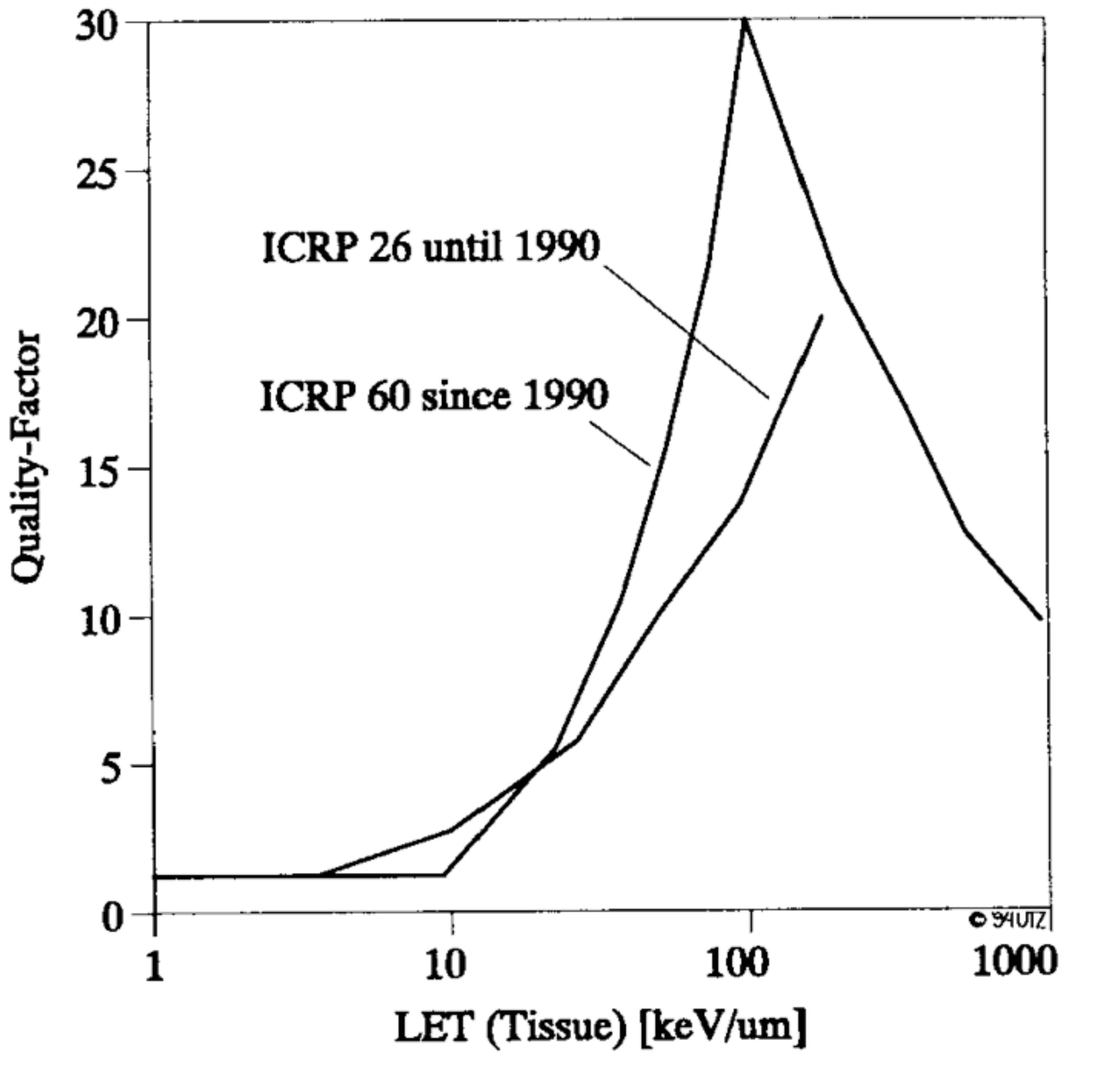
$$1\ Sievert = 1\ \frac{Joule}{kg} = 100\ rem = 10,000\ \frac{ergs}{gm}$$

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

- 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

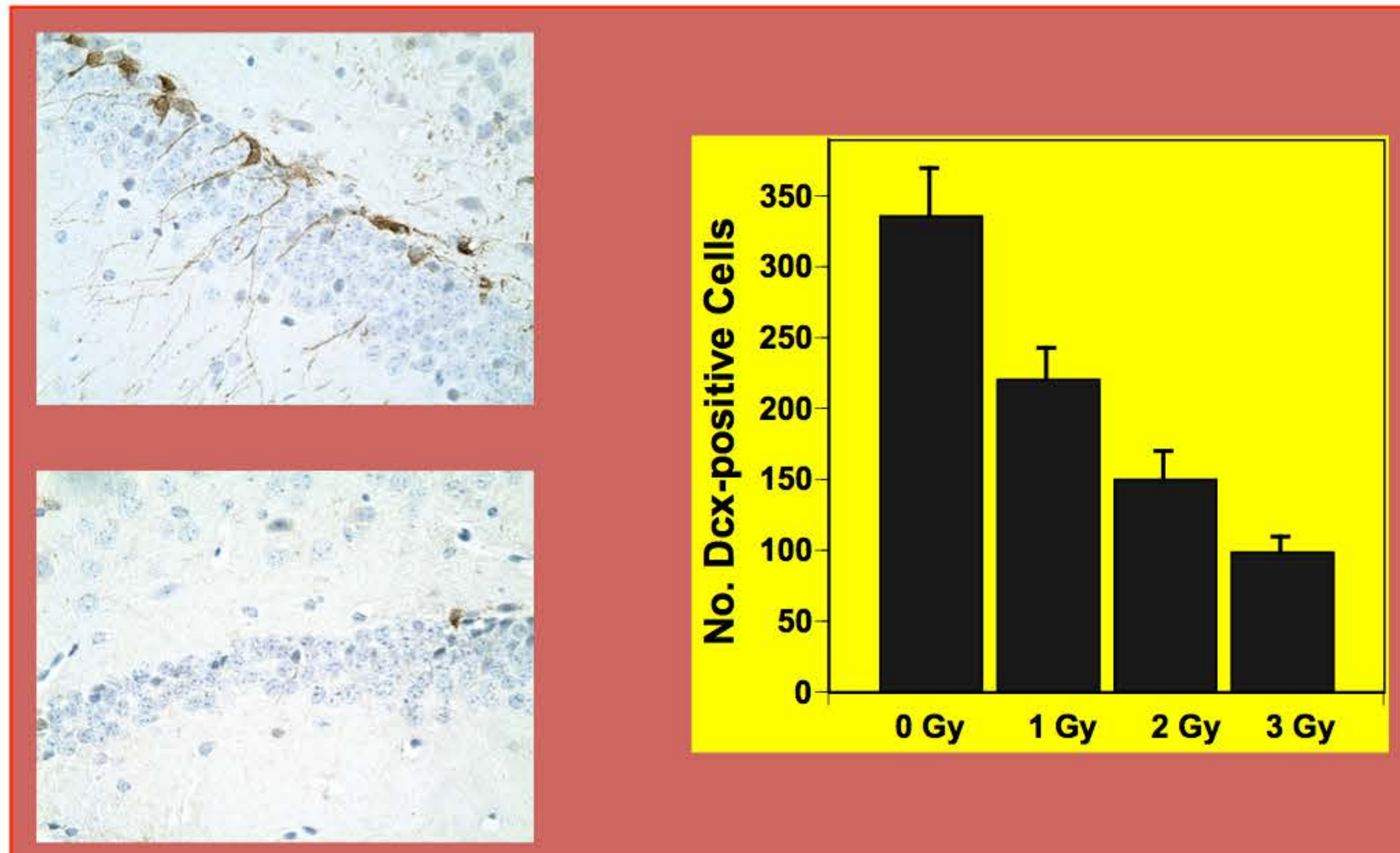
- Radiation carcinogenesis
  - Function of exposure, dosage, LET of radiation
- Radiation mutagenesis
  - Mutations in offspring
  - Mouse experiments show doubling in mutation rate at 15-30 rad (acute), 100 rad (chronic) exposures
- Radiation-induced cataracts
  - Observed correlation at 200 rad (acute),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

Radiation Carcinogenesis

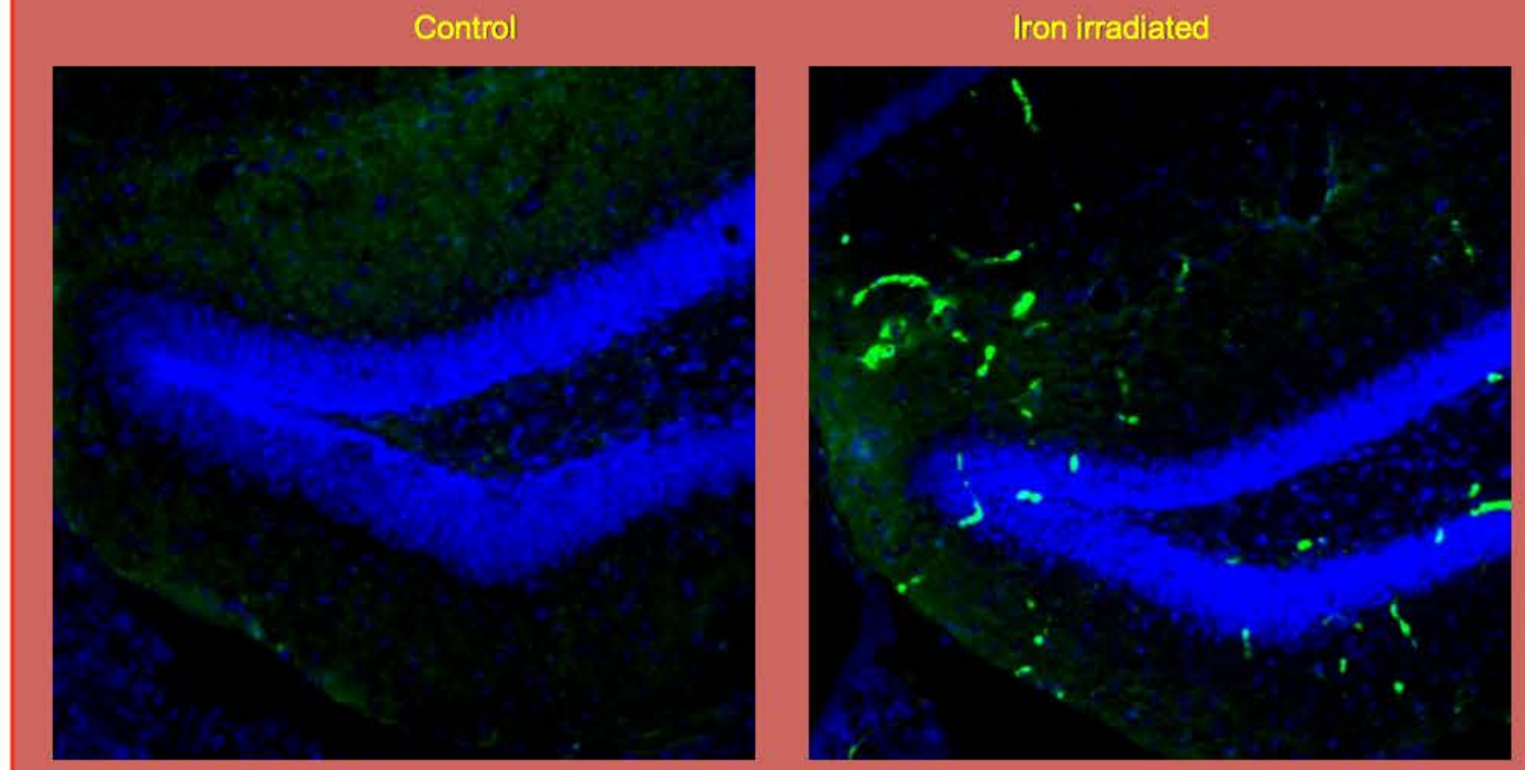
- Manifestations
  - Myelocytic leukemia
  - Cancer of breast, lung, thyroid, and bowel
- Latency in atomic bomb survivors
  - Leukemia: mean 14 yrs, range 5-20 years
  - All other cancers: mean 25 years
- Overall marginal cancer risk
  - 70-165 deaths/million people/rem/year
  - 100,000 people exposed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



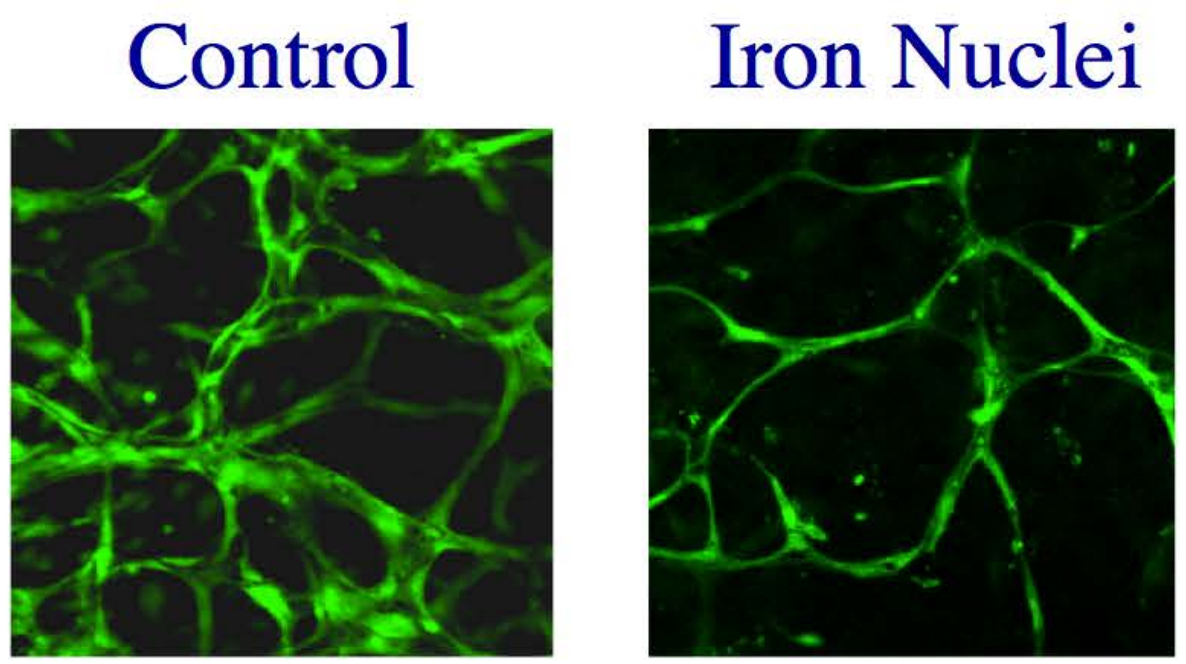
Oxidative Stress (Lipid peroxidation:4-Hydroxynonenal) is Increased in Mouse Hippocampus 9 Months After 2 Gy of ^{56}Fe Irradiation

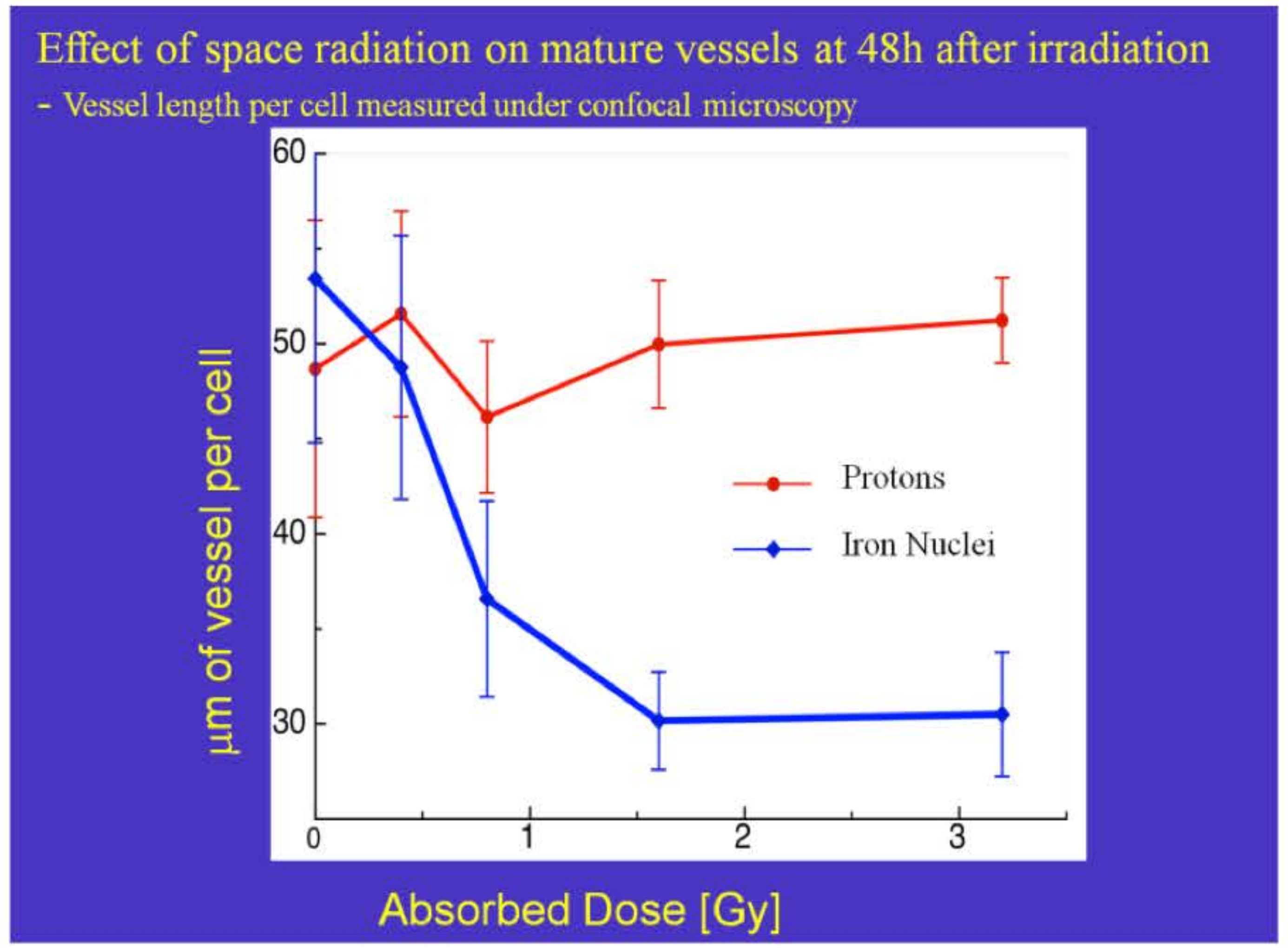
Francis Cucinotta, "What's New in Space Radiation Research for Exploration?" NASA FISO, May 18, 2011

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

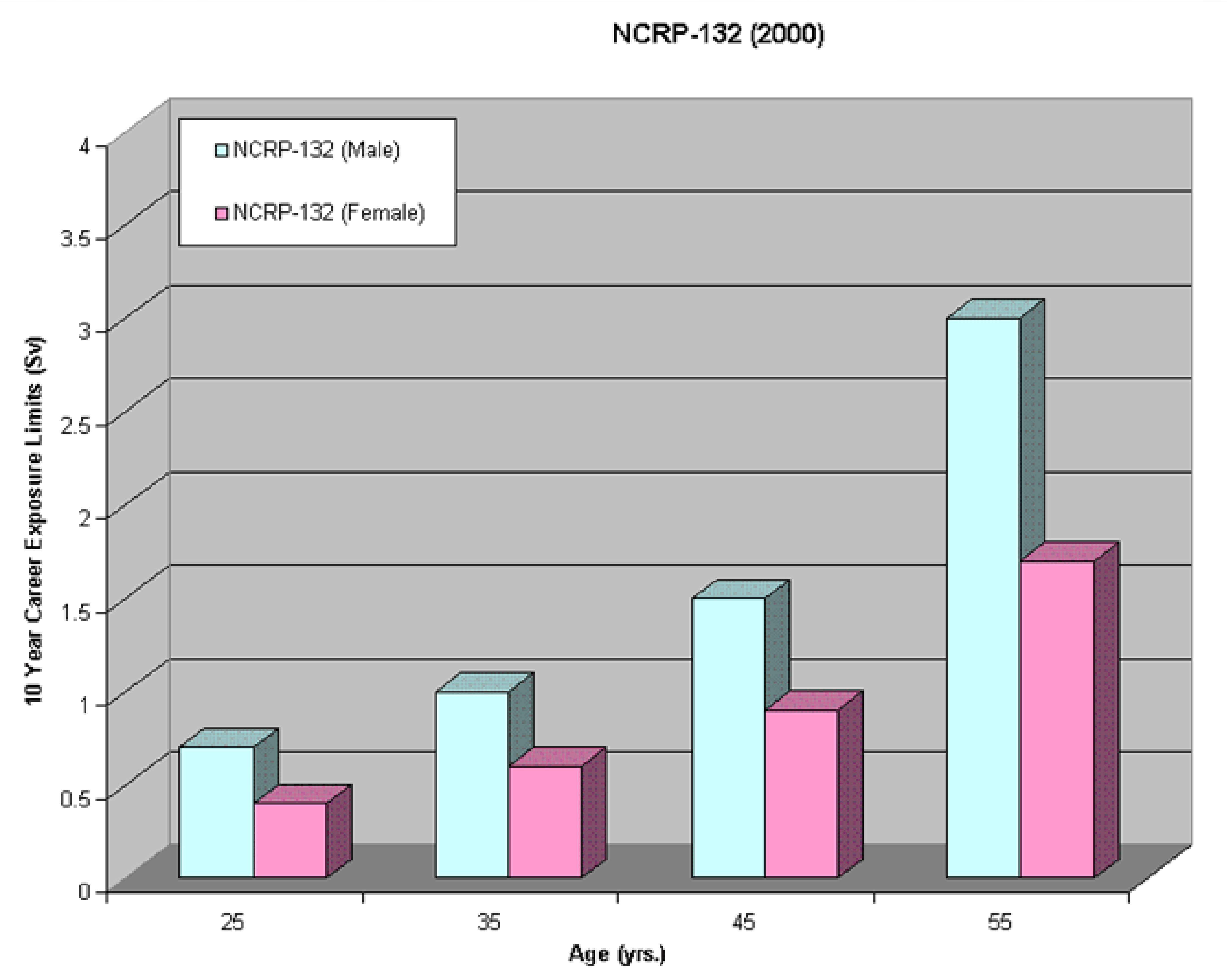
Vasculature Damage by GCR



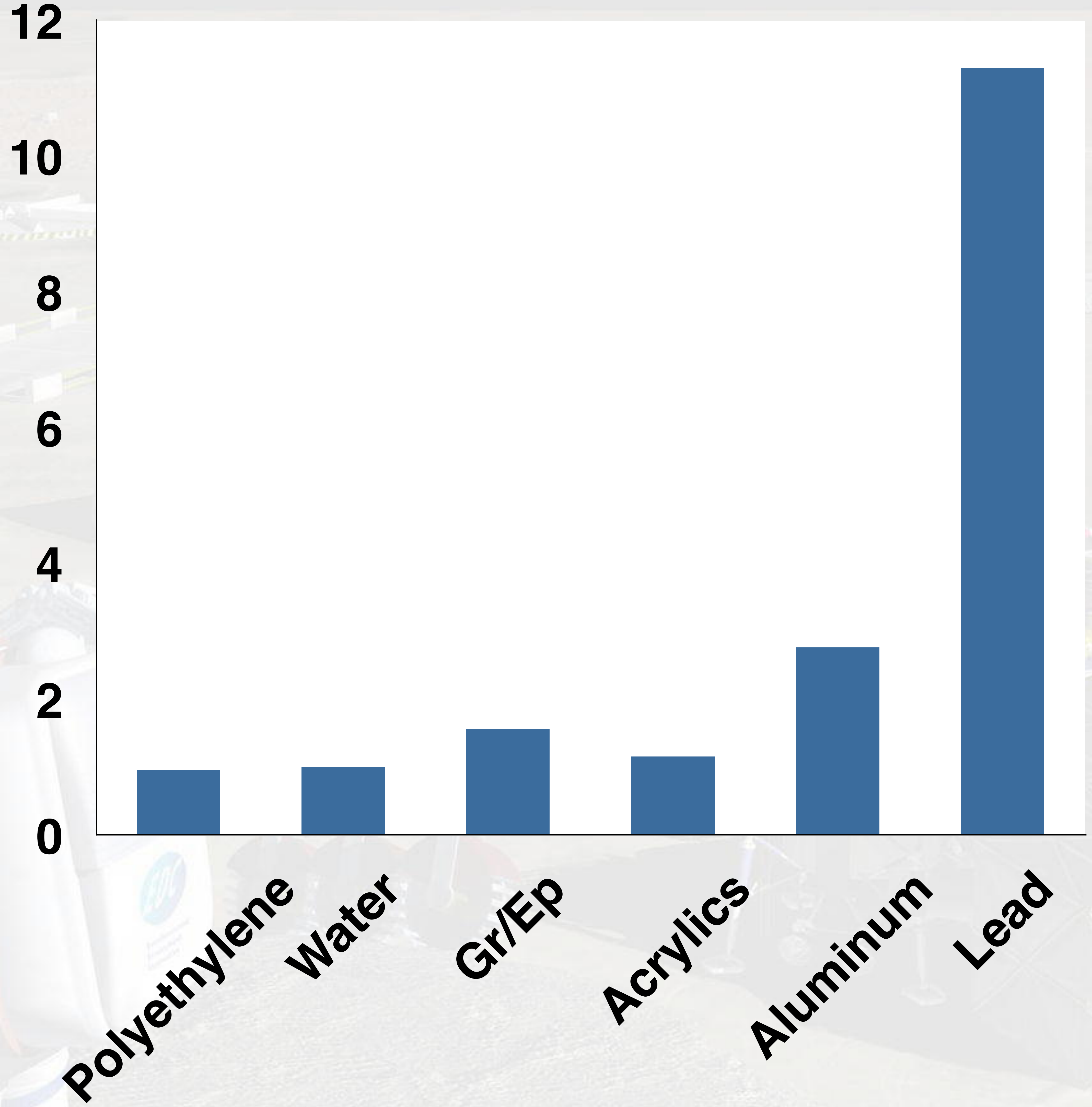


Francis Cucinotta, "What's New in Space Radiation Research for Exploration?" NASA FISO, May 18, 2011

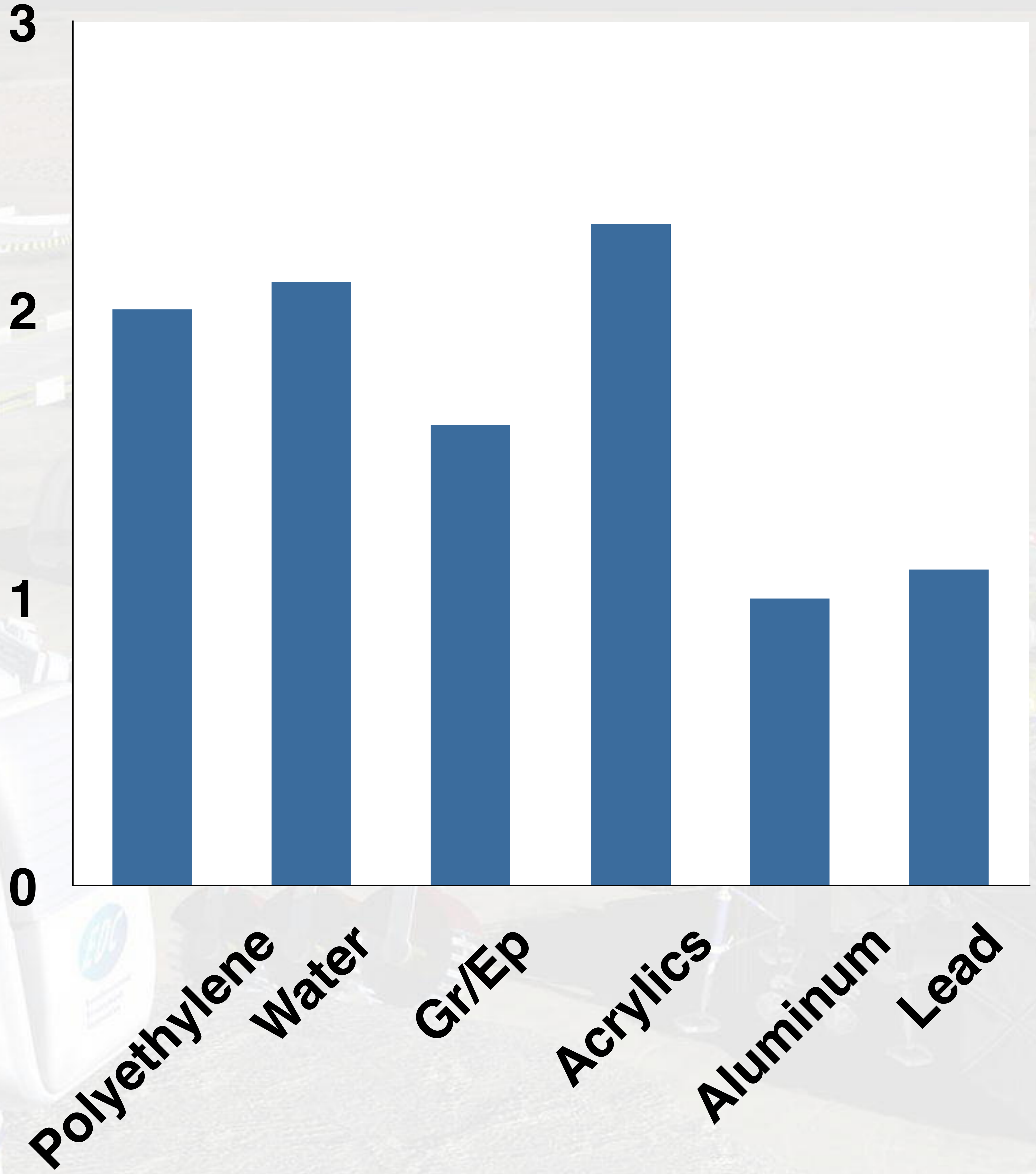
NASA Radiation Dose Limits



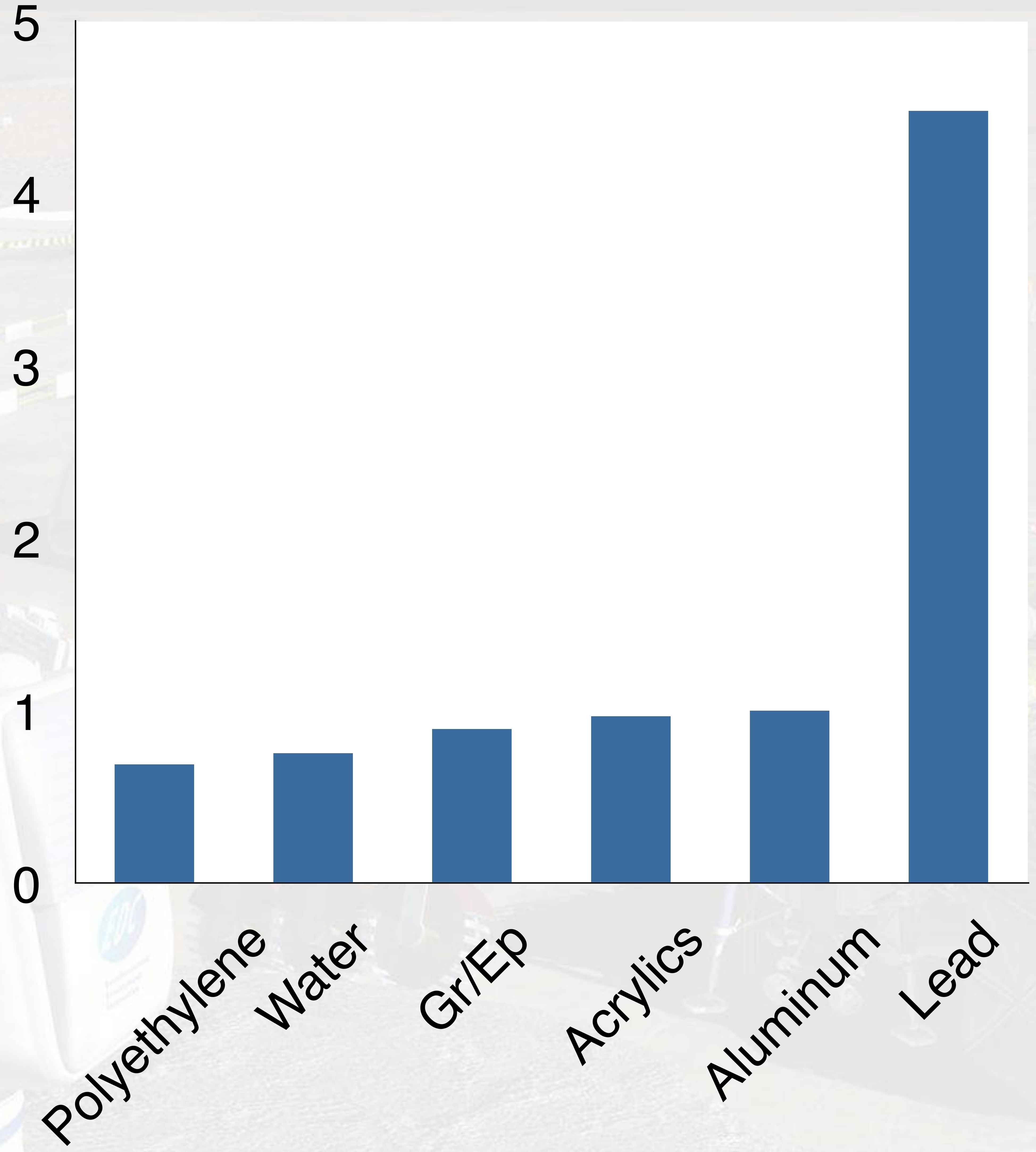
Density of Common Shielding Materials



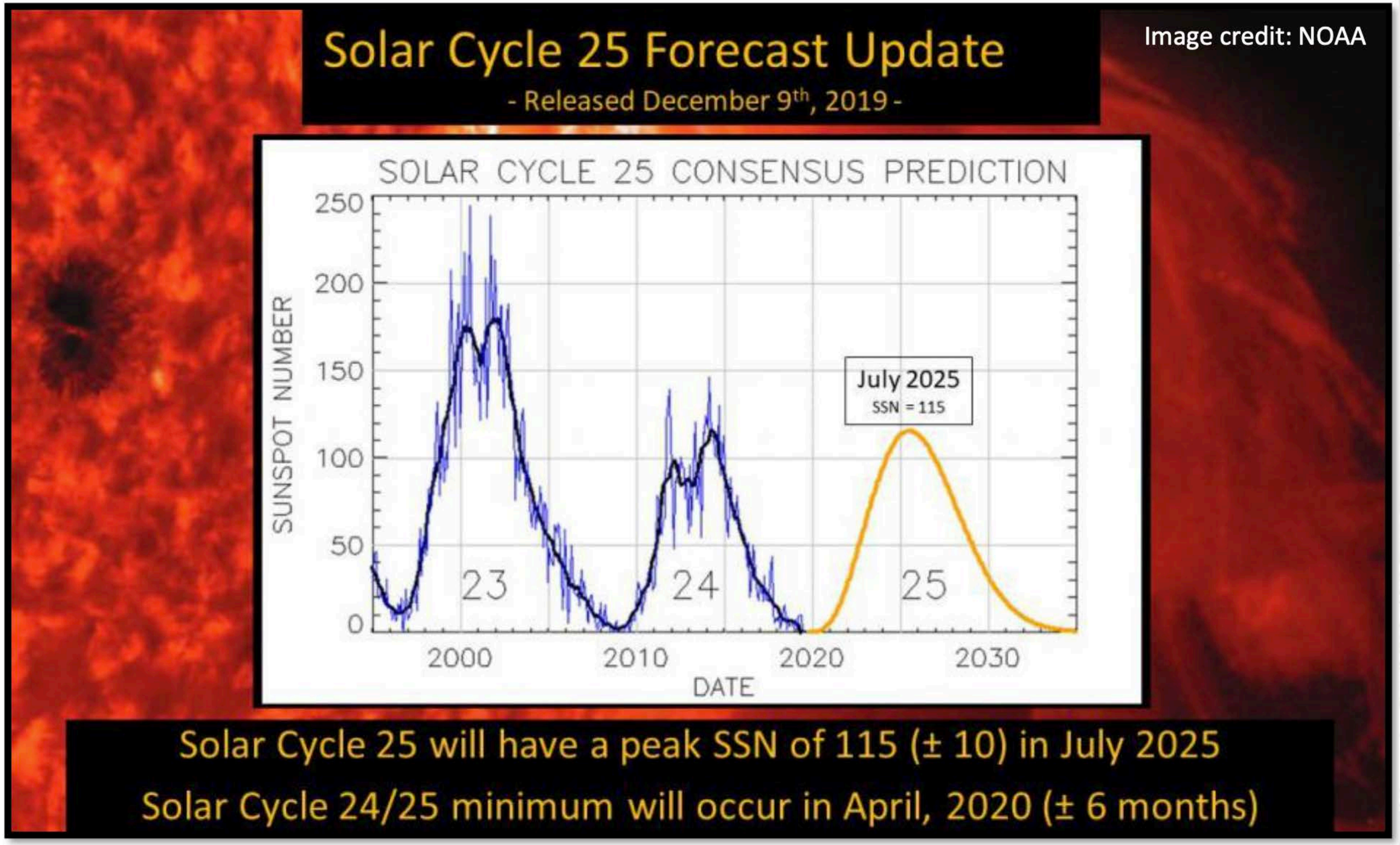
Comparative Thickness of Shields (Al=1)



Comparative Mass for Shielding (Al=1)



Solar Cycles

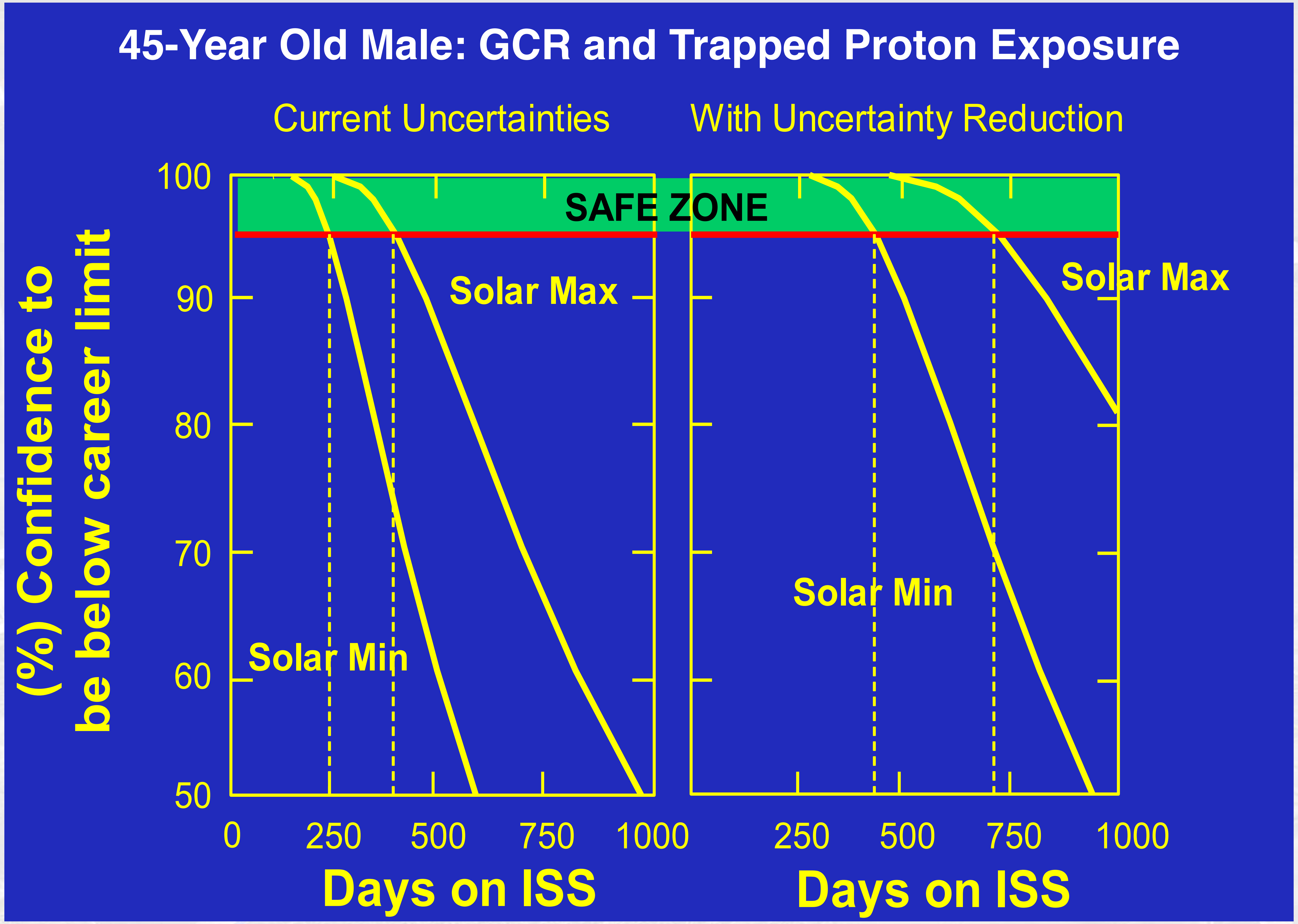


https://www.swpc.noaa.gov/news/solar-cycle-25-forecast-update

Shielding Materials and GCR

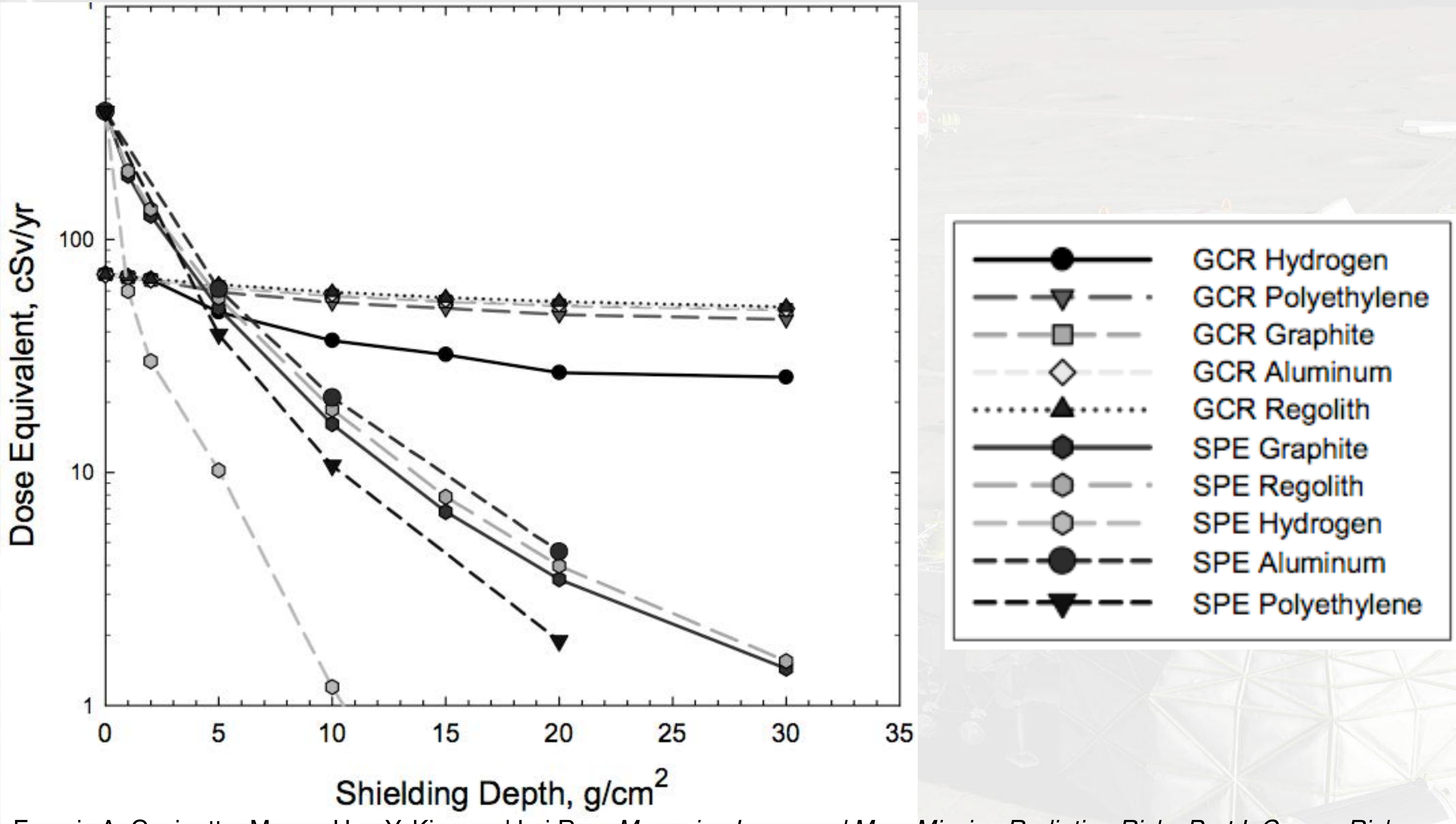
Material		E (Sv) Solar Minimum	E (Sv) SPE + Solar Maximum
10 g/cm²	Liquid H_2	0.40	0.19
	Liquid CH_4	0.50	0.30
	Polyethylene	0.52	0.33
	Water	0.53	0.35
	Epoxy	0.53	0.36
	Aluminum	0.57	0.43
20 g/cm²	Liquid H_2	0.36	0.16
	Liquid CH_4	0.45	0.22
	Polyethylene	0.47	0.24
	Water	0.48	0.25
	Epoxy	0.49	0.26
	Aluminum	0.53	0.30
40 g/cm²	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

SPE and GCR Shielding Effectiveness



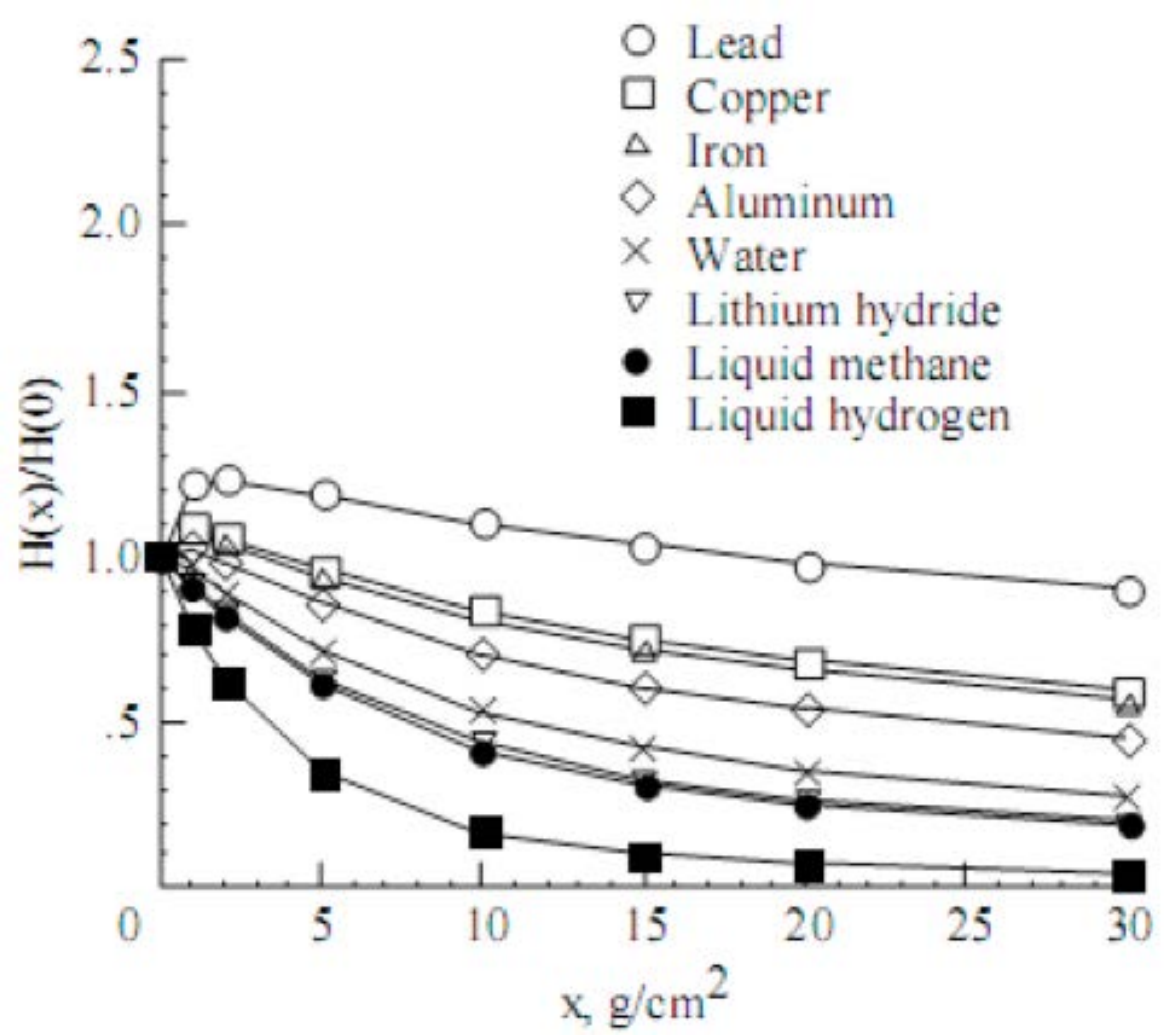
Francis Cucinotta, "What's New in Space Radiation Risk Assessments for Exploration" NASA Future In-Space Operations Telecon, May 18, 2011

Effective Dose Based on Shielding



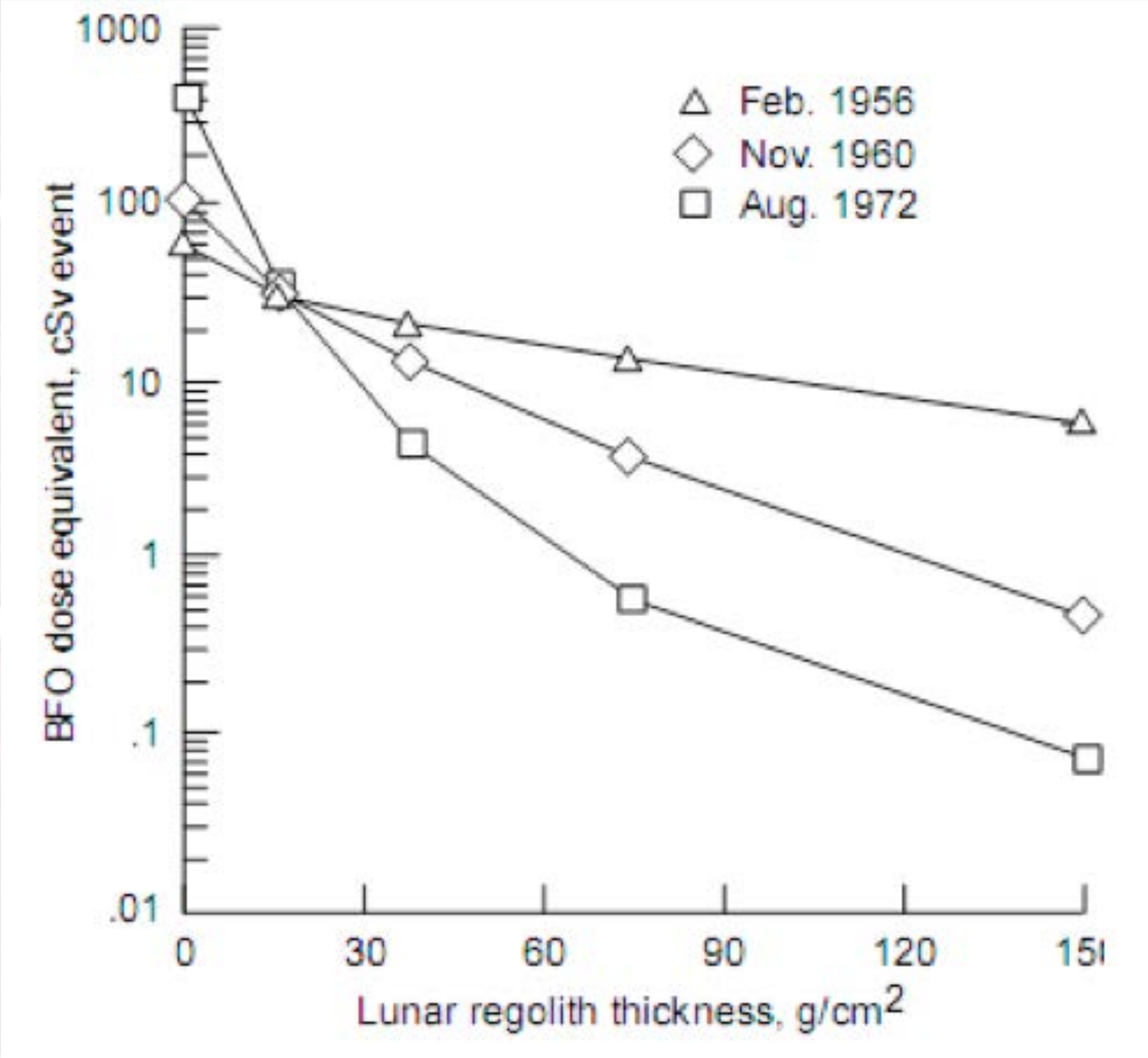
Francis A. Cucinotta, Myung-Hee Y. Kim, and Lei Ren, *Managing Lunar and Mars Mission Radiation Risks Part I: Cancer Risks, Uncertainties, and Shielding Effectiveness* NASA/TP-2005-213164, July, 2005

Shielding Materials Effect on GCR



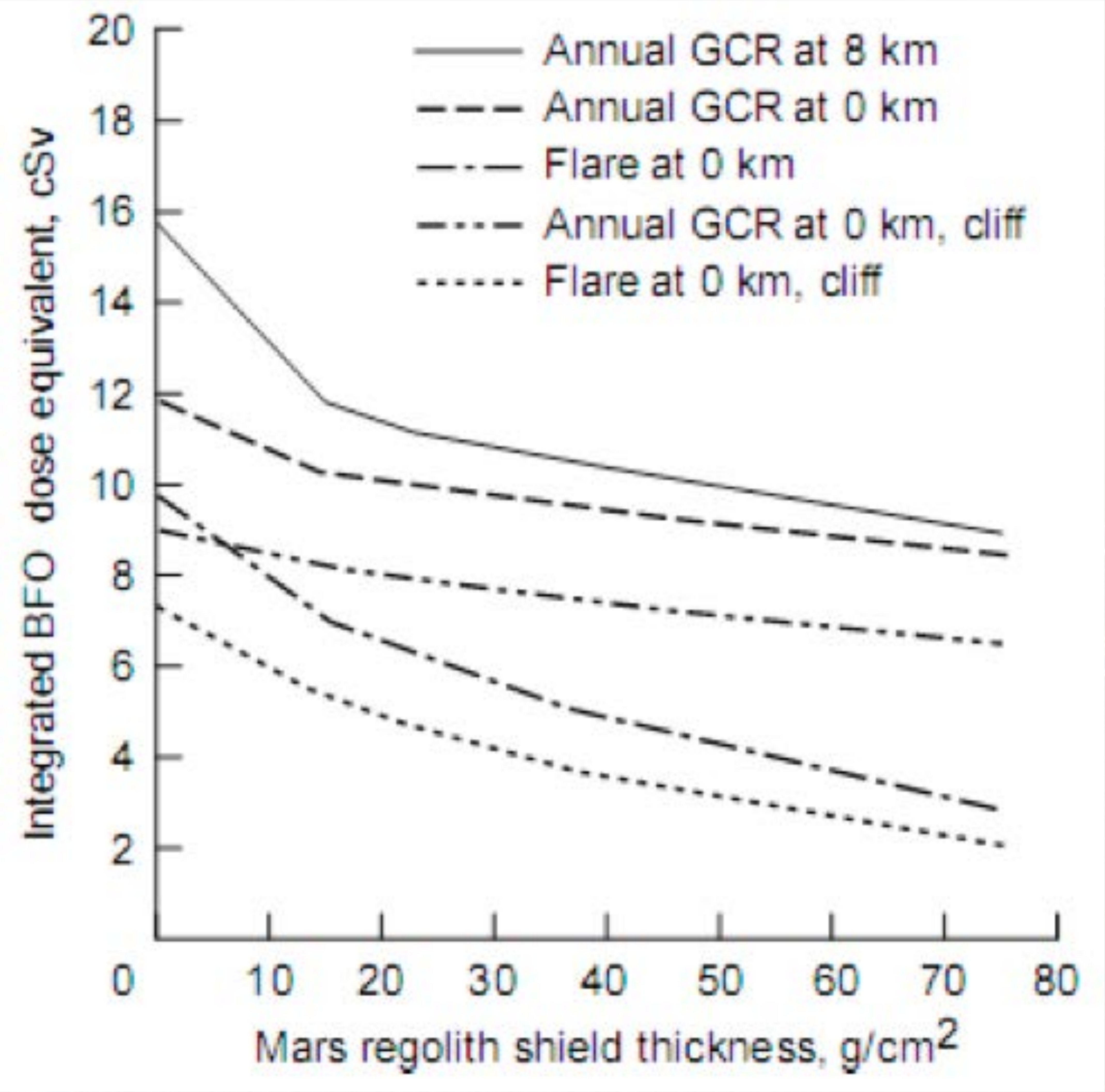
–, *Human Integration Design Handbook*, NASA SP-2010-3407, Jan. 2010

Lunar Regolith Shielding for SPE



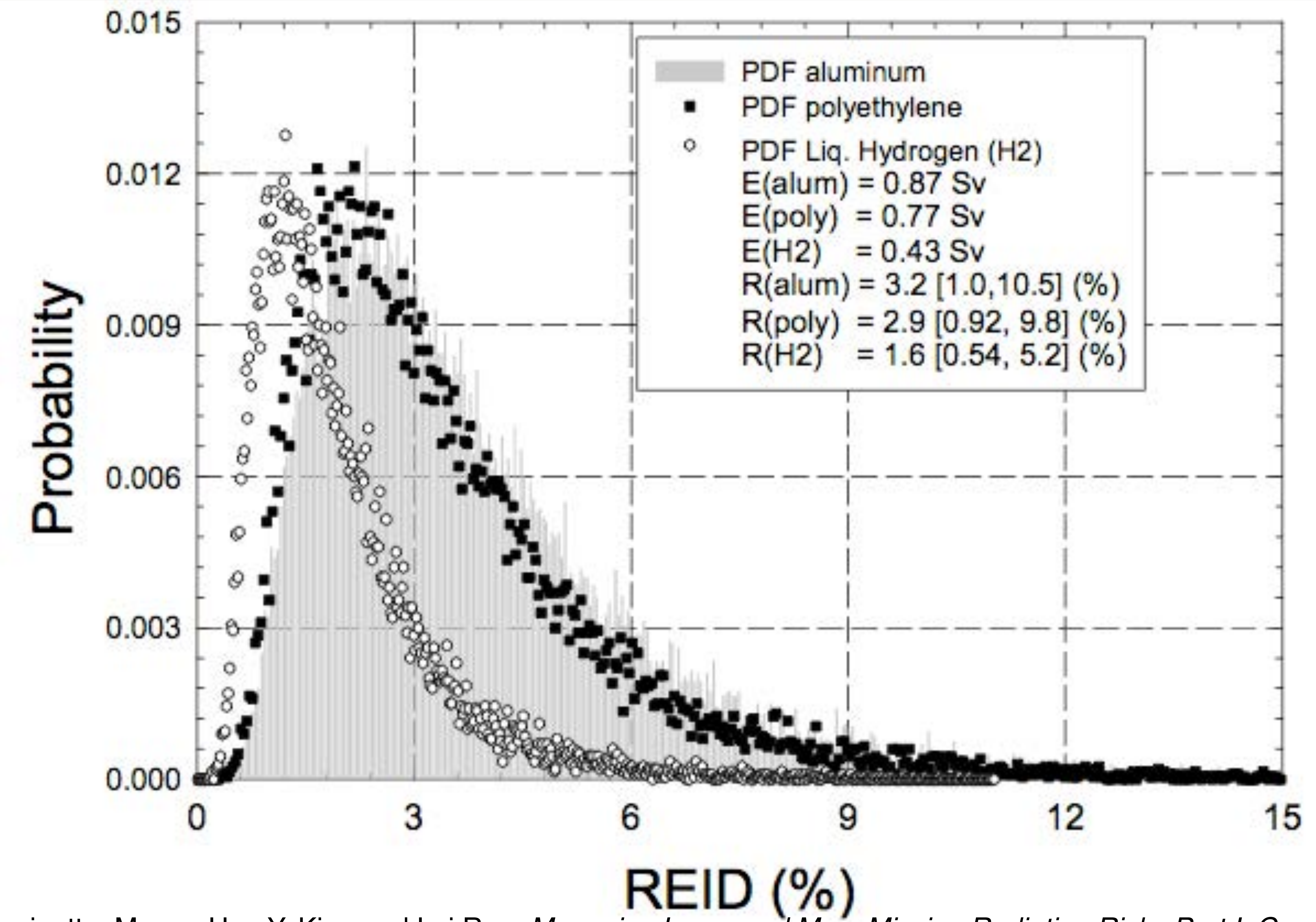
–, *Human Integration Design Handbook*, NASA SP-2010-3407, Jan. 2010

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**

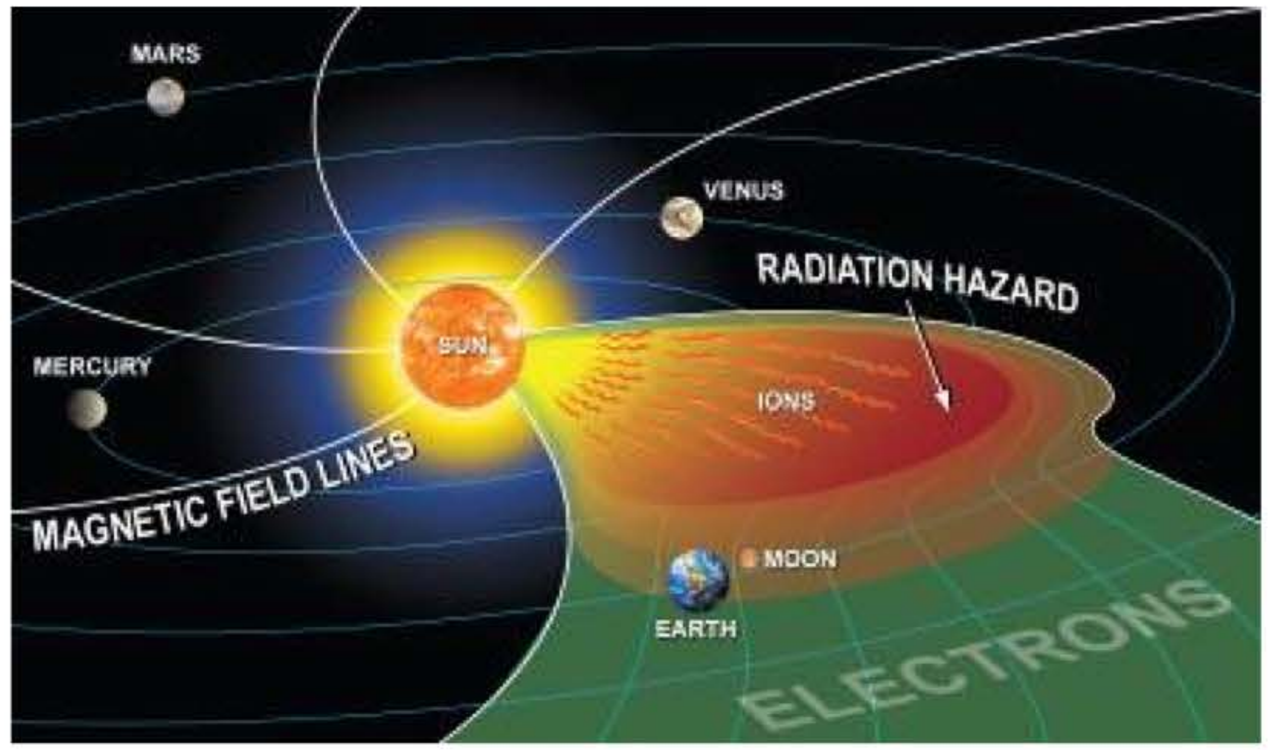
What's New in Space Radiation Research?

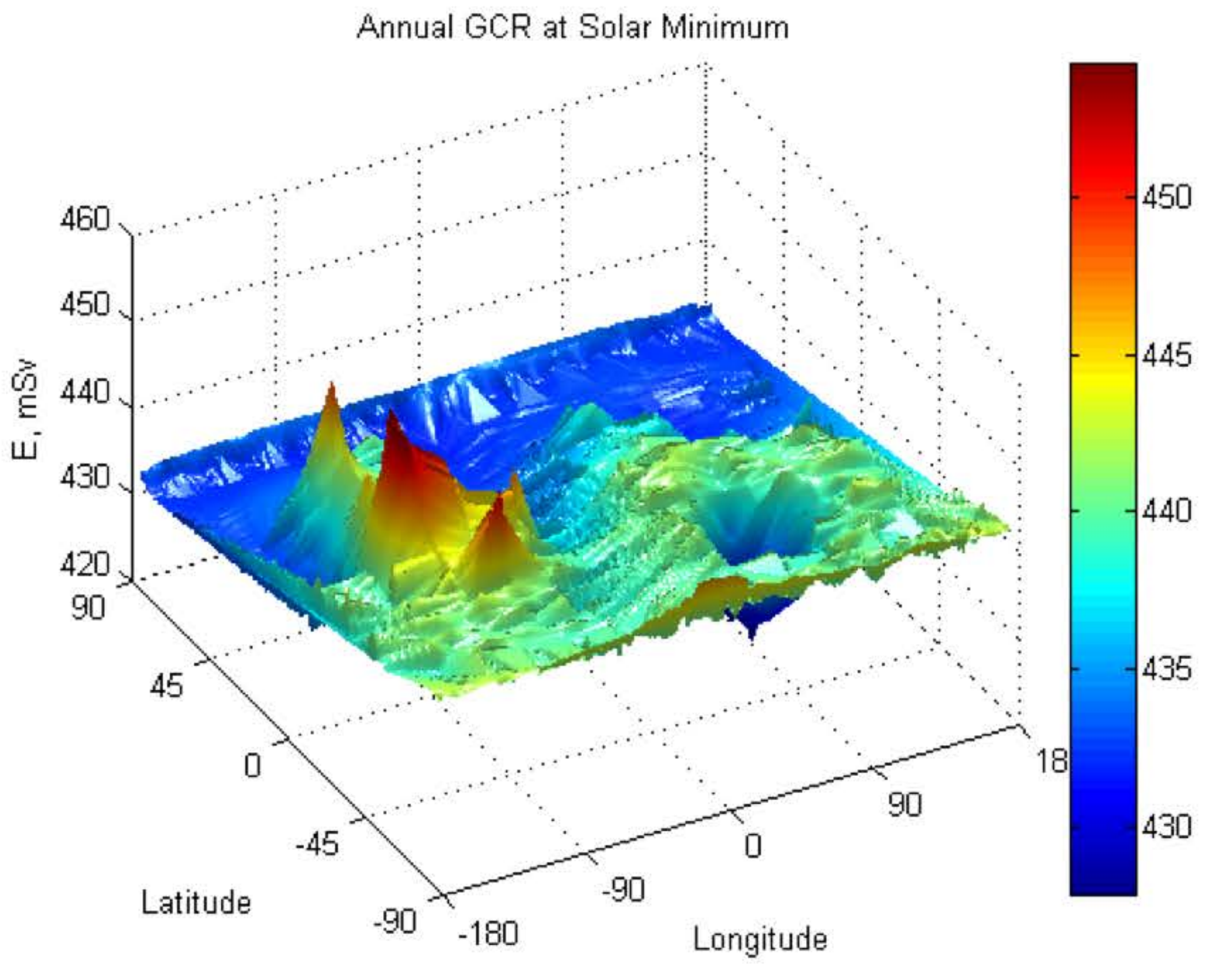
- New Epidemiology data suggests much weaker age dependence on radiation cancer risks
  - Number 1 Trade variable (Astronaut age) is negated
- Probabilistic risk assessments replace "rads and rem"
  - New Quality factors and uncertainty assessments
- Galactic cosmic rays (GCR) are much higher concern 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





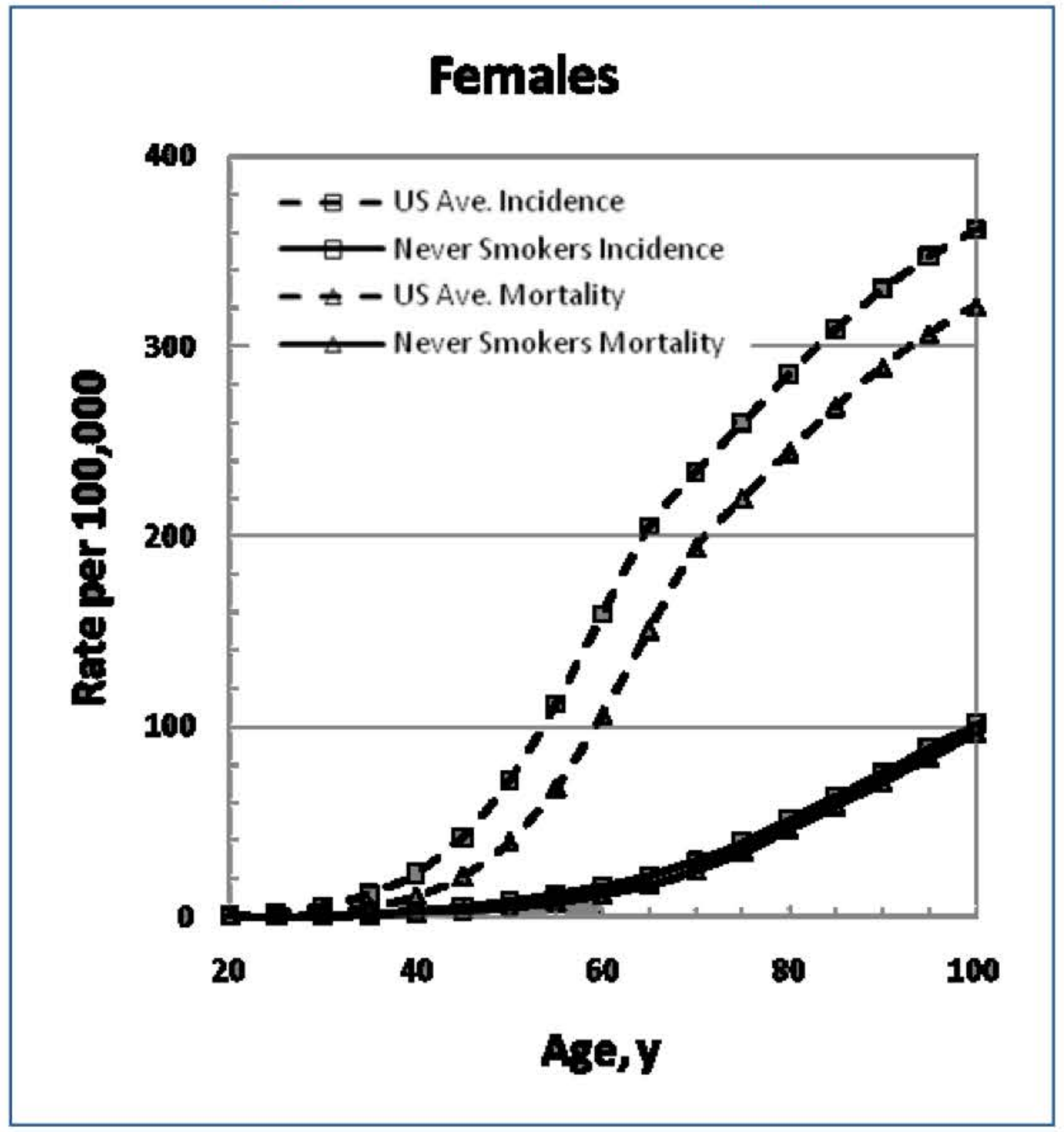
GCR doses on Mars

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

"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/cm^2 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 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

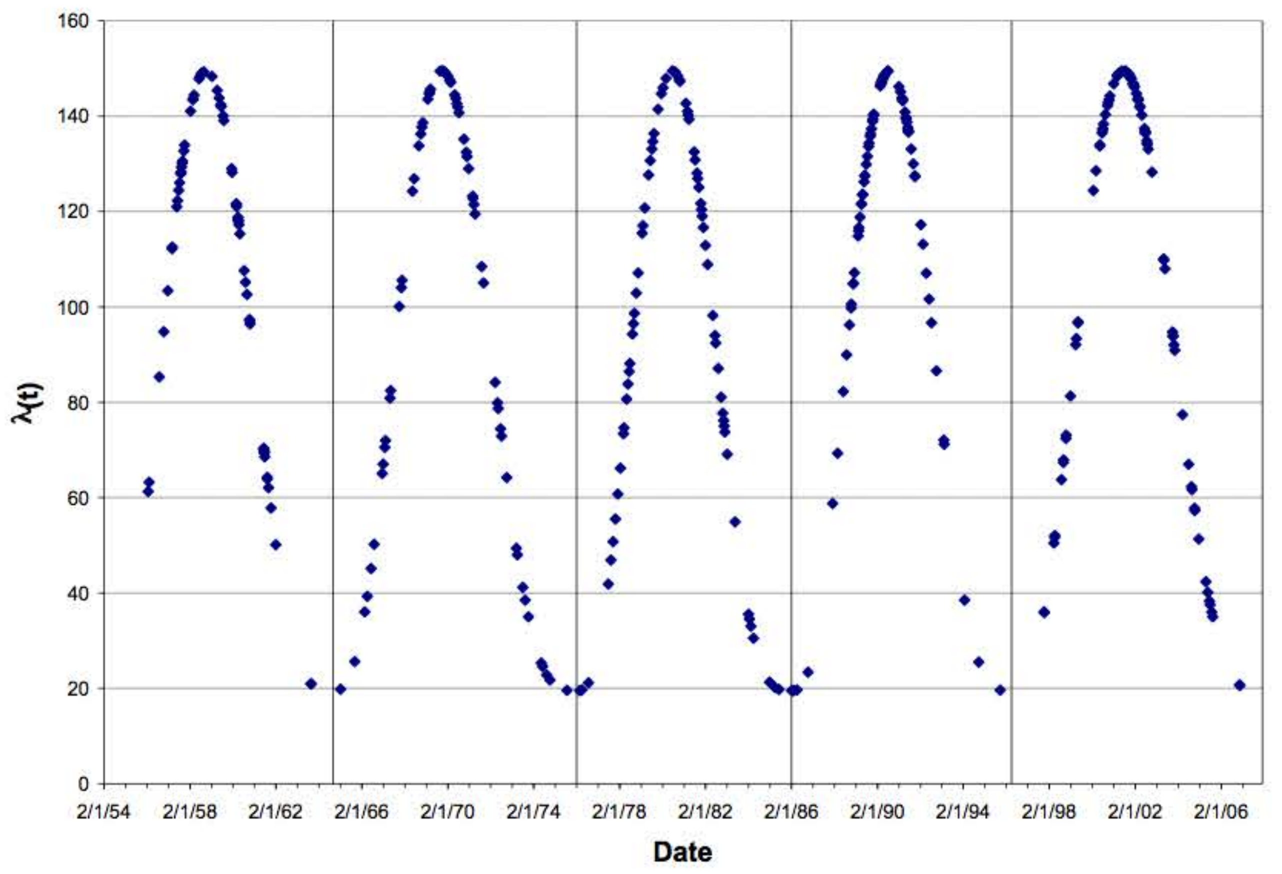
- Radiation sickness if unprotected > 2 hour EVA
- Cancer risk is priority for both EVA and IVA

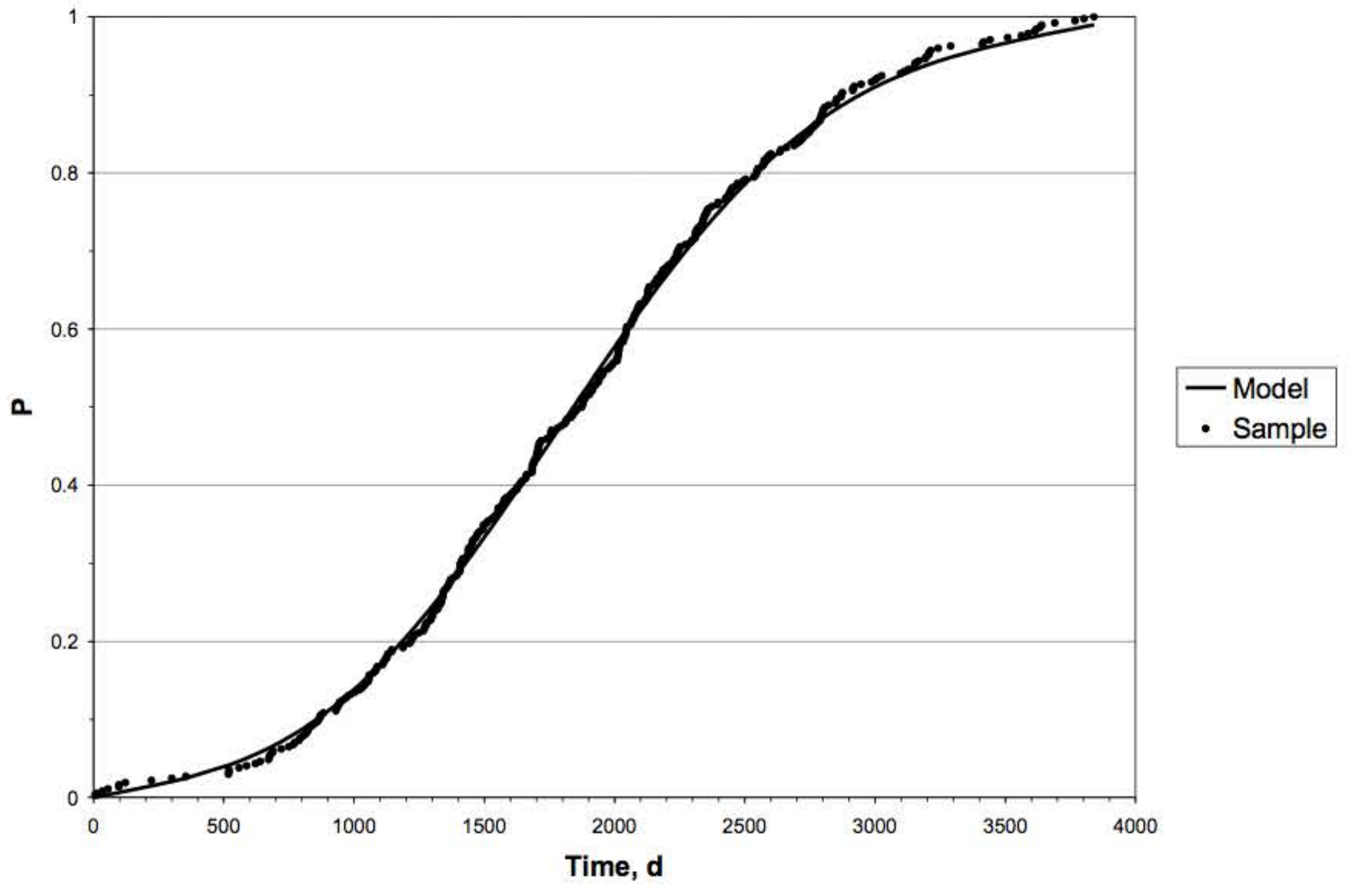
Proper resource management through research:

- 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





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

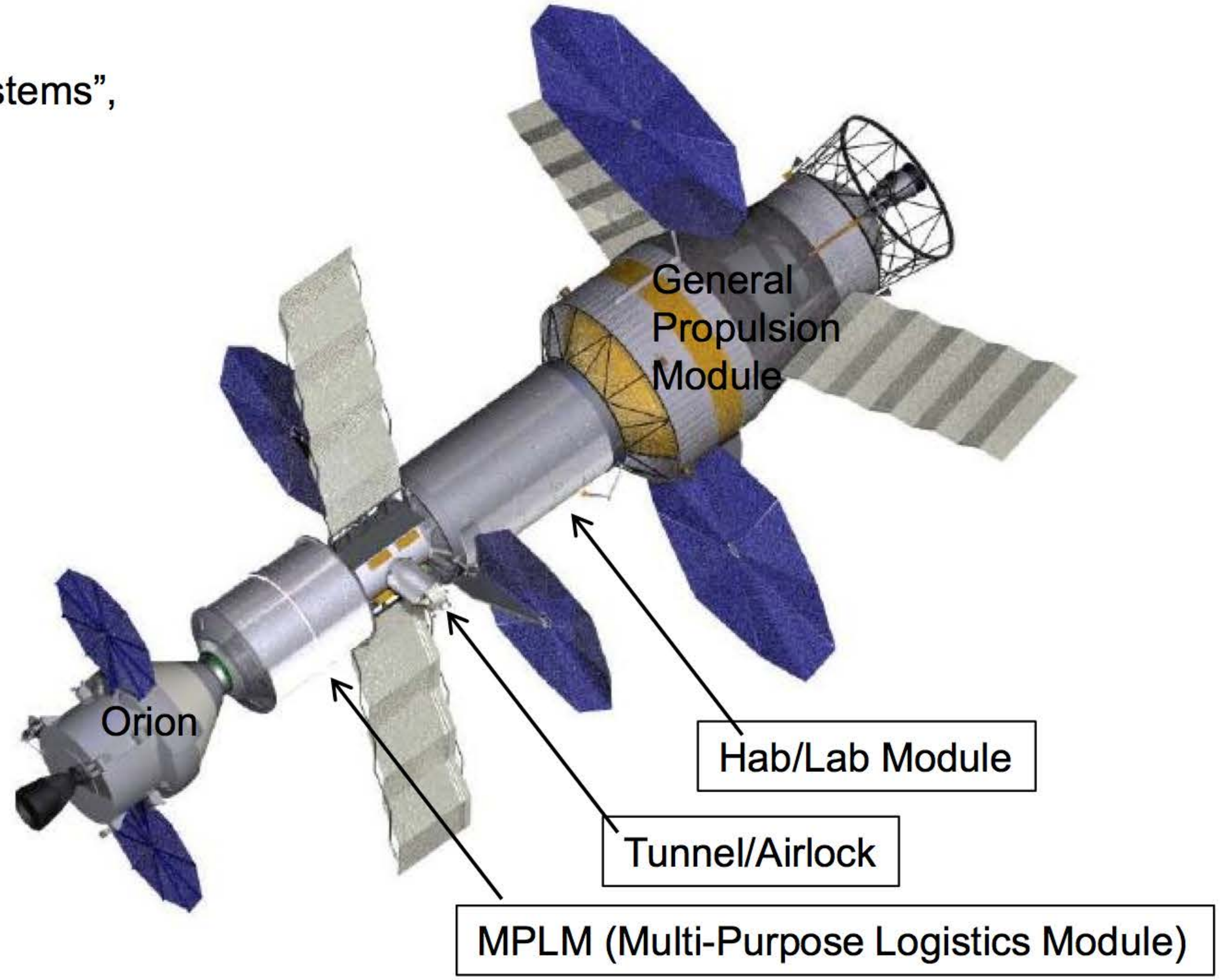
*MSFC study/ ISS-Derived Deep Space Facility

500-Day

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

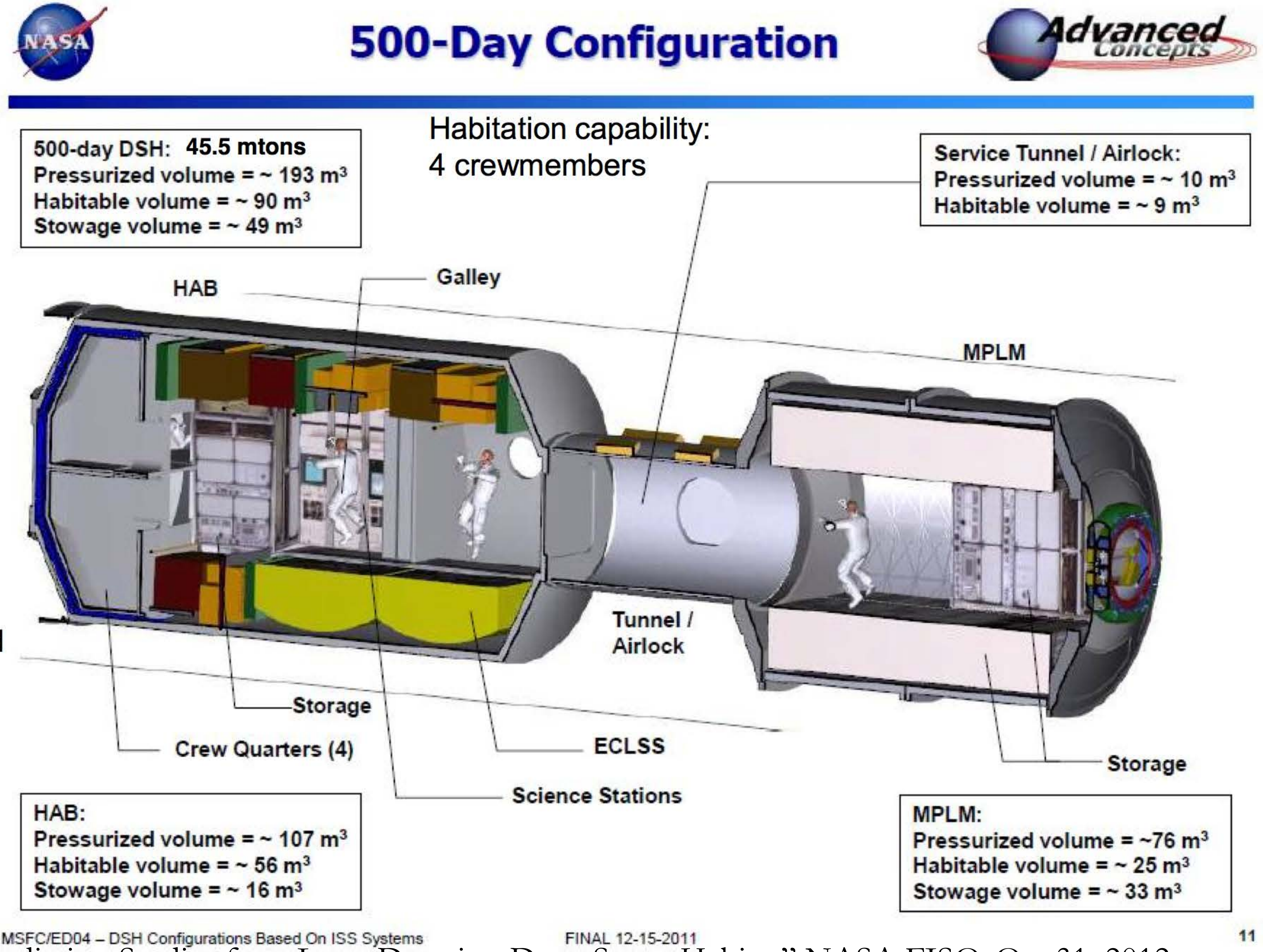
This transit habitat consists of three basic elements:

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

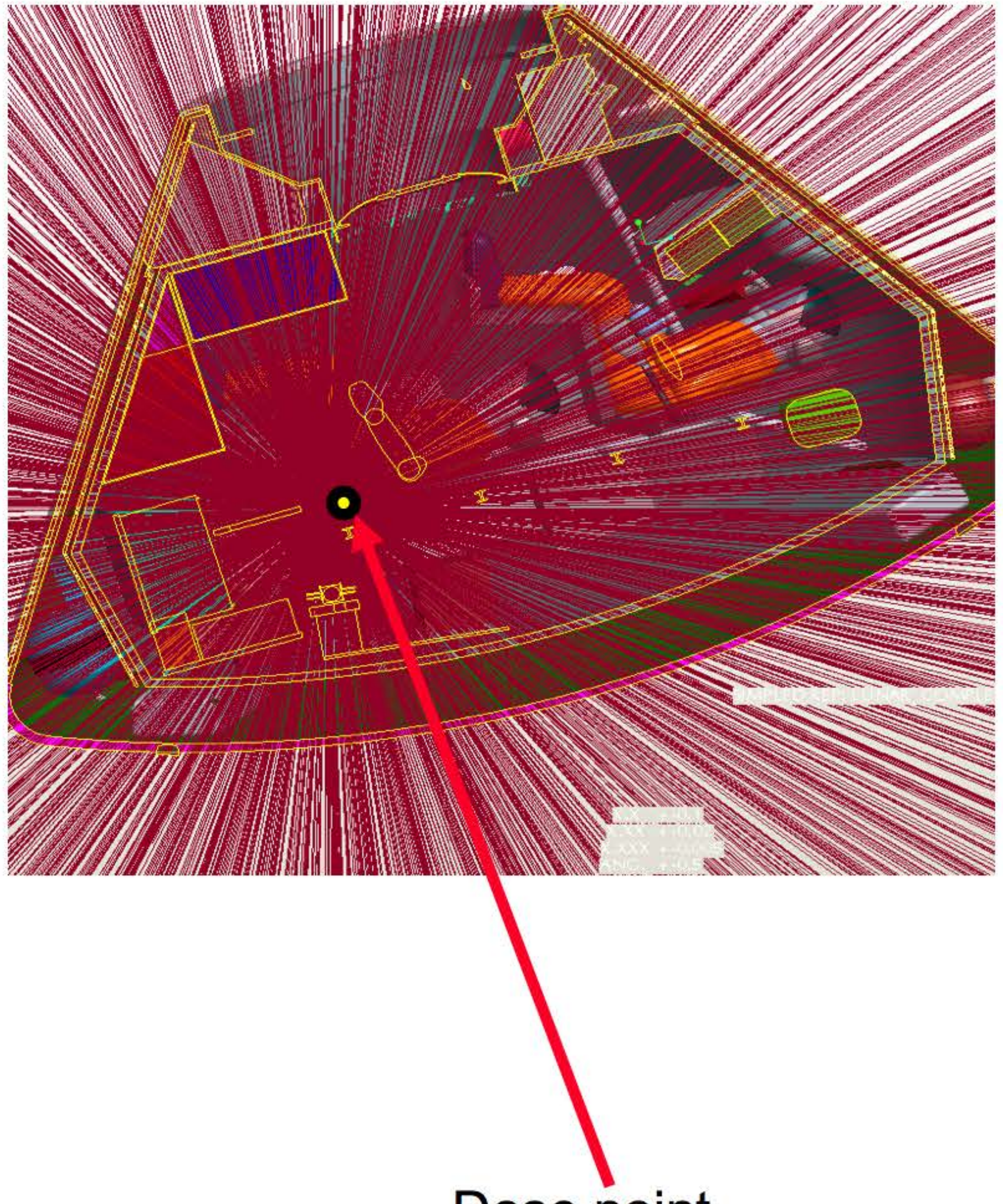


*Reference chart from "DSH Configurations based on ISS Systems", D. Smitherman, et al, 12/2011.

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.



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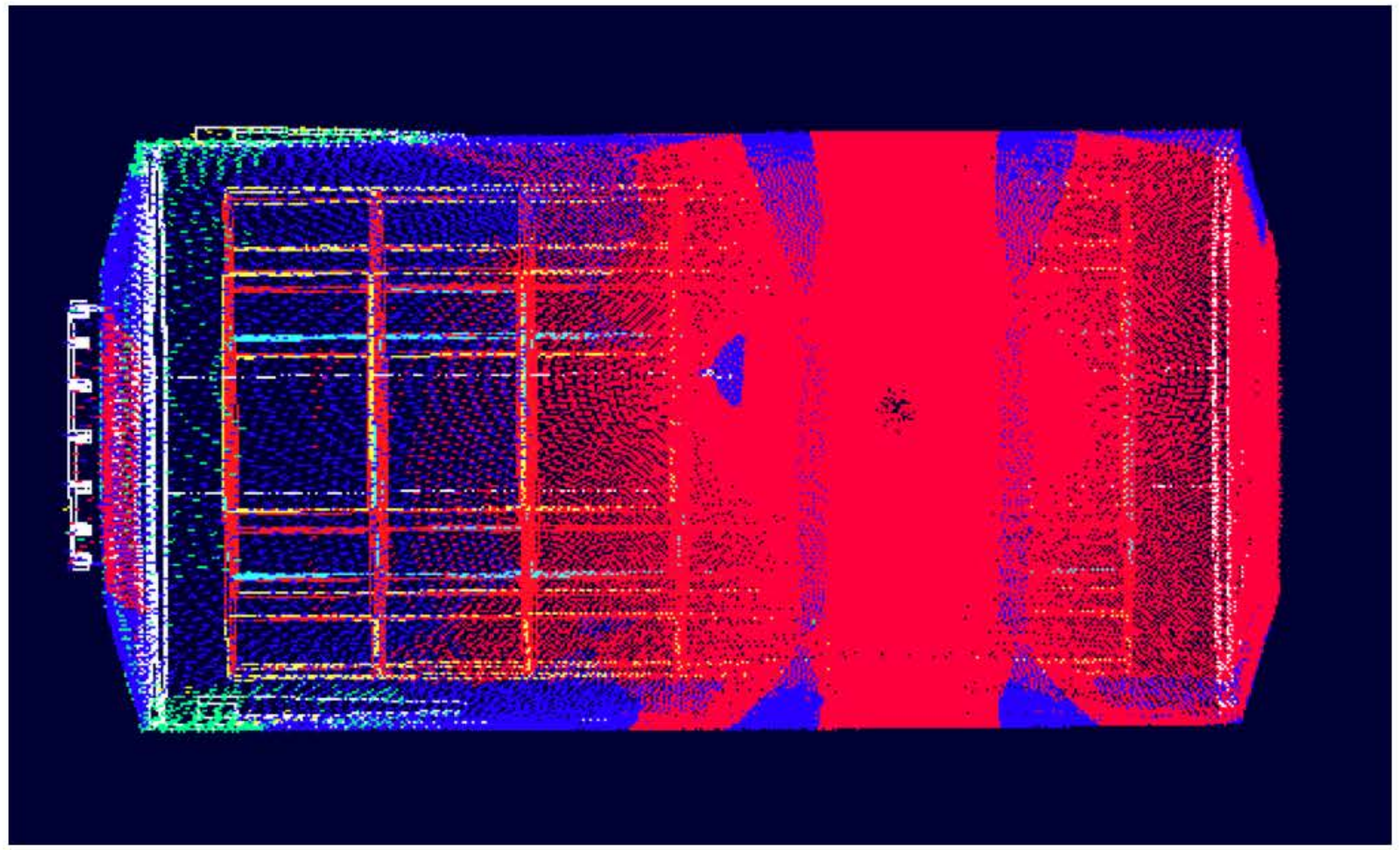
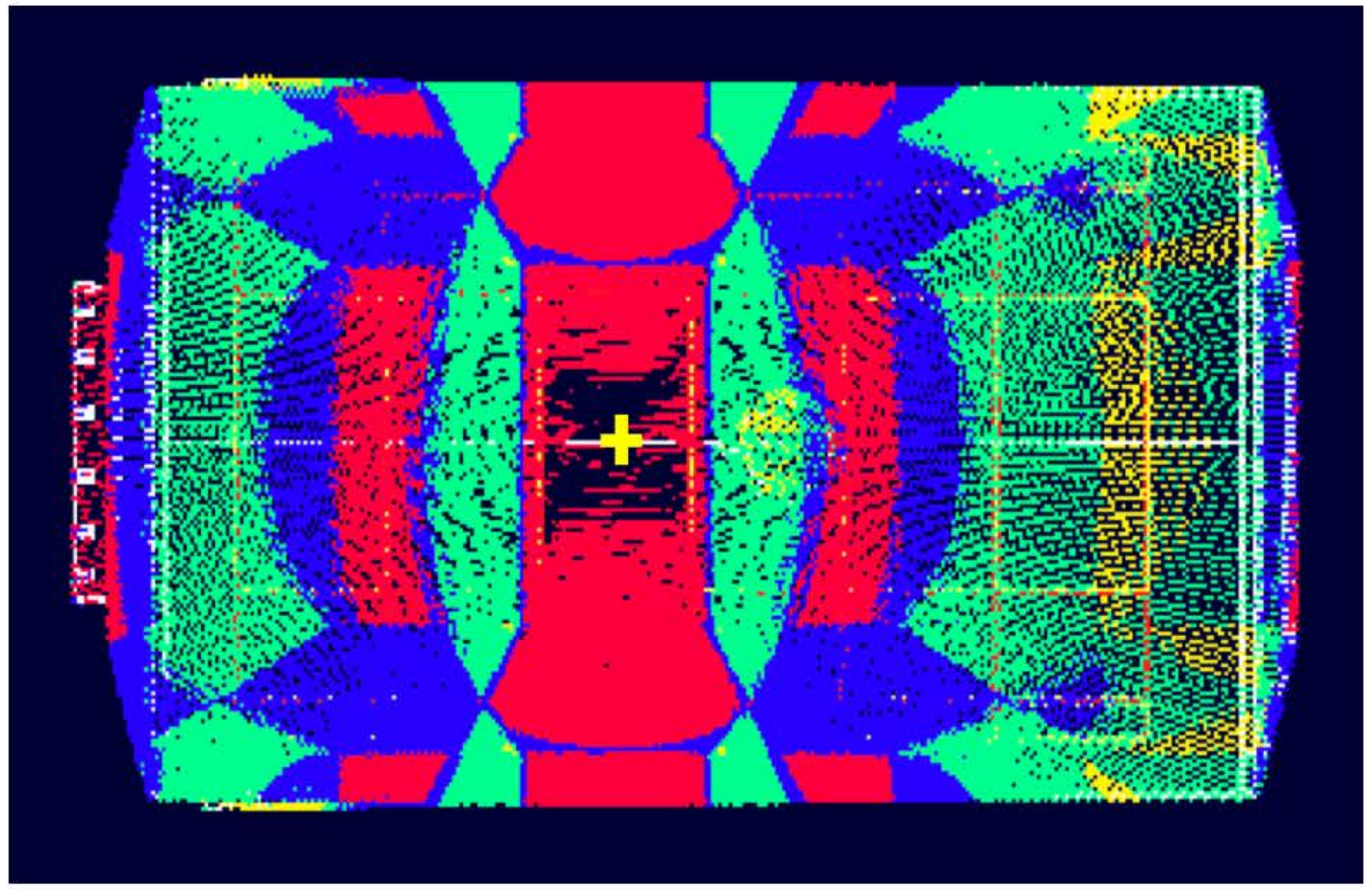
Hot Spots Detection Capabilities

Single dose point Color Coding



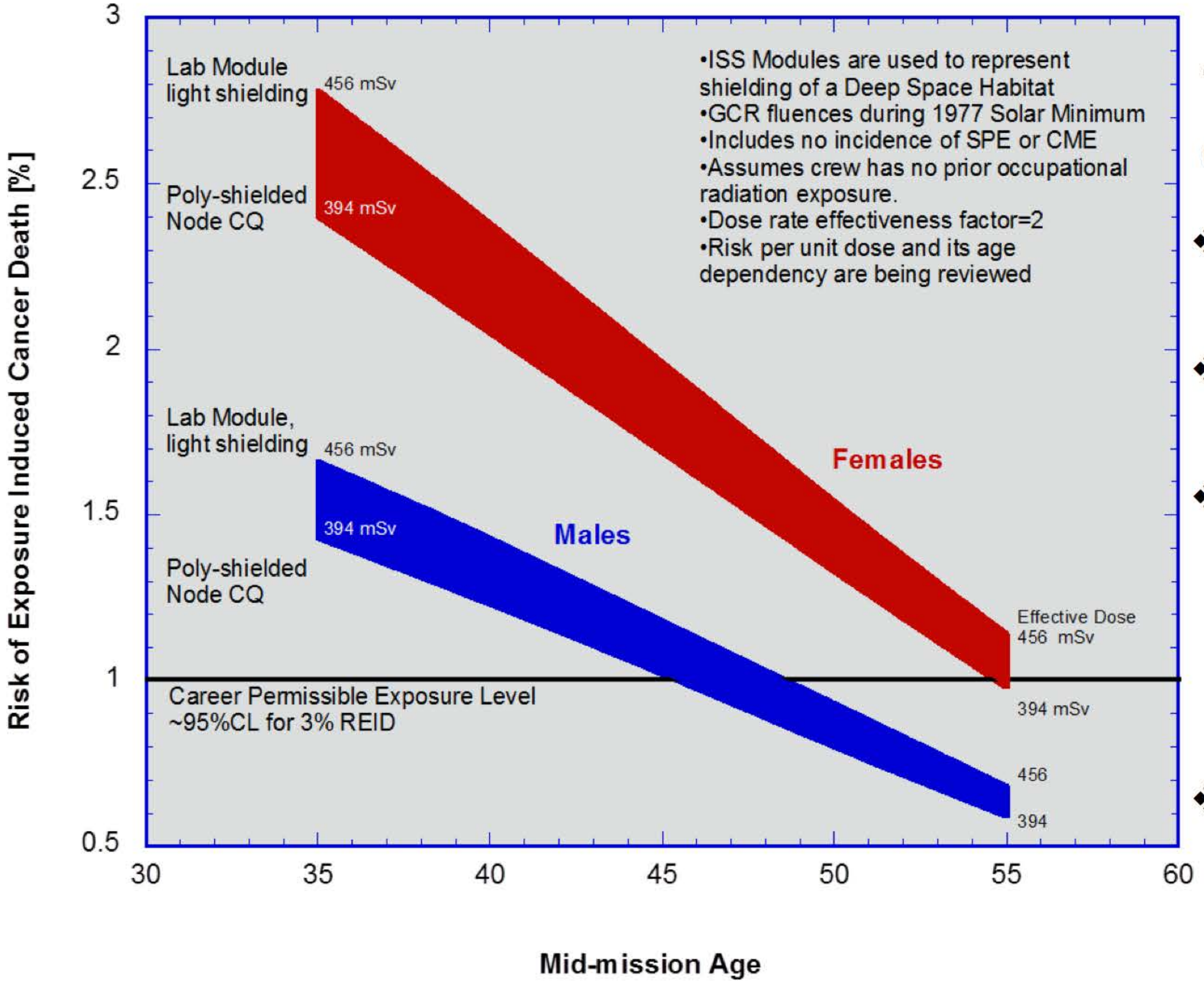


Every ray is color coded according to the areal density value-Shielding- it provides.

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

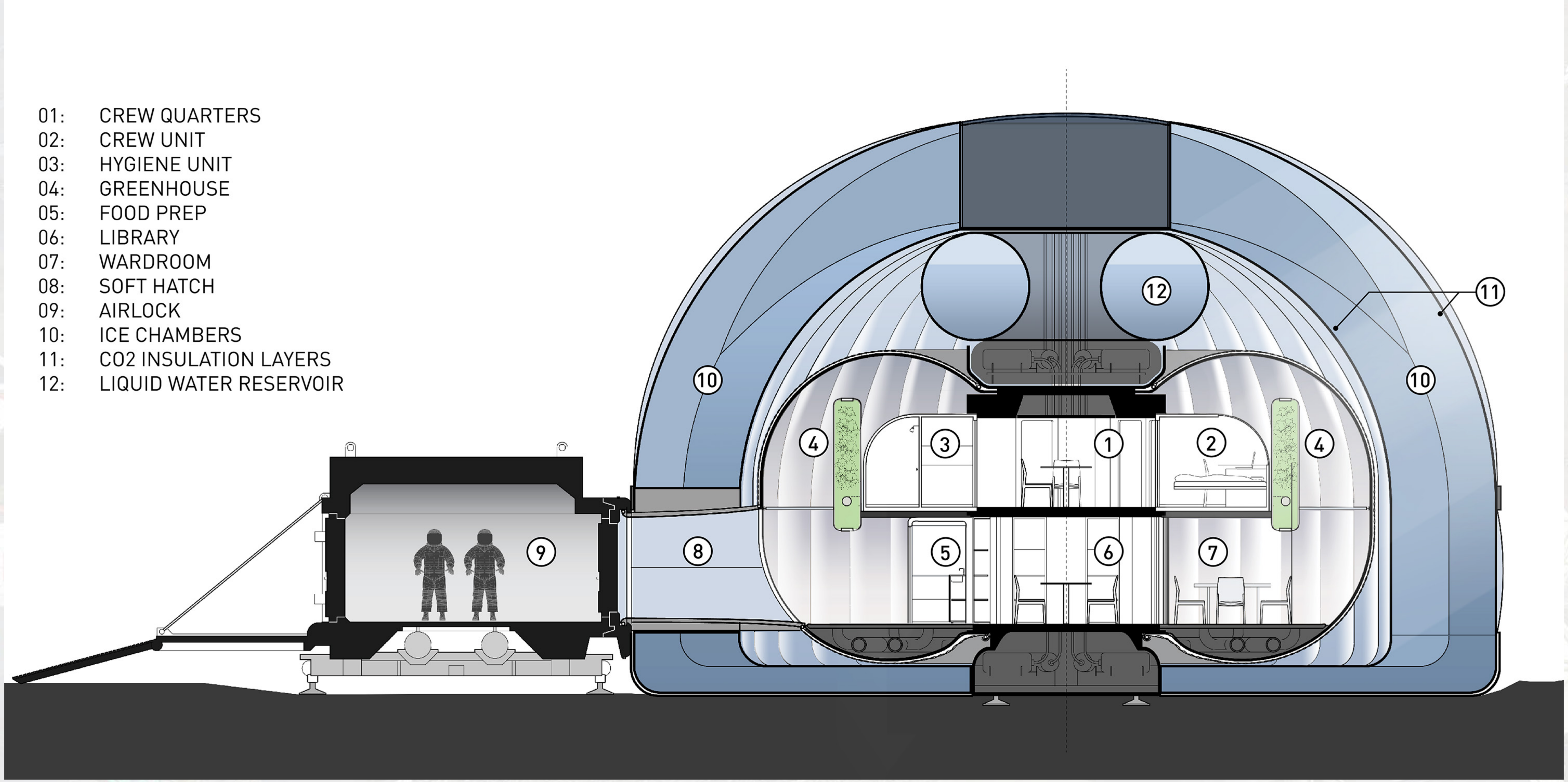
Areal density g/cm²	Aluminum Density = 2.7 g/cm³	Polyethylene or Water Density = 1.0 g/cm³	Liquid Hydrogen Density = 0.07 g/cm³ Boiling point = 20.28° K
1000	370 cm (146 in)	1,000 cm (394 in)	14, 285 cm (5624 in)
500	185 cm (72.8 in)	500 cm (197 in)	7,142 cm (2812 in)
100	37 cm (14.5 in)	100 cm (39.4 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

Early Mars Base Concept

NASA LaRC Ice Home Concept



Lava Tube Exploration

Lave Tubes – Earth and Mars Concept

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)

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

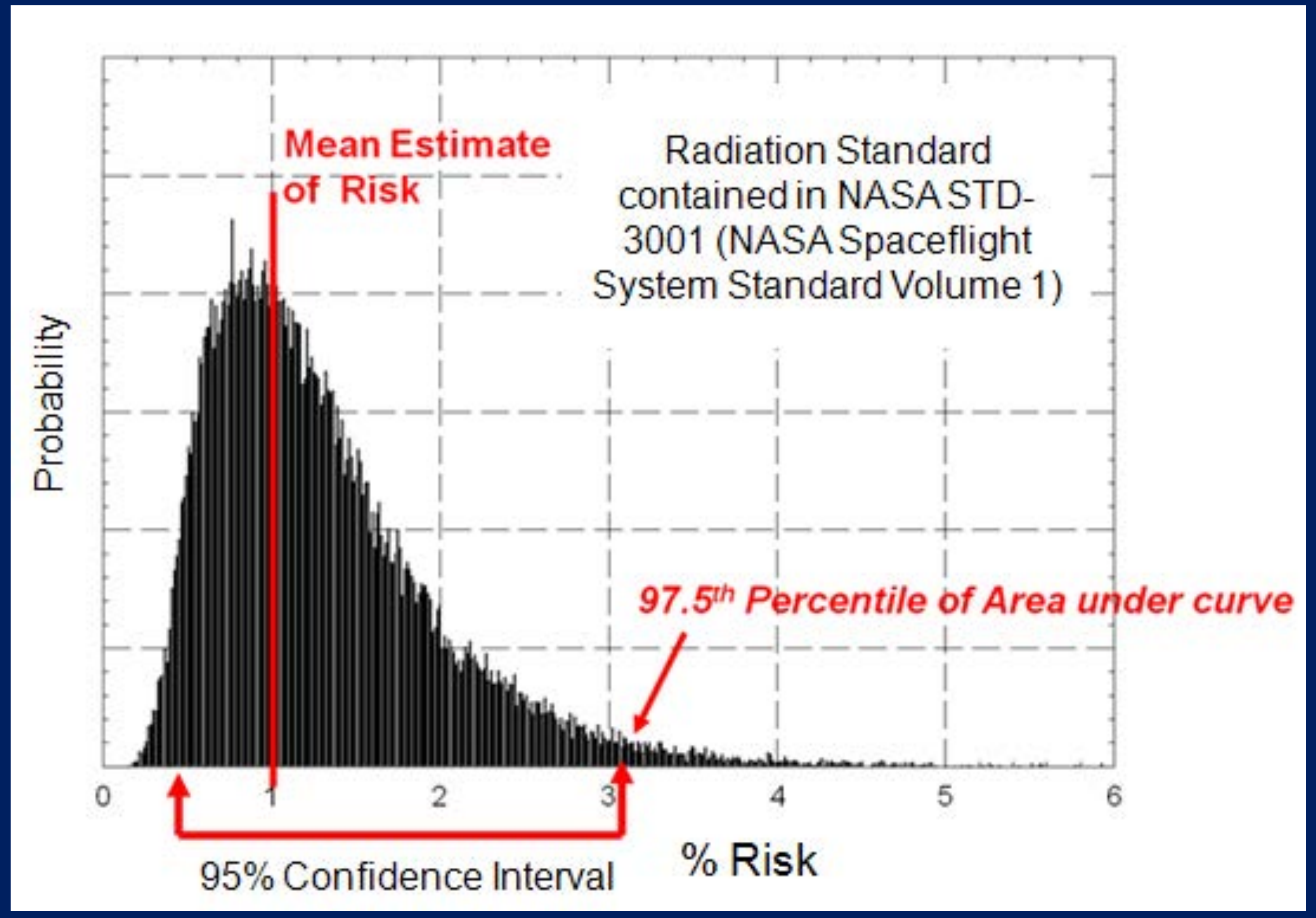
Approach to solve these problems:

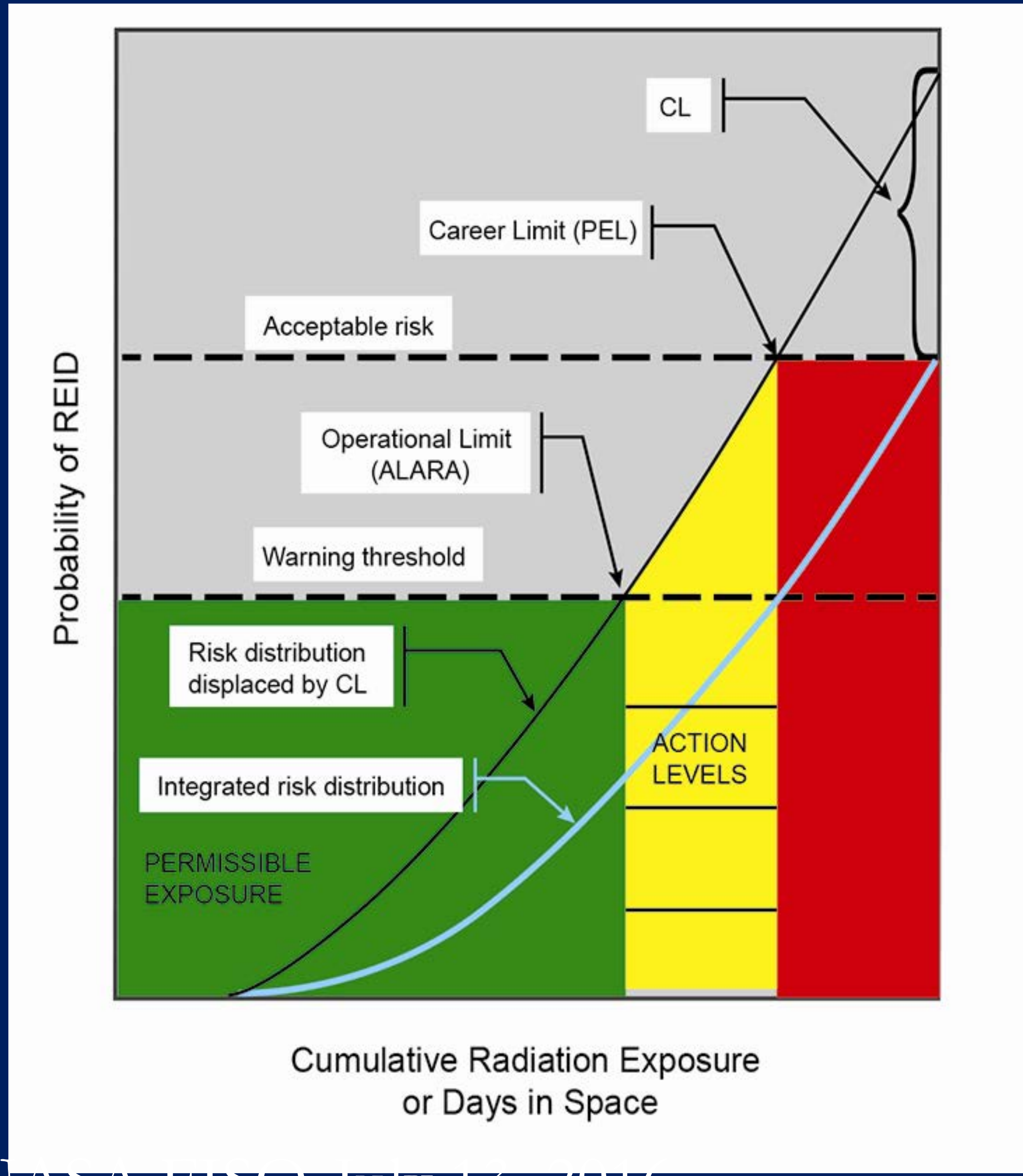
- Probabilistic risk assessment framework for Space Mission Design
- Hypothesis & Ground-based research
- Medical Policy Foundations for Safety

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

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

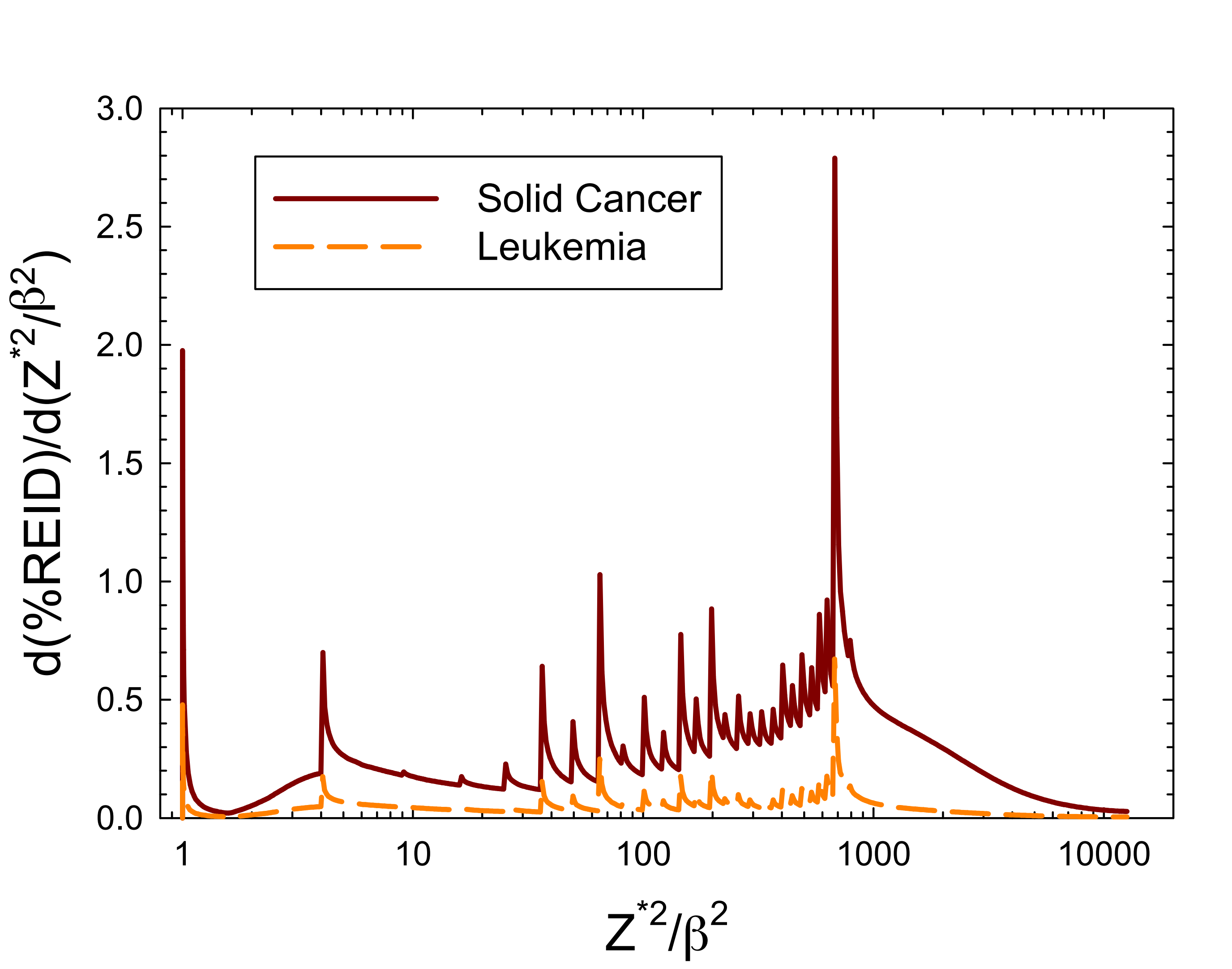
Uncertainties in Space Radiobiology Require New Knowledge and Approaches

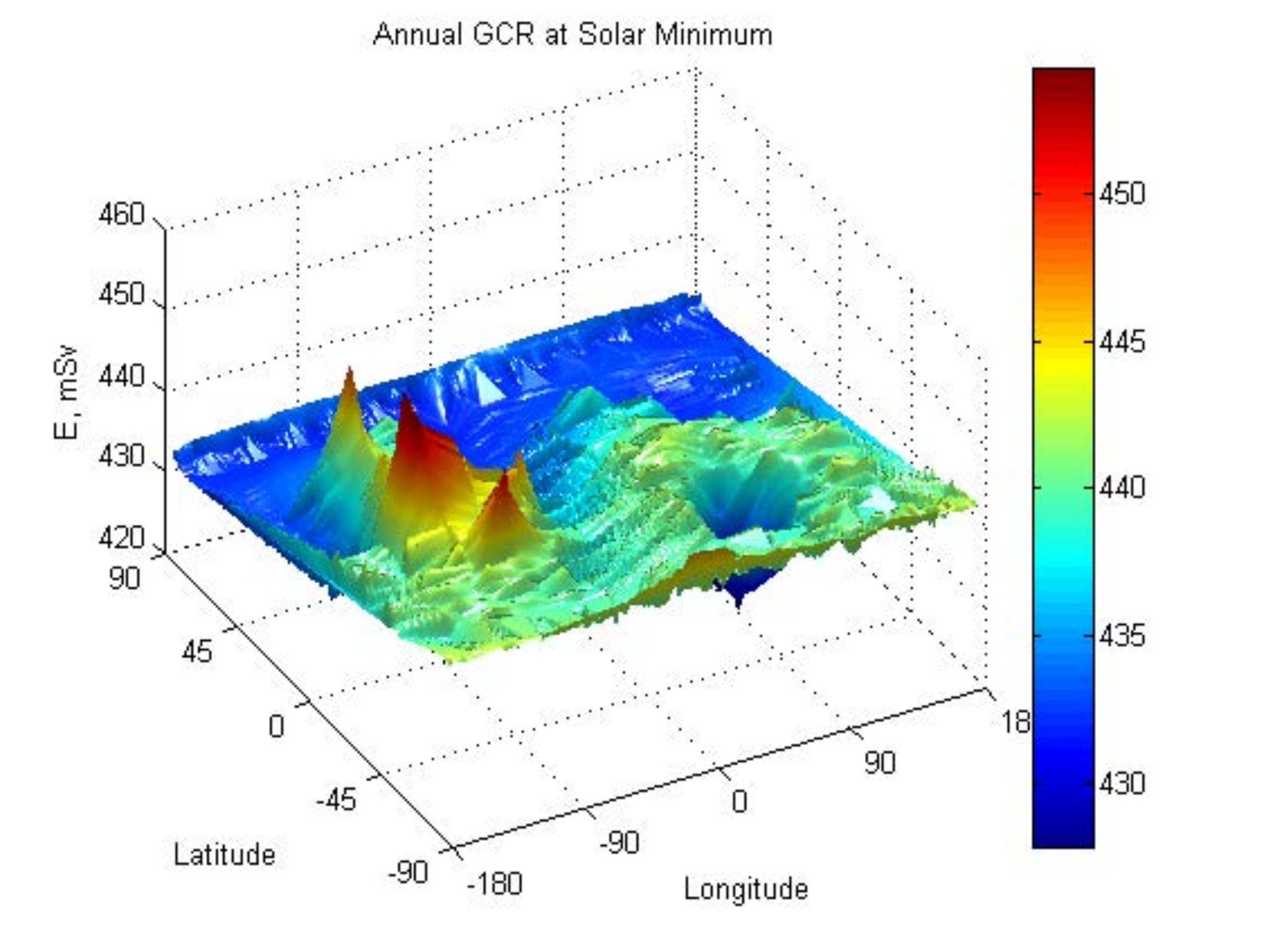
- NCRP Reports 98, 132, 152 noted risk estimates were highly uncertain for Galactic Cosmic Rays (GCR).
  - **Uncertainties too large for Earth based methods to be applied to GCR**
  - **NRC Reports in 1996, 1999 and 2008 echo these concerns**
- All experts agree that knowledge is limited:
  - Unlike 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

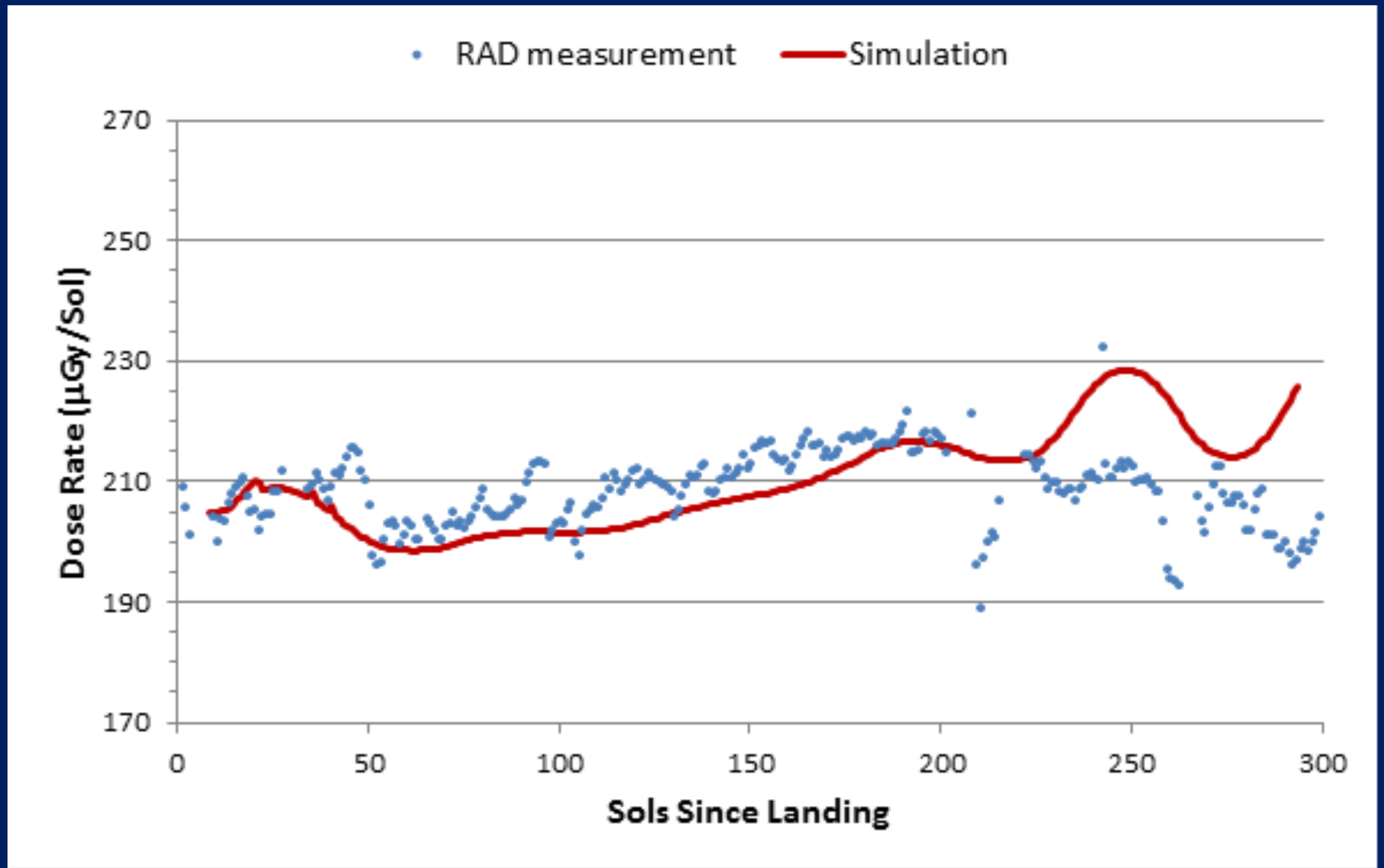
GCR dominate ISS organ risk





GCR doses on Mars

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

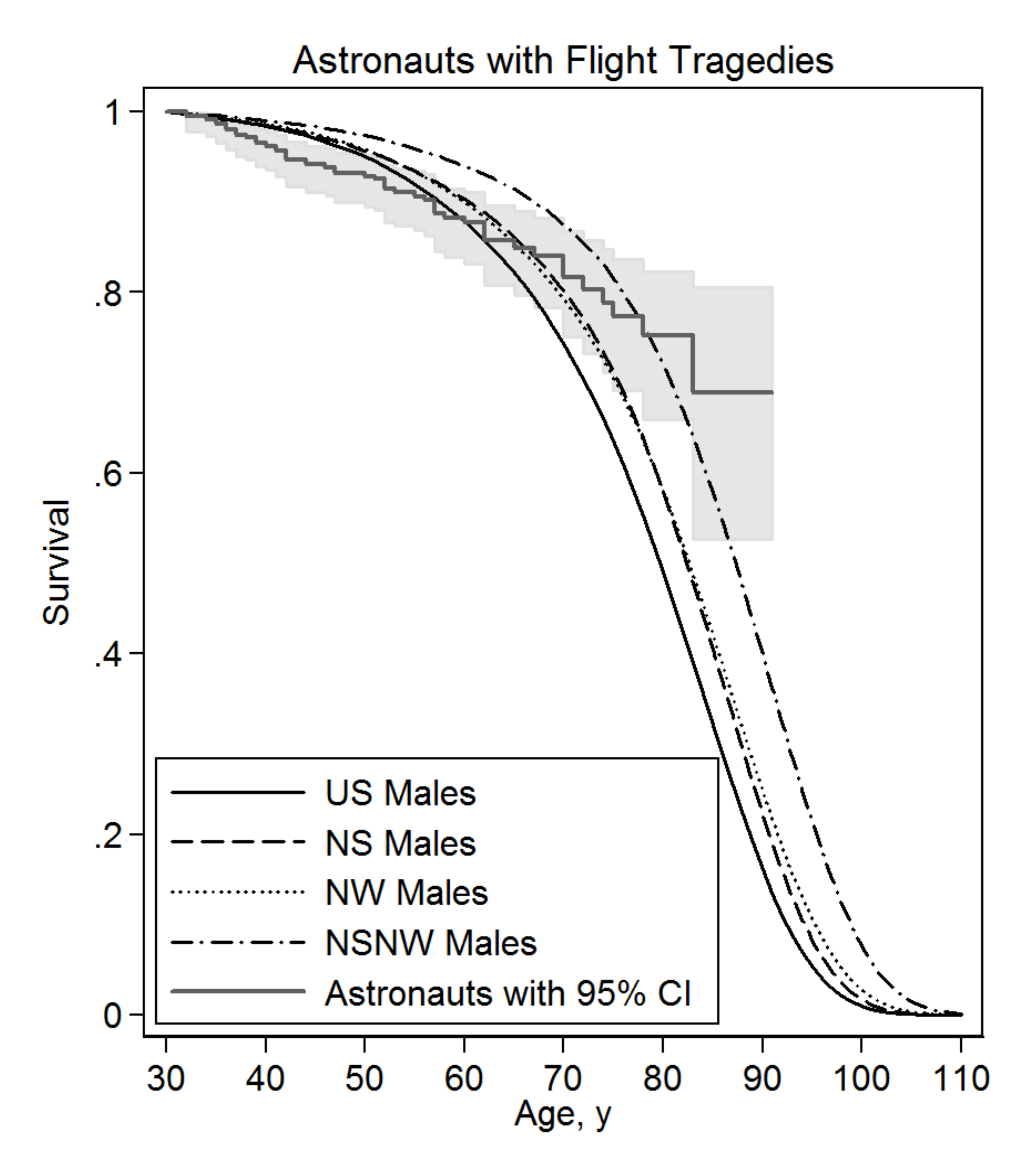


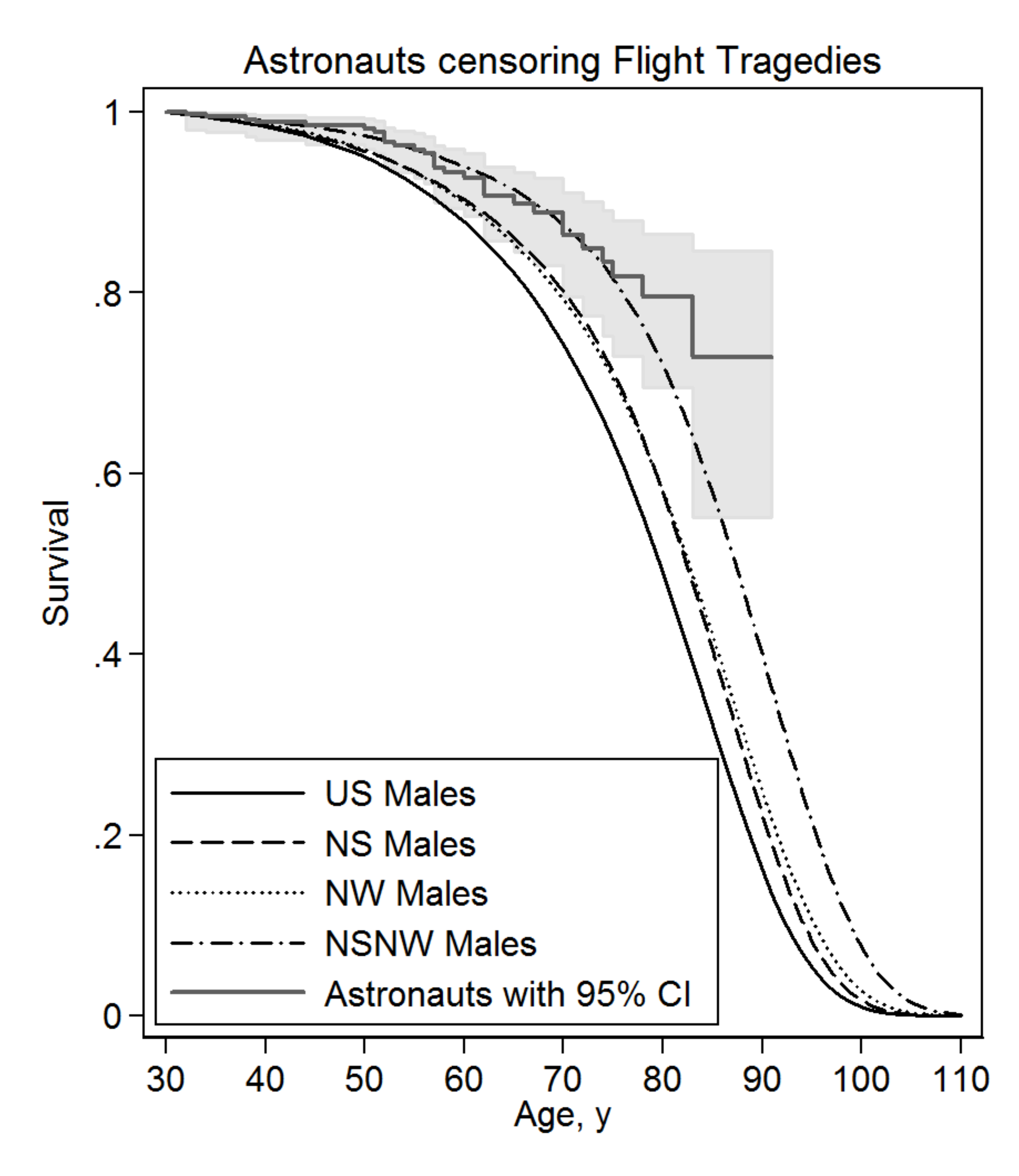
Comparison	GCR Dose Rate (mGy/day)	GCR Dose Equiv. Rate (mSv/day)
Model Cruise to Mars	0.445	1.80
RAD Cruise to Mars (Zeitlin et al. 2013)	0.481±0.08	1.84±0.33
Model Mars surface (Kim et al. 2014)	0.20	0.72
RAD Mars Surface (Hassler et al. 2014)	0.205±0.05	0.70±0.17

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.	1.13 [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**

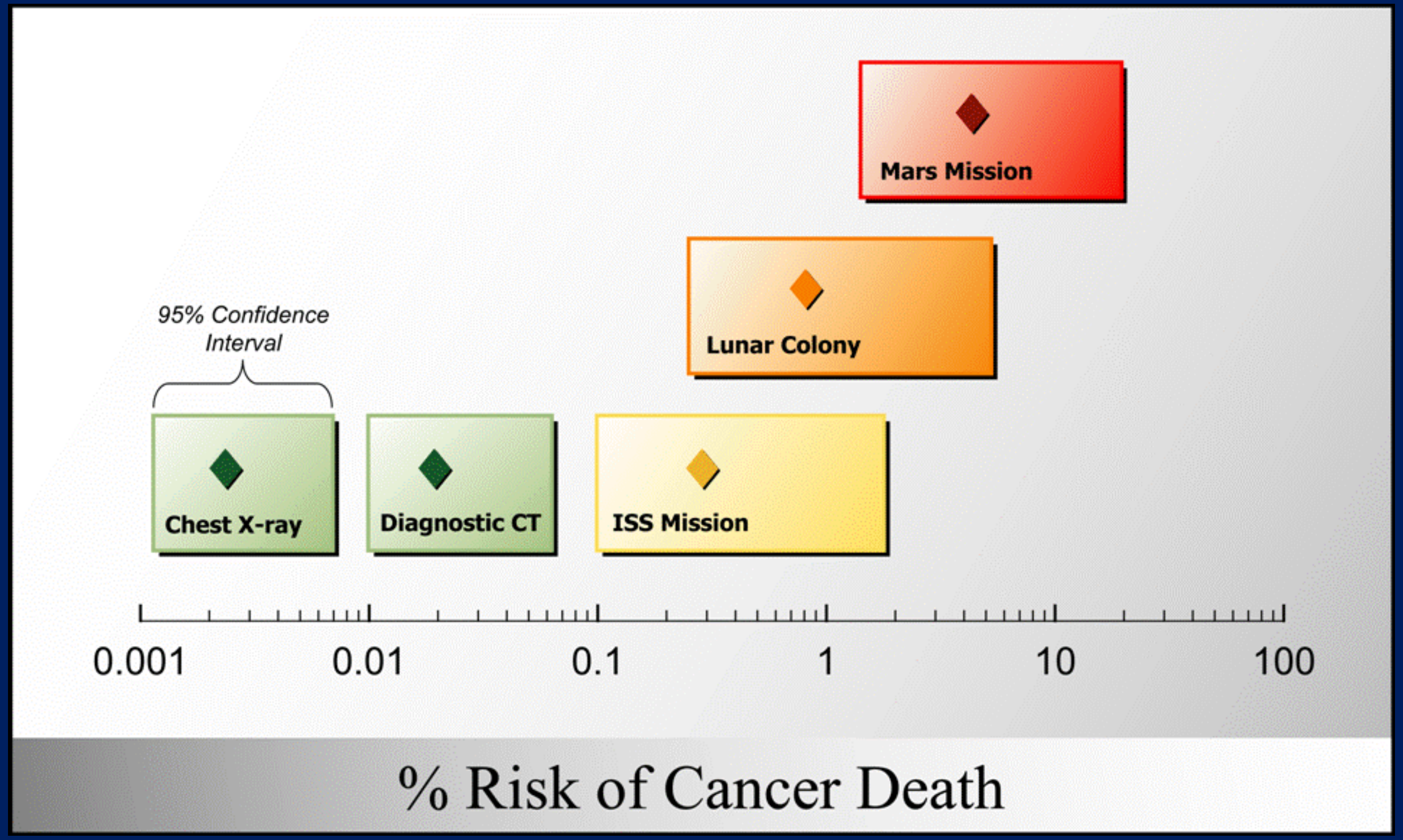
Comparison	*SMR*
Astronauts vs. U.S. avg.	0.33 [0.14, 0.80]
Astronauts vs. NS avg.	0.43 [0.18, 1.04]
Astronauts vs NW avg.	0.47 [0.19, 1.12]
Astronauts vs NS-NW Avg.	0.67 [0.28, 1.62]

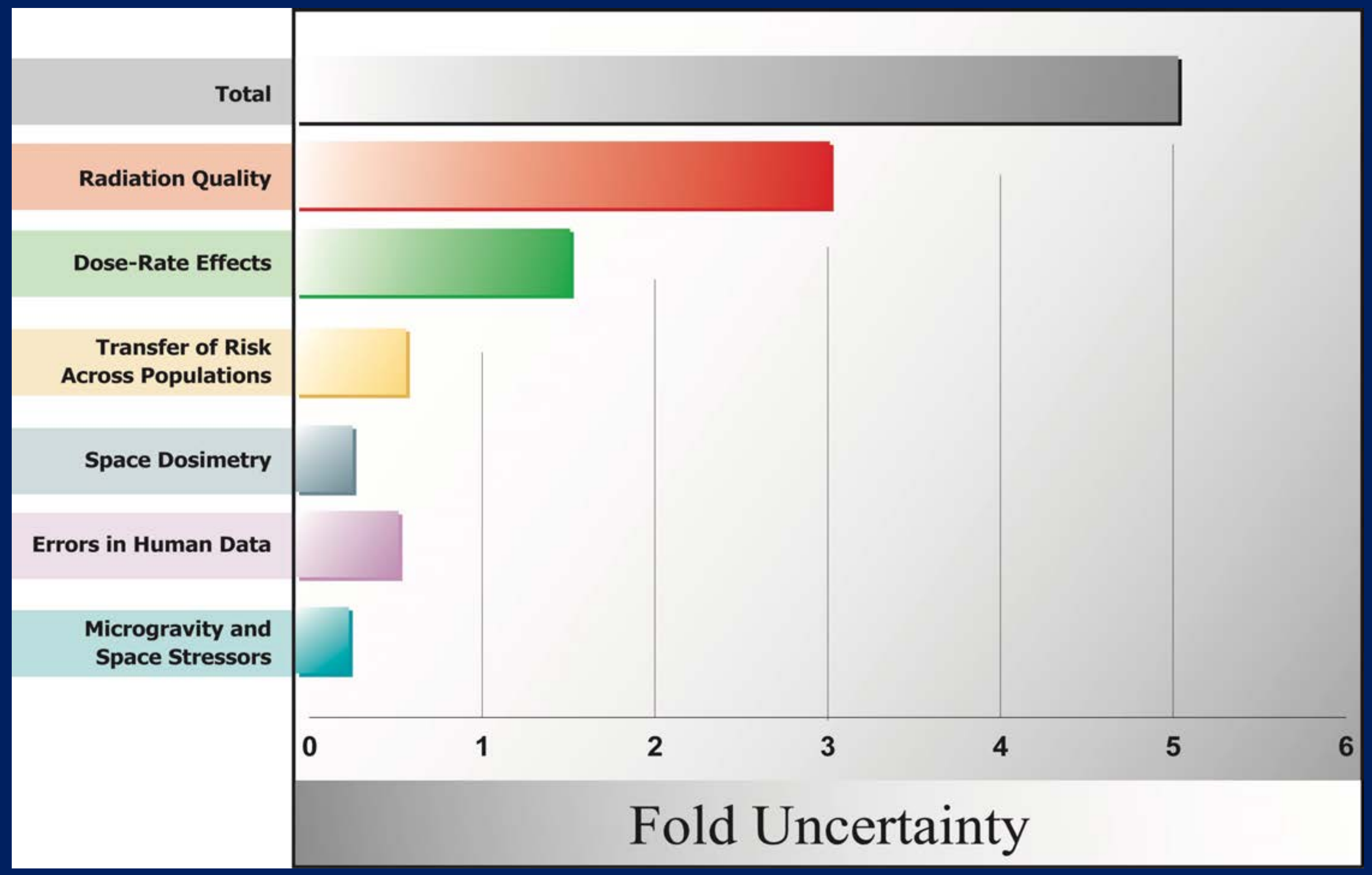
NS = never-smoker, NW = Normal Weight

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

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

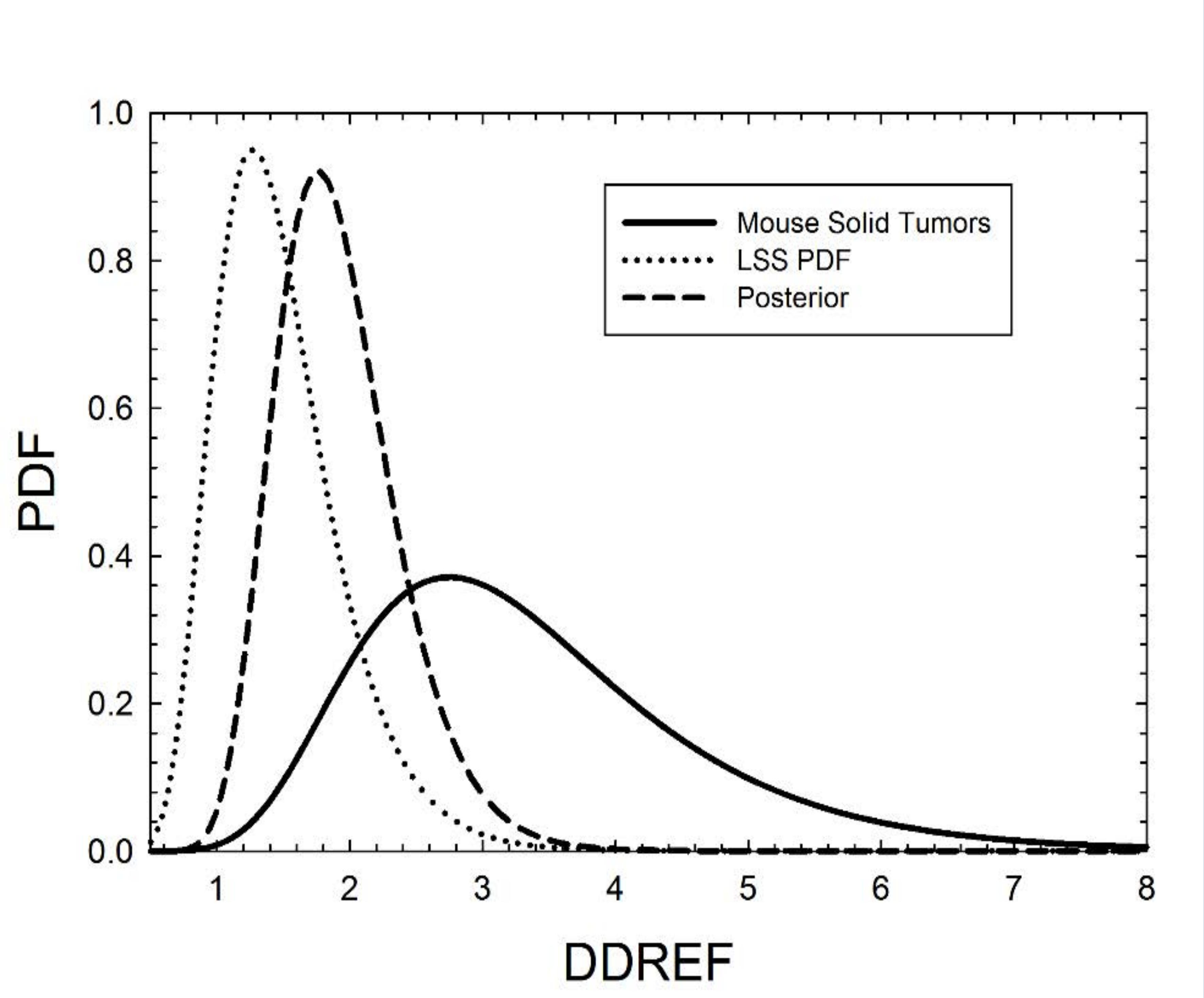




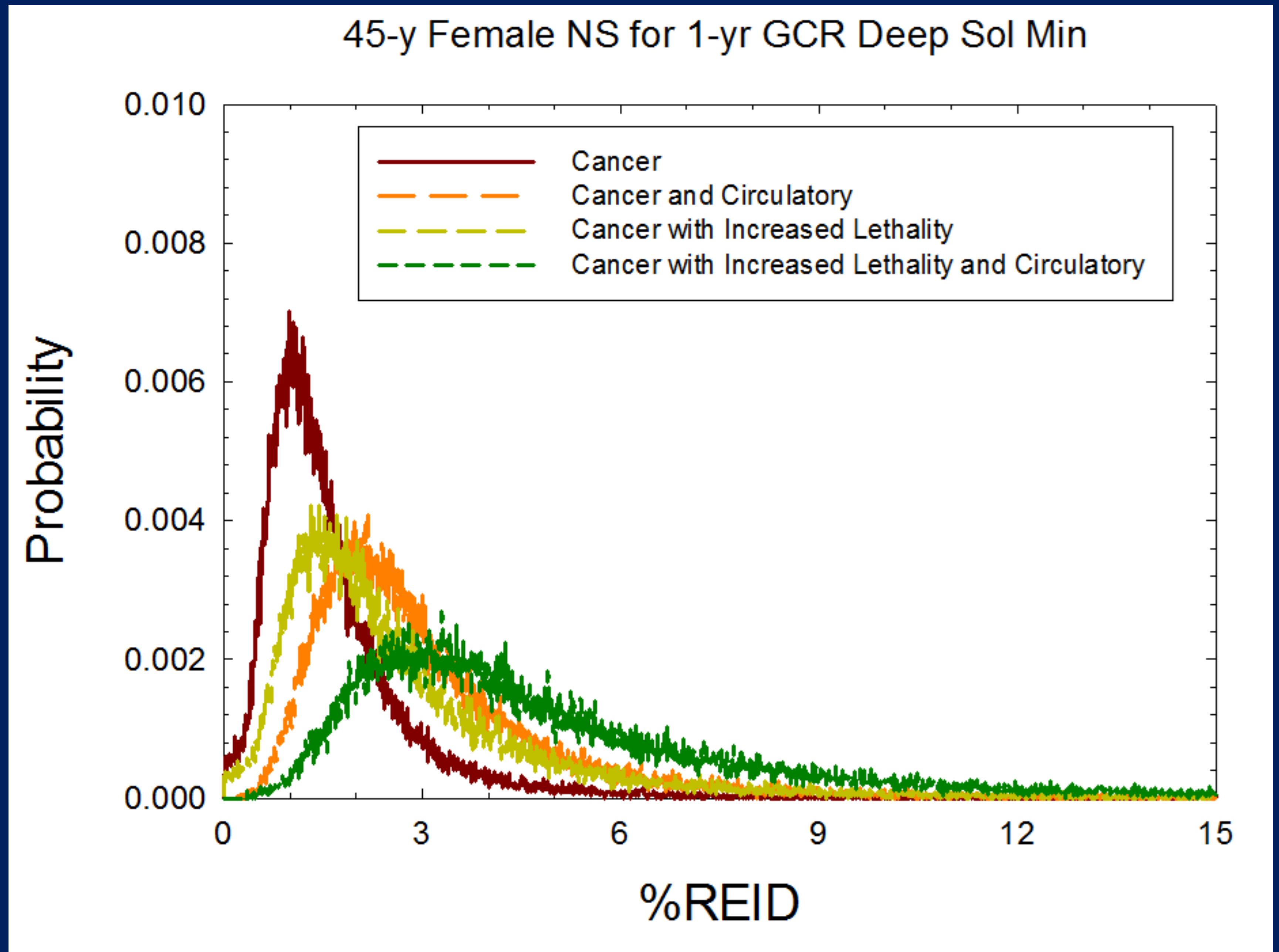
Nature Rev. Cancer (2008)

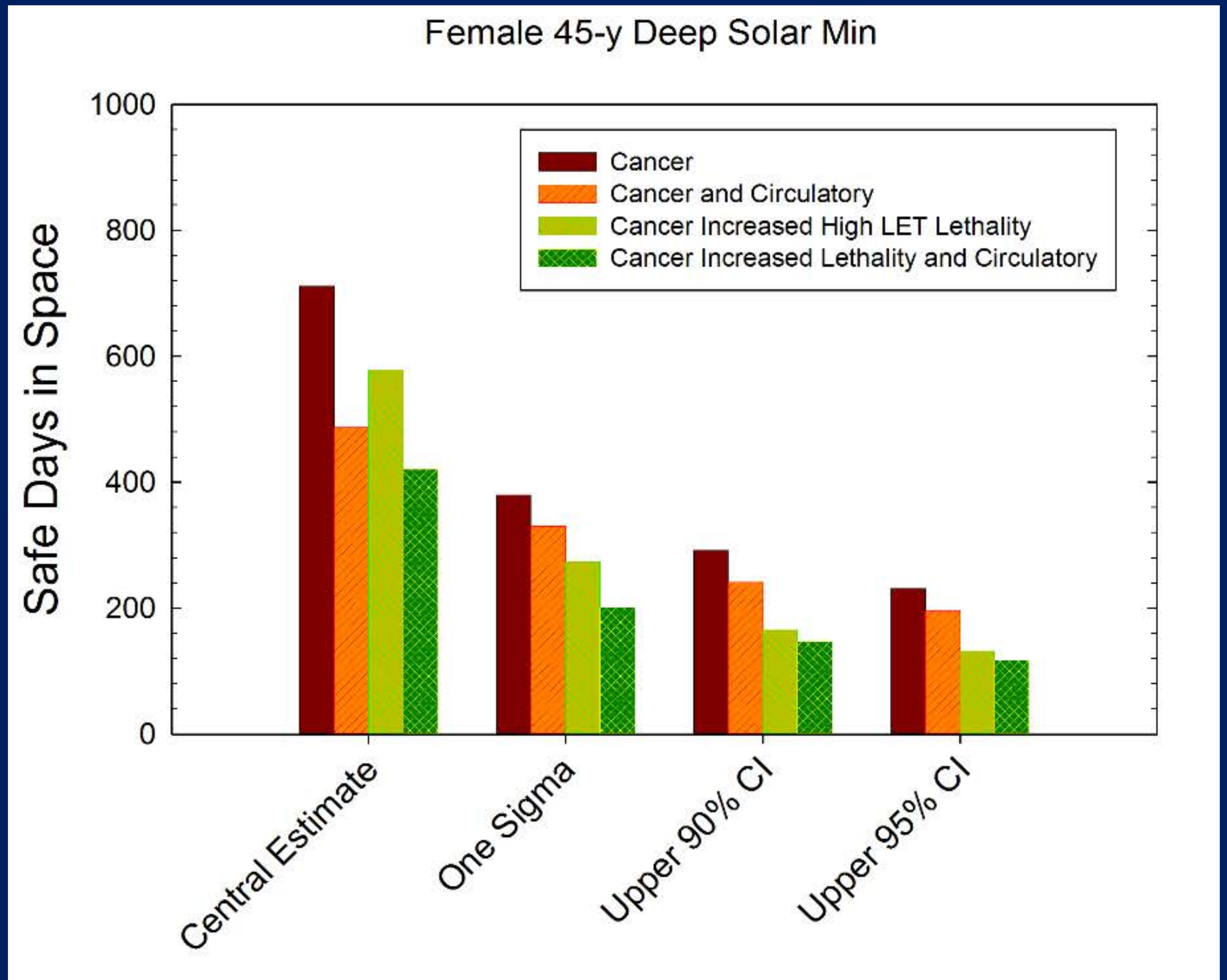
The Dose and Dose-Rate Reduction Effectiveness Factor (DDREF)

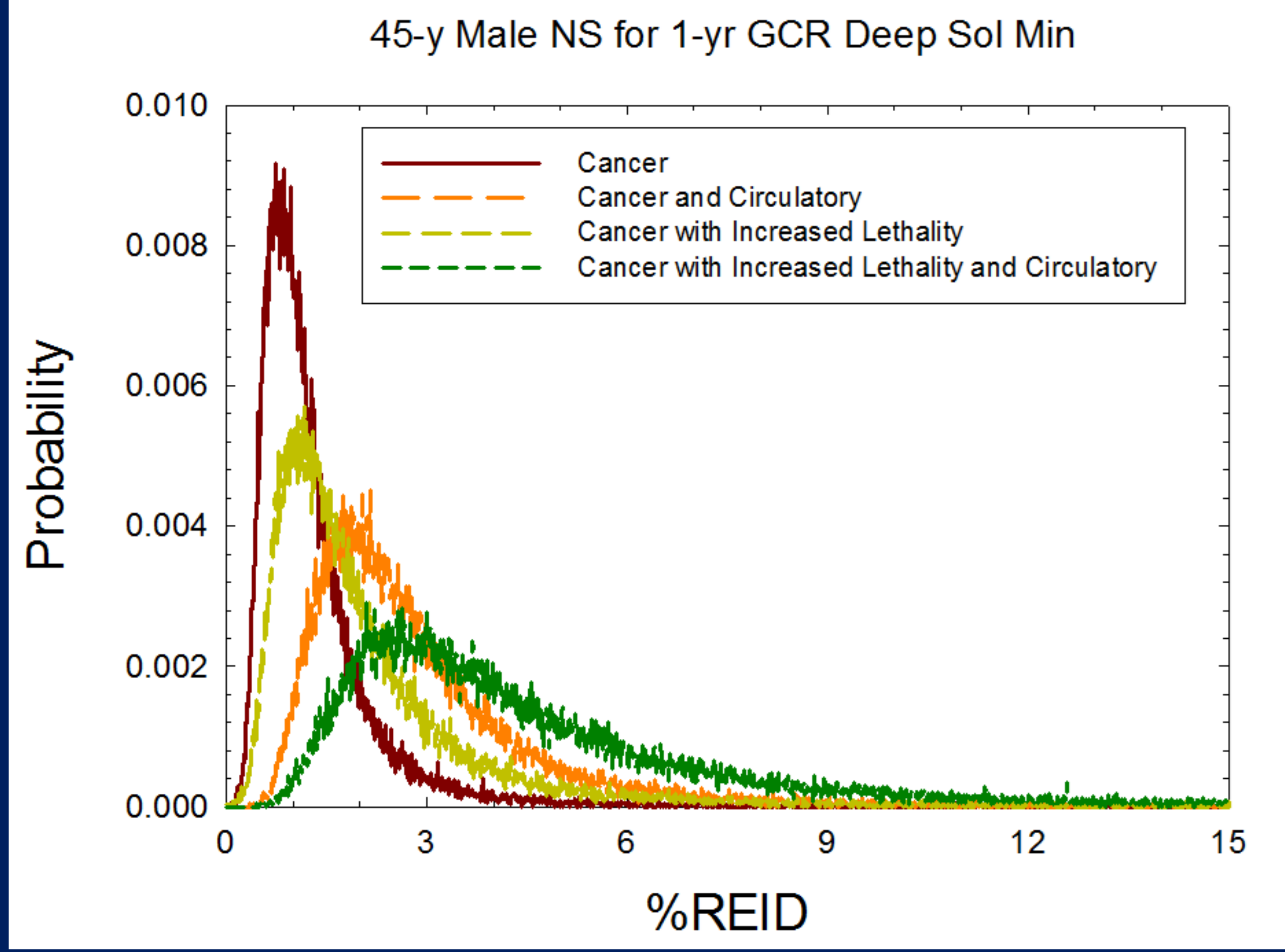
- DDREF reduces cancer risk estimates.
- DDREF estimate from A-bomb survivors is 1.3 in National Academy of Science BEIR VII Report.
- DDREF estimate from animal experiments 2 to 3.

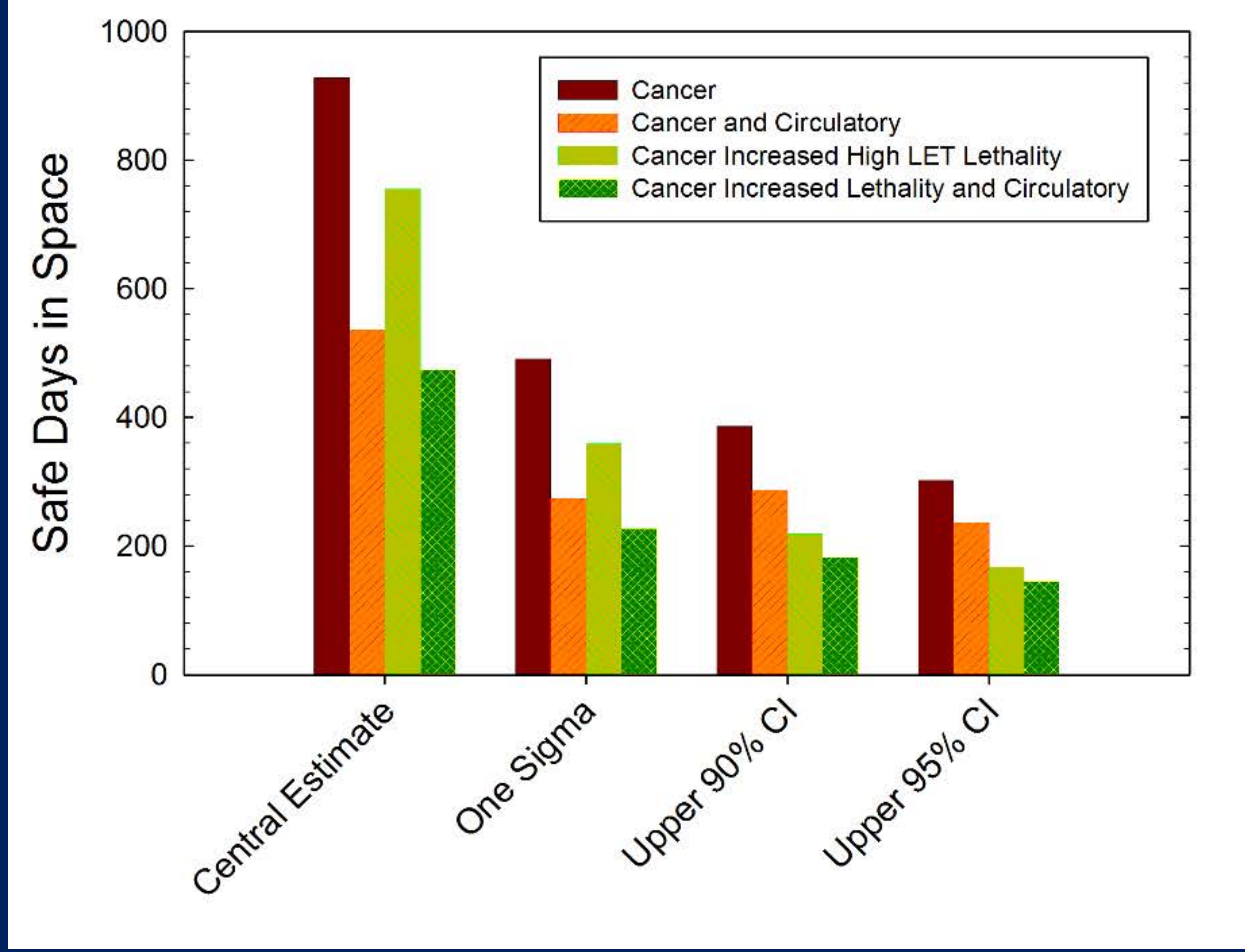


Bayesian Analysis using BEIR VII Prior Distribution and mouse data









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

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]

Major Unanswered Questions in Cancer Risk Estimates

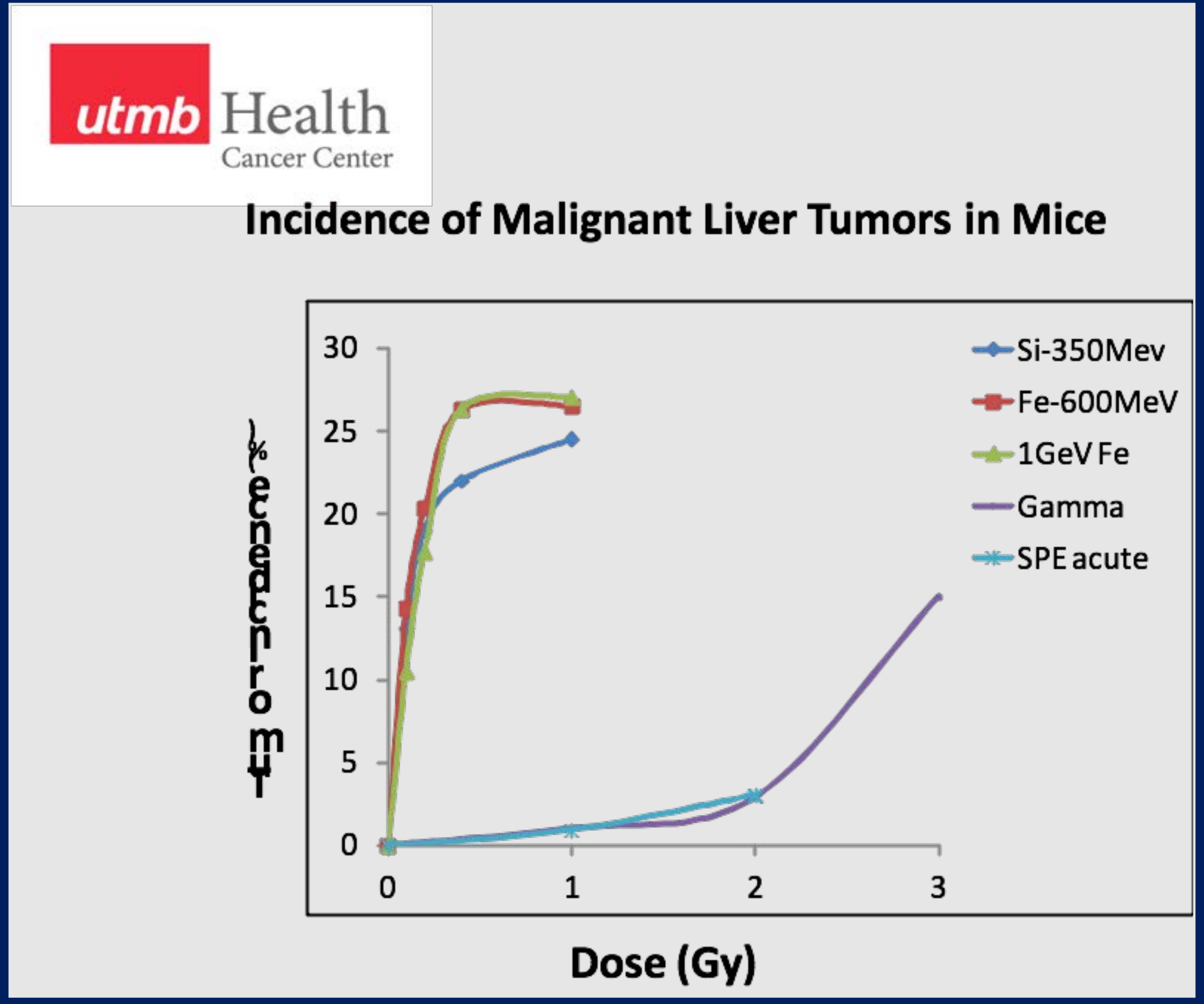
1) There is a lack of Animal Data for Heavy ion quality factors for major tissues in humans (lung, breast, stomach, etc.). Will NASA ever fund such studies?
2) Are the tumors produced by Heavy ions and Neutrons more malignant than that of Gamma-rays?
3) Do Inverse Dose-Rate Effects Occur for High LET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

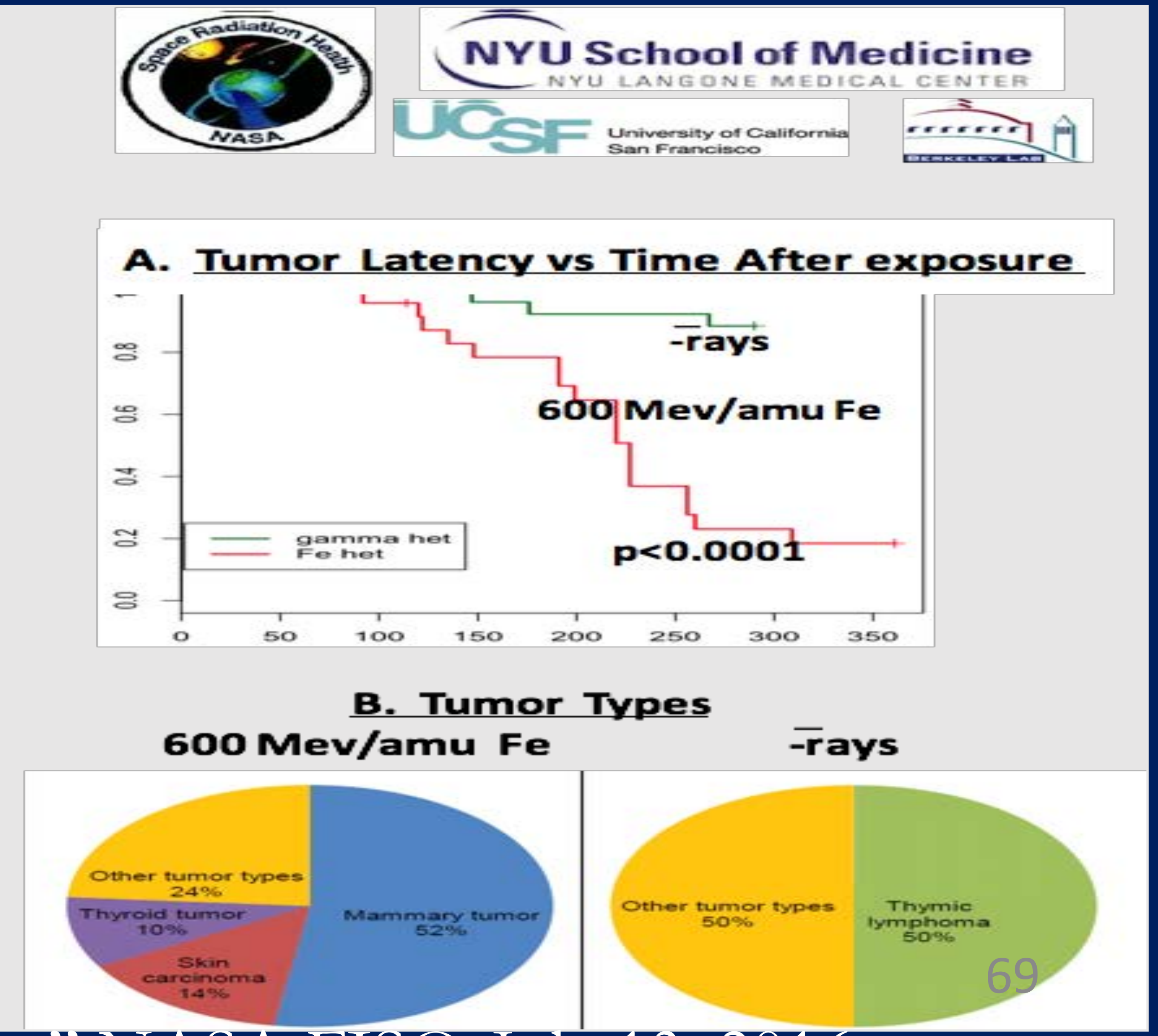
1) Lack of Data for Human Tissues

- 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

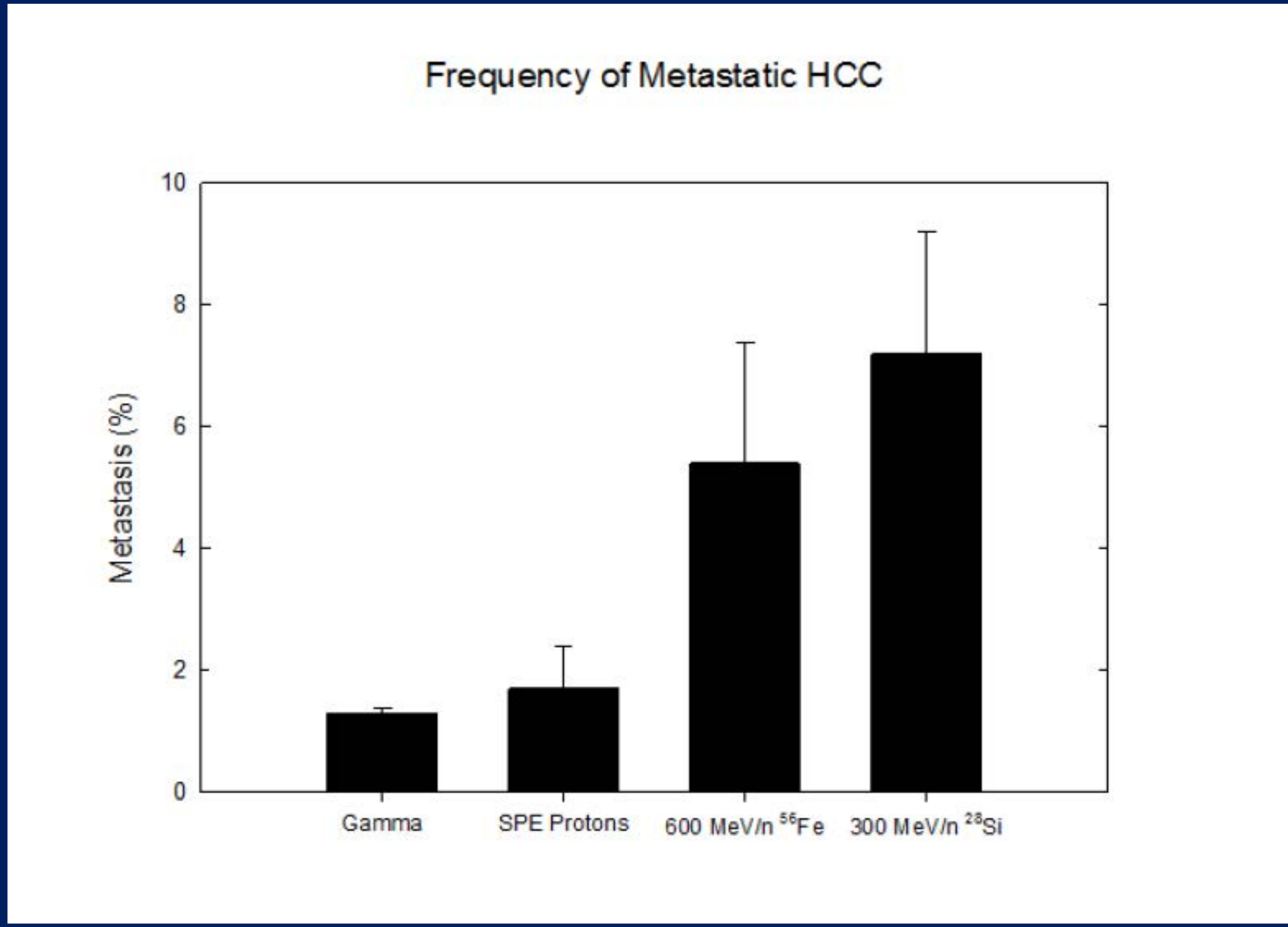
- Risk Models only account for quantitative differences using Quality Factors (QFs) or PDFs
- Issues emerging from research studies of GCR Solid cancer risks
  - Earlier appearance and aggressive tumors not seen with controls, gamma-rays or proton induced tumors
  - Non-linear response at low dose due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

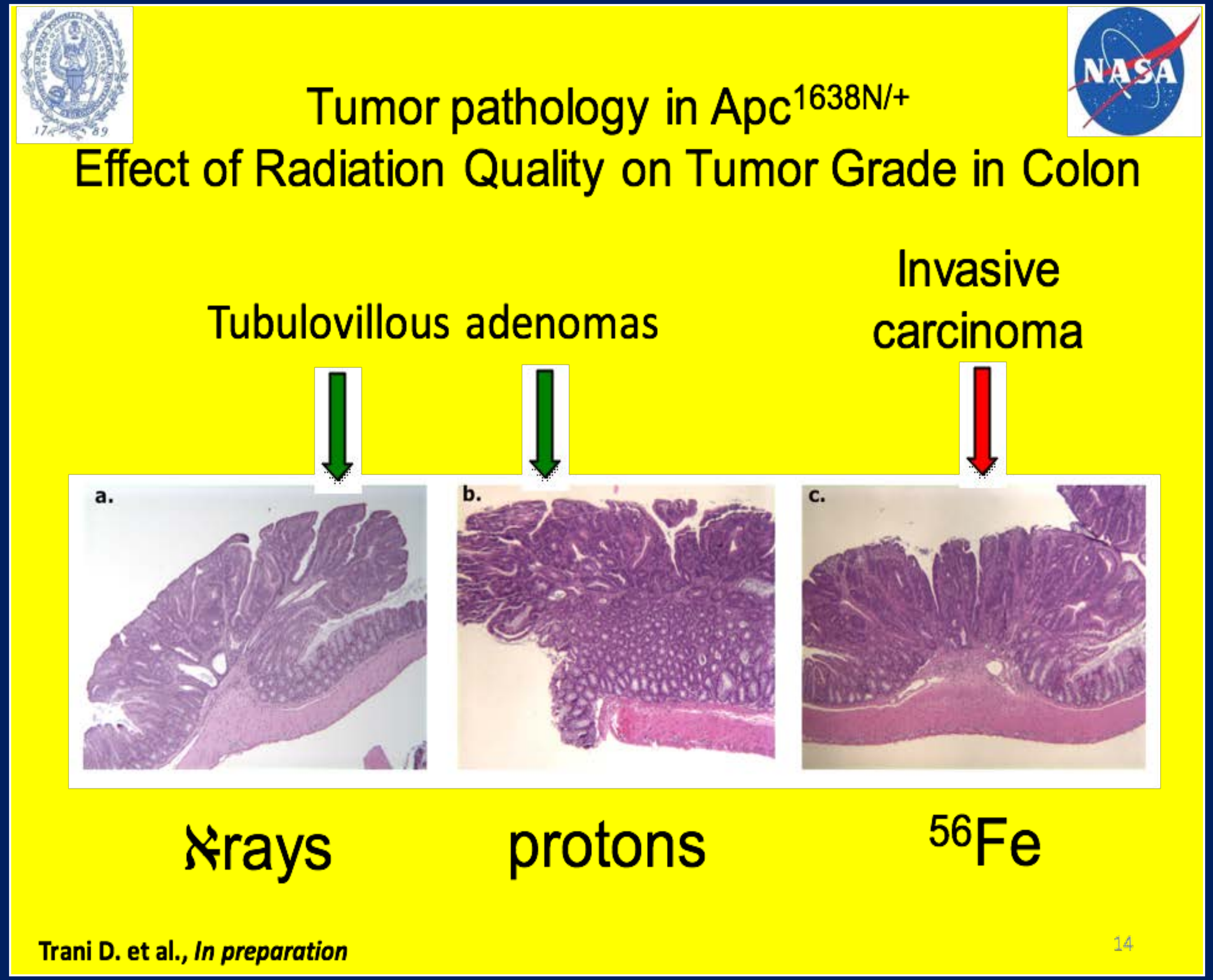




Francis Cucinotta, "New Estimates of Radiation Risks…" NASA FISO, July 13, 2016

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

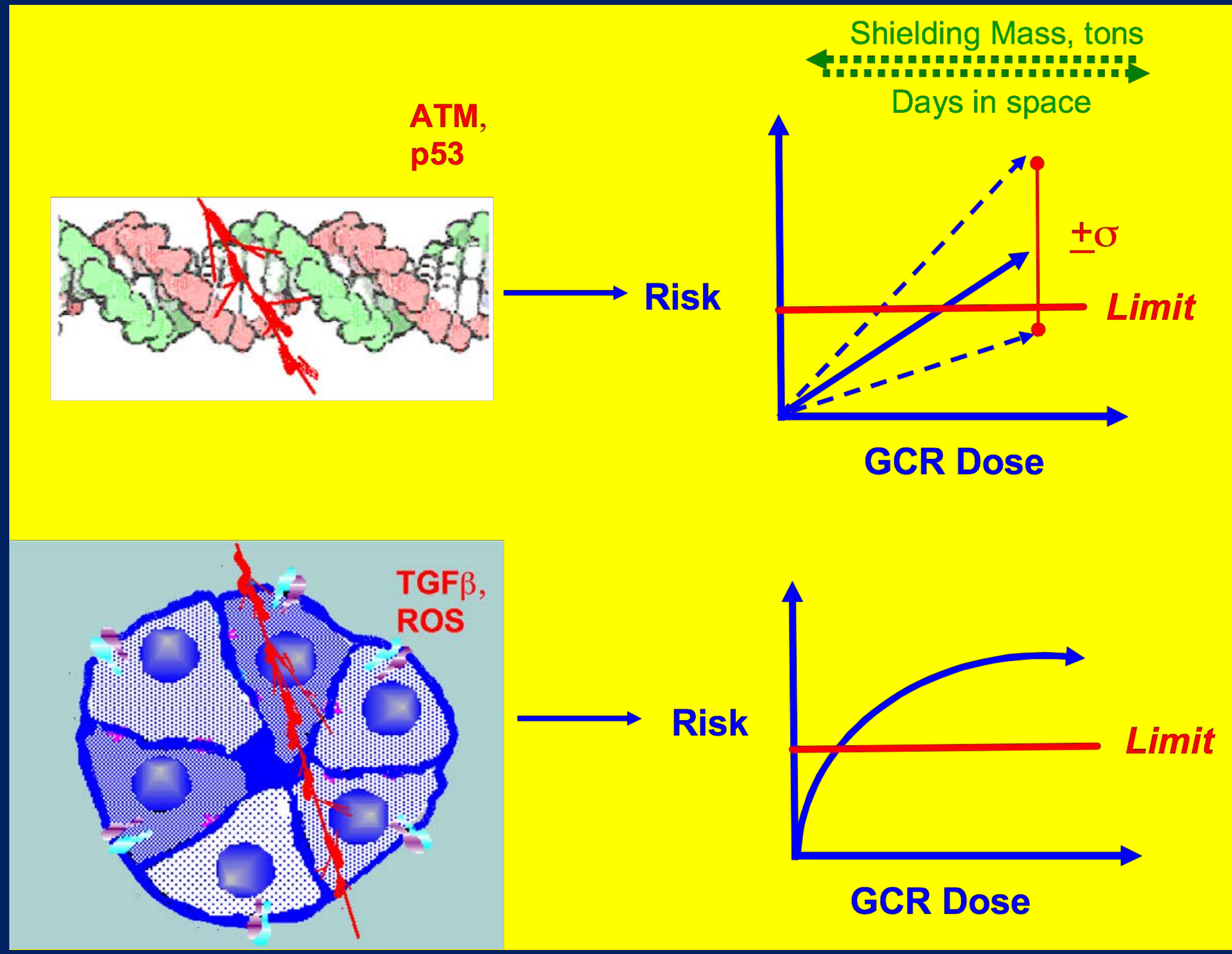
3) Inverse Dose-Rate Effects?

- 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)

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?

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