# Chronic Neutron Radiation Exposure

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**Thomas B. Borak**

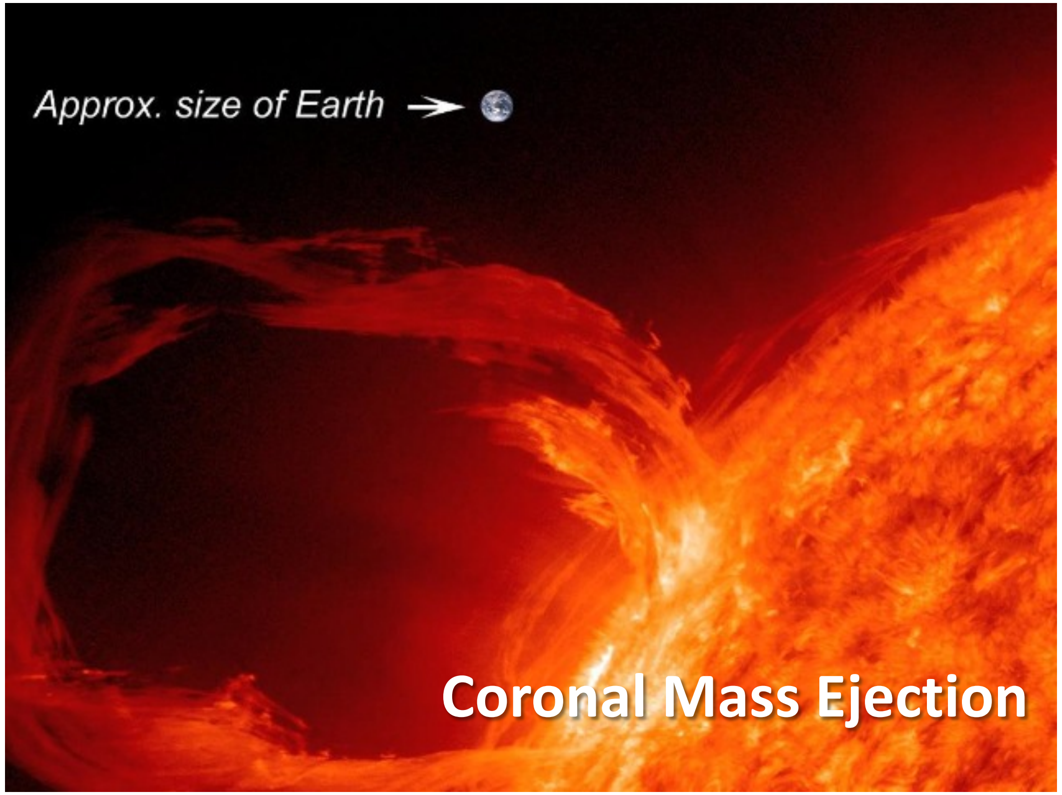
**Red Risk School**
**April 2020**

# TOPICS

- Rationale for using low dose rate neutrons to simulate protracted space radiation exposures
- Status and availability of a low dose rate neutron irradiator facility at CSU
- Early findings from work being done there

# Space Radiation Beyond Low Earth Orbit

- Solar Particle Events



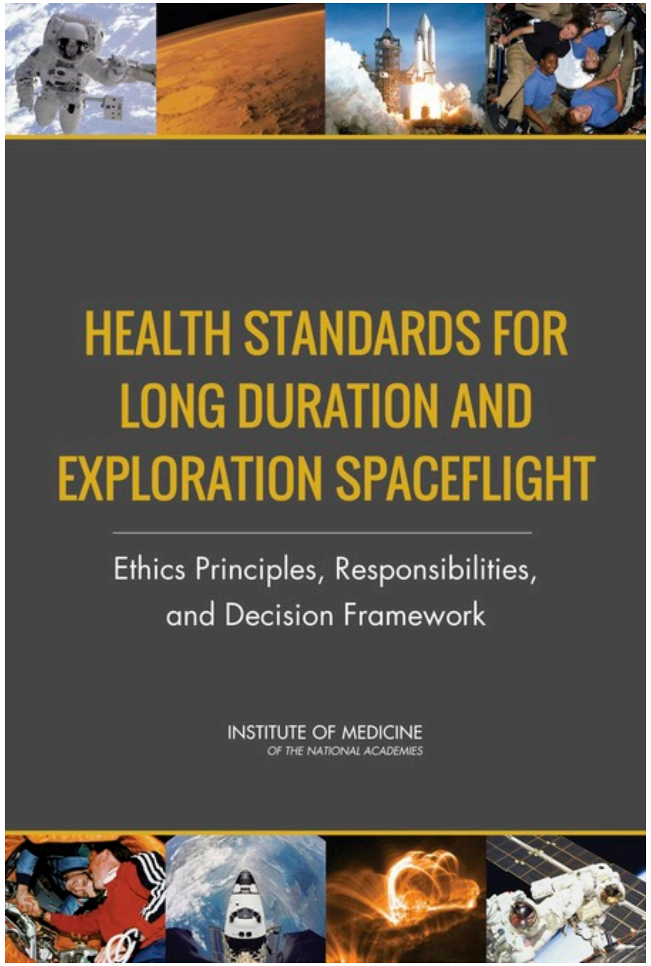

- Galactic Cosmic Radiation


NASA, ESA, HEIC, and The Hubble Heritage Team (STScI/AURA) • Hubble Space Telescope ACS • STScI-PRC05-15

# What amount of fatal cancer risk is acceptable?

## REID

- Risk of Exposure-Induced Death
- Fatal cancer REID is 3% at upper 95% confidence interval
- Permissible exposure limits are for risk, not dose.



# How is the risk calculated?

NASA/TP-2013-217375

**Space Radiation Cancer Risk Projections and Uncertainties – 2012**

*Francis A. Cucinotta*
*NASA Lyndon B. Johnson Space Center*
*Houston, Texas*

*Myung-Hee Y. Kim and Lori J. Chappell*
*U.S.R.A., Division of Space Life Sciences*
*Houston, Texas*

The model is based on epidemiological data from low LET, acute exposures.

OPEN ACCESS Freely available online PLOS ONE

# How Safe Is Safe Enough? Radiation Risk for a Human Mission to Mars

**Francis A. Cucinotta**[1,2]*, **Myung-Hee Y. Kim**[3], **Lori J. Chappell**[3], **Janice L. Huff**[3]

**1** NASA, Lyndon B. Johnson Space Center, Space Radiation Program, Houston, Texas, United States of America, **2** University of Nevada Las Vegas, Department of Health Physics and Diagnostic Sciences, Las Vegas, Nevada, United States of America, **3** Universities Space Research Association, Division of Space Life Sciences, Houston, Texas, United States of America

| Lifetime risks for 940 d Mars Design Reference mission for average solar minimum | | | |
|---|---|---|---|
| | %REID, Cancer | %REID, Circulatory | %REID, Combined |
| | 45-y Females | | |
| U.S. Average | 5.32 [0.95, 14.3] | 1.48 [0.57, 3.05] | 6.57 [1.38, 14.8] |
| Never-Smokers | 3.56 [0.51, 8.87] | 1.55 [0.58, 3.20] | 4.98 [1.77, 10.6] |
| | 45-y Males | | |
| U.S. Average | 3.52 [0.66, 8.23] | 1.53 [0.64, 3.05] | 4.94 [1.91, 9.78] |
| Never-Smokers | 2.75 [0.63, 6.52] | 1.62 [0.68, 3.12] | 4.28 [1.86, 8.22] |

Table 1, truncated

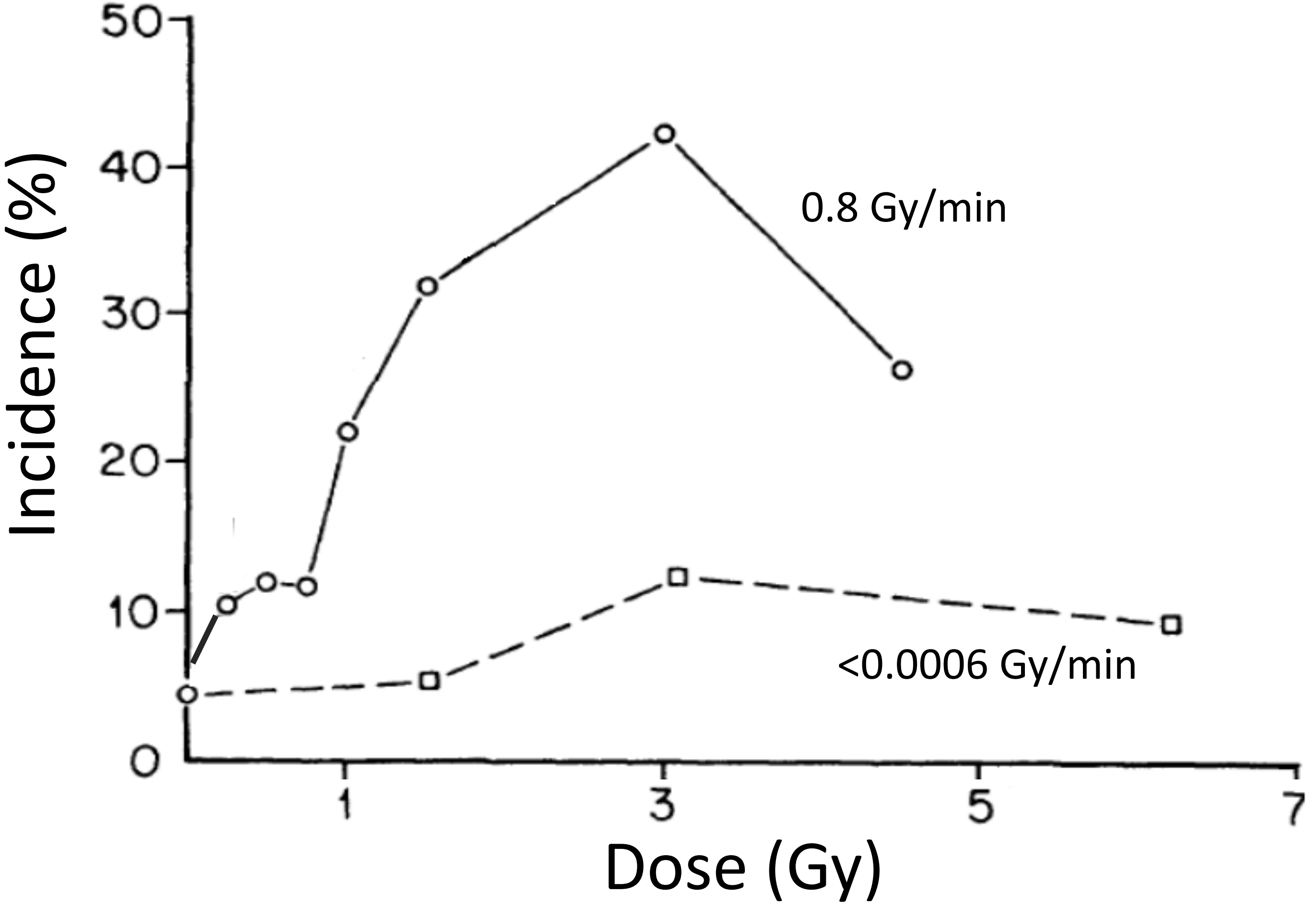
# Major Sources of Uncertainty in the Risk Model

- Radiation Quality Effects
  - Low LET vs high LET
- Dose Rate Effects
  - Acute vs chronic exposures

# Doses and Dose Rates

| Mars Science Lander | GCR Dose Rate (mGy/day) | GCR Dose Equiv. Rate (mSv/day) |
|---|---|---|
| RAD Cruise to Mars (Zeitlin et al. 2013) | 0.481±0.08 | 1.84±0.33 |
| RAD Mars Surface (Hassler et al. 2014) | 0.205±0.05 | 0.70±0.17 |

# Myeloid Leukemia in Male RF/Un Mice



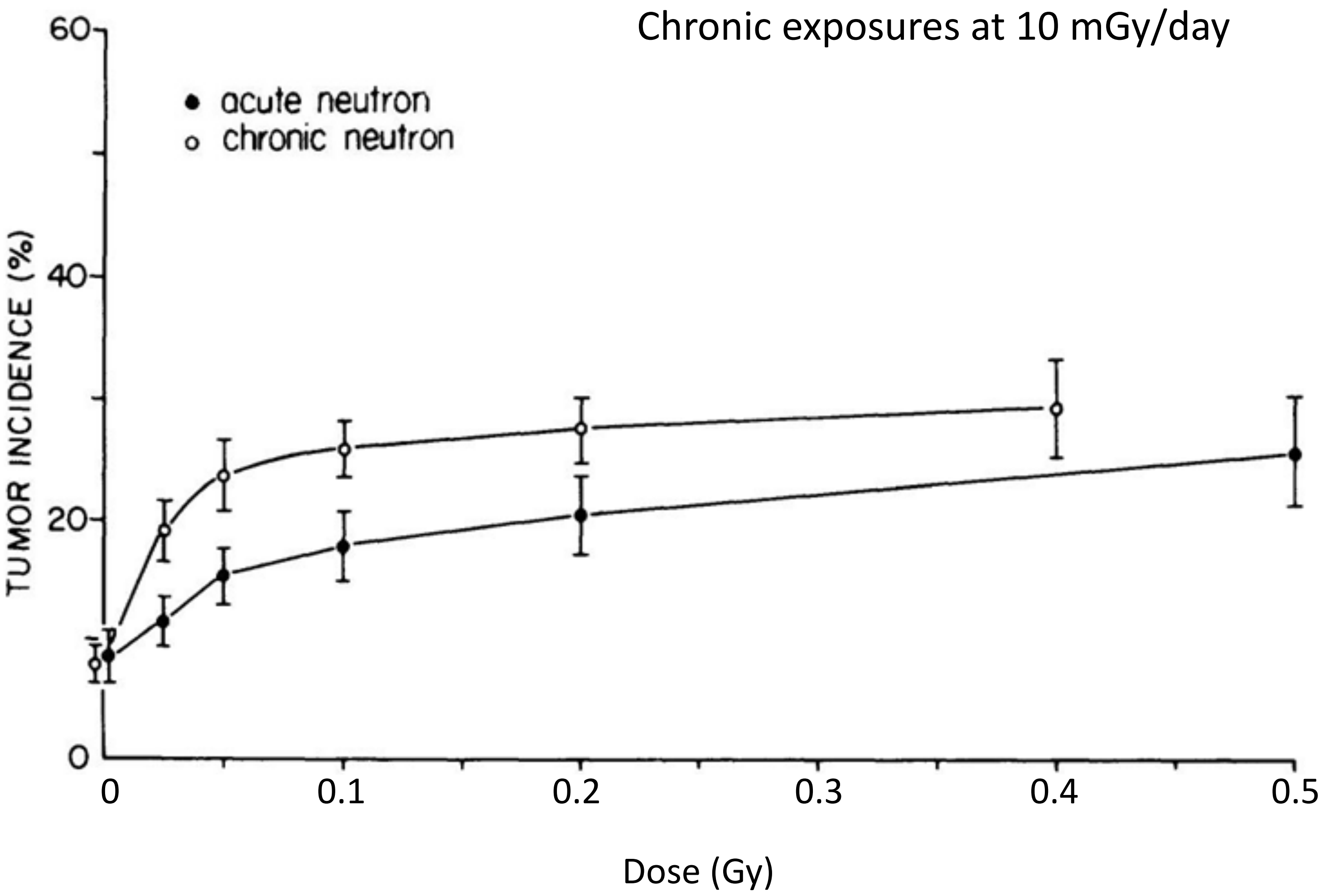

Upton AC, Randolph ML, Conklin JW, Melville GS, Conte FP, Sproul JA. 1970. *Radiat. Res.* 41:467

# Chronic High LET Exposures

- Humans
  - Radium-224
  - Radon progeny
- Rodents
  - Fission neutrons

In some cases, tumor incidence
Increases with protraction – the
"inverse dose rate effect."

# Murine Mammary Tumors



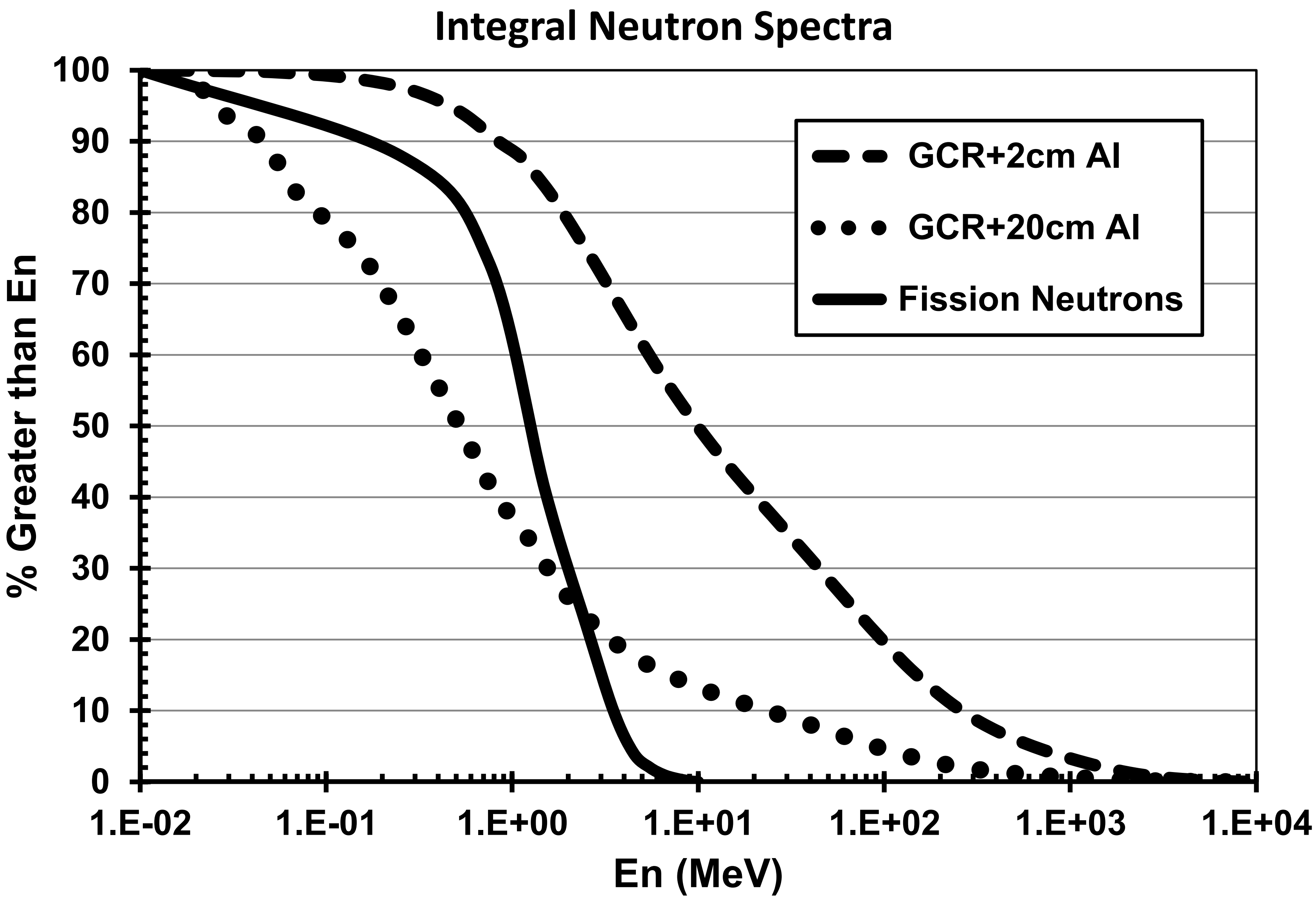

Ullrich, R.L. (1984) Radiation Research 97:587-597.

# Fission Neutrons – Rationale

- Data are needed from animal radiation carcinogenesis studies of high LET exposures delivered at low dose rates for periods up to or exceeding 1 year

# Fission Neutrons – Relevance

- Neutron exposures due to space radiation
- As a model for the high LET effects of HZE ions

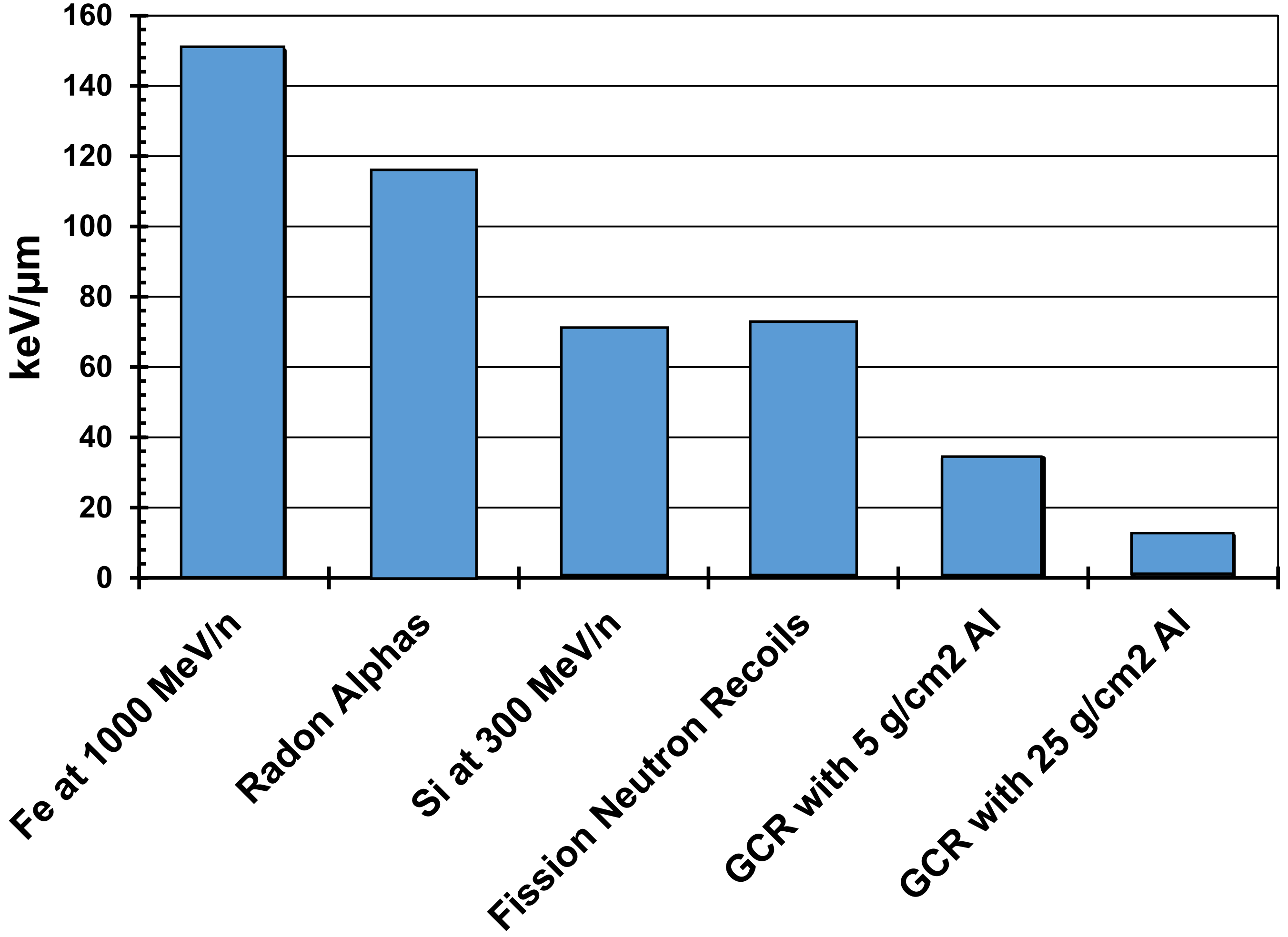



Integral spectra of neutron energies generated by GCR penetrating 2 cm of Al is shown by the dashed line and 20 cm Al by the dotted line. The solid line represents the fission neutron emission spectrum.

# Fission Neutrons – Relevance

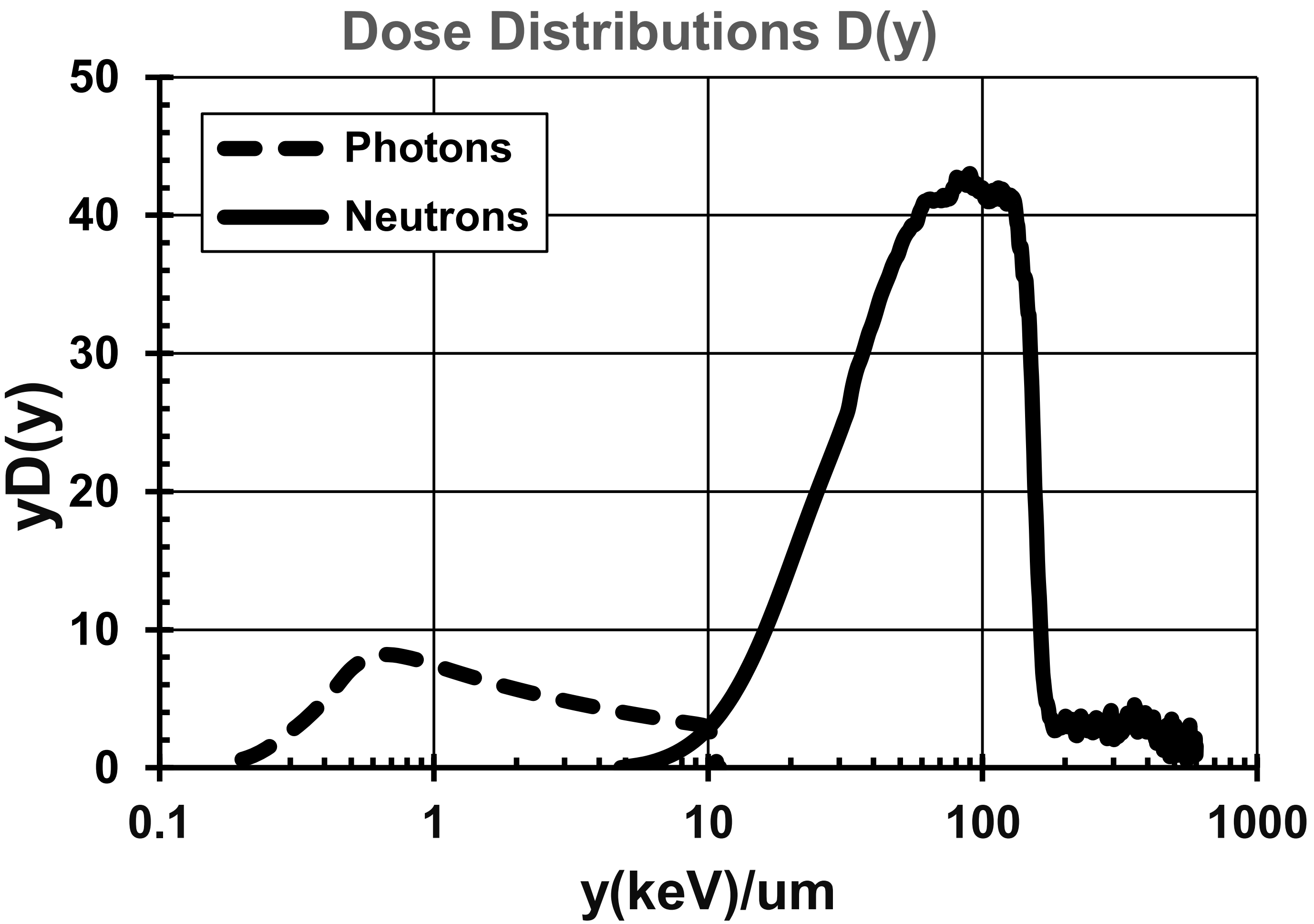
- Neutron exposures due to space radiation
- As a model for the high LET effects of HZE ions

# Dose Averaged LET for Various Radiations

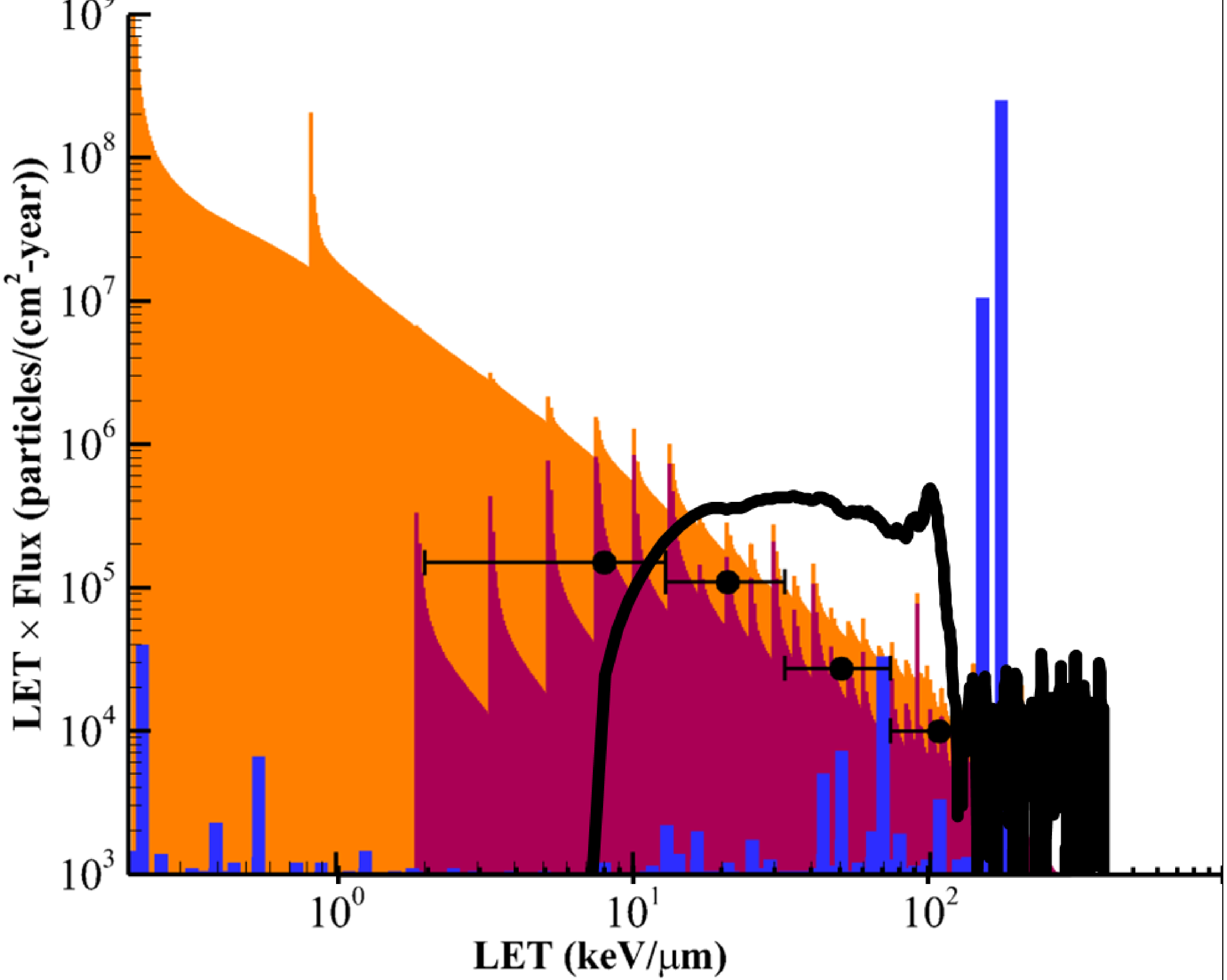


# CSU Foothills Campus

# The Blockhouse




**The dose distributions of lineal energy, D(y) for photons and neutrons.**



LET × Flux (particles/(cm$^2$-year))
$10^9$
$10^8$
$10^7$
$10^6$
$10^5$
$10^4$
$10^3$
$10^0$
$10^1$
$10^2$
LET (keV/μm)

# For more info:

INTERNATIONAL JOURNAL OF RADIATION BIOLOGY
https://doi.org/10.1080/09553002.2019.1688884

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ORIGINAL ARTICLE

## Design and dosimetry of a facility to study health effects following exposures to fission neutrons at low dose rates for long durations

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[a]Department of Environmental and Radiological Health Sciences, Colorado State University, Fort Collins, CO, USA; [b]Department of Nuclear Engineering, University of Tennessee, Knoxville, TN, USA

**ABSTRACT**
**Purpose:** During extended missions into deep space, astronauts will be exposed to a complex radiation field that includes high linear energy transfer (LET) radiation from high energy, heavy ions (HZE particles) at low dose rates of about 0.5 mGy/d for long durations. About 20% of the dose is delivered by ions with LET greater than 10 keV/µm. There are sparse empirical data in any species for carcinogenic effects from whole-body exposures to external sources of mixed or high LET radiation at this level of dose rates. For the induction of solid tumors, acute exposures to HZE ions have been shown to be substantially more effective per unit dose than low LET exposures

**ARTICLE HISTORY**
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Accepted 15 October 2019

**KEYWORDS**
Neutron dosimetry; low dose rate; radiation; high LET

# Ongoing/Completed Projects

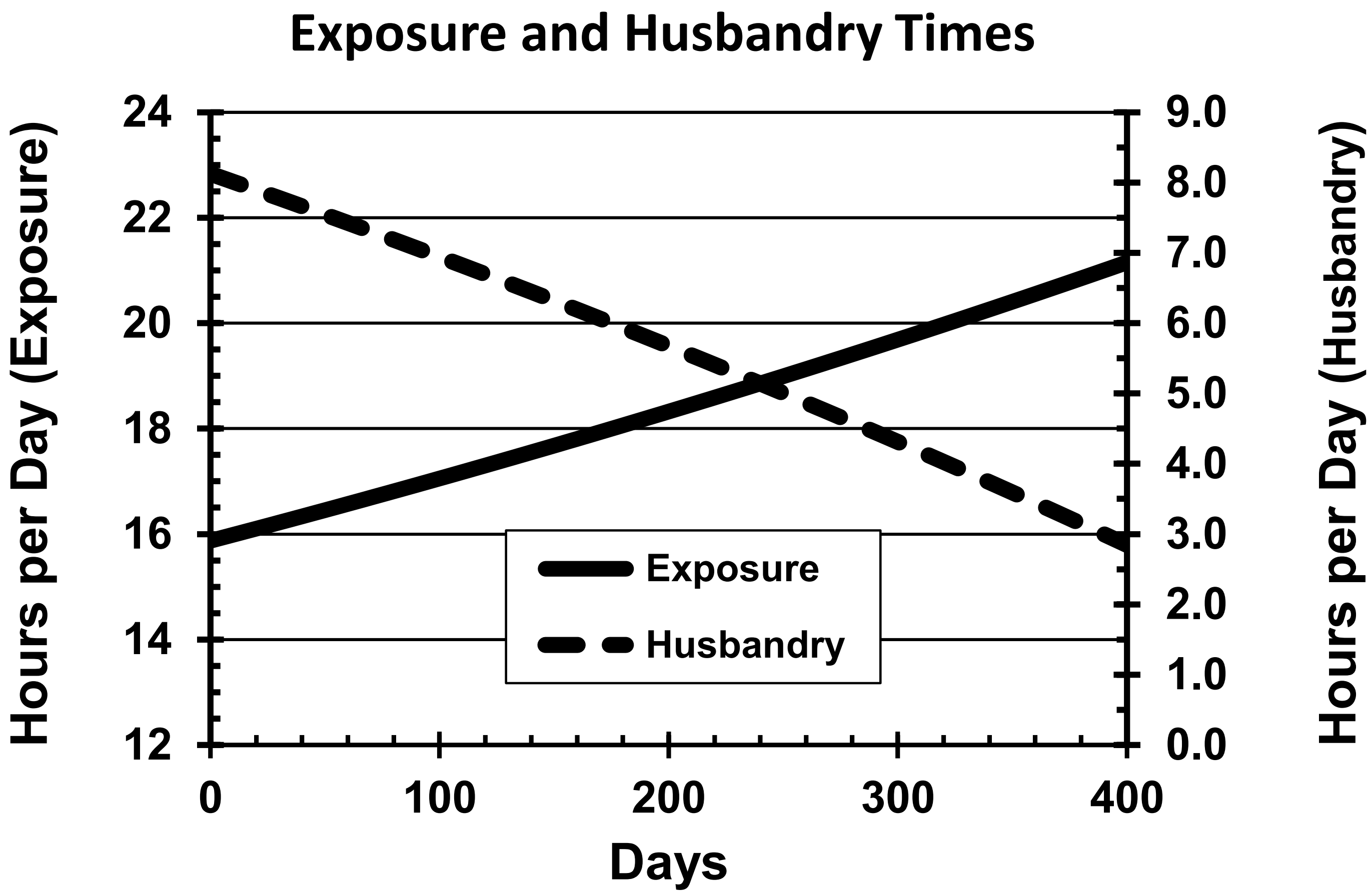
- Carcinogenesis NSCOR  -  Carcinogenesis, Neurobehavioral, Countermeasures
  - CSU
  - OHSU
- University of Arkansas Medical School  -  Cardiovascular
- CNS Function NSCOR  -  CNS Effects
  - UC, Irvine
  - EVMS
  - Loma Linda
- Georgetown University NSCOR - Carcinogenesis
- University of Colorado, Denver  -  *In Utero* Effects

# Support Services

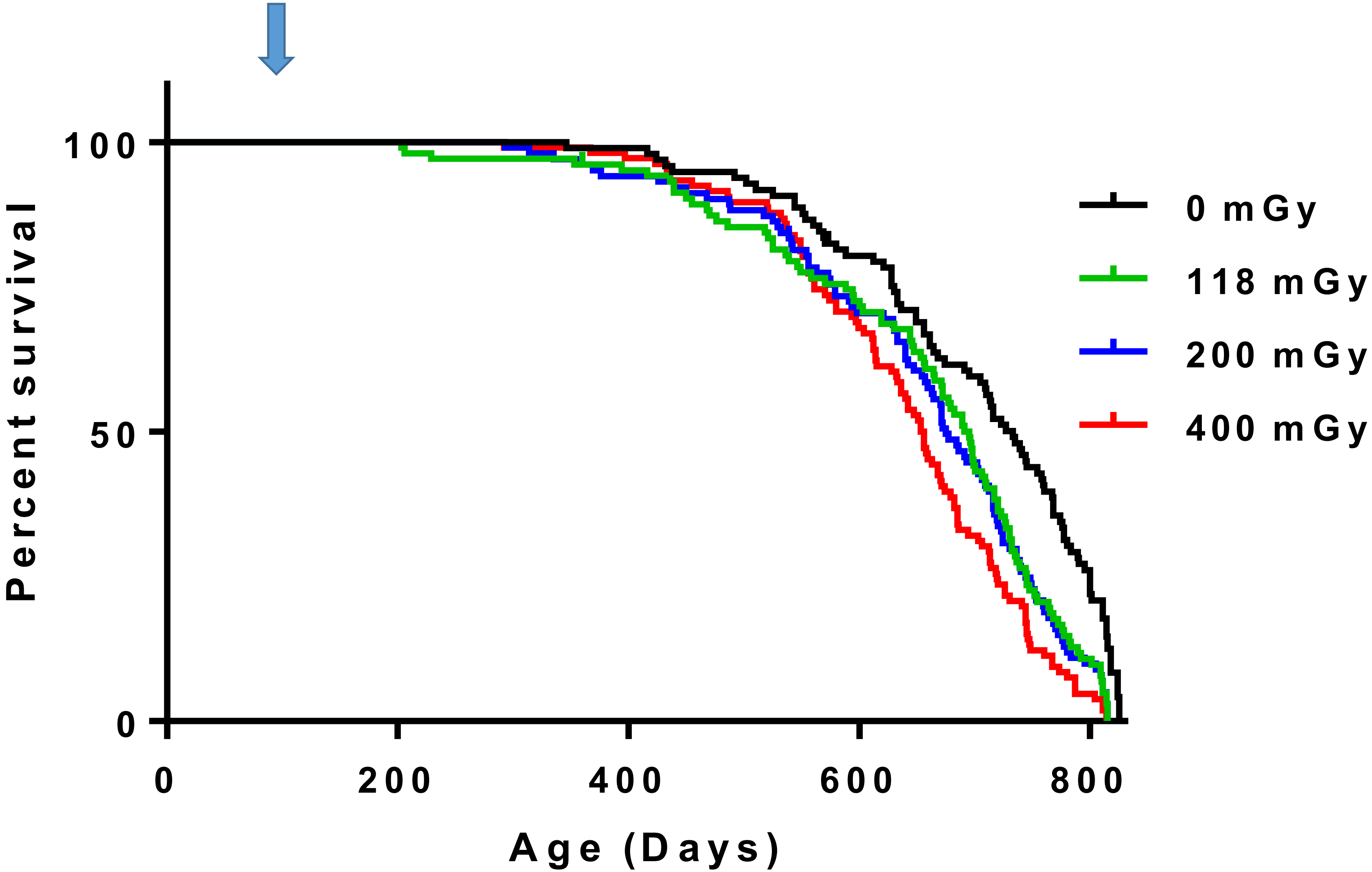
- Animal Care and Use Protocols
- Access
  - Network access (guest associate appointment, eID login and password for access to CSU system)
  - Tech time - Veterinary Residents and Student Hourlies
- Tissue collection and processing
- Equipment and procedure space (Regional Innovation Center)

# CSU Regional Innovation Center

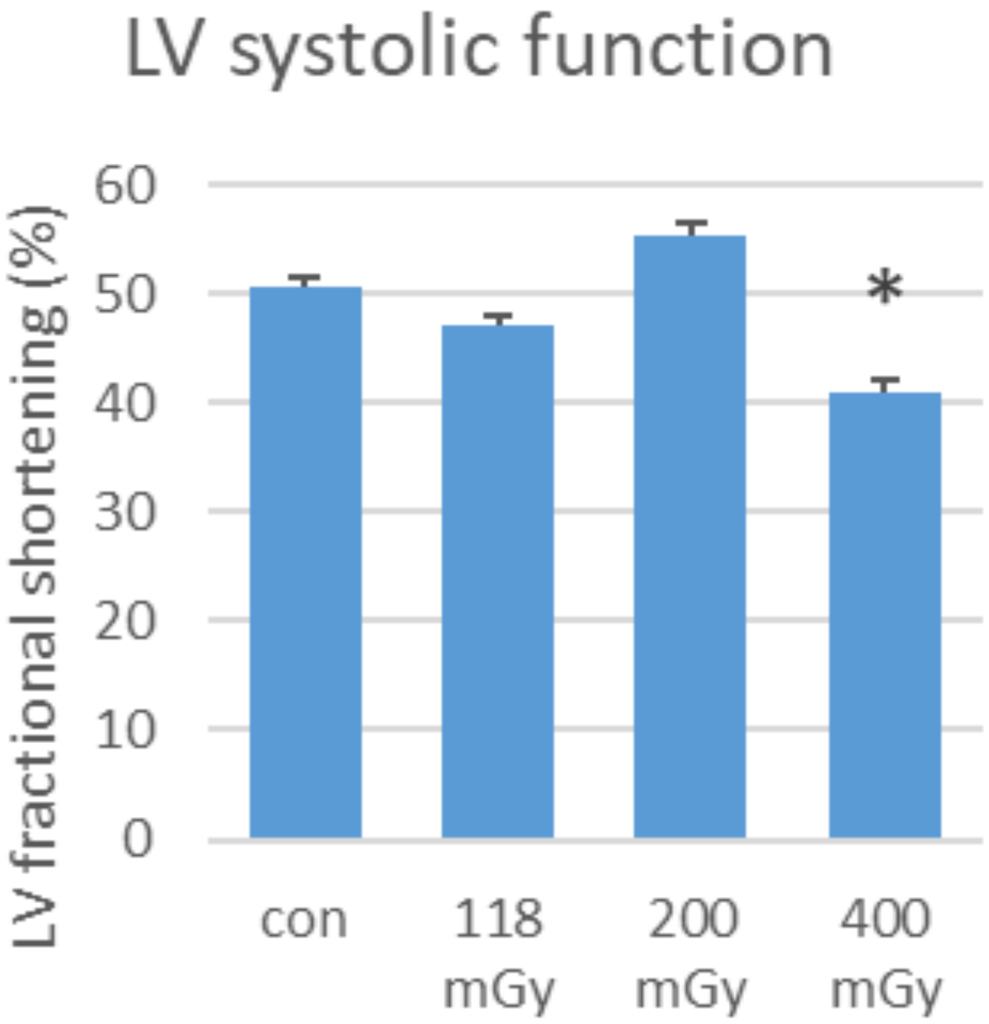
# Status/Availability

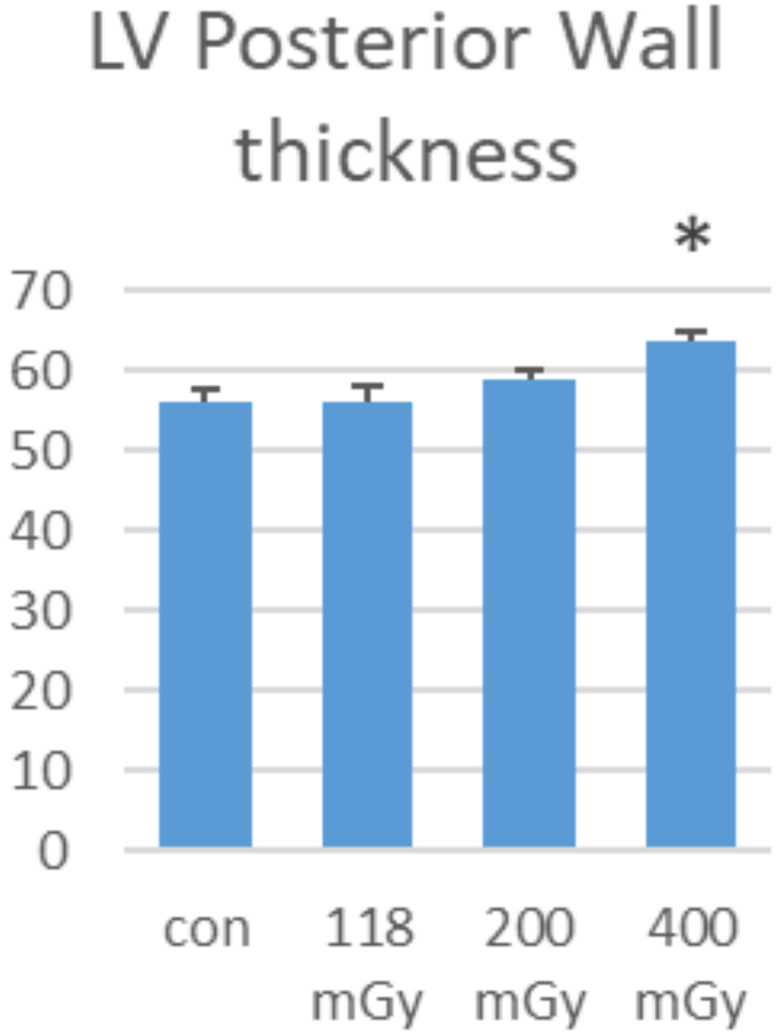


# BALB/c Females Survival



# BALB/c Females 400 Days Post-IR Initiation




Chicco/Boerma

# Neurocognitive/Neurodegenerative

Britten RA, Duncan VD, Fesshaye AS, Wellman LL, Fallgren CM, Sanford LD. Sleep fragmentation exacerbates executive function impairments induced by protracted low dose rate neutron exposure. Int J Radiat Biol. 2019 Dec 6:1-11. doi:10.1080/09553002.2019.1694190. [Epub ahead of print] PubMed PMID: 31724895.

Acharya MM, Baulch JE, Klein PM, Baddour AAD, Apodaca LA, et al. New Concerns for Neurocognitive Function during Deep Space Exposures to Chronic, Low Dose-Rate, Neutron Radiation. eNeuro. 2019 Aug 22;6(4). pii: ENEURO.0094-19.2019. doi: 10.1523/ENEURO.0094-19.2019. Print 2019 Jul/Aug.

# In Utero Exposures

## Study design

- Expose pregnant C57BL/6 mice beginning at E0.5
- Assays at E12.5 and E18.5

## Preliminary results

- No change in initial implantation rate
- Significantly increased early resorption rate
- Significantly decreased placental size
- Decreased maternal weight gain at E12.5, nearly-significant at E18.5
- No change in late resorption rate, fetal weight, or fetal length
- Possible increase in fetal anomalies (study not powered to detect)

Steller/Jansson

# Acknowledgements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  - NASA NNX15AK13G
  - Colorado State University
    - Department of Environmental and Radiological Health Sciences
    - College of Veterinary Medicine and Biosciences
    - Office of the Vice President for Research


QUESTIONS

# EXTRA

# Sarcomas in Patients Treated with Radium-224
# Tumor Incidence Per Unit Dose Increases With Protraction

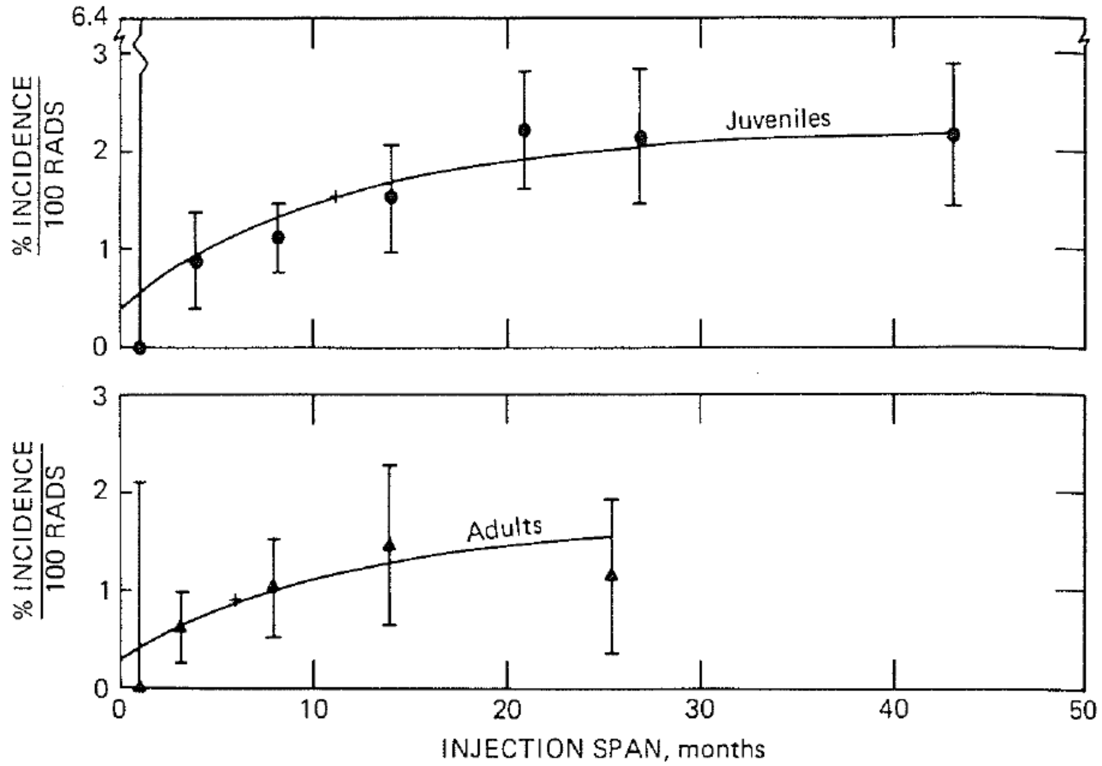



Fig. 1 Bone-sarcoma induction vs. protraction of injections (data from Table 2). The percent incidence per 100 rads tended to increase with injection span for both the juveniles and adults and is reasonably well represented by the fitted curves.

Chmelevsky et al. (1990) Radiation Research S69-S79

# Inverse Dose Rate Effect in Uranium Miners

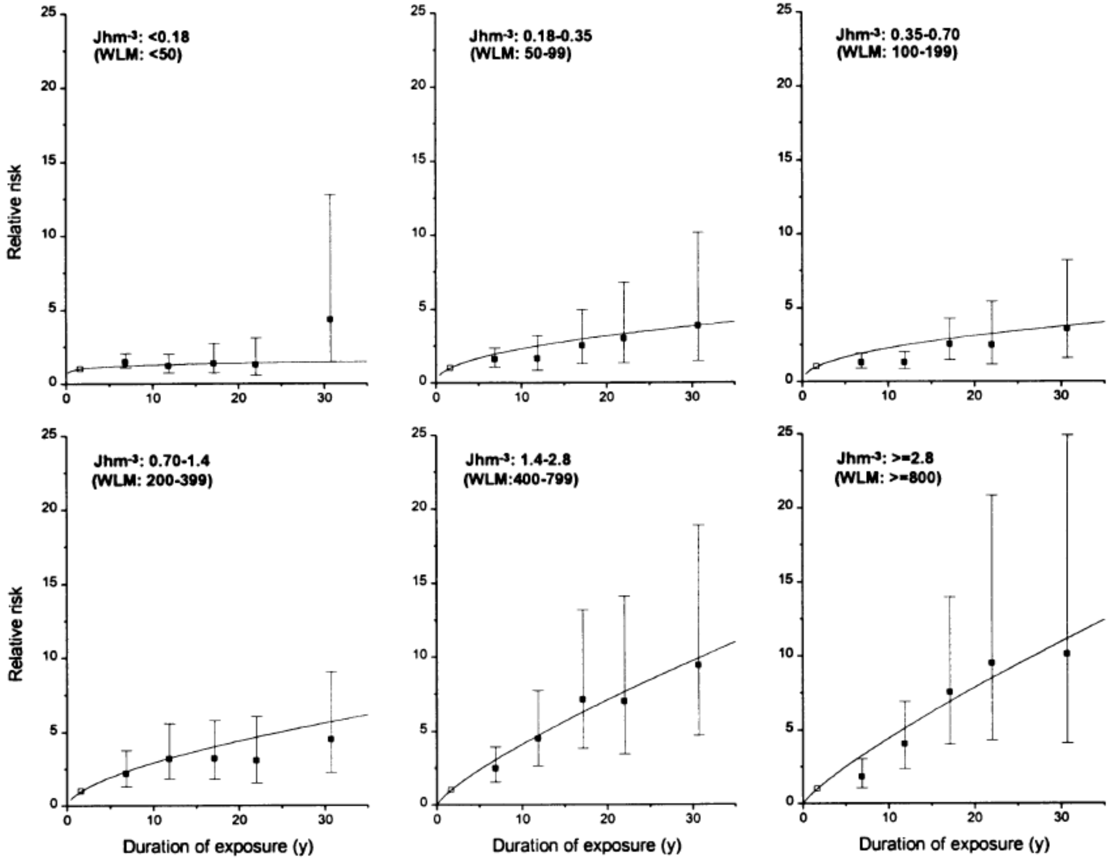



FIGURE 2-3 Relative risks of lung cancer, by duration of exposure, in 11 miner cohorts analyzed by Lubin and others (1995a). Each panel represents a different total exposure. For miners with the highest exposures of > 1.4 $Jhm^{-3}$ (> 400 WLM), there is a marked inverse dose-rate effect. The inverse dose-rate effect is less apparent for miner exposures between 0.18 and 1.4 $Jhm^{-3}$ (50 and 400 WLM) and it is essentially undetectable for exposures under 0.18 $Jhm^{-3}$ (50 WLM).

Lubin, et al.1995 Health Phys. 69:494-500. BEIR VI

# Tumor RBEs for Fission Neutrons

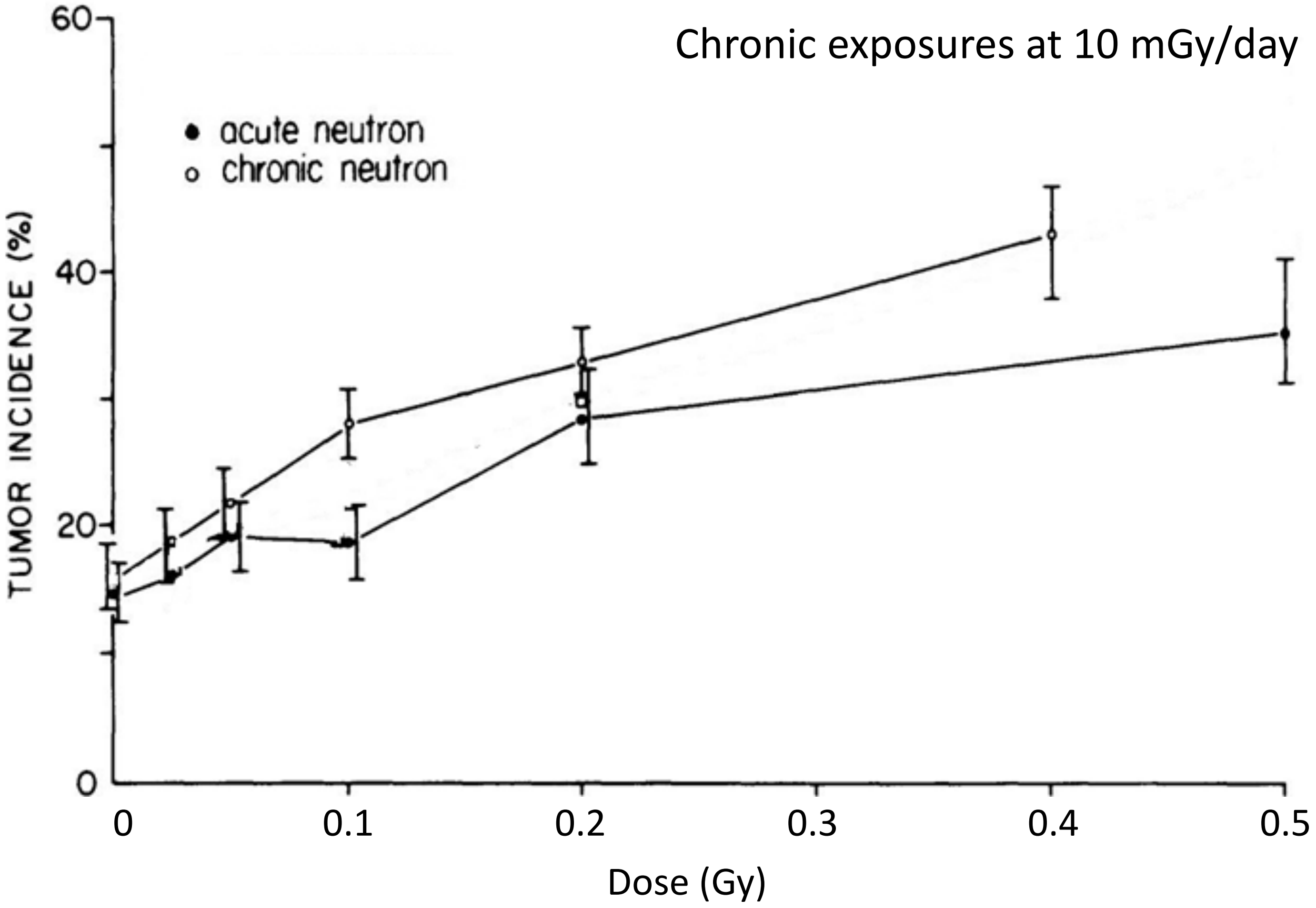
| Strain | Tumor | RBE | Reference |
|---|---|---|---|
| BALB/c mice (F) | Lung | 20 (12 to 30) | Ullrich et al |
| BALB/c mice (F) | Mammary | 27 (13 to 41) | “” |
| B6CF1 mice (M) | Lung | 25 ± 4 | Grahn et al |
| B6CF1 mice (M) | All Epithelial Tumors | 26 ± 4 | “” |
| B6CF1 mice (M) | Vascular Tumors | 15 ± 3 | “” |
| SD rats (M) | Lethal Tumors | >50 | Wolf et al |
| SD rats (M) | Lung | >50 | Lafuma et al |
| SD rats (F) | Mammary | >50 | Shellabarger et al |
| RFM mice (M) | Myeloid Leukemia | 2.8 | Ullrich and Preston |

Modified from Cucinotta et al (2013) NASA/TP-2013-217375.

# Challenges

1. How do we account for the difference in proportion of lifespan exposed between rodents and humans?
2. How do we account for species differences?
3. How do we account for combine stressors?
4. How do we identify effective countermeasures?

# Lung Carcinoma




Ullrich, R.L. (1984) Radiation Research 97:587-597.

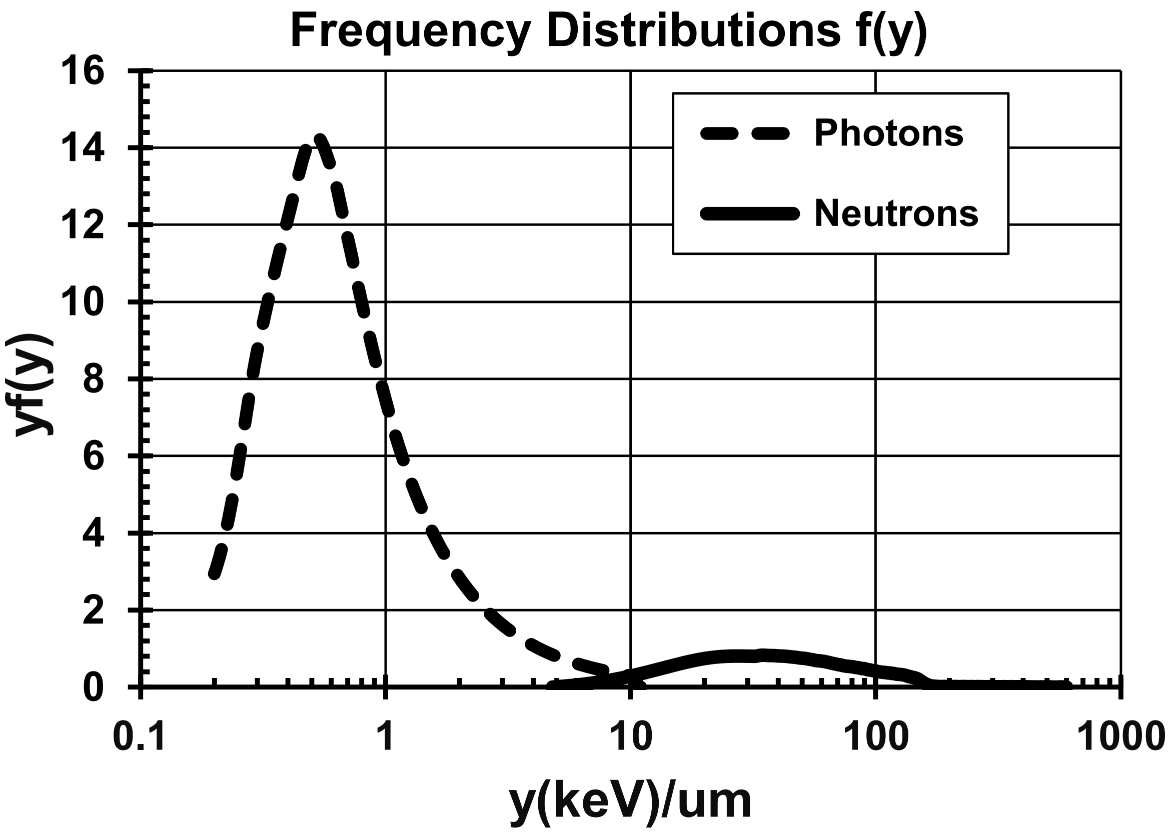



**Figure 18.** The frequency distributions of lineal energy, f(y) for photons and neutrons.