The Biological Effects of Radiation in Space

Radiation Effects

Stochastic effects:
"all or none", can result from the effect on a single cell, e.g., cancer. Cannot predict effect on an individual basis; must use populations and risk probabilities.

Deterministic effects:
severity of the effect increases with increasing dose, e.g., cataracts, erythema.

USAF/NASA Proton Bioeffects Project

Proton energies were chosen to bracket the energies encountered in space:

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Proton energy	Range in tissue
2 MeV	1 cm
55 MeV	2.5 cm
138 MeV	~ 15 cm
250 MeV	~ 40 cm
400 MeV	~ 80 cm
2300 MeV	~ 1000 cm

~ 2000 Rhesus monkeys
~5000 mice

USAF/NASA Proton Bioeffects Project

Dose estimates in a primate head phantom.

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USAF/NASA Proton Bioeffects Project

All endpoints except one, indicated a proton RBE of ~ 1.

Cataract formation is the exception: protons showed an LET dependency.

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Carcinogenesis

See [ALPEN-94] Alpen, E. L, P. Powers-Risius, S. B. Curtis, R. DeGuzman and R J. M. Fry. "Fluence-Based Relative Biological Effectiveness for Charged Particle Carcinogenesis in Mouse Harderian Gland." Advances in Space Research 14 no. 10 (1994): 573-581.

Objective: look at *low doses*

Novel approach: Fluence *versus* dose

Carcinogenesis

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[ALPEN-94] Table 1.

Carcinogenesis

Mouse Harderian gland model.
(secretes, tears, lubricants, hormones)

Within 72 hours, 2 donor pituitary glands implanted into the spleen.

Hormone production promotes the expression of Harderian gland tumors.

Mice sacrificed at 16 months; Harderian glands examined macroscopically and histologically.

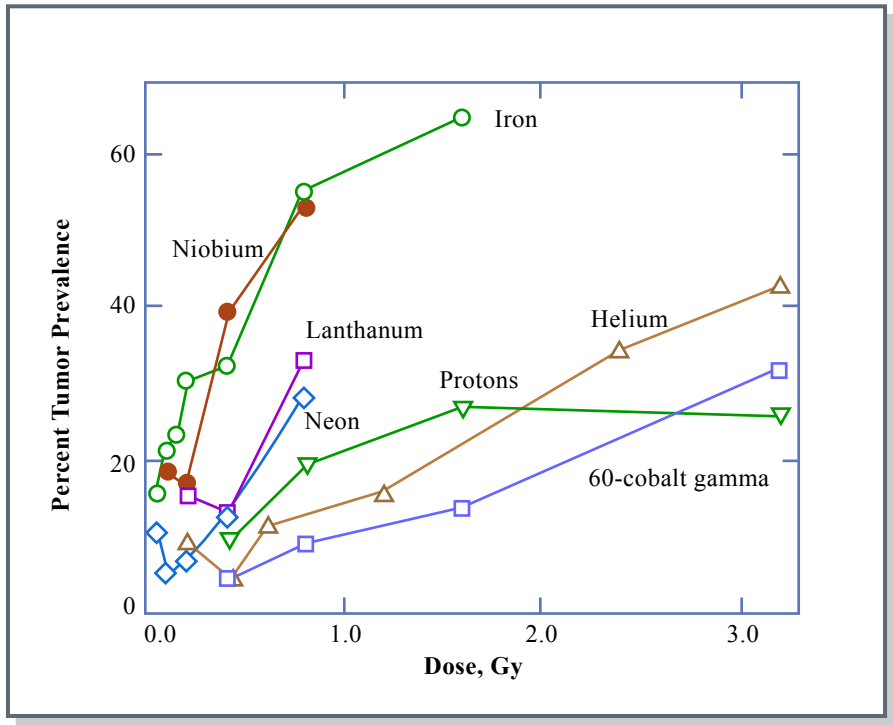


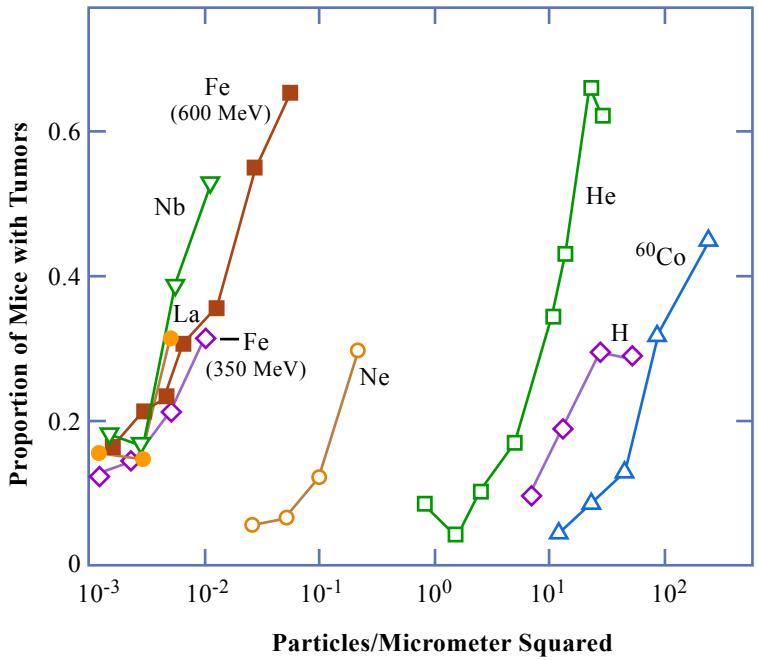
Figure by MIT OCW.

Dose = fluence x LET

Carcinogenesis

Tumor incidence as a function of particle fluence.

Ion	Energy (MeV/a)	LET (keV/µm)
^{60}Co-gamma		0.23
Protons	250	0.4
Helium	228	1.6
Neon	670	25
Iron	600	193
Iron	350	253
Niobium	600	464
Lanthanum	593	953



Carcinogenesis

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Table

- **These are some of the highest RBE values measured in any system.**
- **All tumors were measured, some were benign.**

Carcinogenesis

Cross section = the increase in proportion of animals with Harderian gland tumors per unit fluence.

This is a track penumbra effect.

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Fig. 14.7 in Alpen, E. L. *Radiation Biophysics,* 2nd ed. San Diego, CA: Academic Press, 1998.

Carcinogenesis

The RBEs are significantly higher than other reports with high-LET particles.

The Harderian gland RBEs never dip below 1 at high LET values.

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[ALPEN-94] Fig. 3.

Carcinogenesis

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[ALPEN-94] Table 3.

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[ALPEN-94] Table 4.

Carcinogenesis

Much attention has been drawn to these results.

This is very troubling to NASA.

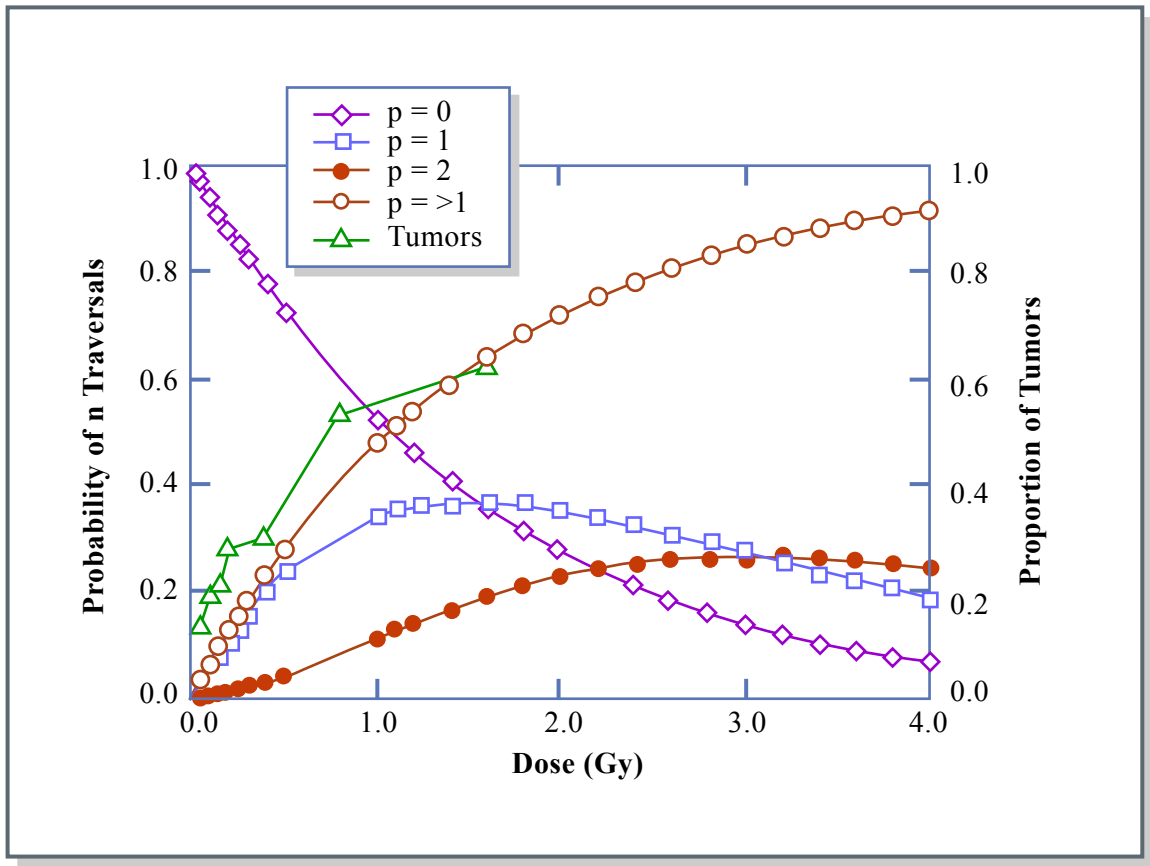

Figure by MIT OCW.

These data suggest that only a single hit by a high-LET iron particle is sufficient to cause transformation and tumor induction.

Skin Cancer

Incidence of skin carcinomas in rats at ~ 1 year after irradiation.

Dose vs fluence?

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[ALPEN-94] Fig. 6.

Cataract Formation

With protons, low dose rate causes less damage.

Iron ions appear much more effective than x-rays for cataract induction.

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[ALPEN-94] Fig. 9.

Chromosome Aberrations

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Premature Aging

See [SHUKITT-HALE]: Shukitt-Hale, Barbara, Gemma Casadeusus, John J. McEwen, Bernard M. Rabin and James A. Joseph. "Spatial Learning and Memory Deficits Induced by Exposure to Iron-56-Particle Radiation." Radiation Research 154 (2000): 28-33.

Previous data from this group has shown:

- Exposure to ^{56}Fe particles disrupts behavior mediated by the dopamine neurotransmitter system. Conditioned Taste Aversion Test.
- ***The changes are similar to those seen in aged rats***.

Current study looks at cognitive function: spatial memory and learning; areas known to be affected in aging.

Rats were tested at 1 month after 1.5 Gy whole-body exposure to 1 GeV/n ^{56}Fe.

Morris Water Maze

Requires rats to use ***spatial learning*** to find a hidden platform just below the surface of a pool and ***remember*** the location from the previous trial.

Testing on 4 consecutive days/6 trials per day.

- Day 1: Trials 1-6; put rat into pool, measure time to find the platform and escape.

- Days 2 and 3: Trial 6; remove platform, measure time spent in quadrant where platform was previously located. ***Measures memory***.

- Day 4: Change location of platform
  - Trials 1-5; measure time to find platform and escape.
  - Trial 6; remove platform, measure time spent searching in the correct quadrant. ***Measures learning***.

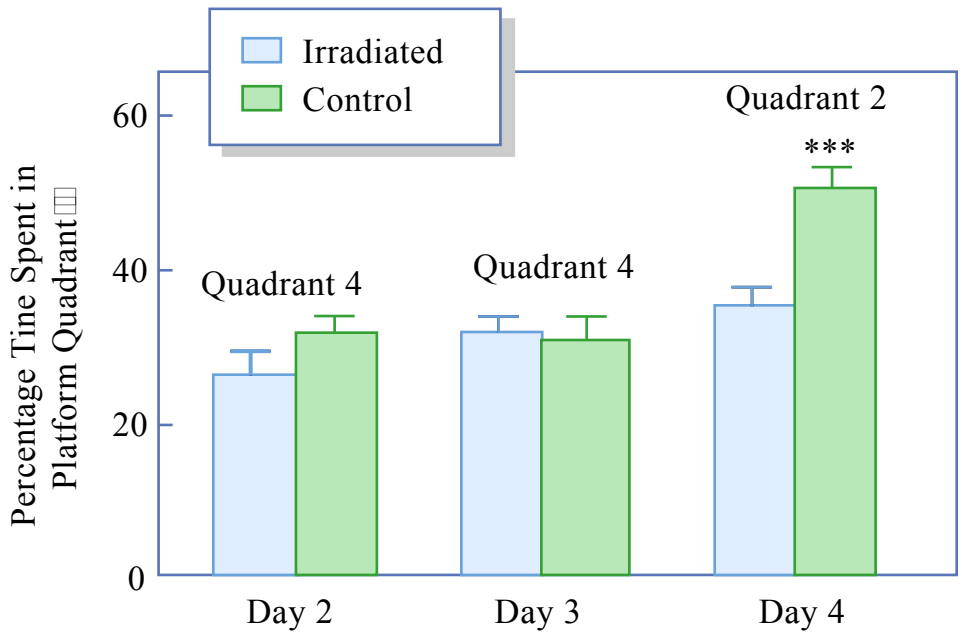
Morris Water Maze

Image removed due to copyright restrictions.
[SHUKITT-HALE] Fig. 1.

Premature Aging

- **The escape platform has been removed.**
- **Measure the time spent searching in the correct location (where the platform used to be).**
- **Control rats are using a spatial strategy**

Irradiated rats are using non-spatial strategy.

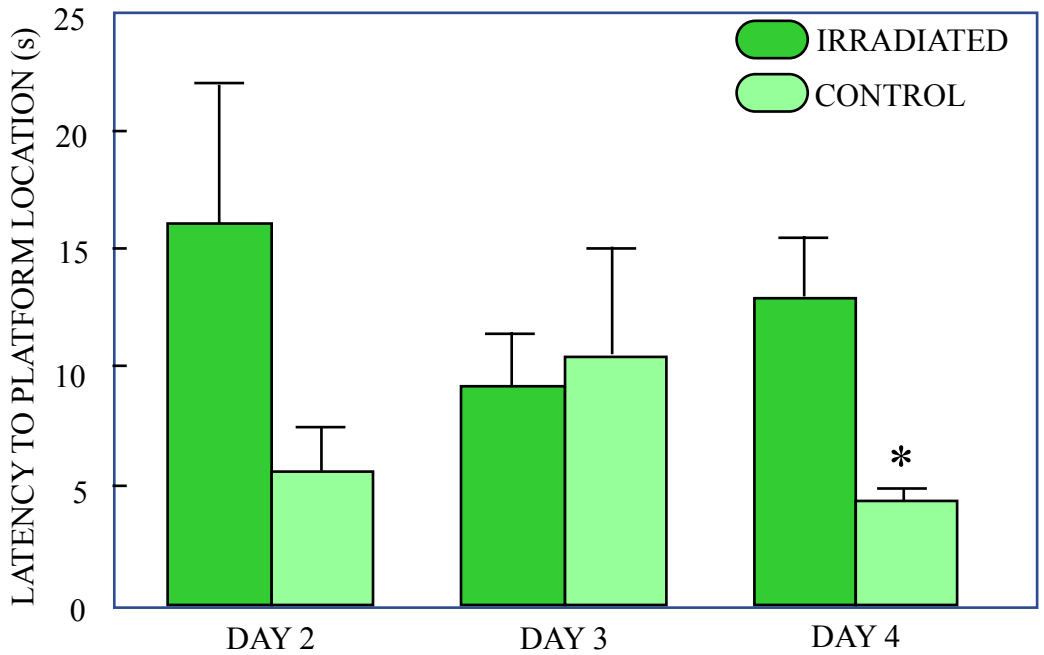


Percentage time (mean + SEM) spent in the quadrant that had previously contained the platform during the probe trials on testing days 2-3 (quadrant 4) and reversal day 4 (quadrant 2) in the Morris water maze for the irradiated and control groups. Asterisks indicate significant differences between the groups (*** $P < 0.001$).

Figure by MIT OCW.

Premature Aging

Control rats have better memory and are using spatial cues for orientation.



Latency to cross (mean + SEM) the previous location of the hidden platform for the first time during the probe trials on testing days 2-4 in the Morris water maze for the irradiated and control group. Asterisks indicate significant differences between the groups (*$p<0.05$).

Figure by MIT OCW.

Conclusions

Whole-body irradiation with 1.5 Gy of ^{56}Fe 1000 MeV/n disrupted spatial memory and learning.

Irradiated rats took longer to learn a new task, and forget the old one, during reversal training.

Irradiated group did not use spatial strategies to find the submerged platform. Random circular swimming.

Both of these are deficits *similar to those seen in aged rats*.

X-rays can produce similar effects, but at doses of 20-30 Gy and not until 200-280 days post irradiation.