Intakes of Plutonium Produce One-Fourth the Risk when Human Susceptibility Data Are Used for Risk Assessment

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Abstract

Cancer is a family of diseases, and it should be obvious that different tissues would have different susceptibility to radiation-induced cancer. Current radiation risk models assume that, while various organs and tissues may have different radiosensitivities, all follow a linear, nonthreshold (LNT) dose-response relationship. A more accurate (if more complicated) risk assessment would account for different shaped dose-response relationships for each cancer type. Since the most compelling risk estimates for radiation carcinogenesis come from human data, we examined the human data for bone cancer and liver cancer caused by intakes of radioactive materials. Excess bone cancer has been seen in radium workers (primarily female dial-painters at the beginning of the 20th century) and plutonium workers at Mayak. Excess liver cancer has been seen in patients administered the radioactive thorium compound Thorotrast for x-ray studies, and also in plutonium workers at Mayak. In each case, there is evidence for, or at least a suggestion of, a threshold dose or dose rate below which there is no excess disease. Since intakes of plutonium produce dose primarily to bone and liver, a threshold in the dose-response relationship for these cancers would directly impact cleanup standards for DOE sites, and radiation protection standards for workers exposed to plutonium. Using state-of-the-art computer codes developed at Pacific Northwest National Laboratory, we show that current cleanup standards for Pu are too *low* by a factor of 4, and worker protection standards are too low by a factor of 13. This work shows that application of radiation-detriment models that incorporate human data for each individual endpoint should be used in radiation risk estimates and standards-setting.

Introduction

- **Cancer is a family of diseases**
  - **different tissues have different susceptibility to radiation**
- ***Current* radiation risk models assume**
  - **various organs and tissues may have different radiosensitivities**
  - **all follow a linear, nonthreshold (LNT) dose-response relationship**
- ***Future* radiation risk models**
  - **more complicated**
  - **more accurate**
  - **account for different shaped dose-response relationships for each cancer type**
  - **some LNT, others nonlinear, still others have thresholds**
- **Human data are most compelling**

The General Linear Model

$$P(n > 0 \mid b, k, D, D_0) = 1 - e^{-(k[D - D_0] + b)}$$

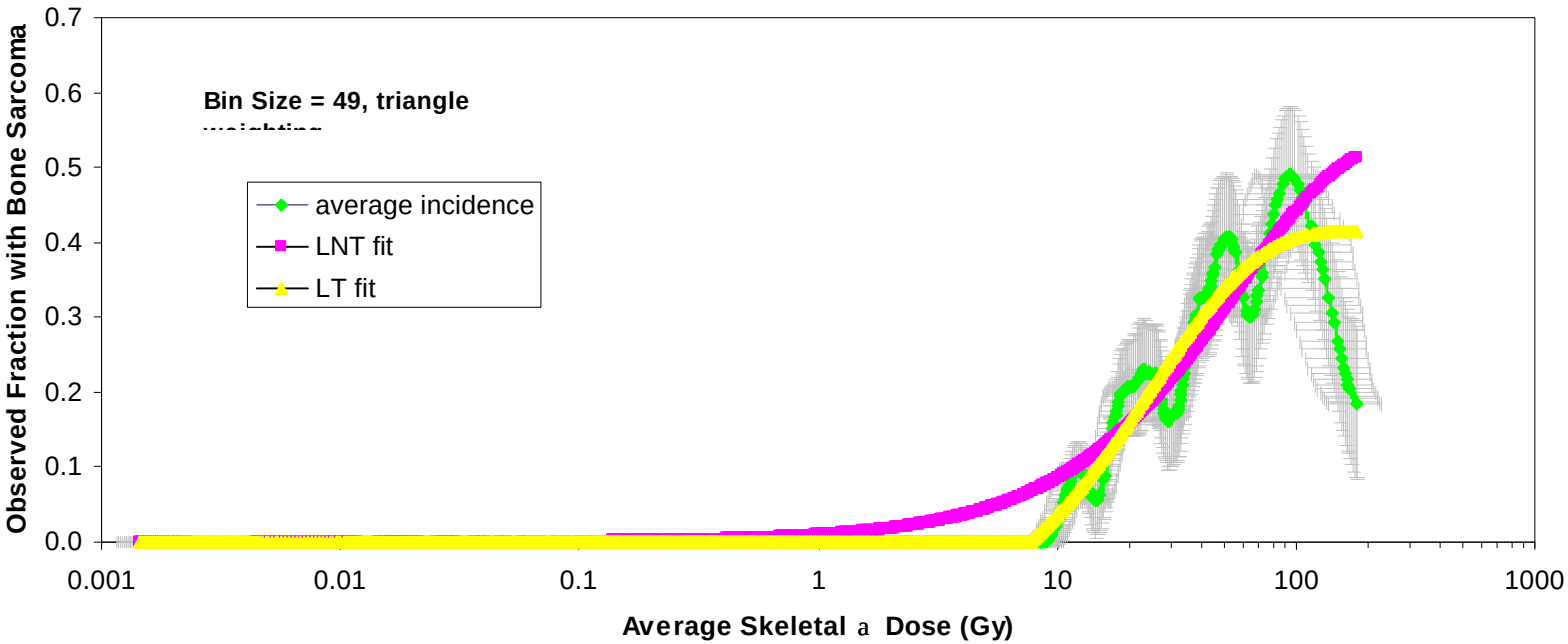
- **where**
  - ***P*** **is the probability of occurrence**
  - ***n*** **is the number of tumors in an individual**
  - ***b*** **is the background incidence rate**
  - ***k*** **is the risk per unit dose (Gy^{-1})**
  - ***D*** **is the dose (Gy)**
  - D_0 **is the threshold dose (Gy)**
    - **if D_0 is 0, then there's no threshold**

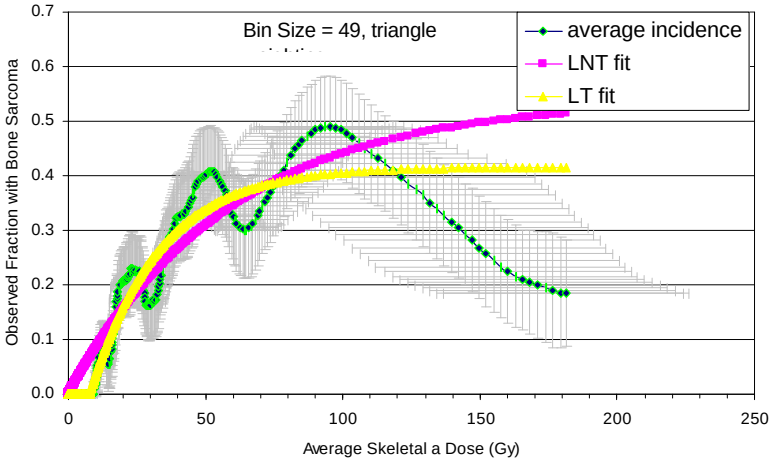
Probable Thresholds

- **Human data suggest *dose* & *dose rate* thresholds for**
  - **Osteosarcoma**
    - **in Ra dial painters (D_0 ~ 8 Gy)**
    - **in Pu-exposed Mayak workers**
  - **Liver cancer**
    - **in Thorotrast patients**
    - **in Pu-exposed Mayak workers**

Model-free data visualization using rolling, weighted averages

2403 Radium Workers

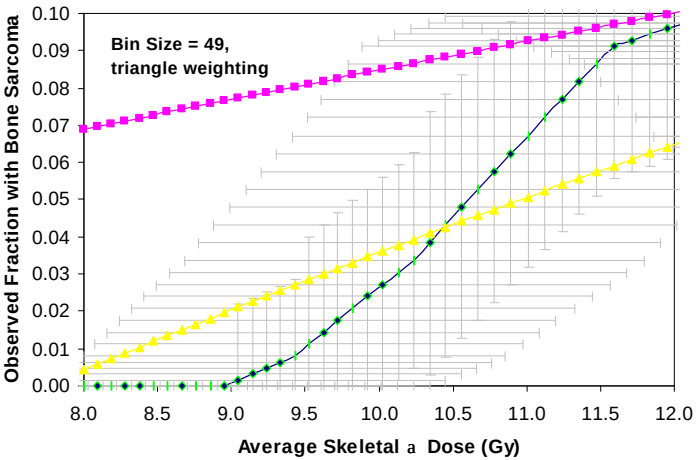




Uncertainty bars:

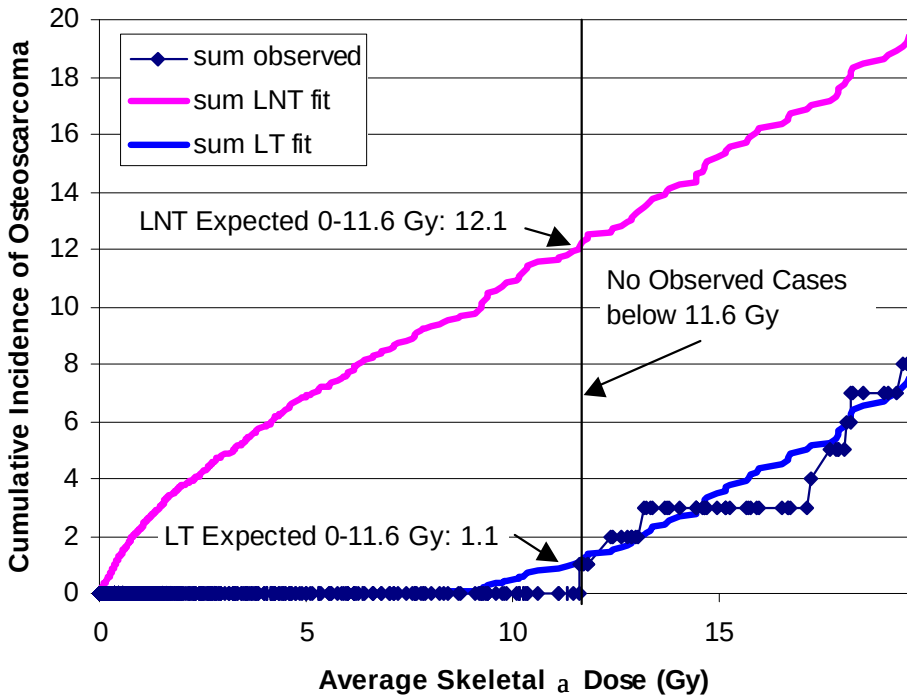
$\pm$ 1 S.D.

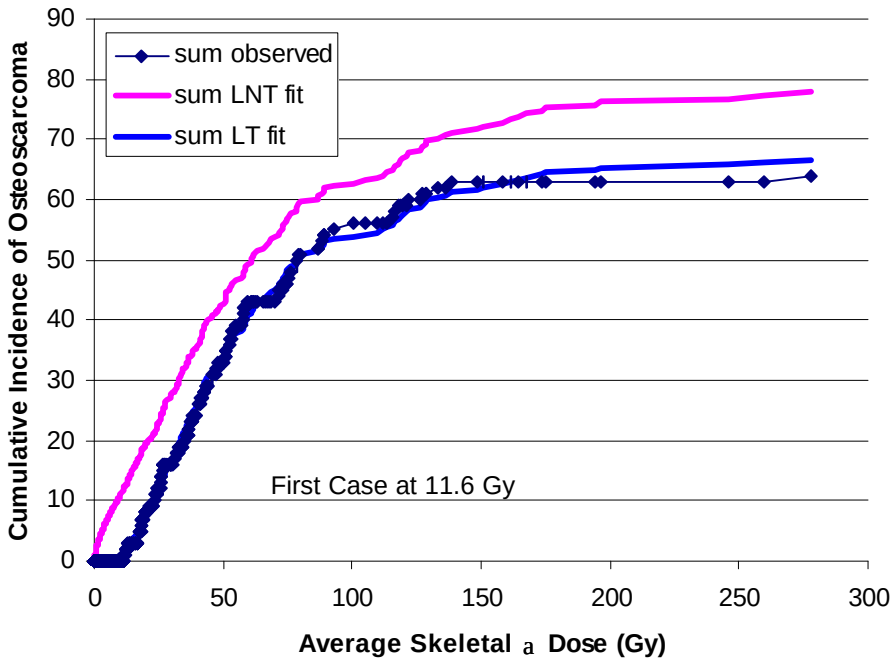
D_0 for LT = 7.73 Gy



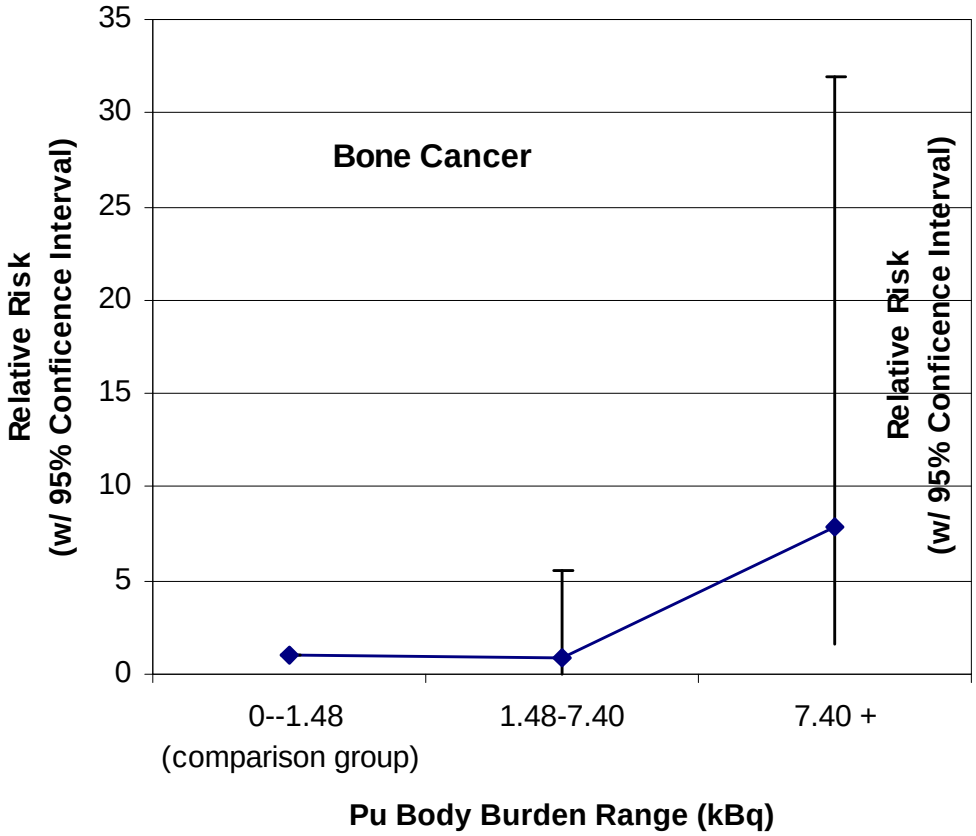
Threshold Likely in Radium Workers

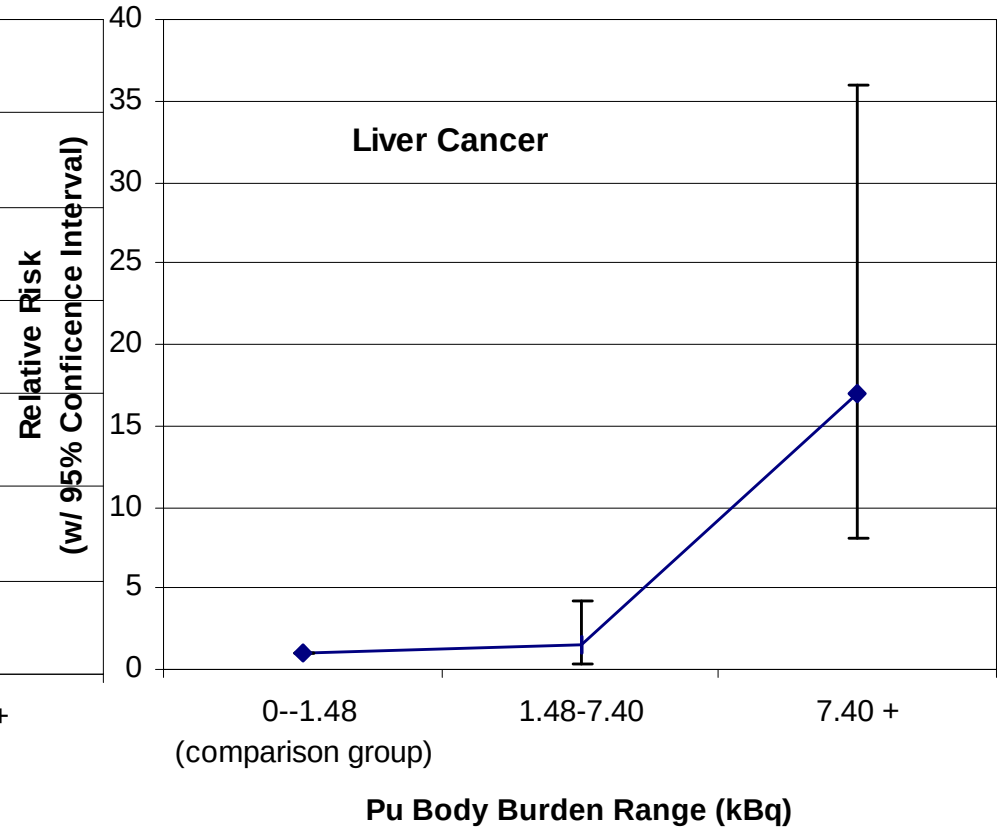
- **LNT model predicts 12 cases when 1 is observed**
- **LNT is not likely to be correct; LT is likely correct**



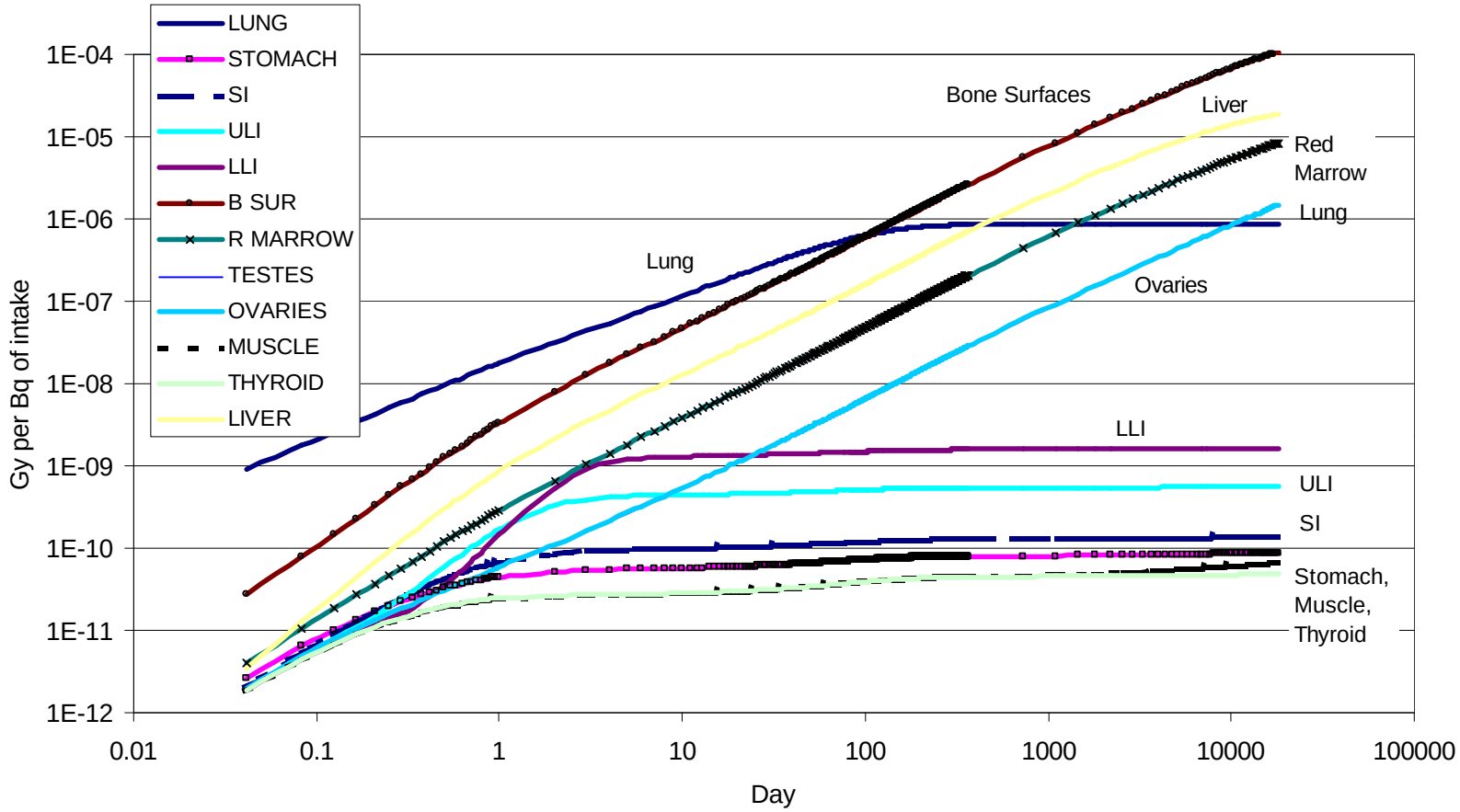


Mayak Workers

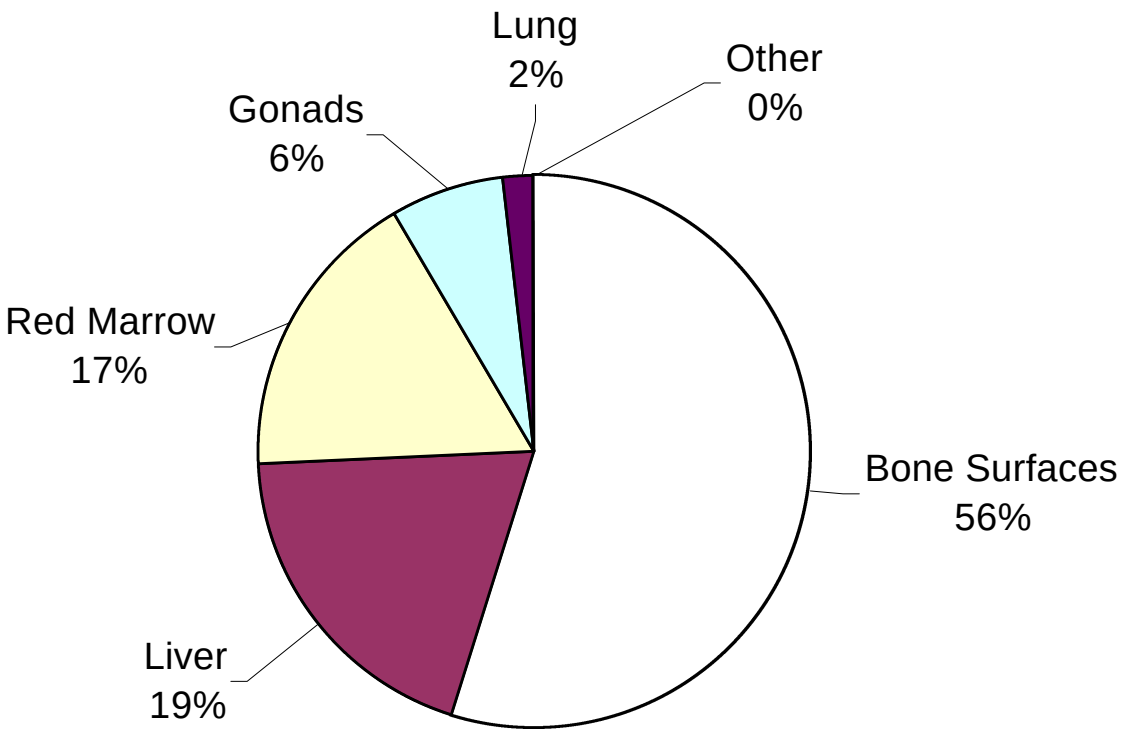




^{239}Pu Organ Cumulative Doses, Acute Inhalation, Class W, f_1 = 0.001



Fraction of *Effective* Dose to Various Tissues from Inhalation of Plutonium



- **bone surfaces and liver account for 75% of *effective* dose**
- **if there's a threshold, only red marrow, gonads, lung, and "other" matter**

Example: Plutonium

- **Internal Pu primarily irradiates bone and liver**
- **If thresholds exist, then only the irradiation that occurs above a certain *dose rate* matters**
- **Dose, especially committed dose, *alone* does not predict risk in this case**
- **Must model entire time course of irradiation in each tissue**
- **There's nothing "linear" about it**

Result: Standards for Human Intakes of Plutonium Increase for *Same Risk*

- **Cleanup standards *increase* by a factor of 4**
  - **environmental standards are based on stochastic effects, i.e., limiting 50-year committed effective dose to 0.05 Sv**
- **Occupational exposure standards *increase* by a factor of 13**
  - **occupational standards are based on deterministic effects, i.e., limiting 50-year committed dose to bone surfaces to 0.5 Sv (0.025 Gy for a-particles)**
- **Higher values for cleanup standards result in**
  - **less cleanup**
  - **lower cost**

Conclusions

- **Different cancer endpoints require different dose-response models**
- **Human data show that cancer dose-response relationships may be**
  - **LNT (Linear-Nonthreshold)**
  - **LQ (Linear-Quadratic)**
  - **LT (Linear-Threshold)**
- **Using cancer-specific dose-response models can result in more accurate risk estimates**
- **For plutonium, dramatic savings in cleanup can be realized from using the correct models based on human data**

References 1

Advisory Committee on Radiological Protection. Biological Effects of Low Doses of Radiation at Low Dose Rate. ACRP-18. Ottawa, Canada: Atomic Energy Control Board of Canada; 1996.

Ames, B.N.; Gold, L.S. Too many rodent carcinogens: mitogenesis increases mutagenesis [published erratum appears in Science 1990 Sep 28;249(4976):1487] [see comments]. Science 249(4972):970-971; 1990.

Andersson, M.; Storm, H.H. Cancer Incidence Among Danish Thorotrast Patients. Journal of the National Cancer Institute 84(17):1318-1325; 1992.

Andersson, M.; Vyberg, M.; Visfeldt, J.; Carstensen, B.; Storm, H.H. Primary Liver Tumors among Danish Patients Exposed to Thorotrast. Radiat. Res. 137:262-273; 1994.

Chomentowski, M.; Kellerer, A.M.; Pierce, D.A. Radiation dose dependences in the atomic bomb survivor cancer mortality data: a model-free visualization. Radiat. Res. 153(3):289-294; 2000.

dos Santos-Silva, I.; Jones, M.; Malveiro, F.; Swerdlow, A. Mortality in the Portuguese thorotrast study. Radiat. Res. 152(6 Suppl):S88-S92; 1999.

Gilbert, E.S.; Koshurnikova, N.A.; Sokolnikov, M.; Khokhryakov, V.F.; Miller, S.; Preston, D.L.; Romanov, S.A.; Shilnikova, N.S.; Suslova, K.G.; Vostrotin, V.V. Liver Cancers in Mayak Workers. Radiat. Res. 246-252; 2000.

International Commission on Radiological Protection (ICRP). 1990 Recommendations of the International Commission on Radiological Protection. ICRP Publication No. 60. Annals of the ICRP 21(1-3); 1991.

Kido, C.; Sasaki, F.; Hirota, Y.; Kiyosawa, K.; Hayashi, S.; Mori, T.; Sobue, T. Cancer mortality of thorotrast patients in Japan: the second series updated 1998. Radiat. Res. 152(6 Suppl):S81-S83; 1999.

Koshurnikova, N.A.; Gilbert, E.S.; Sokolnikov, M.; Khokhryakov, V.F.; Miller, S.; Preston, D.L.; Romanov, S.A.; Shilnikova, N.S.; Suslova, K.G.; Vostrotin, V.V. Bone Cancers in Mayak Workers. Radiat. Res. 237-245; 2000.

References 2

Martling, U.; Mattsson, A.; Travis, L.B.; Holm, L.-E.; Hall, P. Mortality after Long-term Exposure to Radioactive Thorotrast: A Forty-Year Follow-up Survey in Sweden. Radiat. Res. 151:293-299; 1999.

Mori, T.; Fukutomi, K.; Kato, Y.; Hatakeyama, S.; Machinami, R.; Tanooka, H.; Ishikawa, Y.; Kumatori, T. 1998 Results of the First Series of Follow-up Studies on Japanese Thorotrast Patients and their Relationships to an Autopsy Series. Radiat. Res. 152(6 Suppl):S72-S80; 1999b.

Mori, T.; Kido, C.; Fukutomi, K.; Kato, Y.; Hatakeyama, S.; Machinami, R.; Ishikawa, Y.; Kumatori, T.; Sasaki, F.; Hirota, Y.; Kiyosawa, K.; Hayashi, S.; Tanooka, H.; Sobue, T. Summary of entire Japanese thorotrast follow-up study: updated 1998. Radiat. Res. 152(6 Suppl):S84-S87; 1999a.

Napier, B.A.; Peloquin, R.A.; Strenge, D.L.; Ramsdell, J.V. GENII - The Hanford Environmental Radiation Dosimetry Software System. Volume 1: Conceptual Representation. PNL-6584 Vol. 1. Volume 2: Users' Manual. PNL-6584 Vol. 2. Volume 3: Code Maintenance Manual. PNL-6584 Vol. 3. Richland, Washington: Pacific Northwest Laboratory; 1988a-c.

Rowland, R.E. Radium in Humans. A Review of U.S. Studies. ANL/ER-3. Springfield, Virginia: National Technical Information Service; 1994.

Stannard, J.N. Radioactivity and Health, A History, Volume 1: Laboratory Research. Richland, WA: US Department of Energy; 1988.

van Kaick, G.; Dalheimer, A.; Hornik, S.; Kaul, A.; Liebermann, D.; Luhrs, H.; Spiethoff, A.; Wegener, K.; Wesch, H. The german thorotrast study: recent results and assessment of risks. Radiat. Res. 152(6 Suppl):S64-S71; 1999.

van Kaick, G.; Muth, H.; Kaul, A. The German Thorotrast Study. FR of Germany: Commission of the European Communities; 1984.