Low Dose Radiation Research:
"Radiation Dose is More than a Number"

Radiation Dosimetry Standardization Workshop
NCI / NIAID / NIST

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History – Low Dose Program initiated in 1999

"The lowest dose at which a statistically significant radiation risk has been shown is ~ 100 mSv (10 rem) of x-rays."

Bridging Radiation Policy and Science
An international meeting of experts, held
at Airlie House Conference Center
1 – 5 December 1999

History – Low Dose Program initiated in 1999

"The lowest dose at which a statistically significant radiation risk has been shown is ~ 100 mSv (10 rem) of x-rays."

But what do these numbers really mean…??

- **What did they mean in the past?**
- **What do they mean now?**

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DOE's Low Dose Program (1):

- **Focused on very low dose exposures that are encountered by workers in energy production and environmental cleanup**
  - **Less than 0.1 Gy (10 rads)**
  - **Mostly low LET (x- and gamma-ray)**
  - **Higher doses, then titrate down to lower doses**
  - **Low dose rates**
  - **High dose rates**
- **For low dose exposures, the dosimetry is critically important (spatial and temporal)**

DOE's Low Dose Program (2):

- **Biological models include**
  - **Molecular endpoints within single cells** (microbeams)
  - **Cell culture models** (yeast, rodent, human)
  - **3-D tissue models**
    - Rat trachea
    - Matek skin model
    - Ductal mammary epithelia
  - **Animal subjects**
    - rat
    - mouse
    - Medaka and zebrafish
- **Re-analysis of archived tissues and data**
  - **Mega-mouse studies**
  - **Beagle dog studies**
  - **Conducted in the second half of the 20th century**

DOE's Low Dose Program (3):

- **Research to enable mechanism-based models that incorporate both radiobiology and epidemiology**
  - **From cellular and molecular actions within tissues**
  - **To the evolution of cancer as a multi-cellular disease**
  - **… in human populations**

- **Clear understanding of both the biological assumptions and the dosimetry underlying epidemiological analysis in low dose range**

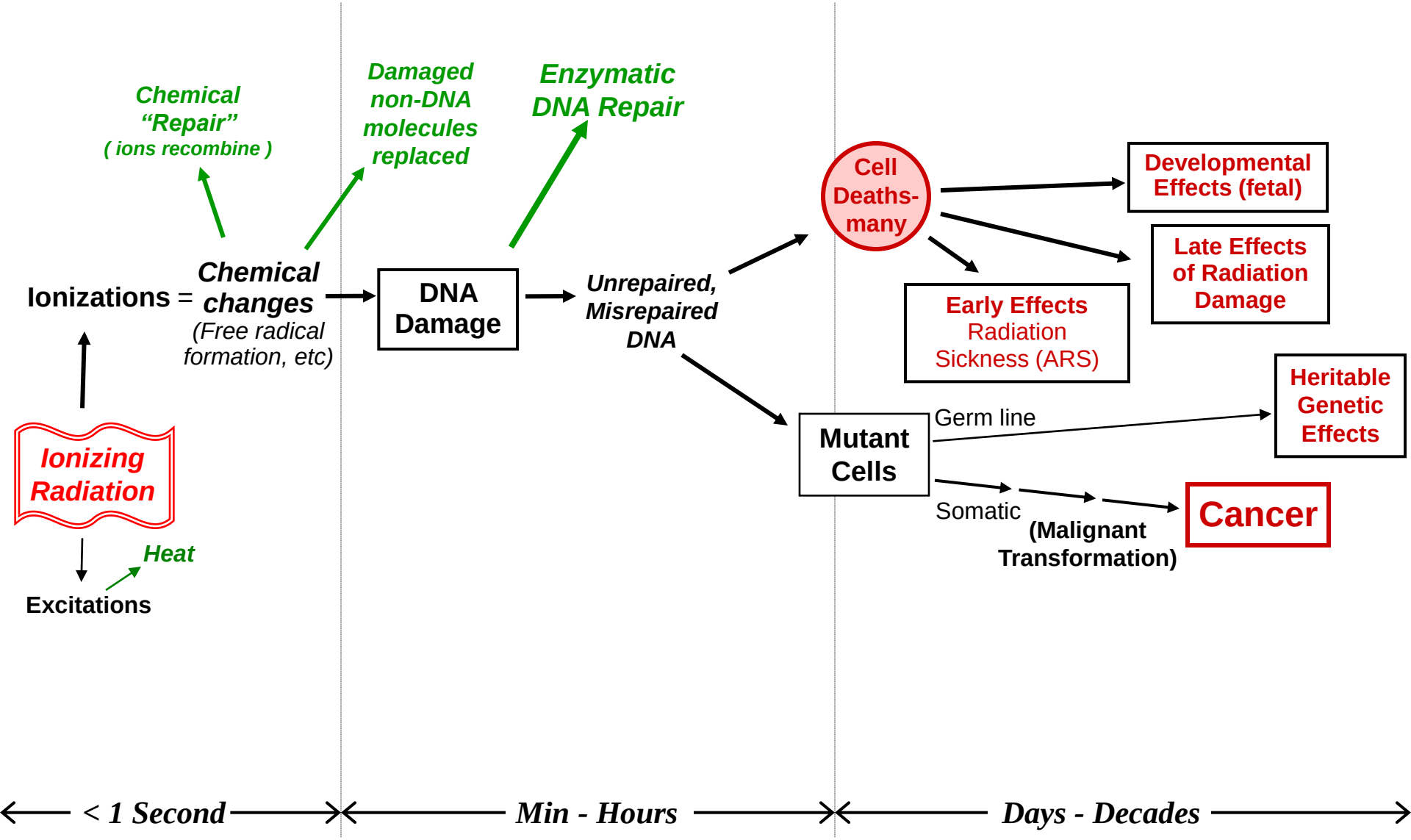
The Underlying Assumption for (Low Dose) Dosimetry:

"If the spatial and temporal distribution of energy deposition events were clearly described, it would improve the understanding of biological mechanisms leading to radiation-induced effects."

Hans-Georg Menzel, 2010 (paraphrased)

End

Classic Paradigm of Radiation Injury (High Dose)



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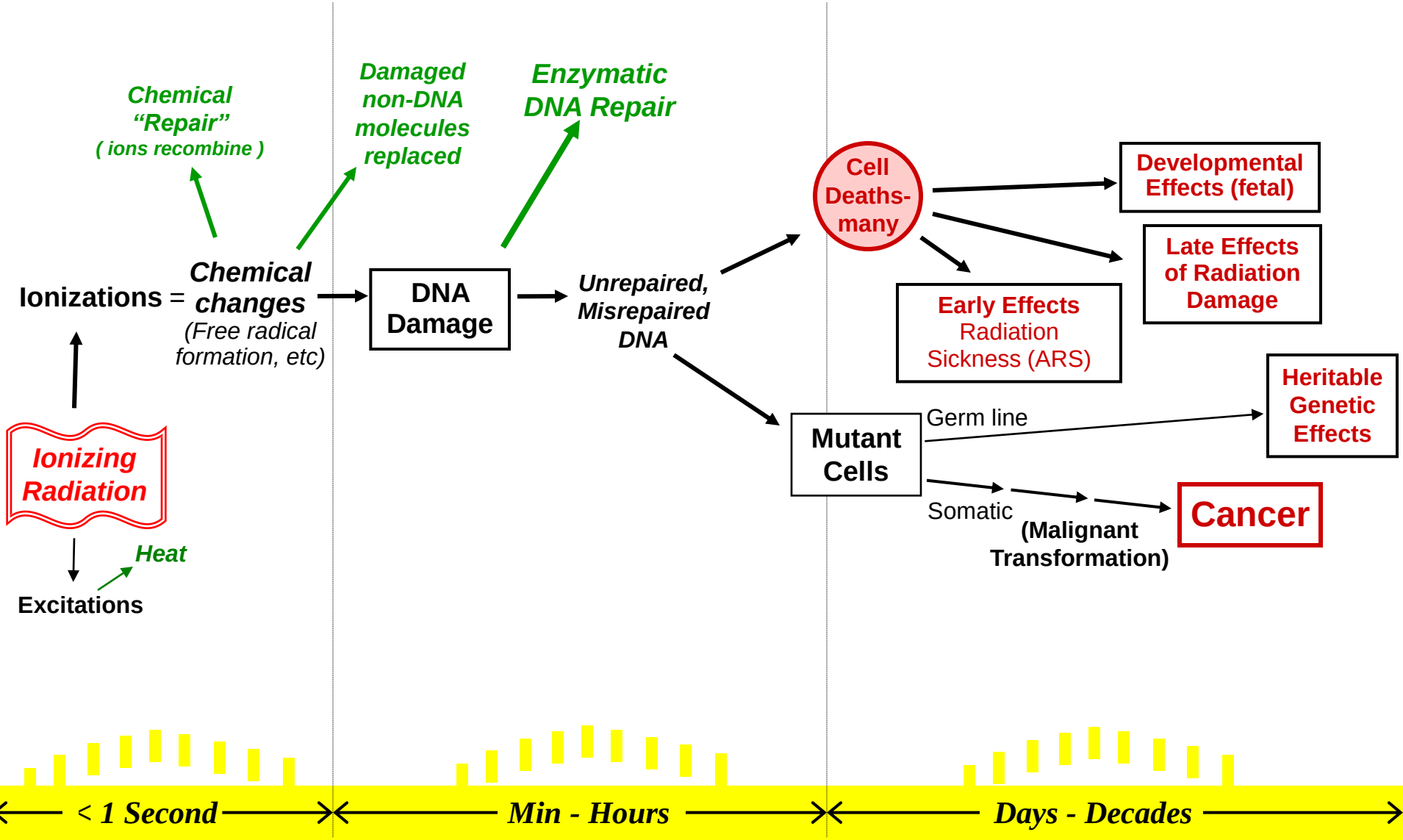
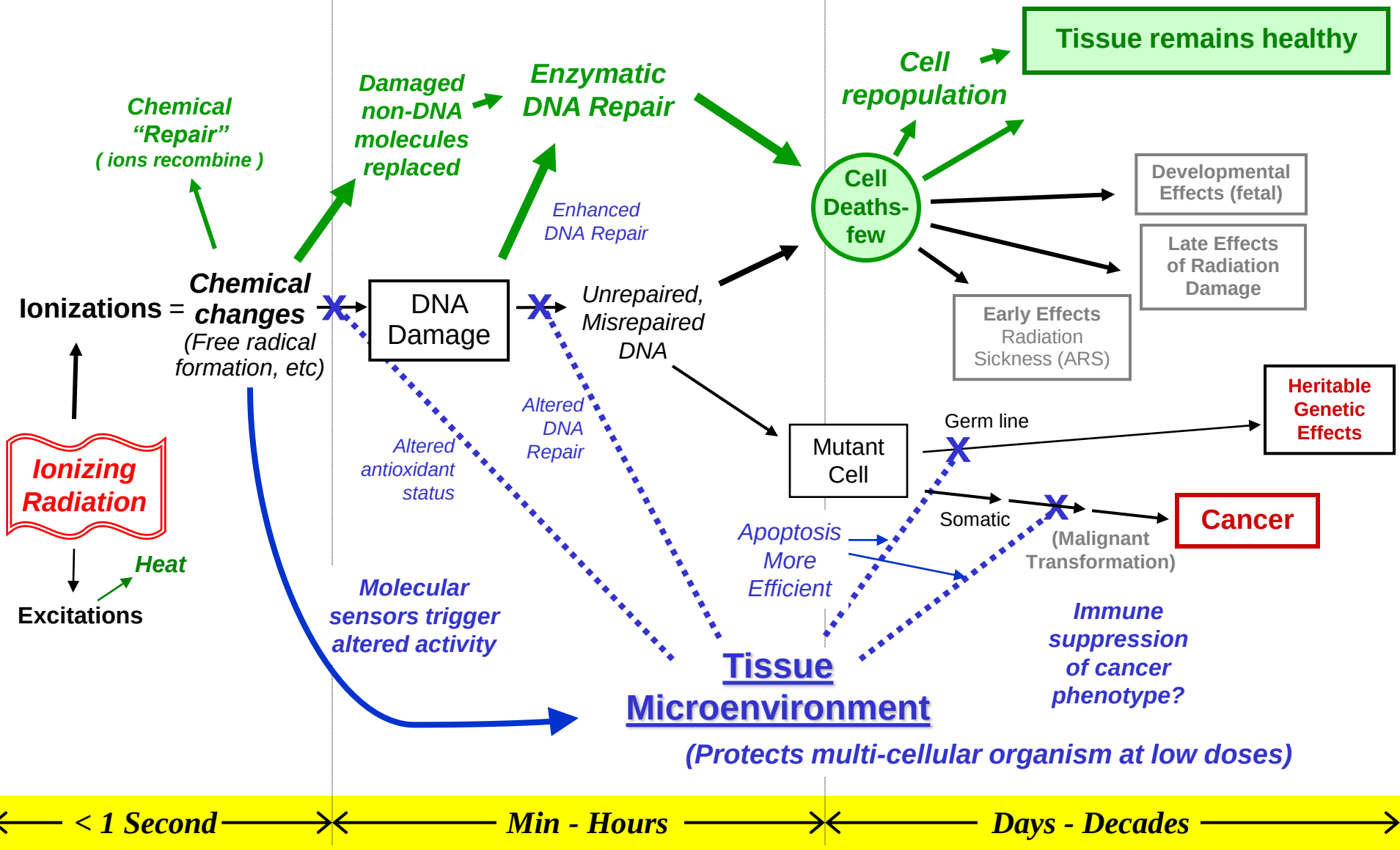


Low Doses show other pathways….



Time Factors:

- **Dose Rates**
  - The biology is clearly different (dose rate effects…)
  - Gamma irradiators change over time (half-lives calculated…)
  - Calibrated radiation-generating machines can drift…

- **Timing of the Experimental Protocol**
  - Dose Fractionation
  - The periods before, between, after each step

- **Daytime, Nighttime**
  - The biology is clearly different (diurnal/nocturnal effects…)
  - The physics

- **Historical Time**
  - The definitions of quantities change
  - New measurement techniques allow improved precision, accuracy
  - Annotation, curation of the literature…

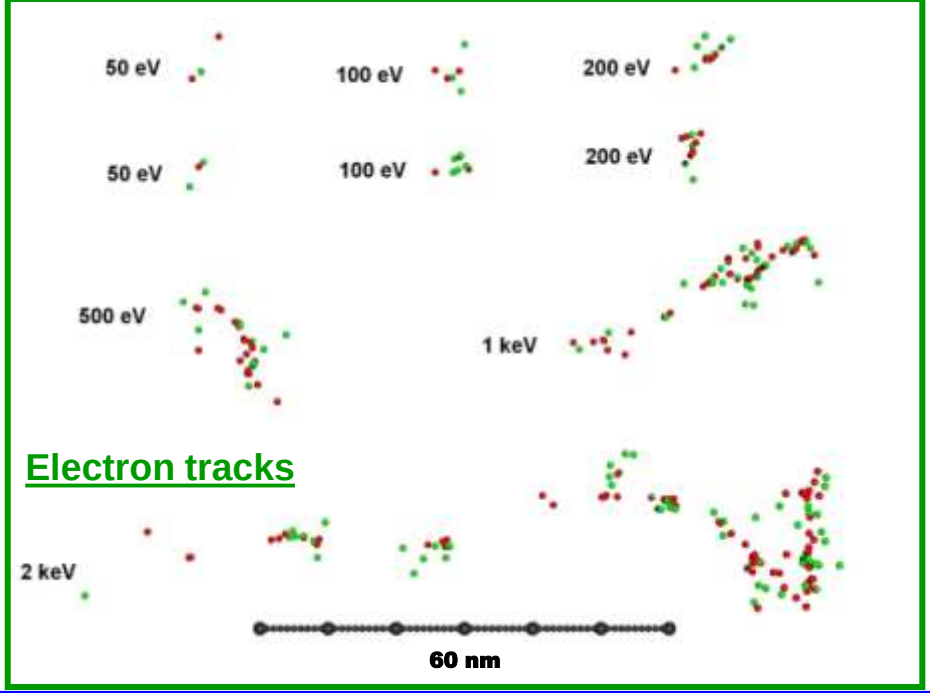
Spatial Factors:

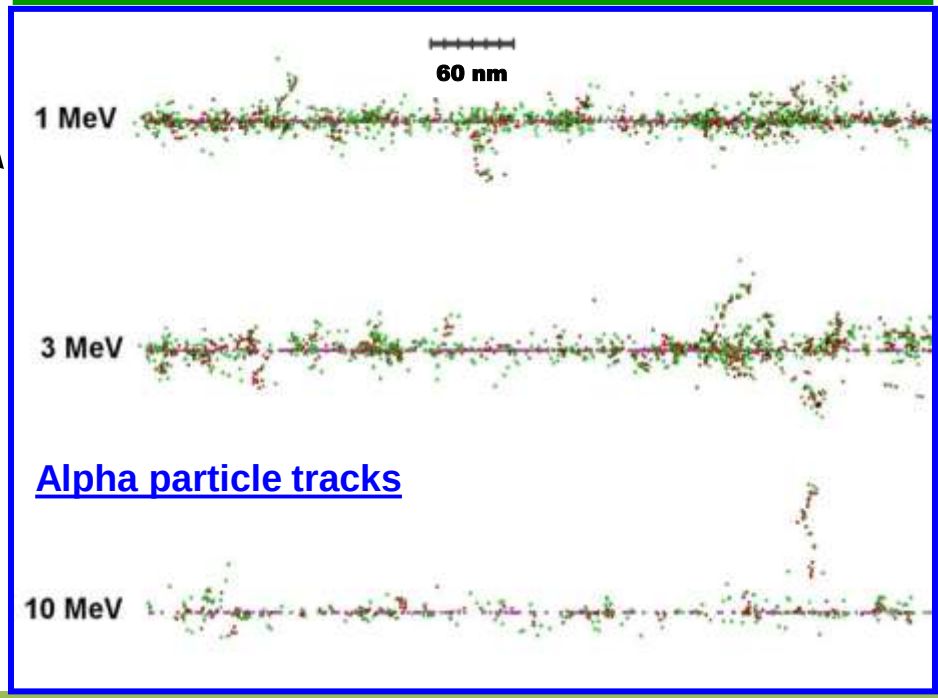
- **Microdosimetry**
  - (Les Braby)
  - Energy distributions
  - Monte Carlo track structure simulations

- **Partial vs. Full**
  - Body of animal subject
  - Cell/tissue culture dish
  - Single cell (intra-, inter-, extra-)

- **Uniform radiation field**
  - To encompass entire subject

- **Background radiation matters**
  - Gamma-rays (soil)
  - Radon
  - Cosmic rays
  - (manmade)

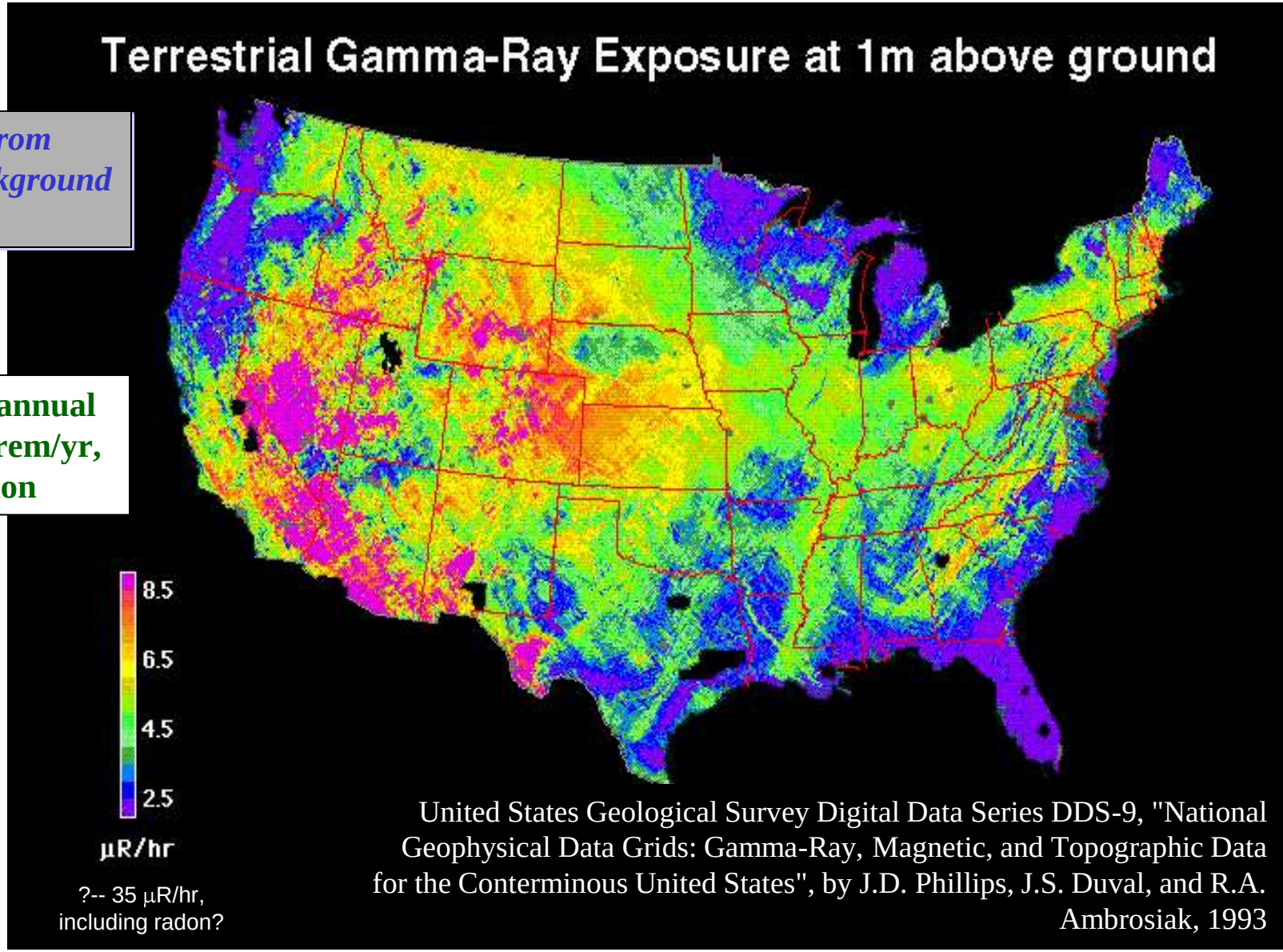




Background Radiation:

Dose Rates from Natural Background USGS

U.S. average annual dose = 310 mrem/yr, including radon



United States Geological Survey Digital Data Series DDS-9, "National Geophysical Data Grids: Gamma-Ray, Magnetic, and Topographic Data for the Conterminous United States", by J.D. Phillips, J.S. Duval, and R.A. Ambrosiak, 1993

Ionizing Radiation Dose Ranges (Rem)

acute exposure = all at once; chronic = hours, days, years

Cancer Radiotherapy — total doses to tumor

Whole body, acute: G-I destruction; lung damage; cognitive dysfunction (death certain in 5 to 12 days)*

Whole body, acute: cerebral/ vascular breakdown (death in 0-5 days)*

⑥ 0 — 2000 — 4000 — 6000 — 8000 — 10,000 rem

Total Body Irradiation (TBI) Therapy

Acute Radiation Syndromes

Life Span Study (A-bomb survivor epidemiology)

Whole body, acute: circulating blood cell death; moderate G-I damage (death probable 2-3 wks)*

Whole body, acute: marked G-I and bone marrow damage (death probable in 1-2 wks)*

Charged particle event (Solar flare) dose on moon, no shielding

Estimated dose for 3-yr Mars mission (current shielding)

⑤ 0 — 200 — 400 — 600 — 800 — 1,000 rem

Early, transient skin erythema (2-24 hr onset)

Temporary epilation (3 wk onset)

Main erythema reaction (10 day onset)

Permanent epilation (3 wk onset)

Human LD_{50} range acute exposure no medical intervention*

Human LD_{50} range acute exposure with medical intervention

*Note: Whole body acute prognoses assume no medical intervention (G-I = gastrointestinal)

Office of Science — U.S. DEPARTMENT OF ENERGY

Cancer Epidemiology

Evidence for small increases in human cancer above 10 rem acute exposure or 20 rem chronic exposure

④ 0 — 10 — 20 — 30 — 40 — 50 — 60 — 70 — 80 — 90 — 100 rem

Typical mission doses on International Space Station (ISS)

Ramsar, Iran high natural bkg/yr

DHS emergency guideline to save a life: 25 rem

Interplanetary Space natural bkg/yr

DOE Low Dose Program

③ E F M I N J K G H L — 0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10 rem

Kerala coast, India high natural bkg/yr

DHS emergency guideline for public relocation: 2 rem/yr (20 mSv/yr)

Guarapari, Brazil high natural bkg/yr

DOE, NRC dose limit for workers: 5 rem/yr (50 mSv/yr)

Typical added annual dose for commercial airline flight crews

Medical Diagnostics (A-O)

see chart >>

② A B C D E F — 0 — 100 — 200 — 300 — 400 — 500 — 600 — 700 — 800 — 900 — 1,000 mrem (1 rem)

Airport x-ray whole body scanner: 0.007 mrem/scan

(Limit = 25 mrem/yr ≈ 4000 scans/yr)

Natural background, USA average ≈ 310 mrem/yr (includes radon)

Yangjiang, China high natural bkg/yr

DOE facility releases

Regulations & Guidelines

① A B — 0 — 10 — 20 — 30 — 40 — 50 — 60 — 70 — 80 — 90 — 100 mrem

Round-trip Los Angeles – New York (≈ 3.7 mrem)

EPA dose limit public drinking water systems: 4 mrem/yr

EPA dose limit from release in air: 10 mrem/yr

NRC cleanup criteria for site decommissioning / unrestricted use: 25 mrem/yr

DOE, NRC dose limit for the public: 100 mrem/yr (1 mSv/yr) (ICRP, NCRP)

Medical Diagnostics rads

(Estimated maximum organ dose)

X-ray films	
A – Chest (PA & Lat)	0.014
B – Dental Panoramic	0.07
C – Lumbar-Sacral Spine	0.2 – 0.3
D – Mammogram	0.2 – 0.4
Radiotracer Imaging	
E – Heart Stress (Tc-99m)	0.6 – 1.2
F – Bone (Tc-99m)	0.4 – 1.5
G – Dual Isotope Stress Test	4.0 – 4.5
H – PET: F-18 FDG (bladder)	5.5 – 8
CT Scans (X-ray) (multiple scan average dose)	
I – Chest	2 – 3
J – Head	3 – 5
K – Abdominal	2.2 – 6
L – Full Body	5 – 10
Fluoroscopy /Procedures	
M – Barium Contrast G.I.	1 – 2.2
N – Cardiac Catheterization	1.2 – 4
O – TIPS Procedure	40 – 140

(TIPS: Transjugular Intrahepatic Porto-systemic Shunt)

LD_{50} = Lethal Dose to 50% (whole body dose that results in lethality to 50% of exposed individuals in 30-60 days)

Dose Equivalent: 100 rem = 1 Sievert = (absorbed dose x radiation quality)

Absorbed Dose: 100 rad = 1 Gray

1 rem ≈ 1 rad for x- and gamma-rays

(" ~ " stands for "approximately equal to")

NOTE: This chart was constructed with the intention of providing a simple, user-friendly, "order-of-magnitude" reference for radiation exposures of interest to scientists, managers, and the general public. In that spirit, most quantities are expressed as "dose equivalent" in the more commonly used radiation protection units, the rem and Sievert. Medical diagnostics are expressed as estimated maximum organ dose; as they are not in "effective dose" they do not imply an estimation of risk (no tissue weighting). Dose limits are in effective dose, but for most radiation types and energies the difference is numerically not significant within this context. It is acknowledged that the decision to use these units is a simplification, and does not address everyone's needs. (NRC = Nuclear Regulatory Commission; EPA = Environmental Protection Agency; DHS = Department of Homeland Security)

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Chart compiled by NF Metting, Office of Science, DOE/BER. "Orders of Magnitude" revised June 2010

http://www.lowdose.energy.gov/

Source: Office of Biological and Environmental Research (BER), Office of Science, U.S. Department of Energy

Ionizing Radiation
Dose Ranges
(Sievert)

acute exposure = all at once; chronic = hours, days, years

Cancer Radiotherapy
total doses to tumor

Whole body, acute: G-I destruction; lung damage; cognitive dysfunction (death certain in 5 to 12 days)*

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Charged particle event (Solar flare) dose on moon, no shielding

⑤ 0 2 4 6 8 10 Sv

Estimated dose for 3-yr Mars mission (current shielding)

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Typical mission doses on International Space Station (ISS)

Ramsar, Iran high natural bkg/yr

DHS emergency guideline to save a life: 250 mSv

Interplanetary Space natural bkg/yr

DOE Low Dose Program

③ E F M I N J K G H L 0 10 20 30 40 50 60 70 80 90 100 mSv

Kerala coast, India high natural bkg/yr

DHS emergency guideline for public relocation: 20 mSv/yr (2 rem/yr)

Guarapari, Brazil high natural bkg/yr

DOE, NRC dose limit for workers: 50 mSv/yr (5 rem/yr)

Typical added annual dose for commercial airline flight crews

Medical Diagnostics (A-O)
see chart >>

② A B C D E F 0 1 2 3 4 5 6 7 8 9 10 mSv

Airport x-ray whole body scanner: 0.00007 mSv/scan (Limit = 0.25 mSv/yr ≈ 4000 scans/yr)

Natural background, USA average ≈ 3.1 mSv/yr (includes radon)

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① A B 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1 mSv

Round-trip Los Angeles – New York (≈ 0.037 mSv)

EPA dose limit public drinking water systems: 0.04 mSv/yr

EPA dose limit from release in air: 0.1 mSv/yr

NRC cleanup criteria for site decommissioning / unrestricted use: 0.25 mSv/yr

DOE, NRC dose limit for the public: 1 mSv/yr (100 mrem/yr) (ICRP, NCRP)

Medical Diagnostics mGy
(Estimated maximum organ dose)

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Source: Office of Biological and Environmental Research (BER), Office of Science, U.S. Department of Energy
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