Slides for Chemical and Biological Effects of Radiation

2024

Effect Timescales

From Turner, J. E. *Atoms, Radiation, and Radiation Protection*.

Times	Events
Physical stage	Formation of H_2O^+, H_2O^*, and subexcitation electrons,
$\lesssim 10^{-15}$ s	e^-, in local track regions ($\lesssim 0.1$ μm)
Prechemical stage	Three initial species replaced by H_3O^+, OH, e^-_{aq}, H,
$\sim 10^{-15}$ s to $\sim 10^{-12}$ s	and H_2
Chemical stage	The four species H_3O^+, OH, e^-_{aq}, and H diffuse and
$\sim 10^{-12}$ s to $\sim 10^{-6}$ s	either react with one another or become widely separated. Intratrack reactions essentially complete by $\sim 10^{-6}$ s
Biological stages	
$\lesssim 10^{-3}$ s	Radical reactions with biological molecules complete
$\lesssim 1$ s	Biochemical changes
Minutes	Cell division affected
Days	Gastrointestinal and central nervous system changes
Weeks	Lung fibrosis develops
Years	Cataracts and cancer may appear; genetic effects in offspring

Physical Stage (<10^{-15} Seconds)

- Two possible things:
- Ionization

$$H_2O \rightarrow H_2O^+$$

- Excitation

$$H_2O \rightarrow H_2O^*$$

Prechemical Stage (10^{-12} Sec)

- Formation of primary free radicals

$$H_2O^+ + H_2O \rightarrow H_3O^+ + OH.$$

$$H_2O^* \rightarrow \begin{cases} H_2O^+ + e^- \\ H + OH \end{cases}$$

Chemical Stage (10^{-6} Sec)

$$OH + OH \rightarrow H_2O_2,$$

$$OH + e^-_{aq} \rightarrow OH^-,$$

$$OH + H \rightarrow H_2O,$$

$$H_3O^+ + e^-_{aq} \rightarrow H + H_2O,$$

$$e^-_{aq} + e^-_{aq} + 2H_2O \rightarrow H_2 + 2OH^-,$$

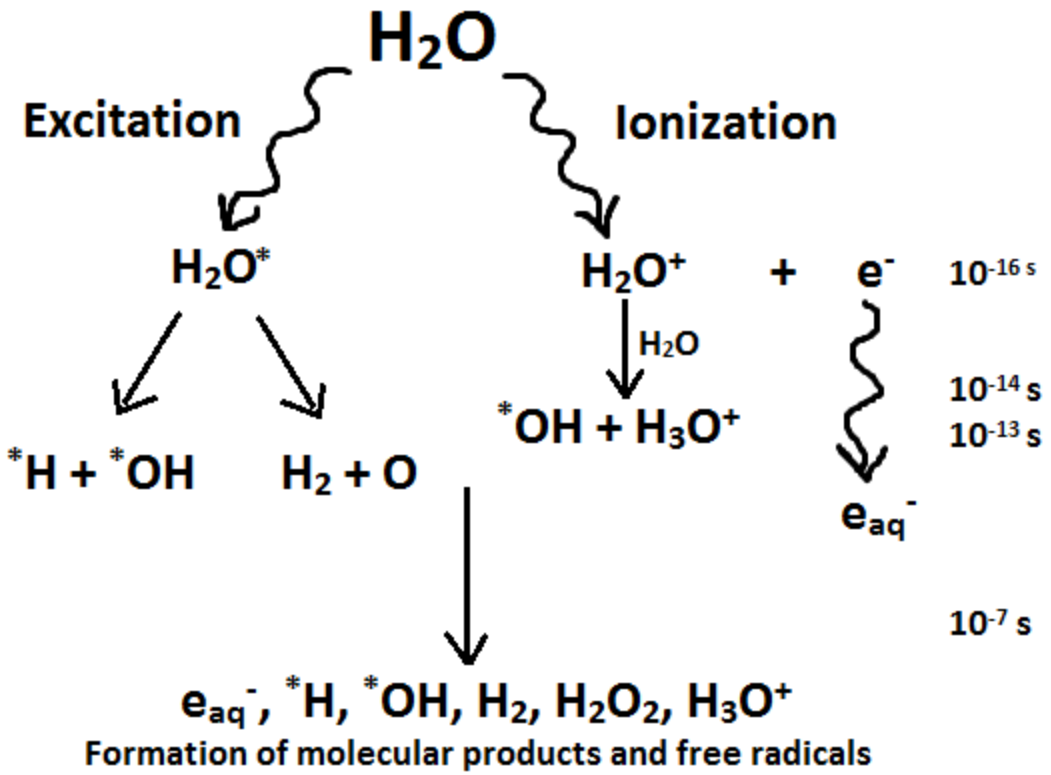
$$e^-_{aq} + H + H_2O \rightarrow H_2 + OH^-,$$

$$H + H \rightarrow H_2.$$

- Each reaction's products can only last so long before recombining with others
- Diffusion out of the "charged particle track" also happens
- This is only a partial set…

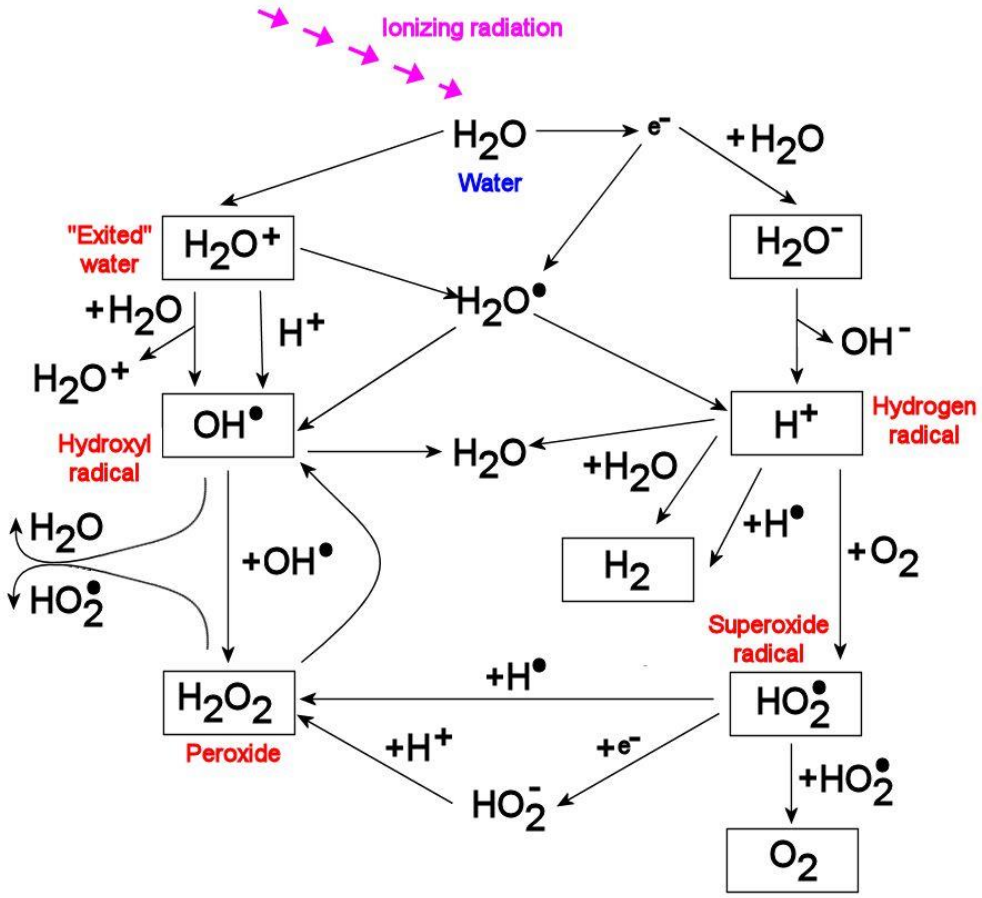
Overall Radiolysis Progression

http://large.stanford.edu/courses/2015/ph241/burkhard1/



Chemical Mechanism Map

http://www.mun.ca/biology/scarr/Radiolysis_of_Water.html



Courtesy of Steven M. Carr. Used with permission.

Chemical Reaction Sets

J. Jarvis, R. G. Ballinger, "RADICAL 1.9 Theory Manual," 2013

No.	Reactions	k_{22}	E_A J x mol^{-1}	k_{288}
1	$OH + OH \rightarrow H_2O_2$	5.5000E+9	7.90E+3	2.540E+10
2	$OH + E^- \rightarrow OH^-$	3.100E+10	1.47E+4	5.345E+11
3	$OH + H \rightarrow H_2O$	9.300E+9	8.20E+3	4.553E+10
4	$OH + HO_2 \rightarrow H_2O + O_2$	7.100E+9	1.42E+4	1.111E+11
5	$OH + O^-_2 \rightarrow O_2 + OH^-$	1.000E+10	1.76E+4	3.024E+11
6	$OH + H_2O_2 \rightarrow HO_2 + H_2O$	2.700E+7	1.42E+4	4.225E+8
7	$OH + H_2 \rightarrow H + H_2O$	3.4000E+7	1.92E+4	1.401E+9
8	$OH + OH^- \rightarrow H_2O + O^-$	1.200E+10	1.42E+4	1.878E+11
9	$OH + HO^-_2 \rightarrow HO_2 + OH^-$	7.500E+9	1.42E+4	1.174E+11
10	$OH + O^- \rightarrow HO^-_2$	1.800E+10	1.42E+4	2.817E+11
11	$O^- + H_2O \rightarrow OH + OH^-$	1.700E+6	Na	1.500E+8
12	$E^- + E^- \rightarrow H_2 + OH^- + OH^-$	5.500E+9	Na	5.500E+9
13	$E^- + H \rightarrow H_2 + OH^- - H_2O$	2.400E+10	1.40E+4	3.613E+11
14	$E^- + O^-_2 \rightarrow HO^-_2 + OH^- - H_2O$	1.300E+10	1.42E+4	2.034E+11
15	$E^- + HO_2 \rightarrow HO^-_2$	2.000E+10	1.42E+4	3.130E+11
16	$E^- + H_2O_2 \rightarrow OH + OH^-$	1.200E+10	1.56E+4	2.463E+11
17	$E^- + O_2 \rightarrow O^-_2$	1.900E+10	1.36E+4	2.647E+11
18	$E^- + H^+ \rightarrow H$	2.300E+10	1.26E+4	2.640E+11
19	$E^- + H_2O \rightarrow H + OH^-$	1.900E+1	1.42E+4	2.973E+2

Diffusion of Radical Species

From Turner, J. E. *Atoms, Radiation, and Radiation Protection*.

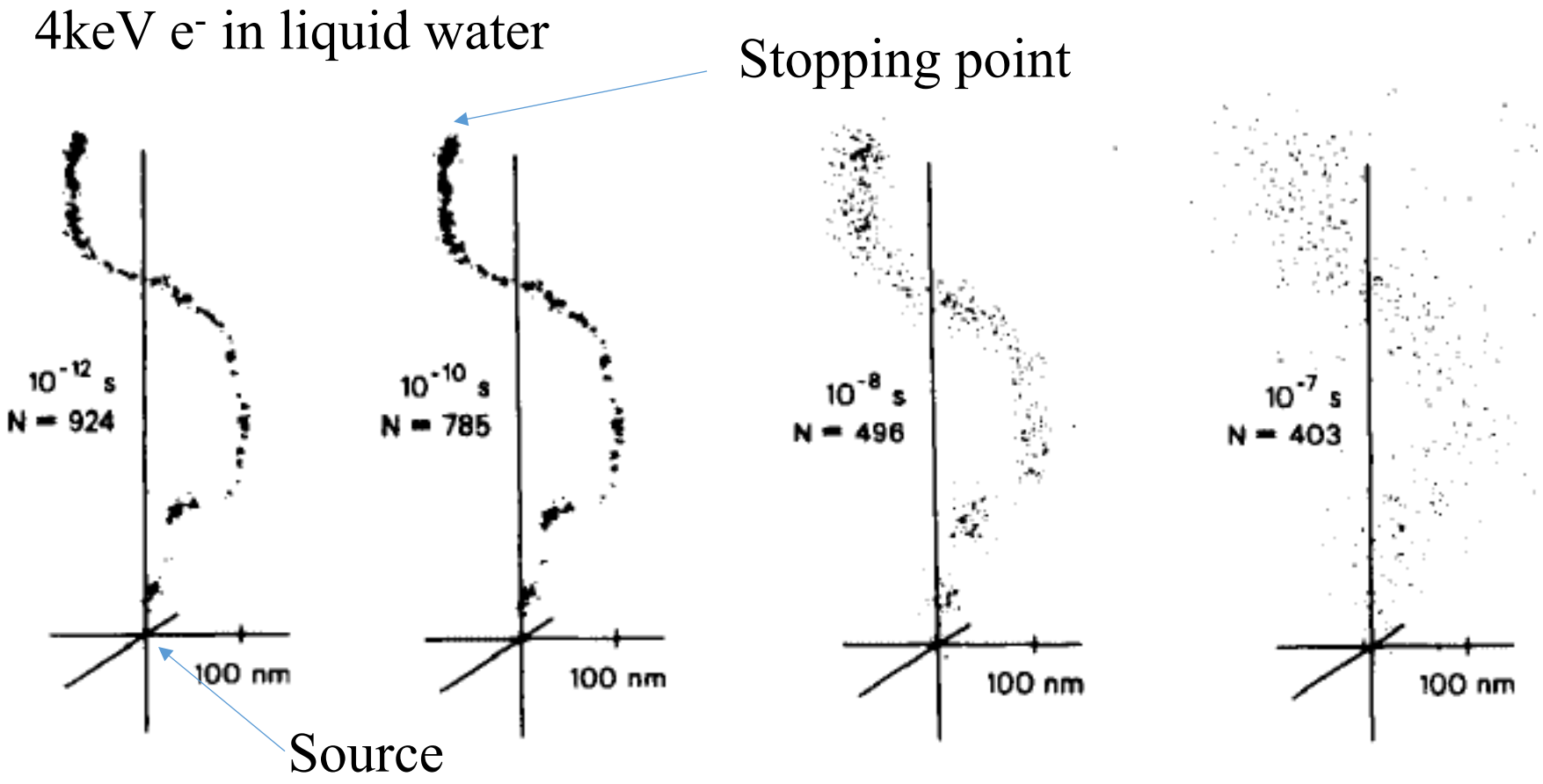
Table 13.2 Diffusion Constants D and Reaction Radii R for Reactive Species

Species	D (10^{-5} cm^2 s^{-1})	R (Å)
OH	2	2.4
e^-_{aq}	5	2.1
H_3O^+	8	0.30
H	8	0.42

$$\frac{\lambda^2}{6\tau} = D.$$

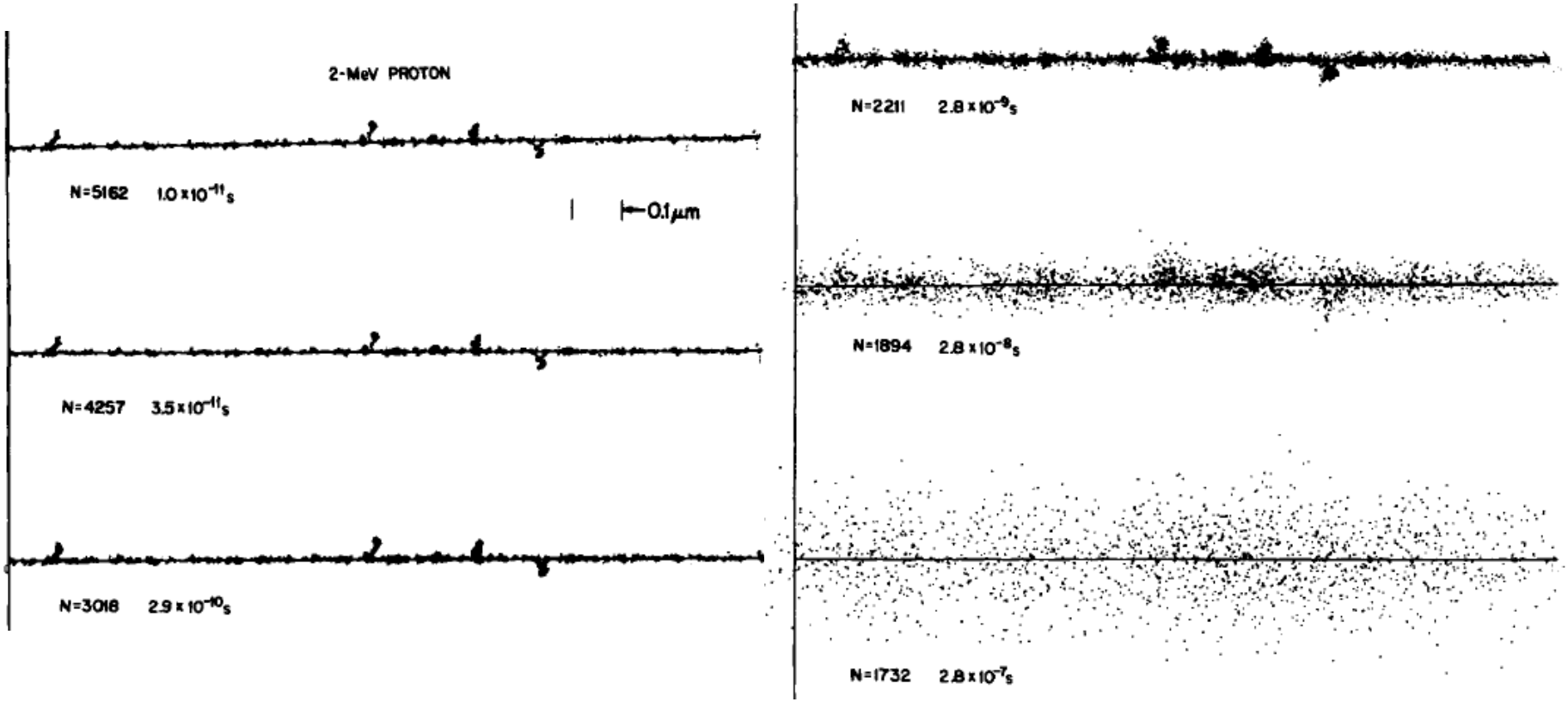
As species diffuse, reactions become less frequent

Charged Particle Tracks (e^-)



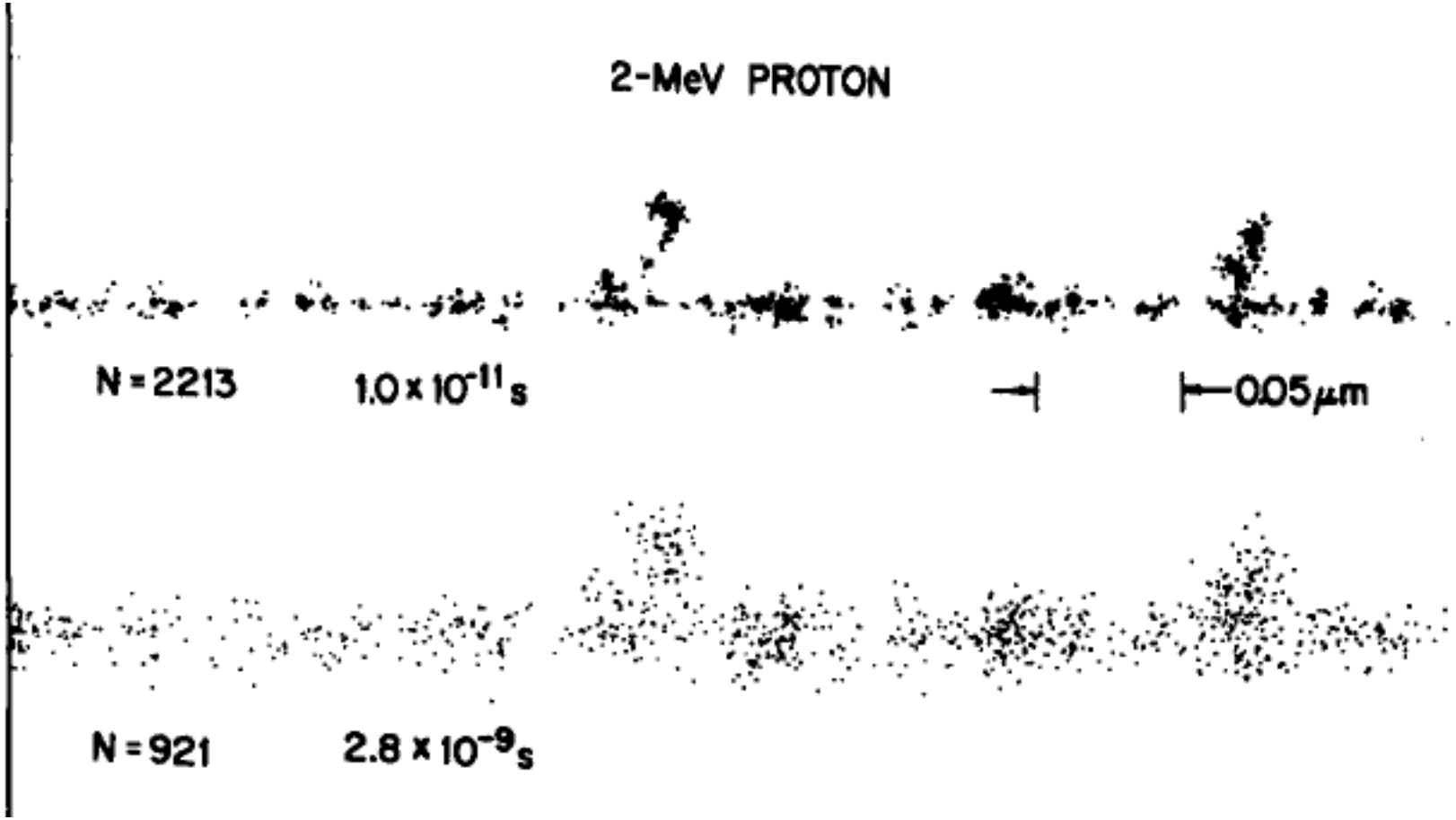
Courtesy of Oak Ridge National Laboratory, U.S. Dept. of Energy.

Charged Particle Tracks (p^+)



Courtesy of Oak Ridge National Laboratory, U.S. Dept. of Energy.

Charged Particle Tracks (p^+), Closeup



Courtesy of Oak Ridge National Laboratory, U.S. Dept. of Energy.

G-Values

- Number of each species present at time t, per 100eV of absorbed energy

Table 13.3 *G* Values (Number per 100 eV) for Various Species in Water at 0.28 μs for Electrons at Several Energies

	Electron Energy (eV)							
Species	**100**	**200**	**500**	**750**	**1000**	**5000**	**10,000**	**20,000**
OH	1.17	0.72	0.46	0.39	0.39	0.74	1.05	1.10
H_3O^+	4.97	5.01	4.88	4.97	4.86	5.03	5.19	5.13
e^-_{aq}	1.87	1.44	0.82	0.71	0.62	0.89	1.18	1.13
H	2.52	2.12	1.96	1.91	1.96	1.93	1.90	1.99
H_2	0.74	0.86	0.99	0.95	0.93	0.84	0.81	0.80
H_2O_2	1.84	2.04	2.04	2.00	1.97	1.86	1.81	1.80
Fe^{3+}	17.9	15.5	12.7	12.3	12.6	12.9	13.9	14.1

G-Values – p^+, Alphas

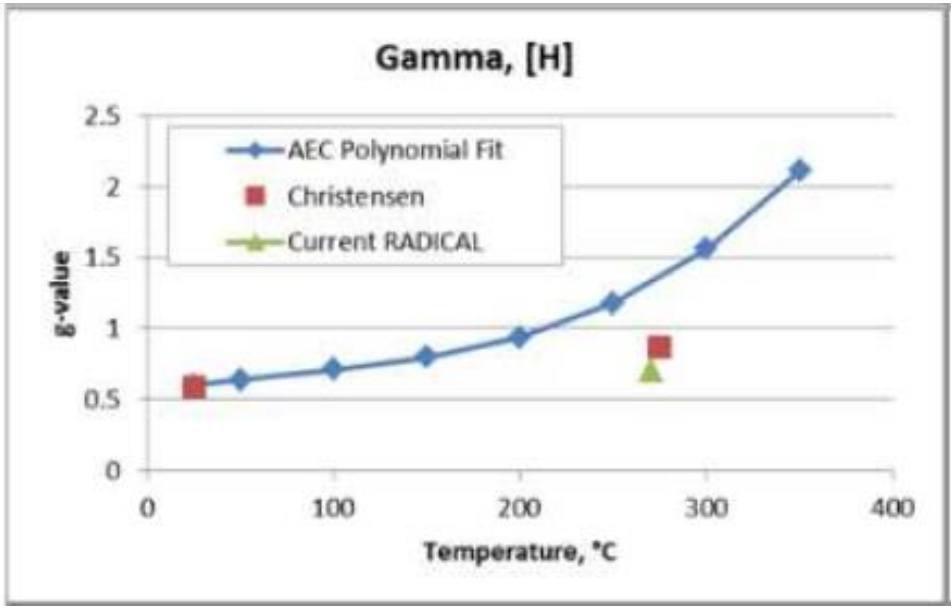
Table 13.4 *G* Values (Number per 100 eV) for Various Species at 10^{-7} s for Protons of Several Energies and for Alpha Particles of the Same Velocities

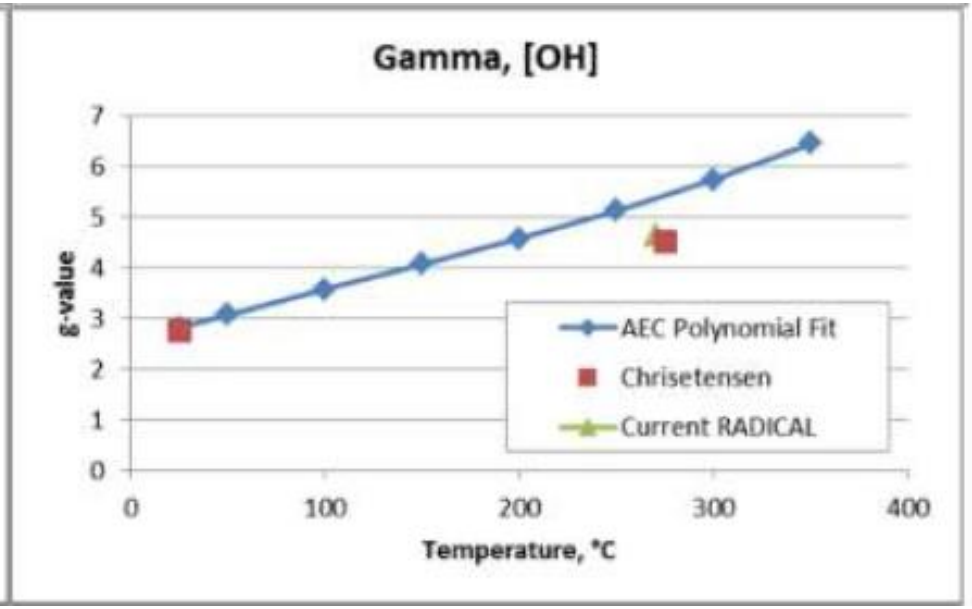
Species	Protons (MeV)				Alpha Particles (MeV)			
Type	1	2	5	10	4	8	20	40
OH	1.05	1.44	2.00	2.49	0.35	0.66	1.15	1.54
H_3O^+	3.53	3.70	3.90	4.11	3.29	3.41	3.55	3.70
e^-_{aq}	0.19	0.40	0.83	1.19	0.02	0.08	0.25	0.46
H	1.37	1.53	1.66	1.81	0.79	1.03	1.33	1.57
H_2	1.22	1.13	1.02	0.93	1.41	1.32	1.19	1.10
H_2O_2	1.48	1.37	1.27	1.18	1.64	1.54	1.41	1.33
Fe^{3+}	8.69	9.97	12.01	13.86	6.07	7.06	8.72	10.31

G-Values vs. Temperature

J. Jarvis, R. G. Ballinger, "RADICAL 1.9 Theory Manual," 2013

- What could be responsible for this increase in G-values vs. temperature?



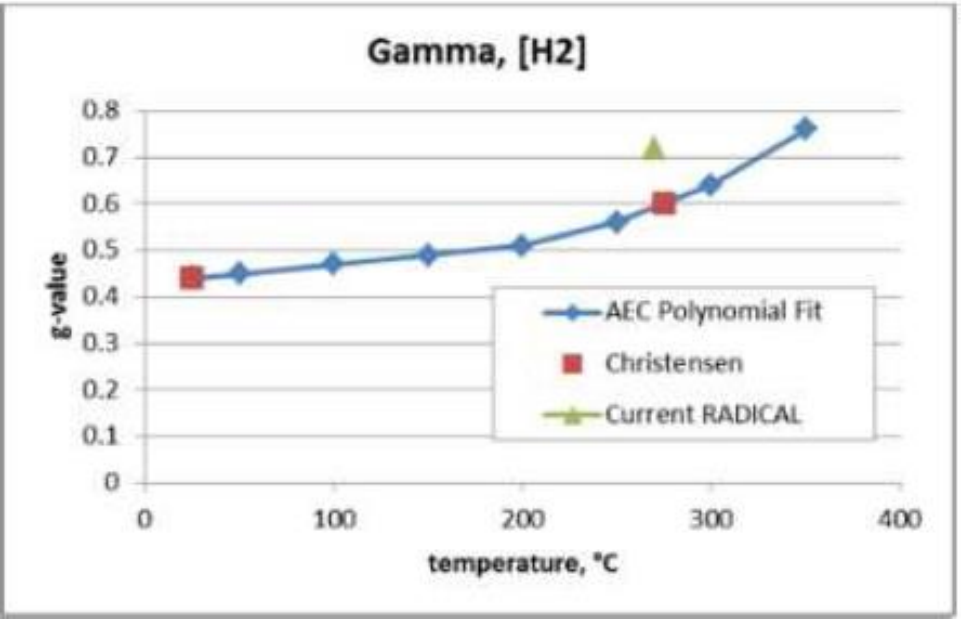


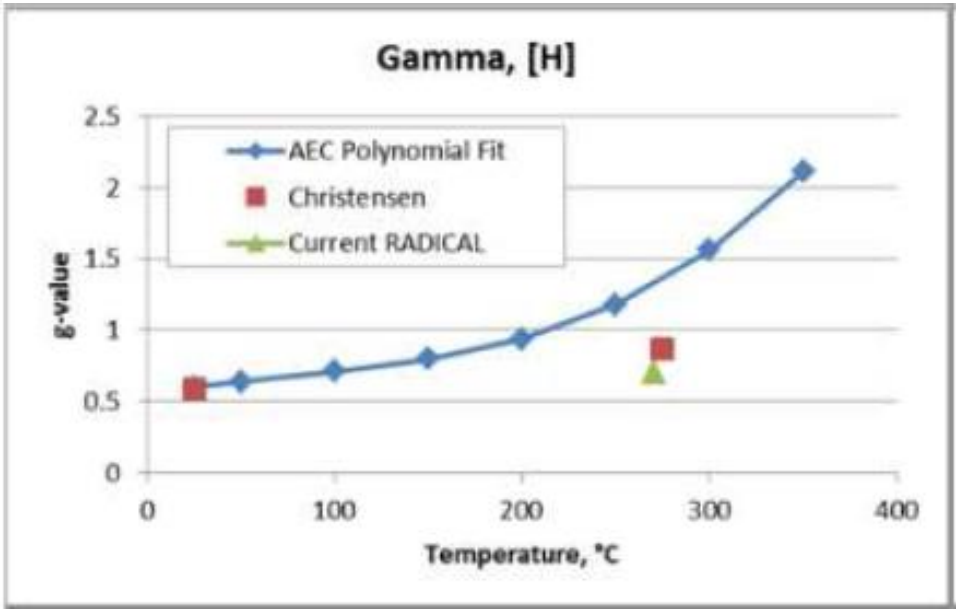
Courtesy of Ronald Ballinger. Used with permission.

G-Values vs. Temperature

J. Jarvis, R. G. Ballinger, "RADICAL 1.9 Theory Manual," 2013

- What could be responsible for this curve shape? What else scales like this with T?

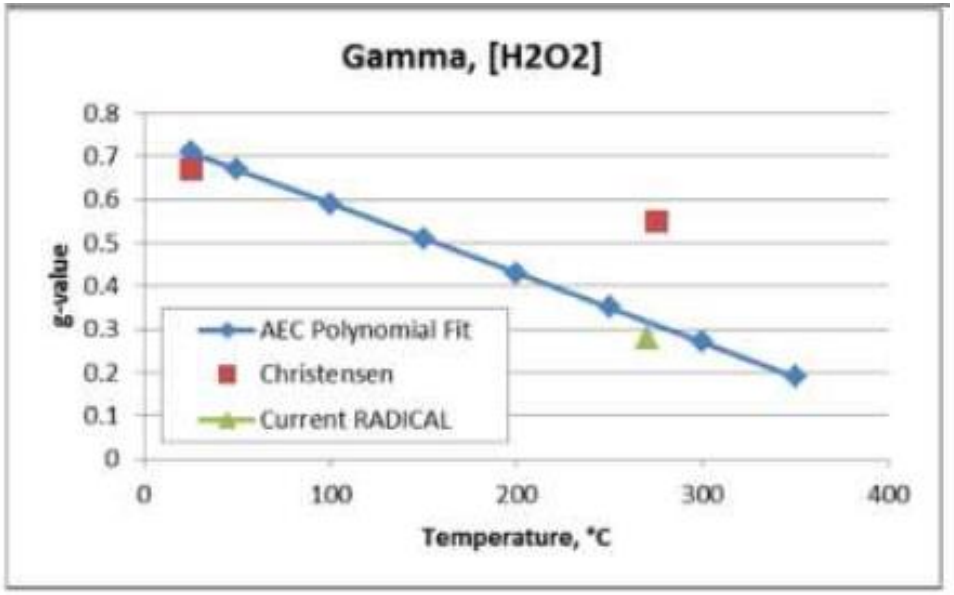


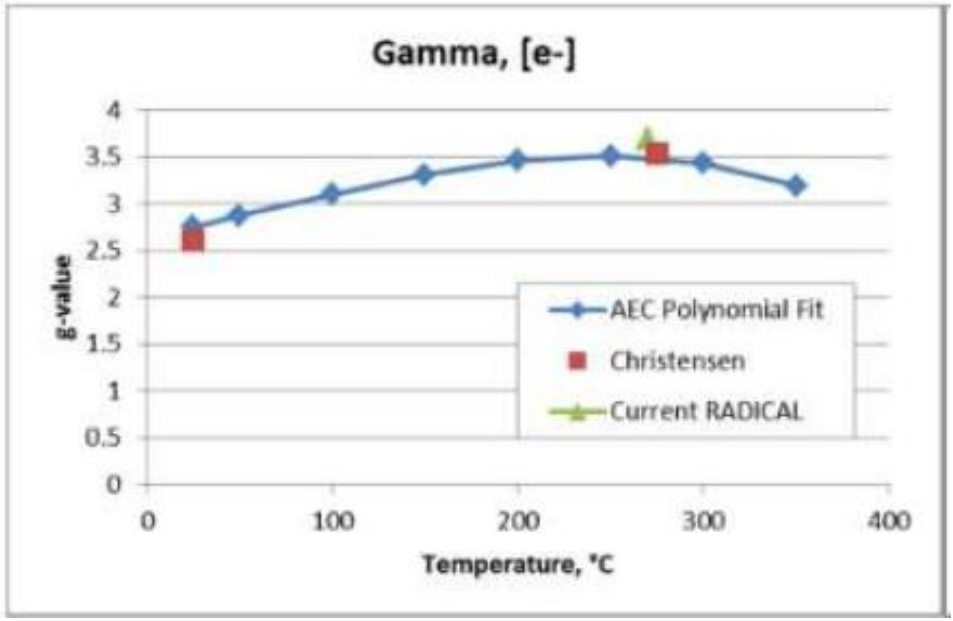


G-Values vs. Temperature

J. Jarvis, R. G. Ballinger, "RADICAL 1.9 Theory Manual," 2013

- What could be responsible for this behavior in G-values vs. temperature?



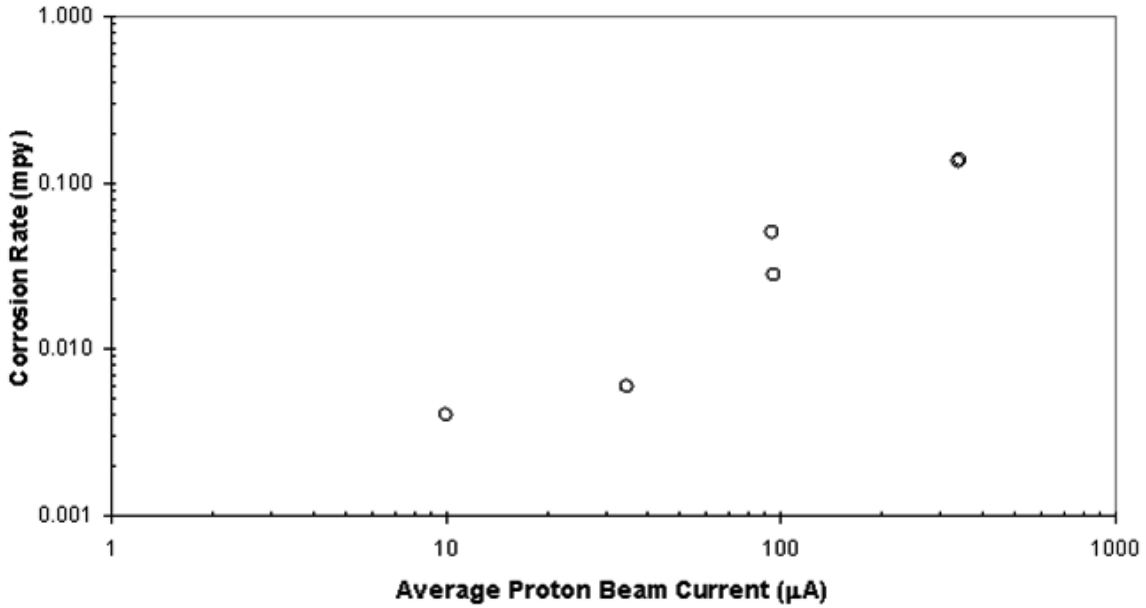


Courtesy of Ronald Ballinger. Used with permission.

An Aside – Reactor Radiolysis

G. T. Chandler et al. "**Corrosion Testing in Support of the Accelerator Production of Tritium Program.**" http://sti.srs.gov/fulltext/ms2000781/ms2000781.html

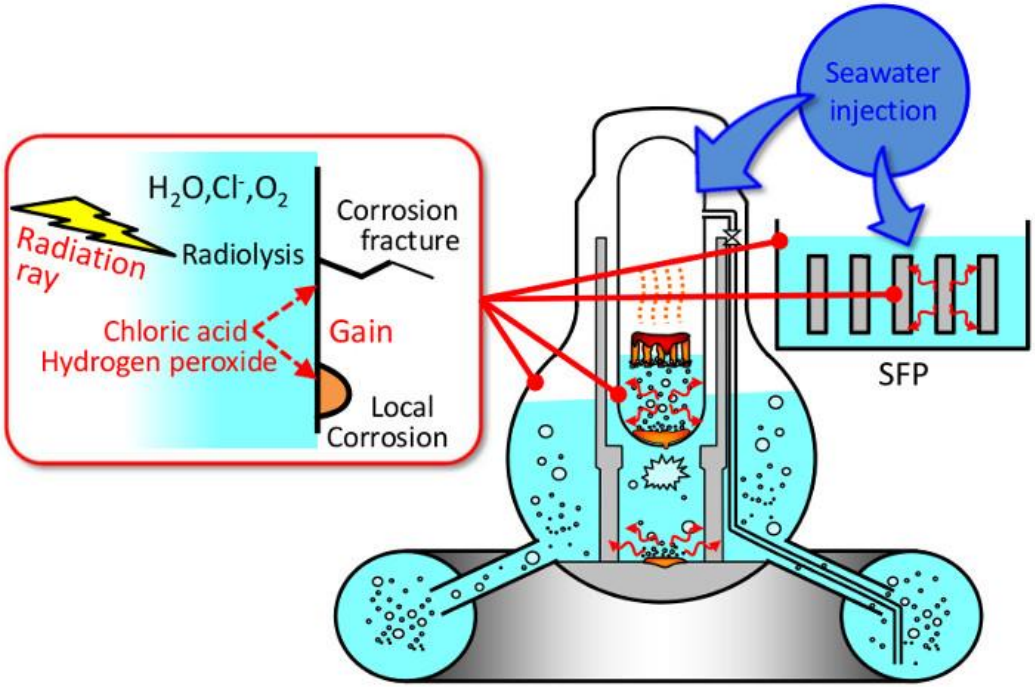
A constant neutron/gamma flux can greatly change local water chemistry near materials



Reactor Radiolysis Even After Shutdown

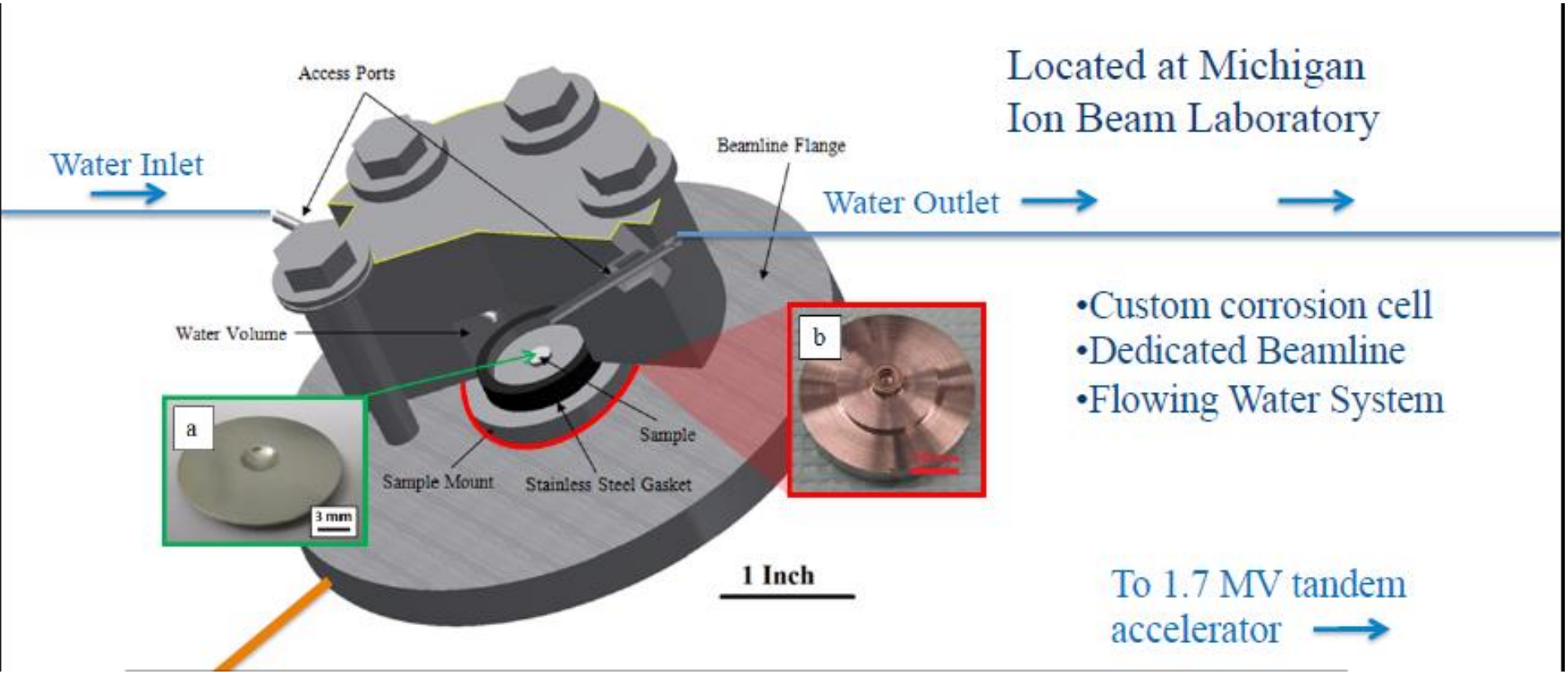
https://www.jaea.go.jp/english/04/ntokai/fukushima/fukushima_04.html

- VERY relevant to Fukushima reactor
- Flooded with seawater, introduces Cl^-



Studying Radiolysis Corrosion

P. Wang, G. S. Was. Corrosion and Hydrogen Pick-up of Zircaloy-4 in Simulated PWR Environment with In-situ Proton Irradiation." CASL Telecon, Aug. 13, 2014.



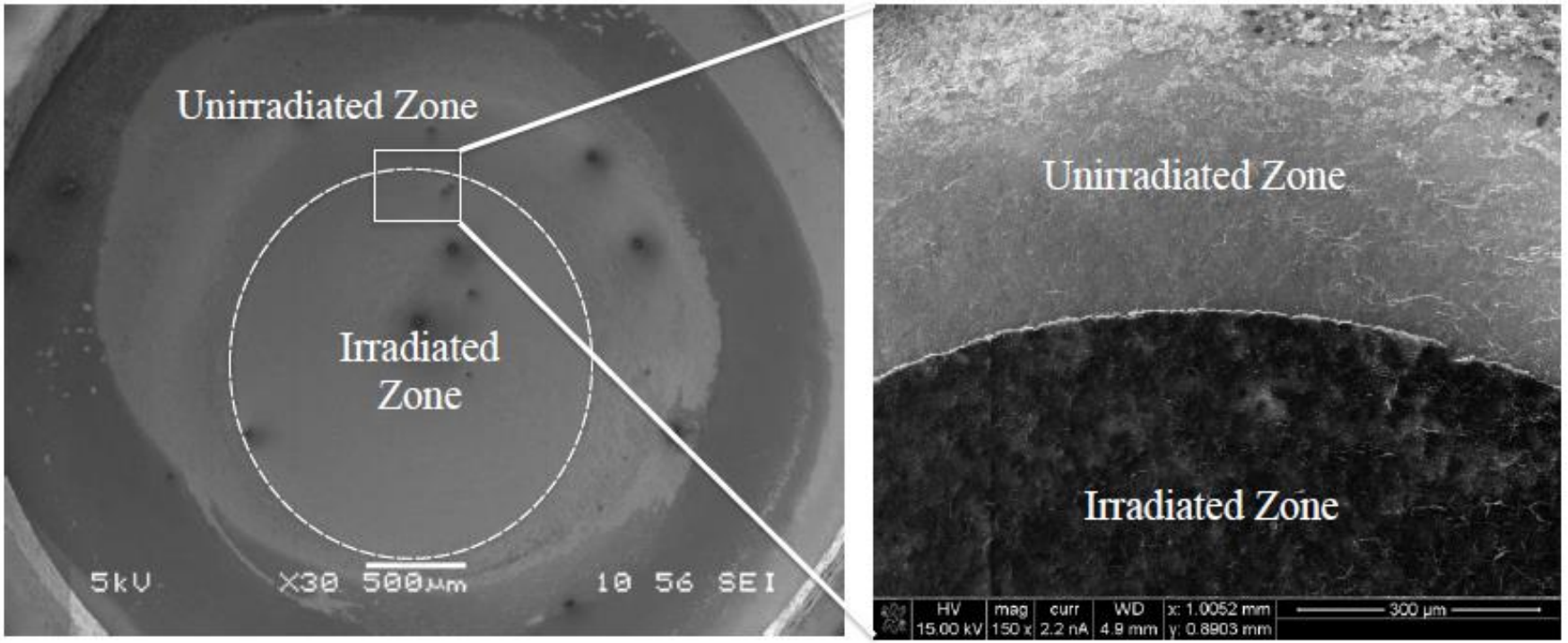
Courtesy of Peng Wang. Used with permission.

Studying Radiolysis Corrosion

P. Wang, G. S. Was. Corrosion and Hydrogen Pick-up of Zircaloy-4 in Simulated PWR Environment with In-situ Proton Irradiation." CASL Telecon, Aug. 13, 2014.

Irradiated Zr-4 Sample IR24

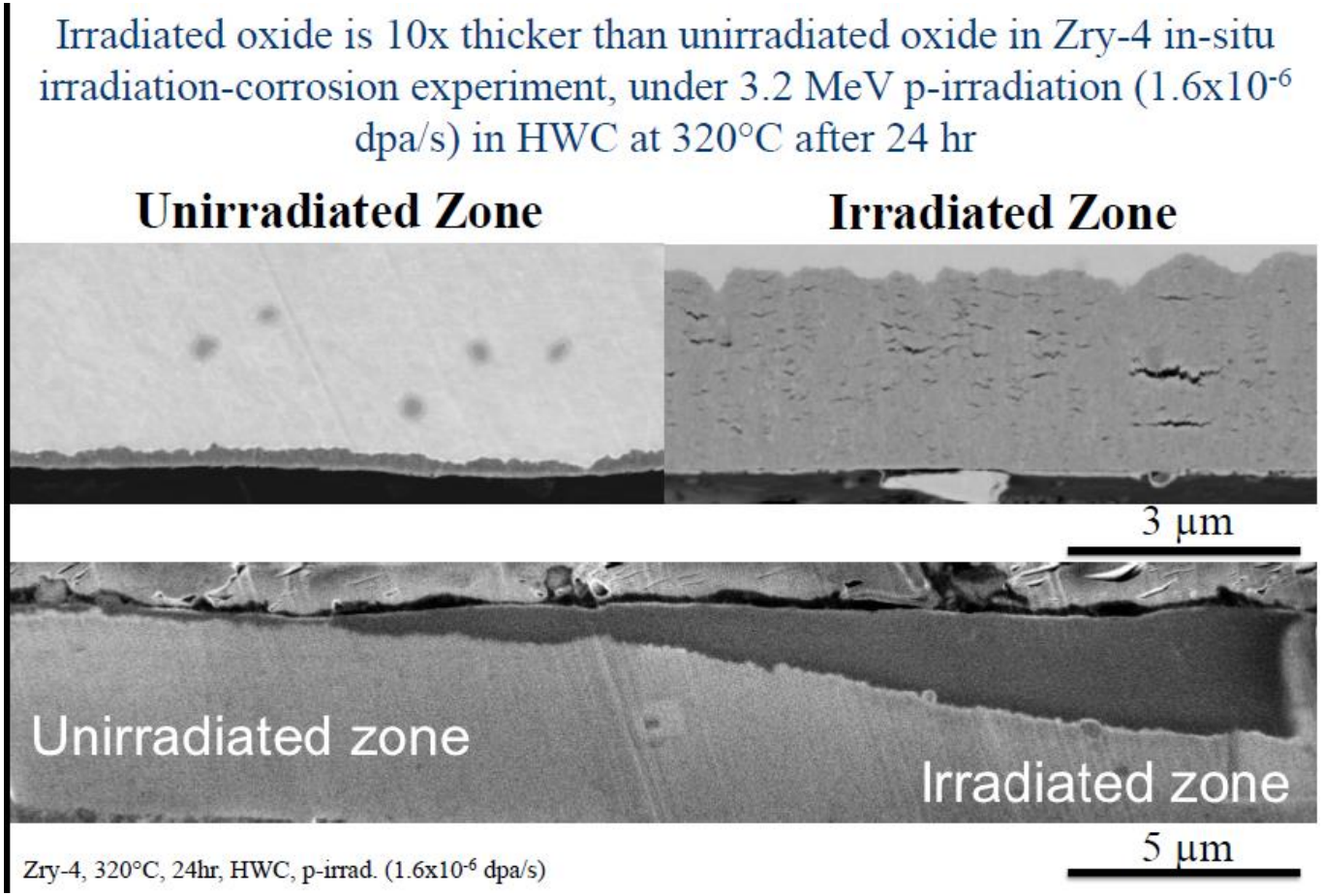
(3ppm H_2, 320°C, 24hr, DI Water, 1.6 x 10^{-6} dpa/s)



Courtesy of Peng Wang. Used with permission.

Irradiation Accelerated Corrosion

P. Wang, G. S. Was. Corrosion and Hydrogen Pick-up of Zircaloy-4 in Simulated PWR Environment with In-situ Proton Irradiation." CASL Telecon, Aug. 13, 2014.

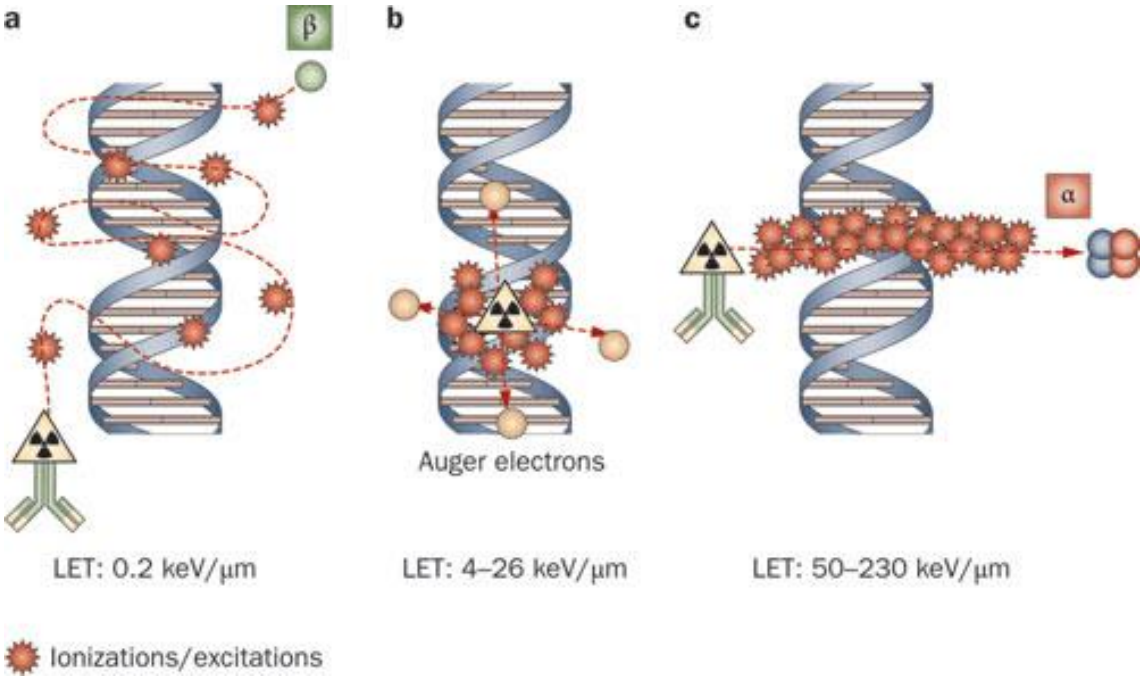


Courtesy of Peng Wang. Used with permission.

Biological Effects

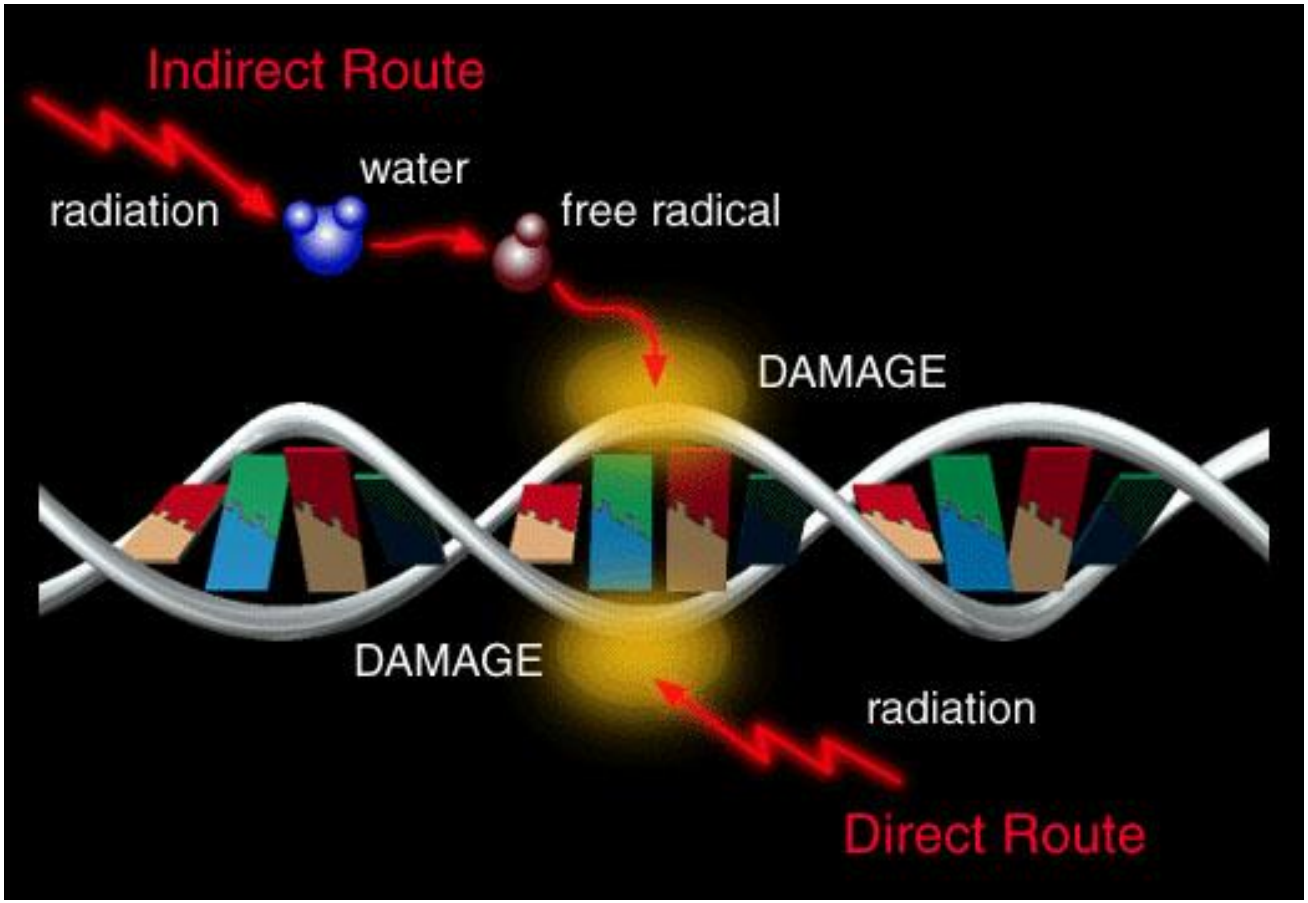
Pouget, J-P., et al. "Clinical radioimmunotherapy—the role of radiobiology."
***Nature Reviews Clinical Oncology* 8 (Dec 2011): 720-734.**

- Low doses, short times: It's all about the DNA



DNA Damage – Direct & Indirect

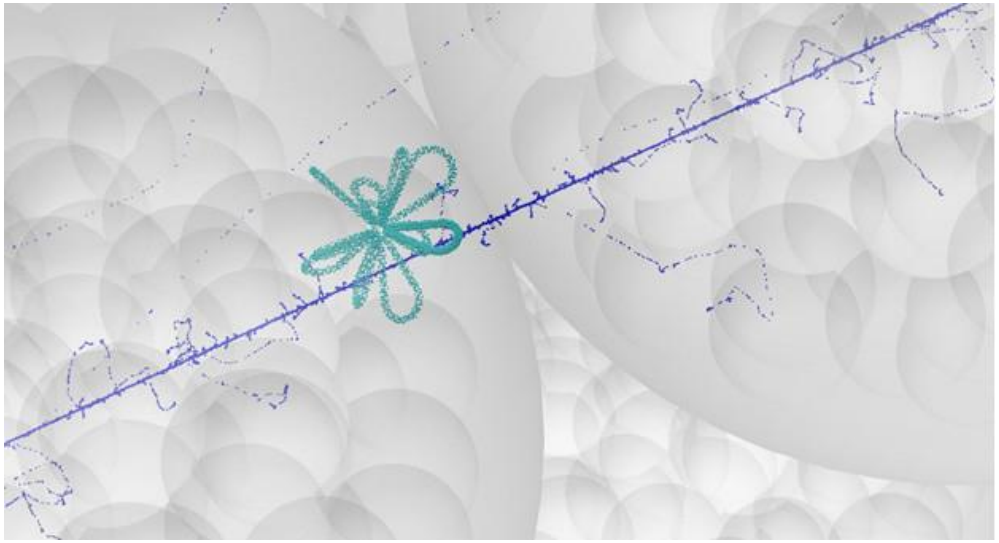
http://www.windows2universe.org/earth/Life/cell_radiation_damage.html



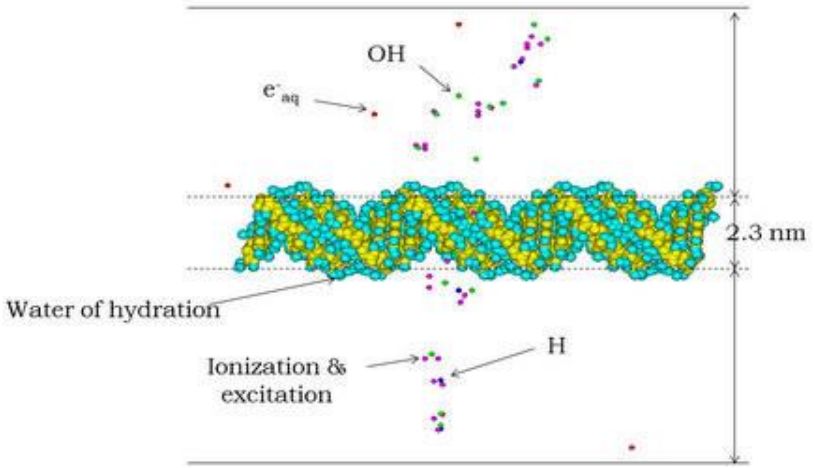
Biological Effects – DNA

http://ki.se/en/onkpat/hooshang-nikjoos-group

DNA modification can cause mutations…



A 10 MeV/u carbon ion track crossing a model of human cell nucleus interacting with chromatin loops in chromosomal domains



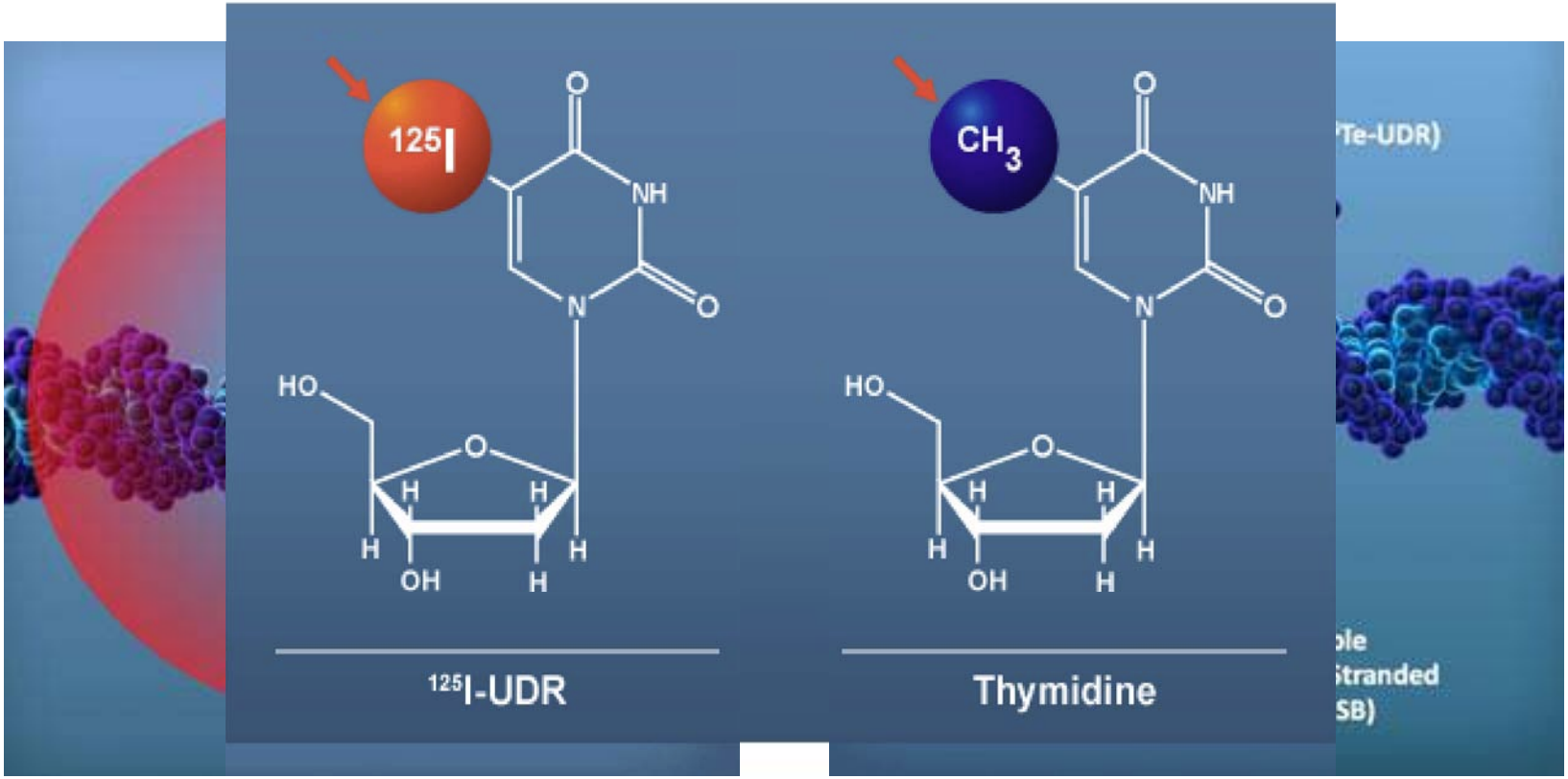
DNA damage by a track of 70keV electron intersecting a DNA segment (only part of the track for direct and radical reactions are shown)

Biological Effects – DNA

Source: Oncotherix

https://web.archive.org/web/20150126015058/http://www.oncotherix.com/incellrt.html

… but it can also be used to kill tumor cells!



Let's Talk Pseudoscience

- Question: Do cell phones cause cancer?
- Answer in the form of a question: Is the radiation ionizing or able to induce electronic excitations?
- Let's read: http://www.globalresearch.ca/44-reasons-to-believe-cell-phones-can-cause-cancer/5420118

Radiofrequency Photons

3kHz to 300GHz (mm to km wavelengths)

CAN be used to cook, induce pain:

Public domain image, from U.S. Department of Defense.

The Active Denial System, an RF generator designed to induce burning sensations on the skin of soldiers

Sources of Human Data

Normal exposure

- Radium dial workers
- Uranium miners
- Radon breathers, medical diagnostics

Accidents

- Atomic bombs
- Nearby nuclear accidents, criticality events

Radium Dial Painters

Ra is a bone-seeking elements (same column as Ca in the periodic table)

Data from bones after death established the first occupational guide, around 0.6mGy/wk

Radon in Smokers vs. Non-Smokers

Turner, J. E. *Atoms, Radiation, and Radiation Protection*. Wiley-VCH, 2007. p. 417

Table 13.5 Estimated Number of Lung-cancer Deaths in 1995 in the U.S. Attributable to Indoor Residential Radon*

Population	Lung-cancer Deaths	Number of Deaths Attributable to Indoor Rn	
		Model 1	Model 2
Total Persons	157,400	21,800	15,400
Ever Smokers	146,400	18,900	13,300
Never Smokers	11,000	2,900	2,100
Male	95,400	12,500	8,800
Ever Smokers	90,600	11,300	7,900
Never Smokers	4,800	1,200	900
Female	62,000	9,300	6,600
Ever Smokers	55,800	7,600	5,400
Never Smokers	6,200	1,700	1,200

Distinguishing Biological Effects

Short-term effects

- Acute radiation sickness
- Due to rapid cell death over short times

Long-term effects

- Called “delayed somatic effects”
- Cancer, mutations, birth defects

Acute Gamma Radiation Syndrome

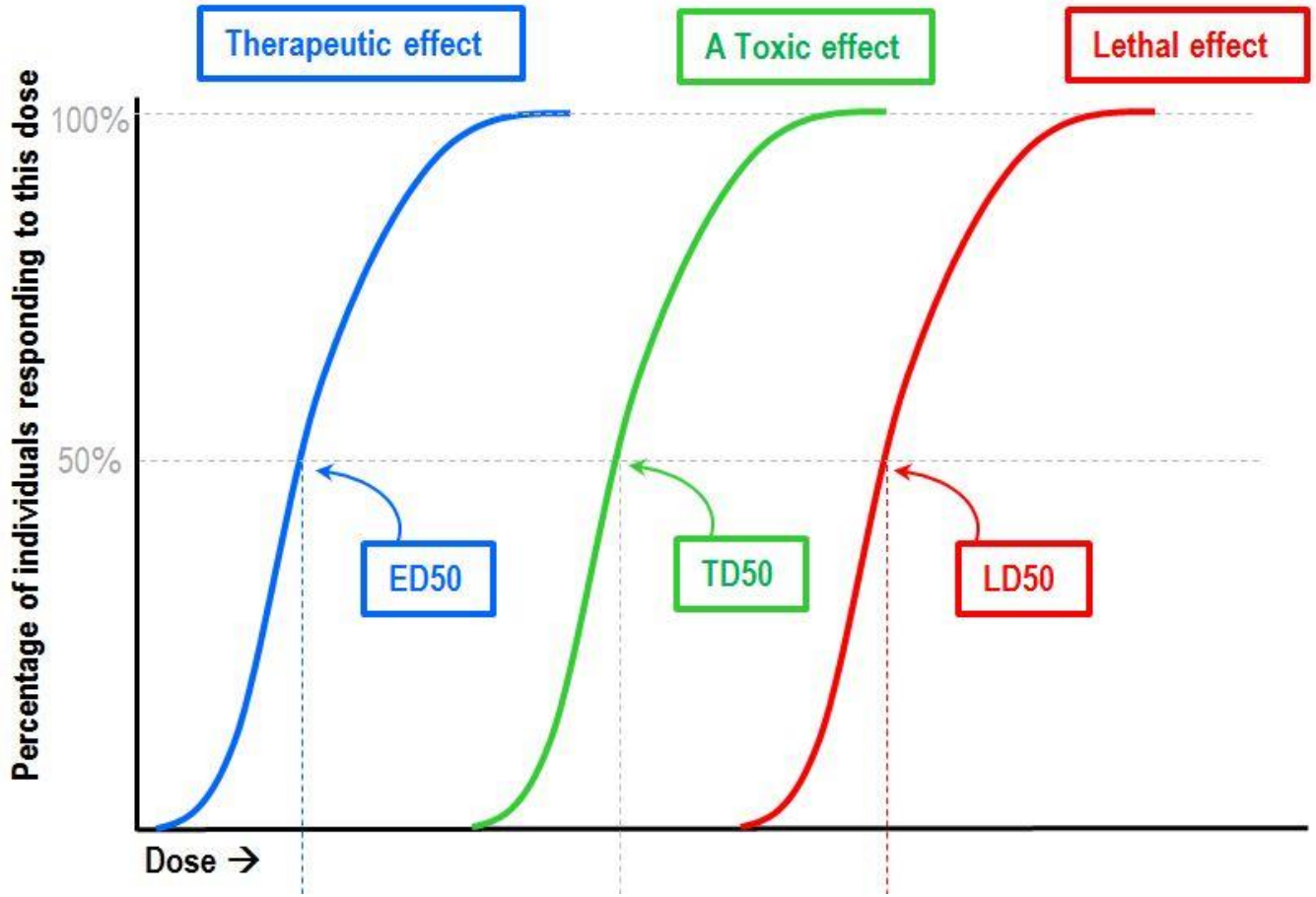
Turner, J. E. *Atoms, Radiation, and Radiation Protection*. Wiley-VCH, 2007. p. 421

Dose (Gy)	Symptoms	Remarks
0–0.25	None	No clinically significant effects.
0.25–1	Mostly none. A few persons may exhibit mild prodromal symptoms, such as nausea and anorexia.	Bone marrow damaged; decrease in red and white blood-cell counts and platelet count. Lymph nodes and spleen injured; lymphocyte count decreases.
1–3	Mild to severe nausea, malaise, anorexia, infection.	Hematologic damage more severe. Recovery probable, though not assured.
3–6	Severe effects as above, plus hemorrhaging, infection, diarrhea, epilation, temporary sterility.	Fatalities will occur in the range 3.5 Gy without treatment.
More than 6	Above symptoms plus impairment of central nervous system; incapacitation at doses above ~10 Gy.	Death expected.

Typical LD50 for acute radiation poisoning

An Aside: The LD50

http://www.derangedphysiology.com/main/core-topics-intensive-care/critical-care-pharmacology/Chapter%202.1.7/median-doses-ld50-ed50-and-td50



Courtesy of Alex Yartsev. Used with permission.

Four Phases of Acute Radiation

- **Prodromal phase**
  - Initial symptoms of exposure, 1-3 days after or sooner
- **Latent phase**
  - Apparent recovery from prodromal symptoms, but lab tests show serious changes in blood & lymph
- **Manifest illness phase**
  - Specific signs of each syndrome appear depending on the dose
- **Final phase**
  - Recovery or death, takes months to years

Acute Radiation Symptoms

Garau, M. M. et al. *Rep. Practical Oncology and Radiotherapy*, 16 no. 4 (2011):123-130

Table 1 – Signs and symptoms of prodromal phase.[4]

Signs and symptoms	Mild (1–2 Gy)	Moderate (2–4 Gy)	Severe (4–6 Gy)	Very severe (6–8 Gy)	Lethal (>8 Gy)
Vomiting					
Onset	≥2 h after exposure	1–2 h after exposure	<1 h after exposure	<30 min after exposure	<10 min after exposure
% of incidence	10–50	70–90	100	100	100
Diarrhea	None	None	Mild	Heavy	Heavy
Onset			3–8 h	1–3 h	Within min
% of incidence			<10	>10	100
Headache	Slight	Mild	Moderate	Severe	Severe
Onset			4–24 h	3–4 h	1–2 h
% of incidence			50	80	80–90
Consciousness	Unaffected	Unaffected	Unaffected	May be altered	Unconsciousnes
Onset					s/min
% of incidence					100 at >50 Gy
Body temperature	Normal	Increased	Fever	High fever	High fever
Onset		1–3 h	1–2 h	<1 h	<1 h
% of incidence		10–80	80–100	100	100

Dose correlates quite well to onset time and severity of symptoms

Acute Radiation Symptoms

Garau, M. M. et al. *Rep. Practical Oncology and Radiotherapy*, 16 no. 4 (2011):123-130

Table 2 – Signs and symptoms of latent phase.[4]

Signs and symptoms	Mild (1–2 Gy)	Moderate (2–4 Gy)	Severe (4–6 Gy)	Very severe (6–8 Gy)	Lethal (>8 Gy)
Latency period	21–35 days	18–28 days	8–18 days	≤7 days	None
Lymphocytes G/L (days 3–6)	0.8–1.5	0.5–0.8	0.3–0.5	0.1–0.3	0.0–0.1
Granulocytes G/L	>2.0	1.5–2.0	1.0–1.5	≤0.5	≤0.1
Diarrhea	None	None	Rare	Appears on days 6–9	Appears on days 4–5
Depilation	None	Moderate, beginning on day 15 or later	Moderate, beginning on day 11–21	Complete earlier than day 11	Complete earlier than day 10

Table 3 – Signs and symptoms of critical phase.[4]

Signs and symptoms	Mild (1–2 Gy)	Moderate (2–4 Gy)	Severe (4–6 Gy)	Very severe (6–8 Gy)	Lethal (>8 Gy)
Onset of symptoms	>30 days	18–28 days	8–18 days	<7 days	<3 days
Clinical manifestations	Fatigue, weakness	Fever, infections, weakness, depilation	High fever, infections, bleeding, depilation	High fever, diarrhea, vomiting, dizziness, desorientation, hypotension	High fever, diarrhea, unconsciousness
Lymphocytes G/L (days 3–6)	0.8–1.5	0.5–0.8	0.3–0.5	0.1–0.3	0.0–0.1
Platelets G/L	60–100	30–60	25–35	15–25	<20
% of incidence	10–25	25–40	40–80	60–80	80–100
Lethality	0%	0–50%	20–70%	50–100%	100%
Onset time		6–8 week	4–8 week	1–2 week	1–2 week

Acute Radiation Symptoms

Garau, M. M. et al. *Rep. Practical Oncology and Radiotherapy*, 16 no. 4 (2011):123-130

Table 4 – The time course and severity of clinical signs and symptoms.

Absorbed dose level	Prodromal phase	Latent phase	Manifest illness	Final phase
0.5–1.5 Gy	Absence of symptoms or nausea and vomiting for 1 day	1 day–several weeks	No symptoms or weakness, nausea and vomiting, temporary hair loss	Recovery
1.5–4 Gy	Nausea, vomiting, fatigue, weakness, diarrhea for up to two days	1–3 weeks	Hematopoietic syndrome (HS): leucopenia and trombocitopenia, hair loss	Recovery possible with supportive care
4–6 Gy	Nausea, vomiting, weakness, diarrhea for up to two days	<1–3 weeks	HS: bleeding, immunosuppression and sepsis, permanent hair loss	Death without supportive care
6–15 Gy	Severe nausea and vomiting, diarrhea in shorter period of time	Several days	HS + gastrointestinal syndrome: diarrhea, bleeding, fluid loss and electrolyte imbalance	Variable with supportive care
>15 Gy	Immediate severe nausea and vomiting	Non-existent	Neurovascular syndrome	Death within 48 h

Leucopenia – reduced white blood cell count
Thrombocitopenia – reduced platelet count

Depilation – hair loss
Hypotension – abnormally low blood pressure

Acute Radiation Syndromes

Garau, M. M. et al. *Rep. Practical Oncology and Radiotherapy*, 16 no. 4 (2011):123-130

- **Hematopoietic**
  - Stem cell creation/division system breaks down, blood cell losses
- **Gastrointestinal**
  - Stem cells in villi fail to reproduce, stopping nutritional uptake
- **Neurovascular (cerebrovascular)**
  - Straight up blasting of endothelial cells, edema (cell fluid leakage) from blood vessels, associated drop in intracranial pressure

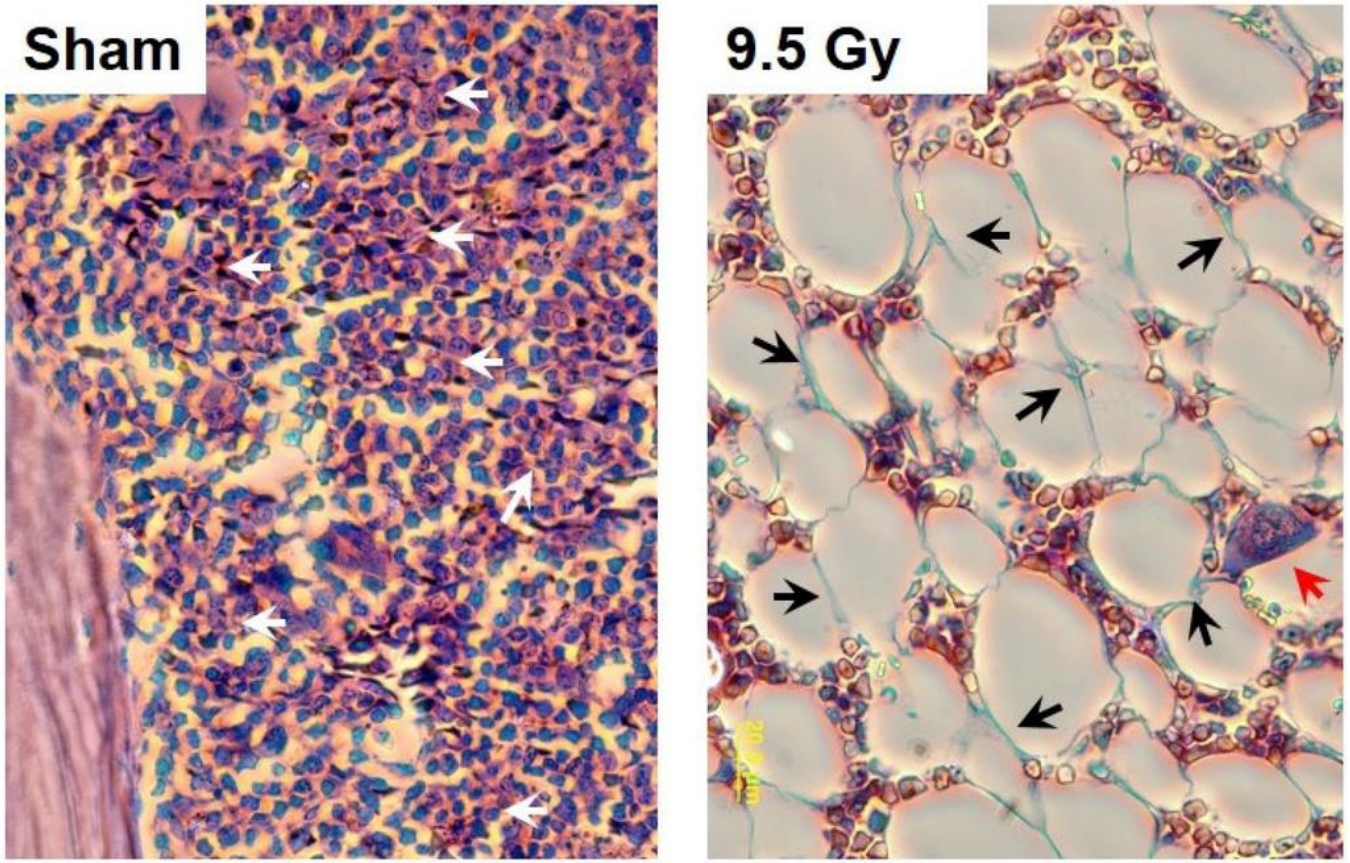
Acute Radiation – Hematopoietic

Garau, M. M. et al. *Rep. Practical Oncology and Radiotherapy*, 16 no. 4 (2011):123-130

- 0.95Gy reduces stem cell count to 37% original levels
  - Surviving cells can redivide quickly to give almost no drop in functionality!
- Hypoplasia/aplasia – Destruction of bone marrow, which makes blood cells (normally full of stem/differentiating cells)
- Decreased white blood cell count (leucopenia)
  - Sudden susceptibility to infections which normally get fought off
- Lymphocytopenia – Decreased specific white blood cell counts
  - T-lymphocytes - Activate cytotoxic cells, "helper" cells, alarm sounders
    - Destruction mimics the symptoms of HIV/AIDS
  - B-lymphocites – "memory" cells that warn the body of pathogens previously seen
    - Destruction mimics immunosupressors
  - Natural killer (NK) lymphocites – Destroy viruses, tumors, fast immune response without T-cell activation

Acute Radiation – Hematopoietic

N. I. Gorbunov, P. Sharma. "Protracted Oxidative Alterations in the Mechanism of Hematopoietic Acute Radiation Syndrome." *Antioxidants*, 4(1):134 (2015).



Mouse bone marrow tissue after 9.5Gy radiation exposure

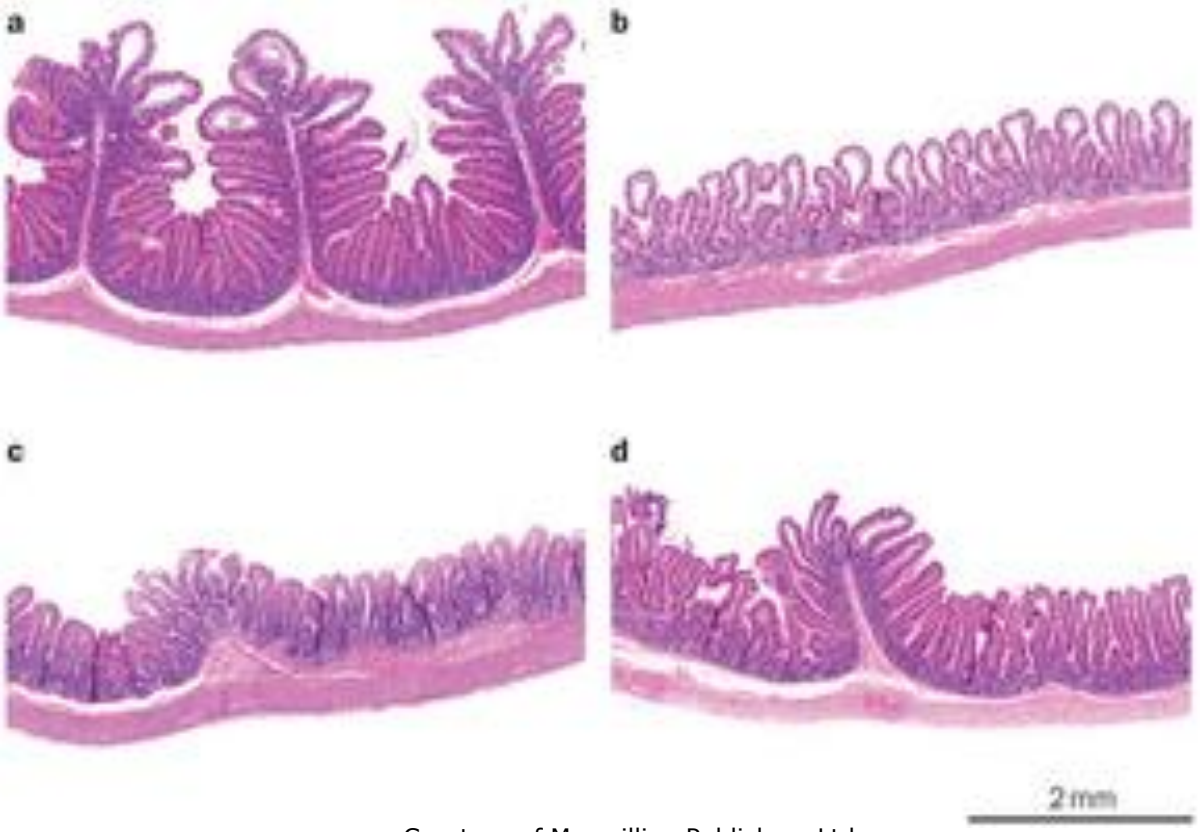
Acute Radiation – Gastrointestinal

Hauer-Jensen, M., et al. "Radiation enteropathy—pathogenesis, treatment and prevention."
***Nat. Rev. Gastroenterol. Hepatol.*, 11:470 (2014).**

- Lack of replacement stem/proliferating cells in the villi, because damaged cells die in mitosis (susceptible stage)
- 7-10 days later, intestinal mucosa disappears (abrasion), causing watery diarrhea, dehydration, electrolyte loss, GI bleeding perforation
- Breakdown of mucus layer, normally an immune component, lets bacteria into the bloodstream (inducing sepsis)
- Works with hematopoietic syndrome to encourage opportunistic infections

Acute Radiation – Gastrointestinal

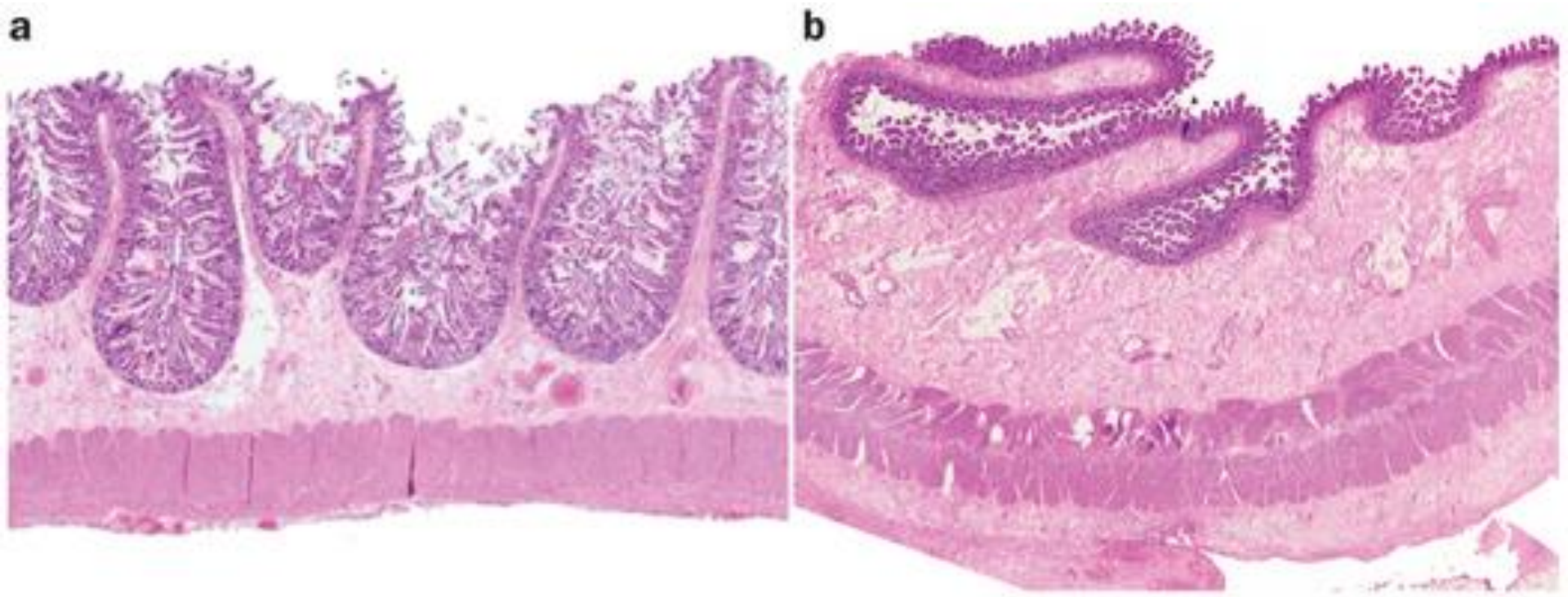
Hauer-Jensen, M., et al. "Radiation enteropathy—pathogenesis, treatment and prevention."
***Nat. Rev. Gastroenterol. Hepatol.*, 11:470 (2014).**



Proximal jejunum from a | unirradiated Rhesus macaque and b–d | Rhesus macaque 4, 7 and 12 days after exposure to single-dose irradiation.

Acute Radiation – Gastrointestinal

Hauer-Jensen, M., et al. "Radiation enteropathy—pathogenesis, treatment and prevention."
***Nat. Rev. Gastroenterol. Hepatol.*, 11:470 (2014).**



Courtesy of Macmillian Publishers Ltd.

a | A healthy intestine and b | intestine from a woman with severe delayed radiation enteropathy; note atrophic mucosa and severe fibrosis in the submucosa and subserosa. Original magnification of both images 0.5x.

Acute Radiation – Neurovascular

Garau, M. M. et al. *Rep. Practical Oncology and Radiotherapy*, 16 no. 4 (2011):123-130

- Mass cell death occurs, affects even non-dividing neurons and endothelial cells (which line blood vessels)
- Massive cell leakage (edema), subsequent drop in blood pressure (little leaks literally everywhere)
- Little/No prodromal or latent phases, as effects are instantaneous

Why the Skin Lesions?

Garau, M. M. et al. *Rep. Practical Oncology and Radiotherapy*, 16 no. 4 (2011):123-130

- Mature skin cells live about three weeks
- Radiation kills basal stem cells, none differentiate into skin cells
- "Moist desquamation" occurs, with blisters & ulcers

Why Always the Vomiting?

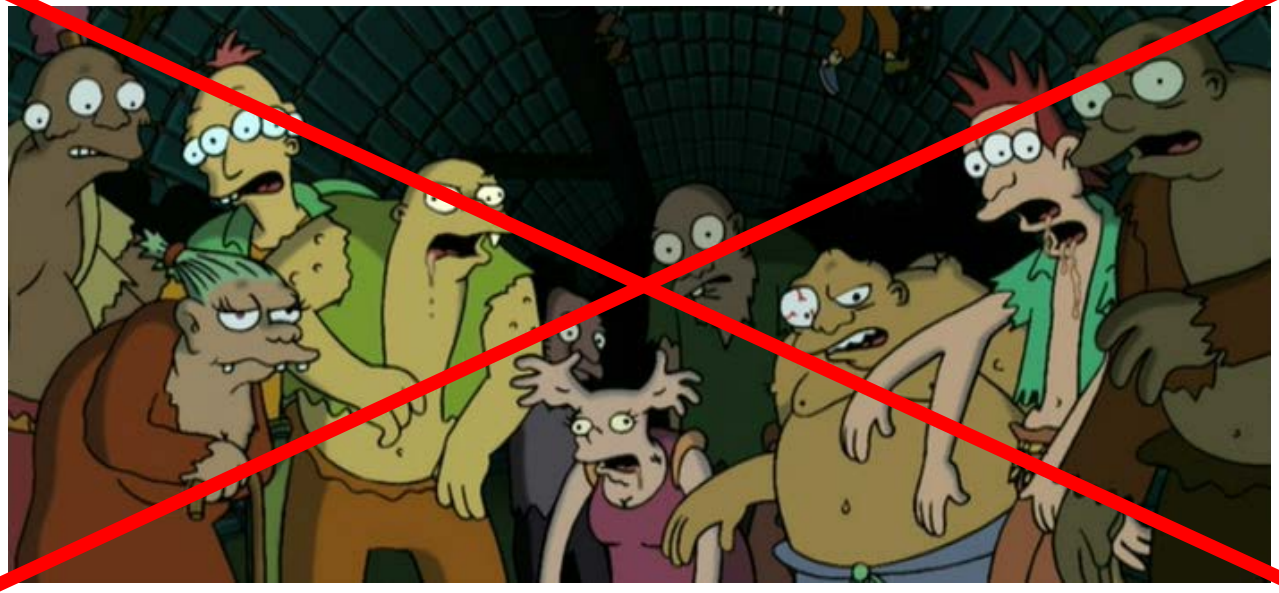
Garau, M. M. et al. *Rep. Practical Oncology and Radiotherapy*, 16 no. 4 (2011):123-130

- We don't really know yet!
- Hypothesis: intestinal cells excrete serotonine, which stimulates the medullary vomiting center, upon irradiation
- Dose correlates inversely with time to vomiting above 1.5Gy

Long Term Effects

http://www.playbuzz.com/tesssb10/futurama-quiz

1. Increased cancer risk
2. Increased teratogenic (birth defect) risk



Statistics on Long Term Effects

ICRP Publication 99, p. 27

- VERY difficult to study/detect increased risk for low doses

Table 2.4. Statistical power calculations for a hypothetical study in which baseline cancer risk, for an (unspecified) subset of cancer sites, is known to be 10%, and the unknown radiation-related excess risk is 10% at 1 Gy and proportional to dose between 0 and 1 Gy

Radiation dose	Excess risk	Total risk	Standard deviation of the estimated excess risk under the null and alternative hypotheses		Population size N needed for 80% power to detect the excess risk at the 5% significance level
1 Gy	10%	20%	$0.316/N^{1/2}$	$0.447/N^{1/2}$	80
100 mGy	1%	11%	$0.316/N^{1/2}$	$0.332/N^{1/2}$	6390
10 mGy	0.1%	10.1%	$0.316/N^{1/2}$	$0.318/N^{1/2}$	620,000
1 mGy	0.01%	10.01%	$0.316/N^{1/2}$	$0.316/N^{1/2}$	61.8 million

Sources of Data on Long Term Effects

ICRP Publication 99, p. 31

Atomic bomb survivor data cancer risk

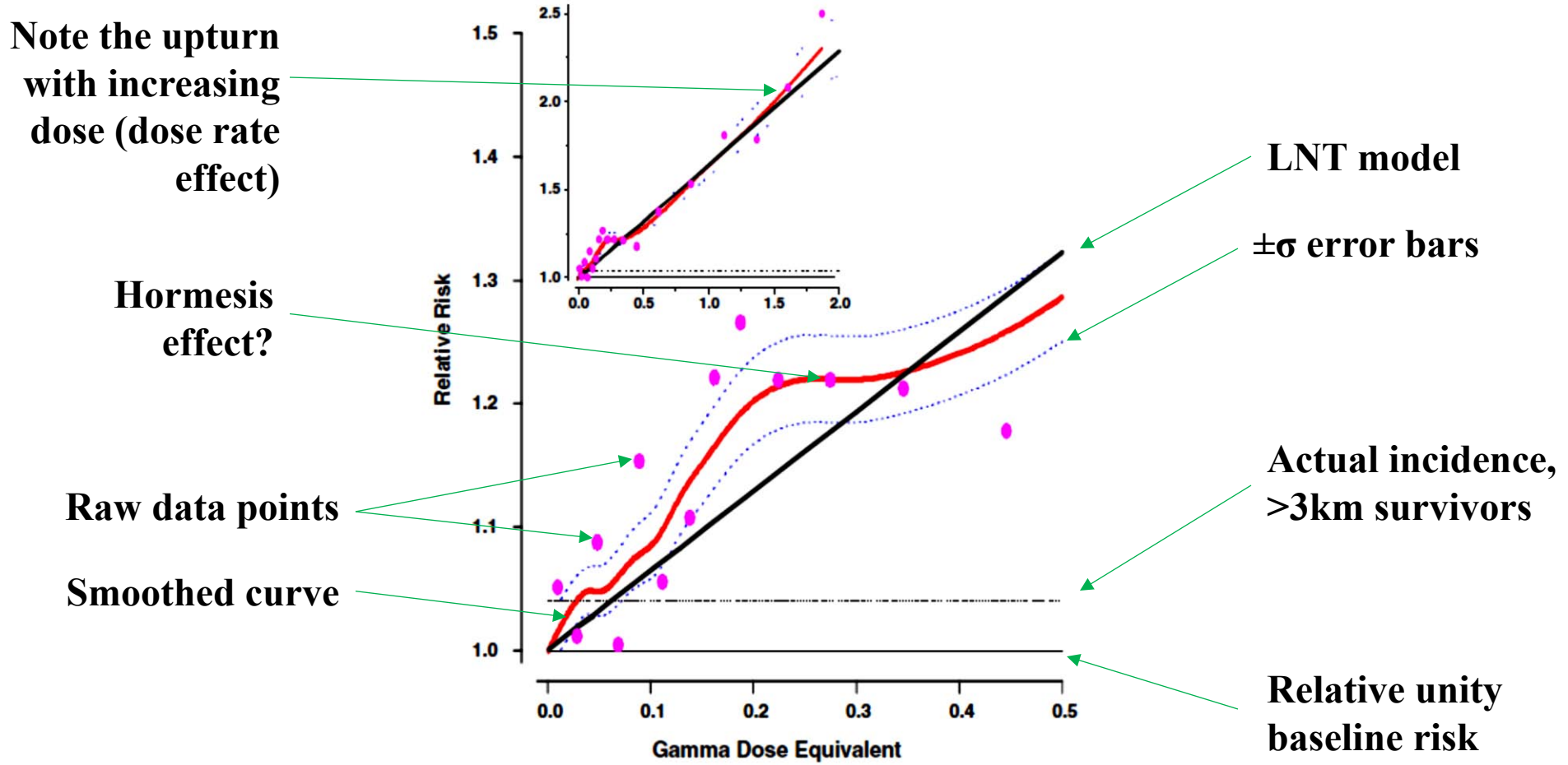
Table 2.5. Distribution of subjects, solid cancers, and estimated radiation-associated, excess solid cancers among 79,901 exposed members of the Life Span Study cohort of Hiroshima and Nagasaki atomic bomb survivors (Pierce and Preston, 2000)

Estimated colon dose	Number of subjects	Number of solid cancers	Estimated number of radiation-associated excess cancers*
Exposed beyond 3000 m	23,493	3230	0
<5 mGy, exposed within 3000 m	10,159	1301	1
5–100 mGy	30,524	4119	77
100–200 mGy	4775	739	60
200–500 mGy	5862	982	164
0.5—1 Gy	3048	582	177
1–2 Gy	1570	376	165
>2 Gy	470	126	80

* Fitted values, linear dose–response relationship.

Total Graphed Atomic Bomb Survivor Risk: Cancers vs. Dose

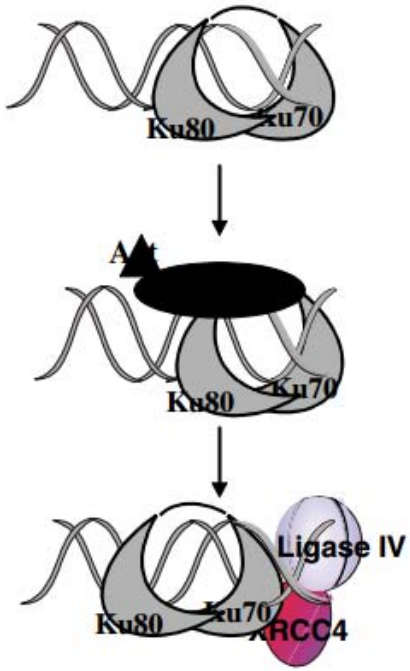
ICRP Publication 99, p. 32



Why the "Hormetic" Effect?

ICRP Publication 99, p. 43

- DNA repair mechanisms *do* exist in the body
- They may be "ramped up" proportionally to exposure



1) Binding of Ku to the double-stranded DNA end. The crystal structure of Ku shows that the DNA passes through a cavity in the structure with Ku encircling the DNA (a single DNA end is shown for simplicity).

2) DNA -PKcs is recruited and the kinase activity activated. Autophosphorylation and phosphorylation of artemis likely ensues, potentially leading to release of DNA -PKcs Artemis nuclease activity may enhance processing of ends.

3) Ku enhances the recruitment of DNA ligase IV/XRCC4 complex and Ku translocates inwards to allow ligase IV/XRCC4 access to the DNA ends.

Note that only a single DNA end is shown for simplicity - one function of DNA -PKcs may be to enhance synapsis of the DNA ends.

Fig. 3.1. Model for DNA non-homologous end-joining. Proposed steps involved in the process.

Why the "Hormetic" Effect?

- DNA damage sensors also exist
- May send a "kill signal" for that cell

***Cell signaling effects may change response at the tissue/organism level compared to single cells

- **See pp. 49-54 of ICRP-99 document**

Multicellular Effects

ICRP Publication 99, p. 69

The bystander effect in irradiated cell populations

(154) The bystander effect of radiation refers to the evidence that damage signals may be transmitted from irradiated to non-irradiated cells in a population, leading to the occurrence of biological effects in cells that receive no radiation exposure.

-Sister chromatid exchanges (SCEs)

DNA Damage in Bystander Cells

ICRP Publication 99, p. 71

Neighboring cells can shift their metabolisms to more oxidative states

(158) DNA damage in bystander cells, however, appears to differ from that occurring in directly irradiated cells; **whereas the mutations induced in directly irradiated cells were primarily partial and total gene deletions, over 90% of those arising in bystander cells were point mutations** (Huo et al., 2001). This would be consistent with the evidence that **oxidative metabolism is upregulated in bystander cells** (Azzam et al., 2002; Narayanan et al., 1997), and has led to the hypothesis that the **point mutations are a result of oxidative base damage occurring in bystander cells** (Huo et al., 2001).

Analyzing The Data – Within 3km Survivors

ICRP Publication 99, p. 33

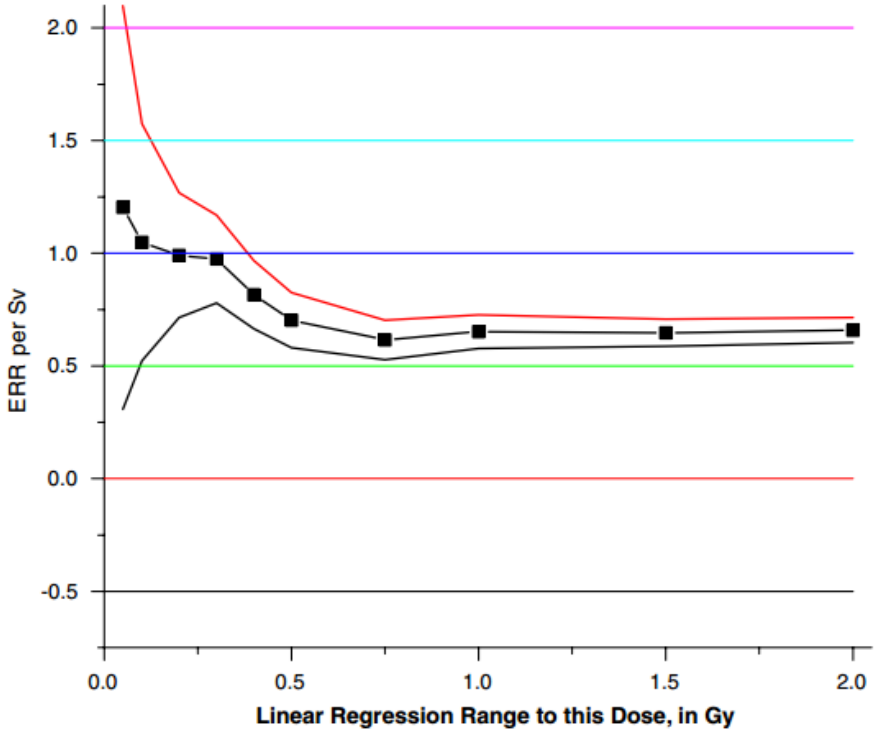


Fig. 2.4. Linear regression estimates of the excess relative risk (ERR) per Gy (points and connecting line, with error bounds of ± one standard error) for solid cancer incidence, based on Poisson regression over dose intervals of differing ranges from zero to the horizontal co-ordinate of the plotted point. The analysis is limited to proximal survivors exposed at distances under 3 km.

Analyzing The Data – ALL Survivors

ICRP Publication 99, p. 34

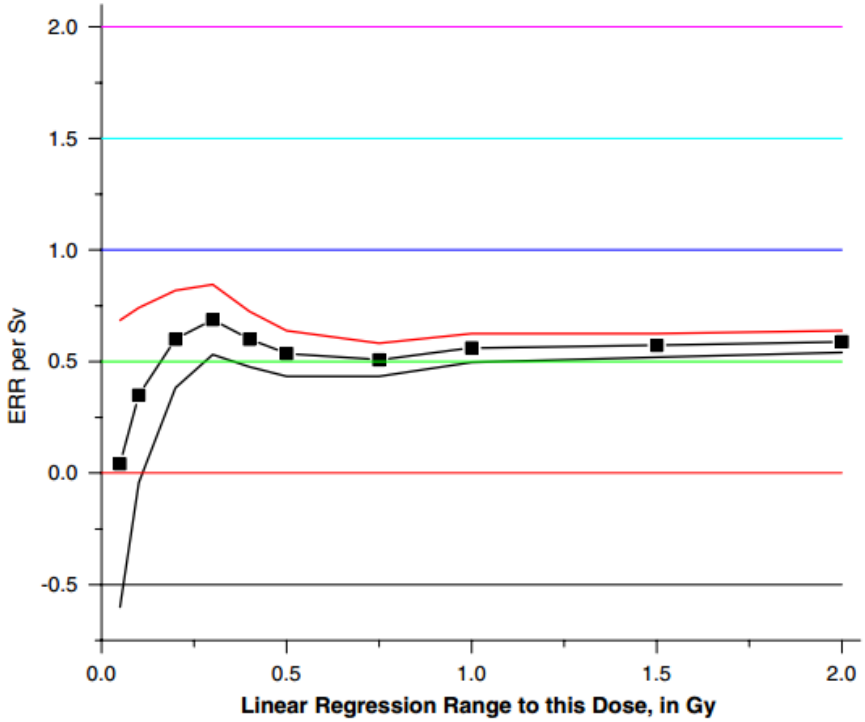
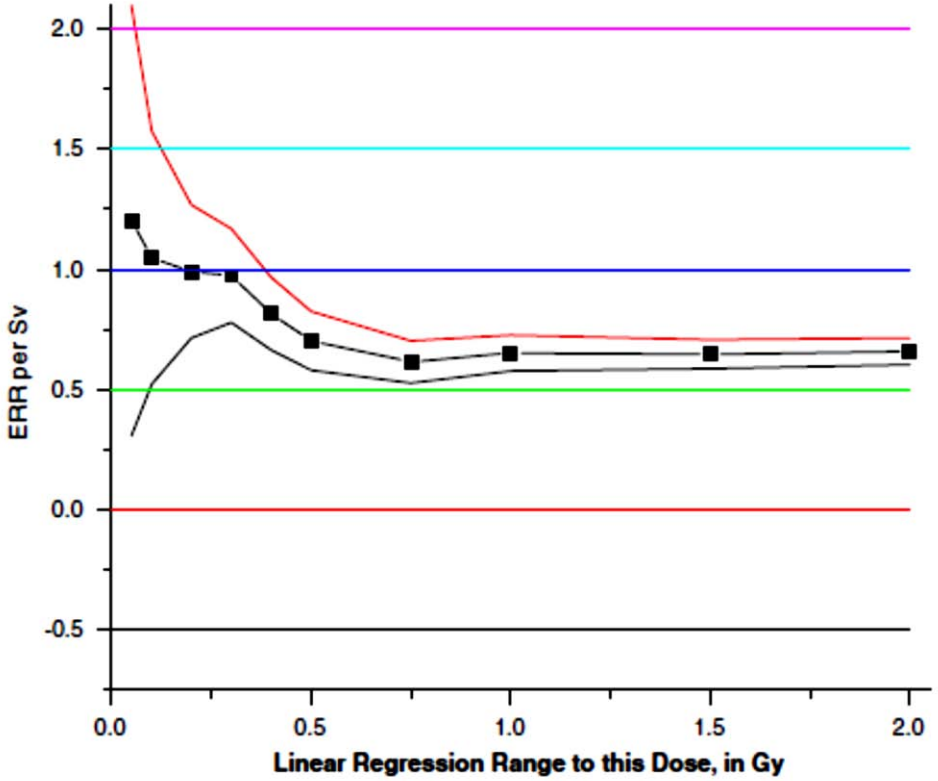


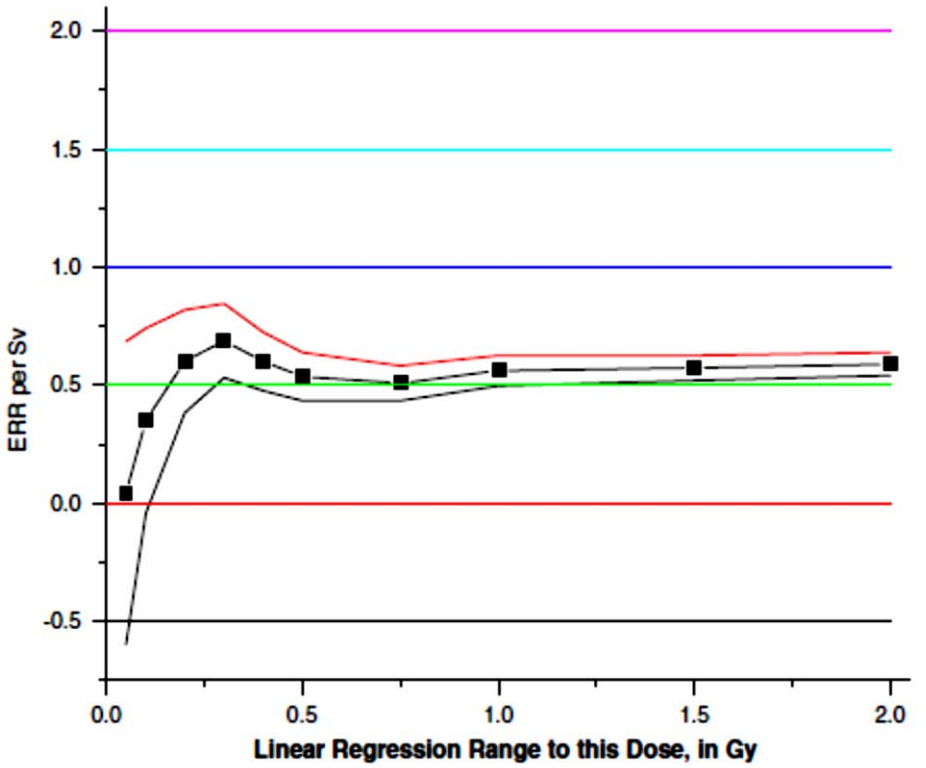
Fig. 2.5. Linear regression estimates of the excess relative risk (ERR) per Gy (points and connecting line, with error bounds of ± one standard error) for solid cancer incidence, based on Poisson regression over dose intervals of differing ranges from zero to the horizontal co-ordinate of the plotted point. The analysis is based on all exposed survivors with estimated radiation doses less than 2 Gy.

What Gives??? Why the Difference?

ICRP Publication 99, p. 33-34



<3km Bomb Survivors



All Bomb Survivors

What Gives??? Why the Difference?

- WAAAY more low-dose survivors outside the 3km radius
- Hiroshima & Nagasaki were urban centers, while surrounding areas were rural

– Due to confounding factors, like

- Lifestyle
- Diet
- Routes of exposure, specific isotopes

Consider the Actual Statistics

ICRP Publication 99, p. 34

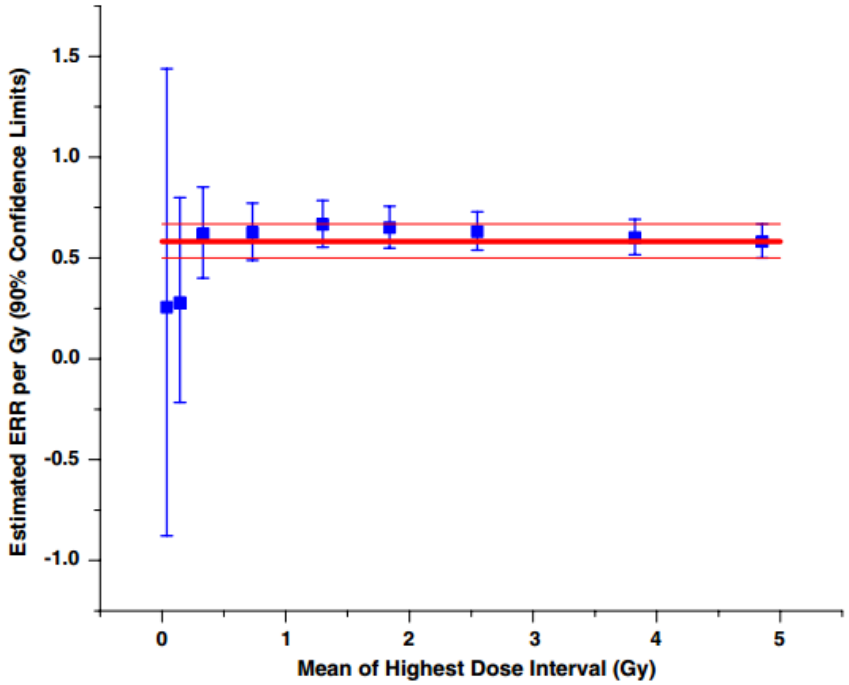


Fig. 2.6. All-age linear regression estimates of excess relative risk (ERR) per Gy for female breast cancer assuming a 12-year minimum latent period, with dose-specific data trimmed from the right. Horizontal placement corresponds to the mean breast tissue dose for the highest neutron-weighted kerma interval included in the regression. Thus, the rightmost point corresponds to the full dose range, the next point to the left to doses under 4 Gy, the next to doses under 3 Gy, and so on.

What Do We Do Next?

ICRP Publication 99, p. 39

2.6. Conclusions: implications for low-dose cancer risk

(73) Epidemiological data from studies of human populations exposed to IR provide direct evidence that such exposure is associated with increased risk of cancer, and reason to believe that **excess risk is not confined to people exposed to very high radiation doses**. Our knowledge of radiation-related risk is highly quantified, more so than for any other common environmental carcinogen, and we have learned much about factors that modify that risk. Our understanding of risks associated with doses commonly encountered in daily life is not insignificant; we know, for example, that such risks are far lower than those observed in populations exposed to hundreds or thousands of mGy. **However, the problem of quantifying risks that are so low as to be practically unobservable, and then recommending policies based on that quantification, is very difficult.**

(74) It is highly likely that there will always be uncertainty about the risk of low doses, and that we will have to come to terms with that uncertainty. One way to do that is to quantify the uncertainty in a manner consistent with mainstream scientific information, and to evaluate actions and policies in terms of plausible probability distributions of risks associated with these actions and policies.

22.01 Introduction to Nuclear Engineering and Ionizing Radiation

Spring 2024