Illinois Institute of Technology

Physics 561

Radiation Biophysics

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Class Overview

- High-LET radiation
  - The Ullrich experiment
  - Large-scale damage to chromosomes
  - Cataracts
- Radionuclides and metabolism
  - Inhaled
  - Ingested
- Break
- Radionuclides, continued
  - Dosimetry and activity
  - Element-specific Issues

The Ullrich Tumor Experiments

- Ullrich found that with low-doses of neutrons, fractionation never diminished incidence of tumors
- With certain types (lung, mammary) there was an enhancement in tumor rate with fractionation
- Dose-response was nonlinear
- Saturation and fall-off of incidence with high doses

Ullrich Experiment: Why?

- Mechanisms of Genetic Damage
- Low vs High LET
  - Low-LET radiation exerts many of its effects at the level of point mutations (single-base substitutions of deletions, or additions)
  - High-LET exerts most of its effects on a more macroscopic scale

Macroscopic Damage to Chromosomes

- First half of chapter 13
- Structural changes in chromosomes
  - Inversions of fragments
  - Multiple hits
  - Isochromatid breaks
  - Dicentrics
  - Minutes
  - Cross over

Cataracts

- Cataracts are common with high-LET radiation
- Reminder: cataracts involve loss of transparency in the lens because problems with differentiation will lead to failure of alignment of the fibers
- Cataracts happened with workers in early accelerator facilities
- RBE values are high, and tend to be higher for lower doses (i.e. low doses cause almost as many cataracts as higher doses)

Cataracts from specific types of radiation

- Neutrons:
  - In animals: cause cataracts with RBE~2 to 100
  - But with humans: cataracts become rare up to 2 Gy, almost universal at D > 11 Gy.
- Argon and iron ions: RBE ~12-40 for low doses (below 0.25 Gy), more like 2-5 for higher doses

Internally Deposited Radionuclides

Why Radionuclides are Studied in the Context of Internal Deposition

- Exposure works differently from external exposure: acts over shorter length scales
- Often involves high-LET forms that wouldn't ever have biological effects if they were external

How do they get in?

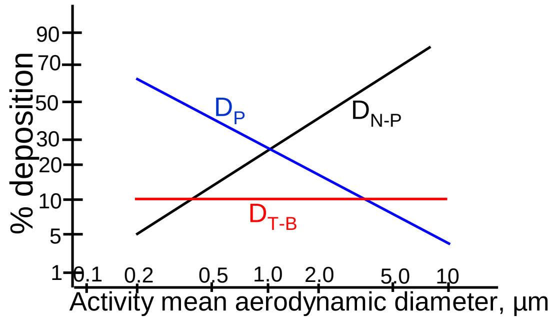
- Ingestion - intake in food & water though GI tract & tracheal clearance
- Inhalation - breathed-in radionuclides traveling through nasophyringeal passages to the lung
- Injection - only intentional - only relevant in a few therapeutic contexts

Ingestion

- Intake through digestive system
- Various fates:
  - Excretion
    - Urine
    - Feces
  - Incorporated into blood,
    e.g. via glutathione conjugation
  - Incorporation into lymph
  - Bile with radionuclides that have collected into the liver out of the circulatory system can be secreted back into the digestive system

Inhalation

- Respiratory system has 3 compartments:
- Nasopharyngeal (NP)
- Tracheobronchial (TB)
- Deep-lung parenchyma (P)
- Deposition (graph sideways from book):



Inhalation: Fate of Radionuclides

- Radionuclides enter respiratory system via nose & mouth
- Travel through trachea
- Either travel farther down to bronchi & lungs or are sent back up to be exhaled or swallowed
- Physical fate primarily function of size & shape
- Size Matters!

What happens to nuclides if they get into the deep lung?

- Fate depends on chemistry
- If particles are moderately to very water-soluble, they pass into the bloodstream readily
  - There's a lot of surfactant (detergent) lining the lung surface that helps to solubilize things
  - once in the blood, the compounds get metabolized or cleared or both
- If the material is very insoluble it gets gobbled up by macrophages
  - Particles go to lymph nodes inside macrophage
  - Ultimately the lymph empties into the blood

Chemistry of Radionuclides: Inhalation, Continued

- Shape matters, too!
- Biological response depends substantially on shape because cells react very differently to needles as compared to cubes
  - Asbestos: caused mostly by needle-shaped fibers, independent of their chemical nature
  - Comparably toxic spheres would be harmless
  - Macrophages respond peculiarly to needle-shaped particles
- Surface area to volume ratios influence biological fate!

Chemistry of Radionuclides: General

- Chemistry is neutron-independent, i.e. every isotope behaves identically (exception: ^{3}H) . . . (until decay occurs)
- Nuclides of elements without ordinary biological function are metabolized approximately like their nearest vertical neighbors in the periodic table
  - Not entirely successful substitutions
  - Sometimes: Very small *discrimination ratio*
- Alkali metals: Li, Na, K, Rb, Cs, Fr
- Elaborate mechanisms for handling K; none for Rb so Rb tends to behave like K.

Chemistry and Metabolism

Periodic Table of the Elements

1 H																	2 He
3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
55 Cs	56 Ba	57 La	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
87 Fr	88 Ra	89 Ac	104 Unq	105 Unp	106 Unh												

Lanthanide Series

58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu

Actinide Series

90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr

Dosimetry with Radionuclides

- Calculations are tricky
- Complications:
  - Variable and organ-dependent rate for isotope to come to specific activity equilibrium, if ever
  - Uneven distribution of nuclide from organ to organ and within an organ
  - Metabolism influences the rate of movement in and out
  - Micro-distribution is non-uniform (e.g. ^{90}Sr in bone)

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Radioactive & Radiochemical Purity

- Radioactive purity: degree to which only one radioisotope is delivered to tissue (^{59}Fe β vs. ^{55}Fe K-capture); see next slide
- Radiochemical purity: the chemical purity of the reagent we are using
  - At high specific activity the emissions themselves can degrade the reagent
  - Example: ^{3}H-labeled thymidine; if it's been around a while, the beta emissions will destroy or modify some of the thymidine!

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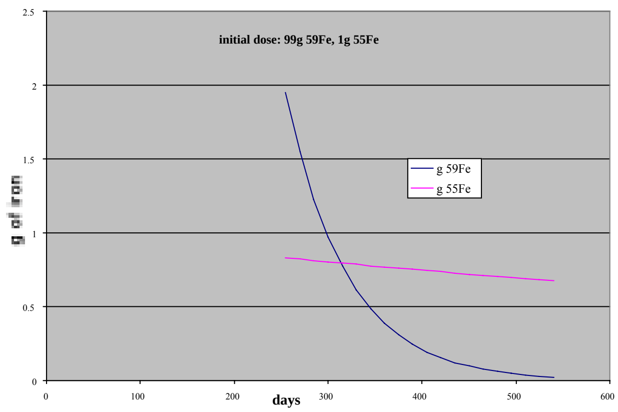
Radioactive Purity: 1% ^{55}Fe vs. 99% ^{59}Fe

- Contaminant predominates later



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Source & Target Regions for Absorbed dose in Tissue

- Absorbed Dose in Target Region:
  $\langle D \rangle = A^{\sim} n E \phi m^{-1}$
  - $A^{\sim}$ = time integral of activity
    i.e. # of disintegrations in source
  - n = < # of ionizing events/ nucl. transf.>
  - E = mean energy per emitted particle
  - ϕ = absorbed fraction in target
  - m = mass of target
- Rewrite in terms of
  $\Phi = \phi / m$ = specific absorbed fraction
  $\Delta = nE$ = total energy released/disintegration:
  $\langle D \rangle = A^{\sim} \Delta \Phi$

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What is A~ ?

- $N = N_0 \exp(-\lambda t)$ describes remaining nuclides as a function of time.
- $A(t) = dN/dt$
- A~ = Integral of A(t) from time t=0 to time t=T
- What we *really* mean by that is the integrated number of disintegrations, i.e. $N_0 - N(T)$
- Aha! That's just $N_0(1-e^{-\lambda T})$
  - This has the nice property that A~(T=0) = 0.
  - It also has the nice property that A~(T=∞) = N_0.

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Metabolism & Clearance

- When a nuclide is present, its concentration or activity decreases due to nuclide decay and biological clearance
- Define effective time constant $\lambda_{eff} = \lambda_b + \lambda_p$ and effective half-life T_{eff}:
  $T_{eff} = 0.693 / \lambda_{eff} = 0.693/(\lambda_b + \lambda_p)$
  $= 0.693/(0.693/T_b + 0.693/T_p)$
  $= 1/(1/T_b + 1/T_p) = T_b T_p/(T_p+T_b)$
- When $T_b >> T_p$, $T_{eff} \sim T_p$ because the denominator becomes essentially T_b.
- When $T_p >> T_b$, $T_{eff} \sim T_b$

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$$\lambda_{eff} = \lambda_B + \lambda_P$$

$$T_{eff} = \frac{0.693}{\lambda_{eff}} = \frac{0.693}{\lambda_B + \lambda_P} =$$

$$= 0.693\left(\frac{1}{\lambda_B + \lambda_P}\right)$$

$$\cancel{= 0.693\left(\frac{\lambda_B \lambda_P}{\lambda_B \lambda_P}\right)}$$

$$= \frac{0.693}{\frac{0.693}{T_B} + \frac{0.693}{T_P}}$$

$$= \frac{1}{\frac{1}{T_B} + \frac{1}{T_P}} = \frac{T_B T_P}{T_P + T_B}$$

Complex Case: ^{99m}Tc

- Three emissions with different activities and energies
- Effective Δ value depends on tabulating individual contributions
- Absorbed dose depends on applying this Δ value in a Monte Carlo analysis of deposition in various organs: see tables 15.2 and 15.3 in the text
- Further variability (beyond limitations of these models) come from the fact that real people aren't identical to the "standard man"

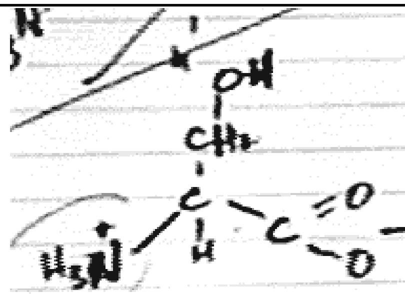
Dosimetry of specific nuclides

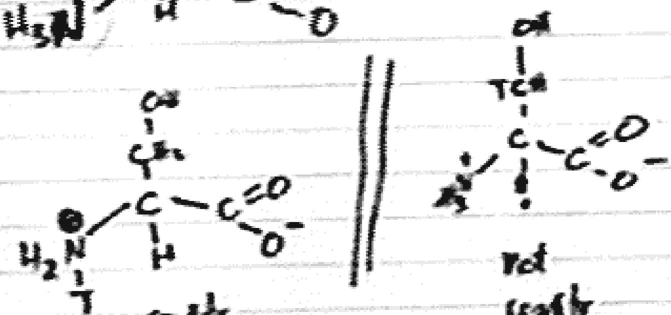
- We describe equivalent dose as
- $H_{T,R} = w_R D_{T,R}$
  where $D_{T,R}$ is the absorbed dose in tissue T from radiation type R, w_R is the radiation weighting factor for this radiation type, and $H_{T,R}$ is the equivalent dose actually experienced by the tissue
- This is similar to the concept of RBE except that it emphasizes that tissues respond differently to different types of radiation.

Tritium

- T_P=12.3y
- Mostly in the form of water
- Turnover: T_B = 10 days, like ordinary water
- Low-energy beta and it's cleared quickly so the hazard is pretty low.
- Some ^{3}H can get incorporated into macromolecules--that could be more severe.
- Hydrogens in different organic molecules have different exchange rates; T~10$_{-10}$s for hydrogens attached to N or O; T ~ minutes or forever for C-H hydrogens.

serine





readily exchanged

H_2O^T

$\tau \sim 10^{-8}$ s

not readily exchanged

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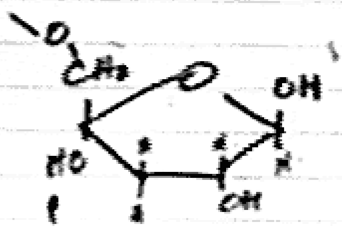
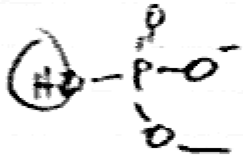
back bone of DNA:



6 not exchangeable
3 are exchangeable



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Krypton and Radon

- ^{85}Kr common in nuclear power
  - Not incorporated in the body much because it's not very reactive
  - Therefore not a serious biological hazard
- Radon *is* important: we'll talk about it in chapter 16.

Alkali Metals

- Sodium isotopes are used in diagnostics
- ^{40}K is an important background irradiator: see chapter 16
- Cesium (and rubidium) are produced in fission.
  - ^{137}Cs ended up in the atmosphere as a component of fallout
  - Behave like potassium
  - T_B ~ 50-150 days
  - T_P ~ 30 y so biological clearance dominates
  - excretion has 2-component model

2 component model:

$$A(t) = A_0\left(e^{-\lambda_1 t} \cdot p_1 + e^{-\lambda_2 t} \cdot p_2\right)$$

$$p_1 + p_2 = 1$$

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Alkaline Earths

- These are typically divalent (2+)
- Be, Mg, Ca not very important except as research subjects
- Sr has practical significance
  - ^{90}Sr is major component of fallout from nuclear weapons testing. T_p = 28 y so it's dangerous
  - ^{89}Sr is important too
  - Sr is a Ca analog and tends to concentrate in tissues where Ca is supposed to concentrate
- ^{140}Ba common in fallout and reactor output; but it has a short half-life
- ^{226}Ra is important too

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Sr and Ra retention and effects

- Ra retiined somewhat less than Sr,
  but a reasonable amount stays around for years
- Did childhood leukemias increase in the US because of fallout in the 1950's? Unclear; it's hard to get unambiguous evidence of environmental effects on human health for anything except smoking.
- Radium dial painters got sarcomas of bone and carcinomas of the sinus epithelium
- ^{224}Ra was used in treatments after WWII
  It can be used to quantitate Pu carcinogenicity

Halogens

- Iodine is concentrated in the thyroid
- ^{131}I is an important fission product
- Short physical half-life (8 days) but it moves quickly through the food chain via milk
- Major releases:
  - Chernobyl (1980's)
  - Windscale nuclear plant in England (1950's)
- Radioactive iodine can be competed away with iodine in table salt