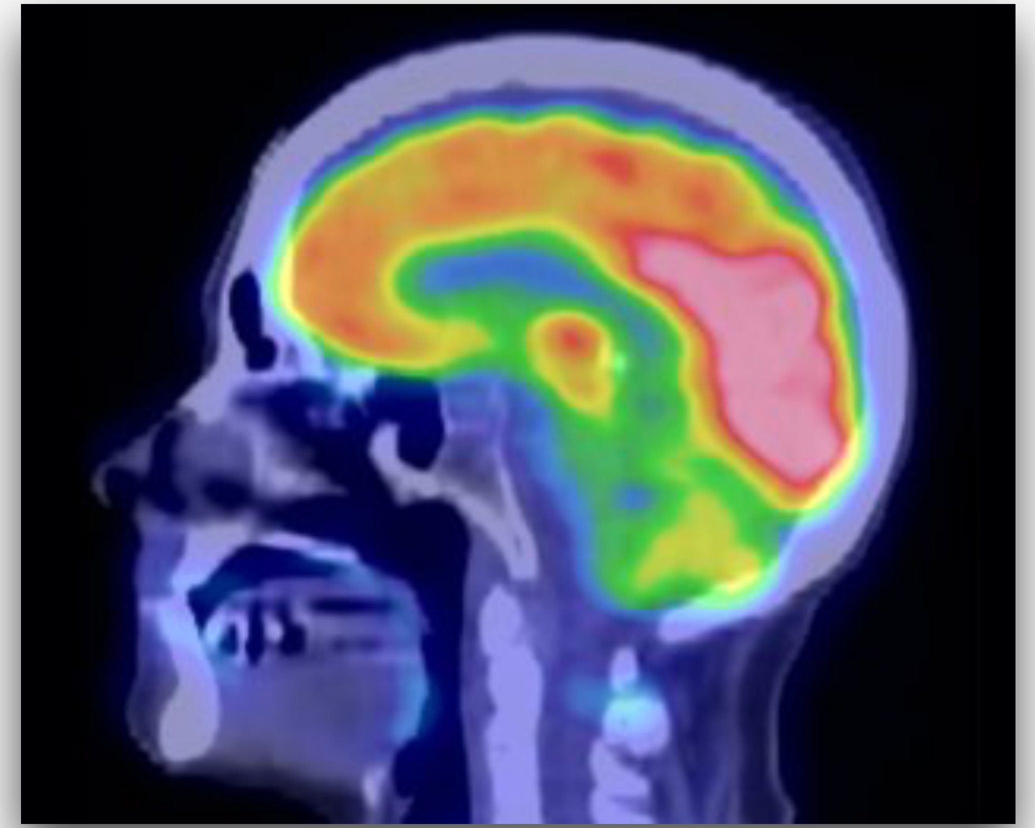
Option D: Medicinal Chemistry

Part D.8

D.8 Nuclear Medicine



- Basics - unstable radioactive nuclei emit radiation in the form of smaller particles
  - alpha, beta, positron, proton, neutron, & gamma are all used in nuclear medicine
  - unstable nuclei have unbalanced forces and excess internal energy - will spontaneously decay (to become stable) - Radioactivity

Types of Radiation

- **alpha** - He-4 nucleus
- **beta** - an electron
- **gamma** - emission of energy as EM waves (photons) - short wavelengths and high frequency
- Nuclear Equations - hmwk - you know how to do these…

a. $^{196}_{82}\mathrm{Pb} + {}^{0}_{-1}\mathrm{e} \rightarrow {}^{196}_{81}\mathrm{Tl}$

b. $^{28}_{15}\mathrm{P} \rightarrow {}^{0}_{+1}\beta + {}^{28}_{14}\mathrm{Si}$

c. $^{226}_{88}\mathrm{Ra} \rightarrow {}^{4}_{2}\alpha + {}^{222}_{86}\mathrm{Rn}$

d. $^{73}_{30}\mathrm{Zn} \rightarrow {}^{0}_{-1}\beta + {}^{73}_{31}\mathrm{Ga}$

Ionizing Effect

- Radioactivity has an ionizing effect - can cause release of non-valence electrons (inside!)
  - causes extremely reactive free radicals
- Free radicals - major effect is on genetic material - DNA
- Ionization Density - high density (alpha) will target cells more closely, lower density (gamma and x-rays) will spread out sparsely within cells
  - high density are more destructive to biological materials - should be avoided, but makes it better for certain treatments

D.8 Nuclear Medicine

Half - life

- A first order reaction where radioactive substances decay at a constant rate dependent upon ONLY the substance that is decaying
- Not affected by changes in temperature, pressure or the presence of other substances
- 50% of the sample will be left after 1 half-life, 25% will be left after 2 half-lives…and so on…Use your brain!

Half-life Equations:

- **Table 1 of Data Booklet!**
  - $t_{1/2} = \ln 2 / k$ (k - rate constant of the half-life)
    - aka $k = 0.693 / t_{1/2}$
  - $N_t = N_0 (0.5)^{t/t_{1/2}}$
    - N_t - amount left at time t
    - N_0 - amount at time = 0
    - t - total time $t_{1/2}$ - half life

N_t/N_0 - proportion remaining

Practice

- An isotope of radium, Ra - 226, has a half life of 1620 years. Calculate the rate constant for the decay of radium - 226.

- What amount of I - 128 will be left when 3.65 mol of this isotope is allowed to decay for 15.0 min? The half-life of I-128 is 25.0 min.

D.8 Nuclear Medicine

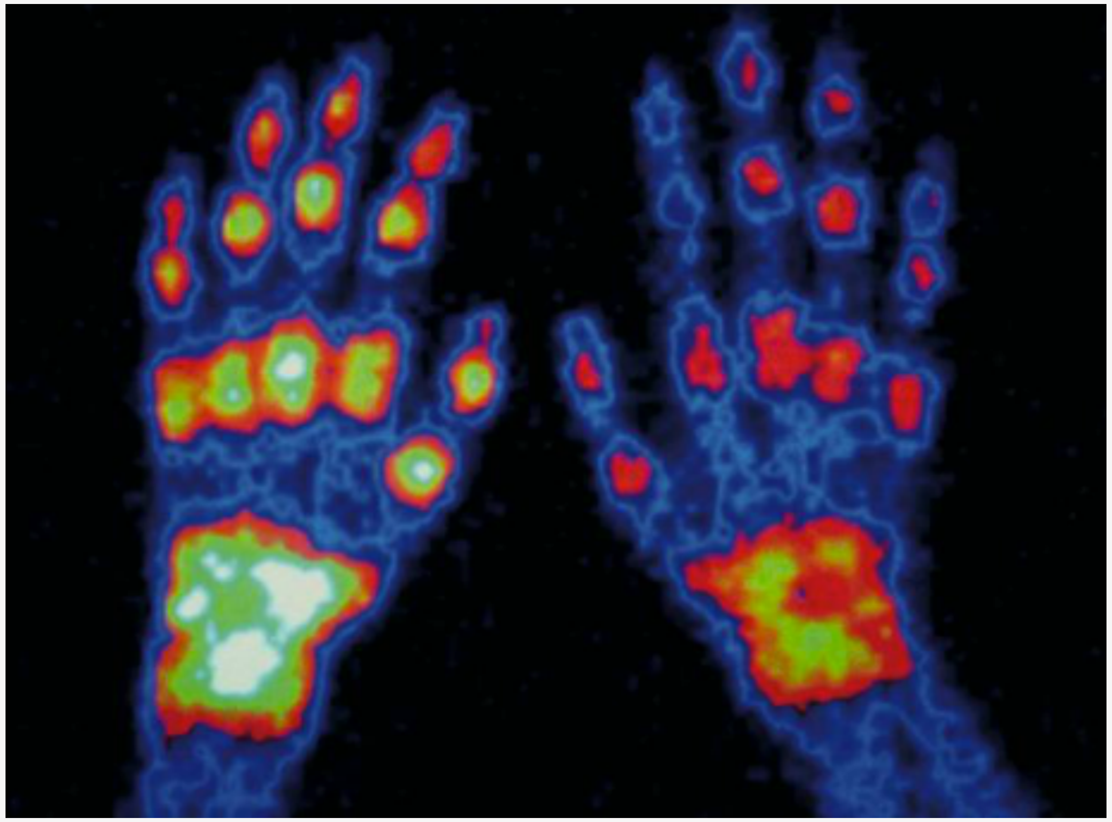
Nuclear Radiation in medical treatment

- Two main types of nuclear medicine
    - Diagnosis
        - provide detailed information about internal organs - known as *nuclear imaging*
    - Treatment
        - mostly cancer, destruction of targeted cells - *radiotherapy*

D.8 Nuclear Medicine

Diagnostic Techniques

- Usually start with attaching a *tracer* to a biologically active molecule - forms a *radiopharmaceutical*
- Detected by a gamma camera
- applies to soft tissue and bones (beyond x-ray!)



D.8 Nuclear Medicine

Design:

- Radiopharmaceutical - target a part of a body where a disease might be - i.e. - iodine in the thyroid OR glucose in the brain
- “hot” or “cold” spots show up in the image where too much or not enough isotope is taken up - either can indicate a malfunction in the organ

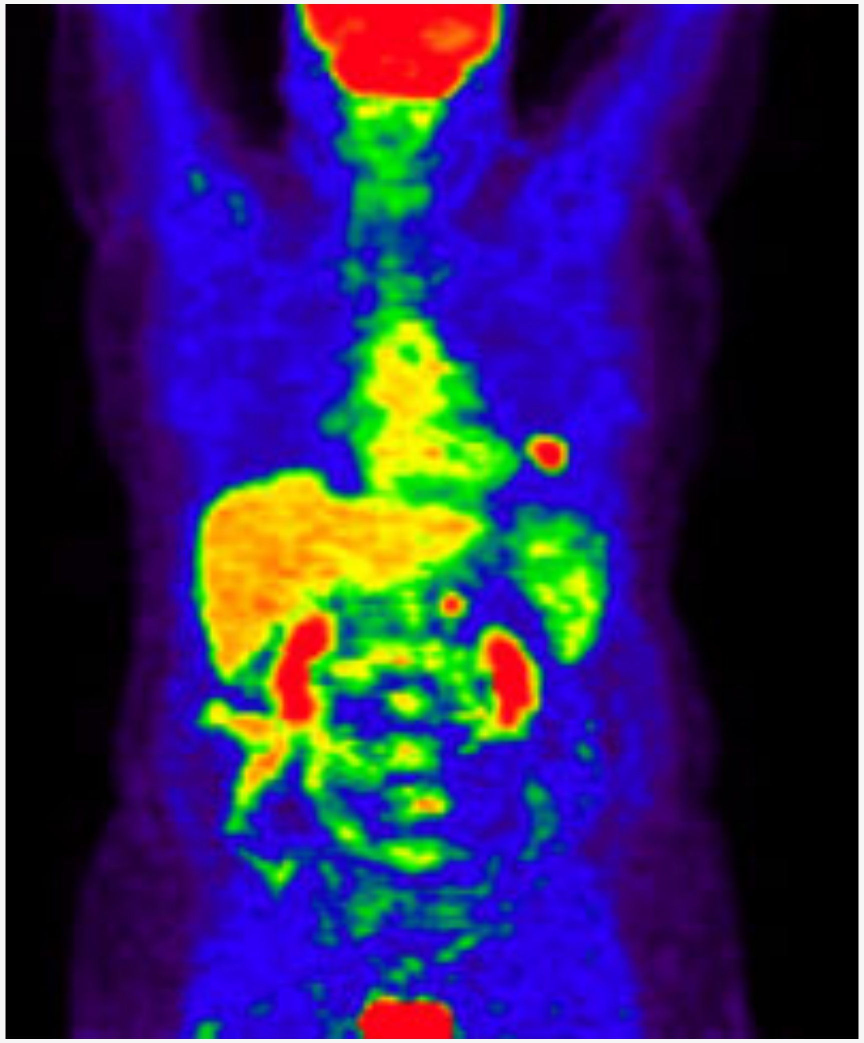
D.8 Nuclear Medicine

Tc - 99

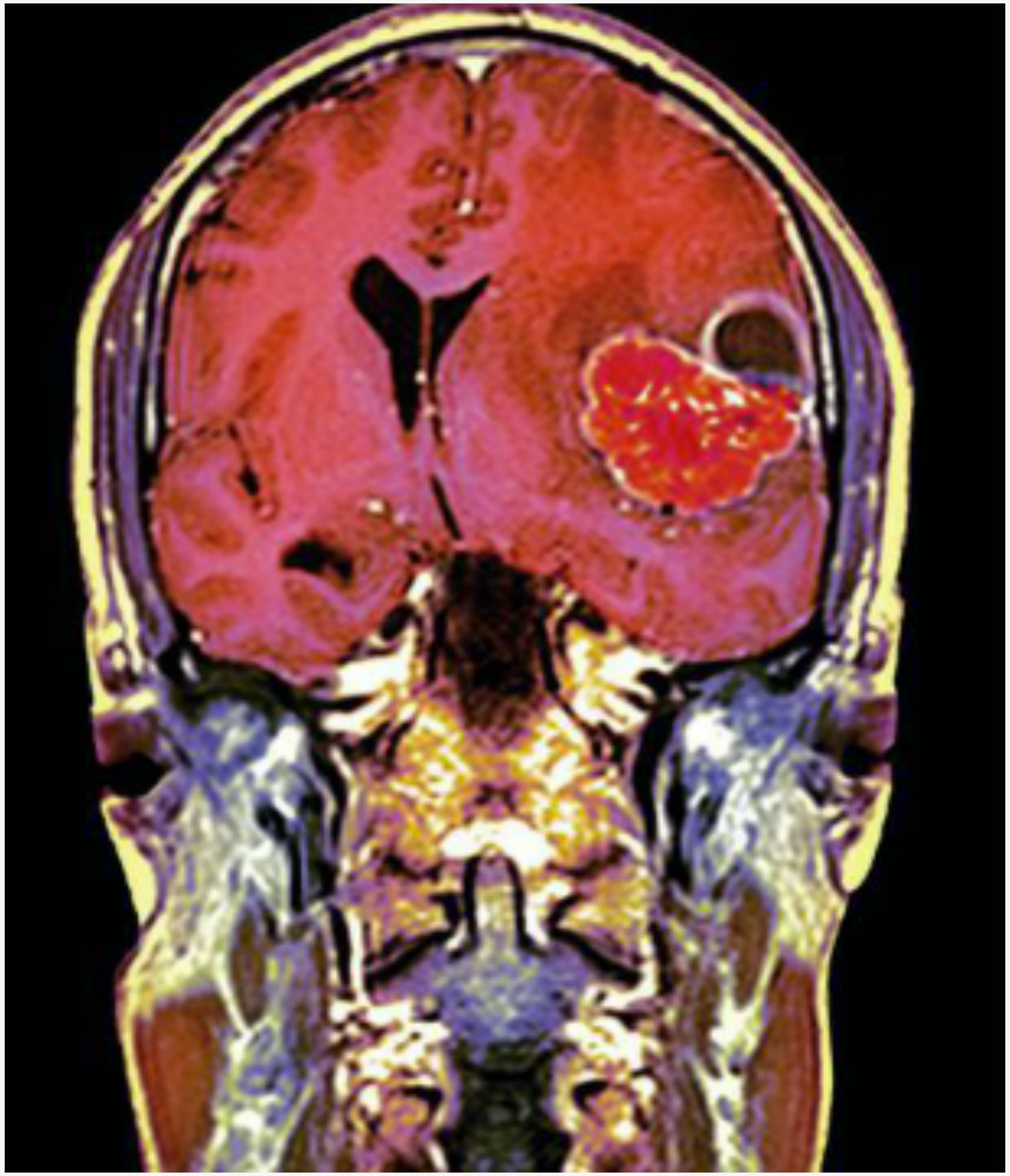
- Technetium-99m - the most widely used radiopharmaceutical in diagnosis (about 80%)
- Tc is artificial and created in nuclear reactors from molybdenum-99 which decays to Tc-99
- Advantages:
  - 6 hour half-life - stays long enough to be seen by scanning equipment, but quick enough to minimize exposure to patient
  - gamma rays and low-energy electrons are released (low dose and can be detected by cameras)
  - Tc is chemically versatile - can be bonded to a range of biologically active substances

Positron Emission Tomography (PET)

- Positrons emitted from the tracer and combine with electrons to form gamma radiation
- Detection by gamma ray cameras allow their position to be precisely determined
- Common tracer - F-18, which is bonded to glucose - uptake of glucose is different in healthy vs. cancer cells



Magnetic Resonance Imaging (MRI)



- An application of NMR spectroscopy - uses H-1 atoms to generate a signal that can be decoded into 2 or 3 dimensional images
- Useful because our body is 70% water (water has hydrogen… duh!)

Magnetic Resonance Imaging (MRI)

- Does not use ionizing radiation
- no known hazards
- can give detailed images of almost any part of the body
- cancer detection, soft tissue injuries or monitoring degenerative diseases

Magnetic Resonance Imaging (MRI)

- Why not NMRI?

D.8 Nuclear Medicine

Radionuclide therapy

- Cancer is difficult to treat because of the rapidly multiplying cells - tumor
  - challenge in treating - killing the tumor while keeping healthy cells alive
- **Radionuclides used in therapy ideally strong beta-emitters that also emit gamma radiation to enable imaging**
  - Lutetium-177 and Yttrium-90

Radionuclide therapy

- 1 - External Radiotherapy or teletherapy
  - An external source of radiation is directed at the cancer site from a radioactive source - usually Cobalt-60 - undergoes beta decay to produce Ni-60
    - $^{60}Co \longrightarrow {}^{60}Ni + {}_{-1}\beta + \gamma$
  - emits gamma radiation which is penetrating and damaging to cancer cells

Radionuclide therapy

- 1 - External Radiotherapy or teletherapy
  - Recent Developments
    - particle accelerators - accelerate electrons aimed at a heavy metal target to produce high energy x-rays - which are precisely directed at the tumor
    - gamma knife radiosurgery: tiny beams of gamma rays focused on tumor from Co-60 sources causing a strong dose where beams converge
  - Reason - more directed/focused radiation for brain cancer patients - can damage healthy cells less this way

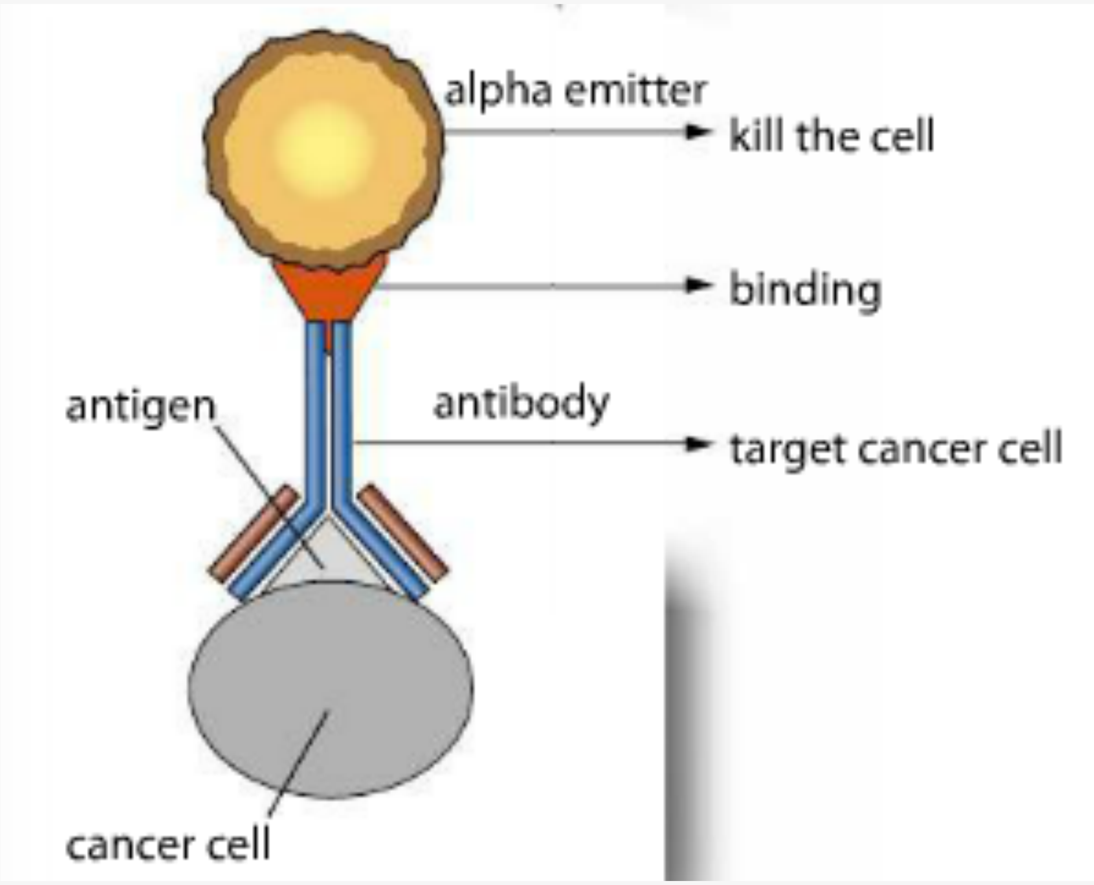
D.8 Nuclear Medicine

Radionuclide therapy

- 2 - Internal Radionuclide therapy
  - either solid form as an implant or as a liquid
  - implant - left near tumor for period of time
    - radioactive wire, seed or tube - gamma or beta emitter
    - sometimes patient is sequestered because they are radioactive
  - liquid - orally or injected
    - P-32 - blood disorders I-131 - thyroid cancer
      Sr-89 - secondary bone cancers (especially pain controls

Internal Radionuclide Therapy

- **Targeted Alpha Therapy** - (TAT)
  - aka - radioimmunotherapy - effective for cancers that have metastasized (spread throughout body)
  - uses alpha-emitting radionuclides directed at a biological target by attaching them to carriers such as antibodies (carry the nuclide to the right place)



Target Alpha Therapy

- Alpha particles are effective because:
  - high ionizing density - high probability of killing cells at the target
  - alpha radiation is short range - minimizes unwanted damage of normal tissue around the cancer cells
- TAT using Lead-212 is showing promise for the treatment of pancreatic, ovarian and melanoma cancers

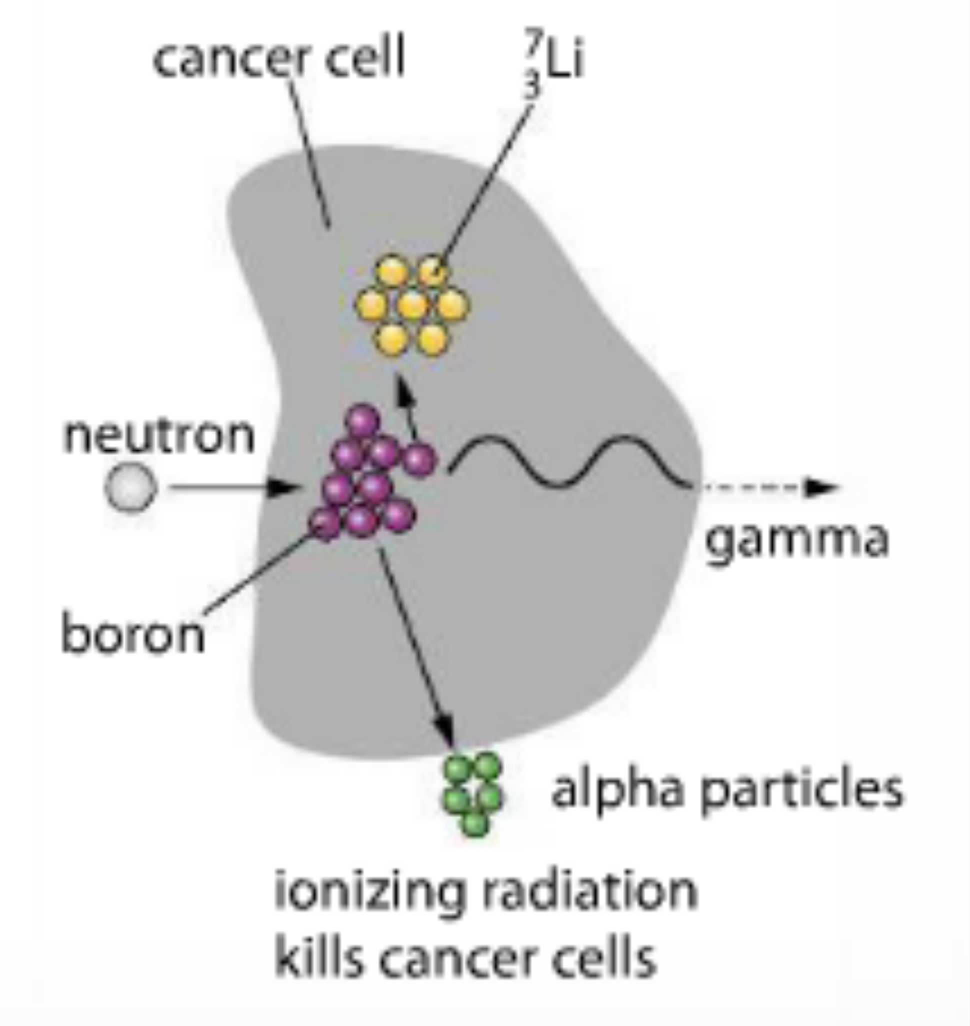
Internal Radionuclide Therapy - cont'd

- **Boron Neutron Capture Therapy** (BNCT)
  - effective for brain and neck tumors
  - non-radioactive Boron-10 is given to patient in a high dose - will concentrate in malignant tumors
  - followed by irradiation with high energy neutrons which are then absorbed by the B-10 (boron neutron capture) - reaction releases alpha particles which are in position to kill the cancer cells
    - $^{10}B + ^{1}n \longrightarrow ^{11}B \longrightarrow ^{4}\alpha + ^{7}Li$

D.8 Nuclear Medicine

BNCT - cont'd

- targeted nature depends on how many healthy cells take up the B-10



- non-radioactive isotopes are being researched for this type of therapy
- Goal: to limit radioactive exposure to the patient and healthy cells

Side Effects of radiotherapy

- External - more general side-effects than internal

- Fatigue - rest and regular hydration are necessary
- Nausea - more common when near digestive system
- sterility - more common when near reproductive system
- skin reaction - red/sore/itchy in local area of radiation