…final slides from lecture 6 last week:

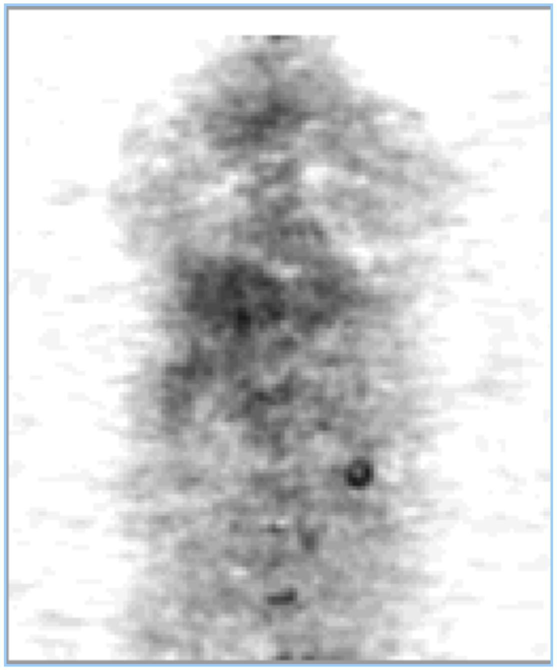
ROC Curves

Larry MacDonald

macdon@uw.edu

May 14, 2013

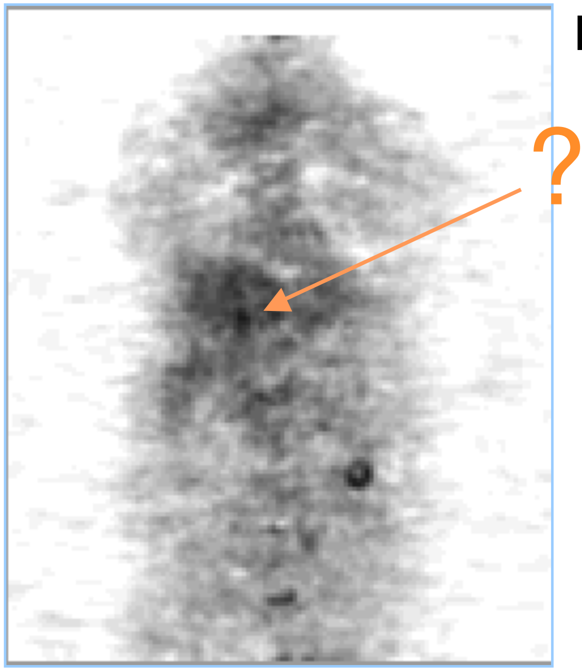
Image quality assessment



Question: which is a better image?

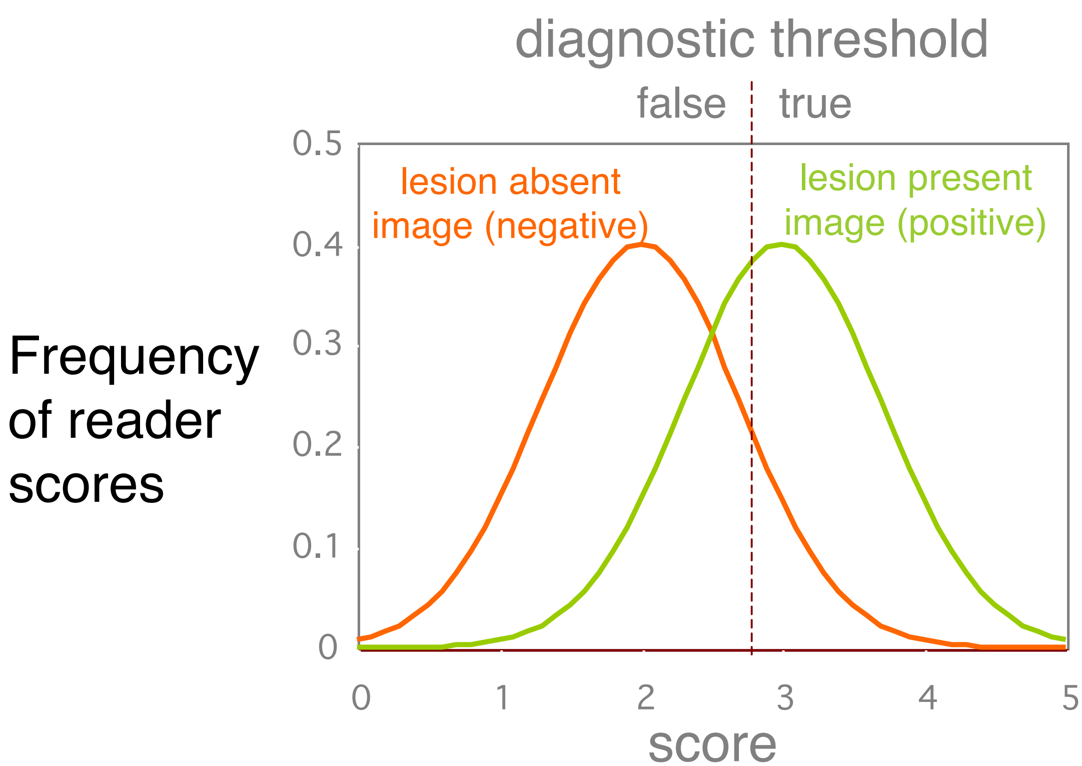
Answer: what are you trying to do?

Quantifying Detection Performance

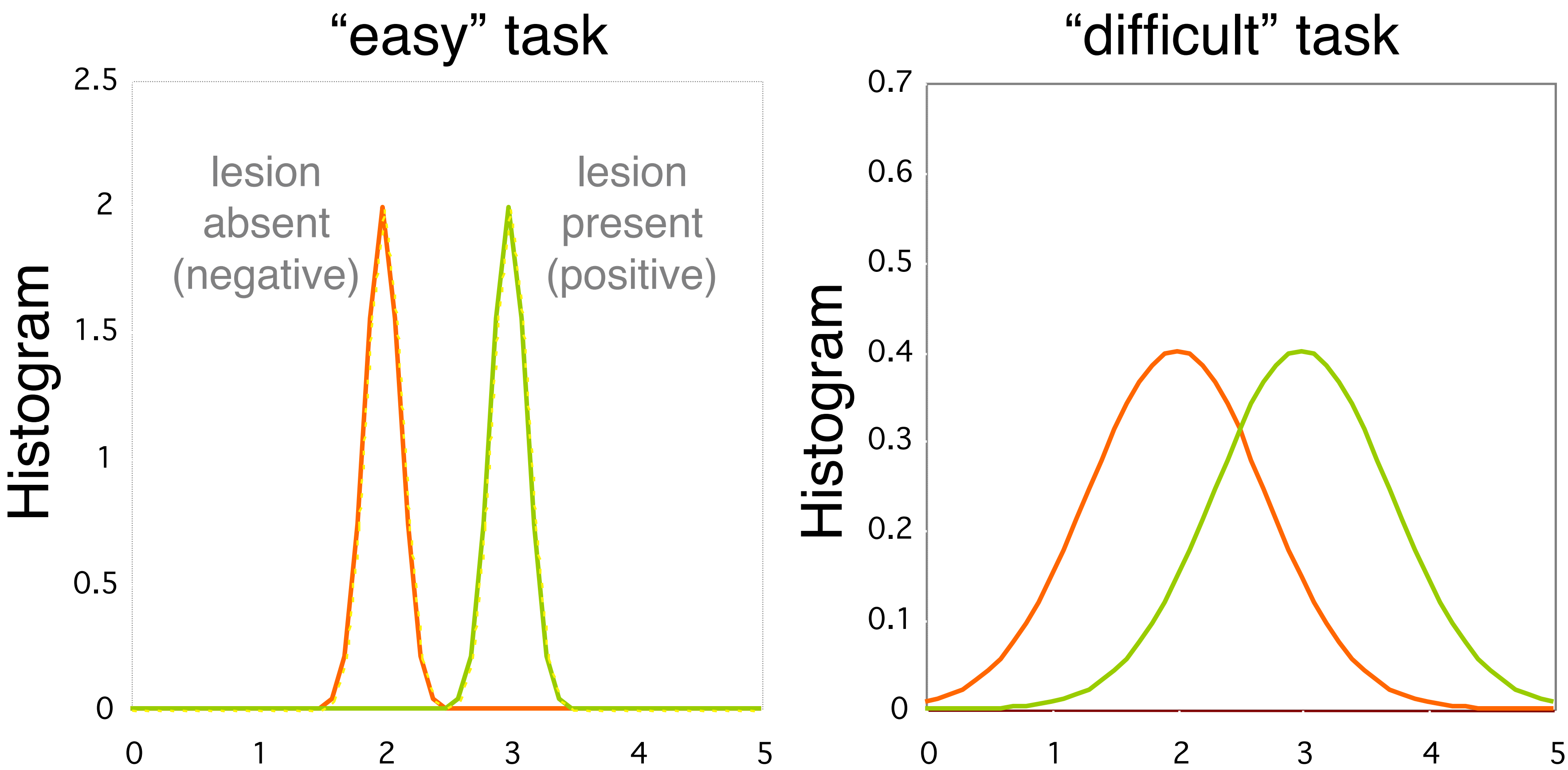


Possible method of reader scoring:

1 = confident lesion absent
2 = probably lesion absent
3 = possibly lesion absent
4 = probably lesion present
5 = confident lesion present



Class Separability (e.g. detectability)



Reader score (1 = confident lesion absent, 5 = confident lesion present)

Quantifying Detection Performance

Is the object present?
("truth" or gold standard)

Does the observer say the object is present?

	Positive	Negative
True	True Positive (TP)	False Positive (FP)
False	False Negative (FN)	True Negative (TN)

Key concepts

- Sensitivity: True positive fraction

  (TPF) = TP/(TP + FN) = TP/P

- Specificity: True negative fraction

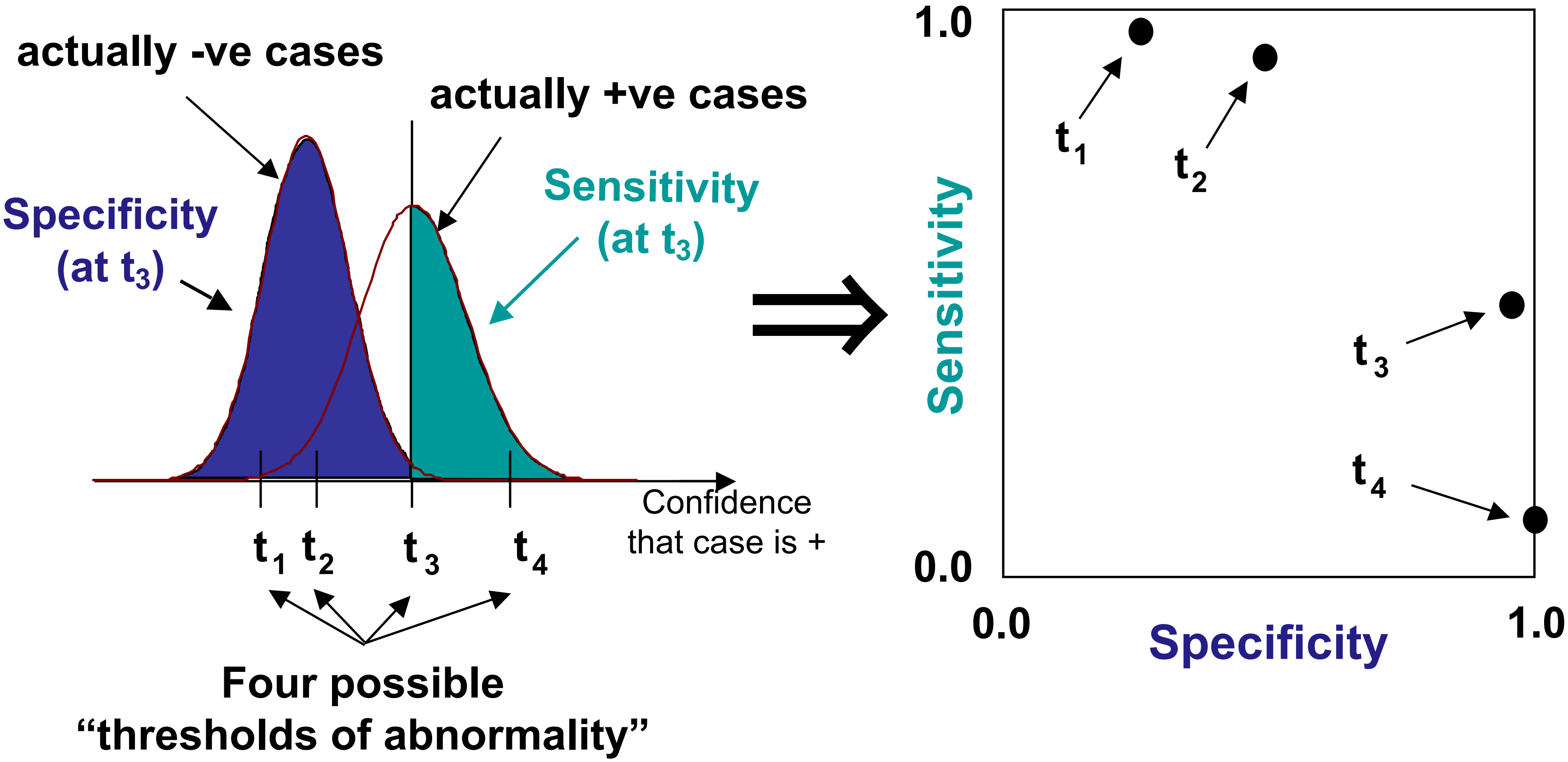
  (TNF) = TN/(TN + FP) = TN/N

- Accuracy = (TP + TN) / (P + N)

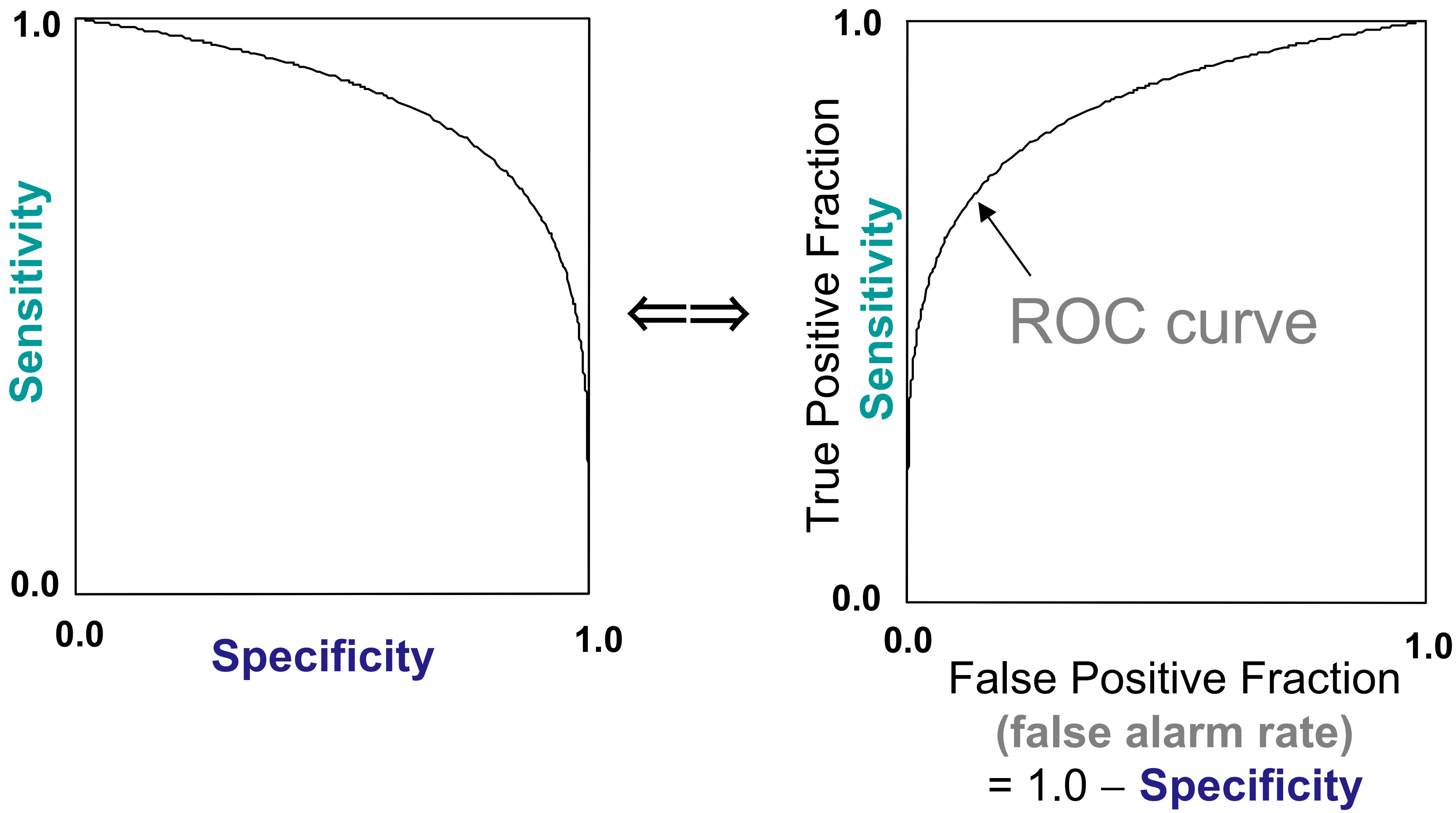
Is the object present?

	Positive	Negative
True	True Positive (TP)	False Positive (FP)
False	False Negative (FN)	True Negative (TN)

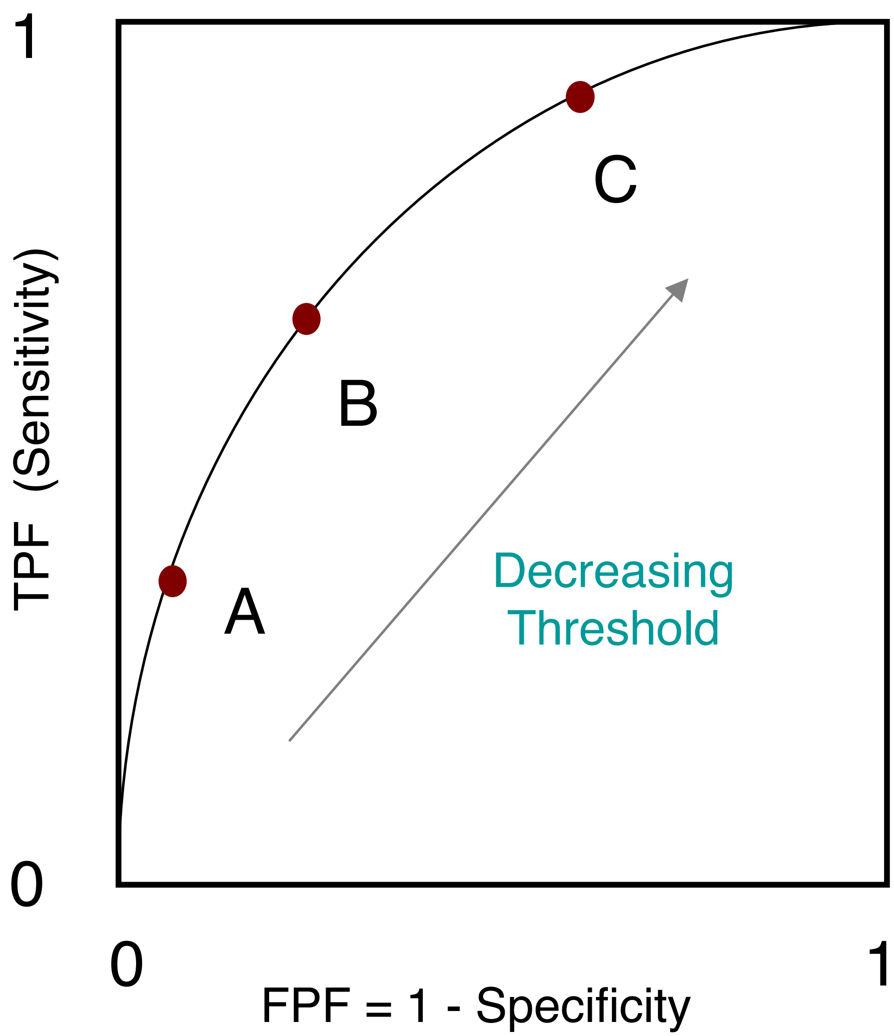
Dependence of Sensitivity and Specificity on "threshold of abnormality":



Receiver Operating Characteristic (ROC) Curve

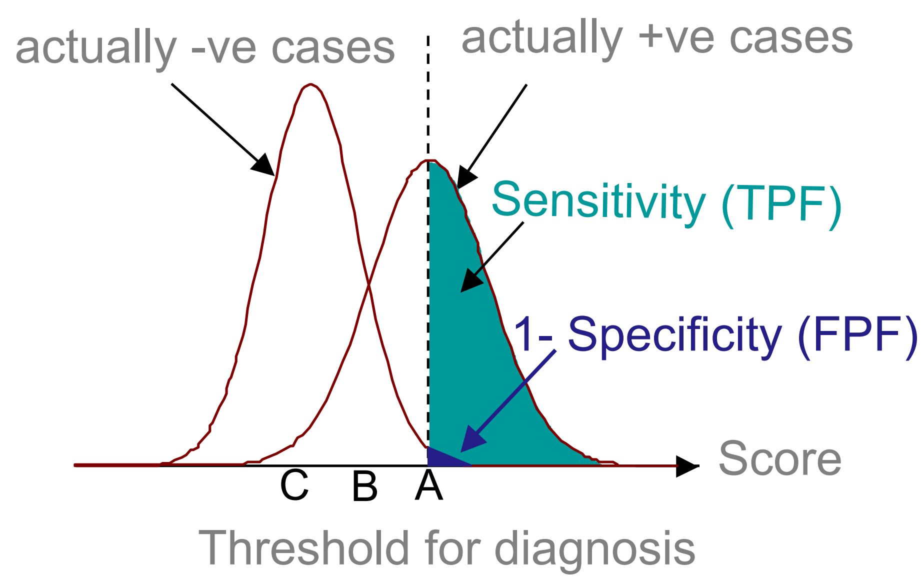


The ROC Curve

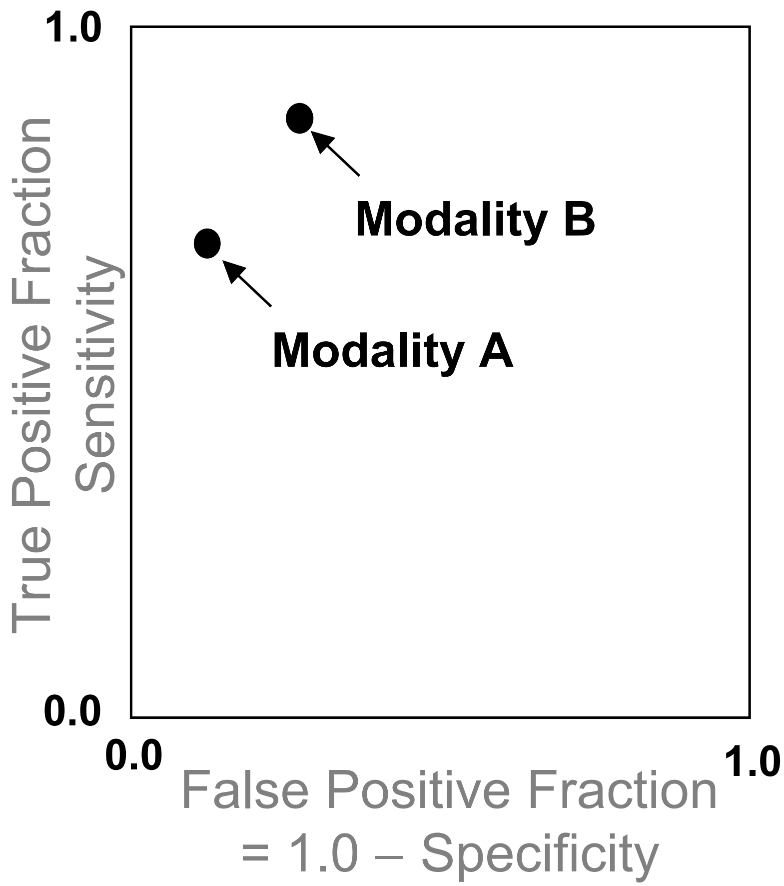


Points A, B, & C correspond to different thresholds

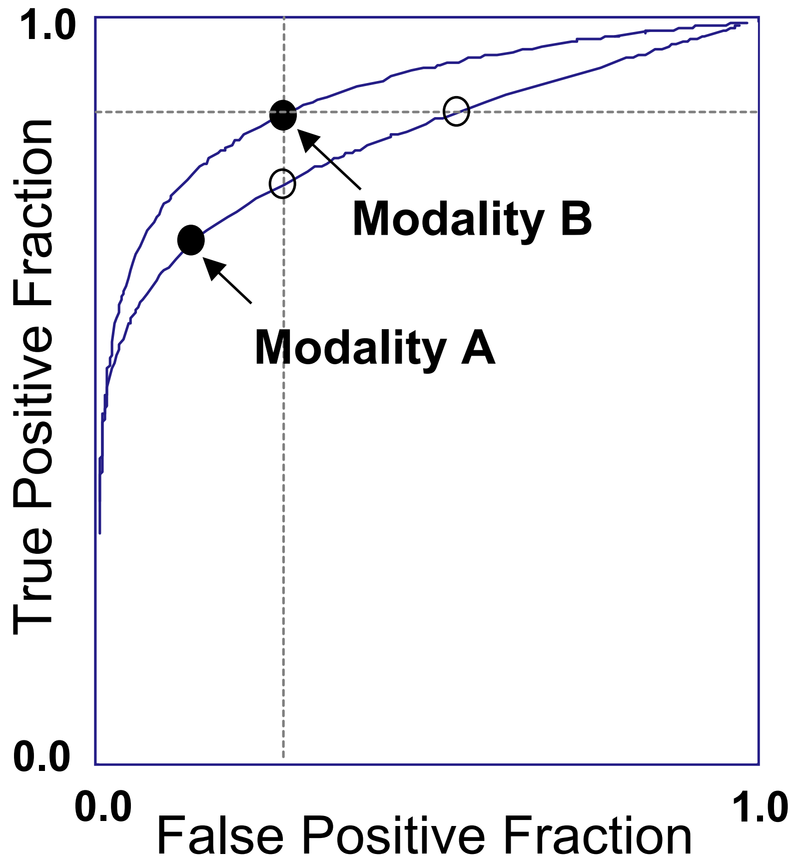
Note, for example, it is always possible to make sensitivity = 1 if the threshold is low enough!



A dilemma: Which modality is better?



The dilemma is resolved after ROCs are determined (one possible scenario):



Conclusion:

Modality B is better, because it can achieve:

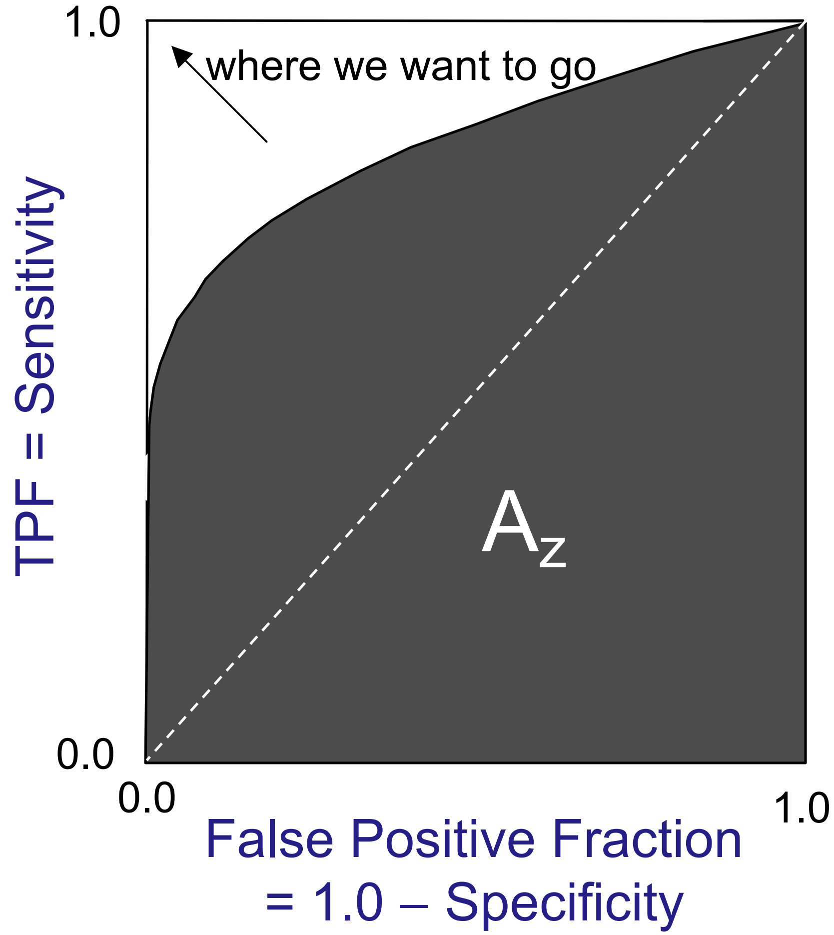
- higher TPF at same FPF, or
- lower FPF at same TPF

However: modality-A and modality-B curves may cross, each being more advantageous in different regions of the TPF-FPF space

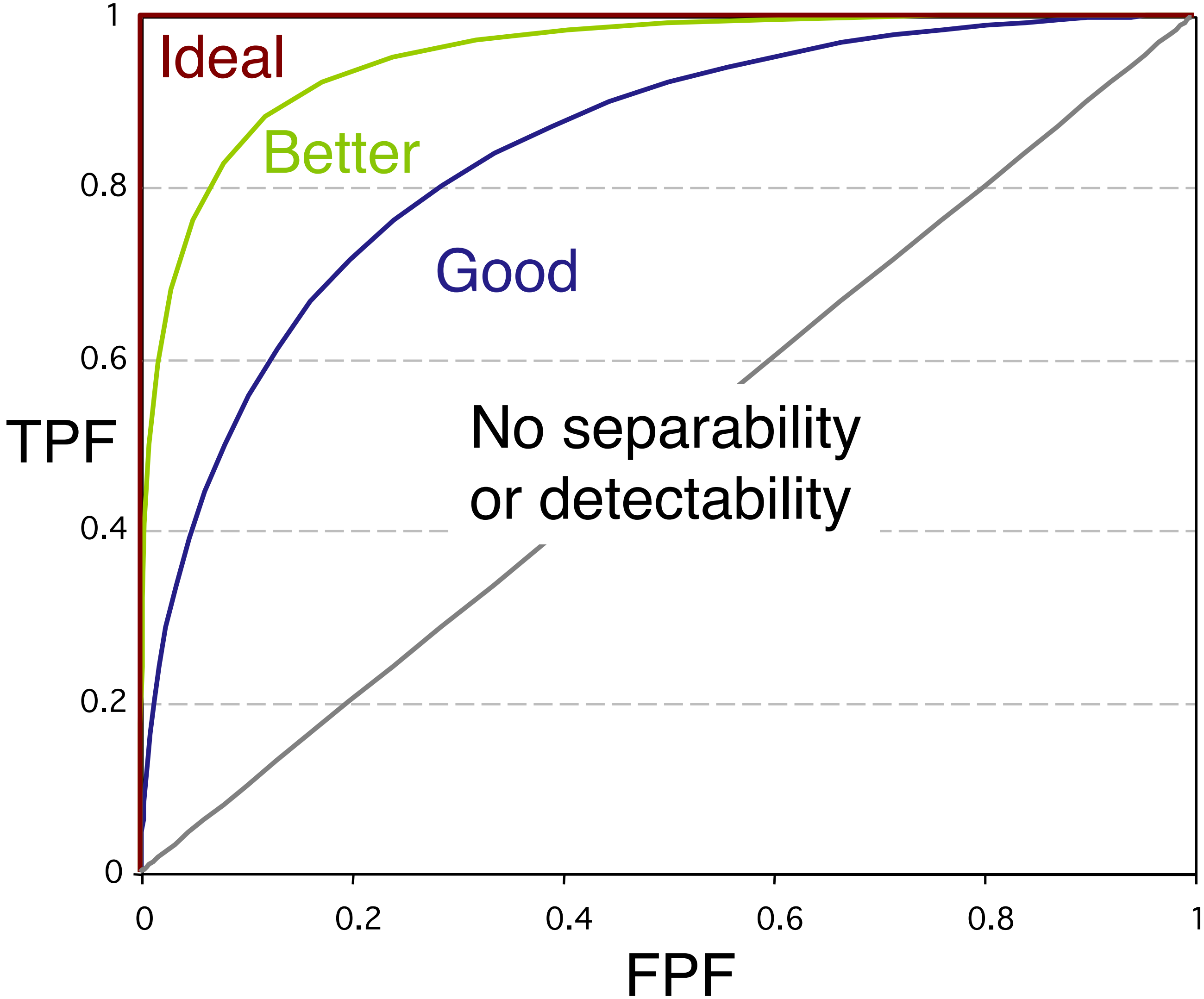
The ROC Area Index (Az)

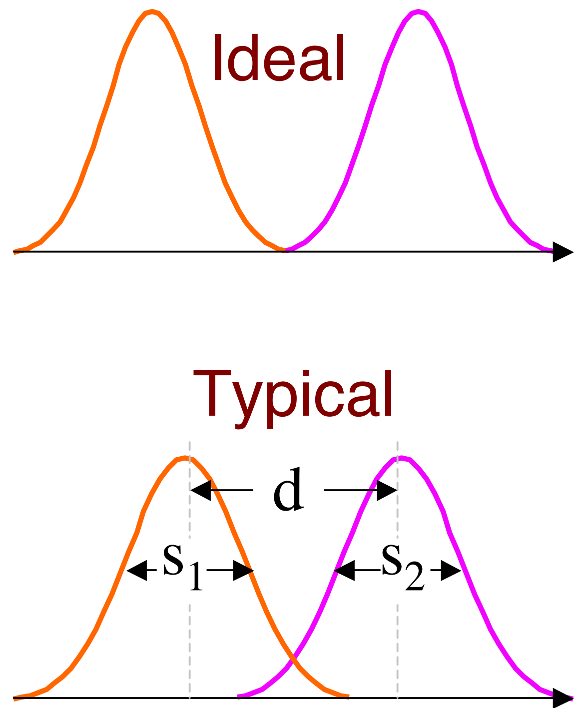
perfect: $A_z = 1.0$

random: $A_z = 0.5$



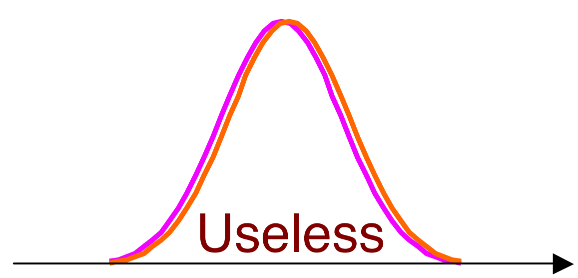
Comparing Imaging Systems





$$SNR = \frac{d}{\sqrt{\left(s_1^2 + s_2^2\right)/2}}$$

(SNR for detection task)



Introduction to Nuclear Physics and Nuclear Decay

Larry MacDonald

macdon@uw.edu

May 14, 2013

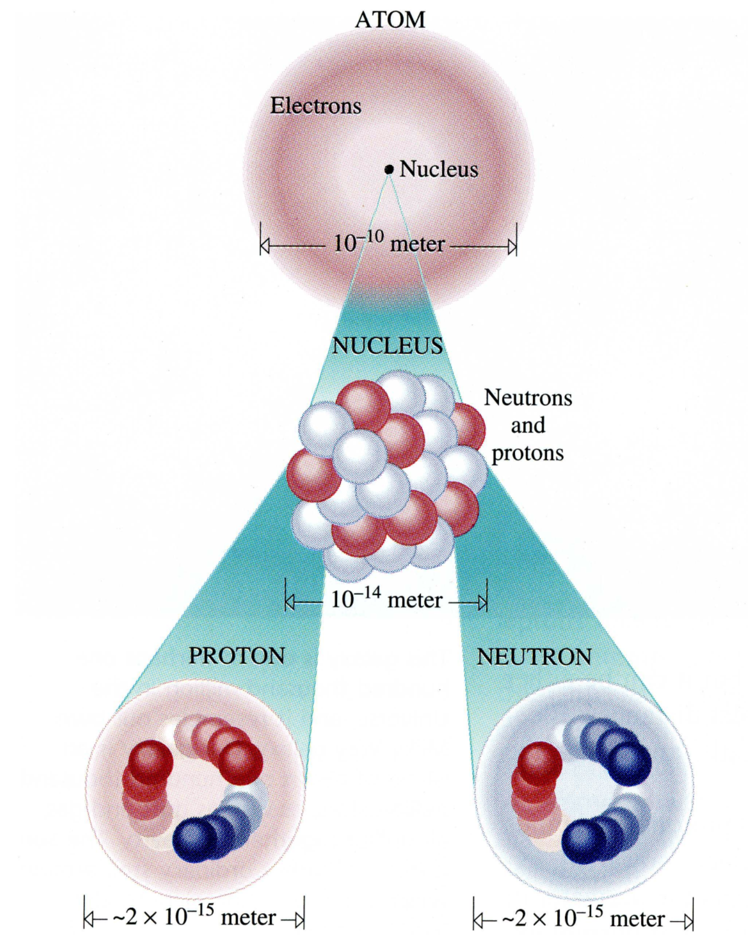
Atoms

•Nucleus: ~10^{-14} m diameter
~10^{17} kg/m^3

•Electron clouds: ~10^{-10} m diameter
(= size of atom)

Nucleons (protons and neutrons) are ~10,000 times smaller than the atom, and ~1800 times more massive than electrons.
(electron size < 10^{-22} m (only an upper limit can be estimated))

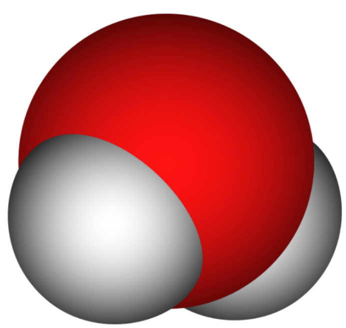
Nuclear and atomic units of length
10^{-15} = femtometer (fm)
10^{-10} = angstrom (Å)



Hecht, *Physics*, 1994

Molecules
water molecule: ~10^{-10} m diameter
~10^3 kg/m^3

mostly empty space
~ one trillionth of volume occupied by mass



Water
(wikipedia)

Table of Elements

Elements distinguished by their numbers of *protons*

Z (*atomic number*) = number of protons in nucleus

N = number of neutrons in nucleus

A (*atomic mass number*) = *Z* + *N*

[*A* is different than, but approximately equal to the *atomic weight* of an atom in amu]

Electrically neural atom, ${}^{A}_{Z}X_{N}$ has *Z* electrons in its atomic orbit. Otherwise it is *ionized*, and holds net electric charge.

X = element symbol

alternative denotations

$${}^{A}_{Z}X_{N} \qquad {}^{A}_{Z}X \qquad {}^{A}X$$

Examples; oxygen, lead

$${}^{16}_{8}O_{8} \qquad {}^{208}_{82}Pb_{126}$$

Standard periodic table

Group → / ↓ Period	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	1 H																	2 He
2	3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
3	11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
4	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
5	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
6	55 Cs	56 Ba	*	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
7	87 Fr	88 Ra	**	104 Rf	105 Db	106 Sg	107 Bh	108 Hs	109 Mt	110 Ds	111 Rg	112 Uub	113 Uut	114 Uuq	115 Uup	116 Uuh	117 Uus	118 Uuo

* Lanthanides	57 La	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
** Actinides	89 Ac	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

Mass and Energy Units
and
Mass-Energy Equivalence

Mass

atomic mass unit, u (or dalton, Da):

$$\text{mass of } ^{12}C \equiv 12.0000 \text{ u} = 19.9265 \times 10^{-27} \text{ kg}$$

Energy

Electron volt, eV $\equiv$ kinetic energy attained by an electron accelerated through 1.0 volt

1 eV $\equiv$ (1.6×10^{-19} Coulomb)*(1.0 volt) = 1.6×10^{-19} J

$$E = mc^2 = \frac{m_0 c^2}{\sqrt{1-\left(\frac{v}{c}\right)^2}}$$

E = total energy (rest mass + kinetic)
m_0 = rest mass
$c = 3 \times 10^8$ m/s
speed of light

mass of proton, m_p	$= 1.6724 \times 10^{-27}$ kg	= 1.007276 u	= 938.3 MeV/c^2
mass of neutron, m_n	$= 1.6747 \times 10^{-27}$ kg	= 1.008655 u	= 939.6 MeV/c^2
mass of electron, m_e	$= 9.108 \times 10^{-31}$ kg	= 0.000548 u	= 0.511 MeV/c^2

Nuclide Groups/Families

A nuclide is a nucleus with a specific Z and A

~1500 nuclides exist

(Periodic Table typically lists distinct Z)

Nuclides with the same:

Z (#protons) are	***Isotopes***
N (#neutrons) are	***Isotones***
A (#nucleons) are	***Isobars***
A, N, and Z are	***Isomers***

A nuclide with the same Z and A (& thus also N) can also exist in different (excited & ground) energy states

Factors in Nuclear Stability

- Nuclear stability represents a balance between:
  - Nuclear "strong force" (basically attractive)
  - Electrostatic interaction (Coulomb force) between protons (repulsive)
  - Pauli exclusion principle
  - Residual interactions ("pairing force", etc.)
- Stability strongly favors N approximately equal to (but slightly larger than) Z. This results in the "band of stability" in the Chart of the Nuclides.

N vs. Z Chart of Nuclides

N > *Z* for the majority
(*N* = *Z* for low *Z* elements)

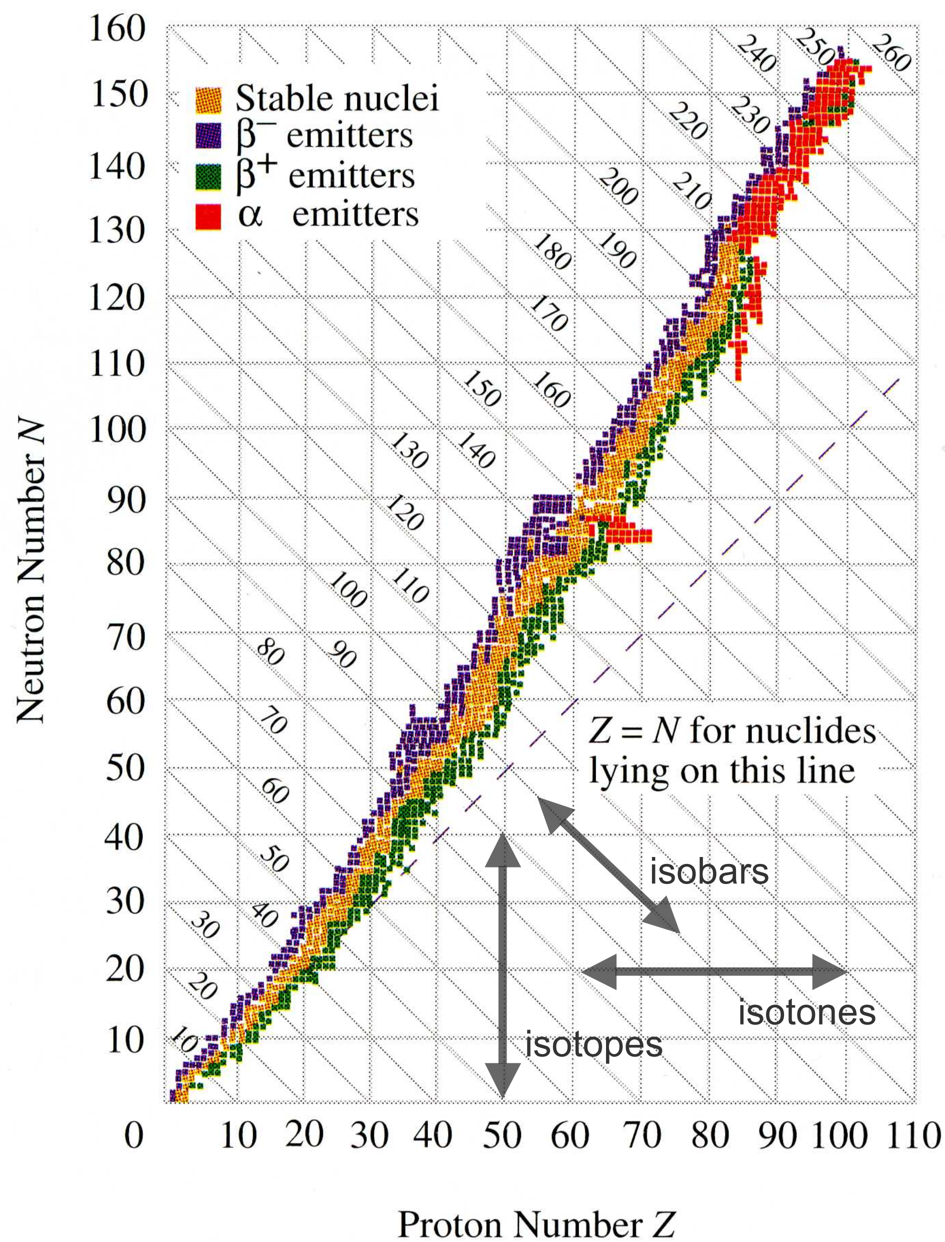
The *line of stability* (gold band) represents the stable nuclei.

Distribution of stable nuclei:

Z	N	#stable nuclei
even	even	165
even	odd	57
odd	even	53
odd	odd	4

279 stable nuclei exist
(all have *Z* < 84)

~1200 unstable (radioactive)
(65 natural, remaining are human-made)



Hecht, *Physics*, 1994

Nuclear Shell Structure

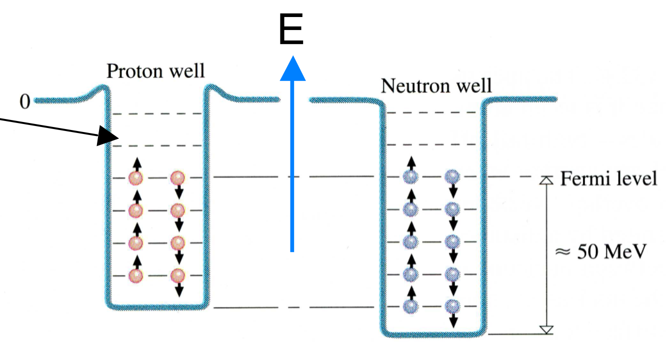
- Similar to atomic structure, the nucleus can be modeled as having quantized allowed energy states (shells) that the nucleons occupy.
- The lowest energy state is the *ground state*.
- Nuclei can exist in *excited states* with energy greater than the ground state.
- Excited nuclear states that exist for > 10^{-12} sec. are *metastable* states (*isomeric*).
- Nucleons held together by the ‘strong force’; short range, but strong.
- This overcomes the repulsive electrostatic force of similar charged protons
- Also similar to atomic theory:
  - → Electrons swirl around in clouds about the nucleus; likewise, the nucleus is a dynamic swirl of nucleons.
  - → Nucleons, like electrons, are paired in energy states - each with opposite spin.
  - → Closed electron shells lead to chemically inert atoms. Magic numbers of nucleons (analogous to closed shells) form particularly stable nuclei.

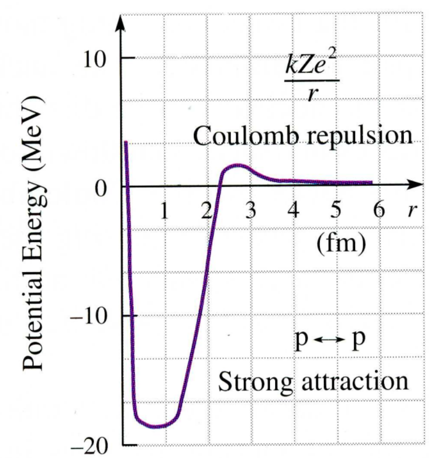
<u>Schematic energy diagrams</u>

E=0: particle is unbound (free)

E<0: particle is bound (e.g. in nucleus, in an atom)

E>0: free & has excess energy (can be potential or kinetic)





Hecht, *Physics*, 1994

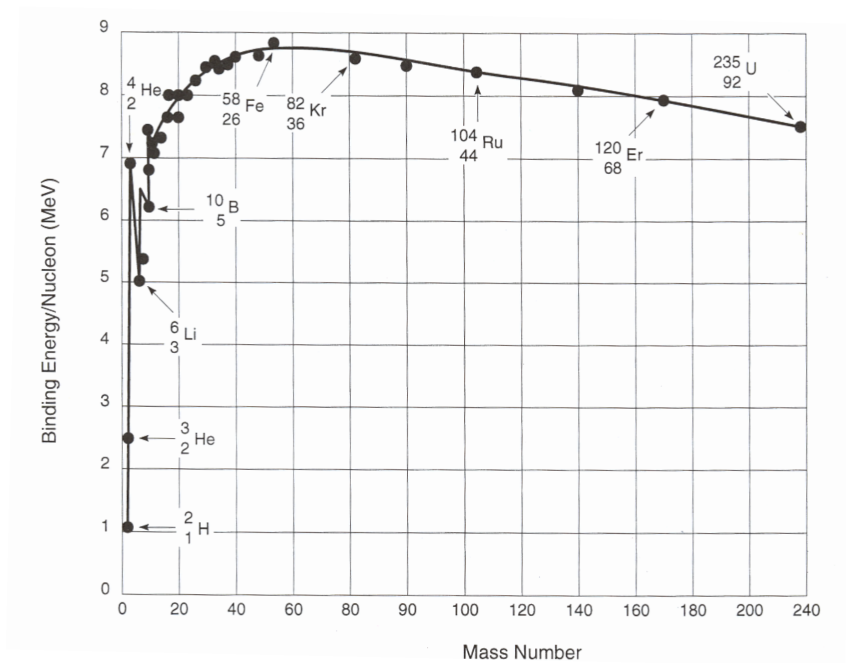
Binding Energy

The mass of a nuclide *is less than* the mass of the sum of the constituents. The difference in energy is the *binding energy*.

The consequence is that energy is liberated when nucleons join to form a nuclide.

The binding energy per nucleon dictates results when nuclides break apart (fission) or fuse together (fusion)

(keep in mind that binding energies are thought of as negative, as in energy level diagrams on previous slide)



Bushberg

Phenomenology of Stability

- Stability strongly favors nuclides with even numbers of protons and/or neutrons
  - ~50% are Even-Even
  - ~25% are Odd-even
  - ~25% are Even-Odd
  - Only 4 out of 266 stable nuclides are Odd-Odd! The heaviest stable Odd-Odd nuclide is ^{14}N.
- "Magic Numbers" -- analogous to closed atomic shells
  - Result in many stable isotopes or isotones
  - Magic nuclei are particularly stable and more "inert"
  - Magic #'s: 2, 8, 20, 28, 50, 82, 126

Nuclear Binding and Stability

- Protons and neutrons are more stable in a nucleus than free. The binding energy is the amount by which the nucleus' energy (i.e. mass) is reduced w.r.t. the combined energy (i.e. mass) of the nucleons.

- Example: N-14 atom - Measured mass of N-14 = 14.00307 u

  mass of 7 protons = 7 * (1.00727 u) = 7.05089 u

  mass of 7 neutrons = 7 * (1.00866 u) = 7.06062 u

  mass of 7 electrons = 7 * (0.00055 u) = 0.00385 u

  mass of component particles of N-14 = 14.11536 u

Binding energy is mass difference: E_{bind} = 0.11229 u = 104.5 MeV

Radioactive Decay

Unstable nuclei change (decay) towards stable states

The transformation involves emission of secondary particles (*radiation*):

$$ {}^{A}_{Z}X \rightarrow {}^{A'}_{Z'}Y^{[*]} + W + Q $$

parent nucleus X	transforms →	daughter nucleus Y [possibly excited *]	+	radiation particle(s) W	+	additional energy liberated in the decay Q

Q can be shared between the *X*, *Y*, and *W* particles. *Y* is frequently unstable itself.

Conservation principles:

the following are conserved in radioactive transitions

- Energy (equivalently, mass)
- Charge
- Linear momentum
- Angular momentum (including intrinsic *spin*)
- Number of nucleons, and lepton number (electron family)

Radioactive Decay Processes

The decay processes are named for the (primary) radiation particle emitted in the transition:

- **alpha** $$ {}^{A}_{Z}X \rightarrow {}^{A-4}_{Z-2}Y + \alpha + Q $$

- **beta**

  isobaric $$ {}^{A}_{Z}X \rightarrow {}^{A}_{Z\mp 1}Y + \beta^{\pm} + \nu + Q $$

  alternative mechanism to β^+ decay is *electron capture*

- **gamma** $$ {}^{A[m]}_{Z}X^{[*]} \rightarrow {}^{A}_{Z}X + \gamma $$

  isomeric

  alternative mechanism is *internal conversion*

Decay Rate

Radionuclide decay probability is constant in time,

thus, the number decaying in a time *dt* is proportional to the number present, *N*, and the amount of time *dt*:

$$-dN = \lambda N \, dt$$

where λ is a radionuclide-dependent proportionality or probability constant
(Question: what are units of λ?)

$$\int \frac{dN}{N} = -\lambda \int dt \qquad\qquad N(t) = N_0 e^{-\lambda t}$$

$N(t)$ = number of radionuclides at time t
N_0 = number at time t = 0
λ = characteristic decay time constant

The *half-life*, $T_{1/2}$, is the time it takes for a sample to decay to one-half of its original number, or half of its original *activity*.

$$T_{1/2} = \frac{\ln(2)}{\lambda} = \frac{0.693}{\lambda} \qquad\qquad N(t) = N_0 2^{-\left(\frac{t}{T_{1/2}}\right)}$$

Probability Distributions

Governing nuclear decay and counting

also very common elsewhere

1. Binomial Distribution

Random independent processes with two possible outcomes

Probability of ***r*** successes in ***n*** tries;
p is probability of success in single trial

$$P_{\text{binomial}}(r) = \frac{n!}{r!(n-r)!} p^r (1-p)^{n-r}$$

2. Poisson Distribution

Approximates binomial distribution when ***n*** is large and ***p*** is small
conditions met by radioactive decay

mean of distribution = μ
variance of distribution = μ

$$P_{\text{Poisson}}(r) = \frac{\mu^r \exp(-\mu)}{r!}$$

3. Gaussian or Normal Distribution

Approximates Poisson distribution if average number of successes is large (e.g. >20)

mean of distribution = μ
variance of distribution = σ^2

$$P_{\text{Gaussian}}(r) = \frac{1}{\sigma\sqrt{2\pi}} \exp\left(-\frac{(r-\mu)^2}{2\sigma^2}\right)$$

Alpha Decay

An alpha particle is two protons and two neutrons
(helium nucleus)

$$\alpha = {}^{4}_{2}\mathrm{He}^{+2}$$

General form of alpha decay process

$${}^{A}_{Z}X \rightarrow {}^{A-4}_{Z-2}Y + \alpha + Q$$

- Alpha particle always carries Q energy as kinetic energy (**monoenergetic**)
- Alpha decay occurs with **heavy nuclides (A > 150)**
- Commonly followed by isomeric emission of photons,
- which can also result in electron emission (see internal conversion slide)

Beta Decay

A beta(minus, β^-) particle is indistinguishable from an electron.

There are also beta(plus, β^+) particles. These are indistinguishable from electrons, *except with positive charge* (of the same magnitude).

In β^- decay, a ***neutron is converted into a proton*** (Z→Z+1, A unchanged)
In β^+ decay, a ***proton is converted into a neutron*** (Z→Z-1, A unchanged)

The general form:

β^- $$ {}^{A}_{Z}X \rightarrow {}^{A}_{Z+1}Y + \beta^- + \bar{\nu}_e + Q $$

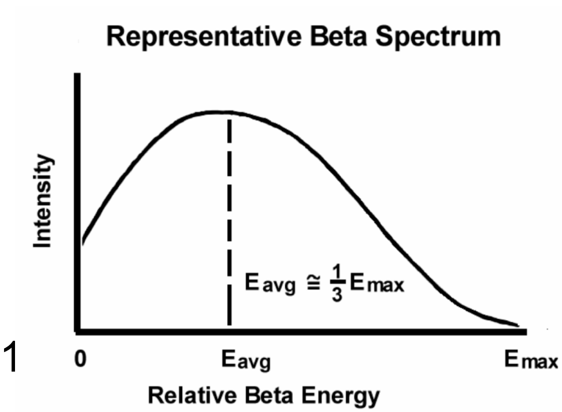
β^+ $$ {}^{A}_{Z}X \rightarrow {}^{A}_{Z-1}Y + \beta^+ + \nu_e + Q $$

e.g. $$ {}^{18}_{9}F \rightarrow {}^{18}_{8}O + \beta^+ + \nu_e + 0.635\,MeV $$

In each case

the fixed Q is shared by β and ν in continuous way

beta particles are emitted with a range of energy



the decay products include a neutrino (ν_e) or an anti-neutrino ($\bar{\nu}_e$)

Neutrinos are leptons with no charge, spin 1/2, and mass < 1

Electron Capture - An alternative and competing mechanism to β+ decay

In electron capture, a **proton + orbital electron convert into a neutron (p + e^- = n)**, rather than a proton converting into p = n + β^+.

A neutrino and additional energy, Q, are also emitted in the electron capture process:

$$ {}_{Z}^{A}X + e^- \rightarrow {}_{Z-1}^{A}Y + \nu_e + Q $$

Capture of an orbital electron creates a vacancy in an inner electron shell, which is filled by another electron from a higher shell. This results in characteristic x-rays, or Auger electrons.

An example of e.c. relevant to nuclear medicine is the following decay:

$$ {}_{81}^{201}Tl + e^- \rightarrow {}_{80}^{201}Hg^* + \nu + Q $$

None of the products of this decay are used in imaging, rather, characteristic x-rays filling the vacancy are detected by gamma cameras.

Characteristic x-rays also mono-energetic (transitions between electron orbits), but several nearby orbital energies can give rise to apparent spread of photon energies.

Gamma Decay

Gamma decay is an isomeric transition that follows the occurrence of alpha or beta decay.

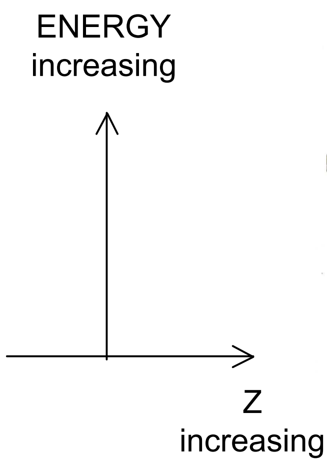
$$^{A[m]}_{Z}X^{[*]} \longrightarrow {}^{A}_{Z}X + \gamma$$

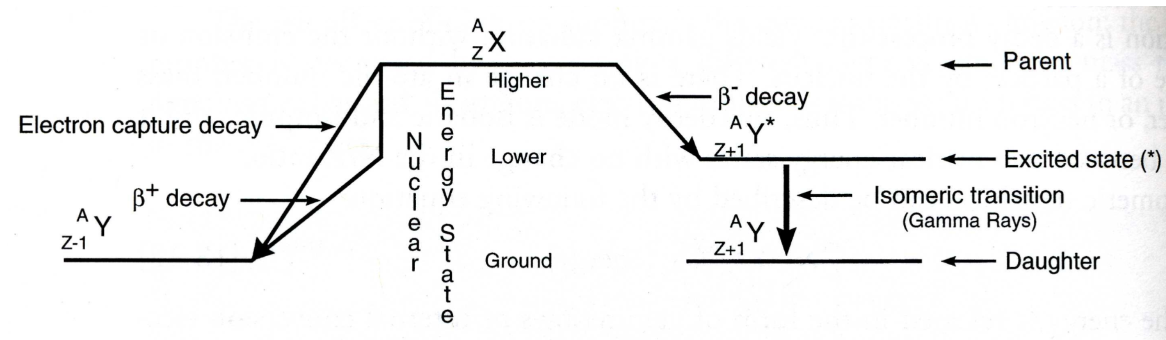
The parent in this case (which is the daughter of the preceding α or β decay, or electron capture) can be in an excited state, * ,that (essentially) immediately transitions to a lower state via emission of a gamma, or it can be in a *metastable* state *m*, which can have a life-time of between 10^{-12} sec. and ~600 years. Decay of metastable states also follow the exponential decay law, and thus have characteristic decay times.

Internal Conversion

- Alternatively, the energy liberated from the isomeric transition can be delivered to an electron ejected from the atom (like Auger electrons vs. char. x-rays).
- Again, electrons rearrange to fill the vacancy left by the i.c. electron, resulting in characteristic x-rays and/or Auger electrons.
- Gamma emission and i.c. electron compete in the same nuclide decay.

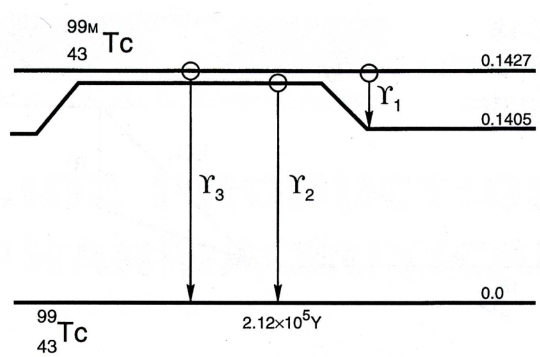
Decay Schemes





Bushberg

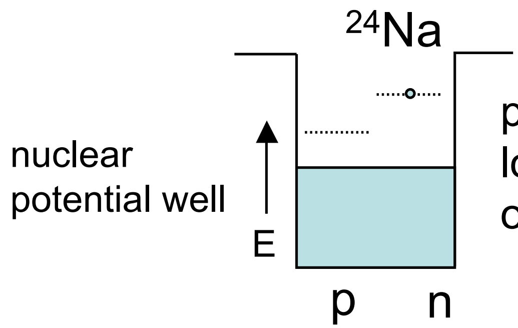
Example: ^{99m}Tc



Decay Data Table

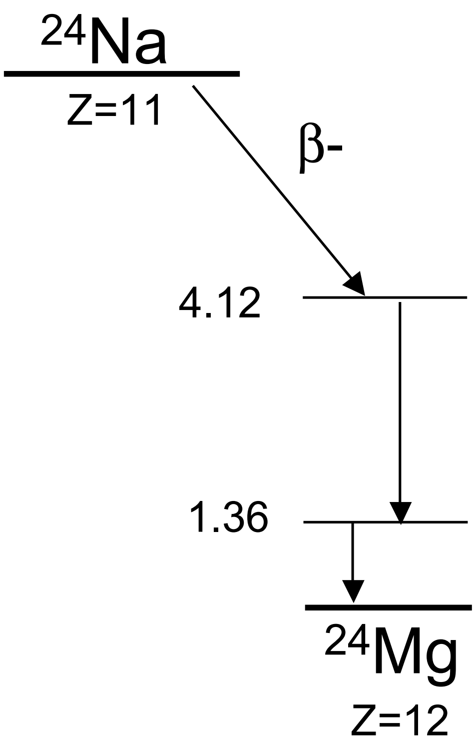
Radiation		**Mean Number per Disintegration**	**Mean Energ per Particl (MeV)**
Gamma	1	0.0000	0.0021
M Int Con Elect		0.9860	0.0016
Gamma	2	0.8787	0.1405
K Int Con Elect		0.0913	0.1194
L Int Con Elect		0.0118	0.1377
M Int Con Elect		0.0039	0.1400
Gamma	3	0.0003	0.1426
K Int Con Elect		0.0088	0.1215
L Int Con Elect		0.0035	0.1398
M Int Con Elect		0.0011	0.1422
K Alpha-1 X-Ray		0.0441	0.0183
K Alpha-2 X-Ray		0.0221	0.0182
K Beta-1 X-Ray		0.0105	0.0206
KLL Auger Elect		0.0152	0.0154
KLX Auger Elect		0.0055	0.0178
LMM Auger Elect		0.1093	0.0019
MXY Auger Elect		1.2359	0.0004

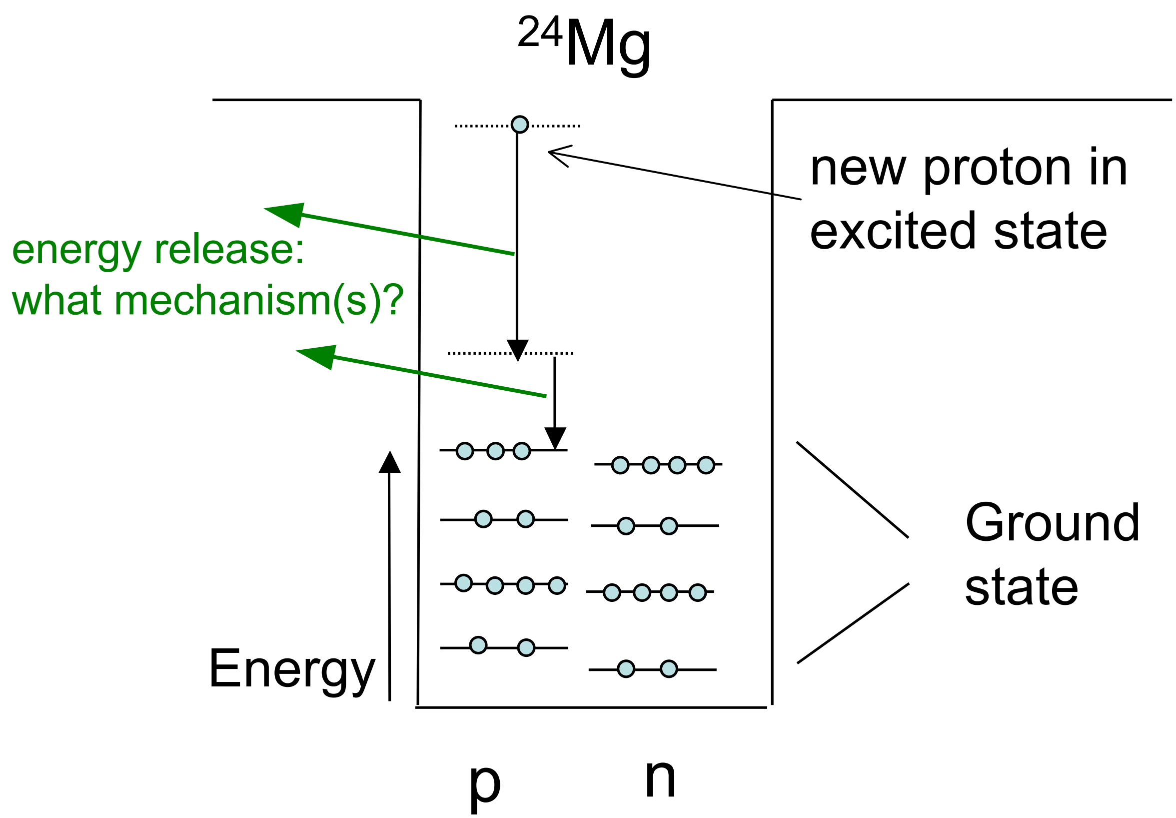
Consider $^{24}Na \rightarrow {}^{24}Mg$



proton level open at a lower energy than an occupied neutron level

$$n \rightarrow p + e^{-} + \bar{\nu}_e$$





Competing Decay Processes

1. Positron decay competes with ___ , and is ___:
(a) Gamma decay, isomeric
(b) Alpha decay, isobaric
(c) Internal conversion, isomeric
(d) Electron capture, isobaric

2. Gamma decay competes with ___ , and is ___:
(a) Auger emission, isomeric
(b) Alpha decay, isobaric
(c) Internal conversion, isomeric
(d) Electron capture, isobaric

3. Alpha decay occurs when:
(a) $Z > N$
(b) $Z = N$
(c) $Z < N$
(d) any Z, N combination

Radionuclide Production

- We would like to use short-lived isotopes to minimize patient radiation dose, but long enough lived to for radiopharmaceutical production & image acquisition
- Unlike an X-ray device, we can't turn off a radionuclide
- Remaining radionuclide in nature are long-lived (short-lived have decayed away)
- So if we want a short-lived isotope we must produce it

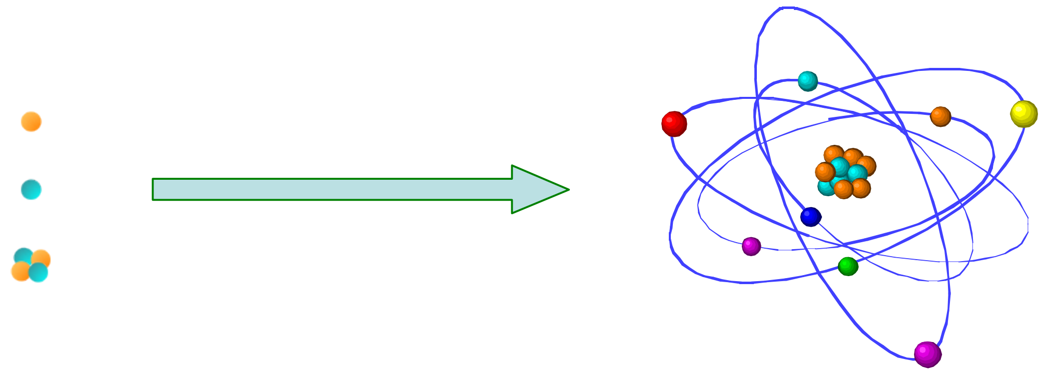
Preferable Characteristics for Nuclear Medicine Imaging Radionuclides

- half-life ~ 1-10 hours ($T_{1/2}$ ~ minutes to days are used)
- emissions:
  - 100-300 keV gamma rays (~50-600 keV are used)
  - positrons (PET)
- no other emissions
- high specific activity (radionuclide fraction of isotope)
- suitable chemical properties for incorporation into biomolecules
  - direct substitution
  - analogs/precursors
  - chelation

Note: different requirements for **therapeutic** radionuclide emissions, e.g. beta-minus & longer-lived

Production: Nuclear Bombardment

Hit nucleus of stable atoms with sub-nuclear particles: neutrons, protons, alpha particles etc.



There are two main methods of performing this bombardment

1. Inserting target in a nuclear reactor - fine for longer-lived isotopes as some time is needed for processing and shipment

We can also use longer-lived isotopes from a nuclear reactor that decay to a short-lived radioisotope in a portable 'generator'

2. Using a charged-particle accelerator called a 'cyclotron' - needed locally for short-lived isotopes ($T_{1/2}$ ~ 1 to 100 min). We have two here at UWMC

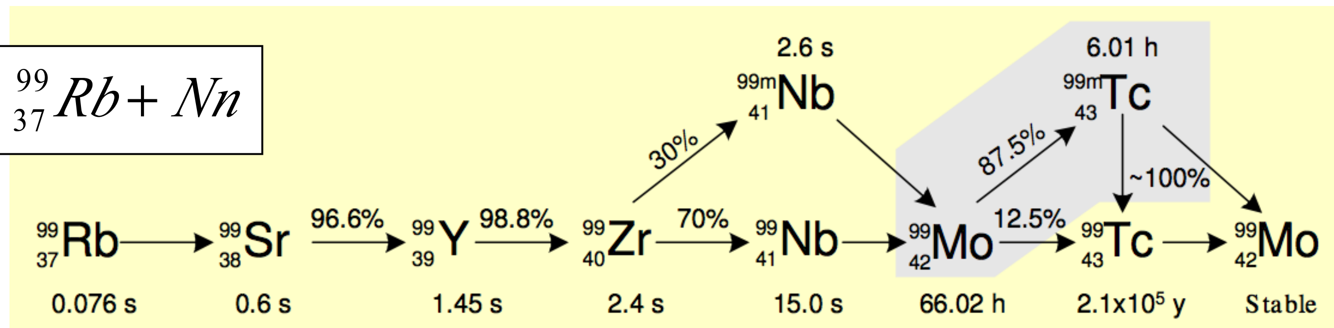
Reactor Produced Isotopes

Fission Fragments

Most important reaction $\quad ^{235}U + n \rightarrow {}^{236}U^*$

decays spontaneously via nuclear fission and a (hopefully) controlled chain reaction producing lots of protons, neutrons, alpha particles etc.

$$^{236}_{92}U^* \rightarrow {}^{137-N}_{55}Cs + {}^{99}_{37}Rb + Nn$$



sample fission product decay chain

1. Fission products always have an **excess of neutrons**, because N/Z is substantially higher for ^{235}U than it is for nuclei falling in the mass range of the fission fragments, even after the fission products have expelled a few neutrons. These radionuclide therefore **tend to decay by beta-minus** emission
2. Fission products **may be carrier free** (no stable isotope of the element of interest is produced), and therefore radionuclides can be produced with **high specific activity** by chemical separation. (Sometimes other isotopes of the element of interest are also produced in the fission fragments. For example, high-specific-activity ^{131}I cannot be produced through fission because of significant contamination from ^{127}I and ^{129}I.)
3. The **lack of specificity of the fission process is a drawback** that results in a relatively **low yield** of the radionuclide of interest among a large amount of other radionuclides.

Reactor Produced Isotopes

Neutron Activation

$$(n,\gamma):\ {}^{A}_{Z}X + n \rightarrow {}^{A+1}_{Z}X^{*} \rightarrow {}^{A+1}_{Z}X + \gamma$$

$$(n,p):\ {}^{A}_{Z}X + n \rightarrow {}^{A}_{Z-1}Y + p$$

1. Because **neutrons are added** to the nucleus, the products of neutron activation generally lie above the line of stability, and thus **tend to decay by β-** emission

2. The most common production mode is by the (n,γ) reaction, and the products of this reaction are **not carrier free** because they are the same chemical element as the bombarded target material. It is possible to produce carrier-free products in a reactor by using the (n,p) reaction (e.g., ^{32}P from ^{32}S) or by activating a short-lived intermediate product, such as ^{131}I from ^{131}Te using the reaction $^{130}\mathrm{Te}(\mathrm{n},\gamma)^{131}\mathrm{Te} \xrightarrow{\beta^-} {}^{131}\mathrm{I}$

3. Even in intense neutron fluxes, only a **very small fraction of the target nuclei actually are activated**, typically 1 : 10^6 to 10^9 Thus an (n,γ) product may have **very low specific activity** because of the overwhelming presence of a large amount of unactivated stable carrier (target material).

Generators

- Use a 'mother' isotope that has a long half-life that decays to a short half-life 'daughter' that can be used for imaging.
- The mother isotope is produced in a nuclear reactor (fission product or by neutron bombardment) and then shipped in a 'generator'.
- As needed, the daughter isotope is 'eluted' and combined into a radiopharmaceutical
- Workhorse of general nuclear medicine

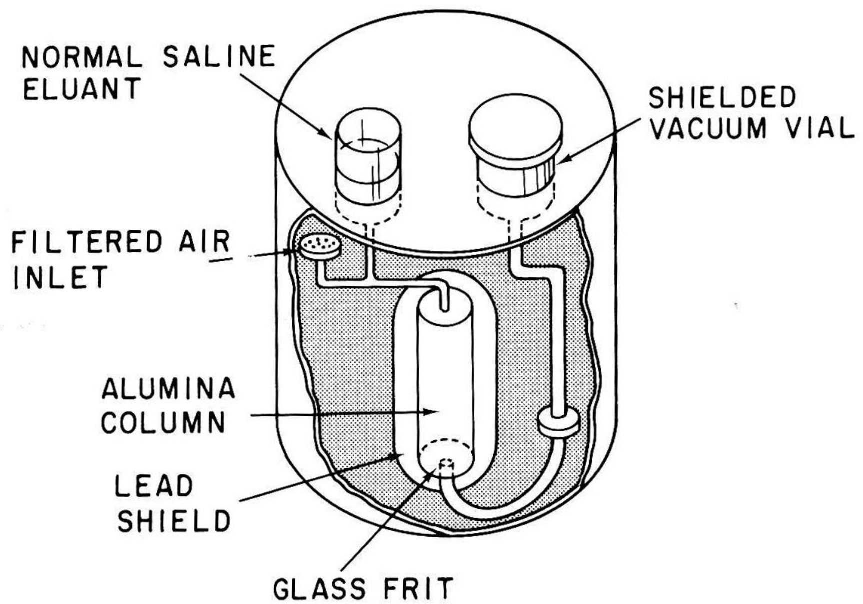


Fig. 7-5. Cross-sectional drawing of a ^{99}Mo-^{99m}Tc generator. (Courtesy of the Society of Nuclear Medicine and Thomas R. Gnau.)

Generator Radionuclides

- ^{99m}Tc (daughter isotopes) generators are by far the most common
- The mother isotope is ^{99}Mo, which is reactor produced by
- – fission product (higher specific activity)
- – neutron bombardment (lower specific activity)
- The generators typically replaced monthly

Table 7-3
Some Radionuclide Generators Used in Nuclear Medicine

Daughter†	Decay Mode	$T_{1/2}$	Parent	$T_{1/2}$
^{68}Ga	β^+,EC	68 min	^{68}Ge	275 days
^{82}Rb	β^+,EC	1.3 min	^{82}Sr	25 days
^{87m}Sr	IT	2.8 hours	^{87}Y	80 hours
^{99m}Tc	IT	6 hours	^{99}Mo	66 hours
^{113m}In	IT	100 min	^{113}Sn	120 days

†Generator product.

EC: electron conversion
IT: isomeric transition

Generator Activity Levels

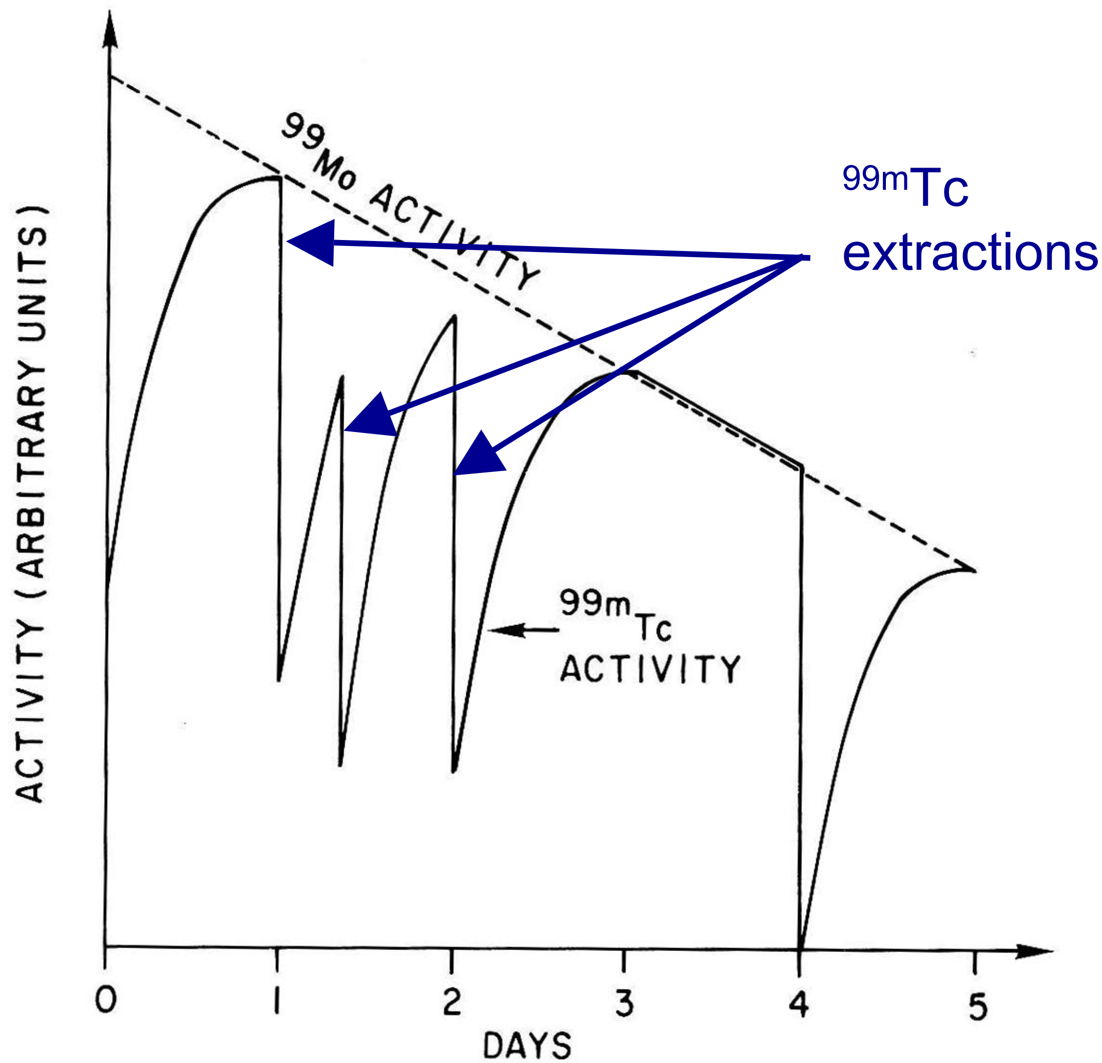


Fig. 7-6. Buildup and decay of ^{99m}Tc generator eluted on days 0, 1, 1.4, 2, and 4.

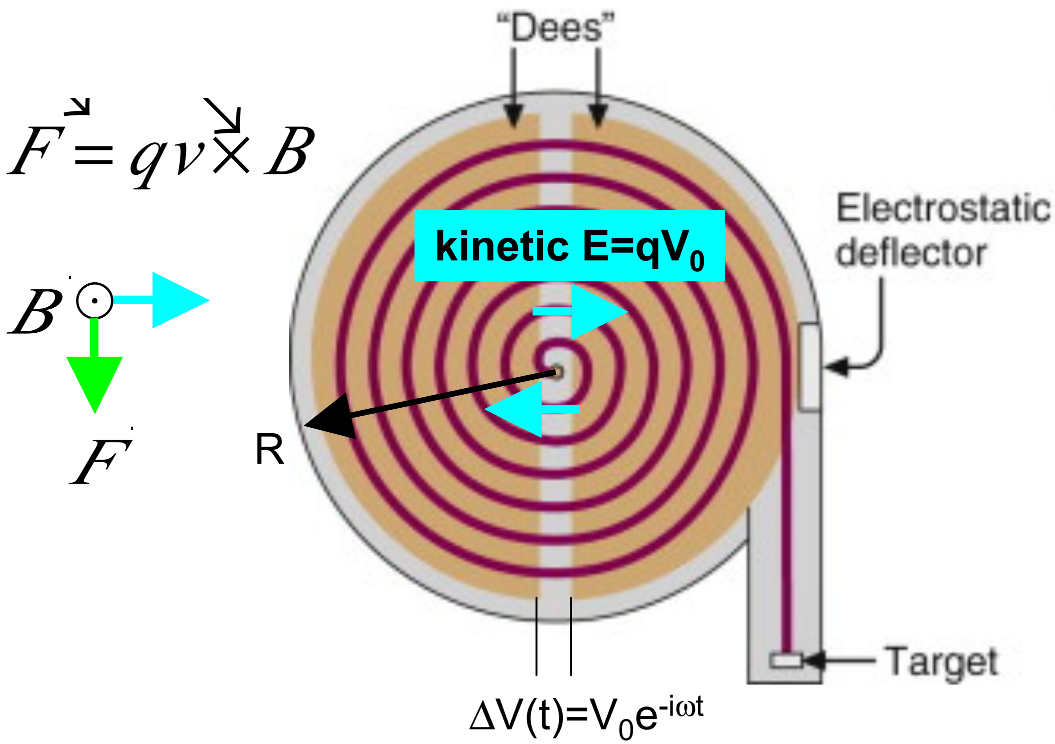
Cyclotron Production

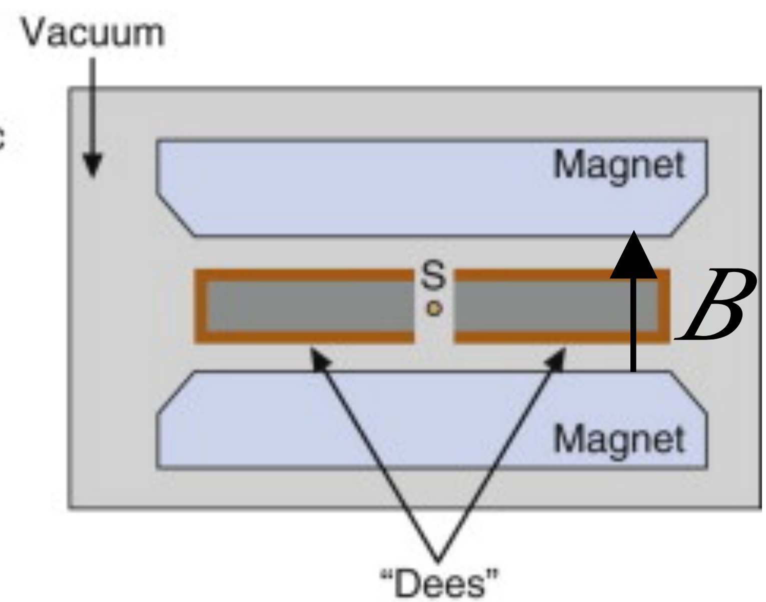
- Typically accelerate protons (H^- ion) using alternating electric fields.
- The magnet is used to bend the path of the charged particle: ΔV(t) frequency is selected to continue acceleration around the Dees
- The proton is then deflected to hit the target

$$E(MeV) \approx 0.0048 \frac{(B \cdot R \cdot Z)^2}{A}$$

B=magnetic field
R=radius
Z,A=atomic,mass #s

$$\vec{F} = q\vec{v} \times B$$





from *Physics in Nuclear Medicine*, Cherry, Sorenson, Phelps, 4th Ed

Cyclotron Products

- Since we are using proton bombardment we **change the element** and typically lie below the line of stability. Thus decay is typically by **positron emission**.
- Cyclotrons can be located locally, thus allowing for short lived isotopes, reducing patient dose.
- Cyclotrons, however, are very expensive to buy and operate. Often there are distribution networks.

Some Cyclotron-produced Radionuclides Used in Nuclear Medicine

Product	Decay Mode	Common Production Reaction	Natural Abundance of Target Isotope (%)
^{11}C	β^+	$^{10}B(d,n)^{11}C$	19.7
		$^{11}B(p,n)^{11}C$	80.3
^{13}N	β^+	$^{12}C(d,n)^{13}N$	98.9
^{15}O	β^+	$^{14}N(d,n)^{15}O$	99.6
^{18}F	β^+,EC	$^{20}Ne(d,\alpha)^{18}F$	90.9
^{22}Na	β^+,EC	$^{23}Na(p,2n)^{22}Na$	100
^{43}K	(β^-,γ)	$^{40}Ar(\alpha,p)^{43}K$	99.6
^{67}Ga	(EC,γ)	$^{68}Zn(p,2n)^{67}Ga$	18.6
^{111}In	(EC,γ)	$^{109}Ag(\alpha,2n)^{111}In$	48.7
		$^{111}Cd(p,n)^{111}In$	12.8
^{123}I	(EC,γ)	$^{122}Te(d,n)^{123}I$	2.5
		$^{124}Te(p,3n)^{123}I$	4.6
^{201}Tl	(EC,γ)	$^{201}Hg(d,2n)^{201}Tl$	13.2

Radionuclides used in Nuclear Medicine Studies

Radionuclide	Decay Mode	Principal Photon Emissions	Half-Life	Primary Use
11-C	β+	511 keV	20.4 min	Imaging
13-N	β+	511 keV	9.97 min	Imaging
15-O	β+	511 keV	2.03 min	Imaging
18-F	β+	511 keV	110 min	Imaging
32-P	β–	—	14.3 d	Therapy
67-Ga	EC	93, 185, 300 keV	3.26 d	Imaging
82-Rb	β+	511 keV	1.25 min	Imaging
89-Sr	β–	—	50.5 d	Therapy
99m-Tc	IT	140 keV	6.02 hr	Imaging
111-In	EC	172, 247 keV	2.83 d	Imaging
123-I	EC	159 keV	13.2 hr	Imaging
125-I	EC	27-30 keV x rays	60.1 d	In vitro assays
131-I	β–	364 keV	8.04 d	Therapy/imaging
153-Sm	β–	41, 103 keV	46.7 hr	Therapy
186-Re	β–	137 keV	3.8 d	Therapy
201-Tl	EC	68-80 keV x rays	3.04 d	Imaging

EC, electron capture; IT, isomeric transition.

Particle Interactions with Matter

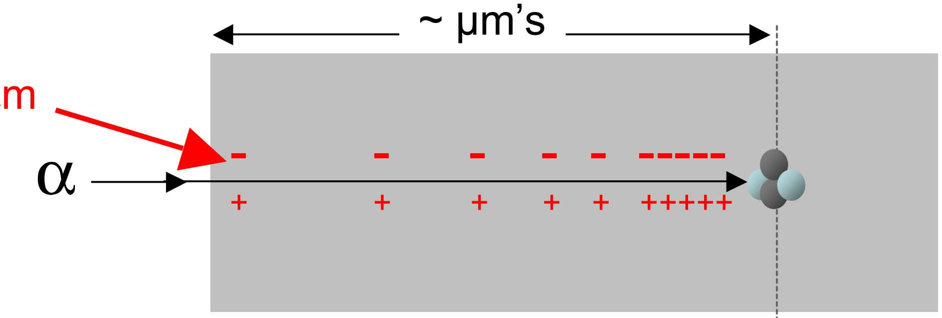
Interactions in Matter: α-rays

- Energy loss is a more or less continuous slowing down process as it travels through matter; linear energy transfer (LET, eV/μm)
- Range (penetration depth) depends only upon its initial energy and its average energy loss rate in the medium; Approx. straight line penetration
- Range for an α particle in tissue is on the order of *μ*m.

Specific Ionization (SI) = (ion pairs generated)/μm

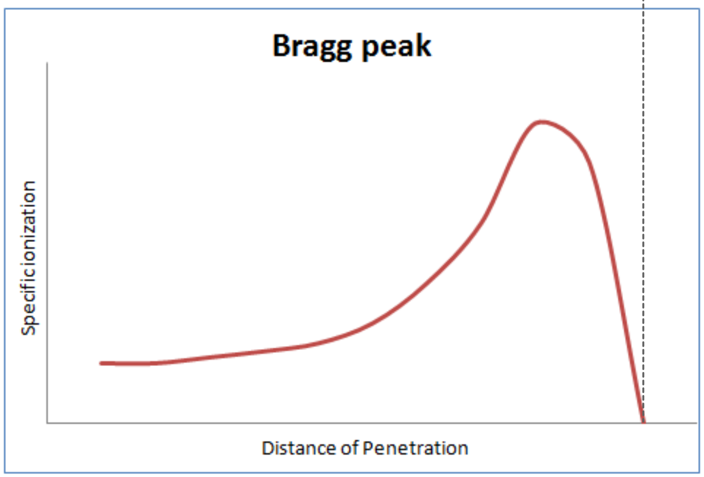
LET = SI * (average eV/ion pair)

∝ (charge)^2/(kinetic energy)



As the α penetrates it slows down, making ionizing collisions more likely, resulting in a peak specific ionization (Bragg peak).

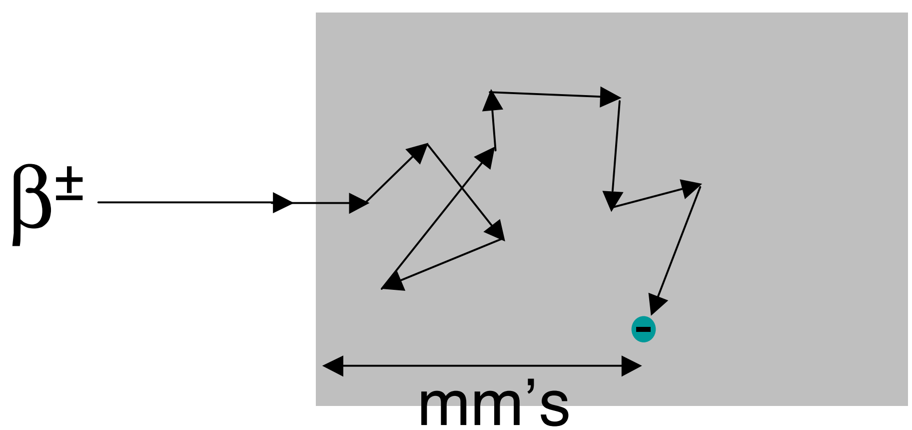
Eventually it slows so much it looses ionizing capability and becomes electrically neutral.



Interactions in Matter: β-rays

Beta particles emitted with a continuous distribution of energies

- β particle ranges vary from one electron to the next, even for βs of the same energy in the same material.
- This is due to different types of scattering events the β encounters (i.e., scattering events, bremsstrahlung-producing collisions, etc.).
- The β **range** is often given as the **maximum distance** the **most energetic** β can travel in the medium.
- The range for β particles emitted in tissue is on the order of mm's.



Interactions in Matter: x- and γ-rays

Exponential absorption/transmission:
(narrow beam geometry)

$$N(x) = N_0 e^{-\mu x}$$ = number remaining after traversing distance x

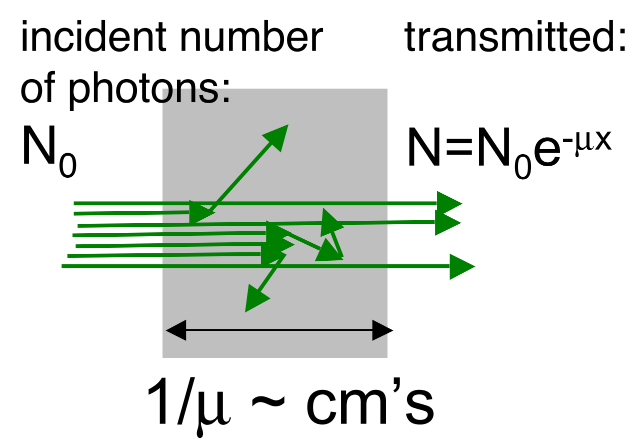
$\mu=\mu(E,Z,\rho,\text{interaction})$; depends on photon energy, material properties, and interaction type

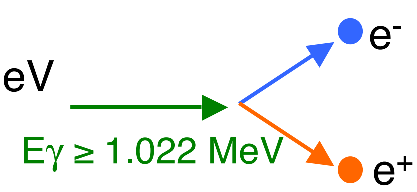
Photoelectric effect
•all photon energy transferred to an electron in a single-interaction
•probability ~ Z^n/E^3 (n~3-5)

Compton scattering
•partial photon energy transferred to e^-, gamma continues in random scattered direction
•all scatter directions possible (0^o-180^o)
→ forward directions preferential

Coherent (Rayleigh) scattering
•photon deflected with very little energy loss
•only significant at low photon energies (<50 keV)

Pair production
•positron-electron pair is created
•requires photons above 1.022 MeV





Linear and Mass Attenuation Coefficients

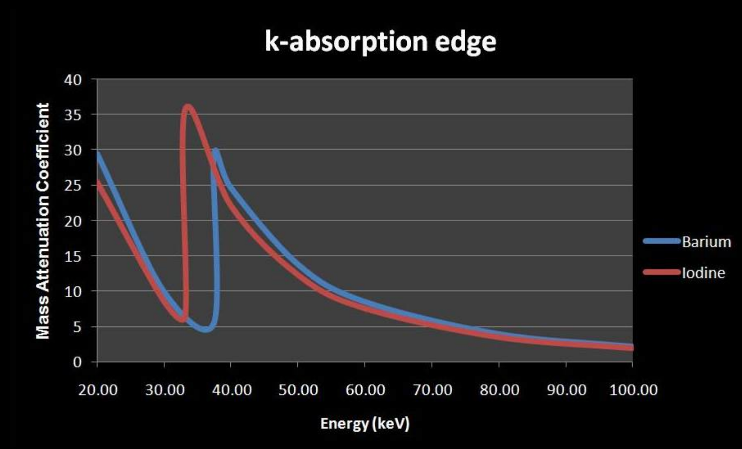
Linear attn. coefficient:

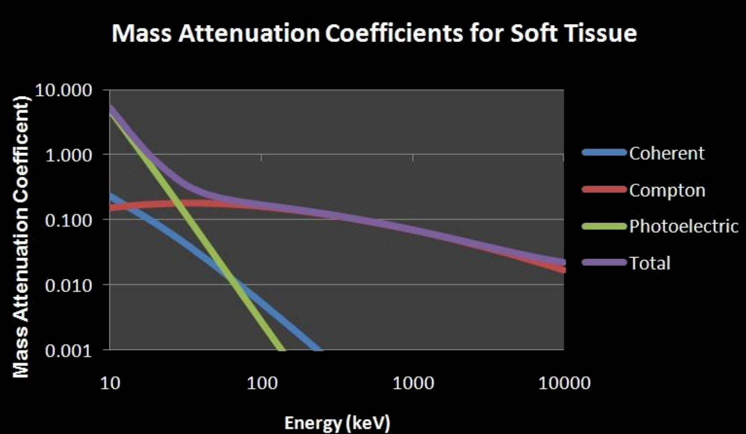
$\mu = \mu(E, Z, \rho, \text{interaction})$; depends on photon energy, material properties, and interaction type

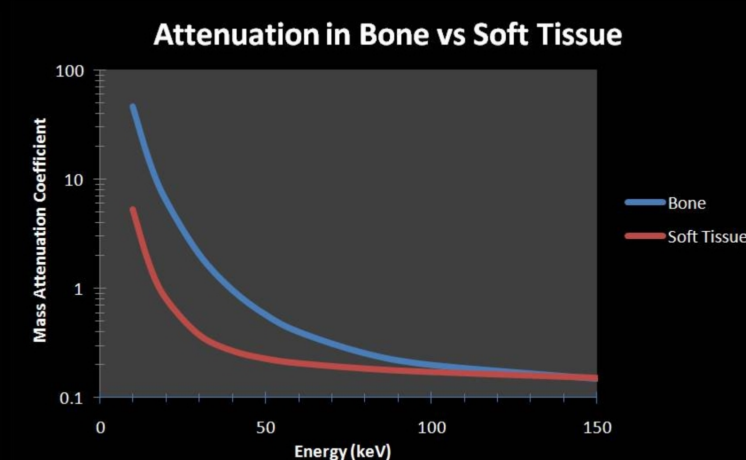
units = inverse length

Mass attn. coefficient = μ/ρ

units = cm^2/g



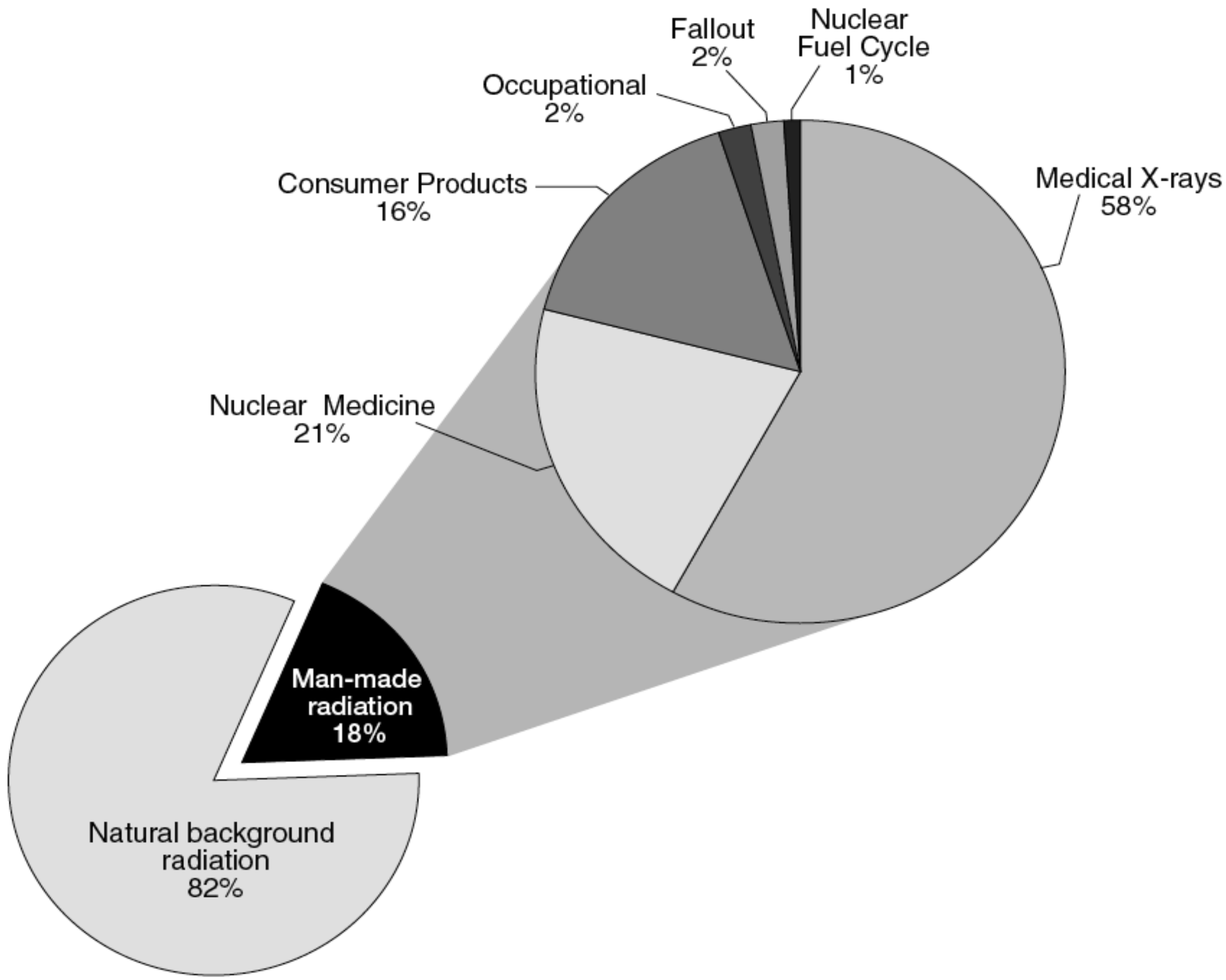




Radiation Dosimetry

a few beginning basics to a complex topic

Sources of Radiation Exposure in U.S.



This figure is based on data from “Ionizing Radiation Exposure of the Population of the United States”, *National Council on Radiation Protection and Measurements*, No.93, 1987.

This figure is based on data from “Ionizing Radiation Exposure of the Population of the United States”, *National Council on Radiation Protection and Measurements*, No.93, 1987.

Dosimetry Descriptors - From Ionizing Radiation

<u>Exposure:</u> Charge per mass of air, **Coulomb/kg** = **3876 roentgens**
Can be measured directly
Does not account for biological effects

<u>Absorbed Dose:</u>
Energy per mass of tissue, Joules/kg = **gray (Gy)** = 100 rads
Usually calculated from exposure measurement
Does not account for biological effects

<u>Equivalent Dose:</u>
(Absorbed Dose) * radiation weighting factor (w_R or Q factor)
Also energy/mass, but units are **sieverts (Sv)** = 100 rem
Biological effects of absorbed dose depend on the type of radiation

<u>Effective Dose:</u>
Sum Over All Tissues[(Equivalent Dose$_T$) * tissue weighting factor (w_T)]
Also measured in **Sv**

The risk of cancer from a dose equivalent depends on the organ receiving the dose. The quantity "effective dose" is used to compare the risks when different organs are irradiated.

Estimating Effective Dose

To go from absorbed dose (Gy) to equivalent dose (Sv), need:

Radiation weighting factors

Type	w_R
Photons	1
Electrons (β), muons	1
Neutrons (varies with energy)	5-20
Protons	5
alpha (α), heavy nuclei	20

For CT and PET, 1Gy = 1Sv

International Commission on Radiological Protection, ICRP, Publ. 60, 1990 (www.icrp.org, *Annals of the ICRP*)

To go from Equivalent Dose (Sv) to Effective Dose (Sv), need:

Tissue weighting factors

Tissue or organ	w_T
Gonads	0.20
Bone marrow (red)	0.12
Colon	0.12
Lung	0.12
Stomach	0.12
Bladder	0.05
Breast	0.05
Liver	0.05
Esophagus	0.05
Thyroid	0.05
Skin	0.01
Bone surface	0.01
Remainder	0.05
Total	**1.00**

$$w_T = \frac{D_{WB}(P)}{D_T(P)}$$

$D_{WB}(P)$= absorbed dose to the *whole body* that has probability *P* of causing cancer

$D_T(P)$ = absorbed dose in a *single organ, T,* that has probability *P* of causing cancer in that organ

ALARA: As Low As Reasonable Achievable

TABLE 23-18. NUCLEAR REGULATORY COMMISSION (NRC) REGULATORY REQUIREMENTS: MAXIMUM PERMISSIBLE DOSE EQUIVALENT LIMITS[a]

Limits	Maximum permissible annual dose limits	
	mSv	rem
Occupational limits		
Total effective dose equivalent	50	5
Total dose equivalent to any individual organ (except lens of eye)	500	50
Dose equivalent to the lens of the eye	150	15
Dose equivalent to the skin or any extremity	500	50
Minor (<18 years old)	10% of adult limits	10% of adult limits
Dose to an embryo/fetus[b]	5 in 9 months	0.5 in 9 months
Nonoccupational (public limits)		
Individual members of the public	1.0/yr	0.1/yr
Unrestricted area	0.02 in any 1 hr[c]	0.002 in any 1 hr[c]

[a]These limits are exclusive of natural background and any dose the individual has received for medical purposes; inclusive of internal committed dose equivalent and external effective dose equivalent (i.e., total effective dose equivalent).

[b]Applies only to conceptus of a worker who declares her pregnancy. If the limit exceeds 4.5 mSv (450 mrem) at declaration, conceptus dose for remainder of gestation is not to exceed 0.5 mSv (50 mrem).

[c]This means the dose to an area (irrespective of occupancy) shall not exceed 0.02 mSv (2 mrem) in any 1 hour. This is not a restriction of instantaneous dose rate to 0.02 mSv/hr (2 mrem/hr).

Shielding

Distance

Exposure time

Average Dose Equivalent

TABLE 23-3. AVERAGE ANNUAL OCCUPATIONAL EFFECTIVE DOSE EQUIVALENT IN THE UNITED STATES

Occupational category	Average annual total effective dose equivalent	
	mSv	mrem
Uranium miners[a]	12.0	1,200
Nuclear power operations[b]	6.0	600
Airline crews	1.7	170
Diagnostic radiology and nuclear medicine techs	1.0	100
Radiologists	0.7	70

Adapted for measurably exposed personnel from National Council on Radiation Protection and Measurements. *Exposure of the U.S. population from occupational radiation.* NCRP report no. 101. Bethesda, MD: National Council on Radiation Protection and Measurements, 1989.
[a]Includes 10 mSv (1 rem) from high LET (α) radiation.
[b]Includes 0.5 mSv (50 mrem) from high LET (α) radiation.
LET, linear energy transfer.

Bushberg et al, The Essential Physics of Medical Imaging, Lippencott, Williams & Wilkins, Philadephia, 2002.

TABLE 9.1. *Characteristics of common radionuclides*

Nuclide	Photons (keV)	Production mode	Decay mode	Half-life ($T_{1/2}$)
^{67}Ga	93, 185, 296, 388	Cyclotron	EC	78 hr
^{99m}Tc	140	Generator	IT	6 hr
^{111}In	173, 247	Cyclotron	EC	68 hr
^{123}I	159	Cyclotron	EC	13 hr
^{125}I	27, 36	Reactor	EC	60 d
^{131}I	364	Fission product	β	8 d
^{133}Xe	80	Fission product	β	5.3 d
^{201}Tl	70, 167	Cyclotron	EC	73 hr

β, beta decay; EC, electron capture; IT, isomeric transition.

Some Reactor-produced Radionuclides Used in Nuclear Medicine and Radiotracer Kinetics

Radionuclide	Decay Mode	Production Reaction	Natural Abundance of Target Isotope (%)	σ_c (b)*
^{14}C	β^-	$^{14}N(n,p)^{14}C$	99.6	1.81
^{24}Na	(β^-,γ)	$^{23}Na(n,\gamma)^{24}Na$	100	0.53
^{32}P	β^-	$^{31}P(n,\gamma)^{32}P$	100	0.19
		$^{32}S(n,p)^{32}P$	95.0	—
^{35}S	β^-	$^{35}Cl(n,p)^{35}S$	75.5	—
^{42}K	(β^-,γ)	$^{41}K(n,\gamma)^{42}K$	6.8	1.2
^{51}Cr	(EC,γ)	$^{50}Cr(n,\gamma)^{51}Cr$	4.3	17
^{59}Fe	(β^-,γ)	$^{58}Fe(n,\gamma)^{59}Fe$	0.3	1.1
^{75}Se	(EC,γ)	$^{74}Se(n,\gamma)^{75}Se$	0.9	30
^{125}I	(EC,γ)	$^{124}Xe(n,\gamma)^{125}Xe \xrightarrow{EC} {}^{125}I$	0.1	110
^{131}I	(β^-,γ)	$^{130}Te(n,\gamma)^{131}Te \xrightarrow{\beta^-} {}^{131}I$	34.5	0.24

*Thermal neutron capture cross-section, in barns, for (n,γ) reactions (see Section D.1).

Properties of Gamma Rays and Beta Rays

Gamma Rays

massless photons travel potentially long distances in body

➔ emitted with single energy (mono-energetic, allows energy discrimination)

➔ penetration is exponential: $N=N_0e^{-\mu(E,Z,\rho,\text{interaction})*x}$

➔ typical ~ cm-to-m penetration, no limits to penetration depth

➔ difficult to collimate – requires high Z &/or high density material (e.g Pb, W)

Beta Rays (e- & e+)

charged particles with mass undergo many interactions in body

➔ emitted with continuous energy distribution (energy discrimination not effective)

➔ no analytical rule for penetration depth (between exp.&linear)

➔ typical ~ mm penetration, maximum penetration depends on particle E

➔ easy to collimate

Highlights

Line of Stability: N = Z for low Z, N > Z for heavier elements (Z > 20)

Isotopes (const. Z, number of protons)

Isotones (const. N, number of neutrons)

Isobars (const. A, number of protons plus neutrons (atomic mass number))

Radioactive Decay

Alpha (2 protons, 2 neutrons)

mono-energetic

followed by other decays

Beta +/-: Z changes by one, emits β, conserve charge

poly-energetic

Beta+ vs. electron capture; nucleus loses unit charge

Gamma: Isomeric transitions between excited states, no change in Z, A, N

mono-energetic

gamma emission vs. internal conversion

Decay Time Dependence

Exponential $$N(t) = N_0 e^{-\lambda t}$$

alternatively (equivalent) $$N(t) = N_0 2^{-\left(\frac{t}{T_{1/2}}\right)}$$

N(t) = number of radionuclides at time t

N_0 = number at time t = 0

λ = characteristic decay time constant

$$T_{1/2} = \frac{\ln(2)}{\lambda} = \frac{0.693}{\lambda}$$

Slide 18 question answers

1. Atomic nuclei are held together by which force(s):
(a) Weak
(b) Strong
(c) Coulomb
(d) Strong & Coulomb
(e) Strong & Weak

- The weak force governs beta decay (topic not covered).
- The Coulomb force tends to push protons apart because of repulsive force between like charges.
- The strong force is an attractive force between protons and neutrons and counters the repulsive Coulomb force to hold nuclei together. More neutrons are needed in heavier elements to provide more strong force to overcome increased repulsive force of larger number of protons in heavy elements.

2. Purple nuclei decay by:
(a) Alpha
(b) Beta+
(c) Beta-
(d) Gamma

- In the N vs Z figure on slide 18 purple nuclei lie above the gold band of stable nuclei; these represent neutron-rich nuclei that need to reduce neutron number (or increase proton number) in order to be stable.
- Beta-minus decay results in a neutron converting into a proton, thus moving the purple-labeled nuclei to a more stable configuration.

3. Green nuclei decay by:
(a) Alpha
(b) Beta+
(c) Beta-
(d) Gamma

- In the N vs Z figure on slide 18 green nuclei lie below the gold band of stable nuclei; these represent proton-rich nuclei that need to reduce proton number (or increase neutron number) in order to be stable.
- Beta-plus (positron) decay results in a proton converting into a neutron, thus moving the green-labeled nuclei to a more stable configuration.

4. Red nuclei decay by:
(a) Alpha
(b) Beta+
(c) Beta-
(d) Gamma

- Alpha decay only occurs for relatively heavy nuclei (A>150).

Slide 19 question answers

1. Positron decay competes with ___ , and is ___:

(a) Gamma decay, isomeric
(b) Alpha decay, isobaric
(c) Internal conversion, isomeric
(d) Electron capture, isobaric

- Electron capture: represents p+e- → n transition rather than p → n+e+ of positron decay; an orbital electron is 'captured' by a proton. Note conservation of charge in each case. In e.c. the disappearance of the orbital electron creates a shell vacancy that is filled by outer shell electrons, resulting in emission of characteristic x-rays (or Auger electrons).
- In each case, e.c., β+, and β- decay, one nucleon is converted to another, so Z and N each change, but A=Z+N remains constant, which is isobaric.

2. Gamma decay competes with ___ , and is
:

(a) Auger emission, isomeric
(b) Alpha decay, isobaric
(c) Internal conversion, isomeric
(d) Electron capture, isobaric

- Internal conversion: energy from nuclear decay is delivered to an orbital electron rather than a gamma-ray photon. The orbital electron is ejected from the atom leaving a vacant inner shell that is filled by outer shell electrons, resulting in emission of characteristic x-rays (or Auger electrons).
- In this case there is no change in Z, N, or A, so the transition is isomeric.

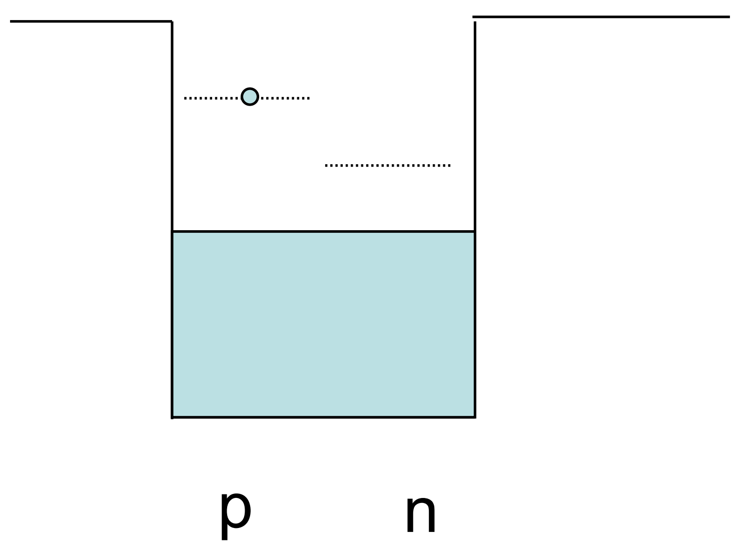
3. Alpha decay occurs when:

(a) Z > N
(b) Z = N
(c) Z < N
(d) any Z, N combination

- Alpha decay only occurs for relatively heavy nuclei (A>150).
- Heavy nuclei have more neutrons than protons in order to provide sufficient attractive strong force between nucleons to overcome high repulsive Coulomb force.

^{18}F to ^{18}O

- Decay occurs because there is a neutron level open at a lower energy than an occupied proton level



$p \to n + e^+ + v$

Positron decay

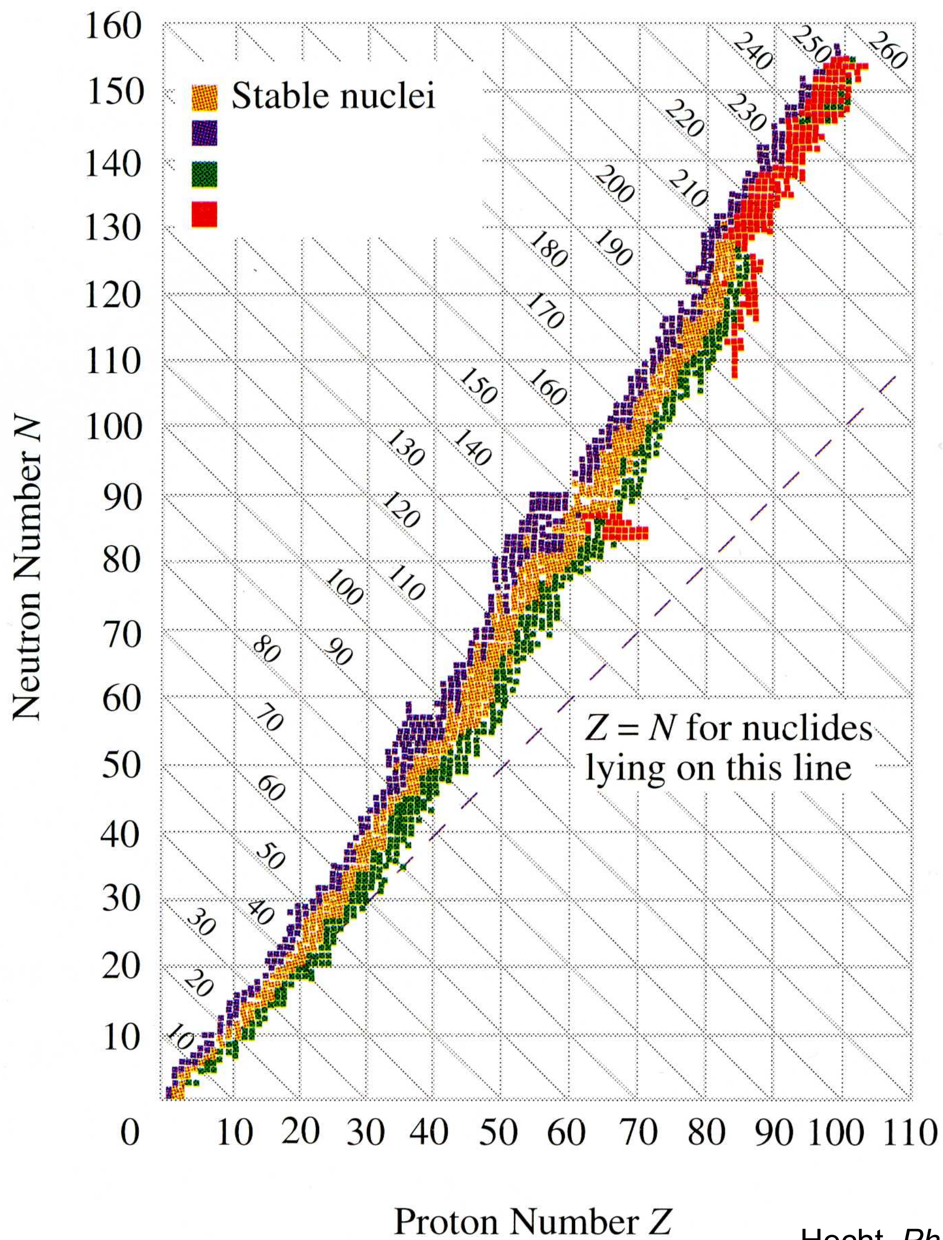
***N* vs. *Z* Chart of Nuclides**

1. Atomic nuclei are held together by which force(s):
(a) Weak
(b) Strong
(c) Coulomb
(d) Strong & Coulomb
(e) Strong & Weak

2. Purple nuclei decay by:
(a) Alpha
(b) Beta+
(c) Beta-
(d) Gamma

3. Green nuclei decay by:
(a) Alpha
(b) Beta+
(c) Beta-
(d) Gamma

4. Red nuclei decay by:
(a) Alpha
(b) Beta+
(c) Beta-
(d) Gamma



Hecht, *Physics*, 1994

Questions

Q1: In heavy nuclei such as ^{235}U:

A. There are more protons than neutrons.

B. Protons and neutrons are equal in number.

C. There are more neutrons than protons.

D. Cannot tell from information given.

C. With higher mass number, more neutrons needed to balance the attraction of all masses (nucleons) with the repulsion between positively charged protons.

Q2: A 10MeV _____ travels at the greatest speed in a vacuum.

A. Alpha particle

B. Neutron

C. Proton

D. Electron

D. The lightest one travels fastest.
(classical or relativistic)

Question and Answer

- 99mTc generators cannot be:
- a. Produced in a cyclotron
- b. Used to dispense more than 1 Ci
- c. Shipped by air
- d. Purchased by licensed users
- e. Used for more than 67 hours

a. ^{99}Mo can be produced in a reactor or from fission products, but it cannot be produced in a cyclotron (^{99}Mo is a beta emitter, requiring the addition of neutrons, not protons).

Raphex Question and Answer

An ideal radiopharmaceutical would have all the following except:

a. Long half-life

b. No particulate emissions

c. Target specificity

d. 150 to 250 keV photons

e. Rapid biological distribution

a: The ideal radionuclide has a short half-life to reduce the radiation dose to the patient