EXUBRION THERAPEUTICS

Authorized User/Radiation Safety Officer Training for Synovetin OA®

Module 2: Radioactivity

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Introduction

- This module introduces basic terminology and common concepts of atomic physics, including atomic structure, radioactivity, and the radiation decay model.
- Upon completion, the reader should be knowledgeable about:
  - Radiation decay
  - Nuclear transformation
  - How to read and understand the decay scheme of various radionuclides.
- Specific properties of Synovetin OA® (tin-117m or ^{117m}Sn) are discussed in the last section.
- Recommended reading:
  - 1.2 NUREG 1556 Vol 7, Revision 1
  - 2.2 Atoms, Radiation, and Radiation Protection (Turner)

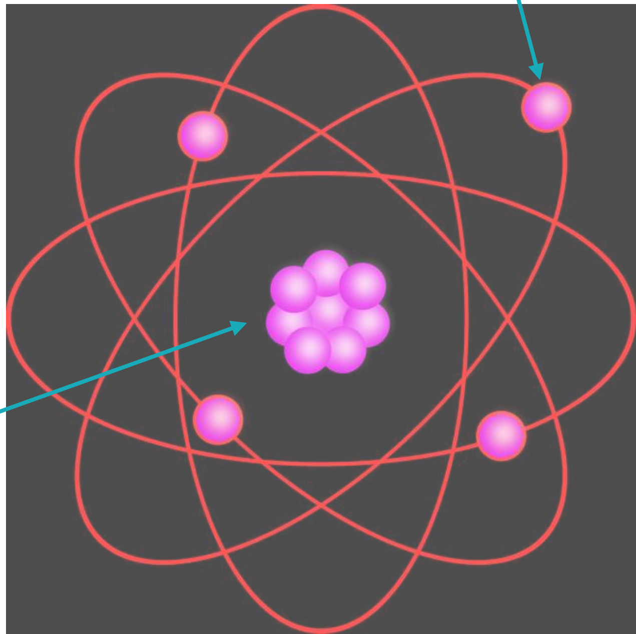
EXUBRION THERAPEUTICS

Outline

- **Part I: The Atom**
  - Atomic structure
  - Atomic number and mass number
  - Chart of nuclides
- **Part II: Radioactive Decay**
  - Activity
  - Half-life
  - Decay equation
  - Alpha decay
  - Beta decay
  - Gamma emission
  - Internal conversion
  - Decay scheme
- **Part III: Properties of Synovetin OA® (^{117m}Sn)**
- **Part IV: Quiz**

Part I: The Atom – Atomic Structure

- Atoms are the basic building blocks of matter and are extremely small units. The diameter of one atom is in the range of 10^{-10} m, or about a million times smaller than human hair.
- In nature, the atom is an electrically neutral particle: it is neither positively nor negatively charged. However, atoms are made up of electrons, protons, and neutrons:
  - An electron has one unit of negative charge.
  - A proton has one unit of positive charge.
  - A neutron is electrically neutral.
- A unit of positive or negative charge is approximately 1.6×10^{-19} coulombs (C). The coulomb is the SI unit of charge.
- Protons and neutrons (called nucleons) are fused together through strong nuclear force to form the center of an atom, or nucleus. A nucleus is positively charged.



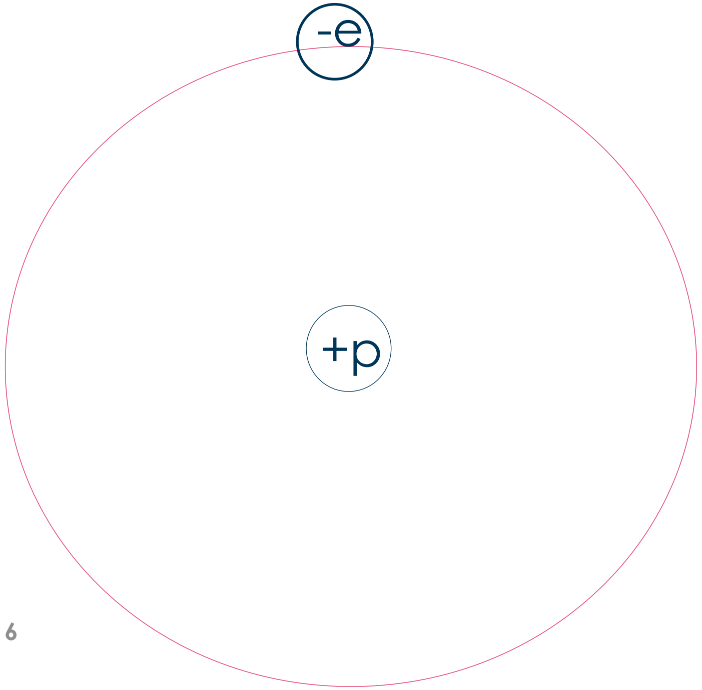
Part I: The Atom – Atomic Structure *(continued)*

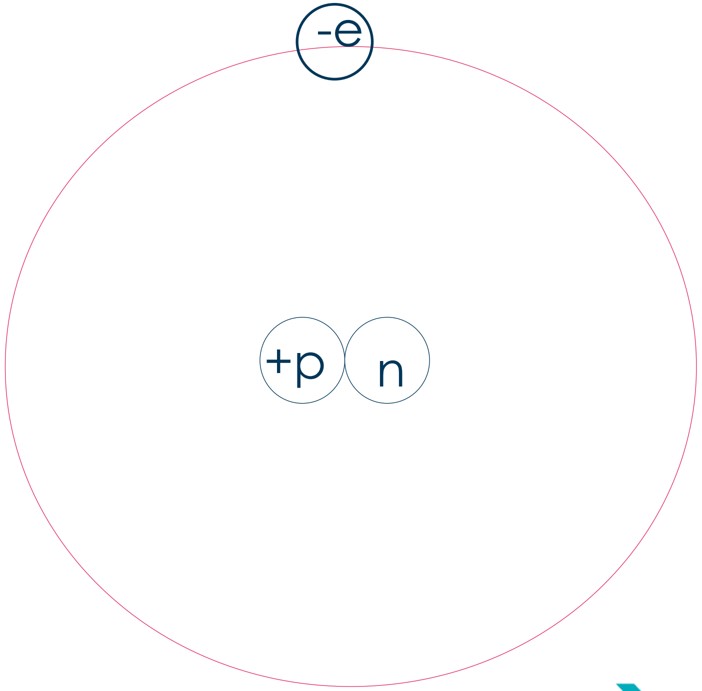
- Most of the mass of an atom is from its nucleus.
- The masses of a proton (m_P) and neutron (m_N) are similar:
  - m_P is about 1.67 x 10^{-27} kg
  - m_N is about 1.69 x 10^{-27} kg
- The mass of an electron (m_e) is much less: about 9.11 x 10^{-31} kg, or 1800 times lighter.
- The negatively charged electrons are attracted to and orbit around the positively charged nucleus by electric force.
- Most atomic events are dictated by the mass of the nucleus through attractive forces between the nucleus and electrons.

Part I: The Atom – Atomic Structure *(continued)*

- The hydrogen atom (below left) - with one electron and one proton - is the simplest example of atomic structure:
  - The nucleus contains just one proton.
  - One electron orbits around the nucleus.
- The Deuterium atom (below right) - with one electron, one neutron, and one proton - is an example of an isotope of Hydrogen:
  - The nucleus contains one proton and one neutron.
  - One electron orbits around the nucleus.

$^{1}_{1}H^{0}$



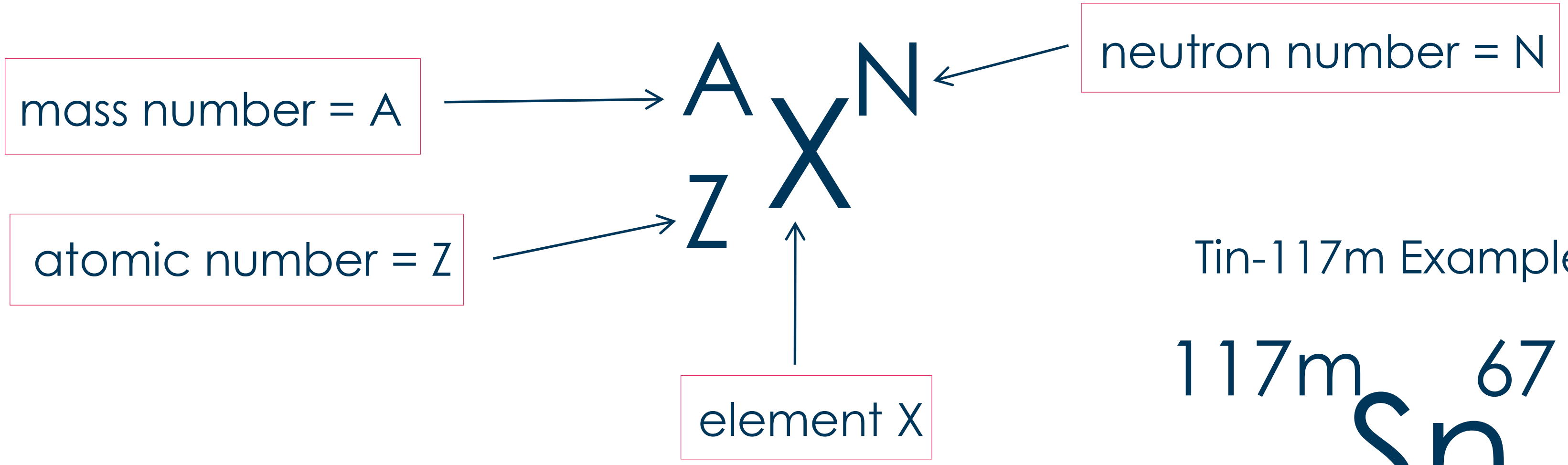


$^{2}_{1}H^{1}$

Isotopes will be further defined in the next few slides

Part I: The Atom – Atomic Number and Mass Number

- Atoms are identified by the **number of protons** they possess. This is called the **atomic number** and is designated by the capital letter **Z**.
- The **number of neutrons** in the atom is designated by the capital letter **N**.
- The **mass number** of an atom is the sum of the number of protons (Z) and neutrons (N). It is designated by the capital letter **A**.
- Therefore, mass number = atomic number + neutron number, or **A = Z + N**.



Tin-117m Example

$${}^{117m}_{50}Sn^{67}$$

Part I: The Atom – Atomic Number and Mass Number *(continued)*

- Atoms with same Z and different N are called **isotopes**.
- Atoms with same N and different Z are called **isotones**.

Example of Isotopes

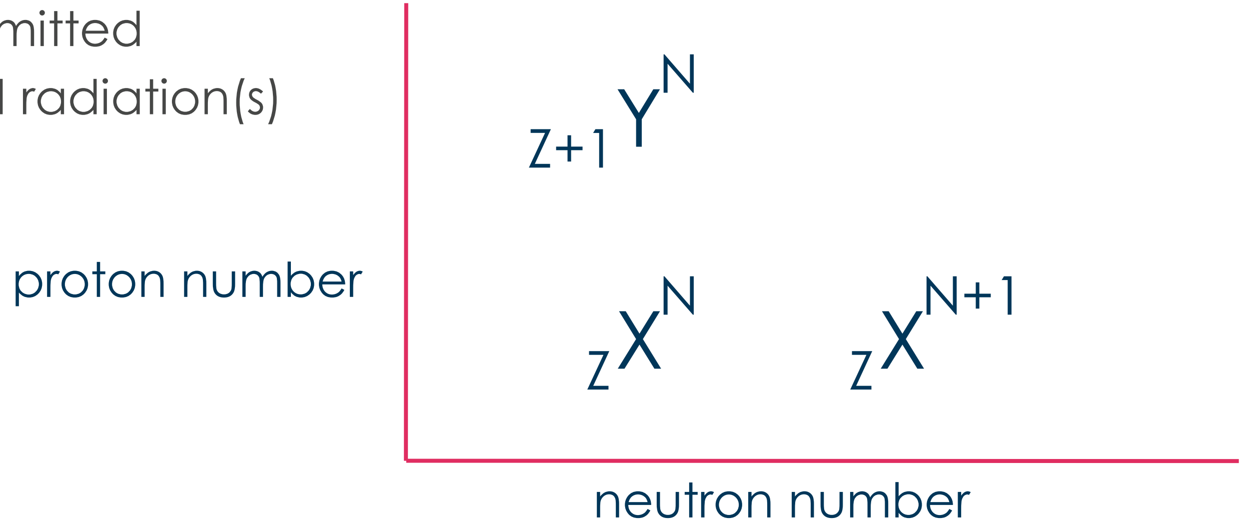
$^{1}_{1}H^{0}$ $^{2}_{1}H^{1}$ $^{3}_{1}H^{2}$

Example of Isotones

$^{12}_{5}B^{7}$ $^{13}_{6}C^{7}$

Part I: The Atom – Chart of Nuclides

- An atom is specified by its proton number and neutron number. An atom with certain P and N is called a **nuclide**.
- A **chart of nuclides** is a map that distinguishes isotopes and isotones:
  - The neutron number increases along the x-axis
  - The proton number increases along the y-axis
  - Isotopes move along the graph below with increasing N or number of neutrons
  - Isotones move along the graph below with increasing P or number of protons
- Note that each radionuclide has unique characteristics, just as each human has a unique signature or fingerprint. These characteristics include:
  - Type(s) of radiation emitted
  - Energy of the emitted radiation(s)
  - Half-life



Part II: Radioactive Decay

- **Radioactive decay** is a process of emitting particles and energy that causes:
  - A nuclide to transform into another nuclide
  - An atom or nucleus to transform from its unstable state to a stable state
- Example of radioactive decay caused by particle emission:
  During naturally occurring radioactive decay of ^{226}Ra, an alpha particle is emitted from a Radium nucleus so that the parent Radium is transformed into Radon (^{222}Rn).
- Example of radioactive decay caused by energy emission:
  The nucleus of the radionuclide ^{99m}Tc (Technetium 99-metastable) is at an unstable energy state. It decays to its ground energy state by emitting excess energy in the form of gamma rays. ^{117m}Sn follows a similar decay process to stable ^{117}Sn.
  - Metastable is a go-between "excited" state when a radionuclide is decaying to a ground state (specific decay processes are explained further in the training module).

Part II: Radioactive Decay – Activity

- A nuclide which experiences a decay process is said to be radioactive.
- **Radioactivity** describes the rate of decay of a radioactive nuclide. It is a measure of the number of disintegrations of atoms or nuclei per unit time.
- The SI unit of activity is the **Becquerel (Bq)**. The Bq describes an extremely small amount of activity: 1 Becquerel = 1 disintegration (or decay) per second.
- The US traditional unit of activity is the **Curie (Ci)**, named after Marie Curie. It was originally used to describe the activity of 1g of ^{226}Ra.
- It is still more common to use Ci in the US: **1 Ci = 3.7×10^{10} Bq.**
- For example, a 3 mCi ^{117m}Sn source of radioactivity experiences a loss of 1.11×10^{8} unstable ^{117m}Sn particles in one second:
  3 mCi = 1.11×10^{8} Bq = 111,000,000 decays per second
    - Note that SI is the abbreviation for the International System of Units.
    - For distance, meters are the SI unit for distance but in the United States we traditionally use feet.

Part II: Radioactive Decay – Half-Life

- As explained on Page 10, radioactive decay is the process of emitting particles and energy of unstable nuclides. The activity diminishes during the decay process as the unstable becomes stable.
- **Half-life ($T_{½}$)** is the time it takes for the number of radioactive nuclides to be reduced by half.
- Half-life is a very important parameter for radioactive decay, as it describes the speed of decay. A short half-life means the unstable nuclides will transform to stable nuclides in a short period of time.

Part II: Radioactive Decay – Decay Equation

- The activity of a radioactive source is calculated by: $\mathbf{A(t)=A_0\ e^{-\lambda t}}$
  - $\mathbf{A_0}$ is the initial activity at time 0
  - **A(t)** is the activity at time t
  - **λ** is the decay constant of the radionuclide
    - The decay constant λ is equal to the natural log of 2 divided by the nuclide specific half-life: $\mathbf{\lambda = ln(2)/T_{1/2}}$
- The **decay equation** is an exponential function with respect to time. The minus sign in the equation indicates that activity decreases with time. At $t = T_{1/2}$, source activity is half of its initial value.

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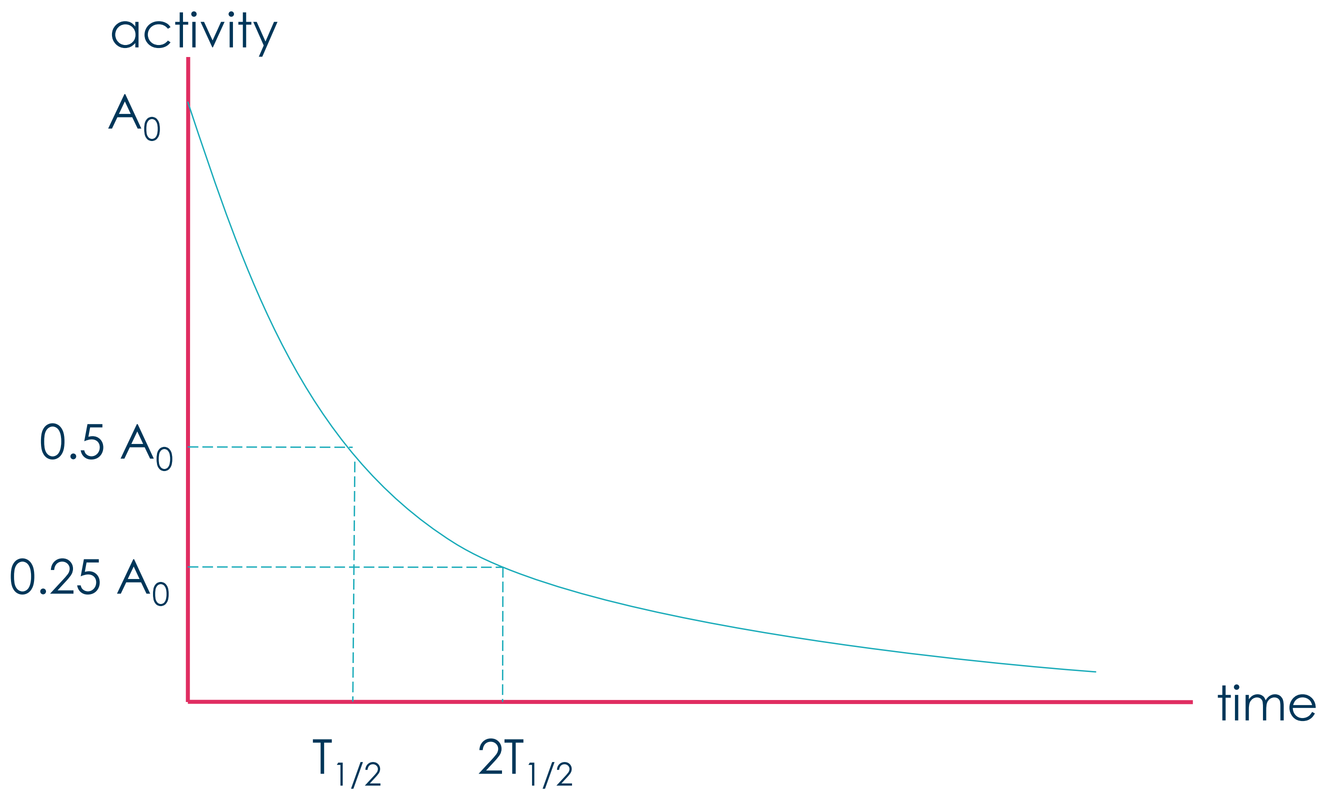
Part II: Radioactive Decay – Decay Equation *(continued)*

- The decay equation is plotted below:
  - At one half-life, the activity drops to half of the initial activity
  - At two half-lives, the activity drops to a quarter of the initial activity



Part II: Radioactive Decay– Alpha Decay

- **Alpha decay** is the spontaneous emission of an alpha particle from a heavy atomic nucleus, for example ^{226}Ra.
- The alpha particle is the same as a Helium nucleus. An alpha particle consists of 2 protons and 2 neutrons and carries a +2 positive charge.
- An alpha particle travels a very short range in tissue, and it can not penetrate the dead layer of skin. However, it has a strong ability to produce intense ion pair tracks when traveling inside tissue. Therefore, the primary biologic concern is internal exposure to alpha emitters.

$$^{A}_{Z}X = {}^{A-4}_{Z-2}Y + [\,^{4}_{2}He]^{2+}$$

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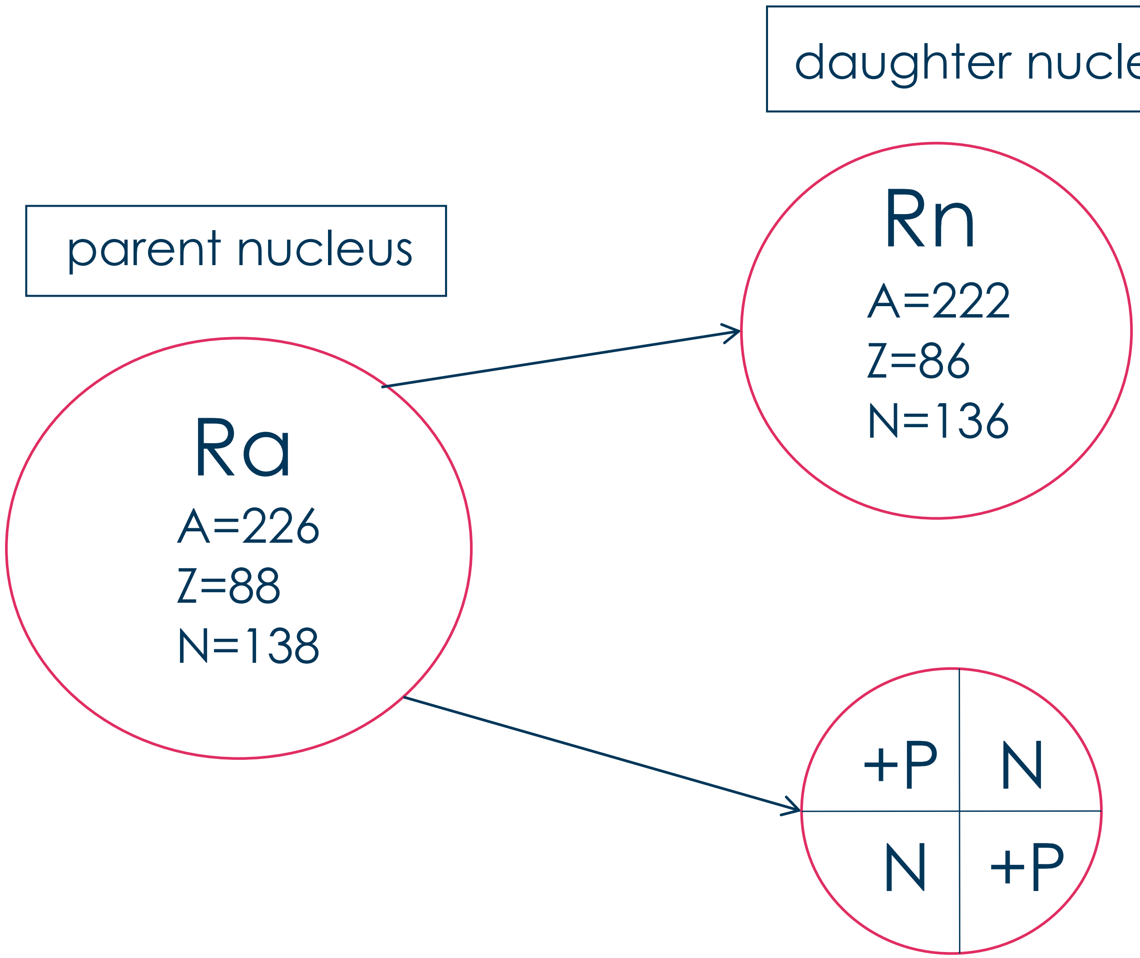
Part II: Radioactive Decay – Alpha Decay *(continued)*

Example of alpha decay process: ^{226}Ra decays to ^{222}Rn, emits $^{4}{}_{2}a^{2+}$



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Part II: Radioactive Decay – Beta Decay

- Another form of radioactive decay is **beta decay**, where the radionuclide emits an electron or positron.
- If a nucleus has an excess number of neutrons compared to the number of protons, an electron is emitted; then a neutron becomes a proton in the nucleus. This nuclear transformation is called **beta minus (β^-)** decay. In this process, an antineutrino particle is emitted from the nucleus. The antineutrino release is not a biological concern.
- If a nucleus has an excess number of protons compared to the number of neutrons, a positron is emitted; then a proton becomes a neutron in the nucleus. This process of nuclear transformation is called **beta plus (β^+)** decay. A neutrino particle is also emitted from the nucleus with β^+.
- The energy of emitted beta particles has a spectral distribution, from 0 to a maximum energy.

Part II: Radioactive Decay – Beta Decay *(continued)*

Beta minus (β^-) decay equation

$$ {}^{A}_{Z}X = {}^{A}_{Z+1}Y + \beta^{-} + v $$

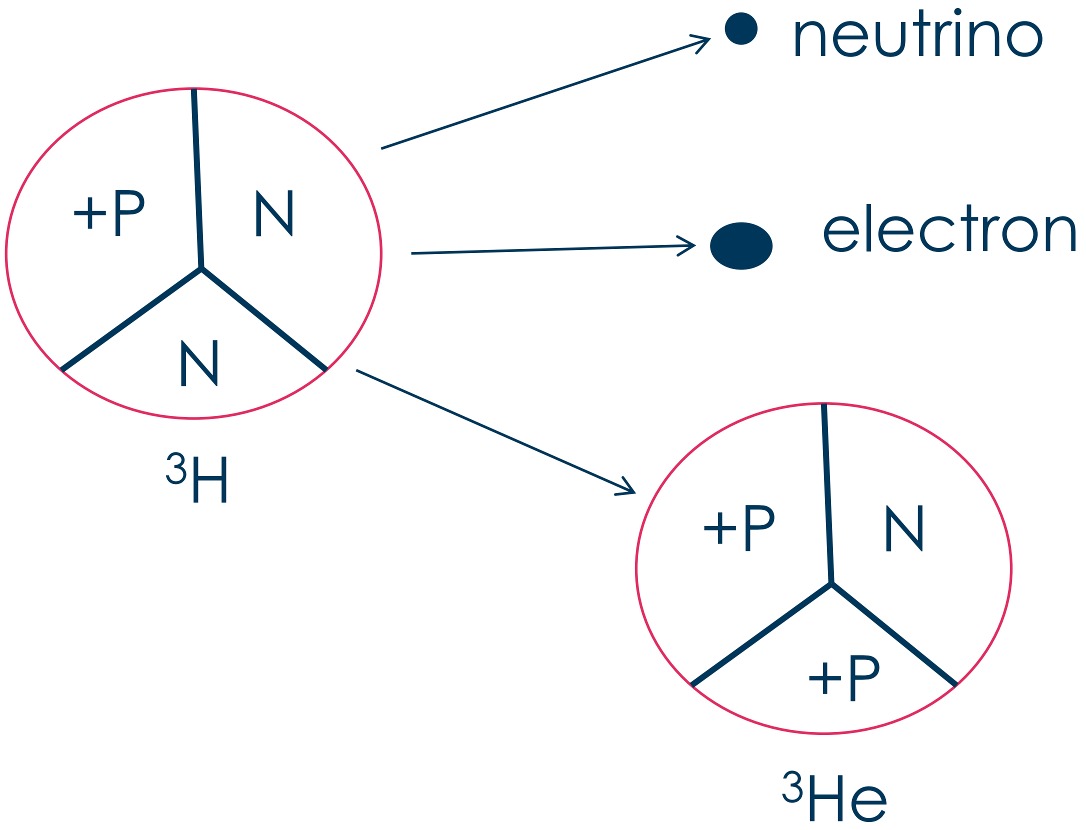
Beta plus (β^+) decay equation

$$ {}^{A}_{Z}X = {}^{A}_{Z-1}Y + \beta^{+} + v $$

*Note that V (or Greek Nu) is the added neutrino / antineutrino release of energy.

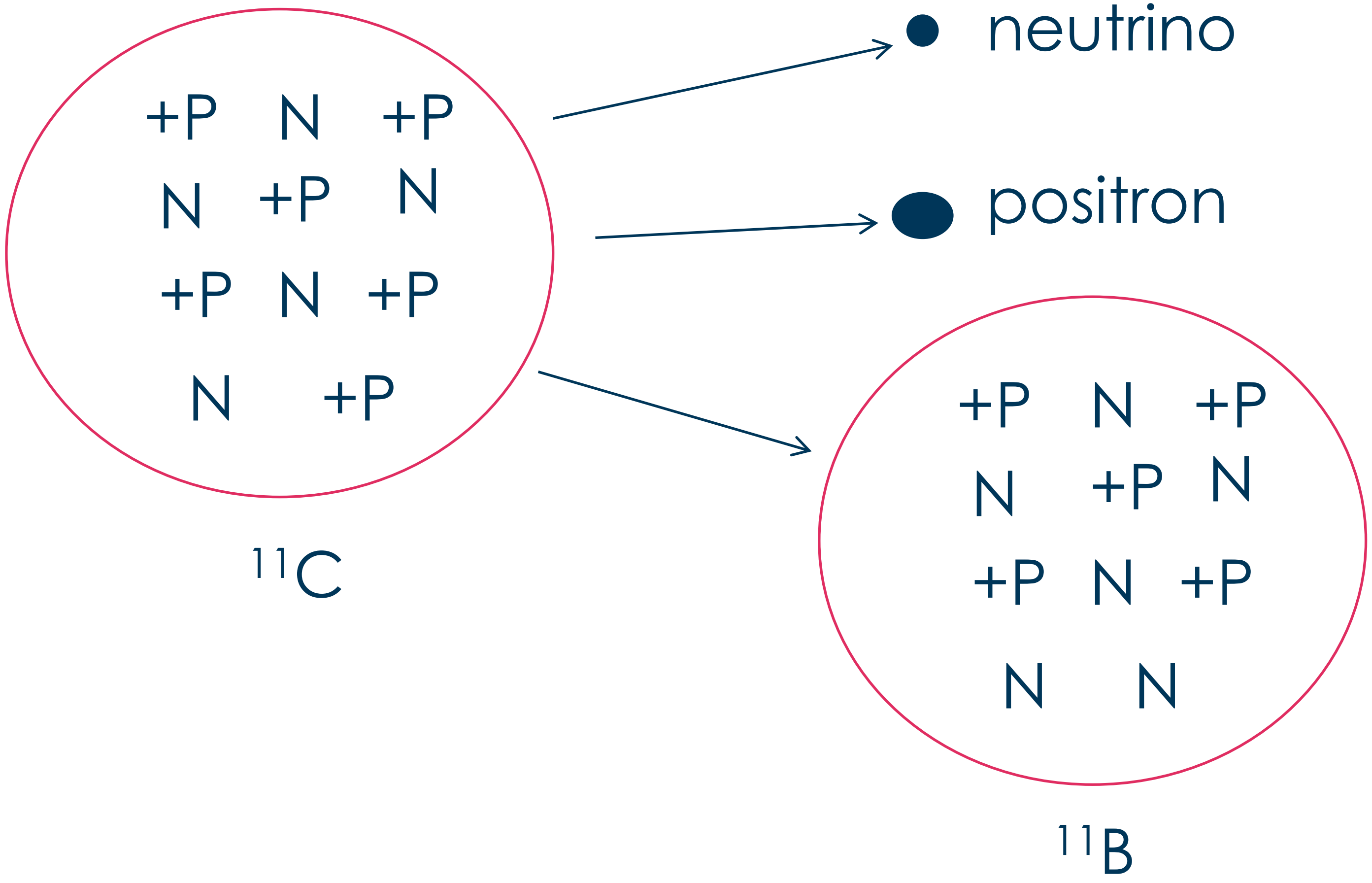
Part II: Radioactive Decay – Beta Decay *(continued)*

- Beta minus (β^-) decay process: parent nuclide Tritium decays to Helium-3



Part II: Radioactive Decay – Beta Decay *(continued)*

- Beta plus (β^+) decay process: a parent nuclide Carbon-11 decays to Boron-11



Radioactive ^{11}C decays to stable ^{11}B through beta plus decay.

Positron: a positively charged electron sometimes denoted as β^+.

Part II: Radioactive Decay – Gamma Emission

- After a nuclear transformation, the daughter nucleus is sometimes in an unstable state.
- The unstable nucleus de-excites excess energy in the form of gamma ray photons. A typical example is when ^{99m}Tc decays to ^{99}Tc by emitting 0.1405 MeV (98.6%) and 0.1426 MeV (1.4%) gamma rays.
- If the gamma ray is not emitted instantaneously from the nucleus with a half life more than (in the order of) 10^{-12} s, the nucleus is said to be in a "metastable" state, denoted by "m". For example, ^{99m}Tc is in the metastable state and decays to the ground state of ^{99}Tc by emitting gamma rays, with a half life of 6 hours.
- Technetium-99m is the most commonly used radioisotope used in human nuclear medicine. It is routinely used in equine nuclear medicine and has a similar gamma energy signature to ^{117m}Sn.

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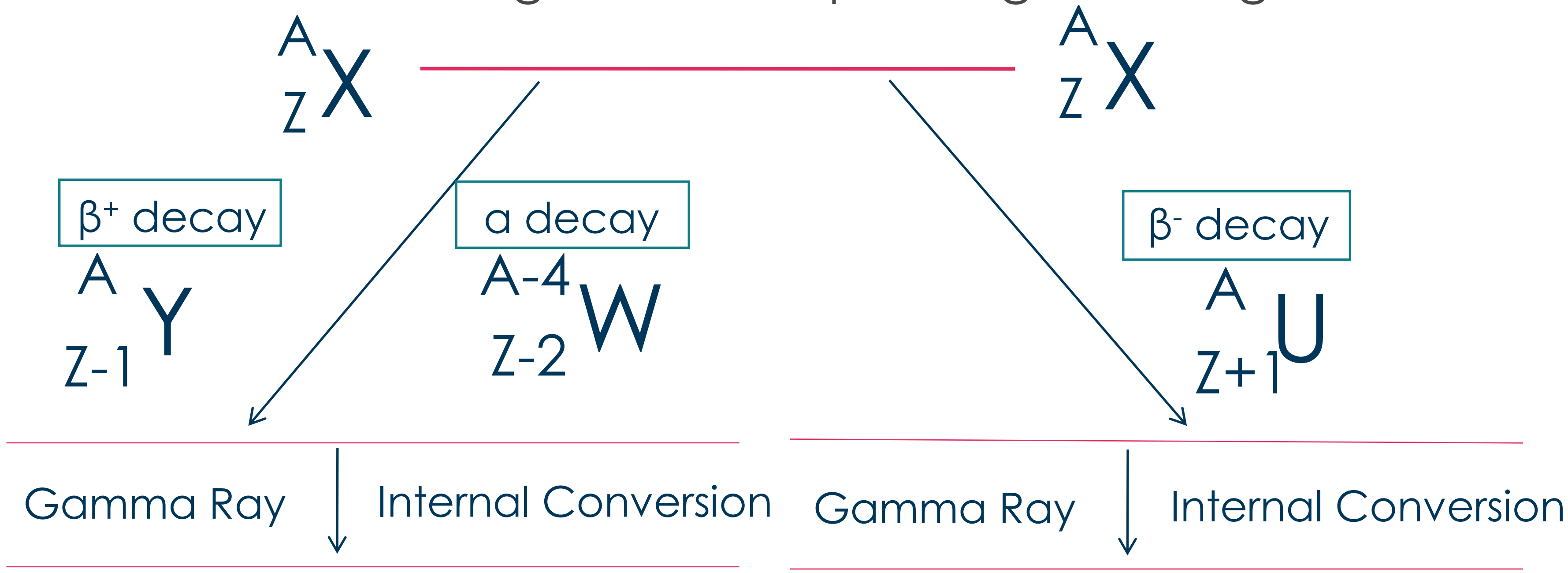
Part II: Radioactive Decay – Internal Conversion

- The de-excitation of a nucleus does not always involve the emission of gamma rays. **Internal conversion (IC)** is an alternative means of releasing excess energy.
- During IC, de-excitation energy is completely transferred to an orbital electron, typically a K, L, or M shell electron. A converted electron is emitted from the nucleus instead of a gamma ray.
- Unlike a beta particle, internal conversion electrons have discrete energies.

Part II: Radioactive Decay– Decay Scheme

- Nuclear decay can be summarized by a “decay scheme”. The decay scheme shows the relevant changes to each component inside the decay pattern.
- The top horizontal line represents the parent nuclide, the bottom horizontal line represents the daughter nuclide, the intermediate line represents a metastable state of the daughter nuclide. A diagonal arrow pointing to the left indicates a decrease in Z and a diagonal arrow pointing to the right indicates an increase in Z.



Where U, Y, and W are different elements

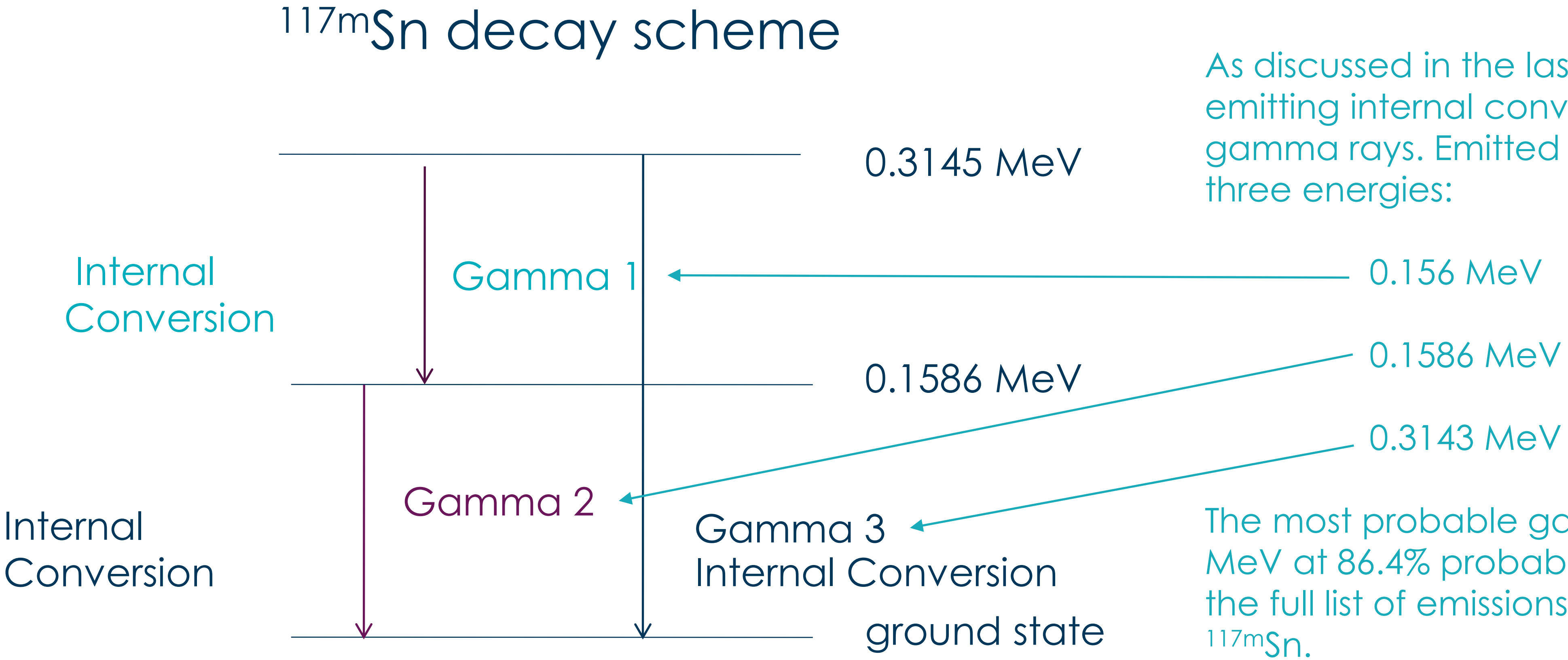
Part III: Properties of ^{117m}Sn

- ^{117m}Sn is the radionuclide in Synovetin OA. Synovetin OA has a physical form of a colloid in ammonium salt.
- ^{117m}Sn emits monoenergetic conversion electrons and gamma radiation. Once injected, these low energy conversion electrons are absorbed in the joint which stimulate a response to reduce inflammation.
- The conversion electron is an alternative decay method competing with gamma decay. It can be thought that some of the gamma rays released from the ^{117m}Sn nuclei hit the orbital electrons of the Tin nucleus and eject electrons out of their orbits to become the released conversion electrons.

Part III: Properties of ^{117m}Sn

- The half life of ^{117m}Sn is 14 days. This means that 3 mCi of ^{117m}Sn becomes 1.5 mCi after 14 days and 0.75 mCi after 14 more days.
- ^{117m}Sn decays by emitting internal conversion electrons and gamma rays. Conversion electrons have discrete energies ranging from 127keV to 158keV, with a total yield of about 114%. Emitted gamma rays contain three energies, 156keV, 158.6keV, and 314.3keV. Among the three energies, 158.6keV is the most abundant with an 86.4% yield, it can be used for diagnostic imaging and verification of an injection site.
  - Note that decay yield or abundance is the fraction of that energy in total decay. A 158.6keV gamma ray with 86.4% abundance means that 86.4% of the time a photon of 158.6keV is emitted, and the other 13.6% of the time the ^{117m}Sn nucleus emits gammas of other energies.

Part III: Properties of ^{117m}Sn (cont)



As discussed in the last slide ^{117m}Sn decays by emitting internal conversion electrons and gamma rays. Emitted gamma rays contain three energies:

The most probable gamma emission is 0.1586 MeV at 86.4% probablility. The next slide shows the full list of emissions and probabilities for ^{117m}Sn.

Part III: Properties of ^{117m}Sn (cont)

- ^{117m}Sn decay energy table, total Internal Conversion electron yield is about 114%

IC = Internal Conversion electron

Radiations	Yield (%)	Energy (keV)
Gamma 1	2.11	156
IC 1, Gamma 1	64.9	126.8
IC 2, Gamma 1	26.2	151.6
IC 3, Gamma 1	5.64	155.1
IC 4, Gamma 1	1.35	155.9
Gamma 2	86.4	158.6
IC 1, Gamma 2	11.7	129.4
IC 2, Gamma 2	1.48	154.1
IC 3, Gamma 2	0.289	157.7
IC 4, Gamma 2	0.0648	158.4
Gamma 3	4.23×10^{-4}	314.3 (very rare)

The IC 1-4 are the internal yields per gamma

Reference:
https://www.orau.org/PTP/PTP%20Library/library/DOE/bnl/nuclidedata/MIRSn117.htm

Conclusion

- Atoms are characterized by atomic number (or proton number Z) and mass number (sum of the number of protons and neutrons).
- Each radionuclide has its own signature with unique characteristics of type of radiation emitted, energy of radiation emitted, and half life.
- The chart of the nuclides is an excellent resource for all things related to radioactivity.
- Half life measures how fast a radionuclide decays. The activity of a radionuclide decreases by half after one half life.
- Nuclear decay is a process of nuclear transformation, including alpha decay, beta minus decay, and beta plus decay.
- A nucleus which is in a metasable state after nuclear transformation releases excess energy by either emitting gamma ray photons and/or internal conversion electrons.
- ^{117m}Sn has a half life of 14 days. It has emissions of discrete internal conversion electrons ranging from 127keV to 158keV and a primary gamma ray emission of 158.6keV.

Recommended Reading:
1.2 NUREG 1556 Vol 7, Revision 1
2.2 Atoms, Radiation, and Radiation Protection - Turner

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