Chapter 14
Nuclear Medicine


Outline

• Introduction
• Radiopharmaceuticals
• Detectors for nuclear medicine
• Counting statistics
• Types of studies
• Absorbed dose from radionulides

Introduction

• The field involving the clinical use of non-sealed radionuclides is referred to as nuclear medicine
• Most of the activities are related to
  – the imaging of internal organs
  – the evaluation of various physiological functions
  – to a lesser degree treatment of specific types of disease
• Typical procedures use a radioactive material (radiopharmaceutical or radiotracer), which is injected into the bloodstream, swallowed, or inhaled as a gas
• This radioactive material accumulates in the organ or area of the body being examined, where it gives off a small amount of energy in the form of gamma rays

Radiopharmaceuticals

• Radiopharmaceuticals are medicinal formulations containing one or more radionuclides
• Once administered to the patient they can localize to specific organs or cellular receptors
• Properties of ideal radiopharmaceutical:
  – Low dose radiation => appropriate half-life
  – High target/non-target activity ratio
  – Low toxicity (including the carrier compound, shelf-life)
  – Cost-effectiveness (available from several manufacturers)

Radiopharmaceuticals production

• Cyclotron
• Nuclear reactor (fission or neutron activation)
• Radionuclide generators

Mechanisms of localization

• Compartmental localization (leakage points to abnormality)
• Phagocytosis
• Cell sequestration (spleen imaging)
• Passive diffusion (often through membranes, e.g., BBB)
• Active transport (membranes with pumps)
• Metabolism (glucose-like molecules, F-18 labelled FDG)
• Capillary blockade/Percusion
• Receptor binding (e.g., antibody-antigen)
• Others

Comprehensive review at: http://pharmacy.unm.edu/nuclear_program/freelessonfiles/Vol16Lesson4.pdf
Radiopharmaceuticals production: Tc-99m generator

- Mo-99 is produced in the fission reaction, and it is then chemically purified and shipped in Tc-99m generators.
  - Molybdate, MoO$_4^{2-}$, is passed on to an anion exchange column of alumina (Al$_2$O$_3$); acid pH promotes binding.
  - As Mo-99 decays it forms pertechnetate TcO$_4^{-}$, which, because of its single charge, is less tightly bound to the alumina. Pouring normal saline solution through the column of immobilized $^{99}$Mo elutes the soluble $^{99m}$Tc.

Detectors in nuclear medicine

- The standard methods for the detection and measurement of radiation are not sensitive enough to detect the emission of a single particle arising from the disintegration of a nucleus.
  - Special gas-filled, scintillating, or semiconductor detectors are used almost exclusively.
  - For visualization of the distribution of activity use computer-aided signal processing (PET scanners, gamma cameras, etc.).

Geiger counter

- Counter filled with a special gas mixture, at $p=10$ cm of Hg.
  - Operated at high voltages, where the passage of each particle creates a controlled avalanche, resulting in a gain of $10^4$-$10^6$.
  - A single particle can produce a pulse of charge in the detectable range (10$^{-10}$ C).

Geiger counters

- Efficiency of gamma counter is very low, ~5%.
  - Efficiency of beta counters is ~100%; their configuration depends on the energy of particles to be detected.

Scintillation detectors

- Scintillating material coupled with a photomultiplier (PM).
  - X-rays -> electrons within the scintillator -> optical photons within the scintillator -> photoelectrons from the photocathode of the PM -> secondary electrons from each dynode -> collected at the final anode of PM.
  - PM multiplication factors ~$10^5$.
  - Pulse size is proportional to the energy of the initial x-ray.

Scintillation detectors

- Figure 14-5: (a) Pulse height distribution for Co-137 and Au-198 obtained on a 100-channels pulse-height analyser using a 0.6 x 4 cm medallion radionuclide window. (b) Comparison of x-ray spectrum of Co-60 observed with a 0.3 mm-thick germanium (120keV) detector and with a 0.3 x 0.3 cm medallion scintillating-spectrometer.
  - Pulse height distributions always have Gaussian shaped peaks and low-energy tails.
Semiconductor detectors

- Ionization produced within the sensitive volume of semiconductor detector is converted directly into a measurable electric pulse
- Fewer losses result in much sharper pulse height spectra
- Sensitivity is typically lower compared to scintillators

Stochastic quantities

- Radiation is random in nature, associated physical quantities are described by probability distributions
- For a “constant” radiation field a number of x-rays observed at a point per unit area and time interval follows Poisson distribution
- For large number of events it may be approximated by normal (Gaussian) distribution, characterized by standard deviation for a single measurement
- \( \sigma = \sqrt{N} \approx \sqrt{N} \)
- \( \% \sigma = \frac{100 \sigma}{N} = \frac{100}{\sqrt{N}} \approx \frac{100}{\sqrt{N}} \)

Statistics of isotope counting

- The probability of observing the value \( N \) when the expected value is \( a \):
  \[ P_N = \frac{a^N e^{-a}}{N!} \]
- For each measurement there is always an error due to statistical fluctuations:
  - Standard deviation \( \sigma = \sqrt{N} \)
  - Probable error \( p = 0.674\sqrt{N} \)

Statistics of isotope counting

- In a normal distribution 68.3% of all measured values fall within 1\( \sigma \) interval on either side of the mean \( a \), 95.5% to be within 2\( \sigma \), and 99.7% to be within interval 3\( \sigma \)
- These are not device-related fluctuations

Standard deviation

- Standard deviation can be estimated from a sample mean value \( a \) determined from a series of measurements, \( \sigma = \sqrt{a} \)
- The sample standard deviation can be constructed from a series of \( N \) measurements of a variable \( x \)
  \[ \sigma_s = \sqrt{\frac{\sum_{i=1}^{N} (x_i - \bar{x})^2}{N-1}} \]

Example 1

- Concerning the Poisson distribution, which one of the following statements is false?
  - A. It is an approximation to the binomial distribution for small sample sizes
  - B. It describes rare and random events
  - C. Radioactive decay as a function of time fits the Poisson distribution
  - D. The standard deviation \( \sigma \) is approximately equal to the square root of the number of counts for large numbers
  - E. The percent standard deviation decreases as the number of counts increases
Example 2

• If the average number of counts in a region of a planar gamma camera image is 25 counts per pixel, what is the percent standard deviation per pixel, assuming Poisson statistics?

A. 0%
B. 10%
C. 20%
D. 50%  

Resolving time and loss of counts

• Most of detectors become unresponsive for a short time after receiving each pulse
  – For Geiger counters resolving time $\tau \sim 100 \mu s$
  – Scintillators $\tau < 10 \mu s$
• At high counting rates some pulses can be missed
• For observed number of counts per second $N_o$, the corrected number of counts $N_c = \frac{N_o}{1 - N_o \tau}$

Uptake and volume studies

• Activity of a sample (P) is compared with a standard source (S) measured in the same geometry
• Thyroid uptake of $^{131}$I taken orally
  \[ \% \text{Uptake} = \frac{P - P_{\text{background}}}{S - S_{\text{background}}} \times 100 \]
• Plasma volume determination by injection of RISA (radioactive iodine-tagged serum albumin)
  \[ \text{Vol} = \frac{S - S_{\text{background}}}{P - P_{\text{background}}} \times \text{Vol}_{\text{relation}} \]

Example 3

• A radioactive sample is counted for 1 minute and produces 900 counts. The background is counted for 10 minutes and produces 100 counts. The net count rate and net standard deviation are about ____ ____ counts.

A. 800, 28
B. 800, 30
C. 890, 28
D. 890, 30
E. 899, 30

\[ N_{\text{corr}} = 900/1 - 100/10 = 890 \]
\[ \sigma = \sqrt{\sigma_i^2 + \sigma_{\text{background}}^2} = \sqrt{N_i^2/N_{\text{background}}^2} = \frac{N_i}{N_{\text{background}}} = \frac{900}{100} = 30 \]

Example 4

• A wipe test over a countertop yields a count rate of 1000 counts per minute in a nuclear medicine clinic that uses $^{99m}$Tc only. If the background is 40 counts per minute and the detector efficiency is 0.8, the activity of the $^{99m}$Tc source corresponding to this surface is ____ Bq.

A. 5
B. 10
C. 20
D. 40
E. 100

\[ N_{\text{corr}} = (N - N_{\text{background}})/\eta = (1000 - 40)/0.8 = \frac{1200 \text{ dpm}}{1200/60 \text{ dps}} = 20 \text{ Bq} \]
Imaging using radioactive materials:

**Rectilinear scanner**

- Computerized Rectilinear Thyroid (CRT) scanner utilizes computer to improve the clarity of thyroid scans and enhance thyroid nodules
- Measures both thyroid function and thyroid size

**Gamma camera**

- Requires positron-emitting isotopes, produced in cyclotrons, have short half-life. Fluorine-18 is the most common ($t_{1/2} \approx 110$ min)
- Positron annihilation results in two $\gamma$-rays emitted at 180° to one another; detectors are arranged to record coincidences
- Regions of high metabolic activity are visible through radioactive labeling

**Positron emission tomography**

- Provides 3D images
- Uses radioactive tracers that emit positrons

**Radioactive tracers**

<table>
<thead>
<tr>
<th>Z</th>
<th>Nuclei</th>
<th>Half-Life</th>
<th>Principle Photon Energy (MeV)</th>
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</thead>
<tbody>
<tr>
<td>53</td>
<td>technetium-99m</td>
<td>6.02 h</td>
<td>biological elimination and physical decay</td>
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<tr>
<td>51</td>
<td>gallium-67</td>
<td>8.04 d</td>
<td>biological elimination and physical decay</td>
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<td>59</td>
<td>indium-111</td>
<td>2.81 d</td>
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<td>81</td>
<td>rubidium-81m</td>
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<td>86</td>
<td>ruthenium-86m</td>
<td>11.4 min</td>
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<td>87</td>
<td>antimony-123</td>
<td>60 min</td>
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</tr>
<tr>
<td>123</td>
<td>technetium-99m</td>
<td>6.02 h</td>
<td>biological elimination and physical decay</td>
</tr>
<tr>
<td>131</td>
<td>iodine-131</td>
<td>66.1 min</td>
<td>biological elimination and physical decay</td>
</tr>
</tbody>
</table>

- Radioactive tags are incorporated in a variety of molecules
- Availability of short half-life isotopes (Tc-99m) allows for shorter image acquisition times, higher resolution

**Radioactive tracers**

- The amount of the radioactive isotope decreases with time by two processes: biological elimination and physical decay
- The effective fraction of the isotope that disappears per unit time

\[
\lambda_{\text{eff}} = \lambda_b + \lambda_p
\]

- The effective half-life is

\[
\frac{1}{T_{\text{eff}}} = \frac{1}{T_b} + \frac{1}{T_p} \Rightarrow T_{\text{eff}} = \frac{T_b \cdot T_p}{T_p + T_b}
\]
Absorbed dose from radionuclides

**Table 16.9**: Input Data for 56Co, Half-Life 6.06h

<table>
<thead>
<tr>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
<th>(4)</th>
<th>Other Nuclear Data</th>
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<tr>
<td>Transition</td>
<td>Mean No. per Disintegration</td>
<td>Energy/MeV</td>
<td>Other Nuclide Data</td>
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<tr>
<td>gamma 1</td>
<td>0.800</td>
<td>0.921</td>
<td>E3</td>
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<tr>
<td>gamma 2</td>
<td>0.800</td>
<td>1.035</td>
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<tr>
<td>gamma 3</td>
<td>0.100</td>
<td>1.600</td>
<td>M1, M2, M3, K1, K2, K3</td>
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<tr>
<td>energy emitted per dis.</td>
<td>(999.1) x (999.1) x (999.1)</td>
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</tbody>
</table>

- A committee of the Society of Nuclear Medicine called MIRD (Medical Internal Radiation Dose) has produced extensive tables for dose calculations for all the commonly used radionuclides.

- The dose calculation involves the detailed physical information about radionuclide, biological information such as the biological half-life, as well as anatomical information concerning the shapes and sizes of different organs, and their locations.

**Summary**

- Radiopharmaceuticals
  - Mechanisms of localization
- Detectors for nuclear medicine
- Counting statistics
- Types of studies
- Absorbed dose from radionuclides