Chapter 14
Nuclear Medicine

Radiation Dosimetry I

http://www.utoledo.edu/med/depts/radther

Outline

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

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

• Shielded vial used to hold reconstituted radiopharmaceuticals
• Using long forceps to handle a vial containing radioactivity

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/Perfusion
• Receptor binding (e.g., antibody-antigen)
• Others

Radiopharmaceuticals production

<table>
<thead>
<tr>
<th>Radiopharmaceuticals production: Tc-99m generator</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mo-99 (t₁/₂=66h) is produced in the fission reaction, it is then chemically purified and shipped in Tc-99m (t₁/₂=6h)</td>
</tr>
<tr>
<td>• Molybdate, MoO₄²⁻ is passed on to an anion exchange column of alumina (Al₂O₃); acid pH promotes binding</td>
</tr>
<tr>
<td>• As Mo-99 decays it forms pertechnetate TcO₄⁻; because of its single charge, it is less tightly bound to the alumina. Pouring normal saline solution through the column of immobilized ⁹⁹Mo elutes the soluble ⁹⁹mTc</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 3.2 Reactors That Irradiate Targets for Global Mo-99 Suppliers as of June 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left: Plot of typical Mo-99 and Tc-99m activity. Right: Image acquired from a Tc-99m cerebral blood flow brain scan of a person with Alzheimer’s disease. The arrows indicate areas of diminished blood flow due to the disease.</td>
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</table>

Detectors in nuclear medicine

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>• 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</td>
</tr>
<tr>
<td>• Special gas-filled, scintillating, or semiconductor detectors are used almost exclusively</td>
</tr>
<tr>
<td>• For visualization of the distribution of activity use computer-aided signal processing (PET scanners, gamma cameras, etc.)</td>
</tr>
</tbody>
</table>

Geiger counter

<table>
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<tr>
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</tr>
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<tbody>
<tr>
<td>• Counter filled with a special gas mixture, at p=10 cm of Hg</td>
</tr>
<tr>
<td>• Operated at high voltages, where the passage of each particle creates a controlled avalanche, resulting in a gain of ~10⁵-10⁷</td>
</tr>
<tr>
<td>• A single particle can produce a pulse of charge in the detectable range (10⁻¹⁰ C)</td>
</tr>
</tbody>
</table>
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 ~10^6
- Pulse size is proportional to the energy of the initial x-ray

Scintillation detectors

- 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

\[ \sigma = \sqrt{N_e} \]

- 100% relative error

\[ \% \sigma = \frac{100}{N_e} \]

Statistics of isotope counting

- The probability of observing the value \( N \) when the expected value is \( \mu \):

\[ P_N = \frac{\mu^N e^{-\mu}}{N!} \]

- For each measurement there is always an error due to statistical fluctuations:
  - Standard deviation
  - Probable error

\[ p = 0.67 \sqrt{N} \]
**Statistics of isotope counting**

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

**Standard deviation**

- Standard deviation can be estimated from a sample mean value \( \bar{a} \) determined from a series of measurements, \( \sigma = \sqrt{\bar{a}} \).
- The sample standard deviation can be constructed from a series of \( N \) measurements of a variable \( x \)

\[
\sigma_x = \sqrt{\frac{\sum_{i=1}^{N} (x_i - \bar{a})^2}{N-1}}
\]

**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 \( \tau \approx 100 \mu s \)
  - Scintillators \( \tau \approx 10 \mu s \)
- At high counting rates some pulses can be missed.
- For observed number of counts per second \( N_0 \), the corrected number of counts

\[
N_c = \frac{N_0}{1 - N_0 \tau}
\]

**Resolving time and loss of counts**

- To determine the resolving experimentally, can use two sources of similar activities.
- For measured number of counts per second \( N_A \), \( N_B \), \( N_{AB} \), the corrected number of counts

\[
\frac{N_A}{1 - N_A \tau} + \frac{N_B}{1 - N_B \tau} = \frac{N_{AB}}{1 - N_{AB} \tau}
\]
- The resolving time:

\[
\tau = \frac{N_A + N_B - N_{AB}}{2N_A N_B}
\]
Uptake and volume studies

• Activity of a sample (P) is compared with a standard source (S) measured in the same geometry
• Thyroid uptake of I-131 taken orally
  \[
  \text{Uptake \%} = \frac{P - P_{\text{bkg}}}{S - S_{\text{bkg}}} \times 100
  \]
• Plasma volume determination by injection of RISA (radioactive iodine-tagged, I-125, serum albumin)
  \[
  \text{Vol} = \frac{S - S_{\text{bkg}}}{P - P_{\text{bkg}}}
  \]

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

\[
N_{\text{corr}} = \frac{900 - 100}{10} \times \frac{1}{10} = 890
\]
\[
\sigma = \sqrt{N_{\text{corr}} + \sigma_{\text{bkg}}} = \sqrt{890 + \frac{100}{10}}
\]

Example 4

• A wipe test over a countertop yields a count rate of 1000 counts per minute in a nuclear medicine clinic that uses \(^{99}\)mTc only. If the background is 40 counts per minute and the detector efficiency is 0.8, the activity of the \(^{99}\)mTc source corresponding to this surface is ____Bq.
  A. 5
  B. 10
  C. 20
  D. 40
  E. 100

\[
N_{\text{corr}} = (N - N_{\text{bkg}}) / \eta = (1000 - 40) / 0.8 = 1200 / 60 = 1200 \text{ dpm} = 20 \text{ Bq}
\]

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

Imaging using radioactive materials: Gamma camera

• 2-D array of PMT’s allows obtaining 3D images
• Used to observe physiological function of different organs
Positron emission tomography

- 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

Images from: The Physics of PET/CT scanners, R.E. Schmitz et al., Dept. of Radiology, Univ. of Washington; Cho, Zang et al. (2011). Fusion of PET and MRI for Hybrid Imaging. 10.1007/978-3-642-15816-2_2.

- The incident annihilation photon (511 keV energy) interacts within scintillator producing tens of thousands visible wavelength photons (~1eV)
- Example of scintillators: BGO = bismuth germinate, NaI(Tl) = thallium-doped sodium iodide, LSO = lutetium oxyorthosilicate, LYSO = lutetium strontium orthosilicate, GSO = gadolinium orthosilicate

- Regions of high metabolic activity appear dark through radioactive labeling
- In raw images lungs and skin show higher tracer uptake than muscle
- Images require attenuation correction based on patient anatomy (use CT image acquired with PET)

Images from: The Physics of PET/CT scanners, R.E. Schmitz et al., Dept. of Radiology, Univ. of Washington

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

Images from: The Physics of PET/CT scanners, R.E. Schmitz et al., Dept. of Radiology, Univ. of Washington

- 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
  \[
  \lambda_{\text{eff}} = \lambda_p + \lambda_b
  \]
- The effective half-life is
  \[
  \frac{1}{T_{\text{eff}}} = \frac{1}{T_b} + \frac{1}{T_p} \quad \Rightarrow \quad T_{\text{eff}} = \frac{T_p \cdot T_b}{T_p + T_b}
  \]

- 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
Absorbed dose from 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.

**Absorbed dose from radionuclides**

<table>
<thead>
<tr>
<th>TABLE 16.4</th>
<th>Originator Dose for Tissue Radiation</th>
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</thead>
<tbody>
<tr>
<td>(1)</td>
<td>(2)</td>
</tr>
<tr>
<td>Mean Energy</td>
<td>Mean Energy</td>
</tr>
<tr>
<td>(MeV)</td>
<td>(MeV)</td>
</tr>
<tr>
<td>3.11</td>
<td>3.11</td>
</tr>
<tr>
<td>5.41</td>
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</tr>
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</table>

*The absorbed dose is calculated using the Monte Carlo method.*

**Absorbed dose from radionuclides**

The absorbed 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.

**Absorbed dose from radionuclides**

<table>
<thead>
<tr>
<th>TABLE 16.5</th>
<th>Absorbed Dose per Unit Accumulated Activity</th>
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<tbody>
<tr>
<td>Isotope</td>
<td>Half-Life</td>
</tr>
<tr>
<td>131I</td>
<td>131I</td>
</tr>
<tr>
<td>131I</td>
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*Calculations for the “standard man” performed by Monte Carlo serve for estimates of absorbed dose.*

**Summary**

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