Dose Estimates for Nuclear Medicine Procedures: What are they? Where do they come from?

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Introduction

• Radiation dosimetry provides fundamental quantities that are essential for radiation protection, risk assessment, and treatment planning

• The science of measuring or calculating radiation dose requires careful accounting of all the physical and biological determinants of dose

• The Medical Internal Radiation Dose Committee of SNM develops standard methods, models, assumptions, nuclear data, mathematical schema, and implementing software needed to assess internal dose from administered radiopharmaceuticals
Why this issue now?


• Americans exposed to more than seven times as much ionizing radiation from medical procedures compared to the early 1980s

• Medical exposure constitutes nearly half of the total radiation exposure of the U.S. population from all background sources combined

• The increase in per capita dose is due to growth in the use of medical imaging procedures (CT and nuclear medicine)
All Exposure Categories
Collective Effective Dose (percent), 2006

- Radon & thoron (background) (37%)
- Computed tomography (medical) (24%)
- Nuclear medicine (medical) (12%)
- Interventional fluoroscopy (medical) (7%)
- Conventional radiography / fluoroscopy (medical) (5%)
- Consumer (2%)
- Occupational (<0.1%)
- Industrial (<0.1%)
- Internal (background) (5%)
- Terrestrial (background) (3%)
- Space (background) (5%)

National Council on Radiation Protection and Measurements
• CT and nuclear medicine contributed 36% of the total radiation exposure and 75 percent of the medical radiation exposure of the U.S. population

• Number of CT scans = 67,000,000/yr (2006) and 72,000,000 CT scans (2008)

• . . . compared to 3,000,000 in 1984

• Number of nuclear medicine procedures = 18 million/yr

• 25% of the medical exposure attributed to x-ray exams
## Typical effective dose (radiology)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>mSv</th>
<th>mrem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest x-ray</td>
<td>0.1</td>
<td>10</td>
</tr>
<tr>
<td>Head CT</td>
<td>1.5</td>
<td>150</td>
</tr>
<tr>
<td>Screening mammography</td>
<td>3</td>
<td>300</td>
</tr>
<tr>
<td>Abdomen CT</td>
<td>5.3</td>
<td>530</td>
</tr>
<tr>
<td>Chest CT</td>
<td>5.8</td>
<td>580</td>
</tr>
<tr>
<td>CT colonography</td>
<td>3.6-8.8</td>
<td>360-880</td>
</tr>
<tr>
<td>Chest, abdomen, and pelvis CT</td>
<td>9.9</td>
<td>990</td>
</tr>
<tr>
<td>Cardiac CT angiogram</td>
<td>6.7-13</td>
<td>670-1300</td>
</tr>
<tr>
<td>Barium enema</td>
<td>15</td>
<td>1500</td>
</tr>
<tr>
<td>Neonatal abdominal CT</td>
<td>20</td>
<td>2000</td>
</tr>
</tbody>
</table>

MIRD Committee
## Typical effective dose (nuclear medicine)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>mSv</th>
<th>mrem</th>
</tr>
</thead>
<tbody>
<tr>
<td>F-18-FDG brain PET</td>
<td>4.9-7.7</td>
<td>490-770</td>
</tr>
<tr>
<td>I-131 thyroid uptake and scan</td>
<td>8.6</td>
<td>860</td>
</tr>
<tr>
<td>Tc-99m sestimibi (parathyroid)</td>
<td>3-9.3</td>
<td>300-930</td>
</tr>
<tr>
<td>Tc-99m myocard. perf. rest</td>
<td>10.2-15.3</td>
<td>1020-1530</td>
</tr>
<tr>
<td>Tc-99m myocard. perf. stress</td>
<td>15.4-25.6</td>
<td>1540-2560</td>
</tr>
<tr>
<td>TI-201 myocard. perf. stress</td>
<td>3.6-8.8</td>
<td>360-880</td>
</tr>
<tr>
<td>N-13 myocard. perf. PET</td>
<td>3-6</td>
<td>300-600</td>
</tr>
<tr>
<td>Tc-99m sulfur colloid (liver)</td>
<td>2.1</td>
<td>210</td>
</tr>
<tr>
<td>Ga-67 infection</td>
<td>18.5-25.9</td>
<td>1850-2590</td>
</tr>
<tr>
<td>Tc-99m MDP (bone scan)</td>
<td>1.5-7.5</td>
<td>150-750</td>
</tr>
</tbody>
</table>

MIRD Committee
Caveats

• Radiation doses in medicine are highly variable due to
  – patient-specific factors: metabolic rate, size, weight
  – machine and operator factors (radiography)
  – choice of isotope and activity administered

• Wide variation in published values due to
  – differences in approach, sources of uncertainty

• Units for effective dose (in Sv, a surrogate of risk) are
  not the same as organ or tissue absorbed dose (in Gy, a
  measure of energy imparted)
Where do we get dosimetry information?

- MIRD Committee calculations, dose-estimate reports for radiopharmaceuticals
- Peer-reviewed literature, journal publications
- Product package inserts based on expert dose assessments
- ICRP Publications 53, 80, 106 (based largely on prior MIRD dose estimates)
- SNM website guidance and physician resources
- RADAR (an SNM Task Group)
- Medical physicists supporting nuclear medicine clinics
Absorbed dose in biological systems

General equation

\[ D = \left( \frac{kAEm}{m} \right) \int_0^t B(t) \, dt \]  

Gy \ (J \ kg^{-1})

where \( k \) is a unit conversion constant
\( A \) is the activity in the organ (Bq)
\( E \) is the total energy emitted (J)
\( f \) is the fraction of energy that is absorbed
\( m \) is the mass of target tissue (g)
\( B(t) \) is the biological retention with time \( t \)
MIRD framework

Rearranged

\[ D = A \int_0^t B(t) dt \left( \frac{kE_f}{m} \right) \]

MIRD Formula

\[ D(r_k \leftarrow r_h) = \tilde{A}_h \sum_i \Delta_i \varphi_i(r_k \leftarrow r_h) / m_k \]

where \( \tilde{A}_h \) is the cumulated activity, \( \Delta_i \) is the mean energy emitted per unit cumulated activity, and \( \varphi(r_k \leftarrow r_h) \) is the absorbed fraction of energy imparted by a source organ.
MIRD schema

- The broad framework for assessing absorbed dose to whole organs, tissue subregions, voxelized tissue structures, and individual cellular compartments
- For use in both diagnostic and therapeutic nuclear medicine
- Simplifies the problem of assessing dose for many different radionuclides--each with its unique radiological characteristics and chemical properties as labeled compound--in the highly diverse biological environment represented by the human body, internal organs, tissues, and fluid compartments
Virtues of the MIRD schema

• The MIRD approach systematically reduces complex dosimetric analyses to methods that are relatively simple without compromising on essential details
  – Is evolving to meet 21st century needs
  – Extends from the whole-organ to the cellular and multi-cellular levels
  – May be applied to uniform or non-uniform radionuclide distributions
• Today—provides a unifying framework for better understanding the risks associated with nuclear medicine (MIRD Pamphlet 21; 2009)
Calculating absorbed dose

Two approaches:

1. Dynamic modeling
2. Direct imaging

Patient-specific methods are preferred over generic model assumptions
1. Dynamic modeling

Requires an appropriate pharmacokinetic or biokinetic model with known parameter values for the model compartments and transfer rates

Example: Biokinetic models established by the International Commission on Radiological Protection (ICRP)

Implemented using modeling software (SAAM II, STELLA)
Dynamic modeling: typical data input

- Intake estimates (inhalation, ingestion, skin)
- Whole body counts
- Chest counts
- Urine sample measurements
- Fecal sample measurements
- Wound counts
- Biokinetic reference data
- Air sample data
- Other environmental measurements
- Animal data assumed applicable to man

Implementation software:  (CINDY, GENMOD, IMBA Expert, IMBA Professional)
2. Direct measurements (MIRD Pamph. 16)

Planar imaging and quantitative SPECT:

- Patient positioning, anterior/posterior geometric means
- Determining the regions of interest for the major organs, tumor, whole body
- Translation from counts to activity
- Calibration against a radionuclide standard
- Background subtraction, attenuation correction
- Marrow and tumor biopsy specimens
- Organ volumetrics by CT scans
- Activity-time curve-fitting
- Area-under-curve analysis
- Dosimetry calculations using the MIRD schema (implemented using software, such as OLINDA-EXM)
Imaging-based time-activity curve

In-111 Day 4, posterior

Time, hr

activity
Relevant dosimetric quantities and units

Sieverts, gray, rem, rads ??
Effective dose, Sv

- For radiation protection planning
  - To compare patient exposures from different procedures
  - For use by institutional review boards and radiation safety committees
- Defined only for stochastic effects (risk of cancer)
  - Does not apply to immediate deterministic effects
  - Not for individual dosimetry
  - Does not express organ or tissue dose
  - Is population-generic, not patient-specific

MIRD Committee
Absorbed dose, Gy

- Is the starting quantity that can be weighted to evaluate effective dose and *stochastic* effects
- Relevant to organ and tumor *deterministic* effects
- For individual patient dosimetry and treatment planning
  - To compare different treatments
  - To evaluate patient-specific factors
  - To maintain complete patient records
Summation

• The biological response to an internalized radiation source is related to the total absorbed dose, localized dose distribution, ionization density, dose rate, tissue radiosensitivity, and biological end-point of interest.

• Ability to accurately assess internal dose and understand the consequences of dose is important for understanding the short- and long-term risks associated with nuclear medicine procedures.

• In therapy, dosimetry is important for ensuring that desirable treatment outcomes can be achieved without exceeding normal tissue tolerances.