Nuclear Regulatory Commission guidance on release of radioactive patients

Dawn Banghart, CHP
Sr. Health Physicist
Alt. Radiation Safety Officer

Can this therapy patient be released?

- Lu-177 Radioactive Octreotate (Lutatheria) will be used to treat patients with neuroendocrine tumors of the small bowel and pancreas.
- Ra223 dichloride (retreatment of prostate cancer spread to bones)

I-131 patients given 100 mCi sometimes can’t be released for at least 24 hours and must stay in a lead lined room at SUH.
Introduction

• Patients that receive therapies using radiopharmaceuticals will expose members their family to radiation and are potentially a significant source of radiation to members of the public (e.g., if traveling by air, sitting next to someone for 5 hours)
• For many decades, patient release criteria was based on the administered activity (ex: patients treated with I-131 sodium iodide used to treat hyperthyroidism or thyroid cancer)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Then</th>
<th>Now (since 1997)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mCi</td>
<td>Exposure to any individual from released patient must be less than 500 mrem</td>
<td></td>
</tr>
<tr>
<td>5 mrem/hr</td>
<td>or dose rate based on isotope*</td>
<td></td>
</tr>
</tbody>
</table>

* From Table U.1, Appendix U, NUREG-1556

Title 10, Code of Federal Regulations, Part 35 ("10 CFR 35")
Medical Use of Byproduct Material

• This part of the 10 CFR code contains requirements and provisions for:
  – Medical use of “byproduct material”
  – Issuance of specific licenses authorizing medical use of this material
• 10 CFR 35 = requirements and provisions for the radiation safety of workers, the general public, patients, and human research subjects
10 CFR 35.75

• A patient administered radioactive materials may be released from controls provided the total “effective” dose to any other individual is unlikely to exceed 5 mSv (500 mrem)

• Regulatory compliance guidance:
  – NUREG 1556, Volume 9, Revision 2, Appendix U
  – *Guide for Diagnostic Nuclear Medicine and Radiopharmaceutical Therapy*

Controversy

• Some argue that 5 mSv is dangerous and that we should return to the old 30 mCi or 5 mR/hr @ 1 m release criteria.

• Some physicists and physicians argue that the 5 mSv limit is well below the threshold of danger.

• Beware: Some patients after receiving your instructions will go straight to a hotel instead of going home. This is not Stanford policy.

• The position of the Health Physics Society:
  – The 5 mSv limit poses no discernible risk to the public and balances safety concerns with benefits to patients, their families and society.
**Benchmark Dose Levels**

- **500 mrem (5 mSv)**
  - “Most exposed” person from patients administered radionuclide therapy

- **300 mrem (3 mSv)**
  - Typical natural background

- **100 mrem (1 mSv)**
  - Members of the public,
    - *Pregnant women,*
    - *children* (*International Recommendations*)

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**Cancer Risk**

- The overall risk of fatal cancer at low doses has been estimated to be 5% per Sievert.
- That predicts one excess fatal cancer in a cohort of 4000 people exposed to 5 mSv. Compare this to the 50% likelihood of developing cancer anyway, half of which cases will be fatal.
- Cancers caused by exposure to ionizing radiation cannot be differentiated from cancers that occur spontaneously in a population.
- For doses below 100 mGy (10,000 mrem) radiation-induced cancer too small to be distinguishable from background.
Examples of Radionuclides or “byproduct material”

- I-131 sodium iodide for thyroid therapy
- I-131-labeled radiopharmaceuticals for treating lymphomas or neuroblastoma (MIBG)
- Sm-153-labeled bone-seeking agents
- Lu-177 Lu-DOTA-Octreotate (Lutathera)
- Ra-223 dichloride
- P-32, Sr-89 and Y-90 (these are pure beta emitters, have no patient release restrictions)

Exposed Persons

- Addressed by NRC guidance
  - Most exposed person
    - Is allowed to receive 5 mSv (500 mrem) on the theory that that person derives some benefit from the exposure.
  - Nursing children
    - Breastfeeding is usually discontinued (Maybe interrupted) to keep the dose to the nursing child below 1 mSv (100 mrem).
- Additional concerns (it is ALARA to keep dose <1 mSv)
  - Members of the public
  - Children (other than nursing)
  - Pregnant Women
  - Fellow Travelers
  - Don’t forget the family pet!
The Patient Release Equation

$$D(\infty) = \frac{34.6 \times \Gamma \times Q_0 \times T_p \times E}{(r)^2}$$

Where $D(\infty)$ = Accumulated exposure at time $t$, in roentgens ($\approx$ rem or rad)

34.6 = Conversion factor from integrating exponential to infinity which converts the physical half-life from days to hours

$\Gamma$ = Specific gamma ray constant for a point source, R/mCi-hr at 1 cm

$Q_0$ = Initial activity of the point source in mCi, at the time of the release

$T_p$ = Physical half-life in days

$E$ = Occupancy Factor at 1 meter

$r$ = Distance from the point source to the point of interest in centimeters

Note: This equation does not apply to patients who are breastfeeding.

NUREG 1556 Patient Release Calculation Assumptions

- Occupancy factor of 0.25 @ 1 m if $T_{phys} > 1$ day (i.e., I-131)
- No self shielding by tissue (of the patient or of the exposed person)
- The patient is modeled as a point source. And, the exposed person is considered a point target.

The above assumptions overestimates dose to the exposed person.
## Occupancy Factors

<table>
<thead>
<tr>
<th>E</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 – 0.75</td>
<td>(18-24 hrs/day) The half-life is &lt; than a day</td>
</tr>
<tr>
<td>0.25</td>
<td>(6 hrs/day) The half-life is &gt; than a day and the patient able to maintain prudent distance from others for 2 days</td>
</tr>
<tr>
<td>0.125</td>
<td>(3 hrs/day) The half-life is &gt; than a day and patient can comply with lifestyle instructions that are consistent with this occupancy factor</td>
</tr>
<tr>
<td>0.75/0.25</td>
<td>For a two compartment thyroidal and non-thyroidal model where one compartment has effective half-life shorter than a day and the other effective half-life is longer than a day (for calculator and info see <a href="http://www.doseinforadar.com/ExposureCalculator.html">http://www.doseinforadar.com/ExposureCalculator.html</a>).</td>
</tr>
</tbody>
</table>

### E = 0.25 (6 hours/day)

- Contingent on the patient being able to maintain a prudent distance from others for at least 2 days.
- Patient must sleep alone for at least the first night and not travel by airplane or mass transportation.
- “Will produce a generally conservative estimate of the dose to family members when instructions on minimizing doses to others are given.” (NRC Regulatory Guide 8.39)
- Example: Patient has a short drive home with their spouse, and can self-isolate in a room away the family. Patient has been given instructions on how to keep the dose he/she gives others as low as possible.
E = 0.125 (3 hours/day)

- If the patient meets all the requirements needed for a factor of 0.25 AND
- Can live alone for first two days.
- Has minimal visits from family and others.
- Example: Patient has a short drive home and lives alone in a studio apartment. Will be completely isolated for multiple days, with the exception of a short visit from their parents on the second day.

E = 0.75 (18 hours/day)

- Typically regarded as overly conservative.
- Used if the patient cannot follow instructions.
- Used if the patient lives in a single room and cannot be separated from family.
- Used if the patient cannot sleep alone.
- Example: Patient lives at home with a pregnant wife and multiple children in a single room. Patient also seems confused about the treatment and radiation safety.
Example using Tc-99m

- $T_p = 0.251$ days
- $\Gamma = 0.76$ rem-cm$^2$/mCi-hr
- $Q_0 = 30$ mCi
- $E = 1.0$
- $R = 100$ cm

\[
D = \frac{34.6 \times (0.76 R \cdot cm^2 / mCi \cdot hr) \times (30 mCi) \times 0.25 d \times 1}{(100 cm)^2}
\]

$D(\infty) = 0.02$ rem = 20 mrem = 0.2 mSv < 500 mrem

Example using I-131

- $T_p = 8.0$ days
- $\Gamma = 2.2$ R-cm$^2$/mCi-hr
- $Q_0 = 30$ mCi
- $E = 0.25$
- $R = 100$ cm

\[
D = \frac{34.6 \times (2.2 R \cdot cm^2 / mCi \cdot hr) \times (30 mCi) \times 8d \times 0.25}{(100 cm)^2}
\]

$D(\infty) = 0.46$ rem = 460 mrem = 4.6 mSv < 500 mrem
**Tc-99m compared to I-131**

- Tc-99m patient’s could be given as much as 760 mCi and be released. 30 mCi of Tc-99m imparts a very modest dose to the most exposed person.
- On the other hand, 30 mCi of I-131 is close to the 500 mrem (5 mSv) limit and 32.7 mCi (1.21 GBq) would reach it.
- The regulatory guide NUREG 1556 Vol 9, Appendix U tabulates the maximum administered activities for many common radionuclides that would give the most exposed person 500 mrem (5 mSv) under these assumptions.

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From regulatory Guide NUREG 1556 Vol 9, Appendix U.1

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Activity At or Below Which Patient May Be Released</th>
<th>Dose Rate at 1 Meter, At or Below Which Patient May Be Released</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ag-111</td>
<td>1.4 mCi</td>
<td>0.08 mrem/hour</td>
</tr>
<tr>
<td>Co-57</td>
<td>55 mCi</td>
<td>0.21 mrem/hour</td>
</tr>
<tr>
<td>Cu-64</td>
<td>4.8 mCi</td>
<td>0.02 mrem/hour</td>
</tr>
<tr>
<td>Cu-67</td>
<td>8.4 mCi</td>
<td>0.27 mrem/hour</td>
</tr>
<tr>
<td>Fe-55</td>
<td>14 mCi</td>
<td>0.22 mrem/hour</td>
</tr>
<tr>
<td>Ga-67</td>
<td>8.7 mCi</td>
<td>0.18 mrem/hour</td>
</tr>
<tr>
<td>In-111</td>
<td>6.6 mCi</td>
<td>0.26 mrem/hour</td>
</tr>
<tr>
<td>Re-186</td>
<td>0.23 mCi</td>
<td>0.01 mrem/hour</td>
</tr>
<tr>
<td>Re-188</td>
<td>0.33 mCi</td>
<td>0.04 mrem/hour</td>
</tr>
<tr>
<td>Re-188/implant</td>
<td>1.2 mCi</td>
<td>0.07 mrem/hour</td>
</tr>
<tr>
<td>Se-75</td>
<td>3.4 mCi</td>
<td>0.01 mrem/hour</td>
</tr>
<tr>
<td>Se-77/implant</td>
<td>0.014 mCi</td>
<td>0.009 mrem/hour</td>
</tr>
<tr>
<td>Se-89</td>
<td>1.5 mCi</td>
<td>0.03 mrem/hour</td>
</tr>
<tr>
<td>Se-90</td>
<td>30 mCi</td>
<td>0.15 mrem/hour</td>
</tr>
<tr>
<td>Se-99/implant</td>
<td>11 mCi</td>
<td>0.17 mrem/hour</td>
</tr>
<tr>
<td>Se-117/implant</td>
<td>0.009 mCi</td>
<td>0.003 mrem/hour</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>0.26 mCi</td>
<td>0.03 mrem/hour</td>
</tr>
<tr>
<td>Tl-201</td>
<td>1.1 mCi</td>
<td>0.04 mrem/hour</td>
</tr>
<tr>
<td>Y-90</td>
<td>3 mCi</td>
<td>0.58 mrem/hour</td>
</tr>
<tr>
<td>Zn-65/implant</td>
<td>0.31 mCi</td>
<td>0.02 mrem/hour</td>
</tr>
</tbody>
</table>

**Hmmm... No Lu-177**
Can go home but must have instructions

- Based on 10 CFR 35.75(b), for some administrations (if the total effective dose equivalent to any other individual is likely to exceed 1 mSv (0.1 rem)) the released patients must be given instructions, including written instructions, on how to maintain doses to other individuals ALARA after the patients are released.
- Table U.2 provides the activity and dose rates at 1 meter above which instructions must be given to patients.
- If the patient is breast-feeding an infant or child, additional instructions may be necessary.

From regulatory Guide NUREG 1556 Vol 9, Appendix U.2
But wait ... there's more

The Two Compartment Model

- For administered activities of NaI\(^{131}\) patient-specific calculations must include:
  - occupancy factors
  - effective half-lives
  - uptake fractions (based on a 2-component, extrathyroidal and intrathyroidal model of I-131 pharmacokinetics)

- \(E_1\) and \(E_2\) = the occupancy factors for the extrathyroidal and intrathyroidal components, respectively

- \(F_1\) and \(F_2\) = the uptake fractions for the extrathyroidal and intrathyroidal components, respectively

- \(T_p\) = physical half-life for I-131 = 8.04 d

- \(T_{1\text{eff}}\) and \(T_{2\text{eff}}\) = effective half-lives (in days) for the extrathyroidal and intrathyroidal components, respectively
• The uptake fractions and effective half-lives can be measured for each patient, or alternatively be taken from Table U.6 (or as shown in below reference).

<table>
<thead>
<tr>
<th>Medical condition</th>
<th>Extraglandular component</th>
<th>Thyroidal component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uptake fraction $F_x$</td>
<td>Effective half-life $T_{1/2}$ (day)</td>
<td>Uptake fraction $F_x$</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>0.20</td>
<td>0.32</td>
</tr>
<tr>
<td>Post-thyroidectomy for thyroid cancer</td>
<td>0.95</td>
<td>0.32</td>
</tr>
</tbody>
</table>

*From Table 6-1 in NRC Regulatory Guide 6.39


• Our equation that looked like this:

$$D(\infty) = \frac{34.6 \times \Gamma \times Q_0 \times T_p \times E}{(r)^2}$$

• Becomes this for NaI $^{131}$I:

$$D(\infty) = \frac{34.6 Q_0}{100cm^2} \left( E_T \frac{T_p}{(0.8)(1-e^{-0.695(0.33)/T_p})} + e^{-0.695(0.33)/T_p}E_T E_{2,T_{14F}} + e^{-0.695(0.33)/T_p}E_T E_{2,T_{2df}} \right)$$

• Using patient data or Table 2 you can use an online calculator such as: http://www.doseinfo-radar.com/ExposureCalculator.html
What about our Lu177?

\[ T_p = 6.6 \text{ days} \]
\[ \Gamma = 0.15 \text{ R-cm}^2/\text{mCi-hr} \]
\[ Q_0 = 200 \text{ mCi} \]
\[ E = 0.25 \]
\[ R = 100 \text{ cm} \]

\[
D = \frac{34.6 \times (0.153 R \cdot \text{cm}^2 / \text{mCi-hr}) \times (200 \text{mCi}) \times 6.7 d \times 0.25}{(100 \text{cm})^2}
\]

\[ D(\infty) = 0.18 \text{ rem (180 mrem, 1.8 mSv)} \]
(The patient can be released but requires instructions)

Example Instructions used at SUH

For 4 days:

Most of the radioiodine is excreted in your urine.

- Drink lots of fluids when awake
- Urinate at least every two hours
- If urine is spilled or splashed on the toilet seat, wash and rinse the area with disposable towels.
- Flush toilet twice

Some of the radioiodine is in your saliva and sweat. To minimize radioiodine contamination in your home:

- Shower once per day (and/or after exercising)
- Use disposable cups, plates, and utensils
- Do not share wash cloths, towels, bathroom cup, or toothbrush
- Sleep in a separate bed
- Wash your clothing, underwear, pajamas, towels, and bed linen separately from your family laundry
- Avoid most physical contact with infants, young children, pregnant women, and pets

The residual radioiodine in your thyroid can expose people near you

- Do not sit within one foot of others for extended periods; such as at a movie theater. (Short periods near others do not cause them too much exposure and is ok.)
Mr. Markey, Representative of Massachusetts:

"My investigation has led me to conclude that the levels of unintentional radiation received by members of the public who have been exposed to patients that have received ‘drive through’ radiation treatments may well exceed international safe levels established for pregnant women and children."

Health Physics Society: The NRC Advisory Committee on the Medical Uses of Isotopes (ACMUI) used the extremely conservative NRC algorithms to evaluate various exposure scenarios from an iodine-131 patient released to a hotel and concluded that the dose to any other individual exposed to the iodine-131 therapy patient is not likely to exceed 1 mSv (U.S. NRC 2010).

Society of Nuclear Medicine: You should ask your doctor for additional instructions if you are planning to use public transportation or stay in a hotel or other non-private lodging.

Hotels & Motels

- Ask if the individual is going to stay at a hotel.
- If they are, instructions must address the potential for exposing other hotel guests and workers.
- For help with instructions contact your Radiation Safety Officer.
- Note: Stanford policy is to have patients stay at SUH and NOT a motel.
Resources include:

- Online calculators such as: [http://www.doseinfo-radar.com/ExposureCalculator.html](http://www.doseinfo-radar.com/ExposureCalculator.html)
- NUREG 1556, Volume 9, Revision 2, Appendix U
- Prepared spreadsheets such as the one used at SUH nuclear medicine
- “how to” articles such as the Journal of Nuclear Medicine Technology:

In Summary

- Patients who receive therapeutic amounts of radiopharmaceuticals are potentially significant source of radiation to family members, the public, and others
- A patient administered radioactive materials may be released from controls provided the total effective dose equivalent to any other individual is not likely to exceed 5 mSv (500 mrem).
- Written instructions shall be provided to the released individual if the total dose to any other individual is likely to exceed 1 mSv (100 mrem).
- A licensee shall maintain a record of the technical basis for authorizing release of an individual, or, authorizing breast-feeding.
• Thanks!