Nuclear Regulatory Commission guidance on release of radioactive patients

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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)

	Release limit for when patients could be let go	
	Then	**Now (since 1997)**
Activity	30 mCi	Exposure to any individual from released patient must be less than 500 mrem
Dose rate at 1 meter	5 mrem/hr	or dose rate based on isotope*

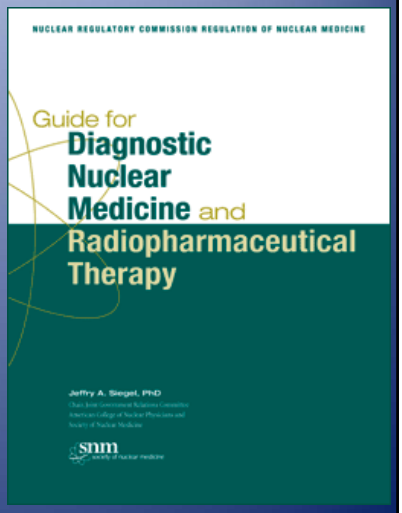
* From Table U.1, Appendix U, NUREG-1556

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

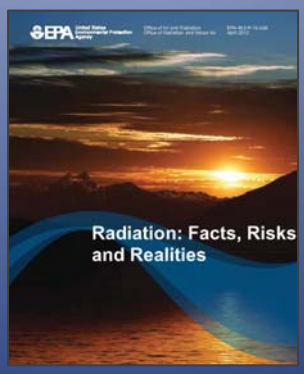
- Some argue that 5 mSv is dangerous and that we should return to the old 30 mCi or 5 mR/hr @ 1 m release criteria.
- Some physicists and physicians argue that the 5 mSv limit is well below the threshold of danger.
- Beware: Some patients after receiving your instructions will go straight to a hotel 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.

HEALTH PHYSICS SOCIETY
FOUNDED 1956

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)

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(∞) = Accumulated exposure at time t, in roentgens (≈ rem or rad)

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

Γ = 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

E	Conditions
1.0 – 0.75 (18-24 hrs/day)	The half-life is < than a day
0.25 (6 hrs/day)	The half-life is > than a day and the patient able to maintain prudent distance from others for 2 days
0.125 (3 hrs/day)	The half-life is > than a day and patient can comply with lifestyle instructions that are consistent with this occupancy factor
0.75/0.25	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 http://www.doseinforadar.com/ExposureCalculator.html).

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

Γ = 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(∞) = 0.02 rem = 20 mrem = 0.2 mSv < 500 mrem

Example using I-131

T_P = 8.0 days

Γ = 2.2 R-cm^2/mCi-hr

Q_0 = 30 mCi

E = 0.25

R = 100 cm

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

D(∞) = 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.

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

Table U.1 Activities and Dose Rates for Authorizing Patient Release†

Radionuclide	COLUMN 1 Activity At or Below Which Patients May Be Released		COLUMN 2 Dose Rate at 1 Meter, At or Below Which Patients May Be Released*	
	(GBq)	(mCi)	(mSv/hr)	(mrem/hr)
Ag-111	19	520	0.08	8
Au-198	3.5	93	0.21	21
Cr-51	4.8	130	0.02	2
Cu-64	8.4	230	0.27	27
Cu-67	14	390	0.22	22
Ga-67	8.7	240	0.18	18
I-123	6	160	0.26	26
I-125	0.25	7	0.01	1
I-125 implant	0.33	9	0.01	1
I-131	1.2	33	0.07	7
In-111	2.4	64	0.2	20
Ir-192 implant	0.074	2	0.008	0.8
P-32	**	**	**	**
Pd-103 implant	1.5	40	0.03	3
Re-186	28	770	0.15	15
Re-188	29	790	0.2	20
Sc-47	11	310	0.17	17
Se-75	0.089	2	0.005	0.5
Sm-153	26	700	0.3	30
Sn-117m	1.1	29	0.04	4
Sr-89	**	**	**	**
Tc-99m	28	760	0.58	58
Tl-201	16	430	0.19	19
Y-90	**	**	**	**
Yb-169	0.37	10	0.02	2

Footnotes for Table U-1

† The activity values were computed based on 5 millisieverts (0.5 rem) total effective dose equivalent.

* If the release is based on the dose rate at 1 meter in Column 2, the licensee must maintain a record as required by 10 CFR 35.75(c), because the measurement includes shielding by tissue. See Item U.3.1, "Records of Release," for information on records.

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

APPENDIX U

Table U.2 Activities and Dose Rates Above Which Instructions Should Be Given When Authorizing Patient Release* *(continued)*

Radionuclide	COLUMN 1 Activity Above Which Instructions Are Required		COLUMN 2 Dose Rate at 1 Meter Above Which Instructions Are Required	
	(GBq)	(mCi)	(mSv/hr)	(mrem/hr)
I-125	0.05	1	0.002	0.2
I-125 implant	0.074	2	0.002	0.2
I-131	0.24	7	0.02	2
In-111	0.47	13	0.04	4
Ir-192 implant	0.011	0.3	0.002	0.2
P-32	**	**	**	**
Pd-103 implant	0.3	8	0.007	0.7
Re-186	5.7	150	0.03	3
Re-188	5.8	160	0.04	4
Sc-47	2.3	62	0.03	3
Se-75	0.018	0.5	0.001	0.1
Sm-153	5.2	140	0.06	6
Sn-117m	0.21	6	0.009	0.9
Sr-89	**	**	**	**
Tc-99m	5.6	150	0.12	12
Tl-201	3.1	85	0.04	4
Y-90	**	**	**	**
Yb-169	0.073	2	0.004	0.4

Footnotes for Table U.2

* The activity values were computed based on 1 millisievert (0.1 rem) total effective dose equivalent.

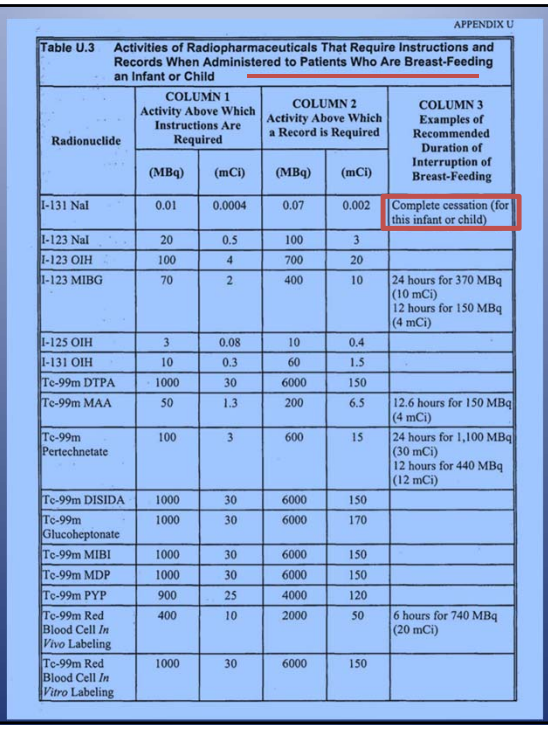
** Activity and dose rate limits are not applicable in this case because of the minimal exposures to members of the public resulting from activities normally administered for diagnostic or therapeutic purposes.

Notes: The values for activity were calculated using Equations U.2 or U.3 and the physical half-life. The values given in SI units (gigabecquerel values) were using conversion factors.

In general, values are rounded to two significant figures; however, values less than 0.37 gigabecquerel (10 millicuries) or 0.1 millisievert (10 millirems) per hour are rounded to one significant figure. Details of the calculations are provided in NUREG-1492.

Agreement State regulations may vary. Agreement State licensees should check their State regulations before using these values.

From regulatory Guide NUREG 1556 Vol 9, Appendix U.



APPENDIX U

Table U.3 Activities of Radiopharmaceuticals That Require Instructions and Records When Administered to Patients Who Are Breast-Feeding an Infant or Child

Radionuclide	COLUMN 1 Activity Above Which Instructions Are Required		COLUMN 2 Activity Above Which a Record is Required		COLUMN 3 Examples of Recommended Duration of Interruption of Breast-Feeding
	(MBq)	(mCi)	(MBq)	(mCi)	
I-131 NaI	0.01	0.0004	0.07	0.002	Complete cessation (for this infant or child)
I-123 NaI	20	0.5	100	3	
I-123 OIH	100	4	700	20	
I-123 MIBG	70	2	400	10	24 hours for 370 MBq (10 mCi) 12 hours for 150 MBq (4 mCi)
I-125 OIH	3	0.08	10	0.4	
I-131 OIH	10	0.3	60	1.5	
Tc-99m DTPA	1000	30	6000	150	
Tc-99m MAA	50	1.3	200	6.5	12.6 hours for 150 MBq (4 mCi)
Tc-99m Pertechnetate	100	3	600	15	24 hours for 1,100 MBq (30 mCi) 12 hours for 440 MBq (12 mCi)
Tc-99m DISIDA	1000	30	6000	150	
Tc-99m Glucoheptonate	1000	30	6000	170	
Tc-99m MIBI	1000	30	6000	150	
Tc-99m MDP	1000	30	6000	150	
Tc-99m PYP	900	25	4000	120	
Tc-99m Red Blood Cell *In Vivo* Labeling	400	10	2000	50	6 hours for 740 MBq (20 mCi)
Tc-99m Red Blood Cell *In Vitro* Labeling	1000	30	6000	150	

But wait … there's more
The Two Compartment Model

- For administered activities of NaI ^{131}I 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_{1eff} and T_{2eff} = 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 2
Uptake Fractions and Effective Half-Lives for Iodine-131*

Medical condition	Extrathyroidal component: Uptake fraction F_1	Extrathyroidal component: Effective half-life T_{1eff} (day)	Thyroidal component: Uptake fraction F_2	Thyroidal component: Effective half-life T_{2eff} (day)
Hyperthyroidism	0.20	0.32	0.80	5.2
Post-thyroidectomy for thyroid cancer	0.95	0.32	0.05	7.3

*From Table B-1 in *NRC Regulatory Guide 8.39.*

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J. Nucl. Med. Technol. December 1, 2000 vol. 28 no. 4 275-279

- 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:

$$D(\infty) = \frac{34.6\Gamma Q_0}{(100cm)^2}\left\{E_1 T_p (0.8)(1 - e^{-0.693(0.33)/T_p}) + e^{-0.693(0.33)/T_p} E_2 F_1 T_{1eff} + e^{-0.693(0.33)/T_p} E_2 F_2 T_{2eff}\right\}$$

- 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 days

Γ = 0.15 R-cm2/mCi-hr

Q_0 = 200 mCi

E = 0.25

R = 100 cm

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

D(∞) = 0.18 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.

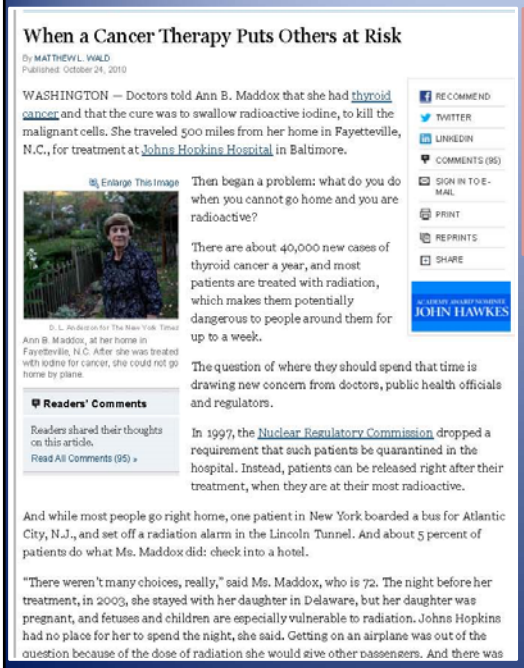
- Drink lots of fluids when awake
- Urinate at least every two hours
- If urine is spilled or splashed on the toilet seat, wash and rinse the area with disposable towels.
- Flush toilet twice

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.)



When a Cancer Therapy Puts Others at Risk

By MATTHEW L. WALD
Published: October 24, 2010

WASHINGTON — Doctors told Ann B. Maddox that she had thyroid cancer and that the cure was to swallow radioactive iodine, to kill the malignant cells. She traveled 500 miles from her home in Fayetteville, N.C., for treatment at Johns Hopkins Hospital in Baltimore.

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D. L. Anderson for The New York Times

Ann B. Maddox, at her home in Fayetteville, N.C. After she was treated with iodine for cancer, she could not go home by plane.

Then began a problem: what do you do when you cannot go home and you are radioactive?

There are about 40,000 new cases of thyroid cancer a year, and most patients are treated with radiation, which makes them potentially dangerous to people around them for up to a week.

The question of where they should spend that time is drawing new concern from doctors, public health officials and regulators.

Readers' Comments

Readers shared their thoughts on this article.

Read All Comments (95) »

In 1997, the Nuclear Regulatory Commission dropped a requirement that such patients be quarantined in the hospital. Instead, patients can be released right after their treatment, when they are at their most radioactive.

And while most people go right home, one patient in New York boarded a bus for Atlantic City, N.J., and set off a radiation alarm in the Lincoln Tunnel. And about 5 percent of patients do what Ms. Maddox did: check into a hotel.

"There weren't many choices, really," said Ms. Maddox, who is 72. The night before her treatment, in 2003, she stayed with her daughter in Delaware, but her daughter was pregnant, and fetuses and children are especially vulnerable to radiation. Johns Hopkins had no place for her to spend the night, she said. Getting on an airplane was out of the question because of the dose of radiation she would give other passengers. And there was

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

- 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:
  - Applying Nuclear Regulatory Commission Guidelines to the Release of Patients Treated with Sodium Iodine-131 (teaching editorial; William K. Tuttle, III, and Paul H. Brown; J Nucl Med Technol 2000; 28:275–279

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!