Standard-Of-Care LutaThera Exposure Rates, Radiation Precaution Durations and Estimated Total Effective Dose Equivalents: One Institution's First Year and a Half Experience

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INTRODUCTION

Lutathera® (^{177}Lu-DOTATATE) is a relatively new standard-of-care (SoC) treatment of somatostatin receptor-positive gastroentero-pancreatic neuroendocrine tumors (GEP-NETs), where the standard treatment regimen consists of four 7.4 GBq (200 mCi) treatments every 8 weeks, on an out-patient basis. Our institution's first SoC Lutathera treatment occurred in July 2018, and up to the present time, over 300 treatments on over 100 patients have been performed. Herein, we describe our first one and a half year results related to the radiation safety of releasing these patients to the general public at the end of the treatment session.

AIM

The purpose of this investigation was to evaluate the radiation safety of treating and releasing Lutathera patients on an out-patient basis, via quantitative analysis of the measured and calculated radioactive patient release parameters over a large number of patients and treatments.

METHOD

1. Descriptive statistics were computed for
   - Exposure rate (mR/h) measured at 1 m (X)
   - Time (hours post-infusion) of release (Trel)
   - Durations (days) of radiation precautions
   - Total effective dose equivalent (mrem TEDE) estimates
2. Calculations based on 1/4th the regulatory TEDE upper limits, i.e.
   - 125 mrem (1.25 mSv) for release with instructions
   - 25 mrem (0.25 mSv) for release without instructions

   (assuming four exposures to the same persons within 6 mos.)
3. Patient-specific release calculations
   - Based on measured X and a fixed 56.1 h T½eff (1)
   - TEDE and patient-specific radiation precaution durations for
     - Most-exposed person
     - Children and pregnant women
     - Fellow travelers

   per NRC guidelines (2), related publications (3,4), lifestyle Q & A
4. Per release means, σ's , minima and maxima computed from
   - 292 treatments on 98 patients
   - July 2018 through January 2020

RESULTS

The prescribed activity for 271 of the 292 treatments was 7.4 GBq (200 mCi). The prescribed activity for the remainder were reduced by a factor of two, i.e., to 3.7 BGq (100 mCi), for patients with below normal renal function (as measured by creatinine clearance, glomerular filtration rate).

The descriptive statistics are shown in the table.

1. X was highly variable, due to:
   - patient-to-patient variation in self-attenuation
   - variable time post-infusion of the measurement

   (Lutathera clearance is bi-exponential, with a fast-component T½ ~2 h. Ergo, rapid fall off in X over the first few hours, until the slow-component dominates.)
2. All radiation precaution durations and TEDE estimates were also highly variable
   - All calculations based on X and a fixed, slow-component T½ (56.1 h)
   - Variation in X translates to variation in calculated durations and TEDEs
   - Fellow traveler TEDE variability also due to patient-to-patient variation in travel arrangements (alone or not, mode, duration, distance from others)
3. However, all TEDE estimates were well below the 100 mrem (1 mSv) regulatory upper limit for release without instructions.
4. The use of a fixed, published slow-component 56.1 h whole body effective T½ for SoC patient release, when post-treatment imaging is not employed, is reasonable. (Mean slow-component T½ from a pre-FDA approval, 13-patient/29-treatment clinical trial with dosimetric analysis [unpublished] was 58.8 h [Fig. 1].)

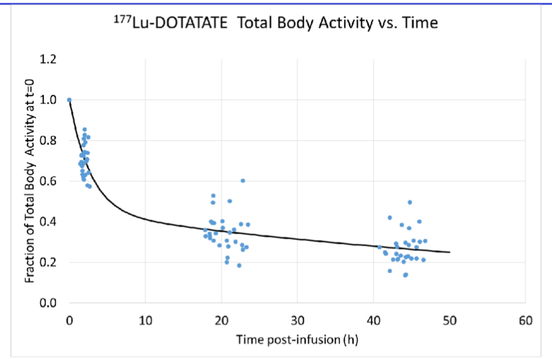
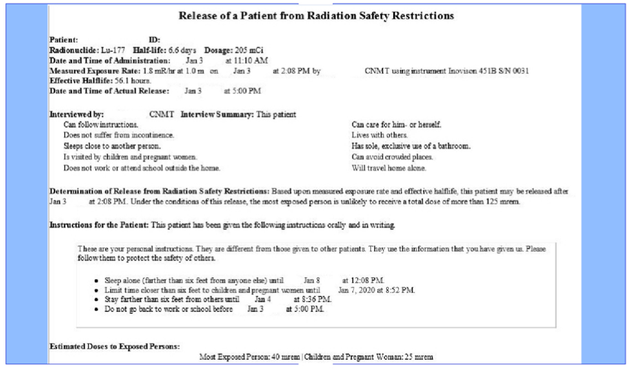


Figure 1. Plot of fraction of initial total body activity vs. time for 13 patients on a ^{177}Lu-DOTATATE trial, who underwent post-therapy dosimetric imaging (29 treatments). A bi-exponential fit is overlaid (T1/2eff: 1.9 h [fast], 59.7 h [slow]).



Release of a Patient from Radiation Safety Restrictions

Patient: **ID:**
Radionuclide: Lu-177 **Half-life:** 6.6 days **Dosage:** 205 mCi
Date and Time of Administration: Jan 3 at 11:10 AM.
Measured Exposure Rate: 1.8 mR/hr at 1.0 m on Jan 3 at 2:08 PM by CNMT using instrument Inovision 451B S/N 0031
Effective Halflife: 56.1 hours.
Date and Time of Actual Release: Jan 3 at 5:00 PM

Interviewed by: CNMT **Interview Summary:** This patient
Can follow instructions. Can care for him- or herself.
Does not suffer from incontinence. Lives with others.
Sleeps close to another person. Has sole, exclusive use of a bathroom.
Is visited by children and pregnant women. Can avoid crowded places.
Does not work or attend school outside the home. Will travel home alone.

Determination of Release from Radiation Safety Restrictions: Based upon measured exposure rate and effective halflife, this patient may be released after Jan 3 at 2:08 PM. Under the conditions of this release, the most exposed person is unlikely to receive a total dose of more than 125 mrem.

Instructions for the Patient: This patient has been given the following instructions orally and in writing.

These are your personal instructions. They are different from those given to other patients. They use the information that you have given us. Please follow them to protect the safety of others.

- Sleep alone (farther than six feet from anyone else) until Jan 8 at 12:08 PM.
- Limit time closer than six feet to children and pregnant women until Jan 7, 2020 at 8:52 PM.
- Stay farther than six feet from others until Jan 8 at 8:26 PM.
- Do not go back to work or school before Jan 3 at 5:00 PM.

Estimated Doses to Exposed Persons:
Most Exposed Person: 40 mrem | Children and Pregnant Woman: 25 mrem

Figure 2. Example documentation of Lutathera patient release, that is signed by the Authorized User and uploaded into the patient's electronic medical record. A copy of the radiation precaution instructions and durations is given to the patient upon release post-treatment.

Safety Parameter	Mean	Standard Deviation	Minimum	Maximum
Exposure Rate (mR/h)	1.70	0.47	0.80	3.10
Time Post-Tx of Release (h)	5.59	0.45	4.53	7.50
Sleeping Alone Duration (d)	4.44	1.20	1.50	7.34
Limiting Children/Pregnant Women Contact Duration (d)	3.41	1.24	1.00	6.84
Avoiding Others Duration (d)	0.95	0.79	0.00	2.95
Avoiding Work or School Duration (d)	0.28	0.61	0.00	2.82
Most-Exposed Person TEDE (mrem)	37.5	9.4	18.0	64.0
Children/Pregnant Women TEDE (mrem)	24.9	0.6	19.0	25.0
Fellow Traveler TEDE (mrem)	8.9	7.6	1.0	25.0

CONCLUSIONS

1. All TEDE estimates were less than 100 mrem (1 mSv).
2. All these Lutathera patients could have been released at the end of treatment without radiation precaution instructions, if the NRC 100 mrem (1 mSv) upper limit for release without instructions was adhered to.
3. If the TEDE upper limits for the most-exposed person and members of the public for release with instructions are reduced by 3/4^{ths}, i.e., to 125 mrem (1.25 mSv) and 25 mrem (0.25 mSv), respectively (to account for potential exposure of the same persons after each treatment within one year), all of these patients could still be released with instructions at end of treatment.

(Note: Dividing the NRC limits for release among four Lutathera treatments within a six-month period is purely voluntary. The current limits are per release, as opposed to either per annum or per annum divided by the number of treatments within any twelve-month period.)

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REFERENCES

1 **C Wehrmann et al**. Results of individual patient dosimetry in peptide receptor radionuclide therapy with ^{177}Lu DOTA-TATE and ^{177}Lu DOTA-NOC. *Cancer Biother Radiopharm 2007; 22: 406–16.*

2 US Nuclear Regulatory Commission guideline NUREG 1556 Volume 9 Revision 2 Appendix U.

3 **JA Siegel et al**. A Practical methodology for patient release after tositumomab and ^{131}I-tositumomab therapy. *J Nucl Med 2002; 43: 354–63.*

4 **LR Coover et al**. Therapeutic ^{131}I in outpatients: a simplified method conforming to the Code of Federal Regulations, Title 10, Part 35.75. *J Nucl Med 2000; 41: 1868–75.*

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