Original Article

Estimation of Whole Body Radiation Exposure to Nuclear Medicine Personnel During Synthesis of ^{177}Lutetium-labeled Radiopharmaceuticals

Geetanjali Arora, Rajesh Mishra, Praveen Kumar, Madhav Yadav, Sanjana Ballal, Chandrasekhar Bal, Nishikant Avinash Damle

Department of Nuclear Medicine, All India Institute of Medical Sciences, New Delhi, India

Abstract

Purpose of the Study: With rapid development in the field of nuclear medicine therapy, radiation safety of the personnel involved in synthesis of radiopharmaceuticals has become imperative. Few studies have been done on estimating the radiation exposure of personnel involved in the radio labeling of ^{177}Lu-compounds in western countries. However, data from the Indian subcontinent are limited. We have estimated whole body radiation exposure to the radiopharmacist involved in the labeling of: ^{177}Lu-DOTATATE, ^{177}Lu-PSMA-617, and ^{177}Lu-EDTMP. **Materials and Methods:** Background radiation was measured by keeping a pocket dosimeter around the workbench when no radioactive work was conducted. The same pocket dosimeter was given to the radiopharmacist performing the labeling of ^{177}Lu-compounds. All radiopharmaceuticals were synthesized by the same radiopharmacist with 3, 1 and 3 year experience, respectively, in radiolabeling the above compounds. **Results:** One Curie (1 Ci) of ^{177}Lu was received fortnightly by our department. Data were collected for 12 syntheses of ^{177}Lu-DOTATATE, 8 syntheses of ^{177}Lu-PSMA-617, and 3 syntheses of ^{177}Lu-EDTMP. Mean time required to complete the synthesis was 0.81, 0.65, and 0.58 h, respectively. Mean whole body radiation exposure was 0.023 ± 0.01 mSv, 0.01 ± 0.002 mSv, and 0.002 ± 0.0006 mSv, respectively. Overall mean radiation dose for all the three ^{177}Lu-compounds was 0.014 mSv. Highest exposure was obtained during the synthesis of ^{177}Lu-DOTATATE. **Conclusion:** Our data suggest that the manual radiolabeling of ^{177}Lu compounds is safe, and the whole body radiation exposure to the involved personnel is well within prescribed limits.

Keywords: *Personnel dosimetry, manual radiolabeling, radionuclide therapy*

Introduction

Personnel monitoring is an intergral part of any radiation safety program. Personnel monitoring aims to keep the occupational radiation exposure as low as reasonably achievable (ALARA) and is based on the principle that the benefits of any intentional or planned exposure to radiation should outweigh the resultant detriment that could arise.[1] Safe radiation work practices and permissible radiation exposure limits have been laid by various national and international regulatory authorities.

As per ICRP recommendations 103 (2007), the equivalent radiation dose to personnel should not exceed 20 mSv/year averaged over 5 years, not exceeding 50 mSv in any year.[2] These limits are aimed at keeping the probability of stochastic effects of radiation to the lowest, while avoiding the occurrence of non-stochastic effects altogether. By defination, any person handling radiation and likely to receive an occupational radiation exposure of more than 1 mSv is liable to be monitored.

In nuclear medicine, personnel involved in synthesis of radiopharmaceuticals, dose administration, and/or scan acquisition are most likely to receive radiation exposure. The risk could be even higher while handling therapeutic radiopharmaceuticals. In the present study, we have focussed on the personnel involved in synthesis of radiopharmaceuticals involving Lu-177 that is DOTATATE/DOTANOC, PSMA-617 and EDTMP. The choice of radiopharmaceuticals was based on the fact that these three radiopharmaceuticals are being routinely synthesized at our department, at the All India Institute of Medical Sciences, New Delhi, India.

Over the last decade, Lu-177 has become the radionuclide of choice for various

Address for correspondence:
Dr. N.A. Damle, Assistant Professor, Department of Nuclear Medicine, AIIMS, New Delhi, India.
E-mail: nkantdamle@gmail.com

Access this article online

Website: www.indjsp.org

DOI: 10.4103/0972-3919.202245

Quick Response Code:

How to cite this article: Arora G, Mishra R, Kumar P, Yadav M, Ballal S, Bal C, Damle NA. Estimation of whole body radiation exposure to nuclear medicine personnel during synthesis of ^{177}lutetium-labeled radiopharmaceuticals. Indian J Nucl Med 2017;32:89-92.

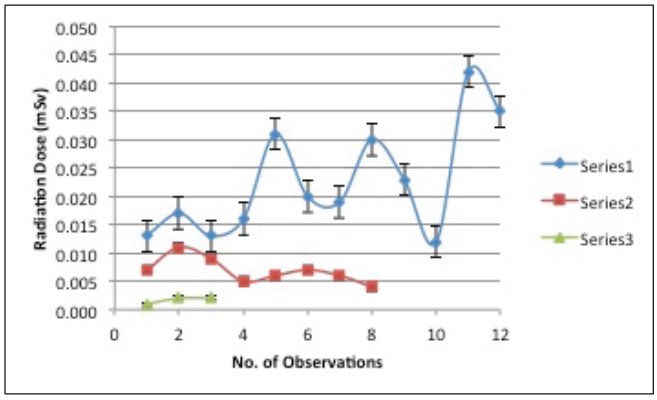

Figure 1: Radiation dose of 177Lu labeled DOTATATE/NOC (series 1), PSMA-617 (series 2) and EDTMP (series 3) with the standard error

radionuclide therapy procedures owing to its ease of large-scale production in moderate flux reactors, favorable radiation characteristics enabling imaging along with therapy (β^-_{max}: 497 keV; γ_1: 113 keV; 6.4% and γ_2: 208 keV; 11%); and sufficiently long half-life (6.7 days) allowing easy transport to centers far off from a reactor site.[3] These economic, characteristic, and logistic advantages of Lu-177 have become even more significant in developing countries, where affordable therapeutic options are always sought.

Although there is a plethora of literature on the internal dosimetry or patient dosimetry with ^{177}Lu-radiopharmceuticals, there is a lesser literature on the personnel dosimetry, especially those involved in synthesis. ^{177}Lu-DOATATATE/DOTANOC, PSMA-617, and EDTMP can be synthesized in automatic or semi-automatic chemistry modules or by manual methods. Since a manual method is more cost effective than automatic or semi-automatic methods, it is the most widely practiced method in developing countries like India. However, it poses a risk of comparatively higher radiation exposure to the personnel involved. Therefore, the present study aims to monitor the radiation dose levels to personnel during manual synthesis of ^{177}Lu-labeled compounds (DOTATATE/DOTANOC, PSMA-617, and EDTMP) and reviews work practices that may reduce the radiation exposure.

Materials and Methods

Lu-177 as $LuCl_3$ was procured from BRIT, Mumbai, India. A digital pocket dosimeter (MYDOSE Mini) was obtained from ALOKA. The precursors used in the synthesis of ^{177}Lu-labeled DOTATATE/DOTANOC and PSMA-617 were obtained from ABX GmbH, Germany, and EDTMP kit was obtained from BRIT/Polatom. All other reagents used in labeling were of analytical grade.

Procedure

Synthesis of Lu-177-labeled DOTATATE, PSMA-617, and EDTMP was carried out by designated skilled personnel at the radio-pharmacy laboratory of the Department of Nuclear Medicine, AIIMS, New Delhi, India. These radiopharmaceuticals were routinely synthesized in our department, on fortnightly basis by manual methods. DOTATATE and DOTANOC were labeled alternatively depending on the availability of precursor. The MYDOSE mini radiation pocket dosimeter was used to measure the radiation exposure. Initially, background radiation of the laboratory, where labeling was carried out, was measured by placing the dosimeter in the laboratory when no radioactive work was being conducted. The background exposure readings were taken at different places around the labeling workbench and mean was calculated.

Personnel were issued a pocket dosimeter prior to the start of labeling procedure. Initial reading of the meter was set at zero every time. Radiation exposure readings recorded in the meter were noted on the completion of labeling process. The total amount of radioactivity handled during labeling and the duration of each labeling procedure were noted.

Table 1: Number of readings of exposure of various radiopharmaceuticals

Radiopharmaceuticals	Number of observations
^{177}Lu-DOTATATE/DOTANOC	2 + 10
^{177}Lu-PSMA-617	8
^{177}Lu-EDTMP	3
Total	23

Statistical Analysis

Descriptive statistic analysis was done for the collected data; and mean, median, standard deviation (SD), and range (minimum to maximum value) were determined. All the readings were expressed as mean ± SD.

Results

A total of 23 readings of radiation exposure were obtained during the labeling of all ^{177}Lu-radiopharmaceuticals put together. Table 1 shows the number of readings obtained for individual radiopharmaceuticals. Background radiation exposure reading was observed to be zero (for 1 hour) around the labeling workbench when no radioactive work was being conducted.

The details of radiation dose during labeling of ^{177}Lu-DOTATATE/NOC, PSMA-617, and EDTMP are given in Table 2, Table 3, and Table 4, respectively. Figure 1 represents the trend of radiation exposure during labeling of the three radiopharmaceuticals.

The mean radiation dose recorded in ^{177}Lu-DOTATATE/NOC labeling was 0.023 ± 0.01 mSv, ^{177}Lu-PSMA-617 was 0.01±0.002, mSv and ^{177}Lu-EDTMP was 0.002 ± 0.0006 mSv and the mean duration of labeling was 0.81, 0.65, and 0.58 h, respectively. The specific activity of Lu-177 was ~19–22 mCi/µgm in all labeling procedures.

The mean estimated radiation dose rate during the three labeling procedures was 0.03 ± 0.01 mSv/h for

Table 2: Radiation exposure during the labeling of ^{177}Lu-DOTATATE/NOC

S.No.	Activity (mCi)	Total duration of RP synthesis (h)	Radiation dose (mSv)	Radiation dose rate (mSv/h)
1.	1024	0.78	0.013	0.02
2.	1097	0.77	0.017	0.02
3.	785	0.75	0.013	0.02
4.	1048	0.78	0.016	0.02
5.	875	0.80	0.031	0.04
6.	654	0.78	0.020	0.03
7.	826	0.92	0.019	0.02
8.	800	0.83	0.030	0.04
9.	1155	0.75	0.023	0.03
10.	540	0.78	0.012	0.02
11.	1170	0.83	0.042	0.05
12.	782	0.90	0.035	0.04
Range	540-1170	0.75-0.92	0.012-0.042	0.02-0.05
Mean	896.33	0.81	0.023	0.03
Median	850.5	0.78	0.019	0.02
SD	201.63	0.05	0.01	0.01

Table 3: Radiation exposure during the labeling of ^{177}Lu-PSMA-617

S.N.	Activity (mCi)	Duration of labeling (h)	Radiation dose (mSv)	Radiation dose rate (mSv/h)
1.	189	0.72	0.007	0.01
2.	200	0.70	0.011	0.02
3.	226	0.75	0.009	0.01
4.	190	0.58	0.005	0.01
5.	180	0.57	0.006	0.01
6.	92	0.60	0.007	0.01
7.	300	0.67	0.006	0.01
8.	147	0.58	0.004	0.01
Range	92–300	0.57–0.75	0.004–0.011	0.01–0.02
Mean	190.5	0.65	0.007	0.01
Median	189.5	0.63	0.006	0.01
SD	59.82	0.07	0.002	0.003

Table 4: Radiation exposure during the labeling of ^{177}Lu-EDTMP

S.No.	Activity (mCi)	Duration of labeling (h)	Radiation dose (mSv)	Radiation dose rate (mSv/h)
1.	80	0.57	0.001	0.0018
2.	83.5	0.58	0.002	0.0034
3.	40	0.58	0.002	0.0034
Range	40–83.5	0.57–0.58	0.1–0.2	0.0018–0.0034
Mean	67.83	0.58	0.002	0.0027
Median	80	0.58	0.002	0.0034
SD	24.17	0.01	0.0006	0.001

DOTATATE/NOC, 0.01 ± 0.003 mSv/h for PSMA-617, and 0.003 ± 0.001 mSv/h for EDTMP. Overall mean radiation dose was 0.014 mSv and duration was 0.72 h.

Discussion

The objective of the study was to evaluate the radiation dose levels to personnel involved in the labeling of ^{177}Lu-labeled radiopharmaceuticals that is DOTATATE/NOC, PSMA-617, and EDTMP. The method of labeling these compounds with Lu-177 may be automated/semi-automated[4,5] or manual. At our department, we perform routine radiolabeling of these compounds with Lu-177 by a manual method, as it is more cost effective and automated modules are not available to us at present. However, in manual labeling procedures, the radiation safety concerns are higher than that in automated or semi-automated methods.

Labeling of ^{177}Lu-DOTATATE/NOC was performed as per the method described by Das *et al.*[6] and that of ^{177}Lu-PSMA-617 was performed by the method described by Ahmadzadehfar *et al.*[7] Automated or semi-automated modules are not available for the labeling of ^{177}Lu-EDTMP, as it is a single step procedure that involves simple addition and incubation of the EDTMP.[8]

Our results suggest that the labeling of ^{177}Lu-DOTATATE/NOC yielded the highest mean radiation dose of 0.023 ± 0.01 mSv, followed by ^{177}Lu-PSMA-617 0.01 ± 0.002 mSv, whereas the dose from the labeling of ^{177}Lu-EDTMP was the lowest 0.002 ± 0.0006 mSv. The reason for the observed trend is the time of radiolabeling, higher the duration of radioactivity handling, higher the radiation exposure. Overall dose trend also follows the same order as can be seen in Figure 1.

One of the most important factors that may affect the radiation dose to personnel in manual methods of radiolabeling is the skill. Different radiation workers have different levels of proficiency and expertise in the handling of radioisotopes that cause the readings to vary greatly among personnel. In our study, we ensured that every time the same radiation worker was involved in the radiolabeling of a particular compound to minimize such inter-personnel variations. However, intra-personnel variations still exist. Furthermore, to maintain uniformity of measurements and minimize the errors, the pocket dosimeter assigned to particular personnel during labeling was kept the same. It was also ensured that through out the observation period (labeling process), the personnel do not carry out any other radiation work or go to any other radiation area that might yield erroneously high reading on the dosimeter.

Other factors that might affect radiation dose are the duration and amount of radioactivity handled during the labeling procedure. Both, radioactivity and mean duration are highest for DOTATATE/NOC (896 mCi; 0.81 h), followed by PSMA-617 (190 mCi; 0.65 h), and EDTMP

(57 mCi; 0.58 h) in our study. This explains the trend of radiation dose for the three procedures.

Overall mean radiation dose for all the three ^{177}Lu-compounds was 0.014 mSv. Our department has a high throughput of patients, and synthesis of ^{177}Lu-compounds is performed once every fortnight, provided there is timely availability of Lu-177 and precursors. Assuming 24 such synthesis every year, the total mean dose to the personnel involved will be ~0.34 mSv. This dose level is far less than the stipulated limit of 20 mSv. Even if in future the synthesis rate increases to once per day and the same radiopharmacist is involved in synthesis, the dose will be ~5.26 mSv. The background activity in the radiolabelling laboratory returned to that existed pre-labeling, that is, zero (for 1 hour) after proper disposal of radioactive vials, syringes, absorbent sheets, gloves, and other contaminated waste. These things were properly sealed, labeled, and stored in a waste disposal room for decay. The reading of the TLD badge of the personnel involved was also within prescribed limits, that is, 0.9 mSv for chest badge for 1 year. It should be noted that this reading includes the radiation expsure to the presonnel from other sources as well apart from the radiolabeling procedures mentioned in this study as the personnel was involved in other departmental work also. This shows that even the manual radio-labeling methods of Lu-177 compounds are safe, provided safe work practices are followed.

The dose can be further reduced by involving staff well trained in good radio-pharmacy practices and radiation safety. Though the procedures are safe even if a single trained staff member conducts all the synthesis, it would be preferable to involve minimum two trained personnel to share and further reduce the radiation burden. The regular use of radiation monitoring devices such as the pocket dosimeters and TLD badges should be encouraged, and radiation surveys should be routinely conducted.

The study was conducted over a period of 6 months and various logistic reasons such as unexpected delay in delivery of Lu-177, or precursors sometimes restricted the regular synthesis of ^{177}Lu-compounds at our department. Hence, not much data points could be collected that is a major limitation of the study. Furthermore, due to unavailability of automated/semi-automated chemistry modules at our department a direct comparison was not possible. However, despite a less number of observations, the study is significant as there are only few similar studies on radiation dose levels to personnel involved in Lu-177 radio-labeling.

Conclusion

Our data suggest that the manual radio-labeling of ^{177}Lu-compounds is safe and the whole body radiation exposure to the involved personnel is well within the prescribed limits of ICRP, i.e., 20 mSv/year (averaged over 5 years). However, the exposure can further be reduced using semi-automated and automated modules, wherever possible.

Financial support and sponsorship

Nil

Conflicts of interest

There are no conflicts of interest

References

1. International basic safety standards for protection against ionizing radiation and for the safety of radiation sources. IAEA, Vienna, Austria. Basic safety standards series no. 115.
2. The 2007 Recommendations of the International Commission on Radiological Protection. Annals of the ICRP, publication 103.
3. Pillai MR, Chakraborty S, Das T, Venkatesh M, Ramamoorthy N. Production logistics of ^{177}Lu for radionuclide therapy. Appl Radiat Isot 2003;59:109-18.
4. Aslani A, Snowdon GM, Bailey DL, Schembri GP, Bailey EA, Pavlakis N, Roach PJ. Lutetium-177 DOTATATE production with an automated radiopharmaceutical synthesis system. Asia Ocean J Nucl Med Biol 2015;3:107-15.
5. Decristoforo C, Summer D, Wurzer A, Haubner R, Virgolini I, Guggenberg EV. Validation of a cassette based fully automated synthesis of ^{177}Lu-PSMA617. World J Nucl Med 2015;14:S3-7.
6. Das T, Chakraborty S, Kallur KG, Venkatesh M, Banerjee S. Preparation of patient doses of (177)Lu-DOTA-TATE using indigenously produced (177)Lu: The Indian experience. Cancer Biother Radiopharm 2011;26:395-400.
7. Ahmadzadehfar H, Rahbar K, Kürpig S, Bögemann M, Claesener M, Eppard E, Gärtner F, Rogenhofer S, Schäfers M, Essler M. Early side effects and first results of radioligand therapy with ^{177}Lu-DKFZ-617 PSMA of castrate-resistant metastatic prostate cancer: a two-centre study. EJNMMI Res 2015;5:36.
8. Agarwal KK, Singla S, Arora G, Bal C. (177) Lu-EDTMP for palliation of pain from bone metastases in patients with prostate and breast cancer: A phase II study 2015. Eur J Nucl Med Mol Imaging 2015;42:79-88.