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Radiation Dose to Nuclear Medicine Technologist During Manual Synthesis of High Specific Activity Non-Carrier Added Lu177 Labelled Radio pharmaceuticals

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Abstract

Introduction: Technologists working in Nuclear Medicine are exposed to radiation when doing tasks such as labeling/synthesis of radiopharmaceuticals, radiopharmaceutical administration, scan acquisition, and radiation survey. When working with therapeutic radiopharmaceuticals, the radiation dose could be significantly higher. The radiation dosage to the technologist in this study involved synthesis of Lu-177-DOTATATE (DOTA-Tyr3-octreotate) and PSMA-617(Prostate specific membrane Antigen) was estimated.

Aim: The purpose of this study is to calculate the whole-body radiation dose to a technologist who is involved in the labelling of two different Lu-177 labelled compounds, namely Lu-177 DOTATATE and Lu-177- PSMA, and to compare the occupational burden to the dose limits recommended by India's Atomic Energy Regulatory Board.

Materials and methods: A survey meter cum contamination monitor was used to detect radiation levels before the start of the labelling in the Hot lab by maintaining it at the area where the technologist generally stands during synthesis. An instant personal monitoring device like electronic pocket dosimeter was used by the technologist at chest level, performing the labelling of Lu177 (135mci to 520mci) received fortnightly by our department. Data were collected for 16 syntheses of Lu-177 DOTATATE and13 syntheses of Lu-177 PSMA-617 followed by the quality control. Mean time required to complete synthesis of Lu-177 DOTATATE and Lu-177 PSMA-617 was 52.68min and 52.39min respectively. Mean whole body radiation dose was 0.041 ± 0.004 mSv and 0.037±0.002mSv. Higher dose was obtained during the synthesis of Lu-177 DOTATATE.

Conclusion: Data suggest that during the manual radio labelling of Lu -177 compounds, the whole-body radiation exposure to technologist is within the limits prescribed by AERB.

Keywords: Radiation • Technologist • Radio pharmaceuticals

Introduction

Technologists working in Nuclear Medicine are exposed to radiation when doing tasks such as labeling/synthesis of radiopharmaceuticals, radiopharmaceutical administration, scan acquisition, and radiation survey. When working with therapeutic radiopharmaceuticals, the radiation dose could be significantly higher.

The dosage of radiation received by technologist during the manual synthesis of Lu-177DOTATATE (DOTA-Tyr3-octreotate) and Lu-177-PSMA-617 (Prostate specific membrane Antigen) was calculated in this work. Personnel monitoring is an important aspect of radiation safety measures. The goal of personnel monitoring is to reduce radiation exposure to a minimum as possible (ALARA). [1]

According to ICRP recommendation 103 (2007), a personnel's effective radiation dosage over five years should not exceed 20mSv, with no more than 50mSv in any single year [2]. As a result, the stochastic chance of radiation impacts will be kept to a minimum, while non-stochastic effects will be completely prevented.

Personnel exposed to radiation are linked with procedures such as labeling of radiopharmaceuticals, dose administration, and/or scan acquisition, especially with therapeutic radiopharmaceuticals. The current study looked at occupational worker exposure to radiation during the production of the DOTATATE (DOTA-Tyr3-octreotate) and

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PSMA-617 radiopharmaceuticals based on lutetium – 177 (Lu-177) (Prostate specific membrane Antigen).

Lu-177 has good physical properties for imaging and therapy (-max: 497 keV; 1: 113 keV; 6.4 percent and 2: 208 keV; 11 percent); and a long half-life (6.7 days), making it easier to transfer to locations far from a reactor site [3].

The most popular way for reactor production of Lu-177 is to directly irradiate high purity Lu-176 via the reaction 176Lu (n,)177Lu, whereas the alternative is to irradiate Yb-176 via the reaction 176Yb (n,)177Yb, which decays with a half-life of 1.9 hours to Lu-177. The latter method has the advantages that (1) there is no carrier lutetium present, and so is referred to as "no-carrier added" lutetium (NCA Lu-177), and (2) there is no 177mLu (meta stable) produced, which has a physical half-life of 160 days. Another benefit of the NCA Lu-177 is that it requires less peptide to label the necessary active amount of Lu-177-DOTATATE and Lu-177-PSMA for the therapy [4].

The specific activity of Lu177 production via the indirect method depends on the amount of lutetium in the target material. Calculations showed that even if only 4.8mg Lu-177 (0.48% by mass) is created from 1g of target material when irradiated with a high-density neutron flux, the Lu-177 specific activity would be significantly reduced.

Lu-177-DOATATATE and PSMA-617 can both be synthesized using automatic, semi-automatic and manual method. When compare to automatic, semi-automatic manual method is more cost effective. However, the employees involved in the synthesis will be exposed to a higher level of radiation. As a result, the goal of this research is to estimate the total radiation exposure to a technologist during manual Lu-177 production [5].

Materials and methods

Lu-177 as LuCl3 was procured from ITG, Germany. NCALu-177 was utilized at our institution. The precursors used in the synthesis of Lu-177 labelled DOTATATE and PSMA-617 were obtained from ABx GmbH Company, Germany. All other reagents used in labelling were of analytical grade. The study was conducted over a period of 20 months (Nov 2017 to June 2019)

Dosimeter and readout system An Electronic Pocket dosimeter (PDM-117) manufactured by ALOKA company was used to measure the dose. The dosimeter was calibrated by Nuvia Company India in January 2016 and recalibrated 2018.A Survey meter (RM-701N) was used. It was calibrated by Nucleonix system, Hyderabad in June 2017 and recalibrated in June 2018.

Procedure: Lu-177-labeled DOTATATE and PSMA-617 was synthesized at the radio-pharmacy laboratory of the Department of Nuclear Medicine, Mahatma Gandhi Cancer Hospital & Research Institute, Visakhapatnam, Andhra Pradesh India. The two radiopharmaceuticals were synthesized by manual method only. A survey cum contamination monitor (RM-701N) was used to measure the background radiation level in the Hot lab before the start of synthesis procedure by keeping it at the location where technologist normally stands during the synthesis. The survey meter was also checked periodically for its accuracy by measuring the exposure rate at 2 meters from the known activity of I-131.As part of the initial laboratory radiation measurement procedures, a survey meter cum contamination monitor was installed. The background exposure readings were taken at different place Electronic pocket dosimeter (PDM-117) was used to measure the radiation dose. The technologist was issued pocket dosimeter before the start of synthesis procedure. Initial reading was set at zero every time. Radiation dose readings recorded were noted on completion of the labelling process. The total amount of radioactivity handled during labelling and the duration of each labelling procedure was noted.

Statistics:

Descriptive statistical 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

S.NO	DATE	Activity (mci)	DURATION (Min)	PRODUCT (mci)	%RCP	RADIATION DOSE (mSv)	EXPOSURE RATE (mSv/Hr)
1	20/11/2017	354	53	351	99.5	0.042	0.06
2	12/02/2018	191	53	175	99.3	0.035	0.05
3	19/03/2018	150	52	144	99.7	0.037	0.04
4	11/04/2018	156	53	143	99.5	0.038	0.04
5	21/05/2018	348	55	325	99.1	0.043	0.05
6	06/06/2018	135	52	130	99.5	0.034	0.04
7	09/07/2018	176	52	170	98.7	0.036	0.04
8	24/09/2018	180	53	177	99.5	0.038	0.04
9	11/03/2019	175	52	165	99.7	0.039	0.03
10	16/04/2019	155	52	147	99.8	0.034	0.04
11	21/05/2019	156	52	150	99.2	0.037	0.04
12	06/06/2019	145	52	135	99.6	0.039	0.03
13	18/06/2019	156	52	150	99.7	0.04	0.04

Table1: Radiation Dose During the synthesis of Lu177-PSMA Labelling.

SNO	DATE	ACTIVITY (mci)	DURATION (Minutes)	PRODUCT (mci)	%RCP	RADIATION DOSE (mSv)	EXPOSURE RATE (mSv/Hr)
1	07/11/2017	320	52	300	99.2	0.042	0.04

2	02/02/2018	220	53	200	99.5	0.035	0.04
3	19/03/2018	190	53	181	99.1	0.03	0.03
4	11/04/2018	446	54	435	99.2	0.046	0.05
5	14/05/2018	520	54	485	99.3	0.053	0.06
6	06/06/2018	145	52	141	99.3	0.04	0.03
7	16/07/2018	370	53	356	99.5	0.046	0.05
8	24/09/2018	295	53	275	99.6	0.041	0.05
9	12/11/2018	183	52	181	99.5	0.042	0.04
10	26/11/2018	181	52	169	99.6	0.042	0.04
11	10/01/2019	146	52	140	99.7	0.043	0.04
12	21/01/2019	165	53	160	99.4	0.04	0.04
13	27/02/2019	265	53	252	99.8	0.041	0.05

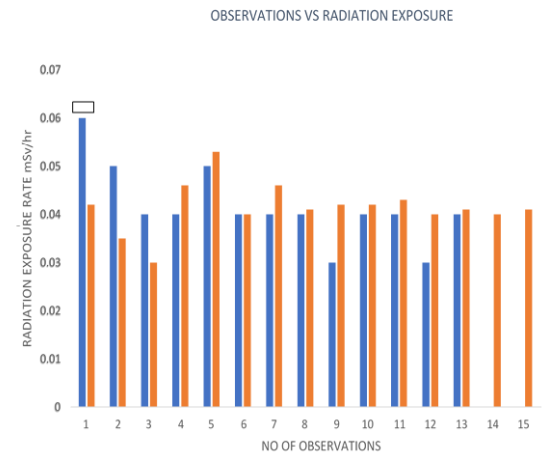
Table2: Radiation Dose During the synthesis of Lu-177-DOTATATE Labelling.

The mean whole-body (chest dose) radiation dose recorded in Lu-177-DOTATATE labelling was 0.041 ± 0.004 mSv and Lu-177-PSMA-617 was 0.037±0.002 mSv and the mean duration of labelling was 52.68min and 52.38 min respectively. The specific activity of Lu-177 was (>3600GBq/mg) in all labelling procedures.

The mean estimated exposure rate during the two labelling procedures was 0.044 ± 0.0089 mSv/hr for DOTATATE and 0.041 ± 0.007 mSv/hr for PSMA-617. Overall mean radiation dose was 0.0425 mSv and duration was 52.53min.

S.NO	OCT-DEC	JAN-MAR	APR-JUNE	JULY-SEPT	OCT-DEC	JAN-MAR	APR-JUNE
CHEST (mSv)	0.25	0.25	0.95	0.55	0.65	0.7	0.8
WRIST (mSv)	3.8	5.85	6.8	7.55	8.7	6.2	7.1

Table3: TLD Dose readings (Oct 2017-June 2019).



Discussion

This study was initiated with the aim to estimate the radiation dose levels to personnel involved in the labelling of 177Lu-labeled radiopharmaceuticals that is DOTATATE and PSMA-617. The method of labelling of the two compounds with Lu-177 can be automated/semi-automated [4,5] or manual. At our department, radio labelling of these compounds was performed with Lu-177 (NCA) by a manual method, as it is cost effective and automated modules are not available at our institute at present. We undertook this study to address the radiation safety concerns is higher than that in automated or semi-automated methods [6].

Lu-177(NCA) providing highest specific activity (>3600GBq/mg) up to 4 to 5 times higher and offers the best preconditions for an efficient radio labelling reaction. It is characterized by a significantly longer shelf life than the CA (carrier added) Lu-177 variant, and also less duration for synthesis. It requires less peptide to label the necessary active amount of Lu-177 -DOTATATE and Lu-177-PSMA-617. As a result, the superior performance creates the best preconditions for efficient radio labelling of bio molecules such as peptides and antibodies. Furthermore, NCA Lutetium-177 provides the highest achievable radio nuclide purity. In comparison, carrier added isotope contains up to 0.1 % metastable Lutetium-177m (t1/2= 160.1 days) and requires costly management and storage of contaminated radioactive waste.

Our results suggest that the mean radiation dose during the labelling was 0.041 ± 0.004 mSv for Lu-177-DOTATATE and0.037±0.002 mSv for Lu-177-PSMA-617.

The reasons for the observed trend in Figure 1 are the time taken for radiolabelling and amount of the radioactivity handled. The highest radiation dose was 0.052 ± 0.0089mSv for Lu-177-DOTATATE (54min&520mCi) and0.043 ± 0.007 mSv for Lu-177-PSMA-617(55 min& 348mCi).

Overall combined mean radiation dose for the two 177Lu-compounds was 0.0425 mSv. Assuming a maximum of 29 such synthesis every year per person, the total mean dose to the personnel involved will be 1.24 mSv.

The reading of the TLD badge of the personnel involved was also within prescribed limits, that is, for 1 year 2.4mSv for chest badge. It should be noted that the above reading includes the radiation dose to

the personnel from other sources as well apart from the radio labelling procedures mentioned in this study. These dose levels are far less than the stipulated AERB limits of 20 mSv/year (averaged over 5 years). The reading of the TLD badge for 1 year was 27.8mSv for wrist badge. This shows that even the manual radio-labelling methods of Lu-177 compounds are safe, provided safe work practices are followed.

Conclusion

This study demonstrates that manual radio-labelling of Lu-177 compounds is safe, and that the whole-body radiation dosage to the personnel participating is well under the ICRP's recommended limits of 20 mSv/year (averaged over 5 years).

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