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Original Article

Estimation of Human-Absorbed Dose of ^{99m}Tc-MAA, Using MIRD Method Based on Animal Data and Comparison with MCNP Simulation Code

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Abstract

Introduction: ^{99m}Tc-Macro Aggregated-Albumin (^{99m}Tc-MAA) has been evaluated as a useful perfusion study agent. In this study, the human absorbed dose of ^{99m}Tc-MAA was estimated with MIRD and MCNP methods based on animal biodistribution data and finally compared with ICRP publication data.

Materials and Methods: In this study, for investigating the biodistribution of ^{99m}Tc-MAA, after radiolabeling of MAA with Technetium-99m, it was injected to mice via the tail vein. After 1-120 min post injection, the mice were sacrificed and some of their tissues dissected and counted for calculating the percentage of the injected dose per gram (% ID/g) and the absorbed dose. Then, the obtained data was converted to equivalent data in human for each tissue.

Results: Dose prediction shows that the highest absorbed dose is observed in the lungs (MIRD: 6.8E-2 mGy/MBq, MCNP: 6.32E-2 mGy/MBq). There is good agreement between the results obtained from MIRD and MCNP simulation for lungs.

Conclusion: According to the present results and comparison with ICRP publication data, animal dissection model and simulation MCNP code can be useful tools for internally-absorbed dose estimation of pulmonary radiopharmaceuticals.

Keywords: MCNP code, MIRD method, Absorbed dose, ^{99m}Tc-MAA

1. Introduction

The lung respiratory function can be studied through perfusion (Q) and ventilation (V) imaging [1]. ^{99m}Tc-Macroaggregated Albumin (^{99m}Tc-MAA) has been well-known as a perfusion agent since 1965 [2]. The radiopharmaceuticals have become the standard for lung perfusion studies and still dominates the global market [3]. Radiopharmaceuticals can deliver radiation dose to organs because of the presence of their radioisotopes. Estimation of the absorbed dose from labeled compound is an important part of the development and usage of new agents [4]. In the field of nuclear medicine, the most commonly used method for obtaining the internal dose estimates is the one developed by the medical internal radiation dose (MIRD) committee. This well-known method is based on the absorbed fractions: it means that a fraction of emitted energy from source tissues is absorbed into target tissues [5, 6].

In addition, simulation with Monte Carlo method is another way. One of the most important codes is MCNP (Monte Carlo

N-particle). This code can be used for some particles' transport [7]. Many studies have been performed for estimating the internal dose after radiopharmaceuticals administration.

Shahbazi-Gahrouei et al. compared the investigation of the organ doses in radioiodine therapy by three methods of calculating, experimental and Monte Carlo simulation [8]. In 2015, Shanehsazzadeh et al. calculated and compared effective dose of different tissues of body, resulting from two radiopharmaceuticals administration, namely ^{99m}Tc-MAA and ^{68}Ga-MAA [6]. The aim of this study was the comparison of estimasted human absorbed dose of ^{99m}Tc-MAA resulting from one MBq after intravenous injection to mice, using MIRD and MCNP simulation code.

2. Materials and Methods

Technetium-99m was prepared by Nuclear Science and Technology Research Institute.

For preparing the ^{99m}Tc-MAA, Technetium-99m was obtained from the ^{99}Mo decay on a column in ^{99}Mo/^{99m}Tc generator. The Technetium-99m was eluted by 0.9% sodium chloride in the form of Na [$^{99m}TcO_4$] solution.

After that, eluted Na [$^{99m}TcO_4$] was added to the reaction vial at room temperature.

After radiolabeling with Technetium-99m, 3.7 MBq activity was injected via the tail vein. After 1, 5, 15, 30, 60 and 120 min post injection, the percentage of the injected dose per gram (% ID/g) was calculated for each organ.

$$ID/g\% = \frac{A_{tissue}/M_{tissue}}{A_{total}} \times 100 \qquad (1)$$

where A_{tissue} is the Technetium-99m activity in the sample, M_{tissue} is the mass of the tissue and A_{total} is the total activity of Technetium-99m injected into the animals [6, 9]. The dose of radiation delivered from a source tissue to a target tissue is dependent on the amount of radioactivity in the source tissue and the time length of the radiopharmaceuticals resides in the source tissue.

The accumulated radioactivity, Ã, can be shown by the eq. (2):

$$\tilde{A}_h = \int_{t_1}^{\infty} \tilde{A}_h(t)\,dt \qquad (2)$$

A_h (t) refers to the activity of each tissue at the time (t). Ã accounts for the radioactivity in the tissue [6, 10]. After calculating the activity for organs at different times, related activity curves were drawn for each. Then, using the curve fitting method (the data points which represent the percentage-injected dose were created and fitted to a mono-exponential, bi-exponential, or uptake and clearance curve), cumulated radioactivity values were obtained.

Some organs were harvested; then for converting accumulated activity of mouse organs to human organs, Sparks and Idogan method [11-14], shown in eq. was used (3):

$$\tilde{A}_{humanorgan} = \tilde{A}_{animalorgan} \times \frac{(organmass/bodymass)_{human}}{(organmass/bodymass)_{animal}} \qquad (3)$$

The radiation-absorbed dose was calculated by MIRD formulation:

$$D_{r_k} = \sum_h \tilde{A}_h S(r_k \leftarrow r_h) \qquad (4)$$

where D_{rk} (rad or Gy) is the absorbed dose of the target organ, Ã is the accumulated activity in source organ (Ci-hr or MBq-sec) and $S(r_k \leftarrow r_h)$ that is called S factor, and is defined as the mean absorbed dose to the target region r_k per unit of accumulated activity in the source region r_h (here are the lungs). The value of S depends on the radiation type, the energy emitted per transformation, the mass of the target organ and the geometry of the mathematical phantoms representing adults and children of various ages. The S factors have been taken from the tables presented in the medical internal radiation

dose No.11 [15] and available in http://doseinforadar.com/RADARphan.html.

This factor represents the physical decay characteristics of the radioisotopes, the range of the emitted radiations, and the organ size. The absorbed dose of different body organs were obtained by converting the mouse results to that of a human and accumulating the activity through both methods (MIRD & MCNP). By considering the type of particle on creating biologic effects, equivalent dose (H) is defined; it is equal to absorbed dose multiplied by the radiation-weighting factor (W).

$$H=D\times W \qquad (5)$$

Weighting factor of Gamma, X-ray and Beta particles is one and for alpha particles it equals 20. The effective absorbed dose (E) of each organ is:

$$E = \sum_T W_T H \qquad (6)$$

Where WT is the tissue-weighting factor according to ICRP106 and H is the equivalent dose [17]. This quantity considers the effect of different beams on tissue types for creation of biologic effects [4, 16-19].

For dose estimation by MCNP simulation code, the absorbed doses of different organs such as lungs, heart, liver, kidneys, spleen, are estimated within an adult male ORNL phantom. MCNP needs the source for a problem to be specified in a user defined input file. In the source card, particle type, source position and distribution, energy, and direction of starting particles were specified. For simulating the present work, it was assumed that the radiopharmaceuticals were uniformly distributed throughout the organs.

The radiopharmaceuticals used in this research emit gamma (^{99m}Tc) radiation. The source energy was chosen based on the 0.14 MeV peak for ^{99m}Tc. Tallies of F6 applied for calculation of absorbed dose in this code. The third method for comparison is ICRP publication data. ICRP publication shows biokinetic models and best estimates of biokinetic data for many radiopharmaceuticals, giving absorbed doses for adults, children and the fetus.

3. Results

Figure 1 shows the percentage of injected dose per gram at times 1, 5, 15, 30, 60 and 120 minutes after intravenous injection of ^{99m}Tc-MAA on various organs of mice.

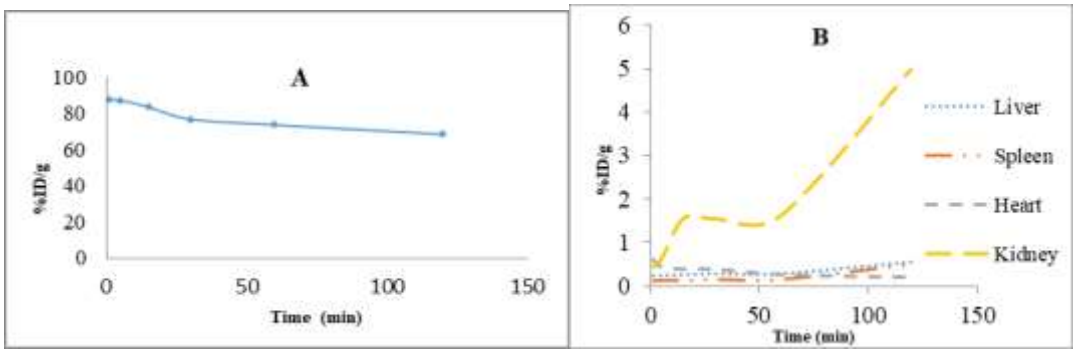

Figure 1. The clearance curves of (A for Lung) and (B for Liver, Heart, kidney and Spleen) after IV injection of 99mTc-MAA. Mean values as the percentage of administered activity per gram (%ID/g)) and the horizontal axis is the times (min) post injections.

After calculating the absorbed dose by MIRD method, the amount of effective absorbed dose of different organs for this pulmonary radiopharmaceutical was obtained. The results of this dosimetry method are indicated in Table 1.

Table 1. Evaluation of human effective dose based on mouse data after intravenous administration of ^{99m}Tc-MAA

Target organs	Mean estimated absorbed dose(mGy/MBq)	WT	Mean effective absorbed dose(mSv/MBq)*
Heart	1.73E-03	0.01	1.73E-05
Lungs	6.80E-02	0.12	8.16E-03
Liver	3.32E-03	0.04	1.32E-04
Spleen	3.09E-03	0.01	3.09E-05
Kidneys	1.26E-03	0.01	1.26E-05

*If injected 1MBq activity of radiotracer

Table 2. Evaluation of human mean absorbed dose based on mouse data after intravenous administration of ^{99m}Tc- MAA using MIRD method and MCNP code and comparison with ICRP's human data.

Target organs	Mean estimated absorbed dose by MIRD (mGy/MBq)	Mean estimated absorbed dose by MCNP code (mGy/MBq)	Mean absorbed dose in ICRP (mGy/MBq)
Heart	1.73E-02	9.80E-03	9.60E-03
Lungs	6.80E-02	6.30E-02	6.70E-02
Liver	3.32E-03	5.90E-03	1.60E-02
Spleen	3.09E-03	5.20E-03	4.40E-03
Kidneys	1.26E-03	2.20E-03	3.70E-03

Then we calculated the absorbed dose by MIRD and MCNP methods and compared them with ICRP dosimetry data in Table 2.

The comparison of human absorbed dose of ^{99m}Tc-MAA by MIRD and MCNP (our estimation) with ^{99m}Tc-MAA (which was in accordance with ICRP publication 53 [18]) is depicted in Figure 2.

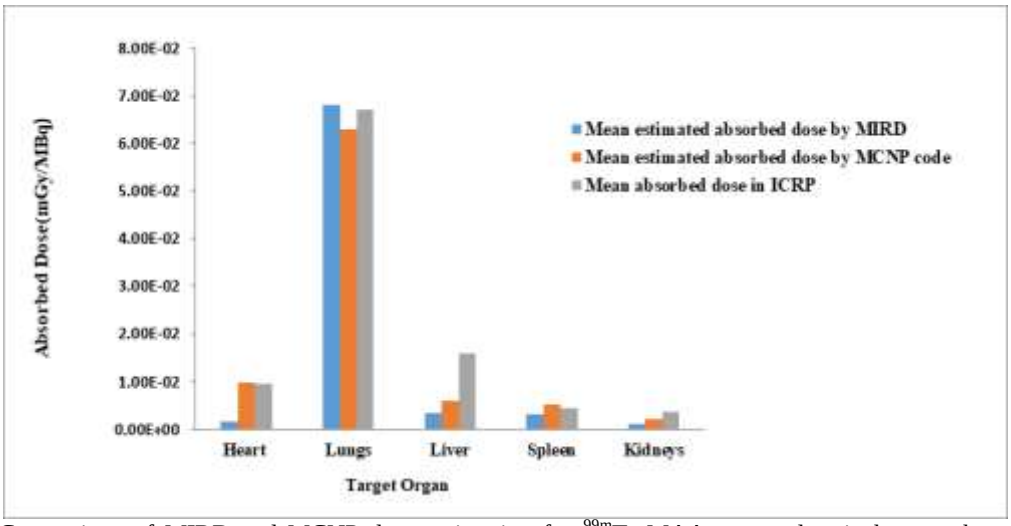

Figure 2. Comparison of MIRD and MCNP dose estimation for ^{99m}Tc-MAA versus data in humans based on ICRP publication data [18].

4. Discussion

Technetium-99m is the most well- known and widely used radioisotope in nuclear medicine for diagnostic procedures. More than 70 percent of nuclear medicine procedures have used it in their clinical application as an imaging agent [20] to estimate the internal radiation dose due to the administration of Technetium-99m to the patients.

Apart from International Commission of Radiation Protection (ICRP) publications,

there are a limited number of documents on radiopharmaceuticals dosimetry in the world.

As mentioned above, the use of a radiopharmaceutical requires investigation of its biodistribution and dosimetry in some models prior to next stage (clinical applications) [16, 17, 21, and 22]. In this study, internal radiation dosimetry of the pulmonary imaging agent, ^{99m}Tc-MAA, was calculated and compared (based on mouse data) through two important methods. Based on the assumption that the biodistribution of radiopharmaceuticals in mouse and in human could be similar (ICRP 103). The dose prediction shows that the highest absorbed dose is observed in the lungs (MIRD: 6.8E-2 mGy/MBq, MCNP: 6.32E-2 mGy/MBq)liver (MIRD: 3.32E-3 mGy/MBq, MCNP: 5.9E-3 mGy/MBq), heart (MIRD: 1.73E-2 mGy/MBq, MCNP: 9.8E-3 mGy/MBq), Spleen (MIRD: 3.09E-3 mGy/MBq, MCNP: 5.20E-3 mGy/MBq) and Kidneys (MIRD: 1.26E-3 mGy/MBq, MCNP: 2.2E-3 mGy/MBq). There is good agreement between the results obtained from MIRD and MCNP simulation for lungs. In addition, as documented in ICRP publication, the highest absorbed dose is observed in the lung, and the tissues that receive the next higher dose are liver, heart, spleen and kidneys. The results of MIRD, MCNP code and ICRP data show an acceptable agreement for ^{99m}Tc-MAA especially in the lungs.

The deviations between the results obtained by three methods can be due to different uncertainties in three methods: mouse to human conversion factor, difference between tissues geometry in human and mouse, etc.

5. Conclusion

Dose estimation shows that the highest absorbed doses are in the Lungs, Liver, heart, Spleen and Kidneys. There is good agreement between the results obtained from MIRD, MCNP simulation and ICRP publication data for lungs. According to the results of the study and comparison results with ICRP data, animal dissection model and simulation MCNP code can be useful tools for internally absorbed dose estimation of pulmonary radiopharmaceuticals.

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Conflict of interest

The authors declare no conflict of interest.

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