Calculation of Intake Retention Fraction and Dose Coefficients for ^{99m}Tc-Labelled Compounds for Internal Exposure of Medical Workers (Post-print)

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Date: 2023-06-18T00:00:00+00:00

Abstract

For recent decades, a considerable amount of 99mTc has been stimulated for diagnosis radiopharmaceuticals because of its physical advantages. The increase in the use of 99mTc makes naturally more chances of internal exposure for not only patients but also medical workers. The patient internal exposure by an intravenous injection has been assessed relatively well with the reports of International Commission on Radiological Protection (ICRP) or Medical Internal Radiation Dose(MIRD). However, there are few studies which can support its accurate assessment for medical worker who treats 99mTc. In spite of the absence of information, the physiological information of each 99mTc-labelled compound for patient, provided by ICRP, can be used optionally for worker exposure because the behaviors after uptake to blood are similar for patient and worker. Using the data, in this study, the data for bioassay were given as the intake whole-body retention and urinary excretion function. We selected the two most frequently used 99mTc-labelled compounds based on statistical data; 99mTc-phosphonate, pertechnetate. The data of the Human Alimentary Tract Model (HATM, publication 100) and the revised Human Respiratory Tract Model (revised HRTM, OIR) were used for compartment models which depict the physiological behavior in body after intake. In case of 99mTc-phosphonate, we adopted the systemic model for patient intake described in ICRP publication 53 based on the assumption that the behaviors after uptake to blood are similar for patient and worker. On the other hand, recent updated systemic model in OIR report could be directly adopted for pertechnetate. We used Birchall' s algorithm for calculation and developed the module which could calculate the retention amounts in each compartment at given time by MATLAB. In addition, we fitted the functions as sum of exponential terms using ORIGIN and the fitting coefficients were provided. We also could calculate the committed

dose coefficients for each compound using SAF values for photons provided by Cristy and Eckerman. The results in this study will be useful to estimate the intake and effective dose for medical field.

Full Text

Preamble

NUCLEAR SCIENCE AND TECHNIQUES 25, S010302 (2014)
Calculation of the intake retention fraction and dose coefficients in 99mTc-labelled compound for internal exposure for medical workers

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(Received June 30, 2013; accepted in revised form October 15, 2014; published online November 25, 2014)

Abstract

Over recent decades, considerable quantities of 99mTc have been used for diagnostic radiopharmaceuticals due to its physical advantages. The increasing use of 99mTc naturally creates more opportunities for internal exposure among both patients and medical workers. Internal exposure in patients from intravenous injection has been relatively well assessed through reports from the International Commission on Radiological Protection (ICRP) and the Medical Internal Radiation Dose (MIRD) committee. However, few studies support accurate assessment for medical workers who handle 99mTc. Despite this information gap, the physiological data for each 99mTc-labelled compound provided by ICRP for patients can be optionally applied to worker exposure because behavior after uptake into the blood is similar for both groups. Using this data, the present study provides bioassay data in the form of intake whole-body retention and urinary excretion functions. We selected the two most frequently used 99mTc-labelled compounds based on statistical data: 99mTc-phosphonate and pertechnetate. The Human Alimentary Tract Model (HATM, Publication 100) and the revised Human Respiratory Tract Model (revised HRTM, OIR) were employed as compartment models depicting physiological behavior in the body after intake. For 99mTc-phosphonate, we adopted the systemic model for patient intake described in ICRP Publication 53, based on the assumption that behavior after uptake into the blood is similar for patients and workers. For pertechnetate, the recent updated systemic model in the OIR report could be directly adopted. We utilized Birchall' s algorithm for calculations and developed a MATLAB module to compute retention amounts in each compartment at given times. Additionally, we fitted the functions as sums of exponential terms using ORIGIN and provided the fitting coefficients. We also calculated committed dose coefficients for each compound using Specific Absorbed Fraction (SAF) values for photons provided by Cristy and Eckerman. The results of this study will be useful for

estimating intake and effective dose in the medical field.

Keywords: Intake retention function, Urinary excretion function, 99mTc, Bioassay, Revised HRTM, HATM, Medical worker, Occupational intakes

DOI: 10.13538/j.1001-8042/nst.25.S010302

Introduction

99mTc, one of the most widely used radiopharmaceuticals, offers significant physical advantages for diagnostic applications. Its 6-hour half-life and negligible beta radiation permit clinicians to administer several millicuries with relatively low radiation burdens. Furthermore, its exclusive emission of 140-keV photons is nearly ideal for gamma camera imaging technology. These characteristics have led to widespread use of 99mTc with various ligands. As 99mTc usage increases, adequate assessment of internal exposure becomes necessary for both patients and medical workers. Internal exposure in patients from intravenous injection has been relatively well assessed through ICRP and MIRD reports. In 2007, ICRP published "Radiation Dose to Patients from Radiopharmaceuticals (ICRP 106 [1])" to provide biokinetic and dosimetric models for 33 radiopharmaceuticals. The systemic models and dose coefficients recommended in ICRP Publications 53 [2], 80 [3], and 106 facilitate assessment of internal exposures for patients receiving 99mTc via intravenous injection.

For medical workers, however, few studies address internal exposure caused by inhalation and ingestion despite predictions of significant exposures. The dose coefficients for 99mTc in ICRP Publication 68 [4] represent the only available information for workers, but these are insufficient for the medical field where various 99mTc-labelled agents are handled, as post-uptake behavior depends on the ligand type. Additionally, recalculations are needed based on new recommendations in ICRP Publication 103 and the OIR report [5], which describe more reliable biokinetic models for occupational intakes. For these reasons, this study aims to calculate intake retention and excretion functions and dose conversion coefficients for internal exposure assessment. The two most frequently used 99mTc-labelled compounds were selected: 99mTc-MDP and pertechnetate, used in bone scans and thyroid scans, respectively. This report provides the fitting coefficients for their whole-body retention and urinary excretion functions along with committed dose conversion coefficients.

II. MATERIALS AND METHODS

A. Selection of 99mTc Radiopharmaceuticals

The Korean Society of Nuclear Medicine documented nuclear medicine scans and their frequency of execution over 51 years in South Korea [6]. This data indicates that bone scans using 99mTc-phosphonates such as 99mTc-MDP, 99mTc-HDP, 99mTc-HDEP, and 99mTc-DDP have been the most frequently performed procedures since 1988. Therefore, most internal exposures of medical workers can

be expected to occur from 99mTc-phosphonates. Furthermore, pertechnetates used for thyroid scans could produce considerable internal exposures because thyroid imaging with pertechnetates is very common. Assessment of pertechnetate is especially important because 99mTc is generated in the pertechnetate form (TcO_4^-). For these reasons, 99mTc-phosphonates and pertechnetate were selected as the compounds of interest in this report. For other 99mTc compounds, bioassay data could be calculated using the same procedure if needed. Nevertheless, we expect that studying these two radiopharmaceuticals can cover most internal intakes of 99mTc.

B. Biokinetic Models for 99mTc-Labelled Compounds

Actual metabolism in the human body, including retention and excretion of materials, is too complex to describe real physiological behaviors accurately. To practically depict metabolism, simple compartment models have been used to calculate retention and excretion in the human body. In 2006, ICRP recommended the HATM (Human Alimentary Tract Model, Publication 100 [7]), which can depict the behavior of ingested materials before uptake into blood. The HATM can describe more realistic behaviors of ingested materials in all alimentary tract regions including the oral cavity, esophagus, stomach, small intestine, right colon, left colon, and rectosigmoid. This updated HATM was adopted in our calculations.

For inhaled materials, the HRTM (Human Respiratory Tract Model) recommended in ICRP Publication 66 [8] could depict deposition and absorption in the respiratory tract. However, the HRTM was revised in the OIR (Occupational Intakes of Radionuclides) draft report, reflecting new recommendations in ICRP 103. The revised HRTM describes post-inhalation behavior more realistically and simply. Therefore, we used the revised HRTM in OIR for more reliable results rather than the original HRTM. This section includes a more detailed review of changes in the revised HRTM and the systemic models that depict behavior after uptake into blood.

1. Systemic Models The physiological behavior of 99mTc compounds after absorption into blood differs depending on the ligand type, making it clear that different systemic models are needed accordingly. First, the systemic model for pertechnetate has been relatively well established because it is the most readily available chemical form and serves as the starting point for technetium chemistry. Additionally, the revised systemic model for technetium provided in OIR was developed based on pertechnetate experimental results and could therefore be directly adopted for occupational intake of pertechnetate. The systemic model for pertechnetate depicted in OIR Part 2 is as follows [12]: The initial distribution of pertechnetate is similar to that of inorganic iodide. Pertechnetate absorbed into blood is selectively concentrated in the thyroid, salivary glands, and stomach wall. In contrast to iodide, pertechnetate trapped by the thyroid is not organically bound but is largely released back to blood over

several hours. Compartments representing the thyroid, salivary glands, stomach wall, and right colon wall were added to the model because they have been identified in human or animal studies as important repositories for pertechnetate. The bone, kidneys, liver, thyroid, and other soft tissues are each divided into multiple compartments representing different phases of retention, and in the case of bone, also different tissue types. The structure of the biokinetic model for systemic technetium used in OIR is shown in Fig. 1 [Figure 1: see original paper].

For 99mTc-phosphonates, the situation is somewhat different. The systemic model recommended in ICRP Publication 53 was developed for patients rather than workers. Nevertheless, we used this model to predict the behavior of material absorbed into blood based on the assumption that behavior after uptake is equivalent regardless of intake route. Additionally, the various 99mTc-phosphonates used for bone imaging have sufficient biokinetic similarity to justify using a common biokinetic model. Therefore, the biokinetic model for 99mTc-phosphonates described in ICRP Publication 53 was used and is shown in Fig. 2 [Figure 2: see original paper]. The main uptake occurs in bone, with a smaller uptake in kidneys, and excretion occurs via the renal system. Transfer rates were calculated using leaving fractions from a transfer compartment and biological half-life.

2. Changes in the Human Respiratory Tract Model Original HRTM: The HRTM described in Publication 66 (ICRP, 1994a) was applied to calculate inhalation dose coefficients and bioassay functions in recent reports. In the original HRTM, the respiratory tract is treated as two tissues: the extrathoracic regions (ET) and the thoracic regions (TH). These tissues are subdivided into regions based mainly on differences in radiation sensitivity. The thoracic regions include bronchial (BB), bronchiolar (bb), alveolar-interstitial (AI), and thoracic lymph nodes (LNT H). The extrathoracic regions include the anterior nasal passage (ET1), posterior nasal passages, pharynx and larynx (ET2), and extrathoracic lymph nodes (LNET).

Deposition: No changes were made to the original HRTM deposition model for aerosols in the revised HRTM, except for the distribution of deposit in the ET airways between regions ET1 and ET2. In ICRP Publication 66, the same deposition fraction was assumed for ET1 and ET2, although the actual deposited amount in ET1 was greater than in ET2. In OIR, however, more realistic fractional deposition in the extrathoracic region is adopted because more realistic transfer rates are available [13] (see below).

Particle Transport: The original HRTM was revised for simpler and more realistic particle transport in the OIR report. The important change is the transfer rate from ET1 to ET2. While transfer was not allowed in the original HRTM, it is now assumed that material deposited in ET1 is cleared at a rate of 2.1 d^{-1} based on recent data; approximately one-third by nose blowing and two-thirds by transfer to ET2. This change will increase systemic uptake in

ET2 and the alimentary tract. In the revised HRTM, slow clearance occurs only in the bronchiolar (bb) region. The rate from bb to BB was decreased by a factor of ten instead of omitting the BB2 and bb2 compartments. Additionally, changes in transfer rates in the alveolar-interstitial region indicate that greater long-term retention in the AI region is assumed.

Absorption to Blood: Absorption into blood of deposited materials has been classified according to absorption speed: F, M, and S. While the absorption parameter values of the original HRTM were not based on experimental data, ICRP recommended more realistic values based on recent data in the revised HRTM. In the OIR report, material-specific parameter values are offered where sufficient information is available, enabling more reliable assessment when material information is known. Material-specific parameters for pertechnetate have been offered as type 'F' in OIR Part 2, whereas 99mTc-phosphonate has been assigned to type 'M' as 'unspecified forms'. Activity Median Aerodynamic Diameter (AMAD) was considered to be 5 µm as recommended for workplace exposures.

3. Calculation of Retention Functions, Excretion Functions, and Dose Coefficients The intake retention and excretion functions can be calculated using the algorithm proposed by Birchall and James [9] with the transfer rates. The algorithm first transforms the rate matrix into a new matrix [A]. If r_{ji} is the transfer rate from compartment i to j and a_{ij} is the value of the elements of matrix [A], respectively, then:

$$a_{ij} = r_{ji}, \text{for } i \neq j$$

$$a_{ij} = -\sum_{\substack{j=1 \\ j \neq i}}^{N} r_{ji}, \text{for } i = j$$

Once matrix [A] is formed, the amount in compartment i at any subsequent time t can be calculated by:

$$q_i = e^{[A]t} q_i(0), \text{for } i \neq j$$

where e^{[A]} is the exponential of matrix [A], and q_i(0) is the column vector of initial amounts in each compartment i when unit activity (1 Bq) is taken into the body. For a biokinetic system consisting of parent and decay products [10], matrix [A] becomes:

$$[A] = \begin{pmatrix} M - \lambda_M I & 0 \\ D & -\lambda_D I \end{pmatrix}$$

where M and λ_M are the rate matrix and decay rate of the parent, and D and λ_D are the rate matrix and decay rate of the decay product, respectively. In this study, the parent and decay product are 99mTc and 99Tc. The retention and excretion functions were calculated every hour up to 20 times the half-life of 99mTc using MATLAB. For use in bioassay, the intake retention function or excretion function, m(t), can be written as:

$$m(t) = \sum_n a_i e^{-\lambda_i t}$$

where a_i and λ_i are fitting coefficients for the i-th term. The fitting was conducted using the ORIGIN program. After obtaining the intake retention and excretion functions, the intake amount of radionuclide, I, can be determined by:

$$I = \frac{M}{m(t)}$$

where M is the measured quantity.

For dose coefficient calculations, SAF values for photons calculated by Cristy and Eckerman were used [11]. However, in some cases, SAF values were surrogated for suitable regions because results were not available for all source and target regions of HATM. For example, SAFs for the upper large intestine (ULI) from Cristy and Eckerman were used for the right colon and left colon, and SAFs for the lower large intestine (LLI) were used for the rectosigmoid colon [13]. In future ICRP reports, however, results calculated using reference voxel phantoms will be published.

The SEE values table was obtained by SEECAL 2.0. The number of nuclear transformations that have occurred up to 50 years in compartment i, U(50), can be calculated by:

$$U(t) = c[A]^{-1}[e^{[A]t} - I]q_i(0)$$

where constant c relates contents to nuclear transformations in the desired units. Dose coefficients can be calculated using U(50) and SEE values with tissue weighting factors, w_T, from ICRP Publication 103. All calculation procedures were implemented in MATLAB.

III. RESULTS AND DISCUSSION

The fitting coefficients of whole-body intake retention functions for 99mTc-phosphonate and pertechnetate are shown in Table 1 for different intake routes. The adjusted coefficients of determination, R^2, verified that the functions fitted

with only two exponential terms are statistically significant. Since the whole-body retention curve has a relatively simple decreasing shape, the fitting coefficients could be obtained easily.

For the urinary excretion function, however, more terms were needed to achieve reliable statistical explanatory power. As shown in Table 2, the daily urinary excretion function was expressed using four exponential terms because urinary excretion exhibits several patterns over time. Table 3 shows the committed dose conversion coefficients calculated based on the OIR models.

Assessments of internal exposures for medical workers who handle 99mTc radiopharmaceuticals can be conducted through whole-body counting or urinary sampling. Thus, the results of this report can be used to estimate radionuclide intake and committed effective dose for inhalation or ingestion.

IV. CONCLUSION

This study provides intake retention and urinary excretion functions with fitting coefficients for assessing internal exposures in medical workers. The results are significant because they adopt revised compartment models based on recent experimental findings. Furthermore, the dose coefficients presented here may be used to estimate internal dose from 99mTc exposure. Although recalculation will be needed after new SAF values derived from reference voxel phantoms are published, we believe the dose coefficients in this report represent the best currently available. Exposures from 99mTc have been considered one of the main intake pathways in the medical field, and internal dosimetry requires the retention and excretion functions developed in this study. Therefore, these results are expected to be useful for assessing internal exposure in medical workers.

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Note: Figure translations are in progress. See original paper for figures.