International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

http://ijpsat.ijsht-journals.org
Vol. 26 No. 2 May 2021, pp.599-602

Calculation Models of Radiopharmaceutical Activities of An Open 4-Compartment Model using The MIRD Method

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Abstract— An open 4-compartment model has been created which includes heart, thyroid, kidney, and liver organs using the MIRD method. Based on the compartment model, models of differential equations can be made as a function of the activities of the four organs. By ignoring the absorption function of radiopharmaceuticals from breast organs (absorption of radiopharmaceuticals by breast organs is very small) and using boundary conditions of the radiopharmaceutical activities function that enters or goes out of the heart organ has the same exponential factor function and ignores all disturbance, we get model of the activity equation is obtained from the heart, thyroid, kidney and liver organs. This activity equation model is only at the conceptual stage of a simple model through simple boundary conditions as well. This model is very difficult to apply to patients because there are many disturbing factors to the dose flow pattern such as organ function abnormalities, internal disease, internal and external disorders, etc.

Keywords— Compartment model, Organs, Differential equations, Radiopharmaceutical activities.

I. INTRODUCTION

Calculation of radiopharmaceutical activities model injected into a patient can be carried out with the open compartment model using the MIRD (Medical Internal Radiation Dosimetry) method [1]. All kinds of radiopharmaceuticals have been produced in line with the need in nuclear medicine, especially to treat cancer [2]. This research focuses on the differential equation of radiopharmaceutical activities as a function of time. When radiopharmaceutical is injected into a patient, it uniformly spreads to all organs such as the heart, kidneys, thyroid and liver as blood plasma activities known as the open compartment system [3]. Energy and radionuclide emission among body organs relates to the function of those organs as source s that emits radionuclides or as target t that absorbs those radionuclides. The function as either source or target organ makes up a differential equation of radionuclides that is interesting for research [4]. However, not all body organs have the ability to emit or adsorb radionuclides. Hence these organs do not belong to either source or target category. A good example of this is the breast [4]. This research using the open compartment system involves organs as source and target, including the heart, kidneys, thyroid, and liver. It disregards the function of breasts.

II. CALCULATION OF DIFFERENTIAL EQUATION FROM ACTIVITIES

The open compartment system using radiopharmaceutical injected into a patient is taken as only spreads to organs such as the heart, kidneys, thyroid, and liver uniformly, whereas the breasts are not taken into account as they cannot function as either the source or target. Other than that, this research also neglects the flow of radiopharmaceuticals from the source kidneys to the target heart, in agreement with the statement by Soenarjo [5]. This means that the illustration for the open 4-compartment with radiopharmaceutical injected to a patient is as shown in Figure 1.

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The differential equation of the open 4-compartment system can be elaborated into 4 differential equations of radiopharmaceutical activities q_1, q_2, q_3, and q_4 of the heart, kidneys, thyroid, and heart, which are written as

$$\frac{dq_1}{dt} = -\left(\lambda_{21} + \lambda_{31} + \lambda_{41}\right) q_1 + \lambda_{13} q_3, \tag{1}$$

$$\frac{dq_2}{dt} = \lambda_{21} q_1 - \lambda_{52} q_2, \tag{2}$$

$$\frac{dq_3}{dt} = \lambda_{31} q_1 - \left(\lambda_{13} + \lambda_{53}\right) q_3, \tag{3}$$

$$\frac{dq_4}{dt} = \lambda_{41} q_1 - \lambda_{54} q_4, \tag{4}$$

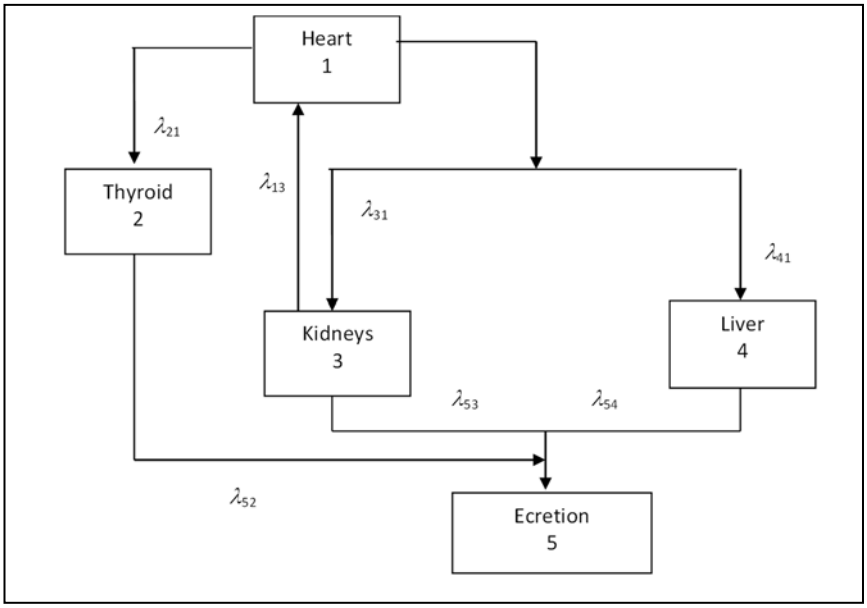

Fig. 1. The open 4-compartment system consists of the heart, kidneys, thyroid, and liver and they detect metabolism of radiopharmaceutical in a patient.

where q_i and λ_{ij} are radiopharmaceutical activities and coefficient of transfer rate for each compartment respectively. By using the relationship between equations (1) and (3) above, we obtain the 2nd order differential equation for activity 1 (heart organ), which can be written as follows,

$$\frac{d^2 q_1}{dt^2} + \left[\lambda_{21} + \lambda_{31} + \lambda_{41} + \lambda_{13} + \lambda_{53}\right] \frac{dq_1}{dt} + \left[\lambda_{21}\lambda_{13} + \lambda_{41}\lambda_{13} + \lambda_{21}\lambda_{53} + \lambda_{31}\lambda_{53} + \lambda_{41}\lambda_{53}\right] q_1 = 0 \cdot \tag{5}$$

The solution to equation (5) for the heart organ case can be expressed in form

$$q_1(t) = Ae^{-\alpha t} + \left(q_{10} - A\right) e^{-\beta t}, \tag{6}$$

where A and q_{10} are constants of the differential equation solution (6) that meet the boundary conditions

$$q_1(0) = q_{10} \cdot \tag{7}$$

The relationship between decay constants α and β in eq. (6) can be written through relationships

$$\alpha + \beta = \lambda_{21} + \lambda_{31} + \lambda_{41} + \lambda_{13} + \lambda_{53}, \tag{8}$$

$$\alpha-\beta=\sqrt{\left[\lambda_{21}+\lambda_{31}+\lambda_{41}+\lambda_{13}+\lambda_{53}\right]^2-4\left[\lambda_{21}\lambda_{13}+\lambda_{41}\lambda_{13}+\lambda_{21}\lambda_{53}+\lambda_{31}\lambda_{53}+\lambda_{41}\lambda_{53}\right]}, \tag{9}$$

with the boundary conditions,

$$\left[\lambda_{21}+\lambda_{31}+\lambda_{41}+\lambda_{13}+\lambda_{53}\right]^2 \geq 4\left[\lambda_{21}\lambda_{13}+\lambda_{41}\lambda_{13}+\lambda_{21}\lambda_{53}+\lambda_{31}\lambda_{53}+\lambda_{41}\lambda_{53}\right]. \tag{10}$$

In eq. (9) we can see that the value of $\alpha \geq \beta$, which shows the exponential decay rate of the component of $Ae^{-\alpha t}$ compared to the component of $\left(q_{10}-A\right)e^{-\beta t}$ in eq. (6). If exponential activity of $Ae^{-\alpha t}$ is an activity originating from the heart that will spread to the thyroid, kidneys and liver, then another exponential factor of $\left(q_{10}-A\right)e^{-\beta t}$ comes from backflow from the kidney to the heart which shows a reduction in the initial total activity value of q_{10} to activity that leaves the heart to the thyroid, kidney and heart.

III. Results of Calculations

Determination of the constants α and β derived from two solutions of differential equations of two graphs of the heart compartment, is quite difficult to measure because usually the graphs presented only consist of one graph of heart compartment. If it is assumed that the value of $\alpha = \beta$ for simplifying the case by assuming that the two radiopharmaceutical activities solutions that enters or goes out of the heart organ has the same exponential factor function, then equation (5) can be expressed as

$$\frac{d^2q_1}{dt^2}+2\alpha\frac{dq_1}{dt}+\alpha^2q_1=0\cdot \tag{11}$$

Because the solution to second-order differential equations requires two solutions with different functions, then the solution of equation (11) can be expressed as,

$$q_1\left(t\right)=\left[tA+q_{10}\right]e^{-\alpha t}, \tag{12}$$

where solution (12) also still meets the boundary requirements (7). In equation (12) it has a part of $q_{10}e^{-\alpha t}$ that leaves the heart towards the thyroid, kidney and liver and the part of $tAe^{-\alpha t}$ that originates from the kidney to the heart. The constant value of A is considered quite small, so there is the following relationship

$$\left[tA+q_{10}\right]e^{-\alpha t}<q_{10}\cdot \tag{13}$$

Equations (2), (3) and (4) contain a part of the heart activity of $q_1(t)$ whose solution is known in equation (12), so that the solution of activities of the $q_2(t)$ (thyroid), $q_3(t)$ (kidney) and $q_4(t)$ (liver) from equations (2), (3) and (4) respectively can be calculated as,

$$q_2\left(t\right)=\left\{\frac{A\lambda_{21}}{\left(\lambda_{52}-\alpha\right)}\left[t-\frac{1}{\left(\lambda_{52}-\alpha\right)}\right]+\frac{\lambda_{21}q_{10}}{\left(\lambda_{52}-\alpha\right)}\right\}e^{-\alpha t}+C_2e^{-\lambda_{52}t}, \tag{14}$$

$$q_3\left(t\right)=\left\{\frac{A\lambda_{31}}{\left(\lambda_{13}+\lambda_{53}-\alpha\right)}\left[t-\frac{1}{\left(\lambda_{13}+\lambda_{53}-\alpha\right)}\right]+\frac{\lambda_{31}q_{10}}{\left(\lambda_{13}+\lambda_{53}-\alpha\right)}\right\}e^{-\alpha t}+C_3e^{-\left(\lambda_{13}+\lambda_{53}\right)t}, \tag{15}$$

$$q_4\left(t\right)=\left\{\frac{A\lambda_{41}}{\left(\lambda_{54}-\alpha\right)}\left[t-\frac{1}{\left(\lambda_{54}-\alpha\right)}\right]+\frac{\lambda_{41}q_{10}}{\left(\lambda_{54}-\alpha\right)}\right\}e^{-\alpha t}+C_4e^{-\lambda_{54}t}, \tag{16}$$

where C_2, C_3 and C_4 are integration constants for $q_2(t)$, $q_3(t)$ and $q_4(t)$ respectively. The solution of organ activities in all equations of (12), (14), (15) and (16) satisfies the condition $\alpha = \beta$, so that equations (8) and (9) will change to a new equation under the condition $\alpha = \beta$ as,

$$\alpha=\tfrac{1}{2}\left(\lambda_{21}+\lambda_{31}+\lambda_{41}+\lambda_{13}+\lambda_{53}\right)=\sqrt{\lambda_{21}\lambda_{13}+\lambda_{41}\lambda_{13}+\lambda_{21}\lambda_{53}+\lambda_{31}\lambda_{53}+\lambda_{41}\lambda_{53}}\,. \tag{17}$$

If equation (12) of the activity of the heart organ has a part of the activity that enters and exits the heart organ, then the equation of activity of the thyroid, kidney and liver organs in equation (14) - (16) shows the part of the organs activity that all the parts come

out of the organs and going to the last organ is the excretion organ as shown in the 4-open compartment model of Figure 1.

IV. Discussion

The calculation of the model of various body organs using the open compartment system using radiopharmaceutical injected into a patient such as MIRD (Medical Internal Radiation Dosimetry) is a calculation model that is very difficult to do because the spread of radiation doses in various organs is influenced by many factors and accompanying disorders such as factors sensitivity to absorption of radiation doses from each organ, internal diseases, internal and external disorders etc. If all the factors that influence the pattern of radiation dose flow can be included, a calculation pattern that is very complex and too difficult to solve in the formulation of the radiation dose activity model for various organs in the body will be created.

The calculation model of the radiopharmaceutical activity of an open 4-compartment model in this paper presents a model of calculation that has experienced many restrictions and simplification of cases and ignores all possible disturbances. Among the simplification and limitation cases in this paper is the neglect of the radiopharmaceutical dosage in the breast organ because the radiopharmaceutical dose received by the breast organ is very little and the assumption that the exponential factor of the activity that exits the heart organ and enters the heart organs is considered the same.

Acknowledgment

This work was financially supported by non-tax revenue (PNBP), Diponegoro University, Semarang, Indonesia under contract No. 1756 N/UN7.5.8/PG/2018.

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