Designing a Computer Code to Calculate the Committed Dose Equivalent to Internal Organs Following the Injection of a Radiopharmaceutical

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Abstract

Radiopharmaceuticals are drugs that contain radioactive isotopes and are used in the nuclear medicine field for diagnostic procedures. There is a demand for an effective software to calculate the Committed Dose Equivalent (CDE) to patients. The designed software would be a useful tool for medical professionals in the nuclear medicine field and for any patient interested in knowing the dose received following the injection of a radiopharmaceutical. The aim is to design an affordable and easy to learn tool to estimate the Committed Dose Equivalent to various organs of interest as well as the total body.

1.0 Introduction

Radiopharmaceuticals are radioactive agents used to diagnose and treat specific medical problems. They may be administered to the patient in various ways such as injection, ingestion, or placed into the eye [1]; the targeted organ determines the type of radiopharmaceutical used and the way it is introduced into the patient's body. The radioactivity is then detected by dedicated imaging equipment and scans are generated. These scans are images of the targeted organs enabling the observation and examination of how the organs are functioning. Moreover, these images enable the detection of cancer or tumors that may be present within an organ. Currently, Technetium-99m (Tc-99m) and Iodine-131 (I-131) are the most commonly used radiopharmaceutical, in Canada Tc-99m is used in over 80% of all nuclear medicine scans [2]. With numerous scans and diagnostic procedures being widely conducted, a demand is present for an effective software to estimate a patient's Committed Dose Equivalent (CDE).

2.0 Methodology

To develop the dose calculator software, the scope was set to include modelling, calculating the activity distribution in regions of interest of the human body, as well as computing the dose based on the distribution of the injected radiopharmaceutical. In order to model the distribution of the radioactive material and determine the localization percentage in each organ, a multi-compartment bio-kinetic model was studied and analyzed. A multi-compartment model, which consists of blocks, each representing one or a group of organs, provides information on the bio-distribution of the radioactive material. The multi-compartment model can be mathematically represented as a system of differential equations which can then be used to calculate the activity and the dose received by the target organs. As a result, a multi-compartment bio-kinetic model of

I-131 was adopted and chosen to build a preliminary design of the software and to be used as a pilot study to perform dose calculations due to its reasonable complexity.

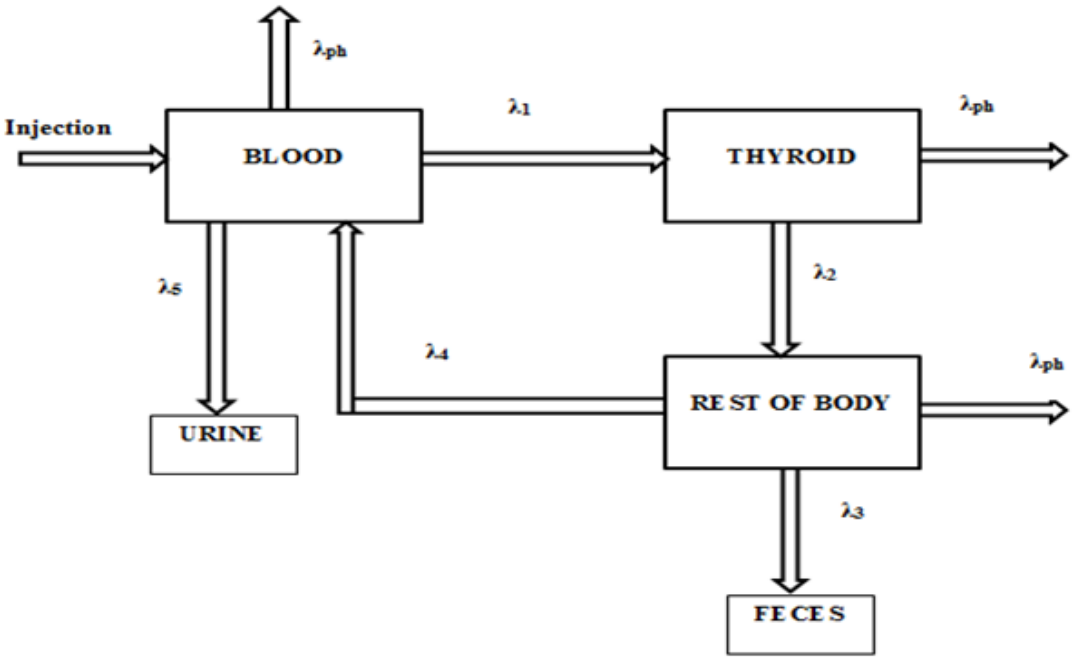

Figure 1 - I-131 Bio-kinetic Model [3]

The bio-kinetic model that is shown above comprises three main compartments which are the blood, the thyroid and the rest of the body. Following the injection, the radioactive material starts its path from the first compartment (Blood), which is then absorbed by the thyroid and lastly by the rest of the body. Each of the arrows represents the decay that the radioactive material undergoes; the λ value associated with each arrow signifies the decay constant. Lambdas from λ_1 to λ_5 represent the biological decay constants of I-131 from one compartment to another. Additionally, the radioactive material undergoes physical decay by emitting gamma rays and other types of ionizing radiation. The decay constant associated with this process is Lambda physical ($\boldsymbol{\lambda_{ph}}$). The bio-kinetic model also considers urine and feces as means of excretion. In order to find the activity in each of the compartments and the dose to other body organs, the number of radioactive nuclides in each compartment had to be found. For this purpose, a system of differential equations that describes the dynamics of the multi-compartment system was developed and numerically solved. In the following differential equations, N values represent the number of radioactive nuclides in that specific compartment:

$$\frac{dN_{Blood}}{dt} = -(\lambda_1 + \lambda_5 + \lambda_{ph}).N_{Blood} + \lambda_4 N_{Body} \quad (1)$$

$$\frac{dN_{Thyroid}}{dt} = -(\lambda_2 + \lambda_{ph}).N_{Thyroid} + \lambda_1 N_{Blood} \quad (2)$$

$$\frac{dN_{Body}}{dt} = -(\lambda_3 + \lambda_4 + \lambda_{ph}).N_{Body} + \lambda_2 N_{Thyroid} \quad (3)$$

2.1 Dose Calculations

Two dose calculating methods were identified and examined. The first method was the Medical Internal Radiation Dose (MIRD) technique. The second method was introduced by the International Commission on Radiological Protection (ICRP). Both approaches were studied and found to be similar in the way of calculating the dose. However, it was decided that the MIRD technique would be used. The Committed Dose Equivalent (CDE) is the effective dose to organs or tissues after introducing radioactive material into the body, integrated over a commitment period which is 50 years for adults and 70 years for children [4]. The CDE ($H_{T,\,t}$) is computed by first calculating the absorbed dose using the following equation [5]:

$$D = S\,(T \leftarrow S) * \int_0^t A.\,dt \tag{4}$$

Where:

- D is the absorbed dose in the target organ in units of Gray (Gy).
- $S(T \leftarrow S)$ is the absorbed dose per activity in units of Gy; the T and S between brackets symbolize the Target and Source tissues, respectively.
- $\int_0^t A.\,dt$ is the cumulated activity of the radioactive material in the source organ; t denotes the commitment period which is determined based on the age of the patient.

In order to calculate the activity in the source organ, the number of radioactive nuclides in that organ has to be found by solving the system of differential equations that was developed for the bio-kinetic model as well as using the following equation [5]:

$$A(t) = \lambda_{ph} * N(t) \tag{5}$$

Where:

- $N(t)$: is the number of radioactive nuclides in the source organ (compartment) at time t.
- λ_{ph}: is the physical decay constant of the radioactive nuclides per unit time.

The S-factor, which is the absorbed dose per activity, is calculated using the following equation [5]:

$$S(T \leftarrow S) = \Delta * \sum_{n=1}^{i} \phi\,(T \leftarrow S) \tag{6}$$

Where:

- $\phi\,(T \leftarrow S)$: is the Specific Absorbed Fraction (kg^{-1}), obtained from MIRD pamphlet 05 tables [5].
- Δ: is the product of the emitted photon energy (E) and its yield (n).

The final step in calculating the Committed Dose Equivalent (CDE) is to multiply the absorbed dose that was found earlier by the radiation weighing factor (W_R) and the tissue weighing factor (W_T) for each of the target organs [5]. Both the radiation and tissue weighing factors are found in the ICRP publication 103 [6].

$$H_{T_t} = D * W_R * W_T \tag{7}$$

2.2 Code

Several programming languages were examined and evaluated based on a predefined criterion. After the evaluation process was completed, it was concluded that C# will serve as the most efficient in meeting the objectives. Once the software is executed, the user has to select a radiopharmaceutical from the drop list. The user then has to input the initial activity being injected. Finally, the user has to select patient's legal gender.

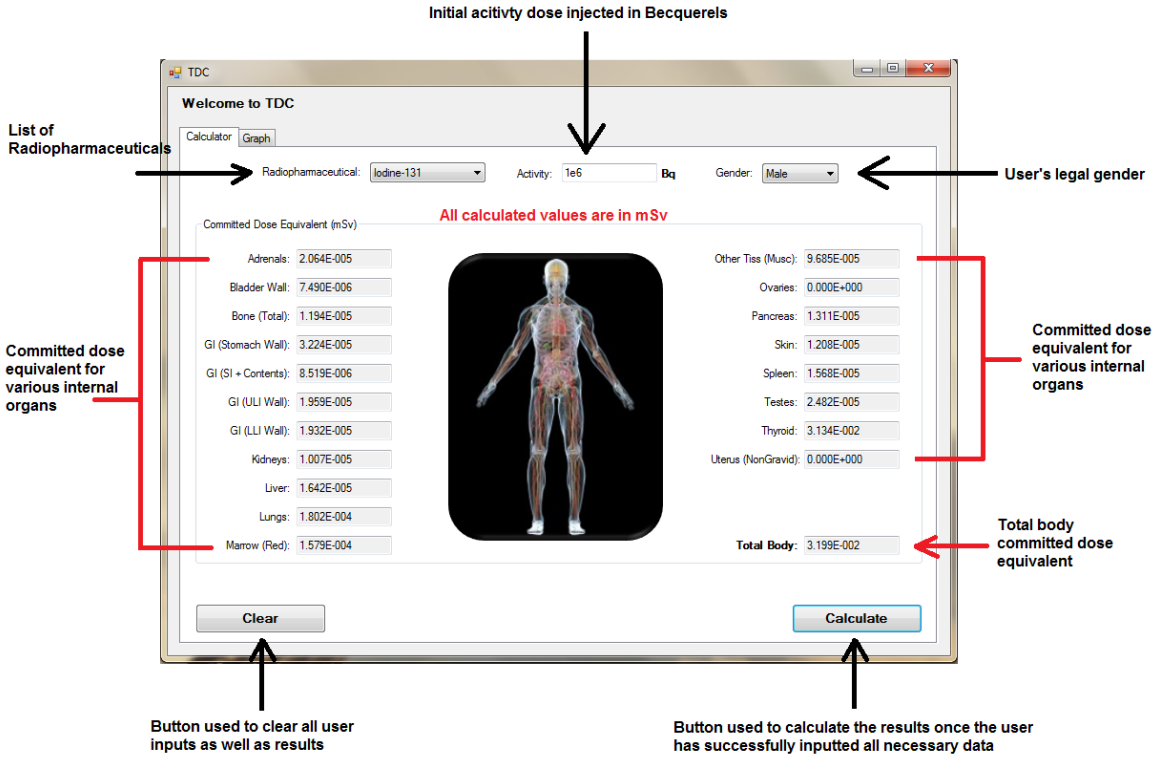

Figure 2 – Software user interface (Tab 1)

Once all three required data have been successfully and correctly inputted, the user will then press the "Calculate" button located at the bottom right corner of the software to obtain the dose results. Figure 2 above shows a test run of the software once the program executable has been run. Since the software is still in beta version, the only available radiopharmaceutical is Iodine-131, which was used as a starting point due to the reasonable complexity of its bio-kinetic model. The inputted activity is then used by the software to calculate the initial number of radionuclides (N_0), which is then used through the system of differential equations shown in section 2.1. The software then utilizes the system of differential equations and various specific absorption factors (from the MIRD pamphlet no.5) to trace the activity throughout the compartments shown in the bio-kinetic model in section 2.1. The software performs 438,000 steps; each step is considered an hour, and collectively are equvalent to 50 years. Once all calculations have been performed, results are then displayed in the 20 textboxes allocated in Tab 1 for various internal organs, as well as the total body. This then allows the user to switch to the second tab by clicking the

"Graph" button. This action generates a line graph that displays the patient's cumulative dose (in mSv) with respect to time.

Various measures have been taken to ensure human errors are minimized. For instance, in the absence of one of the three required inputs, if the user presses "Calculate", an error message will appear notifying the user of that missing variable. All textboxes used to display results have been set to read-only to prevent the user from tampering with the output. The activity textbox shown in the user interface above will only allow numbers and a single input of 'e' (for scientific notation), '**.**' (for decimals), and '**+**' / '**-**'.

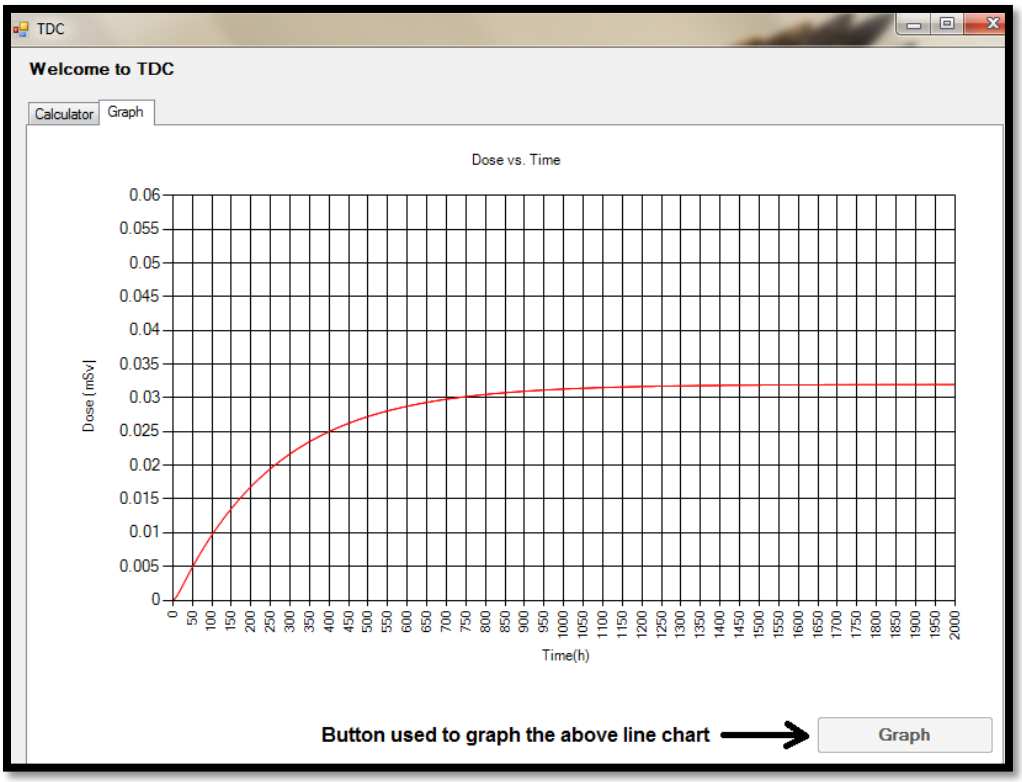

Figure 3- User interface (Tab 2) displaying info graphic

3.0 Results and Discussion

A test run was conducted using an initial activity of one MBq ($1x10^6$ Bq) of I-131 and the following graphs (Figures 4-7) were generated.

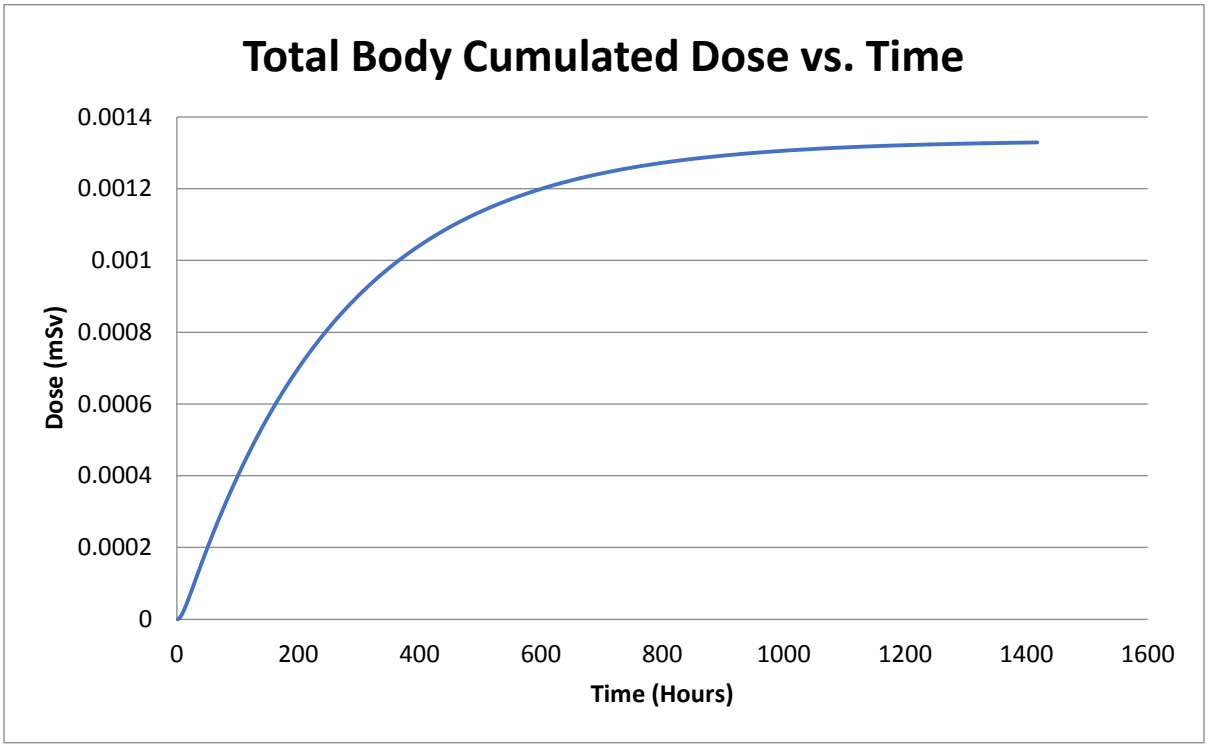

Figure 4 - Graph showing the cumulated dose over time post a one MBq I-131 injection

As shown in Figure 4 above, the cumulated total dose (dose to total body) increases as the emitted radiation is depositing its energy within tissues, the total dose increases over time until it reaches a plateau after a period of time; the accuracy of these results has not been verified yet, and will be done as part of future developments of the software.

The results were obtained from the software and were plotted using Microsoft Excel. Figures 5-7 illustrate the relationship between time and number of radioactive nuclides in each of the three compartments. The N_Blood, N_Thyroid and, N_RoB indicate the number of radioactive nuclides in the Blood, Thyroid and Rest of the Body respectively.

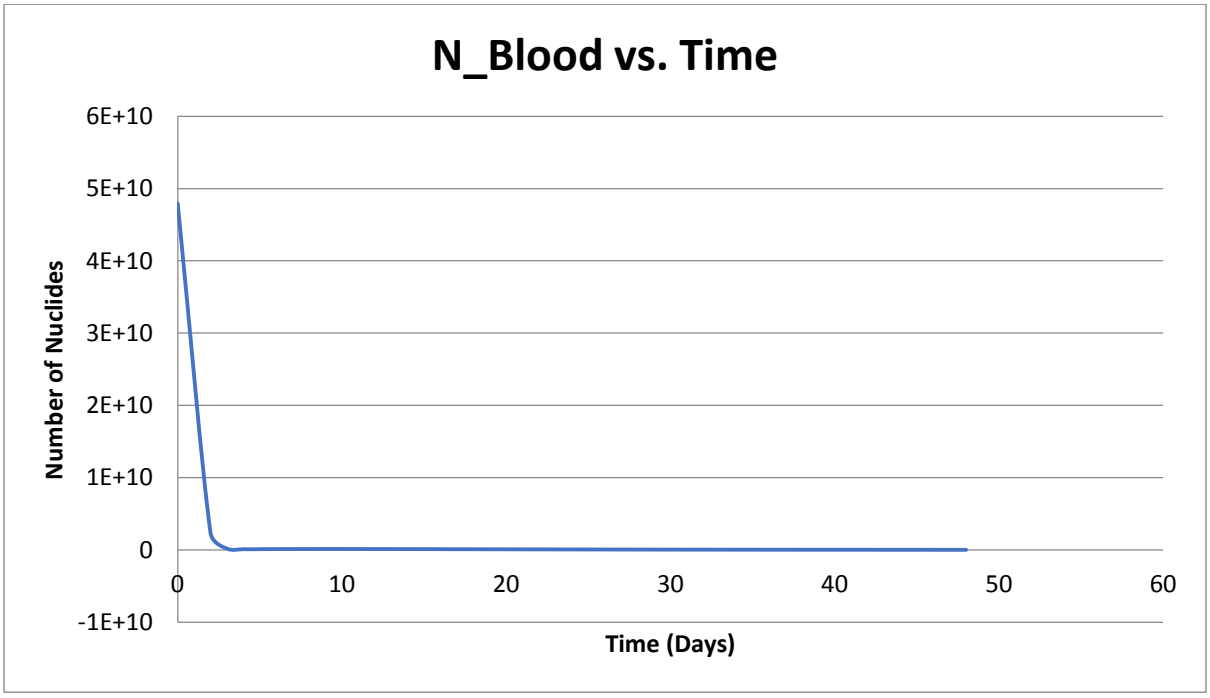

Figure 5- Number of Radioactive Nuclides in the Blood vs. Time

Figure 5 above shows the change in number of radioactive nuclides in the blood compartment (also known as the central compartment) over time. At time=0, the entire amount of the radiopharmaceutical is residing in the blood compartment. As time elapses, the radioactive material decays both biologically and physically causing the number of nuclides to decrease as the curve demonstrates.

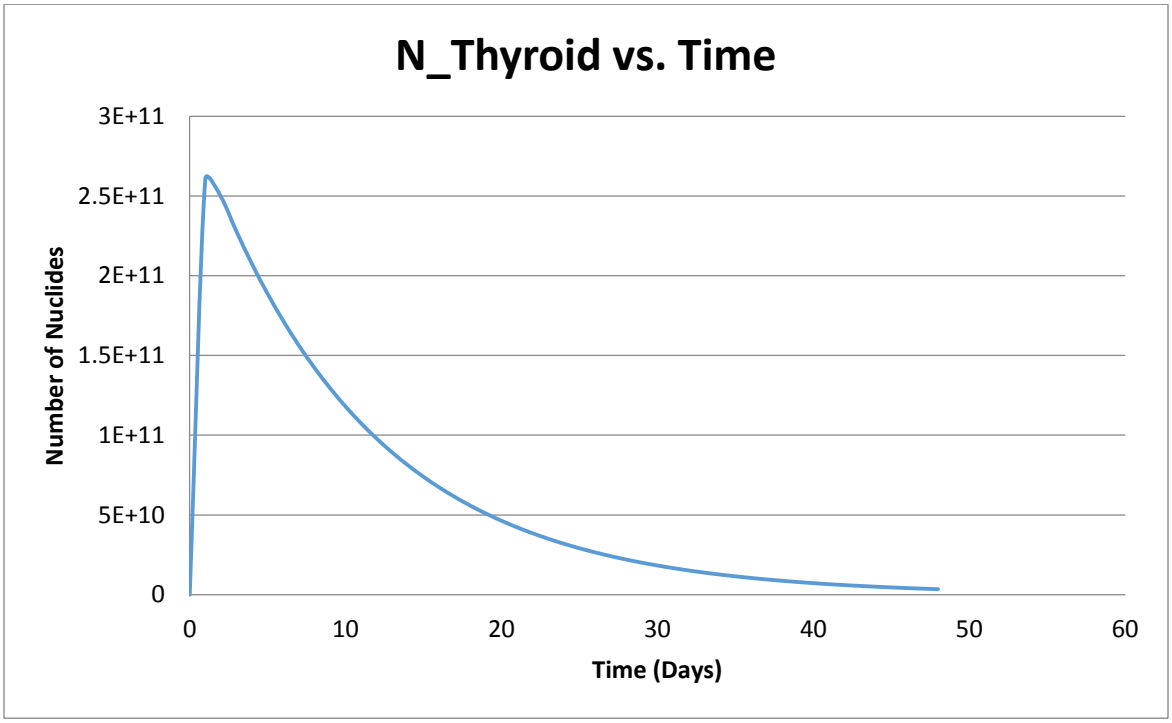

Figure 6 - Number of Radioactive Nuclides in the Thyroid vs. Time

Figure 6 illustrate the change in number of radioactive nuclides in the thyroid. Shortly after the injection, a portion of the radiopharmaceutical starts to biologically decay from the blood compartment into the thyroid, the build-up continues until a peak is reached, then the concentration starts to decrease due to the physical decay as well as the biological decay to other compartments.

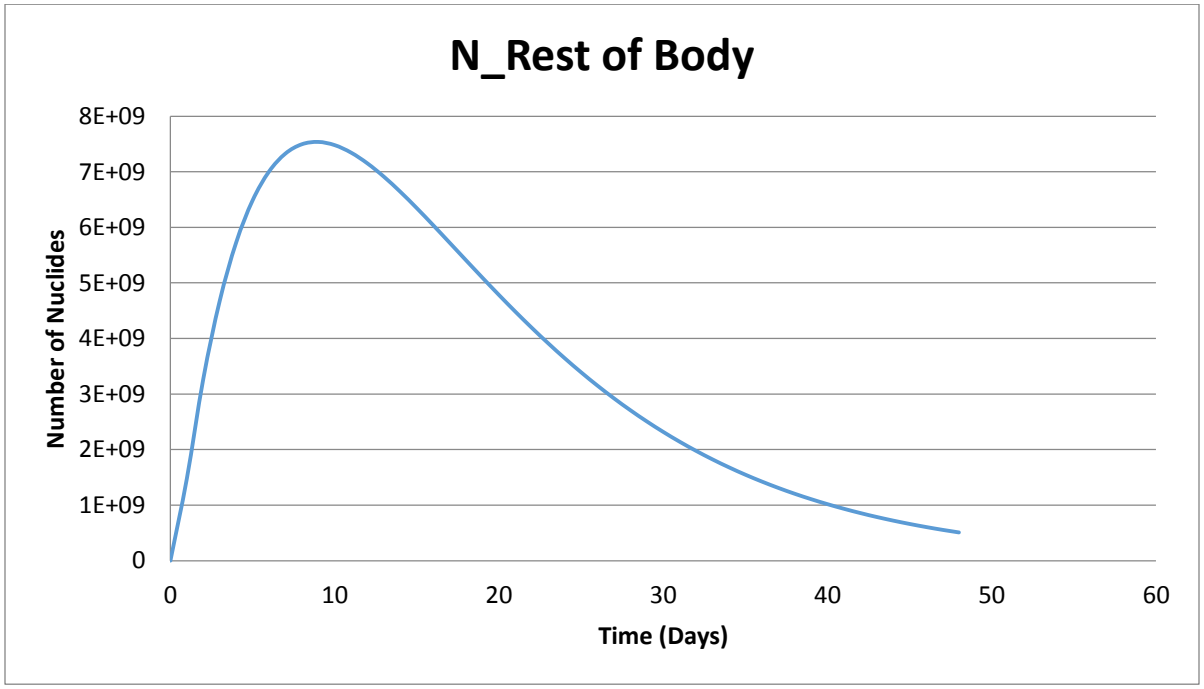

Figure 7- Number of Radioactive Nuclides in the Rest of Body vs. Time

The curve in Figure 7 has a similar shape to Figure 6; the main differences are in the time each compartment took to reach a peak and the number of radioactive nuclides in each compartment.

Numbers of radionuclides in each compartment were plotted because they are a significant variable in the dose calculations. Each of the generated curves had a different profile due to differences in the biological decay constants of the different compartments.

4.0 Conclusion and Future Work

A software to estimate the Committed Dose Equivalent (CDE) was designed and developed in C# programming language and using the MIRD technique as a method of calculating the dose. A bio-kinetic model of I-131 was used to build the preliminary version and as a pilot study in order to calculate the activity in different body regions which was then used to perform the dosimetry. The future work of this research will focus on enhancing the software and include other radiopharmaceuticals such as Tc-99m based radiopharmaceuticals.

5.0 References

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[7] "Chart of Nuclides," National Nuclear Data Center (NNDC).