Tc99m-Sestamibi Dosimetry in Myocardial Perfusion Imaging

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ABSTRACT: *This paper addressed myocardial perfusion imaging providing a spatial dosimetric investigation of the ^{99m}Tc-radiopharmaceutical dose distribution at the myocardium. Radiological data manipulation was performed in order to create a computational voxel model of the heart. A set of images obtained by thoracic angiotomography and abdominal aorta was set up providing anatomic and functional information for heart modeling in SISCODES code. A homogeneous distribution of ^{99m}Tc was assumed into the cardiac muscle. Simulations of the transport of particles through the voxels and the interaction with the heart tissues were performed on the MCNP – Monte Carlo Code. The spatial dose distribution in the heart model is displayed as well as the dose versus volume histogram of the heart muscle. Conclusions: The present computational tools can generate spatial doses distribution in myocardial perfusion imaging. Specially, the dosimetry performed elucidates imparted dose distribution in the myocardial muscle per unit of injected ^{99m}Tc activity, which can contribute to future deterministic effect investigations.*

KEYWORDS – *instrumentation, nuclear medicine, radiation oncology, radiation protection, radiology*

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I. INTRODUCTION

Myocardial perfusion imaging (MPI) becomes an important tool in diagnosis and monitoring patients. On MPIs, a radiopharmaceutical is injected through a peripheral vein and is subsequently captured by myocyte cells of the heart. The uptake radioisotope emits radiation that is converted into a scintigraphic image, generated through a cardiac CT. The images are obtained in two physical patient stages: rest and stress with blood flow increased into the heart. Radiopharmaceuticals accumulate to myocardium in proportion to regional blood flow, which is analyzed in according to a decreasing in the intensity of radioisotope uptake in some part of the heart muscle. When this uptake is transient, coronary ischemia is point out; when it is persistent, fibrosis is the situation. Thus, myocardial perfusion imaging allows the physicians to search the viable areas, separating them from unviable ones. In this case, this procedure is called myocardial viability [1], [2], [3], [4].

The most important clinical application of MIP on stress is the assessment of ischemic heart disease. The Tl-201 or Tc-99m labeled agents are used on this diagnostic. Generally, the correlation between the MPIs in stress condition and angiography findings of the coronary artery with contrast is good. There is sufficient evidence that the finding in MPIs with stress reflects the hemodynamic and functional stenosis of the coronary artery, providing important prognostic information [5]. Regarding the stress images, 75% were acquired with Tc-99m labeled compounds and 25% with Tl-201. SPECT was often used in more than 90% of the studies [5].

Technetium-99m radiopharmaceutical, as a flow tracer, once injected intravenously, is a cationic complex which diffuses passively through the capillary and cell membrane, although less readily than 201Tl, resulting in lower immediate extraction. Within the cell it is localized in the mitochondria, where it is trapped, and retention is based on intact mitochondria, reflecting viable myocytes. Elimination of the radiotracer occurs mostly through the kidneys and the hepatobiliary system [7]. Tc-99m kinetics are affected by viability has important implications for understanding of perfusion tracer kinetics in the setting of acute ischemia and infarction followed by restoration of blood flow and serial determinations of flow in trials of angiogenesis where viability may or may not be present. As observed in study, quantities analysis of Tc-99m washout permits distinguishing between coronary heart disease without previous myocardial infarctions and with previous myocardial infarctions [36].

Despite of the long term of application of MPI, spatial dose distribution at the myocardium during this procedure is poor understood, due to the complex of radiopharmaceutical dynamics in such anatomic dynamic structure [34]. The present paper conducts a heart dosimetric investigation in MPI with Tc-99m radiopharmaceutical in order to elucidate the myocardium spatial imparted dose distribution. Studies demonstrate that technetium-99m glucaric can be used effectively to better detect myocardial infarction in animal models. They show their affinity for necrotic tissues and their apparent advantage in imaging tests when it can be used as an inflammatory marker and severe myocardial ischemia, since it is not picked up by normal tissue [1], [3].

This investigation is justified by the possible induced-radiation deterministic effects especially in the microvasculature of the heart muscles and the modulation of matrix metalloproteinases and citocines [32].

II. METHODS

2.1. Heart model for perfusion image

A set of contrasted CT images of a heart with normal morphology was selected. The contrast was important in order to allow separation among the various cardiac structures. The images were taken from a set of CT sections of an adult chest. Sixty images, each one representing a 2 mm layer, were selected from 355 axial slices of the CT, including the region of interest (heart and part of the mediastinum). The CT images were obtained in DICOM (Digital Imaging and Communications in Medicine) which is the standard for medical images storage and transmission [8].

The select image set was trimmed limiting the heart region. Those were converted to a voxel model of tissues by SISCODES (Computational system for dosimetry in neutron and photon based on stochastic methods) [9], [11]. The SISCODES is a computer system, developed at NRI [12], which allows creating voxel models based on tomography images, simulating a radiotherapy protocol onto voxel model environment, and expressing the simulation results through isodose curves or histograms [9-11]. The images were converted from DICOM to JPEG format since the original format was not compatible with the SISCODES. After that, the tomography images were converted into a three dimensional model based on the grayscale of each image region. This model was then "filled" by the tissues identifying each structure with the aid of the gray tone of the image. The available tissues had its chemical composition and mass density previously entered into SISCODES database, as well as nuclear information, based on data from ICRU-46 [13]. Each tissue has also an associated color, which allows the identification of the distinct tissues used in the model.

A three dimensional visualization of the model was taken on the SOFT-RT software [15], [16]. This software was also developed in house at NRI. It uses OpenGL to render three-dimensional views of the voxel model generated on the SISCODES software.

After identifying each tissue and organ in the model, the dosimetric protocol can be simulated. Later, information of the radioactive sources is incorporated. Each voxel from myocardic muscle received a distributed source of Tc-99m radiopharmaceutical. Thus the activity per unit of mass was homogeneous at all heart muscle, which is a simplification of the complex Tc-99m dynamic on heart. The gamma spectrum from Tc-99m was specified from literature (ENSDF Decay Data in the MIRD - Medical Internal Radiation Dose) [21]. Technetium Tc-99m is provided by 99Mo/99mTc generators and has a half life of 6 h, is a lipophylic cationic (1+) complex that accumulates in the myocardium by passive diffusion, not transported by the Na+–K+–ATPase pump. It indicates the myocardial perfusion abnormalities. After intravenous administration, the blood clearance of 99mTc-sestamibi is rapid with a t1/2 of a few minutes both at stress and rest. The first-pass extraction is almost 50–60%. Myocardial uptake is proportional to regional myocardial blood flow and amounts to about 1.4% of injected dosage during exercise and about 1.0% at rest. Almost 90% of the activity in the cell is bound to proteins in the mitochondria [39].

Finally, the files are exported to a MCNP input file. The resulting input file was simulated in the MCNP5 code [14]. The Monte Carlo (MC) method can be used to simulate theoretically a statistical process, as the interaction of particles with bone and soft tissues, and is particularly interesting for solving complex problems of nuclear transport that cannot be modeled by codes based on deterministic methods. In MC particle transport, each of many particles emitted by Tc-99m is followed throughout its interaction until some terminal event such as absorption, escape, among others. The simulations account for scattering effects near chest and lungs which play an important role in case of Tc-99m. After the simulation, output is exported to SISCODES and the isodose curves of the spatial dose distribution and dose-volume histograms were obtained.

2.2. Imparted dose evaluation

The imparted dose on each voxel of the heart can be obtained multiplying the MCNP simulation providing absorbed dose per unit of particle – F06 (r) multiplied by particle per transition, thus in Gy per transition, by patient´s injected activity (A) in Bq, and by the integral of the percentage of heart uptake over

time, defined by p(t), namely time integral factor. Therefore, the imparted heart dose is expressed as:

$$D = r\, A \int_{t_i}^{t_f} p(t)\, dt \qquad\qquad 1$$

The function p(t) are influenced by two separated mechanisms: the Tc-99m radioactive activity and the sestamibi radiopharmaceutical clinic dynamics. Both mechanisms have exponential behavior, so, p(t) can be expressed as a biexponential function (18):

$$p(t) = C0\, e^{\left(\frac{-\ln(2)t}{c_1}\right)} + C2\, e^{\left(\frac{-\ln(2)t}{c_3}\right)} \qquad\qquad 2$$

where C1 and C3 are constants relatives to half-live of the radiopharmaceutical dynamics and the radioactive decay, and C0 and C2 are the weights of each exponential term.

III. RESULTS

3.1. Heart model

The tissues from the heart voxel model were previously inserted in the SISCODES database. The tissues on the model held its mass density and its chemical weight percentage. Figure 1 shows, respectively, the cardiac tomography imaging and the heart voxel model, in two and three dimensional views. At this figure 1, some sections of the heart voxel model are presented at XY-plane views taken on the SISCODES interface. Also, three dimensional visualizations are depicted from SOFT-RT interface on three distinct perspectives.

Figure 1. Images of the heart respectively in computed tomography (first row), same region on voxel model in SISCODES (second row), and three dimensional view of the voxel model in SOFT-RT (third row).

Sections of the voxel model taken on the MCNP5 interface, after exportation of the model to the stochastic MCNP code, in which simulations took place, can be seen in Figure 2.

Figure 2. Sections of the voxel model taken on the MCNP5 interface, after exportation of the model to the stochastic MCNP code, in which simulations took place

3.2. Spatial dose distribution

The figure 3 presents the percentage isodose areas on the heart sections, following by the value distribution.

The percentage of absorbed dose represented by is based on a maximum value which in this case was 9.9 10-12Gy per particle emission. All values are normalized to the maximum value.
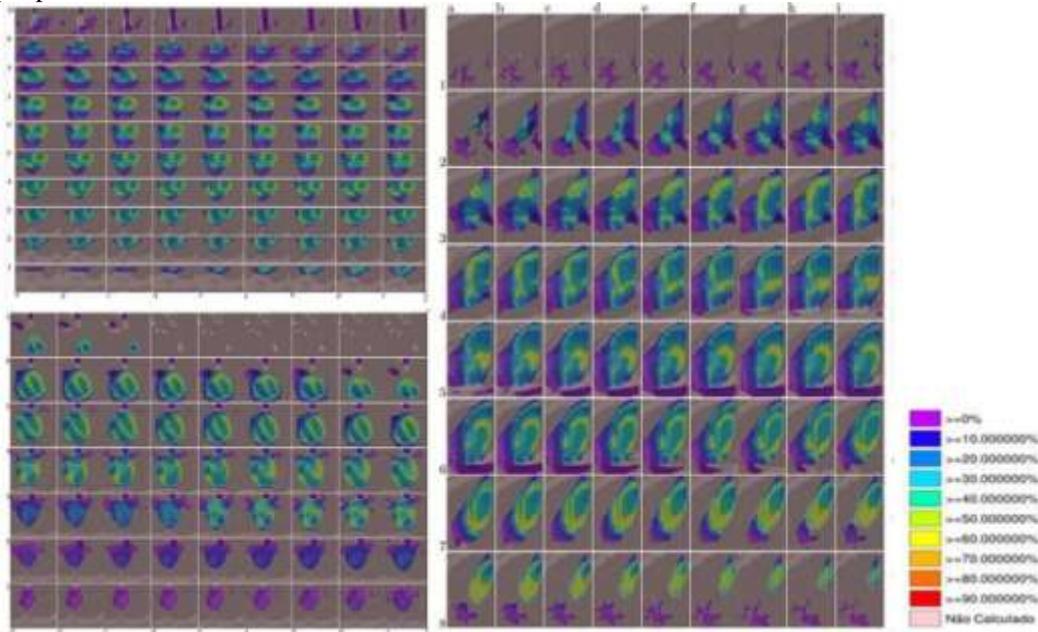
Figure 3. Spatial dose distribution in heart: lateral, saggital and coronal sections.

3.3. Biological and Effective kinetic uptake

In order to obtain imparted dose, the Eq.1 was applied. The C0, C1, C2, C3 in Eq.2 were obtained by non-linear fit to experimental data of heart uptake as function of time, figure 4, and presented by Bristol-Mayer Scribb [39].

These data are shown in figure 4 and table 1.
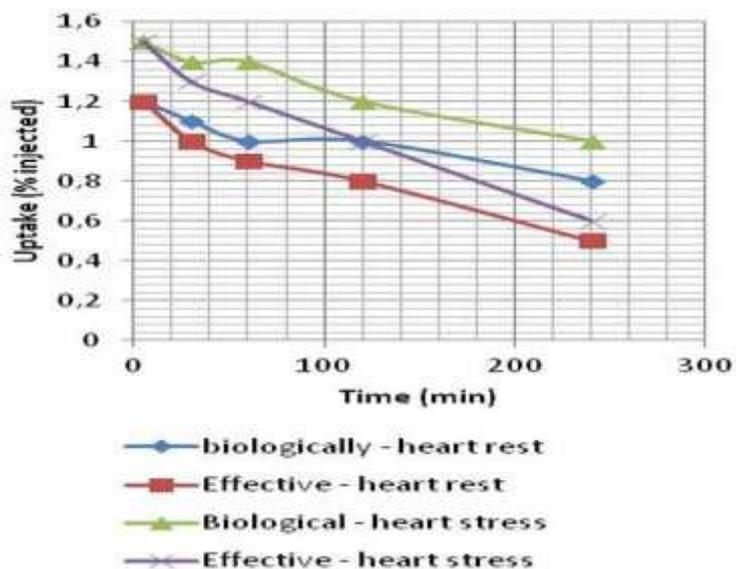
Figure 4. Uptake in function of percentage of activity injected on heart in rest and stress.

Table 1. Experimental data of the technecium heart uptake as function of time at rest and stress.

Time	Heart (rest)		Liver	
	Biological	**Effective**	**Biological**	**Effective**
5	1.2	1.2	19.6	19.4
30	1.1	1.0	12.2	12.2
60	1.0	0.9	5.6	5.6
120	1.0	0.8	2.2	2.2
240	0.8	0.5	0.7	0.7

Time	Heart (stress)		Liver	
	Biological	**Effective**	**Biological**	**Effective**
5	1.5	1.5	5.9	5.8
30	1.4	1.3	4.5	4.2
60	1.4	1.2	2.4	2.1
120	1.2	1.0	0.9	0.7
240	1.0	0.6	0.3	0.2

The integral values of the function p(t) at the interval 0-240 min at the heart for biological and effective were 240 and 204 min.%I on rest and 300 and 252 min.%I on stress, respectively; in which min.%I is the percentage of activity injected. The term 100-1 exists because experimental data are expressed in percentile of total injected activity.

One can see from figure 4 that the isodose curves are so disperse on the heart muscle that it cannot be easily interpreted. Technetium-99m having a half life of 6 h and emitting gamma radiation with energy of 140 keV characteristics that enable the acquisition studies with good quality and low radiation dose. This causes the technetium-99m be the most widely used isotope, which may be administered in the chemical form of sodium pertechnetate or attached to other molecules. Thus, the present study is relevant not only to present imparted dose in the heart but due to the presentation of a new methodology to dose calculation.

IV. CONCLUSIONS

As conclusion, the present computational tool is capable of generating spatial dose distribution at myocardial perfusion imaging protocol. Further studies involving differential uptakes from patient´s images shall be done to obtain dosimetric data for each clinical situation. Specially, the performed dosimetry elucidates spatial imparted dose distribution in the myocardial muscle per unit of injected Tc-99m radiopharmaceutical activity.

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