

**VILNIAUS UNIVERSITETAS
MEDICINOS FAKULTETAS**

Baigiamasis darbas

**Naujos kartos branduolinės medicinos detektorių galimybės širdies ligų diagnostikoje
New Generation Nuclear Medicine Devices for Cardiac Imaging**

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ABSTRACT

Myocardial perfusion scintigraphy is a leading nuclear medicine diagnostic procedure in Vilnius University Hospital Santaros Klinikos, that uses radioactive tracers to provide immensely useful data about perfusion processes in the heart muscle. Soon after the invention of this technique, one of the main tasks for this procedure became reduction of patient received radiation. In the past decade, a lot of upgrades were done to all parts of Single Photon Emission Computed Tomography diagnostic system to keep the patient radiation as low as possible, while preserving the optimal diagnostic quality. The sensitivity of cardiac-centered gamma cameras was increased with newer semiconductor detectors – instead of sodium iodide, new cadmium-zinc-telluride detectors have higher sensitivity, improved energy resolution and eliminates need for photomultiplier tubes. The enriched myocardial count sensitivity of cardiac-centered systems allowed for a decrease in the dose of injected radiopharmaceuticals for myocardial perfusion scintigraphy, resulting in lower radiation exposure to the patient and staff. Accurate dose adaptation to the correctly set parameters of the gamma camera is essential to acquire good quality images with reduced radiation dose to the patient.

In this work we analyze how the radiation exposure tendencies changed over the 2009–2021 period in Vilnius University Hospital Santaros Klinikos Nuclear Medicine department with the introduction of new generation cadmium-zinc-telluride gamma cameras and more accurate calculation of dosage of perfusion tracers using patient weight and body mass index.

SANTRAUKA

Miokardo perfuzijos scintigrafija yra pirmaujanti branduolinės medicinos diagnostinė procedūra Vilniaus Universitetinėje ligoninėje Santaros Klinikos, kurios metu yra naudojami radioaktyvūs farmakologiniai preparatai siekiant gauti nepakeičiamai naudingos informacijos apie perfuzijos procesus širdies raumenyje. Atsiradus šiam diagnostiniam metodui, viena iš pagrindinių užduočių tapo paciento patiriamos apšvitos mažinimas. Per pastarąjį dešimtmetį, vieno fotono emisijos kompiuterinės tomografijos sistema patyrė daug tobulinimų siekiant kiek įmanoma sumažinti radiacijos dozę, išlaikant optimalią diagnostinę kokybę. Apie širdį centruotų gama kamerų jautrumas buvo padidintas atradus naujus puslaidininkių detektorius – naujesni kadmio-cinko-teliurido detektoriai pakeitė natrio jodido kristalus turinčius

detektorius. Šie kristalai turi didesnę jautrumą, didesnę energijos sugerimą ir nereikalauja fotodaugintuvų naudojimo. Didesnis naujos kartos gama kamerų jautrumas leido sumažinti miokardo perfuzijos scintigrafijoje injekuojamų radionuklidų dozę, taip sumažinant paciento gaunamą apšvitą. Pažangesni perfuzijos radiofarmaciniai preparatai ir greitesni vaizdų gavimo protokolai dar labiau sumažino paciento ir darbuotojų patiriamą apšvitą. Tikslus diagnostinei procedūrai reikalingos radionuklidų dozės adaptavimas teisingai nustatytiems gama kameros parametrams yra esminis momentas siekiant gauti geros kokybės vaizdus kartu su sumažinta paciento patiriama radiacine doze.

Šiame darbe mes analizuojame kaip radiacinės apšvitos tendencijos keitėsi Vilniaus Universiteto ligoninės Santaros klinikos Branduolinės medicinos skyriuje nuo 2009 iki 2021 metų, pradėjus naudoti naujos technologinės kartos kadmio-cinko-teliurido gama kameras bei įvedus tikslesnes radiofarmacinių preparatų dozių skaičiavimo formules, paremtas paciento svoriu ir kūno masės indeksu.

Keywords: Myocardial perfusion scintigraphy, single photon emission computed tomography, cardiac radiopharmaceuticals, radiation dose, cadmium-zinc-telluride detectors.

Raktiniai žodžiai: miokardo perfuzijos scintigrafija, vieno fotono emisijos kompiuterinė tomografija, širdies radiofarmaciniai preparatai, apšvitos dozė, kadmio-cinko-teliurido detektoriai

INTRODUCTION

Myocardial perfusion imaging (MPI) plays an important role in coronary artery disease diagnosis, but concerns exist regarding its radiation burden. Technological advancements of new generation cardiac-centered gamma cameras allow to set a new standard in patient received radiation dose when performing myocardial perfusion scintigraphy (1). Moving from conventional gamma cameras to cardiac-centered collimation method in newer generation cameras explains the enhanced count sensitivity (2). The radiation emission sensitivity of conventional gamma cameras is relatively low with only a few parts-per-million (10^{-6}) of injected activities being detected within the myocardial area (2,3). New generation gamma cameras collimators create an orbit that is centered on a heart. This increases emission sensitivity, registers more counts and allows for use of smaller radiopharmaceuticals doses. In new generation gamma cameras, the conventional sodium/iodine (NaI) crystal used for detection of gamma rays has been replaced by a cadmium-zinc-telluride (CZT) crystal. New generation CZT crystal transforms the signal received as gamma rays into electric impulses without the need for photo-detectors. Absence of photo-detectors in CZT crystals using gamma cameras improved energy resolution by a factor of 2, compared with conventional Anger cameras (2). Increased sensitivity of cardiac-centered system allows for technicians to use lesser amount of radiopharmaceuticals for each myocardial perfusion scintigraphy examination and to reduce scan time. The activity of perfusion radiotracer injected to patients should be chosen using ALARA principle (as low as reasonably acceptable), since reduction in activities is always beneficial for a patient. However, quality of the examination should never be impaired by reduction in radiotracer activity. According to the latest myocardial perfusion scintigraphy imaging guidelines, it is recommended to adjust the injected activity to body weight, especially in obese patients and to decrease targeted count level for ultra-low dose protocols (4).

This study investigated how the dose of radiopharmaceuticals used for myocardial perfusion scintigraphy changed from 2009 to 2021 in Vilnius University Hospital Santaros Klinikos (VUHKS) and what impact implementation of CZT gamma cameras and more accurate dose calculation based on body weight and body mass index had on patient-received radiation dose reduction. Calculated contemporary dosing tendencies were compared to the existing national and international guidelines.

METHODS

Study Design

Data from 600 patients was collected retrospectively from Department Nuclear Medicine in VUHKS from 2009-2021 time period. Period was chosen based on the changes in equipment, calculation of doses and transition from two day protocol to one day scanning protocol. The data was managed by the head of Nuclear Medicine Department of Santaros Klinikos. Study was not funded.

Study Population and Methods

Study population: 600 patients that were referred to Nuclear Medicine department of Vilnius University Hospital Santaros Klinikos for myocardial perfusion scintigraphy over the period 2009-2021. Four separate groups from different time periods were analyzed, all consisting of 150 patients. Technetium 99m sestamibi (MIBI) perfusion tracer was used for all studies. Protocols and equipment used in each group are specified in the subgroup subsection below. All the patients had both rest and stress test myocardial perfusion scanning parts performed on them. All patient data was completely anonymical and consent for anonymical use of patient data from bioethics committee of Santaros Klinikos was received in written form. No exclusion criteria were used, because study was conducted retrospectively from the MPS registration list. Differences in age and sex were ignored in this study. Patients were selected at random, therefore groups should represent general population of Lithuania at the selected periods.

Subgroups:

First group had myocardial perfusion scintigraphy performed in year 2009. Equipment used was Single Photon Emission Computed Tomography (SPECT) gamma camera (Infinia, General Electric Healthcare, USA). In this group, a fixed dose of 750 MBq ⁹⁹Tc-MIBI was injected into each individual for stress and rest test. Two day protocol was used: stress test was performed on the first day and rest test was done on the second day. No calculations according to the patient weight or body mass index were done during administration of radiopharmaceuticals.

Second group had myocardial perfusion scintigraphy performed in year 2012. Equipment used was the same as in first group. Imaging protocol was changed from two to one day, with stress test scanned first with a lower dose of radiopharmaceuticals (350MBq) and a rest test carried out later with a bigger dose of radiopharmaceuticals (750MBq). As in

first group, doses were fixed and no calculations according to the patient weight or body mass index were done during administration of radiopharmaceuticals.

Third group had myocardial perfusion scintigraphy performed in year 2013. Gamma camera used for imaging was same as in first and second group. As in second group, one day protocol was used, with stress test performed first, followed by rest test. In this group there was a change in the amount of injected Technetium 99m sestamibi – a transition was made from fixed doses to individual doses for each patients according to their body weight.

Fourth group had myocardial perfusion scintigraphy performed in year 2021. The main MPS equipment was changed to D-SPECT Cardio gamma camera (Spectrum Dynamics, Israel). Same one day protocol was used as in third group. In this group, injected doses of Technetium 99m sestamibi to each individual were calculated according to the body mass index (BMI) of each patient.

Methods: Amounts of injected radiopharmaceuticals from each period were analyzed and compared to each other and the available international and national guidelines.

Data analyzed:

Statistical analysis was conducted by main author of this paper using Microsoft® Excel® for Microsoft 365 MSO (Version 2204 Build 16.0.15128.20158) 64-bit.

Data collected was whether test was stress or rest, dose of radiopharmaceutical injected. In groups where appropriate data was available, weight and height of the patient were also included. Median, mean and quartiles of dose in becquerels units injected into patient were calculated for each group and compared. The calculation of radiopharmaceuticals used per kilogram of patient weight was also conducted and compared to doses recommended by the guidelines for appropriate time period.

Collected dataset of dose injected into patient for each test from each period was tested by Jarque-Bera test of normality.

Study limitations

Although the number of patients (600) in our study is sufficient for statistically reliable evaluation of patient received doses, when divided into subgroups by four different periods, each subgroup consists of 150 patients. Bigger subgroups would present the Lithuanian population of specific periods more accurately. Another limitation is that patient weight data was available for only III and IV group and non-anonymical data of patient height was not available for IV group.

RESULTS

According to Jarque-Bera test of normality, data on ⁹⁹Tc-MIBI dose amount in each period were not normally distributed.

Box and Whisker charts were used for visualization of dose distribution in different periods and different tests (stress and rest) (Figure 1).

Figure 1. Radiotracer dose distribution in groups

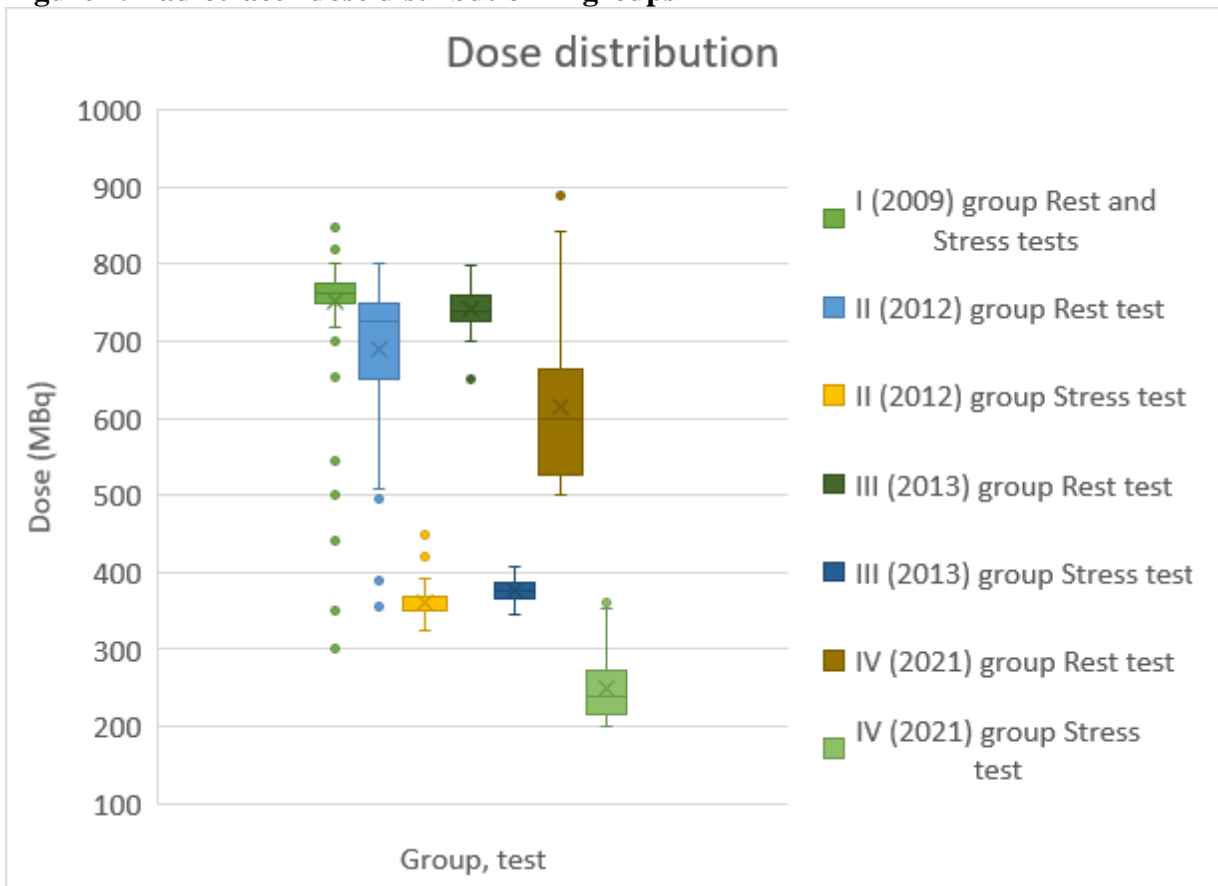
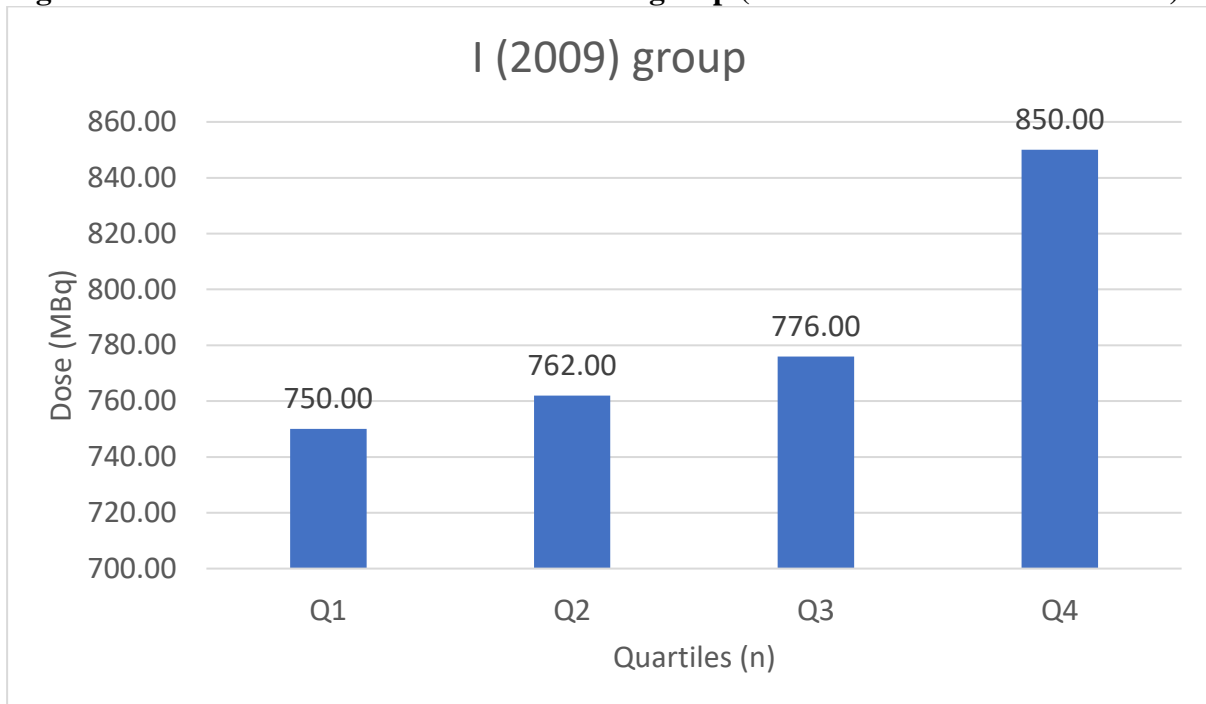


Chart from first period represents doses of radiopharmaceuticals used for both stress and rest test groups, since in 2009 doses used for both tests were identical and fixed at 750MBq. Other groups (II-IV) are presented in separate bars for stress and rest test as 1 day protocol was introduced and different doses were used for each of the tests.

Biggest number of outliers was observed in I group. Dose distribution in other periods of rest and stress tests had a small number of irregularities. Observed number of deviations confirms that data was selected completely randomly and was not adjusted to achieve normal distribution. In group II-IV it is seen that doses used for Stress test were always smaller than doses used for Rest test. This is due to the methodology of myocardial perfusion scintigraphy

test – Stress test is performed first, at a lower dose, and rest test is conducted after that, with a 2-3 times bigger dose than stress test. Bigger dose is necessary to achieve optimal images in rest test, due to the residual dose left in patient after the Stress test.

Figure 2. Radiotracer dose distribution in first group (Stress and Rest tests combined)



Median of injected activities in the first group was 762 MBq (Q1:750 MBq; Q3:776 MBq). Median of the first group was relevant to the usual administered dose of 800 MBq for myocardial perfusion scintigraphy, according to International Atomic Energy Agency (IAEA) guidelines (5). Dose distribution in first period is narrow, with first, second, and third quartiles being distributed very closely to one another (Figure 2). This result is expected when giving standardized doses to all patients.

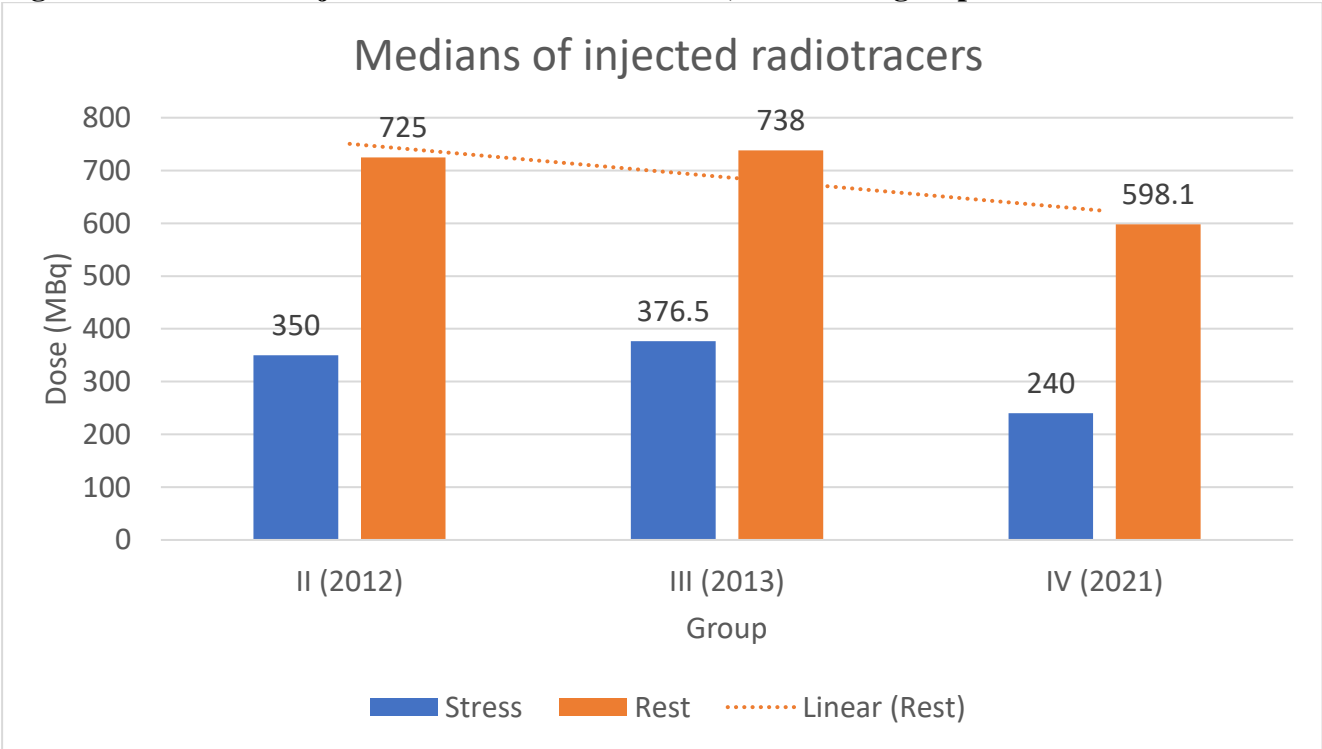
Median of injected activities in second group is 350 MBq (Q1:350 MBq; Q3:350 MBq) for Stress test and 725 MBq (Q1:625 MBq; Q3:750 MBq) for Rest test. Compared to IAEA guidelines, doses used for tests were below recommended maximum dose of radiopharmaceuticals (5). In VUHSK, second injection for Rest test was performed at 2.5 times Stress test dose, to keep radiation exposure as low as possible, following the ALARA principle.

In the third group median of injected activities was 376.5 MBq (Q1:367 MBq; Q3:386.25 MBq) for Stress test, amounting to 4.17MBq/kg and 738 MBq (Q1:726 MBq; Q3:760 MBq) for Rest test, coming at 8.24MBq/kg. As in previous groups, doses

recommended by IAEA for MPS were not exceeded. Median weight in this group was 90kg and median BMI was 29.75.

Fourth group median dose for Stress test was 240 MBq (Q1:218.85 MBq; Q3:271.55 MBq) and 598.1 MBq (Q1:527.5 MBq; Q3:661.3 MBq) for Rest test. Calculated medians of MBq per kilogram were 2.92 MBq/kg and 7.14 MBq/kg for Stress and Rest test, respectively. A large decrease in injected radiopharmaceutical dose can be seen when compared to third period – 30% for Stress test and 13% for Rest test. Such change is a result of dose calculation by body mass index. According to European Association of Nuclear Medicine (EANM) 2015 guidelines, recommended doses for one-day protocol are 250 – 400 MBq for the first injection, three times more for the second injection (author remark: 750 – 1200 MBq) (6), which were not surpassed. Median weight in this group was 82kg. Non-anonymical data of patient height data in this group was not available, therefore it was not possible to calculate BMI.

Figure 3. Medians of injected radiotracer doses for II, III and IV group



Medians of injected activities in Stress and Rest tests are shown in Figure 3. A slight (7.5% for Stress test and 1.8% for Rest test) increase from group II to group III is due to the more accurate calculation of dose needed to inject for specific test – in second group

standardized doses were used for Stress and Rest tests, while in third group doses were adjusted for patient weight.

A noticeable decrease (36.3% for Stress test and 19% for Rest test) in medians from third to fourth group is the result of introduction of new generation of gamma camera with CZT crystals. Comparing II group with fixed doses for each test to fourth group with doses calculated by BMI, a decrease is smaller, but still significant – 31.4% for Stress test and 17.5% for Rest test.

Median trendline is showing a negative slope, which is the result of all the effort in patient received radiation dose reduction – renewed equipment (new generation CZT gamma camera), calculation of doses adopted to patient weight and body mass index, use of ⁹⁹Tc and one day protocol. Benefits of one day protocol are described later in discussion.

Figure 4. Third Quartile of injected radiotracer doses in II, III and IV groups

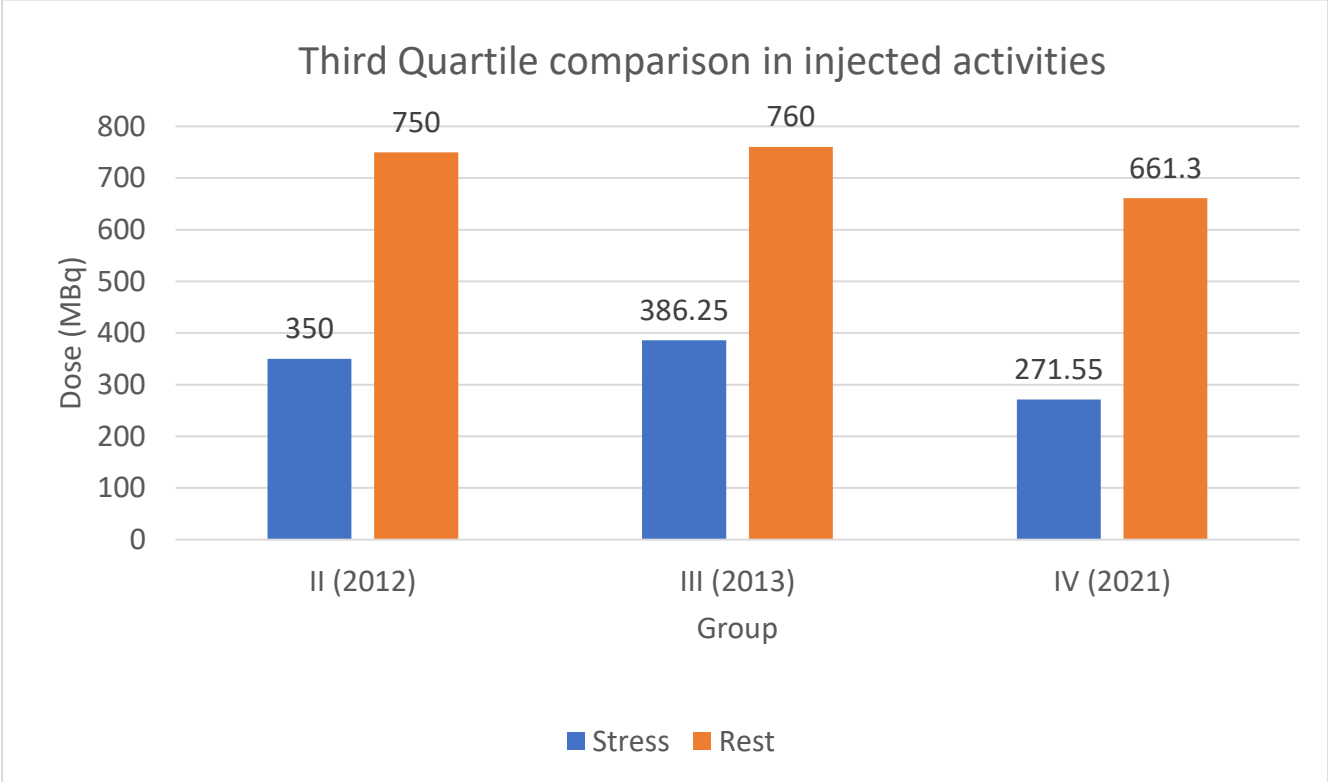


Figure 4 depicts Third Quartiles of injected activities for Stress and Rest test in different groups. Third Quartiles are important for diagnostic reference levels, since diagnostic reference levels are usually calculated based on third quartile. A diagnostic reference level is used as an tool in optimization of protection in the medical exposure of patients for interventional and diagnostic procedures. (6) It is used as a reference level to

indicate, whether a procedure, performed under routine conditions, does not cause unusually high radiation burden for the patient.

Lithuanian National guidelines for diagnostic reference levels state that when performing myocardial perfusion scintigraphy with ^{99}Tc on patient of standard weight (70kg), administered activity should not be greater than: 550 MBq for Stress test using one-day protocol; 700 MBq for Rest test using one-day protocol; 1200 MBq for Stress and Rest test, when using two-day protocol. Diagnostic reference levels for myocardial perfusion scintigraphy using modern gamma cameras with CZT detectors are 450 MBq for Stress test and 650 MBq for Rest test (7).

In Figure 4 we can see that third quartile of Rest test in Third group (760 MBq) was higher than recommended by National guidelines (700 MBq), but it is important to remember that average weight of patients in the third group was 90.4 kg, which is greater than weight of the patient by which doses of administered activities are calculated (70 kg).

Same result is seen in fourth group – dose of administered activities in Rest group (661.3 MBq) is greater than number recommended by National guidelines for Rest tests performed with CZT camera (650 MBq). As in previous group, cause of this is weight of the patients – average in fourth group is 85.13 kg, heavier than patient by which diagnostic reference levels are calculated (70 kg).

It should be mentioned, that if data of administered activities was adjusted for patients with weight of 70 kg, doses in National guidelines would not be exceeded in III and IV groups.

DISCUSSION

Comparison of Myocardial Perfusion Scintigraphy with other imaging modalities of the heart

Myocardial perfusion scanning plays a significant role in diagnostic and therapeutic evaluation of cardiac disease. This imaging modality is in a group of non-invasive imaging tests that can be performed to help clinicians assess blood flow to areas of myocardium. Apart from myocardial perfusion scintigraphy, there are a number of heart structural and functional imaging methods – echocardiography, coronary computed tomographic angiography, cardiac magnetic resonance imaging, invasive coronary angiography. Obtaining and gathering information on perfusion and metabolite uptake from myocardium plays an essential role in determining the appropriate medical treatment or intervention for optimizing one's cardiac health. A variety of clinical symptoms and diseases can be evaluated using myocardial perfusion imaging - symptoms concerning for angina, to rule out acute coronary syndrome as a cause of chest pain, assessing therapeutic outcome after interventions, as well as for assessing for viable or scarred myocardium. This information allows clinicians to better understand patient coronary health, assess risk for future cardiovascular events, evaluate therapeutic response to procedures correcting perfusion defects (such as stenting of coronary arteries) and to prognose potential outcomes of patients.

Among the imaging methods that are able to detect coronary artery disease, coronary computed tomographic angiography and invasive coronary angiography assess coronary anatomy, while the other imaging modalities assess coronary function - stress myocardial perfusion imaging, positron emission tomography, stress cardiac magnetic resonance and echocardiography. Advantage of myocardial perfusion single photon emission computed tomography over invasive diagnostic methods (coronary angiography) is greater safety of non-invasive diagnostic methods and the ability to visualize parts of myocardium that are getting enough perfusion – this information is not available to obtain with coronary angiography. Invasive coronary angiography provides a detail view of main coronary arteries of the heart and is able to find reductions of the lumen in the coronary arteries. Not all reductions of lumen are important. According to Danilo Neglia et al., significant coronary artery disease is defined by invasive coronary angiography as >50% stenosis of the left main stem, >70% stenosis in a major coronary vessel, or 30% to 70% stenosis with fractional flow reserve ≤ 0.8 (8). However, because this imaging method only shows the lumen of the coronary artery, often it is difficult to determine whether narrowing of the targeted vessel is of

clinical significance to the perfusion of the myocardium. When performing invasive coronary angiography a significant stenosis is seen, based on scientific literature it is presumed that the oxygenation of the myocardium supplied by the visualized vessel is corrupted, but this is not a direct parameter but rather an assumption.

As proved by Nakazato et al., MPS performed with CZT detector cameras has a sensitivity of 91%, 88% and 94% and specificity of 59%, 73% and 86% for the detection of significant coronary stenosis per-patient basis upright, supine, or combined acquisitions respectively (9). According to high sensitivity and reasonable specificity, myocardial perfusion scintigraphy can also show significant coronary stenosis, especially when patient is evaluated in combined acquisitions. MPS is especially beneficial in multisegmental coronary disease with different stenosis grades. This noninvasive method helps to determine sites of coronaries to be treatable and helps to consider the safe treatment approach.

Impact of new gamma camera detectors in Myocardial Perfusion scintigraphy

Implimentation of semiconductor CZT detectors has markedly improved stress myocardial SPECT. The new generation gamma camera offers comparable diagnostic performance to that of conventional SPECT cameras, while providing better image quality and quicker image acquisition (1). This due to the improved count sensitivity and spacial resolution. Conventional gamma cameras with sodium/iodine crystals require photo-detectors for conversion of gamma rays into electric impulses that can then be transferred to computer for final proccesing and image reconstruction. In CZT cameras sodium iodine crystals have been replaced with cadmium-zinc-telluride crystals. When photons interact with the CZT in the semiconductor, the incident gamma rays create electron pairs and an electrical signal is produced. The direct conversion of energy in the semiconductor solid-state detectors is characterized by good energy resolution. Clinical applications of the energy resolution is reported to be greater than 6% at 140 keV, which is main energy of ^{99}Tc (10). Flexibility and thinness of CZT cameras was used by manufacturers to create a larger surface area for signal detection, which collimators are focused on the heart region. Larger surface are means higher tomographic radiopharmaceutical radiation emission sensitivity and increased central spacial resolution.

Count sensitivity of new generation gamma camera system using CZT crystals is much greater than conventional SPECT using sodium iodide crystals. On cardiac phantom images new system had a sensitivity of $850 \text{ counts}\cdot\text{s}^{-1}\cdot\text{MBq}^{-1}$, while conventional SPECT had a sensitivity of $130 \text{ counts}\cdot\text{s}^{-1}\cdot\text{MBq}^{-1}$. This difference of sensitivity persists when measuring

myocardial counts normalized to injected activities from human images – 11.4 ± 2.6 counts \cdot s $^{-1}\cdot$ MBq $^{-1}$ for D-SPECT and 0.6 ± 0.1 counts \cdot s $^{-1}\cdot$ MBq $^{-1}$ (respective mean values) (2). Greater count sensitivity of new cameras allow to capture images quicker and to reduce the amount of injected radiopharmaceuticals (11). In a system with higher sensitivity, an image acquired during the same length of time as on a lower-sensitivity system will have more counts and a better signal-to-noise ratio, thus achieving better image resolution and requiring lesser doses of radiopharmaceuticals (12). In MILLISIEVERT study conducted by Einstein et al. in 2014 it was determined that new high-efficiency cameras with specialized collimators and solid-state CZT detectors offer potential to maintain image quality, while reducing administered activity and thus radiation dose to patients (13). The MILLISIEVERT study results are in accordance with our received medians of patient received radiation doses - a noticeable decrease (36.3% for Stress test and 19% for Rest test) in medians from third to fourth group is the result of introduction of new generation of gamma camera with CZT crystals. During these tests, although the dose of injected activities was greatly reduced, image quality remained high.

Central spatial resolution of D-SPECT is 2.5 mm, while conventional SPECT systems typically have resolution of 3.5-4.0 mm, because of the small size of individual detector elements and the geometry of the system (14). Greater spatial resolution of D-SPECT camera allows to differentiate perfusion defects of myocardium more precisely (2). As confirmed by Sharir et al. in a multi-centric study, the extent of myocardial ischemia registered by D-SPECT was slightly but significantly larger, compared to conventional SPECT (15). Another study found good correlations between the extent of stress defects ($r = 0.86$) and infarction area ($r = 0.80$) measured on the D-SPECT, with comparison to lower correlation found on Anger cameras ($r = 0.72$) (14).

Improved gamma camera CZT detectors enable recording times or tracer doses to be reduced, resulting in greater patient comfort and patient radiation exposure (11). Studies have also shown that image quality of D-SPECT is superior to the conventional gamma camera and that high quality images can be generated even in obese patients. Correlations between MPS acquired with each gamma camera was high for summed rest score (SRS; $r = 0.87$), total perfusion deficit (TPD; $r = 0.91$), and LV ejection fraction (LVEF; $r = 0.88$) (13).

Radiation exposure reduction (one day protocols compared to two day protocols and better calculation of injected radiopharmaceuticals calculated by body mass and BMI)

Advancements in technology of myocardial perfusion scintigraphy technology need to be exploited as much as possible, since they allow to reduce radiation exposure to the patient and staff. New technologies allow us to use less harmful radiopharmaceuticals, shorten imaging protocols and reduce doses of injected activities. Selection for a particular patient of the administered activity is complicated since the same administered activity can result in dramatically different count statistics and image quality in different patients due to differences in pharmacokinetics. When choosing what isotope to use for procedure, the goal is compromise between image quality and radiation exposure. Moreover, choice of radiopharmaceuticals and quantity of it depends on the patient body weight, age and the acquisition protocols (1 day or 2 day).

Comparison of ^{99}Tc and ^{201}Tl based radiotracers in Myocardial Perfusion Imaging

Perfusion scanning utilizes various radiopharmaceuticals, which are administered to the patient and allowed to distribute to multiple tissues. In SPECT imaging techniques, common radiopharmaceuticals used include thallium-201 or technetium-based radiotracers, including technetium-99m sestamibi or technetium-99m tetrofosmin (16). ^{99}Tc Technetium isotope agents should be preferred over ^{201}Tl Thallium isotope because of their shorter half-life, significantly lower effective dose, and superior image quality. The average total radiation exposure of a stress/rest perfusion study with recommended injected activities for cardiac-centered cameras is significantly lower with ^{99}Tc labeled radiotracers 6–9 mSv compared to 10–15 mSv with ^{201}Tl (17).

^{99}Tc -sestamibi is a cationic complex uses passive diffusion to fuse passively through the capillary and cell membrane, to later accumulate in mitochondria. These radiopharmaceuticals are injected when the heart is stressed, either by exercise or by pharmacological agents. The uptake of radiotracer indicates areas of perfusion and viable tissue during stress and at rest. Areas of poor perfusion display improved perfusion during rest test, termed reversible ischemia (18). Myocardial uptake of the ^{99}Tc -labelled tracers increases almost proportionately with increase in perfusion.

^{201}Tl thallos chloride was the first radionuclide used widely for myocardial perfusion studies. ^{201}Tl is a potassium analogue and ~60% of the administered activity enters the myocytes via the sodium-potassium, ATPase-dependent exchange mechanism, with the remainder entering passively along an electropotential gradient. After initial Thallium based

radiotracer uptake, prolonged retention depends on the intactness of cell membrane and hence on viability. Retention is the cell lasts several hours. After this phase, a redistribution occurs, since ^{201}Tl is not bound to myocytes or to cells in other tissues. This redistribution/re-availability leads to ^{201}Tl myocardial extraction in regions that were ischaemic when ^{201}Tl was injected at peak stress, thus allowing redistribution images to be acquired that are fairly independent of perfusion and mainly reflect viability. Although this Thallium based radiotracer is good for myocardial perfusion imaging, it does have several limitations. Due to long physical half life, there is a high radiation burden for the patient (17). Also, because of low injected activity, there is low signal-to-noise ratio and suboptimal image quality can be received, especially in obese patients.

Due to these limitations and arguably more important advantages of ^{99}Tc -labelled tracers over ^{201}Tl , the first one is used more commonly, as well as in VUHSK. Main advantages of ^{99}Tc based radiotracers over ^{201}Tl are higher energy of the produced photons, which leads to better quality images because of less attenuation and scatter, as well as the shorter half-life of ^{99}Tc that permits much higher activities to be administered, giving better counting statistics and thus allowing performance of left ventricular ECG gating or first-pass imaging, which provides additional functional information (19).

Differences in one-day and two-day scanning protocols

When performing myocardial perfusion scintigraphy, one-day or two-day scanning protocols are available, with one day protocol meaning that Stress and Rest tests are performed during one day with a few hour interval between them and two day protocol having Stress test done on one day and Rest test on the following day.

A 2-day protocol is preferable because it facilitates comparison between the rest and the stress studies and in addition, keeping the total radiation burden to the patient (and the staff) at a lower level compared with same-day protocols.

Modern semiconductor CZT detectors allow for a 1-day MPI protocol with low dose both during stress and at rest by subtraction of background activity of the preceding stress scan (20). The order of studies in a single-day protocol depends to some extent on the indication for the investigation. If the problem is to detect viable myocardium and reversibility of a defect, in a patient with previous infarction, it may be theoretically preferable to perform the rest study first. Conversely, when the study is performed for the diagnosis of myocardial ischemia, the stress study should be performed first – this both avoids reduction of the contrast of a stress-induced defect by a previous normal rest study and also

obviates the need for an unnecessary rest study, if the stress scan is normal. Many laboratories nowadays consider one day protocol favorable. This protocol is more convenient for the patient and laboratory, since patient only needs to arrive to hospital for one day and the likelihood of patient missing the second part of myocardial perfusion scintigraphy test is extremely slim. Because of this since 2012 one-day protocol is used in VUHSK as well. It should be noted that if the stress examination is performed first, irrespective of a 1- or 2-day protocol, and reported as normal, the rest examination can be omitted (21).

Weight and body mass index-based dose comparison to fixed doses

Calculation of radiotracers used for MPI based on patient weight allows to reduce patient-received radiation greatly and therefore make myocardial perfusion diagnostic test safer.

This can be seen in our results: in first group, where fixed dose of 750MBq was used for Stress and Rest test, median was 762 MBq (Q1:750 MBq; Q3:776 MBq). Median of injected activities in second group, with fixed different doses for Stress and Rest test, was 350 MBq (Q1:350 MBq; Q3:350 MBq) for Stress test and 725 MBq (Q1:625 MBq; Q3:750 MBq) for Rest test. When compared to third group, where dose of injected radiopharmaceuticals was calculated based on weight of the patient, a large decrease in patient-received radiation can be seen – from first group, overall median decreased from 762 MBq to 405 MBq (a 47% change) and from second group, overall median decreased from 437 MBq to 405 MBq (a 7.3% change).

Calculation based on body mass index in fourth group helped to reduce patient-received radiation even further: overall median of mega becquerels received by each kilogram of patients' weight changed from 5.79 MBq/kg to 4.86 MBq/kg, resulting in a 16% decrease.

CONCLUSION

In the light of ever-increasing number of performed diagnostic and interventional radiology procedures, patient-received radiation dose reduction is as important as ever, as radiation is linked to secondary oncological diseases and a decrease in lifespan. Radiation dose reduction performing one-day myocardial perfusion scintigraphy scanning protocol was achieved by implementation of more accurate calculation of modern radiotracers and new generation gamma cameras.

According to analyzed data from VULSK from 2009-2021 period, transition from standardized doses for myocardial perfusion imaging to doses calculated by body weight led to a used radiopharmaceutical dose median decrease of 7.5% for Stress test and 1.8% for Rest test. Following implementation of CZT gamma cameras and dose calculation by body mass index led to a further dose median decrease of 36.3% for Stress test and 19% for Rest test.

In our opinion, to achieve optimal ratio between image quality and dose of radiopharmaceutical, each diagnostic center should harmonize their scanning protocol according to used equipment, required image quality standards and international/national guidelines.

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