SIMULTANEOUS DUAL ISOTOPE (I123/TC99M) CARDIAC SPECT BY USING CZT CAMERA

Dott. Izzo Giacomo, Dott. Buongiorno Pietro, Dott. Cuocolo Alberto, Dott. De Rosa Salvatore

KEYWORDS: spect cardiaca, czt, d-spect,dual isotope (i123/tc99m), medicina nucleare

ABSTRACT

La scintigrafia miocardica con l'utilizzo del sestamibi marcato con Tecnezio 99m e metaiodobenzilguanidina (MIBG) marcata con Iodio123, ha lo scopo di mettere in correlazione lo studio della perfusione cardiaca, ottenuta dalla distribuzione del 99mTc, e la valutazione dell'innervazione cardiaca-simpatica che può essere direttamente studiata con un analogo della noradrenalina radiomarcato con Iodio 123 che riflette l'integrità neuronale visualizzando il recupero e l' uptake nei terminali simpatici cardiaci. Tale studio fatto utilizzando gamma camere di nuova generazione, che adoperano rivelatori composti da cristalli di Tellurio di Cadmio Zincato(CZT) utilizzate esclusivamente per la valutazione miocardica, ha dimostrato come la perfusione combinata all'imaging d' innervazione simpatica, consente la valutazione della discrepanza di innervazione-perfusione.

INTRODUCTION

The left ventricle, and the heart in general, has been the subject of countless studies, both experimental and clinical, with complex conceptual elaborations and formulation of parameters, to assess its function, also the relationship between dysfunction of the autonomic nervous system of the heart, cardiomyopathy and cardiac arrhythmias have been established for some time. The study of myocardial perfusion is a medical-nuclear method that helps cardiology a lot. Myocardial scintigraphy with the use of the sixthibi marked with Tecnetium 99m and metaiodobenzylguanidine (MIBG) marked with Iodine123, aims to correlate the study of cardiac perfusion, obtained from the distribution of 99mTc, and the evaluation of cardiac sympathetic innervation which can be directly studied with a noradrenaline analogue radiolabelled with Iodine 123 which reflects neuronal integrity by displaying recovery and uptake in sympathetic cardiac terminals. This study, carried out using new generation gamma chambers, which use detectors composed of Cadmium Zinc Plated Tellurium (CZT) crystals used exclusively for myocardial evaluation, has shown that perfusion combined with sympathetic innervation imaging, allows the assessment of the discrepancy between innervation and perfusion. It also provides valuable information to evaluate the extent of the pathological area and the prognostic factor of ventricular arrhythmia in the post-infarction myocardium, allowing an accurate study of the myocardium in order to reach diagnosis. In addition, most patients evaluated with 123I-MIBG have ischemic cardiomyopathy with heart failure and have demonstrated a pertinent association between innervating disorder, myocardial alteration and mechanical dychrony. In this clinical context, the double isotope protocol allows a simple and effective corecording of innervation and perfusion studies, and therefore a solid evaluation of the mismatch between them.

NEW DEDICATED MACHINES

Inorganic scintillation detectors have been the default detectors in medical-nuclear imaging for years, despite their limitations, such as: low conversion efficiency, lower sensitivity and reduced spatial resolution. Some of these aspects inevitably involve a higher dose quantity and a low temporal resolution. Over the years, changes have been made to the conventional Anger camera to increase its performance, such as in the case of dedicated imaging systems, particularly in cardio-dedicated systems. Conventional Anger Camera systems are characterized by the presence of NaI(Tl) scintillation crystal coupled to a series of photomultipliers. In scintillation crystals, the conversion of gamma-ray energy into light photons inevitably leads to a loss of signal, as the efficiency of the NaI(Tl) based crystal is equal to -38 luminous photons for 1KeV, moreover not all the luminous photons generated reach the photomultipliers and the quantum conversion efficiency of the photomultipliers is relatively low.

An important innovation has been made with semiconductor detectors. Unlike scintillation detectors, semiconductor detectors are direct conversion detectors, so they do not require the presence of photomultipliers. When a gamma photon interacts with the semiconductor material, by means of a photo- electric or Compton effect, its energy is absorbed, producing a certain number of pairs of positively charged and negatively charged ions (electron pair - gap).

Through the application of an external electric field the ions migrate towards the electrodes of the material, this movement of charges induces a measurable electric signal, from which it will be possible to obtain information on the radiation under exami-

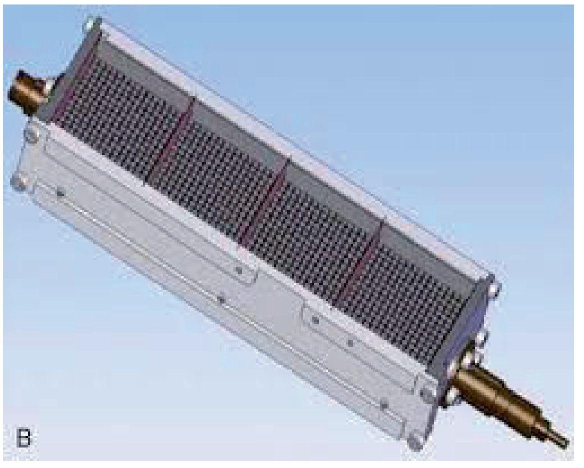

Figure 1 Pixellated CZT detector column.

nation. The semiconductor used in nuclear medical imaging systems is galvanized cadmium tellurium (CZT), a solid-state semiconductor. There are currently two CZT technology devices available on the market: Discovery NM530c (General Eletric Healthcare) and D-SPECT (Spectrum Dynamics), the two devices differ in their geometry, sensitivity (4 times improved with DNM-530c and almost 7 times improved with DSPECT) and spatial resolution (6.7 mm with DNM-530c and 8.6 mm with DSPECT), which leads to images with different degrees of sharpness and contrast-to-noise ratios.

The Discovery NM530c developed by GE Healthcare, using Alcyone technology, consists of a set of 19 pinholes collimators, each coupled with 4 pixel CZT solid state detectors. Each detector consists of 1024 CZT elements, measuring 2.46x2.46x5 mm, which are arranged in a set of 32x32 elements, measuring approximately 80x80mm. All 19 collimators are focused on a spherical region that delimits the heart of the patient, in this system the detectors and collimators do not move during acquisition but remain stationary. The multi-pinholes detectors are positioned so as to obtain a three-dimensional geometry acquisition: 9 of these detectors are positioned perpendicularly to the long axis of the patient, 5 of them are oriented above and the other 5 below the axis. The use of multiple simultaneously acquired projections improves the overall sensitivity of the system and it has been shown that the combination of CZT detectors with pinholes collimators further improves the energy resolution.

The patient performs the examination in a supine or possibly prone position with his arms above his head. A pre-scan is performed before the examination to locate the position of the heart and make sure it is centered in the field of view. Although this system uses pinholes collimators, the heart does not appear enlarged in the image matrix because the distance between the heart and collimators is greater than the distance between the collimator and the underlying detector.

The D-SPECT produced by Spectrum Dynamics is an innovative cardio-dedicated SPECT system. The new camera features a compact gantry design with 9 independent vertical columns of pixelated CZT detectors, arranged in a 90° curve configuration useful for conforming to the patient's left hemithorax. Each column consists of a set of 1024 elements (16x64) based on CZT, each element or pixel has dimensions of 2.46x2.46x5mm and are arranged in a set such that the dimensions of the column are 40mm wide x 120mm long. During acquisition each detector block rotates around its own axis in sync with the other 8 blocks, so that photons coming from a given position are detected at multiple angles from multiple columns simultaneously. The collimator used by D-SPECT is made of tungsten and has large parallel holes of square shape, these are shorter (length equal to 21.7mm) and wider (diameter 2.26mm) than those of LEHR collimators in conventional SPECT systems, which in contrast are longer (45mm) and smaller (1.6mm).

Each hole in the collimator is paired with each pixel of CZT. The collimation system and the dedicated geometry of the scanner surrounding the patient allow for better photon collection, increasing sensitivity from 5 to more times than the conventional camera range.

The increased sensitivity results in a reduced dose of radio medication to be administered (up to 2 mCi) and a shorter imaging time required, while maintaining high image quality. The loss of spatial resolution

Figure 2 Discovery NM530c.

Figure 3 Gantry D-SPECT with 9 detection columns.

that follows the increase in sensitivity is preserved by specific algorithms of reconstruction that recover the resolution. The significant gains in detector performance combined with specific reconstruction algorithms allow to improve the diagnostic accuracy of cardiac imaging and at the same time to reduce the dose of radiant exposure for the patient and staff and to lower the acquisition time. The high sensitivity of the D- SPECT allows to obtain, in addition to the information related to myocardial perfusion and left ventricular function, the reserve of coronary flow, increasing the diagnostic capabilities of cardiac nuclear imaging.

POTENTIAL OF THE NEW CARDIO-DEDICATED MACHINES

The CZT-based detector offers several advantages, first of all is the conversion of the energy, deposited by gamma rays, directly into pairs of ions without the aid of photomultipliers and also has a better detection efficiency thanks to the high atomic number (Cadmium 48, Zinc 30, Tellurium 52) and the high density (5.78 g/cm3), in fact, the energy required to create a gap-electron pair is low and produces an ionization every 3- 5eV of energy absorbed by the radiation. All this gives the system greater compactness, greater efficiency in signal collection, but above all better image quality due to increased sensitivity, high energy resolution and high spatial resolution. Thanks to the better performance of the system, direct benefits are obtained for the patient, such as the reduced dose of radio medication administered, and therefore less exposure to radiation for the patient and staff, and shorter data acquisition times that allow to reduce artifacts due to patient movement during acquisition, another feature of CZT detectors is that they allow simultaneous imaging procedures with the use of double radioisotope.

As a result, the advent of these CZT detectors has led to improved image quality and a reduction in the time taken to capture radiation exposure. In patients with known or suspected coronary artery disease, rapid imaging of myocardial perfusion using CZT detectors has provided better diagnostic accuracy with better regional sensitivity than in conventional Anger chambers.

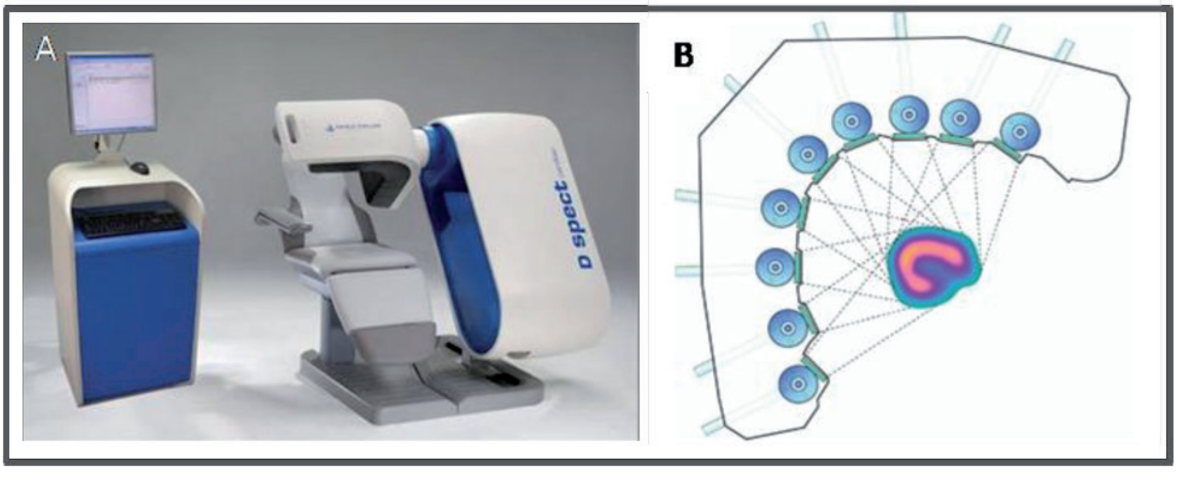

Figure 4 D-SPECT and heart-focused CZT detectors.

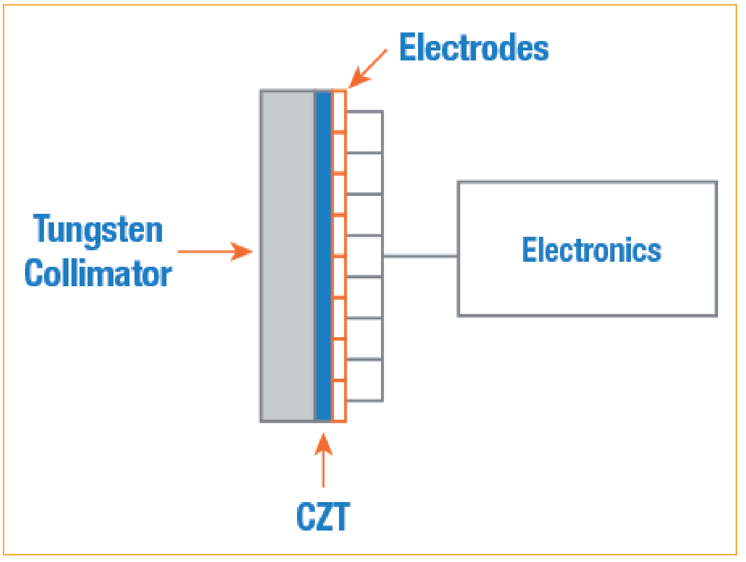

Figure 2 D-SPECT schematic structure.

IMAGING OF MYOCARDIC PERFUSION/INNERVATION WITH DOUBLE ISOTOPE 99MTC-SESTAMIBI/123I-MIBG

Patient preparation is one of the most important steps in order to obtain an optimal examination to allow an optimal diagnosis.
One of the first things to do is to block the thyroid: this is done by taking two capsules of potassium iodide, Lugol, on the evening of the day before the scan and two capsules on the evening of the day of the scan. This is important in order to limit the absorption of Iodine123 by the thyroid, which physiologically tends to absorb it.
Patients should be advised not to take over-the-counter medications such as nasal drops and cough mixtures in the 3 days prior to scanning.
The patient is also invited to discontinue therapy with nitro-derivatives at least twelve or twenty-four hours before the examination, beta-blockers for at least forty-eight or seventy-two hours, and calcium antagonists between twelve and twenty-four hours before the examination, it is also recommended to avoid the intake of drinks and foods containing caffeine for at least twelve hours. The treatment of diabetes can be performed as well as maintaining a normal diet on the day of scanning, also reminds patients receiving treatment with Dipyridamole or Xanthine that they must discontinue the drug for at least 24 hours before scanning.
Once the patient has been well prepared and informed about the examination he will perform, he begins to place a needle-cannula, a peripheral venous catheter, for the intravenous administration of radiopharmaceuticals. The examination will be divided into two phases.
The first phase will begin after positioning the needle-cannula and with the injection of 150 MBq of 123I-MIBG, the acquisition of the early MIBG scan with D-SPECT is performed, the acquisition time is 15 minutes in supine position.
The next step is to inject the 99mTc-MIBI with activity equal to 330 MBq, the patient must not move from the position in which it was placed for the duration of the examination.
Immediately after injection, the MIBI Gated scan starts at rest and has an acquisition time of 10 minutes.

After completing the MIBI scan, the patient will wait in the waiting room while analyzing the data collected in this first step.
Scanning results are acceptable when extra-cardiac activity does not interfere with left ventricle uptake, if the results are not satisfactory the acquisition phase is repeated.
The second phase of the examination is carried out 4 hours after the first acquisition.

Drug stress is induced by using dipyridamole to acquire the stress phase of perfusion. You inject 800 MBq 99mTc-MIBI for the acquisition of stress and you wait 45 minutes before you can perform the scan that lasts about 10 minutes.
Repeating the same positioning of rest during the acquisition of stress, will ensure the achievement of results without the effect of positioning problems, such as different angles or alterations of the left ventricle within the FOV which will be the same for both acquisitions.
During acquisitions, the patient is placed on an adjustable chair, which can be tilted by several degrees allowing both sitting and supine acquisition. This feature is useful in the case of false positives due to the attenuation of the gamma photons due to the presence of soft tissues, the examination is regained by repositioning the patient at a different angle, so as to discriminate the attenuation of the photons from the real defects. The patient rests his arms above the gantry and the open design of the system also reduces the effects of claustrophobia and increases the comfort for the patient, this results in fewer artifacts caused by his possible movements during the acquisition. At the beginning of each examination a rapid prescan is performed, from which a preliminary image of the distribution of activity in the myocardium is obtained; this image is useful to identify the position of the heart and to set the limits of movement of the detectors; an ROIis defined in which the entire study organ is included, so that the columns of CZT detectors acquire the data of the ROI rather than from the external regions. This process is called ROI-centric, because the scanning field is limited only to the myocardial region, In addition a simultaneous double isotope protocol provides a clearer 99mTc-MIBI image and a perfect recording to define the contours of the heart on the image and then accurately measures the heart absorption 123I-MIBG The data is collected in list mode, ie all acquired data is saved in a list mode, this provides the ability to reformulate the data by changing different parameters and thus greater flexibility in how they can be used for the formulation of ‘image. They are then reconstructed using the iterative Broadview algorithm, from the D-SPECT system based on the OSEM (Ordered Subset Expectation Maximization) approach with resolution recovery and noise regularization.

HMR calculated using planar imaging with conventional gamma camera (A) Tomographic imaging with D-SPECT (E), with trans-axial reconstructed images

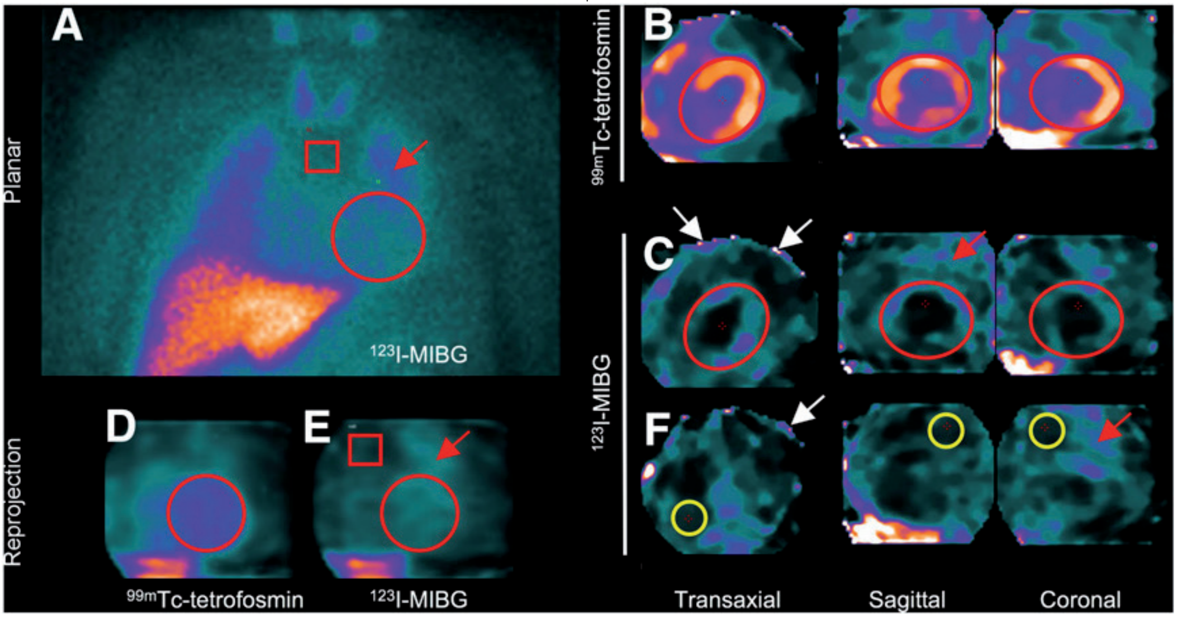

Figure 6 Patient with ischemic heart failure (left ventricle FE 44%

(C and F) Imaging with 99mTc allowed the positioning of planar cardiac ROI (D) and tomographic cardiac ROI (B) ROI were placed on images with 123I (E or C). Mediastinal ROI (E and F) on 123I images. Pulmonary activity (red arrows) and truncation artifacts (white arrows) can cause measurement errors)

NEW SOFTWARE FOR IMAGE PROCESSING

The visual interpretation of the images, obtained from the study, depends on the experience and knowledge of the physician and is therefore subject to inter-observer variability, which is why in nuclear cardiology have been developed several software packages for automatic quantification, so as to make the interpretations, inherent to perfusion and myocardial function, more standardized. The commercially available software programs are: QPS/QGS (Cedars-Sinai Medical Center, Los Aangeles, CA, USA), Corridor 4DM (4DM; INVIA Medical Imaging Solutions, Ann Arbor, MI, USA) and Emory Cardiac toolbox (ECTb; Syntermed, Atlanta, GA, USA). QPS (Quantitative Perfusion SPECT) is the most used algorithm in clinical practice, where the representation of the distribution of counts of the left ventricle takes place within a single circular image divided into 17 or 20 segments, called polar map or bull's eye, where the outermost part represents the ventricular base and the central portion the apex. Each segment is assigned a score, indicating the perfusion present, on a scale from 0 to 5 points. The objective of the quantification of myocardial perfusion is the regional classification of myocardial tissue as: normal, scarring or ischaemic, so that the severity, size and reversibility of the defect can be described. The sum of all the scores of the polar maps representing the acquisition after stress and at rest are indicated respectively by the parameters SSS (Summed Stress Score) and SRS (Summed Rest Score), the difference between the two parameters gives the SDS (Summed Difference Score) whic represents the reversibility index of the perfusive defect. The QGS (Quantitative

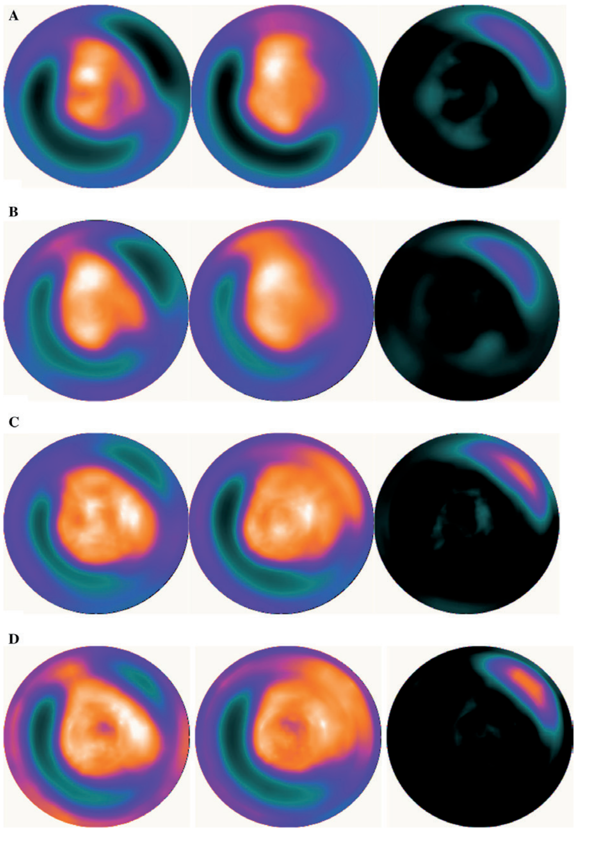

Figure 7

A. Double acquisition with ^{123I} and ^{99mTc} with DNM 530c

B. Double acquisition with ^{123I} and ^{99mTc} with D-SPECT

C. Simultaneous acquisition with double isotope with DNM 530c

D. Simultaneous acquisition with double isotope with DSPECT)

Gated SPECT) is based on the same principle as QPS and generates automatic segmentation, quantification and gated analysis, in which the acquisition is performed by synchronizing it with the patient's electrocardiographic signal, R-wave. Polar maps are also used in this case and the segmentary scores related to kinetics can be included in a scale of values ranging from 0 to 5, where 0 indicates a normal contractility and 5 dyskinesia. From the sum of the segmentary scores we obtain the SMS (Summed Motion Score) which expresses the degree of anomaly of the Chinese of the left ventricle in basal conditions and after stress. Another parameter obtainable through QGS is the STS (Summed Thickening Score) that expresses the alteration of the wall thickness. Other parameters that can be obtained are the ejection fraction (EF) and the telesystolic and telediastolic ventricular volumes (EDV and ESV), which allow to give an additional value to the diagnosis and prognosis of the patient.

The Corridor 4DM is a software for the quantification, revision and visualization of perfusion and cardiac function. Based on iterative algorithms, 4DM accurately quantifies nuclear studies and allows high quality image visualizations resulting in more precise quantitative measurements with consequent improvement in coronary heart disease detection. Provides perfusion studies, flow and functionality configurable in a single application with customizable reporting modules. Determines systolic and diastolic evaluation parameters for gated studies with ECG synchronization, plus manages thickening and motion data.

Finally, the Emory Cardiac Toolbox also allows to perform both a functional and a perfusional analysis on cardiological tomographic studies.

CONCLUSIONS

In the present study, we performed simultaneous double isotope D-SPECT acquisitions with 99mTc-mibi and 123I-MIBG, this acquisition allowed the simultaneous evaluation of innervation and cardiac function. A previous study showed that in a double simultaneous isotope condition, the presence of 123I did not have an impact on the evaluation of the left ventricle within the 99mTc energy window for dedicated CZT equipment. In addition, a simultaneous double isotope protocol provides a clearer 99mTc-MIBI image and a perfect recording to define the contours of the heart on the image and thus accurately measures 123I-MIBG cardiac absorption. The amount of activity 99mTc had an impact on the ratio 99mTc / 123I and did not interfere with the detector's energy resolution, changing only the size and not the width of the photon peak. Finally, capturing SPECT and planar images using the Anger camera typically takes 30-45 min. On the contrary, acquisition with CZT cameras usually takes 10 minutes; the latter is much more convenient for patients with heart failure. In the field of multimodal non-invasive imaging in cardiology, the use of new cardio-dedicated methods is an ambitious opportunity. In this panorama of innovation and prospects, the role of TSRM is of great importance in order to optimize the resources available to provide the nuclear physician and the clinician with increasingly reliable information, ensuring greater comfort and less exposure to radiation to patients and healthcare professionals.

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