Optimization of a protocol for myocardial perfusion scintigraphy by using an anthropomorphic phantom*

Estudo de otimização de protocolo em cintilografia de perfusão miocárdica com a utilização de um simulador antropomórfico

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Abstract

Objective: To develop a study aiming at optimizing myocardial perfusion imaging.

Materials and Methods: Imaging of an anthropomorphic thorax phantom with a GE SPECT Ventri gamma camera, with varied activities and acquisition times, in order to evaluate the influence of these parameters on the quality of the reconstructed medical images. The ^{99m}Tc-sestamibi radiotracer was utilized, and then the images were clinically evaluated on the basis of data such as summed stress score, and on the technical image quality and perfusion. The software ImageJ was utilized in the data quantification.

Results: The results demonstrated that for the standard acquisition time utilized in the procedure (15 seconds per angle), the injected activity could be reduced by 33.34%. Additionally, even if the standard scan time is reduced by 53.34% (7 seconds per angle), the standard injected activity could still be reduced by 16.67%, without impairing the image quality and the diagnostic reliability.

Conclusion: The described method and respective results provide a basis for the development of a clinical trial of patients in an optimized protocol.

Keywords: Myocardial perfusion imaging; Optimization; Anthropomorphic phantom.

Resumo

Objetivo: Realizar um estudo de otimização de exames de cintilografia de perfusão miocárdica.

Materiais e Métodos: Foram adquiridas imagens de um objeto simulador antropomórfico de tórax contendo coração, pulmões, fígado e coluna vertebral, em uma gama câmara SPECT GE modelo Ventri, utilizando-se diferentes atividades e variando-se os tempos de aquisição, de forma a verificar a influência destes parâmetros na qualidade da imagem clínica reconstruída. Foi utilizado o radiofármaco ^{99m}Tc-sestamibi e os testes realizados foram avaliados clinicamente a partir de notas, tanto para o *summed stress score* quanto para a qualidade técnica da imagem e perfusão. As quantificações foram realizadas pelo *software* ImageJ.

Resultados: Os resultados demonstraram que, para o tempo padrão utilizado na realização dos exames de 15 segundos por ângulo, a atividade injetada poderia ser reduzida em 33,34%. Além disso, se o tempo usual de exame for reduzido em 54,34% (7 segundos por ângulo), ainda assim a atividade padrão injetada poderia ser reduzida em 16,67%, sem prejudicar a qualidade da imagem e a confiabilidade do diagnóstico.

Conclusão: O método desenvolvido e os resultados obtidos podem ser utilizados para o desenvolvimento de um estudo clínico de pacientes em um protocolo otimizado.

Unitermos: Cintilografia de perfusão miocárdica; Otimização; Simulador antropomórfico.

INTRODUCTION

Coronary arterial disease (CAD) is the main cause of death among men and women in the world, according to the World Health Organization(1). Estimates indicate that approximately one individual dies every 40 seconds on account of cardiovascular diseases(2).

The greater prevalence of CAD in male individuals caused this disease to be underdiagnosed and undertreated in women, in spite of being an important morbimortality factor in this population. This is due to the fact that the greatest part of the studies in the literature approaching diagnosis, treatment and prognosis of CAD has contemplated a relatively small number of women. Thus, the obtained re-

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sults in such studies cannot always be extrapolated to this population.

The diagnosis of CAD in women is always a challenge. The clinical presentation is late (approximately 10 to 15 years after the men's) and the symptoms are usually atypical. For being more elderly, women present with a greater number of comorbidities and worse prognosis. It is important to remind that the prevalence of CAD after the 7th decade of life is similar in men and women, and once it is diagnosed, the prognosis is worse in women. In developed countries, more than 50% of the women die on account of cardiovascular diseases, and sudden deaths are responsible for 35% of the mortality[3].

Myocardial perfusion scintigraphy (MPS) is a noninvasive imaging method with high diagnostic and prognostic value, and it is widely validated in clinical practice both for men and women[4–6]. Such nuclear medicine imaging method relies on the utilization of a gamma camera and a radiopharmaceutical. Currently, ^{99m}Tc-sestamibi is the most used radiopharmaceutical in this procedure. The two-day protocol includes recommended activities of 888 to 1,332 MBq, according to the American Society of Nuclear Cardiology[7], and 600 to 900 MBq, as stated by the European Council on Nuclear Cardiology (ECNC), that also recommends a time of 25 seconds per acquisition as ideal for cardiac SPECT[8].

The present study was aimed to the optimization of ^{99m}Tc-sestamibi MPS by varying the activities and acquisition times, and verifying the influence of such parameters on the image quality in a cardiac anthropomorphic phantom.

MATERIALS AND METHODS

Anthropomorphic phantom

A Data Spectrum ECT/TOR/P model anthropomorphic phantom was utilized, simulating the upper part of a medium to large-sized individual's chest. Such a phantom comprises heart simulators (with the possibility of attaching lesions of different sizes), lungs, liver, and dorsal spine (Figure 1).

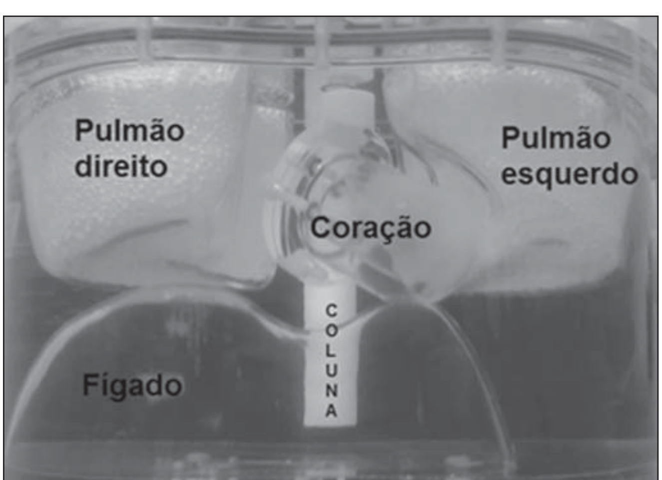

Figure 1. Anterior view of the ECT/TOR/P model anthropomorphic phantom, Data Spectrum Corporation.

Equipment and imaging protocol

The nuclear medicine imaging system was a GE Healthcare Ventri model gamma camera with SPECT (single photon emission tomography) comprising a fixed 90° dual-head system and an image processing software, Xeleris2 (release 2.151). Each detector has a 370 × 190 mm rectangular field of view (FOV) of a 9.5 mm-thick NaI(Tl) crystal.

The two-day protocol included the following characteristics:

- Simulated wait time for the performance of the scan: 60 minutes.
- Patient's positioning: supine and prone.
- Matrix: 64 × 64.
- Zoom: 1.0.
- Pixel size: 6.4 mm.
- Voxel size: 6.40 × 6.40 × 1 mm.
- Orbit: 180°.
- Number of projections: 60 (30 per detector, with two detectors at a 90° geometry).
- Energy window: 140 keV ± 10%.
- Contour: circular.
- Acquisition technique: step-and-shoot.
- Collimator: low energy high resolution (LEHR) parallel holes.

Different activities were utilized not only to reduce the doses received by patients, respecting the international ALARA (as low as reasonably achievable) concept, but also to meet possible restrictions in the radiopharmaceuticals supply, as it recently occurred during the so-called "generator crisis" (2010/2011).

Image acquisitions were also performed with different projection times, in order to analyze whether the usual acquisition time could be optimized, both for the patient's comfort as well as for the reduction of motion artifacts which may lead to scan repetition.

Simulated variations

- Injected activity: 555 to 1,110 MBq (15 to 30 mCi).
- Time per projection: 7 to 20 seconds (standard: 15 seconds).

Image processing and reconstruction

The images were iteratively reconstructed with the aid of the software Evolution for Cardiac from GE Healthcare, a recently introduced algorithm for cardiac images reconstruction. Such algorithm incorporates RR (resolution recovery) and MAP (maximum a posteriori) type noise regularization, allowing the SPECT images to be acquired in half the time compared with standard OSEM (ordered subset expectation maximization) algorithm, being known as HT (half time acquisition)[9].

Preparation of the anthropomorphic phantom

Measurements were performed with and without insertion of heart lesions, in order to simulate healthy individuals and the ones with CAD. For the studies that simulated hypo-uptake, a 1.0 cm-thick solid-type lesion with 2 cm in length was inserted in the lower basal region of the cardiac phantom.

The radioactivity concentration in the cardiac phantom followed the pharmaceutical biodistribution[10,11]. The details of the activity in each organ are individually presented on Table 1. The concentration ratio (MBq/ml) between heart:liver:body was 12:8:1. According to the literature, the concentration ratio (MBq/ml) myocardium/liver is 1.3 ± 0.1[10–12].

Table 1—Activities injected into each organ individually for each simulation.

Phantom	Total activity (MBq)	Activity injected in the organ (MBq)
Heart	1,110	17.76 ± 0.89
	925	12.17 ± 0.61
	740	8.69 ± 0.43
	555	6.52 ± 0.33
Liver	1,110	124.54 ± 6.23
	925	80.66 ± 4.03
	740	52.98 ± 2.65
	555	39.74 ± 1.99
Body	1,110	153.55 ± 7.68
	925	76.22 ± 3.81
	740	56.61 ± 2.83
	555	42.46 ± 2.12

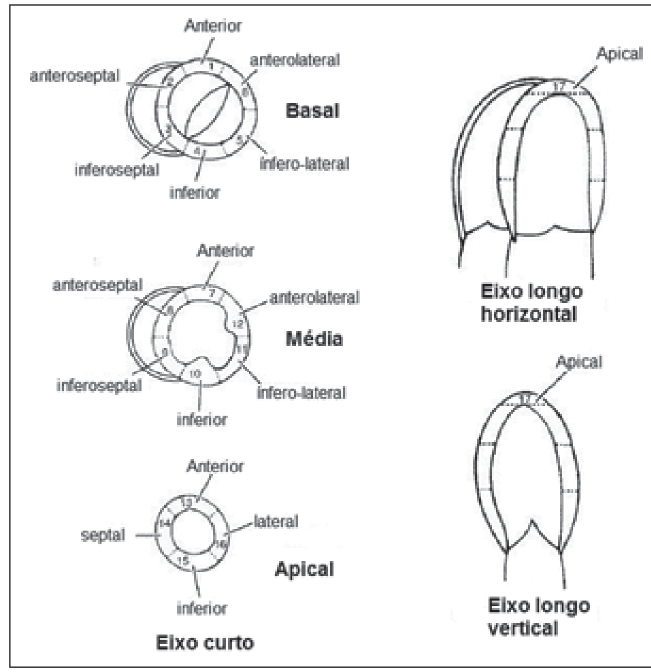

Figure 2. Image of left ventricle with recommended terminology of the 17 segments for tomographic images of the heart.

Image evaluation method

Qualitative and semi-quantitative analyses: scores on medical evaluation

The clinical evaluation was blindly performed by an experienced nuclear cardiologist, i.e., without any knowledge on the parameters utilized in the images acquisition. The scores considered three criteria, as follows:

- Technical quality of the images (evaluation of noise, artifacts and contrast), based on the letters A, B and C: A – excellent quality, without any image characteristic that might impair interpretation of the study; B – good quality, with presence of some characteristic(s) that might eventually impair the interpretation of the study; C – bad quality, impairing interpretation of the study.
- Perfusion: normal – homogeneous radiotracer uptake; abnormal – heterogeneous radiotracer uptake.
- Summed stress score (SSS).

The semi-quantitative evaluation is aimed at standardizing the segmental analysis of the left ventricle (LV) and the lower subjectivity in the interpretation. A system of scores for the 17 segments of the LV which considers three sections in the smaller axis (apical, median and basal) and a section on the long vertical axis, is utilized as shown on Figure 2.

Each one of the 17 segments is scored according to the radiopharmaceutical uptake, as follows: 0 (zero) = normal; 1 (one) = slight reduction in the radiopharmaceutical uptake; 2 (two) = moderate reduction in the radiopharmaceutical uptake; 3 (three) = significant reduction in radiopharmaceutical uptake; 4 (four) = absence of radiopharmaceutical uptake.

The sum of the values attributed to each representative segment of the stress phase is called SSS. The values between 0 and 4 are considered as normal or equivocal (possibility of attenuation artifact) and SSS values > 4 are considered as altered.

Semi-quantitative analysis with software

The software analysis was performed with the aid of the software ImageJ. Short and long vertical axes images were selected for analysis resulting from processing, with 600% zoom. Customized regions of interest (ROI) were delimited for each one of the 17 segments. Such ROI were defined with the assistance of a nuclear cardiologist, being repeated in an identical manner in all heart images. The sum of the pixel count values in each ROI were graphically represented, comparing the phantom with a patients' data bank.

Validation of the method

In order to validate the data obtained with the phantom, the results were compared with those from a group of female patients with pre-test low probability of CAD, according with the criteria by Diamond et al.[12]. A total of 40 studies were used and originated a databank representative of the normal radiotracer uptake on each one of the analyzed 17 LV segments. The mean age of the patients selected as standard databank was 57.3 years (36–69 years); mean body mass index of 25.40 (19–37); and mean injected activity of 811.78 MBq (699.30–1,013.80 MBq). Such data were collected from the databank of the clinic where the study was performed.

RESULTS

Initially, the activities and acquisition times were varied in the phantom without heart lesions. The scores from the evaluations performed by the cardiologist regarding technical image quality, evaluation of perfusion and SSS value (observer-dependent) obtained for activities from 555 to 925 MBq and acquisition times from 7 to 20 seconds per projection can be observed on Table 2.

The investigation performed with a lesion in the inferobasal region of the heart was not performed with 555 MBq (15 mCi) due to the results from the first part of the study. Likewise, the images were not acquired in the prone position with more than 7 seconds per projection. The cardiologist evaluation scores for simulation with lesion can be seen on Table 3.

By simulating the usually administered activity of 1,110 MBq, the acquisition time could be reduced to 7 seconds per projection, which is a reduction of 53.34% of the time used in the standard protocol, without changing the possibility of identifying the lesion, as demonstrated on Figure 3.

The ROI delineated for quantification at ImageJ can be observed on Figure 4. The counts for each segment were used to compare with the data from patients in the normality databank.

In order to validate the data, the counts for each segment of the heart phantom were compared with those from the normality databank by the ImageJ software. The chart on Figure 5 shows such comparison.

The lesion positioned in the inferobasal region of the phantom was the only count with a value below those of the databank, as this comprised data from healthy patients. The injected activity in the phantom was 1,110 MBq, demonstrating that this is the actual activity administered in the patients.

DISCUSSION

The results demonstrated that the scan cannot be performed with 555 MBq (15 mCi) of injected activity, as the technical quality of the image is not appropriate for an accurate diagnosis, according to the acquisition protocols adopted in the present study. In the images acquired with the phantom in ventral decubitus (prone), with 740, 925 and 1,110 MBq, no change was observed in the image quality, even for acquisitions with 7 seconds per projection.

It was observed that the injected activity could be reduced to 740 MBq (33.34% reduction) if the acquisition time remained the same as the usual time of 15 seconds per projection. For a time shorter than this, the lesion may be masked by the lack of counting statistics. Nevertheless, the activity

Table 2—Medical evaluation scores, with the heart phantom without lesion.

555 MBq (without lesion)	Simulation	Supine 7 s/p	Supine 10 s/p	Supine 15 s/p	Supine 20 s/p	Prone 7 s/p	Prone 10 s/p	Prone 15 s/p	Prone 20 s/p
	Technical quality	C	B	B	B	B	B	C	C
	Perfusion	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal
	SSS	2	3	2	2	1	1	2	1
740 MBq (without lesion)	Simulation	Supine 7 s/p	Supine 10 s/p	Supine 15 s/p	Supine 20 s/p	Prone 7 s/p	Prone 10 s/p	Prone 15 s/p	Prone 20 s/p
	Technical quality	B	A	A	A	B	A	A	A
	Perfusion	Abnormal	Abnormal	Abnormal	Normal	Normal	Normal	Normal	Normal
	SSS	1	2	1	0	0	0	0	0
925 MBq (without lesion)	Simulation	Supine 7 s/p	Supine 10 s/p	Supine 15 s/p	Supine 20 s/p	Prone 7 s/p	Prone 10 s/p	Prone 15 s/p	Prone 20 s/p
	Technical quality	A	A	A	A	A	A	A	A
	Perfusion	Abnormal	Abnormal	Normal	Normal	Normal	Normal	Normal	Normal
	SSS	1	2	0	0	0	0	0	0

s/p, seconds per projection.

Table 3—Scores given by medical evaluation, with the heart phantom without lesion.

740 MBq (with lesion)	Simulation	Supine 7 s/p	Supine 10 s/p	Supine 15 s/p	Supine 20 s/p	Prone 7 s/p
	Technical quality	B	B	A	A	B
	Perfusion	Abnormal	Normal	Abnormal	Abnormal	Abnormal
	SSS	4	0	2	2	2
925 MBq (with lesion)	Simulation	Supine 7 s/p	Supine 10 s/p	Supine 15 s/p	Supine 20 s/p	Prone 7 s/p
	Technical quality	B	A	A	A	B
	Perfusion	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal
	SSS	2	2	2	2	2
1,110 MBq (with lesion)	Simulation	Supine 7 s/p	Supine 10 s/p	Supine 15 s/p	Supine 20 s/p	Prone 7 s/p
	Technical quality	A	A	A	A	A
	Perfusion	Abnormal	Abnormal	Abnormal	Abnormal	Abnormal
	SSS	3	2	2	2	2

s/p, seconds per projection.

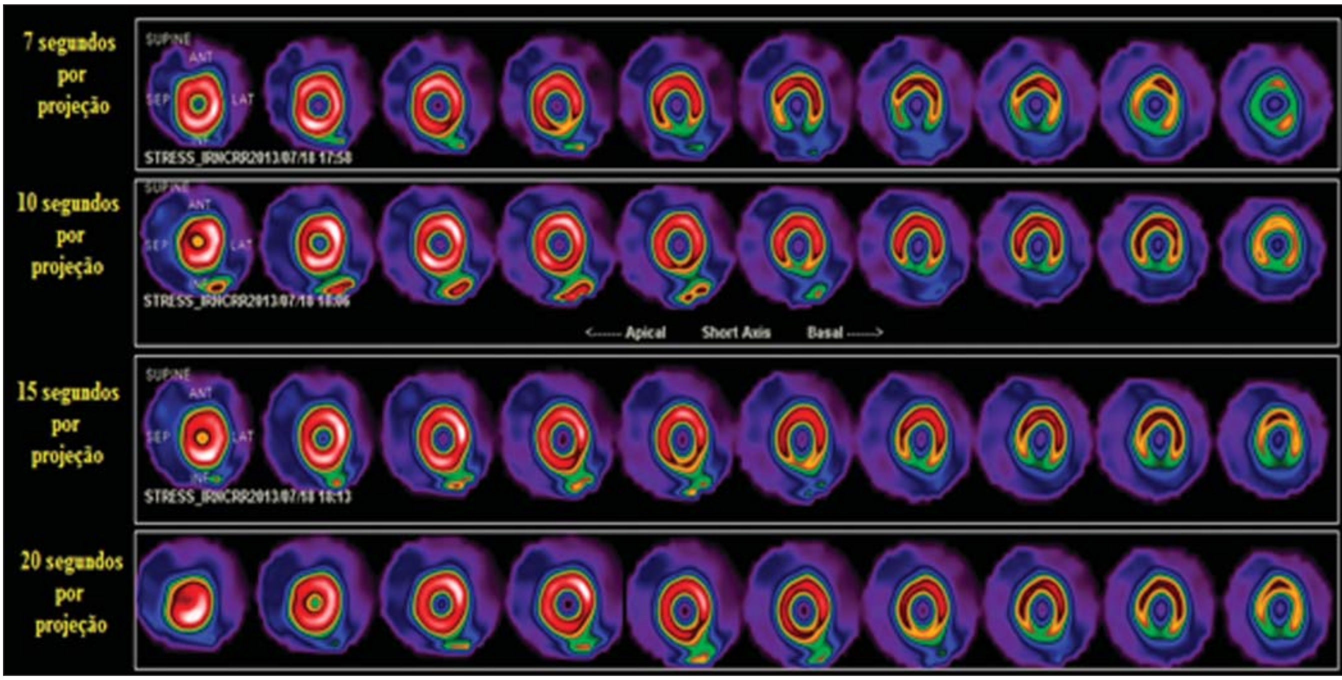

Figure 3. Processed images of the heart phantom with a lesion in the inferobasal segment, with times varying between 7 and 20 seconds per projection, highlighting that the protocol's standard time is 15 seconds.

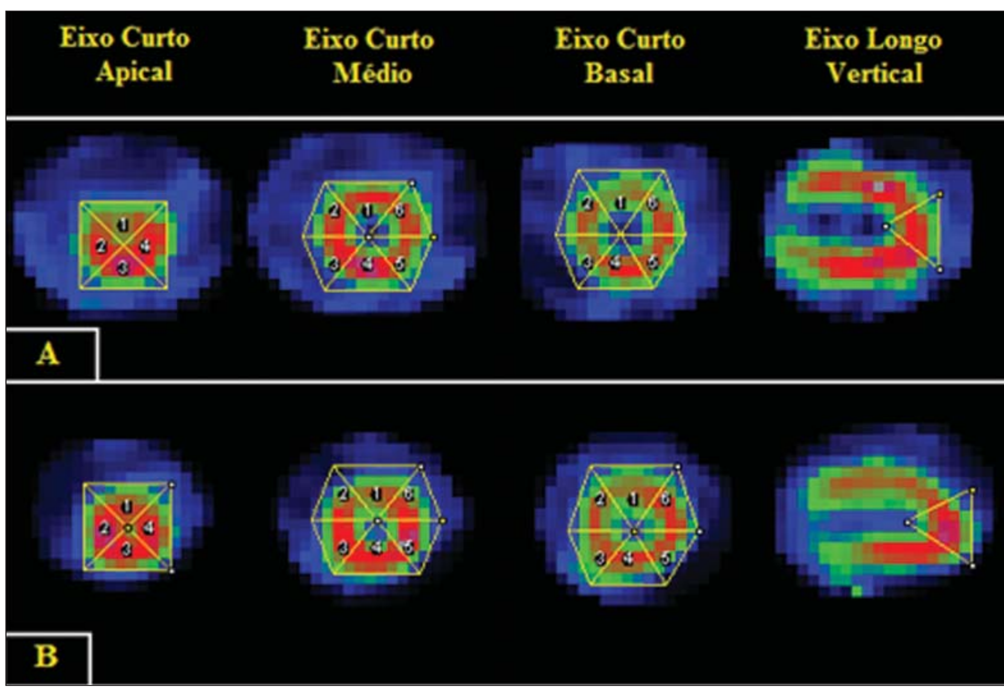

Figure 4. Regions of interest delineated for each one of the 17 segments of the heart by the ImageJ software. **A:** Anthropomorphic heart phantom. **B:** Patient's exam.

could be reduced to 925 MBq (16.67% reduction) and 53.34% reduction in acquisition time with no change in image quality and with the lesion still being properly diagnosed. With the usual injected activity of 1,110 MBq, the acquisition time could be reduced to 7 seconds per projection both in the supine and in the prone positions (reduction of 53.34%), without any change in image quality and in the diagnostic accuracy of the method.

The chart on Figure 5 shows the count on each one of the 17 heart segments for the normality databank, considering the count on the same segments of the heart phantom. The values observed were within the mean value of the counts considering the standard deviation, which confirms the validity of the proposed phantom usage.

CONCLUSION

The present study demonstrated that the ECT/TOR/P Data Spectrum anthropomorphic phantom appropriately reproduces patients, within the mean and standard deviation of a randomly selected sample. After validation, activity and

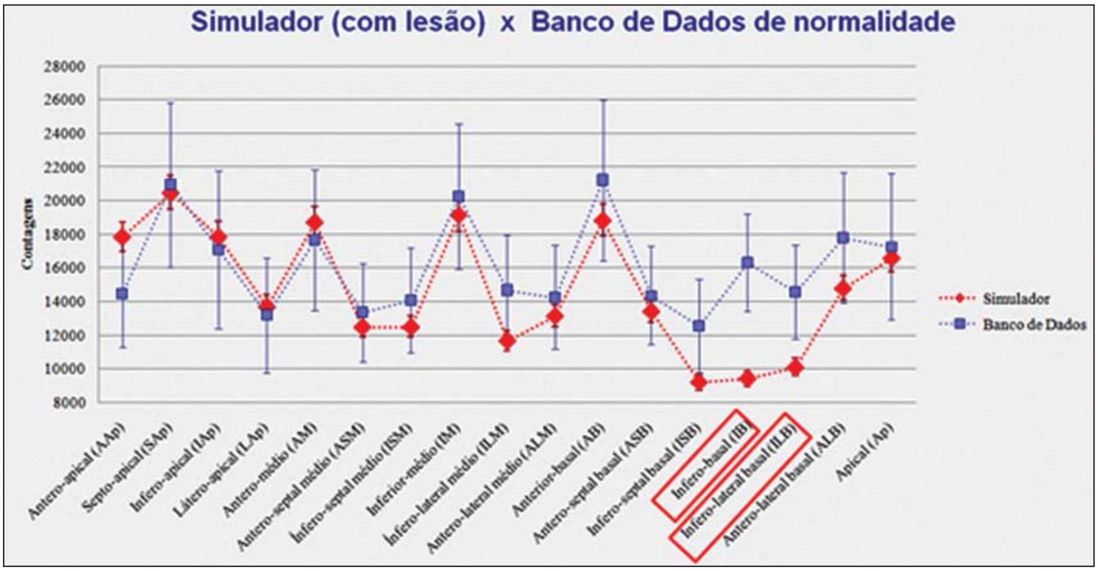

Figure 5. Count values at the 17 segments compared with the databank. The lesion on the heart phantom is observed as well as its influence on neighboring segments.

time parameters were varied for the two-day protocol study in MPS. The results demonstrated that for the same time currently used for the exam, the injected activity could be reduced in up to 33.34%. If the acquisition time is also reduced (to 53.34% of the usual time), the activity could be reduced up to 16.67% of the usual injected activity, without any change in the image quality and in the diagnosis. The images acquired in ventral decubitus (prone) demonstrated improvement in relation to those acquired only in supine position, complementing the exam. A deeper study of optimization based on positioning is currently underway and should produce more results for the present investigation on the two-day protocol for this type of exam. Such results serve as grounds for the undertaking of clinical studies involving patients for definition of an optimized protocol.

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