Influence of SPECT reconstruction algorithms in the improvement of SNR in cardiac imaging

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Abstract

Cardiac SPECT images often suffer from a number of degrading factors including depth-dependent spatial blurring, attenuation, scatter and low data counts. Thus, researchers have been working on developing a variety of reconstruction methods incorporating scatter correction (SC), resolution recovery (RR), noise supression and attenuation correction (AC). The goal of this work is to study the accuracy of absolute and relative measurements, and how these degrading factors impact on the reconstructed myocardium when different methods are used for half-time acquisitions. The reconstruction software used were WBR (UltraSPECT, Ltd.) and Evolution for Cardiac (GE Healthcare) with and without CT-based AC. The comparison between algorithms was made based on raw and normalized counts, severity and SRS values. Overall, some statistically significant differences were noted between parameters obtained with different methods, which makes decision only based on them somewhat unreliable. The results obtained confirm the usefulness of AC in addition to RR, but they should be evaluated next to NC images to avoid undervaluation of a lesion. The assessment of the RCA and LCX territory seems to benefit most from it.

Keywords: SPECT, Attenuation correction, WBR, Evolution

1. Background

Coronary Artery Disease (CAD) is a process in which the coronary arteries become partially or completely obstructed by the accumulation of plaque (accumulation of lipids, complex carbohydrates, and calcium deposits) on the inner wall of the arteries supplying blood to the heart. Without proper blood flow, the cardiac muscle will not receive oxygen and other vital nutrients that makes the heart work properly, hence, possibly creating an array of heart problems that can lead to death. When the insufficient blood flow to the heart is only temporary and reversible is called ischemia, however if the heart suffers an infarction, the damage made to the muscle is irreversible and permanent, on the other hand, if there is enough perfusion to keep the cells alive but not enough to allow a fully functional contraction of the heart muscle, it is still considered a viable myocardium. Therefore, is necessary to have an imaging technique capable of setting apart ischemic, viable, and infarcted myocardium as each one has a different impact on the patient's treatment and prognosis. Myocardial perfusion SPECT is considered an excellent non-invasive method for the diagnosis of CAD, prediction of disease prognosis, selection of patients for revascularisation and assessment of acute coronary syndromes [1]. Numerous studies have assessed the relative accuracy of SPECT imaging reporting a sensitivity and specificity of $87-89\%$ and $73-75\%$, respectively, dependent of the radionuclide chosen and stress modality [2]. During this procedure the patient is injected intravenously with a radiopharmaceutical tracer that is taken up in the heart muscle (myocardium), to evaluate regional coronary blood flow usually at rest and after stress. This compound is a pharmaceutically-active molecule labeled with a single-photon emitter, that is a radionuclide tracer that emits one gamma-ray per radioactive decay. This molecule is chosen on the basis of its preferential localization in a given organ, or its participation in a physiological process. In cardiac imaging procedures, the most common used radiopharmaceutical tracers are thallium chloride (^{201}Tl), technetium (^{99m}Tc) sestamibi and tetrofosmin. After the administration of the radiopharmaceutical tracer, its distribution within the myocardium (which is dependent on myocardial blood flow) is imaged by the SPECT system. The image acquisition is performed by rotating a camera around a point (center of rotation) located within a stationary patient so that multiple two-dimensional

projections can be acquired at different angles covering an angular range of 180° or 360° (at equal angular steps). The data acquired in this projections is reconstructed into tomographic slices using a mathematical reconstruction algorithm and realigned to 3 cardiac planes: horizontal, short-axis and horizontal long-axis.

1.0.1 Mode of operation

The gamma camera system has basically two functions: the detection of single photons events and the measurement of its energy and position. Its main components are the scintillation crystal, collimator, an array of photomultiplier tubes (PMTs), a pulse height analyzer and an analogue electronics for position encoding. The first piece of hardware met by the gamma rays is the collimator, which is one of the most important features of the system as is used to define the direction of the detected gamma rays. By regulating which gamma rays get through, the collimator forms a projected image of the gamma distribution on the surface of the scintillation crystal made of sodium iodide, doped with thallium NaI(Tl). When the gamma rays interact with the crystal, thousands of photons with wavelength of visible light are emitted. This light pulses, whose yield is proportional to the energy absorbed from the incident photon, are then optically guided through an array of photomultiplier tubes (PMT) system in which they are converted into an electrical signal through the production of photoelectrons in the photocathode. The output of each photomultiplier tube is an electric signal proportional to the intensity of the light that arrived at the tube. The multiplier section of the PMT amplifies the electronic signal so the current is sufficiently large to be used by conventional electronic circuits. In order to produce an image, we need more than just the intensity of the detected photons, we need to know from where they came from. The position is determined using the pulses that occur at the anodes of the phototube array. The output of the PMTs is mapped by a network of electric resistors, weighted according to the spatial position of the PMTs in the x-axis and y-axis of the coordinate system of the array. There are 4 position signals, labeled X^+, X^-, Y^+ and Y^-, and one energy signal Z that indicates the energy of the incident photon or pulse height. This helps to identify the position of an event by applying a simple formula per coordinate based on the relative amount of current received by each resistor. Because gamma camera operates in pulse mode we can treat the light photons from a single event as a unit. Most gamma rays interactions (the ones that don't suffer compton scattering), generates a larger signal in the PMT above the place where the interaction happened while the surrounding PMTs will receive smaller amounts of light. The position signal has to be normalized by dividing the position signals by the energy signal (Z). The next step is the Pulse Height Analyzer (PHA) that determines the amplitude of the pulses, which correlate with the gamma ray's energy.

1.0.2 Collimator

In order to create an image, the photons emitted at the source should hit the detector in a predictable position. However, as with all forms of electromagnetic radiation, photons are emitted isotropically so, simply using a detector wouldn't result in an image. Some photons escape the patient without interaction, some scatter within the patient before escaping, and some are absorbed within the patient. Also, many of the photons escaping the patient are not detected because they are emitted in directions away from the detector. The geometry of the collimator ensures that the position of the photon is well determined. Unfortunately, this technique is an inefficient method because many potentially useful photons are absorbed by the collimator and don't contribute towards the image formation. A heavy price is paid for using collimation - the vast majority typically well over 99.95% of emitted photons is wasted. Thus collimation, although essential to image formation, severely limits the performance of these devices. The design of the collimator depends on the gamma-ray energy and the trade-off between photon count sensitivity and spatial resolution. It is impossible to optimize both parameters. SPECT sensitivity describes the probability of detecting a photon incident upon the detector, commonly quantified as the number of detected counts per unit time per unit source activity for a specified energy window and geometry of measurement (system sensitivity). In order to have better sensitivity, the collimator hole size has to be bigger and the hole length shortened so that less photons are absorbed by the collimator.

1.0.3 Energy discrimination

Usually, the spectrum includes the total energy photopeak without any interaction before reaching the crystal and a background of lower energies due to the partial absorption of gamma by compton scattering. Because the path of a gamma photon changes after undergoing Compton scattering, it is impossible to locate where it came from. In order to have a final image with decent resolution, we have to avoid all events registered that don't correspond to the absorption by photoelectric effect of gamma photons with the total emission energy.

Thus, energy discrimination is important for imaging because provides a mean to reject the gamma-rays that lost their positional information. This is accomplished by placing a *window* for the adequate double threshold energy. If the event amplitude Z falls within the PHA settings, the event is accepted. Usually the values for a gamma camera *window* (difference between lower and upper-level discriminators) are within 20% ($\pm$10%) of the photopeak energy in the pulse height spectrum. Furthermore, more than just one window can be used, for instance, if the isotope used has more than one gamma-ray emission.

2. Radionuclides in SPECT

The most important radionuclide in Nuclear medicine and the one used in this study is technetium-99m (^{99m}Tc). ^{99m}Tc has all the right properties, with 140 keV gamma photons convenient for detection and has a half life of 6.03 hours [3] that allows a fast clearing from the body after an imaging process. This isotope of technetium can bind chemically to many biological active molecules making it suitable for many medical exams and is easily available from a ^{99}Mo generator that can be stored in a radiopharmacy. The next table shows the properties of different radionuclides used in Nuclear Medicine.

3. Iterative reconstruction technique

As computer technology started to improve, the interest in these reconstruction methods in SPECT increased because of the need to compensate the various image degrading effects in SPECT imaging process. The most important method are the Statistical techniques, who differ between those who assume Gaussian noise (involving least squares solutions) and those who assume Poisson noise (involving maximum likelihood solutions). The most used reconstruction algorithm is the *Maximum Likelihood Expectation Maximization algorithm* (MLEM) [4] and its accelerated form *Ordered Subsets Expectation Maximization* (OSEM) [5]. Since SPECT projection data is severely affected by Poisson noise, an advantage of these algorithms is the treatment of data according to the Poisson nature of the measures.

3.0.4 Maximum Likelihood Expectation Maximization algorithm (MLEM)

Iterative reconstruction is based upon the premise that if estimated profiles are generated by forward projecting an initial estimate of the image. These estimated profiles can be compared with the real profiles, to generate a profile error. Then, image errors can be generated by back projecting these profiles errors in order to update that first image estimate. This process is repeated until the best possible solution is reached. Iterative reconstruction methods are more flexible and allow the incorporation of models capable of correct some of the image degradation effects.

1. First, an estimate of the activity distribution within the patient is made, which is denoted by $f^*(x, y)$. The first estimate is very simple, usually, a nonzero image that has the same total projection counts as the measured projection data.
2. The estimate is then forward projected to estimate what the detectors would measure given the initial object i. In order for this to occur accurately, a model of the emission and detection process must be incorporated, the 'system matrix' into which alterations for attenuation, scatter and loss of resolution with depth can be included.
3. The estimated projections are then compared with the measured projections and any discrepancies in projection space are back-projected to give discrepancies in image space.
4. The differences between the estimated and actual projections are used to adjust the estimated image to achieve closer agreement.
5. The update-and-compare process is repeated until the difference between the estimated and acquired projections is minimal or until a fixed number of iterations have been achieved.

4. Sources of degradation and their impact in SPECT

The ideal scenario for a SPECT would be that all gamma rays emitted by the decaying tracer could escape the body and be detected by the gamma camera. However, realistically, the gamma photons emitted are deeply affected by the interaction with tissue within the patient's body (photon attenuation and scattering), by the inaccuracy of the collimator (blurring) and also by noise in part because of the reduction of counted events after collimation. After all, it's impossible to obtain high quality SPECT images without having in consideration these phenomenons and their possible corrections. Therefore, it's important to take into account these sources of image degradation:

a) the attenuation of the photons traveling toward the detector;

b) collimation, uniformity and stability of a gamma camera;

c) parameters related to corrupt recorded events due to different physical interaction of gamma rays.

d) the partial volume effect (PVE) as a consequence of the finite spatial resolution of the gamma camera due to detector blurring and non-ideal collimation.

d) factors related to the patient movement and positioning.

Although physicians have learned how to detect the related artifacts, it's likely that, in some cases

they still affect the patient's diagnosis. On the other hand, in order to achieve right quantitative SPECT analysis, the data acquired has to contain a great amount of correct information. As a result, is really important to understand all the effects that cause deterioration of the reconstructed image.

5. Commercial Software

One of the biggest limitations of SPECT-MPI is a trade-off between image-acquisition time and noise levels. Therefore, because of the advantages of a shorter acquisition time are significant, new SPECT reconstruction algorithms have been improved in order to provide a better image quality despite poor count statistics. The new algorithms allow lower count-density cardiac SPECT acquisitions to be processed with resolution recovery (RR) and noise-reduction techniques. Most manufactures of SPECT cameras have already implemented these new improvements into MLEM or OSEM algorithm. In this study, the commercial reconstruction software used are Evolution (GE Healthcare) [6] and Wide Beam Reconstruction (UltraSPECT) [7]. Clinical trials comparing these algorithms with conventional SPECT reconstruction showed that:

- Acquisition time can be decreased to half without compromising qualitative or quantitative diagnostic performance [8, 9, 10];
- Acquisition time can be decreased to a quarter if the reconstruction is optimized for the reduced count density [11];
- Can provide similar diagnostic quality whether imaging time is reduced by half or a half-dose is injected [9, 12]

5.1. Evolution for Cardiac

GE Healthcare (Waukesh, WI) has developed a new reconstruction algorithm, Evolution for Cardiac, that incorporates RR and a maximum *a posteriori* (MAP) noise regularization. The Evolution approach focuses on CDR compensation by integrating the collimator-detector response in the iterative algorithm. The PSF is stored in a lookup table and the radial distance of the detector is obtained as part of the projection data. The collimator-specific data are embedded in the software, also in the form of look-up tables that are part of the reconstruction package. Therefore, during the reconstruction process, collimator length and septa thickness, intrinsic resolution, crystal thickness and collimator-detector gap are all taken into account. Furthermore, acquisition parameters like the distance from the center of rotation to the collimator for every acquired projection, are retrieved directly from the raw projection data [13]. At the same time, Evolution software incorporates noise suppression since MLEM algorithm converges to a quantitatively unbiased but noisy image. Because noise tends to propagate during image reconstruction resulting in a potential compromise between the noise level and quantitative accuracy. This method suppresses the impact of noise by incorporating a maximum *a posteriori* (MAP) algorithm. Bayes theorem allows to introduce in the reconstruction process a prior distribution that describes properties of the unknown image. Maximization of this *a posteriori* probability over the set of possible images results in a MAP estimate [14]. The main idea behind this method is that, at the end of each iteration, there have been calculated OSEM and Bayesian coefficients. The next image is a pixel by pixel product of the current image and the two sets of coefficients. Then, the current image is compared with the prior, and if the image is locally monotonous, the coefficients generated by the prior are all unity and the OSEM coefficients are not changed. Only, when non-monotonous structures start to develop along the iterations, does the prior modify the corresponding OSEM coefficients, in order to remove these structures from the image of the next iteration step. There are two tasks that are clearly separated: the OSEM part is responsible for the generation of a quantitatively correct image and the median root prior (MRP) tends to remove the unwanted noise without blurring the locally monotonous structures [14]. Attenuation correction (AC) with Evolution for Cardiac also includes scatter correction based on a dual-energy window where the scatter estimation is added to the estimated projection as opposed to subtracting the scatter from the original projections, as is implemented in regular iterative reconstruction with scatter correction [6].

5.2. Wide Beam Reconstruction (WBR)

The WBR software (UltraSPECT Limited, Haifa, Israel) is another iterative reconstruction method that includes RR and noise reduction in order to improve image quality in studies with fewer photons counts. The WBR algorithm is also an OSEM-based algorithm that models the physics and geometry of the acquisition for resolution recovery in a similar way than the previously described method. Therefore, during the reconstruction process, data representing the relationship between each projection pixel and reconstructed voxel is modified according to collimator's geometry. These pixel-voxel weights correspond to the solid angles between each detector pixel and each body voxel and are calculated analytically [15]. On top of that, if the angular position is not available from the acquisition parameters, WBR uses a simple algorithm capable of calculating the body contour of the patient from which the distance of the detector to the body determined [16]. Thus, resolution recovery yields images of improved spatial resolution and

with less noise when compared with other similar techniques [8]. Noise compensation with WBR can suppress noise and enhance the signal-to-noise ratio (SNR) by modeling the statistical characteristics of the emission process and of the detected data. Most RR methods use the Poisson distribution to describe the emission-detection statistical model. However, WBR regularizes the likelihood objective function with a combination of Poisson and Gaussian distributions. If a higher weight is given to the Gaussian component, high-frequency components in the projections are suppressed. On the other hand, if higher weight is given to Poisson's component, then, results in recovery of high-frequency signal. The balance between these two components is determined by Fourier's analysis of a projection to determine the SNR that is present in the acquired data and the approximate statistical distribution. This way, no post filter is applied and the parameters defining resolution and noise are chosen according to the data analysis and desired smoothness. WBR utilizes a stand-alone running hardware workstation (Xpress.cardiac) and can reconstruct data acquired from most scanners with standard collimator design.

5.3. Quantitative analysis

In SPECT imaging, detailed analysis of shapes and values of the region of interest (ROIs) of the image is important for diagnoses but high-accuracy quantification is, however, very difficult to achieve. The quantification is affected by the degradation of the image introduced by statistical noise, attenuation, collimator/detector response and scattering effects. These factors affect image contrast by reducing the connection between image counts and activity concentration, thus for a more reliable quantification, it is necessary to correct them using compensation algorithms. As a result, this work will focus on the analysis of the images processed by different software in order to compare the quantitative differences that arrive from each of them. In order to have a quantitative analysis, each data point on the polar map is assigned a number and color corresponding to the radiotracer activity at that point. The use of two-dimensional polar map coordinates allows comparison of count intensities between different patients. First, before any comparison is made, image intensities need to be normalized, with activity being calculated as a percentage of the maximal left ventricular uptake. The meaning of each score is as follow:

$0 : \geq 80\%$- normal;

$1 : 70\% - 80\%$ - mild decrease;

$2 : 60\% - 70\%$ - moderate decrease;

$3 : 50\% - 60\%$ - severe decrease;

$4 : < 50\%$ - absence of detectable radiotracer uptake.

6. Clinical study

This study was designed to determine whether similar absolute and relative quantification such as raw and normalized counts, severity and SRS parameters could be achieved with half-time acquisitions. Therefore, WBR (UltraSpect, Haifa) and Evolution for Cardiac (GE Healthcare) (IRACRR and IRNCRR) were compared in order to evaluate the contribution of RR and AC in SPECT images quantification. The comparison made between WBR and IRNCRR had the purpose of evaluating both algorithms' resolution recover. A similar study was made between both GE algorithms, IRACRR and IRNCRR, so as to compare RR results with and without attenuation correction. Last, WBR and IRACRR were also analyzed since their credited as state-of-the-art iterative algorithms for SPECT reconstruction. All aforementioned advances have contributed greatly to the change from evaluation by visual interpretation alone, towards describing perfusion in conjugation with automated quantification as an aid to clinical diagnosis. Absolute and relative quantification of MPI has reduced inter-and intra observer variability, and allows the possibility to study and compare parameters in the same patient or between a group. The objective of myocardial perfusion quantification is the regional classification of the myocardial tissue as being normal, scar, or ischemic, thus, the visual representation of quantitative values obtained from SPECT images is an important part of the evaluation process. According to standard quantification protocols, each rest and stress scan data is resolved into a polar map based on derived measures of defect size, severity, and reversibility. The quantified measures are accomplished by comparing each segment of the polar map with measurements made from a population that is known to be normal (patients with low pretest likelihood ($\leq 5\%$) of CAD).

Population

Overall, for this study, we evaluated 73 patients who were scheduled to have myocardial perfusion SPECT for suspected or known CAD at the Atomedical Laboratory in Lisbon, Portugal. However, 23 of these scans had to be excluded, because in those cases, WBR scan frame had the maximal pixel count outside of the myocardium (i.e., the stomach, bowel, or liver), thus assigning a lower intensity value to the myocardium pixels. The purpose of this study was to assess the impact of these softwares according to patient's sex and site of CAD for 'overweight' patients. Therefore, the main selection factor for this study was body mass index $BMI. > 31\, Kg/m^{-2}$ with the total of 50 patients, 25 women and 25 men, with the following charac-

teristics:

	Women		Men	
N	25		25	
Age (y)	$68,6$	$\pm 9,5$	$63,7$	$\pm 11,3$
BMI (Kg/m^{-2})	$36,5$	$\pm 3,8$	$35,7$	$\pm 4,2$

Table 1: Characteristics of the patients.

Image acquisition protocols
All acquisition were performed with GE Optima NM/CT 640 Gamma Camera system 20 minutes after injection of approximately 7 mCi ^{99m}Tc - tetrosfosmin (GE Healthcare). The images were acquired with a low-energy high-resolution collimator (LEHR), 64×64 matrix, an elliptic orbit with step-and-shoot acquisition at 3° intervals over 180 °, 60 projections and 9-13 s per projection using a 20% energy window centered on the 140 keV photopeak of ^{99m}Tc. The patients were in supine position on the table with his or her arms raised straight above the head. The SPECT image set was reconstructed on a dedicated workstation (Xeleris, GE Healthcare, Haifa, Israel), using WBR and Evolution for Cardiac recommended manufacturer RR and noise-reduction parameters and with and without CT-based AC (12 iterations and 10 subsets). At the end of each acquisition a single low-dose CT scan (100 keV; 1,0 mA; 0,2-0,3 mS) of the chest was performed in order to obtain attenuation maps automatically applied by the processing software to correct the emission data. The myocardial perfusion imaging dataset is carefully co-registered with the CT attenuation map to produce the attenuation-corrected images. The comparisons were made between thr territories associated to the various coronary arteries, RCA - right coronary artery; LCX - left circumflex artery; LAD - left anterior descending artery.

Raw counts
All reconstruction processes were done with half-time protocol, therefore with low count statistics in comparison with standard FBP reconstruction. Raw counts obtained by WBR, IRACRR and IRNCRR were all significantly different ($p < 0,05$). WBR reconstruction clearly had the best results averaging around 1000 more counts than IRACRR and 2000 more than IRNCRR. Therefore, WBR resolution recover and noise suppression is able to recover better the loss of resolution at different source-detector distances during the procedure than Evolution for Cardiac with or without using CT for AC. For Evolution for Cardiac algorithms, the difference between IRACRR and IRNCRR raw counts was around 1000. Since the main difference between these two methods is the inclusion or not of attenuation correction, is fair to state that the extra raw counts are a consequence of its use. Overall, from the data collected, there is no obvious relationship between these algorithms with an exception of IRACRR and IRNCRR correlation for women (r=$0,75 \sim 0,80$). A similar result could be expected for men's raw counts but their relationship is only average (r=$0,56 \sim 0,62$).

Normalized Counts
Quantification of myocardial activity is conventionally measured relative to the region of most intense uptake (brightest pixel count). Therefore, each raw data set is normalized to the maximum myocardial tracer content in the LV in order to be compared with a database obtained from subjects with expected normal perfusion. This study showed that for LAD territory, all comparisons were within 95% CI limits, with an exception of WBR & IRNCRR comparison for men's perfusion data. For this particular situation, IRNCRR algorithms gives an average perfusion of $80,8\%$ and the addition of AC decreases the perfusion value in $1,68\%$. Although for women, the difference is not statistically significant, the use of AC in this territory increases the perfusion,on average, $1,5\%$ from IRNCRR and $1,9\%$ from WBR. For LCX territory, mean perfusion values were the lowest for IRNCRR and the highest for IRACRR, with a statistically significant bias between them of $3,5\%$ for women and $3,7\%$ for men. In this case, for women, WBR algorithm had a good agreement with IRACRR while for men, WBR mean average was closer to the IRNCRR one. RCA's mean perfusion values, for men, are significantly different between all 3 algorithms. For this LV territory, it's obvious the difference between IRACRR algorithm and both WBR and IRNCRR. The difference between Evolution for cardiac with and without AC (IRACRR-IRNCRR) perfusion values is 10%. The perfusion obtained with WBR algorithm had on average minus 12% than IRACRR and was closer to the IRNCRR mean with only minus $1,8\%$. Similar results are also observed for women perfusion values, however, the differences between IRACRR and both IRNCRR and WBR are $3,8\%$ and $3,3\%$, respectively. Overall, for normalized counts, we encountered clear discrepancies between perfusion values acquired by these 3 algorithms. Attenuation of photons within the body is recognized as a major factor limiting SPECT detection of myocardial perfusion defects. This is particularly important in low-count studies such as this one since it can compromise image quality because of the increased noise due to low statistics and blur from scattered photons. The main purpose of this

study was to evaluate absolute and relative quantitative parameters that are generally used to classify normal or abnormal myocardial perfusion within clinical setting. In particular, to determine whether those parameters differ significantly between attenuation corrected and non corrected images in patients with high BMI. Attenuation artifacts caused by the highly nonuniform tissue composition of the thorax has a big impact in diagnostic accuracy of SPECT and although the true prevalence is unknown some reports estimate they appear in between 20% to 50% of the studies [17]. The most frequently identified sources of artifacts are breast tissue in women and in the by the left hemidiaphragm in men. Breast attenuation often appear as a region with decreased count density along the anterior wall of the LV (mostly in LAD territory) although depending on their density, shape and position relative to the myocardium, lateral wall, septum, and even the apex can be affected. Attenuation by subdiaphragmatic structures commonly affect the assessment in regions associated with RCA and LCX. Several studies reported that attenuation correction improves primarily specificity in the RCA territory [17] [18]. However, it can be said that some studies describe different results for the influence of AC in the sensibility to detect CAD in the LAD and LCX. For instance, Vidal et al. showed that AC actually reduced the detectability of the defects in the LAD region and reported that a significant loss of sensitivity in the LAD territory followed the increase of RCA specificity with the application of attenuation correction [19]. In our study, first and foremost, it's plainly evident the influence of attenuation correction in the estimation of radiotracer uptake for LCX and in RCA territories. The results presented showed that images reconstructed with AC had an improvement in perfusion, in particular, RCA territory in men. Furthermore, a higher percentage of perfusion was obtained for 65% and 73% of the studies reconstructed with IRACRR in comparison with WBR and IRNCRR, respectively. Looking at the Bland-Altman plot for normalized counts it's possible to see some significant differences in perfusion for IRACRR and IRNCRR comparison. By comparing BA plots 95% CI limits for men and women, we get that the mean bias for women LAD territory is positive $(1,5\%)$, which means that in average, perfusion values obtained with AC are bigger than without AC as was expected. On the other hand, for men we have a mean bias between IRACRR and IRNCRR of $-1,7\%$, hence for most studies, we get higher perfusion values for IRNCRR than with IRACRR. Since, for men in particular, we have that with AC there was a considerable positive bias for both RCA and LCX, in which often perfusion differences were about 15% higher than those without AC. It is possible that over-correction of the inferior wall (RCA) resulted in a relative decrease in tracer distribution in the LAD territory when the brightest pixel used for normalization was, for NC images, in a position where AC didn't enhanced greatly the artificially reconstructed counts. When territories like RCA are intensified, the maximum myocardial tracer content can be in a different place and have a significantly higher value with AC. Thus, a region in the LV where for NC images showed a bright color indicating high perfusion can, in AC images, have decrease relative perfusion values or look like it has less tracer uptake due to bigger contrast between over-corrected areas and areas where the perfusion values are normal but the color scheme of the polar map changed. Therefore, it's fair to consider that when RCA territory is overcorrected, the polar maps might show decreased uptake in the AC corrected images for LAD. As a way of avoiding misinterpretation, IRACRR should be interpreted with IRNCRR or WBR reconstructed images.

Severity

First, women's LAD territory, showed a good agreement between WBR, IRACRR DB 2 and IRNCRR where their mean's difference are close to 0 with $p > 0,963$. For men, there is also a good agreement between IRACRR DB 2 and IRNCRR, although WBR's severity average differs significantly from IRNCRR and also has a considerable gap to IRACRR DB 2 results, yet not statistically significant. While, for women, AC doesn't seem to have a big impact since its results are close to those algorithms without AC, for men, WBR results have, on average, plus $0,320SD$ than IRACRR DB 2. The use of DB 2 for IRACRR algorithm creates a polar map with, in average, less $0,240SD$ than with DB 1 for women and plus $0,184SD$ for men. Similar to LAD, LCX territory for women had a good agreement between WBR, IRACRR DB 2 and IRNCRR. AC doesn't seem to have a big impact in the women's LCX territory since its results are close to those algorithms without AC. However for men, despite WBR and IRNCRR having good agreement, WBR results have, on average, plus $0,400SD$ than IRACRR DB 2, which is statistically significant. RCA territory had the most significant differences between algorithms and it's the most affected by attenuation correction. IRACRR with DB 2 corrects IRNCRR, on average, by $-0,428SD$ for women and $-0,560SD$ for men, which are both statistically significant. WBR comparison with IRACRR DB 2 yields contrary results, with plus $0,392SD$ for women and plus $0,188SD$ for men. Moreover, the high perfusion values obtained with IRACRR for men, described earlier, are interpreted similarly

by WBR algorithm despite having, on average, a 12% perfusion difference in this territory. Thus, is likely that some of those large difference in trace uptake are due to over-correction of the RCA territory for men, because otherwise, we would see a more pronounce difference between IRACRR and WBR severity measures. On the other hand, the difference in perfusion between WBR and IRACRR for women still differs significantly, on average, for severity polar map results. In this case, WBR algorithm has a better agreement with IRNCRR than with IRACRR, independently of the DB used. This result demonstrates that AC for women RCA territory may not be very beneficial. The use of DB 2 for IRACRR algorithm creates a polar map with, in average, only plus $0,072SD$ than with DB 1 for women and plus $1,452SD$ for men. For women's RCA, the choice of DB 1 and DB 2 for IRACRR doesn't have a big effect in severity results. Overall, for men, IRACRR DB 2 gives smaller severity results than IRNCRR and WBR, while for women, that difference is not as evident but happens regularly for RCA territory.

Summed Rest Scores (SRS)

The differences between SRS are closely related to severity results, thus, most considerations abovementioned also apply for this section. For women's LAD, SRS don't differ significantly between the 3 algorithms, thus are not typically changed by the use of AC whereas for men, a considerable bias can be seen between WBR and IRACRR DB 2. WBR algorithm scores, on average, $0,880$ more than Evolution with attenuation correction. Furthermore, men's SRS scores of IRACRR with DB 1 differ significantly when compared with DB 2 for LAD and LCX. The choice of DB can have a big influence in clinical diagnostic since with DB 1, IRACRR scores are $0,920$ less than with DB 2 for LAD and $0,640$ for LCX. Attenuation correction also has a bigger impact in LCX scores for men than for women. For men, IRACRR DB 2 also gives a score $0,800$ lower, on average, than IRNCRR algorithm. Therefore, despite severity results agreement between this pair, the correspondent SRS differs significantly. WBR and IRNCRR seem to have the identical interpretation for SRS on women's LAD and RCA territories, only in LCX appears a significant difference where IRNCRR scores were $0,560$ higher than WBR. Finally, for RCA territory, both WBR and IRNCRR attribute, on average, 1 score more than IRACRR DB 2 for women patients. SRS values attributed by IRACRR DB 2 are, regularly, significantly smaller hence, the consequences of AC can be different for each LV territory. What appeared as a perfusion defect in NC images, can become a near-normal homogeneous uptake with AC and be diagnosed often as normal. Thus, AC has to be used carefully as it can overlook possible significant lesions. Additionally, a comparison between SRS and clinical diagnoses were made in terms of sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV). The values obtained for these parameters are meant to give us an idea of how the summed rest scores agree with the physician diagnosis for each patient. Since abnormal clinical diagnoses for men were only 3, sensitivity results were heavily affected by a minor change. Typically, AC adjusts the intensity of the myocardial perfusion image to reflect the estimated magnitude of soft tissue attenuation on different regions of the LV. Thus, the relative uniformity of the tracer distribution in patients is improved, resulting in a better diagnostic accuracy [20, 21, 22], which usually results in fewer false-positives tests (higher specificity). These results are in concordance with the studies mentioned above, in which the specificity was higher with the use of AC. On the contrary, the sensitivity decreased in comparison with IRNCRR and WBR, hence it shows, without knowledge of the expected changes in activity distribution that occur with the use of AC, some MPI results can be misleading and cause to incorrectly misjudge a lesion. A closer look to IRACRR DB 2 false-negatives (3 for women's data and 1 for men's data) showed that the main difference was the under valorization of SRS values for LAD. Describing SRS values, only for LAD territory, in the vector form of (WBR,IRNCRR,IRACRR DB 2) for each study, the SRS values for the false negatives were (5,6,1), (7,7,1), (3,2,0),(5,5,1). With an exception of the third vector, the SRS results for LAD were enough, under the conditions adopted, to consider them as abnormal studies. Thus, part of the loss of sensitivity can be due to misjudgment of the LAD territory. Therefore, it is understandable the contradictory opinions about the influence and benefits of AC in SPECT-MPI, where some report good improvements [20, 21, 22] and others do not find much difference between them [17, 19, 23].

7. Conclusions

Due to their well-documented beneficial effect on image quality, the use of resolution recover and attenuation correction in SPECT have become widely used in Nuclear Medicine. This study compared LV quantitative parameters determined by 2 new methodologies, half-time Evolution for Cardiac and WBR reconstruction. The quality of the images, obtained with these half-time acquisitions, were for all studies equivalent or superior to that usually achieved with full-time acquisitions processed with FBP. In this work, the techniques described were

validated only for the single SPECT\CT system - the GE Optima NM\CT 640 Gamma Camera system (GE Healthcare) with high-resolution parallel-hole collimators manufactured specifically for that camera. Because resolution recovery and noise reduction are modeled specifically for each camera and collimator, these results may not coincide to other cameras and collimators. The first conclusion to be drawn was that, overall, WBR reconstruction algorithm had significant higher number of raw counts than Evolution for Cardiac with and without AC. Furthermore, we have that the addition of AC to SPECT images resulted on average, 5 times more raw counts. Some statistically significant differences were noted, between quantitative parameters of raw, normalized counts, severity and SRS values, obtained with the different reconstruction software, which makes decision fully based on them somewhat unreliable. This was true, specially, for RCA and LCX territory. In general, the results of our study confirm the usefulness of attenuation correction in addition to resolution recover in SPECT images. The assessment of the RCA territory seems to benefit most from it, which is in agreement with the results of other studies using various systems for attenuation correction [21, 22]. Because quantitative parameters attributed by Evolution with the use of AC are typically significantly smaller than for NC images, the consequences of AC can be different for each LV territory. Thus, what appeared as a perfusion defect in NC images can become a near-normal homogeneous uptake with AC and be diagnose often as normal. For this reason, AC has to be used carefully as it can overlook possible significant lesions. On the other hand, these difficulties in the interpretation of AC images can disappear in a matter of time if its use eventually becomes standard practice. Now, most physicians are used and prepared to evaluate in a certain matter the different color patterns showed in each study, based on their knowledge of where some attenuation or artifacts can appear in the LV. Because AC images have different standards, NM physicians may take some time to assimilate those differences. Because of the lack of an independent standard, it remains uncertain which of the approaches yields a more accurate result in this small number of cases. Further investigation with an independent standard such as PET would be necessary to settle this question. Therefore, as is the case for existing commercially available algorithms to evaluate LV function, the interpreting physician must be aware of these methodological differences and interpret scans accordingly. The phantom study showed that the raw data registered, for 4 acquisitions over a time period, with both Evolution for Cardiac algorithms follow the decay ^{99m}Tc. On the other hand, for WBR algorithm, the same acquisitions yield a number of raw counts approximately constant. The small number of subjects studied is a major limitation of the study and subsequent large scale clinical implementation of this novel image reconstruction algorithm requires a further larger patient study rigorously tested in standardized conditions.

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