Prone Myocardial Perfusion Imaging and Breast Attenuation: A Phantom Study

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Abstract: Background: Soft tissue attenuation artifacts are the most common cause of misinterpretation in myocardial perfusion imaging (MPI). Few studies assessing the value of prone imaging in women have been published. Breast attenuation artifacts can be present in up to 40% of the MPI studies in women.

Objectives: This study aimed at evaluating the potential impact of prone MPI on breast attenuation, with a critical analysis of activity optimization and breast size influence.

Methods: MPI of an Anthropomorphic Torso Phantom with silicone breast prostheses and equivalent adipose tissue was compared to a standard MPI database.

Results: A medical qualitative and semiquantitative analysis demonstrated higher uptake in the LV anterior segments in the prone position for all injected activities. An artificial myocardial lesion was diagnosable in the right segment in all images, which shows that prone positioning would not mask a true lesion and it assists the cardiologist with a more accurate analysis. These results showed that it is possible to optimize the activity to be injected by up to 55.6% when using combined supine-prone images.

Conclusion: Prone position has a high impact on the interpretation of MPI in female patients since it reduces the breast attenuation artifacts, and optimizes the radiation protection of the patient and all staff involved in the procedure, making it more cost-effective.

Keywords: Myocardial perfusion imaging, prone imaging, breast attenuation artifacts, activity optimization, breast size influence, anthropomorphic torso phantom, radiation protection.

1. INTRODUCTION

Cardiac imaging techniques such as Myocardial Perfusion SPECT Imaging (MPI), coronary catheterization, and PET/CT (Positron Emission Tomography) expose patients to radiation levels as high as 24 mSv per exam, and MPI performed with two radionuclides is at the top of these exposure rates [1]. The use of ⁹⁹mTc can lead to an effective dose of 16.3 mSv, and when combined with ²⁰¹Tl (dual-isotope protocol), it can reach 24.1 mSv [2, 3]. Therefore, one of the most critical issues regarding radiation protection that nuclear cardiologists should be continuously working on is how can MPI be optimized in a way that we inject less activity, maintaining the diagnostic accuracy [2].

MPI is an accurate and reliable diagnostic imaging technique for coronary artery disease (CAD), with well-recognized prognostic value [4]. However, the accuracy of the method is adversely affected by gender-specific factors in women [5-7]. Soft tissue attenuation artifacts are a limitation of MPI, affecting its accuracy mostly due to a decrease in specificity [8-12]. Several techniques have been used to identify these artifacts such as ECG-gating, attenuation-correction methods and prone imaging position [13].

Breast attenuation artifacts can be present in up to 40% of the MPI studies in women, decreasing counts in the anterior, anteroseptal or lateral wall of the left ventricle (LV) resulting in potential perfusion artifacts in the left anterior descending artery or left circumflex artery territories [11, 12, 14-19]. When there is a thick layer of breast tissue, radiation might be scattered and not captured by a gamma camera,
which can cause increasing false-positives or negatives, if this effect is overestimated. Therefore, for young women with large breasts, it can be quite challenging to get a conclusive diagnosis on the anterior wall [20, 21].

Supine position is usually used for MPI exams. However, this position is often associated with diaphragmatic attenuation [24-26] of the LV in the inferior wall, most commonly seen in men, and breast attenuation of the LV anterior in females [27]. Segall and Davis [28] first described the use of prone position imaging in MPI. Slomka et al. [19] showed that the combined quantitative analysis of prone and supine images in women yields significantly increased specificity and normalcy rates without compromising sensitivity for CAD detection. Glavam et al. [29] demonstrated that prone imaging has an impact on the interpretation of MPI images in women with suspected CAD. There were statistically significant differences between the average values of the summed stress (SSS) and summed difference (SDS) scores in supine and prone position. Lower perfusion score values in prone position images suggest less influence of soft tissue attenuation in that position. Also, 48.3% of the studies, initially considered as equivocal due to suspected soft tissue attenuation in supine position, were reclassified as normal after the combined analyses with prone images. In the last decade, a few studies have demonstrated that the combination of supine and prone positions is recommended, when possible, for patients with large breasts [19]. Ramos et al. and previous studies demonstrated with anthropomorphic phantoms that there are still opportunities to improve MPI protocols regarding injected activity, acquisition time and positioning [20, 30].

This study aimed to evaluate the potential impact of prone position imaging on breast attenuation, with a critical analysis of activity optimization and breast size influence.

2. MATERIALS AND METHODS

2.1. Image Acquisition

The study was performed in a two-detector Ventri™ gamma camera from GE Healthcare, and the reconstruction software was Xeleris™. The local two-day Protocol was performed, which is based on the ASNC guidelines [2]. The study used iterative reconstruction OSEM with attenuation, scatter, and resolution corrections, 64x64 matrix, 180° orbit, thirty projections per detector, step-and-shoot acquisition, pixel size of 6.4 mm. Technetium-99m MIBI was used in this study since it is the most used radiopharmaceutical for this procedure. Two-day protocol includes activities from 600 to 1332 MBq (16.2 to 36 mCi), based on international guidelines [2, 31].

2.2. Anthropomorphic Phantom

An Anthropomorphic Torso Phantom© (ECT/TOR/P, Data Spectrum Co.) (Fig. 1a), which simulates upper torso of average to large male/female patient (38 x 26 cm), was provided to evaluate perfusion. It has a heart insert which was used both with and without a solid artificial defect (1.0 cm thickness, 2 cm length).

Two external silicone breast prostheses in four different sizes were attached to the phantom, (Siligel Mamma© from Ortho Pauher) to analyze breast attenuation: S (small), M (medium), L (large) and XL (extra-large) corresponding to cup sizes from A to DD (Table 1). The equivalence between breast prostheses and breast tissues was analyzed by Computed Tomography in Hounsfield Units (HU), which matched the mean -200 ± 40 HU of the patients breast from a local database developed to validate the experiments.

The use of adipose tissue was also necessary since the body fat causes a significant attenuation in clinical practice [32]. A polymeric rubber (white arrow, Fig. 1b) was developed and attached to the phantom, and its composition and density were analyzed by X-ray fluorescence technique in a chemistry lab. The attenuation coefficients from equivalent adipose tissue were compared with the one from the database by CT to guarantee the equivalency.

Fig. (1). a) Anthropomorphic torso phantom ECT/TOR/P, Data spectrum corporation. b) The phantom in a Ventri GE gamma camera, with breast (black arrow) and adipose (white arrow) equivalent tissues. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

The concentration ratio for Myocardium: Liver: Background was 20:15:5, with total activity ranging from 740 to 1110 MBq (20 to 30 mCi). This concentration followed the
biodistribution of MIBI recommended by the phantom manufacturer, which means it does not represent an individual quantification of the patients’ specific biological uptake and wash out; however, this concentration was also verified during the validation process described here, and patient data was comparable to the activity concentration into the myocardium insert of the phantom [33].

2.3. Phantom Validation with Database

The results were compared to a group of healthy and low pre-test probability of CAD female patients, according to the criteria of Diamond and Forrester [34] to validate the obtained data. Forty randomly chosen retrospective exams (2010-2011) represented the standard range of the population, composing a local database (Table 2) [29] that could represent the normal uptake of the radiotracer in each LV segment analyzed. The counts in the segments were statistically compared with the ones from the phantom through T-Test (Software SPSS). The null hypothesis - H0 - was made to test the ability of the anthropomorphic phantom to simulate the cohort built with the database of patients, i.e., to validate its simulation ability. The mean injected activity in these patients was 925 MBq (25 mCi). This part of the study was analyzed and approved by an Ethics Committee.

2.4. Qualitative and Semiquantitative Medical Assessment

Two nuclear cardiology physicians blindly analyzed the phantom images which were anonymized separately and randomly, without the knowledge of position and breast size. The score of the medical assessment was divided into three categories:

1- Technical image quality (noise, artifacts, contrast).
   A = Excellent quality, nothing that could compromise the interpretation.
   B = Good quality, but with the presence of something that could jeopardize the interpretation.
   C = Bad quality, interpretation is compromised.

2- Perfusion.
   Normal = Homogeneous radiopharmaceutical uptake within all LV segments.
   Abnormal = Heterogeneous radiopharmaceutical uptake within all LV segments.

3- SSS (Summed Stress Score).

Table 2. Characteristics of the local database of patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean and Standard Deviation (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45.5 ± 10.6</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>25.0 ± 1.4</td>
</tr>
<tr>
<td>Bra Size</td>
<td>43 ± 1.0</td>
</tr>
</tbody>
</table>

2.5. Semiquantitative Software Assessment

To validate the findings in the images, counting profiles for supine and prone positions were built with the software ImageJ by fixed Regions of Interest (ROI) in each of the 17 segments of the myocardium from the American Heart Association [35] (Fig. 2) to compare the phantom images with the standard patient database.

The categorical variables, such as contrast, are reported as percentages. The percent contrast for each cold lesion was calculated by NEMA NU2 Equation 1 [36].

\[ Q_{c,j} = \left( 1 - \frac{C_{c,j}}{C_{b,j}} \right) \times 100\% \] (1)

Where:

\( C_{c,j} \) is the average counts in the ROI for lesion \( j \).
\( C_{b,j} \) is the average of the background ROI counts for lesion \( j \).

In myocardial perfusion imaging, the contrast between the target and the background is the signal-to-noise ratio. Since this was a study performed with a gamma camera
without a CT, we considered the background radiation as the noise in the phantoms images, i.e. the uptake in non-myocardial tissues.

The study had two sections:

I – Phantom validation: A fixed activity of 740 MBq and four breast sizes to evaluate their attenuation influence in prone positions.

II – Radiation exposure: Three activities (740, 925 and 1110 MBq) and extra-large breast to evaluate activity optimization between supine and prone positions.

3. RESULTS

3.1. Phantom Validation

All LV segments were analysed for each breast size, and when compared with the patient database, the results showed a $p > 0.05$; the lowest $p$-value was 0.20 in BAS segment, and the highest was 0.98 in ApL segment, showing weak evidence against the $H_0$, which means the countings in those patients were statistically equal to the ones in the phantom, and presented enough degree of normalcy to be used in comparison with the simulations.

Fig. (3) shows the software semiquantification of the 17 segments with different breast sizes and the database of patients. Simulations were capable of mimicking the physiological behavior of the LV segments from the database since the concentration ratio was statistically alike ($p > 0.05$).

However, the simulation that used the XL breasts (blue circles in Fig. 3) behaved differently from the other sizes, including the database, especially in the apex region (ApA, ApS, ApI, ApL), which shows that for this group there could be breast attenuation artifacts compromising the MPI results.

3.2. Activity Optimization and Comparison Between Supine and Prone Positions

3.2.1. Qualitative and Semiquantitative Medical Assessments

Fig. (4) shows the tomographic images of the phantom with XL breasts in supine and prone positions for each injected activity, and Table 3, the qualitative and semiquantitative medical assessment.

From Fig. (4), shows an increased perfusion uptake, mostly in anterior and inferior LV segments in short axis for prone position for 740 and 925 MBq of injected activities. This can be assigned to the breast tissue flattening when the phantom is set in this position, reducing the thickness which the radiation needs to pass through. The medical assessment of the supine images (Table 3) showed a mildly abnormal perfusion due to breast attenuation, and the prone images resulted in normal perfusion with a mild reduction in the basal anterior segment uptake.
Fig. (4). Tomographic images of the phantom with XL breasts in supine and prone positions for each injected activity. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

### Table 3. Medical assessment of the images in Fig. (4).

<table>
<thead>
<tr>
<th>Simulation with 740 MBq</th>
<th>Supine</th>
<th>Prone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical quality of the image</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Perfusion</td>
<td>Abnormal</td>
<td>Normal</td>
</tr>
<tr>
<td>SSS</td>
<td>5, being ApA = 1, MA = 1, BA = 1, BAL = 1, MAS = 1</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Simulation with 950 MBq</th>
<th>Supine</th>
<th>Prone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical quality of the image</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Perfusion</td>
<td>Abnormal</td>
<td>Abnormal</td>
</tr>
<tr>
<td>SSS</td>
<td>4, being ApA = 1, MA = 1, BA = 2, BI = 1</td>
<td>1, being BA = 1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Simulation with 1110 MBq</th>
<th>Supine</th>
<th>Prone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical quality of the image</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Perfusion</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>SSS</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
However, for 1110 MBq (Fig. 4) there is no perfusion increase when in prone position and there is no difference in the medical assessment as well. Both positions showed an SSS equal to zero, with normal perfusion, which is due to the higher injected activity that overcame breast tissue attenuation.

### 3.2.2. Semiquantitative Software Assessment by Injected Activities

For 740 MBq (Fig. 5) the counting was higher for prone position in LV segments ApA, ApI, MI, MIL, MAL, BA, BIS, BI and BAL, which showed a greater uptake in those areas. This difference was more significant (21.8% more...
uptake for prone) in the Mid Inferior segment than in the other ones.

For 925 MBq (Fig. 5) besides ApL, ApL, MIS, and MI which were statistically equal, all other segments presented higher uptake for prone position when compared to supine. The most considerable difference was in the Mid Anterior segment, with 39.3% higher uptake for prone.

For 1110 MBq, there was no improvement in image quality (Fig. 4) nor SSS (Table 3) or software counting (Fig. 5), when using both positioning.

The statistical signal to noise ratio measured into the concerned segments was an average of 30.82 ± 1.35% higher for prone position, which means there is a higher uptake for this position.

3.3. Study of Myocardial Abnormality – Artificial Defect

It is critical to demonstrate that there would be no error or misjudgment with prone positioning, i.e., lower uptake perfusion caused by a lesion should not be masked. Therefore, simulations with artificial defects were necessary to determine the real meaning of prone imaging and its impact.

An artificial lesion was placed in the Basal Inferior (BI) segment and simulations were made with XL breasts. Fig. (6) shows the images for both the positions and Table 4 shows the qualitative blind medical assessment of these images.

The lesion was diagnosable in the right segment for different injected activities, which shows that prone positioning would not mask a true lesion and it fundamentally assists the cardiologist with a more accurate analysis.

4. DISCUSSION

The high cost of the new scanners and the existence of a large set of conventional equipment create a barrier to the rapid dissemination of this new technology. While it is clear
that there is still a need to optimize dose and time for MPI on conventional scanners, it is not so clear what would be the most effective approach to validate it and introduce it into the clinical practice. Some recent studies have been following the approach of new software for reconstruction [37, 38].

The results of the present study focused on demonstrating that the prone imaging has a high impact on breast attenuation artifacts, caused mainly by extra-large breasts in the MPI interpretation.

The average count of radiotracer in each of the 17 segments of the phantom’s cardiac insert was compared to a standard database, and a similar pattern of radiotracer uptake was observed, validating the developed set up in this study.

Visual and semi-quantitative medical analysis showed low MIBI uptake in the anterior wall of the phantom’s cardiac insert for supine position, and normal uptake for prone imaging. Therefore, the phantom is capable of mimicking the breast attenuation, and prone imaging helps to identify this artifact.

Supine-prone image acquisitions are feasible, cost-effective and do not expose patients to an extra dose of radiation [39-41]. Recent studies concluded that when the two sets of images are available for analysis, the observer confidence in interpretation increases significantly [42, 43] and the rate of invasive coronary angiography after MPI is reduced [44]. Furthermore, previous authors showed that prone positioning has a high impact on the interpretation of MPI, mainly for younger female patients with larger breast sizes. A recent research from 2018 concluded however that further studies should be done to identify patients who should be preferentially imaged in the prone position to minimize scan time and improve clinical interpretive confidence [43].

The present study showed that it is possible to reduce the activity to be injected by up to 55.56% when compared to the 1332 MBq of maximum activity used in many facilities that follow ASNC protocols [2]. This reduction is meaningful when it comes to radiation protection of the patient, carers, and workers, and it helps to maintain the exposure as low as possible. The optimized protocol from this study is consistent with the purpose of MPI, and takes into account the state of technology with economic considerations, making it more cost-effective. Prone position is indispensable when using lower activities such as 925 MBq or 740 MBq since supine images showed decreased uptake, which could be mistaken as early ischemia. There is limited evidence in the literature demonstrating activities to be injected for optimal images in the different settings of MPI, as stated in the European Association of Nuclear Medicine - EANM - procedural guidelines from 2015 [47].

This study showed that it was possible to interpret and diagnose artificial lesions in every simulation; independently on how low was the injected activity (down to 740 MBq). In these cases, by adding prone images, the interpretation did not cover any lesion, helping the cardiologist to give a more accurate diagnosis.

Since the set up developed here - Anthropomorphic phantom with breast and adipose equivalent tissues - was validated to simulate real conditions observed during MPI acquisitions in women, this method could be replicated for other machines and settings. The phantom and the materials used to simulate the attenuation by breast and adipose tissues are commercially available.

CONCLUSION

(1) An anthropomorphic phantom needs breast and adipose equivalent tissues to be capable of simulating MPI with breast attenuation artifacts. (2) A combined supine-prone positioning has a high impact on the interpretation of MPI, mainly for younger female patients with larger breast sizes. (3) This type of MPI interpretation has a direct influence on patient dose since less than half of the activity needs to be injected to provide high-quality images.

LIST OF ABBREVIATIONS

ASNC = American Society of Nuclear Cardiology.
Ap = Apex
ApA = Apical Anterior
ApS = Apical Septal
ApI = Apical Inferior
ApL = Apical Lateral
BA = Basal Anterior
BI = Basal Inferior
BIS = Basal Inferoseptal
BAL = Basal Anterolateral
BAS = Basal Anterosetal
BIL = Basal Inferolateral
CAD = Coronary Artery Disease
ECG = Electrocardiogram
EANM = European Association of Nuclear Medicine
LV = Left Ventricle
MA = Mid Anterior
MPI = Myocardial Perfusion SPECT Imaging
MIL = Mid Inferolateral
MAS = Mid Anteroseptal
MIS = Mid Inferoseptal
MI = Mid Inferior
MAL = Mid Anterolateral
MIBI = Methoxyisobutylisonitrile
NEMA = National Electrical Manufacturer Association
PET/CT = Positron Emission Tomography–Computed Tomography
ROI = Regions of Interest
SSS = Summed Stress Score
SDS = Summed Difference Score
SPSS = Statistical Package for Social Sciences
99mTc = Technetium-99m
201TI = Thallium-201
XL = Extra Large

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Ethics Committee for Human Experimentation from the Hospital Copa D’Or, in Rio de Janeiro, Brazil (Reference Number: 308.130).

HUMAN AND ANIMAL RIGHTS

No animals were used in this study. The reported experiments on humans were followed in accordance with the ethical standards of the committee responsible for human experimentation (institutional national), and with the Helsinki Declaration of 1975, as revised in 2008 (http://www.wma.net/).

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author SMOR, upon request.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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