Hellenic J Cardiol 48: 211-217, 2007

Original Research

# Clinical Usefulness of Attenuation and Scatter Correction in Tl-201 SPECT Studies Using Coronary Angiography as a Reference

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Key words:
**Attenuation and scatter correction, myocardial SPECT studies, thallium 201, gadolinium 153 transmission.**

*Manuscript received:*
February 28, 2007;
*Accepted:*
April 25, 2007.

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**Introduction:** The aim of this investigation was to evaluate the clinical usefulness of both attenuation and scatter correction in $^{201}$Tl SPECT studies.

**Methods:** We studied 102 patients (76 males, 26 females, mean age 54 years) who underwent coronary angiography prior to or after a scintigraphic examination. A $^{201}$Tl one-day protocol was used. Simultaneous transmission-emission images were obtained by a γ-camera equipped with an attenuation and scatter correction system based on two moving collimated $^{153}$Gd rod sources. Stress and delay reconstructed images, uncorrected for attenuation and scatter, were diagnosed. One month later, stress and delay reconstructed images corrected for attenuation and scatter were diagnosed by the same readers. The results were compared using the coronary angiography findings as reference. A stenosis 50% or larger was considered significant.

**Results:** Attenuation and scatter corrected images demonstrated a significant increase in specificity for findings in the right coronary artery territory, i.e. 89% vs. 41% for uncorrected images ($p<0.05$), with a non-significant loss in sensitivity from 96% to 89%. When we split the population on a gender basis, statistically significant differences in specificity between corrected and non-corrected images were observed in the left anterior descending territory for the females (100% vs. 42%) and in the right coronary artery territory for males (87% vs. 26%).

**Conclusion:** Attenuation and scatter correction in $^{201}$Tl SPECT studies may significantly decrease false positive lesions in the inferior wall as well as in the anterior in females.

Single photon emission computed tomographic (SPECT) imaging with technetium 99m ($^{99m}$Tc) agents or thallium 201 ($^{201}$Tl) is widely used to estimate the presence and extent of coronary heart disease. Although the sensitivity of cardiac SPECT is high, the specificity ranges from 40% to 90% because of imaging artefacts mimicking either reversible or fixed defects.[1] Experienced readers can recognise these artefacts most of the time, but less experienced interpreters may lead patients to unnecessary catheterisation.

Among the most widely recognised sources of artifacts are breast and diaphragmatic attenuation, lateral chest attenuation in obese persons and photon scatter from adjacent structures.[2] Decreased image activity in the anterior and upper septal wall can be caused by increased breast attenuation. Also, decreased image activity in the inferior wall can be produced by diaphragmatic attenuation. Artefacts resulting from lateral fat pads may appear as defects in the lateral cardiac wall. The probability of photon absorption decreases as photon energy increases, and this is the reason why attenuation artefacts are less critical in $^{99m}$Tc SPECT than in $^{201}$Tl SPECT imaging,[3] but still important. In addition, Compton scatter decreases overall image resolution and contrast. Just as with attenuation, the deleterious effects of scatter are more evident in SPECT imaging with $^{201}$Tl than with $^{99m}$Tc.

Several methods have been proposed to solve the diagnostic confusion caused by attenuation or/and scatter. A popular approach is based on the use of planar imaging, breast binding, prone position and gated SPECT images. However, several limitations of these techniques have been reported: a) the prone position increases camera to chest wall distance and reduces image resolution; b) artefacts may also be caused by the sternum and ribs; c) breast binding increases the thickness of the breast; and d) normal regional wall motion on a gated SPECT study after stress is not helpful in distinguishing artefact from ischaemia in the presence of a reversible perfusion defect. None of these techniques provides unequivocal answers at all times.[4]

To date a number of methods have been developed in order to reduce the artificial change in activity caused by attenuation and scatter, so that the image more accurately represents the actual activity in the myocardium. Several types of systems with transmission hardware modifications and external sources have been used in clinical practice. The most widely used external source is gadolinium 153 ($^{153}$Gd, 100 keV), while cobalt 57 ($^{57}$Co, 122 keV), americium 241 ($^{241}$Am, 60 keV), barium 133 ($^{133}$Ba, 360 KeV) and $^{99m}$Tc (140 keV) have also been used.[5] The success of attenuation correction in clinical studies has been variable, with some reports being positive[6-12] and others negative[13-16] or without benefit.[17-18] But the studies comparing both attenuation and scatter correction are few.[19-22]

The aim of our study was to evaluate the clinical usefulness of a commercially available system for both attenuation and scatter correction based on two moving $^{153}$Gd collimated rod sources in $^{201}$Tl scintigraphy using coronary angiography as a reference.

## Materials and methods

### *Patient population characteristics*

Participants in the current study were 102 patients (76 males, 26 females; mean age 54 years) seen in daily clinical practice, who underwent coronary angiography within 3 weeks prior to or after the scintigraphic study without any change in cardiac condition or treatment. The most common reason for referral was for the diagnosis of chest pain (67 patients, 66%), which included both typical and atypical angina. Twenty-eight patients (27%) had a prior myocardial infarction and were referred for risk stratification. Another 7% (7 patients) were referred for assessment following coronary artery bypass grafting and/or percutaneous transluminal coronary angioplasty. Of the total study population, 46 patients (34 males, 12 females) were found to have significant (≥50%) coronary artery disease (CAD) on angiography, whereas 56 patients (55%) had no significant CAD. Most of the patients underwent an exercise test according to the Bruce protocol (achieving 85% of maximum age-adjusted predicted heart rate), but in 17 patients pharmacological vasodilatation with dipyridamole or adenosine was used as stress method because of neurological, orthopaedic, or peripheral vascular problems. All patients were intravenously injected with 111 MBq $^{201}$Tl one minute before termination of exercise. Images were obtained approximately 5 minutes after the injection of thallium at stress and four hours later at rest.

### *Instrumentation and scintigraphic data acquisition*

An L-shaped dual head γ-camera system (Optima NX, General Electric, Milwaukee, USA), dedicated for cardiac SPECT studies in our institution, was used. This camera is equipped with an attenuation and scatter correction system based on transmission scan acquisition. Acquisition of transmission images was implemented by a dual transmission source system. Opposite each detector, a box containing a collimated $^{153}$Gd rod source was mounted on the Optima NX gantry. The source is mechanically moved at constant speed along the long axis of the patient. The source is stored in a shielded parking position when not in use. Transmission images are generated by the $^{153}$Gd photons emitted from the rod sources, transmitted through the patient's thorax and detected by the crystal.

Patient data acquisition was performed using simultaneous interleaved acquisition mode. Namely, emission and transmission images were both acquired sequentially in one gantry stop and data acquisition was complete after one gantry rotation. Thirty-two projections were acquired through a 30% window centered on the 70 KeV peak and 20% on the 167 KeV peak in 16 stops over 180 degrees (90 degrees per head) extending from 45 degrees left posterior oblique to 45 degrees right anterior oblique in step and shoot mode with a 64x64 pixel matrix and zoom of one. The emission and transmission scan image acquisition time was set to 30 s/stop and 5 s/stop, respectively. These values are recommended by the manufacturer for $^{201}$Tl cardiac perfusion studies. A transmission scan equal to 5 s/stop has been found to result in sufficiently good image quality even for obese patients.[23] Transmission and emission images were acquired with the low energy general purpose detector collimators.

The ability of the camera to acquire up to four images simultaneously at different energy windows, coupled with the use of electronic image masking which follows source motion, allowed reduction of crosstalk from the emission scan into the transmission image. Multiple window acquisition also allowed final myocardial perfusion images to be corrected for both attenuation and scatter effects. The dual-window scatter correction was used. The dual-window technique makes the assumption that the scattered photons in the scatter window are linearly proportional to the scattered photons in the photo peak window.[24] Raw emission and transmission images were transferred to a Genie (General Electric, Milwaukee, USA) processing and review station. Transmission data were used to derive maps of attenuation coefficients through filtered back-projection. Attenuation and scatter-corrected myocardium SPECT images were derived using the attenuation maps and an iterative reconstruction processing method. Images not corrected for attenuation and scatter effects were also reconstructed. When necessary, images were motion corrected manually.

### *Evaluation of SPECT images*

Both uncorrected and corrected SPECT images (for attenuation and scatter) were uniformly reoriented to the short, vertical and horizontal axes for display and interpretation and studies with low count density or excessive patient motion were not included in the study. Stress and delay reconstructed images, uncorrected for attenuation and scatter, were diagnosed. One month later, stress and delay reconstructed images corrected for attenuation and scatter were diagnosed by the same readers. The readers were blinded to the angiographic findings, did not know the patient's gender and did not view the rotating projections to evaluate breast or diaphragmatic attenuation. Agreement was obtained between the readers in all cases. Each set of images was scored as: definitely normal, probably normal, equivocal, probably abnormal or definitely abnormal, using a nine-segment polar map (basal and distal anterior, lateral, inferior and septal walls and the apex). Equivocal images due to apical defects were considered as probably normal. These findings were compared using the angiography findings as reference. A reduction in vessel diameter of 50% or more was considered significant. To correlate results with vessel territories, anterior, septal and apical segments were assigned to the left anterior descending artery (LAD), lateral segments to the left circumflex artery (LCx) and inferior segments to the right coronary artery (RCA).

### *Statistical analysis*

Data analysis was carried out using the SYSTAT 8.0 for windows statistical software package (SPSS Inc, Chicago IL, USA). Results were expressed as mean ± standard deviation unless otherwise indicated. Receiver operating characteristics (ROC) analysis was used to compare the diagnostic value of the uncorrected images versus the attenuation and scatter corrected images. A p-value $<0.05$ was the criterion of significance.

## Results

### *Coronary angiography*

For comparison with the SPECT findings, lesions of the posterior descending branch were recorded as RCA. Left main coronary lesions were recorded as LAD and/or LCx disease. Diagonal lesions were considered as LAD and obtuse marginal arteries were considered as LCx.

In our population, 57 patients demonstrated no haemodynamically significant coronary lesions, 24 patients had single-vessel disease, 13 patients had 2-vessel disease and 8 patients had 3-vessel disease (i.e. ≥50 % stenosis in 0, 1, 2 and 3 coronary territories, respective-

**Table 1.** Global sensitivity and specificity on Tl-201 SPECT studies with (A&S cor) and without (non-cor) attenuation and scatter correction. Note that there is a statistically significant difference ($p<0.05$) only in specificity for findings in the RCA territory. LAD – left anterior descending artery; LCx – left circumflex artery; RCA – right coronary artery.

| | Sensitivity | | Specificity | |
|---|---|---|---|---|
| | non-cor | A&S cor | non-cor | A&S cor |
| LAD | 84% | 79% | 84% | 98% |
| LCx | 85% | 85% | 99% | 100% |
| RCA | 96% | 89% | 41% | 89% |

ly). Twenty-eight patients had stenosis of the RCA, 19 had stenosis of the LAD and 13 had stenosis of the LCx. No patient had left main artery disease.

### *Scintigraphic findings*

Of the total of 57 patients without CAD a normal SPECT study without attenuation and scatter correction was found in 19 patients, whereas in attenuation and scatter corrected studies 31 more patients had normal findings. Of these 50 patients, 32 were interpreted as definitely normal and the remaining 18 as probably normal due to apical artefacts.

In 24 patients with single-vessel disease, the attenuation and scatter correction study failed to detect 2 patients (1 with LAD stenosis, 1 with RCA stenosis), while in non-corrected studies, 7 patients without RCA stenosis (6 patients with LAD and 1 with LCx stenosis) were interpreted as probably abnormal in the inferior wall also. No differences in specificity and sensitivity were observed in 21 patients with 2 or 3-vessel disease.

Figures 1 to 3 show SPECT studies with and without attenuation and scatter correction.

Statistical testing of ROC curve areas showed that defect detection performance improved with attenuation and scatter correction when compared with performance without correction in the RCA region (Figure 4). Attenuation and scatter corrected images demonstrated a significant increase in specificity for findings in the RCA territory, i.e. 89% compared to 41% for uncorrected images ($p<0.0001$), with a non-significant loss in sensitivity from 96% to 89%. No significant differences in specificity and sensitivity were observed for findings in the other regions, when the attenuation and scatter corrected images were viewed instead of the uncorrected image set (Table 1).

When we split the population on a gender basis, statistically significant differences between corrected and non-corrected images were observed in the LAD territory for the females and in the RCA territory for males (Figures 5, 6).

An important negative result (of attenuation and

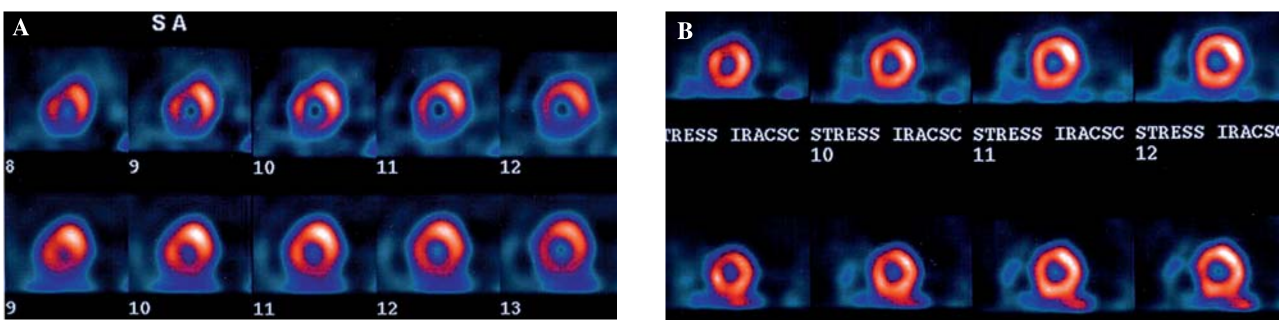


**Figure 1.** A 68-year-old male with chest pain underwent an exercise test according to the Bruce protocol. Panel A: on non-attenuation and scatter-corrected images (first row stress images, second row rest images), a reversible defect in the inferior wall was detected. Panel B: attenuation and scatter corrected images (first row stress images, second row rest images), reveal no perfusion abnormalities. The interpretation was normal. The patient had normal coronary angiographic findings.

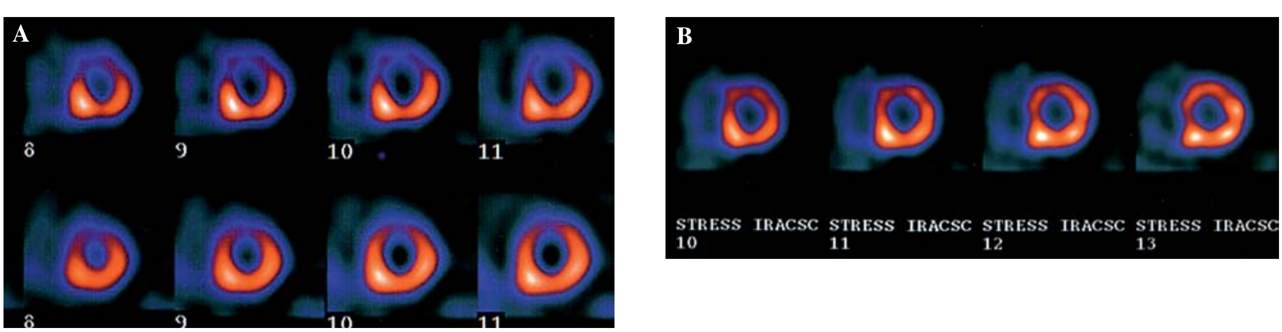


**Figure 2.** A 59-year-old female with non-anginal chest pain underwent pharmacological vasodilatation with dipyridamole because of orthopaedic problems. Panel A: on non-attenuation and scatter-corrected images (first row stress images, second row rest images), a reversible defect in the anterior wall was detected. Panel B: attenuation and scatter corrected images (stress images), reveal no perfusion abnormalities. The interpretation was normal. The patient had normal coronary angiographic findings.

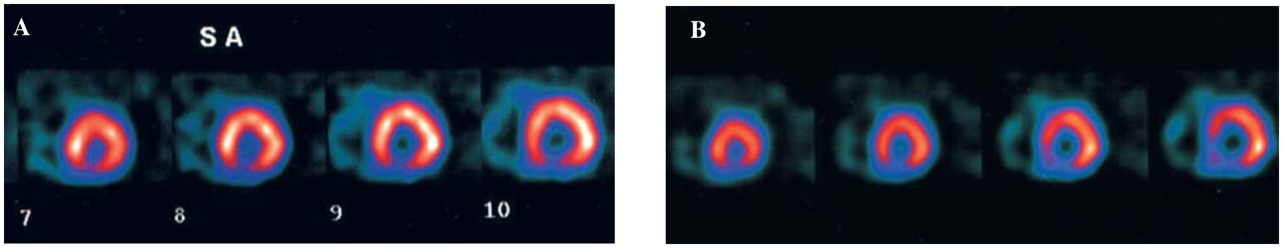


**Figure 3.** A 66-year-old male with chest pain underwent an exercise test according to the Bruce protocol. Panel A: on non-attenuation and scatter-corrected images (stress), a defect in the inferior wall was detected. Panel B: attenuation and scatter corrected images (stress) show a defect in the inferior wall as well the basal-septal region. The interpretation was abnormal. The patient had an 80% stenosis of the right coronary artery.

scatter correction with this method) was the creation of apical artefacts (false positive findings), which occurred in six subjects (two fixed defects, two reversible defects and two defects as reverse redistribution).

## Discussion

Methods that use transmission imaging for attenuation correction in SPECT were first investigated in the 1980s. In the past few years a wide range of equipment has been designed for transmission imaging with SPECT scanners. In our study we chose to validate the most widely used transmission source: $^{153}$Gd. The emission energies of 97 KeV and 103 KeV allow energy discrimination from both the 140 KeV photons of $^{99m}$Tc and the 72 KeV photons of $^{201}$Tl. $^{153}$Gd has a long half life of 242 days so it requires replacement infrequently and it is not expensive to manufacture.[25] According to Perisinakis et al,[26] the patient radiation exposure from the transmission scan is negligible compared to that from the radiopharmaceutical injected. Transmission data acquisition contributes to total radiation-induced fatal cancer risk from a cardiac SPECT procedure by less than $10^{-3}$ and to total genetic defect risk by less than $10^{5}$.

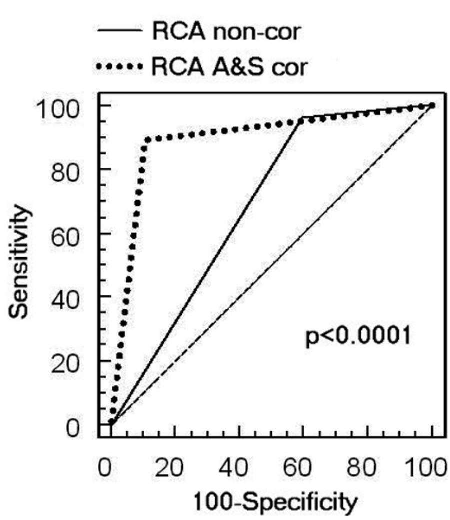


**Figure 4.** Receiver operating characteristics (ROC) analysis comparing the diagnostic value of the non-corrected images (non-cor) versus the attenuation and scatter corrected images (A&S cor) in the right coronary artery (RCA) region.

The ROC curves of non-corrected and attenuation and scatter-corrected studies confirmed an enhanced specificity with attenuation correction, particularly in areas supplied by the RCA. This result is comparable to that of Kluge et al,[27] who used $^{99m}$Tc-tetrofosmin and a system similar to ours, and to that of Vidal et al,[6] who used a different method of transmission scanning with $^{99m}$Tc and confirmed the increase in specificity for findings in the RCA territory but found it "deleterious" for the LAD territory assessment. The present study reveals an increased specificity for findings in the RCA territory, i.e. 91% compared to 41% for uncorrected images ($p<0.05$), with no significant differences in specificity for the other territories. The low specificity of data uncorrected for attenuation may be explained by the methodology of the protocol. The interpreters were unaware of any of the patients' data and the identification was removed. This kind of interpretation was necessary for an unbiased evaluation of each correction method and is not used in everyday routine.

The success of attenuation correction in clinical studies has been variable, with some reports positive [6-12] and others negative[13-16] or without benefit.[17-18] However, studies comparing both attenuation and scatter correction are few.[19-22]

A study by Ficaro et al[28] was performed without scatter correction and was among the most encouraging. The most important result of this study was the enhanced detection of multi-vessel stenoses with attenuation correction SPECT. In our study, patients with two- or three-vessel disease did not show significant differ-

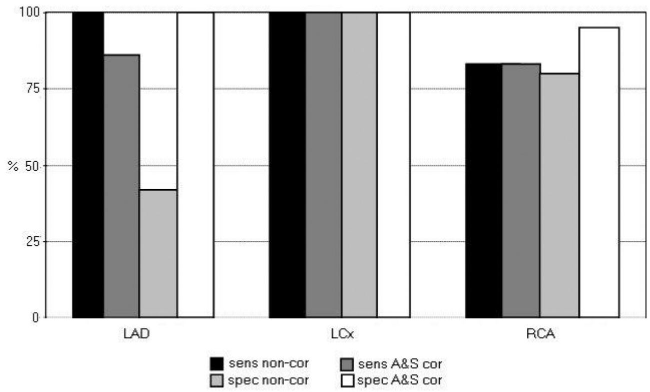


**Figure 5.** Sensitivity and specificity on Tl-201 SPECT studies with (A&S cor) and without (non-cor) attenuation and scatter correction in women. Note that there is a statistically significant difference ($p<0.01$) only in specificity for findings in the LAD territory. LAD – left anterior descending artery; LCx – left circumflex artery; RCA – right coronary artery.

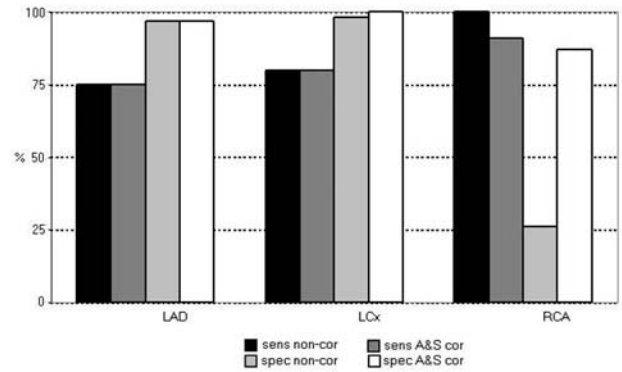


**Figure 6.** Sensitivity and specificity on Tl-201 SPECT studies with (A&S cor) and without (non-cor) attenuation and scatter correction in men. Note that there is a statistically significant difference ($p<0.001$) only in specificity for findings in the RCA territory. LAD – left anterior descending artery; LCx – left circumflex artery; RCA – right coronary artery.

ences in specificity and sensitivity in attenuation and scatter-corrected images compared to uncorrected images.

Several studies of healthy individuals[29] or patients[9,11,12,18,25,30] have been published with attenuation correction but without scatter correction. An overcorrection of inferior wall attenuation was documented. The relative increase in inferior wall counts was most likely caused by scattered photons coming from activity in structures near the heart, such as the liver and intestines. In our study this problem was overcome by the use of a scatter correction method. The combination of scatter and attenuation correction demonstrated an improvement in corrected image homogeneity.[19] In fact, the ratio of scattered photons included in the energy window (scatter fraction) is typically 0.34 for $^{99m}Tc$ and 0.95 for $^{201}Tl$.[20,21] In some patients the photon scatter effect is more severe in attenuation-corrected images. Because the attenuation correction procedure cannot distinguish scattered from non-scattered photons, both components are equally amplified during attenuation correction. As a result, the scattered radiation is more prominently displayed in the attenuation corrected images and poses a larger problem in the interpretation of these images compared with the uncorrected images. After attenuation correction, the abdominal activity, normally suppressed by the homogeneous attenuation below the heart, may be increased relative to the myocardial walls. It is thus evident that photo peak scatter compensation is essential for accurate attenuation compensation.[31]

As in earlier reports,[9,22,23,30,31] we also noted that attenuation correction sometimes leads to apical defects, which were considered to be related to the thinner apical wall and to the partial volume effect. The apical region is the shallowest portion of the heart and is the least impacted by attenuation. Thus, the apical region is artificially enhanced by attenuation. When the deeper portions of the heart are brought back to equal sensitivity with the apex through attenuation correction, the apical region counts appear suppressed compared with the thicker portions of the myocardium. This behaviour requires the physician interpreting the attenuation correction SPECT to recognise mild reductions in apical activity as normal. That is why, in our study, in attenuation and scatter correction images all the equivocal images due to apical defects were considered as probably normal.

Like Ficaro et al[9] and unlike Pretorius et al[22] and Dondi et al[32] we observed that the application of attenuation and scatter correction resulted in statistically significant differences between the male and female patients in the RCA and LAD territories, respectively.

## *Conclusion*

Attenuation and scatter correction using a collimated $^{153}Gd$ rod source increases the specificity for the RCA territory. Further studies are required to confirm the possibility that the present correction method affects coronary artery disease detection in the anterior wall in women.

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