

# Reduced-time myocardial perfusion study processed with “Myovation Evolution” — assessment of diagnostic efficacy

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## Abstract

**BACKGROUND:** While assessing images using standard segmental method, we felt that some defects were either underscored or missed. So this work is intended to compare results of low count myocardial perfusion studies (MPS) processed with „Myovation Evolution”, applying complete evaluation of all available slices, with full count studies and assess impact of reduction of counts on diagnostic efficacy of the study.

**MATERIAL AND METHODS:** A retrospective study was conducted in a group of 95 patients (56 males, age  $62 \pm 9$  years, BMI  $28 \pm 4$ ) with known or suspected CAD, without clinical history or any signs of a previous myocardial infarction. All patients underwent coronary angiography (CA) within 3 months of MPS. CA was used as a reference method for diagnostic performance of MPS. Patients underwent a stress/rest 2-day MPS. Both studies were performed twice, with normal (25 s) and shortened (13 s) time/projection. Studies were processed using Myovation protocol (OSEM, 2 iterations, 10 subsets) for full time (FT) studies and a Myovation Evolution protocol for half time (HT) studies (OSEM, 12 iterations, 10 subsets, Resolution Recovery). Reconstructed images, with and without attenuation correction (AC), were evaluated by 2 experienced nuclear medicine specialists (a consensus) visually, taking into account all available slices, in a 5-grade scale (normal, probably normal, equivocal, probably abnormal and abnormal). Study results were additionally dichotomized as normal or abnormal. Perfusion defects were assigned to coronary arteries.

**RESULTS:** An exact agreement between FT and HT study assessment, without AC, amounted to 66%, with AC it grew to 79%,  $p = 0.05$ . In studies without AC 10 perfusion defects were found only in HT studies in RCA area in male patients. A higher percentage of studies with perfusion defects in RCA area visible only in HT studies was found among discordant (7/25, 28%) than concordant results (3/70, 4%),  $p = 0.003$ . AC reduced this difference. HT study provided lower accuracy in detection of CAD than FT study (58% vs. 68%,  $p = 0.034$ ). AC reduced this difference considerably. Dichotomized assessment agreed in 81% of studies without AC and in 87% with AC.

**CONCLUSIONS:** Myovation Evolution protocol requires application of AC otherwise perfusion defects in RCA area in male patients are falsely detected. Shortened studies reconstructed with „Myovation Evolution” package without AC reveal a tendency toward reduction of accuracy of the study in detection of CAD. AC makes up for this reduction.

**KEY words:** myocardial perfusion imaging, Myovation Evolution, attenuation correction, dose reduction

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## Background

Diagnostic and prognostic usefulness of myocardial perfusion imaging, a non-invasive study presenting myocardial perfusion at cardiomyocyte level, is nowadays beyond question [1, 2]. However, a quickly growing number of imaging studies applying ionizing radiation forces a tendency toward reduction of patient exposure [3]. This proceeding is in agreement with a fundamental rule of radiological protection that patient exposure should be as low as reasonably achievable. It applies also to patients with coronary artery disease (CAD), a considerable part of whom undergo repeat diagnostic and therapeutic procedures using ionizing radiation. In case of radionuclide studies, reduction of radiation dose implies administration of lower radiopharmaceutical activity, which is especially important when technetium-99m labeled tracers are used because of periodic problems with availability of this radionuclide [4]. However, quality of radionuclide images, also of SPECT studies, depends on the level of a statistical noise which is reduced with the number of acquired gamma rays forming images. For this reason projection images containing reduced number of counts (as a result of lower activity or shortening of acquisition time) require a specialized reconstruction software preserving good quality of reconstructed SPECT images.

A rapid development of image processing methods encouraged introduction of advanced software into tomographic image reconstruction. A sophisticated software making use of three-dimensional reconstruction procedure including resolution recovery was introduced which, together with noise regularization methods, preserves good quality of reconstructed images in spite of reduction of counts in raw projections. As examples of implementations of this procedure „Evolution for Cardiac” by GE Healthcare, „Astonish” by Philips and „Flash3D” by Siemens can be mentioned.

We showed in our previous publication concerning this topic [5], that making use of „Myovation Evolution”, a part of „Evolution for Cardiac” package, requires application of attenuation correction (AC). In the present work image evaluation method taking into account all available slices in all three planes instead of only four selected slices used in a standard method was applied. Previously, while assessing images with the standard method, we felt that some defects were either underscored or missed. This work is intended to compare results of reduced- and full-time studies and also compare their diagnostic efficacies with and without AC giving stronger arguments in favor of this correction.

## Material and methods

A retrospective study was conducted in a group of 95 patients (56 males and 39 females, aged  $62 \pm 9$  years, BMI:  $28 \pm 4$ ) with known or suspected CAD, without clinical history, electrocardiographic or echocardiographic signs of a previous myocardial infarction or any other factors affecting myocardial perfusion, like cardiomyopathy, severe aortic valve disease or left bundle branch block or a history of CABG. All patients underwent coronary angiography less than 3 months before or after myocardial perfusion imaging. The study was approved by the Medical University Bioethics Committee.

## Myocardial perfusion imaging — study acquisition and reconstruction

Study acquisition and reconstruction was presented in details in our previous publication [5]. In short: SPECT/CT studies were acquired with a hybrid Infinia 2 Hawkeye 4 (GE Healthcare) camera after administration of  $^{99m}\text{Tc}$ -MIBI, in activity of 11 MBq per kilogram of body mass. A 2-day study protocol was applied. Before stress study a physical exercise or a dipyridamole infusion was used. A standard acquisition (25 seconds per projection) was complimented with shortened one (13 s). Aside from specified above acquisitions a low dose CT study (140 keV, 2.5 mA) was carried out that was afterwards used for correction of gamma rays attenuation inside a patient body (attenuation correction — AC).

Studies were processed on GE Xeleris™2 work station, using Myovation protocol (OSEM with 2 iterations and 10 subsets) for full time (FT) studies and a Myovation Evolution protocol dedicated to shortened studies (OSEM with 12 iterations, 10 subsets) implementing resolution recovery and noise regularization procedure for processing of half time (HT) studies. Besides, if projection images or sinogram showed patient movement, a correcting procedure called “Motion Correction” was applied. Every time attenuation correction was used, an alignment of emission and transmission slices was visually checked and corrected, if necessary. After reconstruction images were filtered using a 3D Butterworth filter with following parameters: cutoff frequency — 0.52, order 5.

## Myocardial perfusion imaging — evaluation of study

Reconstructed images were evaluated by consensus of 2 experienced nuclear medicine specialists taking into account all available short axis, coronal and sagittal slices. Interpreters were informed only of a patient sex and if attenuation correction was applied during study reconstruction; they were not aware of a study protocol (FT or HT) or results of coronary angiography. Myocardial perfusion was assessed in a 5-grade scale: 0 — normal (N), 1 — probably normal (PN), 2 — equivocal (EQ), 3 — probably abnormal (PA) and 4 — abnormal (A). If perfusion defects were observed, their location was assigned to one or more of three coronary arteries: left anterior descending (LAD), left circumflex (LCx) or right (RCA). Study results were additionally divided into normal and abnormal, after grouping of 0 and 1 results into a category of normal and 2, 3 and 4 into a category of abnormal findings.

After at least 2 months FT images were interpreted again by the same specialists. Based on those results, repeatability of FT study interpretations was obtained that was afterwards treated as a reference value for the agreement between FT and HT study results.

## Coronary angiography

Invasive contrast coronary angiography was performed according to standard percutaneous techniques, with each arterial segment visualized in at least 2 perpendicular planes. Angiograms were analyzed by experienced angiographers unaware of SPECT imaging findings. Significant CAD was defined as  $> 70\%$  luminal diameter narrowing by visual inspection in at least one of the three coronary arteries (LAD, Cx and RCA) and  $> 50\%$  in the left main coronary artery. Coronary angiography findings were subsequently used as a reference for the analysis of diagnostic performance of myocardial perfusion study protocols.

**Table 1.** Cross tabulation of FT and HT (A) and FTAC and HTAC (B) studies assessment. Results with agreement beyond  $\pm 1$  range are shown with smaller numbers. N — normal, PN — probably normal, EQ — equivocal, PA — probably abnormal and A — abnormal

A FT vs. HT kappa 0.52 Exact agreement 66% Agreement $\pm 1$ –74%		HT				
		N	PN	EQ	PA	A
FT	N	27	1	6	1	1
	PN		1	1	2	
	EQ	2	1	4		6
	PA	1	3	1	1	2
	A			3	1	30

B FTAC vs. HTAC kappa 0.63 Exact agreement 79% Agreement $\pm 1$ –88%		HTAC				
		N	PN	EQ	PA	A
FTAC	N	47	2	1	2	
	PN	2	1	1		2
	EQ	2		1		1
	PA	2			2	1
	A		2		3	23

### Statistical analysis

Agreement between results was assessed with cross tabulation and Cohen's kappa coefficients. Agreement between dichotomized results was assessed using 95% confidence intervals for binomial distributions. Indices of diagnostic efficacy in detection of CAD were obtained based on ROC analysis. Statistical significance of differences between indices of diagnostic efficacy was assessed with McNemar's test for paired proportions.

## Results

### Coronary angiography

In 37 patients (37 out of 95, 39%) coronary angiography revealed critical stenosis of at least one coronary artery, so results of these studies were considered positive. Studies of remaining 58 (61%) patients were negative. Among positive results critical stenosis was found in 20 LAD, 9 Cx and 19 RCA arteries. In 26 patients one artery was stenosed and in 11 — two.

### Perfusion study

An exact agreement between FT and HT study assessment, without AC (Table 1A) amounted to 66% (kappa 0.52), whereas after application of AC (Table 1B) it grew to 79% (kappa 0.63). This improvement of agreement turned out statistically significant ( $p = 0.05$ ). Agreement within  $\pm 1$  grade without AC was equal to 74%, whereas with AC — 88%.

After application of AC during study reconstruction, number of studies assessed concordantly was almost twice as high as without AC — Table 2. At the same time AC strongly reduced numbers of studies with uncertain results, i.e. probably normal (PN), equivocal (E) and probably abnormal (PA), from 25 and 26 in FT and HT studies to 15 in both studies reconstructed with AC (FTAC and HTAC).

**Table 2.** Numbers of full time and half time studies, reconstructed without AC and with AC, concordantly assessed as normal and with uncertain interpretation

	Without AC	With AC
Concordantly assessed as normal (N)	27	47
Uncertain results (PN, EQ, PA)	FT: 25 HT: 26	FTAC: 15 HTAC: 15

### Location of perfusion defects

In studies without AC the most apparent asymmetry can be observed in Table 3 in RCA area, where 10 small perfusion defects were found only in HT studies. From those 10 defects 8 were detected in males and only 2 were confirmed by coronary angiography. Seven out of those 8 defects, as falsely positive, compromised specificity of a HT study in relation to coronary angiography.

Seven out of those 10 defects were found among 25 discordant results (numbers on light background in Table 1A), and the remaining 3 were among 70 concordant results (numbers on dark background in Table 1A). It points at a higher percentage of studies with perfusion defects in RCA area visible only in HT studies among discordant results (7 out of 25, 28%) than among concordant results (3 out of 70, 4%),  $p = 0.003$ , and therefore may be one of causes of limited agreement between assessments of FT and HT studies.

No relationship between occurrence of false positive defect in inferior wall in HT study and patient obesity expressed in terms of a body mass index was found.

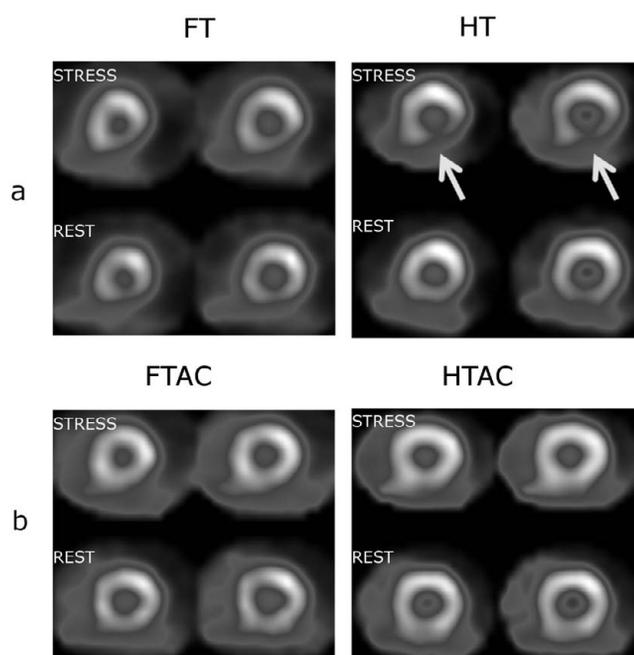
Application of AC reduced the mentioned above asymmetry in detection of perfusion defects in the inferior wall (Table 3B). An example of a difference in infero-lateral wall in FT and HT studies can be observed in Figure 1A. AC reduced this difference (Figure 1B).

**Table 3.** Cross tabulation of perfusion defect locations in studies without AC (A) and with AC (B)

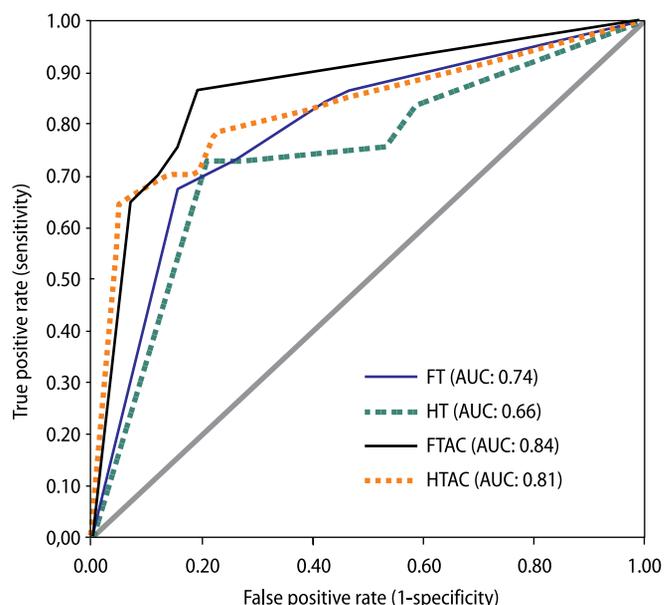
A FT vs. HT		HT			
	–	LAD	LCx	RCA	
–		2	1	10	
LAD	3	18			
LCx	1		6		
RCA	2			36	

B FTAC vs. HTAC		HTAC			
	–	LAD	LCx	RCA	
–		3		5	
LAD	4	12			
LCx	1		7		
RCA	3			20	

**Figure 1A.** FT study (assessed as normal) and HT study (assessed as probably abnormal, with perfusion defect in infero-lateral wall — arrows); **B.** Attenuation correction filled in perfusion defect (both studies assessed as normal)**Diagnostic efficacy of normal and shortened studies**

ROC analysis (Figure 2) enabled comparison of areas under those curves as well as indices of diagnostic efficacy in detection of CAD (Figure 3). Areas under ROC curves in shortened studies were smaller than in full time studies, with and without AC, although these differences did not attain statistical significance. HT study provided lower indices of diagnostic efficacy than FT study, although only a difference between accuracies of methods turned out statistically significant ( $p = 0.034$ ). Attenuation correction reduced differences between diagnostic efficacies considerably and

**Figure 2.** ROC curves for 4 methods used for myocardial perfusion assessment. AUC — area under ROC curve

statistically significantly improved specificities of both FTAC and HTAC methods ( $p < 0.01$ ).

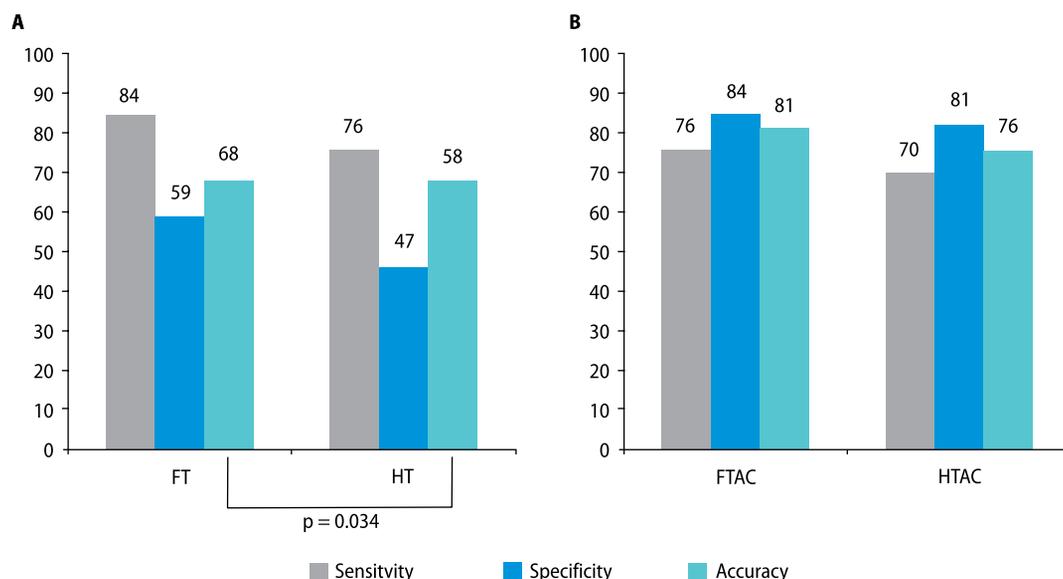
A dichotomous categorization of results into normal and abnormal (Table 4) provided agreement in 81% of studies without AC (kappa 0.61) and in 87% (kappa 0.74) of studies with AC.

**Repeatability of study assessment**

Table 5A presents agreement between FTAC and HTAC studies (87%), the same as Table 4B, but this time along with repeatability of assessments of FTAC studies (91%) — Table 5B. Ninety five percent confidence intervals calculated for agreement between FTAC and HTAC studies ( $CI_{95\%}$  [80–94]) and repeatability of FTAC study ( $CI_{95\%}$  [85–97]) overlap to a large extent. This fact does not allow to reject a hypothesis that agreement between FTAC and HTAC study results is not worse than repeatability of FTAC study interpretations.

**Discussion**

Software providing reconstructed images of good quality obtained from studies consisting of lower numbers of counts is very helpful in every day practice of nuclear medicine departments. On the one hand, it permits to administer a lower activity of a radiopharmaceutical reducing patient radiation dose. On the other hand, shortening of a study acquisition becomes possible resulting in the improvement of patient's comfort. If a typical, full time imaging procedure is applied, making use of a dual head Anger gamma camera, a patient is supposed to lie motionless with his left arm above head for about 15 minutes. It is very demanding and uncomfortable for considerable number of patients. Although new, semiconductor-based gamma cameras with much higher sensitivity are being introduced now into practice, they still form only a small part of instrumentation used in nuclear medicine.



**Figure 3.** Diagnostic efficacy of **A.** full time (FT) and half time (HT) studies without attenuation correction and **B.** full time study with attenuation correction (FTAC) and half time study with attenuation correction (HTAC). Attenuation correction statistically significantly improved specificities and accuracies of both FTAC and HTAC methods ( $p < 0.01$ )

**Table 4.** Cross tabulation after dichotomous categorization of study results into normal and abnormal without **(A)** and with **(B)** attenuation correction

<b>A</b> FT vs. HT		HT	
		Normal results	Abnormal results
kappa 0.61			
Agreement 81%			
FT	Normal results	29	11
	Abnormal results	7	48

<b>B</b> FTAC vs. HTAC		HTAC	
		Normal results	Abnormal results
kappa 0.73			
Agreement 87%			
FTAC	Normal results	52	6
	Abnormal results	6	31

**Table 5.** Cross tabulation after dichotomous categorization of FTAC and HTAC studies **(A)** vs. FTAC and FTAC study — repeat assessment **(B)**

<b>A</b> FTAC vs. HTAC		HTAC	
		Normal results	Abnormal results
kappa 0.73			
Agreement 87%			
FTAC	Normal results	52	6
	Abnormal results	6	31

<b>B</b> FTAC vs. FTAC		FTAC	
		Normal results	Abnormal results
kappa 0.80			
Repeatability 91%			
FTAC	Normal results	52	6
	Abnormal results	3	34

According to our previous publication concerning this topic [5], reconstructed images obtained from shortened studies were

of good quality, comparable with full time studies. This good quality was attained thanks to implementation of three-dimensional reconstruction procedure with resolution recovery. However, if one of studies is reconstructed with a software using resolution recovery (shortened study) and the other one without it (full time study), differences between reconstructed images are unavoidable. Therefore, a question arises whether those differences are clinically important.

In a visual assessment, taking into account all available slices of studies reconstructed without AC an exact agreement in a 5-grade scale amounting to 66% (in the range  $\pm 1$  to 74%) was attained, and if AC was applied during study reconstruction it was improved to 79% (in the range  $\pm 1$  to 88%). A more frequent detection of perfusion defects in the inferior wall in half time study in male patients, not supported by coronary angiography results, was identified as one of causes of discordances between interpretations of full time and half time studies reconstructed without AC. Those defects were small but were observed consistently in a shortened study. Attenuation correction reduced differences between full time and half time studies to a large extent.

After dichotomous categorization of study results into normal and abnormal ones attenuation correction improved an agreement from 81% to 87%. Those values are not as high as the ones presented by Ali et al. [6], Valenta et al. [7], and Armstrong et al. [8], who also made use of „Evolution for Cardiac“ software package. They obtained agreement between full time and half time studies equal to 95% without AC and 96% with AC [6], 96% with 100% agreement in a clinical interpretation [7], and 83% to 96% (in case of acceptance of minor inconsistencies) [8]. A more detailed analysis of results presented in specified above publications was provided in our previous publication [5].

Only in a publication by Lawson et al. [9], presenting results of a multi-center trial conducted in sixteen nuclear medicine departments in Great Britain a lower agreement between full and half time studies were obtained. In 41% of patients results of standard and shortened stud-

ies differed, and in 10% in a clinically significant way. In general, results of our work agree with the ones obtained by Lawson et al.

Patients after myocardial infarction were not accepted in our work in order to avoid a difficulty of interpretation caused by overlapping of stress induced hypoperfusion with post-infarction scar because results of myocardial perfusion imaging were compared with coronary angiography. In this way indices of diagnostic efficacy in detection of CAD for all applied methods (full time and half time, with and without AC) were obtained. Although Gutstein et al. [10] studied a diagnostic efficacy of low count studies reconstructed with Myovation Evolution protocol in relation to coronary angiography and obtained sensitivity and specificity equal to 89% and 75%, respectively, their studied material was small, especially a group of patients without critical stenoses of arteries, which consisted of 16 people. Besides, they did not apply attenuation correction while reconstructing studies. To our knowledge this is the first publication presenting not only agreement between results of full and reduced count studies processed with „Evolution for Cardiac” software package, but also comparing their diagnostic efficacy with and without attenuation correction. Other results of works comparing diagnostic efficacy of full and reduced count studies can be found in the literature [11, 12], but they do not concern „Evolution for Cardiac” software.

Areas under ROC curves obtained for different reconstruction methods turned out lower for shortened than for full time studies although no statistical significance was attained. Moreover, indices of diagnostic efficacy of a shortened study processed without AC turned out lower than those of a full time study although a difference attained statistical significance only for accuracy of both methods. Study results point to slightly different pattern of perfusion image in inferior wall in male patients, of a study reconstructed with Myovation Evolution protocol. This seemingly lower uptake of a tracer may be misinterpreted as perfusion defect. Study results point to negative effect of false defects visible in inferior wall in HT study, not confirmed by coronary angiography, on diagnostic accuracy of the study. Interestingly, no relationship between occurrence of those defects and patient obesity expressed in terms of a body mass index was found. The same trend (lower indices of diagnostic efficacy obtained for a shortened study) although less noticeable, could be observed in our previous work presenting results of interpretation of studies of the same patients but using different, segmental method [5]. Attenuation correction reduced differences between indices of diagnostic efficacy of full time and half time studies considerably.

Results of the present work also show that agreement between visual assessment of FTAC and HTAC studies (87%) is not statistically significantly different from repeatability of a dual assessment of FTAC study (91%). These results should be interpreted in such a way that possible real differences between images in full time and half time studies are not so significant as to surpass the subjectivity of a visual method used for study evaluation. More objective, quantitative method was not available at the time of this project due to lack of normal data base dedicated to studies processed with Myovation Evolution software.

Application of a method taking into account all available slices, not only those used in a segmental method, followed our observation that in many cases sagittal and coronal slices make visual evaluation of perfusion images much more confident.

## Conclusions

Myovation Evolution protocol dedicated to reconstruction of myocardial perfusion studies with reduced number of counts should include attenuation correction, otherwise a perfusion pattern in inferior wall in male patients may be misinterpreted as abnormal. Discordances observed during visual assessment of normal and reduced count studies reconstructed with AC are statistically not significantly larger than disagreements between dual assessment of a full count study. Shortened studies reconstructed with „Myovation Evolution” package without AC reveal a tendency toward reduction of accuracy of the study in detection of CAD. Attenuation correction makes up for this reduction.

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