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Original

Comparison of shortened gated myocardial perfusion imaging processed with „Myovation Evolution" with full time study

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Abstract

BACKGROUND: The work compares the results of shortened gated myocardial perfusion imaging (MPI), processed with „Myovation Evolution" software, with a study performed in a standard way.

MATERIAL AND METHODS: A retrospective study was conducted in a group of 95 patients (56 males and 39 females, age 62 ± 9 years, BMI 28 ± 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 MPI. CA was used as a reference for diagnostic performance of MPI. Patients underwent a stress/rest 2-day MPI. Both studies were performed twice, with normal (25s) and shortened (13s) time per projection. Studies were processed using Myovation protocol (OSEM with 2 iterations and 10 subsets) for full time (FT) studies and a Myovation Evolution protocol dedicated to half time (HT) studies (OSEM with 12 iterations, 10 subsets). Reconstructed images, with and without attenuation correction (AC), were evaluated by 2 experienced nuclear medicine specialists (a consensus), with regard to image quality and perfusion, evaluated using a visual semi-quantitative method, applying a standard division of myocardium into 17 segments. Perfusion was assessed in every segment using a standard 5 grade scale. Summed stress scores were calculated for every patient and threshold values for detection of CAD were selected based on ROC analysis with CA treated as a reference method. After 2 months FT images were interpreted again by the same specialists.

RESULTS: The quality of images obtained from shortened and normal studies was equally good. All correlation coefficients between segmental scorings of FT and HT studies were high and statistically significant. Correlation coefficients between corresponding segments in FTAC and HTAC (i.e. with AC) studies were systematically higher than without AC. The agreement between FT and HT study results was equal to 81% for FT and HT studies and to 86% for FTAC and HTAC studies ($p = 0.40$). The repeatability of FTAC study assessments was equal to 94%. 95-percent confidence intervals calculated for agreement between FTAC and HTAC studies and the repeatability of FTAC study overlapped considerably. Correlation coefficients for EDV, ESV and EF values between FT and HT were high: 0.93, 0.96 and 0.88, respectively.

CONCLUSION: Myovation Evolution protocol used for reconstruction of myocardial perfusion studies with reduced number of counts requires AC. The agreement between the results of visual assessment of normal and reduced count studies is high and not worse than the agreement between repeat assessment of a full time study.

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

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Background

Myocardial perfusion imaging is a non-invasive study revealing perfusion at a cardiomyocyte level. Thanks to its high diagnostic efficacy the study has gained approval in many countries. Perfusion image together with its quantitative analysis provide valuable data facilitating diagnosis of coronary artery disease (CAD), the assessment of the efficacy of its therapy as well as prognosis of adverse cardiac events [1, 2]. However, a relatively long SPECT study acquisition is considered its drawback. It is especially true for Anger gamma cameras with scintillation detectors still widely used in nuclear medicine departments. In case of this study it is necessary for a patient to lie motionless with left arm behind the head for about 15 minutes. Moreover, a pronounced trend toward a radiation dose reduction due to a rapid increase in the number of studies making use of ionizing radiation can be noted [3]. When 99m-technetium labeled radiopharmaceuticals are used, patient effective dose is assessed to be about 12mSv [4]. Although this dose is quite low, a trend toward dose reduction is noted in all imaging methods using ionizing radiation. In case of radionuclide studies dose reduction can be attained by administration of a lower radiopharmaceutical activity. However, this approach results in a study consisting of a smaller number of counts. As can be inferred from information presented above, there is a need for image reconstruction methods preserving good image quality in spite of reduced number of counts collected during study acquisition.

The producers of software dedicated to SPECT studies meet those expectations by the refinement of image reconstruction methods. New approaches can reduce image noise without a degradation of its resolution. An example of such a software can be found in the „Evolution for Cardiac" package (GE Xeleris^{TM}2*)* as a myocardial perfusion imaging reconstruction software "Myovation Evolution". If a diagnostic value of images reconstructed with this software were close to value of images obtained in a standard way, it would be possible to shorten study acquisition or administer a lower activity of a radiopharmaceutical resulting in reduction of patient radiation dose. This work intends to compare results of shortened myocardial perfusion study processed with „Myovation Evolution" software with a study performed in a standard way.

Material and methods

A retrospective study was conducted in a group of 95 patients (56 males and 39 females, age 62 ± 9 years, BMI: 28 ± 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 Study — Acquisition and Reconstruction

Patients underwent a stress/rest double day myocardial perfusion imaging. In 74 (78%) patients an exercise stress test according to Bruce protocol was performed and the remaining ones had a dipyridamole infusion (0.56–0.70 mg/kg in 4 min.). Beta blockers, nitrates, calcium channel blockers and trimetazidine were discontinued for 48 hours before a stress study. Radiopharmaceutical — Tc-99m methoxy-isobutyl-isonitryl (MIBI), in activity of 11 MBq per kilogram of body mass, was administered intravenously at peak stress or 3–6 minutes after dipyridamole infusion. After administration of a radiopharmaceutical patients ate a fatty meal to accelerate hepatobiliary clearance of the tracer. Stress study acquisition was started 45 minutes and rest study — 1 hour after administration of a radiopharmaceutical. Gated SPECT/CT studies were performed with a hybrid Infinia Hawkeye 4 (GE) camera, equipped with low energy high resolution (LEHR) collimators set in L-mode. Study protocol consisted of acquisition of 60 projections in a matrix 64 × 64 (zoom 1.28) using „step & shoot" mode and a circular orbit. Cardiac cycles were divided into 8 time intervals. Stress as well as rest studies were performed twice, with normal (25s) and shortened (13s) time per projection. Aside from specified above acquisitions: standard (FT — full time) and shortened (HT — half time), a low dose CT study (140 keV, 2.5 mA) was carried out that was afterwards used for attenuation correction — AC).

Studies were processed on GE Xeleris^{TM}2 work station, using Myovation protocol (OSEM with 2 iterations and 10 subsets) for FT studies and a Myovation Evolution protocol dedicated to shortened studies (OSEM with 12 iterations, 10 subsets) for processing of HT studies. Myovation Evolution software makes use of resolution recovery (RR), correcting for the phenomenon of resolution distortion with growing distance between imaged object and a collimator. 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. In case of misalignment, CT slices were manually shifted and after a proper alignment a repeat reconstruction was performed. After reconstruction images were filtered using 3D Butterworth filter with following parameters: for gated studies cutoff frequency 0.4/order 10, for non-gated images 0.52/5. End-diastolic and end-systolic volumes (EDV and ESV) as well as ejection fraction (EF) were calculated making use of QGS/QPS protocol applied to rest studies. All studies were processed by the same operator.

Myocardial Perfusion Study — Image Assessment

Reconstructed images were evaluated by 2 experienced nuclear medicine specialists (a consensus), with regard to image quality, assessed as good, medium or bad, as well as perfusion. 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 evaluated using a visual semi-quantitative method, applying a standard division of myocardium into 17 segments [5]. Perfusion was assessed in every segment in a 5 grade scale: 0 — normal, 1 — slight (equivocal) reduction, 2 — moderate reduction, 3 — severe reduction of uptake, 4 — absence of radiopharmaceutical uptake. In order to compare segmental scorings of FT and HT studies, stress and rest images were pooled together and Spearman's correlation coefficients between scoring in respective segments were obtained. Next, summed stress scores (SSS) were calculated for every patient and threshold values for detection of CAD were selected based on ROC analysis with coronary angiography treated as a reference method. Analyses of agreement of FT and HT studies and repeatability of FT were based on application of those threshold values.

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 which was afterwards treated as a reference value for the agreement between FT and HT study results.

Coronary angiography

Invasive 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.

Statistical analysis

The analysis of correlation between segmental scorings in FT and HT studies used Spearman's correlation coefficients. 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. Correlations between ESV, EDV and EF in FT and HT studies were examined using Pearson's correlation coefficients.

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. The 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 arteries.

Myocardial Perfusion Study

The quality of images obtained from shortened, as well as normal studies, was good (Figure 1).

All correlation coefficients between segmental scorings of FT and HT studies turned out high and statistically significant (Figure 2). It is worth noticing that correlation coefficient in medium inferior segment in subgroup of males was quite low (0.55), and only slightly higher (0.71) in the remaining two segments of inferior wall (apical and basal). Moreover, correlation coefficients between corresponding segments in FTAC and HTAC studies (i.e. with attenuation correction) are systematically higher than without this correction pointing to higher agreement of perfusion assessment in segments. After grouping of segments into corresponding artery areas correlation coefficients were calculated again, for segments belonging to these three areas. All values were high and statistically significant (Tab. 1). The lowest value (0.73) was obtained for RCA area in studies without attenuation correction, in subgroup of males. Attenuation correction improved agreement of scoring in this area (correlation coefficient increased to 0.85).

Summed Stress Score

Summed stress score (SSS) was accepted as an index allowing to detect coronary artery disease. In studies without attenuation correction (FT and HT), median values of SSS were the same and

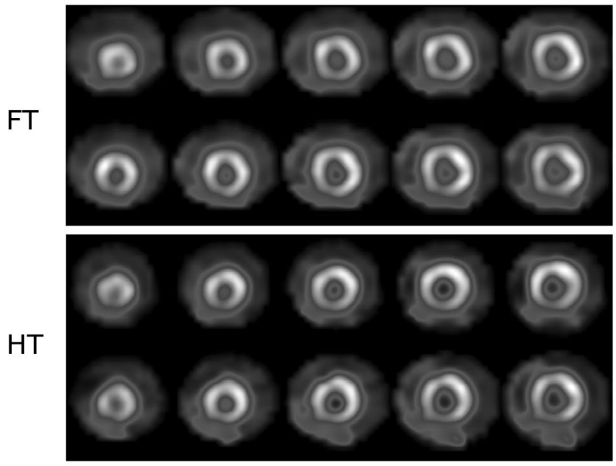

Figure 1. Image presents good quality of full time and half time studies

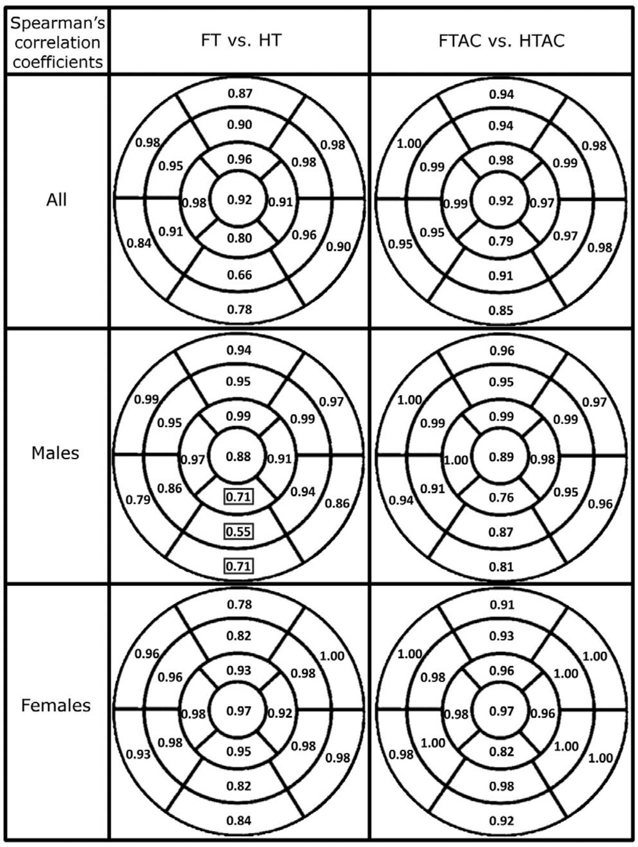

Figure 2. Spearman's correlation coefficients for segmental assessment of myocardial perfusion

Table 1. Spearman's correlation coefficients between full time and half time studies, for segments grouped according to their assignment to three coronary arteries

Artery	All		Males		Females	
	NC	AC	NC	AC	NC	AC
LAD	0.94	0.97	0.95	0.97	0.91	0.96
RCA	0.80	0.89	0.73	0.85	0.90	0.94
LCx	0.95	0.98	0.93	0.97	0.97	0.99

equal to 3, whereas in studies with attenuation correction (FTAC and HTAC) they both fell to 0. Spearman's correlation between SSS values calculated from FT and HT studies was high and amounted to 0.82 ($p < 0.01$) and from FTAC and HTAC studies — 0.83 ($p < 0.01$).

Table 2 presents threshold SSS values accepted for detection of CAD with respective indices of diagnostic efficacy. In studies without attenuation correction a threshold value of 3 and in studies with attenuation correction a threshold value of 2 were accepted. Lower threshold value for studies with attenuation correction is a consequence of lower median SSS value for those studies as well as evidently lower sensitivity of those studies for threshold value of 3.

The indices of diagnostic efficacy did not differ significantly between FT and HT studies, although a HT method provided a slightly lower sensitivity, specificity and accuracy without attenuation correction and sensitivity and accuracy with attenuation correction, as well as lower values of areas under respective ROC curves. Application of attenuation correction provided a higher specificity of FTAC as compared with FT method ($p = 0.01$) and of HTAC in comparison with HT method ($p = 0.004$).

The agreement between full time and shortened study results is presented in Table 3. It was equal to 81% (kappa 0.62) for studies without attenuation correction (FT and HT) and to 86% (kappa 0.70) for studies with attenuation correction (FTAC and HTAC), although the improvement of agreement was not statistically significant ($p = 0.40$). Table 4 presents the same as Table 3B agreement between FTAC and HTAC studies (86%), but this time along with repeatability of FTAC study (94%). Figure 3 shows that 95-percent confidence intervals calculated for agreement between FTAC and HTAC studies ($CI_{95\%}$ [79–93]) and repeatability of FTAC study ($CI_{95\%}$ [89–99]) 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.

Left ventricular contractility

Gated study acquisition enabled assessment of left ventricular end-diastolic volume (EDV), end-systolic volume (ESV) and ejection fraction (EF) for shortened and full-time studies. Correlation coefficients for those values between FT and HT turned out to be high: for EDV — 0.93, ESV — 0.96 and EF — 0.88. Figure 4 presents linear regression for end-diastolic volume, end-systolic volume and ejection fraction as well as Bland-Altman plot for ejection fraction. Mean systematic difference between ejection fraction values calculated from FT and HT studies was very small (0.61 percentage points) and standard deviation of differences was equal to 4.13 percentage points.

Discussion

The introduction of resolution recovery (RR) to the reconstruction of SPECT images is an obvious step toward the improvement of this software. It is well known that in conventional gamma cameras with scintillation crystal and parallel-hole collimator resolution is compromised with growing detector to object distance. When this effect is taken into account during iterative reconstruction process, images reproduce actual distribution of activity inside a patient body with higher accuracy. In case of acquisition of lower than standard number of counts, application of RR complimented with noise regularization method indicates a good quality of reconstructed images. The producers of software implemented this method to reconstruction software packages, some of them as a part of software dedicated to particular gamma cameras (GE Healthcare „Evolution for Cardiac", Siemens „Flash3D", Philips „Astonish", Digirad „nSPEED"), another ones as standalone implementations (UltraSPECT „WBR", Hermes Medical Solutions „Hybrid Recon — Cardiology"). In the present work, as in most communications concerning this topic [6–9], shortening of acquisition time was used as a method for reduction of counts in projection images. Some authors [10] attained reduction of counts by lowering of activity of administered radiopharmaceutical.

One of the criteria used for comparison between shortened and full-time study acquisitions was a quality of reconstructed images.

Table 2. Threshold values of SSS accepted for detection of CAD together with sensitivity. specificity and accuracy of applied methods. AUC — area under ROC curve

SSS	FT AUC: 0.77			HT AUC: 0.73			FTAC AUC: 0.80			HTAC AUC: 0.75		
	SENS.	SPEC.	ACC.	SENS.	SPEC.	ACC.	SENS.	SPEC.	ACC.	SENS.	SPEC.	ACC.
0	1.00	0.00	0.39	1.00	0.00	0.39	1.00	0.00	0.39	1.00	0.00	0.39
1	0.95	0.34	0.58	0.86	0.31	0.53	0.76	0.72	0.74	0.70	0.71	0.71
2	0.84	0.52	0.64	0.81	0.43	0.58	0.68	0.81	0.76	0.62	0.81	0.74
3	0.76	0.62	0.67	0.70	0.57	0.62	0.65	0.90	0.80	0.49	0.88	0.73
4	0.70	0.72	0.72	0.68	0.72	0.71	0.59	0.90	0.78	0.43	0.91	0.73
5	0.62	0.78	0.72	0.65	0.79	0.74	0.51	0.93	0.77	0.35	0.95	0.72
6	0.54	0.84	0.73	0.49	0.83	0.69	0.43	0.95	0.75	0.30	0.95	0.69
7	0.46	0.86	0.71	0.49	0.88	0.73	0.38	0.95	0.73	0.30	0.97	0.71

Table 3. A cross tabulation of study results after dichotomous categorization without (**A**) and with (**B**) attenuation correction

A	FT vs. HT kappa 0.62 agreement 81%	HT Normal result SSS < 3	HT Abnormal result SSS ≥ 3
FT	Normal result SSS < 3	36	10
	Abnormal result SSS ≥ 3	8	41

B	FTAC vs. HTAC kappa 0.70 agreement 86%	HTAC Normal result SSS < 2	HTAC Abnormal result SSS ≥ 2
FTAC	Normal result SSS < 2	54	6
	Abnormal result SSS ≥ 2	7	28

Table 4. Cross tabulation after dichotomous categorization of FTAC and HTAC studies (**A**) vs. FTAC and FTAC study — repeat assessment (**B**)

A	FTAC vs. HTAC kappa 0.70 agreement 86%	HTAC Normal result SSS < 2	HTAC Abnormal result SSS ≥ 2
FTAC	Normal result SSS < 2	54	6
	Abnormal result SSS ≥ 2	7	28

B	FTAC vs.FTAC kappa 0.87 repeatability 94%	FTAC Normal result SSS < 2	FTAC Abnormal result SSS ≥ 2
FTAC	Normal result SSS < 2	55	4
	Abnormal result SSS ≥ 2	2	34

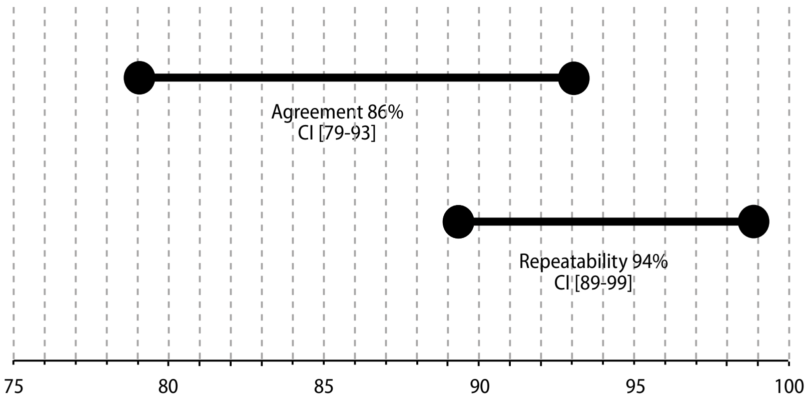

Figure 3. 95%-confidence intervals for repeatability of visual assessment of FTAC study (as in Table 4A) and agreement of assessment of FTAC and HTAC studies (as in Table 4B)

Similarly to another communications [6, 7, 11], image interpreters did not have objections to reconstructed image quality. Moreover, they could not say whether reconstructed images were obtained from full or half time study. Worse image quality was observed only in raw image projections as a consequence of less counts.

Myocardial perfusion studies were evaluated in the present work in the form of a widely accepted 17-model, constructed of short axis slices and in case of an apex — a vertical long axis slice. Perfusion in every segment was assessed visually in a 5 grade scale (from 0 to 4).

A categorization of study results into normal and abnormal ones enabled the assessment of the concordance between full time and half time study results. It was equal to 81% for studies without attenuation correction and increased to 86% as a result of this correction. Although the improvement of agreement was not statistically significant, if taken together with increase of segmental correlation coefficients after application of attenuation correction, especially in males, it should be treated as a real trend. Moreover, the results of the present work indicate that the agreement between visual assessments of FTAC and HTAC studies (86%) does not differ significantly from repeatability of FTAC study assessments (94%). These results should be interpreted in such a way that possible real differences between images in full time and half time studies are lost in the subjectivity of a visual method used for study evaluation.

The agreement of interpretations of full time and half time studies presented in this work is not so good as the one presented by Ali et al. [6]. They published in 2009 a work comparing results of shortened studies processed with „Evolution for Cardiac" package (GE Healthcare) with results of studies acquired and processed in a standard way (FBP, OSEM), making use of a 1-day study protocol and applying attenuation correction. In shortened studies time per projection was reduced from 25s to 15s for rest and 10s for stress studies. Full time and half time studies were performed in 112 patients (among which 23 had a history of a myocardial infarction). In addition, in order to check

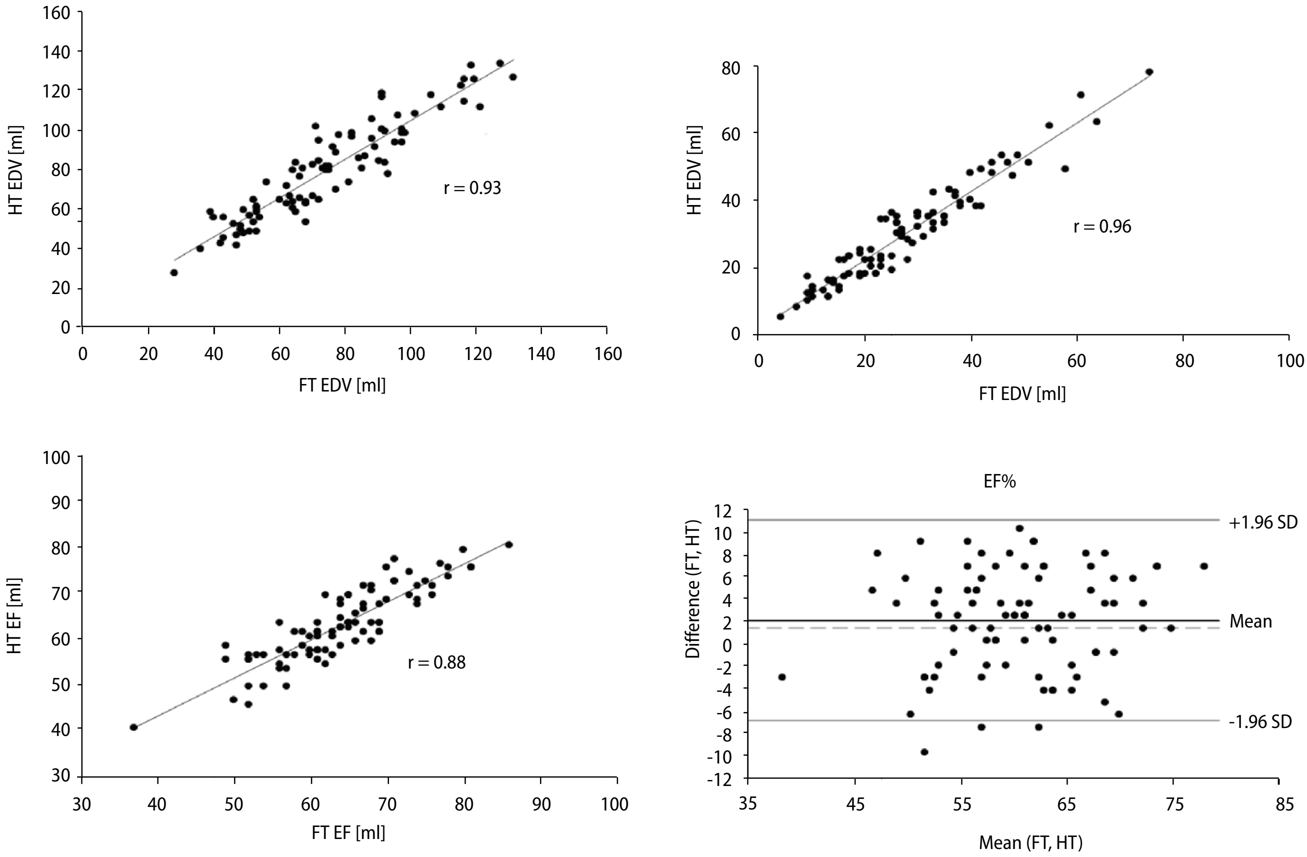

Figure 4. Linear regression for EDV, ESV and EF values and Bland-Altman chart for EF obtained from FT and HT studies

repeatability of results of standard studies, in 100 patients a full time study was acquired twice. Authors communicate on high correlations between perfusion parameters (SSS, SRS and SDS) obtained from visual analysis of 17 segments of full time and half time studies. Excepting segmental perfusion assessment, study analysis took into account also wall motion and TID (transient ischemic dilation) index. A very high concordance between study results (95% without and 96% with attenuation correction, also 98% repeatability) was obtained. Authors claim that concordance of interpretations of full time and half time studies was not worse than concordance of interpretations of repeated full time studies. Unfortunately, no results presenting agreement of perfusion alone in both studies were presented.

Another work applying „Evolution for Cardiac" package was published in 2010 by Valenta et al. [7]. Authors present the results of studies performed in a group of 50 patients (9 after myocardial infarction). One-day study protocol was applied, with reduced time per projection from 25s to 15s for rest and 10s for stress studies. Image quality as well as perfusion were assessed visually. Images were reconstructed and analyzed without and with attenuation correction. Concordance between the results of perfusion assessments (based on inspection of all slices) was again as high as 96%. Small differences were observed in two studies, but were considered clinically insignificant. In this way a 100% concordance was obtained. In a quantitative analysis a 20-segment model of left ventricular myocardium was used. Percentage uptake of a radiopharmaceutical in segments of normal and shortened studies was compared. Correlation coefficients for most of segments were high.

In 2012 Armstrong et al. [11] studied 53 patients, applying a 2-day protocol. They reduced counts in every study by taking every other time bin from the 16-bin data set or rejecting every other projection from full-count data. Reconstructed studies making use of „Evolution for Cardiac" package were obtained. The comparison of perfusion (in a 4-grade scale) revealed an 83% agreement and in case of the acceptance of minor inconsistencies (± 1) — 96%. Authors admit application of attenuation correction in a part of studied patients but do not reveal if this correction was taken into account during image interpretation. They also suggest study acquisition to be shortened by 33% instead of 50% of time because in their opinion low number of counts affects negatively agreement between studies in question. In our work a lower concordance between results of normal and shortened studies was observed in spite of much higher (approximately twice) activities administered.

Finally, in 2014 Lawson et al. [12] published results of wide, multi-center trial that aimed at verification of a usefulness of myocardial perfusion image reconstruction methods applying resolution recovery. Sixteen nuclear medicine departments in Great Britain, which routinely performed myocardial perfusion imaging, took part in the study. Altogether 769 studies were analyzed. A specialized software simulating half-count data was applied. Several types of dedicated software provided by various vendors were applied, among them also „Evolution for Cardiac" (GE Healthcare), applied to 421 studies. Resulting images were compared with standard ones. In 171 patients (41%) results of standard and shortened studies differed and in 42 (10%) in a clinically significant way. The multi-center character of the study and a relatively large number of patients make this study highly reliable. In general, the results of our work agree with the ones obtained by Lawson et al., although their results differed considerably among departments.

Criteria of inclusion applied in this work were passed by 95 patients. All of them underwent coronary angiography which was treated as a verification while assessing diagnostic efficacy of applied methods in detection of coronary artery disease. Patients after myocardial infarction were not accepted in order to avoid a difficulty of interpretation caused by overlapping of stress induced hypoperfusion with post-infarction scar. It is possible that elimination of patients after myocardial infarction decreased the agreement between the results of full- and half-time studies because in this way patients with evidently abnormal perfusion were removed from the material.

Indices of diagnostic efficacy in detection of coronary artery disease (especially a sensitivity) obtained in this work turned out quite low. However, in this case differences between indices obtained for FT and HT methods are more important than their absolute values. Sensitivity, specificity and accuracy of HT and HTAC were slightly lower than of FT and FTAC studies, respective differences were statistically insignificant.

As for left ventricular contractility, high correlations between EDV, ESV and EF values in normal and shortened studies were observed. Moreover, only a small dispersion and no systematic differences between ejection fraction values obtained from both studies were found. However, it is worth mentioning that in a studied group of people no patients after myocardial infarction were included. This patient selection reduced probability of observing a higher disagreement.

Based on presented results the following conclusions can be drawn from this work:

Myovation Evolution protocol dedicated to reconstruction of myocardial perfusion studies with reduced number of counts requires an application of attenuation correction. The agreement between results of visual assessment of normal and reduced count studies is high and not worse than agreement between repeat assessment of a full time study. In the next stage we plan to assess results of the study in another, probably more objective way, by comparing them to normal data bases.

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