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Quantification of left ventricular volumes and ejection fraction from gated ^{99m}Tc-MIBI SPECT: MRI validation of the EXINI heart software package

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Summary

The aim of the study was to validate the accuracy of the EXINI heart software (EXINI) package in assessing left ventricular end-diastolic/systolic volumes (EDV, ESV) and ejection fraction (LVEF) from gated ^{99m}Tc-MIBI single-photon emission tomography (SPECT). Cardiac magnetic resonance imaging (cMRI) was used as reference. Furthermore, effects of perfusion defects and image quality in SPECT on correlation between gated SPECT and magnetic resonance imaging were investigated.

Methods: Seventy patients were examined using gated SPECT (rest study, eight gates per cardiac cycle). EDV, ESV and LVEF were calculated from gated SPECT using EXINI. Directly before or after SPECT, cMRI (20 gates cardiac per cycle) was performed. EDV, ESV and LVEF were calculated using Simpson's rule. Perfusion defects were quantified using the summed-rest-score (SRS). Total number of myocardial counts were used to rate image quality.

Results: Correlation between results of gated SPECT and cMRI was high for EDV ($R = 0{\cdot}89$) and ESV ($R = 0{\cdot}94$) and good for LVEF ($R = 0{\cdot}78$). ESV (EXINI 54 ± 31 ml versus cMRI 57 ± 34 ml) and LVEF (EXINI 62·9 ± 11·7% versus cMRI 60·6 ± 13·9%) did not differ significantly whereas EXINI overestimated EDV significantly compared with cMRI (EXINI 144 ± 41 ml versus cMRI 137 ± 36 ml; $P<0{\cdot}005$). No correlation was found between absolute differences of the results given by gated SPECT and cMRI and SRS or total myocardial counts ($R < 0{\cdot}18$).

Conclusion: End-diastolic volume, ESV and LVEF calculated from gated SPECT using EXINI agree with cMRI over a wide range of values. Correlation between both the methods was good for EDV and ESV, and acceptable for LVEF. No relevant influence of image quality or SRS on the accuracy of EXINI results was found.

Introduction

The existence and extent of regional and global cardiac dysfunction in coronary artery disease are a diagnostic criterion of heart failure. Furthermore, they also provide essential information on the expected clinical outcome. Left ventricular volumes and ejection fraction as indicators of impaired systolic function proved to be especially powerful and reliable predictors of poor long-term prognosis (Hammermeister *et al.*, 1979; White *et al.*, 1987; Yamaguchi *et al.*, 1998). Electrocardiographically gated single-photon emission tomography (gated SPECT), a technique primary used for diagnostic work-up of coronary artery disease, allows myocardial perfusion imaging (Smanio *et al.*, 1997) with subsequent analysis of regional wall motion, regional wall thickening and calculation of global function from end-diastolic and end-systolic volumes (EDV, ESV) as well as Left ventricular ejection fraction (LVEF) (Germano *et al.*, 1995; Iskandrian *et al.*, 1998; Faber *et al.*, 1999; Ficaro *et al.*, 1999). This integrated approach combining analysis of perfusion and function proved useful in tissue characterization (DePuey & Rozanski, 1995) and prognosis prediction (Sharir *et al.*, 1999). Algorithms for automated left ventricle segmentation from gated SPECT images have recently been developed. Their accuracy for the assessment of left ventricle (LV) volumes and LVEF was assessed compared to functional imaging tools such as radionuclide ventriculography and cardiac magnetic resonance imaging (cMRI) (Vaduganathan *et al.*, 1998; Faber *et al.*, 2001; Ficaro *et al.*, 2003; Lum & Coel, 2003; Lipke *et al.*, 2004). The segmentation algorithms tested accurately provided parameters of LV dysfunction, but are inherently restricted by tracer accumulation defects and the low resolution of SPECT, which restricts exact classification of endo- and epicardial contours. Since the algorithms differ both generally in computation and in their mode of application, one can expect results to differ depending on the patient group. Accordingly, comparative studies have shown different results for absolute quantification of LV volumes and LVEF given by different software (Faber *et al.*, 2001; Nakajima *et al.*, 2001; Ficaro *et al.*, 2003; Lum & Coel, 2003).

In this study, the quantification software EXINI heart 3·1 (EXINI Diagnostics AB, Lund, Sweden) was validated for measuring EDV, ESV and LVEF against cMRI as reference. The software is based on the active shape algorithm. This technique fitted a non-geometrical, heart-shaped model to the left ventricle in the three-dimensional (3D) image space (Lomsky *et al.*, 2005). The EXINI heart results were also compared with published results from a cMRI validation study (Schaefer *et al.*, 2005) based on same gated SPECT data analysed using QGS (Cedars-Sinai Medical Center, Los Angeles, CA, USA), 4D-MSPECT (University of Michigan Medical Center, Ann Arbor, MI, USA) and the Emory Cardiac Tool Box (ECTB; Emroy University Hospital, Atlanta, GA, USA) to investigate software-specific characteristics. cMRI is best suited as reference because assessment of cardiac volumes and function by cMRI does not rely on geometrical assumptions of left ventricular shape (Dulce *et al.*, 1993; Barkhausen *et al.*, 2001). As perfusion defects interfere with finding contours on SPECT, the possible influences of such defects were examined by correlating the absolute differences between gated SPECT and magnetic resonance imaging (MRI) with the summed-rest-score (SRS), a measure of the extent and depth of perfusion defects on SPECT. Furthermore, as reduced SPECT image quality may also influence contour finding, a possible effect of total number of myocardial counts as a measure of image quality on the difference between gated SPECT and cMRI was investigated.

Materials and methods

Patients

The study comprised 70 patients (54 male, 16 female, mean age 59·7 ± 12·4 years, range 33–82 years) without MRI contraindications referred for routine stress–rest myocardial perfusion imaging using ^{99m}Tc-MIBI SPECT. The 2-day SPECT protocol started with the stress part. Rest gated SPECT and cMRI studies were carried out on a separate day. All patients gave informed consent. Coronary artery disease was suspected in 29 patients. Of the 41 patients with known coronary artery disease, 27 had a history of at least one myocardial infarction and 11 had received a coronary artery bypass graft.

Gated ^{99m}Tc-MIBI SPECT

Gated acquisition (64 × 64 matrix) was done on a Siemens Multispect 3 (triple-head gamma-camera; Siemens Gammasonics Inc., Hoffman Estates, IL, USA) 60 min after intravenous administration of 446 ± 32 MBq ^{99m}Tc-MIBI, with 20 views of 30 s per view and a zoom factor of 1·23. The cardiac cycle was divided into eight equally spaced intervals. All gates were reconstructed using filtered back projection (third order Butterworth filter, critical frequency 0·5; Siemens ICON software). The data sets were transferred to a Siemens ICON system (Siemens Gammasonics Inc.) where they were reoriented using transversal planes, first parallel to the septum and then parallel to the inferior wall. The reoriented short-axis data sets (voxel size 5·8 × 5·8 × 5·8 mm^3) were stored for analysis and in the DICOM data format. Gated SPECT images were analysed for EDV, ESV and LVEF using the EXINI heart software package (version 3·1) (EXINI Diagnostics AB). We are not using the EXINI heart manual correction option to minimize operator influence in case of inadequate anatomical delineation, a clearly inappropriate contour finding did not occur. EDV and ESV values are given in ml, LVEF values in %. SRS was calculated automatically from the gated SPECT images using the 4D-MSPECT algorithm based on an institutional normal database and a 20-segment model (see Knollmann *et al.* 2008). Furthermore, total number of myocardial counts were calculated using a region-of-interest (ROI) technique and the non-gated short-axis data sets.

Cardiac magnetic resonance imaging methodology and data analysis

Directly before or after rest SPECT imaging, all patients underwent cMRI on a 1·5 Tesla Gyroscan ACS-NT unit (Philips Medical Systems, Best, the Netherlands). MRI was carried out with a five-element cardiac phased-array coil and ECG triggering. A balanced fast-field echo sequence (Plein *et al.*, 2001) was used in all patients, with repetition per echo time of 3·1/1·5 ms, flip angle 65°, matrix 256 × 256 (field of view 350–400 mm) and slice thickness 8 mm. Each slice was acquired in a separate breath-hold cycle at end expiration. Twenty phases were obtained per cardiac cycle. Integrated sensitivity encoding technology reduced acquisition time for most patients. Based on the vertical and horizontal long axes of the left ventricle, the true short axis was determined covering the left ventricle from base to apex. Functional analysis of MRI data was done on a separate workstation using MASS 5·0 (Medis Medical Imaging Systems, Leiden, the Netherlands). After determining the cardiac base and apex, the end diastole was defined as the first gate in each series and the end-systolic phase as the image with the smallest ventricular volume. Left ventricular volumes were outlined by manually tracing the endocardial contours of the end-diastolic and end-systolic phase with the trabeculation and papillary muscles being segmented as part of the myocardium. EDV and ESV were then automatically computed in ml using modified Simpson's rule (Dulce *et al.*, 1993) by summing the cross-sectional areas outlined by the endocardial borders of all short-axis slices included in the analysis. The ejection fraction was expressed in % and calculated as the stroke volume divided by the EDV.

Statistical analysis

All statistical analyses were performed using SPSS 14 (SPSS Inc., Chicago, IL, USA). Data are shown as mean ± standard deviation. Mean EDV, ESV and LVEF were tested for significance using a t-test for paired samples. A significance level of $P<0{\cdot}05$ was accepted as significant after applying the Bonferroni–Holm correction for multiple comparisons. The degree of agreement was evaluated according to Bland & Altman, (1986). Bland–Altman limits (BAL) (mean of the differences ± 2 standard deviations of the differences) are shown in the figures. Pearson correlation coefficients were also calculated. Absolute difference between gated SPECT and MRI results were correlated with SRS and total number of myocardial counts.

Results

Mean end-diastolic volume, end-systolic volumes and left ventricular ejection fraction

The results of patients from our previous study using 4D-MSPECT, QGS and ECTB (Schaefer *et al*., 2005) are shown in Table 1 in comparison with cMRI and EXINI heart. EDV ranged from 75 to 280 ml for EXINI heart and from 66 to 234 ml for cMRI. The EXINI heart EDV (144 ± 41 ml) was significantly higher than that from cMRI (137 ± 36 ml) ($P<0{\cdot}005$). End-systolic volumes range were 14–159 ml (EXINI heart) and 16–162 ml (cMRI). There was no significant difference between ESV obtained from EXINI and cMRI (EXINI heart 54 ± 31 ml, cMRI 57 ± 34 ml). LVEF ranged 29–86% (EXINI heart) and 25–83% (cMRI). No significant differences were found for LVEF obtained from EXINI heart and cMRI (EXINI heart 62·9 ± 11·7%, cMRI 60·6 ± 13·9%).

Correlation and regression analysis of gated SPECT versus cardiac magnetic resonance imaging

Correlation and regression analysis of EDV, ESV and LVEF calculated from all 70 patients using EXINI heart and cMRI are given in Table 2. This Table also shows the results from our previous study using 4D-MSPECT, QGS and ECTB (Schaefer *et al*., 2005) in comparison with cMRI. The EDV correlated very well between gated SPECT using EXINI heart and cMRI (Table 2, Fig. 1a). The regression line was fairly close to the line of identity ($R = 0{\cdot}89$, slope = 1·02, intercept = 4·38 ml, $P<0{\cdot}005$). The Bland–Altman plot (Fig. 1b) shows moderate wide limits. By comparison, 4D-MSPECT, QGS and ECTB yielded similar regression coefficients (Table 2) and similar to slightly smaller (QGS) width of BAL. The ESV also correlated very well between gated SPECT using EXINI heart and cMRI (Table 2, Fig. 2a). The regression line deviated from the line of identity with a slope lower than 1 ($R = 0{\cdot}94$, slope = 0·85, intercept = 6·13 ml, $P<0{\cdot}005$). The corresponding Bland–Altman plot (Fig. 2b) shows moderatly wide limits. 4D-MSPECT, QGS and ECTB gave similar regression coefficients (Table 2) and similar to slightly smaller (QGS) width of the BAL. The correlation between LVEF derived from gated SPECT using EXINI heart and cMRI was acceptable. LVEF tended to be slightly overestimated by EXINI heart. The regression line deviated from the line of identity with a slope distinctly lower than 1 ($R = 0{\cdot}78$, slope = 0·62, intercept = 23·08 ml, $P<0{\cdot}005$). The respective Bland–Altman plot shows relatively wide limits. The other three algorithms – 4D-MSPECT, QGS and ECTB – gave better correlation coefficients and smaller Bland–Altman limits than did EXINI heart (Table 2).

Table 2 Results of regression analysis between cMRI (x-axis) and gated SPECT (y-axis).

	EXINI heart	4D-MSPECT	QGS	ECTB
EDV				
Correlation coefficient R	0·89	0·88	0·92	0·90
Slope of regression line	1·02	1·03	1·00	1·08
y - intercept of regression line	4·4 ml	−14·0 ml	−16·0 ml	−18·0 ml
Width of BAL	73 ml	79 ml	59 ml	74 ml
ESV				
Correlation coefficient R	0·94	0·96	0·96	0·94
Slope of regression line	0·85	1·01	0·93	1·02
y - intercept of regression line	6·1 ml	−2·0 ml	−7·0 ml	−6·0 ml
Width of BAL	47 ml	41 ml	38 ml	49 ml
LVEF				
Correlation coefficient R	0·78	0·87	0·89	0·85
Slope of regression line	0·66	0·79	0·73	0·83
y - intercept of regression line	23·1%	11·0%	9·0%	13·0%
Width of BAL	34%	27%	25%	30%

Given are correlation coefficients, slopes and y-intercepts. In addition widths of Bland–Altman limits (BAL) for end-diastolic⁄systolic volumes (EDV, ESV) and left ventricular ejection fraction (LVEF) calculated by gated SPECT (EXINI heart, 4D-MSPECT, QGS and ECTB) and cMRI are listed.

Influence of image quality and perfusion deficits (summed-rest-score) on accuracy of gated SPECT results

Correlation analysis between absolute differences of the results (gated SPECT versus cMRI) and absolute total number of myocardial counts yielded no significant correlation for neither

Table 1 Mean values (±standard deviation) for end-diastolic⁄systolic volumes (EDV, ESV) and left ventricular ejection fraction (LVEF) calculated by gated single-photon emission tomography (EXINI heart, 4D-MSPECT, QGS and ECTB) and cMRI.

	EXINI heart	4D-MSPECT	QGS	ECTB	cMRI
EDV	144 ± 41 ml	127 ± 42 ml	120 ± 38 ml	131 ± 43 ml	137 ± 36 ml
ESV	54 ± 31 ml	56 ± 36 ml	60 ± 33 ml	53 ± 37 ml	57 ± 34 ml
LVEF	62·9% ± 11·7%	59·0% ± 12·7%	53·2% ± 11·5%	62·7% ± 13·7%	60·6% ± 13·9%

parameter (EDV: R = −0·04, P = 0·8; ESV: R = −0·04, P = 0·8; LVEF: R = 0·10, P = 0·4) (Figs 1–3c). Correlation analysis between absolute differences of the results (gated SPECT versus cMRI) and SRS yielded no significant correlation for neither parameter (EDV: R = 0·18, P = 0·1; ESV: R = 0·13, P = 0·3; LVEF: R = 0·08, P = 0·5) (Figs 1–3d).

Discussion

The main aim of this study was validating the segmentation algorithm EXINI heart for assessing EDV, ESV and LVEF from gated perfusion SPECT. The relative peformance of EXINI heart, compared with 4D-MSPECT, QGS and ECTB was also examined. cMRI is the accepted standard for measuring global function (Dulce *et al.*, 1993), even when the used cMRI quantification is not based on a true 3D-data set, limiting the comparability to true 3D SPECT data. The results show that EXINI heart can be used to reliably determine EDV, ESV and LVEF from gated SPECT. Even though the overall performance of EXINI heart is similar to that of 4D-MSPECT, QGS and ECTB (Schaefer *et al.*, 2005), the results are different for all four algorithms and therefore not interchangeable. Mean EDV, ESV and LVEF calculated using EXINI heart differed from the cMRI-derived values, as did the values obtained using 4D-MSPECT, QGS and ECTB. Also, EDV was significantly overestimated by EXINI heart while they were underestimated by the other three algorithms, especially by QGS. More insight into the relative performance of EXINI heart was gained from correlation and regression analysis. EXINI heart data for EDV, ESV and, to a lesser extent, LVEF correlated quite well with cMRI data. ESV showed the best correlation to cMRI while those for EDV and LVEF were lower. This fairly agrees with our previous investigations (Schaefer *et al.*, 2005) for 4D-MSPECT, QGS and ECTB, with best correlations for ESV and slightly lower correlations for EDV and LVEF. The better correlation between gated SPECT and cMRI for ESV can easily be explained by the fact that the thickened wall in the end-systolic phase facilitates contour finding. The correlation of LVEF versus cMRI was slightly higher for QGS than for 4D-MSPECT and ECTB, which in turn showed a higher correlation than EXINI heart. The slope of the regression line (EXINI heart 0·66) was distinctly lower than expected. This effect was less pronounced for the other algorithms but can for all algorithms at least partly explained by the fact that the temporal resolution of cMRI is 2·5-fold higher than that of gated SPECT (20 versus eight gates cardiac per cycle), which causes LVEF to be underestimated when using gated SPECT with only eight gates cardiac per cycle, particularly in patients whose ventricles are contracting well. Nevertheless, in this context it is hard to explain why the average LVEF results from EXINI heart are higher than those from cMRI, but in comparison with the other algorithms EXINI heart overestimates the LVEF nearly identically like the ECTB algorithm.

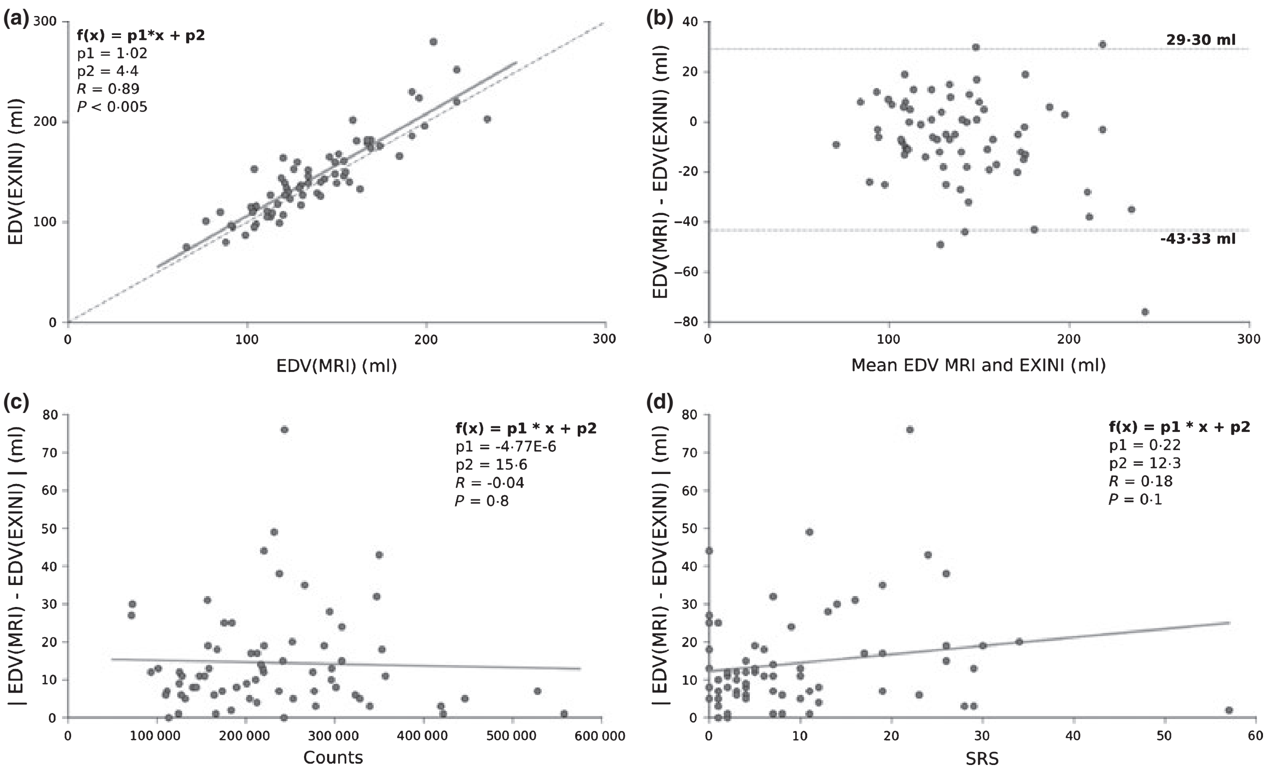

Figure 1 Correlation analysis of end-diastolic volume (EDV) from gated single-photon emission tomography (gated SPECT) and cardiac magnetic resonance imaging (cMRI) using EXINI heart (a). Bland–Altman plot for comparing EXINI heart and cMRI (b). Correlation analysis of absolute EDV differences (cMRI and gated SPECT) versus counts (c) and versus summed rest score (SRS) (d).

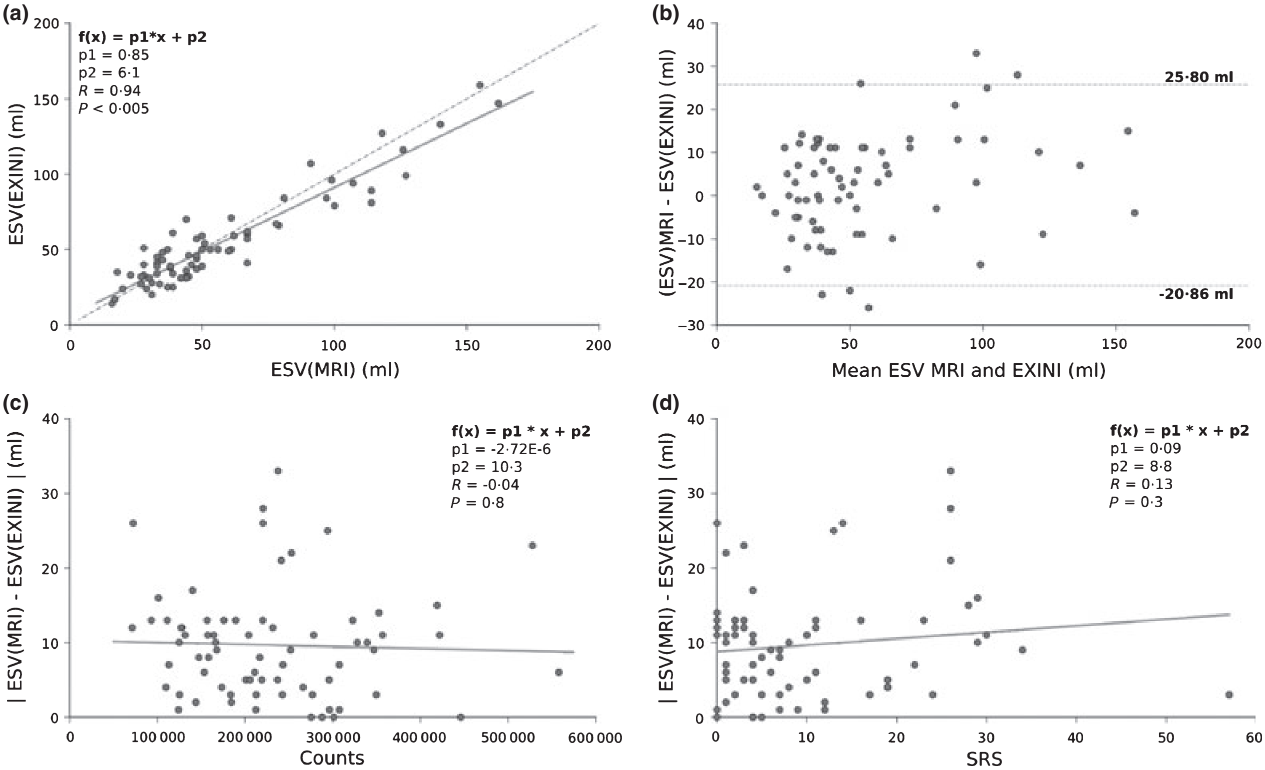

Figure 2 Correlation analysis of end-systolic volume (ESV) from gated single-photon emission tomography(gated SPECT) and cardiac magnetic resonance imaging (cMRI) using EXINI heart (a). Bland–Altman plot for comparing EXINI heart and cMRI (b). Correlation analysis of absolute ESV differences (cMRI and gated SPECT) versus counts (c) and versus summed rest score (SRS) (d).

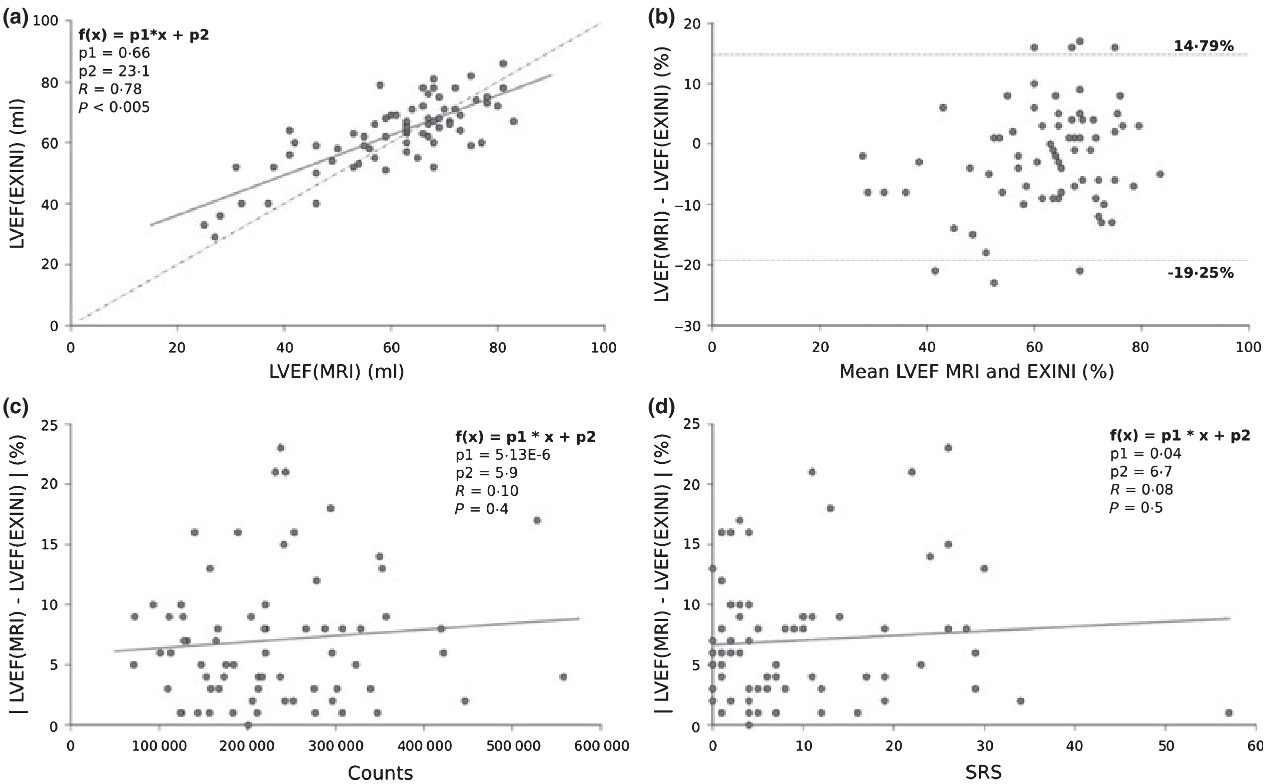

Figure 3 Correlation analysis of left ventricular ejection fraction (LVEF) from gated single-photon emission tomography (gated SPECT) and cardiac magnetic resonance imaging (cMRI) using EXINI heart (a). Bland–Altman plot for comparing EXINI heart and cMRI (b). Correlation analysis of absolute LVEF differences (cMRI and gated SPECT) versus counts (c) and versus summed rest score (SRS) (d).

A promising result is that neither the presence of perfusions deficits nor the low total number of counts in the myocardium had a negative effect on the accuracy of the gated SPECT results calculated with EXINI heart. This proves that the contour-finding algorithm is robust even in the presence of low-count areas or in studies with reduced statistics (e.g. obese patients).

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