

# Gated Myocardial Perfusion SPECT: Algorithm-Specific Influence of Reorientation on Calculation of Left Ventricular Volumes and Ejection Fraction

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Gated myocardial perfusion SPECT allows calculation of end-diastolic and end-systolic volumes (EDV and ESV, respectively) and left ventricular ejection fraction (LVEF). The quantification algorithms QGS (quantitative gated SPECT), 4D-MSPECT, and CARE heart show a good correlation with cardiac MRI. Nevertheless, differences in contour finding suggest algorithm-specific effects if heart axes vary. The effect of tilting heart axes on gated SPECT was quantified as a possible source of error. **Methods:** Sixty men underwent gated SPECT (450 MBq of <sup>99m</sup>Tc-tetrofosmin or sestamibi, 8 gates/cycle). After correct reorientation ( $R_0$ ), datasets were tilted by 5°, 10°, 15°, 20°, 30°, and 45° along both long axes ( $R_5$ ,  $R_{10}$ ,  $R_{15}$ ,  $R_{20}$ ,  $R_{30}$ , and  $R_{45}$ , respectively). EDV, ESV, and LVEF were calculated using QGS, 4D-MSPECT, and CARE heart. Because a 15° tilt could be a maximum possible misreorientation in routine,  $R_0$  and  $R_{15}$  results were analyzed in detail. Absolute-difference values between results of tilted and correctly reoriented datasets were calculated for all tilts and algorithms. **Results:** QGS and CARE heart succeeded for  $R_0$  and  $R_{15}$  in all cases, whereas 4D-MSPECT failed to find the basal plane in 1 case (patient B).  $R^2$  values between paired  $R_{15}/R_0$  results were 0.992 (QGS), 0.796 (4D-MSPECT;  $R^2 = 0.919$  in  $n = 59$  after exclusion of the failed case), and 0.916 (CARE heart) for EDV; 0.994 (QGS), 0.852 (4D-MSPECT;  $R^2 = 0.906$  in  $n = 59$ ), and 0.899 (CARE heart) for ESV; and 0.988 (QGS), 0.814 (4D-MSPECT;  $R^2 = 0.810$  in  $n = 59$ ), and 0.746 (CARE heart) for LVEF. Concerning all levels of misreorientation, 1 patient was excluded for all algorithms because of multiple problems in contour finding; additionally for 4D-MSPECT patient B was excluded. In the 45° group, QGS succeeded in 58 of 59 cases, 4D-MSPECT in 58 of 58, and CARE heart in 33 of 59. Mean absolute differences for EDV ranged from  $5.1 \pm 4.1$  to  $12.8 \pm 10.5$  mL for QGS, from  $6.7 \pm 6.3$  to  $34.2 \pm 20.7$  mL for 4D-MSPECT, and from  $5.4 \pm 5.6$  to  $25.2 \pm 16.1$  mL for CARE heart (tilts between 5° and 45°). Mean absolute differences for ESV ranged from  $4.1 \pm 3.7$  to  $8.0 \pm 9.4$  mL for QGS, from  $5.6 \pm 8.0$  to  $10.0 \pm 10.5$  mL for 4D-MSPECT, and from  $5.4 \pm 5.6$  to  $25.5 \pm 16.1$  mL for CARE heart. Mean absolute differences for LVEF ranged from  $1.1\% \pm 1.0\%$  to  $2.2\% \pm 1.8\%$  for QGS, from  $4.0\% \pm 3.5\%$  to  $8.0\% \pm 7.1\%$

for 4D-MSPECT, and from  $3.4\% \pm 2.9\%$  to  $9.2\% \pm 6.0\%$  for CARE heart. **Conclusion:** Despite tilted heart axes, QGS showed stable results even when using tilts up to 45°. 4D-MSPECT and CARE heart results varied with reorientation of the heart axis, implying that published validation results apply to correctly reoriented data only.

**Key Words:** gated SPECT; QGS; 4D-MSPECT; CARE heart; reorientation

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**E**lectrocardiographically gated SPECT allows myocardial perfusion imaging (1,2) with simultaneous analysis of regional wall motion and thickening, calculation of global function from end-diastolic and end-systolic volumes (EDV and ESV, respectively), and left ventricular ejection fraction (LVEF) (3). In myocardial perfusion imaging, gated SPECT data acquisition with the option of calculating EDV, ESV, and LVEF has been established and validated (4). EDV, ESV, and LVEF serve as indicators of impaired systolic function and as powerful and reliable predictors of long-term prognosis (5–7). They are parameters of proven prognostic and therapeutic relevance for different cardiac diseases (8,9). The quantification algorithms QGS (quantitative gated SPECT) (3), 4D-MSPECT (10), and CARE heart (11) have been validated by cardiac MRI (12). Agreement of gated SPECT results with reference methods is good if the heart axis is defined by trained investigators.

The 3 algorithms rely on different methods of identifying endo- and epicardial contours. QGS uses a 3-dimensional model of the heart without specific geometric assumptions of horizontal or transversal long axes. QGS is easy to use, and its quantification routine does not appear susceptible to reorientation errors for gated PET studies (13). On the other hand, 4D-MSPECT requires the heart base to be perpendicular to the chosen long axes. Finally, CARE heart uses an active shape algorithm which has been “trained” on cases that were properly reoriented (Lars Edenbrandt, written communication, January 2008).

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Because of these different approaches, it was expected that an incorrect choice of heart axes leads to algorithm-specific influences on contour finding and hence on estimation of EDV, ESV, and LVEF. So far, to the best of our knowledge, no study has been done on the effect of differences in heart axis reorientation on the results of automatic quantification for gated myocardial perfusion SPECT. Thus, it was the aim of the present study to examine possible algorithm-specific effects of heart axis reorientation on left ventricular volumes and functional parameters.

## MATERIALS AND METHODS

### Study Population

The study population comprised 60 men (mean age,  $61 \pm 12$  y; range, 34–79 y) referred for routine myocardial perfusion imaging using gated  $^{99m}\text{Tc}$ -tetrofosmin or  $^{99m}\text{Tc}$ -sestamibi SPECT. Nineteen patients were referred for myocardial SPECT because of suspected coronary artery disease, and 41 had confirmed coronary artery disease. The SPECT protocol usually started with the stress part, followed by gated SPECT at rest a few days later (2-d protocol).

### Gated $^{99m}\text{Tc}$ -Tetrofosmin/Sestamibi SPECT: Acquisition and Data Analysis

Gated acquisitions ( $64 \times 64$  matrix) were done on a MultiSPECT 3 (triple-head  $\gamma$ -camera; Siemens Gammasonics Inc.) 60 min after intravenous administration of 450 MBq of  $^{99m}\text{Tc}$ -tetrofosmin or  $^{99m}\text{Tc}$ -sestamibi at rest. Sixty views at 30 s/view were acquired using a zoom factor of 1.23. The cardiac cycle was divided into 8 equally spaced intervals. All frames were reconstructed using filtered backprojection (third-order Butterworth filter; critical frequency, 0.5 Nyquist).

The datasets were transferred to an ICON system (Siemens Gammasonics Inc.) and reoriented by experienced technologists, first along the septum and then along the inferior wall. The reoriented

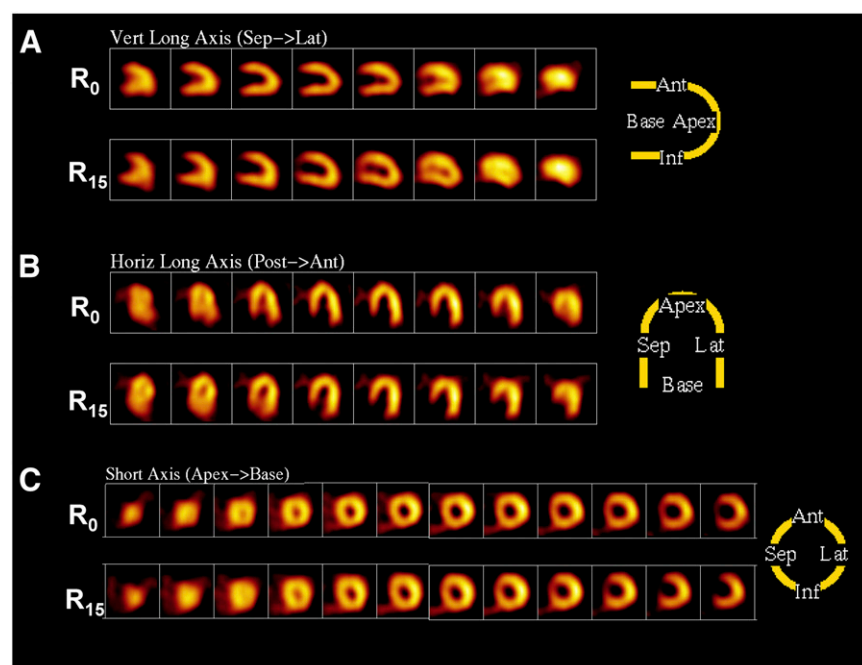
short-axis ( $R_0$ ) datasets (voxel size,  $5.8 \times 5.8 \times 5.8$  mm) were stored for analysis. Reorientation was controlled by a physician experienced in nuclear cardiology. All  $R_0$  datasets were then tilted automatically in the direction of the inferior and lateral walls by  $5^\circ$ ,  $10^\circ$ ,  $15^\circ$ ,  $20^\circ$ ,  $30^\circ$ , and  $45^\circ$  each, yielding a total of 360  $R_5$ ,  $R_{10}$ ,  $R_{15}$ ,  $R_{20}$ ,  $R_{30}$ , and  $R_{45}$  datasets, respectively, and stored for further analysis.

Gated SPECT images were analyzed for EDV, ESV, and LVEF using QGS (Cedars-Sinai Medical Center), 4D-MSPECT (version 2.1.6.5; University of Michigan Medical Center), and CARE heart (version 3.0.1; WeAidU), recently renamed EXINI heart (<http://www.exini.com>). All algorithms were used in full automatic processing mode without manual interaction. EDV and ESV values are given in milliliters, and LVEF values in percentages.

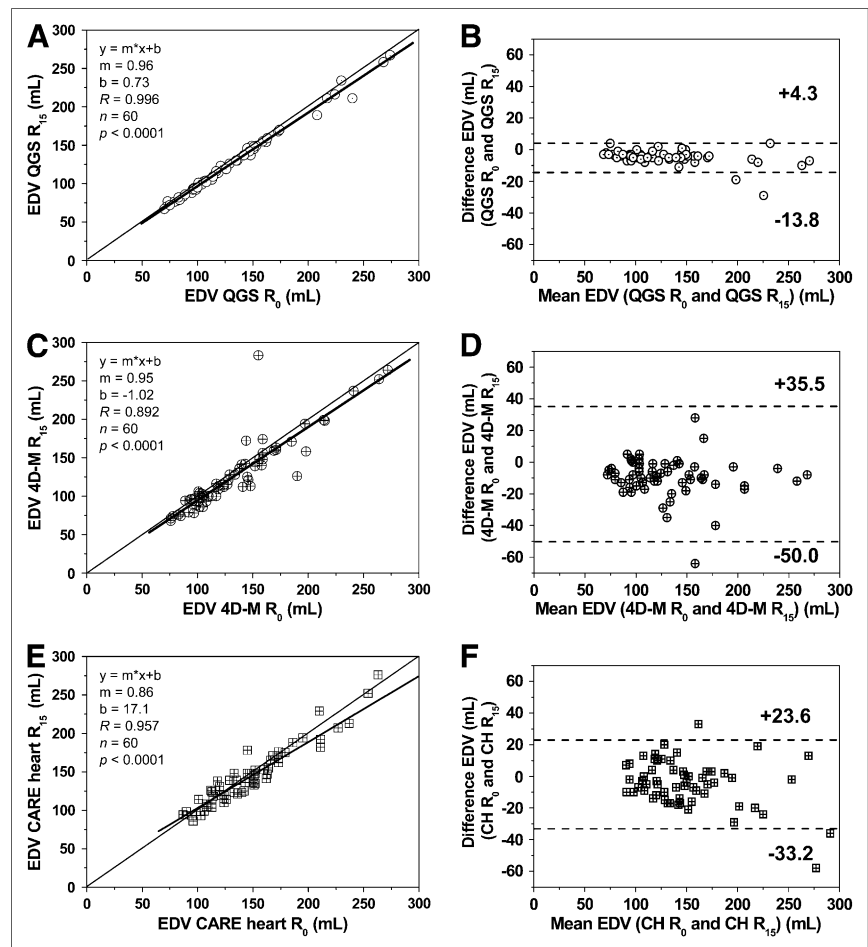
### Statistical Analysis

All statistical analyses were done using SPSS 10 (SPSS Inc.) and Origin 6.1 G (OriginLab Corp.). Mean values ( $\pm$ SD) of EDV, ESV, and LVEF were calculated for all tilts and, regarding  $R_0$  and  $R_{15}$ , tested for significant differences using the *t* test for paired samples. A *P* value of less than 0.05 after Bonferroni adjustment for multiple comparisons was accepted as significant.  $R_0$  and  $R_{15}$  results were chosen for illustration because a misreorientation of  $15^\circ$  was considered the maximum that can occur in daily routine (example of a  $15^\circ$  tilt is shown in Fig. 1). The  $R_0$  and  $R_{15}$  results are shown in Figures 2–4 as scatter plots and Bland–Altman plots. The degree of agreement was calculated according to Bland and Altman (14), and Bland–Altman limits were calculated (mean of the differences  $\pm 1.96 \times$  SD of the differences). Pearson correlation coefficients were also calculated. The number of patients differing by more than 10 mL for EDV or ESV and by more than 5% for LVEF was determined for the  $R_0$  and  $R_{15}$  results.

Figure 5 shows box plots of the mean absolute differences between  $R_{5-45}$  and  $R_0$  results for all algorithms and all parameters.



**FIGURE 1.** Sample of correctly reoriented ( $R_0$ ) and  $15^\circ$ -tilted ( $R_{15}$ ) SPECT data. Images show vertical long axis (A), horizontal long axis (B), and short axis (C).



**FIGURE 2.** EDV correlation analysis using QGS (A), 4D-MSPECT (C), and CARE heart (E) calculated from  $R_{15}$  vs.  $R_0$  data. Bland-Altman plots show  $R_0$  and  $R_{15}$  differences vs. mean EDV using QGS (B), 4D-MSPECT (D), and CARE heart (F). Outlier of 4D-MSPECT is beyond limits to avoid too narrow scaling of axes. CH = CARE heart.

## RESULTS

### Mean EDV, ESV, and LVEF for $R_0$ and $R_{15}$

Analysis of  $R_0$  datasets was done using QGS and yielded the following means: EDV,  $129.6 \pm 48.7$  mL; ESV,  $75.4 \pm 45.4$  mL; LVEF,  $45.5\% \pm 13.1\%$ . Analysis of the  $R_{15}$  datasets yielded  $125.0 \pm 46.8$  mL for EDV ( $P < 0.001$  vs.  $R_0$ ),  $71.8 \pm 43.3$  mL for ESV ( $P < 0.001$  vs.  $R_0$ ), and  $46.2\% \pm 13.4\%$  for LVEF ( $P < 0.001$  vs.  $R_0$ ). Only 4 patients showed an absolute difference of 10 mL or more between  $R_0$  and  $R_{15}$  for EDV and ESV. The absolute difference for LVEF did not exceed 5% in any case.

When 4D-MSPECT was used, the basal plane was not correctly identified in 1 dataset. The results for the remaining 59 patients are shown in parentheses. Analyses of  $R_0$  datasets yielded  $136.4 \pm 44.8$  mL for EDV ( $136.1 \pm 45.1$  mL),  $67.8 \pm 41.0$  mL for ESV ( $67.2 \pm 41.1$  mL), and  $53.7\% \pm 13.8\%$  for LVEF ( $54.0\% \pm 13.7\%$ ). These results did not differ significantly from the results of the  $R_{15}$  datasets:  $129.2 \pm 48.0$  mL for EDV ( $126.6 \pm 43.9$  mL),  $62.3 \pm 39.9$  mL for ESV ( $60.4 \pm 37.6$  mL), and  $55.3\% \pm 13.9\%$  for LVEF ( $55.6\% \pm 13.8\%$ ). Thirty-one patients showed an absolute difference of 10 mL or more between  $R_0$  and  $R_{15}$  for EDV and 18 for ESV. For LVEF, 28 patients showed absolute differences of 5% or

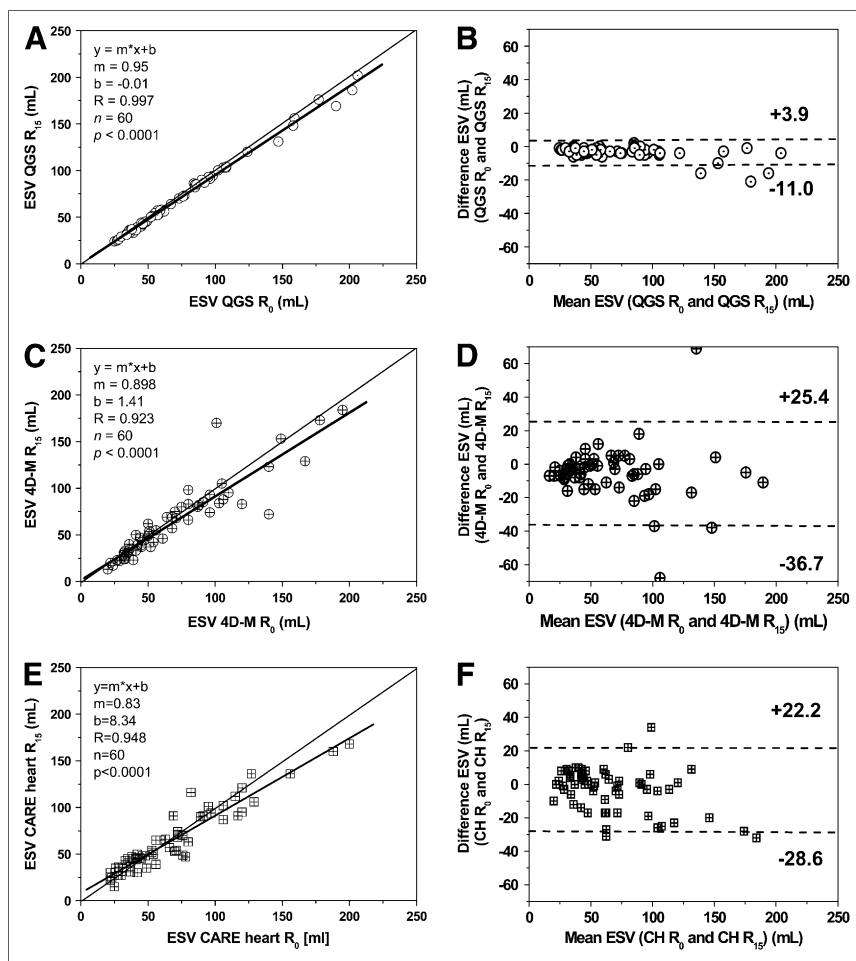
more (analysis of the aforementioned outlier always yielded suprathreshold absolute difference values).

When CARE heart was used, analysis of the  $R_0$  datasets yielded means of  $153.1 \pm 49.1$  mL for EDV,  $67.7 \pm 40.0$  mL for ESV, and  $57.6\% \pm 14.1\%$  for LVEF—values that did not differ significantly from the means of the  $R_{15}$  datasets:  $148.5 \pm 44.0$  mL for EDV,  $64.5 \pm 34.7$  mL for ESV, and  $57.7\% \pm 13.3\%$  for LVEF. Thirty-two patients showed an absolute difference of 10 mL or more between  $R_0$  and  $R_{15}$  for EDV and 20 patients for ESV. Thirty patients showed absolute LVEF differences of 5% or more.

### Correlation Analysis for $R_0$ and $R_{15}$

Correlation analysis of the QGS results ( $R_{15}$  vs.  $R_0$ ) showed a high correlation ( $R^2$ )—0.992 for EDV, 0.994 for ESV, and 0.988 for LVEF (Figs. 2A, 3A, and Fig. 4A, respectively)—with narrow Bland-Altman limits: 18.2 mL for EDV, 14.8 mL for ESV, and 5.6% for LVEF (Figs. 2B, 3B, and 4B, respectively).

Including all 60 patients, corresponding correlation analysis of the 4D-MSPECT results yielded considerably lower  $R^2$  values of 0.796 for EDV, 0.852 for ESV, and 0.814 for LVEF (Figs. 2C, 3C, and 4C, respectively), with wide Bland-Altman



**FIGURE 3.** ESV correlation analysis using QGS (A), 4D-MSPECT (C), and CARE heart (E) calculated from  $R_{15}$  vs.  $R_0$  data. Bland–Altman plots show  $R_0$  and  $R_{15}$  differences vs. mean ESV using QGS (B), 4D-MSPECT (D), and CARE heart (F). CH = CARE heart.

limits: 85.5 mL for EDV, 62.1 mL for ESV, and 23.8% for LVEF (Figs. 2D, 3D, and 4D, respectively). However, when the aforementioned outlier was excluded, results for EDV and ESV were better, although still inferior to QGS. For the remaining 59 patients,  $R^2$  values were 0.919 for EDV, 0.906 for ESV, and 0.810 for LVEF. Bland–Altman limits were 50.0 mL for EDV, 49.6 mL for ESV, and 24.2% for LVEF.

CARE heart provided results that were comparable to 4D-MSPECT but inferior to QGS. Correlation analyses yielded a fair to good correlation ( $R^2$  values: 0.916 for EDV, 0.899 for ESV, and 0.746 for LVEF; Figs. 2E, 3E, and 4E, respectively), with wide Bland–Altman limits: 56.8 mL for EDV, 50.8 mL for ESV, and 28.1% for LVEF (Figs. 2F, 3F, and 4F, respectively).

#### Different Degrees of Tilt: Absolute Difference Values

Regarding the various levels of misreorientation, 1 patient was excluded for all algorithms because of multiple failures in contour finding. Additionally, for 4D-MSPECT the patient in whom the basal plane was not correctly identified was excluded.

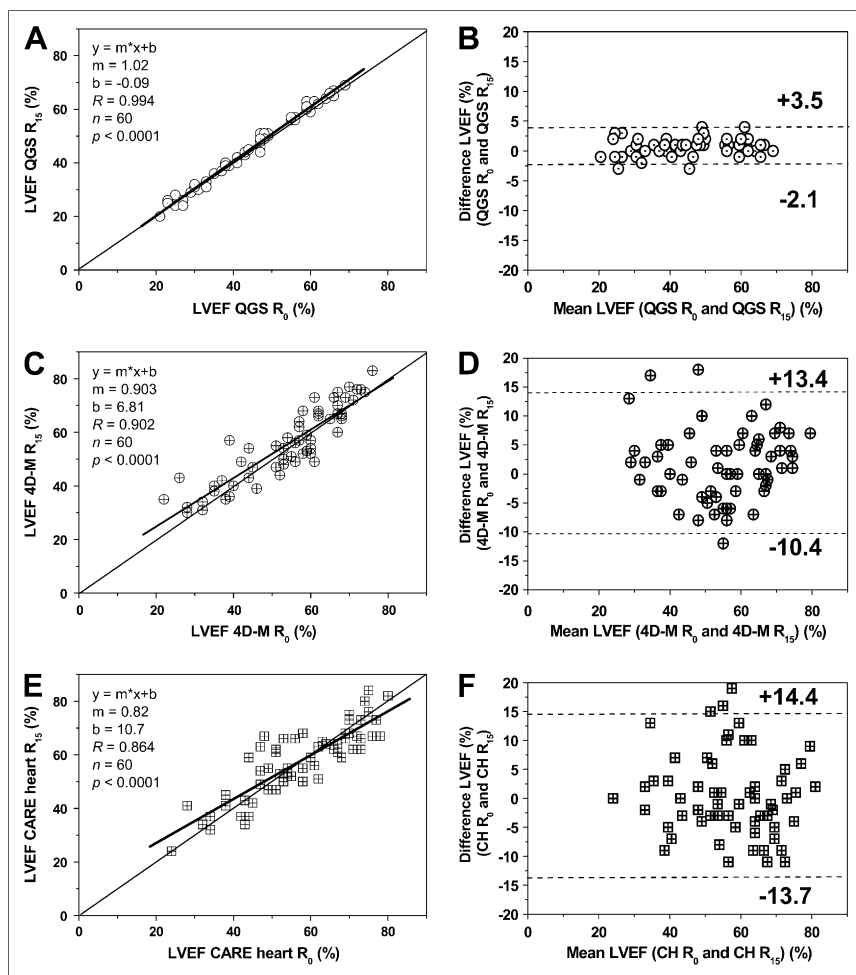
QGS succeeded (i.e., the algorithm converged and provided reasonable results) in 59 of 59 cases up to a 30° tilt. In the 45° tilt group, the algorithm failed in 1 of 59 patients. For 4D-MSPECT, all 58 patients were successfully analyzed for

all tilts. CARE heart case failure rates for groups were 1 of 59 for  $R_{20}$ , 10 of 59 for  $R_{30}$ , and 26 of 59 for  $R_{45}$ .

Mean absolute EDV difference ranges for 5°–45° tilts were  $5.1 \pm 4.1$  to  $12.8 \pm 10.5$  mL for QGS,  $6.7 \pm 6.3$  to  $34.2 \pm 20.7$  mL for 4D-MSPECT, and  $5.4 \pm 5.6$  to  $25.2 \pm 16.1$  mL for CARE heart. Likewise, mean absolute ESV difference ranges were  $4.1 \pm 3.7$  to  $8.0 \pm 9.4$  mL for QGS,  $5.6 \pm 8.0$  to  $10.0 \pm 10.5$  mL for 4D-MSPECT, and  $5.4 \pm 5.6$  to  $25.5 \pm 16.1$  mL for CARE heart. The corresponding mean absolute LVEF difference ranges were  $1.1\% \pm 1.0\%$  to  $2.2\% \pm 1.8\%$  for QGS,  $4.0\% \pm 3.5\%$  to  $8.0\% \pm 7.1\%$  for 4D-MSPECT, and  $3.4\% \pm 2.9\%$  to  $9.2\% \pm 6.0\%$  for CARE heart. These results are shown as box plots in Figure 5, which clearly shows that the QGS results were more stable (EDV, ESV, and LVEF) over the entire range of tilts than were the 4D-MSPECT and CARE heart results, which showed similar behavior to each other.

#### DISCUSSION

Electrocardiographically gated SPECT allows myocardial perfusion imaging with simultaneous calculation of parameters of left ventricular function (EDV, ESV, and LVEF). Several studies have shown the accuracy of gated SPECT values, especially compared with cardiac MRI (4,12,15,16).



**FIGURE 4.** LVEF correlation analysis using QGS (A), 4D-MSPECT (C), and CARE heart (E) calculated from  $R_{15}$  vs.  $R_0$  data. Bland-Altman plots of the  $R_0$  and  $R_{15}$  differences vs. mean LVEF using QGS (B), 4D-MSPECT (D), and CARE heart (F). CH = CARE heart.

The aim of the present study was to determine the influence of differences in heart axis reorientation on the calculation of EDV, ESV, and LVEF from gated SPECT data using 3 different quantification algorithms that rely on different contour-finding approaches. To that end, functional parameters were calculated from the correctly reoriented and artificially tilted datasets of a large cohort (60 patients), and the results of 3 standard software programs (QGS, 4D-MSPECT, and CARE heart) were compared.

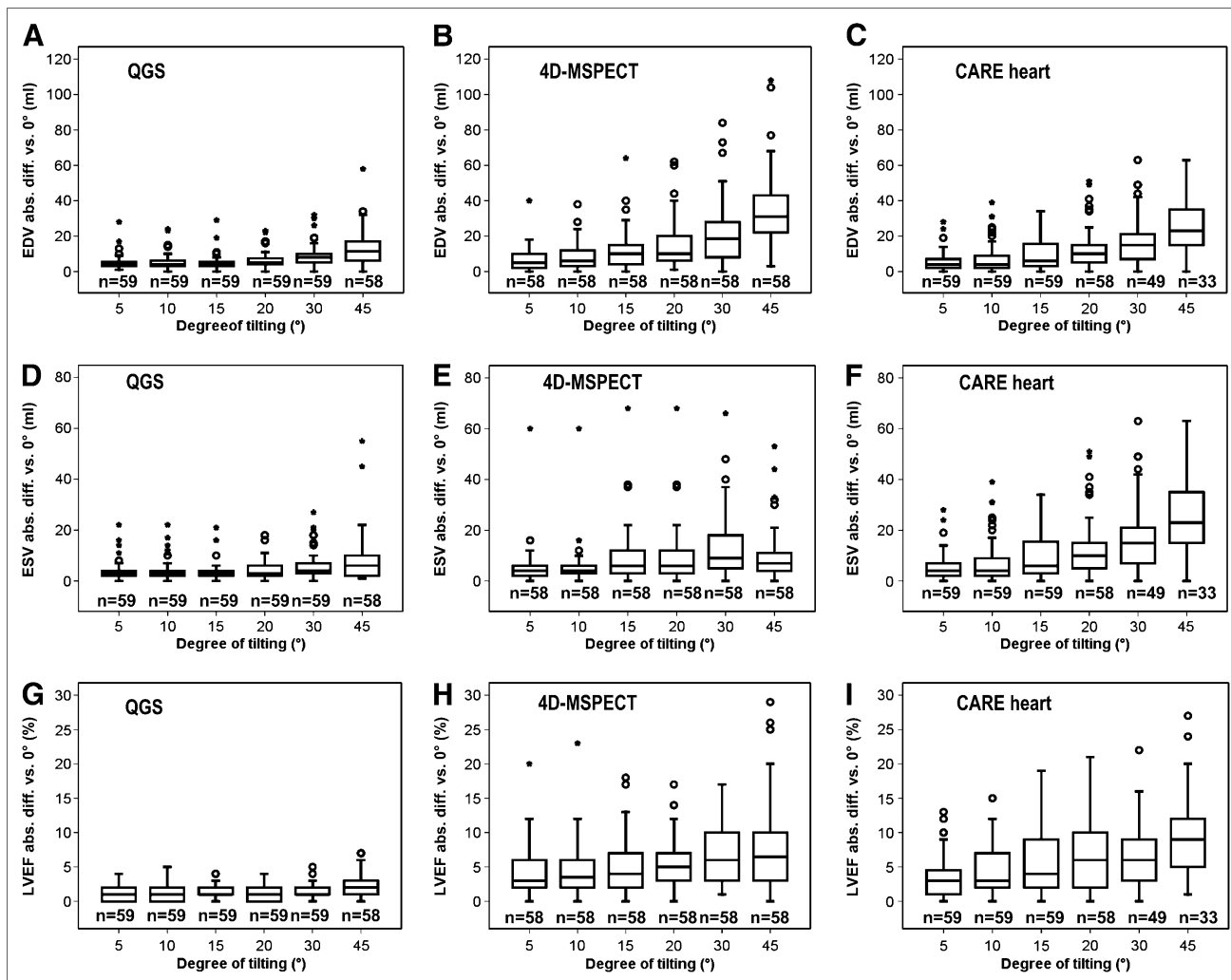
Correlation between results from correctly reoriented and  $15^\circ$ -tilted datasets (assessed using the  $R^2$  value) were best for QGS, as shown in the detailed analysis. Accordingly, QGS Bland-Altman limits were the narrowest for all 3 left ventricular parameters. Compared with QGS, the correlation of 4D-MSPECT and CARE heart results was distinctly lower whereas the Bland-Altman limits were considerably wider for all parameters. The number of patients with clinically relevant absolute EDV or ESV differences (i.e.,  $\geq 10$  mL) between the results of  $R_0$  versus  $R_{15}$  datasets was low for QGS (only 4 patients) and 5- to 8-fold higher for CARE heart and 4D-MSPECT. The absolute LVEF  $R_0$ - $R_{15}$  difference never exceeded the clinically relevant threshold of 5% (17)

when QGS was used, although nearly half the patients differed by 5% or more for the other 2 algorithms.

Additional analysis of SPECT data that had been tilted between  $5^\circ$  and  $45^\circ$  (an upper value never reached in clinical practice) showed increasing mean absolute differences with rising tilt levels for all 3 algorithms (compared with correctly reoriented data). The smallest changes were seen for QGS, whereas mean absolute differences rose more steeply for 4D-MSPECT and CARE heart (Fig. 5, box plots).

QGS provided the most stable and most consistent results over the entire tilt range, even when analyzing data tilted by  $45^\circ$ . 4D-MSPECT and CARE heart were less reliable with tilted datasets; especially for the  $30^\circ$ - $45^\circ$  range, causing 26 patients to be excluded with CARE heart (due to problems with finding the heart contour).

Taken together, these results show that CARE heart and 4D-MSPECT depend far more strongly on correct heart axis reorientation than QGS does. This is in line with the initial assumption of algorithm-specific effects. CARE heart is trained on correctly reoriented datasets, a condition that is not met if the axes are chosen incorrectly. 4D-MSPECT assumed the basal plane to be perpendicular to the long axes, another condition that is not met if the axes are chosen incorrectly.



**FIGURE 5.** Summary of effect of heart axis tilting on left ventricular functional parameters assessed using QGS, 4D-MSPECT, and CARE heart. SPECT datasets were tilted along each long axis by 5°–45°. EDV, ESV, and LVEF were assessed using these 3 algorithms and compared with results from original, correctly reoriented SPECT datasets as reference. Box plots show absolute EDV (A–C), ESV (D–F), and LVEF (G–I) differences (y-axis) for each tilt level (x-axis) for each algorithm (QGS: A, D, and G; 4D-MSPECT: B, E, and H; CARE heart: C, F, and I). y-axes were scaled identically for all parameters. Number below each box plot is number of datasets successfully analyzed (i.e., algorithm converged and gave reasonable results). Height of box indicates interquartile range (25%–75%); line within box, median (i.e., 50% quartile). Upper and lower whiskers include all measurements within 1.5 times interquartile range from either side of box (data points in this range are not considered outliers). Data points falling in 1.5–3 interquartile range above box are considered mild outliers (circles); those exceeding 3 interquartile range, extreme outliers (asterisks).

These results stress the importance of accurately reorienting SPECT datasets before using them for automatic analyses, especially regarding 4D-MSPECT and CARE heart. Inaccurately defining the heart axes in clinical routine may lead to incorrect EDV, ESV, and LVEF results, which in turn can influence diagnosis or therapy planning.

## CONCLUSION

QGS gave stable results despite tilted heart axes. 4D-MSPECT and CARE heart results depended greatly on reorientation. Hence, for those 2 algorithms, published validation results apply only to correctly reoriented data. The importance of correct reorientation must be stressed to avoid

miscalculation of the left ventricular parameters EDV, ESV, and LVEF.

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