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# Evaluation of Left Ventricular Function by 64-Multidetector Computed Tomography in Patients Undergoing Totally Endoscopic Coronary Artery Bypass Grafting

**Alexander Spoeck,**[1] Johannes Bonatti, MD,[2] Guy J. Friedrich, MD,[3] Thomas Schachner, MD,[2]
Nikolaos Bonaros, MD,[2] Gudrun M. Feuchtner, MD[1]

Departments of [1]Radiology II, [2]Cardiac Surgery, and [3]Cardiology, Innsbruck Medical University,
Innsbruck, Austria

## ABSTRACT

**Objectives:** The goal of this study was to quantify left ventricular (LV) function with automated 3-dimensional volume segmentation by 64-slice computed tomography (CT) in patients undergoing totally endoscopic coronary artery bypass grafting (CABG).

**Methods:** We used 64-multidetector CT coronary angiography to examine 63 patients with >70% coronary stenosis who were undergoing totally endoscopic CABG for single-vessel disease (left internal mammary artery to left anterior descending coronary artery) or multivessel disease with the da Vinci robotic surgical device (arrested heart approach). CT measurements were compared with cineventriculography results in 20 patients.

**Results:** The intraobserver variability values for the end-systolic volume (ESV) and the end-diastolic volume (EDV) were excellent (7.2% and 5.2%, respectively). Bland-Altman plots showed good upper and lower limits of agreement (ESV, +9% and –3.3%, respectively; EDV, +17% and –5.9%). Intraobserver variability for the LV ejection fraction (LVEF) was 4.8% with narrow limits of agreement (+7.8%, –2.2%). The mean postprocessing time was 6.5 minutes. Mean values (±SD) were 62.7% ± 12% (range, 23%-86%) for LVEF, 98.4 mL ± 29 mL for EDV, and 38.3 mL ± 23 mL for ESV. The LVEF obtained via CT was moderately but significantly correlated with the invasive cineventriculogram ($r = 0.51$; $P = .02$; limits of agreement, +18.7% and –18.4%).

**Conclusion:**. Through the use of automated LV volume segmentation, 64-slice CT permits fast quantification of LV function in patients with coronary artery disease undergoing totally endoscopic CABG grafting, enabling a comprehensive evaluation of coronary arteries and bypass grafts.

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*Correspondence: Gudrun M. Feuchtner, MD, Ao. Prof., Department of Radiology II, Innsbruck Medical University, Anichstrasse 35, A-6020 Innsbruck, Austria; 0043-512-504-81898; fax: 0043-512-504-24029 (e-mail: Gudrun.Feuchtner@i-med.ac.at).*

## INTRODUCTION

Totally endoscopic coronary artery bypass grafting (CABG) surgery with the da Vinci robotic device (Intuitive Surgical, Mountain View, CA, USA) is a promising and innovative technique for minimally invasive CABG without opening the chest. Accurate measurement of left ventricular (LV) function is important before CABG surgery in predicting, for example, early hospital mortality or long-term survival and to define medication and treatment strategies [Eagle 2004].

The presence of ischemic regional wall-motion abnormalities in patients with coronary artery disease can negatively influence the accuracy of measurements of LV function via conventional methods such as 2-dimensional echocardiography [Bartel 2007], yielding high interobserver variability of 5% to 34% [Jenkins 2007]. Two-dimensional echocardiography is routinely used in clinical practice for assessing LV function [Schiller 1991], but it has limitations because of the method's dependence on the level of the observer's experience, transducer position, and the patient's size and morphology.

Cineventriculography is commonly used in clinical practice for quantifying LV function, because such patients require cardiac catheterization anyway. The accuracy of cineventriculography also is limited, however, by its being based on 2-dimensional biplane projections that do not precisely display true 3-dimensional (3D) LV volumes. Cardiac magnetic resonance (CMR) imaging serves as the gold standard method for quantifying LV function, but its availability is often limited in clinical practice.

Sixty-four–slice computed tomography (CT) is an emerging imaging modality for the noninvasive assessment of coronary arteries [Hendel 2006] and bypass graft patency [Martuscelli 2004; Anders 2006; Feuchtner 2007a; Schachner 2007]. Through the use of retrospective electrocardiographic (ECG) gating over the entire cardiac cycle, comprehensive measurement of LV volumes has become feasible.

Thus far, time-consuming image postprocessing, such as manual contour tracking, has been the main factor limiting the routine clinical use of CT. Advances in postprocessing software tools allow fast automated segmentation of LV volumes via the use of an automated 3D region-growing algorithm based on CT densities (in Hounsfield units [HU]). This module enables quantification of the LV ejection fraction

(LVEF), the end-systolic volume (ESV), the end-diastolic volume (EDV), and the myocardial mass. Therefore, the purposes of this study were to assess the feasibility and reproducibility of measurements of LV function by using automated 3D volume segmentation in patients who had coronary artery disease and were scheduled for totally endoscopic CABG grafting, and to compare 64-slice CT with the invasive cineventriculography approach.

## METHODS

### Study Population

Sixty-three patients were examined between November 2005 and July 2007. Demographic data and patient characteristics are summarized in Table 1. All patients had coronary artery disease (either single- or double-vessel disease) with at least one hemodynamically significant stenosis of >70% confirmed by invasive angiography. Bypass grafting was indicated in all patients because percutaneous coronary intervention was either unsuccessful or not possible. The patients were referred for CT angiography before and/or after minimally invasive totally endoscopic CABG with the da Vinci robotic device [Argenziano 2006] and the arrested-heart approach (ESTECH cannula; ESTECH, San Ramon, CA, USA) for preoperative planning and/or postoperative assessment of bypass graft patency [Feuchtner 2007b]. Eight patients had had a previous myocardial infarction more than 3 weeks before the CT scan. All patients gave written informed consent.

Patient-exclusion criteria were renal dysfunction (serum creatinine >1.2 mg/dL), hyperthyroidism, known iodine allergy, pregnancy, and multiple myeloma. Twenty patients underwent an invasive angiography examination within a maximum of 5 days before or after CT evaluation.

Table 1. Demographic Data for the Study Population (N = 63)*

| | |
|---|---|
| Age, y | 61 ± 9 (42-77) |
| Sex, n | |
| Male | 50 (79%) |
| Female | 13 (21%) |
| Body weight, kg | 85.3 ± 18 (50-153) |
| Body mass index, kg/m$^2$ | 28.5 ± 4.9 (20.8-48.8) |
| Cardiovascular risk profile | |
| Arterial hypertension | 94% |
| Cigarette smoking | 65% |
| Positive family history | 48% |
| Hypercholesterolemia | 88% |
| Diabetes | 14% |
| STEMI/NSTEMI, n | |
| <3 wk before CT examination | 0 (0%) |
| >3 wk before CT examination | 8 (13%) |
| Vessel disease, n | |
| Single | 33 (52%) |
| Double | 24 (38%) |
| Triple | 6 (10%) |

*Data are presented as the mean ± SD (range) where indicated. STEMI indicates ST-elevation myocardial infarction; NSTEMI, non–ST-elevation myocardial infarction; CT, computed tomography.

### CT Examination Technique

CT scanning was performed with a multidetector CT scanner (Sensation 64; Siemens Medical Systems, Forchheim, Germany) with 32-row detector collimation that acquired 64 × 0.6-mm slices by using the *z*-axis flying-focus technique, a table-translation speed of 3.8 mm/rotation, and a gantry-rotation time of 0.33 seconds. The tube current of 120 kV and 600 to 900 mA was dependent on the patient's sex, the patient's body size and mass, and the scan-range length. "ECG pulsing" (ECG tube current modulation) was applied if the heart rate was <65 beats/minute (bpm). Scan direction was craniocaudally during mid breath-hold. A bolus of 90 to 120 mL of iodine contrast agent, either iodixanol (Visipaque 320; GE Healthcare, Piscataway, NJ, USA) or iomeprol (Iomeron 400; Bracco Diagnostics, Princeton, NJ, USA), was injected with a power injector into an antecubital vein with a 20-gauge cannula at a flow rate of 4.5 to 6 mL/second. The amount of contrast agent injected depended on the scan-range length (iodine-delivery rate of approximately 1.5 g iodine per second as recommended for CT coronary angiography) and body mass (1-1.2 mL/kg). The scan was started automatically by applying a bolus-tracking technique (ascending aorta; threshold, 100 HU) as previously described for coronary CT angiography [Cademartiri 2004]. A β-blocker was given intravenously before the CT scan if the heart rate was >75 bpm (5-10 mL metoprolol [Beloc]; Schering, Kenilworth, NJ, USA).

### CT Image Reconstruction, Postprocessing, and Analysis

By using retrospective ECG gating, we reconstructed a data set containing transaxial slices at every 10% of the R-R interval (effective slice width, 1.5 mm; increment, 1.2 mm; medium-smooth convolution kernel, B30f) and transferred it to an external workstation (Leonardo; Siemens Medical Solutions, Erlangen, Germany). The images were reviewed with dedicated software (Circulation, version 1.0; Siemens Medical Solutions) at every 10% of the steps of the cardiac cycle. The most appropriate phase of end-systole and end-diastole was chosen for calculating LV volumes (70%-80% of the R-R interval for end-diastole and 20%-30% of the R-R interval for end-systole).

The LV was segmented by applying a dedicated automated volume-segmentation module based on Hounsfield units and a 3D region-growing algorithm [Muhlenbruch 2006] (Figure 1). The segmentation result was checked by scrolling through all transaxial images on multiplanar reformations and was adjusted individually (either expanded or contracted). After this step, we again checked the segmentation result and judged it as either "accurate" or "inaccurate." If we judged the segmentation result as "inaccurate," we performed an image-quality analysis as follows: (1) LV enhancement was evaluated as either "homogeneous" or "inhomogeneous." In the case of inhomogeneous enhancement, we measured the CT densities (in Hounsfield units) of differently attenuating regions for round-shaped regions of interest. (2) We maintained detailed records of the presence and characteristics of artifacts.

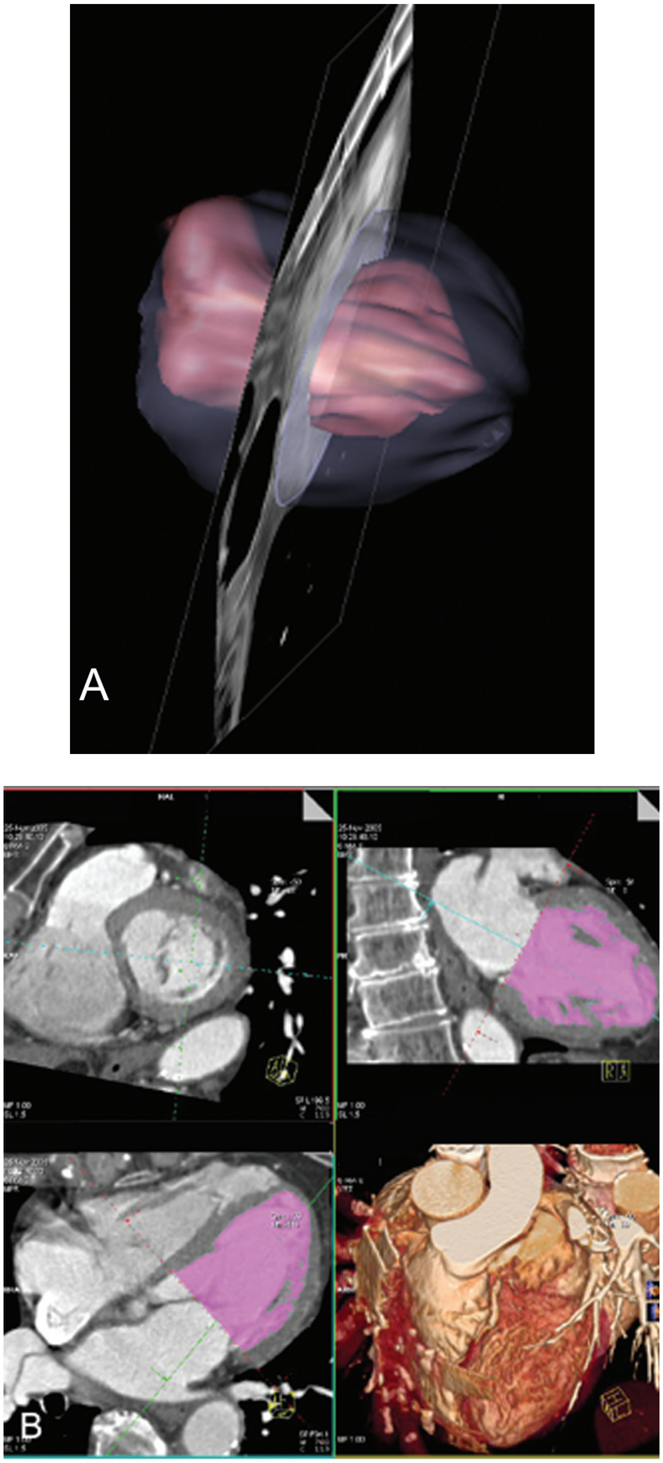

Figure 1. A, Three-dimensional (3D) left ventricular (LV) volume segmentation produced by the volume-rendering technique from a computed tomography data set. B, Automated volume segmentation by using a 3D region-growing algorithm. This software necessitates only the definition of the mitral valve level (red dashed line). The LV end-diastolic and end-systolic volumes are segmented automatically from the CT densities (in Hounsfield units; rose color). Upper left, short-axis view; upper right, 2-chamber view; bottom left, 4-chamber view.

The LV volumes at end-systole (20%-30% of the R-R interval; we adopted a "best fit" approach by using the smallest volume at the best image quality) and end-diastole (70%-80% of end-diastole; the best-fit approach was the use of the widest volume and the best image quality) were calculated automatically by multiplying the intrinsic voxel size of the CT scanner (approximately 0.4 $\text{mm}^3$) by the number of voxels within the segmented volume.

The LVEF was automatically calculated as a percentage from the LV EDV and ESV according to the formula:

$$\text{LVEF (\%)} = \frac{(\text{LV EDV}) - (\text{LV ESV})}{\text{LV EDV}} \times 100$$

One reviewer (A.S.) repeated the LV function measurements (LVEF, EDV, ESV).

### *Invasive Angiography*

An experienced cardiologist (G.F.) performed invasive angiography via a 7F catheter with femoral access in the left or right groin by means of the Judkins technique and a standard fluoroscopy unit (Axiom; Siemens Medical Solutions). Biplane ventriculograms were acquired in standardized 60° left anterior oblique and 30° right anterior oblique projections after the injection of iodine contrast agent (40-60 mL Visipaque). LV ESV and EDV volumes were calculated by the area-length method:

$$V = \frac{8 \cdot F^2}{3 \cdot \pi \cdot L}$$

### *Statistical Analysis*

Statistical analysis was performed with SPSS software (version 14.0.1; SPSS, Chicago, IL, USA). Quantitative variables were expressed as the mean ± SD. Testing checked that the data were consistent with a normal distribution.

The intraobserver variation (the mean of differences between corresponding observations divided by the mean of all observations) was expressed as a percentage. The correlation between the first and the second measurements of LV function was expressed as the Pearson correlation coefficient, and a 2-tailed $P$ value of <.05 was considered statistically significant. However, because the Pearson test has limited statistical power [Bland 1999], we used the Bland-Altman plot to evaluate the accuracy of agreement of repeated measurements [Bland 1986]. The coefficient of repeatability ($CR$) was calculated as 1.96 (or 2) times the SDs of the differences between the 2 measurements ($d_2$ and $d_1$), as follows:

$$CR = 1.96 \times \sqrt{\frac{\sum (d_2 - d_1)^2}{n - 1}}$$

The Mann-Whitney $U$ test was used to test the significance of LVEF differences between patients with inadequate and adequate segmentation results.

The intermodality agreement of the CT and invasive ventriculogram results was evaluated by linear regression analysis with the Pearson correlation coefficient and by the Bland-Altman plot by plotting the differences between the multislice CT and invasive ventriculography results against the means. The mean of the difference with a bias of ±1.96 SDs denotes the limits of agreement (ie, the 95% confidence interval).

## RESULTS

### *Reproducibility of LV Function Measurements with 64-Slice CT*

Overall, measurements of LV function were successfully performed in all 63 patients. Mean (±SD) values were 62.7% ± 12.1% (range, 23%-86%) for LVEF, 98.4 mL ± 28.5 mL (range, 51-217 mL) for EDV, and 38.3 mL ± 22.9 mL (range,10-140 mL) for ESV. Table 2 presents the results in detail.

**LV Ejection Fraction.** The mean intraobserver variability for LVEF was 4.8% ± 5.3% (range, 0%-30.3%), and the absolute mean for the 63 patients was 2.8%. The correlation of 2 independent measurements was excellent ($r = 0.98$; $P < .001$), and the Bland-Altman plot showed narrow limits of agreement (upper limit, 7.8%; lower limit, –2.2%) (Figure 2A).

For 6 of the 63 patients, the intraobserver variability for the LVEF was >10% (mean, 16.8%; range, 10.6%-30.3%). In these 6 patients, inhomogeneous filling of the LV (mean difference in CT densities, 150 ± 38 HU) and/or motion blurring were noted. These findings produced insufficient segmentation results for evaluating LV volumes. The mean LVEF for these 6 patients (44.9% ± 11%) was significantly lower ($P < .0001$) than those of patients with adequate ventricular volume segmentation results (64.6% ± 10.6%). This is because the low EF had caused suboptimal timing of the contrast agent bolus such that the contrast agent had already washed out of the LV.

**LV Volumes.** The mean intraobserver variability for the LV ESV was 7.2% ± 5.7%, and the absolute variability was 2.84 mL ± 3.1 mL. For the LV EDV, the intraobserver variability was 5.2% ± 4.8%, and the absolute variability in volumes was 5.55 mL ± 5.86 mL. The correlation of 2 independent measurements was excellent for both the LV EDV ($r = 0.98$; $P < .0001$) and the LV ESV ($r = 0.99$; $P < .0001$). Bland-Altman plots showed narrow limits of agreement (Figures 2B and 2C).

The mean postprocessing time was 6.5 minutes (range, 4.2-20 minutes) for the 63 patients. The mean heart rate during CT scanning was 60.5 bpm (range, 42-82 bpm). All patients were in sinus rhythm.

### *Measurements of LV Function with 64-Slice CT versus with Invasive Cineventriculography*

We selected 20 patients who required no pretreatment with β-blockers and who had undergone invasive angiography within 5 days. The LVEF measured by CT was moderately correlated with that obtained with cineventriculography ($r = 0.51$, Pearson correlation; $P = .01$; Figure 3A). The Bland-Altman plot (Figure 3B) showed moderate limits of agreement (upper limit, 18.7%; lower limit, –18.4%). We observed a slight LVEF overestimation (0.9%) with CT scanning and placed 19 of the 20 patients within the limits of agreement. The mean heart rate during CT scanning was 63 bpm (range, 42-65 bpm). All patients were in sinus rhythm.

## DISCUSSION

Our results indicate that measurement of LV function via automated 3D volume segmentation with 64-slice CT is feasible and fast in patients who have ischemic heart disease and are undergoing totally endoscopic CABG surgery. The main advantage of 64-slice CT over other modalities is that it provides a comprehensive coronary CT angiography examination that permits simultaneous evaluation of both coronary arteries and patencies of coronary bypass grafts (Figure 4). Quality control of bypass graft patency is particularly important following innovative coronary-revascularization techniques, such as totally endoscopic CABG.

The intraobserver variability observed in our study is consistent with the findings of a study that used 16-slice CT [Dewey 2006]. This study found a better agreement of CT with CMR, compared with echocardiography and cineventriculography, indicating that CT produces highly accurate LVEF measurements, similar to those obtained with CMR. Similar to our study, these investigators also reported moderate limits of agreement in the Bland-Altman plot when they compared cineventriculography with CMR (upper limit, 19%; lower limit, 16%) and a slight tendency (4%) for CT to overestimate the LVEF. The prevalence of "significant" coronary stenosis in this study was only 50%, however, and whether the degree of

Table 2. Reproducibility of Measurements of Left Ventricular (LV) Function by 64-Slice Computed Tomography in 63 Patients*

| | 1st Measurement | 2nd Measurement | Mean of 1st and 2nd Measurements | Intraobserver Variability | *P*† | Limits of Agreement (95% CI)‡ |
|---|---|---|---|---|---|---|
| LVEF, % | 64.2 ± 11.6 | 61.3 ± 12.5 | 62.7 ± 12.0 | 4.8% ± 5.3% | <.001 | +7.8; –2.2 |
| LV ESV, mL | 39.7 ± 23.8 | 36.9 ± 22.0 | 38.3 ± 22.9 | 7.2% ± 5.7% | <.0001 | +9.0; –3.3 |
| LV EDV, mL | 101.2 ± 29.8 | 95.6 ± 27 S | 98.4 ± 28.3 | 5.2% ± 4.8% | <.0001 | 17.1; –5.9 |

*Data are presented as the mean ± SD. CI indicates confidence interval; LVEF, LV ejection fraction; ESV, end-systolic volume; EDV, end-diastolic volume.

†Pearson correlation.

‡Limits of agreement (equal to the 95% CI) are obtained via the Bland-Altman plot. Data are presented as the upper and lower limits of agreement.

stenosis was hemodynamically relevant (ie, >70%) is not known. Ischemic wall-motion abnormalities, which occur in the presence of hemodynamically relevant stenosis of >70%, are known to influence the accuracy of measurements of LV function. Consequently, we recruited only patients with proven hemodynamically significant stenosis of >70%. Furthermore, the older 16-slice CT technology used in the study of Dewey et al [2006] is limited by a lower temporal resolution.

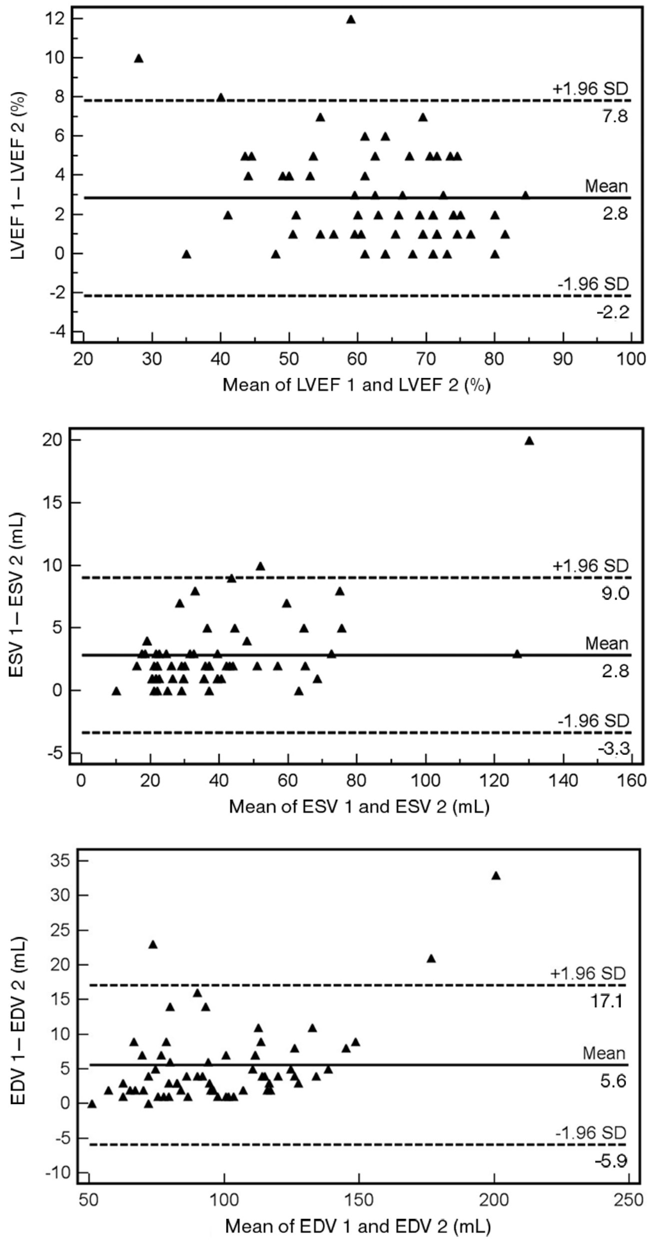

Figure 2. Agreement of repeated measurements of left ventricular (LV) function by computed tomography, as illustrated by Bland-Altman plots. A, LV ejection fraction (LVEF). Repeatability was excellent with narrow limits of agreement. B, LV end-systolic volume (ESV). The agreement was excellent with narrow limits of agreement (±1.96 SDs) (upper, +9.0%; lower, −3.3%). Two patients were placed outside the limits of agreement; the systolic image quality was hampered by motion artifacts in both patients. C, Repeated measurements of LV end-diastolic volume (EDV) showed good agreement, but 3 patients were placed outside the limits of agreement because of inhomogeneous filling of the LV owing to suboptimal timing of the contrast agent bolus caused by a low EF.

Recent advances in multislice CT technology have improved both spatial and temporal resolutions to 0.4 $mm^3$ and >105 milliseconds, respectively. Higher temporal resolution reduces motion artifacts, especially during systole. A newly introduced postprocessing module based on automated volume segmentation was used in our study. A study of manual contour tracking by 16-slice CT has shown the method not to be highly accurate compared with CMR [Mahnken 2005], and it is time-consuming in practice.

Few studies have assessed the accuracy of CT for evaluating LV function. Most have used the 16-slice CT technology, and data obtained with 64-slice CT have been limited.

Belge et al [2006] also demonstrated an excellent correlation between 16-slice CT and the CMR reference standard ($r$ = 0.95 for the LVEF) in 40 patients with a normal LV function.

Butler et al [2007] reported good interobserver correlations of measurements of LV function obtained with 64-slice CT in 25 patients ($r$ = 0.72-0.84) with markedly reduced LV function (EF <45%) and described moderate agreement with echocardiography results ($r$ = 0.67). Another study [Ferencik 2007] investigated 20 patients with severe heart failure before heart transplantation and showed even lower correlations ($r$ = 0.49-0.54) with echocardiography. However, echocardiography is known to have the highest interobserver variability in the presence of wall-motion abnormalities [Bartel 2007] and severe LV dysfunction. In patients with significant coronary stenosis, ischemic damage of the LV myocardium that produces wall-motion abnormalities can significantly influence the reproducibility of LVEF, EDV, and ESV measurements [Bartel 2007].

In addition, the correlation coefficient ($r$) has limited statistical power to test the intermodality agreement. In this setting, Bland-Altman plots are preferred for drawing such conclusions [Bland 1999].

Wu et al [2007] have recently published excellent results for comparisons of 64-slice CT with the reference CMR method for 41 patients. An evaluation of regional wall-motion abnormalities also showed promising results in this study.

### *Limitations*

**Radiation Dose.** Radiation exposure during a 64-slice CT scan ranges between 9.4 mSv and 14.8 mSv (mean, 11 mSv) [Hausleiter 2006]. ECG tube current modulation, which reduces the radiation exposure approximately 45% to 48%, is an important consideration and should be applied. Adapting the tube current (effective milliamperes) to the patient's sex and body mass/size is important to reduce radiation exposure, and this precaution was taken in our study (range, 600-900 effective mA).

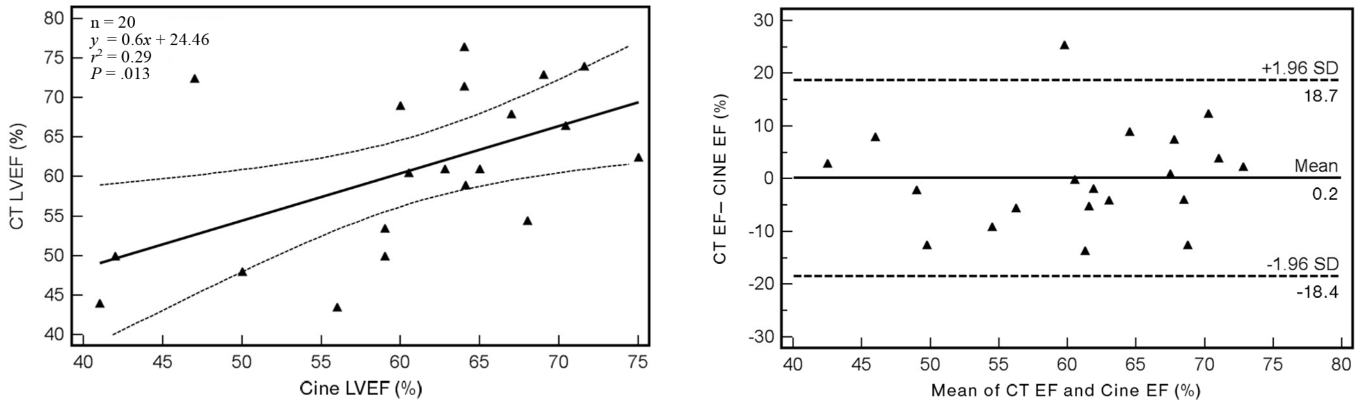

Figure 3. Left ventricular ejection fraction (LVEF) measurements: 64-slice computed tomography (CT) versus invasive cineventriculography (Cine). A, A moderate correlation was noted in the linear regression analysis ($P = .01$). Dashed lines indicate the 95% confidence interval. B, Bland-Altman Plot shows a moderate agreement between CT and cineventriculography with 19 of 20 patients placed within the limits of agreement. Limits of agreement were large (upper, +18.7%; lower, −18.4%). A slight tendency toward CT overestimation of the LVEF (+0.2%) was noted.

**Homogeneous LV Attenuation.** We have used a standard CT protocol, as recommended for coronary CT angiography [Cademartiri 2004], and the amount of contrast agent was adjusted individually on the basis of scan-range length and body mass index. In patients with LV dysfunction (LVEF <45%), however, we have found incomplete filling of the LV, which caused inaccurate LV volume segmentation and yielded high intraobserver variabilities (>10%). This result is probably explained by suboptimal timing of the contrast bolus, which produced a partially washed out LV by the time the scan was performed, and is related to a longer time-to-peak-enhancement curve in cases of low cardiac output. Thus, we suggest that increasing the amount of contrast agent by approximately 10 to 20 mL might solve this problem.

Figure 4. Comprehensive evaluation of coronary bypass graft patency by 64-slice computed tomography. The left internal mammary artery (LIMA) was grafted to the left anterior descending coronary artery (LAD) (white arrows) because the stent in the LAD was occluded. Three-dimensional volume-rendering technique.

***β*-Blockers.** β-Blockers are frequently necessary for controlling the heart rate before the CT scan to guarantee good image quality; however, the negative chronotropic and inotropic effects of β-blockers influence the measurement and lead to CT overestimates of LV function compared with CMR [Schlosser 2007]. Therefore, none of the patients in whom CT was directly compared with invasive angiography received any premedication with β-blockers.

## CONCLUSION

Sixty-four–slice CT allows reproducible and fast measurements of LV function in patients who have ischemic coronary heart disease and are undergoing totally endoscopic CABG surgery. A coronary CT angiography examination protocol allows a comprehensive evaluation of coronary arteries and patencies of coronary artery bypass grafts.

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