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Noel C.F. Codella
Weill Cornell Medical College

Hae Yeoun Lee
Weill Cornell Medical College

David S. Fieno
Heart South Cardiovascular Group

Debbie W. Chen
Weill Cornell Medical College

Sandra M. Hurtado Rua
Cleveland State University, s.hurtadorua@csuohio.edu

See last page for additional authors

Authors
Noel C.F. Codella, Hae Yeoun Lee, David S. Fieno, Debbie W. Chen, Sandra M. Hurtado Rua, Minisha Kochar, John Paul Finn, Robert Judd, Parag Goyal, Jesse Schenendorf, Matthew D. Cham, Richard B. Devereux, Martin Prince, Yi Wang, and Jonathan W. Weinsaft

Improved Left Ventricular Mass Quantification With Partial Voxel Interpolation

In Vivo and Necropsy Validation of a Novel Cardiac MRI Segmentation Algorithm

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Background—Cardiac magnetic resonance (CMR) typically quantifies LV mass (LVM) by means of manual planimetry (MP), but this approach is time-consuming and does not account for partial voxel components— myocardium admixed with blood in a single voxel. Automated segmentation (AS) can account for partial voxels, but this has not been used for LVM quantification. This study used automated CMR segmentation to test the influence of partial voxels on quantification of LVM.

Methods and Results—LVM was quantified by AS and MP in 126 consecutive patients and 10 laboratory animals undergoing CMR. AS yielded both partial voxel (AS_{PV}) and full voxel (AS_{FV}) measurements. Methods were independently compared with LVM quantified on echocardiography (echo) and an ex vivo standard of LVM at necropsy. AS quantified LVM in all patients, yielding a 12-fold decrease in processing time versus MP (0:21±0:04 versus 4:18±1:02 minutes; $P<0.001$). AS_{FV} mass (136±35 g) was slightly lower than MP (139±35; $\Delta=3\pm9$ g, $P<0.001$). Both methods yielded similar proportions of patients with LV remodeling ($P=0.73$) and hypertrophy ($P=1.00$). Regarding partial voxel segmentation, AS_{PV} yielded higher LVM (159±38 g) than MP ($\Delta=20\pm10$ g) and AS_{FV} ($\Delta=23\pm6$ g, both $P<0.001$), corresponding to relative increases of 14% and 17%. In multivariable analysis, magnitude of difference between AS_{PV} and AS_{FV} correlated with larger voxel size (partial $r=0.37$, $P<0.001$) even after controlling for LV chamber volume ($r=0.28$, $P=0.002$) and total LVM ($r=0.19$, $P=0.03$). Among patients, AS_{PV} yielded better agreement with echo ($\Delta=20\pm25$ g) than did AS_{FV} ($\Delta=43\pm24$ g) or MP ($\Delta=40\pm22$ g, both $P<0.001$). Among laboratory animals, AS_{PV} and ex vivo results were similar ($\Delta=1\pm3$ g, $P=0.3$), whereas AS_{FV} (6±3 g, $P<0.001$) and MP (4±5 g, $P=0.02$) yielded small but significant differences with LVM at necropsy.

Conclusions—Automated segmentation of myocardial partial voxels yields a 14–17% increase in LVM versus full voxel segmentation, with increased differences correlated with lower spatial resolution. Partial voxel segmentation yields improved CMR agreement with echo and necropsy-verified LVM. **(*Circ Cardiovasc Imaging*. 2012;5:137-146.)**

Key Words: left ventricular mass ■ cardiovascular magnetic resonance ■ echocardiography

Left ventricular mass (LVM) is widely used to guide clinical decision-making and prognostic assessment.[1,2] Cardiac magnetic resonance (CMR) is well suited to assess LVM because it provides high-resolution tomographic imaging that enables volumetric quantification without geometric assumptions. LVM quantification on CMR is typically done using manual planimetry (MP), whereby myocardial borders are traced by hand. Although MP has the potential to be highly detailed, it can be time-consuming, especially when LV chamber dilation is present.[3] MP can be especially challenging with respect to LV trabeculations, which contribute to LVM but are irregular in shape and can be difficult to discern from LV blood pool. Although MP of trabeculae has been reported to decrease CMR reproducibility and prolong

MP processing time,[4,5] failure to account for trabeculae yields increased discordance with necropsy-verified LVM and alters clinical classifications for patients with LV remodeling, in whom trabecular size and complexity are increased.[6–8]

Clinical Perspective on p 146

Automated segmentation (AS) can rapidly quantify highly detailed structures within the heart and elsewhere. Recent AS advances have enabled quantification of partial voxels—discrete structures admixed within a single imaging voxel. This approach fundamentally differs from conventional (full voxel) analysis, whereby regions are partitioned in a binary manner, based on location in relation to manual or automated contours. Though new to CMR, partial voxel segmentation has been successfully applied to other organs: Neurological studies have shown this to be useful for segmentation of tissue borders and irregularly contoured structures.[9–12] By extension, partial voxel segmentation holds particular relevance for LVM as it can account for endocardial irregularities and LV trabeculae.

AS algorithms have recently been developed that can simultaneously perform full and partial voxel segmentation of routine cine-CMR (steady-state free precession [SSFP]) images.[13,14] Instead of generating shape-based contours that mimic MP, the algorithms measure statistics regarding signal intensities of blood and myocardium, and, from this, perform voxel-by-voxel segmentation whereby partial voxel content of each substance is quantified for every LV voxel. In an initial validation study, partial voxel segmentation closely agreed with ex vivo phantom volumes and was applied in vivo for LV chamber quantification.[13] However, to date, partial voxel segmentation has not been used to measure LVM.

This study tested LVM segmentation among clinical patients and laboratory animals undergoing CMR. In patients, echocardiography (echo) was performed within 1 day of CMR and used as a clinical comparator for LVM. In laboratory animals, euthanasia was performed after CMR and segmentation results were compared with ex vivo LV weight. The aim was to examine the impact of partial voxel segmentation on CMR quantification of LVM.

Methods

Clinical Protocol

The study sample comprised consecutive patients enrolled in a post–myocardial infarction (MI) registry who underwent CMR and echo within a 1-day interval.[15] Imaging was performed between September 2006 and April 2010 at Weill Cornell Medical College. The study was conducted in accordance with the Weill Cornell Institutional Review Board; written informed consent was obtained at study enrollment.

CMR Image Acquisition

CMR was performed at 1.5 T (General Electric), using a standard 2-dimensional SSFP pulse sequence. Short-axis SSFP images were acquired from the mitral annulus through the LV apex. Typical SSFP parameters were repetition time, 3.5 ms; echo time, 1.6 ms; flip angle, 60°; temporal resolution, 30–50 ms; and in-plane spatial resolution, 1.6×1.3 mm. Images were acquired with a slice thickness of 6.0 mm and interslice gap of 4.0 mm. CMR imaging was performed without adjunctive contrast (gadolinium) administration.

LVM Quantification

LVM was quantified on CMR, using MP and AS. AS segmentation was performed with simultaneous calculation of LVM based on full (AS_{FV}) and partial (AS_{PV}) voxel calculated myocardial content.

AS and MP were performed independently, blinded to results of the other method. For each, contiguous end-diastolic short-axis images were segmented from LV base through apex. Basal and apical images of all patient exams were defined in accordance with established clinical criteria,[4,8] with the basal LV defined by the basal-most image encompassing at least 50% of circumferential myocardium. To directly compare AS with MP while minimizing potential confounding by slice and phase variance, basal-apical slice position and end-diastolic phase were held constant between methods. LVM was calculated as the product of myocardial specific gravity (1.05) and volume by each segmentation method.

Manual Planimetry

MP was performed in accordance with standard clinical practice, with LVM quantified by planimetry of end-diastolic endocardial and epicardial borders. Papillary muscles and trabeculae were included within myocardial contours; trabeculae were defined as myocardium protruding from the circumferential contour of the LV endocardium with similar signal intensity to the adjacent LV wall.[4,8] Planimetry was performed using commercial software (ReportCARD 4.0, General Electric). MP was also used to quantify LV dimensions, volumes, and total endocardial surface area—defined as the area of planimetered endocardial surface for each slice, summed across all 2D slices. Segmentation was performed by physicians (Drs Weinsaft and Cham) with American College of Cardiology/American Heart Association (ACC/AHA)level III training in CMR.

Automated Segmentation

Automated LVM quantification was performed using integrated endocardial and epicardial segmentation, based on previously established algorithms.[13,14] User input included identification of slices to be segmented and definition of the mitral and aortic valve annuli.

For endocardium, segmentation was performed using a geometry-independent algorithm that quantifies the mixture of blood and myocardium in each LV pixel.[13,14] Segmentation is accomplished by automatically computing blood and myocardial signal intensity distributions for each image individually (Figure 1A) and subsequently using that information to determine partial voxel content—defined as per voxel myocardial (or blood) content—for every voxel comprising the LV. The algorithm outputs 2 endocardial measurements: (1) "partial voxel" analysis consisting of the sum of partial blood voxel contents of every voxel ($ENDO_{PV}$) and (2) "full voxel" analysis consisting of the sum of all voxels with any fractional blood content ($ENDO_{FV}$). Full voxel analysis closely mimics MP, which partitions myocardium and cavity in a binary manner, with trabeculae included in LVM when contiguous in shape or of similar signal intensity to surrounding LV myocardium.[4,7,8,16] Figures 1B and 1C provide an illustration of partial voxel content as quantified by the segmentation algorithm.

For epicardium, segmentation was performed using an active contour model that uses location and signal intensity information resulting from the endocardial segmentation, in addition to signal intensity and edges at the epicardial-pericardial interface.[14] LVM was calculated on the basis of epicardial volume subtracted by either $ENDO_{PV}$ or $ENDO_{FV}$, respectively.

Intraobserver and interobserver reproducibility of automated and manual CMR methods were tested among a random sample of 20 patients.

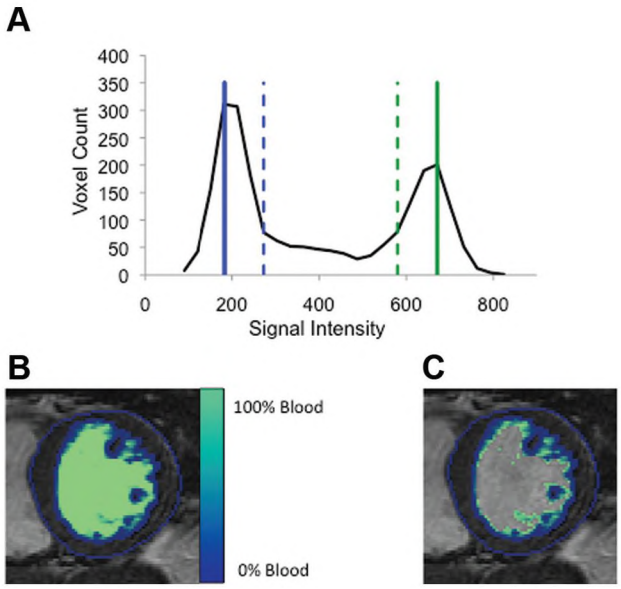

Figure 1. Automated segmentation algorithm. **A**, Representative histogram generated by automated segmentation (AS). **Solid blue line** indicates myocardial mean signal intensity; **dotted blue line**, 2 SD above myocardial mean (all intensities below this threshold considered full myocardial voxels by AS). **Solid green line** indicates full-blood mean signal intensity; **dotted green line**, 2 SD below blood mean (all intensities above this threshold considered full-blood voxels). Blood and myocardial partial voxel content is linearly interpolated between dotted blue and dotted green lines. **B**, Endocardial voxel content and epicardial contour as calculated by AS. Endocardial voxel content is displayed on a voxel-by-voxel basis, with colors mapped from blue to green, which represents 100% myocardium (0% blood) to 100% blood (0% myocardium), respectively. Epicardial contour is displayed as a **blue outline**. **C**, Identical steady-state free precession image with all endocardial voxels containing 100% blood removed from the display-only voxels containing less than 100% blood remain in the endocardial segmentation, and the epicardial contour is maintained as the **outer outline**.

Validation Protocol

Each method—MP, as well as AS_{FV} and AS_{PV}—was compared with 2 standards for LVM, described as follows.

Clinical Validation: Echocardiography

Echocardiography was performed within 1 day of CMR in all patients. LVM was quantified in accordance with established consensus guidelines[17]: Linear measurements on 2D and M-mode echo were used to calculate LVM using a standard formula $(0.8*\{1.04[(LVIDd+PWTd+SWTd)^3-(LVIDd)^3]\}+0.6$ g), developed and validated on the basis of necropsy-verified LV weight.[18–21] Echo analysis was performed blinded to CMR data.

Two-dimensional and M-mode linear measurements by the designated ACC/AHA level III–certified echo reader for the current study (Dr Devereux) have been previously shown to be closely correlated to each other in a series of 196 adults ($r=0.967$, $P<0.001$, mean $\Delta=0.4$ g, SD=10.2 g; P=NS).[22] Among 22 participants in another study,[23] LVM calculated from 2D linear measurements by the same reader (Dr Devereux) yielded values close to those obtained with use of M-mode recordings by a second reader ($r=0.94$, $P<0.001$; mean $\Delta=0.9$ g, SD=9.5 g, P=NS). Excellent reproducibility between measurements by a single experienced reader from separate echocardiograms has previously been shown in a series of 183 hypertensive adults for LVM (intraclass correlation coefficient [ρ]=0.93, $P<0.001$, mean $\Delta=1.7$ g, SD=18 g, P=NS) as well as LV chamber and wall dimensions ($\rho=0.83$–0.87), using echo methods applied in the current study.[24]

Table 1. Patient Characteristics

Age, y	57±13
Male sex	81% (102)
Atherosclerosis risk factors	
Hypertension	44% (55)
Hyperlipidemia	48% (61)
Diabetes mellitus	20% (25)
Tobacco use	34% (43)
Family history	27% (34)
Coronary artery disease history	
Prior myocardial infarction	6% (7)
Prior coronary revascularization	10% (12)
Cardiovascular medications	
Beta-Blocker	98% (124)
ACE inhibitor/ARB	71% (89)
HMG-CoA reductase inhibitor	97% (122)
Aspirin	100% (126)
Thienopyridines	94% (119)
Myocardial infarct parameters	
Infarct-related artery	
Left anterior descending	63% (80)
Right coronary	29% (36)
Left circumflex	8% (10)
Infarct size, % myocardium	17±10
Post–myocardial infarction interval, d	26±8
LV chamber size and function	
Cardiovascular magnetic resonance	
Ejection fraction, %	51±11
End-diastolic volume, mL	154±44
End-systolic volume, mL	77±37
Echocardiography	
Ejection fraction, %	48±11
End-diastolic diameter, cm	5.7±0.5
End-systolic diameter, cm	4.3±0.6

ACE indicates angiotensin-converting enzyme; ARB, angiotension II receptor blocker; LV, left ventricular.

Ex Vivo Validation: Necropsy

Necropsy validation of LVM was obtained in a preexisting cohort of animals that underwent CMR immediately before euthanasia, with confirmation of LVM based on ex vivo weight.[6,25] Necropsy specimens were weighed within 30 minutes of animal euthanasia. For the current study, CMR images were retrieved from image archives, analyzed by MP and AS, and compared with necropsy-verified LV weight. To directly compare CMR methods with total LV weight at necropsy, segmentation of animal exams was performed with inclusion of all slices containing LV myocardium. Basal-apical slice position and segmentation phases were matched between CMR methods.

Statistical Methods

Continuous variables (expressed as mean±SD) were compared using paired Student t test for 2-group comparisons. Categorical variables were compared using McNemar test for paired proportions. All continuous variables had qq plots and histograms suggesting normality. Processing time and LV volume were compared using bivariate correlation coefficients and linear mixed-effects models.

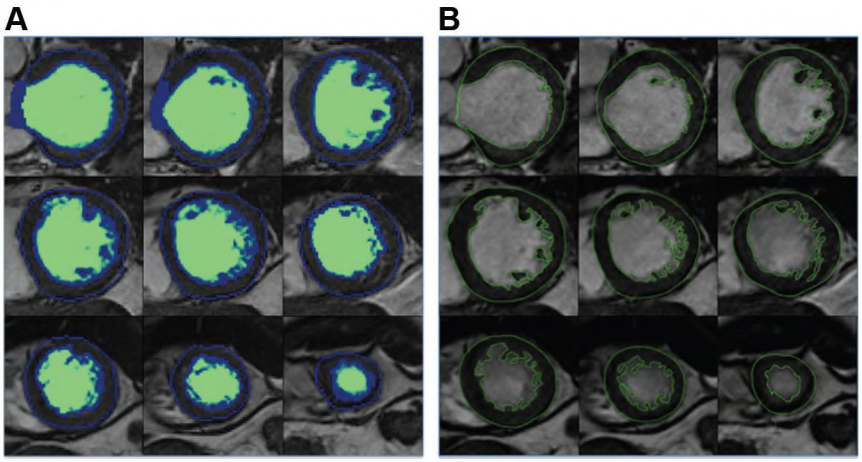

Figure 2. Typical example. Typical short-axis images demonstrating automated segmentation (AS) (**A**) and manual planimetry (MP) (**B**) segmentation, both of which account for myocardial trabeculae and papillary muscles. In this example, left ventricular mass by AS_{FV} (75.0 g/m^2) and MP (74.6 g/m^2) closely agreed, whereas AS_{PV} yielded higher mass (86.4 g/m^2), respectively, corresponding to relative differences of 15% and 16% with AS_{FV} and MP.

Multivariable linear regression analyses were used to evaluate associations between continuous variables.

Comparison of mean LVM by each quantification method was assessed using a linear mixed-effects model (taking into account the fact that echo, MP, AS_{FV}, and AS_{PV} measurements are correlated within patients/animals) with an unconstrained covariance matrix. Multiple comparisons procedures were used to control for family-wise error rate: For patient data, adjustment was done using the Tukey-Kramer multiple comparison procedure, which enabled primary comparison to the reference of echo as well as relative differences between CMR methods. For animal data, CMR methods were compared with necropsy reference with adjustment using the Dunett-Hsu multiple comparison procedure. Two-sided $P<0.05$ indicated statistical significance. Calculations were performed using SPSS 12.0 (SPSS Inc, Chicago, IL) and SAS 9.2 (SAS Inc, Cary, NC).

Results

Patient Sample

LVM segmentation was tested in 126 consecutive patients undergoing CMR as part of an ongoing study examining post-MI LV remodeling.[15] No patients were excluded on the basis of clinical characteristics or image processing results. Table 1 details patient characteristics.

Automated LVM Segmentation

AS successfully quantified LVM in all cases. Of the total 1127 images (126 exams, 8.9±0.9 images/examination), 51 (4.5%) required endocardial corrections, 74 (6.6%) epicardial corrections, and 107 (9.5%) delineation of the basal LV outflow tract. In aggregate, 60% of exams required no manual adjustment apart from identification of LV images and truncation of the LV outflow tract. For the remainder, epicardial or endocardial contours were manually adjusted based on visual inspection (1.0±1.6 adjustments per examination, 58% epicardial). Endocardial or epicardial corrections were deemed necessary when automated segmentation failed to truncate the myocardial border with either LV cavity or pericardium (ie, due to temporal blurring and/or indistinct anatomic boundaries). Total processing time, including AS, visual inspection, and any manual adjustment, was under 1 minute in all cases.

Figure 2 provides a typical example of LVM segmentation by AS compared with MP.

Full Voxel Segmentation

Table 2 reports LVM quantification by AS_{FV} and MP. LVM was slightly lower by AS_{FV}, with average differences between methods (3±9 g, 1.6±4.7 g/m^2, $P<0.001$) corresponding to 6±4% of LVM by MP. When established CMR-based cutoffs were applied,[26,27] both methods yielded similar proportions of patients meeting criteria for LV hypertrophy ($P=1.00$) and chamber remodeling ($P=0.73$).

Also shown in Figure 3A, processing time for AS was over 12-fold lower versus MP (0:21±0:04 versus 4:18±1:02 minutes), corresponding to an average time savings of nearly 4 minutes (Δ=3:58±1:02, $P<0.001$). Processing time correlated with LV chamber size for MP ($r=0.57$, $P<0.001$) and AS ($r=0.24$, $P=0.007$). However, as shown in corresponding scatterplots for each method (Figure 3B), regression slopes were >30-fold higher for MP (0.89) compared with AS (0.03), reflecting a markedly higher proportionate increase in processing time in relation to chamber size.

Partial Voxel Segmentation

AS was also used to calculate LVM with incorporation of myocardial partial voxels (AS_{PV}). Table 3 compares AS_{PV} with MP and AS_{FV}. As shown, LVM by AS_{PV} was higher compared with either MP (Δ=20±10 g) or AS_{FV} (Δ=23±6

Table 2. Conventional LV Mass Segmentation: LV Segmentation Results

	Manual Planimetry	Automated Segmentation, Full Voxel	Δ	*P*
LV mass, g	139.1±35.1	135.9±35.0	3.1±9.3 g	<0.001†
LV mass index, g/m^2	71.1±15.1	69.5±15.3	1.6±4.7 g/m^2	<0.001†
Diagnostic classifications*				
LV chamber remodeling	57% (72)	56% (70)	2% (2)	0.73
LV hypertrophy	3% (4)	4% (5)	1% (1)	1.00

LV indicates left ventricular.

*Based on previously established, population-based, cardiac magnetic resonance cutoffs.[26,27]

†*P* value <0.05 (data presented as mean±SD).

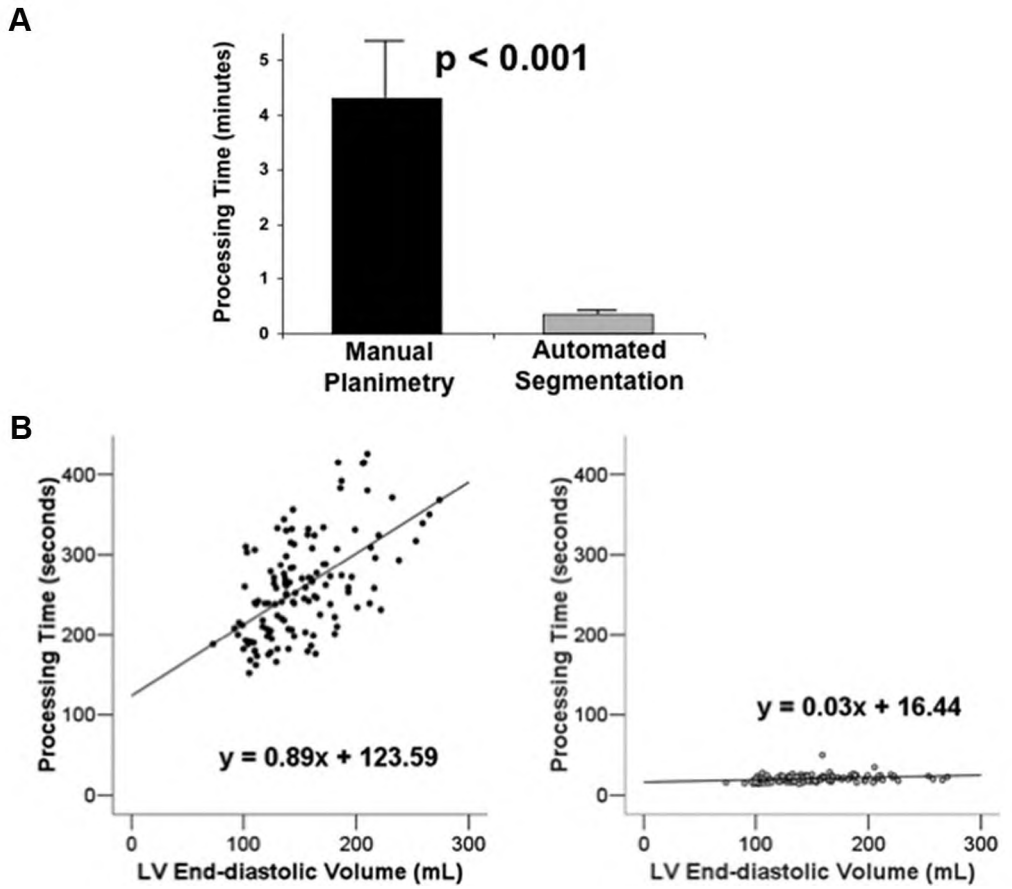

Figure 3. Processing time. **A**, Processing time for manual planimetry (MP) (**black bar**) and automated segmentation (AS) (**gray bar**). Data shown as mean±SD. **B**, Corresponding scatterplots for MP (**left**) and AS (**right**) relating left ventricular (LV) chamber volume (*x*-axis) to processing time (*y*-axis) for each method.

g, $P<0.001$), corresponding to relative differences of 14% and 17%, respectively. LVM by AS_{PV} yielded a similar proportion of patients (5%) meeting established criteria for LV hypertrophy[26] compared with either MP (3%; $P=0.50$) or AS_{FV} (4%; $P=1.00$). However, AS_{PV} yielded a markedly lower proportion of patients (26%) meeting established criteria for LV chamber remodeling[27] than did MP (57%; $P<0.001$) or AS_{FV} (56%; $P<0.001$).

In multivariable analysis, magnitude of difference between AS_{PV} and AS_{FV} independently correlated with larger voxel size (partial $r=0.37$, $P<0.001$) even after controlling for LV chamber volume ($r=0.28$, $P=0.002$) and LVM ($r=0.19$, $P=0.03$) as quantified by the standard of full voxel segmentation (model $r=0.64$, $P<0.001$).

All segmentation methods demonstrated good intrareader and inter-reader reproducibility, although limits of agreement were smaller for both AS_{FV} and AS_{PV} by AS compared with MP (Figure 4).

Validation

Each CMR segmentation method was independently compared with 2 standards: (1) a clinical standard of LVM measured on echo and (2) an ex vivo standard of LVM as weighed at time of necropsy.

LVM by Echocardiography

Echo was performed within 1 day of CMR in all patients (97% same day); 96% of echoes (n=121) were technically sufficient to quantify LVM. The most common reasons for technically insufficient echoes (4%) were poor endocardial definition or off-axis imaging.

Table 3. Comparison of Full and Partial Voxel–Adjusted LV Mass

	Partial Voxel AS_{PV}	AS_{FV}			MP		
	Mean±SD	Mean±SD	Δ*	*P**	Mean±SD	Δ*	*P**
LV mass, g	158.7±37.9	135.9±34.9	22.8±5.5	<0.001	139.1±35.1	19.7±10.1	<0.001
LV mass index, g/m^2	81.2±16.2	69.5±15.3	11.7±2.4	<0.001	71.1±15.1	10.1±5.0	<0.001

LV indicates left ventricular; AS, automated segmentation; MP, manual planimetry.

*Difference (mean±SD) vs partial voxel–adjusted LV mass (*P* values adjusted for multiple comparisons).

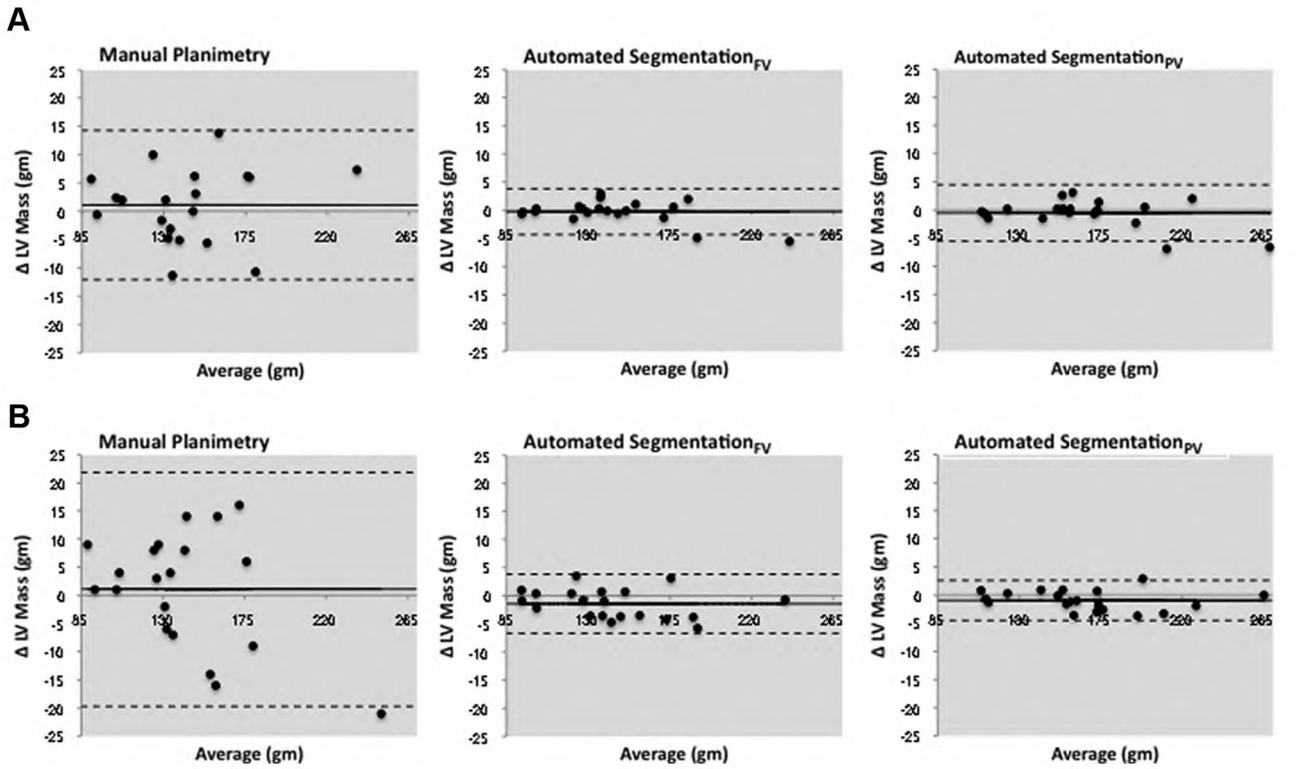

Figure 4. Reproducibility. Bland-Altman plots demonstrating reproducibility data for each segmentation method. Data shown as mean±2 SD. **A**, provides intraobserver data, demonstrating that mean differences for all methods were small (MP: 1.1 g, automated segmentation $[AS]_{FV}$: −0.3 g, AS_{PV} −0.6 g), although limits of agreement were narrower for AS_{FV} (−4.3 to 3.8 g) and AS_{PV} (−5.6 to 4.5 g) compared with MP (−12.1 to 14.3 g). Interobserver measurements (**B**) demonstrated similar findings. LV indicates left ventricular; CMR, cardiac magnetic resonance; MP, manual planimetry.

Figure 5A shows LVM results by each method, demonstrating that echo yielded higher LVM than did all CMR segmentation methods ($P<0.001$). However, as shown in Figure 5B, mean differences between CMR and echo were smallest with LVM_{PV} ($\Delta=20\pm25$ g, 11 ± 13 g/m^2) compared with LVM_{FV} by either AS ($\Delta=43\pm24$ g, 22 ± 12 g/m^2) or MP ($\Delta=40\pm22$ g, 20 ± 12 g/m^2) (both $P<0.001$).

LV Weight at Necropsy

LVM segmentation methods were also tested in a preexisting cohort of 10 animals (8 dogs, 2 pigs) that underwent CMR before euthanasia. Figure 6 shows results of each CMR method compared with the reference standard of ex vivo LV weight: LVM averaged 70 ± 13 g at necropsy and 69 ± 14 g by LVM_{PV}, reflecting nonsignificant absolute and relative differences of 1 ± 3 g and $4\pm3\%$ ($P=0.54$). Automated LVM_{FV} was lower (63 ± 14 g) and yielded significant differences (7 ± 3 g, $10\pm6\%$) with ex vivo LV weight ($P<0.001$). MP paralleled automated full voxel data, as reflected by lower LVM (65 ± 16 g) that differed significantly (4 ± 5 g, $8\pm7\%$; $P=0.049$) from ex vivo results.

Discussion

This study is the first to examine partial voxel segmentation for automated LVM quantification. There are several key findings: First, among the consecutive series of post-MI patients studied, AS using full voxel analysis (AS_{FV}) yielded similar results to manual planimetry (MP), with small albeit statistically significant, absolute differences (3 ± 9 g, $P<0.001$). Both methods yielded similar results concerning classification of patients with LV remodeling ($P=0.73$) or hypertrophy ($P=1.00$). Second, AS using partial voxel analysis (AS_{PV}) yielded larger LVM than AS using full voxel analysis ($\Delta=23\pm6$ g) or MP ($\Delta=20\pm10$ g; both $P<0.001$). Magnitude of difference between AS_{PV} and AS_{FV} independently correlated with larger voxel size (partial $r=0.37$, $P<0.001$) even after controlling for LV chamber volume ($r=0.28$, $P=0.002$) and LVM ($r=0.19$, $P=0.03$) (model $r=0.64$, $P<0.001$). Third, AS_{PV} yielded better agreement with the clinical standard of LVM by echo and smaller differences with LV weight at necropsy.

Regarding necropsy data, automated segmentation was applied to a preexisting CMR dataset in which actual LV weight was verified ex vivo. Results demonstrated that partial voxel segmentation yielded nonsignificant differences with necropsy-evidenced LVM (1 ± 3 g, $P=0.3$), whereas full voxel yielded small but significant differences when either AS (6 ± 3 g, $P<0.001$) or MP (4 ± 5 g, $P=0.02$) were used. This finding is consistent with prior cine-CMR (SSFP) studies that have reported small mean differences between CMR and necropsy LVM but have noted variability ranging from -0.8 ± 2.6 to 0.2 ± 8.4 g with MP and -10.6 ± 7.1 to 4.2 ± 7.1 g with AS.[6,28,29] Although the reasons for variable differences in CMR and necropsy results are not certain, this may relate to animal and study specific differences in spatial resolution, image quality, or interval between imaging and necropsy with resultant postmortem changes in LVM.

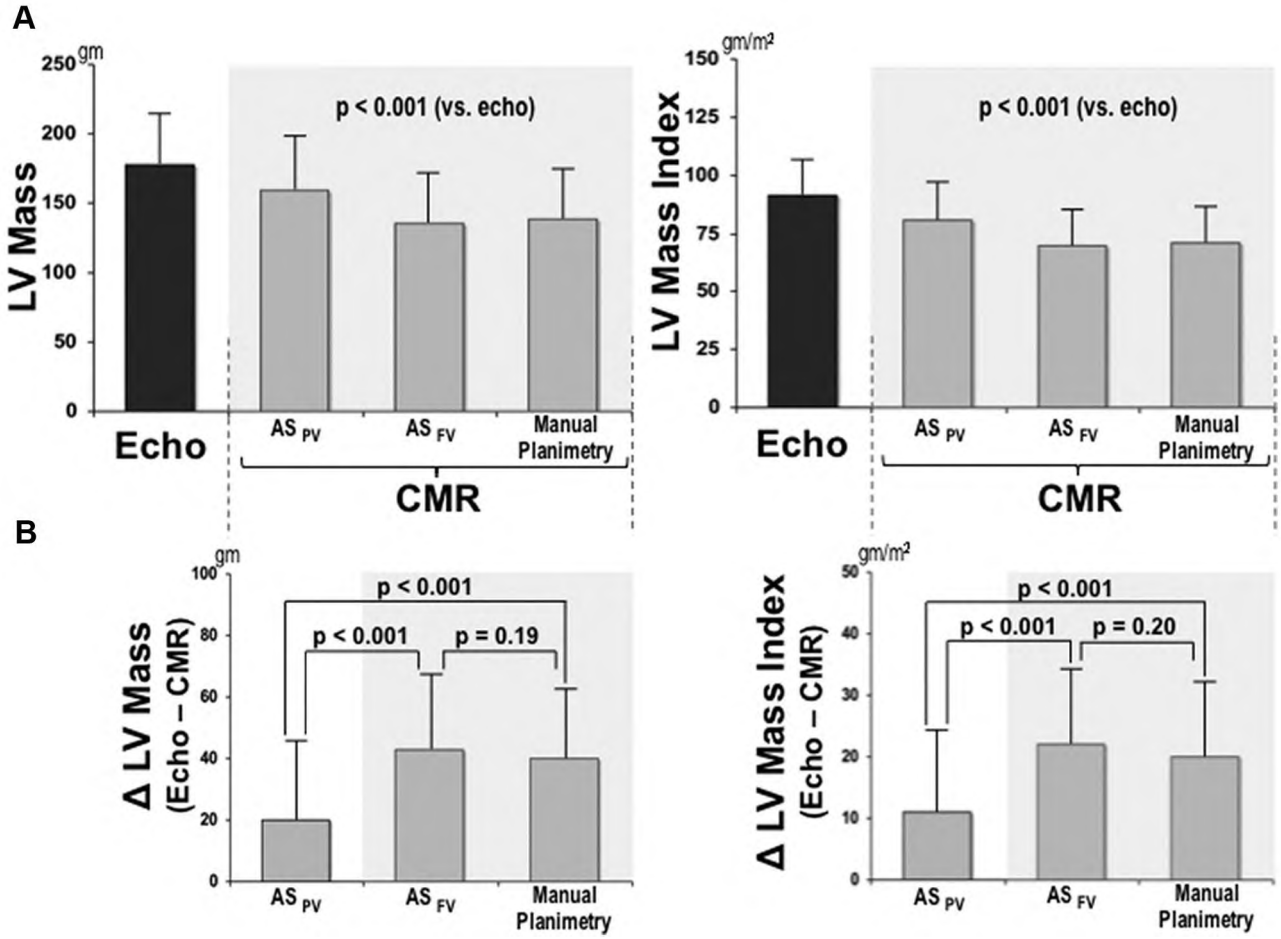

Figure 5. Comparison to echocardiography. **A**, Mean left ventricular mass (LVM) by each cardiac magnetic resonance (CMR) segmentation method (**gray bars**) compared with echo (**black bar**) among patient cohort (n=121). **B**, Mean LVM difference between each CMR method and echo, demonstrating smaller differences with automated segmentation $(AS)_{PV}$ as compared with AS_{FV} or manual planimetry ($P<0.001$; all probability values adjusted for multiple comparisons).

To further test CMR segmentation versus an independent clinical reference, patient results were compared with LVM as quantified by echo. Findings demonstrated that whereas all CMR methods yielded lower LVM than echo, partial voxel analysis yielded smaller mean differences (20±25 g, 11±13 g/m^2, $P<0.001$) than did AS full voxel (43±24 g, 22±12 g/m^2) or MP (40±22 g, 20±12 g/m^2). Prior comparative studies have used MP and also reported lower LVM by CMR,[30–32] although variance has been larger than in our study, as evidenced by mean differences of 37±39 g/m^2 in cohorts with valvular heart disease and 58±63 g (data reported unindexed) in heart transplant patients.[31,33]

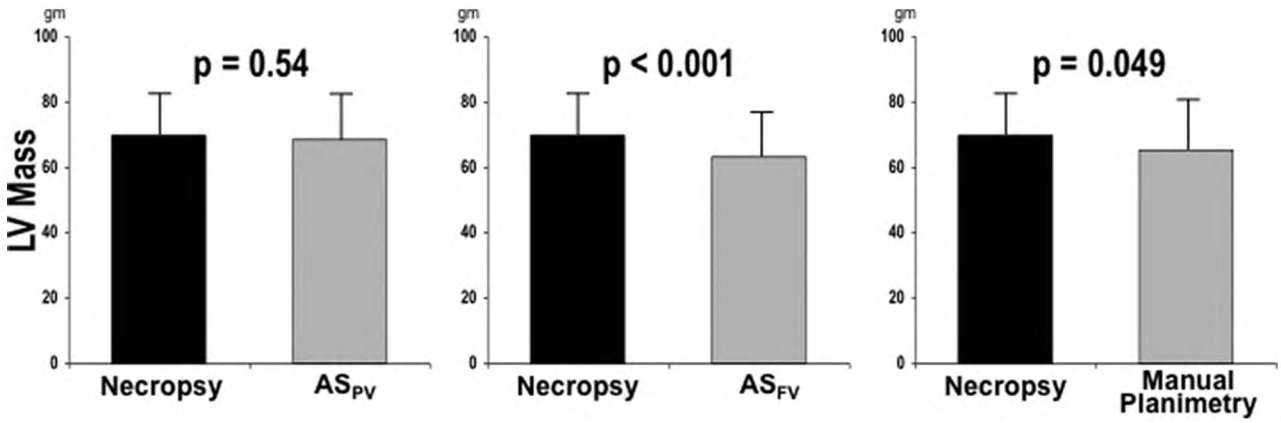

Figure 6. Comparison to necropsy. Left ventricular (LV) mass by each cardiac magnetic resonance segmentation method (**gray bars**) compared with necropsy-derived LV weight (**black bar**) among animal cohort (n=10). Only automated segmentation $(AS)_{PV}$ yielded nonsignificant differences with LV weight at necropsy (all probability values adjusted for multiple comparisons).

Our data shed new light on prior comparative studies, which have commonly attributed LVM differences between modalities to echo-specific factors. Certainly, it is important to recognize that echo-based calculations employ geometric assumptions whereas CMR quantifies LVM based on actual planimetry of myocardial borders: Both off axis imaging and image quality can affect echo measurements, whereas CMR provides high resolution imaging with great precision for detecting small differences in LVM.[33] However, prior papers have demonstrated systematically lower LVM by CMR versus echo,[30–32] suggesting intrinsic biases not fully explained by echo alone in context of several studies showing unbiased estimation of echo-derived LVM versus necropsy-verified LV weight.[18,19,21]

Our results suggest that previously reported differences between CMR and echo may be partially attributable to the approach used for CMR segmentation, with agreement improved through quantification of myocardial partial voxel content. Although reasons for improved agreement between echo and partial voxel CMR are uncertain, we speculate that this may be due to the fact that echo-formulas use linear measurements to calculate LVM based on models derived from actual LV weight (ie, trabeculae inclusive) at necropsy,[18,19,21] an approach that can yield error on an individual patient basis but provide generally accurate LVM when measured for overall populations. Partial voxel CMR calculates LVM without geometric assumptions while accounting for detailed components of LV myocardium (ie, trabeculae) that can be difficult to trace manually but contribute to overall LV weight, resulting in higher LVM values for individual patients and across populations. These issues may explain improved agreement between partial voxel CMR and echo, as well as residual differences between modalities. Consistent with this, our group's prior research has demonstrated that failure to segment trabecular volume on CMR yields increased discrepancy with linear echo formulas for LVM.[8] As multimodality imaging is increasingly being used to guide patient care, the ability of partial voxel CMR segmentation to yield improved agreement with echo-derived LVM is of substantial clinical importance.

Beyond partial voxel segmentation, a novel feature of the AS algorithm tested in this study is that no geometric assumptions regarding endocardial shape are used.[13] This differs from several prior AS algorithms, which have used shape-based constraints regarding LV border geometry.[34–38] In contradistinction, the algorithm tested in this study relies on only one fundamental assumption—LV blood is enclosed by LV myocardium. On this basis, AS is performed using an automated effusion-threshold–based approach that relies on intrinsic differences in signal intensity between blood and myocardium rather than shape-based algorithmic constraints. This feature is complementary to partial voxel segmentation, in that it enables LV segmentation independent of remodeling-associated changes in LV contours. Moreover, the current algorithm segmented all cases in less than 1 minute, a considerable time saving compared with MP. Whereas few prior studies have reported actual processing times, we note that mean processing time for AS in the current study (0:21±0:04) was far lower than that reported for prior shape-based AS algorithms (5:00±0:18 minutes).[29]

Concerning clinical performance, study results demonstrate the utility of geometry-independent effusion-threshold segmentation. Among the consecutive series of 126 patients tested, AS was successful in all cases and required minimal user corrections. Absolute differences between AS_{FV} and MP were significant but small ($\Delta=3\pm9$ g, $P<0.001$), resulting in nonsignificant differences when established CMR criteria for LV hypertrophy and remodeling were applied. The relative agreement between MP and AS_{FV} can be explained at least in part by the similarities between the two techniques. When performing MP, an operator visually discerns LV myocardium from blood, based on shape or signal intensity,[4,7,8,16] with regions of similar signal intensity partitioned together. With this approach, voxels that contain any amount of fractional blood content (and thus exhibit higher signal intensity than the adjacent myocardium) are included in blood volume, even though they may also include fractional myocardial content. Similarly, AS_{FV} uses an algorithm that simply counts the number of voxels with any fractional blood content; thus, it labels regions that are inherently brighter than LV myocardium (due to fractional blood content) as blood, even though they may also contain fractional myocardial content. In contrast, partial voxel segmentation allows fractional quantifications of both blood and myocardium within each voxel region. Thus, AS_{PV} would be expected to be of incremental utility when increased voxel size results in juxtaposition of myocardium and blood within a single voxel—a phenomenon that is not accounted for by MP or full voxel analysis. Consistent with this, our results demonstrate that differences between full and partial voxel segmentation correlate with larger voxel size ($r=0.37$, $P<0.001$) even after controlling for LV cavity size and total LVM.

Several limitations should be recognized. First, clinical performance of CMR segmentation was tested among patients in a post-MI registry, the majority (81%) of whom were male. Although this enabled us to test segmentation among patients with MI-associated LV remodeling, further study is needed to evaluate partial voxel segmentation in broad population-based cohorts. Second, although results demonstrate that partial voxel segmentation yields better agreement with independent standards of echo and necropsy quantified LVM, clinical outcomes data were not obtained and the predictive value of partial versus full voxel CMR segmentation results is not known. Finally, although geometry-independent partial voxel segmentation was shown to perform robustly, minimal user interaction is still required to identify the actual LV slices to be segmented.

In summary, this study demonstrates that partial voxel automated segmentation is a promising improvement for LVM quantification. Future research is necessary to test whether partial voxel–adjusted LVM provides incremental utility versus full voxel assessment for clinical prognostic assessment.

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Disclosures

The authors' institution (Weill Cornell) has submitted a patent for the automated segmentation algorithm described in this study.

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CLINICAL PERSPECTIVE

Left ventricular mass (LVM) is widely used to guide clinical decision-making and prognostic assessment. Cardiac magnetic resonance (CMR) is well suited to assess LVM because it provides high-resolution tomographic imaging that enables volumetric quantification without geometric assumptions. CMR typically quantifies LVM by manual planimetry (MP) of LV chamber contours: This approach is widely used in clinical practice but can be time-consuming, challenging with respect to planimetry of irregularly contoured trabeculae, and limited in its ability to account for myocardial partial voxels—myocardium admixed with blood in a single voxel. Recent advances in automated segmentation (AS) have enabled quantification of partial voxel components. This study tested a novel AS algorithm that can quantify LVM while accounting for myocardial partial voxels. Among laboratory animals undergoing CMR before euthanasia, LVM quantified using AS-based partial voxel segmentation (AS_{PV}) yielded nonsignificant differences with LV weight at necropsy, whereas both conventional AS and MP yielded small but significant underestimations. Among patients undergoing CMR within 1 day of echocardiography, AS_{PV} yielded significantly smaller differences with echocardiography-quantified LVM than did either conventional AS or MP. AS was successful in all patients, required minimal manual adjustments (1.0 ± 1.6 per examination), and yielded a 12-fold reduction in processing time versus MP ($0:21 \pm 0:04$ versus $4:18 \pm 1:02$ minutes; $P<0.001$). These results support use of automated partial voxel segmentation for quantification of LVM, demonstrating that this method markedly reduces CMR processing time among clinical patients while yielding improved agreement with independent references of both echocardiography and necropsy-verified LVM.