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Improved approach to quantitative cardiac volumetrics using automatic thresholding and manual trimming: a cardiovascular MRI study

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Abstract. To establish the clinical validity and accuracy of automatic thresholding and manual trimming (ATMT) by comparing the method with the conventional contouring method for *in vivo* cardiac volume measurements. CMR was performed on 40 subjects (30 patients and 10 controls) using steady-state free precession cine sequences with slices oriented in the short-axis and acquired contiguously from base to apex. Left ventricular (LV) volumes, end-diastolic volume, end-systolic volume, and stroke volume (SV) were obtained with ATMT and with the conventional contouring method. Additionally, SV was measured independently using CMR phase velocity mapping (PVM) of the aorta for validation. Three methods of calculating SV were compared by applying Bland–Altman analysis. The Bland–Altman standard deviation of variation (SD) and offset bias for LV SV for the three sets of data were: ATMT-PVM (7.65, -0.82), ATMT-contours (7.85, -5.78), and contour-PVM (11.01, 4.97), respectively. Equating the observed range to the error contribution of each approach, the error magnitude of ATMT:PVM:contours was in the ratio 1:2.4:2.5. Use of ATMT for measuring ventricular volumes accommodates trabeculae and papillary structures more intuitively than contemporary contouring methods. This results in lower variation when analyzing cardiac structure and function and consequently improved accuracy in assessing chamber volumes. © 2018 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: [10.1117/1.JMI.5.1.014004](https://doi.org/10.1117/1.JMI.5.1.014004)]

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1 Introduction

Historically, in cardiac magnetic resonance (CMR) imaging, segmentation techniques were utilized to delineate the blood pool and the myocardium.¹ Many of the techniques employed region-growing, edge detection, and intensity thresholding. These approaches sought to identify blood pool and myocardium based on absolute intensity levels and signal gradients among image regions. Most, if not all, of these approaches were abandoned due to the poor image contrast of gradient-recalled echo (GRE). This limitation gave way to the contouring approach (contours) applied on GRE images to obtain cardiac volumetric quantification of chambers and myocardium. However, since blood flow contributed in a nonuniform manner to GRE images, contours tended to register higher mass and lower cardiac volumes than were present.² Consequently, many of the automatic contour approaches³ inherently rely on geometric assumptions concerning the shape and degree of curvature of the ventricle and other structures and thereby avoiding reliance on robust contrast at all points of the blood–myocardium interface. More recently, steady-state free precession (SSFP) gained popularity due to its excellent signal-to-noise ratio, much improved temporal and spatial resolution and improved blood/myocardial contrast. Heart volumes are traditionally measured using contouring methods applied to contiguous slice image data. The recommended approach of obtaining these measurements is evaluating

a stack of, typically, contiguous short-axis images acquired from base to apex.^{4,5} They are usually measured using commercial software programs for drawing automatic or semiautomatic contours of both epicardial and endocardial borders at end-diastole (ED) and at end-systole (ES). The most practical method of measuring left ventricular (LV) mass is to include both papillary muscles and trabeculae with the blood pool (Fig. 1). This is typically accomplished by drawing a contour to sculpt out the root of the papillary muscles where they are attached to the myocardium and include them as part of the blood pool.^{6,7} In routine clinical practice, this approach has been largely adhered to but has led to a situation whereby there are no widely agreed upon standards for software packages to separately treat papillary muscles. As well, it is intuitive that including or excluding papillary muscle will lead to decrease or increase in LV ejection fraction (EF) unrelated to intrinsic contractility. Due to the often tedious effort required in manually drawing the contours, only a token effort is made in the software regarding the capture of papillary muscles, whereby it is anticipated that only a single root and head of papillary muscle are present, which is not always the case.

Another, and more fundamental, reason that the papillary muscles are usually excluded from the identification of myocardium is that they and the trabeculae are not commonly regarded as “working myocardium.” That is, these ill-defined structures do not significantly contribute to the muscular contraction during systolic ejection (Fig. 1). Thus, LV mass quantification typically focuses on identifying the working myocardium, since it

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Fig. 1 Working myocardium: (a) endocardial and epicardial boundaries in the end systolic (ES) and (b) end diastolic (ED) phases showing the assignment of papillary muscle and trabeculae, which are excluded from the identification of “working myocardium.” (c) Endocardial and epicardial boundaries in the ES and (d) ED phases showing the appreciable volume occupied by the papillary muscle and trabeculae in addition to identifying the working myocardium.

forms the perfusion burden of the ventricle. Further, even when interest is focused on calculation of the chamber function, with special attention paid to the EF, this is usually performed, not to identify the fraction of blood ejected, but to assess the status of the working myocardium. That is, the contouring method focuses attention on the working myocardium rather than the volume of blood pumped. However, trabeculae and papillary muscles occupy appreciable volume in the ventricular chamber. Thus, it is expected that the contours, which are drawn under these assumptions and aims, are expected to overestimate the chamber end-diastolic volume (EDV) and end-systolic volume (ESV), which in turn influence the accuracy with which stroke volume (SV) and EF are calculated.^{8,9}

Finally, the original regression equations establishing LV mass by echocardiography and autopsy were determined by excluding papillary muscles,¹⁰ which was later extended to CMR volumetric quantification using gradient echo imaging. However, since SSFP contrast is dominated by T1 and T2 properties, the flow-related contribution to contrast is dramatically diminished. Thus, there remain widespread opportunities for more complete incorporation of all myocardial elements in the quantification of LV mass, and by extension, leading to a more correct assessment of LV function; an integral clinical aim. Accordingly, we revisited the original idea of edge detection and signal thresholding methods¹¹ to devise automatic thresholding and manual trimming (ATMT) for assessment of cardiac chamber volumes. Previously, we applied the ATMT approach to show that it identified myocardial mass with more accuracy than contours when applied to *ex vivo* hearts (removed for transplantation).¹² This approach led to a high degree of correlation between CMR mass and autopsy mass for the LV and RV; a first in human CMR. We hypothesize that the ATMT approach accommodates both trabeculae and papillary muscles and is ideally suited for quantification of cardiac chamber volumes *in vivo* and is more accurate than the traditional contour approach.

We further hypothesize that ATMT will accurately portray LV volumes against external standards.

2 Methods

In this IRB-approved retrospective study, we considered a patient cohort ($N = 30$) between the ages 49 ± 16.5 (50% females), with essentially no evidence of left-sided valvular disease (Table 1) and a volunteer control group without any cardiovascular disease ($n = 10$). The entire group underwent CMR imaging (GE, 1.5 T, Milwaukee, Wisconsin) using the standard SSFP approach (TR/TE/flip angle 4.2/2.1/45; FOV 350 mm, matrix 224×224 , scan percentage 75%): slices oriented parallel to the LV short-axis, applied contiguously from above the base to below the apex (slice thickness 8 mm and gap 0 mm) and phase velocity mapping (PVM) obtained through ascending aorta. Three methods were used for LV chamber volumetric analysis: contouring method, ATMT method, and PVM. A full range of slices containing the LV chamber was identified and these slices were by design kept common for all the methods described as follows:

2.1 Contours

A semiautomatic contouring method was applied to the end-diastolic and end-systolic frames using commercially available software (qMass, Medis, Leiden, The Netherlands) (Fig. 1). ESV, EDV, and SV were then measured. The papillary muscles were included in the volume of the LV cavity. The volumes obtained by this approach were within the normal range and inter- and intraobserver variability for this approach has been previously established.⁷

2.2 ATMT

The ATMT approach is a method applied to the same range of slices identified for contouring as follows: using an image analysis program provided with our scanner, the selected slices and the region of interest are loaded [Fig. 2(a)]. Using the scalpel tool, a region of interest encompassing the left ventricle is selected to give a three-dimensional (3-D) model [Fig. 2(b)].

Table 1 Patient demographics.

Variables	$N = 30$ (%)
Female	15 (50)
Age	49 ± 16.5
Body mass index	29.4 ± 6.6
Ejection fraction	50 ± 18.8
Cardiomyopathy	10 (33.3)
Hypertension	7 (23.3)
Coronary artery disease	3 (10)
Heart failure	3 (10)
Other	7 (23.3)

Note: Data presented are means $\pm$ SD for continuous variables. N (%) for dichotomous variables.

Fig. 2 ATMT steps: (a) Initial selection of the region of interest in 3-D model. (b) Trimmed region of the heart in 3-D model. (c) Upper and lower thresholds applied, resulting in removing the papillary muscle and trabeculae (dark regions). (d) LV region is identified and trimmed by successively removing extracardiac features (green shading).

The window width and level (W/L) setting in any imaging modality determines how clearly pathologies and other anatomical structures present in an image. Incorrect W/L settings may result in pathologies and other essential anatomical structures not being displayed correctly. Hence, it is very essential in any imaging modality to have the correct W/L settings so that all the relevant features are displayed clearly. Thresholding is a process wherein all the voxels with values outside the selected threshold range are removed from the 3-D volume. Automatic thresholding involves adjusting a range of voxel values by means of “minimum value” and “maximum value” (slider) on the threshold panel. By setting upper and lower myocardial signal intensities, we can visually delineate blood pool from myocardium and other solid structures [Fig. 2(c)]. Having established the threshold limits that exclude trabecular and papillary muscles from the blood pool, the manual trimming was achieved by removing extraneous tissue signal with an interactive scalpel tool [Fig. 2(d)]. At the end of this iterative process, the LV signal was rendered in a full 3-D model [Figs. 2(a)–2(d)]. The pixels in the identified blood pool were summed and multiplied by the voxel dimensions to calculate the end-diastolic and end-systolic blood pool volumes. For both contouring and ATMT methods, SV was calculated as the subtraction of the ESV from the EDV. This process was independently repeated (ATMT1 and ATMT2) for the entire patient cohort to establish interobserver variability by a second observer (Table 2). The reanalysis was double-blinded to avoid any bias.

2.3 Phase Velocity Mapping

PVM analysis was performed using commercially available software (qFlow, Medis, Leiden, The Netherlands). These images were acquired through the ascending aorta and oriented perpendicular to the primary axis of the aorta for quantitation of forward SV as a validation step. SV was obtained from the PVM images by outlining the aorta in each image frame and calculating the forward flow volume using qMass. Under ideal conditions, SVs obtained by contouring and ATMT methods should be identical to the SV obtained by PVM.^{13,14} Interobserver

Table 2 ESV and EDV-ATMT versus contours.

	ESV		EDV	
	All	Control	All	Control
SD	10.32	5.85	12.55	6.91
Bias	−15.94	−13.16	−21.12	−14.26
Range	40.47	22.94	49.21	27.10
R ²	0.96	0.91	0.93	0.97
Slope	0.86	0.82	0.80	0.84

Table 3 A three-way comparison of SV using ATMT, PVM, and contour methods.

	SD	Bias	Range	R ²	Slope
Contour versus PVM	11.01	4.97	43.15	0.78	0.83
ATMT versus PVM	7.65	-0.82	30.00	0.89	0.89
ATMT versus contour	7.85	-5.78	30.78	0.87	0.86
ATMT1 versus ATMT2	7.97	0.53	31.24	0.89	0.88

and intraobserver variability of SV obtained from PVM was reported by earlier studies with excellent reproducibility ($0.61 \pm 1.15\%$).^{15,16}

3 Statistical Analysis

Linear regression was performed to assess the correlation for each pair of comparisons. Bland–Altman plots were used to determine the bias and the range of 95% of the data points. The Bland–Altman method calculates the mean difference between two different measuring techniques (i.e., the “bias”) and the 95% limits of agreement (± 2 SD).¹⁷ The Bland–Altman analysis is partly visual, in that if there is a systematic variation this offset would appear as an off-axis skewing of the data. Apart from the systematic bias, and in the absence of obvious skewing, the Bland–Altman range can be used to judge the noise level of the two contributing measurements. In this manner, a three-way comparison of SV was performed. Formally, it follows that the series of Bland–Altman plots arranged from least to maximum

variation identify the relative noise contribution of each separate approach.

4 Results

A total of 40 subjects successfully underwent clinical CMR imaging and EDV and ESV were measured using standard contouring along with ATMT. While not formally calculated, the time to perform manual contouring and ATMT was comparable, $\sim 10 \pm 2.5$ min, depending on the complexity of the study.

4.1 Component Volumes

LV chamber volumes were obtained using ATMT and contours method. The values obtained with ATMT (Tables 2 and 3) were in accordance with normal ranges obtained *in vivo*.¹⁸ The ESV measured by ATMT-contours for all subjects had a Bland–Altman bias and SD of -15.94 mL and 10.32 mL, respectively, with an excellent coefficient of determination, $r^2 = 0.96$, while the ESV measured for the control group had the bias and range of -13.16 mL and 5.85 mL, respectively, and $r^2 = 0.91$ (Fig. 3 and Table 3). Similarly, EDV measured for the entire group by ATMT-contours had Bland–Altman bias and SD of -21.12 mL and 12.55 mL with a coefficient of determination, $r^2 = 0.93$, while the EDV measured for the control group had the bias and SD of -14.26 mL and 6.91 mL, respectively, and $r^2 = 0.97$ (Fig. 4 and Table 3). Separately, SV by PVM was compared to the SV of manual contouring and ATMT. The range and correlation of SV were compared in multiple two-way comparisons: contour-PVM, ATMT-PVM, and ATMT-contour (Fig. 5). Bland–Altman analysis of SV for ATMT-PVM had an SD and bias (7.65 , -0.82) that are lower than those obtained for

Fig. 3 End systolic volume: (a) Bland–Altman plot comparing ESV obtained from ATMT and contour methods for the entire patient population ($n = 30$) and (b) for the control group ($n = 10$) showing bias and standard deviation of -15.94 mL and 10.32 mL, respectively. (c) Corresponding linear regression analysis comparing ATMT and contour methods for ESV for the entire patient population ($n = 30$) and (d) the control group ($n = 10$) showing correlation R^2 of 0.96 and 0.91 , respectively.

Fig. 4 EDV: (a) Bland–Altman plot comparing EDV obtained from ATMT and contour methods for the entire patient population ($n = 30$) and (b) for the control group ($n = 10$) showing bias and standard deviation of -21.12 mL and 12.55 mL and -14.26 mL and 6.91 mL, respectively. (c) Corresponding linear regression analysis comparing ATMT and contour methods for EDV for the entire patient population ($n = 30$) and (d) the control group ($n = 10$) showing correlation R^2 of 0.93 and 0.97 , respectively.

Fig. 5 Stroke volume: top row: Bland–Altman plots for SV comparing (a) contour and ATMT, (b) ATMT and PVM, and (c) ATMT and contour methods. Bottom row: (d–f) corresponding linear regression analysis for SV displaying correlation R^2 values.

comparison of contour-PVM ($11.01, 4.97$) and ATMT-contour ($7.85, -5.78$) as shown in Table 2. To attribute the proportionality of errors to each method, we assess the error (ϵ), as a first-order approximation, to the range in the Bland–Altman analysis (Table 2)

$$\epsilon_A + \epsilon_P = 7.65, \quad (1)$$

$$\epsilon_A + \epsilon_P = 7.85, \quad (2)$$

$$\epsilon_A + \epsilon_P = 7.85, \quad (3)$$

where ε_A is the error term for ATMT, ε_C is the error term for contouring, and ε_P is the error term for PVM method. Solving for the aforementioned three equations, we get

$$\varepsilon_A = 2.2, \quad (4)$$

$$\varepsilon_P = 5.4, \quad (5)$$

$$\varepsilon_C = 5.6. \quad (6)$$

When expressed as ratios, we get

$$\varepsilon_A : \varepsilon_P : \varepsilon_C \text{ as } 1:2.4:2.5. \quad (7)$$

The correlation plot r^2 value for ATMT-PVM (0.89) was stronger than contouring-PVM (0.78) or contouring-ATMT (0.87) (Fig. 5 and Table 2).

5 Discussion

Here, we have revisited the original contrast driven extraction of cardiac blood volumes using SSFP imaging. By design, the slice selection was consistent between ATMT and contour analysis on a per patient basis. Thus, the slices contributing to the volume by ATMT and contouring methods were identical and any differences between the two were due to the treatment of papillary and trabeculae tissue.^{19,20} It is also shown in the literature that the error terms in consideration with and without papillary and trabeculae were virtually identical.⁴ This demonstrates the inherent difficulty of manually directing contour boundaries to accommodate papillary and trabeculae tissue, while the more signal-driven ATMT approach inherently excludes these structures from the blood volume measurement.

5.1 ATMT versus Contours

From the statement Eq. (7), we have shown that

$$\varepsilon_A : \varepsilon_P : \varepsilon_C \text{ as } 1:2.4:2.6.$$

The many potential sources of error²¹ in measuring cardiac volumetrics include the correct identification of the basal slice and extent of its features within the slice, delineating myocardium from blood-pool, the inclusion/exclusion of papillary muscles (which is further complicated by issues of whether they are contiguous to the myocardium or separated), trabeculae and partial volume errors near regions of high curvature^{22–24} and perhaps most importantly, consistency of registration of the acquisition to the heart during multiple breath holds. We have eliminated any errors from slice selection for both ED and ES frames as they were kept constant between approaches on a patient basis. In general, for an irregular-shaped object, multiple observers would tend to be more in agreement in measurement of the area than the boundary length, since the boundary length can extended to infinity due to the fractal nature and the scale of boundaries.²⁵ This explains the error term, 1:2.6, and the accuracy of ATMT approach when compared to contours in volumetric measurements.

As an independent measure of SV we used PVM. The potential errors of PVM include temporal and spatial blood flow acceleration, partial volume, slice orientation with respect to flow direction, and slice position relative to valvular plane. In the absence of valvular disease, the SV measured at the aorta and the volume ejected by the left ventricle should both

match. Gratifyingly, in the Bland–Altman analysis, the bias term in ATMT-PVM comparison was practically negligible (-0.82 mL) (Table 2 and Fig. 5) indicating that this assumption was indeed true on average. Not surprisingly, the BA analysis of contours-PVM exhibited a substantial increase in bias (~ 5 mL), which can be attributed to the papillary and trabeculae structures. Further, as the published literatures states that the cardiac volumes are virtually unchanged irrespective of whether papillary muscle were considered or not, which illustrates the difficulty in trying to manually address this issue.⁴

5.2 End-Diastolic and End-Systolic Volumes

When the relative error terms were calculated using the SV data, we showed that the contour method had a much higher error term than the ATMT approach [Eqs. (4)–(6)]. When comparing ATMT versus contours for ESV and EDV, we see that the error in EDV (taken as the data range in the Bland–Altman analysis) is $\sim 23\%$ higher than the ESV comparative error (Table 3). Under the assumption that the error contribution is higher for the contour method, this implies that attempts to compensate for papillary muscle and trabeculae are less successful during diastole. This is also reflected in the higher bias in EDV data than in ESV data (Figs. 3 and 4).

5.3 Working versus Volumetric Myocardium

Historically, the role of contouring technique was used to identify working myocardium by defining the ventricular chamber. This method captures wall motion abnormalities and assumes a smooth-walled ventricle, not taking into account trabeculae and valvular apparatus. However, this method does not measure the actual perfusion needed by the entire myocardium including papillary and trabecular muscles. The ATMT approach, by contrast identifies the blood volume of the heart chamber, which better agrees with the flow volume seen in the aorta. If we were to ask ourselves which of these two techniques identify wall motion abnormalities more accurately, we can find the answer by looking at which technique inherently tackles the problem. Consider that the contouring method is used to: (1) assess the EF of the “working myocardium,” i.e., the muscular contraction of myocardium and (2) to assess LV chamber volumetrics, i.e., blood volume. These conflicting requirements may contribute to the inaccuracies in performing each measurement, leading the user to err on one side or another in an inconsistent manner depending on the perceived use for the data. Typically, differences on the order of 10% between the ventricular SV and aortic SV are expected. When stroke volume is compared in a three-way fashion with the measurements obtained from ATMT, contour and also independently measured by PVM, we can show less variation in ATMT. The Bland–Altman plot of SV obtained from ATMT and PVM shows lower bias and SD (-0.82 , 7.65) when compared with that of contour and PVM (4.97, 11.01) (Fig. 5 and Table 2).

Hence, we are overloading the contour technique when we use it to describe both the working myocardium and blood chamber volumetric, when in actuality it was not designed to measure blood volume in the chamber.

5.4 Limitations

By design, we have included that same slice selection for contouring and ATMT methods in identifying the basal and apical

slices. It is possible that a free selection of these slices might have produced different results, particularly with regard to agreement between aortic forward blood flow volume and ventricular SV. Here, we were limited to a three-way Bland–Altman comparison, but if the RV and MPA were also included, we could have added more cross-checks between measurements in the absence of right-sided valvular disease. While 3-D data were extracted by both contours and ATMT, no shape analysis was used to enhance accuracy by potentially reducing partial-volume error.

6 Conclusions

Previously, we showed that the ATMT approach when applied to explanted hearts was more accurate than the contour approach at assessing cardiac mass¹² and here we extend those findings to *in vivo* cases. Based on multiple comparison metrics with independent measures, the ATMT approach is more accurate and reproducible for quantification of LV chamber volumes. Further, using the high contrast of SSFP imaging, the ATMT processing time is comparable to that of the contouring approach. The performance of this method will significantly improve when coupled with acquisition of short-axis slices using compressed sensing in a single breathhold, errors due to respiratory motion are thereby dramatically reduced.²⁶ We can expect substantially improved results when compressed sensing used with ATMT becomes mainstream. This will mark a new paradigm shift by not assuming “one method measures all,” instead use the most accurate method for that characteristic measurement. This approach, once replicated, should be considered for routine clinical practice to measure cardiac structure and function. The future direction for this work is to further differentiate between the assessments of ventricular function versus ventricular chamber volumes. Initially, we plan to further assess the impact of additional sources of error in the acquisition and measurement methods, and propose approaches to recognize their presence and remedy. Continuing, we plan to investigate approaches to assess ventricular function that are insensitive to errors in ventricular volume assessment.

Disclosures

The authors declare that they have no competing interests.

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