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Comparison of 3D Echocardiographic Derived Indices Using Fully Automatic Left Ventricular Endocardial Tracing (Heart Model) and Semi-Automatic Tracing (3DQ-ADV)

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Abstract

Aims. The availability of a true 3D dataset provides an opportunity for automation of left ventricular (LV) and left atrial (LA) measurements. Although manual and automated measurements of 3D volumes are known to correlate, the variance is an important parameter for the individual patient. The reasons for discrepancies remain unexplained. We hence aim to explain the disagreement between automated and manual LV and LA volumes.

Methods and Results. 355 patients underwent standard clinical echo, with offline analysis in both fully- (Heart Model, Philips), and semi-automated (3DQ-Adv, Philips) assessment of routine indices of LV and LA function and shape. Each image was classified according to quality using a 4-point scale as well as the American Society for Echocardiography guidelines for appropriate use of contrast. Bland Altman plots were used to assess agreement, and t-tests were used to assess differences in agreement. Predictors of volume discrepancy were sought with linear regression.

Measures of LV and LA volumes were greater with automatic than semi-automatic assessment. The difference in left ventricular end diastolic volume was dependent on the number of regional wall motion abnormalities (RWMA) (β=0.59, $p<0.04$), and image quality (β=19.71, $p=0.02$). RWMA predicted the difference in left ventricular end systolic volume (β=0.83, $p<0.01$), and left atrial end systolic volume (β=-1.01 $p<0.01$).

Conclusion. LV and LA volumes were higher with automatic than semi-automatic assessment. Image quality and RWMA may contribute to this discrepancy. These limitations need to be addressed before fully automatic assessment of 3D echocardiograms can be used in the clinic.

Keywords. 3D Echocardiography, LV endocardial border delineation, left ventricular volumes

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Introduction.

Recent guidelines have recommended 3D echocardiography (3DE) as the preferred technique for the calculation of LV volumes [1]. Because this method does not use geometric assumptions, it is a more accurate method of assessing LV morphology and function than 2DE [2]. However, in addition to limitations relating to user dependence and spatial resolution [3], the time required for image processing continues to be an important barrier to the adoption of 3DE.

The current era of artificial intelligence (AI) promises to automate components of imaging, thereby

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improving efficiency and access to care. An early application of AI has been the process of fully automatic (FA) chamber segmentation of the LV for volume analysis by 3DE [4,5]. This contrasts with the standard approach of user-derived (semi-automated, SA) guidance of marking fiducial points, and modification of an automated traces. Previous studies have demonstrated similarity between mean values of LV volumes between semi- and fully-automated analysis, but less attention has been directed towards situations where the results show variance [6], and explanations for these differences need to be better understood before such a tool can be used to help clinical decision making. No studies have yet defined what individual and imaging-based factors may be driving this discrepancy, although potential contributors include image quality (itself associated with body mass index, and individual patient anatomy[7]), as well as heart rate. Understanding these factors might enable correction for the discrepancy between fully- and semi-automated measures of 3D volumes, which could facilitate the appropriate introduction of FA chamber segmentation into clinical practice [6-8]. We hypothesized that certain individual and imaging factors contribute to the discrepancies between fully- and semi-automated LV volumes. Accordingly, we sought to compare both approaches for measurement of LV and LA volumes, describe the discrepancies, and to identify the contributing factors.

Methods.

Ethics. This study was approved by the institutional ethics committees of both institutions.

Patient selection. 355 patients were identified from the 3D echocardiography database of two large tertiary centres (The Princess Alexandra Hospital, Brisbane, Australia and The Baker Heart and Diabetes Institute, Melbourne, Australia). The only inclusion criterion was that the patient had to have had at least one 3D transthoracic echocardiogram which was compatible with fully automated analysis. Limited demographic and clinical data was obtained from the patient database of each institution. A patient was considered to have valvular disease if the severity of regurgitation or stenosis present was more than mild, and this was assessed by the treating cardiologist.

Imaging assessment. All 3D echocardiograms were assessed offline in QLAB (Philips, Best, Netherlands), using both the Heart model (HM, fully-automated) and standard user guided (3DQ-ADV) software. The attributes of HM have been well described previously [8]. Briefly, the program uses adaptive analytics to place endocardial boundaries in the LV and LA. It then automatically detects end-systole and end-diastole, and hence creates a mesh model of the cardiac chambers at both time points, from which volumes are calculated directly. In order to accurately assess the ability of HM to work as a truly automatic tool for LV function and volume assessment, manual boundary correction was not completed in the current study (see Fig 1). HM has a slider setting which allows the user to adjust the endocardial border from the innermost tissue-blood barrier to the compact LV

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myocardium. There is limited data and no consensus in the literature on the most advantageous settings to adjust the slider to, and it was hence left on the default setting of 50/50.

3DQ-ADV is a semi-automatic algorithm which detects the LV endocardium. Users are first required to select the end-diastolic and end-systolic frame in an apical 4- and 2-chamber views. Two markers are then placed on each side of the mitral annulus in both views, as well as an apex marker. The program then automatically traces the endocardial boundaries, with an option to correct manually if the operator was not satisfied that the endocardial boundaries had been appropriately traced.

Each image was classified according to quality (1 = all segments visible, 2 = 1 or 2 segments undefined without impacting the overall diagnostic quality of the study, 3 = an entire LV wall or LV apex was undefined, 4 = >1 LV wall or 1 LV wall + apex undefined). Image quality was also graded based on the American Society of Echocardiography (ASE) guidelines for appropriate use of contrast (unsatisfactory = > 2 segments undefined) (see Fig 2).

Reproducibility. The reproducibility of left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV), ejection fraction (EF), and stroke volume (SV) using 3DQ-ADV were assessed using a randomly derived subgroup of 30 patients.

Statistics. Bland Altman plots and paired t-tests were used to assess the level of agreement between volumes as measured by automatic and semi-automatic echocardiography. Paired wilcoxon sign rank tests were used where normality could not be assumed. Unpaired T-tests were used when comparing differences in mean difference between studies of different image quality. Variables are presented as mean±sd for normally distributed variables, and median[IQR] for non-normally distributed variables. Appropriate transformations were used to transform non-normally distributed variables to normally distributed variables for correlation and regression analysis. The log transformation was used on left atrial end systolic volume (LAESV), LVEDV, and LVESV. Standard linear regression was used to determine predictors of volume discrepancy between the two techniques. All analysis was completed in a blinded fashion. Interobserver variability was assessed using ICC statistics. Variables which were likely to influence LV volume measurements were included in the multivariable analysis – these included image quality, heart rate, gender, sphericity index, and body mass index. A significant difference between volumes was defined as present if there was a discrepancy between Heart Model and 3DQ-ADV greater than 10ml. to further characterise the factors influencing any difference seen between techniques, Individuals were classified into two groups – ‘discrepancy present’ and ‘discrepancy not present’. Poisson regression with robust standard errors was used to predict discrepancy status, and prevalence ratios (PR) are hence reported.

Results.

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Study population. There was a moderate prevalence of regional wall motion abnormalities (29.5%), and these appeared to be distributed equally throughout the various LV regions. As expected with 3D echocardiograms, overall image quality was low (Table 1). There was mild prevalence of valvular disease, with mitral regurgitation being the most common (9.2%).

LV structure and function. LVEDV was higher when assessed by HM than 3DQ-ADV (130.0 [56.0] mls vs 106.1 [44.9] mls, $p<0.01$), as was LVESV (58 [40.0]mls vs, 49.0 [35.0] mls $p<0.01$). EF was also significantly higher when assessed with Heart Model than 3DQ-ADV (54.0±12.5% vs 50.0±13.6%, $p<0.01$). There was a marked difference in stroke volume between Heart Model and 3DQ-ADV (71.4±23.5mls vs 53.9±22.2mls , $p<0.01$).

LV volumes correlated between automatic and semi-automatic endocardial tracking, although the relationships seen with EF and SV were considerably weaker (Table 2). Automatic measures of LV structure and function were greater than those for semi-automatic measurements (Table 2 and Figure 3). The discrepancy between the two techniques was larger in images of poor quality for all standard measurements other than LVESV and LAESV (Table 3).

Features associated with differences in LV measurements. The degree of difference of LVEDV between the methods was associated with the number of regional wall motion abnormalities ($\beta=0.59$, $p<0.04$), and image quality ($\beta=19.71$, $p=0.02$). The difference in LVESV was only dependent on the number of regional wall motion abnormalities ($\beta=0.83$, $p<0.01$), and the difference in EF was dependent on image quality ($\beta=6.40$ $p=0.01$), and the number of regional wall motion abnormalities ($\beta=-0.32$ $p=0.04$).

When LVEDV discrepancy was assessed as a dichotomous variable, there were no significant predictors found. When LVESV discrepancy was assessed as a dichotomous variable, male sex (PR = 1.8, $p <0.01$), and the number of regional wall motion abnormalities (PR = 1.02, $p = 0.02$), although the magnitude of effect was small. Image quality was borderline significant (PR = 1.1, $p = 0.06$)

There were a number of cases where the automatic algorithm did not appropriately track the endocardium. The most commonly encountered problem was inappropriate approximation of the LV apex, and mitral annulus (Fig 4).

LA measurements. LAESV was significantly higher when assessed with HM than 3DQ-ADV (68 [34.3] mls vs 41.2 [29.8] mls, $p<0.01$). Fully- and semi-automatic measurement of LA volumes correlated significantly (Table 2), although HM significantly presented higher LA volumes (Table 2). The degree of agreement did not appear to be dependent on image quality. On multivariable analysis, only the number of LV regional wall motion abnormalities were predictive of the difference in LAESV ($\beta=-1.01$ $p<0.01$).

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There were no significant predictors of difference in LAESV when assessed as a dichotomous variable.

LA tracking was very often inadequate, with boundaries being drawn outside the image window. There were a number of cases where the LV endocardium was approximated in images of inadequate quality to allow meaningful analysis (Fig 5).

Interobserver variability. Interobserver agreement (ND, VA) for the assessment of left ventricular end diastolic volumes using 3DQ-ADV was high (ICC=0.81 [0.64, 0.91]). This was paralleled in LVESV (ICC = 0.93 [0.87, 0.97]), SV (0.44 [0.10, 0.69]), and EF (ICC = 0.84 [0.69, 0.92]).

Discussion.

The main findings of this study were that automatic tracking of the LV and LA endocardium resulted in significantly higher values for LV and LA volumes when compared to semi-automatic techniques. As expected, measures of LV and LA volumes and function correlated significantly between techniques. The main drivers of this discrepancy appeared to be poor image quality, and the presence of RWMAs. It may be that image quality and wall motion abnormalities are influencing where automatic segmentation algorithms are placing LV and LA boundaries – an important direction for further investigation. The large discrepancy between techniques limits the clinical utility of fully automatic techniques in the clinic, and hence the practical implementation of 3DE into routine practice.

Discrepancies in the previous HM literature. The literature shows some variability in the relation between fully- and semi-automated 3D measurements in previous reports. Some studies have reported that HM presents artificially low volumes [6,9]. This is likely due to the selection of images (only images with good image quality were acceptable), and the extensive use of manually corrected endocardial traces. Furthermore, many patients with common cardiovascular issues were excluded. Further studies [8,10,11] have shown that when compared to manual 3D measurements, HM systematically presented higher LV volumes, although to a lesser degree than reported in the current study, perhaps because of the selection of high quality studies. Interestingly, these studies also report biases which were higher in patients with regional wall motion abnormalities. When patients with a variety of cardiovascular diseases were included, HM was found to present artificially high volumes, with large biases, even in images of reasonable quality [12]. These limitations must be addressed before large scale implementation of automated 3DE occurs in the clinic.

Causes of discrepancies. The drivers of the discrepancy between HM and 3DQ-ADV were found to be image quality, the number of regional wall motion abnormalities, and BMI. Similar studies [10,13] have shown that image quality has a major effect on the accuracy of automatic detection of the endocardium. The endocardial tracking algorithm misrepresents the endocardium in some cases. A

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poorly visualized apex and mitral annulus appear to result in the greatest discrepancy between techniques. These results imply that while HM may be useful in optimal conditions, it has shortcomings when applied to a sample of patients representative of a typical clinical cohort. The need for contour manipulation has been previously emphasised, even in a cohort where most major cardiac pathology was excluded and all echocardiograms were of excellent quality [6,8]. This was very evident in the current study, with automatic estimation of endocardial borders very often being inappropriate. Previous studies [7,14,15] have shown that completely autonomous algorithms capable of tracking the endocardium still require corrections, particularly in patients with cardiovascular disease. Automatic border detection needs to be improved before HM can be used routinely in a clinical setting.

Limitations. There was no 'gold standard' reference method such as cardiac MRI available for inclusion in the current study.

Conclusion. HM systematically presented higher values for LV and LA function and structure in a large unselected cohort. The drivers of this discrepancy related to both patient factors and imaging-specific factors. The difference in volumes between the techniques limits the clinical applicability of fully automatic chamber detection, and leaves the large scale clinical application of 3DE difficult.

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Author Contributions.

ND: Concept and designs, data analysis and interpretation, data acquisition, drafting article, approval of article, statistics, ethical approval.

VA – Concept and designs, data acquisition data analysis and interpretation, drafting article, approval of article, critical revision.

JN- data acquisition, data analysis and interpretation, drafting article, approval of article, critical revision.

MM- data acquisition, data analysis and interpretation, drafting article, approval of article, critical revision.

TM - Concept and design, data analysis and interpretation, drafting article, approval of article, statistics, ethical approval.

SW - Concept and design, data analysis and interpretation, drafting article, approval of article, statistics, ethical approval.

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Tables.

Table 1 – Baseline demographic and clinical parameters for the study population. BMI = Body Mass Index. There was a moderate prevalence of both valvular disease and regional wall motion abnormalities. Image quality was varied amongst studies, but as expected with true 3D datasets, there was a significant portion with poorly imaged regions.

Variable	N (%)
Regional Wall motion Abnormalities	104 (29.5)
Sex Male	213 (61)
Aortic Regurgitation	12 (3.6)
Aortic Stenosis	10 (3)
Mitral Regurgitation	31 (9.2)
Mitral Stenosis	1 (0.3)
Tricuspid Regurgitation	24 (7.1)
Tricuspid Stenosis	0 (0)
Pulmonary regurgitation	0 (0)
Pulmonary stenosis	0 (0)
Inferior Wall Motion Abnormality	56 (19.0)
Anterior Wall motion Abnormality	54 (18.3)
Lateral Wall motion abnormality	55 (18.6)
Septal wall motion abnormality	57 (19.3)
Apical wall motion abnormality	54 (18.3)
ASE image quality satisfactory	108 (30.7)
Image quality 1	59 (17.5)

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Image quality 2	140 (41.5)
Image quality 3	107 (31.8)
Image quality 4	31 (9.2)
Long Axis cm (mean±sd)	8.9±1.1
Short Axis cm (mean±sd)	4.3±0.8
Sphericity Index (mean±sd)	0.5±0.1
Height m (mean±sd)	1.7±0.1
Weight Kg (mean±sd)	79.9±18.5
BMI Kg/m^2 (mean±sd)	27.7±6.0
Age years (mean±sd)	61.9±16.7

Table 2 – Comparison of HM and 3DQ-ADV. LVEDV = Left Ventricular End Diastolic Volume, LVESV = Left Ventricular End Systolic Volume, EF = Ejection Fraction, SV = Stroke Volume, LAESV = Left Atrial end systolic volume, HM = Heart Model, R = Correlation coefficient. Measures of left ventricular volumes correlated significantly between automatic and semi-automatic as well as invasive methods. Automatic assessment presented significantly higher volumes.

	LVEDV (ml)	LVESV (ml)	EF (%)	SV (ml)	LAESV (ml)
R (3DQADV vs HM)	0.86 (0.83, 0.89), p<0.01	0.80 (0.77, 0.84), p<0.01	0.39 (0.30, 0.48), p <0.01	0.42 (0.33, 0.50), p<0.01	0.74 (0.69, 0.79), p<0.01
Bias [limits of agreement]	27 ml [-21ml, 74ml]	9ml [-37ml, 55ml]	4% [-24%, 32%]	18ml [-30ml, 66ml]	24ml [-17ml, 66ml]

Variable	Quality 1 or 2	Quality 3 or 4	P-Value	ASE Satisfactory	ASE not Satisfactory	P-Value

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Mean Diff LVEDV mls (mean±SD)	22.0ml±17.3ml	33.3ml±30.6ml	<0.01	21.6ml±18.1ml	28.8ml±26.3ml	<0.01
Mean Diff LVESV mls (mean±SD)	8.1ml±17.0ml	9.2ml±30.5ml	0.71	5.95ml±17.3ml	8.55ml±25.9ml	0.29
Mean Diff EF % (mean±SD)	2.2%±11.8%	7.3%±16.9%	<0.01	3.51%±11.7%	5.24%±15.3%	0.26
Mean Diff LAESV mls (mean±SD)	23.3ml±19.9ml	25.9ml±24.3ml	0.36	22.0ml±21.5ml	25.3ml±21.4ml	0.23
Mean Diff SV mls (mean±SD)	13.9ml±16.0ml	24.2ml±32.6ml	<0.01	15.6ml±15.8ml	20.2ml±27.7ml	0.06

Table 3 – Mean differences by image quality. LVEDV = Left Ventricular End Diastolic Volume, LVESV = Left Ventricular End Systolic Volume, EF = Ejection Fraction, SV = Stroke Volume, LAESV = Left Atrial end systolic volume, ASE = American Society for Echocardiography. It can be seen that mean differences were larger in images with poor quality, this difference appeared to be most marked in LVEDV.

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Figure Legends.

Figure 1 – Example of Heart Model automatic tracing in three planes (A,B,C). Heart Model is a novel computer program which automatically traces the endocardium in the left ventricle and left atrium throughout the cardiac cycle (pink lines). This allows automatic calculation of left atrial and left ventricular volumes. A 3D model is presented in D which can be viewed in all axis. LV = left ventricle, LA = left atrium, RV = right ventricle, RA = right atrium.

Figure 2 – Example of the 4 difference classes of image quality. A – Image quality grade 1 as all regions are defined. image quality grade 4 as both the lateral wall and apex are not appropriately imaged. B – image quality grade 2 as there is some loss of the mid regions, although the endocardial outline can still be appreciated. C – Image quality grade 3 as the apex is not adequately imaged. D – Image quality grade 4 as multiple regions are not visible making the image difficult to interpret. LV = left ventricle, LA = left atrium, RV = right ventricle, RA = right atrium.

Figure 3 – Bland Altman Analysis for the comparison between fully automatic and semi- automatic left ventricle (LV) and left atrial (LA) tracing. A = Bland Altman plot for left atrial end systolic volume, B = Bland Altman for left ventricular end diastolic volume, C = Bland Altman for left ventricular end systolic volume, D = Bland Altman for ejection fraction, E = Bland Altman for stroke volume. Heart Model systematically presented higher volumes as can be seen from the uniformly positive biases. The limits of agreement were wide throughout all analysis.

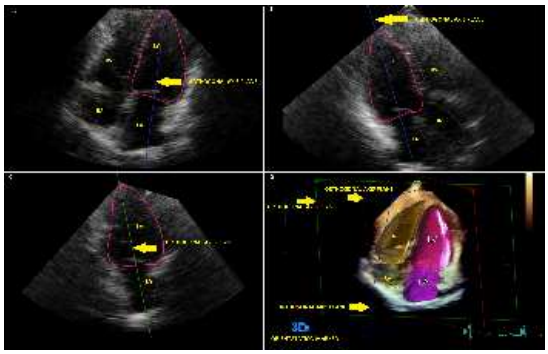
Figure 4 – Poor mitral annulus tracking. It can be seen from this figure that heart model has inappropriately drawn the mitral annulus at the level of the papillary muscles within the left ventricle. Figures A,B,C are diastolic traces which show approximately correct placement of the mitral annulus (MA) as indicated by green arrows. Figures D,E,F are systolic traces of the same ventricle which shows grossly misplaced mitral annulus approximations (red arrows). It can also be seen that the LV apex is also mistraced in the systolic figures (true apex indicated by blue circle, while the Heart Model (HM) approximation of the apex is indicated by an orange circle. . LV = left ventricle, LA = left atrium, RV = right ventricle, RA = right atrium.

Figure 5 – Poor atrial tracking. From this example it can be seen that heart model has approximated atrial boundaries in regions of very poor signal quality in 3 different planes (A,B,C), and completely misrepresented the endocardial borders in each. . LV = left ventricle, LA = left atrium, RV = right ventricle, RA = right atrium.

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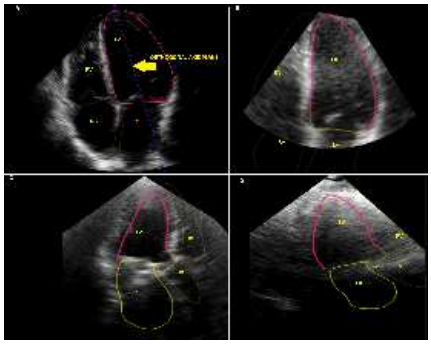
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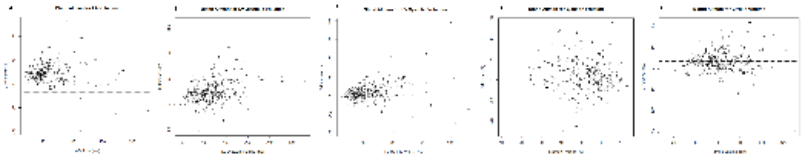
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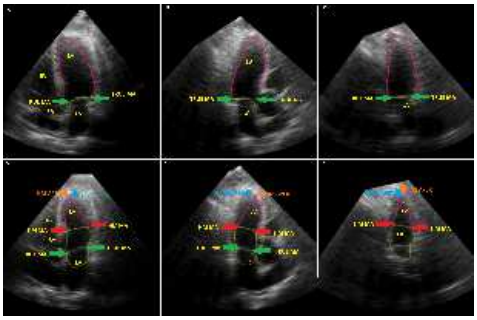


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