Comparing a Knowledge-based 3D Reconstruction Algorithm to TomTec 3D Echocardiogram Algorithm in Measuring Left Cardiac Chamber Volumes in the Pediatric population

Attila Ahmad[1], Sachie Shigemitsu[1], Yozo Termachi[1], Jonathan Windram[1], Nee Scze Khoo[1], Tim Colen[1], and Luke Eckersley[1]

[1]University of Alberta

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Abstract

Background: Three-dimensional echocardiography (3DE) is an emerging method for volumetric cardiac measurements; however, few vendor-neutral analysis packages exist. Ventripoint Medical System Plus (VMS3.0+) proprietary software utilizes a validated MRI database of normal ventricular and atrial morphologies to calculate chamber volumes. This study aimed to compare left ventricular (LV) and atrial (LA) volumes obtained using VMS3.0+ to Tomtec echocardiography analysis software. **Methods**: Healthy controls (n=98) aged 0 to 18 years were prospectively recruited and 3D DICOM datasets focused on the LV and LA acquired. LV and LA volumes and ejection fractions were measured using TomTec Image Arena 3D LV analysis package and using VMS3.0+. Pearson correlation coefficients, Bland-Altman's plots and intraclass coefficients (ICC) were calculated, along with analysis time. **Results**: There was a very good correlation between VMS and Tomtec LV systolic ($r^2 = 0.88$, ICC 0.89 [95% CI 0.81,0.94]), and diastolic ($r^2 = 0.88$, ICC 0.90 [95% CI 0.77,0.95]) volumes, and between VMS and Tomtec LA diastolic ($r^2 =0.75$, ICC 0.89 [95% CI 0.81,0.93]) and systolic ($r^2 =0.88$, ICC 0.91 [95% CI 0.78,0.96]) volumes on linear regression models. Natural log transformations eliminated heteroscedasticity, and power transformations provided best fit. The time (mins) to analyze volumes using VMS were less than using Tomtec (LV VMS 2.3±0.5, Tomtec 3.3±0.8, $p<0.001$; LA: VMS 1.9±0.4, Tomtec 3.4±1.0, $p<0.001$). **Conclusions**: There was very good correlation between knowledge-based (VMS3.0+) and 3D (Tomtec) algorithms when measuring 3D echocardiography derived LA and LV volumes in pediatric patients. VMS was slightly faster than Tomtec in analyzing volumetric measurements.

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Affiliations:

1. University of Alberta, Edmonton, AB, Canada.

2. Stollery Children's Hospital, Edmonton, AB, Canada.

3. Mazankawski Heart Institute, Edmonton, AB, Canada

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Correspondence: Dr. Luke Eckersley. Division of Pediatric Cardiology, Department of Pediatrics, University of Alberta, Faculty of Medicine and Dentistry. 8440-112th Street, Edmonton, AB Canada, T6G 2G3, Phone:

(780) 407-3963 Email: leckersl@ualberta.ca

Authors contribution

Sachie Shigemitsu and Yozo Termachi : prospective acquisition of 3D imaging. Nee Khoo and Tim Colen: design and oversight of prospective acquisition of normal 3D study. Jonathan Windram: expertise and liaison in Ventripoint software. Attila Ahmad and Luke Eckersley: study design, data analysis and manuscript preparation.

Key words: 3D Echocardiogram, LV function, LA function, knowledge-based 3D Reconstruction, TomTec 4D arena, normal values

ABSTRACT :

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Methods :

Healthy controls (n=98) aged 0 to 18 years were prospectively recruited and 3D DICOM datasets focused on the LV and LA acquired. LV and LA volumes and ejection fractions were measured using TomTec Image Arena 3D LV analysis package and using VMS3.0+. Pearson correlation coefficients, Bland-Altman's plots and intraclass coefficients (ICC) were calculated, along with analysis time.

Results :

There was a very good correlation between VMS and Tomtec LV systolic (r^2 = 0.88, ICC 0.89 [95% CI 0.81,0.94]), and diastolic (r^2 = 0.88, ICC 0.90 [95% CI 0.77,0.95]) volumes, and between VMS and Tomtec LA diastolic (r^2 =0.75, ICC 0.89 [95% CI 0.81,0.93]) and systolic (r^2 =0.88, ICC 0.91 [95% CI 0.78,0.96]) volumes on linear regression models. Natural log transformations eliminated heteroscedasticity, and power transformations provided best fit. The time (mins) to analyze volumes using VMS were less than using Tomtec (LV VMS 2.3±0.5, Tomtec 3.3±0.8, $p<0.001$; LA: VMS 1.9±0.4, Tomtec 3.4±1.0, $p<0.001$).

Conclusions :

There was very good correlation between knowledge-based (VMS3.0+) and 3D (Tomtec) algorithms when measuring 3D echocardiography derived LA and LV volumes in pediatric patients. VMS was slightly faster than Tomtec in analyzing volumetric measurements.

INTRODUCTION

Accurate and reproducible measurements of cardiac chambers are a vital component of diagnosis, prognostication, medical management, and surgical referral in congenital as well as acquired heart diseases in children[1, 2,3,4,5]. Three-dimensional volumetric echocardiography (3DE) is an emerging alternative to two-dimensional echocardiography (2DE) which makes fewer geometric assumptions regarding chamber shapes and may provide benefits in accuracy and reproducibility compared to 2DE[6,7,8].

It is therefore important to establish that commercially available algorithms for 3D measurement of cardiac chambers produce comparable results. Both TomTec 4D LV-Analysis software and Philips QLAB LV 3D underestimate LV volumes compared to MRI and have relatively wide inter-vendor limits of agreement in neonates and infants[9]. Although left atrial (LA) 3DE volumetric analysis packages exist, most studies have used LV packages[6,7].

Knowledge-based reconstruction (KBR) is an alternative volumetric methodology whereby 2DE images tracked in 3D space via a magnetic localizer are reconstructed into a 3D dataset from which volumes can be measured, thus overcoming the temporal and spatial resolution issues of 3DE. Ventripoint Medical Systems (VMS+ 3.0, (Ventripoint Diagnostics Ltd., Toronto ON), utilizes a piecewise smooth subdivision surface algorithm and an MRI-derived catalogue of heart datasets to reconstruct a unique cardiac chamber rendering for each patient. VMS software includes specific algorithms for all four cardiac chambers and has been previously validated for right and left ventricular volume measurements[10,11,12]. 3DE data and 3D MRI datasets can also be imported into VMS3.0 for analysis, however no validation of the resultant chamber volumes has been made against other 3DE analysis software.

This study aimed to compare 3DE dataset derived LA and LV volumetric measurement using VMS3.0 and TomTec 4D LV-analysis software. We hypothesized that VMS would offer an alternative volumetric measurement technique for cardiac chambers using a semi-automated software algorithm with results comparable to TomTec.

Materials & methods

Population :

Healthy pediatric patients aged 0-18 years referred for murmurs, syncope or chest pain with normal hearts identified by 2DE during their routine clinical evaluation were recruited for an additional research echocardiogram. Clinical data were taken from the medical records and included age, sex, weight, height, and medical history. Anyone with insufficient image quality precluding measurement using either software was excluded. The study was approved by the Institutional Ethics Review Board.

Real-Time Three-Dimensional Echocardiography :

The 3DE data sets were obtained using iE33 or Epic C7 machines (Philips, Andover, MA) with a matrix transducer X5 or X7. Apical 4 chamber view full volume acquisitions to include the entire LV were obtained. Full volume acquisitions were over 4-7 consecutive beats with no significant stitch artifact. The same process was completed for the LA.

3D volumetric data analysis :

Uncompressed 3D DICOM datasets focused on the LV or LA were imported into Tomtec Image Arena. LV and LA end systolic (ES) and end diastolic (ED) volumes and ejection fractions (EF) were measured using TomTec Image Arena 3D LV analysis package. A single cardiac cycle was defined using mitral valve (MV) closure. For the LV, the apex and aortic valve (AoV) were defined, and automated tracking was adjusted visually against the 2D imaging planes (four, three and two chamber apical views).

The same 3D DICOMs datasets were imported into VMS software, and reference points from recreated four, three and two chamber view imaging planes were manually placed at the AoV, MV, apex and LA and LV chamber walls as per the VMS protocol at both end systole and end diastole. The software generates a KBR-derived ESV and EDV and ejection fraction for each chamber (Figure 1).

The time taken to complete LA and LV volumetric analysis via TomTec and VMS were recorded.

Statistical Methods :

To adequately assess technique differences across a range of ages, sex and BSA with a power of 0.8 and alpha of 0.05, and assuming a standard deviation of 15% within techniques, 101 patients were included in this study.

The relationship between end-diastolic and end-systolic values with body surface area was assessed using linear regression modelling, with Breusch-Pagan testing for heteroscedasticity. Logarithmic transformation was used to reduce heteroskedasticity where present, and optimal regression with BSA was identified using curve-fitting.

Analysis time between Tomtec and VMS was compared using a non-paired Student's t-test. Linear regression models were used to compare the two software measurements of LV and LA ES and ED volumes and EF. Intraclass coefficients (ICC) were calculated, and Bland-Altman plots constructed for comparison of the two software algorithms. For interobserver agreement (IOA) and intra-observer agreement (IAOA), we randomly selected subjects for reanalysis by two of the investigators, LE & AA (IOA – LE, IAOA AA), and a two-way agreement model with 95% confidence interval and constructed Bland-Altman plots were used. All statistical analysis was performed using StataIC 14 (College Station, Texas).

RESULTS

Population

One hundred and one children with structurally normal hearts were included in the LV analysis and 98 in the LA analysis. Of the subjects, 51 (51%) were female and 49 (49%) were male. The median and range for height was 127cm (57 – 195cm) and for weight was 25kg (5.2 – 139kg). Body surface areas between 0.5 and 1kg/m2 composed the greatest proportion of the group (42%) whereas BSA <0.5kg/m2 were less well represented (12%) (Table 1).

Assessment of regression

The end-diastolic and end-systolic measurements were first regressed against BSA and tested for heteroscedasticity. All measurements demonstrated a strong correlation with BSA. Both TT derived and VMS derived LV and LA EDV showed significant heteroscedasticity using the Breusch-Pagan F-statistic. Power transformation provided the best model for the relationship between BSA and all volumes, however, heteroscedasticity was accentuated. A log-log transformation of volumes and BSA eliminated heteroscedasticity with acceptable overall residuals (Table 2). Average, standard deviations and upper and lower normal ranges for values indexed using the optimal power transformation are shown in Table 3 and 4. Calculation of z-scores for study values using the best fit power regression revealed that 5 - 6% of diastolic and systolic study values using either technique fell beyond the 2 standard deviation range (Table 3).

Agreement and reliability

LA Volumes: There was very good to excellent correlations between VMS and Tomtec measuring LA systolic and diastolic volumes: LAESV ICC 0.94 (95% CI 0.90,0.96), LAEDV ICC 0.87 (95% CI 0.81, 0.91). On average Tomtec LA measurements were greater than VMS measurements with a small mean bias: LAESV (mean difference 6.6±1.9% (limits of agreement 44%, -31%), LAEDV (mean difference 6.5% (95% CI 47%, -60%). The Pearson correlation coefficient for LA ESV was 0.94 and for LA EDV was 0.87

LV Volumes: Tomtec derived ventricular measurements were higher than VMS measurements on average, with no difference in variability. The mean bias between Tomtec and VMS measurements of LVEDVi was 7.5ml±9.2ml or 15.5±1.9% (limits of agreement: 52.9%, -22.3%), and LVESV was 1.7ml±4.2ml or 7.3±2.0%, (limits of agreement 47.1, -32.5%) (Table 3, Figure 1). There was very good to excellent correlations between VMS and Tomtec measurements of LV systolic and diastolic volumes: LV systolic ICC 0.93 (95% CI 0.89, 0.95), LV diastolic ICC 0.92 (95% CI 0.79, 0.96). The Pearson correlation coefficient for LVEDV was 0.94, and for LVESV was 0.94. LV and LA linear regression scatter plots are displayed in Figure 2.

Efficiency :

VMS analysis time was shorter than Tomtec for both the LA and LV (Table 5). LV analysis time (total EDV and ESV) using TomTec vs VMS analysis time had an estimated difference of 0.75 minutes (95% CI 0.56, 0.94, $p<0.0001$) For LA analysis time, there was an estimated difference between TomTec and VMS of 1.23 minutes (95% CI 1.01,1.45, $p<0.0001$).

Reproducibility :

Interobserver Agreement (IOA): We used a two-way agreement model with 95% confidence interval to report IOA completed on 23 Tomtec analyses and 18 VMS analyses of the LV and LA. There was excellent IOA for Tomtec LAESV (ICC 0.96 (95% CI 0.90 – 0.98)), VMS LAESV (ICC 0.90 (95% CI 0.75 – 0.96)) and VMS LAEDV (ICC 0.92 (95% CI 0.64 – 0.98). There was good IOA for Tomtec LA EDV (ICC 0.84 (95% CI 0.13, 0.95), with several outliers accounting for wide confidence intervals. There was excellent IOA for TomTec LVEDV (ICC 0.95 (95% CI 0.56 – 0.98)), VMS LVEDV (ICC 0.97 (95% CI 0.90 – 0.98)) and VMS LVESV (ICC 0.96 (95% CI 0.90 – 0.99)) and good IOA for LVESV (ICC 0.77 (95% CI 0.53 – 0.89). LA & LV interobserver regression analysis and Bland-Altman plots of agreement are displayed on Figures 3 and 4 respectively.

Intra-observer agreement (IAOA): We used two-way agreement model with 95% confidence interval to report IAOA completed on 21 studies. There was excellent IAOA for VMS LAESV (ICC 0.99 (95% CI 0.95 – 1.0) and VMS LAEDV (ICC 0.96 (95% CI 0.76 – 0.99). There was also excellent IAOA agreement for TomTec LAESV ICC 0.96 (95% CI 0.91 – 0.98) and good agreement for LAEDV (ICC 0.86 (95% CI 0.52 – 0.95)). VMS and TT LA intra-observer regression analysis and LA Bland-Altman plots of agreement are displayed on Figure 5 and 6 respectively. TomTec LV intra-observer agreement was performed as part of a multicenter study[13].

DISCUSSION

In this study, we demonstrate strong agreement between Tomtec Image Arena and VMS+ 3.0 for left ventricular and left atrial volumetric calculations from pediatric 3D DICOM datasets over a wide range of age and BSA. We provide formulas for linear, optimally curve-fitted, and log-log transformed regressions using both software algorithms, and the distribution parameters (average, standard deviations) for the indexed values from the optimal fit regression. This permits calculation of normal ranges and z-scores specific to the algorithms used. We also demonstrate excellent to good inter and intraobserver agreement for these techniques by intraclass correlation.

Three-dimensional echocardiographic imaging has emerged as a useful adjust to standard 2-dimensional echocardiography in volumetric measurement, and in some cases is promoted as the preferable method. Its main advantage is measurement of the atrial or ventricular chamber without reliance on geometric assumptions and (usually) only two 2D imaging planes. The replicability of 3DE volumetric measurement of the LV has been shown to be superior to 2D calculations and 3D LV volumes are more comparable to those derived from the gold standard, cardiac magnetic resonance imaging (CMR)[5,6, 7,25,26,27]. Therefore 3DE volumetric imaging is becoming an important tool in risk stratification, pre-procedural planning, and assessment of treatment in pediatric and adult cardiac populations. 3DE offers a relatively inexpensive and readily available tool at the bedside to assess cardiac chamber volumes and a viable alternative modality when CMR is not feasible or contraindicated.

Measurement of the LA volume has been increasingly recognized as an important component of echocardiographic analysis, with robust data showing prognostic importance in cardiac failure, as well as in assessment of progressive mitral valve disease. Assessment of the phases of LA function (reservoir, conduit and atrial contraction), while beyond the scope of this study, can be assessed with 3DE. Changes in these phases may provide useful early warnings of progressive disease before detectable LV diastolic function becomes apparent.

This study, to the best of our knowledge, is the first to compare TomTec to VMS software in measuring left cardiac chambers. Given that TomTec software has been previously validated against CMR in recently published multi-center studies in pediatrics; we provide in this study an alternative software algorithm to currently available software with comparable accuracy and efficiency in measuring left cardiac chambers using real time 3DE. Both algorithms performed particularly well in patients with smaller BSA compared to larger BSA. This could be in part due to higher spatial and temporal resolution images obtained in smaller children, and the smaller chest excursion during breathing, leading to fewer stitch artifacts. It was true despite the higher heart rates in younger children, and the benefits of older patient cooperation and ability to understand instruction for breath holding during multi-beat acquisitions. Tomtec LA and LV measurements were on average slightly higher than VMS measurements which should be considered when using the two software interchangeably.

In considering utility in clinical practice, both VMS+ 3.0 and Tomtec Image Arena have quick post processing times (VMS on average being slightly faster, Table 5) for both LV & LA with means between 1.5 - 2 minutes for VMS and 3 minutes for TomTec for each chamber. Our analysis time did not include the time required to import datasets into the offline software packages, which may be longer than the analysis time itself. Integration of 3DE analysis packages with general echocardiographic reporting software, allowing direct launch of the analysis, and automatic upload of the measurements obtained can help to streamline this process, and encourages routine usage of these tools. Direct measurement on echocardiographic imaging modalities can also facilitate this process for some workflows.

Study limitations

This study utilized a prospectively acquired single dataset of 3DE images in normal children, and therefore the findings need to be validated among cases with abnormal volumes, as agreement may diverge outside of the normal ranges. This was not a study on feasibility, and therefore we did not attempt to capture the number of children in which insufficient image quality could be obtained. We did not compare the two software directly to CMR which is considered the current reference standard, however, given TomTec 4D LV-analysis has been directly compared in previous large studies in measuring both LA and LV volumes and ejection/emptying fraction, we felt it was reasonable to use it as a reference[6,7]. We also acknowledge that 3DE has limitations related to the temporal resolution and spatial lateral resolution in the depth.

Future directions

Future work will focus on comparison of prospectively acquired KBR and 3DE datasets, to further validate the Ventripoint KBR platform and VMS+ 3.0 software as alternatives to atrial and ventricular volumes measured using MRI and 3DE. The availability of multiple validated analysis packages will encourage work in pediatric echocardiography that assesses 3DE volumetrics assessment as a prognostic and treatment indicator and may lead to inclusion of these parameters in future echocardiographic guidelines to aid in clinical decision making.

Conclusion

In conclusion, 3DE left heart volumes measured using VMS+ 3.0 and TomTec Image Arena are comparable, with excellent to good reproducibility. VMS+ 3.0 is associated with slightly shorted analysis time, although results can be obtained efficiently using both systems.

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Table 1: Study patient characteristics.

Total group (n)		101
Gender	Female	51 (51%)
	Male	50 (49%)
Age	<1 year	11 (11%)
	1 - 5 years	31 (32%)
	6 – 12 years	41 (40%)
	13 - 18 years	18 (17%)
Height(cm)	Mean (SD)	128±34
	Median [Min, Max]	127 [57, 195]
Weight(kg)	Mean (SD)	33±23.7
	Median [Min, Max]	25 [5.2, 139]
BSA (kg/m2)	Mean (SD)	1.06 ± 0.50
	<0.5	12 (12%)
	0.5 – 1	42 (42%)
	1 – 1.5	25 (25%)
	>1.5	22 (22%)

SD: standard deviation, min: minimum, max: maximum, BSA: body surface area.

Dependent variable	Independent variable	r^2	p-value	Coefficient (b1)	Intercept (b0)	Robust SE of coefficient
TT LVEDV	BSA	0.83	<0.0001	62.80102	-6.87617	5.167519
Ln(TT EDV)	Ln(BSA)	0.91	<0.0001	1.269637	3.974738	0.0561246
TT LVEDV	b0*(BSA^b1)	0.96	<0.0001	1.054172	56.40865	0.0931908 / 1.204307
VMS LVEDV	BSA	0.89	<0.0001	61.43118	-12.7263	3.406664
Ln(VMS EDV)	Ln(BSA)	0.93	<0.0001	1.344509	3.82453	0.0420661
VMS LVEDV	b0*(BSA^b1)	0.97	<0.0001	1.1937558	48.16209	0.0881996 / 1.21647
TT LVESV	BSA	0.77	<0.0001	27.26819	-5.05474	2.416927
Ln(TT LVESV)	Ln(BSA)	0.85	<0.0001	1.262735	3.0324	0.0553847
TT LVESV	b0*(BSA^b1)	0.93	<0.0001	1.1630229	22.05374	0.1212076/ 0.7257536
VMS LVESV	BSA	0.86	<0.0001	25.38475	-4.74177	1.410101
Ln(VMS ESV)	Ln(BSA)	0.91	<0.0001	1.349213	2.963445	0.0494901
VMS LVESV	b0*(BSA^b1)	0.96	<0.0001	1.15831	20.53851	0.0681439 / 0.501224
TT LAESV	BSA	0.85	<0.0001	25.30602	-3.52493	1.181858
Ln(TT LAESV)	Ln(BSA)	0.88	<0.0001	1.223491	3.031821	0.0471771
TT LAESV	b0*(BSA^b1)	0.96	<0.0001	1.132366	21.54519	0.0446251 / 0.541359
VMS LAESV	BSA	0.78	<0.0001	23.55753	-3.05372	1.498966
Ln(VMS LAESV)	Ln(BSA)	0.86	<0.0001	1.226555	2.964109	0.050976
VMS LAESV	b0*(BSA^b1)	0.94	<0.0001	1.119447	20.31953	0.0569337 / 0.6141348

Dependent variable	Independent variable	r^2	p-value	Coefficient (b1)	Intercept (b0)	Robust SE of coefficient
TT LAEDV	BSA	0.79	<0.0001	9.946382	-2.42243	0.6897877
Ln (TT LAEDV)	Ln(BSA)	0.87	<0.0001	1.427431	1.92521	0.0557446
TT LAEDV	b0*(BSA^b1)	0.93	<0.0001	1.270034	7.316284	0.0657074 / 0.2407124
VMS LAEDV	BSA	0.74	<0.0001	9.308305	-1.44972	0.6147768
Ln (VMS LAEDV)	Ln(BSA)	0.83	<0.0001	1.303145	1.984423	0.0629305
VMS LAEDV	b0*(BSA^b1)	0.92	<0.0001	1.138106	7.795621	0.0663989 / 0.2965523

Table 2: Tomtec and Ventripoint-derived algorithms for left ventricular and left atrial volumes: relationship with body surface area

Absolute and percentage differences are calculated as VMS -Tomtec. Indexing: TT LVEDV: BSA^1.05172. VMS LVEDV: BSA^1.1937558. TT LVESV: BSA^1.1630229, VMS LVESV: BSA^1.15831. ULOA Upper limit of agreement. LLOA Lower limit of agreement: Represents Average ± 1.96 x SD. VMS: Ventripoint software VMS 3.0, TT: Tomtec Image Arena, LV: left ventricle, LA: left atrium, EDV: end diastolic volume, ESV: end systolic volume, EF: ejection fraction, BSA: body surface area. 95% CI Ninety-five percent confidence intervals (1.96 SD +/- mean), Ln: natural logarithm.

Table 3 : Left ventricular volumes and agreement between Tomtec and Ventripoint algorithm

	Average (SEM)	**SD**	**ULOA / 95%CI**	**LLOA / 95% CI**	**Study v**
TT LVEDVi (ml/m^2)	54 (1.1)	11.1	75.8	32.2	6%
VMS LVEDVi (ml/m^2)	46.4 (0.9)	8.9	63.9	28.9	5%
absolute difference LVEDVi (ml/m^2)	-7.5 (0.9)	9.3	10.6	-25.7	
EDV percentage difference	-15.5 (1.9)	19.2	22.3	-52.9	
TT LVESVi (ml/m^2)	21.4 (0.5)	5.4	32.1	10.8	6%
VMS LVESVi (ml/m^2)	19.7 (0.4)	4.3	28.1	11.3	5%
absolute difference ESVi (ml/m^2)	-1.7 (0.4)	4.2	6.6	-9.9	
ESV percentage difference	-7.3 (20.3)	20.3	32.5	-47.1	
TT Ejection Fraction (%)	60.4 (0.7)	7.2	74.5	46.2	
VMS Ejection Fraction (%)	56.4 (0.4)	3.7	63.7	49.1	
EF absolute difference (%)	4.0 (0.8)	-8.1	11.9	-19.8	

Absolute and percentage differences are calculated as VMS - Tomtec. Indexing: TT LVEDV: BSA^1.05172. VMS LVEDV: BSA^1.1937558. TT LVESV: BSA^1.1630229, VMS LVESV: BSA^1.15831. ULOA Upper limit of agreement. LLOA Lower limit of agreement: Represents Average ± 1.96 x SD. VMS: Ventripoint software VMS 3.0, TT: TomTec Image Arena, LV: left ventricle, LA: left atrium, EDV: end diastolic volume, ESV: end systolic volume, EF: ejection fraction, BSA: body surface area. 95% CI Ninety-five percent confidence intervals (1.96 SD +/- mean), SD: standard deviation, SEM: standard error of the mean

Table 4 : Left atrial volumes and agreement between Tomtec and Ventripoint algorithm

	Average (SEM)	**SD**	**ULOA**	**LLOA**
TT LAEDVi (ml/m^2)	7.1 (0.2)	2	11	3.2
VMS LAEDVi (ml/m^2)	7.5 (0.24)	2.4	12.2	2.8
absolute difference LAEDVi (ml/m^2)	-0.5 (0.21)	2.1	3.7	-4.6
EDV percentage difference	-6.5 (2.8)	27	47	-60
TT LAESVi (ml/m^2)	21.1 (0.46)	4.6	30.1	12.1
VMS LAESVi (ml/m^2)	19.9 (0.51)	5	29.7	10.1
absolute difference ESVi (ml/m^2)	1.3 (0.39)	3.8	8.8	-6.2

	Average (SEM)	SD	ULOA	LLOA
ESV percentage difference	6.6 (1.9)	19	44	-31
TT LA Emptying Fraction (%)	67 (0.7)	6.6	80	54
VMS LA Emptying Fraction (%)	62 (0.6)	6.1	74	50
LA EF absolute difference (%)	5.0 (0.8)	7.6	19	-10

Absolute and percentage differences are calculated as Tomtec – VMS. Indexing: TT LAEDV: BSAˆ1.270034. VMS LAEDV: BSAˆ1.138106. TT LAESV: BSAˆ1.132366, VMS LAESV: BSAˆ1.119447. ULOA Upper limit of agreement. LLOA Lower limit of agreement: Represents Average ± 1.96 x SD. VMS: Ventripoint software, TT: TomTec Image Arena, LV: left ventricle, LA: left atrium, EDV: end diastolic volume, ESV: end systolic volume, EF: ejection fraction, BSA: body surface area, SD: standard deviation, SEM: standard error of the mean

Table 5 : Measurement times for LV and LA volume measurements.

	Mean (SD)	Median [Min, Max]	Average Difference (95% CI)	p-value
VMS LA (mins)	1.60 (0.37)	1.46 (1.1, 2.39)	1.23 (1.01,1.45)	p<0.0001
TT LA (mins)	3.04 (0.98)	2.92 (1.68, 7.73)		
VMS LV (mins)	2.39 (0.10)	2.41 (1.48, 5.1)	0.75 (0.56, 0.94)	p<0.0001
TT LV (mins)	3.14 (0.18)	3.1 (1.1, 3.58)		

Mean, median presented. SD: standard deviation. VMS: Ventripoint software, TT: TomTec 4D LV Image Arena, LV: left ventricle, LA: left atrium.

Figure legends:

Figure 1. LA & LV Bland-Altman plots VMS-TT: Solid lines represent predicted means, dashed lines represent 95% prediction limits, and dots represent individual measurements. The plots depict percentage of deference in means com. VMS: Ventripoint software, TT: TomTec 4D LV Image Arena, LV: left ventricle, LA: left atrium, EF= ejection fraction, EDV: end diastolic volume, ESV: end systolic function

Figure 2: LA & LV linear regression scatter plots VMS-TT: VMS: Ventripoint software, TT: TomTec 4D LV Image Arena, LV: left ventricle, LA: left atrium, EF= ejection fraction, EDV: end diastolic volume, ESV: end systolic function.

Figure 3. VMS-calculated LA volumes - Interobserver regression and Bland-Altman plots:

For Bland -Altman plots, Solid lines represent predicted means, dashed lines represent 95% prediction limits, and dots represent individual measurements. VMS: Ventripoint software, TT: TomTec 4D LV Image Arena, LV: left ventricle, LA: left atrium, EF= ejection fraction.

4. Figure 3. VMS-calculated LV volumes - Interobserver regression and Bland-Altman plots:

For Bland -Altman plots, Solid lines represent predicted means, dashed lines represent 95% prediction limits, and dots represent individual measurements. VMS: Ventripoint software, TT: TomTec 4D LV Image Arena, LV: left ventricle, LA: left atrium, EF= ejection fraction, EDV: end diastolic volume, ESV: end systolic function.

Figure 5. VMS-calculated LA volumes - intra-observer regression and Bland-Altman plots:

For Bland -Altman plots, Solid lines represent predicted means, dashed lines represent 95% prediction limits, and dots represent individual measurements. VMS: Ventripoint software, TT: TomTec 4D LV Image Arena, LV: left ventricle, LA: left atrium, EF= ejection fraction, EDV: end diastolic volume, ESV: end systolic function.

Figure 6. Tomtec-calculated LA volumes - intra-observer regression and Bland-Altman plots:

For Bland -Altman plots, Solid lines represent predicted means, dashed lines represent 95% prediction limits, and dots represent individual measurements. VMS: Ventripoint software, TT: TomTec 4D LV Image Arena, LV: left ventricle, LA: left atrium, EF= ejection fraction, EDV: end diastolic volume, ESV: end systolic function.

Figure 1. LA & LV Bland-Altman plots VMS-TT.

VMS:

Figure 2: LA & LV linear regression scatter plots VMS-TT:

Figure 3. VMS-calculated LA volumes - Interobserver regression and Bland-Altman plots:

4. Figure 3. VMS-calculated LV volumes - Interobserver regression and Bland-Altman plots:

Figure 5. VMS-calculated LA volumes - intra-observer regression and Bland-Altman plots:

Figure 6. Tomtec-calculated LA volumes - intra-observer regression and Bland-Altman plots: