



## Reproducibility of Semi-automated Three-dimensional Volumetric Analysis using Cardiac Computed Tomography in Patients With Left Ventricular Assist Device<sup>☆</sup>

Gauravpal S. Gill<sup>a</sup>, Gaby Weissman<sup>a</sup>, Yael F. Meirovich<sup>b</sup>, Diego Medvedofsky<sup>a</sup>, Selma F. Mohammed<sup>a,c</sup>, Ron Waksman<sup>a</sup>, Hector M. Garcia-Garcia<sup>a,b,\*</sup>

<sup>a</sup> MedStar Washington Hospital Center, Washington, D.C., United States of America

<sup>b</sup> MedStar Cardiovascular Research Network, Washington, D.C., United States of America

<sup>c</sup> MedStar Advanced Heart Failure Program, Washington, D.C., United States of America

### ARTICLE INFO

#### Article history:

Received 11 January 2019

Accepted 18 January 2019>

#### Keywords:

Volumetric analysis

Cardiac computed tomography

Left ventricular assist device

### ABSTRACT

**Background:** Multi-detector gated cardiac computed tomography (CCT) allows three-dimensional (3D) quantification of cardiac chambers and is clinically indicated to assess left ventricular assist device (LVAD) malfunction and complications. Automated volumetric analysis is, however, disrupted by inflow cannula artifact in patients with LVAD. With this study, we evaluated intra-observer variability in semi-automated 3D cardiac volumetric analysis using CCT in patients with LVADs.

**Methods:** Ten clinically indicated CCTs were studied retrospectively from 9 patients with LVADs. 3D chamber quantification included left and right ventricles end-systolic and end-diastolic volumes (ESV, EDV); and left and right atrial ESV. Derived measurements included cardiac output (CO), ejection fraction (EF), and stroke volume (SV). Automated volumetric analysis was performed, and manual corrections were added when necessary. Absolute and relative differences, Bland-Altman plots, and interclass correlation coefficients (ICCs) were used to assess intra-observer reproducibility for these measurements.

**Results:** Intra-observer reproducibility was excellent for volumetric (ICC >0.99) and derived data (ICC >0.91). Comparing right vs left heart volumetric assessments, the former had a higher relative difference (atria 2.8% vs 1.6%, ESV 3.0% vs 1.9%, EDV 2.7% vs 1.3%), which also translated to a greater relative difference in right-side derived data (CO 11.1% vs. 8.8%, EF 10.5% vs. 9.9%, SV 10.9% vs. 9.0%). The mean difference in left ventricular ejection fraction was 0.4% (limits of agreement [LOA]: −2 and 3.2) and right ventricular ejection fraction was 1.2% (LOA: −4.7 and 7.1).

**Conclusions:** Our results for semi-automated 3D volumetric analysis showed excellent reproducibility for both volumetric and derived data.

**Summary:** Electrocardiography-gated cardiac computed tomography with semi-automated volumetric analysis has excellent reproducibility in patients with left ventricular assist device making it imaging modality of choice for functional assessment in this patient population, where cardiac magnetic resonance imaging is contraindicated and transthoracic echocardiography may be limited by poor acoustic windows.

© 2019 Elsevier Inc. All rights reserved.

### 1. Introduction

Computed Tomography (CT) is an essential diagnostic study in today's clinical practice. This imaging modality has gained considerable attention over the past decade for its applicability in management of cardiovascular disease due to its increase availability and non-invasive nature. In patients

with systolic heart failure and left ventricular assist device (LVAD) implant, the clinical indication of cardiac CT (CCT) is for evaluation of device position, dysfunction, and thrombus formation [1,2].

Contrast between endocardial border and chamber cavity allows for delineation of cardiac chambers, thus permitting volumetric and functional analyses. Despite the fact that cardiac magnetic resonance

<sup>☆</sup> Disclosures: Ron Waksman: Advisory Board: Abbott Vascular, Amgen, Boston Scientific, Medtronic, Philips Volcano, Pi-Cardia LTD, Cardioset; Consultant: Abbott Vascular, Amgen, Biosensors, Biotronik, Boston Scientific, Medtronic, Philips Volcano, Pi-Cardia LTD, Cardioset; Grant support: Abbott Vascular, AstraZeneca, Biosensors, Biotronik, Boston Scientific, Chiesi; Speakers bureau: AstraZeneca, Chiesi; Investor: MedAlliance. All other authors have no conflicts to disclose.

\* Corresponding author at: MedStar Washington Hospital Center, 110 Irving St., NW, Suite 4B-1, Washington, DC 20010, United States of America.

E-mail address: [hector.m.garciagarcia@medstar.net](mailto:hector.m.garciagarcia@medstar.net) (H.M. Garcia-Garcia).

**Table 1**  
Baseline characteristics.

Variable	Median or n (%)
Age (years)	61
Male	9 (90%)
Heart failure etiology	
Ischemic cardiomyopathy	4 (40%)
Non-ischemic cardiomyopathy	6 (60%)
Race	
African-American	8 (80%)
Caucasian	1 (10%)
Hispanic	1 (10%)
Type of LVAD	
HeartWare	7 (70%)
HeartMate II	3 (30%)

imaging (CMR) is the gold standard for ventricular function analysis, it is contraindicated in patients with a metal LVAD implant. This renders CCT as the best imaging modality for the estimation of cardiac chamber volume and derived functional measurements [3–5]. When compared to its alternative, the transthoracic echocardiography, CCT, while being more expensive and limited in availability, allows for a better visualization of right ventricular morphology and assessment of function and is not limited by poor acoustic windows [6,7].

Traditionally, manual volumetric measurements with CCT use modified Simpson's summation of discs method where assumptions in chamber shapes are used to calculate volumes, while in automated analysis using various commercially available electrocardiography

(ECG)-gated software, accurate assessments through multi-slice images are available in a timely manner.

The objective of this study is to evaluate the intra-observer variability in quantitative three-dimensional (3D) volumetric analysis of all 4 cardiac chambers using electrocardiographic-gated CCT in patients with LVADs [8].

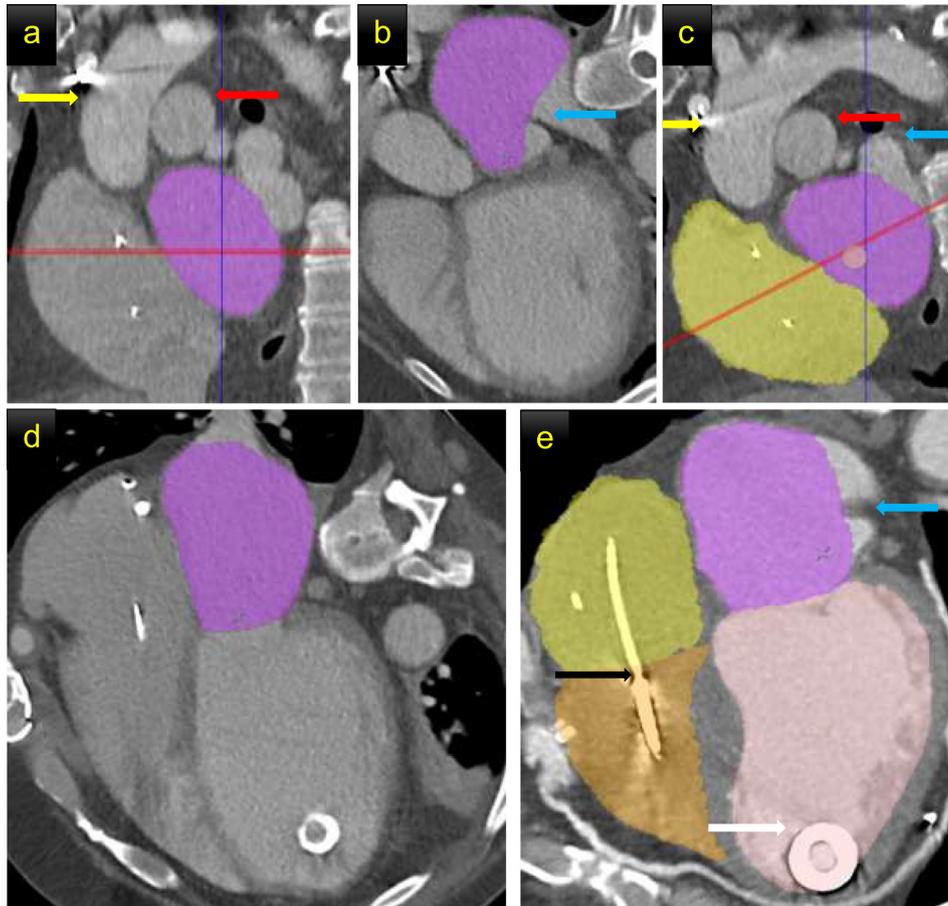
## 2. Methods

### 2.1. Study population

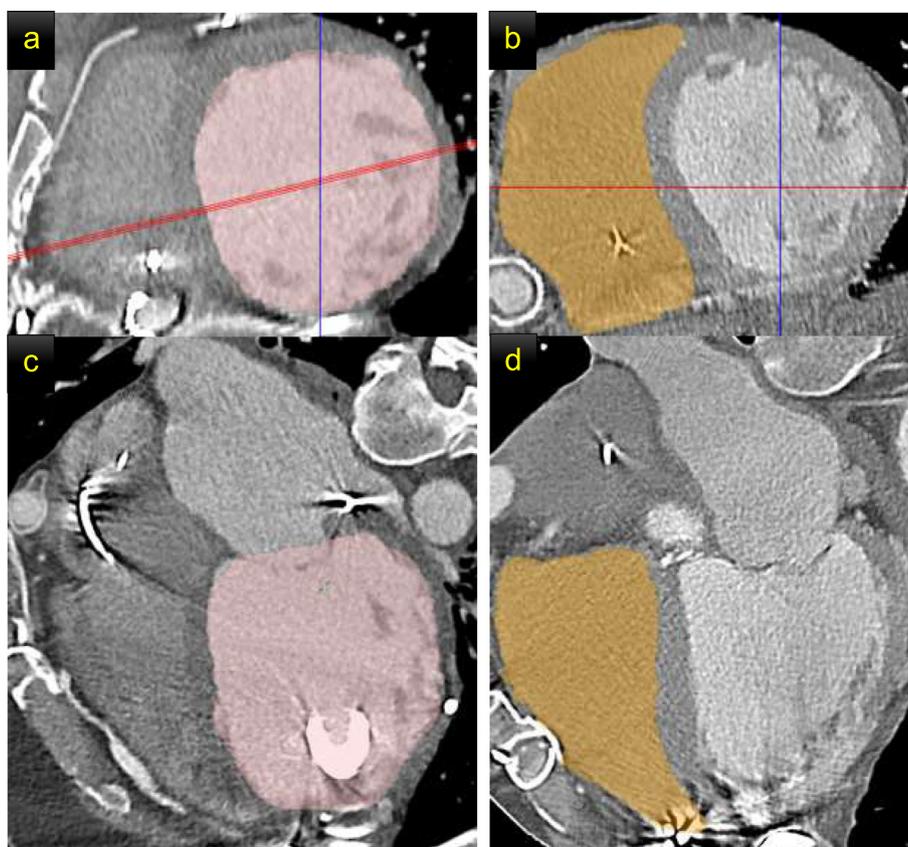
Patient cohort was selected from among those being routinely followed at the MedStar Advance Heart Failure Program and who underwent CCT. Ten high quality clinically-indicated ECG-gated CCTs with right and left heart contrast enhancement were chosen for this study from patients with HeartWare (70%) and HeartMate II (30%) LVADs (Table 1).

### 2.2. Imaging protocol

CCT was performed on a 256-slice CT scanner with 0.625 mm detector collimation (Philips Brilliance iCT v. 3.2). Imaging technique included ECG-gated 256-slice high-resolution helical CT scanning of the chest from lung apices to diaphragm, and high-resolution thin cut axial images were reconstructed at <1 mm slice thickness using iterative algorithm in different phases from 0 to 90% (at increments of 10%) within R-R interval and analyzed used Philips IntelliSpace Portal 7.0 software.



**Fig. 1.** Semi-automated atrial analysis with Philips IntelliSpace Portal 7.0 software. Left atrium (purple) in images a-e; right atrium (yellow) in images c and e; left (pink) and right ventricles (orange) in image e; pulmonary artery (yellow arrow) and aorta (red arrow) in images a and c; left atrial appendage (blue arrow) in images b, c and e; right ventricular pacer artifact (black arrow) and left ventricular assist device outflow canula artifact (white arrow) in image e.



**Fig. 2.** Semi-automated ventricular analysis with Philips IntelliSpace Portal 7.0 software. Left ventricular cavity (pink) in images a and c; and right ventricular cavity (orange) in images b and d.

### 2.3. Assessment of atrial and ventricle volumes

Phases corresponding to end-systole and end-diastole were determined manually by measuring maximal left ventricular (LV) cavity diameter in different ECG-gated phases described above.

Left and right atrial volumes were measured at end-systole using Philips IntelliSpace Portal 7.0 software-based endocardial border detection with manual correction while excluding pulmonary veins and appendages. Basal limits were defined by atrio-ventricular margins marked at the level of mitral and tricuspid valve rings, respectively (Fig. 1).

Similarly, left and right ventricular volumes were measured at the end-systole and end-diastole using the aforementioned software with manual correction for automated endocardial border detection. Papillary muscles and trabeculations were included in the LV cavity volume (Fig. 2). Myocardial trabeculae and moderator band were included in right ventricular cavity volume. Interpolation method was used for demarcation of LV chamber margins in apical area due to artifact from the presence of inflow cannula.

Data, including stroke volume, ejection fraction, and cardiac output, were derived from measured volumes in the software (Fig. 3).

### 2.4. Statistical analysis

The intra-observer reproducibility was performed by a single observer twice at an interval of 30 days. We presented continuous variables from measured and derived data as either mean  $\pm$  standard deviations (SDs) or median depending on the distribution of the data; absolute and relative differences between first and second time of analysis were calculated. Inter-class coefficients (ICCs) and 95% confidence intervals (CIs) were analyzed with IBM SPSS Statistics Version 23 (Table 2). Limits of agreement (LOA), defined as the mean difference of measurements during first and second analysis  $\pm$  1.96 SD, were calculated, and Bland-Altman plots were generated using Microsoft Excel to assess for concordance (Figs. 4 and 5).

	Based on Heart Segmentation	
	Left	Right
ES Ventricular Volume (Phase 40%)	299.3 ml	222.9 ml
ED Ventricular Volume (Phase 90%)	328.2 ml	257.7 ml
Ventricular Stroke Volume	28.8 ml	34.8 ml
Ventricular Ejection Fraction	8 %	13 %
Ventricular Cardiac Output	2.0 L/min	2.4 L/min

**Fig. 3.** Software based 3-dimensional volume and derived measurements with automated calculations using ECG-gated coronary CTA.

**Table 2**

Volumetric and derived functional measurements of 4-cardiac chambers for heart failure patients with LVAD implant calculated using 3-dimensional volumetric analysis.

Variables	1st analysis	2nd analysis	Difference absolute relative (%)		ICC (95% CI)
<b>Volumetric measurements</b>					
LAESV (mL)	154.7 (±67.1)	154.4 (±65.8)	0.3 (±3.2)	1.6	0.999 (0.996–1.000)
RAESV (mL)	209.2 (±81.7)	208.7 (±83.9)	0.5 (±6.7)	2.8	0.998 (0.994–1.000)
LVEDV (mL)	422.5 (±167.5)	423.2 (±162.5)	-0.7 (±7.6)	1.3	1.000 (0.998–1.000)
LVESV (mL)	371.1 (±158.2)	373.6 (±154.8)	-2.4 (±8.6)	1.9	0.999 (0.997–1.000)
RVEDV (mL)	287.8 (±96.6)	286.0 (±101.0)	1.8 (±9.8)	2.7	0.998 (0.991–0.999)
RVESV (mL)	212.2 (±91.4)	214.3 (±92.5)	-2.1 (±7.6)	3.0	0.998 (0.994–1.000)
<b>Derived measurements</b>					
RVCO (L/min)	6.3 (±1.8)	6.0 (±1.8)	0.3 (±0.9)	11.1	0.939 (0.770–0.985)
LVCO (L/min)	4.3 (±1.6)	4.2 (±1.4)	0.1 (±0.5)	8.8	0.974 (0.902–0.993)
RVEF (%)	27.8 (±7.9)	26.5 (±6.9)	1.2 (±3.0)	10.5	0.947 (0.801–0.987)
LVEF (%)	13.2 (±4.6)	12.8 (±4.7)	0.4 (±1.5)	9.9	0.982 (0.928–0.995)
RVSV (mL)	75.6 (±19.9)	71.7 (±17.0)	3.9 (±10.3)	10.9	0.912 (0.670–0.978)
LVSV (mL)	51.3 (±16.0)	49.6 (±14.1)	1.7 (±5.6)	9.0	0.964 (0.864–0.991)

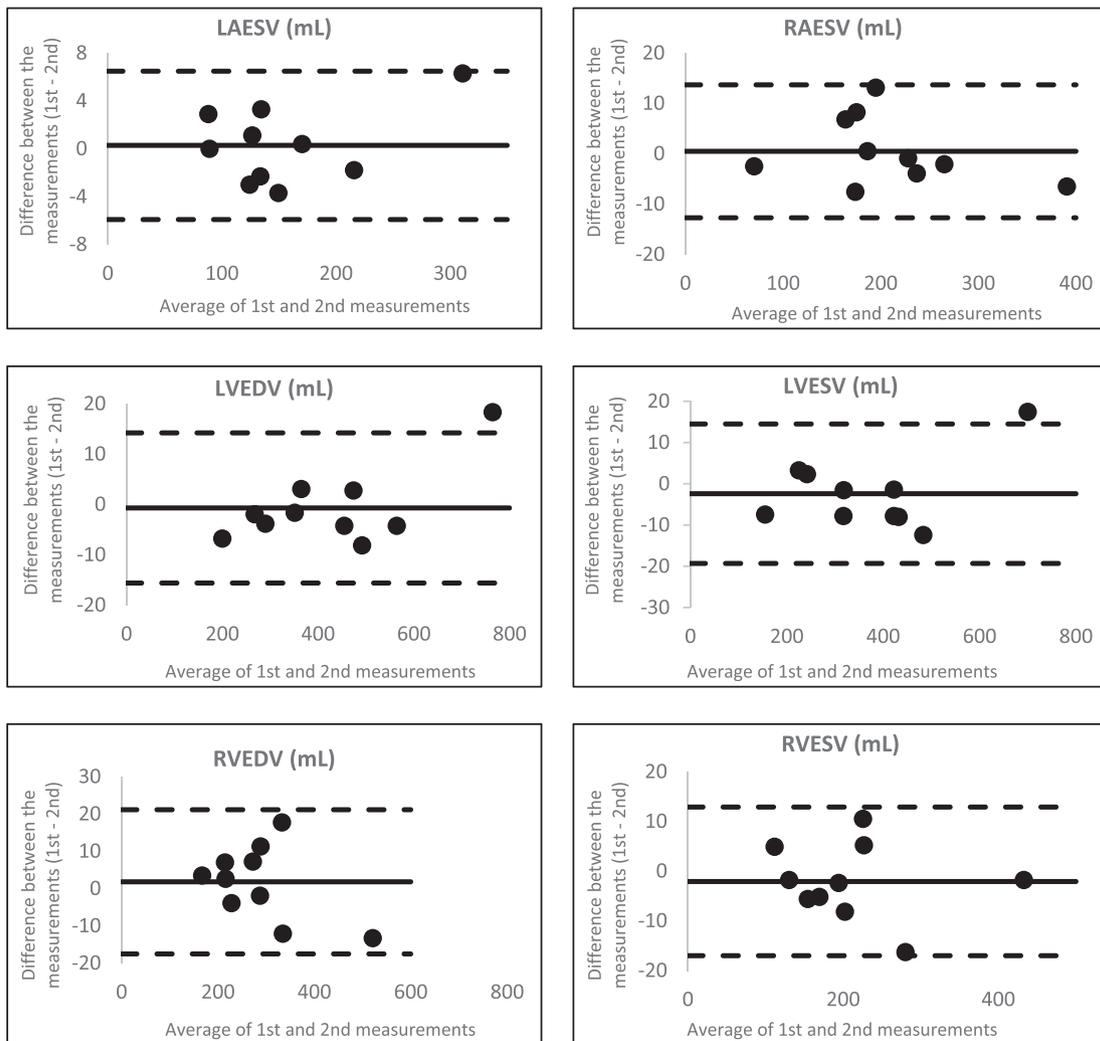
ICC = Inter-class Correlation Coefficient; LAESV = Left Atrial End Systolic Volume; RAESV = Right Atrial End Systolic Volume; LVEDV = Left Ventricular End Diastolic Volume; LVESV = Left Ventricular End Systolic Volume; RVEDV = Right Ventricular End Diastolic Volume; RVESV = Right Ventricular End Systolic Volume; RVCO = Right Ventricular Cardiac Output; LVCO = Left Ventricular Cardiac Output; RVEF = Right Ventricular Ejection Fraction; LVEF = Left Ventricular Ejection Fraction; RVSV = Right Ventricular Stroke Volume; LVSV = Left Ventricular Stroke Volume.

**3. Results**

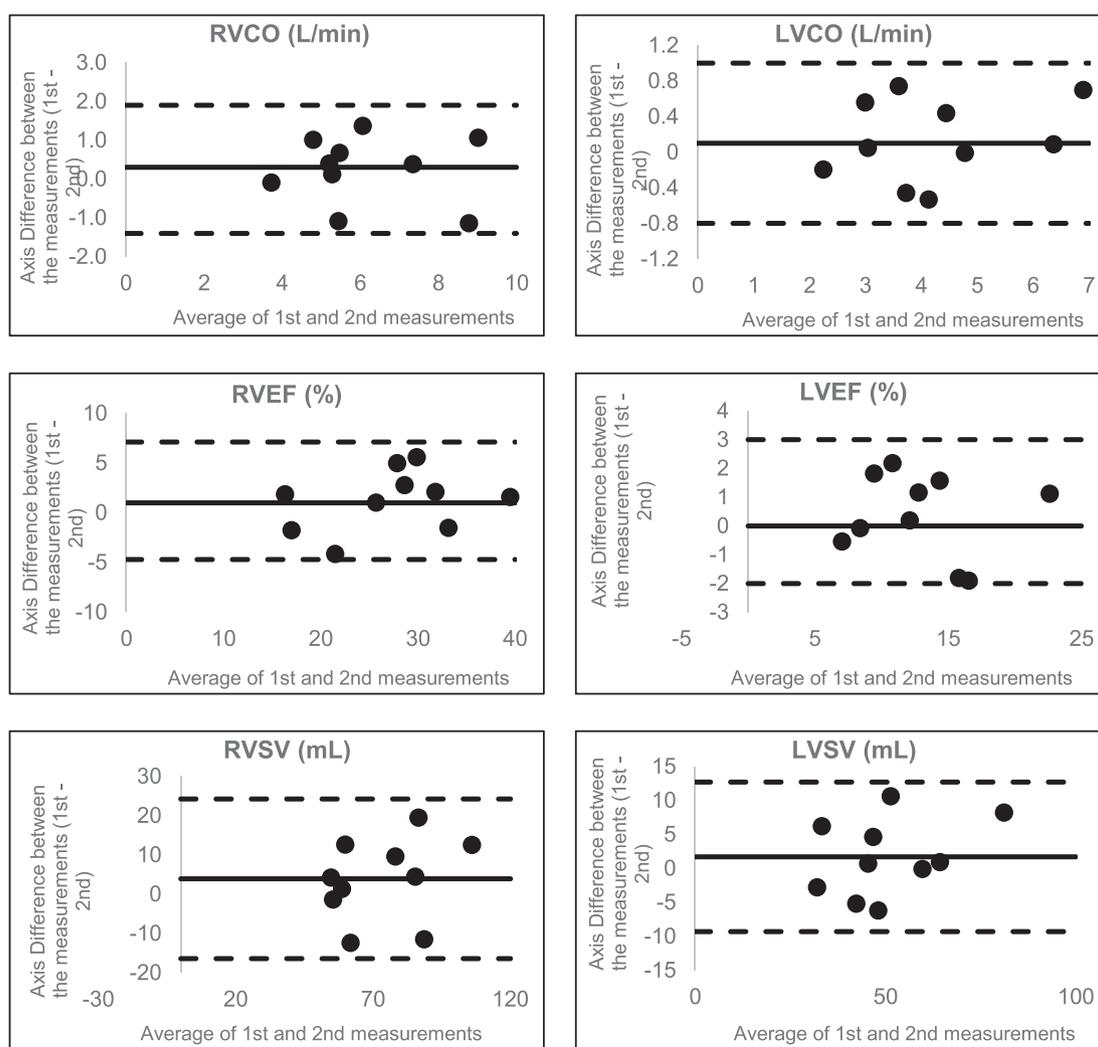
The median age of study population was 61 years with 80% African American, 90% male, and 40% having ischemic cardiomyopathy as the

cause of heart failure. Ten CCTs from 9 patients, performed at a median of 1079 days from device implantation, were analyzed (Table 1).

Intra-observer reproducibility was excellent for volumetric (widest ICC range 0.991–0.999 for right ventricular end-diastolic volume) and



**Fig. 4.** Bland-Altman plots depicting intra-observer agreement for volume measurements. LAESV = Left Atrial End Systolic Volume; RAESV = Right Atrial End Systolic Volume; LVEDV = Left Ventricular End Diastolic Volume; LVESV = Left Ventricular End Systolic Volume; RVEDV = Right Ventricular End Diastolic Volume; RVESV = Right Ventricular End Systolic Volume.



**Fig. 5.** Bland-Altman plots depicting intra-observer agreement for derived measurements. RVCO = Right Ventricular Cardiac Output; LVCO = Left Ventricular Cardiac Output; RVEF = Right Ventricular Ejection Fraction; LVEF = Left Ventricular Ejection Fraction; RSV = Right Ventricular Stroke Volume; LSV = Left Ventricular Stroke Volume.

derived data (widest ICC range 0.670–0.978 for right ventricular stroke volume).

Minimum relative difference in volumetric data was seen in left ventricular end-diastolic volume at 1.3%, while maximum difference was seen in right ventricular end-systolic volume at 3%. Similar difference in reproducibility between left and right chamber volumes were also seen in atrial measurements as well, with relative difference in measurements for left atrial end-systolic volume at 1.6% and right atrial end-systolic volume at 2.8% (Table 2).

As expected, derived data showed higher relative differences, with the greatest difference in right ventricular cardiac output (11.1%). Also, as mentioned above, the right-side volumetric assessments had a higher relative difference when compared to left chambers (2.7–3.0% vs 1.3–1.9%) which translated to greater relative difference in derived data (10.5–11.1% vs 8.8–9.9%) as well (Table 2).

Results of intra-observer agreements in functional assessment were promising with mean difference in left ventricular ejection fraction at 0.4% (LOA:  $-2$  and  $3.2$ ) and in right ventricular ejection fraction at 1.2% (LOA:  $-4.7$  and  $7.1$ ) (Fig. 5).

#### 4. Discussion

Our study using semi-automated analysis showed excellent reproducibility for volumetric measurement of cardiac chambers and for left and right heart functional measurements, even in the presence of

significant artifact from LVAD outflow canula and the right ventricular pacer wire.

CMR is the gold standard for cardiac volumetric functional analysis; however, it cannot be performed in patients with LVADs. While evaluating for device-related complications in these patients, CCT is the modality of choice and is frequently performed to assess device position, dysfunction, and thrombus formation in addition to standard structural analysis [1,2].

ECG-gated CCT provides images through different phases of the cardiac cycle, which allows for the assessment of volumes, and has previously been shown to produce results comparable to CMR for volumetric analysis in patients without these devices [9–11]. Traditionally for volumetric analysis using this modality, manual assessment with modified Simpson's method of disc summation is used, which relies on assumption of chamber shapes for calculations [8]. In this study, 3D automated volumetric measurements were subjected to manual correction due to loss in cavity-endocardial border distinction caused by significant artifact from device and right ventricular pacer wire. We used the interpolation technique to define limits of left ventricular cavity in frames with artifact. This allowed for chamber quantification without geometric assumptions.

An alternate imaging modality which is less expensive and more widely available is the echocardiography. However, CT images allow for better visualization and are not limited by poor acoustic windows [6,7]. In addition, volume analysis by echocardiogram also includes

application of the modified Simpson's method of disc summation, hence, making assumptions in cavity shapes.

In this study, LOA demonstrated by Bland-Altman plots were narrow, and ICCs were excellent ( $>0.9$ ) for volumetric and derived functional data from both left and right cardiac chambers. ICCs were also higher than those reported in the study by Garcia-Alvarez et al. where modified Simpson's method was used to measure right ventricular volumes (Table 2 and Fig. 4) [7]. Although it had higher relative differences, derived functional data showed high ICCs, and the reproducibility was acceptable (Table 2).

Results of this study were significant for consistently higher relative differences in right cardiac volume and derived functional data, which can be attributed to poorer contrast enhancement of endocardial border in right-sided chambers when compared to the left. Also, derived measurements showed greater differences, likely due to extremely low ejection fractions in these patients.

Using the multiplanar 3D analysis with interpolation as opposed to modified Simpson's method may have a potential drawback, namely difficulty in delineation of cavity limits in areas on metal artifact. However, maneuverability of the images along different axis allows for minimizing this artifact, thus resulting in high reproducibility, as in this study.

CCTs have a growing availability today, especially in institutions catering to LVAD populations. Studying the reproducibility of volumetric analysis in this population is important for designing longitudinal studies in the future. This modality can help identify cardiac response to continuous flow with a more reliable assessment of remodeling in all 4 chambers while defining cavity margins in multiple planes.

#### 4.1. Study limitations

Being that the study is retrospective, image protocol was not optimized to enhance the right cardiac chambers, leading to poor visualization and higher variability on the side. Small sample size of the study and limitation to intra-observer reproducibility may be taken into account when interpreting the results of this study.

## 5. Conclusion

Three-dimensional volumetric analysis using CCT, otherwise clinically indicated for LVAD population, showed high reproducibility in our study with narrow LOA and high ICCs. This imaging modality would be a good choice for longitudinal studies designed to assess cardiac remodeling in response to pressure and flow changes in the heart.

## References

- [1] Mishkin JD, Enriquez JR, Meyer DM, et al. Utilization of cardiac computed tomography angiography for the diagnosis of left ventricular assist device thrombosis. *Circ Heart Fail* 2012;5:e27–9.
- [2] Raman SV, Sahu A, Merchant AZ, Lbt Louis, Firstenberg MS, Sun B. Noninvasive assessment of left ventricular assist devices with cardiovascular computed tomography and impact on management. *J Heart Lung Transplant* 2010;29:79–85.
- [3] Kim SS, Ko SM, Song MG, Kim JS. Assessment of global function of left ventricle with dual-source CT in patients with severe arrhythmia: a comparison with the use of two-dimensional transthoracic echocardiography. *Int J Cardiovasc Imaging* 2010;26:213–21.
- [4] Stolzmann P, Scheffel H, Trindade PT, et al. Left ventricular and left atrial dimensions and volumes: comparison between dual-source CT and echocardiography. *Invest Radiol* 2008;43:284–9.
- [5] Takx RA, Moscariello A, Schoepf UJ, et al. Quantification of left and right ventricular function and myocardial mass: comparison of low-radiation dose 2nd generation dual-source CT and cardiac MRI. *Eur J Radiol* 2012;81:e598–604.
- [6] Asferg C, Usinger L, Kristensen TS, Abdulla J. Accuracy of multi-slice computed tomography for measurement of left ventricular ejection fraction compared with cardiac magnetic resonance imaging and two-dimensional transthoracic echocardiography: a systematic review and meta-analysis. *Eur J Radiol* 2012;81:e757–62.
- [7] Garcia-Alvarez A, Fernandez-Friera L, Lau JF, et al. Evaluation of right ventricular function and post-operative findings using cardiac computed tomography in patients with left ventricular assist devices. *J Heart Lung Transplant* 2011;30:896–903.
- [8] Rizvi A, Deano RC, Bachman DP, Xiong G, Min JK, Truong QA. Analysis of ventricular function by CT. *J Cardiovasc Comput Tomogr* 2015;9:1–12.
- [9] Nasir K, Katz R, Mao S, et al. Comparison of left ventricular size by computed tomography with magnetic resonance imaging measures of left ventricle mass and volumes: the multi-ethnic study of atherosclerosis. *J Cardiovasc Comput Tomogr* 2008;2:141–8.
- [10] Schlosser T, Mohrs OK, Magedanz A, Voigtlander T, Schermund A, Barkhausen J. Assessment of left ventricular function and mass in patients undergoing computed tomography (CT) coronary angiography using 64-detector-row CT: comparison to magnetic resonance imaging. *Acta Radiol* 2007;48:30–5.
- [11] Busch S, Johnson TR, Wintersperger BJ, et al. Quantitative assessment of left ventricular function with dual-source CT in comparison to cardiac magnetic resonance imaging: initial findings. *Eur Radiol* 2008;18:570–5.