#### NEW TECHNOLOGIES IN ECHO AND CV IMAGING: LUXURY OR NECESSITY? Automated measurement of left ventricular ejection fraction and volume

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**31**GIORNATE CARDIOLOGICHE TORINESI

*Everything you always wanted to know about* Cardiovascular Medicine

> Mauro Rinaldi CO-PRESIDENTS Fiorenzo Gaita Sebastiano Marra

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# **DISCLOSURE INFORMATION**

## Mauro Pepi

negli ultimi due anni ho avuto i seguenti rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:

\_\_\_Nessun conflitto interesse\_\_\_\_\_

# IMAGING CARDIOVASCOLARE2D 0 3D ?

ISSOD RECESSIE









LAD

#### **Methods**

#### Importance of Imaging Method Over Imaging Modality in Noninvasive Determination of Left Ventricular Volumes and Ejection Fraction Assessment by Two- and Three-Dimensional Echocardiography and Magnetic Resonance Imaging Michael L. Chuang, MS,\* Mark G. Hibberd, MD, PHD,\* Carol J. Salton, BA,\* Raymond A. Beaudin, MS,† Marilyn F. Riley, BS,\* Robert A. Parker, ScD,‡ Pamela S. Douglas, MD, FACC,\* Warren J. Manning, MD, FACC\*§ Boston and Andover, Massachusetts

- Volumetric 3D (Free-hand technique) correlated with Volumetric MRI in pts with normal or dilated LV.

- Agreement is poor between Biplane and volumetric methods (regardless of imaging modalities).

# REPRODUCIBILITY OF ECHO and MRI Left ventricular VOLUMES

## VolMRI BipMRI 3DEcho BipEcho

Interobserver EDV Interobserver ESV Intraobserver EDV Intraobserver ESV

3,5%	9,4%	4%	17,5%
4,8%	12,9%	5,6%	24,3%
2,6%	8,1%	3,2%	17,3%
3,5%	10,5%	4,2%	22,4%

Interobserver EF Intraobserver EF

3,6%	13,4%	8,3%	17,8%
5,1%	13%	6,9%	13,4%

Chuang et al JACC 2000

# 2D vs 3D LV assessment: state of the art

#### <u>2D</u>

- Foreshortening → volumes underestimation
- Reproducibility → reader dependent
- Time consuming → multiple measurements



#### <u>3D</u>

- Accurate
- Reproducible
- Time saving???



#### GUIDELINES AND STANDARDS

#### EAE/ASE Recommendations for Image Acquisition and Display Using Three-Dimensional Echocardiography 2012

Roberto M. Lang, MD, FASE, \*<sup>‡</sup> Luigi P. Badano, MD, FESC, <sup>†‡</sup> Wendy Tsang, MD, \* David H. Adams, MD, \*
Eustachio Agricola, MD, <sup>†</sup> Thomas Buck, MD, FESC, <sup>†</sup> Francesco F. Faletra, MD, <sup>†</sup> Andreas Franke, MD, FESC, <sup>†</sup>
Judy Hung, MD, FASE, \* Leopoldo Pérez de Isla, MD, PhD, FESC, <sup>†</sup> Otto Kamp, MD, PhD, FESC, <sup>†</sup>
Jaroslaw D. Kasprzak, MD, FESC, <sup>†</sup> Patrizio Lancellotti, MD, PhD, FESC, <sup>†</sup> Thomas H. Marwick, MBBS, PhD, \*
Marti L. McCulloch, RDCS, FASE, \* Mark J. Monaghan, PhD, FESC, <sup>†</sup> Petros Nihoyannopoulos, MD, FESC, <sup>†</sup>
Natesa G. Pandian, MD, \* Patricia A. Pellikka, MD, FASE, \* Mauro Pepi, MD, FESC, <sup>†</sup>
David A. Roberson, MD, FASE, \* Stanton K. Shernan, MD, FASE, \* Girish S. Shirali, MBBS, FASE, \*
Lissa Sugeng, MD, \* Folkert J. Ten Cate, MD, <sup>†</sup> Mani A. Vannan, MBBS, FASE, \*
Jose Luis Zamorano, MD, FESC, FASE, <sup>†</sup> and William A. Zoghbi, MD, FASE \*, *Chicago and Oak Lawn, Illinois; Padua and Milan, Italy; New York, New York; Essen and Hannover, Germany; Lugano, Switzerland; Boston, Massachusetts; Madrid, Spain; Amsterdam and Rotterdam, The Netherlands; Lodz, Poland; Liege, Belgium; Cleveland, Ohio; Houston, Texas; London, United Kingdom; Rochester, Minnesota; Charleston, South Carolina; New Haven, Connecticut; Morrisville, North Carolina* 



(J Am Soc Echocardiogr 2012;25:3-46.)

Currently, <u>3D TTE</u> and TEE assessment of LV volumes and EF <u>is recommended over the use of</u> <u>2D echo</u>, as it has been clearly demonstrated to provide more accurate and reproducible measurements

FOCUS TOPIC: RIGHT VENTRICULAR VOLUME AND FUNCTION

Reference Values for Right Ventricular Volumes and Ejection Fraction With Real-Time Three-Dimensional Echocardiography: Evaluation in a Large Series of Normal Subjects

Gloria Tamborini, MD, Nina Ajmone Marsan, MD, Paola Gripari, MD, Francesco Maffessanti, MS, Denise Brusoni, MD, Manuela Muratori, MD, Enrico G. Caiani, PhD, Cesare Fiorentini, MD, and Mauro Pepi, *Milan, Italy* 

**JASE 2010** 



#### Age-, Body Size-, and Sex-Specific Reference Values for Right Ventricular Volumes and Ejection Fraction by Three-Dimensional Echocardiography

#### A Multicenter Echocardiographic Study in 507 Healthy Volunteers

Francesco Maffessanti, PhD\*; Denisa Muraru, MD\*; Roberta Esposito, MD; Paola Gripari, MD; Davide Ermacora, MD; Ciro Santoro, MD; Gloria Tamborini, MD; Maurizio Galderisi, MD; Mauro Pepi, MD; Luigi P. Badano, MD



Circulation CV Imaging 2013



	RV EDV, mL		RV ESV, mL		RV SV, mL		RV EF, %	
Normative equations (ASBa)	β (95% Cl)	<i>R</i> <sup>2</sup>	β (95% Cl)	<b>R</b> <sup>2</sup>	β (95% Cl)	<i>R</i> <sup>2</sup>	β (95% Cl)	R
Women	120.4·Age-0.24·BSA1.02		66.2·Age <sup>-0.39</sup> ·BSA <sup>1.23</sup>		55.2·Age <sup>-0.14</sup> ·BSA <sup>0.94</sup>		45.9·Age <sup>0.10</sup>	
Men	134.9·Age <sup>-0.24</sup> ·BSA <sup>1.02</sup>		79.3·Age <sup>-0.39</sup> ·BSA <sup>1.23</sup>		59.0-Age <sup>-0.14</sup> -BSA <sup>0.94</sup>		43.8·Age <sup>0.10</sup>	
) echo	Women 20 10 10 10 10 10 10 10 10 10 1	5 5 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Men of the the the the the the the the the the		Women (u) (u) (u) (u) (u) (u) (u) (u) (u) (u)	(iii)/M <sup>2</sup> ) Age (ye	Men 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
/IRI			Women Women Age (yezrs) <sup>4</sup> <sup>2</sup>		Men 5 5 5 5 5 5 5 5 5 5 5 5 5			
Normative equa	tions for RV para	ameter	s (N=441)*		Kawut et	al. Cir	culation 20 <sup>2</sup>	11
	ppRV mass army		nnRVEDV				RVEF	

RVEDV (mL)/(31.50· Age-0.258Ht1.582Wt0.382)

Women

Men

RV mass (g)/(10.59-Age<sup>-0.320</sup>Ht<sup>1.135</sup>Wt<sup>0.315</sup>)

RV mass (g)/(11.25·

Age<sup>-0.320</sup>Ht<sup>1.135</sup>Wt<sup>0.315</sup>)

RVEDV (mL)/(27.94 · Age-0.258Ht1.582Wt0.382) RVEF (%)/(75.19 · Age0.0706Ht-0.00771Wt-0.0782)

Normative equations for RV parameters (N=507) Maffessanti, Muraru et al. Circ Imag. 2013

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RVEF (%)/ (71.52· Age<sup>0.0706</sup>Ht<sup>-0.00771</sup>Wt<sup>-0.0782</sup>)







Ottima correlazione ECO 3D vs CMR (specie EF) con lieve sottostima VOLUMI VS e VOLUMI VD



Low reproducibility

LV diastolic volume Underestimation

- 33 ml
- Contrast Agent
  - **-18** ml

Higher reproducibility Than 2D and lower underestimation of LV volumes Vs CMR



**Gold standard** 

Low interobserver and intra-observer variability

#### MAINLY INTRAOPERATIVE/Monitoring interventional procedures



#### MAINLY ROUTINE TRANSTHORACIC



3,000 elements and breakthrough PureWave xMATRIX technology, the X5-1 supports virtually any cardiac ultrasound exam, including 3D, 2D, color flow, Mmode, PW/CW Doppler, Tissue Doppler imaging, and contrast-enhanced exams.

Sonde Switch 2D/3D

#### FLOW-CHART PROTOCOLLO TEE o TTE



# Fully Automated Cardiac Chamber Quantification



#### **ARTICLE IN PRESS**

JACC: CARDIOVASCULAR IMAGING © 2016 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION PUBLISHED BY ELSEVIER VOL. ■, NO. ■, 2016 ISSN 1936-878X/\$36.00 http://dx.doi.org/10.1016/j.jcmg.2015.12.020

#### Transthoracic 3D Echocardiographic Left Heart Chamber Quantification Using an Automated Adaptive Analytics Algorithm

Wendy Tsang, MD, MS,<sup>a,b</sup> Ivan S. Salgo, MD, MS,<sup>c</sup> Diego Medvedofsky, MD,<sup>b</sup> Masaaki Takeuchi, MD, PhD,<sup>b</sup> David Prater, BS,<sup>c</sup> Lynn Weinert, BSc,<sup>b</sup> Megan Yamat, RDCS,<sup>b</sup> Victor Mor-Avi, PhD,<sup>b</sup> Amit R. Patel, MD,<sup>b</sup> Roberto M. Lang, MD<sup>b</sup>

PROTOCOL 1: 3DE MANUAL REFERENCE STANDARD. 104 consecutive patients

## PROTOCOL 2: CMR REFERENCE STANDARD.

# The concept of Machine-learning

- The prototype 3DE software involves an automated analysis that simultaneously detects LV and LA endocardial surfaces by using an adaptive analytics algorithm.
- The program identifies LV end-diastole using the electrocardiogram and determines global cardiac shape orientation.
- Preliminary end-systolic and end-diastolic LV and LA models are then built by using automatic endocardial surface detection in conjunction with information from a 3DE database, which consists of LA and LV end-diastolic and endsystolic shapes from approximately 1,000 3D TTE datasets of varying image quality in patients with a wide range of function and morphologies





The program matches features from the LV volume being analyzed to selected shapes in the database. This selected model is then locally adapted to the patient's LV volume by using a series of adaptations



TABLE 2	3DE Model	Comparison	Versus	Manual	3D	Measurements
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	Averaged Automated 3DE Program	Averaged Manual 3DE Reference Standard	Correlation	Bias	LOA (2 SDs)
LVEF, %					
No contour adjustment	$40 \pm 16$	$46\pm16^{\ast}$	0.87	-6	16
With contour adjustment	$42\pm16$	$46\pm16^{\ast}$	0.92	-4	12
LVEDV, ml					
No contour adjustment	$163\pm73$	$\textbf{161} \pm \textbf{71}$	0.96	2	40
With contour adjustment	$173\pm75$	$161\pm71^{*}$	0.97	12	36
LVESV, ml					
No contour adjustment	$105\pm67$	$95 \pm 66^*$	0.95	10	40
With contour adjustment	$108\pm70$	$95\pm66^{*}$	0.96	13	36
LAV at LVES, ml					
No contour adjustment	$85\pm34$	$76 \pm 31^*$	0.95	10	20
With contour adjustment	$93\pm37$	$76 \pm 31^*$	0.96	17	24

Ottima correlazione 3D automatico vs 3D manuale

The average 3DE volume rate was 16+ 6 Hz (median 15; interquartile range: 11 to 21). Twelve (8%) datasets had a volume rate <10 Hz.



3D transthoracic echocardiography (TTE) LA and LV analysis time using the manual method and the automated method with and without contour adjustment. Abbreviations as in Figures 1 and 2.

# Robust 3D quantification of cardiac chambers for everyday clinical practice.

### « Static» Heart Model

New automated software to obtain LV volumes from real time 3DE acquisitions using a model based adaptive analytic algorithm.



JACC: CARDIOVASCULAR IMAGING © 2016 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION PUBLISHED BY ELSEVIER VOL. ■, NO. ■, 2016 ISSN 1936-878X/\$36.00 http://dx.doi.org/10.1016/i.icmg.2015.12.020

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European Heart Journal - Cardiovascular Imaging (2017) **0**, 1–12 doi:10.1093/ehjci/jew328

Three-dimensional echocardiographic quantification of the left-heart chambers using an automated adaptive analytics algorithm: multicentre validation study

Diego Medvedofsky<sup>1</sup>, Victor Mor-Avi<sup>1</sup>\*, Mihaela Amzulescu<sup>2</sup>, Covadonga Fernández-Golfín<sup>3</sup>, Rocio Hinojar<sup>3</sup>, Mark J. Monaghan<sup>4</sup>, Kyoko Otani<sup>5</sup>, Joseph Reiken<sup>4</sup>, Masaaki Takeuchi<sup>5</sup>, Wendy Tsang<sup>6</sup>, Jean-Louis Vanoverschelde<sup>2</sup>, Mathivathana Indraiith<sup>4</sup>, Lynn Weinert<sup>1</sup>, Jose Luis Zamorano<sup>3</sup>, and

Feasibility and Accuracy of Automated Software for Transthoracic Three-Dimensional Left Ventricular Volume and Function Analysis: Comparisons with Two-Dimensional Echocardiography, Three-Dimensional Transthoracic Manual Method, and Cardiac Magnetic Resonance Imaging

Gloria Tamborini, MD, Concetta Piazzese, PhD, Roberto M. Lang, MD, Manuela Muratori, MD, Elisa Chiorino, MD, Massimo Mapelli, MD, Laura Fusini, MD, Sarah Ghulam Ali, MD, Paola Gripari, MD, Gianluca Pontone, MD, Daniele Andreini, MD, and Mauro Pepi, MD, *Milan, Italy; and Chicago, Illinois* 

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Feasibility and Accuracy of Automated Software for Transthoracic Three-Dimensional Left Ventricular Volume and Function Analysis: Comparisons with Two-Dimensional Echocardiography, Three-Dimensional Transthoracic Manual Method, and Cardiac Magnetic Resonance Imaging

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Optimization of the user-adjustable slider position improved the correlation and markedly reduced the bias between the MBA and 3DFV or CMR.

The MBA is highly feasible, reproducible, and rapid, and it correlates highly with the traditional 3DFV method.



The study included 194 patients. LV volumes and ejection fraction were obtained with automatic HM and compared to 2DE biplane method (2DBP), 3DE tracings modality (3DFV) and cardiac magnetic <u>resonan</u>ce (**CMR**) measurements (90 pts).



## Versus





### HM acquisition and reconstruction time .

# processing time of 29±10 sec.





#### HeartModel

#### Manual global Editing:

# 3-fold cross validation Vs ECHO o RMN ?

• A slider may be freely moved from the default position to arbitrarily optimize LV border identification and different slider positions can be preset to user's preference.







	Find t	he Ball	0
		Reset Level	
Unlock Trick	:	ON	
Smile Quotes	:	ON	
More Fast and F	urious :	ON	



С a S U a

à



Scienza



#### Bland Altman analysis of **conventional 3D full volume (3DFV)** measurements vs HM (top panels) and HM measurement optimized (HM opt)



(by changing the slider position from default location (50) to the theoretical ideal level identified with three-fold cross-validation test in order to improve the correlation between HM and 3DFV measurements: <u>39 for end diastolic</u> <u>frame and 22 for end systolic frame (bottom panels).</u>

# Bland Altman analysis of HM (top panels) and HM measurement optimized (HM opt) vs CMRI



(by changing the slider position from default location (50) to the theoretical ideal level identified with **three-fold cross-validation test** in order to improve the correlation between HM and 3DFV measurements: 75 **for end diastolic frame and 57 for end systolic frame (bottom panels)**.

## One reason for this consistent underestimation is the poor differentiation $\longrightarrow$ between the compacted myocardium and trabeculae on TTE,

especially during systole, that results in less precise endocardial border identification compared with CMR



The new automated method may better compared to «traditional» 3D TTE volumes or CMR values depending on inclusion or exclusion of trabeculae (sliders and setting of border detection)

# From static to « Dynamic» Heart Model»

2018



EUROPEAN Heart Journal - Cardiovascular Imaging (2018) 0, 1–9 European Society doi:10.1093/ehjci/jey137 of Cardiology

# Machine learning based automated dynamic quantification of left heart chamber volumes

Akhil Narang<sup>1</sup>, Victor Mor-Avi<sup>1</sup>\*, Aldo Prado<sup>2</sup>, Valentina Volpato<sup>1,3</sup>, David Prater<sup>4</sup>, Gloria Tamborini<sup>3</sup>, Laura Fusini<sup>3</sup>, Mauro Pepi<sup>3</sup>, Neha Goyal<sup>1</sup>, Karima Addetia<sup>1</sup>, Alexandra Gonçalves<sup>4</sup>, Amit R. Patel<sup>1</sup>, and Roberto M. Lang<sup>1</sup>

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Received 27 July 2018; editorial decision 2 September 2018; accepted 13 September 2018

# The automated ML algorithm can quickly measure **dynamic LV and LA volumes** and accurately analyse ejection/filling parameters. Incorporation of this algorithm into the clinical workflow may increase the utilization of 3DE imaging.

# **Clinical implications**

- Field of interest (potentially all cardiovascular pathologies)
- Rapid assessment of LV and LA volumes
- and function
- Cardiomyopathies
- LV dysfunction
- Valve diseases





#### ONE Tranthoracic PROBE: Comprehensive 2D 3D morphologic and functional assessment of MV anatomy and LV and LA function

3D : not only MV morphology, but also LV and LA volumes and function



## Case report : MV prolapse Comprehensive 2D 3D morphologic and functional assessment of MV anatomy and LV and LA function





Easy 3D morphologic reconstruction of the MV from the LA: Surgical view





P2 flail with partial eversion towards P1 3D Transthoracic photorealistic rendering with virtual light source



# From the 4 chamber view we launch Dynamic Heart Model Acquisition



Dynamic HM acquisition and reconstruction time .

#### **Processing time of 35 sec. (after 4 chamber acquisition)**

LV volumes and curves; LA volume and curves LV mass









178 ml

64 ml

m

60

30



# LA volumes and

#### curve

Maximum and minimum volumes (Vmax, Vmin) and filing fraction, volume at 50% FT, volumes at 25%, 50%, and 75% emptying time, volume at diastasis, passive emptying volume (PEV), and active emptying volume (AEV)



LV VOLUMES AND CURVE : (EDV, ESV) and (EF), volume at 50% ejection time (ET), volumes at 25%, 50%, and 75% filling time (FT), volume at diastasis, rapid filling volume (RFV), and atrial filling volume (AFV)





Feasibility And Accuracy Of Automated Software For Transthoracic 3D Left Ventricular And Atrial Volumes And Function Analysis In Degenerative MV Regurgitation



Automatic volumes were feasible in **111 patients** (93%), with a mean processing time of 29 + **10 sec**.



Good correlations between MBA LV volumes and 3D standard echo or CMR further improved by optimization of sliders.

# Excellent correlation between MBA and CMR/3D standard ECHO for Left atrial volumes













#### Table 4 Normal ranges and severity partition cutoff values for 2DE-derived LV EF and LA volume

	Male				Female			
	Normal	Mildly	Moderately	Severely	Normal	Mildly	Moderately	Severely
	range	abnormal	abnormal	abnormal	range	abnormal	abnormal	abnormal
LV EF (%)	52–72	41–51	30–40	<30	54–74	41–53	30–40	<30
Maximum LA volume/BSA (mL/m²)	16–34	35–41	42–48	>48	16–34	35–41	42–48	>48

It has been demonstrated that LA volumes have a very important role in diagnosis and prognosis of several

pathologies.

## We have to move from 2D to 3D assessment

Left atrial reverse remodeling and functional improvement after mitral valve repair in degenerative mitral regurgitation: a realtime three-dimensional echocardiography study.

Nina Ajmone Marsan<sup>1</sup>, Francesco Maffessanti<sup>2</sup>, Gloria Tamborini<sup>1</sup>, Paola Gripari<sup>1</sup>, Enrico Caiani<sup>2</sup>, Laura Fusini<sup>2</sup>, Manuela Muratori<sup>1</sup>, Marco Zanobini<sup>1</sup>, Francesco Alamanni<sup>1</sup>, Mauro Pepi<sup>1</sup>. 3D Transthoracic ECHO ideal method for pre-operative an follow-up of LEFT ATRIAL VOLUME



Marsan Am Heart 2011

# **3D LA Al-based Analysis: Auto-strain**



**Normal Subject** 

Differences in LA curves (reservoir and atrial contraction)

# In pts with MV prolapse an severe MR

### Model of volume overload

MBA-derived LV volumes and EF correlated significantly with all evaluated methods, with slight overestimation of two-dimensional biplane and slight underestimation of CMR volumes measurements.

Optimization of slider position improved the correlations and markedly reduced the bias between the MBA and 3DFV or CMR.

# The accuracy of LA volumes by MBA was optimal.

Feasibility and accuracy of the new automated software Dynamic Heart Model in an unselected population.

L. Manfredonia, L. Fusini, V. Mantegazza, V. Volpato, M. Muratori, G. Tamborini, M. Pepi (Abstract accepted EuroeCHO 2019)

91 consecutive unselected patients (80% in sinus rhythm, 20% in atrial fibrillation)

DHM was feasible in 79/91 cases (87%).

Physiological curves of LA and LV were plausible

## New data on Dynamic Heart Model

# 403 unselected pts

Patients	Age	Acquisition	Feasibility	High Quality
121	73 + 14	30 + 30	85%	68%



## 3D LV AI-based Analysis: Dynamic Heart Model Aortic Stenosis



**3D LV AI-based Analysis: Auto-strain** 



**Revision and Editing** 

# Apical aneurysm



# Aortic stenosis and Amylodosis



# **Miocarditis**

140





Battito attuale

DOI: 10.1111/echo.14234

#### ORIGINAL INVESTIGATION

WILEY Echocardiography

#### Automated, machine learning-based, 3D echocardiographic quantification of left ventricular mass





FIGURE 4 Bland-Altman analysis (left) and linear correlation analysis (right) comparing the automated algorithm (HeartModel, HM, Philips Healthcare) (top) and conventional 3DE volumetric analysis (bottom) with cardiac magnetic resonance (CMR) reference for left ventricular mass quantification 3D Echocardiography analysis of LV mass using novel ML-based algorithm is feasible, fast, and accurate and may thus facilitate the incorporation of 3DE measurements of LV mass into clinical practice.

# HOCM LV mass 217 gr



# Improvement Spatial Resolution with the new probes and Dynamic HM



















# A bioengeneering dream....







#### Courtesy of Francesco Maffessanti; 2008

# **2017: Che cosa ci riserva il futuro ?**

# Fully Automated Cardiac Chamber Quantification ??



Courtesy prof. Lang 2017

# 2019 !!!: <u>Case report . 25 Minutes</u> Young Athlete : LVEF 60%; RVEF 55%; GS: -23; Normal LA (plus all standard measurements)









There is nothing like a dream to create the future. Victor Hugo

