

4D Analysis of Ventricular Function: Is It Ready for Clinical Practice ?

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- No Disclosure

3DE Assessment of LV Volume and Fx

Why LV volume and fx matter?

Accurate assessment is crucial in management of patients with CVD

- decision of optimal time for
CRT & ICD in systolic HF, valve replacement in VHD
- prediction of prognosis in
systolic HF, ischemic HD
- follow-up after
CRT and stem cell therapy

2DE method for LV volume & fx

biplane Simpson's method

Two major sources of error

- **Unguided image position:**

operator dependent variability of image acquisition

apical foreshortening

> low reproducibility

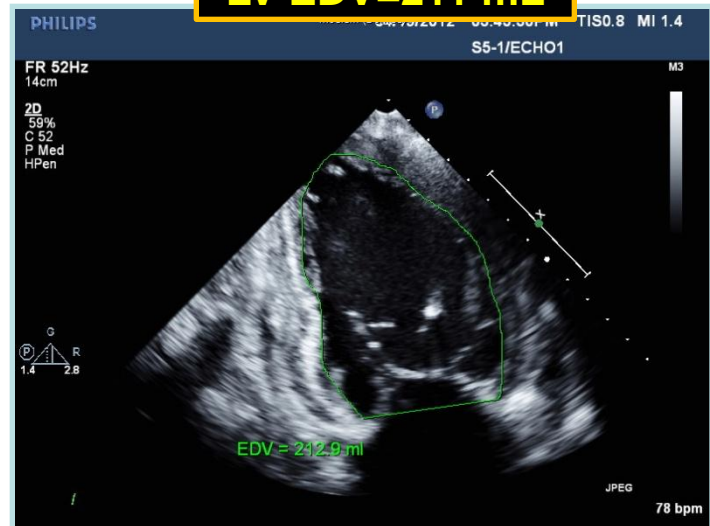
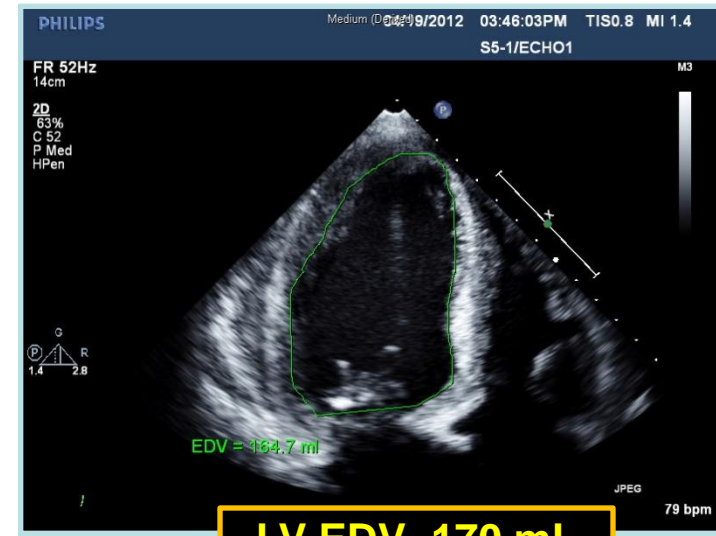
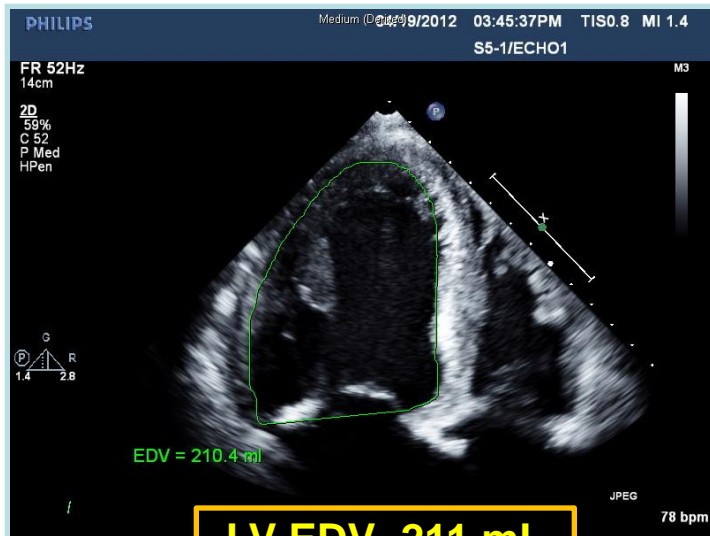


foreshortened apex

- **Geometric assumption**

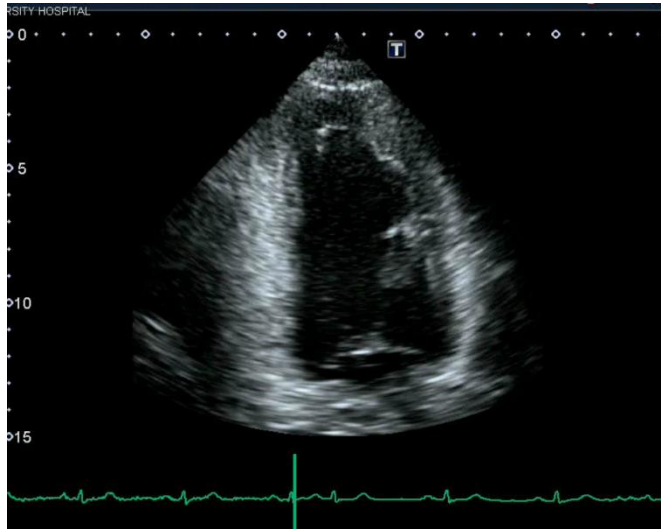
> inaccurate particularly in asymmetrical LV

Low reproducibility due to operator dependent variability

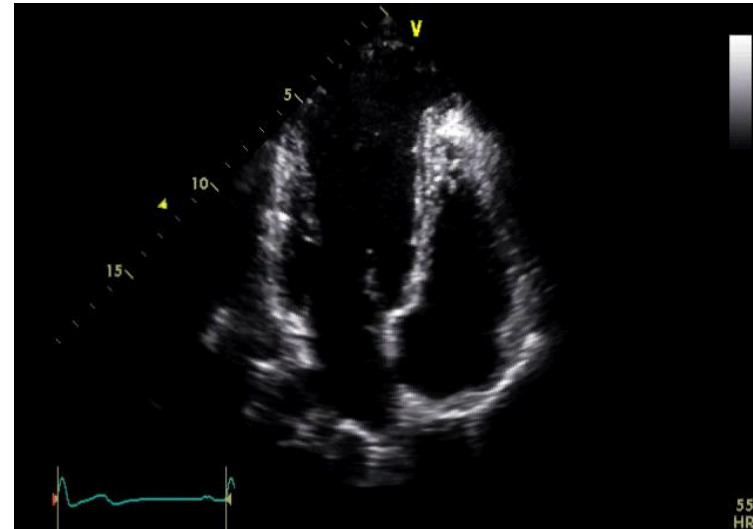


Inaccuracy due to geometric assumption

- Particularly in case with asymmetrical LV



RWMA



Aneurysm

Exaggerated underestimation of LV volume in patients with asymmetrical LV

Variable	Multiplane RT3DE			Multiplane RT3DE		
	2DE	6 planes	8 planes	2DE	6 planes	8 planes
EDV						
Mean (mL)	91.5 ± 20.9	124.8 ± 26.1	129.1 ± 26.7	155.8 ± 55.4	203.6 ± 64.6	206.7 ± 67.5
r	0.50	0.98	0.99	0.79	0.96	0.97
SEE (mL)	14.7	3.7	3.5	20.3	11.3	10.5
P	.002	<.0001	<.0001	<.0001	<.0001	<.0001
RMS percentage error	36	6	4	33	10	9
Bias (mL)	-38.8	-5.6	-1.2	-57.7	-9.9	-6.8
Width of limits of agreement	-89.4 to 11.7	-16.5 to 5.3	-10.9 to 8.5	-138.7 to 23.3	48.6 to 28.6	-41.6 to 28.0
ESV						
Mean (mL)	30.0 ± 9.7	48.7 ± 13.8	51.1 ± 11.9	96.4 ± 51.2	131.6 ± 62.7	134.2 ± 65.7
r	0.53	0.89	0.95	0.86	0.97	0.97
SEE (mL)	5.1	4.0	2.4	10.3	6.2	6.1
P	.001	<.0001	<.0001	<.0001	<.0001	<.0001
RMS percentage error	52	16	12	41	15	13
Bias (mL)	-24.6	-4.9	-3.5	-45.5	-10.2	-7.6
Width of limits of agreement	-50.7 to 1.5	-18.9 to 9.1	-14.8 to 7.8	-117.9 to 27.0	-46.0 to 25.5	-40.3 to 24.9
EF						
Mean (mL)	67.5 ± 6.6	60.4 ± 6.3	60.5 ± 5.2	42.0 ± 17.4	38.5 ± 14.2	38.5 ± 14.3
r	0.23	0.60	0.79	0.86	0.89	0.90
SEE (mL)	10.4	8.1	5.2	4.0	2.9	2.8
P	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001
RMS percentage error	21	10	8	27	20	19
Bias (mL)	9.1	2.0	2.1	4.6	1.1	1.1
Width of limits of agreement	-6.6 to 24.8	-9.1 to 13.1	-5.5 to 9.7	-13.3 to 22.5	-13.5 to 15.7	-12.8 to 14.9

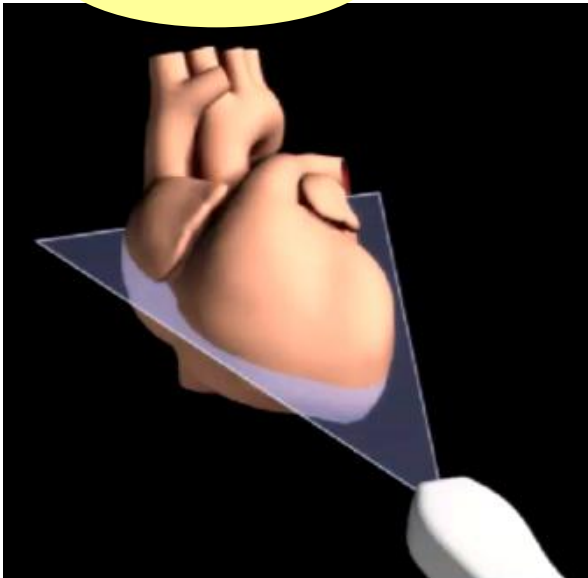
Normal

MI

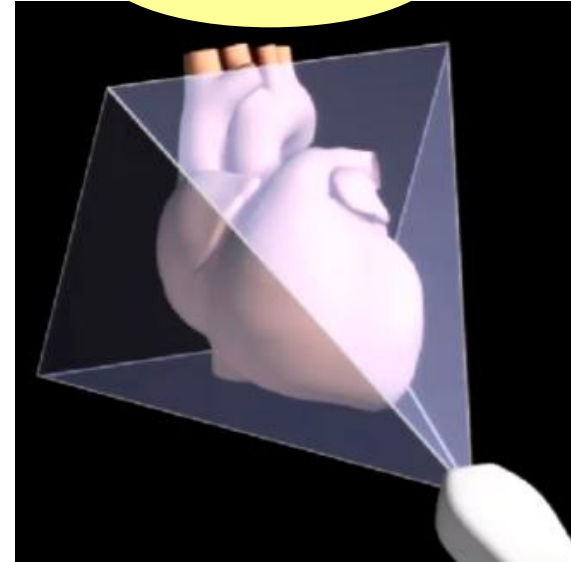
2D Echo vs. 3D Echo

- Acquisition of volumetric dataset of Whole LV
 - ✓ avoid errors or variation by operator
 - ✓ no need for geometric assumption

2D echo

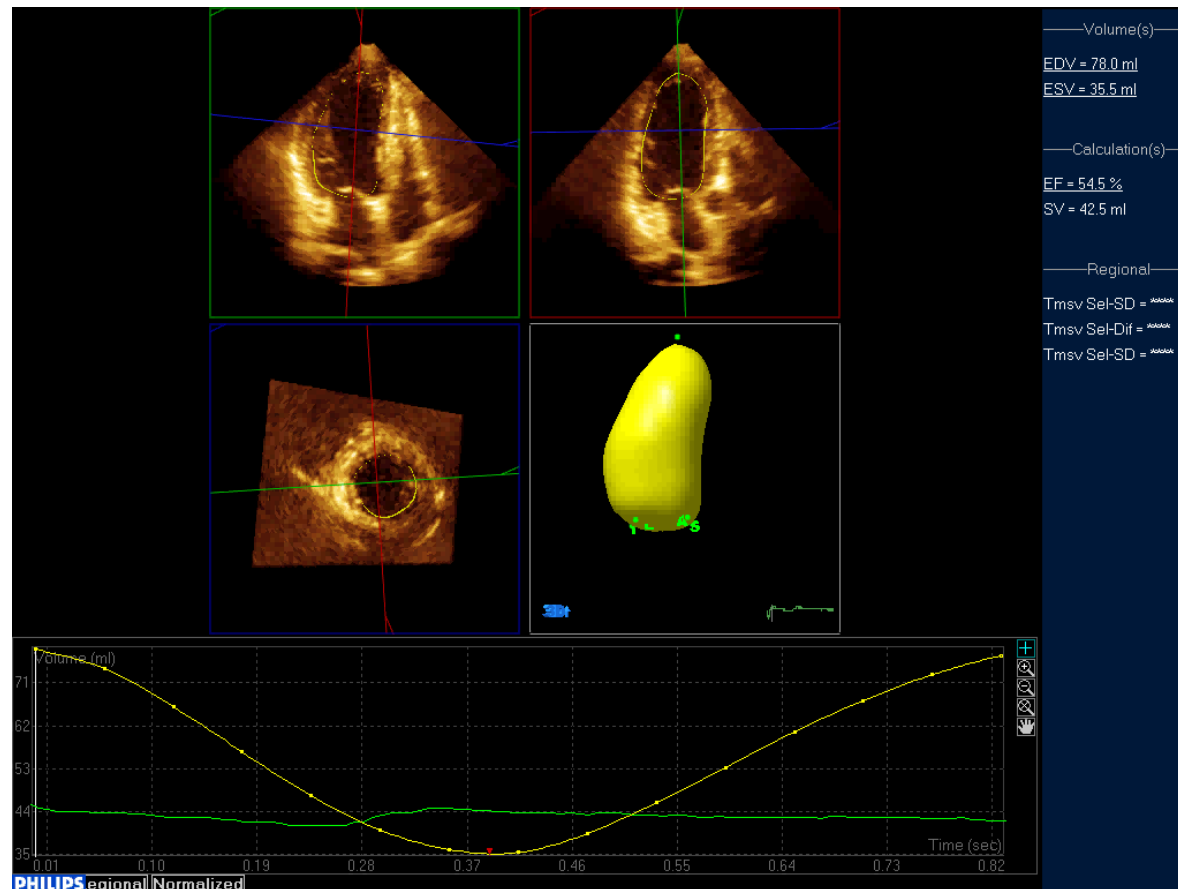


3D echo



3DE: LV volume by semi-automated border tracing of whole LV endocardium

- 5 points algorithm



3DE: LV volume by semi-automated border tracing of whole LV endocardium

- 2 points algorithm

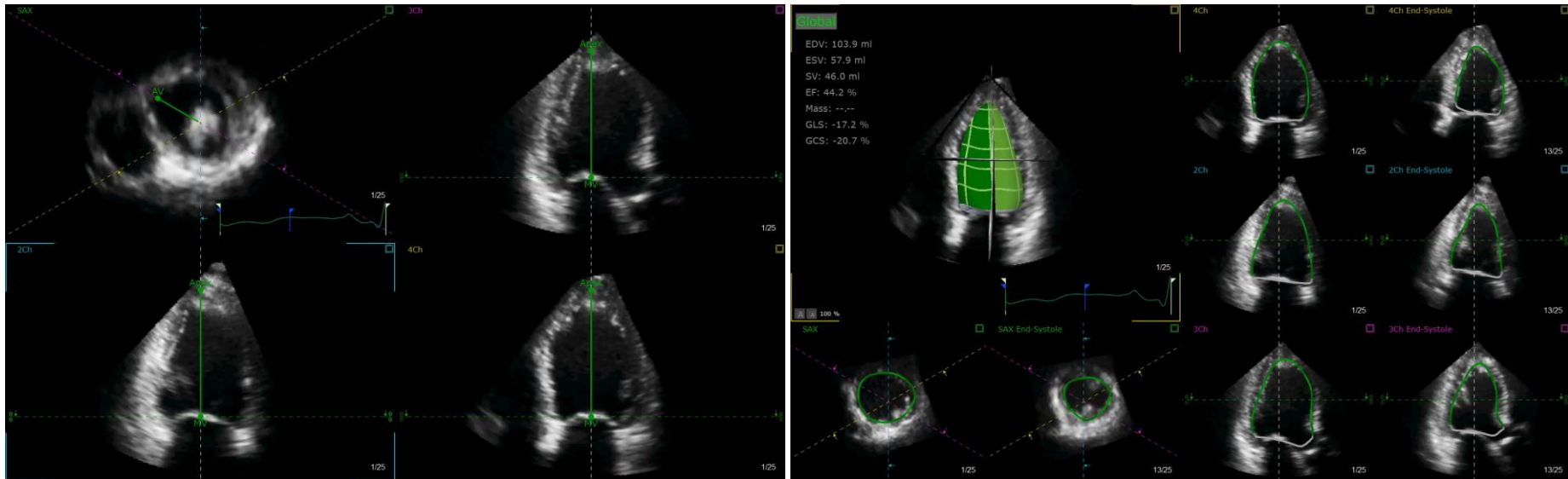


GE., 4D Auto LVQ

3DE: LV volume by semi-automated border tracing of whole LV endocardium

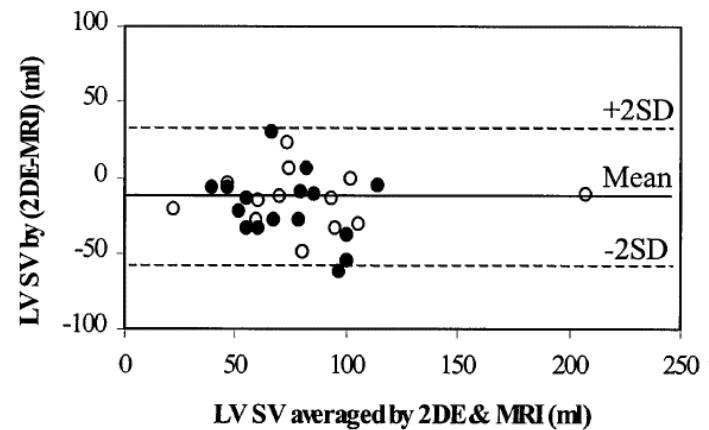
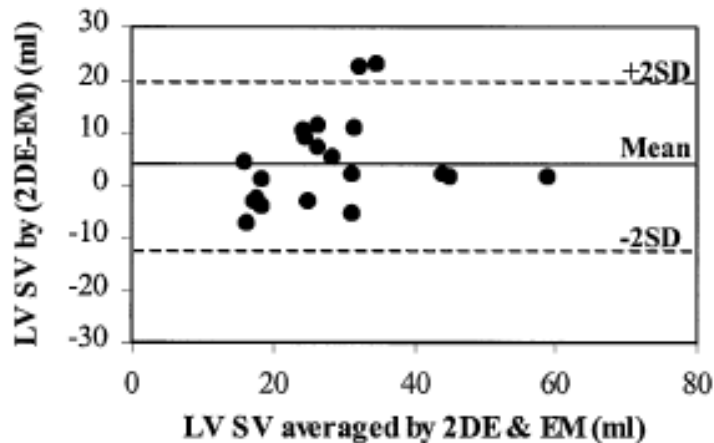
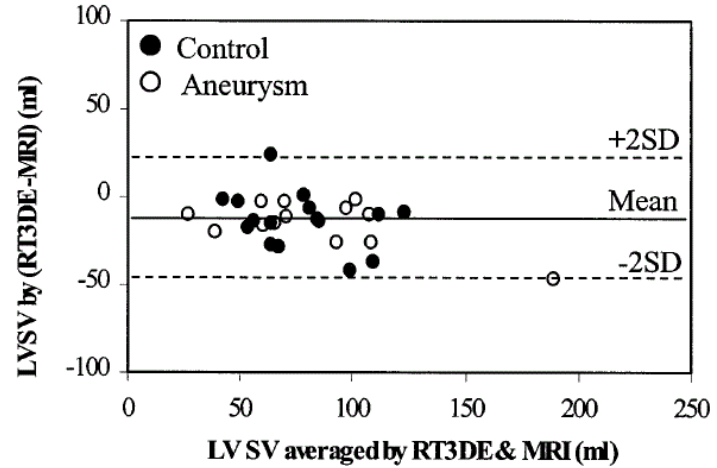
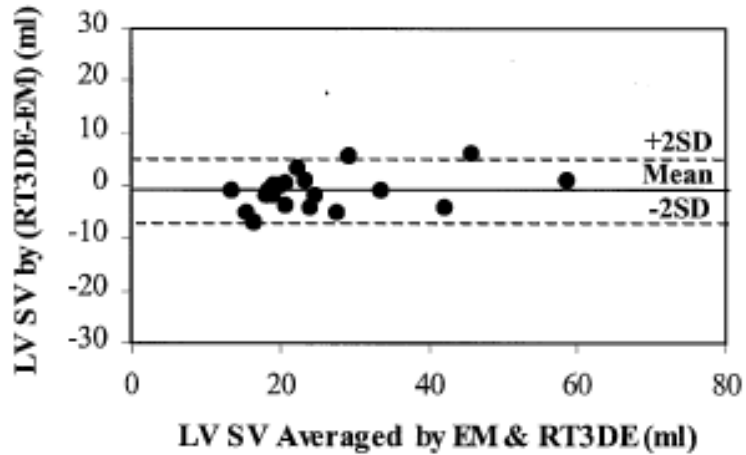
LV volume close to actual volume even in pt with MI

- 2 points algorithm



TomTec, 4D LV analysis

Accuracy of 3DE vs. 2DE for LV volume in LV aneurysm



Lower Variability of 3DE vs. 2DE

Inter-observer agreement 3DE vs. 2DE

	RT-3DE		2DE		Difference in Interobserver Agreement for RT-3DE and 2DE	
End-diastolic volume (ml)	$r = 0.95^*$	-3 ± 10	$r = 0.76^*$	13 ± 17	$Z = 6.4$	$p < 0.01$
End-systolic volume (ml)	$r = 0.97^*$	-2 ± 6	$r = 0.79^*$	-9 ± 13	$Z = 7.8$	$p < 0.01$
Ejection fraction (%)	$r = 0.88^*$	0 ± 3	$r = 0.61^\dagger$	2 ± 8	$Z = 5.1$	$p < 0.01$
LV mass (g)	$r = 0.96^*$	-1 ± 11	$r = 0.75^*$	-5 ± 23	$Z = 7.4$	$p < 0.01$

* $p < 0.01$; $^\dagger p < 0.03$.

Intra-observer agreement 3DE vs. 2DE

	RT-3DE		2DE		Difference in Intraobserver Agreement for RT-3DE and 2DE	
End-diastolic volume (ml)	$r = 0.98^*$	-1 ± 6	$r = 0.90^*$	-5 ± 9	$Z = 6.3$	$p < 0.01$
End-systolic volume (ml)	$r = 0.98^*$	-2 ± 6	$r = 0.86^*$	0 ± 10	$Z = 7.7$	$p < 0.01$
Ejection fraction (%)	$r = 0.97^*$	1 ± 2	$r = 0.61^\dagger$	-2 ± 6	$Z = 10.5$	$p < 0.01$
LV mass (g)	$r = 0.96^*$	-5 ± 8	$r = 0.84^*$	-12 ± 24	$Z = 5.5$	$p < 0.01$

* $p < 0.01$; $^\dagger p < 0.03$.

Lower Test-retest Variability of 3DE vs. 2DE

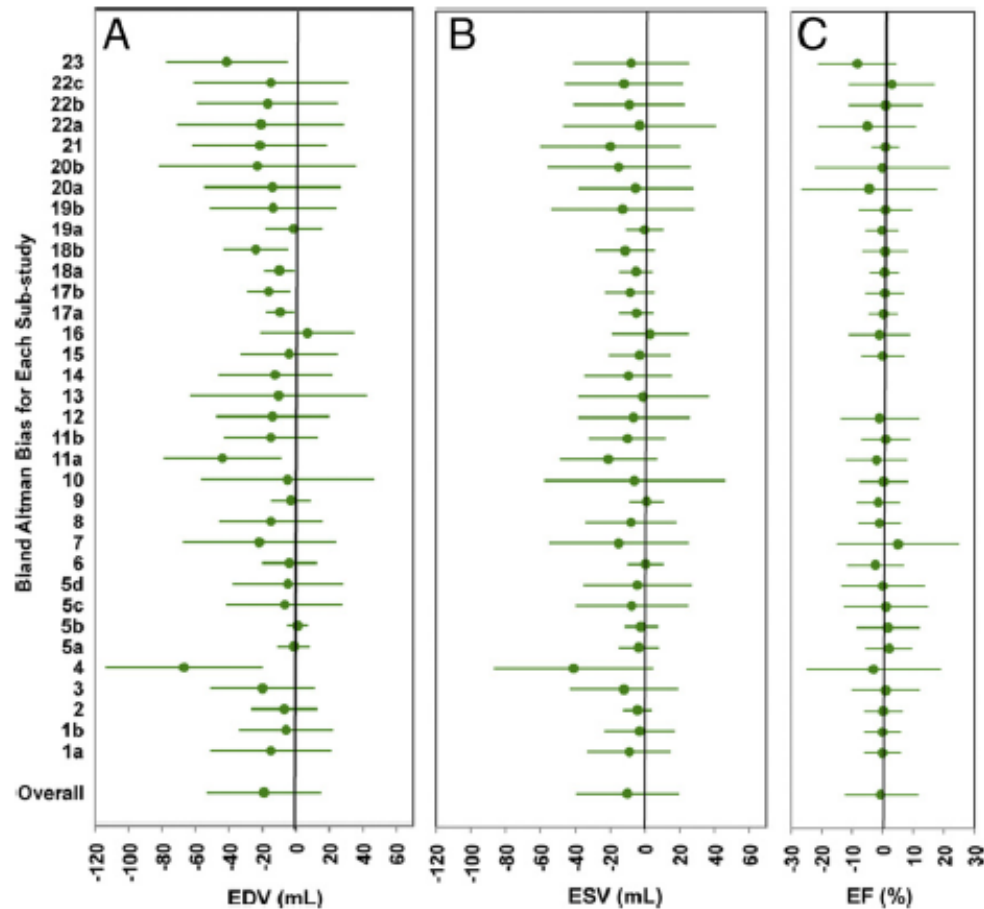
Test-retest variability with 2DE and 3DE (n: 20)

	RT3DE		2DE		p Value (RT3D vs 2DE)
	Mean Difference	Correlation	Mean Difference	Correlation	
End-diastolic volume (ml)	-12 ± 68	r = 0.33, p = 0.15	-34 ± 54	r = 0.13, p = 0.58	Z = 0.87, p = 0.39
End-systolic volume (ml)	1 ± 20	r = 0.62, p <0.01	-11 ± 36	r = -0.23, p = 0.34	Z = 2.02, p = 0.06
Ejection fraction (%)	-4 ± 7	r = 0.63, p <0.01	5 ± 21	r = 0.07, p = 0.78	Z = 2.77, p = 0.01
LV mass (g)	12 ± 38	r = 0.57, p <0.01	57 ± 94	r = -0.006, p = 0.79	Z = 2.41, p = 0.03

- Lower test-retest variability in serial estimation of LV volume in pts with MI
- 3DE is more reliable in f/u assessment of LV volume than 2DE

Performance of 3-Dimensional Echocardiography in Measuring Left Ventricular Volumes and Ejection Fraction

A Systematic Review and Meta-Analysis

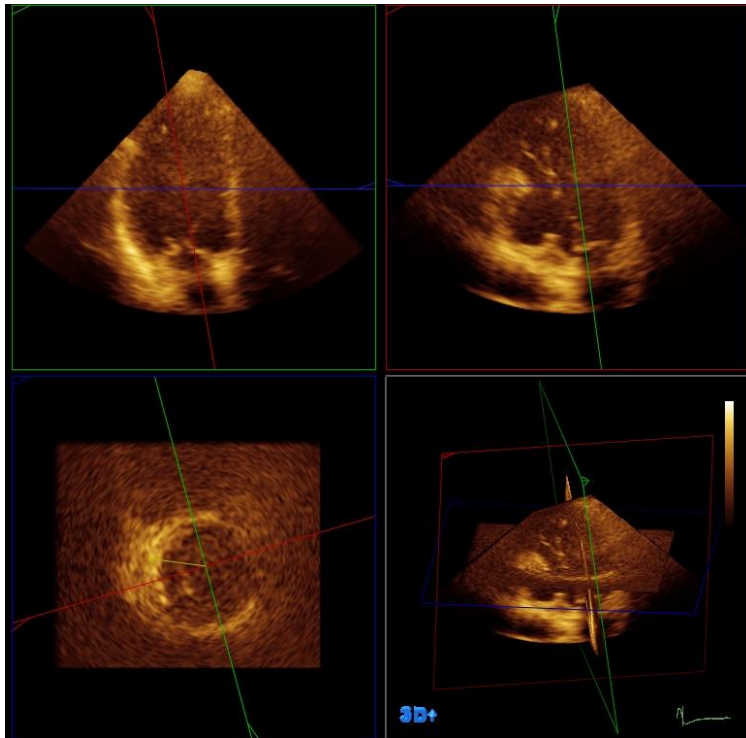


Underestimation of LV volume of 3DE

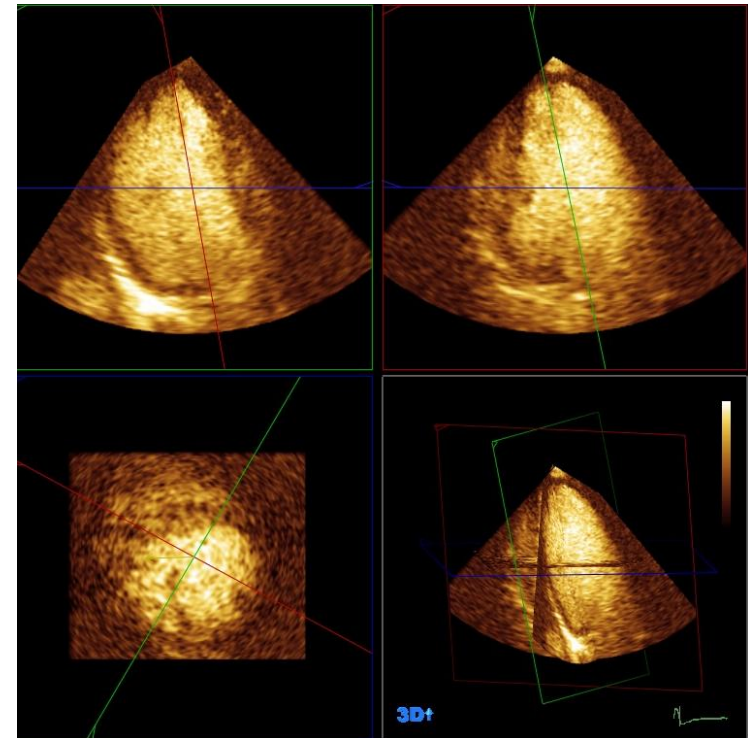


Contrast 3DE

N-3DE



CE-3DE



More clear visualization of endocardium with excluding trabeculae

Diagnostic Value of Three-Dimensional Contrast-Enhanced Echocardiography for Left Ventricular Volume and Ejection Fraction Measurement in Patients With Poor Acoustic Windows: A Comparison of Echocardiography and Magnetic Resonance Imaging

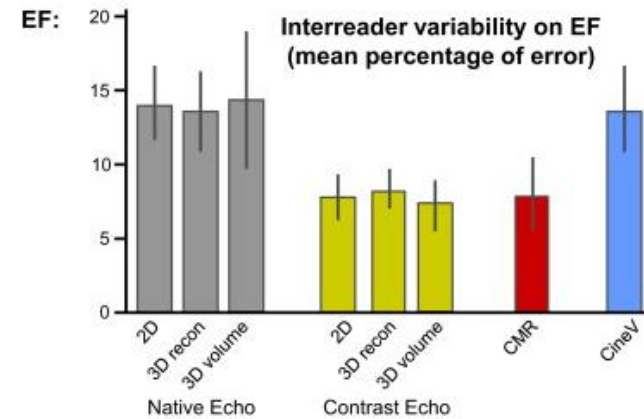
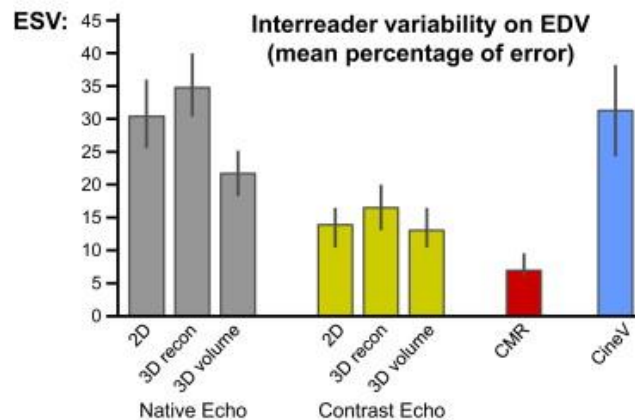
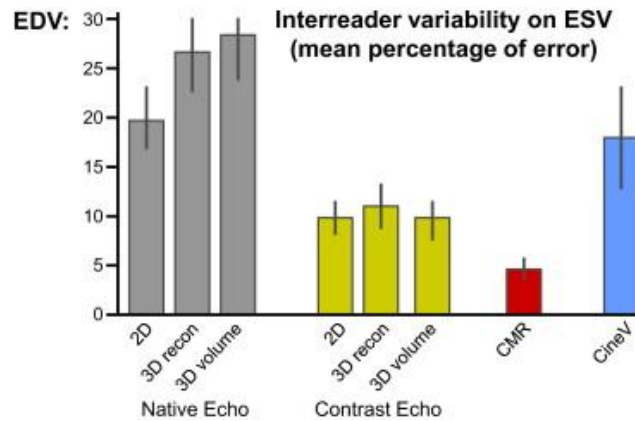
KSC 2015

Underestimation was dramatically reduced when using C3DE

Average volume difference from CMR

Factor	2DE	3DE	C3DE	MRI Volume (mL)
EDV bias (mL) (% of MRI EDV)				EDV
All patients	76 ± 40 (35 ± 19)	59.8 ± 89 (27 ± 22)	28 ± 62.6 (13 ± 15)	216 ± 85
EDV > 250 mL	119 ± 23 (37 ± 7)	109 ± 39 (34 ± 13)	43 ± 35 (14 ± 11)	315 ± 40
EDV < 150 mL	42 ± 17 (36 ± 15)	39 ± 20 (34 ± 18)	9 ± 14 (7 ± 12)	114 ± 23
Group A	92 ± 38 (37 ± 35)	68 ± 36 (28 ± 15)	37 ± 34 (15 ± 14)	243 ± 84
Group B	62 ± 40 (32 ± 29)	57 ± 50 (30 ± 26)	22 ± 30 (11 ± 16)	190 ± 82
HCM	51 ± 24 (37 ± 19)	42 ± 21 (30 ± 15)	17 ± 22 (12 ± 16)	138 ± 36
ICM	99 ± 39 (36 ± 15)	88 ± 58 (32 ± 22)	35 ± 38 (13 ± 14)	269 ± 76
DCM	85 ± 44 (35 ± 18)	60 ± 46 (23 ± 18)	35 ± 32 (14 ± 13)	253 ± 68
3DE	68 ± 38 (33 ± 19)	60 ± 45 (29 ± 22)	28 ± 29 (14 ± 14)	206 ± 86
No 3DE*	99 ± 40 (41 ± 17)	NA	29 ± 35 (12 ± 16)	242 ± 80
ESV bias (mL) (% of MRI ESV)				ESV
All patients	45 ± 45 (35 ± 35)	33 ± 37 (25 ± 29)	17.76 ± 23 (14 ± 18)	129 ± 94
EDV > 250 mL	92 ± 21 (39 ± 9)	78 ± 32 (33 ± 14)	33 ± 27 (14 ± 12)	234 ± 61
EDV < 150 mL	11 ± 6 (30 ± 16)	11 ± 5 (31 ± 14)	4 ± 5 (12 ± 14)	36 ± 21
Group A	66 ± 53 (41 ± 33)	43 ± 33 (26 ± 20)	26 ± 28 (16 ± 17)	162 ± 100
Group B	27 ± 28 (27 ± 29)	28 ± 40 (29 ± 42)	11 ± 16 (11 ± 17)	97 ± 84
HCM	12 ± 9 (38 ± 27)	12 ± 5 (35 ± 14)	5 ± 6 (15 ± 17)	33 ± 11
ICM	80 ± 50 (41 ± 26)	66 ± 43 (33 ± 22)	27 ± 29 (14 ± 15)	197 ± 82
DCM	52 ± 36 (30 ± 22)	32 ± 38 (19 ± 22)	24 ± 21 (14 ± 12)	171 ± 63
3DE	35 ± 33 (31 ± 28)	33 ± 37 (28 ± 32)	16 ± 20 (14 ± 18)	115 ± 92
No 3DE*	77 ± 63 (47 ± 39)	NA	22 ± 29 (14 ± 18)	162 ± 96

Reduced inter-observer variability with contrast enhancement




Normal values of 3DE derived LV volume and EF

No significant difference in 3DE derived LV volume and EF between studies

	Aune <i>et al.</i> (2010)	Fukuda <i>et al.</i> (2012)	Chahal <i>et al.</i> (2012)	Muraru <i>et al.</i> (2013)
Number of subjects	166	410	978	226
Ethnic makeup of population	Scandinavian	Japanese	51% European white, 49% Asian Indian	White European
EDVi (mL/m ²)				
Men, mean (LLN, ULN)	66 (46, 86)	50 (26, 74)	White: 49 (31, 67); Indian: 41 (23, 59)	63 (41, 85)
Women, mean (LLN, ULN)	58 (42, 74)	46 (28, 64)	White: 42 (26, 58); Indian: 39 (23, 55)	56 (40, 78)
ESVi (mL/m ²)				
Men, mean (LLN, ULN)	29 (17, 41)	19 (9, 29)	White: 19 (9, 29); Indian: 16 (6, 26)	24 (14, 34)
Women, mean (LLN, ULN)	23 (13, 33)	17 (9, 25)	White: 16 (8, 24); Indian: 15 (7, 23)	20 (12, 28)
EF (%)				
Men, mean (LLN, ULN)	57 (49, 65)	61 (53, 69)	White: 61 (49, 73); Indian: 62 (52, 72)	62 (54, 70)
Women, mean (LLN, ULN)	61 (49, 73)	63 (55, 71)	White: 62 (52, 72); Indian: 62 (52, 72)	65 (57, 73)

Recommendations for LV volume and function quantification in adults: An update from ASE and EACVI

JASE 2015

Technique	Advantages	Limitations
<p>3D data sets</p> 	<ul style="list-style-type: none"> • No geometrical assumption • Unaffected by foreshortening • More accurate and reproducible compared to other imaging modalities 	<ul style="list-style-type: none"> • Lower temporal resolution • Less published data on normal values • Image quality dependent

- **Recommendation:**

In laboratories with experience in 3DE, 3D LV volumes is recommended when feasible depending on image quality

- In patients with good image quality, 3DE-based EF is accurate and reproducible and should be used when available and feasible

3DE Assessment of RV Volume and Fx

Why RV matters?

- RV is not just a conduit of blood flow: It has its unique function
- Prognostic significance in various clinical settings
- Risk stratification or guide to optimal therapy

Why RV volume and fx matter?

- In a study of pulmonary HIBP, absolute RV volumes and fx by MRI were found to predict prognosis stronger than conventional echo parameters or pulmonary pr.

Moledina S, Circ Cardiovasc Imaging 2013

- Multi-center study demonstrated that RV fx and its changes over 1yr paralleled changes in functional class and survival

Peacock AJ. Circ Cardiovasc Imaging 2014

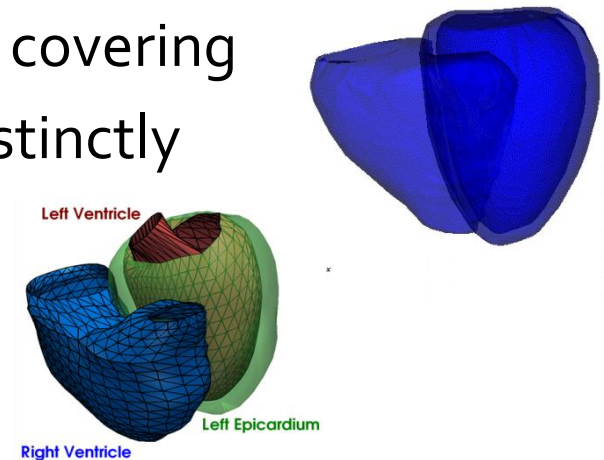
- The outcome of HF therapy with LV assist devices critically depends on RV function

Hayek S, Circ Cardiovasc Imaging 2014

No RV volume and EF is possible based on 2DE

- **Considerably difficult structure to visualize**

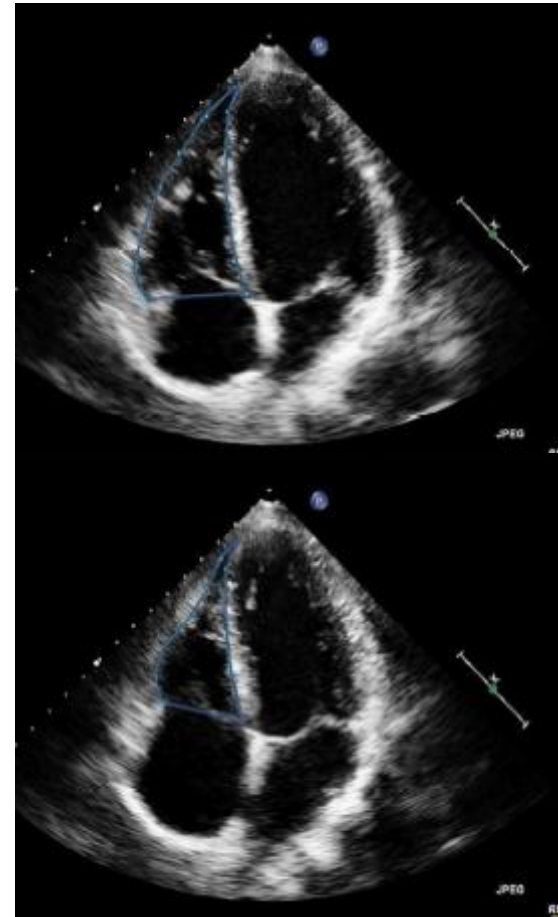
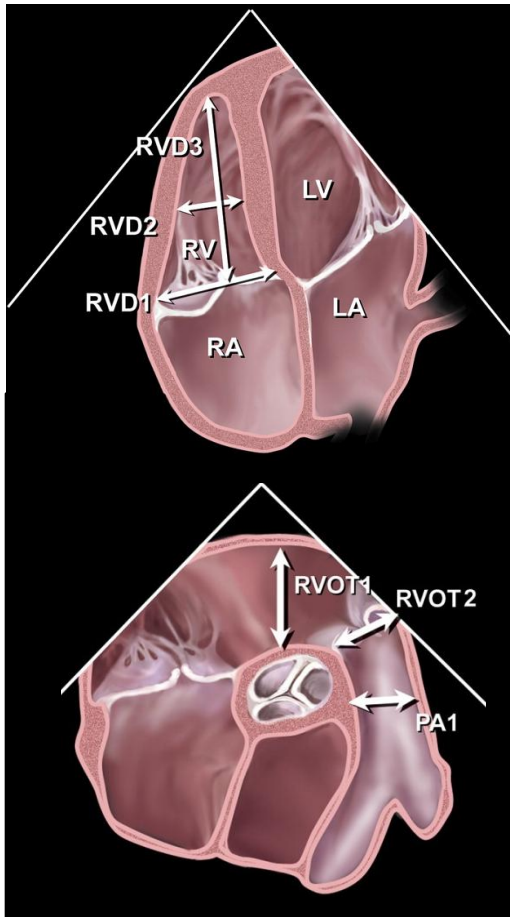
A crescent-shaped and triangular body covering part of the circumference of LV with distinctly separated inflow and outflow



- **Geometric assumption is not applicable for calculating RV volume**

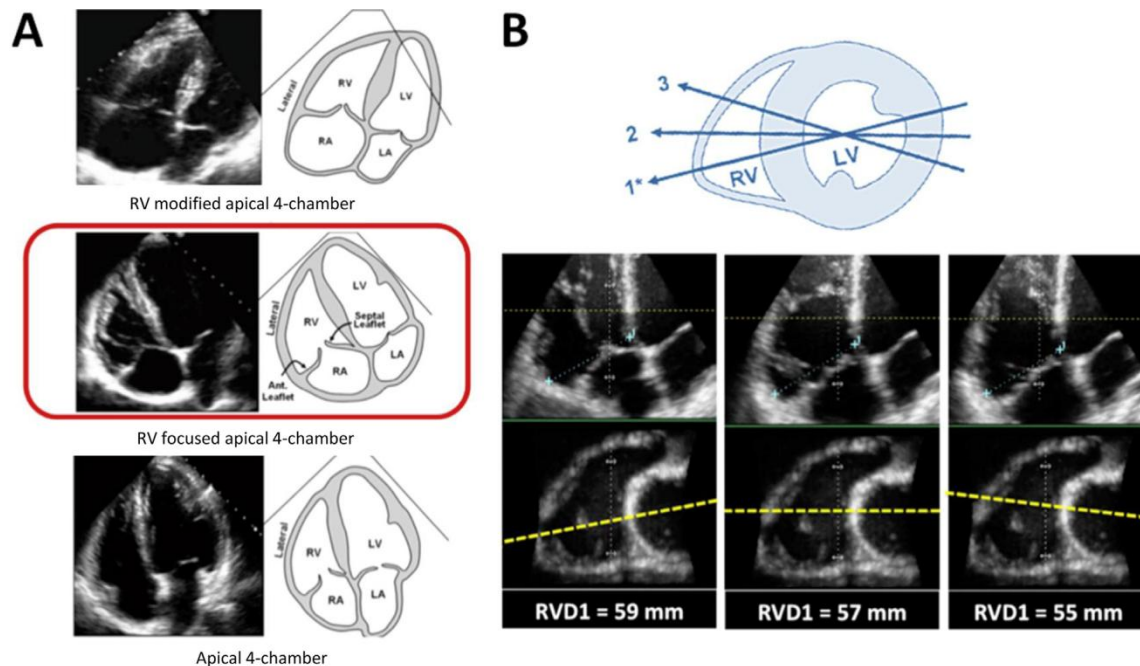
2DE Assessment of RV

RV Size: by RV Dimension & Area



Pitfall of RV sizing on apical 4ch plane

- Given the RV's complex geometry, RV dimensions and areas in apical 4ch plane can vary significantly with minor rotations in transducer position

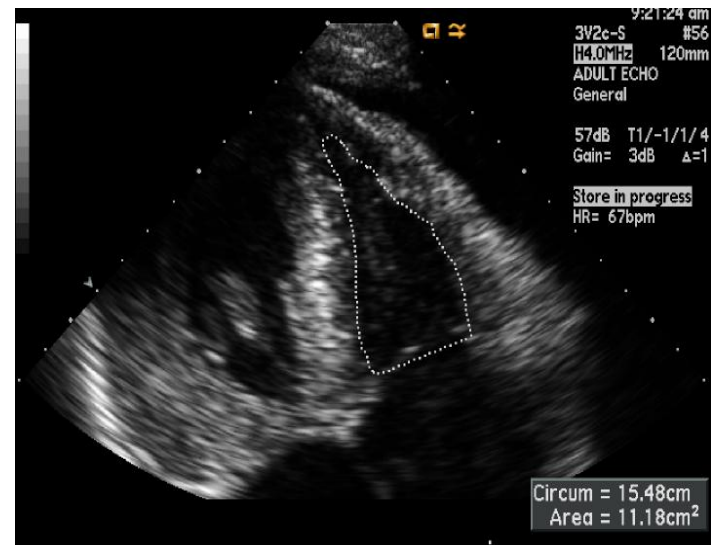
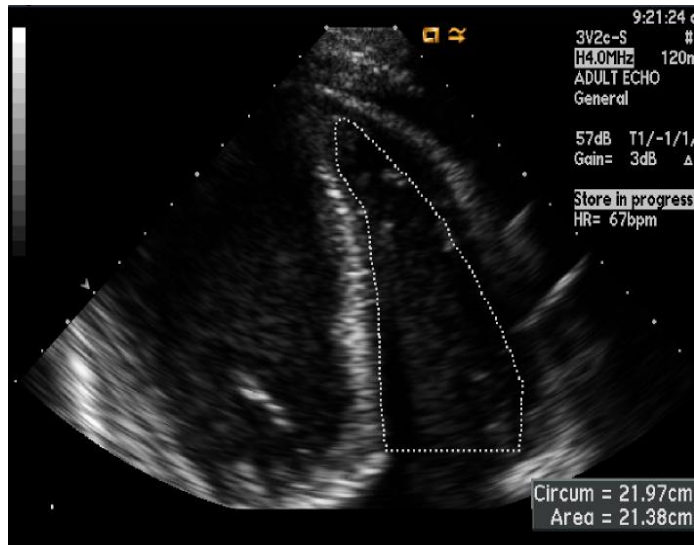


RV Size Measurements

Measurement	Normal value	Limitation
RV 1 (RV basal diameter)	<4.2 cm	Influenced by probe rotation Requires RV-focused view
RV 2 (midcavity diameter)	<3.5 cm	Level of measurement not clearly defined (level LV papillary muscles) Normal value?
RV 3 (base-apex RV length)	<8.6 cm	Influenced by probe rotation Definition of RV apex?
RV end-diastolic area	<28 cm ²	Influenced by probe rotation Definition of trabeculations can be difficult
RVOT parasternal short axis just proximal to pulmonary valve	2.7 cm	Often difficult endocardial definition Limited normative data

RV Function

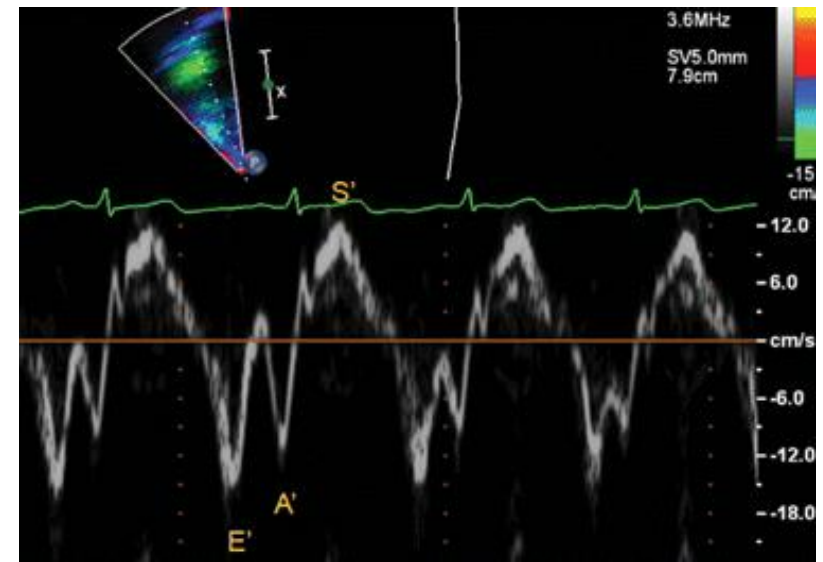
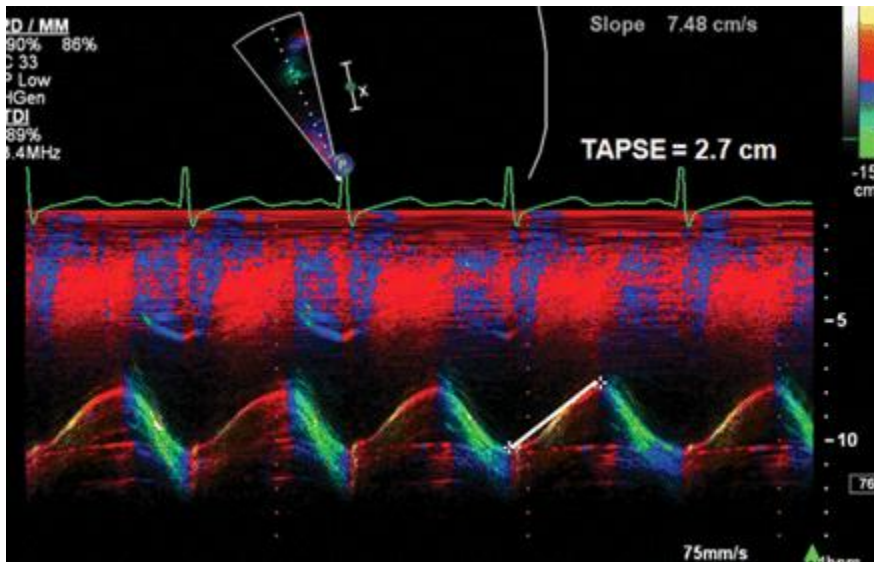
Fractional Area Change (FAC)



$$\frac{(\text{End-diastolic area}) - (\text{end-systolic area})}{(\text{end-systolic area})} \times 100$$

RV Function

Longitudinal RV wall systolic fx: TAPSE & Lateral TA Velocity

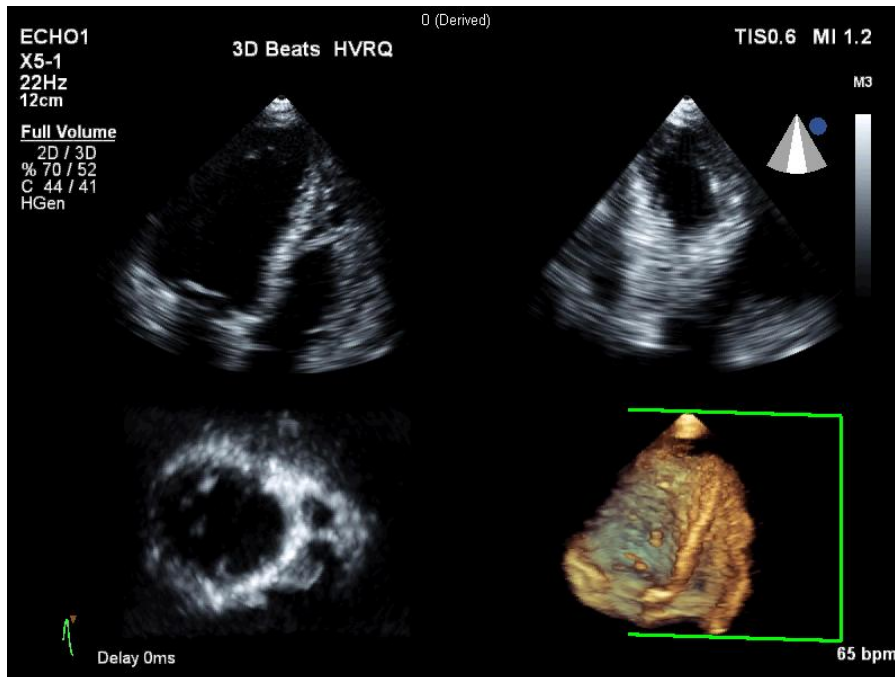


- Fundamentally problematic, because they consider only a section of RV
- RV free wall motion can be induced passively by LV lateral wall contraction

RV functional measurements

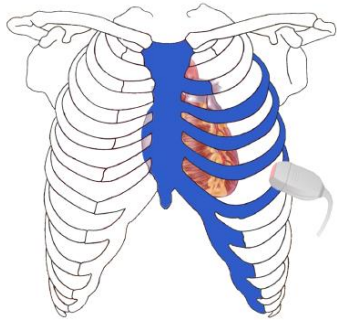
Measurement	Normal value	Limitation
%FAC	>35%	<p>Endocardial border detection can be difficult especially in systole</p> <hr/> <p>Load-dependent</p> <hr/> <p>No imaging of the outflow tract</p>
TAPSE	>16 mm	<p>Influenced by direction of motion (alignment)</p> <hr/> <p>Influenced by loading and tricuspid regurgitation</p> <hr/> <p>No imaging of the outflow tract</p>
Peak systolic tissue Doppler velocity tricuspid annulus	>10 cm/s	<p>Influenced by alignment with the motion</p> <hr/> <p>Influenced by loading conditions</p> <hr/> <p>Only one single segment used for global function</p>

RV volume with 3DE

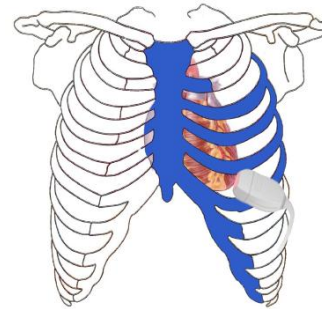


- Gets a full volume dataset of RV in a single shot
- Avoid many of limitations of 2DE in the assessment of RV volume & function

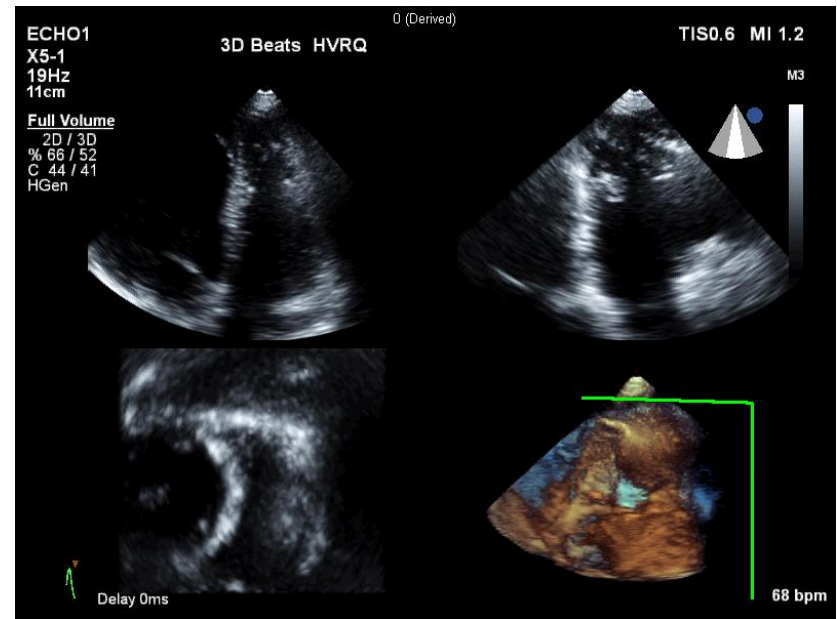
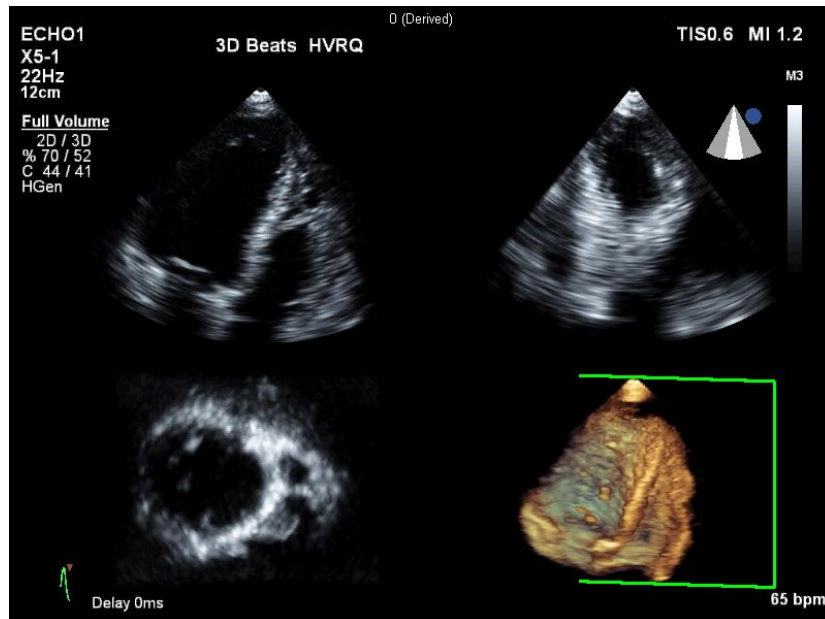
3DE acquisition of full volume dataset of RV two probe position



Lateral apical view

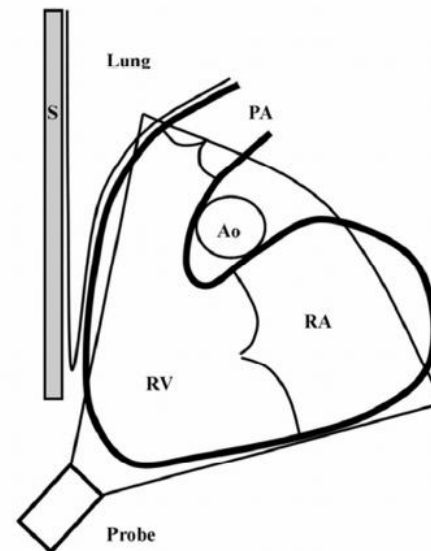
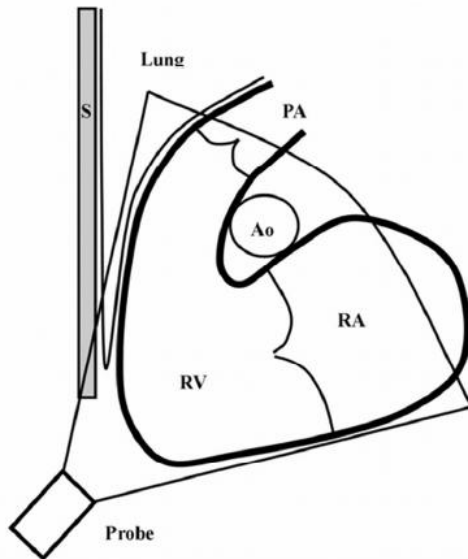


Medial apical view

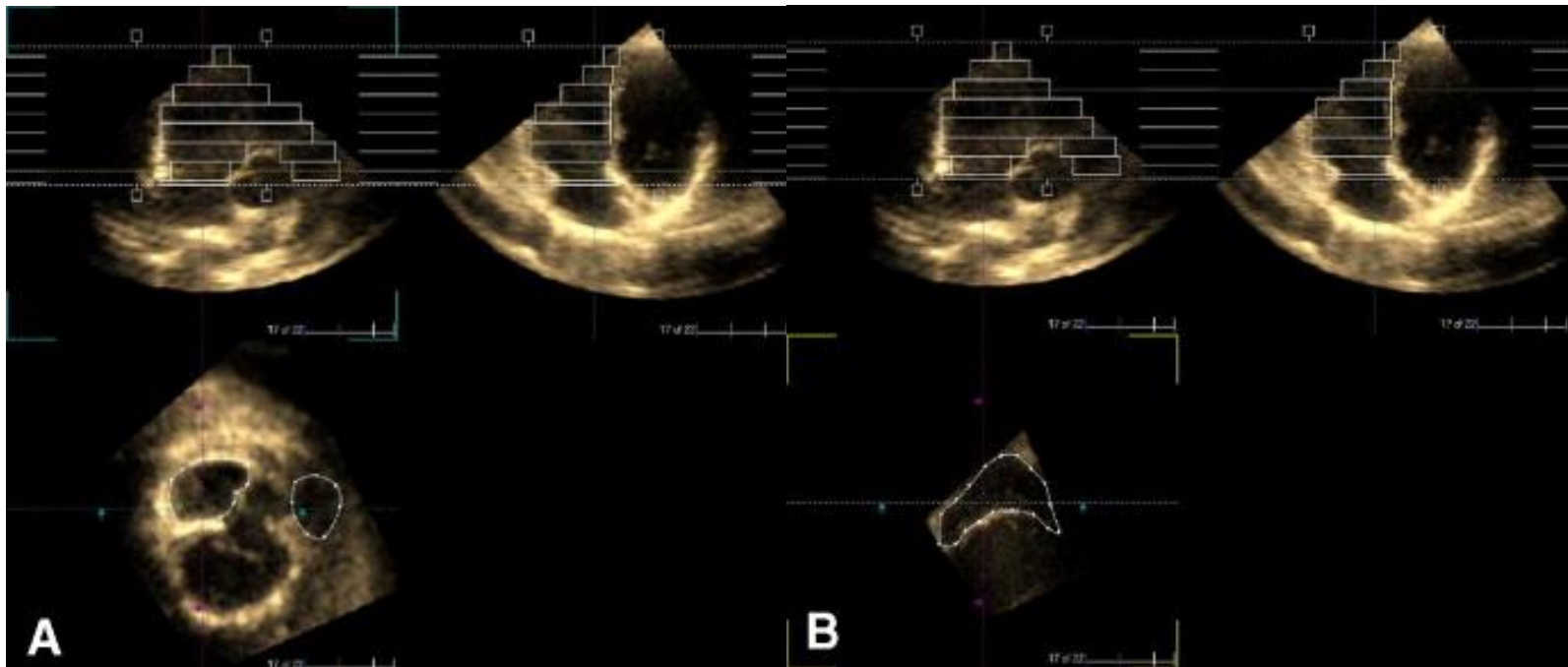


Difficulty to get the whole RV

- Located behind the sternum and may be obscured by ribs, sternum, or lung in apical views
- Anatomically separated inflow and outflow tracts
- Narrow sector angle of 3DE probe particularly in pts with large RV



Offline Assessment of 3D RV volume by disc summation method



Semi-automated RV volume by software designed specifically for RV volume

Automatic contour proposal after contour drawing in ap4ch, sagittal and coronal view at ED and ES

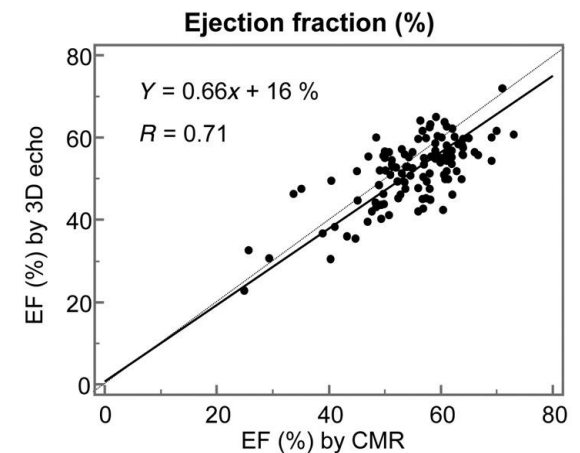
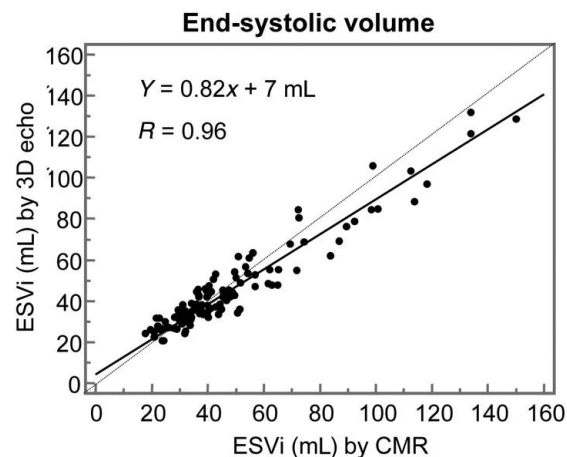
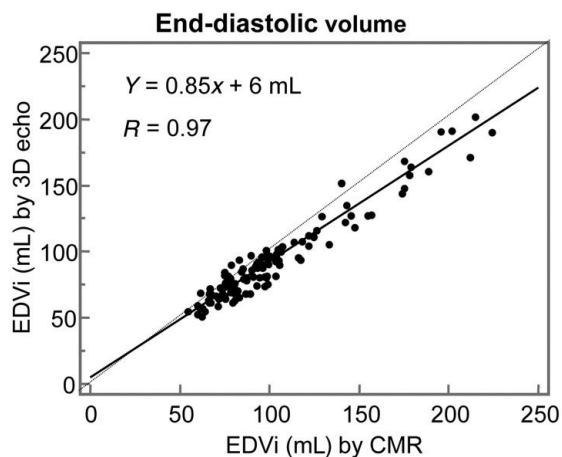


TomTec, 4D RV-function

Right ventricular quantification in clinical practice: two-dimensional vs. three-dimensional echocardiography compared with cardiac magnetic resonance imaging

Heleen B. van der Zwaan^{1*}, Marcel L. Geleijnse¹, Jackie S. McGhie¹, Eric Boersma², Willem A. Helbing^{3,4}, Folkert J. Meijboom⁵, and Jolien W. Roos-Hesselink¹ *Euro J Echo. 2011*

3DE showed reasonable limits of agreement with CMR

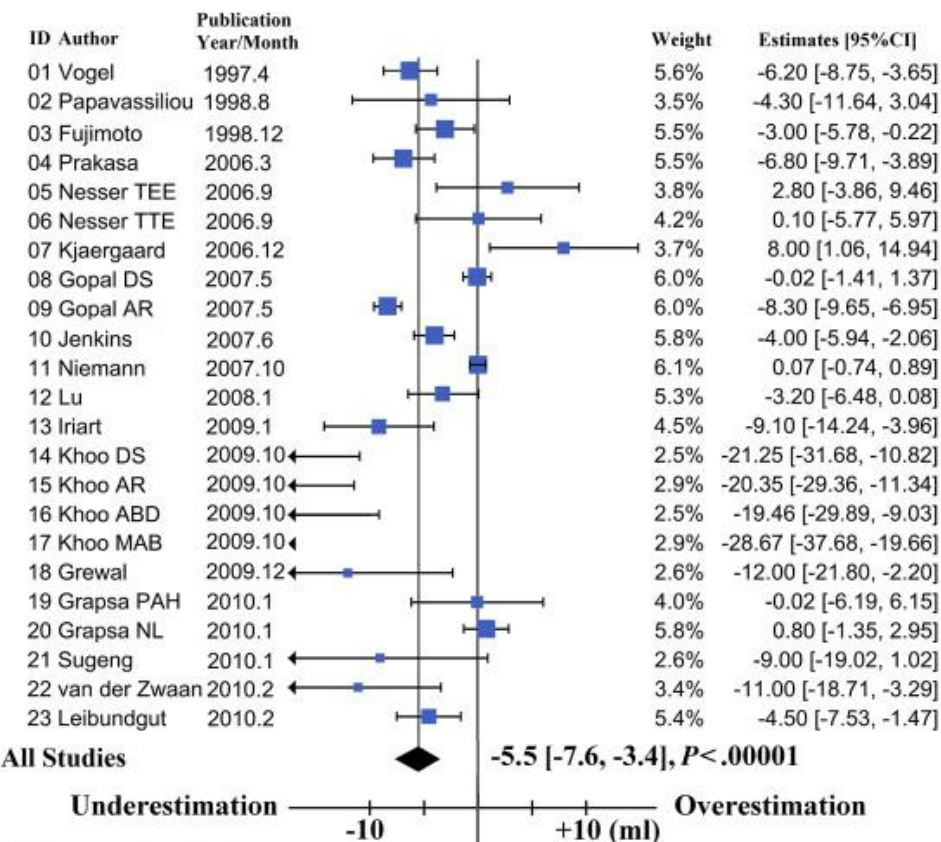


Accuracy of Right Ventricular Volumes and Function Determined by Three-Dimensional Echocardiography in Comparison with Magnetic Resonance Imaging: A Meta-Analysis Study

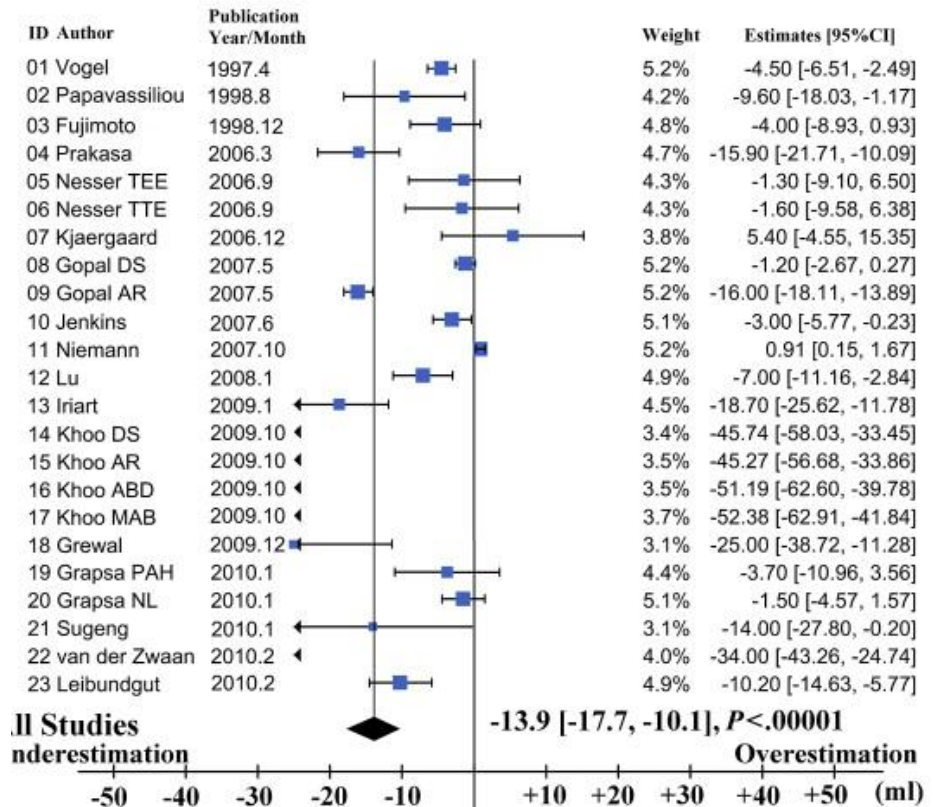
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Difference in RVESV between 3DE and MRI



Difference in RVEDV between 3DE and MRI



Normal range of 3DE derive RV volume and fx by gender and age decade

- Normal values for 3DE derived RV volumes and EF showed dependency on gender and age

Age (y)	n (women, men)	RV EDV (mL/m ²)		RV ESV (mL/m ²)		RV EF (%)	
		Women	Men	Women	Men	Women	Men
<30	102 (45, 57)	53 (38, 78)	66 (42, 100)	20 (8, 45)	28 (16, 52)	60 (43, 82)	56 (42, 68)
30–39	96 (50, 46)	50 (38, 77)	58 (35, 85)	18 (11, 38)	23 (12, 38)	63 (50, 78)	60 (47, 74)
40–49	96 (53, 43)	50 (34, 65)	54 (36, 78)	18 (8, 27)	21 (11, 33)	65 (49, 80)	59 (51, 75)
50–59	88 (47, 41)	49 (37, 69)	53 (36, 76)	18 (11, 29)	19 (10, 37)	62 (46, 76)	62 (45, 74)
60–69	69 (39, 30)	46 (26, 64)	52 (37, 86)	17 (8, 26)	19 (10, 36)	61 (50, 79)	63 (49, 79)
≥70	37 (23, 14)	43 (25, 62)	54 (31, 68)	12 (7, 21)	18 (7, 28)	71 (57, 82)	65 (55, 76)

Data are expressed as median (5th, 95th percentile).

Normal values of 3DE derived RV volume from healthy adults: 50% difference between studies

	Gopal 2007 (33)	Aune 2009 (46)	van der Zwaan 2011 (34)	Tamborini 2010 (35)
RVEDV [mL]		77 ± 23		86 ± 21
RVEDVI [mL/m ²]	70 ± 14	40 ± 11	75 ± 12	49 ± 10
RVESV [mL]		30 ± 12		29 ± 11
RVESVI [mL/m ²]	33 ± 10	16 ± 6	33 ± 7	16 ± 6
RVEF [%]	53 ± 10	61 ± 10	57 ± 4	67 ± 8
N	71	166	31	245

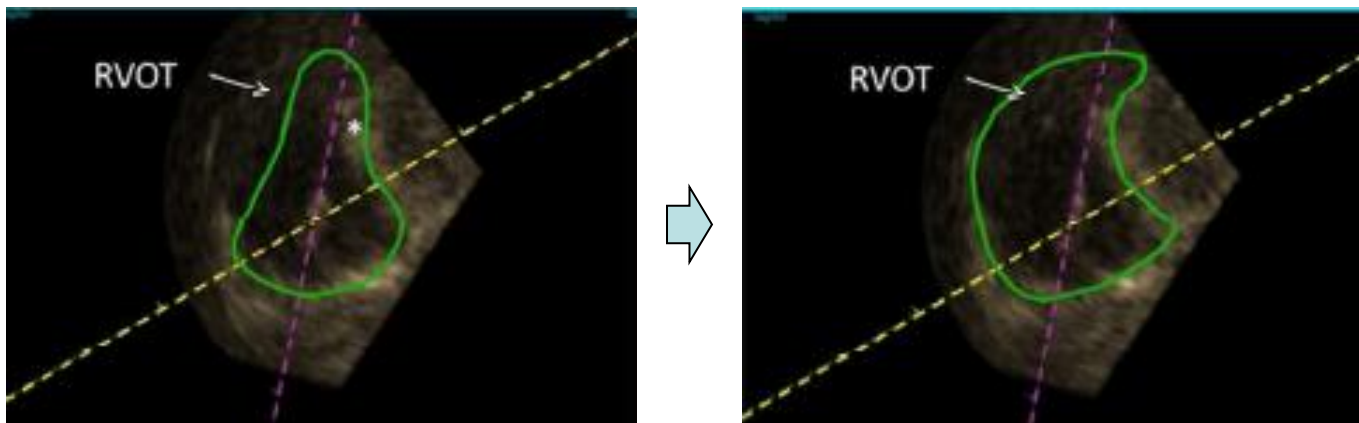
- Cohorts difference in height and BSA
- Difference in image quality and software for volume calculation

Gopal, J Am Soc Echo 2007, Van der zwaan, Eur J Echo 2011

Tamborini, J Am Soc Echo 2010, Aune, Cardiovasc Ultrasound 2009

Differing levels of manual correction of automated tracking algorithm

- Manual contour tracking corrections lead to higher calculated volumes by avoiding "streamlined" RV contours
- Semi-automated delineation of RV with manual correction is needed particularly for ant part of RVOT

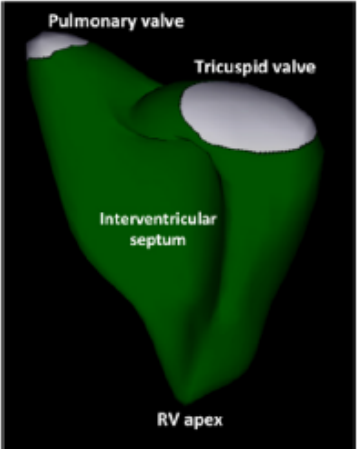


Several issues limiting clinical implementation of 3DE for RV volume

- Lack of methodologic standardization: several different methods were used (method of disks, surface modeling)
- Difficulty in visualizing some RV segments (RV anterior wall and RVOT) due to being shadowed by sternum and ribs as well as its narrow sector angle particularly for the large RV
- Requirement of pretty long learning curve to achieve intra-observer reliability
- Lack of large population-based normative values

Recommendations for RV volume in adults: An update from ASE and EACVI

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Echocardiographic imaging	Recommended methods	Advantages	Limitations
3DE RV volumes 	<ul style="list-style-type: none"> • Dedicated multibeam 3D acquisition, with minimal depth and sector angle (for a temporal resolution > 20–25 volumes/sec) that encompasses entire RV cavity • Automatically identified timing of end-diastole and end-systole should be verified • Myocardial trabeculae and moderator band should be included in the cavity 	<ul style="list-style-type: none"> • Unique measures of RV global size that includes inflow, outflow and apical regions • Independent of geometric assumptions • Validated against cardiac magnetic resonance 	<ul style="list-style-type: none"> • Dependent on image quality, regular rhythm, patient cooperation • Needs specific 3D echocardiographic equipment and training • Reference values established in few publications

• Recommendations

In laboratories with experience in 3DE, when RV volumes is clinically important, 3D RV volumes is recommended.

Upper limit of RV volume: RV ESVs: 44 & RV EDVs: 87 mL/m² in men

RV ESVs: 36 RV EDVs: 74 mL/m² in women

Take Home Messages

- 3DE offers better accuracy, precision and lower variance in measuring ventricular volumes compared with 2DE which are particularly important in a real-world practice
- For the assessment of LV, 3DE derived LV volume and EF already became standard measurement
- For the assessment of RV, RV size and systolic fx by conventional 2DE parameters are still standard despite their problematic limitations, whereas 3DE derived RV volume and EF are the newcomers

Take Home Messages

- 3DE still has several limitations, which will be minimized or overcome with full understanding the limitations and further improvements of 3DE technology
- Future advance in 3DE technology together with tremendous amount of data validating its clinical use in terms of accuracy, efficiency, and novelty will determine position of 3DE as a standard reference technique for both LV and RV volume and fx