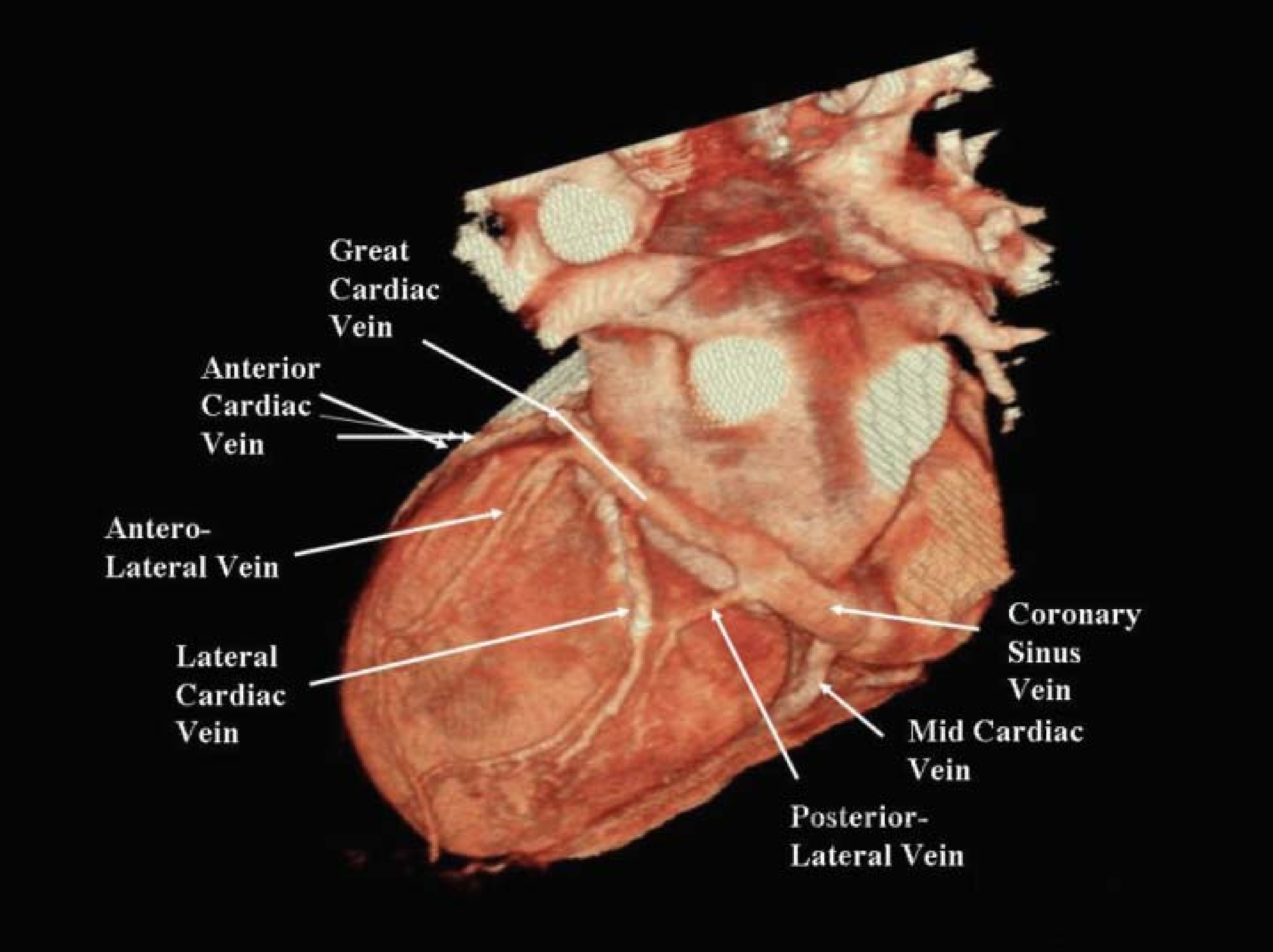
Cardiac Resynchronization Therapy(CRT) in Congenital Heart Disease

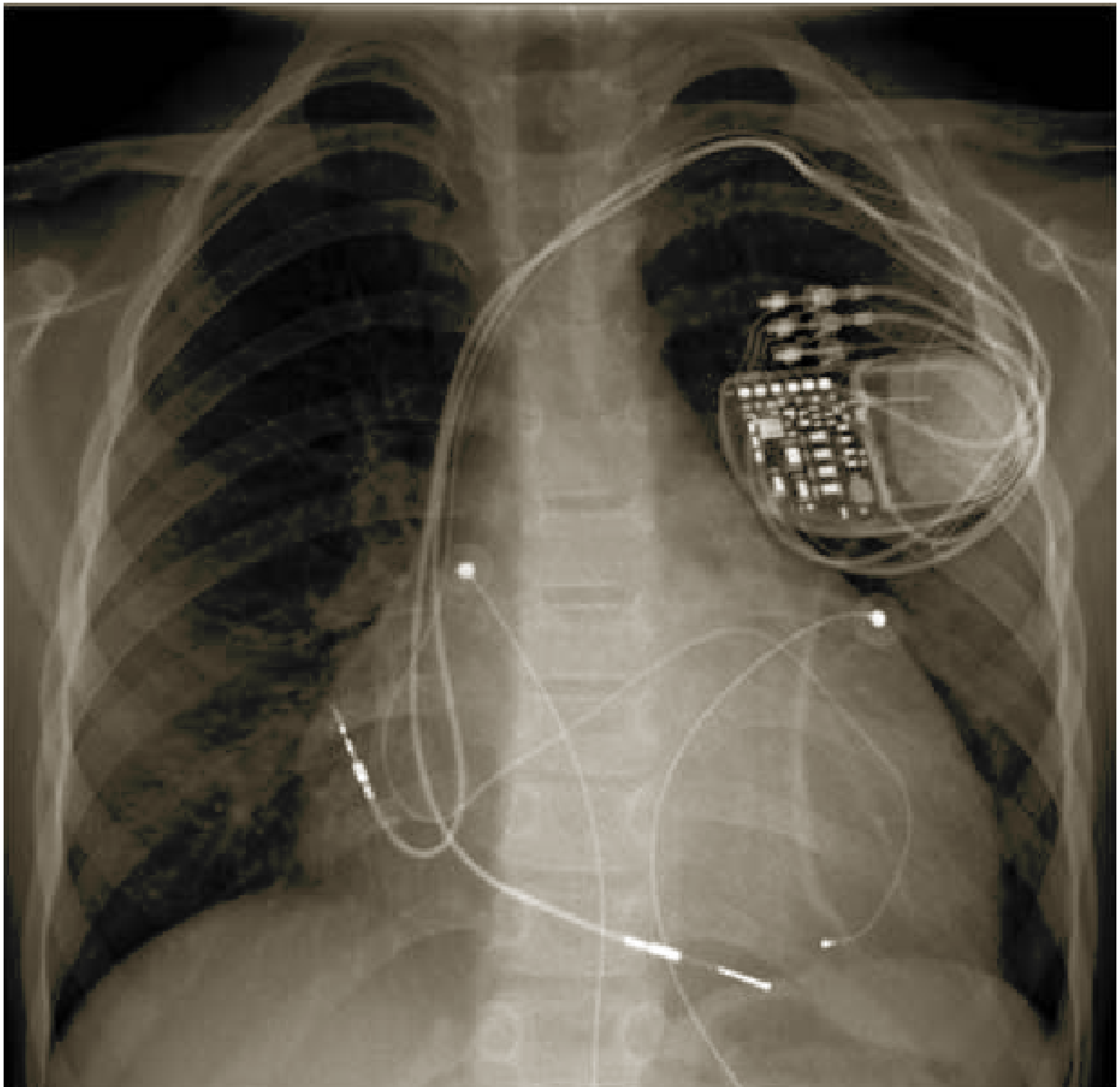
Advanced alternative therapy for congestive heart failure with cardiac dyssynchrony

Pacing lead insertion

- Transvenous Vs. epicardial approach

- Lead positions
  - In right ventricle
    - Apex
    - Outflow tract
    - Anterior free wall
  - In left ventricle
    through coronary sinus to branches
    (mainly posterolateral / lateral cardiac veins)


Great Cardiac Vein
Anterior Cardiac Vein
Antero-Lateral Vein
Lateral Cardiac Vein
Coronary Sinus Vein
Mid Cardiac Vein
Posterior-Lateral Vein

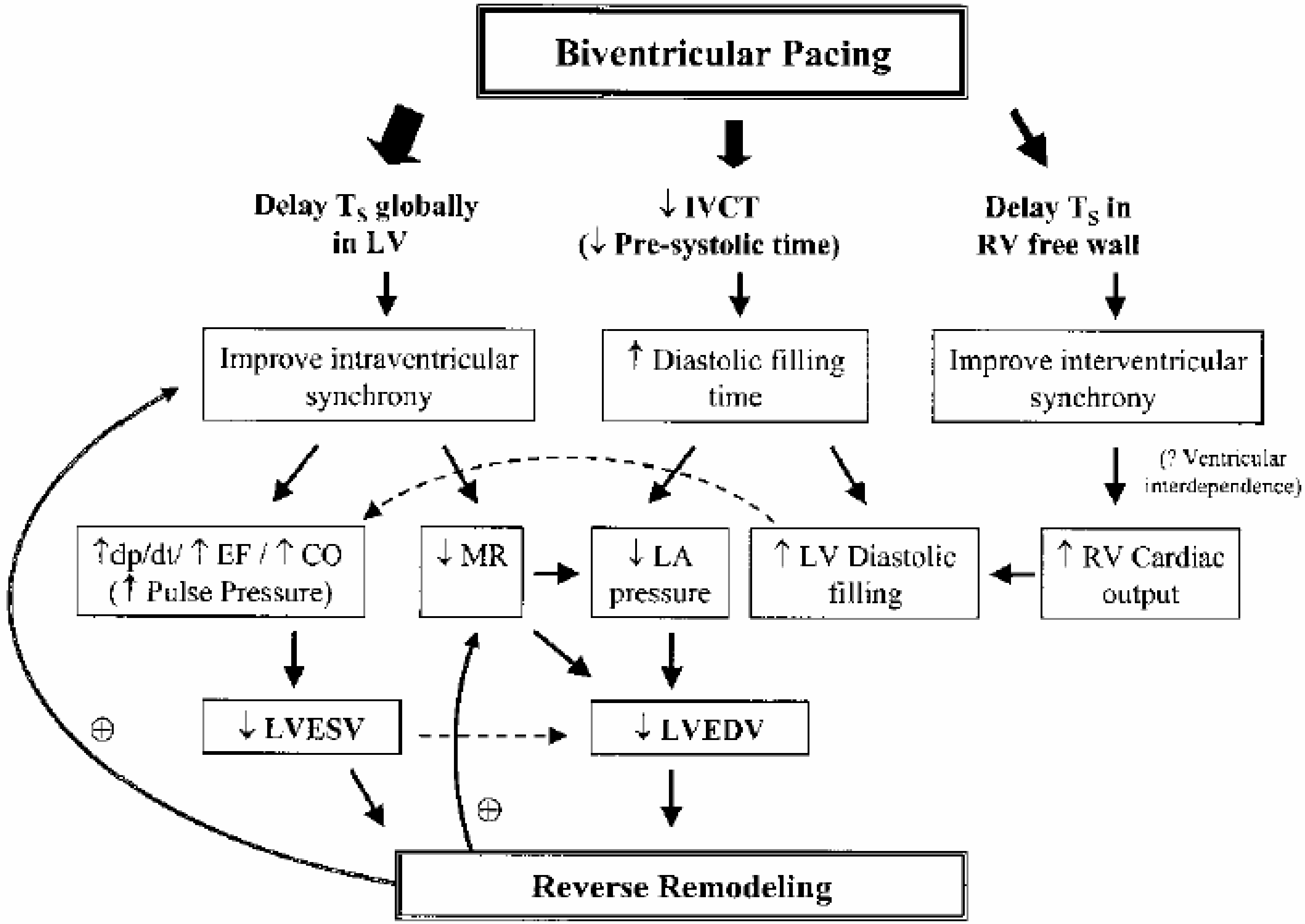


The 3 chamber pacemaker system implanted through the left subclavian vein has a bipolar atrial screw-in lead at the free right atrial wall, a tined bipolar lead at the right ventricular apex and a unipolar coronary sinus lead running to the dorsolateral portion of the LV in an epicardial vein.

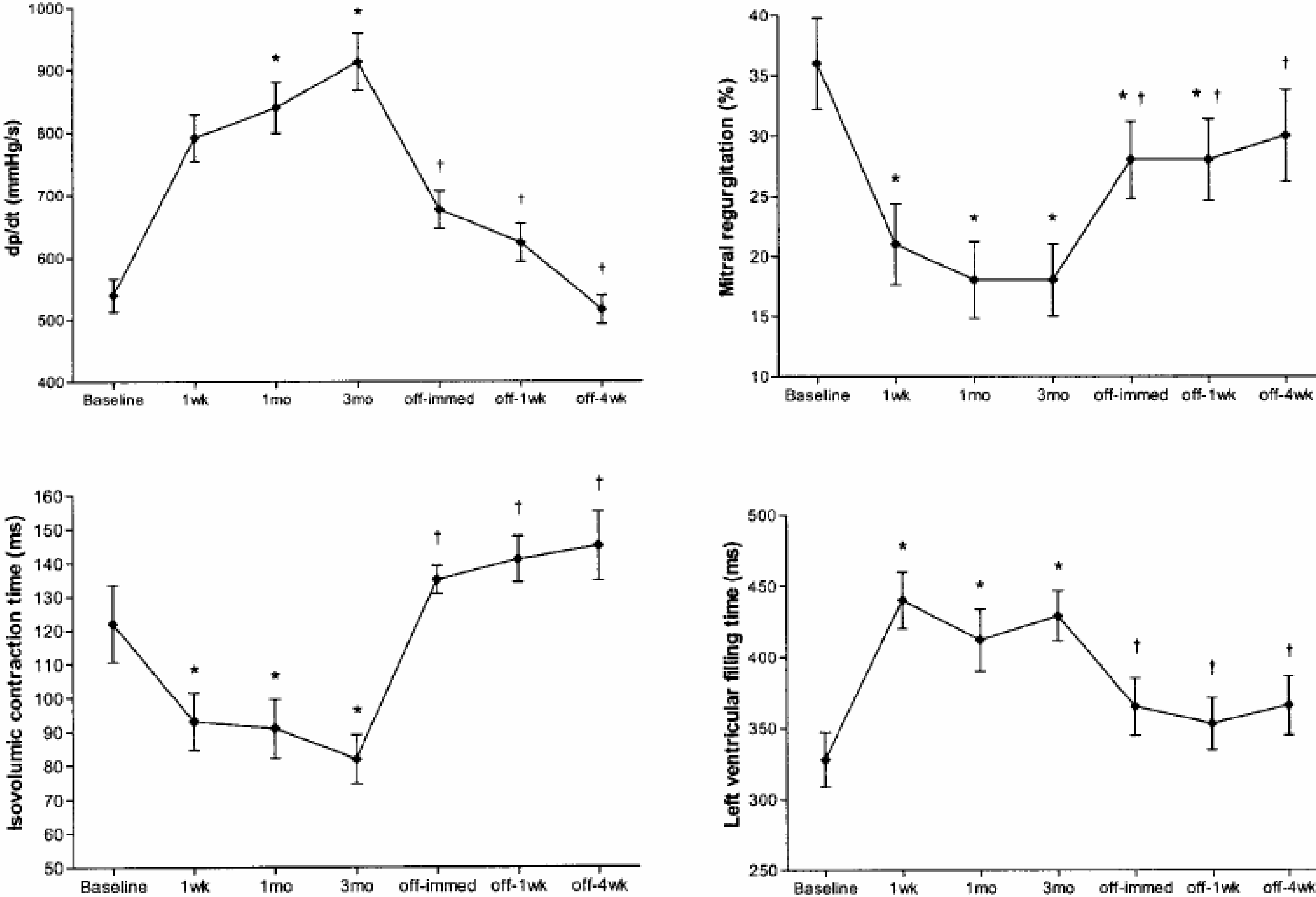
FDA labeling criteria for CRT

NYHA functional class III or IV
QRS duration > 130 milliseconds
Left ventricular ejection fraction of ≤ 0.35
Optimized medical therapy
Normal sinus rhythm

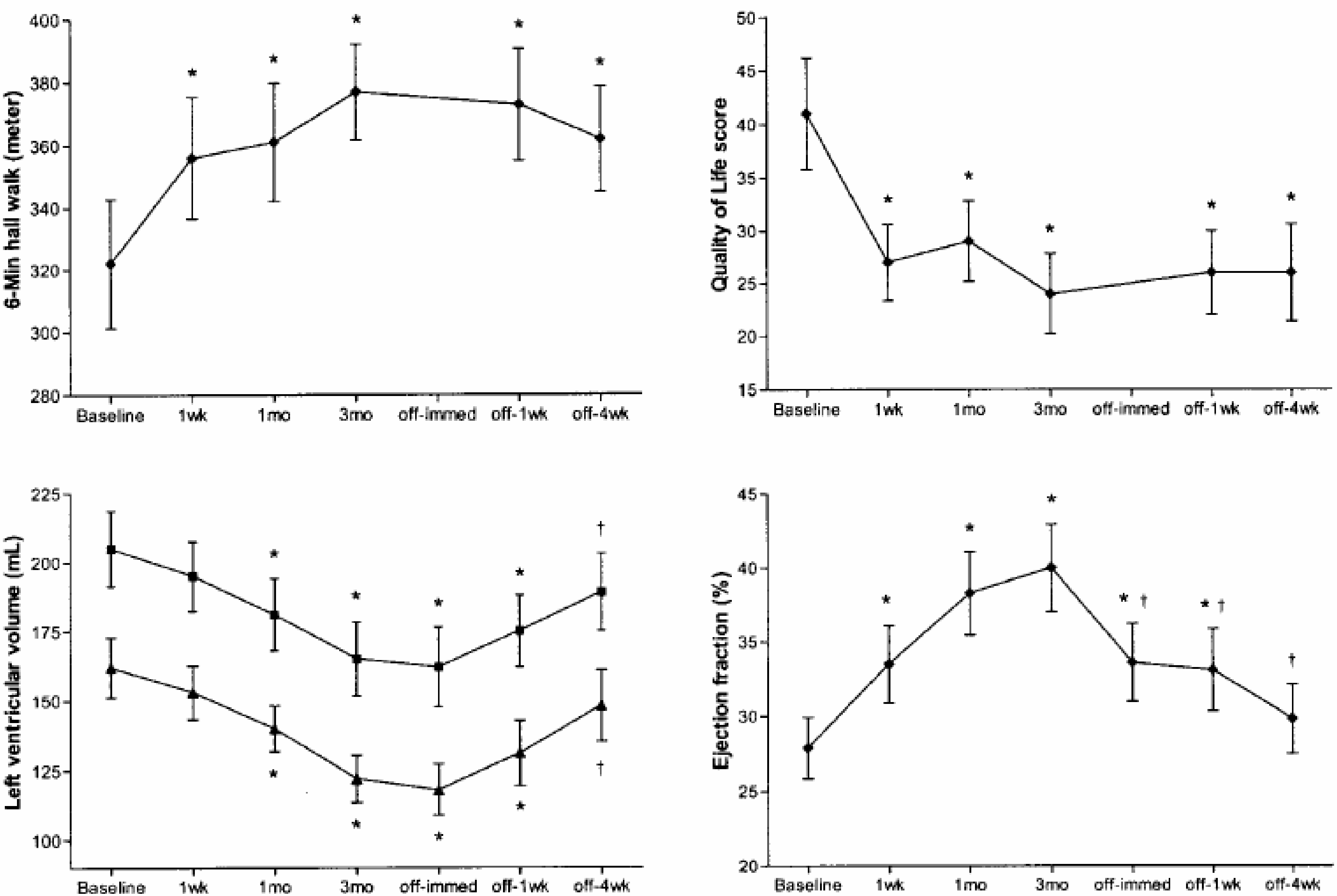
Proposed mechanisms of benefit from CRT



Ts: time to peak sustained systolic contraction, IVCT: isovolumic contraction time, EF: ejection fraction, CO: cardiac output, MR: mitral regurgitation (Circulation 2002;105:438-45)



dp/dt (mmHg/s)
1000
900
800
700
600
500
400
Baseline
1wk
1mo
3mo
off-immed
off-1wk
off-4wk
Mitral regurgitation (%)
40
35
30
25
20
15
10
Baseline
1wk
1mo
3mo
off-immed
off-1wk
off-4wk
Isovolumic contraction time (ms)
160
150
140
130
120
110
100
90
80
70
60
50
Baseline
1wk
1mo
3mo
off-immed
off-1wk
off-4wk
Left ventricular filling time (ms)
500
450
400
350
300
250
Baseline
1wk
1mo
3mo
off-immed
off-1wk
off-4wk

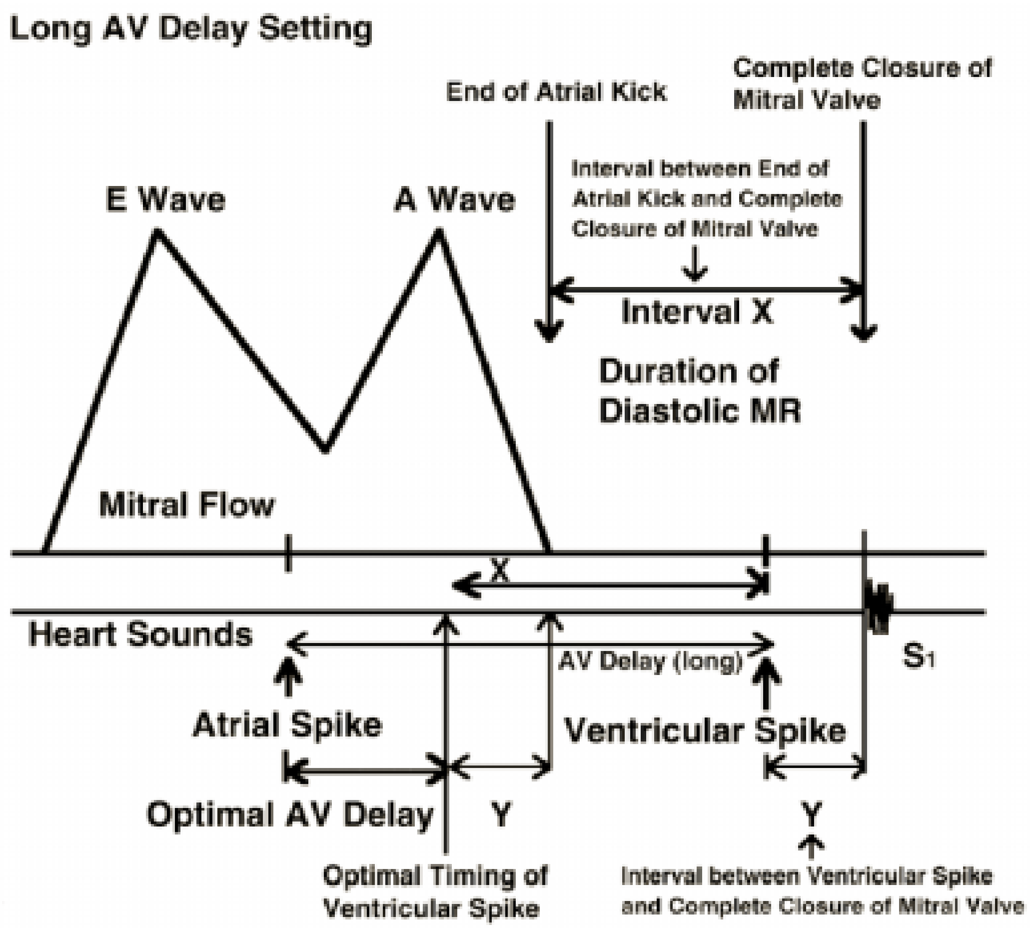


6-Min hall walk (meter)
400
380
360
340
320
300
280
Baseline
1wk
1mo
3mo
off-immed
off-1wk
off-4wk
Quality of Life score
50
45
40
35
30
25
20
15
Left ventricular volume (mL)
225
200
175
150
125
100
Ejection fraction (%)
45
40
35
30
25
20

Cardiac Dyssynchrony

AV dyssynchrony
Interventricular dyssynchrony
Intraventricular dyssynchrony

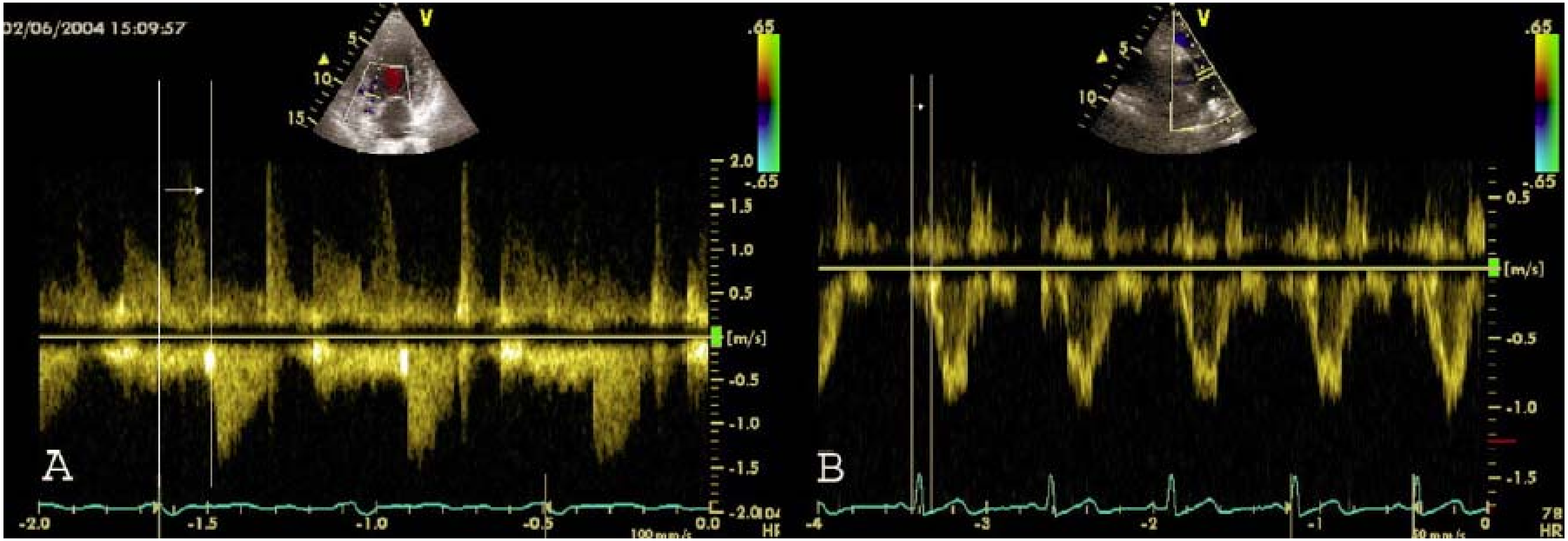
Optimization of AV delay



Optimal AV Delay = AV Delay(long) - Interval X

(Cir J 2005;69:201-4)

Interventricular Dyssynchrony

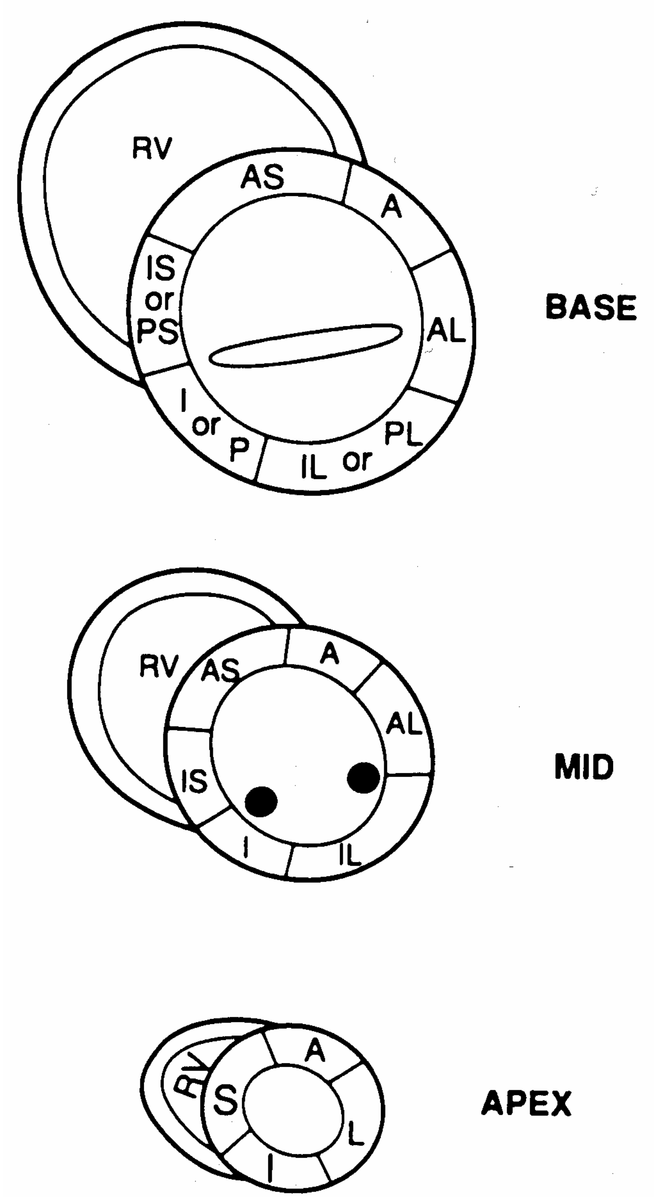


A. PW Doppler in aortic outflow tract. The measured time from onset of QRS to the onset of PW curve is LV preejection period(PEP).
B. PW Doppler in RV outflow tract. The measured time from onset of QRS to the onset of PW curve is RV PEP.

The difference between LV PEP and RV PEP is used to decide interventricular synchronicity (≥ 40msec).

Evaluation of Intraventricular Dyssynchrony

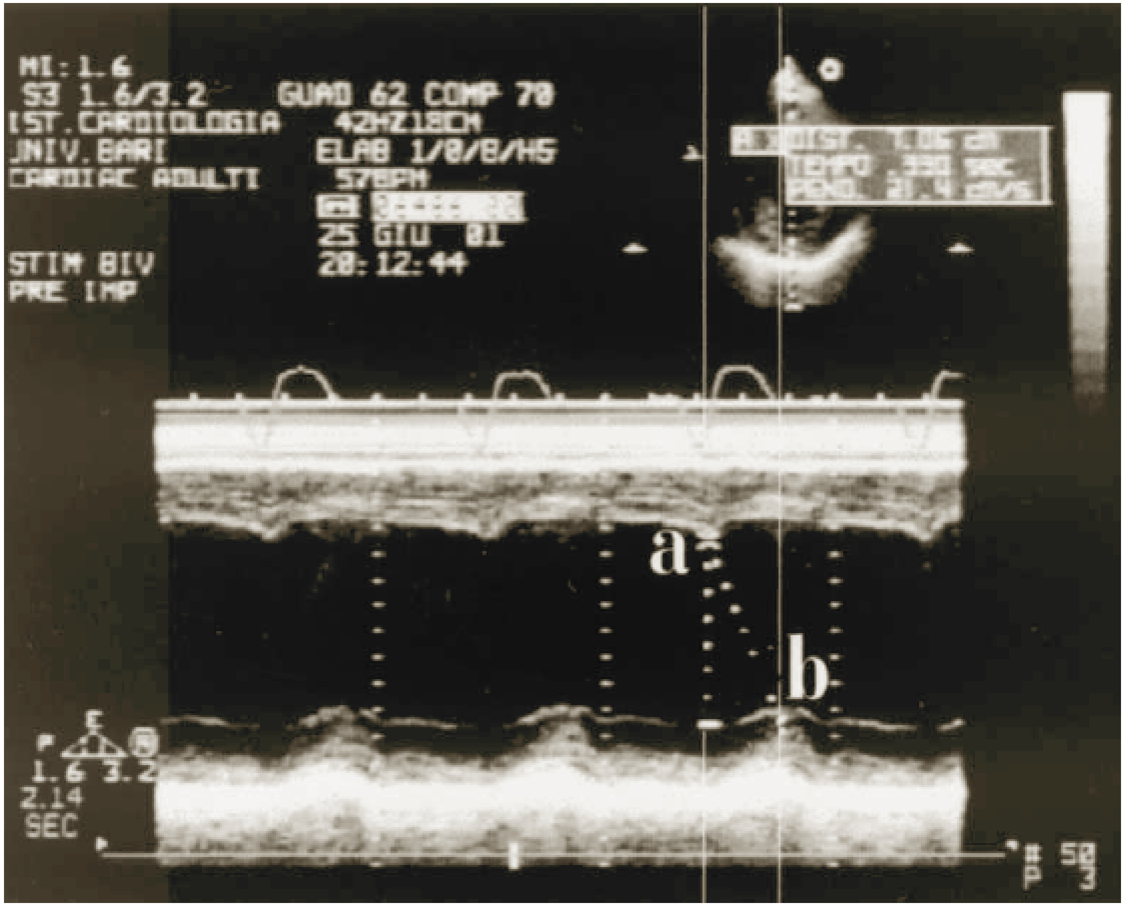
- QRS duration
- Conventional Echocardiography
- Methods associated with Tissue Doppler examination
- Other methods (tagged MRI, biventricular pressure measurements)



16 segments model recommended by American Society of Echocardiography

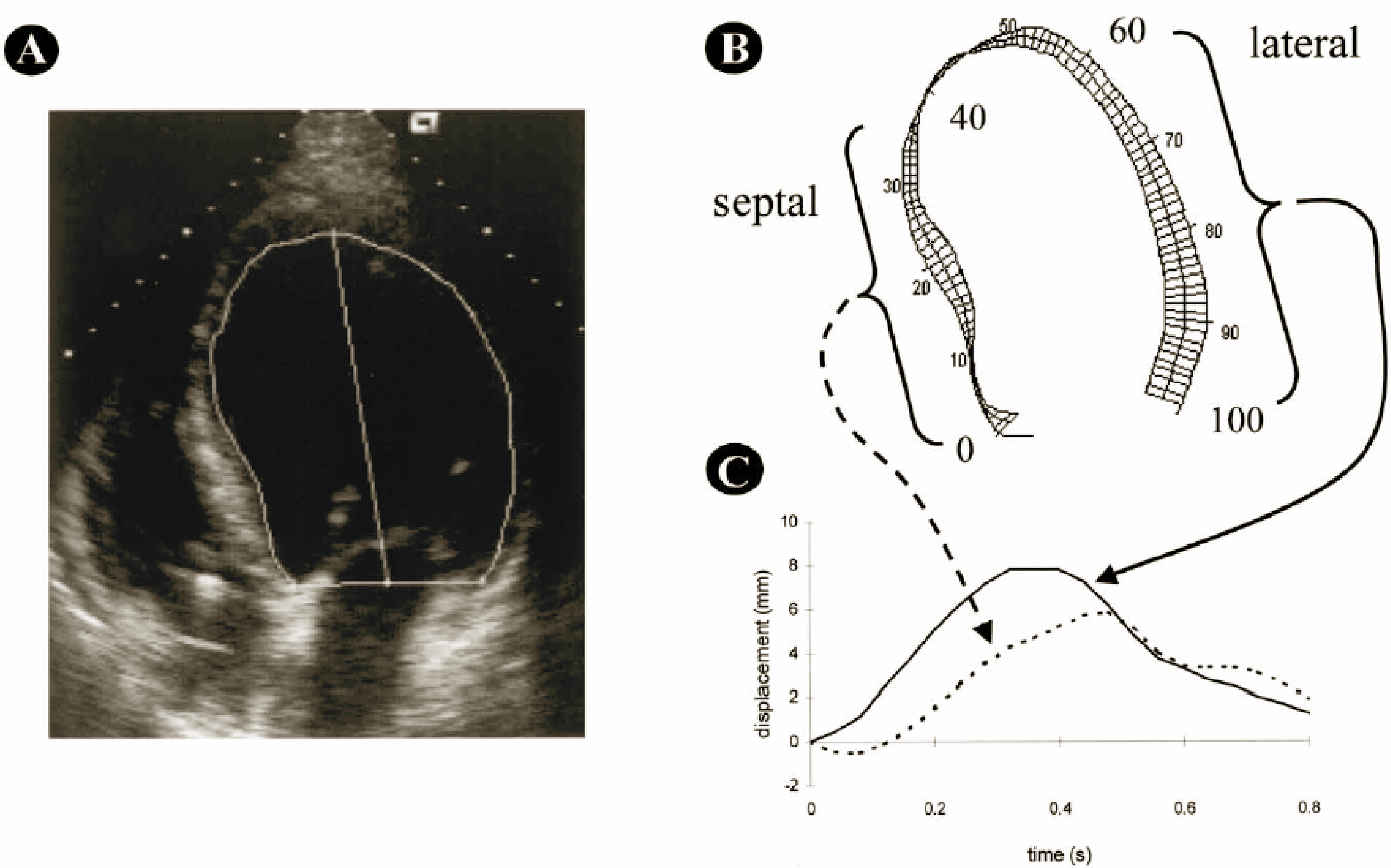
- A : anterior, AS : anteroseptal, IS/PS : infero- posteroseptal, I/P : inferior/posterior, IL/PL : infero- posterolateral, AL : anterolateral, L : lateral, S : septal
- Apical 4 chamber view
  Apical 2 chamber view
  Apical long axis view

Septal-to-posterior wall motion delay



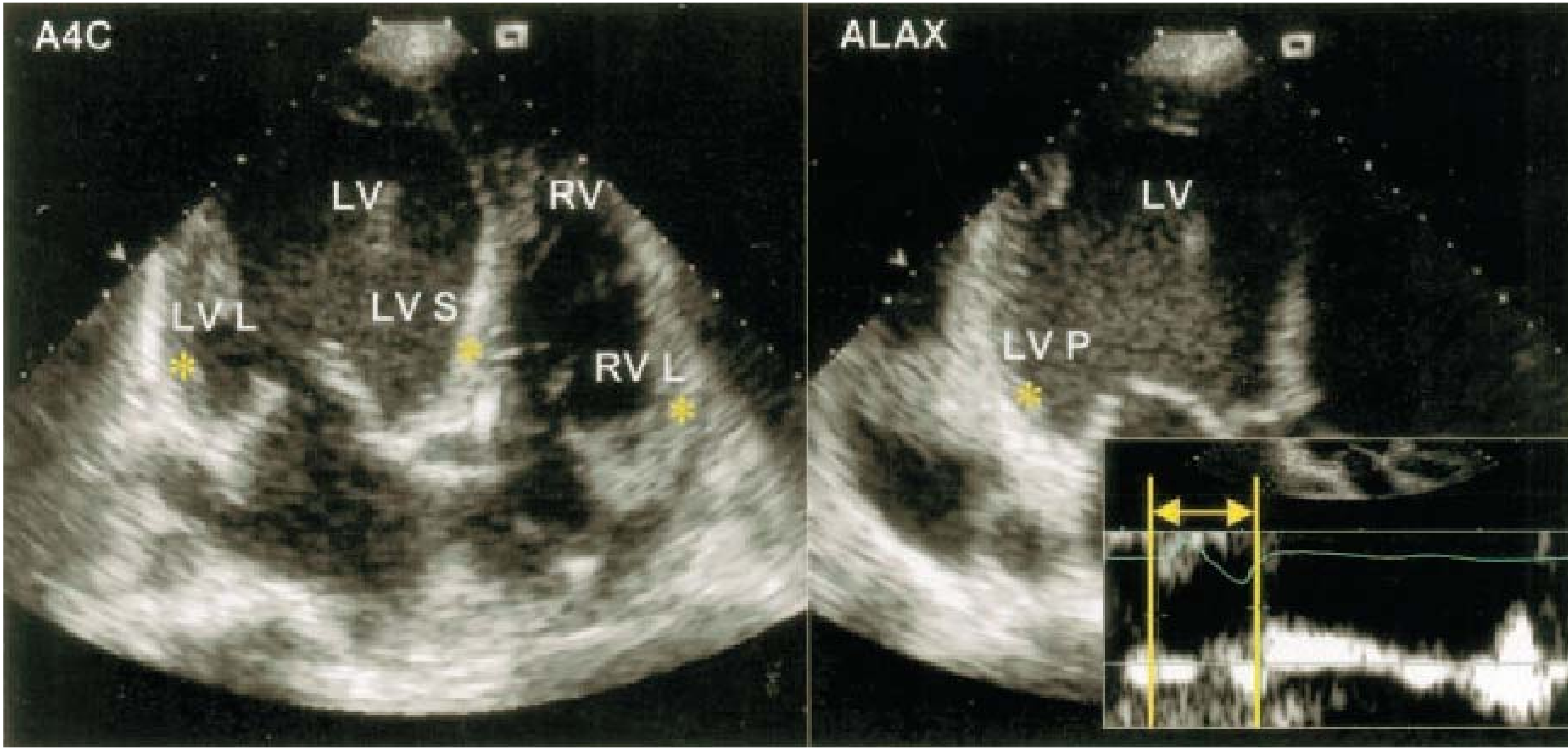
- The maximal posterior displacement of the septum (a) and the posterior wall (b).
- Cut-off value : 130msec (J Am Coll Cardiol 2005;45:65-9)

Septal-lateral phase angle difference



(A) End-diastolic image (apical 4 chamber view) with manually drawn LV endocardial tracing. (B) LV wall motion displacement for 100 endocardial segments. (C) Septal And lateral wall motion averaged for 40 septal and lateral segments and 3~7 cycles. (J Am Coll Cardiol 2002;40:536-45)

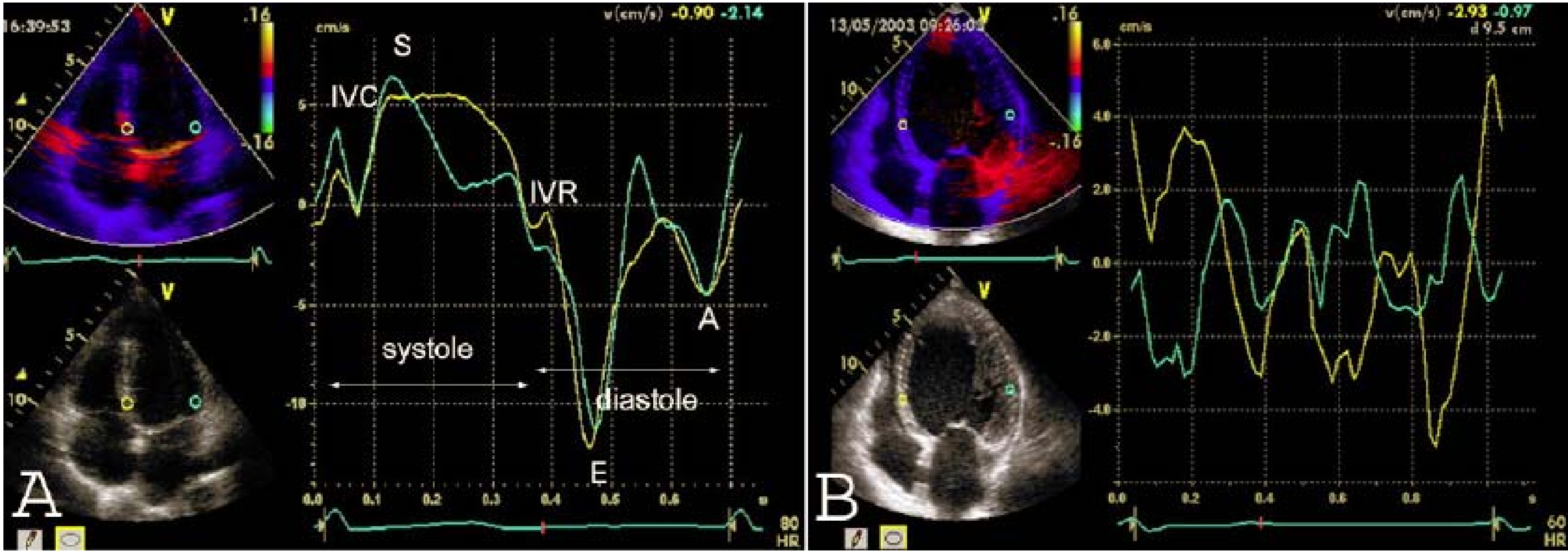
Pulsed-wave Tissue Doppler Imaging (TDI)



- Electromechanical delay (EMD) : the time interval between onset of QRS complex and onset of regional velocity of myocardial systolic shortening at TDI.
- Intraventricular dyssynchrony : difference between longest and shortest regional EMD in LV segments.
- Interventricular dyssynchrony : difference between regional EMD in RV lateral segment and most delayed from LV segments.

(Circulation 2004;109:978-83)

2D Tissue Doppler Imaging



A) Normal control patients. There is a synchronous myocardial velocity in the septal (=yellow) and the lateral (=green curve) segment.

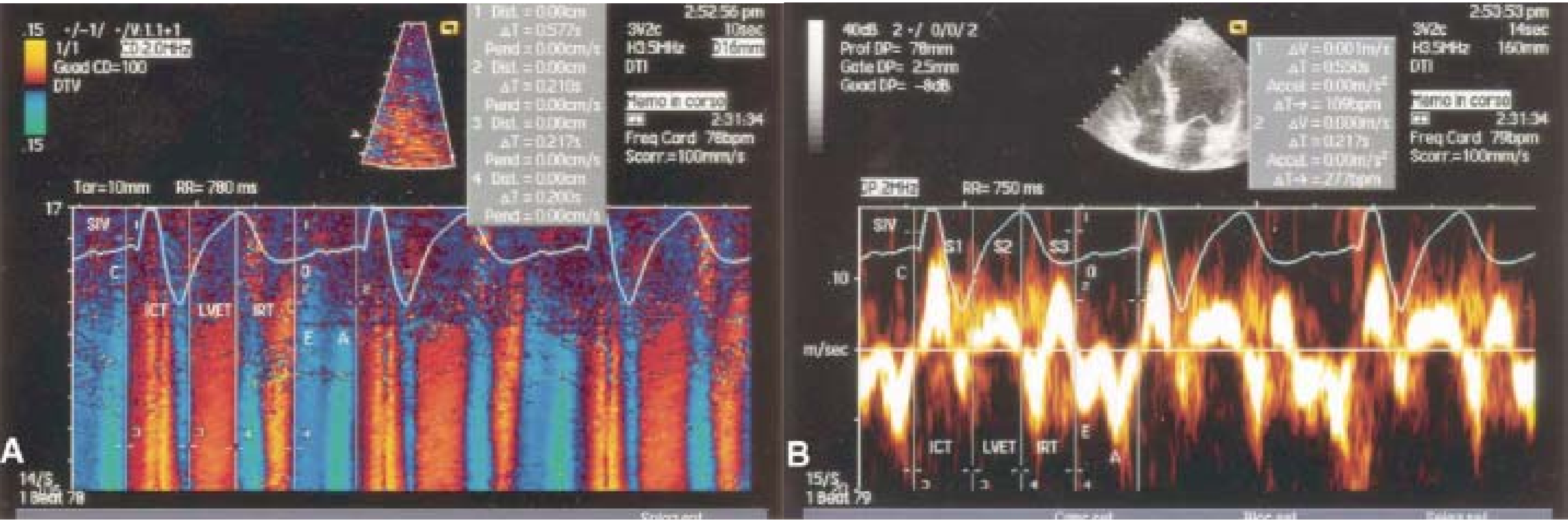
B) There is asynchronous myocardial velocity in the septal and the lateral segment

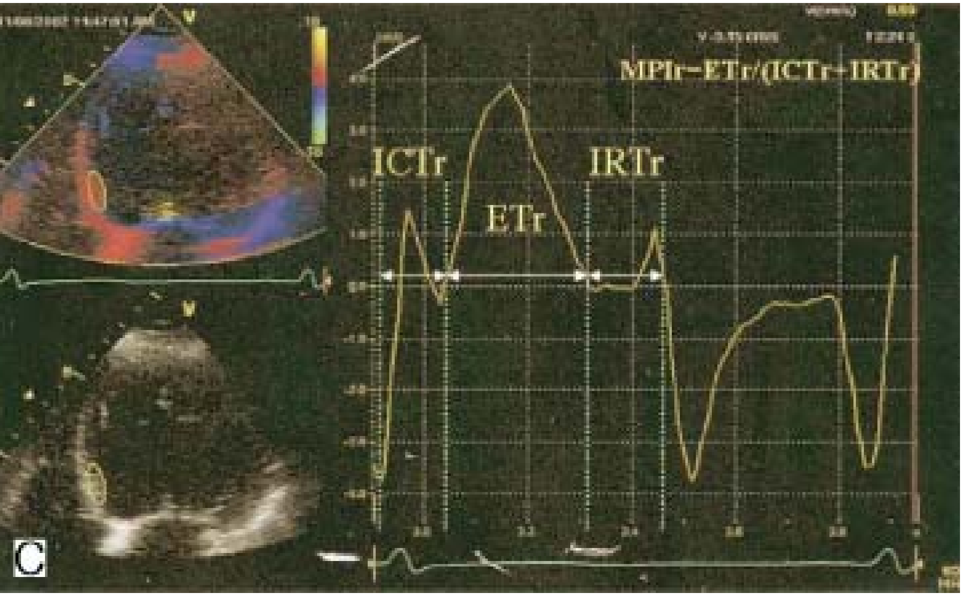
(Cardiovascular Ultrasound 2004;2:17-29)

- Difference in septal-lateral time-to-peak TDI,
  Cut-off > 60msec
  (Cardiovascular Ultrasound 2004;2:17-29)

- Dyssynchrony / asynchrony index (Ts-SD) :
  Standard deviation of 12 LV segments' time to peak regional myocardial contraction (Ts).
  Cut-off > 32.6 msec
  (Am J Cardiol 2002;91:684-8)

- Mean regional myocardial performance index, &
  Difference between regional Q-wave to peak systolic displacement time
  (J Am Soc Echocardiogr 2004;17:845-50)

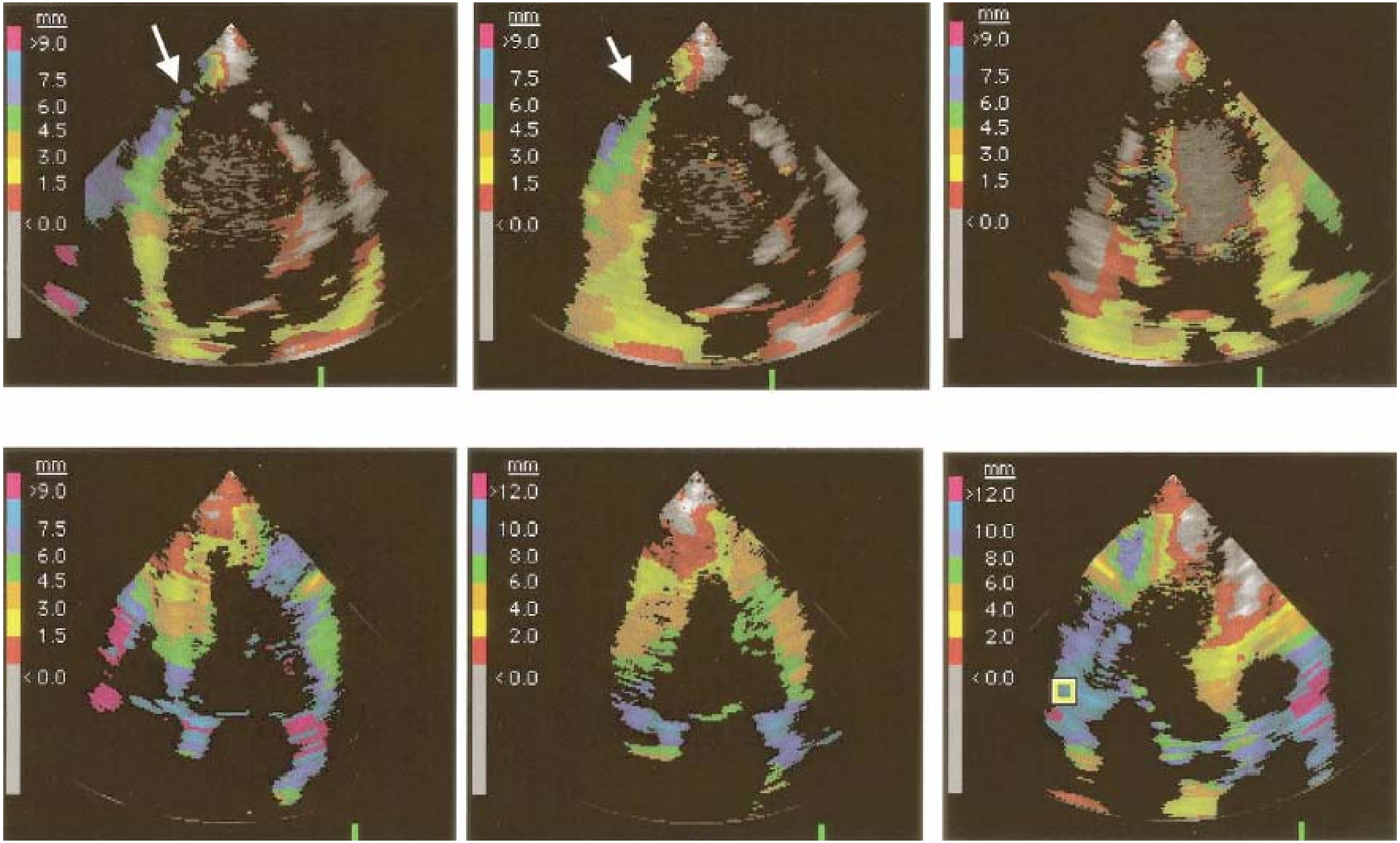




A. Color tissue M-mode of septum
B. PW tissue Doppler of basal septum
C. Tissue velocity of basal septum in TDI

ICT : isovolumic contraction time, LVET : LV ejection time, IRT : isovolumic relaxation time, E : early wave, A : atrial wave, MPIr : regional myocardial performance index, ICTr : regional ICT, ETr : regional ET, IRTr : regional IRT

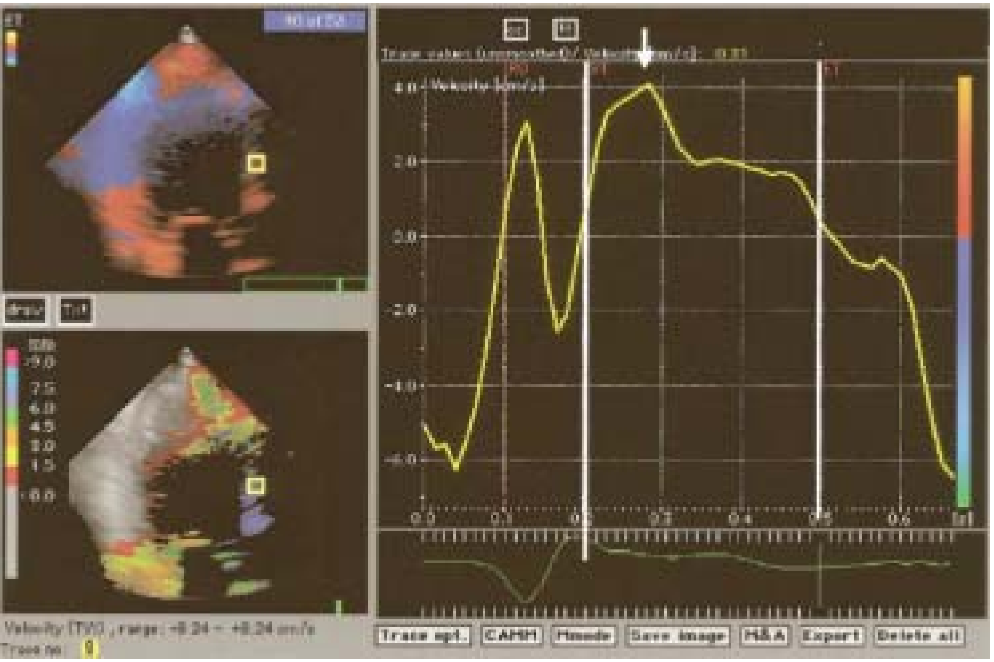
Tissue tracking (TT) image

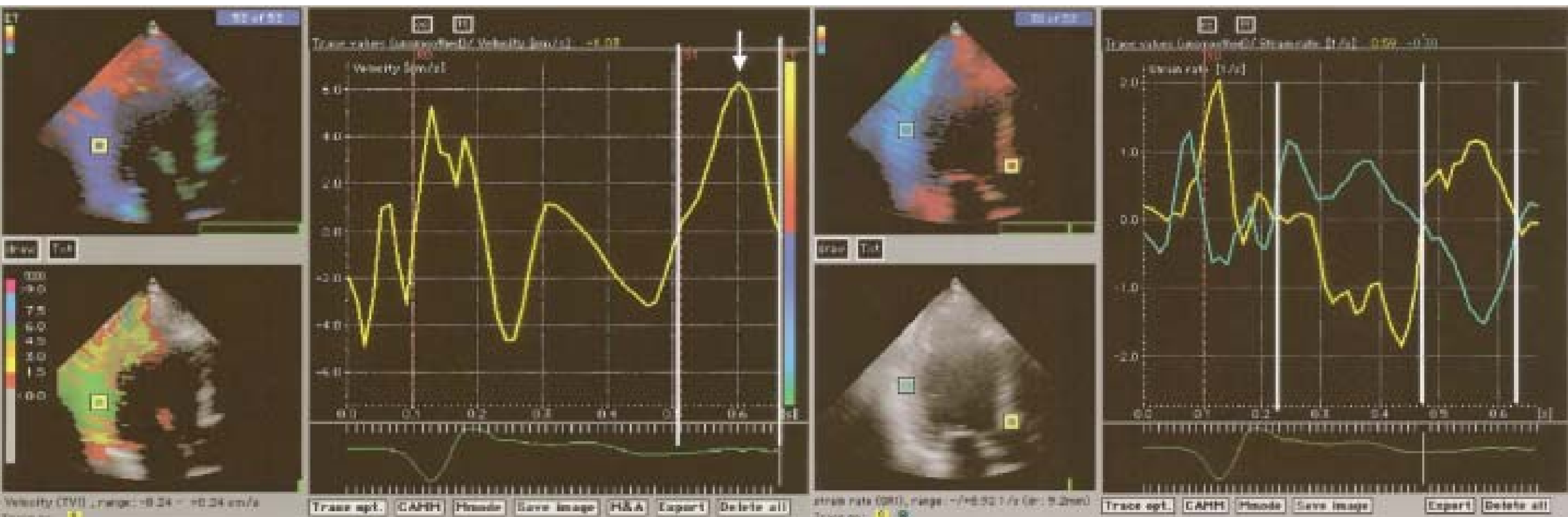


The upper panels represent the 3 apical views in systolic in a patient with DCMP before CRT. The lower panels show corresponding view after 1 year of CRT. (J Am Coll Cardiol 2002;40:723-30)

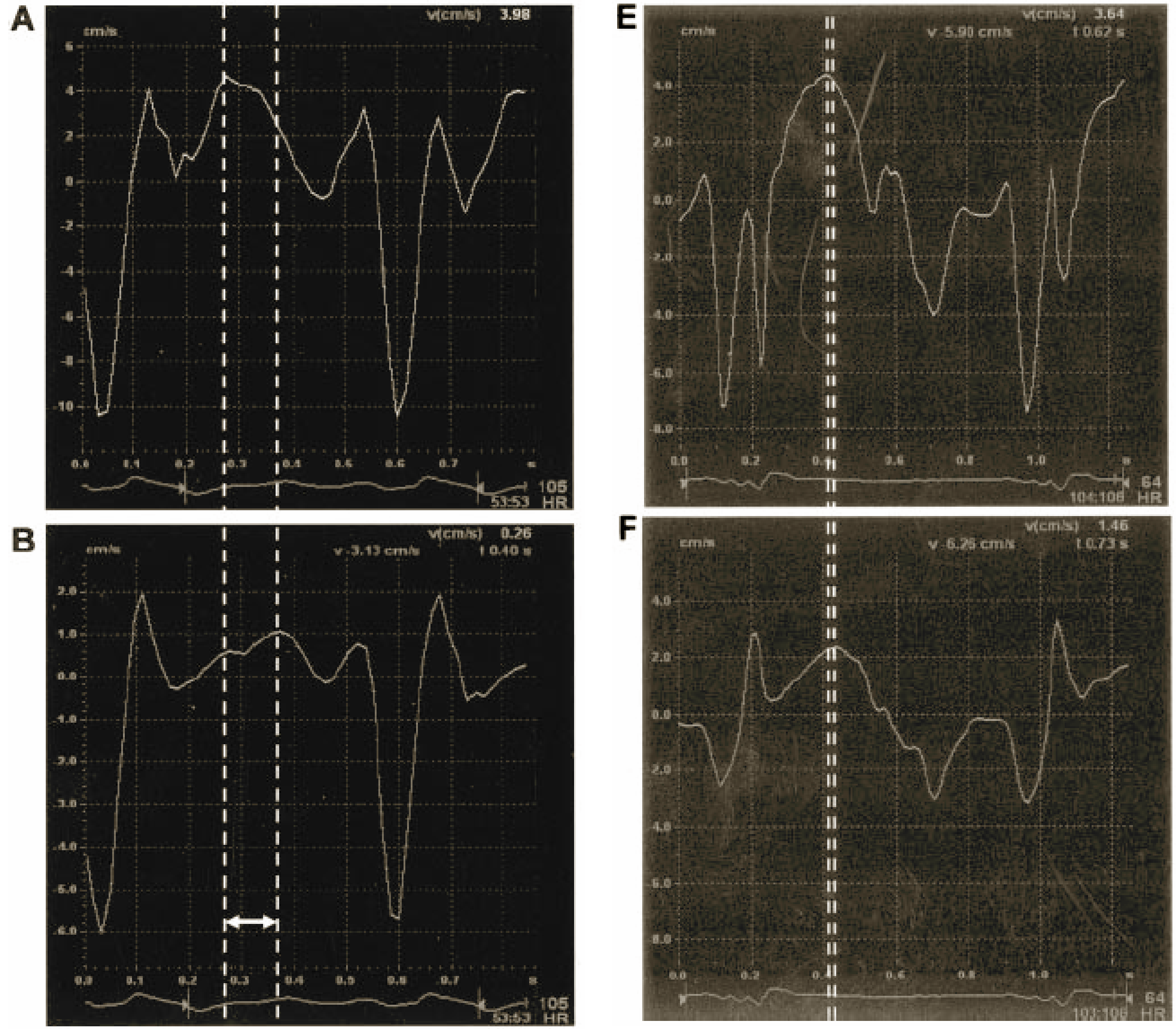
Detection of delayed longitudinal contraction

(J Am Coll Cardiol 2002;40:723-30)

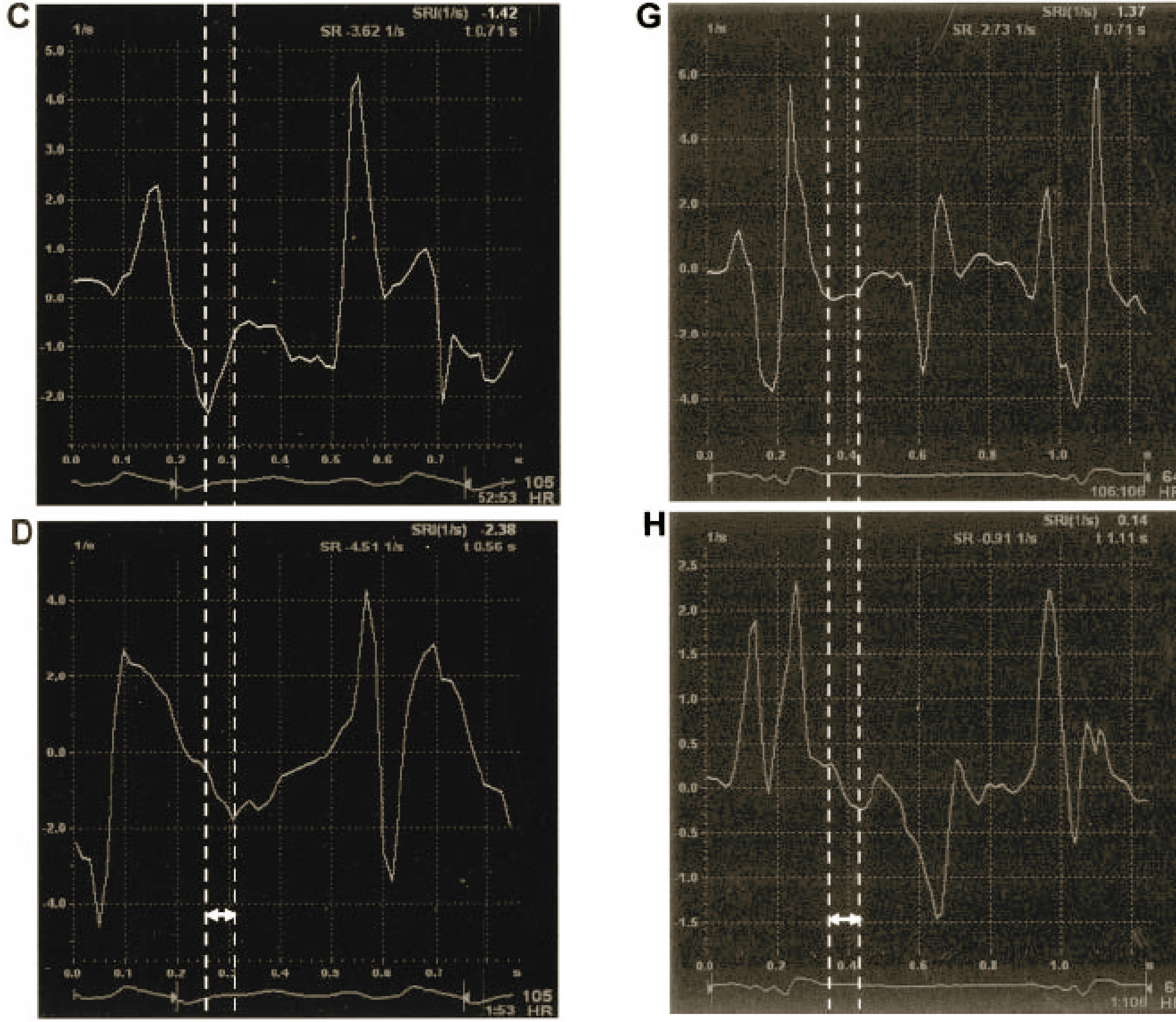




TDI is superior to SRI ?



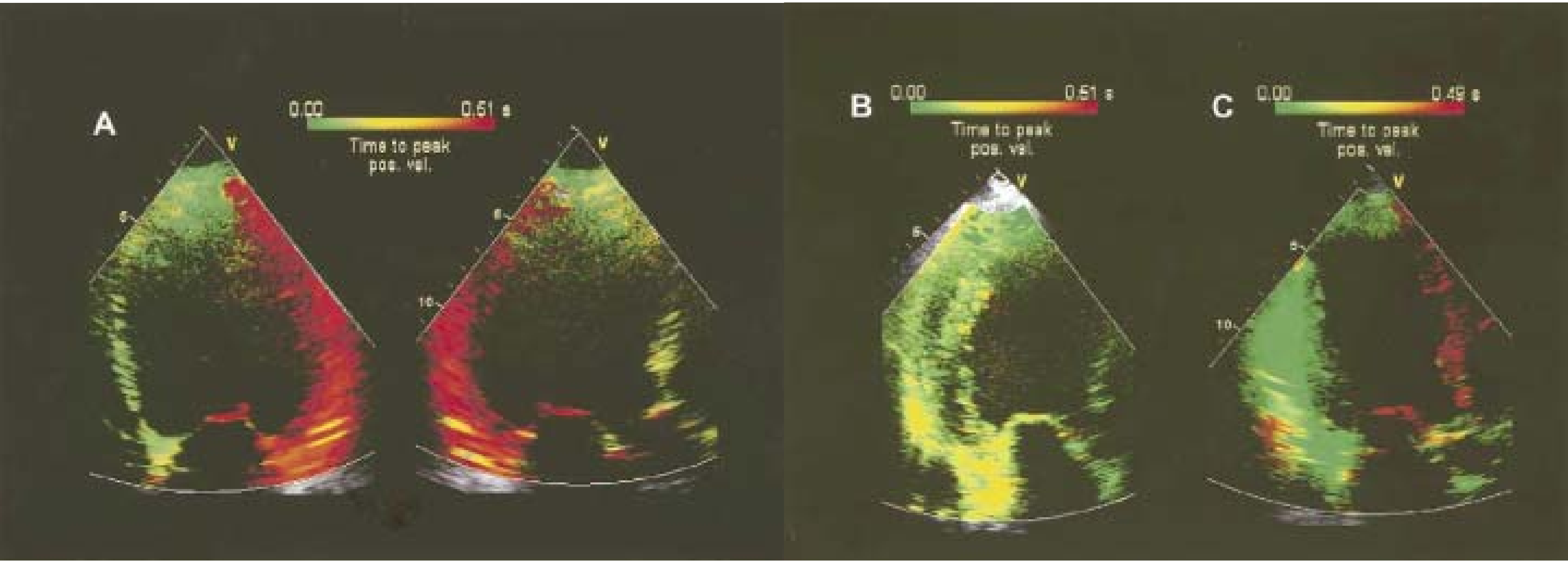
- Analyses of TDI in a patient. Before CRT, peak contraction of basal septal segment (A) is 102ms earlier than basal lateral segment (B). After CRT, nearly exact timing of peak contraction in 2 segments (E & F).



- Analyses of SRI in same patient. Before CRT, there is a 38 ms lateral wall delay in peak strain rate (C & D). After CRT, basal lateral segment remains delayed over septal segment by 48 ms.

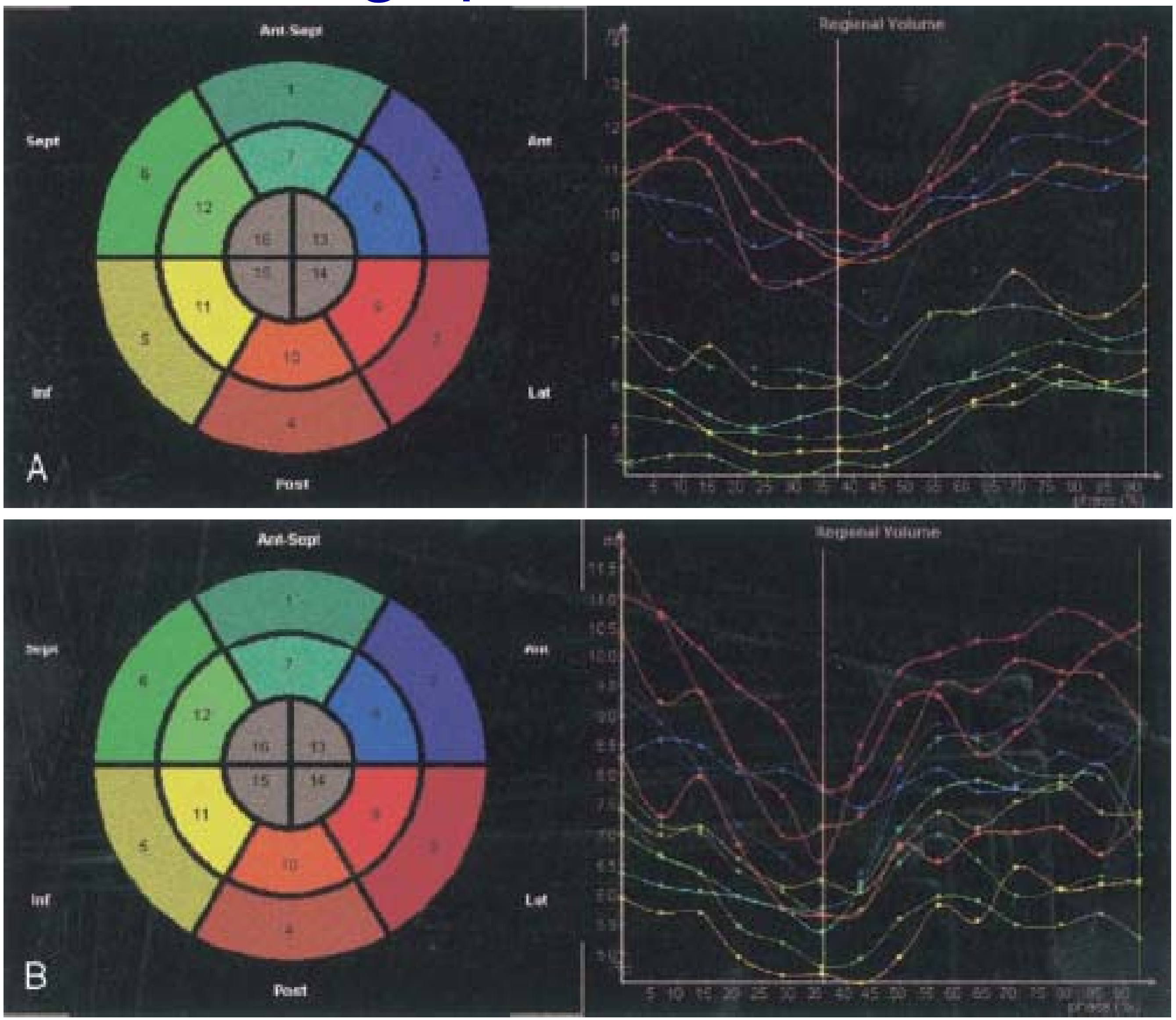
(Circulation 2004;110:66-73)

Tissue synchronization imaging



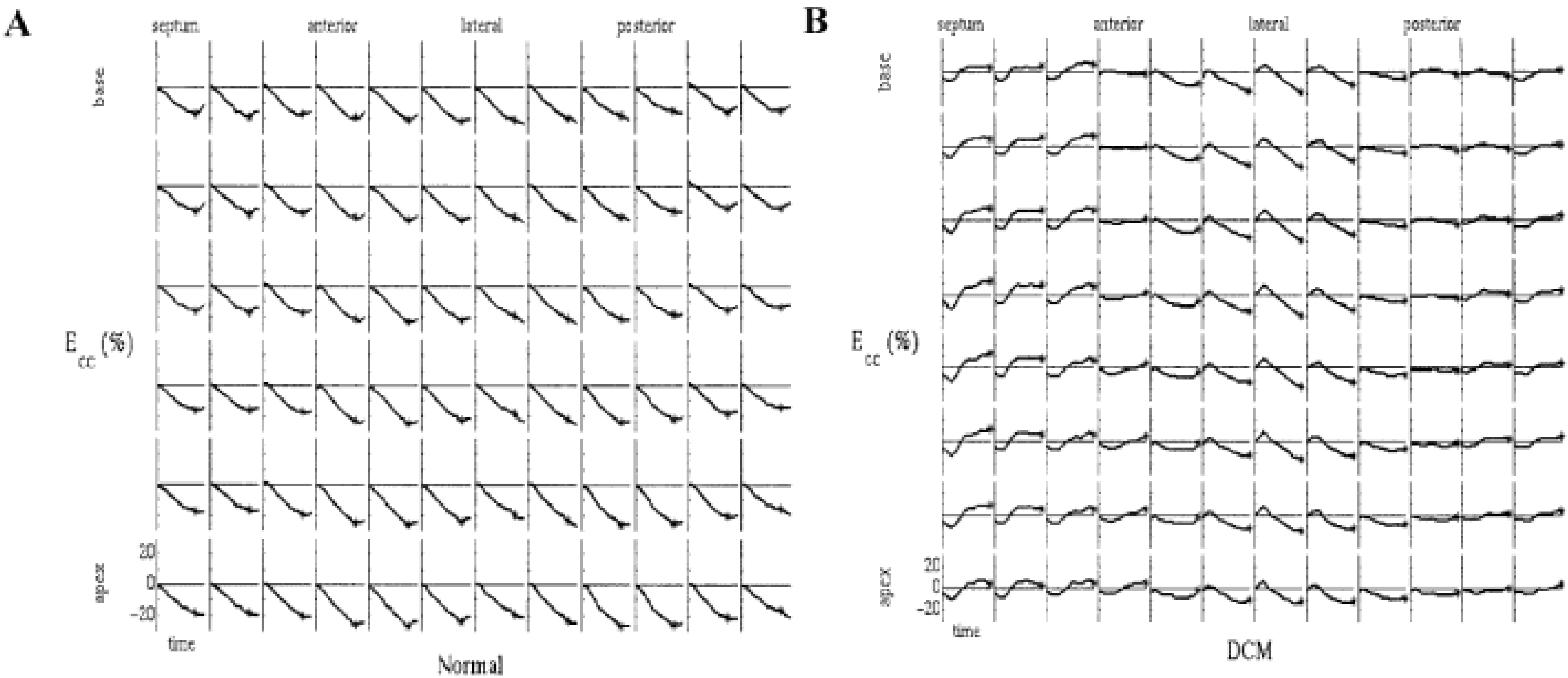
(A) Apical 4 chamber view (left) and apical long axis view (right) from the same patient, before CRT. (B) Apical long axis view from a patient who had no acute response to CRT, demonstrating no significant delay in anteroseptal and posterior walls. (C) Apical long axis view from a different patient with no response to CRT, demonstrating a reversed delay in the anterior septum rather than the posterior wall.
(Am J Cardiol 2004;93:1178-81)

3D echocardiographic method



(A) Regional volumetric curves of 12 segments in a patient showing asynchronous LV contraction in CRT-off mode. (B) The same patient showing reduction of LV asynchrony in CRT-on mode. (Am J Cardiol 2995;95:126-9)

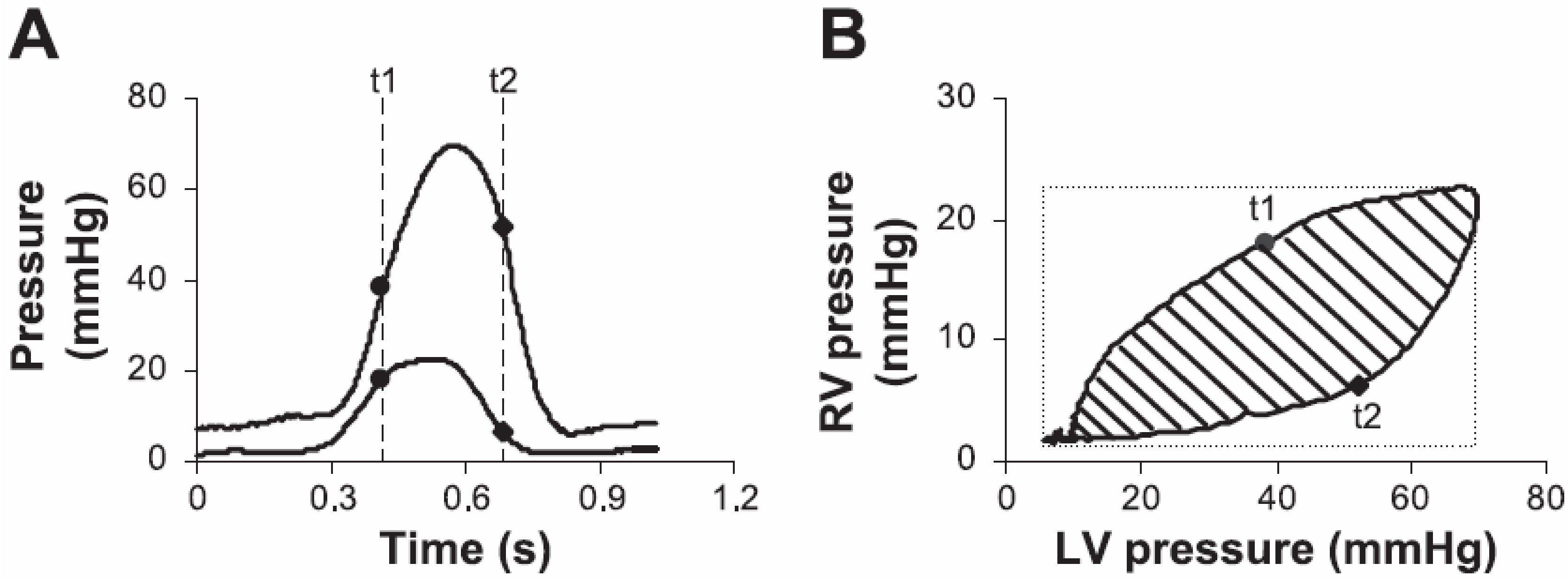
Tagged MRI method



- Representative strain maps derived by TMRI for representative control (A) and DCMP (B) hearts are shown. DCMP heart displays marked regional variability in magnitude and temporal strain pattern.
- The time of maximal negative Ecc(circumferential strain) was determined for the whole ventricle. Strains at all sites were assessed at this time (yielding Ecc*). The coefficient of variation of these strains ($CV_{Ecc^*}=SD_{Ecc^*}$/mean $Ecc^* \times 100\%$) indexed dyssynchrony.

(Circulation 2000;101:2703-9)

Normalized pressure-pressure (NPP) loop



- (A) Simultaneous recordings of LV(top) and RV(bottom) pressures during one cardiac cycle. The RV pressure changes precede those in the LV. (B) PP loop made from the pressure traces in A by plotting the RV pressure (y-axis) against the LV pressure (x-axis).
- Npp loop area =

  PP loop area / [LVPmax-LVPmin)×(RVPmax-RVPmin)]

(Am J Physiol Heart Cir Physiol 2003;285:H2788-96)

Studies of cardiac resynchronization therapy in children

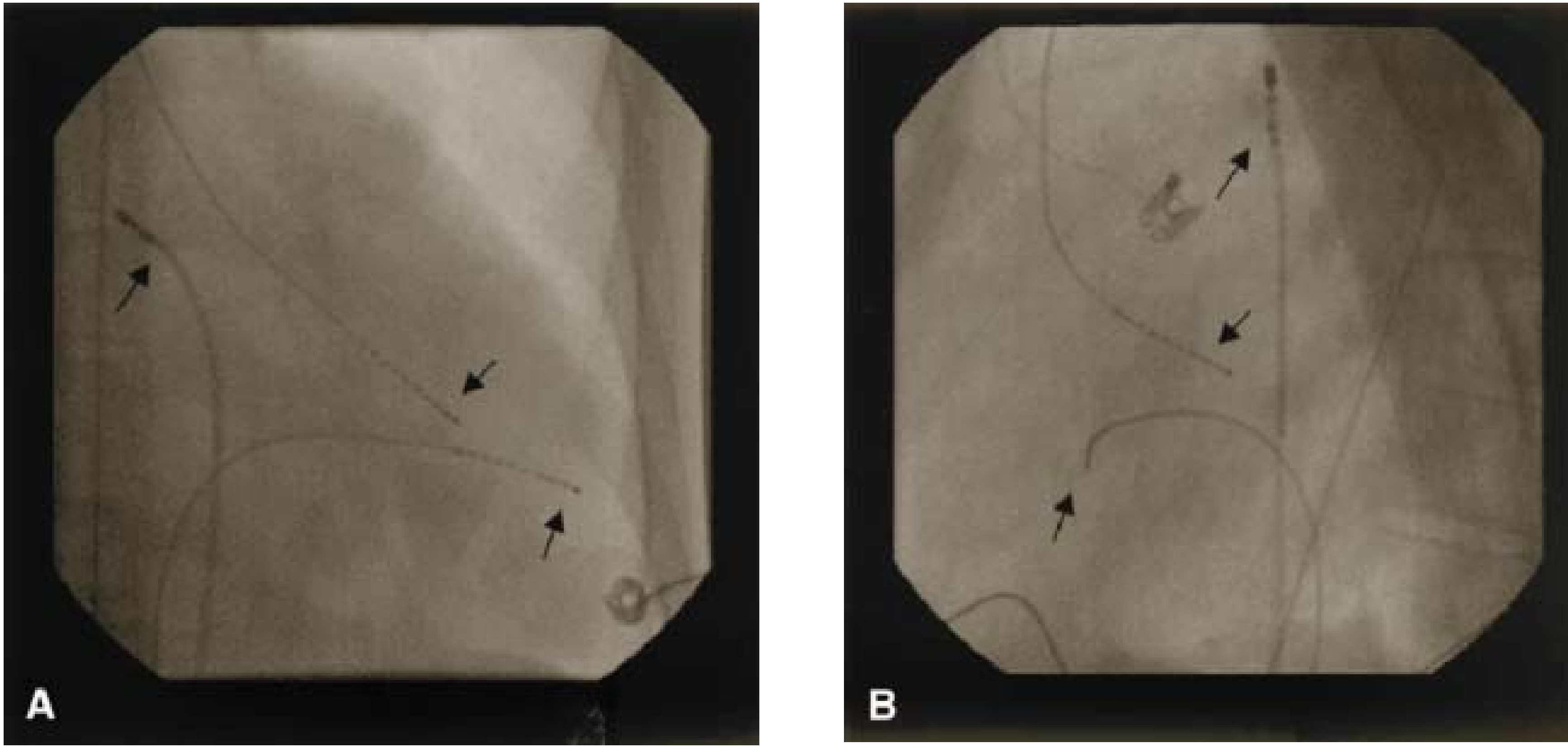
Janousek J et al. Am J Cardiol 2001;88:145-52

- Patients : 20 Children aged 3.4 months to 14 years, studied 1 to 120 hours after arrival to ICU from surgery for congenital heart defects.
  - Atrioventricular &/or inter/intraventricular dyssynchrony
  - Need for inotropics
- Diagnosis : TOF(8), TGA(1), truncus arteriosus(2), AVSD(3), DORV(3), VSD(2), pulmonary atresia(1)
- Dyssynchrony evauation method : QRS duration
- Benefits : Arterial systolic & mean pressure ↑, Pulse pressure ↑
- Follow up periods : 3 hours ~ 45 days

Senzaki H et al.
J Thorac Cardiovasc Surg 2004;127:287-8

- Patient : 18 year old man with asplenia sydrome. BCPS had been performed when he was 8 years old, but this was reversed because of anastomosis site aneurysm formation. After that he was repeatedly hospitalized because of worsening heart failure associated with AV regurgitation and cyanosis. QRS duration 180msec

- Benefits : ejection fraction (20→45%), dP/dt (321mmHg/s ↑), end systolic elastance (5.7→10mmHg/cm^2), aortic pressure (19mmHg ↑), NYHA class IV→II

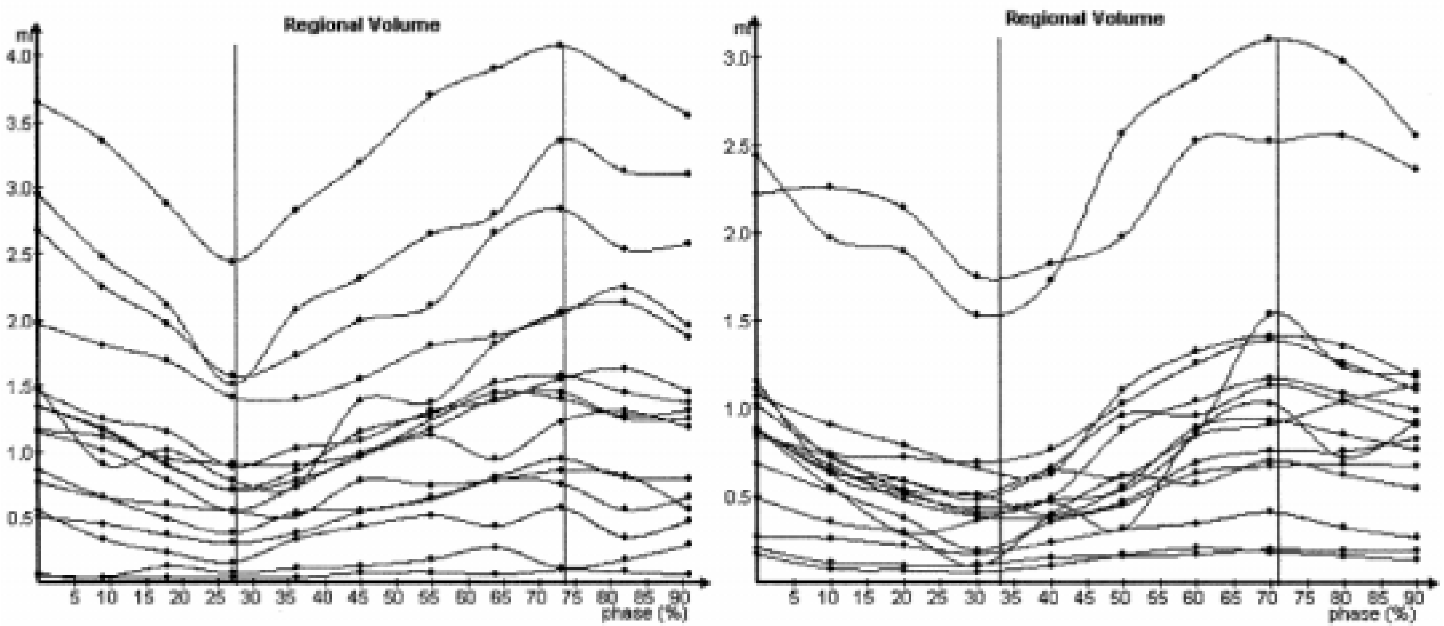


- Biventricular pacing sites : right and left side of ventricle, selected by determining which epicardial site provided the maximal rise in aortic pressure.

A : AP veiw, B : lateral view, arrows : leads

Bacha EA et al.
Ann Thorac Surg 2004;78:1678-83

- CRT after single ventricle palliation surgery
- Dyssynchrony evaluation method : real time 3D echocardiography
- Index of asynchrony : standard deviation of the mean time from end-diastole (maximum volume status) to end ejection (minimum volume status)



Asynchrony index: 4.2

Asynchrony index: 2.8

Surgery	Diagnosis Dx	Number of Patients	Mean Age (mo)	Mean POD	Mean QRS Pre (ms)	Mean QRS Post (ms)	Mean SBP Pre (mm Hg)	Mean SBP Post (mm Hg)	Mean CI Pre ($L \cdot min^{-1} \cdot m^{-2}$)	Mean CI Post ($L \cdot min^{-1} \cdot m^{-2}$)	Mean % Change CI
Norwood	HLHS	4	0.6	1	87	70	60	68	2.7	3.1	17
BDG	HLHS/other SV	9	7.1	2.1	88	72	96	104	3.5	4.1	15
Fontan	HLHS/other SV	8	27.5	4.2	96	71	83	89.5	2.8	3.1	12.3
Fontan revision	SV	3	80	1	97	73	94	102	3.5	4.1	17.5
SVR	HLHS, sp Fontan	1	48	1	120	80	110	110	5.1	6.3	23.8
BTS	TA, PA	1	12	5	90	70	68	72	3.8	4.4	16
Mean			28.7	2.6	93.9	71.7	86.3	93.8	3.2	3.7	15.1
SD			35.3		17.5	10.8	20.0	20.2	0.86	1.0	9.4
p value						<0.001		<0.001		<0.001	

BDG : bidirectional Glenn, BTS : Blalock-Taussig shunt,
CI : cardiac index,
POD : postoperative day,
Pre : preoperative,
SVR : semilunar valve replacement

Abdel-Rahman U et al. Pediatr Cardiol 2002;23:553-4

- Patient : 6 month old infant with TOF complicated by LPA atresia. After corrective operation, weaning from extracorporeal circulation was impossible due to LV output failure based on rhythm disturbances and reduced LV function with a dilated LV. And intermittent complete AV block was present.

- Benefits : successful weaning from extracorporeal circulation.
- Follow up periods : 5 days

Zimmerman FJ et al. Ann Thorac Surg 2003;75:1775-80

- Patients : 29 Children aged 1 week to 17 years, undergoing surgery for congenital heart diseases
  - Whose QRS duration greator than the upper limits for age.
  - Expected to develop Bundle branch block or interventricular block as a result of the planned surgery.

- Diagnosis : HLHS (5), SV, Fontan candidate (6). DORV (2), tricuspid atresia, TOF (6), AVSD, VSD (2), valve repair (3), Ross Op (2)

- Dyssynchrony evauation method : QRS duration

- Benefits : systolic BP ↑, cardiac index ↑
- Follow up periods : 20 minutes

Roofthooft MTR et al. PACE 2003;26:2042-4

- Patient : A 2 months year old girl.

  Initial diagnosis was coarctation of aorta, subaortic AS, arch hypoplasia, and VSD. At the age of 3 weeks, corrctive operation underwent. The postoperative course complicated by a CAVB and a permanent DDD pacemaker implanted. She discharged in good condition, but was readmitted 3 weeks later for congestive heart failure.

- Dyssynchrony evauation method :

  M-mode echocardiography.

- Benefits : subjective symptoms improved, improved mitral regurgitation, ejection fraction ↑
- Follow up periods : 6 months

Blom NA et al.
J Cardiovasc Electrophysiol 2003;14:1110-2

- Patient : A 6 year old boy presented with heart failure after surgery. Initial diagnosis was multiple VSD and severe MR. During the 1st year of life, a PAB procedure was performed. At age 2 years, corrective surgery (MVR included) was done. 6 Months later, 3rd operation for residual apical VSD closure was done. Over the following years, he developed congestive heart failure
- Dyssynchrony evauation method : septal-to-lateral delay through TDI

- Benefits : subjective symptoms improved, compensatory growth, ejection fraction ↑, LVEDD↓
- Follow up periods : 1 year

Strieper M et al. Am J Cardiol 2004;94:1352-4

TABLE 1 Patient Characteristics

Patient Number	Age at Transplant (yrs)/Sex	Patient Length of f/u Post Implant (mo)	Cardiac Disease	Electrical Diagnosis	Length of Pacing Pre CRT (mo)	LV Leads	Clinical Status (post CRT)
1	2.3/F	13	ALCA/MVR	SCHB	–	Epicardial	Alive
2	4.3/M	8	TOF	SCHB	45	Epicardial	Alive
3	5.1/F	19	d-TGA/VSD/PS	SCHB	41	Epicardial	Alive
4	7.3/M	—	ASD	SCHB	24	Epicardial	Died
5	13.8/M	22	PA/VSD	SCHB	117	Endocardial	Alive
6	16.4/M	4	VSD	RBBB	–	Endocardial	HT
7	28/F	72	l-TGA/VSD	SCHB	96 VVIR 96 DDD	Endocardial	Alive

ASD = atrial septal defect; ALCA = anomalus left coronary artery; d-TGA = transposition great arteries; F/u = follow-up; HT = heart transplant; LV = left ventricular; MVR = mitral valve replacement; PA = pulmonary atresia; PS = pulmonary stenosis; RBBB = right bundle branch block; SCHB = surgical complete hear block; TOF = tetralogy of Fallot; VSD = ventricular septal defect.

TABLE 2 Electrocardiographic and Echocardiographic Parameters

Patient Number	QRS Duration (ms)		LVEDd (cm)			LVEDs (cm)			EF (%)		
	Pre	Post CRT	Pre	Acute	Late	Pre	Acute	Late	Pre	Acute	Late
1	160	80	3.8	3.7	3.4	3.2	3.4	2.3	35	22	68
2	320	100	5.0	4.4	5.2	4.9	4.2	4.2	6	11	23
3	120	120	6.2	4.6	4.8	5.7	3.9	4.3	17	24	37
4	280	120	5.8	5.8	—	5.5	5.5	—	14	16	Died
5	240	150	7.6	6.2	4.8	7.2	5.6	4.4	12	26	22
6	220	180	6.7	6.6	6.7	5.8	6.0	6.6	28	25	03
7	160	150	7.0	6.5	6.7	6.5	4.9	4.8	10	28	20
Mean	208*	117*	5.9†	5.2	4.8†	5.5‡	4.6	3.9‡	16‡	23	36‡
95% CI	144–281	84–164	4.7–7.1	4.0–6.4	3.6–6.1	4.5–6.5	3.5–5.6	2.8–5.1	5–26	13–34	18–54

*p <0.03; †p = 0.05; ‡p <0.05.
CI = confidence interval; EF = ejection fraction; LVEDd = left ventricular end-diastolic dimension; LVEDs = left ventricular end-systolic dimension.

Janousek J et al. J Am Coll Cardiol 2004;44:1927-31

Pt. No.	Age (yrs)	Diagnosis	Previous Surgical Procedures	Concurrent Surgical Procedures	NYHA Functional Class	Baseline Rhythm	QRS (ms)	LV Lead	RV Lead
1	13	TGA, VSD	Senning, patch, PA banding	PA debanding	II	RBBB	140	—	RAS, RPL
2	10	CTGA, VSD, TV regurgitation	—	Patch, TV plasty	II	3°AVB/DDD	140	LAL	RAL, RPL
3	22	TGA	Senning	—	II	3°AVB/DDD	180	LMVS	RAL, RPL
4	12	TGA, VSD	Senning, patch	PA banding	II	3°AVB/DDD	190	LMVS	RL
5	29	TGA	Mustard	—	III	1°AVB, RBBB	150	LMVS	RL, RP
6	18	CTGA, VSD, PS, TV regurgitation	Patch, TV replacement, LV-PA conduit	—	II	3°AVB/DDD	180	LVA	RL
7	9	CTGA, TV regurgitation	—	TV replacement	II	3°AVB/DDD	170	LL	RL
8	7	DORV, ventricular inversion	Kawashima	Pacing lead revision	II	3°AVB/DDD	140	LVA	RL

AVB : AV block, CTGA : corrected TGA, LAL : left anterolateral, LL : left lateral, LMVS : left mid-ventricular septum, LVA : LV apex, RAL : right anterolateral, RAS : right anteroseptal, RL : right lateral, RP : right posterior, RPL : right posterolateral

Acute Hemodynamics Effects of CRT

Parameter	CRT Off Mean (SD)	CRT On Mean (SD)	% Change	p Value
QRS interval (ms)	161 (21)	116 (22)	−28.0	0.002†
Interventricular mechanical delay (ms)	median 60	median 50	−16.7	0.047‡
Dyssynchrony index (ms)	138 (59)	64 (21)	−53.6	0.042†
RV filling time (% RR)	45.1 (6.5)	50.0 (6.1)	10.9	0.002†
Tei index	median 0.65	median 0.60	−7.7	0.008‡
RV +dP/dt (mm Hg/s)	630 (142)	919 (211)	45.9	0.007†
Aortic VTI (cm)	17.2 (6.2)	18.4 (6.8)	7.0	0.028†
RV EF (%)*	41.5 (8.1)	45.5 (6.4)	9.6	0.04†

*Measured at a median of 3.8 months after initiation of CRT; †paired *t* test; ‡Wilcoxon signed rank test.

CRT = cardiac resynchronization therapy; EF = ejection fraction; RR = RR interval; RV = right ventricular; SD = standard deviation; VTI = velocity-time integral.

Mid-Term Changes Associated With CRT

	Prior to CRT Mean (SD)	End of Follow-Up Mean (SD)	% Change	p Value
TV regurgitation (grade)	2.1 (1.0)	1.6 (1.4)	—	NS†
RV end-diastolic area (cm^2/m^2 BSA)	27.3 (5.4)	28.4 (7.0)	4.0	NS†
RV fractional area of change (%)	median 18.1	median 29.5	63.0	0.008‡
NYHA functional class	2.0	1.3	—	0.008‡

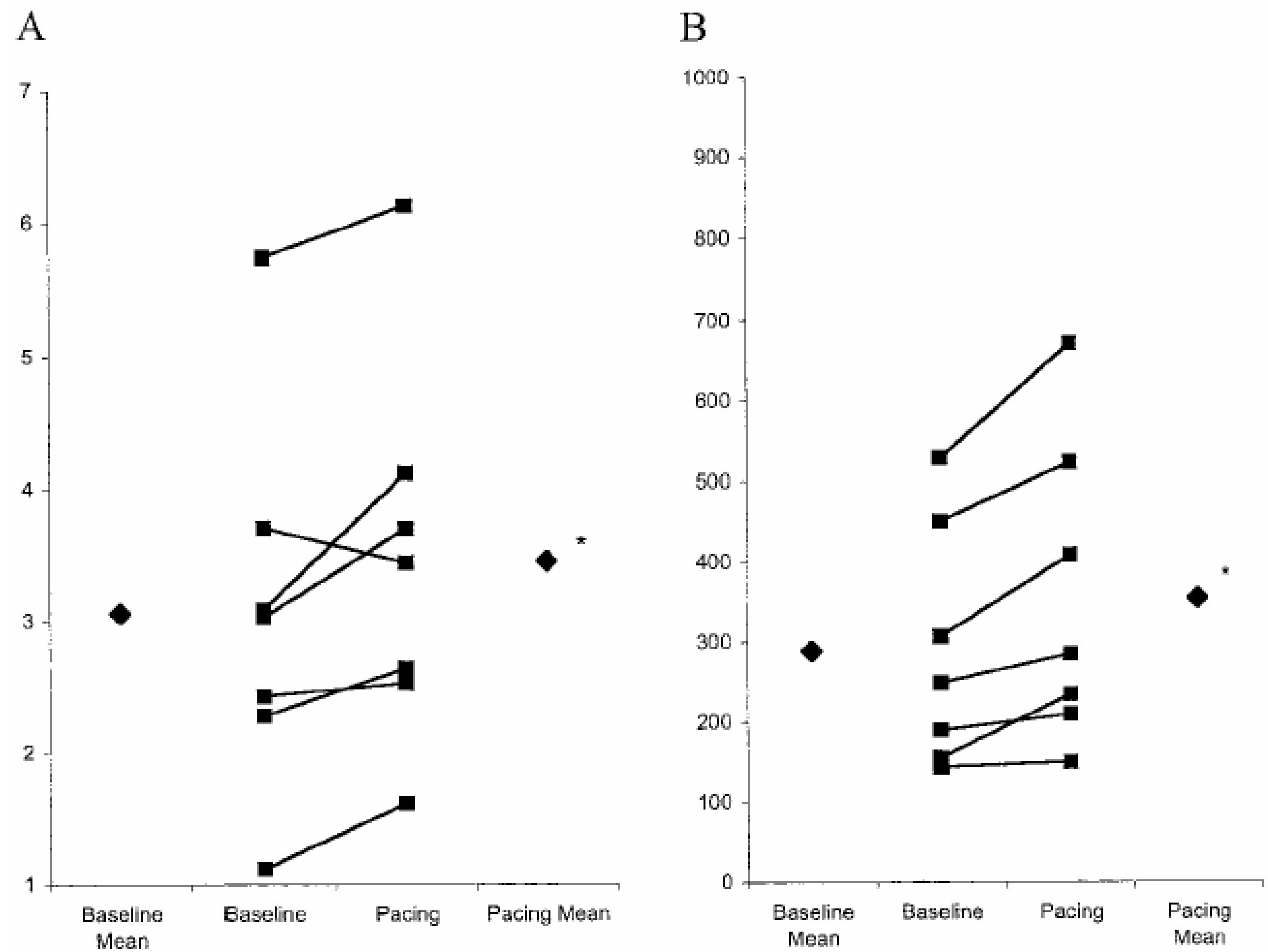
BSA = body surface area; NS = not significant; other abbreviations and footnotes as in Tables 1 and 2.

Dubin AM et al. Circulation 2003;107:2287-9

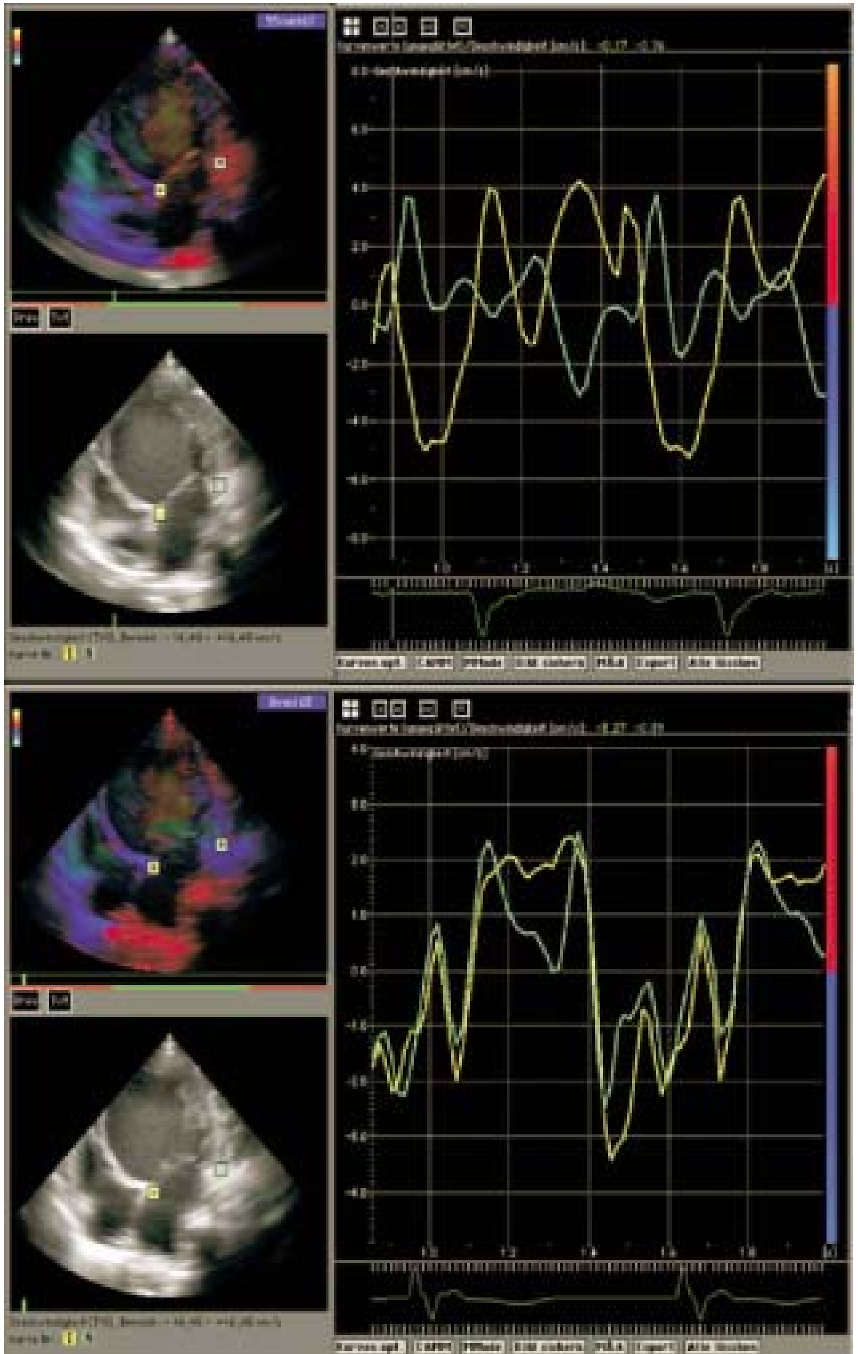
- 7 Patients (4 males)
- Diagnosis included TOF and AS status after Ross procedure.
- RBBB, sinus rhythm RV dysfunction

Baseline Characteristics and Hemodynamic Data of Study Subjects

	Mean (SD)	Minimum	Maximum
Age, y	23.6 (18.7)	1.7	53
Height, cm	147 (42)	70	178
Weight, kg	66.5 (38)	9.3	81
Baseline cycle length, ms	828 (123)	590	1000
QRS duration, ms	166 (39)	140	200
Hemoglobin, gm/dL	13.2 (2.8)	10	17
NYHA class	2–4	2	4
Cardiac index, L/min per m^2	2.85 (1.19)	1.12	4.60
Systolic blood pressure, mm Hg	114 (23)	90	148
Diastolic blood pressure, mm Hg	69 (14)	54	88
RV peak pressure, mm Hg	54 (36)	26	130
RV/LV ratio	0.47 (0.25)	0.18	0.94
RV minimum pressure, mm Hg	4 (5)	0	12
RV end-diastolic pressure, mm Hg	14 (9)	5	28
RV dP/dt_{max}, mm Hg/s	289 (151)	149	548



Change in cardiac index (A) and dP/dt (B) achieved with DOO pacing as compared with AOO pacing.
Cardiac index in L/min/m^2, dP/dt in mmHg/sec



Nurnberg JH et al. Z Kardiol 2005;94:44-8

- Patient : 9 year old boy(height 140cm, weight 30kg) with dilated cardiomyopathy.

Tissue Doppler echocardiography	Before CRT	After CRT	Effect
Interventricular delay [ms]	17	2	+
LV lateral s-wave [cm/s]	0.33	0.32	=
LV septal s-wave [cm/s]	2.2	2.9	(+)
LV lateral e-wave [cm/s]	1.95	4.5	++
LV septal e-wave [cm/s]	2.2	5.6	++
LV Tei index	0.52	0.28	+
Exercise testing (Jones protocol)	**Before CRT**	**After CRT**	**Effect**
Capacity [w/kg]	1.8	2.1	(+)
VO_2 max [ml/min/kg]	21.8	30.9	+

Summary

- There are many methods to evaluate cardiac dyssynchrony. Evidence is accumulating that echocardiography, especially TDI may be the ideal technique to identify responders to CRT and to reevaluate the recipients

- CRT applications in children :
  - As a method of post-op care
  - As a alternate therapy for heart failure in children with single ventricle physiology and with systemic right ventricle.
  - To improve LV function in children, had conventional pacemakers.
  - As a RV function improving method in children with RV dysfunction.