Predictors of Good Responders of CRT : Role of Echo, MRI and CT

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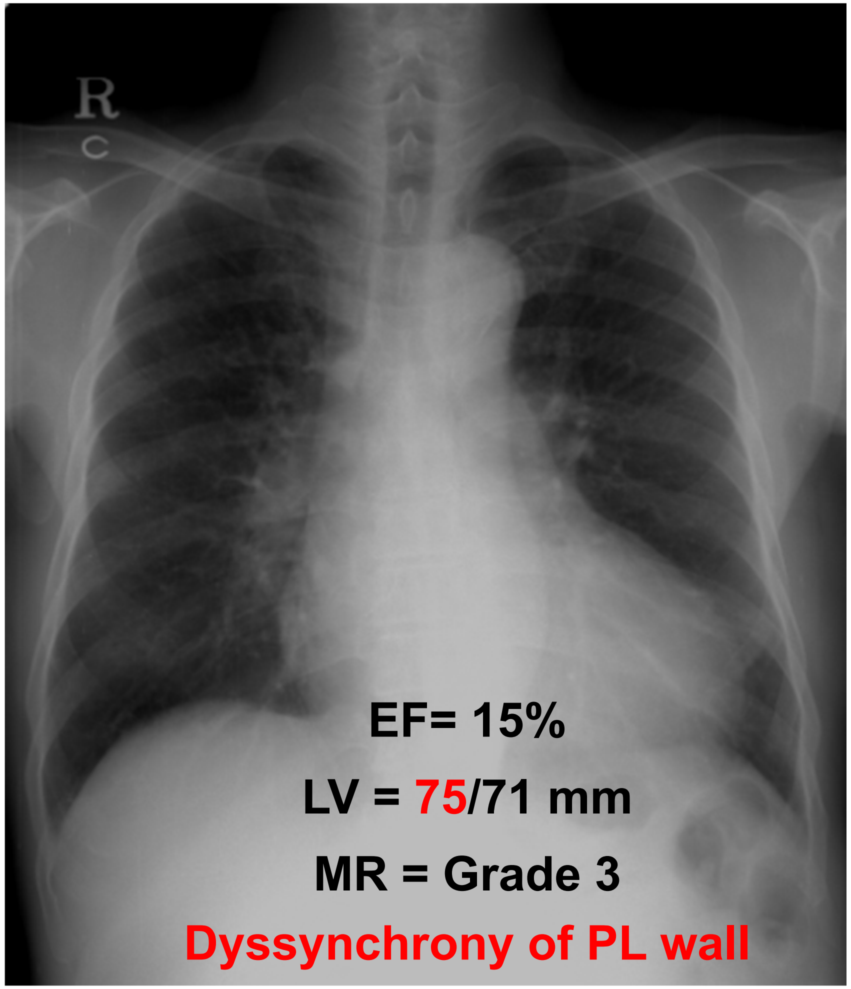
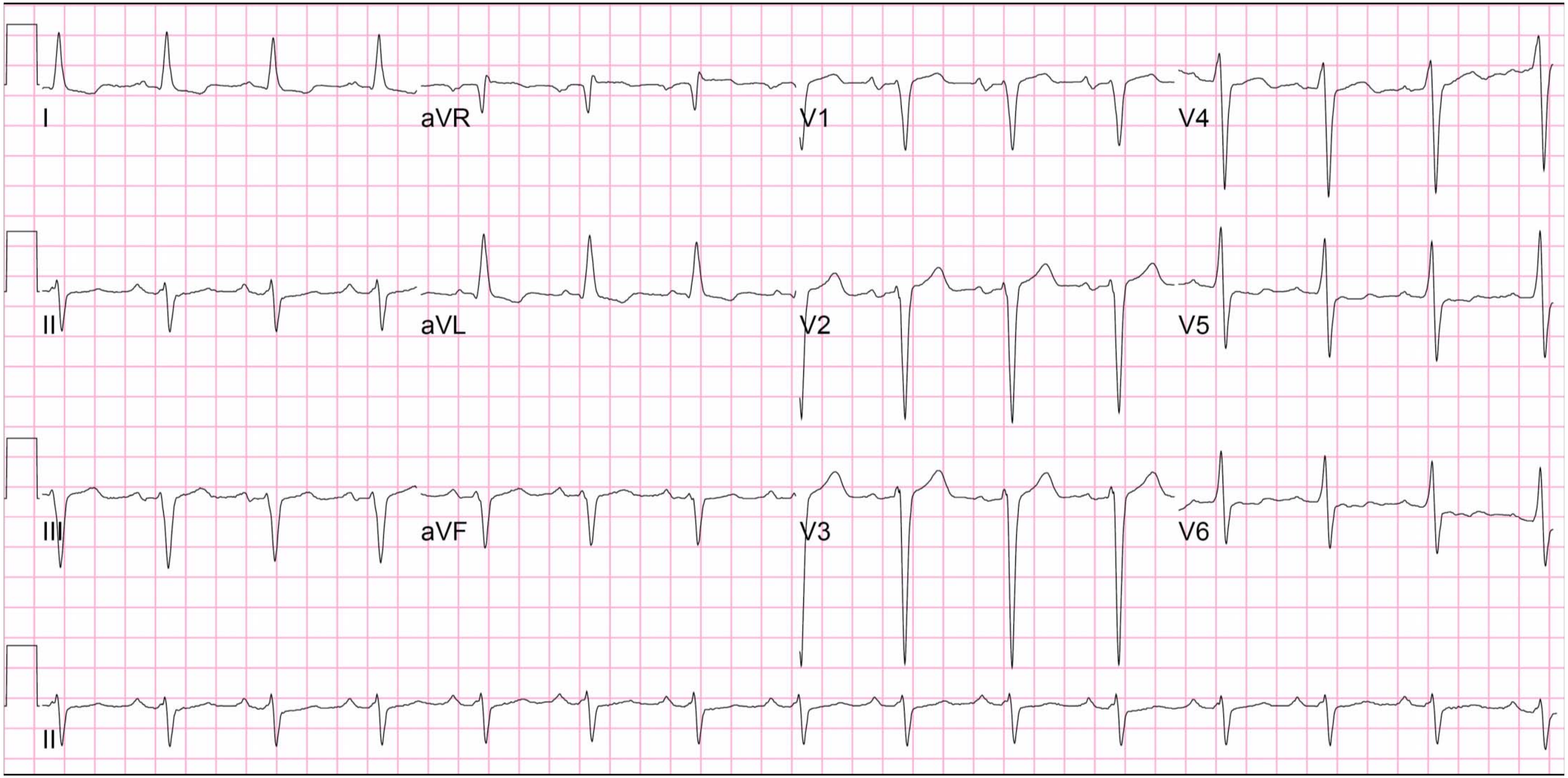
CASE

- **M/66**
- **Dyspnea/DOE for 5 years**
- **Hospital admissions**
  - ➢ **3 times/1 year**
- **Past History :**
  - ➢ **DCMP: 3 years**
  - ➢ **Hypertension : 20 years**
  - ➢ **Smoking : 40 pack years**
  - ➢ **Alcohol : Social drinking**
- **NT-proBNP 2,717 pg/mL**
- **Medication**
  - ➢ **Beta blocker, ACEI, Diuretics**



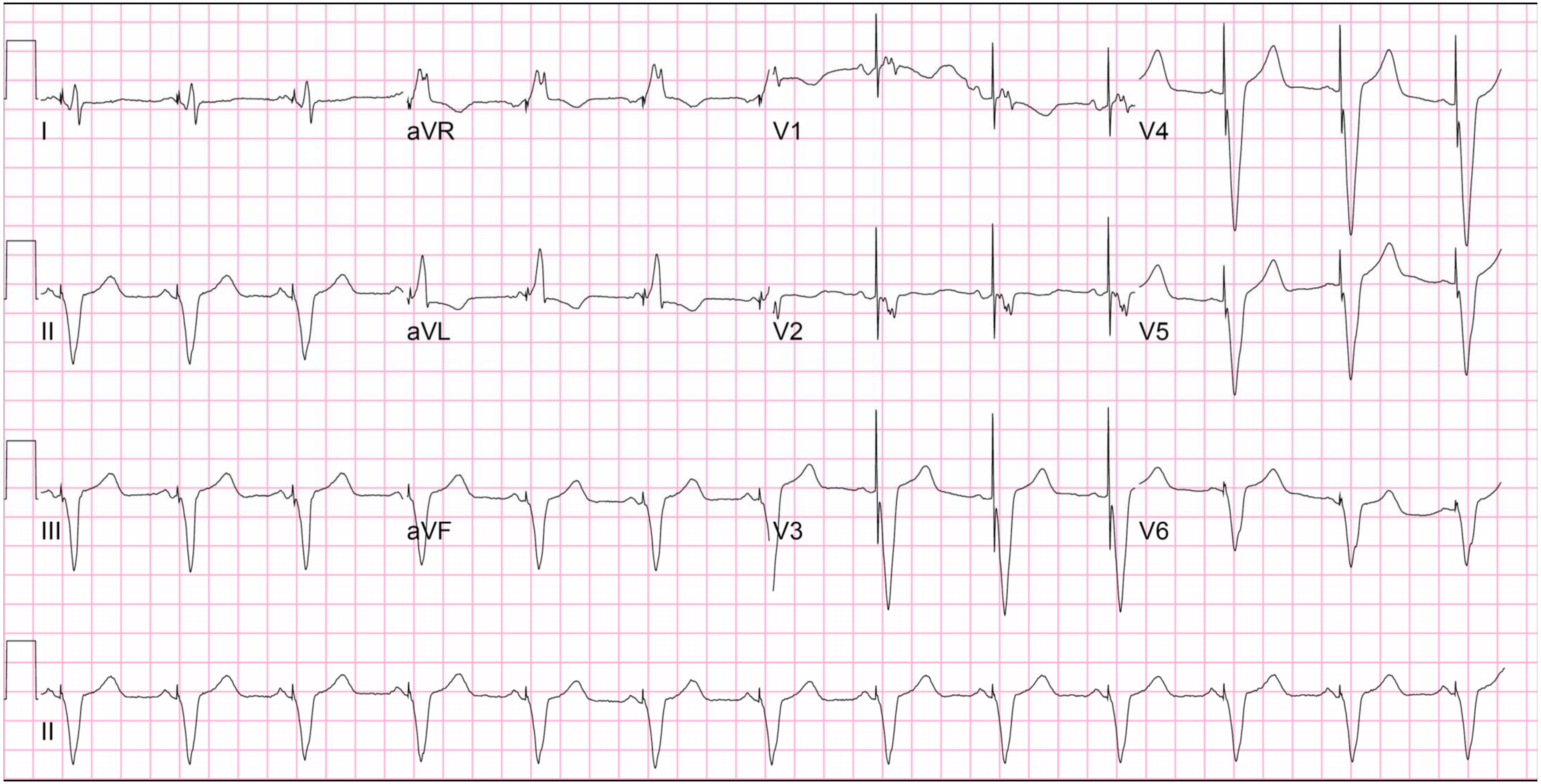
EKG

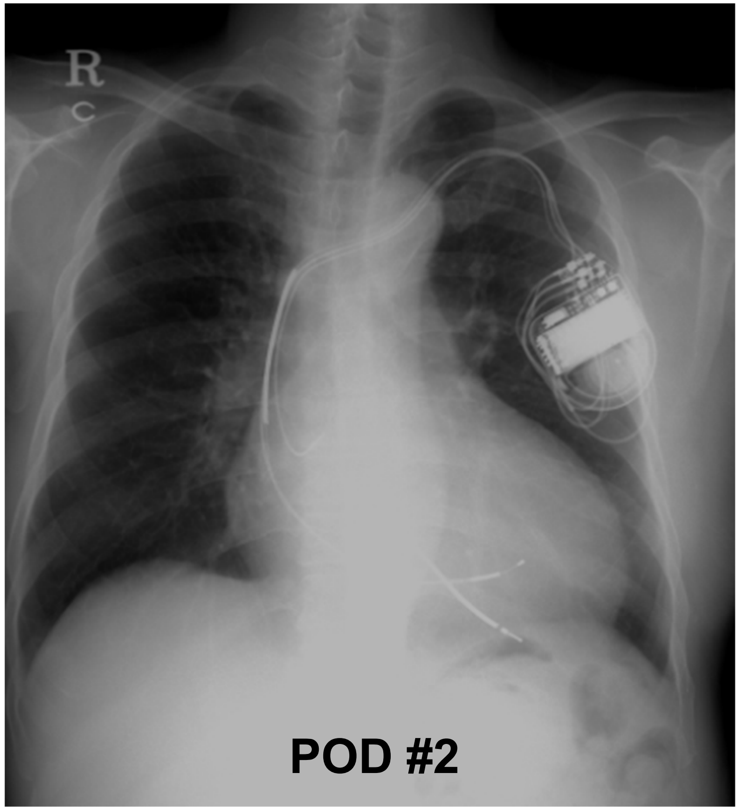
QRS =132 ms

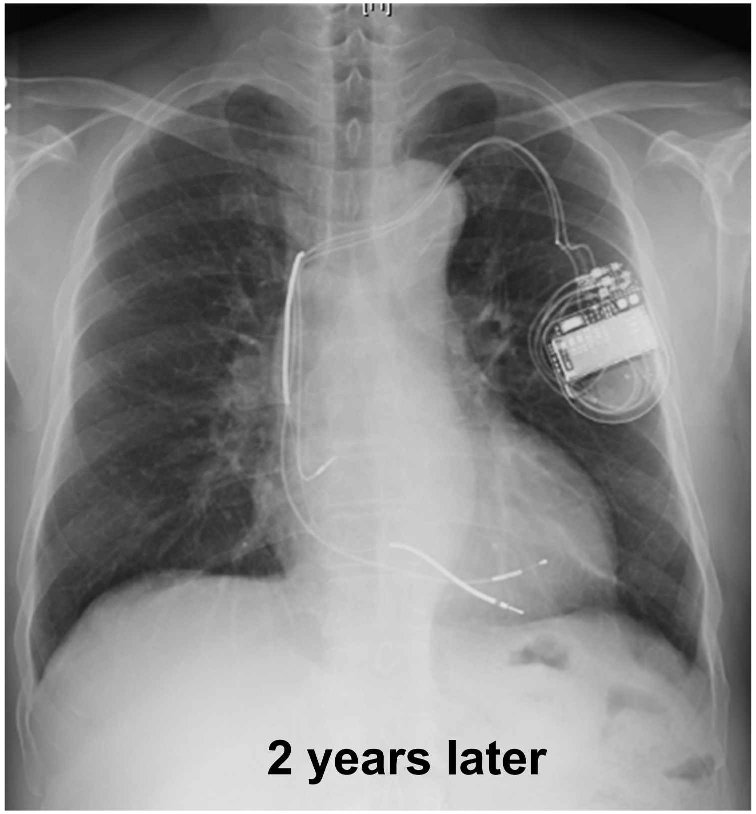


EKG after CRTD implantation

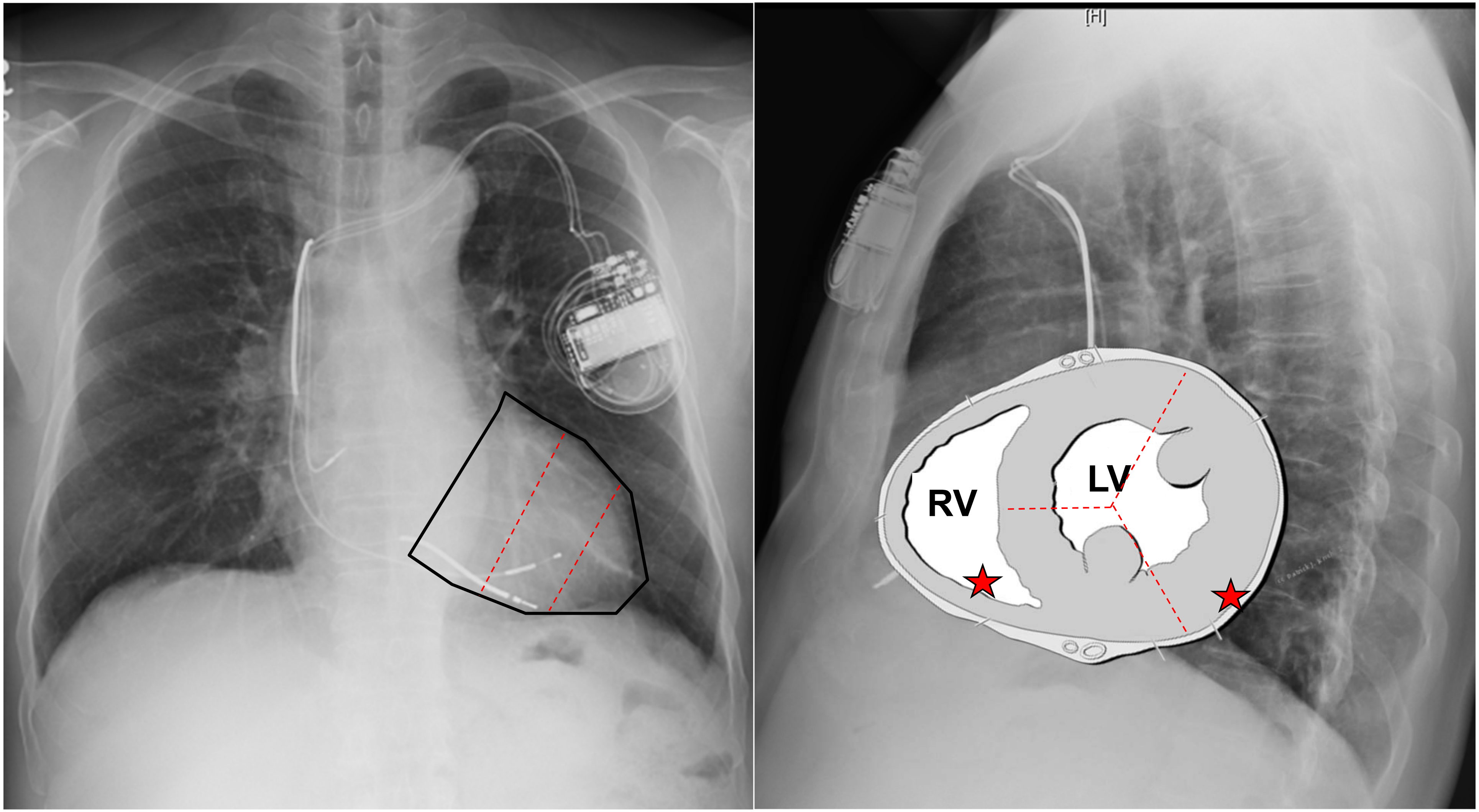
QRS 170 ms







Echocardiography	Before CRT	2 years later
QRS duration	132 mm	170 mm
LV ejection fraction	15%	39%
LVEDD/SD	75/71 mm	67/53 mm
Mitral regurgitation	Grade 3	Trivial
RVP	53 mmHg	19 mmHg


[H]
RV
LV

2008 AHA/ACC/ESC Indication

- Class 1
  - NYHA class III-IV
  - QRS > 120 ms
  - EF < 35%
  - Refractory to Medical Therapy
  - In Sinus Rhythm
- Class 2a
  - In AF or RV pacing induced

HF patients with wide QRS

- Morbidity and mortality -

- **COMPANION Study**
  - N = 1,520 (NYHA III-IV, LVEF ≤ 35%, QRS ≥ 120 ms)
  - ↓ Primary end point (death, hospitalization):
    - CRT (-19%, Hazard ratio 0.81, p=0.014),
    - CRT + ICD (-20%, Hazard ratio 0.81, p=0.014)
  - All cause mortality: Significant reduction in CRT + ICD
- **CARE-HF Study**
  - N = 813 (NYHA III-IV, LVEF ≤ 35%, LV ESD ≥ 55 mm, QRS ≥ 120 ms)
  - Primary end point (death, hospitalization):
    - CRT (39%), Medical (55%)

N Engl J Med 2004;350:2140-50.
N Engl J Med 2005;352:1539-49.

모든 환자가 CRT에 반응하는지?

CRT Non-responders

- **Prevalence:**
  - **30% by clinical or 40% by echo response of LV reverse remodeling**
- **Definition of Non-responders:**
  - **Acute hemodynamics: +dp/dt, pulse pressure**
  - **Functional: NYHA class/ 6 MHW/ Composite Clinical Score**
  - **Volumetric/ Echo: LVESV, EF, SV**
- ***Relatively lack of consensus!***

Prevalence of CRT Non-reponsers: Hemodynamics, clinical or volumetric

Author (Year)	N	FU period	Definition of responders	No. (%) of non-responders
Auricchio A (2002)	39	Acute	↑Pulse pressure > 5%	12/39 (31%)
Nelson GS (2000)	23	Acute	Δdp/dt ≥ 25%	6/22 (27%)
Alonso C (1999)	26	12 mo	Survivor, ↓NYHA ≥1 class, ≥ 10% VO2 max	7/26 (27%)
Reuter S (2002)	102	12 mo	↓NYHA & ↑QOL	18/102 (18%)
Abraham WT (2002)	228 (Rx arm)	6 mo	Clinical Composite response	75/228 (33%)
Young JB (2003)	187 (Rx arm)	6 mo	Clinical Composite response	62/187 (33%)
Stellbrink (2001)	25	6 mo	LVVs (ΔLVVs < 15%)	9/25 (36%)
Yu CM (2003)	30	3 mo	LVVs (ΔLVVs < 15%)	13/30 (43%)
Yu CM (2003)	54	3 mo	LVVs (ΔLVVs < 15%)	23/54 (43%)
Notabartolo (2004)	49	3 mo	LVVs (ΔLVVs < 15%)	20/49 (41%)

Predictors of Non-response to CRT

- Ischemic heart disease
- Severe mitral regurgitation
- LV end-diastolic diameter ≥ 75 mm
- Pre-implantation apical wall motion abnormality
- Posterolateral ventricular scar

Diaz-Infante E, et al. Am J Cardiol, 2005; 95: 1436–1440.
Buch E, et al. Heart Rhythm, 2007; 4: 1300–1305.

The Advantage of Echocardiography

Echo Predictors of CRT Response

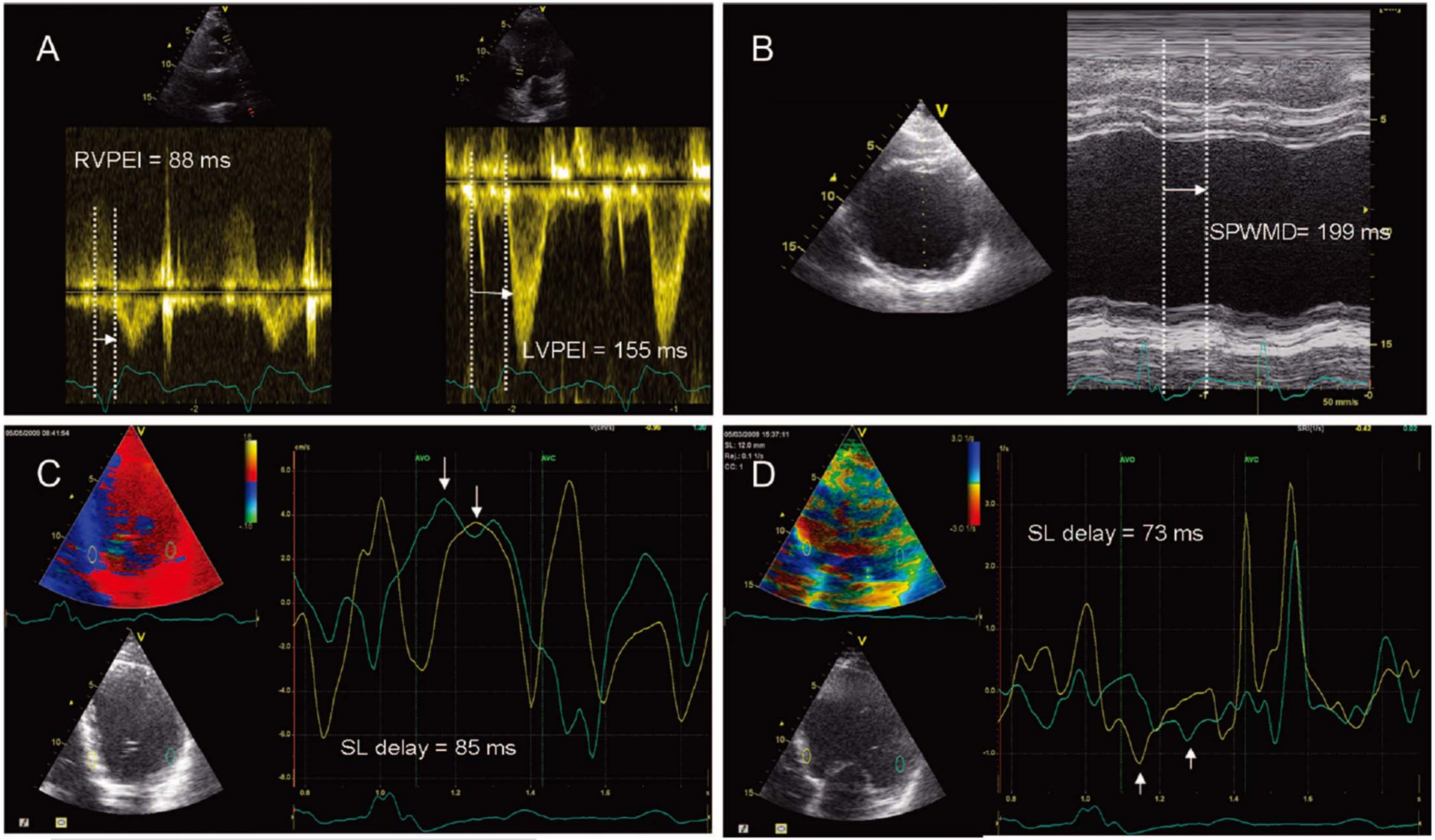
- American Society of Echo Dyssynchrony Guideline paper -

- **Inter-ventricular:**
  - **Doppler echo – IVMD > 40ms**
- **Radial delay:**
  - **M-mode – SPWMD > 130ms**
  - **2D Speckle tracking – Sept-to-post radial & delay > 130ms**
- **Longitudinal delay:**
  - **TDI – Septal-to-lateral delay > 65ms**
  - **TDI – Ts-SD of 12 segments > 33ms**
  - **TDI – Ts-Diff of 12 segments > 100ms**

- **IVMD: Interventricular mechanical delay**
- **SPWMD: septal-posterior wall motion delay**
- **Ts : the time to peak myocardial systolic velocity**

A. IVMD ≥ 40ms

B. SPWMD ≥ 130ms



C. Ts-(lateral-septal) > 65ms

C. Peak Strain Rate -(lateral-septal)

Delgado V, et al. Circulation 2011;123:640-655

Results of the Predictors of Response to CRT (PROSPECT) Trial

Eugene S. Chung, MD; Angel R. Leon, MD; Luigi Tavazzi, MD; Jing-Ping Sun, MD; Petros Nihoyannopoulos, MD; John Merlino, MD; William T. Abraham, MD; Stefano Ghio, MD; Christophe Leclercq, MD; Jeroen J. Bax, MD; Cheuk-Man Yu, MD, FRCP; John Gorcsan III, MD; Martin St John Sutton, FRCP; Johan De Sutter, MD, PhD; Jaime Murillo, MD

Interobserver and Intraobserver Variability Summary

Echocardiographic Measure	Intraobserver CV, %	Interobserver CV, %	Interobserver κ Coefficient*
SPWMD	24.3	72.1	0.35
Ts-SD	11.4	33.7	0.15
Ts-peak (basal)	15.8	31.9	0.25

An adjusted coefficient of variation (CV), defined as the ratio of the SD and the mean of absolute readings for each echocardiographic parameter.

Circulation 2008;117:2608-2616

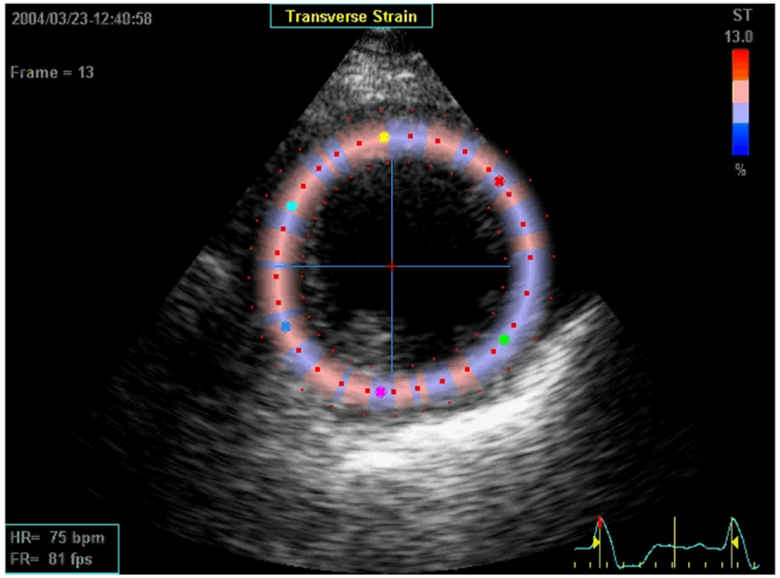
Echocardiography Type	Dyssynchrony Measure	Evaluable Echocardiograms, (yield) %	Sensitivity	Specificity	AUC	*P* for AUC
M mode	SPWMD	71.7	55.4	50.0	0.54	0.27
Pulsed Doppler	IVMD	92.4	55.2	56.4	0.58	0.013
	LVFT/RR	85.3	36.3	76.6	0.57	0.032
	LPEI	94.6	66.3	47.1	0.60	0.001
M mode+Doppler	LVEC	67.7	6.3	91.7	0.52	0.63
TDI, published	Ts (Lat-Sep)	66.8	42.4	56.9	0.50	0.85
	Ts-SD	50.0	74.1	35.8	0.60	0.034
	PVD	81.4	67.6	37.8	0.51	0.89
TDI+SRI	DLC	81.1	41.7	60.4	0.51	0.75
TDI, median value used as cutoff	Ts-peak displacement	37.4	54.8	56.1	0.56	0.32
	Ts-peak basal	82.0	51.9	53.8	0.55	0.19
	Ts-onset basal	82.0	54.1	60.4	0.58	0.047

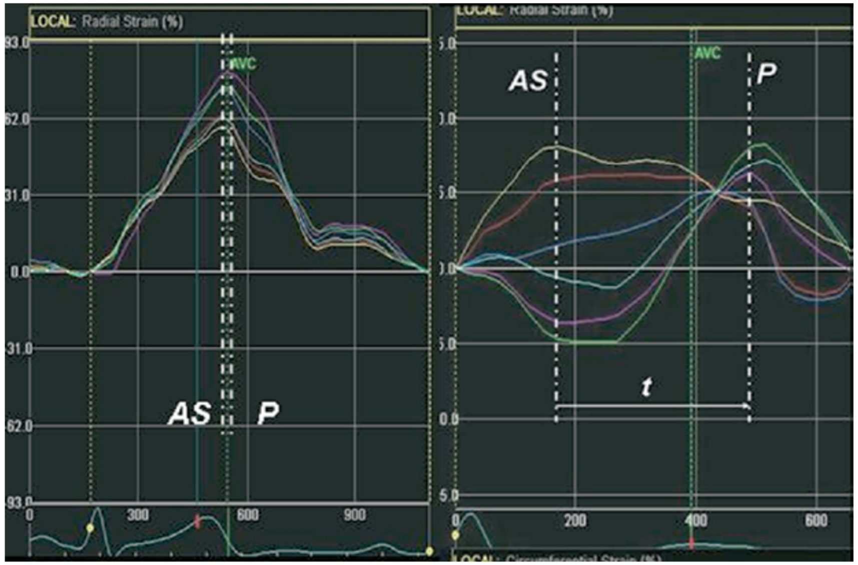
No Single Echo Measure of Dyssynchrony may be recommended to improve patient selection for CRT!

Circulation 2008;117:2608-2616

Assessment of Left Ventricular Dyssynchrony by Speckle Tracking Strain Imaging

Comparison Between Longitudinal, Circumferential, and Radial Strain in Cardiac Resynchronization Therapy

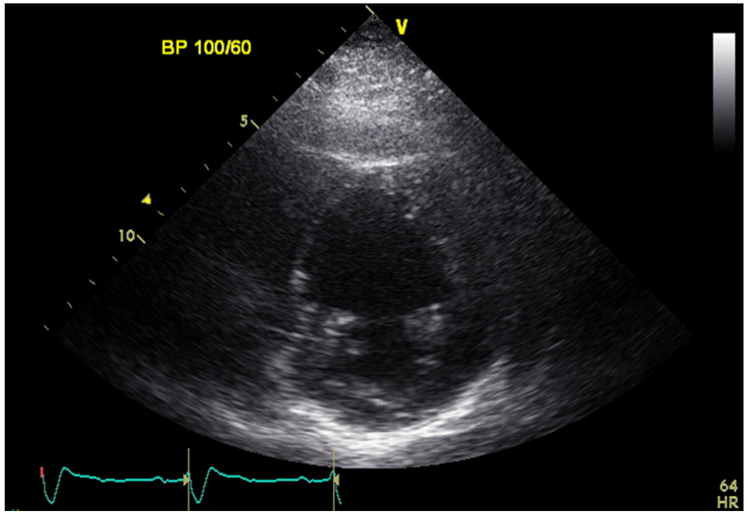


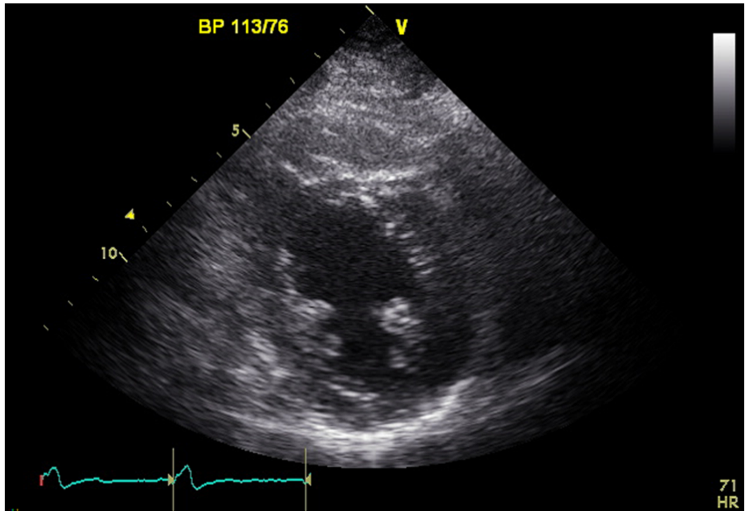


Radial dyssynchrony (130 ms):
sensitivity of 83% specificity of 80%
for prediction of CRT response

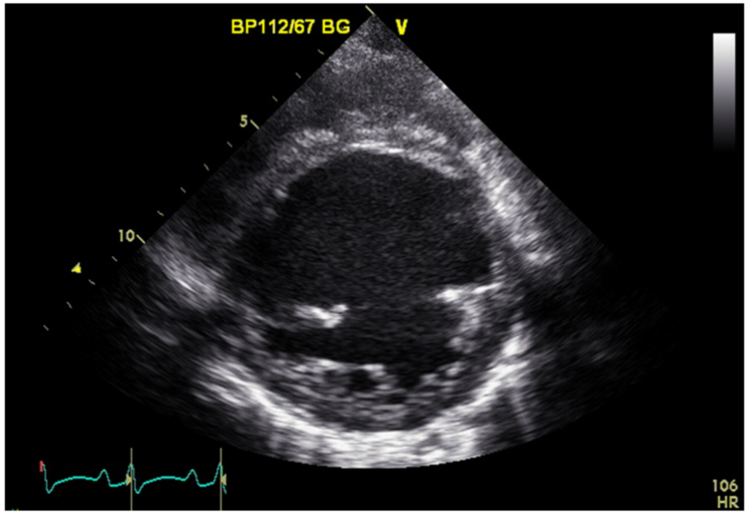
Delgado V J Am Coll Cardiol 2008;51:1944-52.

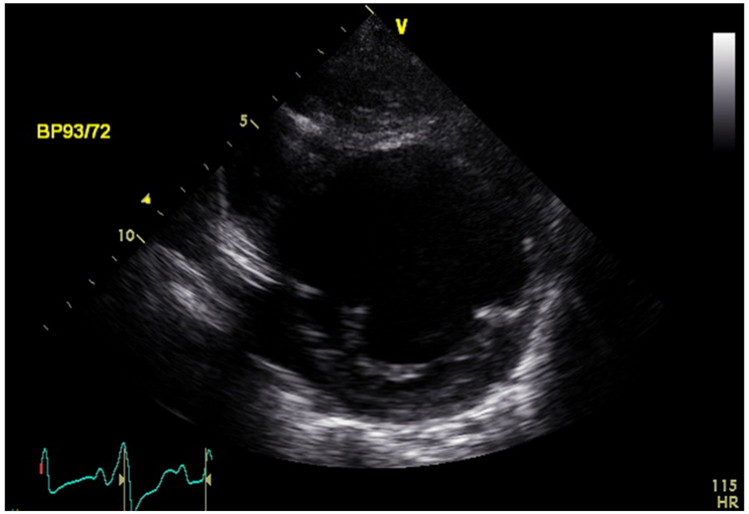
Before CRT **Responder (5076881)** **After CRT**



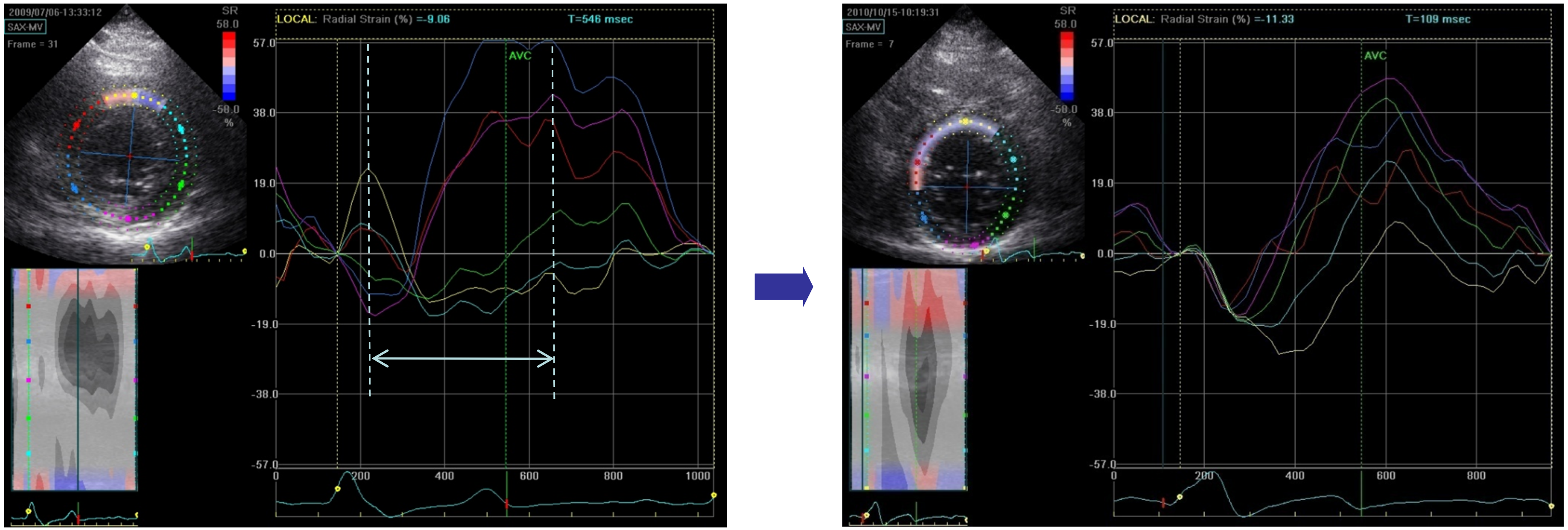


Non-responder (2834120)

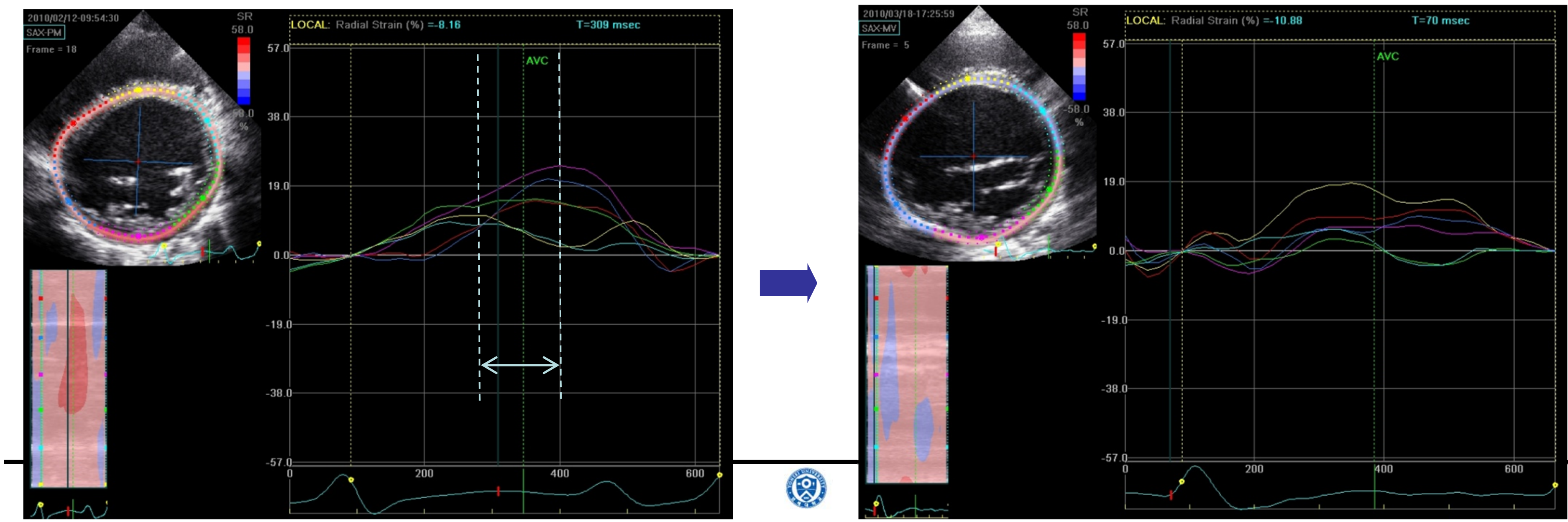




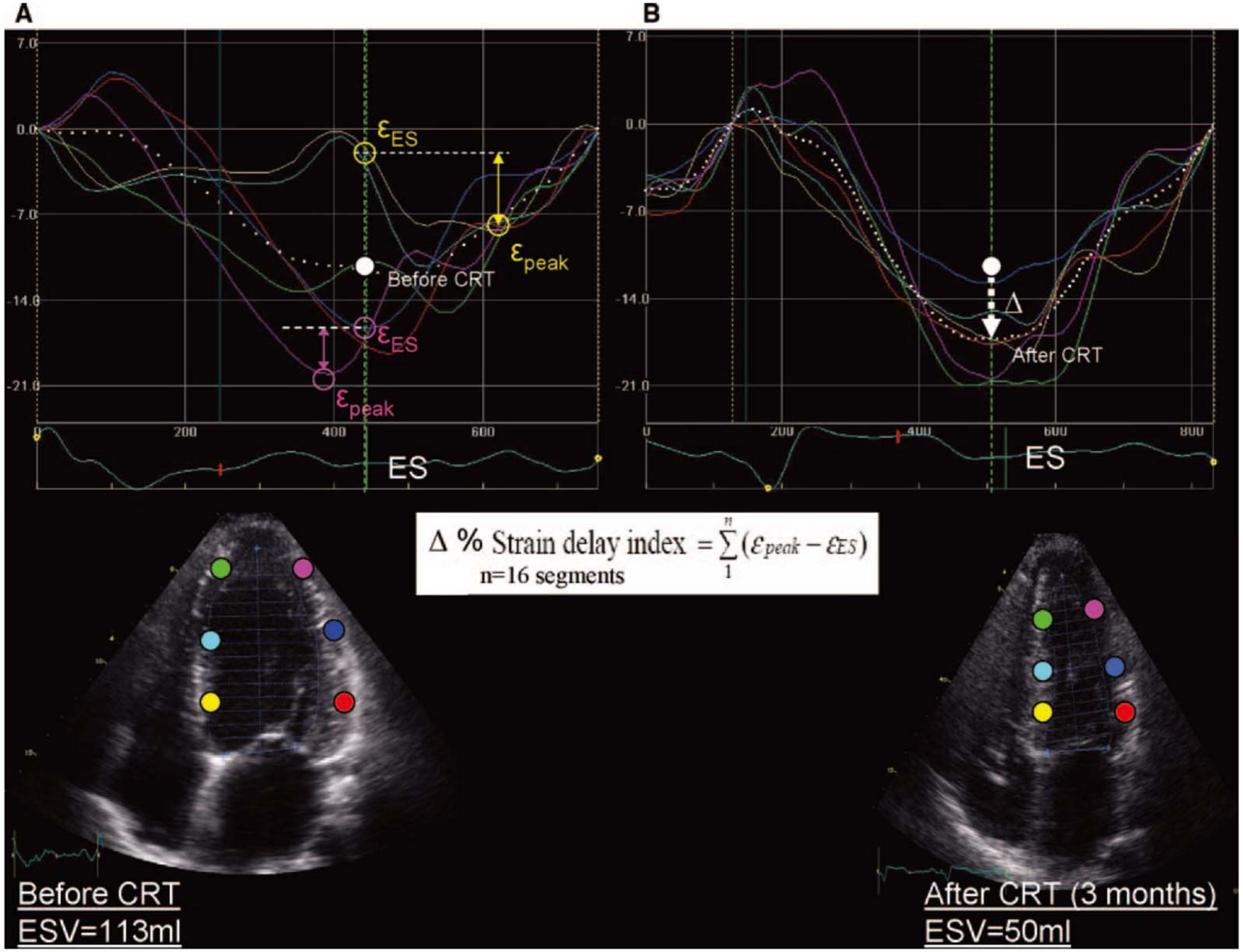
Before CRT **Responder (5076881)** **After CRT**



Non-responder (2834120)

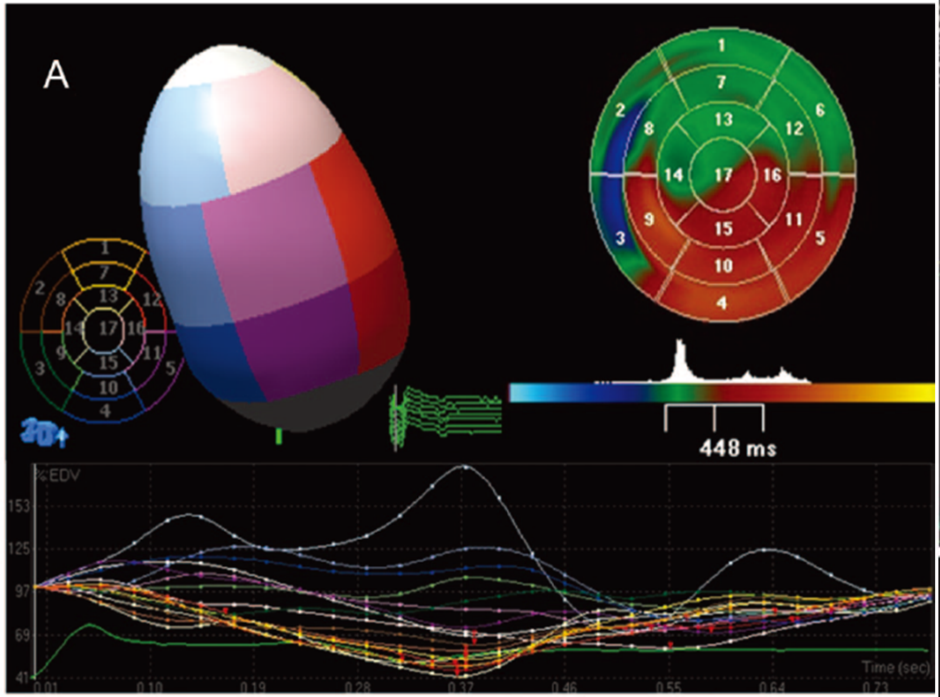


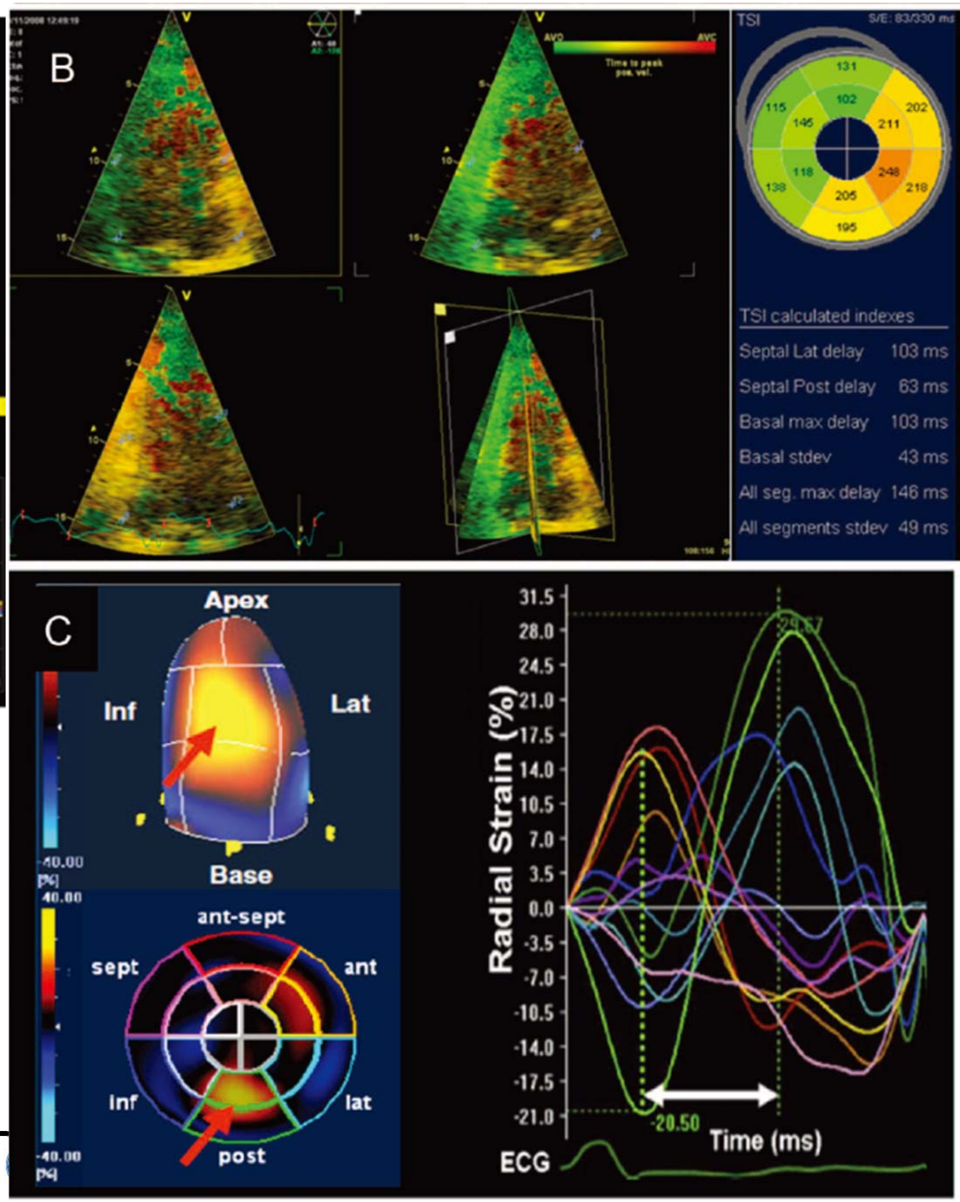
Longitudinal strain delay index



Lim P, *Circulation.* 2008;118:1130 –1137.

3D echocardiographic imaging techniques





Green: the earliest
Orange/red: the latest activated segments

Delgado V, et al. Circulation 2011;123:640-655

The Advantage of MRI

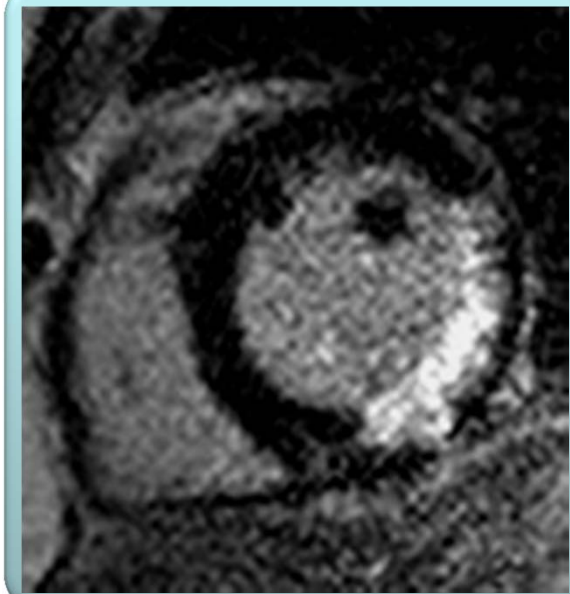
Cardiac MRI in Ischemic Heart Disease

Cine MRI

Morphology and Function

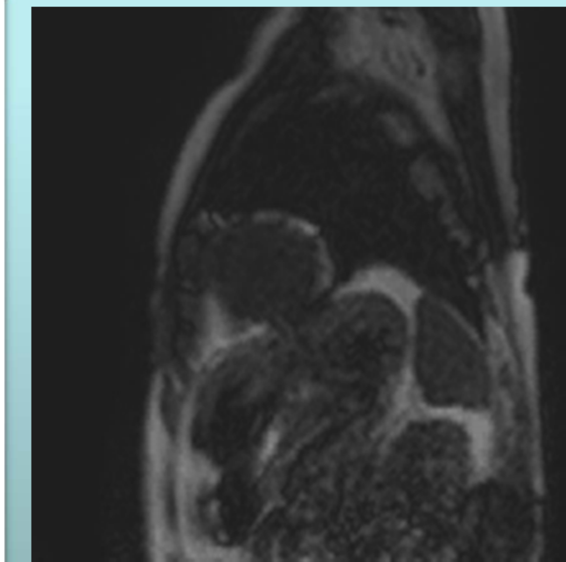
DE MRI

Infarction size/ viability



Perfusion MRI

Perfusion



CLINICAL RESEARCH

Cardiac Magnetic Resonance Assessment of Dyssynchrony and Myocardial Scar Predicts Function Class Improvement Following Cardiac Resynchronization Therapy

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Robert H. Helm, MD,* Robert G. Weiss, MD,* Joao A. Lima, MD,* Ronald D. Berger, MD, PhD,*
Gordon F. Tomaselli, MD, FAHA, FACC, FHRS,* David A. Bluemke, MD, PhD, FAHA,§
Henry R. Halperin, MD, FAHA,*†§ Theodore Abraham, MBBS, MD, *
David A. Kass, MD, FAHA,*†‡ Albert C. Lardo, PhD, FACC, FAHA*†‡

Baltimore, Maryland

OBJECTIVES We tested a circumferential mechanical dyssynchrony index (circumferential uniformity ratio estimate [CURE]; 0 to 1, 1 = synchrony) derived from magnetic resonance-myocardial tagging (MR-MT) for predicting clinical function class improvement following cardiac resynchronization therapy (CRT).

BACKGROUND There remains a significant nonresponse rate to CRT. MR-MT provides high quality mechanical activation data throughout the heart, and delayed enhancement cardiac magnetic resonance (DE-CMR) offers precise characterization of myocardial scar.

METHODS MR-MT was performed in 2 cohorts of heart failure patients with: 1) a CRT heart failure cohort (n = 20; left ventricular ejection fraction of 0.23 ± 0.057) to evaluate the role of MR-MT and DE-CMR prior to CRT; and 2) a multimodality cohort (n = 27; ejection fraction of 0.20 ± 0.066) to compare MR-MT and tissue Doppler imaging septal-lateral delay for assessment of mechanical dyssynchrony. MR-MT was also performed in 9 healthy control subjects.

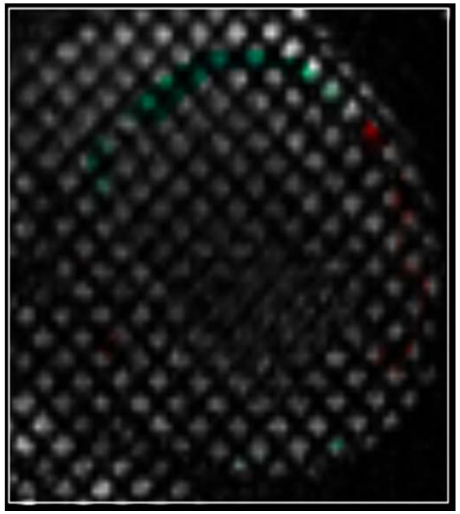
RESULTS MR-MT showed that control subjects had highly synchronous contraction (CURE 0.96 ± 0.01), but tissue Doppler imaging indicated dyssynchrony in 44%. Using a cutoff of <0.75 for CURE based on receiver-operator characteristic analysis (area under the curve: 0.889), 56% of patients tested positive for mechanical dyssynchrony, and the MR-MT CURE predicted improved function class with 90% accuracy (positive and predictive values: 87%, 100%); adding DE-CMR (% total scar <15%) data improved accuracy further to 95% (positive and negative predictive values: 93%, 100%). The correlation between CURE and QRS duration was modest in all cardiomyopathy subjects (r = 0.58, p < 0.001). The multimodality cohort showed a 30% discordance rate between CURE and tissue Doppler imaging septal-lateral delay.

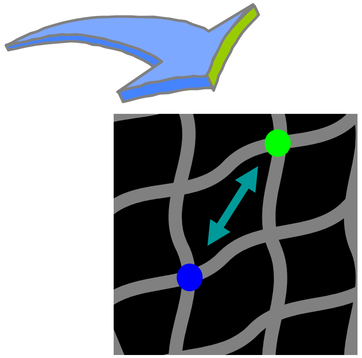
CONCLUSIONS The MR-MT assessment of circumferential mechanical dyssynchrony predicts improvement in function class after CRT. The addition of scar imaging by DE-CMR further improves this predictive value. (J Am Coll Cardiol Img 2008;1:561–8)

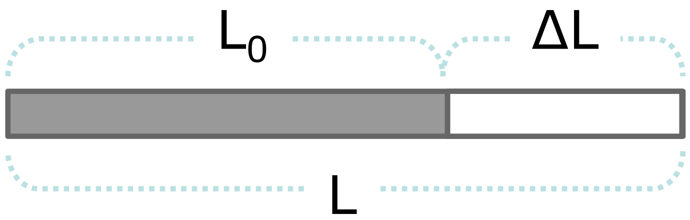
The magnetic resonance-myocardial tagging (MR-MT) assessment of circumferential mechanical dyssynchrony predicts improvement in function class after CRT.

The addition of scar imaging by DE-CMR further improves this predictive value.

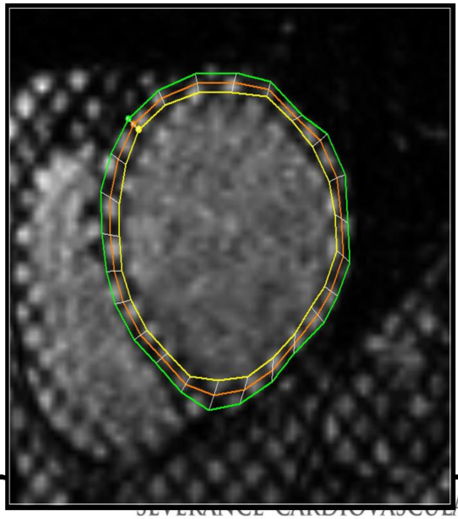
HARmonic Phase analysis of tagged MRI

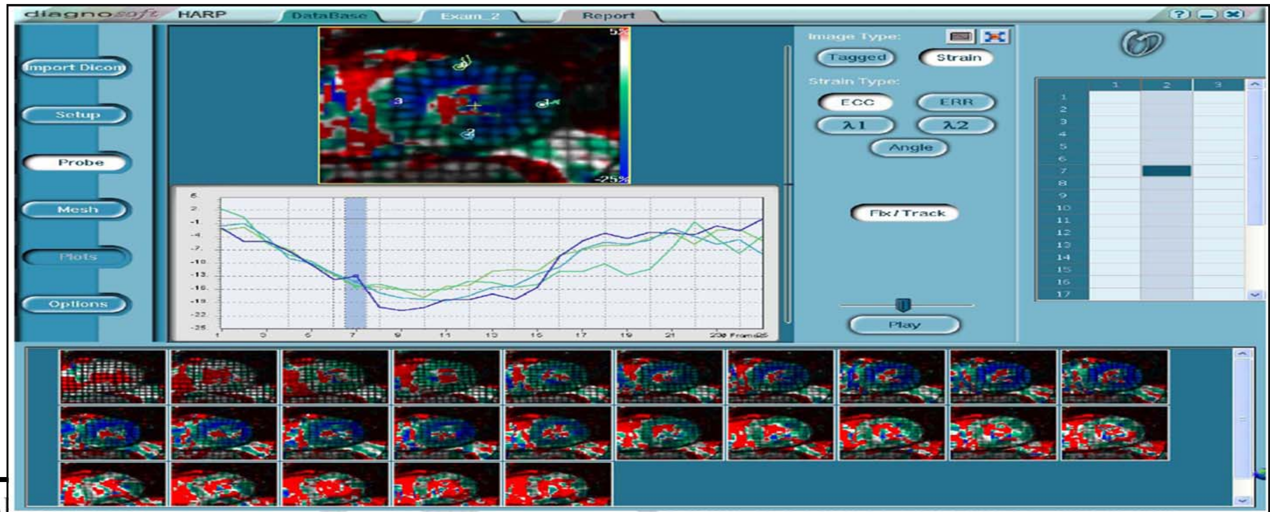




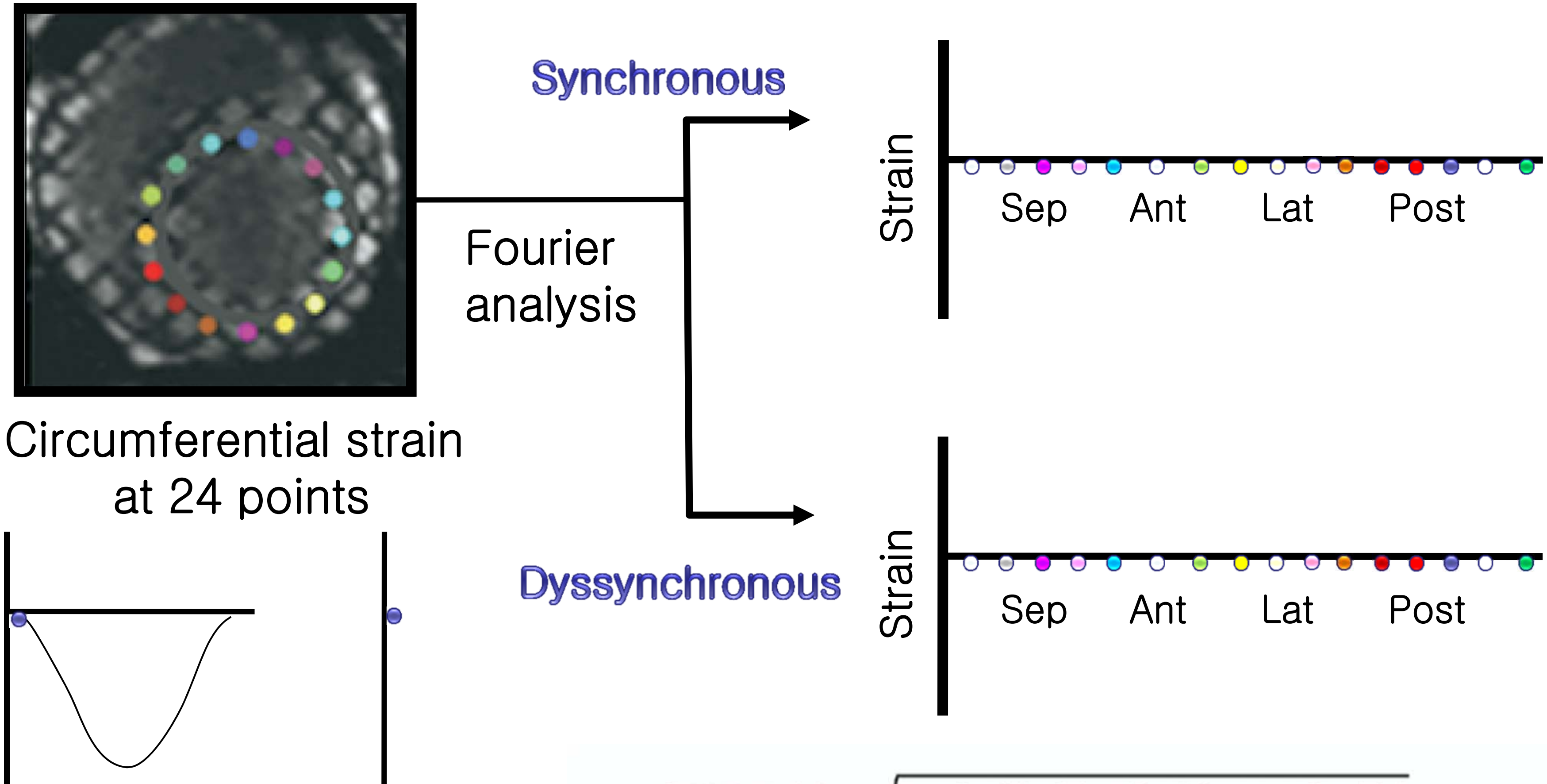


$$\text{Strain } (\varepsilon) = \frac{L - L_0}{L_0} = \frac{\Delta L}{L_0}$$



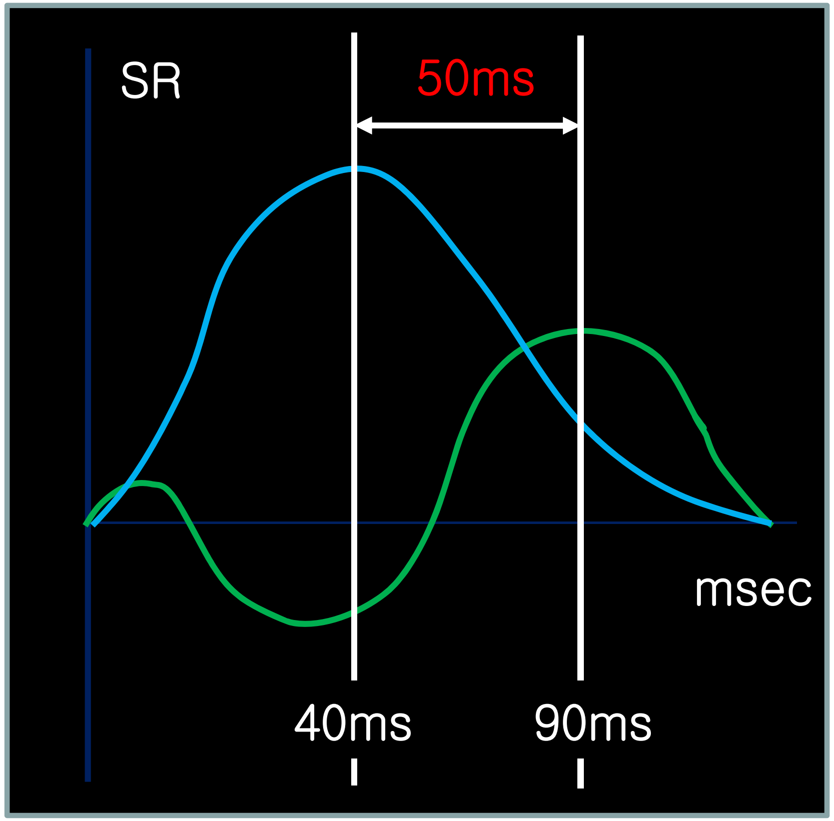


LV dyssynchrony index
CURE (Circumferential Uniformity Ratio Estimate)



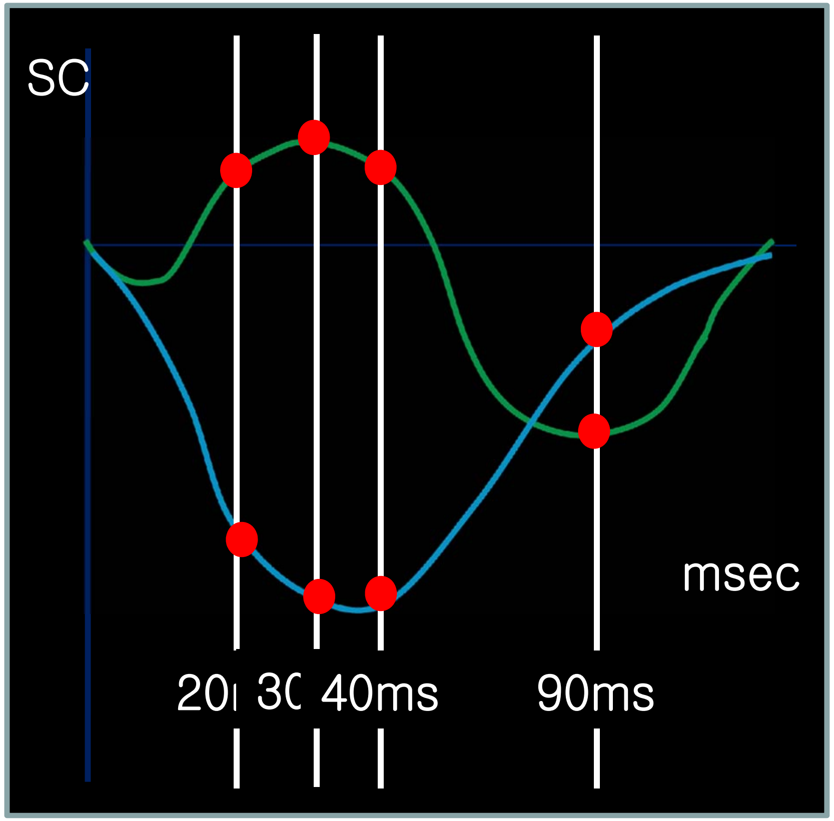
$$\mathrm{CURE}\ (t) = \sqrt{\Sigma\, S_0(t) \,/\, (\Sigma\, S_0(t) + \Sigma\, S_1(t))}$$

Maximal Difference of Radial Strain



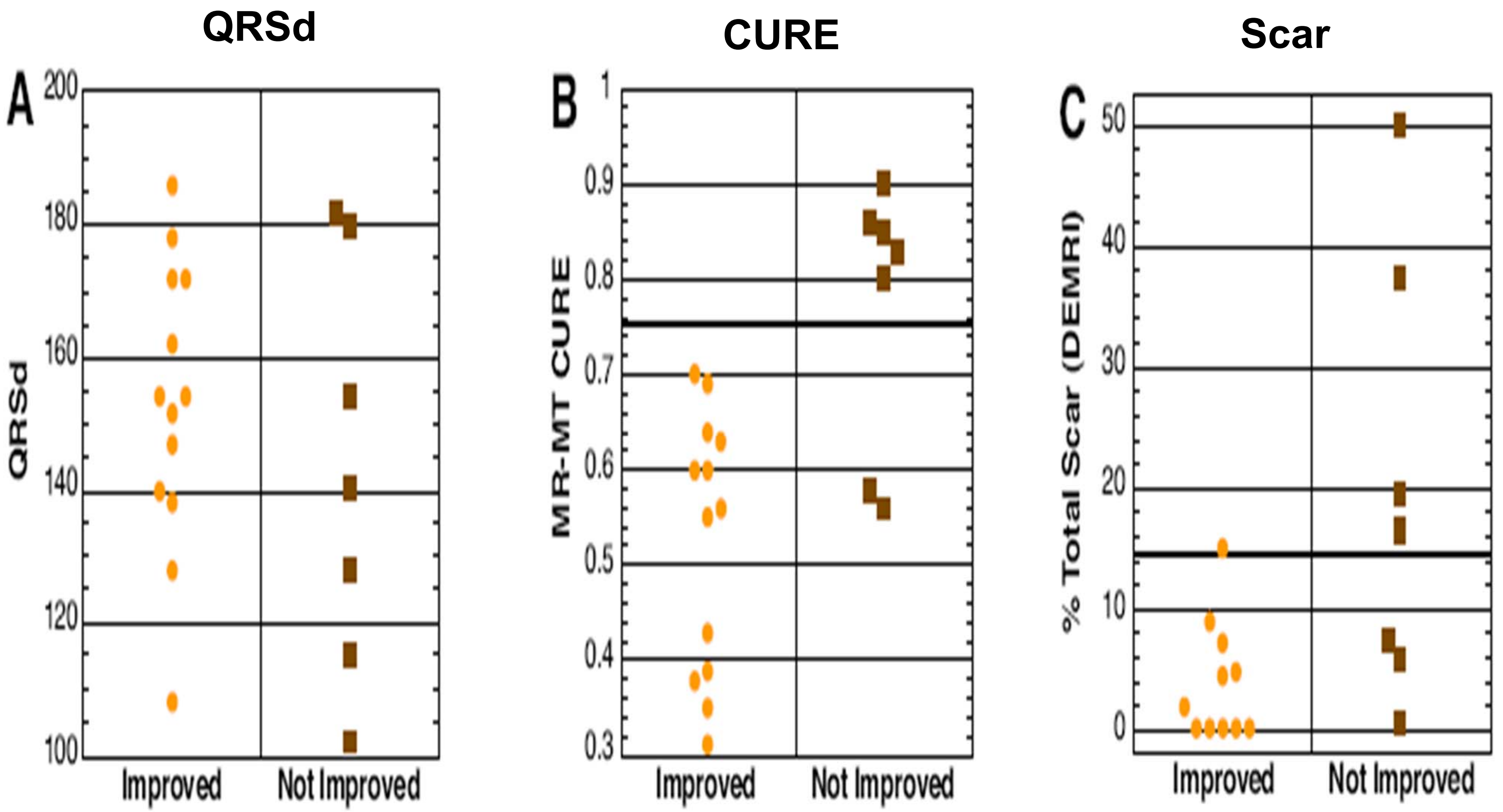
Relative time interval (Δtime)
“Define peak strain” is very important

CURE



Relative deformation at each time point
Not include Δtime
→ “Define peak strain” is less important

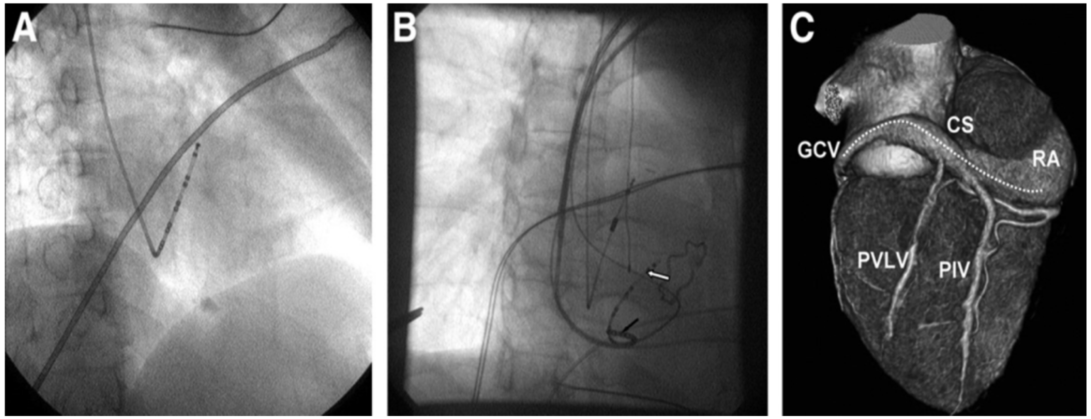
Clinical Response to CRT Based on CMR Findings



The Advantage of Cardiac CT

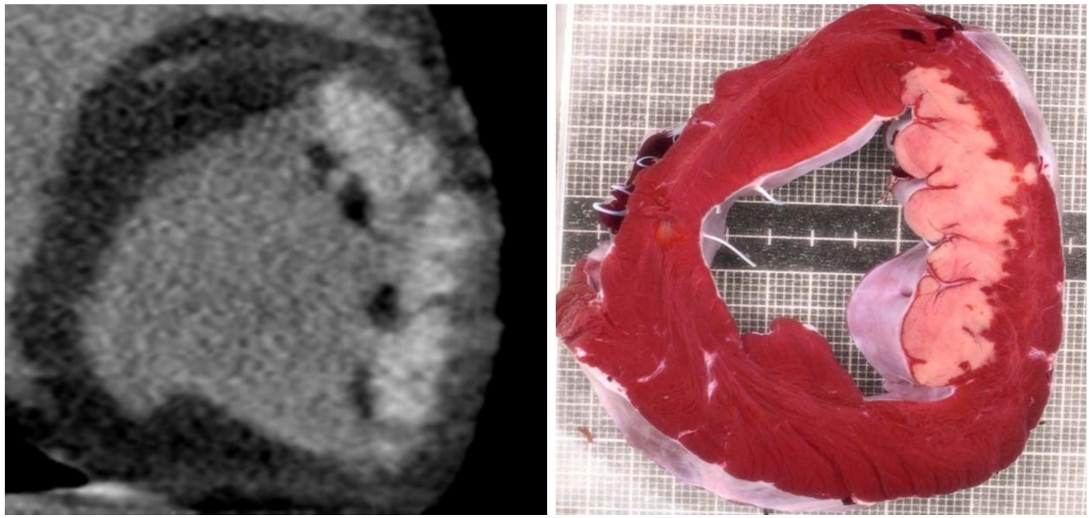
The Advantage of Cardiac CT

Coronary venous anatomy



JACC Cardiovascular Imaging 2009

Viable myocardium



Circulation 2006

Radiology

Reperfused Myocardial Infarction: Contrast-enhanced 64-Section CT in Comparison to MR Imaging[1]

Koen Nieman, MD, PhD
Michael D. Shapiro, DO
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Suhny Abbara, MD
Udo Hoffmann, MD
Herman K. Gold, MD
Ik-Kyung Jang, MD, PhD
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Ricardo C. Cury, MD

ORIGINAL RESEARCH ■ CARDIAC IMAGING

Purpose: To prospectively compare 64-section multidetector computed tomography (CT) and cardiac magnetic resonance (MR) imaging for the early assessment of myocardial enhancement and infarct size after acute reperfused myocardial infarction (MI).

Materials and Methods: The study was HIPAA compliant and was approved by the institutional review board. All participants gave written informed consent. Twenty-one patients (18 men; mean age, 60 years ± 13 [standard deviation]) were examined with 64-section multidetector CT and cardiac MR imaging 5 days or fewer after a first reperfused MI. Multidetector CT was performed during the first pass of contrast material to assess myocardial perfusion and detect microvascular obstruction (no reflow). In 15 patients, a second scan was performed 7 minutes later to assess total infarct size by using delayed hyperenhancement. Early hypoenhancement and delayed hyperenhancement were compared between multidetector CT and cardiac MR imaging with Pearson correlation coefficient and Bland-Altman analysis.

Results: Early hypoenhancement was recognized on all multidetector CT and cardiac MR images. Delayed hyperenhancement was observed with cardiac MR imaging at all examinations and with multidetector CT at 11 of 15 examinations. While signal intensity differences between hypoperfused and normal myocardium were comparable for first-pass multidetector CT and cardiac MR imaging, cardiac MR imaging had a far better contrast-to-noise ratio (CNR) for delayed acquisitions than did CT ($P < .001$). Hypoenhanced areas (as a percentage of left ventricular mass) at first-pass multidetector CT (11% ± 6) correlated well with those at first-pass cardiac MR imaging (7% ± 4, $R^2 = 0.72$). Delayed-enhancement multidetector CT (13% ± 9) correlated well with delayed-enhancement cardiac MR imaging (15% ± 7, $R^2 = 0.55$). Quantification of delayed hypoenhancement ($n = 12$) had very good correlation between multidetector CT (4% ± 4) and cardiac MR imaging (3% ± 2) ($R^2 = 0.85$).

Conclusion: Early and late hypoenhancement showed good CNR and correlated well between multidetector CT and cardiac MR imaging.

[1] From the Cardiac MRI-PET-CT Program, Department of Radiology (K.N., M.D.S., M.F., C.H.N., S.A., U.H., T.J.B., R.C.C.) and the Cardiology Division (H.K.G., I.K.J.), Massachusetts General Hospital and Harvard Medical School, 165 Cambridge St, Boston, MA 02114. Received February 17, 2007; revision requested April 26; revision received July 3; accepted August 1; final version accepted September 25. K.N. supported by the Interuniversity Cardiology Institute of the Netherlands, Utrecht, the Netherlands. **Address correspondence to** K.N. (e-mail: *koennieman@hotmail.com*).

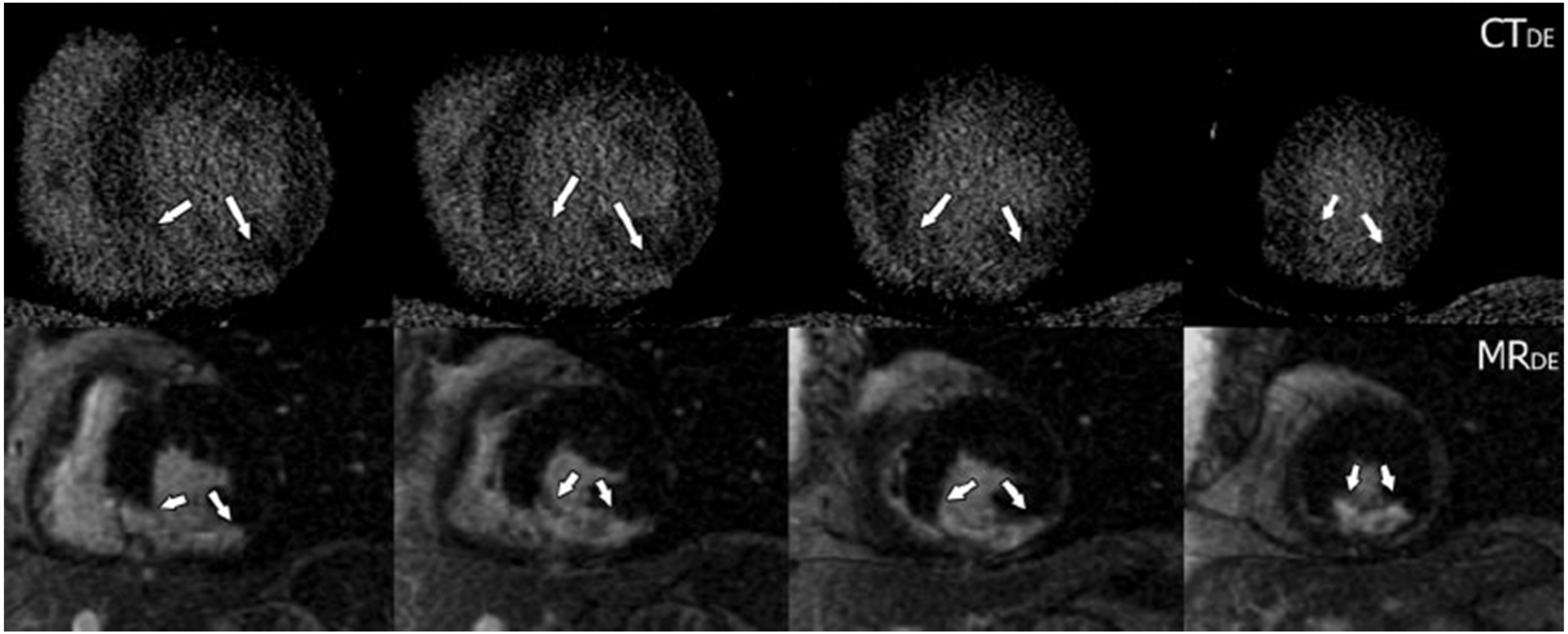
Radiology: Volume 247: Number 1—April 2008 49

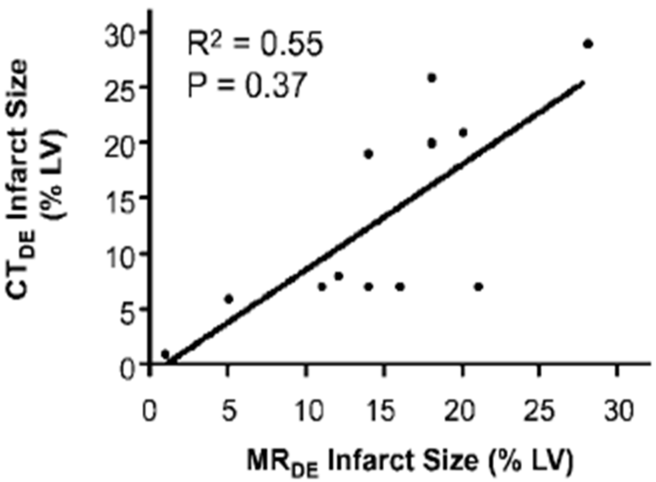
Delayed-enhancement CT acquisition:

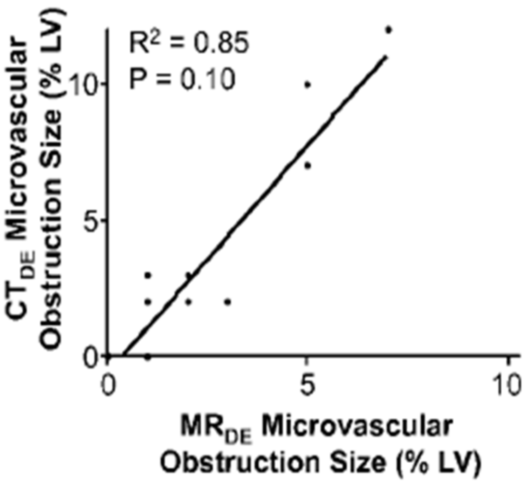
A second scan was performed 7 minutes after contrast injection.

To minimize radiation exposure, a wider detector collimation (24x1.2 mm) and lower tube output were used (100 kV, 800 mAs).

The calculated radiation dose was 4.5 mSv±2.4.







Radiology 2008;247:49-56

Imaging-based Prediction of Response to Cardiac ReSynchronization (IMPRESS) Study

Patients (N=30)

Subjects who meet classic indication for CRT

1. NYHA III or IV
2. ≤35%
3. ≥120 ms

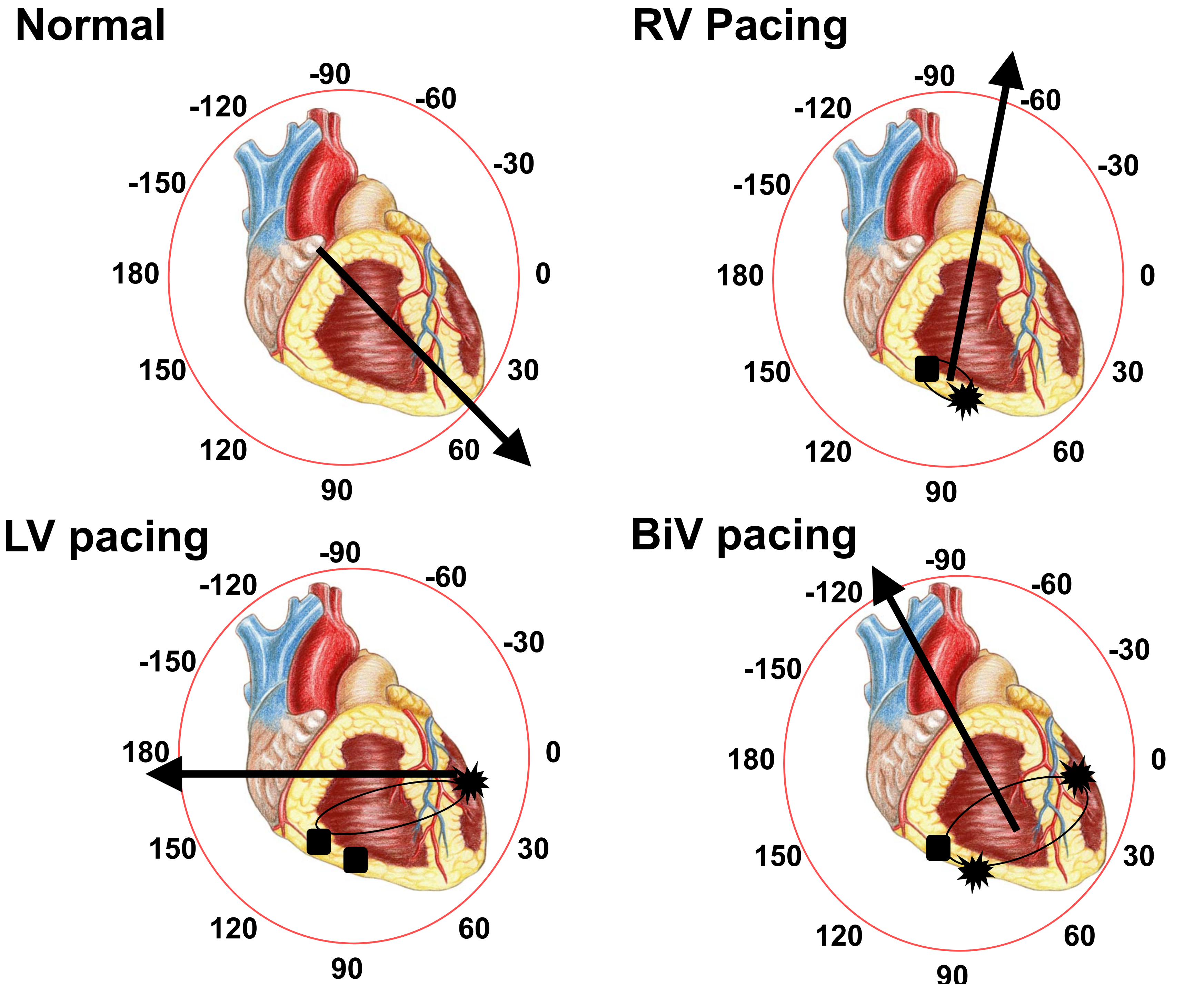
Work-up

TTE, CMR, Cardiac CT

Differential Diagnosis of Non-Responders

- Lack of mechanical dyssynchrony despite LBBB
- Large area of scar from prior M.I.
- Poor LV lead location

- **LV lead dislodgment or loss of capture**
- **Pacemaker inhibited a significant portion of the time**
  - **Atrial fibrillation with intact conduction**
  - **Automatic mode switch**
  - **Sinus rate > Maximum Tracking Rate**
- **Inappropriate AV and VV delays**


Normal
-90
-120
-60
-30
-150
180
0
150
30
120
60
90
RV Pacing
-90
-120
-60
-30
-150
180
0
150
30
120
60
90
LV pacing
-90
-120
-60
-30
-150
180
0
150
30
120
60
90
BiV pacing
-90
-120
-60
-30
-150
180
0
150
30
120
60
90

“Takehome massage”

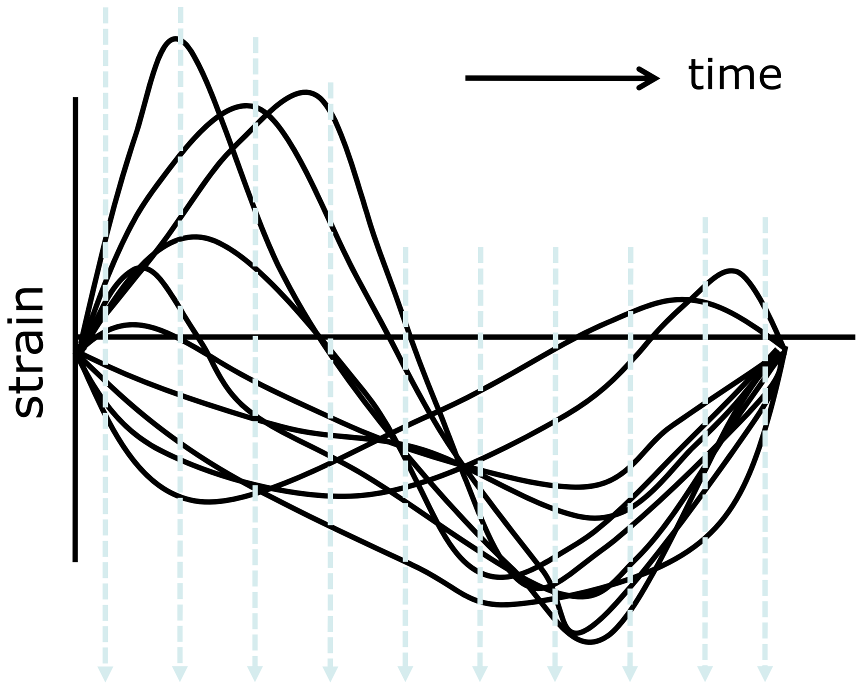
1) CRT의 Class I 적응증 환자의 30-40%는 치료에 반응하지 않는 non-responder이다.

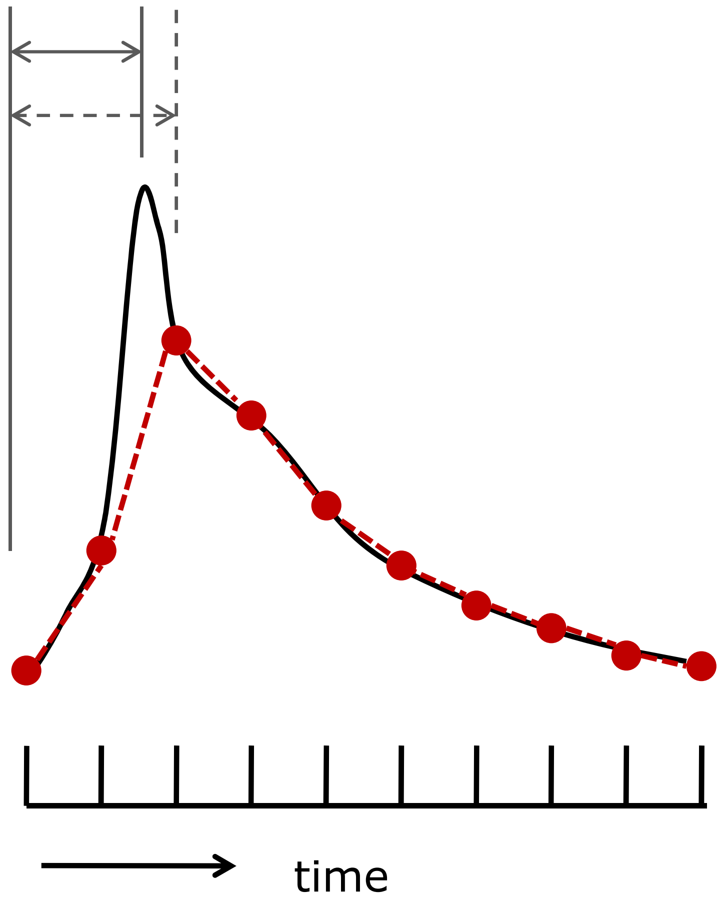
2) 초기 소규모 연구에서는 ECHO, MRI, CT가 non-responder 예측에 도움이 된다고 하였으나, 아직까지 역할은 불분명하다.

3) 최근에 ECHO의 speckle tracking strain imaging, MRI의 CURE index 등이 새로운 방법이 연구되고 있다.

Thanks for your attention!

Assessing Mechanical Synchrony from Strain with CURE (Circumferential Uniformity Ratio Estimate)





$$\text{CURE}(t) = \sqrt{\Sigma S_S(t)/(\Sigma S_S(t) + \Sigma S_D(t))}$$

1 = pure synchrony , 0 = pure dyssynchrony

Circumferential systolic dyssynchrony index (SDI)