How to Use Echocardiography for Cardiac Resynchronization Therapy

John Gorcsan, MD
University of Pittsburgh, Pittsburgh, PA

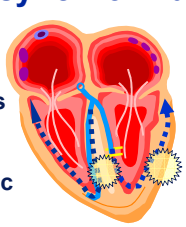
Disclosures:

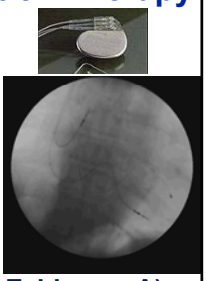
Research Grant Support: Biotronik, GE, Medtronic, St. Jude, Toshiba

AHA/ACC/ESC Guidelines for Cardiac Resynchronization Therapy

Patients with:

- NYHA class III or IV symptoms
- LVEF ≤ 35%
- QRS ≥ 120 msec

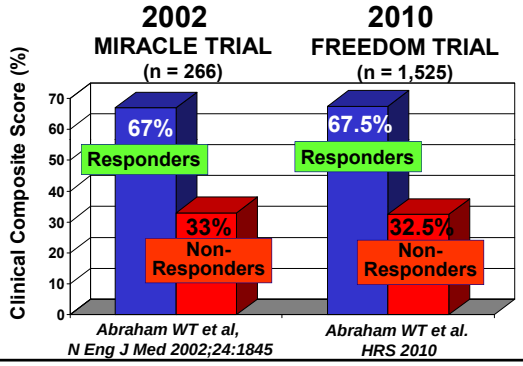




(Class I indication. Level of Evidence: A)

HOW FAR HAVE WE COME WITH CRT ?

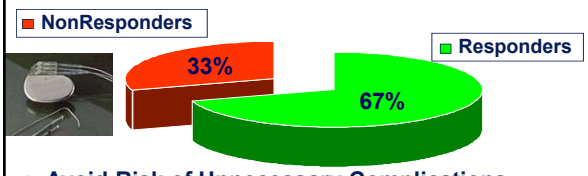
CLINICAL COMPOSITE SCORE



Abraham WT et al, N Eng J Med 2002;24:1845

Abraham WT et al. HRS 2010

WHY TRY TO IMPROVE PATIENT SELECTION FOR CRT ?

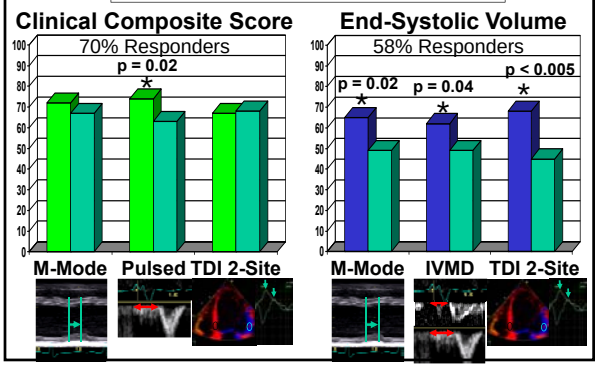


- Avoid Risk of Unnecessary Complications
  - Coronary Sinus Dissection
  - Perforation - Tamponade
  - Death
- Cost Savings $10-15,000 extra per CRT-D Implant

Abraham W. et al Circulation 2007

PROSPECT: CRT *Response at 6 Months*

n = 426 Dyssynchrony No Dyssynchrony



Circulation

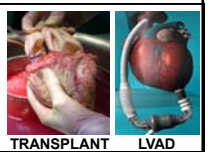
DYSSYNCHRONY-CRT LONG-TERM SURVIVAL STUDY

n = 229 Consecutive Patients
Routine CRT Indications

- NYHA: III (89%), IV (11%)
- QRS (ms) 160 ± 28, EF (%) 25 ± 7, 58% Ischemic

Primary Events (4 yrs)

- 49 Deaths
- 9 Heart Transplants
- 6 Left Ventricular Assist Devices

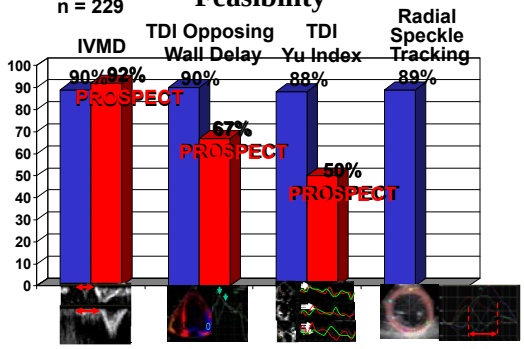


Gorcsan et al. Circulation 2010;112 (Nov.9)

DYSSYNCHRONY-CRT LONG-TERM SURVIVAL STUDY

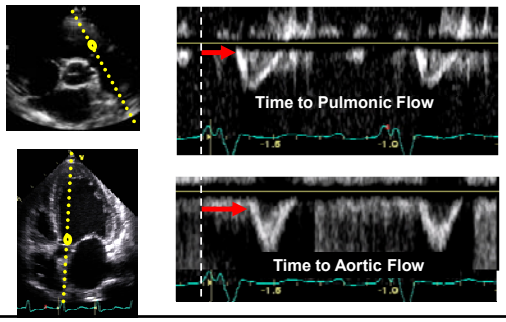
Feasibility

n = 229

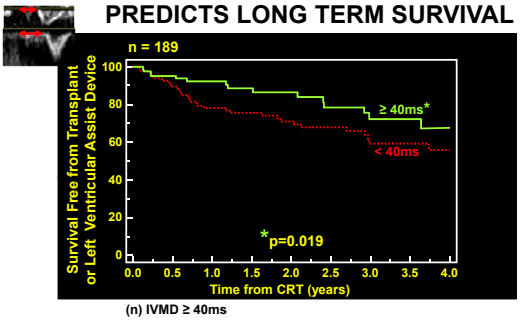


Gorcsan et al. Circulation 2010;112 (Nov.9)

Routine Pulsed Doppler INTERVENTRICULAR MECHANICAL DELAY



INTERVENTRICULAR MECHANICAL DELAY PREDICTS LONG TERM SURVIVAL

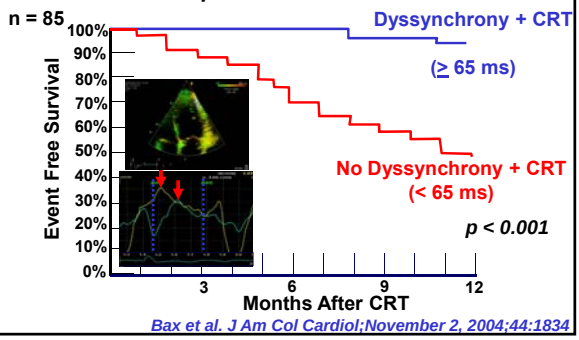


(n) IVMD ≥ 40ms
83 68 54 43 34 29 23 16 10
(n) IVMD < 40ms
97 83 65 52 47 36 27 19 11

Gorcsan et al. Circulation 2010;112 (Nov.9)

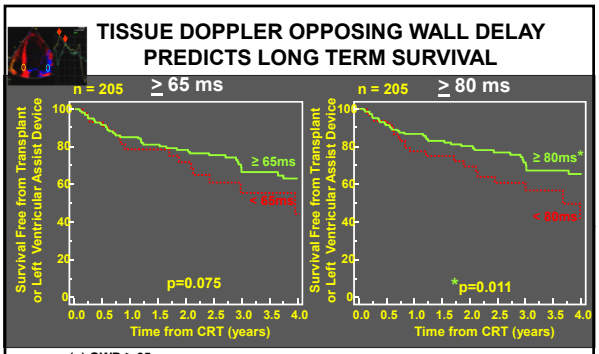
TISSUE DOPPLER LONGITUDINAL VELOCITY OPPOSING WALL DELAY PREDICTS PROGNOSIS

Death or Hospitalization For Heart Failure



Bax et al. J Am Col Cardiol;November 2, 2004;44:1834

TISSUE DOPPLER OPPOSING WALL DELAY PREDICTS LONG TERM SURVIVAL

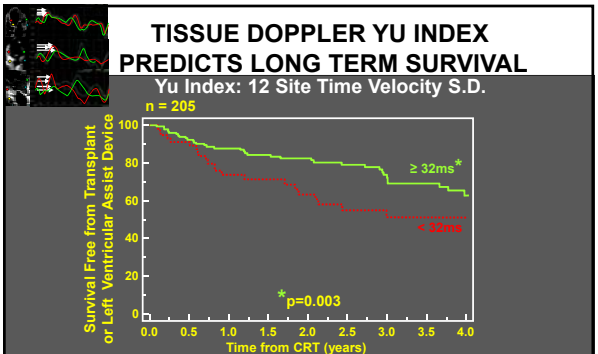


(n) OWD ≥ 65ms
160 134 111 93 80 68 52 41 25
(n) OWD < 65ms
45 40 30 23 21 14 10 6 4

(n) OWD ≥ 80ms
142 120 103 88 76 64 48 39 24
(n) OWD < 80ms
63 54 38 28 25 18 14 8 5

Gorcsan et al. Circulation 2010;112 (Nov.9)

TISSUE DOPPLER YU INDEX PREDICTS LONG TERM SURVIVAL

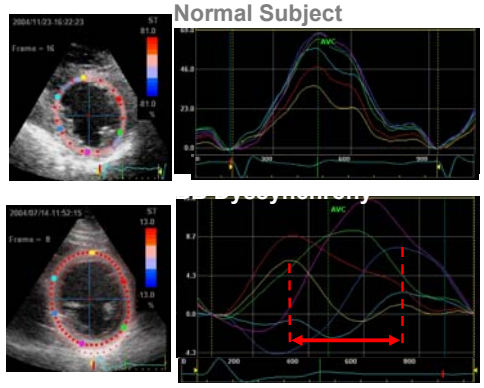


(n) Yu Index ≥ 32ms
148 126 107 89 77 65 48 39 24
(n) Yu Index < 32ms
57 48 34 27 24 17 14 8 5

Gorcsan et al. Circulation 2010;112 (Nov.9)

SPECKLE TRACKING RADIAL STRAIN

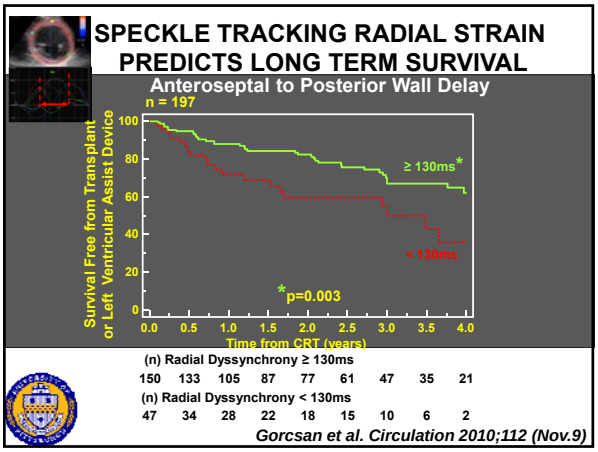
Normal Subject



Suffoletto M…Gorcsan et al. Circulation 2006 (Feb 21)

SPECKLE TRACKING RADIAL STRAIN PREDICTS LONG TERM SURVIVAL

Anteroseptal to Posterior Wall Delay



(n) Radial Dyssynchrony ≥ 130ms
150 133 105 87 77 61 47 35 21
(n) Radial Dyssynchrony < 130ms
47 34 28 22 18 15 10 6 2

Gorcsan et al. Circulation 2010;112 (Nov.9)

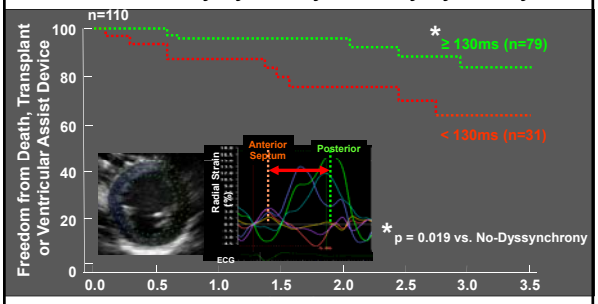
Speckle Tracking And Resynchronization (STAR) Study

- 132 CRT pts. were prospective enrolled in the multicenter international "STAR Study":
  - University of Linz, Linz Austria
  - University Hospital Essen, Essen Germany
  - University of Pittsburgh, Pittsburgh, PA USA
- Age 66±13 years; 39% female
- All were NYHA class III or IV
- EF 24 ± 7 %, all ≤ 35%
- QRS duration 158 ± 26 ms, all ≥ 120ms

Tanaka…Gorcsan et al. European Heart Journal June 8, 2010 FAST TRACK

LONG-TERM OUTCOME AFTER CRT

Radial Dyssynchrony vs. No-Dyssynchorny

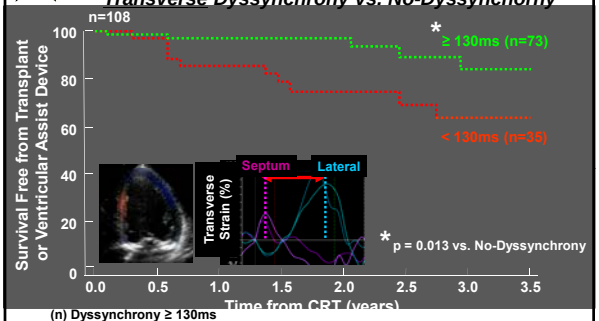


(n) Dyssynchrony ≥ 130ms
79 70 53 36 27 21 19 17
(n) No-Dyssynchrony < 130ms
31 29 26 19 16 11 8 7

Tanaka…Gorcsan et al. European Heart Journal June 8, 2010 FAST TRACK

LONG-TERM OUTCOME AFTER CRT

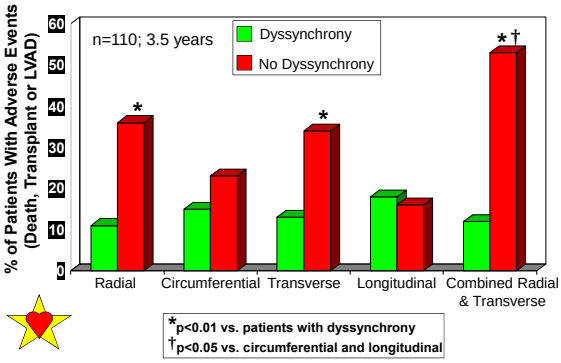
Transverse Dyssynchrony vs. No-Dyssynchorny



(n) Dyssynchrony ≥ 130ms
73 65 52 36 28 19 16 14
(n) No-Dyssynchrony < 130ms
35 34 27 19 15 13 11 10

Tanaka…Gorcsan et al. European Heart Journal June 8, 2010 FAST TRACK

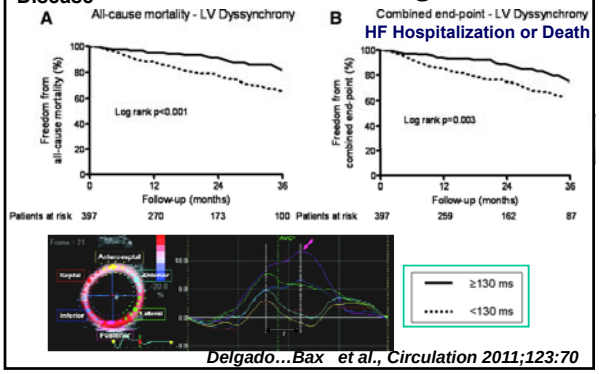
Absence of Dyssynchrony is Associated with Serious Clinical Events After CRT



*p<0.01 vs. patients with dyssynchrony
†p<0.05 vs. circumferential and longitudinal

n = 397 Ischemic Disease

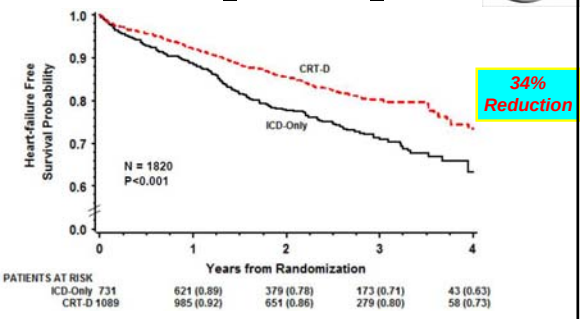
Association of Dyssynchrony with Outcome Following CRT



Delgado…Bax et al., Circulation 2011;123:70

MADIT CRT Trial

- 1,820 patients NYHA Class I or II
- Wide QRS ≥ 130 ms, EF ≤ 30%



Moss et al. N Engl J Med. 2009;361(14):1329-38.

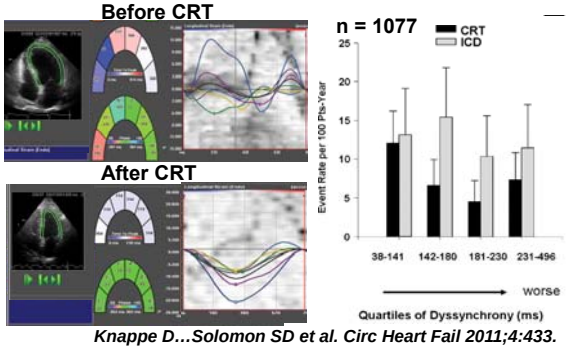
Circulation
Heart Failure
Journal of the American Heart Association
American Heart Association
Learn and Live

Dyssynchrony, Contractile Function, and Response to Cardiac Resynchronization Therapy

Dorit Knappe, Anne-Catherine Poulcur, Amal M. Shah, Susan Cheng, Hajime Uno, W. Jackson Hall, Mikhail Bourgoun, Elyse Foster, Wojciech Zareba, Ilan Goldenberg, Scott McNitt, Marc A. Pfeffer, Arthur J. Moss, Scott D. Solomon and for the Multicenter Automatic Defibrillator Implantation Trial –Cardiac Resynchronization Therapy Investigators

Circ Heart Fail 2011;4;433-440; originally published online May 22, 2011;
DOI: 10.1161/CIRCHEARTFAILURE.111.962902
Circulation: Heart Failure is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 75514

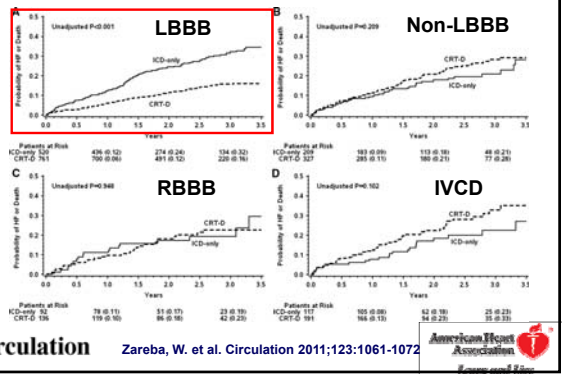
MADIT-CRT Longitudinal Dyssynchrony Associated with Lower Event Rate



Knappe D…Solomon SD et al. Circ Heart Fail 2011;4:433.

MADIT-CRT: QRS Morphology

Benefits Seen in LBBB Patients



Circulation Zareba, W. et al. Circulation 2011;123:1061-1072

September 16, 2010
WASHINGTON

FDA expands approval of implants for heart failure

The Food and Drug Administration approved 3 implantable heart devices (cardiac resynchronization therapy defibrillators) from Boston Scientific Corp. for a new use in treating heart failure patients. The devices are implanted in the upper chest and use electrical signals to shock the heart and correct irregular beats and then coordinate its pumping action.

The FDA approved the products for:
A new indication in patients with mild or asymptomatic heart failure with left bundle branch block.

That condition reduces the heart's pumping ability by delaying the electrical activation of its left ventricle. This means portions of the left ventricle contract later than the rest of the heart muscle. Previously the devices were only approved to treat patients with more severe heart failure. Boston Scientific said in a separate statement that the approval makes its devices the only ones approved by the FDA for all four classes of heart failure, as categorized by the New York Heart Association. The FDA based its approval on an 1,800-patient study that followed patients with left bundle branch block for three years. Patients implanted with a combination resynchronization-defibrillator had a 57 percent lower rate of death and heart failure than patients who only received a defibrillator.

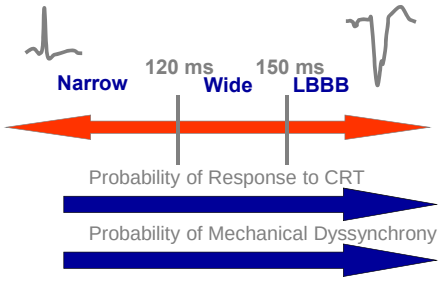
MY REALITY CHECK

Class III-IV HF

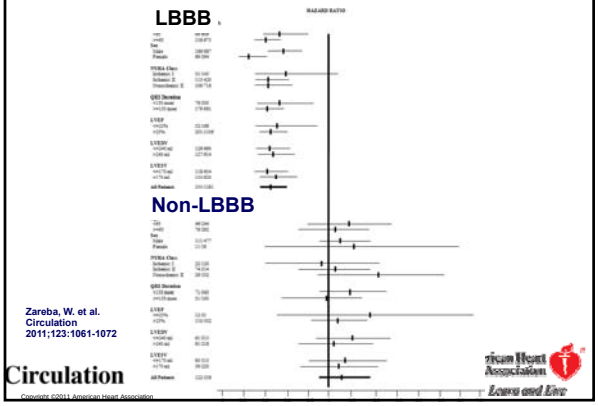
Wide QRS > 150 ms or LBBB

Echo Dyssynchrony is Unlikely to Change Clinical Practice in the Near Future

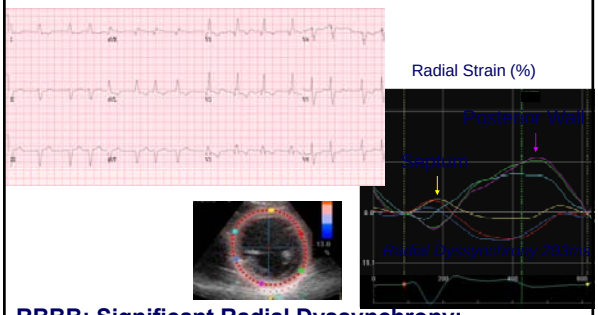
QRS Width as a Surrogate for Dyssynchrony



MADIT-CRT: LBBB vs. Non-LBBB

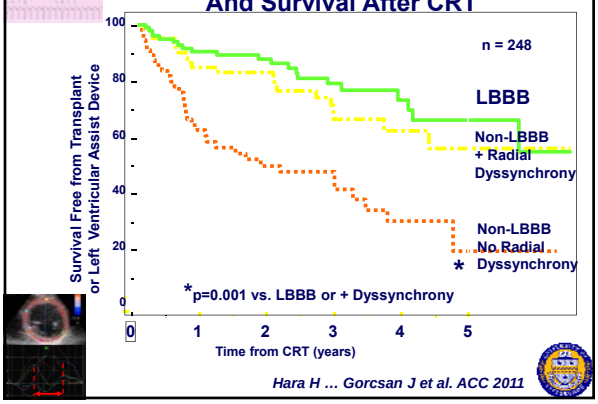


RBBB Patient who had CRT



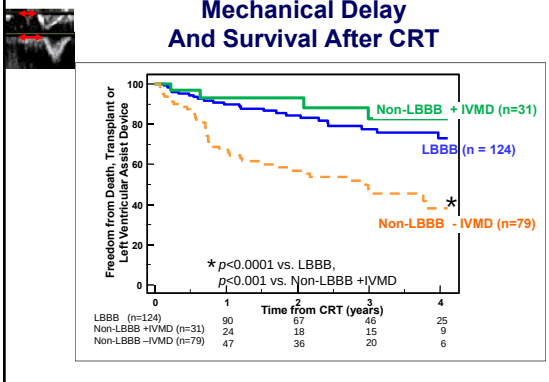
RBBB: Significant Radial Dyssynchrony; Long-term survivor 3 years; EF improved from 17% to 40% after CRT.

QRS Morphology, Radial Dyssynchrony And Survival After CRT



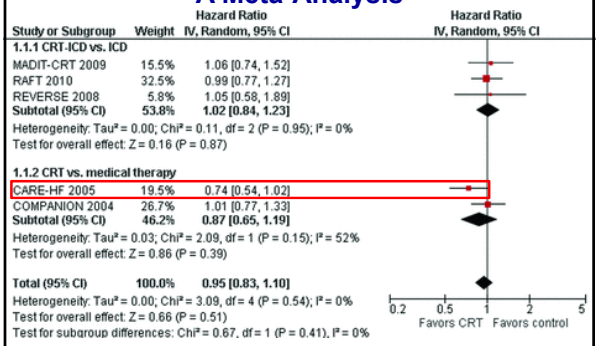
Hara H … Gorcsan J et al. ACC 2011

QRS Morphology, Interventricular Mechanical Delay And Survival After CRT



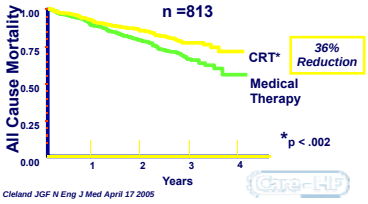
Hara H … Gorcsan J et al. ACC 2011

The Benefit of CRT in QRS Duration <150 ms
A Meta-Analysis



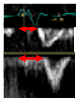
Stavrakis S et al. Journal of Cardiovascular Electrophysiology 2011 Vol 1: 1-9

CARE-HF
Required Dyssynchrony for Narrower QRS



QRS 120 - 150 ms (2 of 3):

- IVMD > 40 ms
- Preejection Delay > 140 ms
- M-mode Posterior Lateral Wall Delay

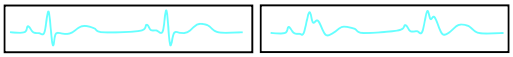


BORDERLINE QRS PATIENTS

n = 187 Heart Failure Patients Referred for CRT

	Borderline QRS 100-130ms (n = 72)	Wide QRS >130ms (n = 115)
Age (years)	60 ± 11	64 ± 11
Female	15 (32%)	37 (34%)
NYHA	III - IV	III - IV
Ischemic CM	55%	58%
EF (%)	24 ± 5	24 ± 6
QRS (ms)	115 ±8 *	168 ±26

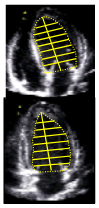
* p<0.01 vs. wide QRS

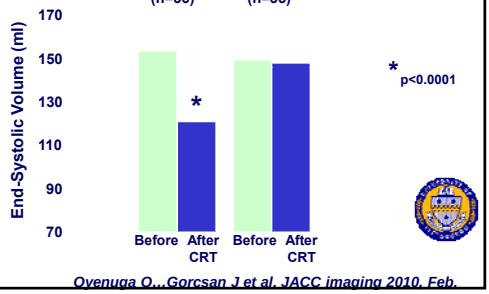


Oyenuga O...Gorcsan J et al. JACC imaging 2010. Feb.

RADIAL DYSSYNCHRONY PREDICTS REVERSE REMODELING IN BORDERLINE QRS PATIENTS

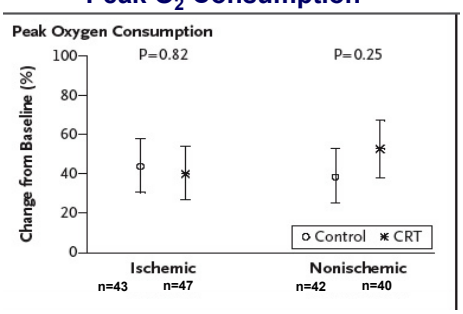
n = 72





Oyenuga O...Gorcsan J et al. JACC imaging 2010. Feb.

RethinQ Results
Primary End-Point
Peak O_2 Consumption

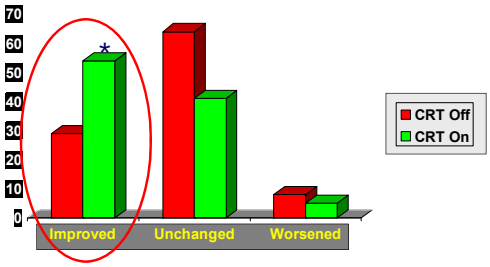


Beshai et al. NEJM Nov. 6, 2007

RETHINQ RANDOMIZED TRIAL EFFECTS ON NYHA CLASS

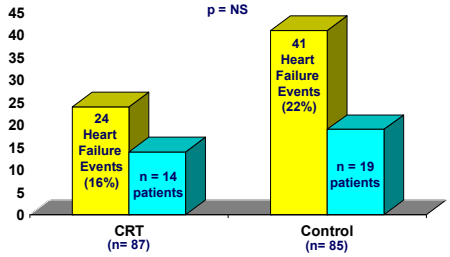
n = 156 *6 month Follow-Up*

* p < 0.006



Beshai et al. N Eng J Med 2007; 357:2461-2471

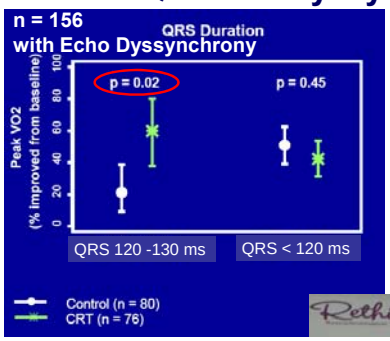
Heart Failure Events In RethinQ After 6 Months



Beshai et al. N Eng J Med 2007; 357:2461-2471

"There were 24 heart-failure events requiring intravenous therapy in 14 patients in the CRT group (16.1%) and 41 events in 19 patients in the control group (22.3%), but the difference was not significant."

RETHINQ RANDOMIZED TRIAL Narrow QRS and Dyssynchrony



EchoCRT Narrow QRS Trial

– Randomized (1:1), prospective, double-blinded, multi-center, international trial.

NYHA Class III-IV, EF ≤ 35%, QRS < 130 ms

• Tissue Doppler OW Delay ≥ 80ms

OR

• Speckle Tracking Radial Strain AS-P Delay ≥ 130ms

Primary Endpoint

– Evaluate the effect of CRT=ON versus CRT=OFF in time to event of a combined endpoint of death or first hospitalization for worsening HF.

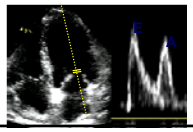
GOAL: Randomize ~1250 pts worldwide; 1100 with 2 yr. follow-up

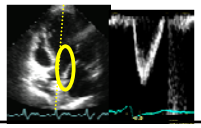
Journal of the JASE American Society of Echocardiography

Echocardiography for Cardiac Resynchronization Therapy: Recommendations for Performance and Reporting
A Report from the *American Society of Echocardiography*
Dyssynchrony Writing Group
Endorsed by the Heart Rhythm Society

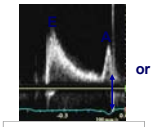
John Gorcsan, Theodore Abraham, Deborah A. Agler, Jeroen J. Bax, Genevieve Derumeaux, Richard A. Grimm, Randy Martin, Jonathan S. Steinberg, Martin St. John Sutton, Cheuk-Man Yu

JASE 2008 Volume 21, (March 2008) pages 191-213



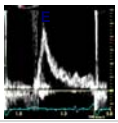


Arrange for AV Programming if:



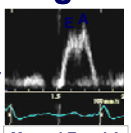
Truncated A Wave
AV Too Short

or



Absent A Wave
AV Much Too Short

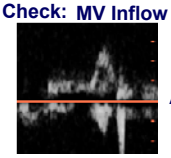
or



Merged E and A
AV Too Long

AV Optimization

Check: MV Inflow

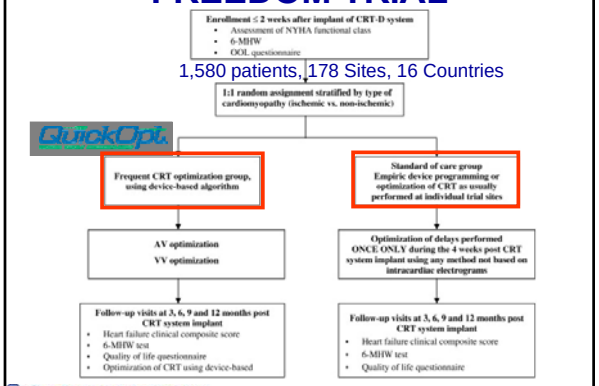


Program AV Delays:

- 100 ms
- 120 ms
- 140 ms
- 160 ms
- 180 ms
- 200 ms
- 220 ms

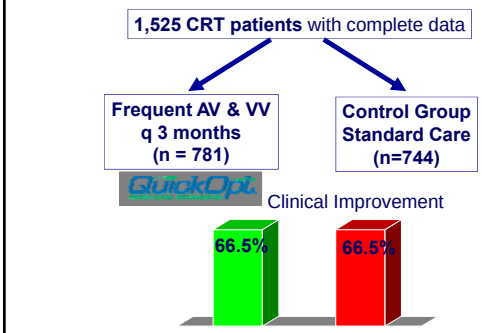
From J. Gorcsan

FREEDOM TRIAL



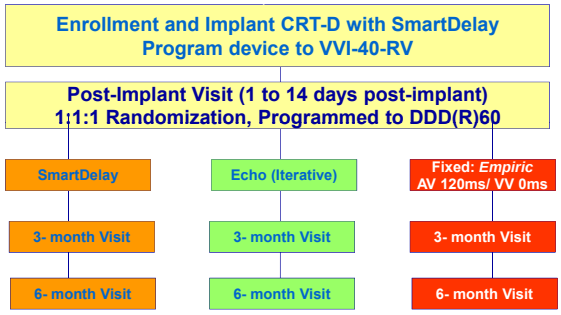
ST. JUDE MEDICAL *Abraham WT et al. Am Heart J 2010;159:944-948*

FREEDOM TRIAL



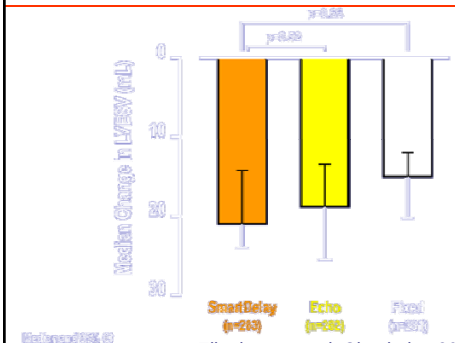
ST. JUDE MEDICAL *Abraham WT et al. HRS 2010*

SMART AV DELAY Randomized Trial: Empiric vs. Echo-Guided vs. Device-Based



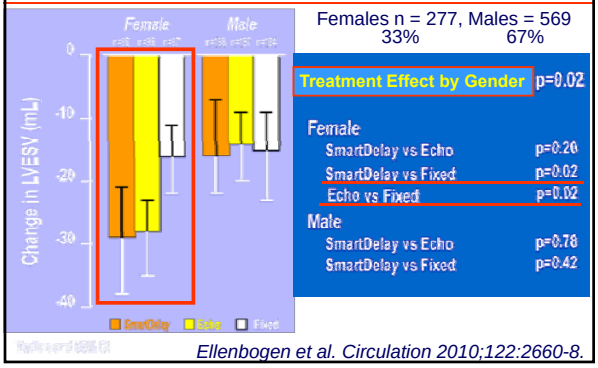
Ellenbogen et al. Circulation 2010;122:2660-8.

SMART AV Trial Primary Endpoint – LVESV



Ellenbogen et al. Circulation 2010;122:2660-8.

SMART AV Trial Primary Endpoint LVESV: Gender Subgroup

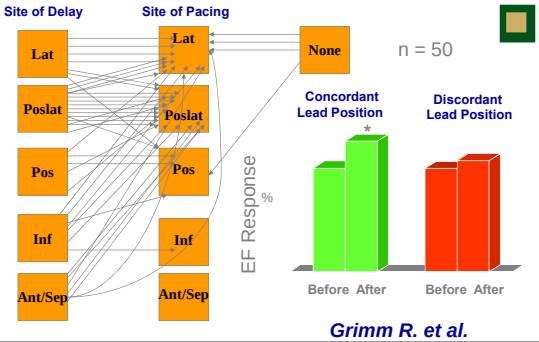


Females n = 277, Males = 569
33% 67%

Treatment Effect by Gender	p=0.02
Female	
SmartDelay vs Echo	p=0.20
SmartDelay vs Fixed	p=0.02
Echo vs Fixed	p=0.02
Male	
SmartDelay vs Echo	p=0.78
SmartDelay vs Fixed	p=0.42

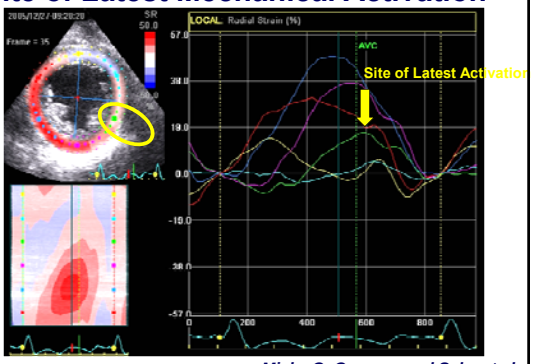
Ellenbogen et al. Circulation 2010;122:2660-8.

Effect of Concordance of Site of Latest Activation with LV Lead



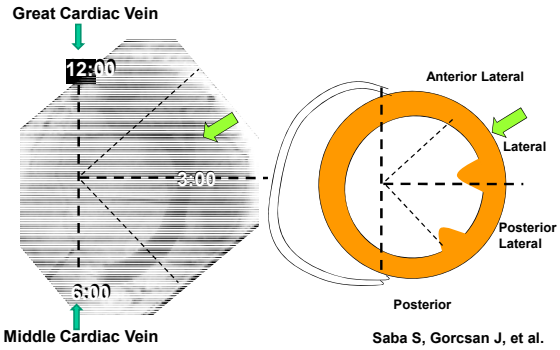
Grimm R. et al.

Speckle Tracking Strain Localization of Site of Latest Mechanical Activation



Miske G, Gorcsan and Saba et al.

Echo-Fluoro Alignment LAO View

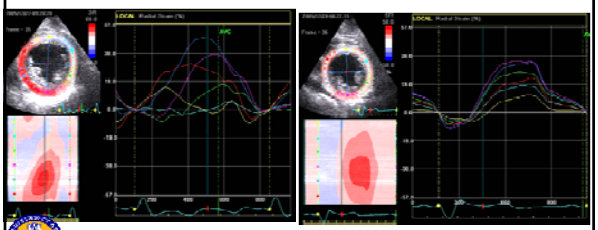


Saba S, Gorcsan J, et al.

EXACT CONCORDANCE OF LV LEAD POSITION

ACUTE IMPROVEMENTS IN LV SYNCHRONY

BASELINE DAY AFTER CRT

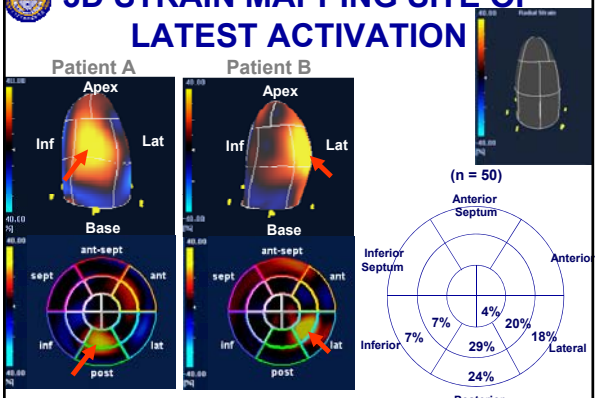


Lead Placement Exact Match with Site of Latest Mechanical Activation

Miske G, Gorcsan and Saba et al. ACC 2010

3D STRAIN MAPPING SITE OF LATEST ACTIVATION

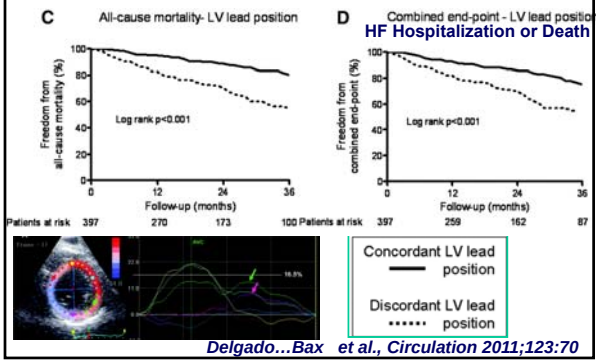
Patient A Patient B



Tanaka, H... Gorcsan J et al. Am J Cardiol 2009

LV Lead Position and Site of Latest Mechanical Activation

n = 397

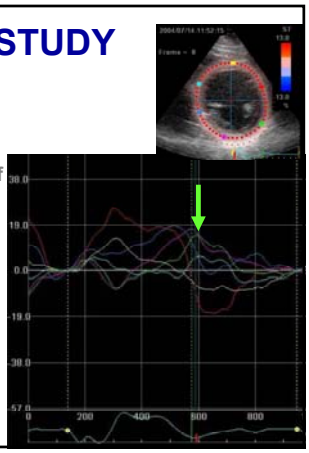


Delgado...Bax et al., Circulation 2011;123:70

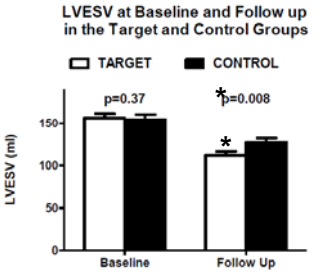
TARGET STUDY

- 220 CRT patients
- Randomized LV Lead:
  - Speckle Tracking Site of latest activation >10% thickening
  - Routine Control
- Primary end-point: ≥15% Reduction in LV end systolic volume at 6 months

Khan et al. ACC 2011



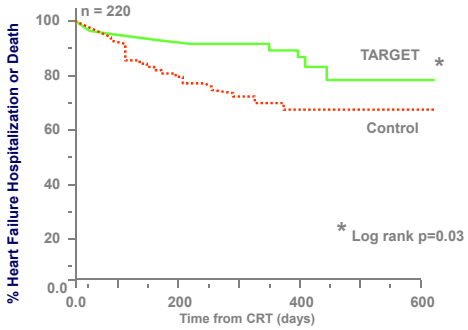
TARGET
Primary End-Point Results



- TARGET ESV response rate ≥15%: 70% vs. 55% in control (p=0.03)
- TARGET Clinical response rate ≥ 1 NYHA Class: 83% vs. 65% in control (p=0.003)

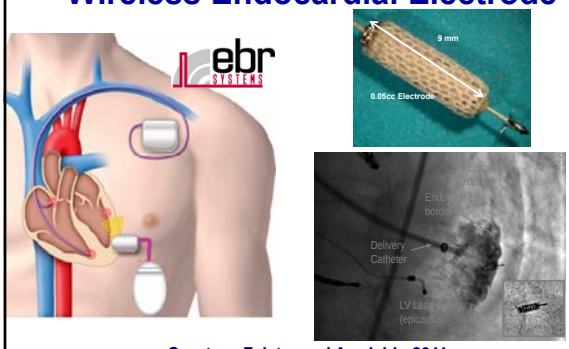
Khan et al. ACC 2011

TARGET: Secondary End-Point
HF Hospitalization or Death



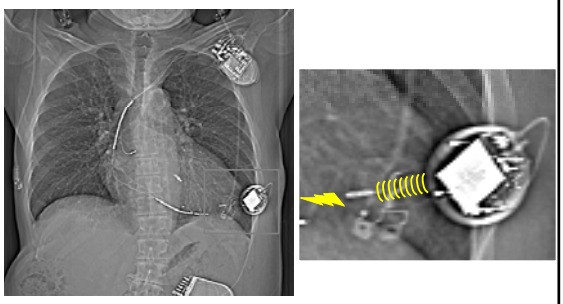
Khan et al. ACC 2011

The Future ?
Wireless Endocardial Electrode

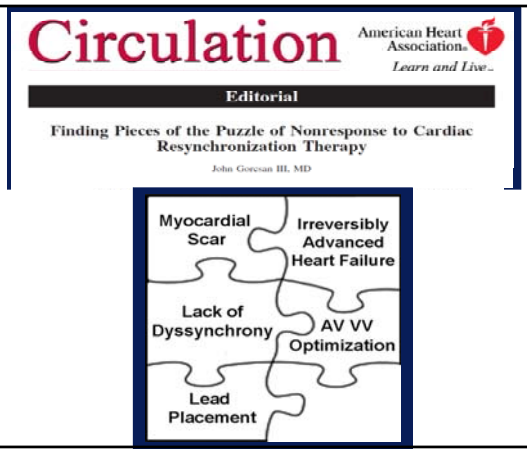


Courtesy Faletra and Aurrichio 2011

Wireless Endocardial Electrode
Ultrasound Triggered Electrical Stimulation



Courtesy Faletra and Aurrichio 2011



TAKE HOME MESSAGES

1. There is an abundance of evidence that dyssynchrony by echo is associated with long term outcome after CRT.
2. Opportunities for Dyssynchrony by Echo to Influence Patient Care for CRT:
   - Non-LBBB
   - Borderline QRS Width (110-130 ms)
   - Narrow QRS Width (< 130 ms)

   Randomized Clinical Trials are Underway
3. Imaging Site of Latest Activation to Assist in Guiding Optimal LV Lead Position.
4. Future Applications for Echo in CRT Will Continue to Emerge