Resynchronization Therapy in Children with Cardiomyopathy and Reduced Ejection Fraction

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No Disclosures

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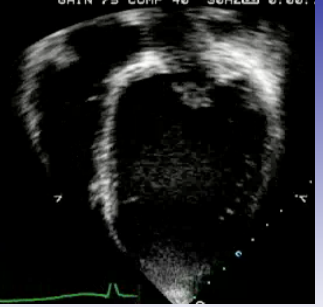
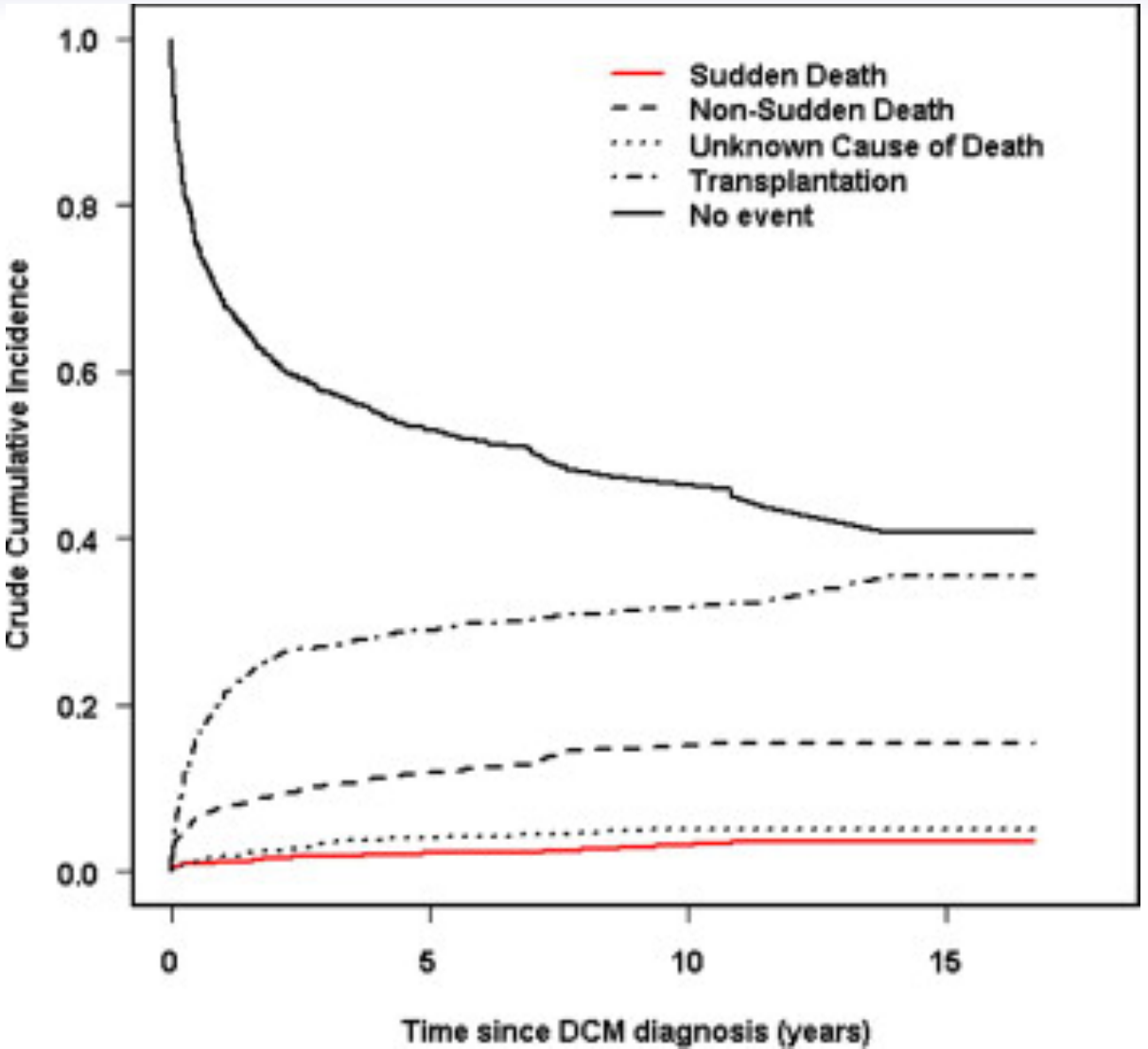
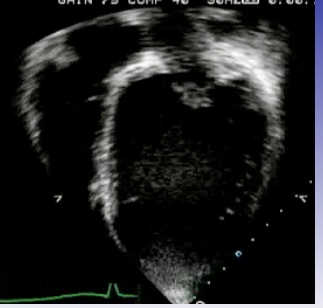


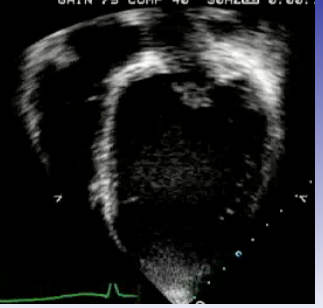
Competing risks analysis for sudden cardiac death, non-sudden cardiac death, unknown cause of death, and cardiac transplantation





Hemodynamic Management

- Patients with left ventricular failure often have regional dyskinesis associated with bundle branch block or IVCD
- Discoordinated contraction sequence results in decreased stroke volume
- Resynchronization therapy normalizes the ventricular activation sequence and improves hemodynamics

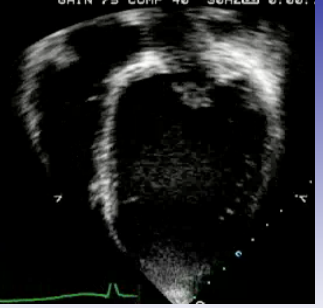


Dyssynchronous Heart Failure

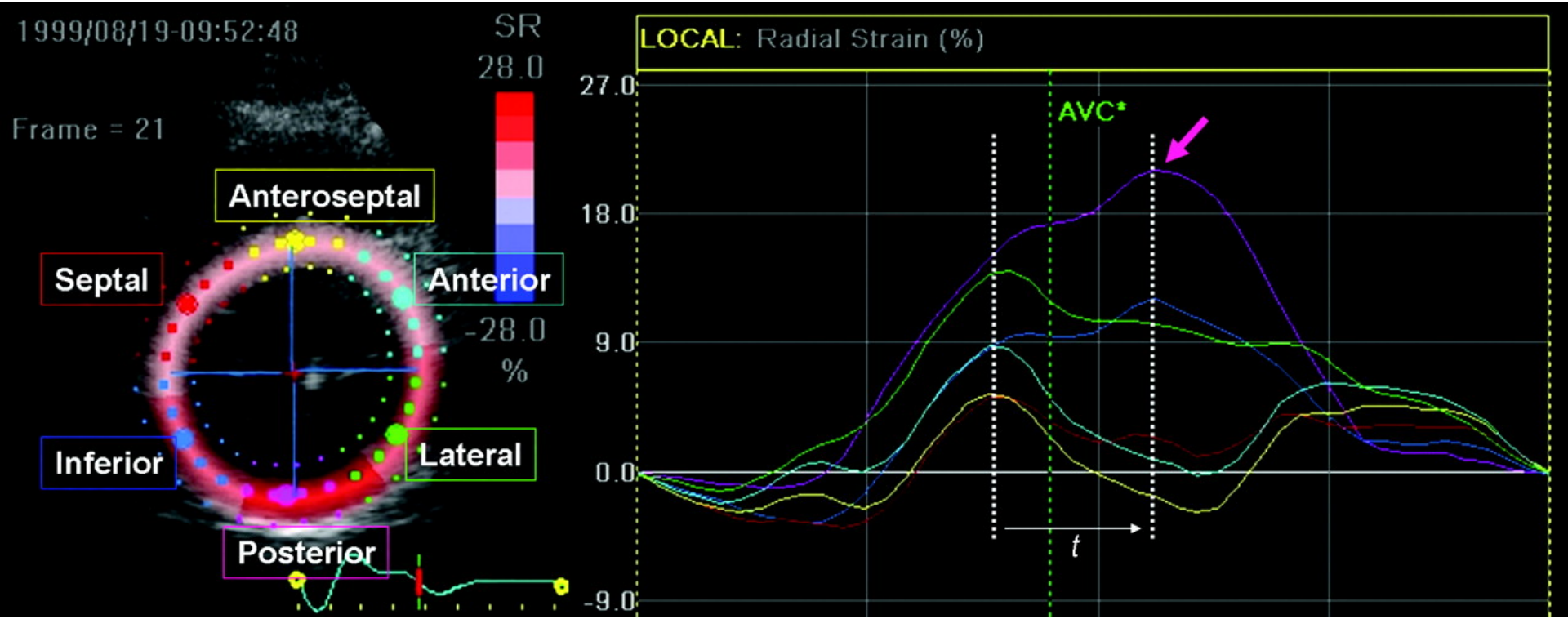
Electrical and mechanical dyssynchrony can lead to heart failure

- Dyssynchrony characterized by early and late activated areas of the ventricle
- Relaxation of early activated areas occur when late activated areas contracting
- This leads to unbalanced preload
  - Asymmetric hypertrophy
  - Ventricular remodeling.
  - Inefficient myocardial work
  - Cellular remodeling

Prinzen 1999



LV radial dyssynchrony by 2-dimensional speckle tracking



Victoria Delgado et al. Circulation. 2011;123:70-78

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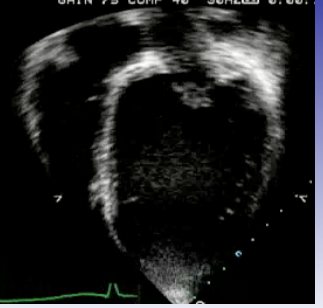
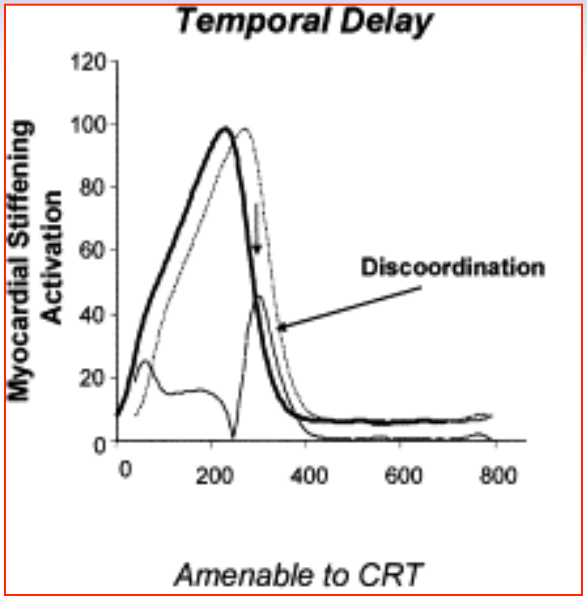
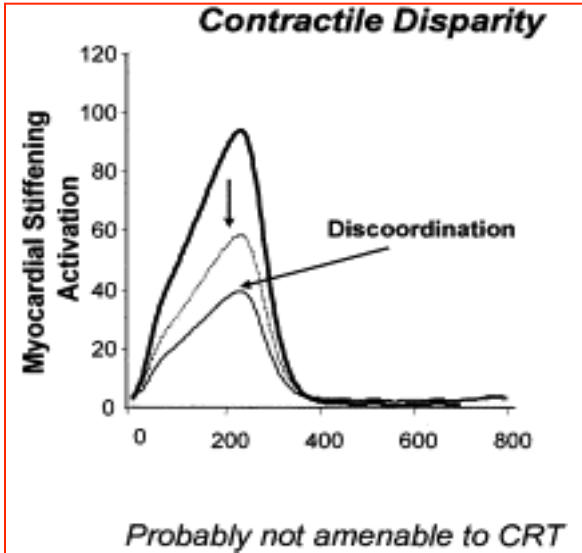
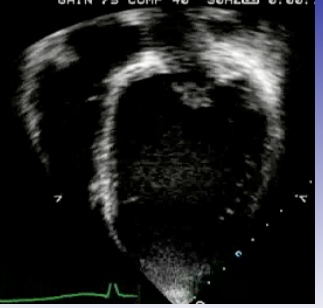


Dyssynchronous Heart Failure

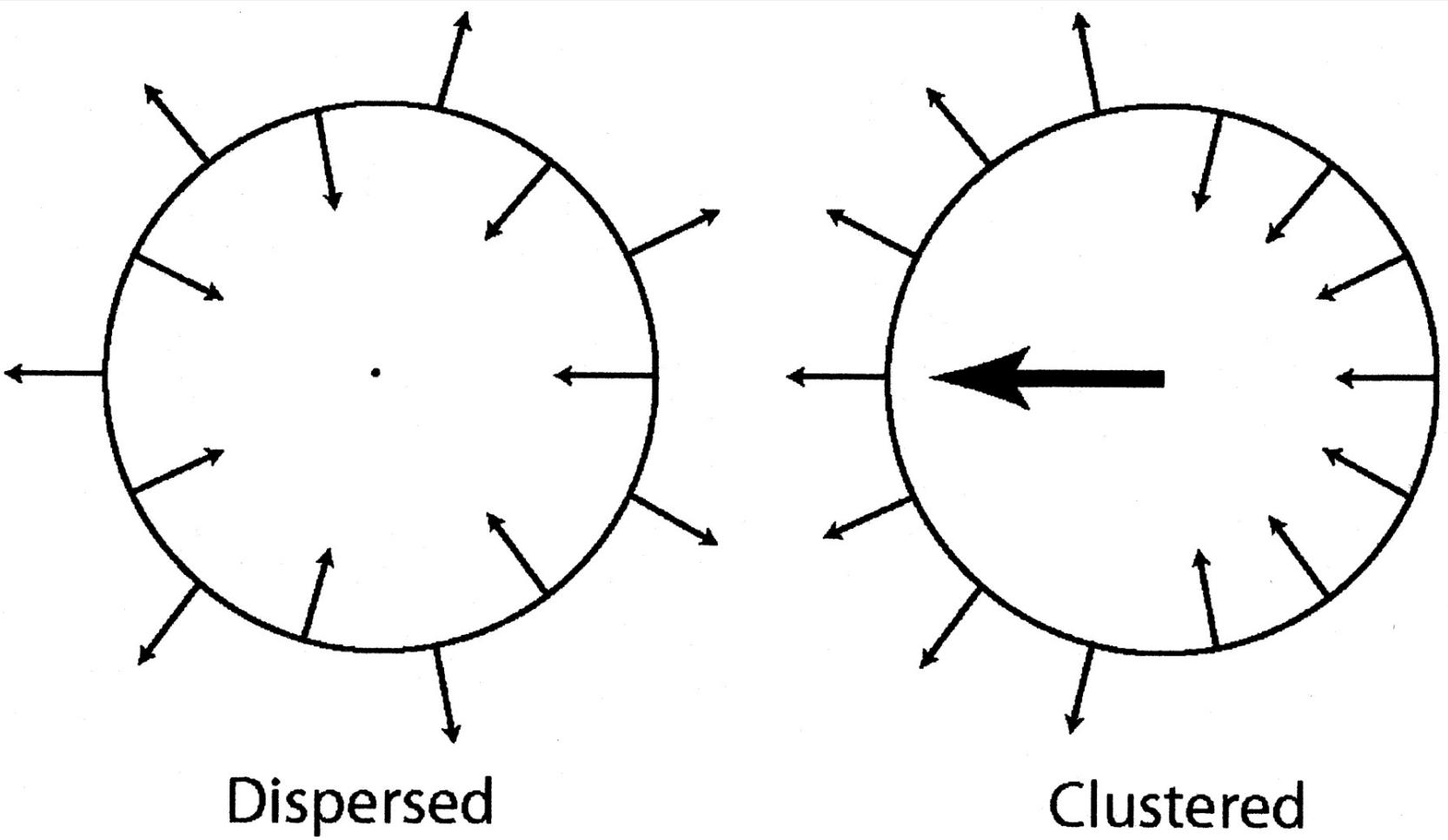
- Not all dyssynchrony the same
  - Electrical dyssynchrony secondary to late ventricular activation
    - Secondary to scar, dilatation, ischemia
    - Can result in mechanical dyssynchrony
    - Mechanical dyssynchrony is “clustered” – amenable to CRT
  - Mechanical dyssynchrony may have several causes
    - Secondary to electrical dyssynchrony
    - Secondary to primary muscle issues and contractile disparities
    - Mechanical dyssynchrony is dispersed– not amenable to CRT



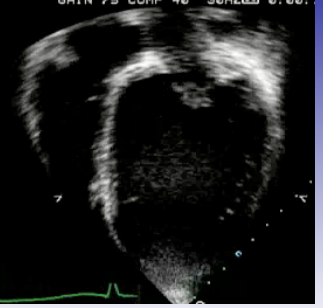




Dispersed vs Clustered Dyssynchrony



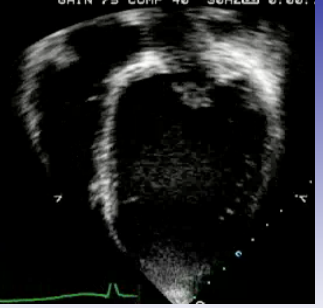
Helm et al, Circulation 2005



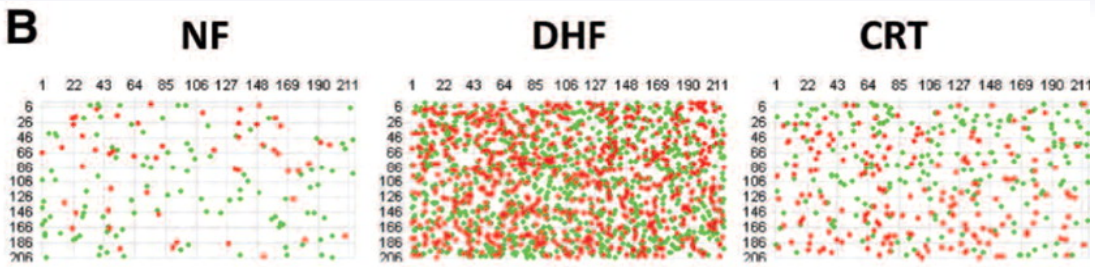
Dyssynchronous Heart Failure

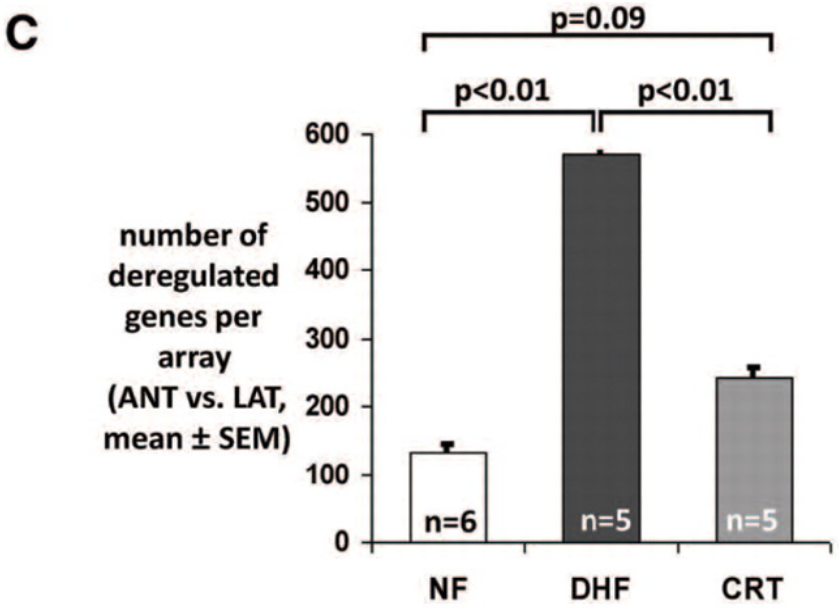
- Cellular remodeling
  - Increased levels of mediators of fibrosis and apoptosis in late contracting segments
  - Decreased calcium cycling in cell, resulting in impaired excitation-contraction coupling
  - Reduction in beta-adrenereceptor gene expression
  - Connexin-43 down regulation in late contracting segments with a consequent reduction in myocardial conduction velocity

Chakir 2008 Vanderheyden 2008
Mullens 2008 Spragg 2003



Dyssynchrony leads to increased regional heterogeneity in gene expression





Partially reduced with CRT

Hana Cho et al. Circ Arrhythm Electrophysiol. 2012;5:594-603

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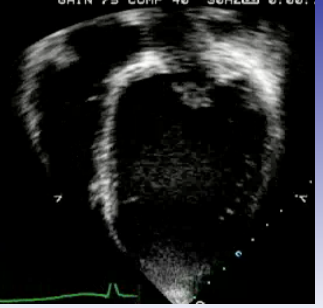
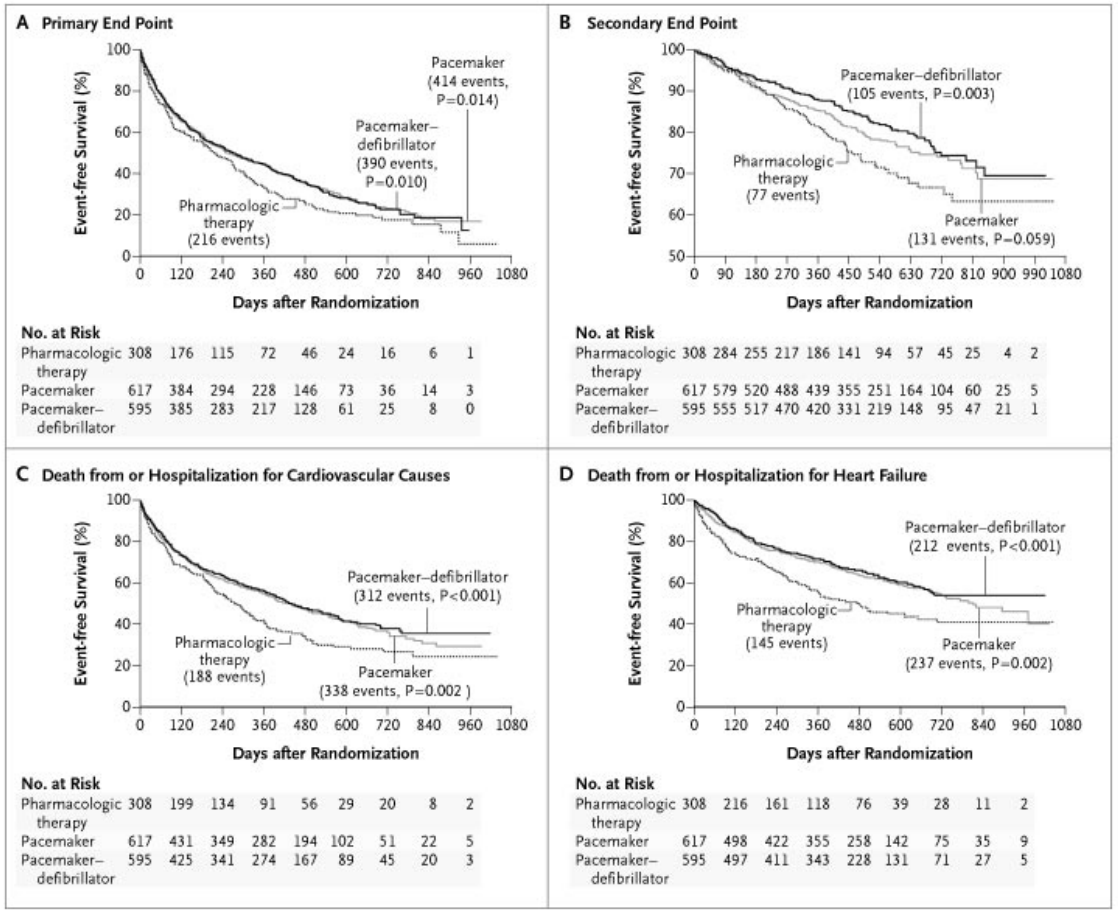
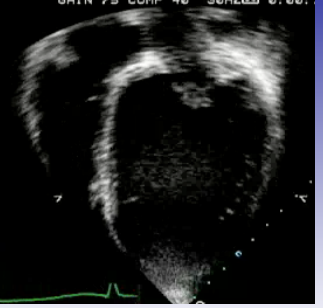


Efficacy of CRT in Adults

- Multiple adult studies have assessed efficacy and safety of resynchronization therapy
  - MIRACLE - 453 patients with improvement in QOL and 6 minute walk
  - COMPANION - 1500 patients with reduction in mortality
    - 24% with CRT
    - 36% with CRT/ICD



NEJM 2002,2004

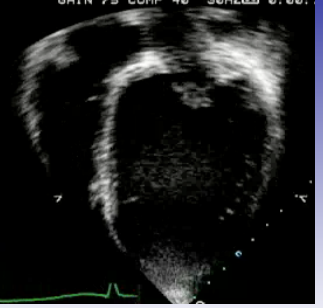


Pediatric vs. Adult

Adult and Pediatric patients quite different

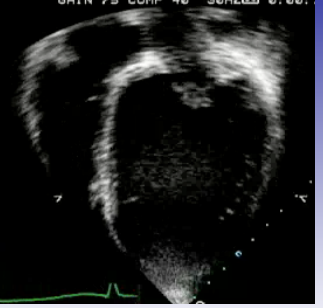
- Pediatric patients unlikely to meet adult criteria for resynchronization
- Schiller looked at a heart failure registry of all pediatric patients with dilated cardiomyopathy
  - 52 patients
  - All patients with mean EF of 25%
  - No patients met criteria for prolonged QRS on first visit
  - No patient had a LBBB on ECG

Schiller JCE 2015



Clinical Studies in Pediatrics

- Dubin: 2005
  - 16 (15.5%) DCM, 14 (13.6%) CCAVB
- Cecchin: 2009
  - 10 (16.7%) DCM, 4 (6.7%) CCAVB
- Janousek: 2009
  - 10 (9.2%) DCM, 12 (11%) CCAVB
- Perera: 2013
  - 10 (14.9%) DCM, 7 (10.4%) CCAVB

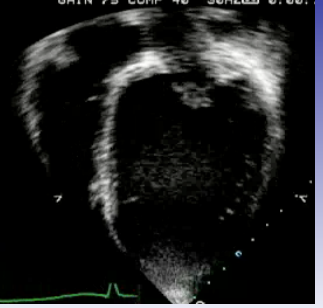


Responders after resynchronization

- Janousek and colleagues looked at 109 patients in pediatrics with CRT
- Median age of 16.9 yrs

  (.24-73.8)
- Median follow-up of 7.5 months
- Able to identify several predictors of non-response
  - Dilated CM
  - Poor NYHA class
- Strongest predictor of response
  - Systemic LV

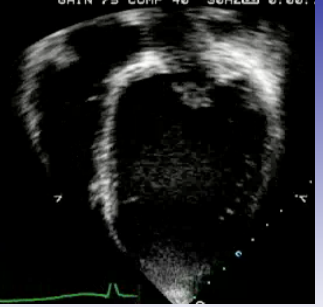
Janousek 2009

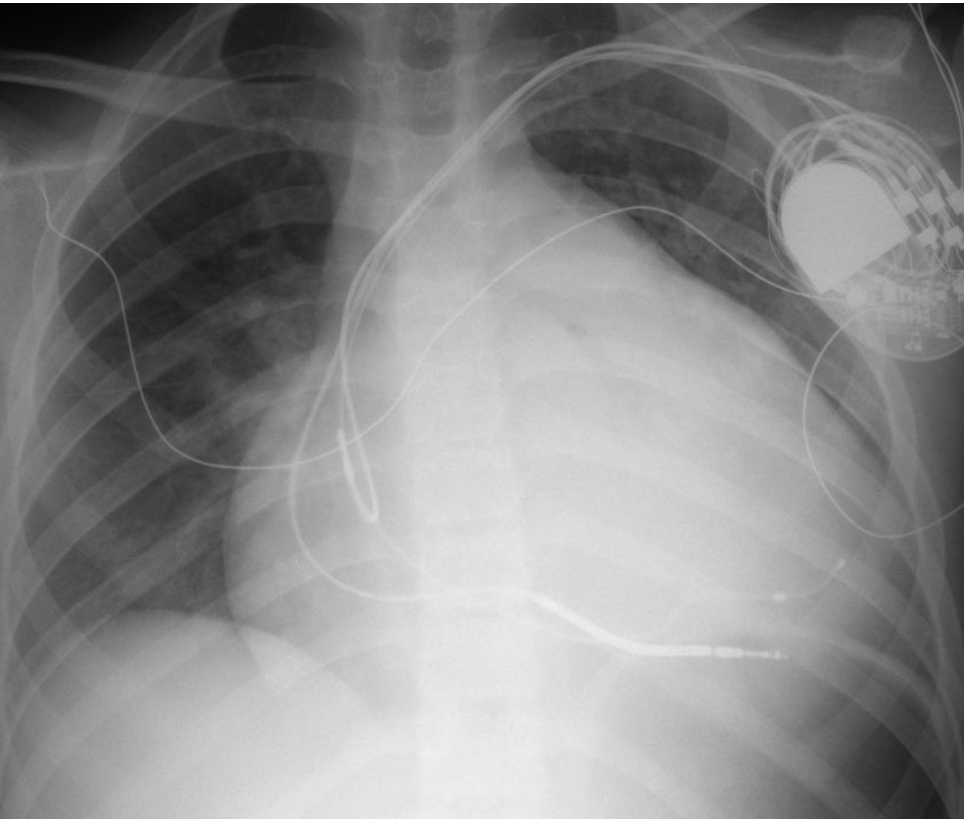


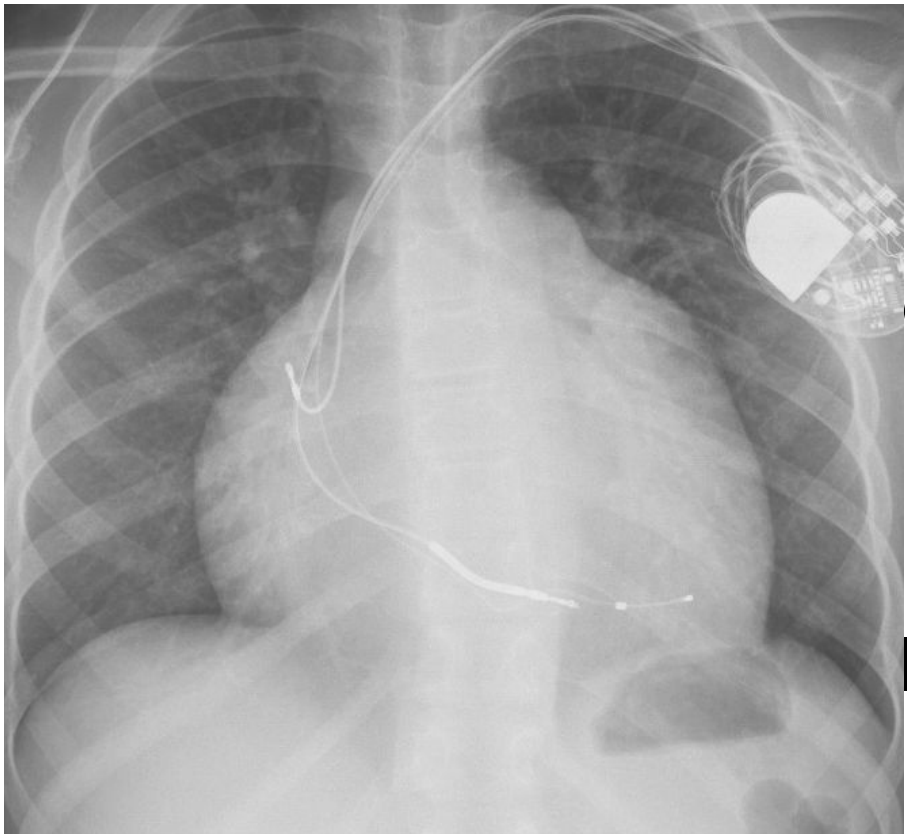
Mechanical vs Electrical Dyssynchrony?

- Friedberg et al:
  - 65% of pediatric DCM patients had mechanical dyssynchrony
  - Median QRSd was only 84 ms
  - Mechanical dyssynchrony did not correlate with QRSd
- Chen et al:
  - 18% of ped DCM patients have a QRSd >120 ms
  - However average QRSd for cohort of 89 DCM patients = 93 ms
  - QRSd did not correlate with intraventricular mechanical dyssynchrony.

- This is in contrast to studies in adult DCM patients demonstrating average QRSd >150 milliseconds







Thank You