Cardiac Resynchronization Therapy
Programming and Optimization of Biventricular Stimulation

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WHAT YOU NEED TO KNOW ABOUT CRT PROGRAMMING AND OPTIMIZATION

Marleen Irwin
Disclosure-of-Relationship

Marleen Irwin,
participant in industry sponsored education
Medtronic & St. Jude Canada

Cardiac Resynchronization Therapy:
Optimization of Biventricular Stimulation
Chronic Congestive Heart Failure:

Heart failure....a pathophysiological state in which an abnormality of cardiac function is responsible for the failure of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues.

A state of chronic adrenergic stimulation.
Ventricular Dyssynchrony:
Incidence

• **Age**
  - 1% in < 50 years of age
  - 5% in 50 - 70 years of age
  - 10-15% in the >70 age range

• **Gender**

• **Race**
HF Incidence and Prevalence

• Prevalence
  – Worldwide, 23 million\(^1\)
  – Canada, 350,000
  – United States, 5 million\(^2\)

• Incidence
  – Worldwide, 2 million new cases annually\(^1\)

• HF afflicts 1000 out of every 100,000 over age 65 \(^2\)

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1 World Health Statistics, World Health Organization,
2 American Heart Association, 2001 Heart and Stroke Statistical Update.
Traditional CHF Rx: Summary

• Early diagnosis imperative
• Multidisciplinary approach essential
• Drugs proven to ↓ mortality most important
  – ACEI, β blockers, amiodarone, aldactone
• ↑ QOL: Digoxin, diuretics

Can cardiac resynchronization Rx [CRT] improve QOL?
Typical population

(73%) male; (36%) female

mean age 61 ±3.8 years

LVEF < 35%

NYHA III & IV

QRS > 180ms or bundle branch block pattern

PR interval > 250 ms
Cardiac Resynchronization Therapy

LBBB
Prognosis with Ventricular Dyssynchrony

1 Year Survival

P < 0.001

11% QRS < 120 ms
16% QRS > 120 ms

Long-term (45 Mo) Survival

P < 0.001

34% QRS < 120 ms
49% QRS > 120 ms

N=5,517

Iuliano et al. *AHJ* 2002;143:1085-91
N=669
Is Heart Failure Bad?

YES!
EVOLUTION OF CLINICAL STAGES

- Normal
  - No symptoms
  - Normal exercise
  - Normal LV fxn

- Asymptomatic LV Dysfunction
  - No symptoms
  - Normal exercise
  - Abnormal LV fxn

- Compensated CHF
  - No symptoms
  - Exercise
  - Abnormal LV fxn

- Decompensated CHF
  - Symptoms
  - Exercise
  - Abnormal LV fxn

- Refractory CHF
  - Symptoms not controlled with treatment
It is about remodeling...
• Atrial synchronous cardiac resynchronization therapy (CRT) is an accepted therapeutic option for patients with first degree AV block, intraventricular conduction delay (IVCD) and drug refractory chronic congestive heart failure, and provides a demonstrated functional benefit in a subset of individuals with ventricular dysynchrony.
Role of Echo Guided Cardiac Resynchronization Therapy

- Patient Selection
- LV & RV Lead Positioning
- Device Timing Optimization
Selection of best LV lead location

Stimulation at the site of latest activation of the LV free wall has provided greatest improvement in pulse pressure & LV +dP/dT

1 - lateral/marginal cardiac vein
2 - posterior-lateral cardiac vein
3 - posterior cardiac vein
4 - middle cardiac vein
5 - great cardiac vein
Figure 6: When the LV lead tip is at the site of latest activation, the LV electrogram signal will intersect the latter part of the QRS on the ECG.
Congestive Heart Failure

- Predicted to be the major worldwide cardiovascular problem of the next few decades.
- Increase due to general aging population and the improved treatment of myocardial infarction; patients surviving the acute event, yet with a damaged heart.
Response to CRT

- Many patients derive considerable benefits from CRT
  - morbidity, mortality, and quality of life

- Challenge: Converting non-responders to responders!
CRT Optimization

• Programming may specifically meet the needs of an individual patient who has been classified as a “non-responder”

• Two main device-based approaches
  – Promoting right – left ventricular synchronized depolarization
  – Optimizing timing
    • AV timing
    • VV timing
Promoting ventricular synchronization

- RV and LV stimulation 100% of the time

Telemetered Diagnostic Data
Promoting ventricular synchronization:

AV Interval

- AV interval programming for both
  - Paced AV
  - Sensed AV
Promoting ventricular synchronization: AV modification to maintain ventricular pacing

- AV interval modification algorithms will encourage a forced ventricular output [Pace stimulation] whenever an intrinsic ventricular event is sensed

  - Negative AV hysteresis
  - Ventricular “PACE” enabled
Negative AV Hysteresis
Timing Optimization

• Precise timing of ventricular contractions
• Allow for
  – Adequate time for passive filling of the ventricles
  – Avoid intrinsic depolarization
  – Interventricular contraction of RV and LV
# Measuring Mechanical Dyssynchrony

<table>
<thead>
<tr>
<th></th>
<th>+ Pros</th>
<th>- Cons</th>
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<tr>
<td><strong>ECG</strong></td>
<td>• simple, widely available</td>
<td>• may lack specificity</td>
</tr>
<tr>
<td></td>
<td>• defined (120 ms)</td>
<td>• QRS duration non-specific</td>
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<tr>
<td><strong>MRI (tagged)</strong></td>
<td>• 3-D</td>
<td>• resolution/frame rate/#cycles used</td>
</tr>
<tr>
<td></td>
<td>• accurate</td>
<td>• no post-implant data</td>
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<tr>
<td></td>
<td></td>
<td>• expensive</td>
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<tr>
<td><strong>Radionuclide venography</strong></td>
<td>• improved border detection</td>
<td>• invasive</td>
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<tr>
<td></td>
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<td>• few tissue movement algorithms</td>
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<tr>
<td><strong>Echo-based</strong></td>
<td>• widely available/clinical</td>
<td>• accuracy and reproducibility</td>
</tr>
<tr>
<td></td>
<td>• simplicity</td>
<td>• varying techniques, not all available</td>
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<tr>
<td></td>
<td>• time-dependent algorithms</td>
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Elements of Cardiac Dyssynchrony

Deleterious Effects of Ventricular Dyssynchrony on Cardiac Function

- Reduced diastolic filling time
- Weakened contractility
- Protracted mitral regurgitation
- Post systolic regional contraction

= Diminished stroke volume

Let's look at it this way...
Echo guided variables

- **Mitral regurgitation** – **MR**
- **Septal to posterior wall motion delay** - **SPWMD**
  intraventricular conduction delay
- **Interventricular Mechanical Delay** **IVD**
  as a marker for ventricular dysynchrony measured from the
  onset of QRS to aortic outflow and QRS to pulmonic flow
- **Velocity Time Integral** – **VTI**
  as a marker for stroke volume and cardiac output
  and optimized atrioventricular timing interval
Echo Based Techniques to Measure Cardiac Dyssynchrony

- **Atrio-ventricular**
  - 2D Doppler
    - LV filling time
    - E/A ratio

- **Inter-ventricular**
  - 2D Doppler: Inter-ventricular mechanical delay (IVMD)
  - Tissue Doppler Imaging: myocardial strain

- **Intra-ventricular**
  - M-mode: Septal to posterior wall motion delay (SPWMD)
  - 2D Doppler: Aortic pre-ejection interval (APEI)
  - Contrast: systolic regional fractional area
  - 2D with wall motion phase analysis
  - Tissue Doppler Imaging:
    - 5 segment grading
    - Myocardial strain rate
    - Time to peak or start of systolic contraction
Echo Guided Optimization

“Gold standard” of device timing optimization

- Mitral velocity Doppler echo is used for AV timing optimization
  - Sensed and paced AV delays

- Aortic velocity time integral (VTI) for VV timing
  - RV and LV synchronization
Reduction of intra and interventricular asynchrony (IVCD) along with optimization of the paced atrio-ventricular delay (AVI) is believed to be a mechanism for improvement.

Therefore...

with the subsequent optimization of the timing of sequential left ventricular to right ventricular (V-V) stimulation a reduced intraventricular asynchrony may be achieved.
Goals of AV Optimization

- Allow adequate time for passive filling of the ventricles
  - atrial diastole
- Allow adequate time for a complete atrial contraction
  - atrial contribution to ventricular filling
- Allow for ventricular contraction
  - Ventricular systole

When AV timing is not optimized and is too short
- Ventricular filling time may be cut short
- The atrial kick can be cut short
- Hemodynamics can be impaired

If AV timing is too long, intrinsic ventricular activity can break through
Echo Doppler Waveform

- Isovolumetric Contraction
- Aortic Flow
- Isovolumetric Relaxation
Delayed LV activation due to IVCD

**IVCD**

- LV activation is delayed, resulting in early passive LV filling and the atrial “kick” occurring simultaneously.
- Therefore, a diminished transmitral blood flow and decreased preloading of the LV.

Doppler echo of transmitral blood flow

Fusion of the E and A waves decreased transmitral flow and diminished preload of the LV.
Delayed LV activation due to IVCD

With synchronized LV RV stimulation

- LV and RV activation is simultaneous, resulting in LV contraction and earlier relaxation which increases LV filling time.
- With optimized AV delay, the return of normal E and A wave separation

Doppler echo of transmitral blood flow

Normalized E and A wave separation an increased LV filling time
Optimized AVI results in separation of the early filling and atrial contraction, normalizing the filling pattern.
Mitral Velocity Doppler Echo

AV interval – too long
Echo for CRT Optimization

AV interval – too short

Observe the A wave is cut off

Aortic Flow

Aortic Flow
Trans-mitral Flow
AV Delay Optimization Methods

- **Trans-mitral Flow Duration**
  - Iterative method. Assess filling patterns at various AV delays.
  - “Ritter” method. Formula derived optimum from a short AV delay and a long AV delay.

- **Trans-mitral Flow Volume**
  - Select maximum mitral VTI from tested AV delays
  - Concordant with invasively measured maximum dP/dt²

Too short AV delay. E and A waves separated, but A wave is truncated.

Too long AV delay. E and A waves fused, filling time reduced.

“Just Right” AV delay. BiV pacing sustained, active filling maintained.

Optimization of AV Timing with MVDE

- Measure the intrinsic PR; program the AV delay to a shorter value
- Using mitral velocity Doppler echo (MVDE), record and observe the E and A waves
- Shorten the AV delay in steps of 20 ms until A waves cut off—the AV delay is too short
- Now step up the AV delay in 10 ms steps until you see E and A waves without A-wave cutoff

That point is the optimized AV delay
Septal to posterior wall motion delay - SPWMD

- M-mode echocardiography allows noninvasive quantification of the degree of ventricular asynchrony by assessing the time delay from septal to posterior wall motion peak systolic contraction and may help identify potential responders to CRT.
Septal Dyskinesis - Timing “mismatch”

**IVCD**

- abnormal activation-contraction sequence between the septum and the LV posterior free wall
- the septum moves away from the LV free wall during systole
- thus, diminished septal contribution to LV stroke volume

Marked degree of paradoxical septal motion (PSM).

Makaryus, Amgad N., Arduini, Armando D., Mallin, Jason, Chung, Erica, Kort, Smadar, Shi, Qiuhu, Jadonath, Ram & Mangion, Judy
Echocardiographic Features of Patients With Heart Failure Who May Benefit From Biventricular Pacing.
Intra-ventricular Dyssynchrony
Septal-Posterior Wall Motion Delay

- Difference in times from peak excursions of the septum and of the posterior wall at the papillary muscle level
- SPWMD ≥ 130 ms predicted response (LVEDVi) to CRT in study of 25 pts with QRS ≥ 140 ms
  - From parasternal short-axis view at papillary muscle level

Parasternal Long-axis View Shown

SPWMD 80ms vs 150ms @ V-V 40
V-V 4   SPWMD 320ms

V-V 40   SPWMD 390ms

Paradoxical septal wall motion
The velocity time integral (VTI) is directly proportional to the stroke volume ejected through the valve and if the area of the vessel is accurately measured and the VTI is the maximum which can be recorded from the site, the stroke volume is then calculated.
VTI

Doppler Profile of Aortic Valve Flow of Varying AV Interval

A surrogate for the stroke volume Velocity Time Interval (VTI) of aortic valve flow;

- less with short AVI,
- optimized at AVI 150ms

Resynchronization Therapy for Heart Failure
L A Saxon, T DeMarco, et.al.
Educational Content from the HRS website
Aortic VTI

Sensed AV Delay = 180 ms
VTI = 16 cm

Sensed AV Delay = 160 ms
VTI = 22 cm

SV = VTI x A
CO = SV x HR
Using VTI Doppler Echo for VV Timing

- Optimize the sensed and paced AV delays
- Measure the VTI while adjusting the interventricular settings
  - Do LV first and measure VTI values for 20, 40, 60 and 80 ms
  - Record the offset value that produces the greatest VTI value
- Repeat with the RV but this time, adjust the AV delay
  - To adjust the AV delay, subtract the interventricular delay from the AV delay
  - For example, to test RV first, 20 ms with AV delay of 130 reprogram the AV delay to 110 ms (130 minus 20)
  - Record the VTI scores
- Optimal VV timing delay is the one that produces the greatest VTI value
V-V 4ms  VTI SV 34ml

V-V 40ms  VTI SV 40ml
Programming VV Timing Optimization
VV Timing Considerations

- VV timing may vary over time particularly with disease progression or reverse remodeling.
- Echo remains the gold standard of VV timing optimization.
- Some programmer based algorithms correlates with echo results.
- The location and etiology of the delayed longitudinal contraction of the heart may play a role in VV timing; “a developing story”
Optimizing VV Delay Based on Aortic VTI

- Obtain Pulsed Wave Doppler of LVOT with several different sequential ventricular paced intervals
- Select the setting yielding the largest VTI as the optimal paced interval
A novel echocardiographic technique for assessment of regional systolic tissue velocity, providing measurements of time to peak systolic velocity represented as a colorized image used as a surrogate marker of the degree of left ventricular dysynchrony.
Intra-ventricular Dyssynchrony
Tissue Doppler Imaging

- A standard deviation of 32.6 ms in differences in time to peak systolic contraction (velocity) between 12 LV segments predicted response (LVESV) to CRT in 30 pts. Yu CM et al. Am J Cardiol 2002;91:684–688

- % of 6 basal LV segments with contraction after aortic valve closure measured using strain rate* predicted change in LVEF with CRT in 20 pts. Søgaard P, et al. JACC 2002;40:723–730

* Uses tissue velocity data to calculate regional deformation rates. May be less influenced by translational motion or tethering.
Tissue Doppler Imaging (TDI)

- TDI measures the actual contraction patterns at different regions of the ventricle
  - TDI can measure dyssynchronous or delayed contraction patterns
LV=RV

V. C  excellent synchronization
<table>
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<tr>
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<th>Time To Peak</th>
<th>Peak Velocity</th>
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<tbody>
<tr>
<td>6</td>
<td>95.74 ms</td>
<td>6.02 cm/s</td>
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<tr>
<td>5</td>
<td>123.54 ms</td>
<td>6.31 cm/s</td>
</tr>
<tr>
<td>4</td>
<td>116.59 ms</td>
<td>11.54 cm/s</td>
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<tr>
<td>3</td>
<td>158.20 ms</td>
<td>1.14 cm/s</td>
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<tr>
<td>2</td>
<td>269.43 ms</td>
<td>2.82 cm/s</td>
</tr>
<tr>
<td>1</td>
<td>276.48 ms</td>
<td>4.79 cm/s</td>
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B. G  Delayed septal contraction.
CRT Device Optimization with Echo Potential Targets

- Stroke Volume (Aortic VTI)
- Trans-mitral Flow
- Intra-Ventricular Synchrony
How Important is Timing Optimization?

- Studies suggest that CRT timing optimization improves response.
- AV and VV timing optimization were shown to improve LVEF scores.
- Since CRT non-response is a clinical challenge and since some patients seem to improve markedly with CRT timing optimization, it is an important clinical consideration.

![Graph showing Mean LVEF (%) for Rosario and Sogaard with Baseline, AV OPT, and VV OPT categories.](image)
Considerations

Presenting baseline CRT programmed parameters

- AV interval optimization
  - The Ritter method
  - aortic velocity time integral (VTI)

- Ventricular dysynchrony
  - M-Mode SPWMD; septal to posterior wall motion delay
  - IVD - QRS to aortic outflow - QRS to pulmonic flow
  - TSI reviewed during
    - LVRV simultaneous pacing
    - Left ventricle “first”
    - Right ventricle “first”
Methods for review of non-responders

- Acute changes in SPWMD and Aortic VTI measured during sinus rhythm (SR), RV, LV and RV=LV pacing

- AV delay may be optimized using Mitral Velocity Time Integral (VTI)
  - AV delays:
    - Short (50ms)
    - Intermediate (110ms)
    - Long (150ms)

- Interventricular delay (IVD), as a marker for dysynchrony, measured from the onset of QRS to aortic outflow and QRS to pulmonic flow

- SV and IVD may be improved using
  - echo guided aortic VTI and SPWMD
Outcomes

- There appears to be a reduction in time delay from the septal to posterior wall motion peak systolic contraction (SPWMD) with LV and LV+RV pacing, compared to SR with IVCD and RV pacing.
Effect of Pacing Site on Intraventricular Asynchrony (SPWMD msec)

Site of Pacing

- Intrinsic
- RV
- LV
- LV+RV

Pts

1 2 3 4 5 6 7
Effect of Pacing Sequence on Interventricular Asynchrony (IVD) ms

Site of Pacing

Pts

1 2 3 4 5 6 7

Intrinsic RV LV LV+RV

IVD ms

0 20 40 60 80 100 120 140 160
It has been shown that there may be a trend toward incremental improvement, if aortic velocity time integral (VTI), which correlates with cardiac output/stroke volume is used as a marker for optimized AV interval and V-V interval timing.

Short and intermediate AV delays appear to have the greatest improvements in diastolic filling parameters compared to long AV delay.
Effect of AV Delay on Mitral Velocity Time Integral (VTI) cm
Poor Quality of Life for HF patients

Overall perception of health

- General population: 70
- Depression: 58
- Angina: 56
- AF symptomatic: 52
- Valve disease symptomatic: 48
- Chronic Bronchitis: 48
- Heart Failure NYHA Class II: 55
- Heart Failure NYHA Class III: 45
- Heart Failure NYHA Class IV: 36

Adjusted SF 36 means

QOL  PCS8

5 - 10 point increase is meaningful
LV RV stimulation

Intraventricular pacing delay of left ventricular to right ventricular pacing activation (V-V ms) is believed to be patient specific and may be optimized using echocardiography techniques such as SPWMD, and TSI for objective quantification of the degree of improvement in left ventricular dysynchrony.
Conclusions for echo guided programming...

- *Optimization* of the timing of sequential left ventricular to right ventricular (V-V) pacing and the hypothesis that this may reduce intraventricular asynchrony, has resulted in a number of echocardiography clinical reviews to attempt to objectively select:
  - the optimal intraventricular timing for left ventricular to right ventricular contraction, and
  - to estimate improvements in systolic function during Cardiac Resynchronization Therapy

- To that end, if a synchronized timing delay is optimal for systolic function (V-V 20ms or 40ms) then anodal stimulation should be assessed and avoided...
Biventricular pacing LVRV with Ring to Tip configuration and a programmed V-V 16ms
LV only with Ring to Tip configuration
Never the less...It may be all about the synchrony
What can we milk from the data?
Is Heart Failure Bad?

YES!
Summary

- Interventricular delay (IVD) as a marker for ventricular dysynchrony and SPWMD appear to be promising measures of intra and inter-ventricular asynchrony to assist with tailoring CRT programming for improvements in synchrony and systolic function.

- Aortic velocity time integral (VTI) as a marker for improvement in stroke volume also appears to be promising in guiding AV interval programming.
Follow-up Care

- Standard medical management of CHF as defined by practice guidelines
- Standard device follow-up as defined by practice guidelines
  - Goal is to achieve 100% LV and RV stimulation to deliver therapy; optimize V-V interval
  - AV interval optimization is recommended to achieve maximum diastolic filling time
  - Review quality of life and activities of daily living
Collaboration = Synchronization

- The impact of collaborative care of the heart failure patient has been shown to significantly improve survival compared to those followed by family physicians alone....
Cardiac Resynchronization Therapy

**Goals**

- Improve hemodynamics
- Improve Quality of Life
Biventricular pacing AVI -30, VV-4
Summary

- Large number of patients studied in RCTs
- Concordant proof that CRT improves quality of life, exercise capacity, functional capacity; persist through 1 year
- CRT reduces the risk of mortality and heart failure due to worsening HF
- CRT + ICD reduces risk of mortality
- CRT improves cardiac function and structure
Cardiac Resynchronization Therapy for Chronic Congestive Heart Failure

Quality of Life
AV optimization
Ventricular resynchronization
Heart Rate Variability
Reduced hospital visitations
Referral to Heart Function clinics
Thank you
谢谢

XI E-XI E NI
Thank you
Figure 15. Biventricular Stimulation-Shared Cathode Bipolar (Tip Electrode) This AP image demonstrates an LV branch vein unipolar lead in a lateral coronary sinus vein and an RV bipolar lead in the RV apex. Biventricular stimulation is achieved using a shared cathodal bipolar configuration.
LV only with Unipolar
Aortic Velocity Time Integral (VTI)

- Time integral [speed] of blood flow past the aortic valve during systole
- Aortic VTI is surrogate for stroke volume; cardiac output (CO)
- Using Aortic VTI Echo, adjust the AV delay until the greatest possible VTI value, which would correspond to an increased CO