Optimizing CRT: a clinical must?

P.G. Golzio
AOU Molinette
Torino -Italy
CRT optimization: the “Guidelines”

*Guidelines for cardiac pacing & CRT (in collaboration with EHRA)*

They simply recommend post-implant programming of the optimal AVD & VVD prior to hospital discharge ... *(very generic statement!)*

*“Echo for CRT: recommendations for performance & reporting” (Dyssynchrony Writing Group)*

They don’t formally recommend AVD optimization, but provides GLs on how it can be performed using Ritter, Iterative or ‘Simplified’ methods. Similarly, they acknowledge VVD optimization may have hemodynamic benefits but without sufficient data regarding any long-term benefits.

2009 Focused Update: ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults
A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012
*The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology.*

2010 Focused Update of ESC guidelines on device therapy in heart failure

Not a single word about CRT optimization!!
Although the importance of AV synchrony is unquestioned, the need for routine, systematic AV delay optimization in all patients undergoing CRT remains controversial.

The role of routine VV optimization is even less clear.
CRT optimization: the Opinions from Experts

...[...]... CRT is an effective therapy in general, and implant rates are strikingly growing ...

The majority of CRT pts enjoy symptomatic improvement, but ... approximately 30% of individuals reap no benefit ...

Many potential reasons for NON-response to CRT, including inappropriate pacing parameters for a given pt (⇒ in other words, NEED for “CRT customization”)

Theoretically, optimizing in the post-implant (AVD & VVD) yields to maximize cardiac performance ⇒ should maximise the clinical benefits from CRT.

However, rationale & methods for routine CRT optimization have been the subjects of recent debate ...[...]...

Optimizing atrioventricular and interventricular intervals following cardiac resynchronization therapy


Nayar V, Khan FZ, Pugh PJ. Expert Rev Cardiovasc 2011
WHY should we customize CRT settings?
the “EP” point of view

Atrioventricular and interventricular delay optimization in cardiac resynchronization therapy: physiological principles and selection of available methods

Physiological rationale for optimization

As outlined above, from a physiological point of view, it seems reasonable to assume that correction of atrio-, inter- and intraventricular dyssynchrony improves cardiac function and efficiency. In the contemporary era of CRT, this can be achieved by programming both AV and VV timings.

It should be stressed that intrinsic AV, programmed AV and programmed VV delay can all influence ventricular activation and filling. Thus, depending on the device settings, there can be up to three activation fronts that potentially determine the degree of intraventricular dyssynchrony: intrinsic right bundle branch activation, right and left ventricular pacing, respectively (Fig. 1) [16].

Houthuizen P & al. HF Reviews 2011
WHY should we customize CRT settings?

the “Echo” point of view

A. Optimal AV delay

B. Long AV delay

C. Short AV delay

Optimizing atrioventricular and interventricular intervals following cardiac resynchronization therapy


Nayar V, Khan FZ, Pugh PJ.
Expert Rev Cardiovasc Ther 2011

Figure 1. Effect of varying the atrioventricular interval on the mitral inflow
“AVD value” vs “Mitral Inflow & Hemodynamics” (movements of mitral leaflets vs AVD value)

AVD optimization in sequential & BiV pacing, although widely recommended, is often poorly performed in clinical practice as an improper setting can reduce the success of the pacing therapy.

Despite the several methods proposed, the AVD is frequently programmed in an empirical way or left to a predefined value (usually the manufacturer’s setting), without considering the different variables involved in this context:

- intra- and inter-individual variability of the EM events;
- peculiarities of several CMP;
- spontaneous inter-atrial and AV conduction characteristics;
- medical therapy;
- pacing mode.

...[...][...]

Antonini L & al. Europace 2012 July (background & critical review)
Need for V pacing & “AVD issue” (AVB/CRT pts): Approaches & Methods

NON-device-based methods (formulas & iterative)

• Very efficient to observe ACUTE effects, but ...
• Inter- & Intra-Operator variability
• Controversial results (*long-term performance?*)
• Optimization under specific in-Lab conditions (*at rest*)
• Resource-consuming (*manpower/time*)
• Repeated evaluations needed over time ⇒ *limit their applicability in clinical practice*

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**Table 1** Methods for atrioventricular setting

<table>
<thead>
<tr>
<th>References and methods</th>
<th>Methodology</th>
<th>Type</th>
<th>Used in</th>
<th>Compared</th>
<th>Trials</th>
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<tbody>
<tr>
<td>Ismer^5</td>
<td>Echo and</td>
<td>Formula Opt. AV = AEA -</td>
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<td>Formulas</td>
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<td>Antonini L &amp; al.</td>
<td>Formulas</td>
<td>DDD</td>
<td>Ritter</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Antonini L & al. Europace 2012 July (background & critical review)**

**FORMULAS** (predefined)

**ITERATIVE methods**

**AUTOMATIC methods**

**FIXED** (the most used ... )
Conclusions

CRT therapy is an effective, important treatment strategy in selected patients with systolic heart failure; however, even in the properly selected patient population with optimal implant results, there is a significant proportion of poor responders. The role and efficacy of AV and VV optimization in improving clinical outcomes in CRT remains unclear. In addition, there are many methods that can be employed with no clear superior technique. There seems to be acute hemodynamic benefits to optimizing these timing intervals, but it has not been adequately proven that these changes translate into long-term clinical improvement. Certainly, improperly programmed AV and VV delays can result in a loss of diastolic filling and suboptimal resynchronization, which logically could result in clinical deterioration; however, what is not clear is that routinely “tweaking” these parameters is effective or necessary. At this time, conservative nominal values or simple and rapid methods to optimize CRT timing intervals seem most practical. In addition, a protocol-driven, multidisciplinary approach to address CRT nonresponders seems promising but needs further study.
AV AND VV DELAY OPTIMIZATION IN LANDMARK CLINICAL TRIALS
AV/VV delay optimization in RCTs on CRT

**CONTAK CD** (JACC 2003; 42:1454-59)  
No AV optimization

**PATH-CHF** (Am J Cardiol 1999; 83:13035)  
**PATH-CHF II** (Circulation 2001; 104:3026-29)  
AV optimization by invasive method

**COMPANION** (NEJM 2004; 350:2140-50)  
AV optimization by EGM

**MUSTIC SR** (NEJM 2001; 344:873-80)  
**MIRACLE** (NEJM 2002; 346:1845-5)  
**CARE-HF** (NEJM 2005; 352:1539-49)  
**InSync III** (JACC 2005; 46:2348-56)  
AV optimization by echocardiography

**PROSPECT** (Circulation 2008; 117:2608-16)  
**REVERSE** (Circulation 2009; 120:1858-65)  
**MADIT CRT** (NEJM 2009; 361:1329-38)  
*optional VV opt at 6 months*
AV AND VV DELAY OPTIMIZATION IN REAL WORLD
European CRT Survey

(141 centres from 13 countries in western europe)

AV optimization was performed in 78% of patients
International CRT Survey
(108 investigators from 16 countries)

AV opt before discharge

Lack of time 56%
Unqualified staff 26%

13% Systematically
20% Selectively
80% Never
Time needed for AV and VV optimizing by echocardiography

- Mitral inflow iterative method (AV) + Aortic outflow VTI method (VV)
- Three replicates at each AV/VV delay setting (average)
- Supine at rest

![Diagram showing time needed for AV and AV + VV optimization. AV optimization: 15.5 ± 4 min, AV + VV optimization: 25.5 ± 5 min.]
Impact of averaging multiple replicates on reproducibility

- 1 measurement: Reliability for true optimal value = 50%
- 10 measurements: Reliability for true optimal value = 75%
- 100 measurements: Reliability for true optimal value = 100%
OPTIMIZATION FOR ATRIAL SENSING/PACING
Landmark RCTs

COMPANION (NEJM 2004; 350:2140-50)
PATH-CHF (Am J Cardiol 1999;83:1303)
PATH-CHF II (Circulation 2001;104:3026-29)
MUSTIC SR (NEJM 2001; 344:873-80)
MIRACLE (NEJM 2002; 346:1845-5)
CARE-HF (NEJM 2004; 352:1539-49)
InSync III (JACC 2005; 46:2348-56)
PROSPECT (Circulation 2008;117:2608-16)
REVERSE (Circulation 2009;120:1858-65)
MADIT CRT (NEJM 2009; 361:1329-38)

All optimized for sensed AV delay only!
Additional delays introduced by artificial pacing

DDD  VDD

Atrial transport delay

124 ms  85 ms

△ 40 ms

A-Pace  A-Sense
CRT-AVO study

Optimal AV Delay
During Atrial Pacing and Atrial Sensing

- Atrial Sensing: 134 ± 45 ms
- Atrial Pacing: 208 ± 62 ms

Mean optimal AVD offset: 75 ± 40 ms

(p < 0.0001)
OPTIMIZATION OVER THE TIME
Re-assessment of optimal AV delay over the time in RCTs

**MIRACLE** (NEJM 2002; 346:1845-5)  
**CARE-HF** (NEJM 2005; 352:1539-49)  
re-optimized at 3, 6, 9, 18 months
Temporal variation of optimal AV delay

Changes of optimal AV delay at long-term (16±11 months) follow up
Temporal variation of optimal VV delays

Distribution of VV delay variations respect to previous programmed values

A difference > 40 ms in optimal VV delay was in 57% of pts
Factors limiting routine AV/VV delays optimization in CRT

- Cultural limits (experienced staff)
- Organizational limits (time-consuming, training, equipment)
- Limited controlled evidence (long-term validation)
- Tecnological limits (variation over time, exercise)
DEVICE-BASED METHODS
Device-based methods: QuickOpt (SJM)
Electronic Optimization of AV Delay

“The paced and sensed RA-LA activation time at the time of implant eliminates the need for echo based AV optimization.”¹

The EGM duration represents the sum of right and left atrial activation.

The QuickOpt™ algorithm utilizes this measurement to calculate the proper AV delay allowing for full valve closure which occurs prior to full completion of electrical activity.

The device IEGM looks across local right atrial activation as well as far-field left atrial activation.

¹ Worley, et.al "Optimization of cardiac resynchronization: left atrial electrograms measured at implant eliminates the need for echo and identifies patients where AV optimization is not possible" Journal of Cardiac Failure Aug. 2004 Vol. 10, Issue 4, Pg 562
Paced and sensed tests are performed to characterize the conduction properties of the ventricles.

\[ VV_{opt} = 0.5 \times (\Delta + \varepsilon) \]

\( \Delta \) is related to the intrinsic depolarization
\( \varepsilon \) is a correction term depending on wave front velocity

© 2006 St. Jude Medical
V-V optimization:
intrinsic depolarization term ($\Delta$)
V-V optimization: wave fronts velocities ($\varepsilon$)

$\varepsilon = IVCD_{LR} - IVCD_{RL}$
FREEDOM trial: Design / Objs

QuickOpt (SJM)

- Prospective, randomized (1:1), double-blinded, multicenter study
- Treatment: **frequent optimization using QuickOpt®** timing @ every FU visit
- Controls: **Empiric programming or one-time optimization** using a non-IEGM method (usually echo) within first month
- FU duration: **12 months**

**Primary Endpoint**
HF clinical composite score (CCS) as defined by Packer*:
- hospitalization
- all-cause mortality
- NYHA class
- Pt Global Assessment

**Secondary Endpoints**
- All-cause, CV & HF mortality
- All-cause, CV & HFH

* Packer M. J Card Fail 2001
Conclusions applicable to clinical practice:

- EASINESS of USE
- NON-INFERIORITY vs SoC (clinical endpoint @ 1Y)
Device-based methods: SmartDelay (BSx)

How does SmartDelay work?

Data Collection

Start SmartDelay

Test: sensed AV intervals

Test: paced AV interval

LV lead location

“Anterior”  “Free Wall”

SmartDelay adjusts suggestions for currently programmed LV Offset

Input temporary LRL

Calculation of Interventricular Timing occurs

SmartDelay Suggestions:
1) Paced AV Delay
2) Sensed AV Delay
SmartDelay concept is not new to CRT patients

Boston Scientific’s optimization algorithm has evolved in the last decade, and some basic elements of the formula upon which the feature was designed were used to recommend AV delays in clinical trials:

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Time Period</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMPANION 1,2</td>
<td>1999 – 2003</td>
<td>1200+</td>
</tr>
<tr>
<td>DECREASE-HF 3,4</td>
<td>2003 – 2005</td>
<td>300+</td>
</tr>
<tr>
<td>RENEWAL 3 AVT Study 5</td>
<td>2003 – 2005</td>
<td>130+</td>
</tr>
</tbody>
</table>

Boston Scientific conducted the CRTAVO study to evaluate SmartDelay and compare it to other AV optimization methods. Using an invasive catheter to measure LV \((dP/dt)_\text{max}\), the CRTAVO study compared several AV delay optimization methods:

- SmartDelay optimization [manual mode]
- Echo optimization [stroke volume calculation by aortic VTI]
- Ritter method [echo-based technique]
- Fixed AV Delay values [100, 120, 140, and 160 ms]

(Note: SmartDelay was referred to in the CRTAVO study as EEHF+)
In the CRTAVO study, SmartDelay optimization for atrial sensing was 98% correlated to the accurate and reliable invasive pressure measurement — LV (dP/dt)_{max}. For atrial pacing, the correlation was 96%.¹

1. CRTAVO data were prospectively collected. However, the data analyses were not pre-specified. Refer to Appendix F of the COGNIS System Guide for clinical data on the hemodynamic performance of this feature.
Aims to optimize:

- Paced AVD (PAVD) & Sensed AVD (SAVD)
- V Pacing Chamber (BiV or LV only) & LV Offset

Suggested Sensed AVD (SAVD) & Paced AVD (PAVD) [@ user-defined HR]:

- the calculated AVDs further refined based on Suggested “Pacing Chamber” and “LV Offset” to find-out the final suggested optimal PAVD & SAVD:

\[
AVD_{(p,s)} = 0.757 \times AVI_{(p,s)} - 0.728 \times QRS + 71.3 \text{ (ms)}
\]

Full test duration = **2.5 min** (pt @ rest, normal breathing, NO talking)
Boston Scientific conducted the SMART-AV study to assess the effects of three methods for optimizing AV delay timing during CRT, and if more frequent re-optimization can improve clinical outcomes.

- **Baseline Evaluation**
  *To document inclusion / exclusion criteria and establish baseline heart status* *

- **Randomization (1:1:1 SmartDelay: Echo: Fixed)**
  *1 – 14 days post implant*

  - AV Delay Optimized Quarterly Using SmartDelay
  - AV Delay Optimized Using Echo (Iterative Method)
  - AV Delay Fixed at 120ms with 0 Offset

- **Clinic Follow-up Visits**
  *3 month and 6 months post implant*
Clinical Support: SMART-AV

Study population

1060 Patients Enrolled

1014 Patients Implanted

Not implanted = 46
Screening Failure = 27
Withdrawn by physician/Sponsor = 15
Withdraw consent = 4

980 Patients Randomized

332 Assigned to SmartDelay (SD)
Received allocated intervention = 332
Lost to follow-up = 24
Withdrawn by physician/Sponsor = 22
Lost = 2
Discontinued intervention = 7
Death = 7
No. Included in Analysis = 283
No. Excluded From Analysis = 18
Lost = 18

323 Assigned to Echo
Received allocated intervention = 323
Lost to follow-up = 12
Withdrawn by physician/Sponsor = 12
Discontinued intervention = 15
Death = 15
No. Included in Analysis = 282
No. Excluded From Analysis = 14
Lost = 14

325 Assigned to Fixed
Received allocated intervention = 325
Lost to follow-up = 20
Withdrawn by physician/Sponsor = 19
Lost = 1
Discontinued intervention = 6
Death = 6
No. Included in Analysis = 281
No. Excluded From Analysis = 18
Lost = 18
SMART-AV: LV remodeling (all p=ns)

Some comments:

• LVESV & LVEF: clear TREND in favour of optimizing AVD (echo or SD) vs Fixed AVD

• Was this study powered enough to get significant results?

• In other words: correct statistical assumptions?
SmartDelay does NOT significantly improve LVESV vs either the Echo-optimized or the “Fixed-AVD” approach.

NO significant differences in the 2-ary structural or functional endpoints by optimization group.

Subgroups: wide QRS duration, LBBB, non-ischemic CMP, and F gender responded more favorably to CRT (observed in general CRT registries).

Conclusions applicable to Clinical Practice:
- EASINESS of USE (1-button, 2.5 min)
- NON-INFERIORITY vs Echo methods (or fixed AVD) in terms of remodeling endpoints @ 6M
### AUTOMATIC haemodynamic-driven methods: the SonR technology (SORIN Group)

<table>
<thead>
<tr>
<th>Year</th>
<th>Lead</th>
<th>Fixation</th>
<th>Introducer</th>
<th>Chamber</th>
<th>Device</th>
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<tbody>
<tr>
<td>1995</td>
<td>BEST</td>
<td>Tined</td>
<td>13 Fr</td>
<td>RV</td>
<td>Living DR (PM)</td>
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<tr>
<td>2000-2004</td>
<td>Minibest</td>
<td>Tined/Screw</td>
<td>11 Fr</td>
<td>RV</td>
<td>NewLiving DR (PM, 2002); Living CHF CRT-P (2004)</td>
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<tr>
<td>2005-2007</td>
<td>Microbest</td>
<td>Tined/Screw</td>
<td>9 Fr</td>
<td>RV</td>
<td>NewLiving DR NewLiving CHF (CRT-P)</td>
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<tr>
<td>2008-2010</td>
<td>SonRfix</td>
<td>Screw</td>
<td>9 Fr</td>
<td>RA</td>
<td>Investigat. Device Only (NewLiving/Paradym)</td>
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<tr>
<td>2011</td>
<td>SonRtip</td>
<td>Screw</td>
<td>9 Fr</td>
<td>RA</td>
<td>Paradym RF SonR CRT-D</td>
</tr>
</tbody>
</table>

**Endocardial acceleration** sensor (correlated with LVdP/dt): combines LV contractility & LV filling to optimize CRT settings

**Contractility** ↔ **LV filling**
Optimization of **VVD at rest** (atrium paced OR sensed condition)

Optimization of **AVD at rest** (both atrium paced AND sensed conditions)

Optimization of **AVD under effort**:
1. the user defines an “effort target HR” *(programmable; default 90bpm)*
2. optimization done only if pt’s HR > “effort target HR”

Procedure **AUTOMATICALLY** repeated on a **WEEKLY** basis
in pts with a true LBBB (w spontaneous RV activation front), “synchronized LV pacing” is a recommendable option alternative to the standard BiV pacing

KEY elements of the downloadable “AdaptivCRT” algorithm:

1. evaluation of intrinsic conduction
2. determination & update of pacing configuration:
   - LV or BiV
   - AV delays (p/s)
   - VV delay

AUTOMATIC methods: Adaptive-CRT algo (Mdt)

**BACKGROUND:**
In pts with SR & normal AV conduction, pacing only the LV with appropriate AVDs can result in superior LV & RV function compared to standard BiV pacing.

**OBJECTIVE:**
To evaluate the **Adaptive CRT (a-CRT) algorithm** for CRT that provides automatic:
- ambulatory **selection** between synchronized LV or BiV pacing;
- ambulatory dynamic **optimization** of AVD & VVD.

**METHODS:**
- n=522 CRT-D pts, randomized (2:1) to (a-CRT) vs Echo-optimized BiV pacing (Echo);
- FU visits @ 1M, 3M, and 6M post-randomization.
RESULTS: the study met all 3 non-inferiority 1-ary objectives:

a) % CLINICAL RESPONSE to CRT @ 6M (Packer’s combined endpoint):

Non-inferiority P = 0.0007

73.6% 72.5%

b) a-CRT and Echo-optim. settings resulted in SIMILAR CARDIAC PERFORMANCE:

high Concordance Correlation Coefficient, Ao-VTI @ a-CRT vs. @ Echo settings (at randomization & 6M after);

c) a-CRT did NOT result in inappropriate device settings.

AUTOMATIC methods: “Adaptive-CRT” study (Mdt)
<table>
<thead>
<tr>
<th>Based on</th>
<th>QuickOpt (SJM)</th>
<th>SmartDelay (BSx)</th>
<th>AdaptivCRT (Mdt)</th>
<th>SonR (Sorin-G)</th>
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<tr>
<td>IEGM measures</td>
<td>IEGM measures</td>
<td>IEGM measures</td>
<td>Hemodynamic (SonR) sensor (contractility)</td>
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<th>Programming</th>
<th>1 parameter: “Timing optimization”</th>
<th>Paced HR + 1 parameter: “CRT optimization”</th>
<th>1 parameter (downloadable sw)</th>
<th>1 parameter: “SonR CRT optimization”</th>
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<th>Only @ REST; Paced &amp; sensed</th>
<th>Only @ REST; Paced &amp; sensed</th>
<th>@ REST &amp; under EFFORT; Paced &amp; sensed</th>
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<th>OK (LV synchro or BiV)</th>
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<th>In-clinic (@ FU) vs Ambulatory (Automatic)</th>
<th>In-clinic</th>
<th>In-clinic</th>
<th>Ambulatory (downloadable sw)</th>
<th>In-clinic + Ambulatory (Weekly)</th>
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<th>Outcomes from trials: SAFETY</th>
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<th>OK</th>
<th>OK (downloadable sw)</th>
<th>OK</th>
</tr>
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</table>

| Outcomes from trials: EFFICACY | AV & VV opt @ FU visits NON-INFERIOR to clinical practice (0 or 1 echo) clinically @ 1Y (FREEDOM) | AV opt @ FU visits EQUIVALENT to ECHO-guided or Empiric programming, structurally & functionally @ 6M (SMART-AV) | Adaptive-CRT approach is NON-INFERIOR to Echo-optimized BiV, clinically @ 6M (Adaptive-CRT) | AV (weekly) & VV (@ FU visits) optimization by SonR is SUPERIOR to clinical practice, clinically @ 1Y (CLEAR pilot) |
CONCLUSIONS
Conclusions (1/2)

• Post-implant optimization of CRT programming is **NOT universally performed**
• Optimizing AVD & VVD **theoretically improves** cardiac performance
• Optimization is **most commonly** performed using **ECHO** but many NON-echo methods are available
• **Paucity of data to recommend the use** of any one method

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**Expert Reviews**

Optimizing atrioventricular and interventricular intervals following cardiac resynchronization therapy


Nayar V, Khan FZ, Pugh PJ. *Expert Rev Cardiovasc Ther 2011*
Conclusions (2/2)

- Many non-randomized studies have demonstrated **hemodynamic & symptomatic benefit** from **AVD** optimization

- **Contradictory evidence** for the hemodynamic effects of **VVD** optimization

- **No long-term data** for optimization, but landmark CRT trials have included AVD optimization in their protocols

- **Guidelines** vary in their emphasis for recommending optimization

- **AUTOMATED built-in optimization** within CRT devices likely to become predominant mode of optimization

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**Optimizing atrioventricular and interventricular intervals following cardiac resynchronization therapy**

*Nayar V, Khan FZ, Pugh PJ. Expert Rev Cardiovasc Ther 2011*
Thank you for Your attention!
CRT optimization: the “Common Sense”

Post-implant AVD & VVD optimization in CRT patients produces **ACUTE HEMODYNAMIC benefits**; optimal values change according to:
1. time from implant
2. effort vs resting phases
3. paced vs sensed atrial activity

**ECHO optimization** methods are time- & resource-consuming, they are NON-frequently used (“FREEDOM survey”), often ONLY in NR pts ⇒ Need for **automatic built-in methods within CRT devices**

A strategy with **in-hospital** (only @ FU visit) **device-based** optimization (IEGM-based), when **compared with ECHO** methods, produces the same hemodynamic (**SMART-AV**) & clinical (**FREEDOM/Adaptive-CRT**) benefits

It is NOT clear whether an **ambulatory CONTINUOUS adaptive AV/VV device-based optimization** (not only during FU) translates acute hemodynamic benefits into mid- & **long-term CLINICAL BENEFIT**
Subgroups of pts who may benefit more?

The LVESV response rate for SD vs. fixed increased as QLV prolonged. In the highest quartile of QLV, SD had a greater than 6 fold increase in odds ratio for a LVESV response vs. fixed.
How do short (or very short) AVDs perform in clinical practice?

ATRIOVENTRICULAR DELAY AND THE RISK OF HEART FAILURE AND DEATH IN MADIT-CRT

Andrew J. Brenyo, MD, Christine Tompkins, MD, FHRS, Alon Barsheshet, MD, Mohan Rathi, MD, Yuming Huang, MD, Scott McNitt, MS, Wojciech Zareba, MD, and Ilan Goldenberg, MD. University of Rochester

Introduction: The optimal atrioventricular (AV) delay in cardiac resynchronization therapy (CRT) remains to be determined. We hypothesized that shorter AV delay would improve the response to CRT through an increase in biventricular pacing and degree of resynchronization.

Methods: The effect of short AV delay defined as AVD < 100 ms (n = 308) on the risk of heart failure heart failure or death in comparison to AVD > 100 ms (n = 724) was assessed in the CRT arm of MADIT-CRT. The risk of HF or death and death alone were assessed in the CRT-only group (n = 711). Left ventricular (LV) remodeling was analyzed comparing baseline to 1 year data.

Results: Kaplan-Meier survival analysis (Figure) demonstrated the rate of HF or death at 3 years was lowest (p < 0.001) with a short AV delay (<100 msec), intermediate with a long AV delay, and highest for CRT-only group (p < 0.001 for the overall difference). Compared to CRT patients with both short and long AV delays, patients with short AV delay had significant reductions in the risk of HF or death at 3 years of 0.42, p < 0.001; and 0.70, p = 0.001; respectively. In the CRT group a short AV delay was associated with a significant 40% reduction in the risk of HF or death alone compared to long AV delay. Additionally, short AV delay was also associated with a substantial reduction in LV systolic volume (34%) compared to long AV delay (10%, p < 0.005) and CRT-only (10%, p < 0.005).

Conclusions: Short AV delay is associated with a more substantial reduction in HF and death in patients with mild heart failure receiving CRT. This is possibly due to an increased frequency of biventricular pacing resulting in more favorable LV remodeling.

Brenyo AJ & al. HRS 2012 abstracts
Did the patient die?
Hospitalized for worsening HF?
Crossover due to worsening HF?
Worsening NYHA Classification?
Moderately or markedly worse on Patient Global Assessment?

Answer YES to Any
Patient classified as worsened

Answer NO to ALL

Improved NYHA Classification?
Moderately or markedly improved on Patient Global Global Assessment?

Answer YES to Any
Patient classified as improved

Answer NO to ALL
Patient classified as unchanged