Simposio: The “Hemodynamic Approach” to improve CRT
Torino, 25/10/2012
Centro Congressi Unione Industriale

Optimizing CRT: a clinical must?

P.G. Golzio
AOU Molinette
Torino -Italy

CRT optimization: the "Guidelines"

Vardas PE & al. Europace 2007;9(10):959-998.

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!)*

Gorcsan J III & al. J. Am. Soc. Echocardiogr. 2008;21(3):191-213.

"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.

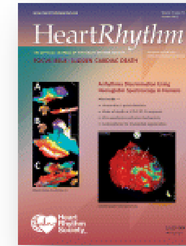
2010 Focused Update of ESC guidelines on device therapy in heart failure

Not a single word about CRT optimization !!

2012 EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: implant and follow-up recommendations and management

Developed in partnership with the European Heart Rhythm Association (EHRA), A registered branch of the European Society of Cardiology (ESC), and the Heart Rhythm Society; and in collaboration with the Heart Failure Society of America (HFSA), the American Society of Echocardiography (ASE), the American Heart Association (AHA), the European Association of Echocardiography (EAE) of the ESC and the Heart Failure Association of the ESC (HFA).

Endorsed by the governing bodies of EACVI, AHA, ASE, HFSA, HFA, EHRA, and HRS



(Heart Rhythm 2012;9:1524 –1576)

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.

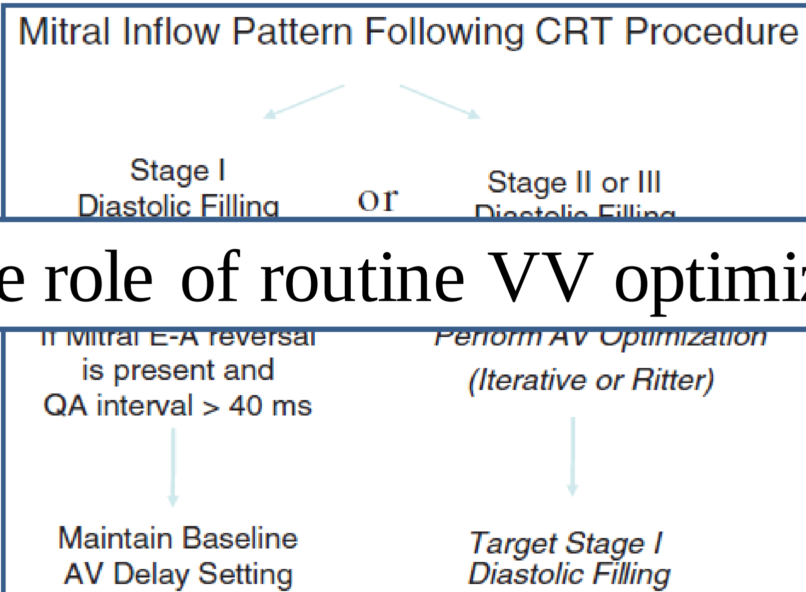


Figure 6 Algorithm for echo guided candidacy for atrioventricular (AV) optimization determined from mitral inflow pattern post-cardiac resynchronization therapy (CRT) implant (adapted from American Society of Echocardiography Dyssynchrony Guidelines, 2008).

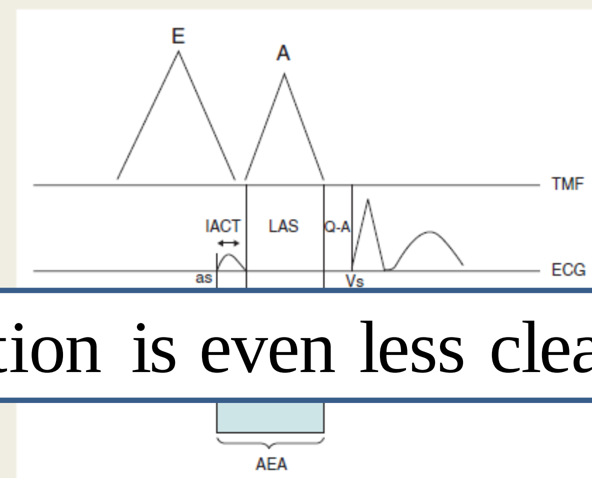


Figure 2 Atrial electromechanical action. Atrial electromechanical action is the interval between the atrial pacing artefact (spike) on the electrocardiogram and the end of the A-wave of the pulsed Doppler transmitral flow. E, E-wave; A, A-wave; as, atrial spike; vs, ventricular spike; IACT, interatrial conduction time; LAS, left atrial systole; AEA, atrial electromechanical action; Q-A, interval between the Q-wave or the ventricular spike and the end of the A-wave; TMF, transmitral flow; ECG, surface electrocardiogram; LAE, left atrial electrogram; LAP, left atrial potential. Blue area = AEA.

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** …[…]…

EXPERT REVIEWS

Optimizing atrioventricular and interventricular intervals following cardiac resynchronization therapy

Expert Rev. Cardiovasc. Ther. 9(2), 185–197 (2011)

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

WHY should we customize CRT settings ?

the "EP" point of view

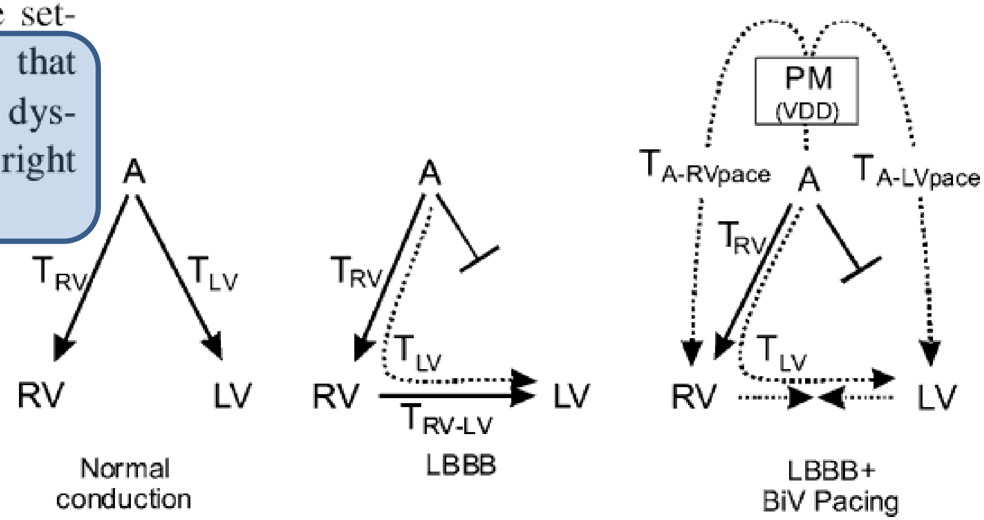
Atrioventricular and interventricular delay optimization in cardiac resynchronization therapy: physiological principles ... of available methods

Houthuizen P & al. HF Reviews 2011

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].



WHY should we customize CRT settings ?
the "Echo" point of view

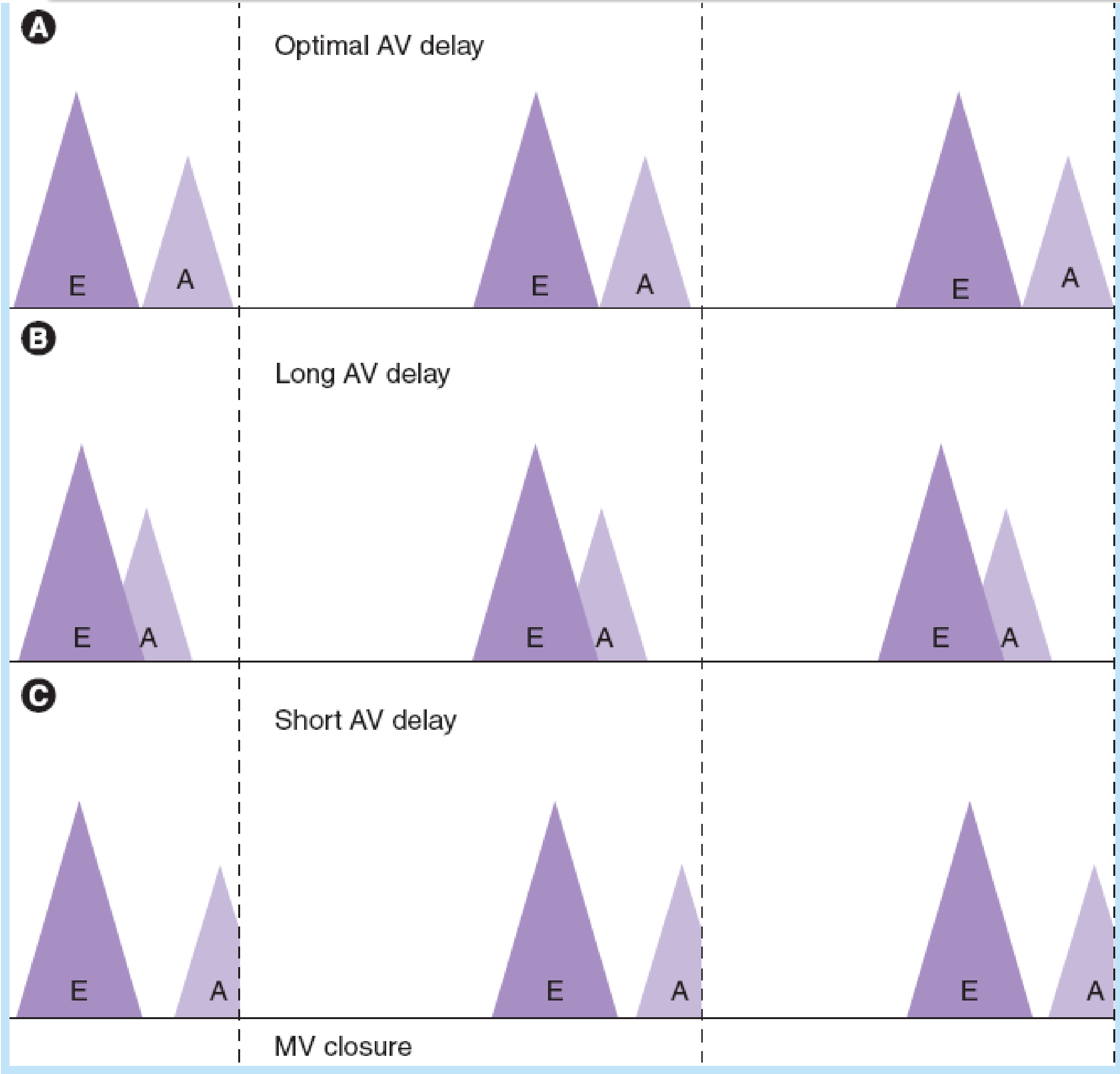


Figure 1. Effect of varying the atrioventricular interval on the mitral inflow

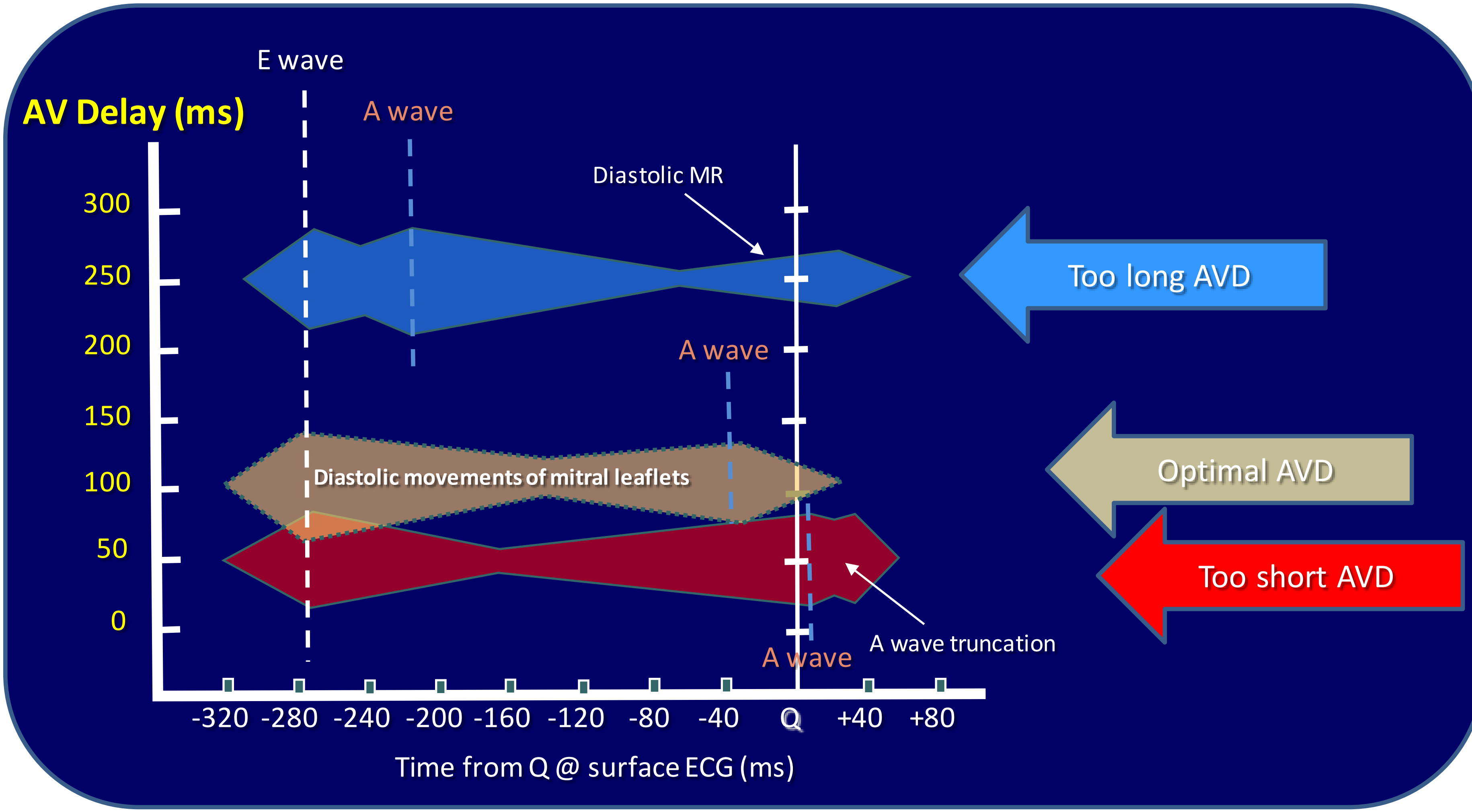
Optimizing atrioventricular and interventricular intervals following cardiac resynchronization therapy

Expert Rev. Cardiovasc. Ther. 9(2), 185–197 (2011)

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

“AVD value” vs “Mitral Inflow & Hemodynamics”

(movements of mitral leaflets vs AVD value)



Wexler LF & al. Circulation 1982;66:235-43

EUROPEAN SOCIETY OF CARDIOLOGY®

Europace (2012) **14**, 929–938
doi:10.1093/eupace/eur425

REVIEW

Optimization of the atrioventricular delay in sequential and biventricular pacing: physiological bases, critical review, and new purposes

Lanfranco Antonini*, Antonio Auriti, Vincenzo Pasceri, Antonella Meo, Christian Pristipino, Antonio Varveri, Salvatore Greco, and Massimo Santini

…[…]… 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

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

Table 1 Methods for atrioventricular setting

References and methods	Methodology	Type	Used in	Compared	Trials
Ismer[5]	Echo and	Formula Opt. AV = AEA –	DDD,	No	
FPPG	Plethysmography			pressure	
ICG[20]	Impedance	Iterative	DDD, CRT	Ritter	
PEA[21]	Mechanical acceleration	Automatic	DDD, CRT	Ritter	CLEAR[22]
Quick Opt[23]	Intracardiac electrogram	Automatic	CRT	Ao VTI, Standard	FREEDOM[24]
EEHF[25]	Intrinsic measures	Automatic	CRT	Standard, Ritter, Ao VTI	
SMARTDelay[26]	Intracardiac electrogram	Automatic	CRT	DFT, Standard	SMARTAV[27]
Standard	Fixed predefined	Fixed	DDD, CRT	Ao VTI, Doppler dP/dt, EEHF, DFT, Ritter	

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*

FORMULAS (predefined)

ITERATIVE methods

AUTOMATIC methods

FIXED (the most used …)

CRT customization is effective or necessary?

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.

Editor: Stephen C. Hammill, M.D.

ation Therapy: Importance
meters

R. GOLD, M.D., Ph.D.

y of South Carolina, Charleston, South Carolina, USA

One of the basic tenets of cardiac resyn-
ed parameters is important to maximize
ntricular (VV) timing intervals have been
iety of techniques have been described to
s have demonstrated acute hemodynamic
efit have been lacking. Echocardiography-
hnique has been shown to be superior. In
time-consuming. Device-based algorithms
owever, their clinical value has also been
iques for CRT optimization and evaluate
, Vol. 23, pp. 110-118, January 2012)

A, Gold MR, JCE 2012 Jan (Clinical Review)

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) * **PROSPECT** (Circulation 2008;117:2608-16) **REVERSE** (Circulation 2009;120:1858-65) **MADIT CRT** (NEJM 2009; 361:1329-38)	AV optimization by echocardiography

* optional VV opt at 6 months

AV AND VV DELAY OPTIMIZATION IN REAL WORLD

Dickstein et al. – *Eur Heart J* 2009;30:2450-60

European CRT Survey

(141 centres from 13 countries in western europe)

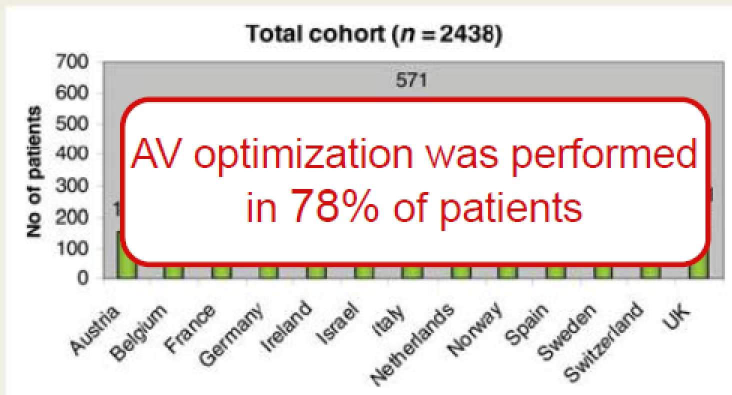


Figure 1 Country distribution of patients included in the CRT Survey.

Gras et al. - *PACE* 2009;32:S236–S239

International CRT Survey

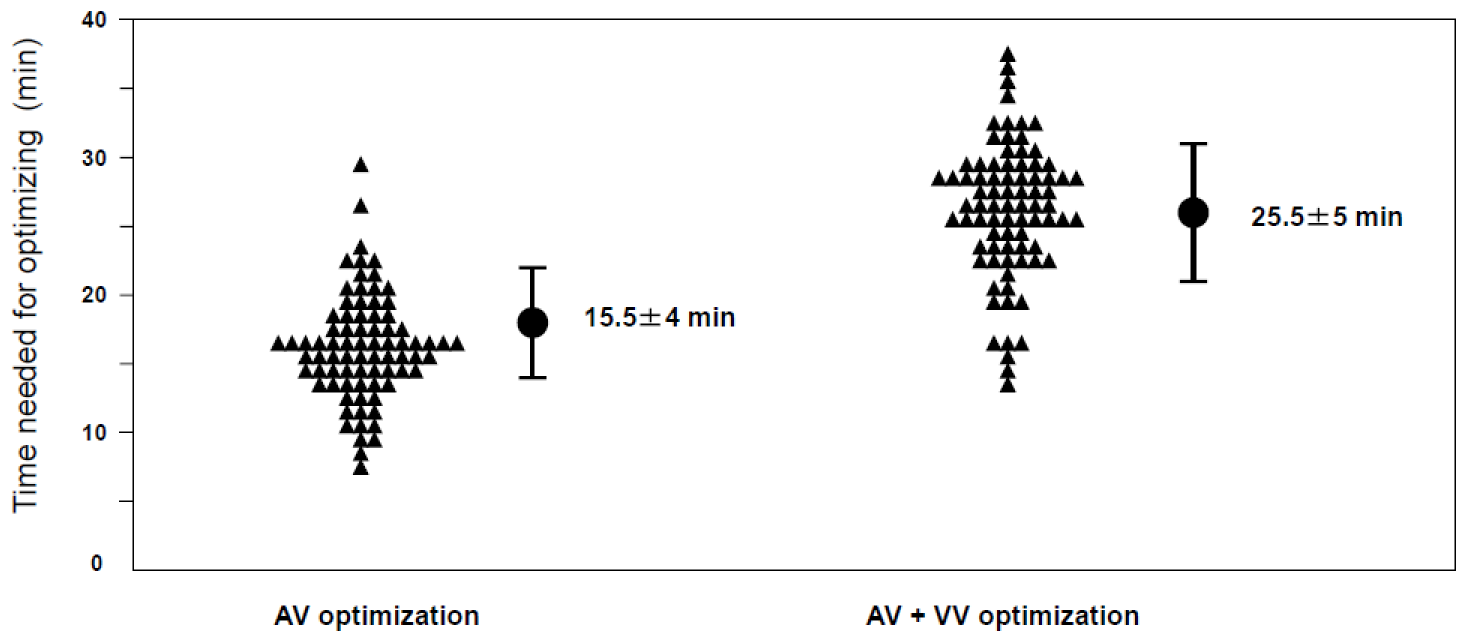
(108 investigators from 16 countries)

AV opt before discharge

Lack of time 56%
Unqualified staff 26%

Time needed for AV and VV optimizing by echocardiography

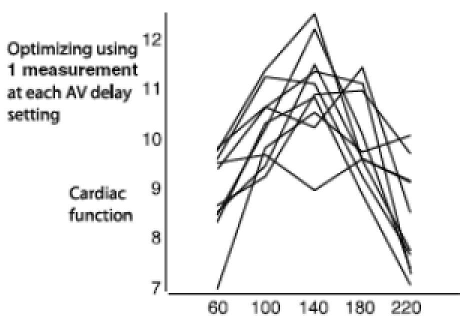
- Mitral inflow iterative method (AV) + Aortic outflow VTI method (VV)
- Three replicates at each AV/VV delay setting (average)
- Supine at rest



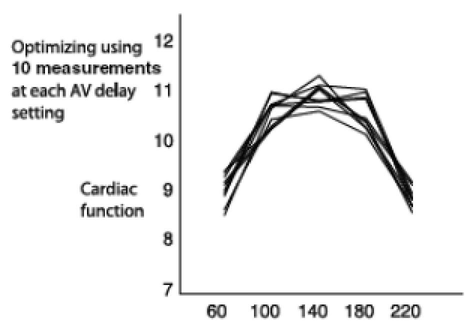
Pabari et al. – *Heart Fail Rev,* November 2010

Impact of averaging multiple replicates on reproducibility

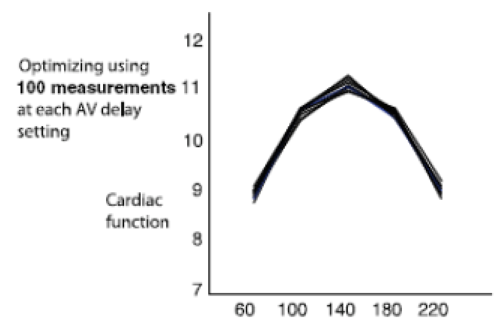
1 measurement



10 measurements



100 measurements



Reliability for true optimal value

50%

75%

100%

OPTIMIZATION FOR ATRIAL SENSING/PACING

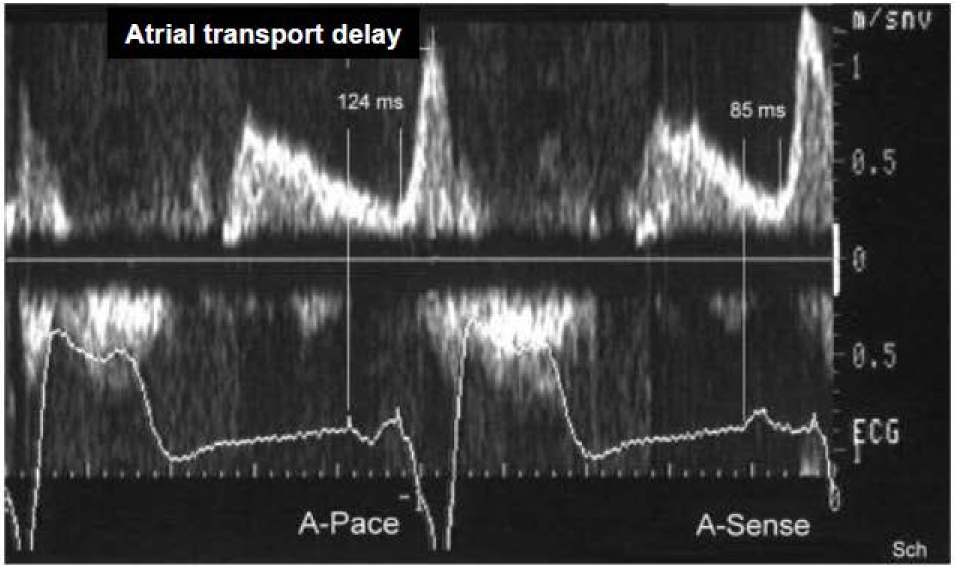
Landmark RCTs

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)

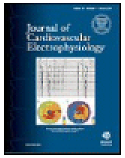
All optimized for sensed AV delay only !

Additional delays introduced by artificial pacing

DDD VDD



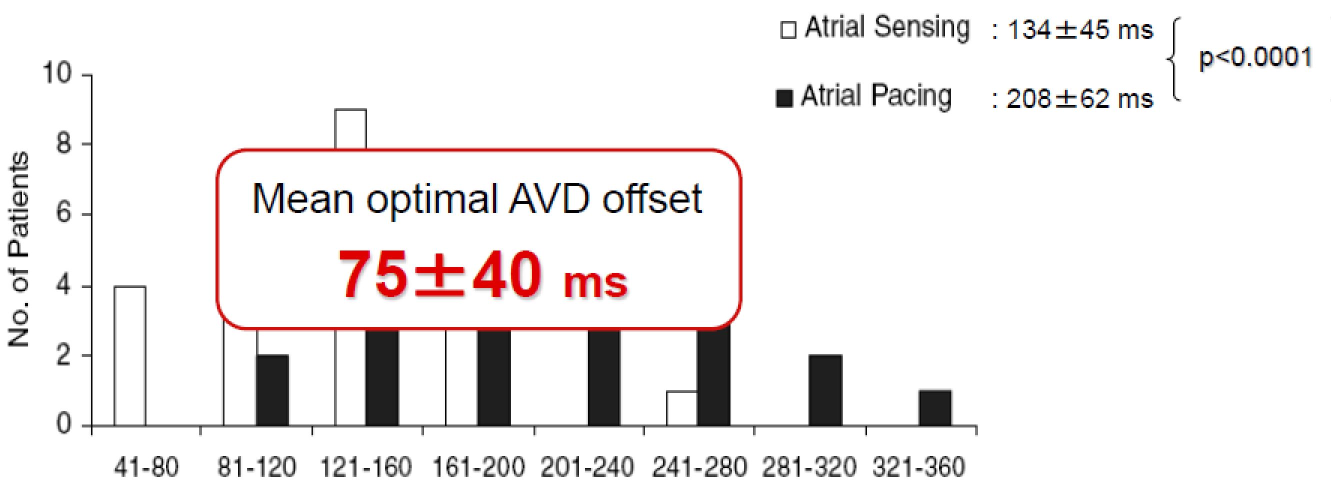
Δ 40 ms



Gold et al. - *J Cardiovasc Electrophysiol* 2007;18:490-96

CRT-AVO study

Optimal AV Delay
During Arial Pacing and Atrial Sensing



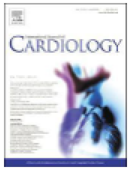
OPTIMIZATION OVER THE TIME

Re-assessment of optimal AV delay over the time in RCTs

MIRACLE (NEJM 2002; 346:1845-5)

CARE-HF (NEJM 2005; 352:1539-49)

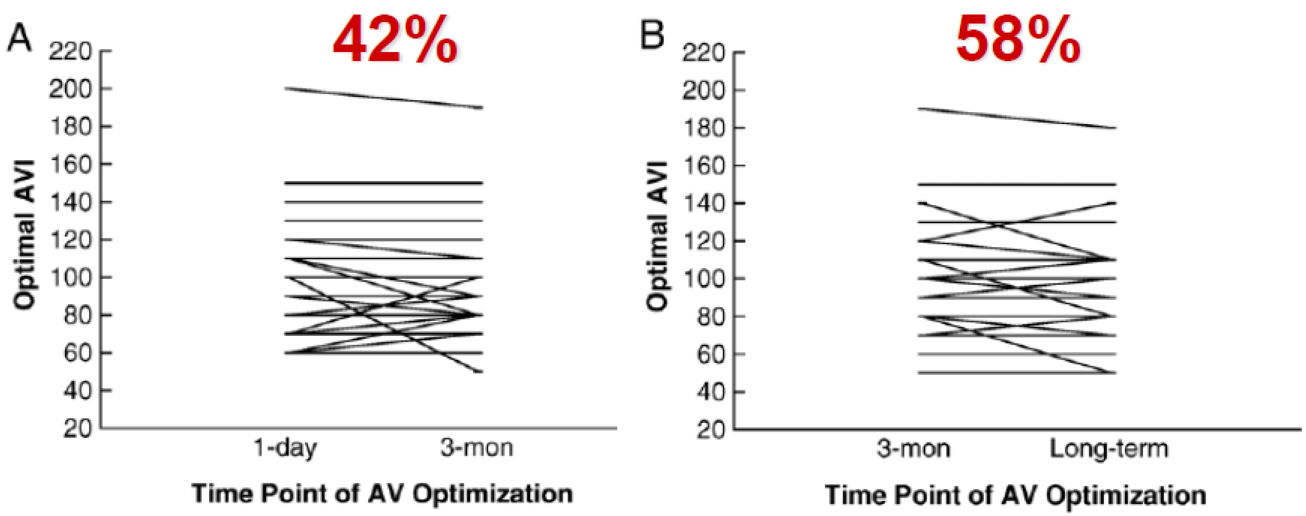
→ re-optimized at 3,6,9,18 months

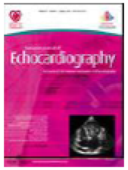


Zhang et al. – *Int J Cardiol* 2008;124:211-7

Temporal variation of optimal AV delay

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

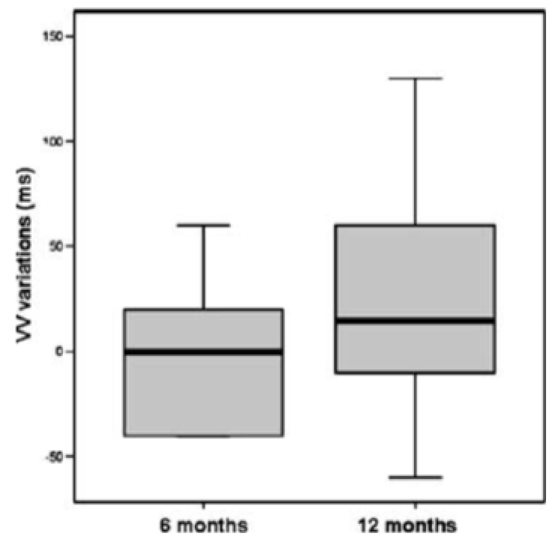




Valzania et al. – *Echocardiography* 2007; 24:933-39

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

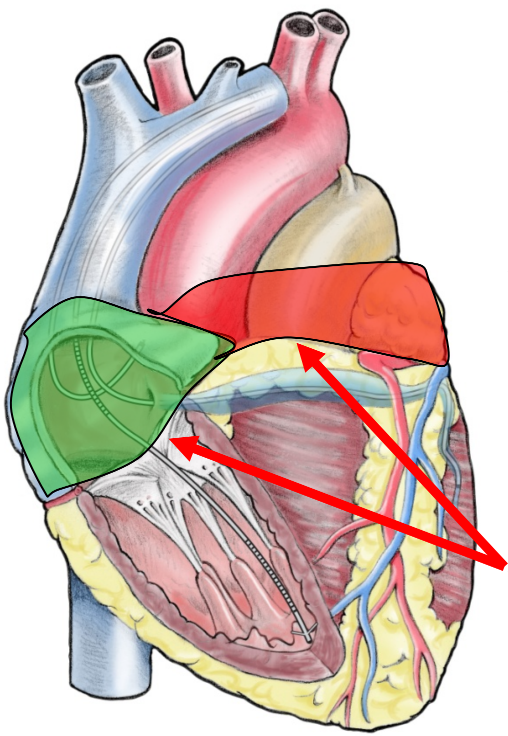
- Cultural limits (experienced staff)
- Organizational limits (time-consuming, training, equipment)
- Limited controlled evidence (long-term validation)
- Tecnological limits (variation over time, exercise)

DEVICE-BASED METHODS

Device-based methods: QuickOpt (SJM)

Electronic Optimization of AV Delay

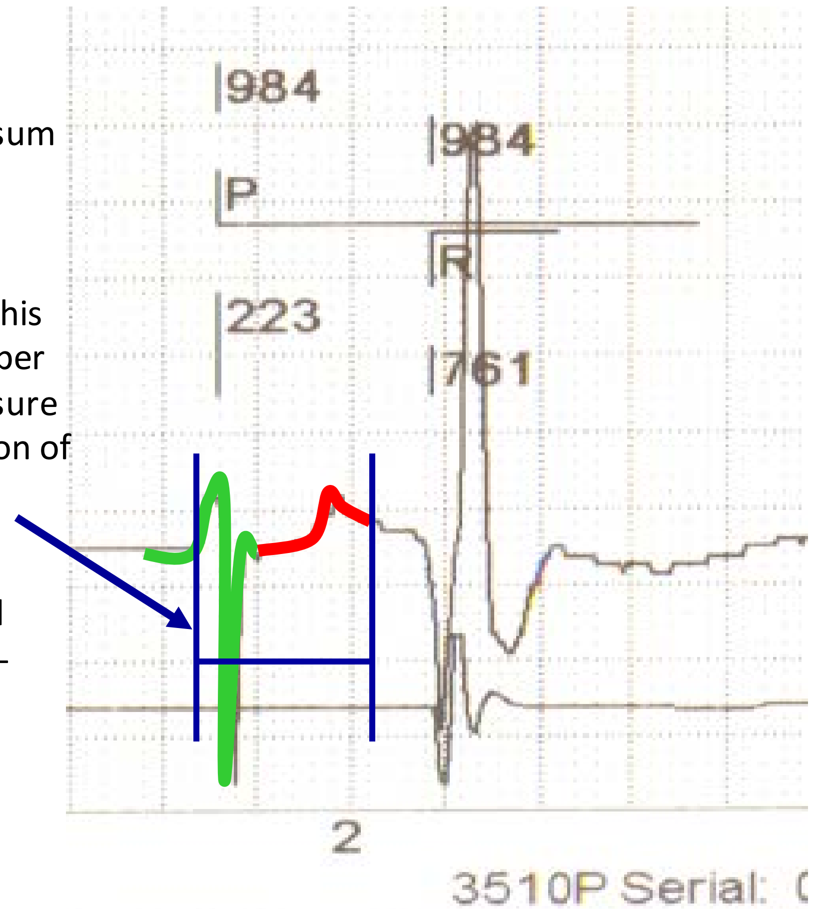
"Measuring the paced and sensed RA-LA activation time at the time of implant eliminates the need for echo based AV optimization."[1]



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

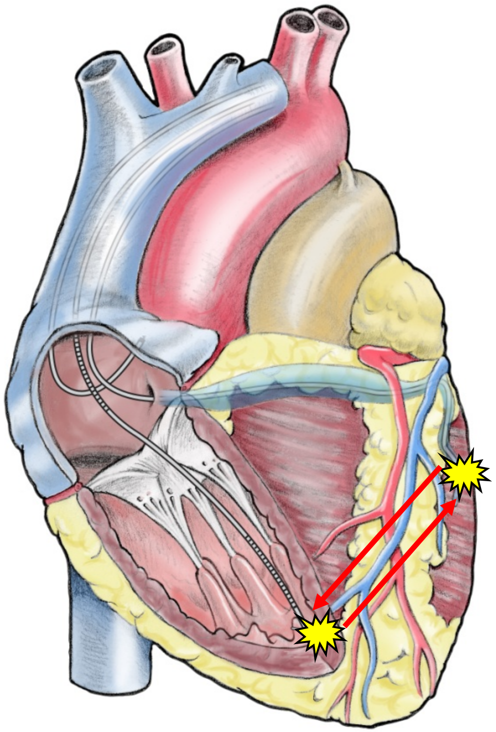
The QuickOpt™ algorithm utilizes this measurement to calculate the proper AV delay allowing for full valve closure which occurs prior to full completion of electrical activity.

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

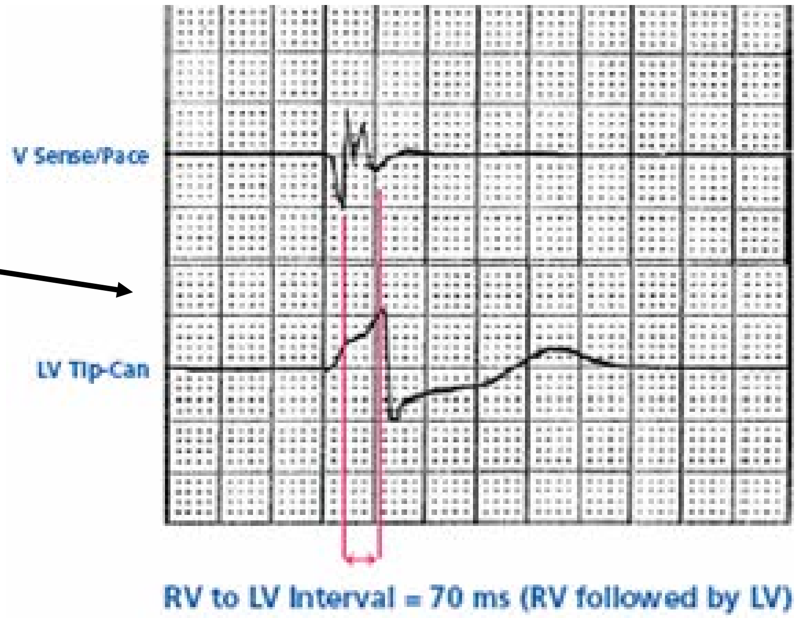


1. Worley, et.al "Optimization of cardiac resynchronization: left atrial electrograms measured at implant eliminates the need for echo and identifies patients where AV optimization is not possible" *Journal of Cardiac Failure Aug. 2004 Vol. 10, Issue 4, Pg S62*

Electronic Optimization of VV Delay



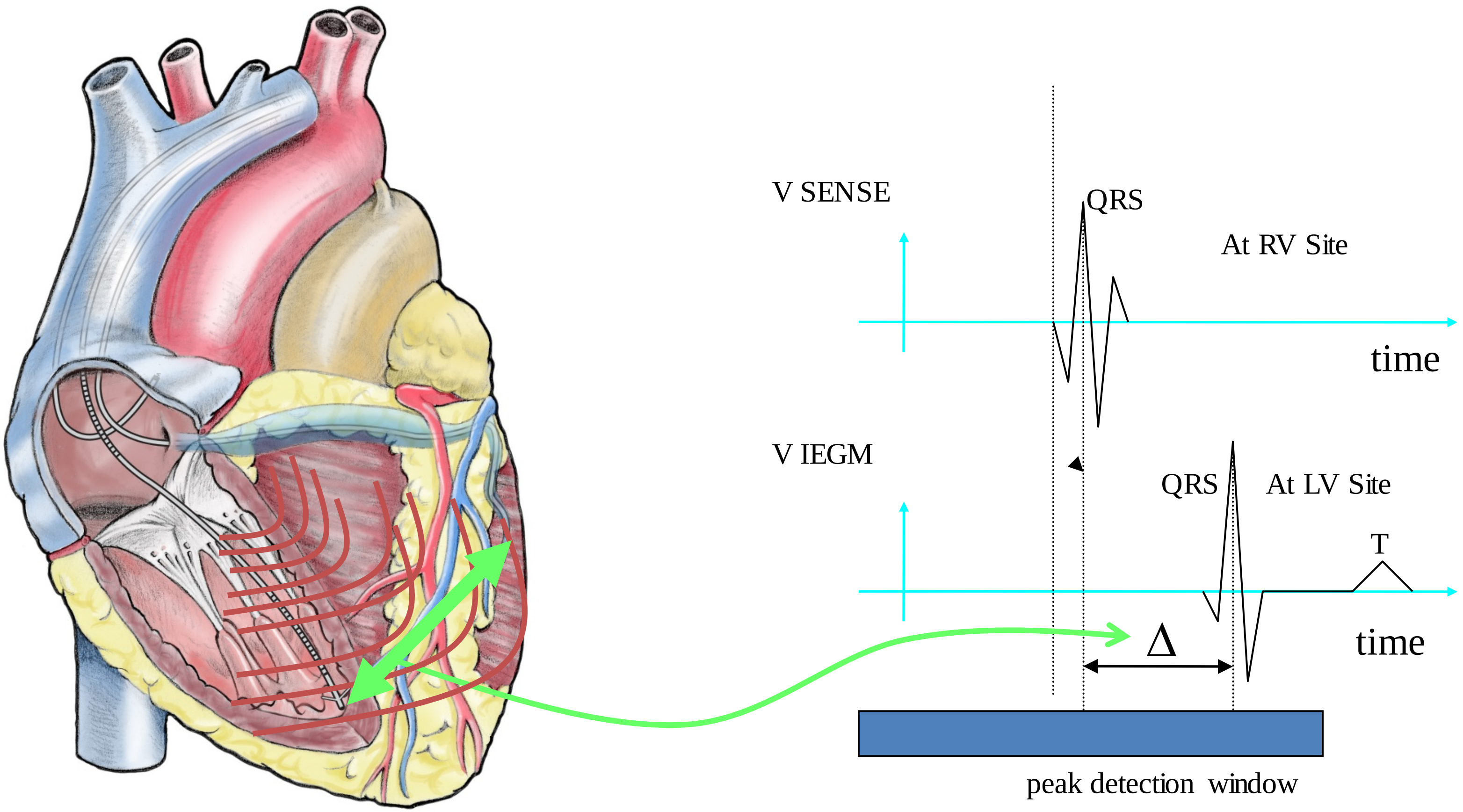
Paced and sensed tests are performed to characterize the conduction properties of the ventricles.



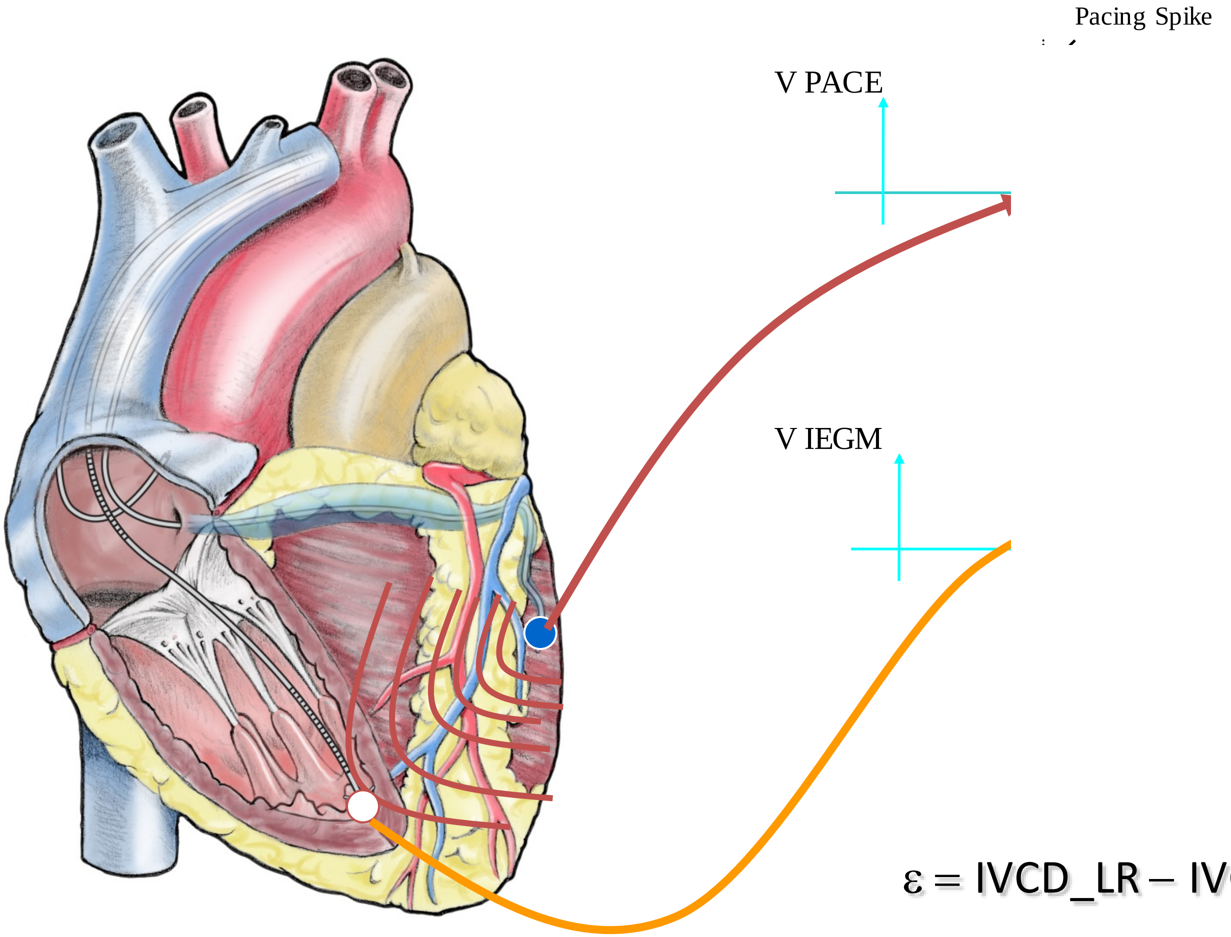
$VV_{opt} = 0.5 \times (\Delta + \varepsilon)$

Δ is related to the intrinsic depolarization
ε is a correction term depending on wave front velocity

V-V optimization: intrinsic depolarization term (Δ)



V-V optimization:
wave fronts velocities (ε)



$\varepsilon = IVCD\_LR - IVCD\_RL$

FREEDOM trial: Design / Objs

QuickOpt (SJM)

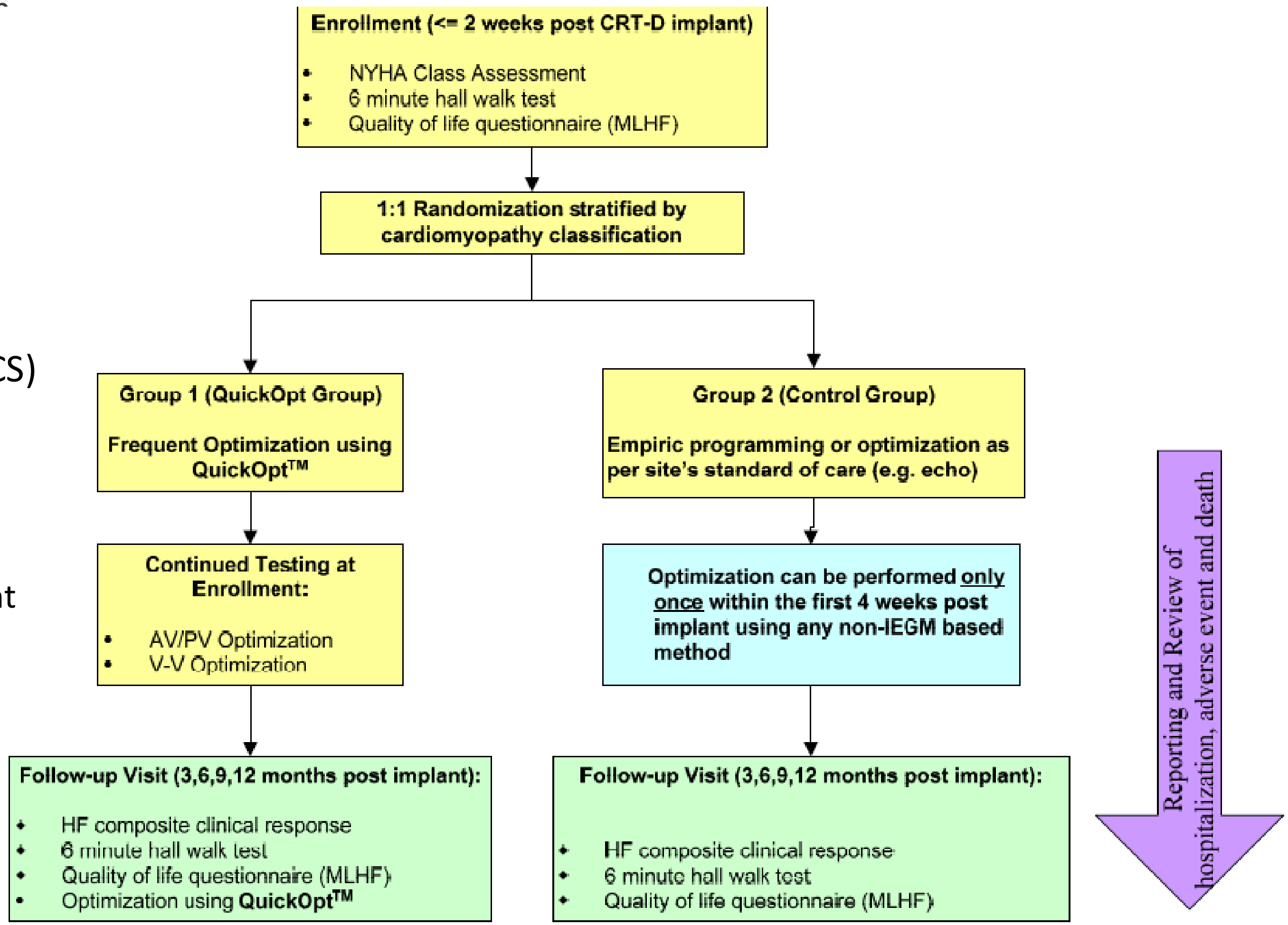
FREEDOM Trial

ST. JUDE MEDICAL
MORE CONTROL. LESS RISK.

- 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*

FREEDOM trial: Outcomes

QuickOpt (SJM)

FREEDOM Trial

ST. JUDE MEDICAL
MORE CONTROL. LESS RISK.

Intention-to-Treat

	QuickOpt Optimization Treatment group		Control group		
Heart Failure Clinical Composite Score	n	%	n	%	p-value
Improved	551	**67.52%**	559	**67.51%**	0.50
Unchanged	76	9.31%	86	10.39%	
Worsened	189	23.16%	183	22.10%	

ALL randomized pts

Conclusions applicable to clinical practice:

- EASINESS of USE
- NON-INFERIORITY vs SoC (clinical endpoint @ 1Y)

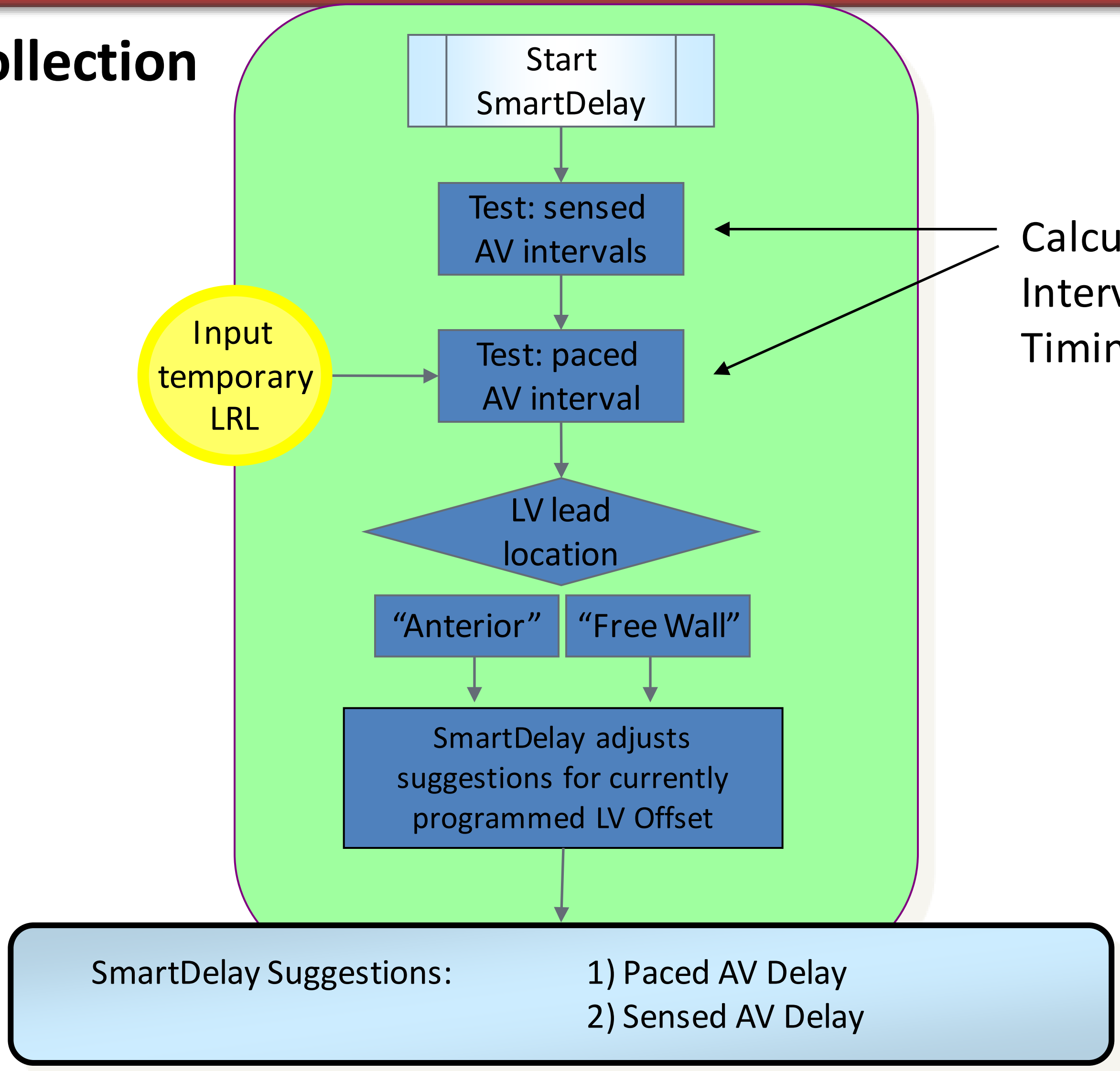
	Treatment group		
Heart Failure Clinical Composite Score	%	%	p-value
Improved	**71.29%**	**68.82%**	0.25
Unchanged	5.50%	4.78%	
Worsened	23.21%	26.40%	
Total	100%	100%	

ALL pts who strictly followed the protocol

Device-based methods: SmartDelay (BSx)

How does SmartDelay work?

Data Collection



Calculation of Interventricular Timing occurs

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:

COMPANION [1,2]	**1999 – 2003**	1200+ patients
DECREASE-HF [3,4]	**2003 – 2005**	300+ patients
RENEWAL 3 AVT Study [5]	**2003 – 2005**	130+ patients

1. Bristow MR et al. *J Card Fail* 6: 276-285., 2000.
2. Bristow MR et al. *N Engl J Med* 350: 2140-2150, 2004.
3. De Lurgio DB et al. *J Card Fail* 11: 233-239, 2005.
4. Rao RK et al. *Circulation* 115: 2136-2144, 2007.
5. Saxon LA et al. *J Cardiovasc Electrophysiol* 17: 520-525, 2006.

Clinical Support: CRTAVO

Overview of CRTAVO – An Acute Study

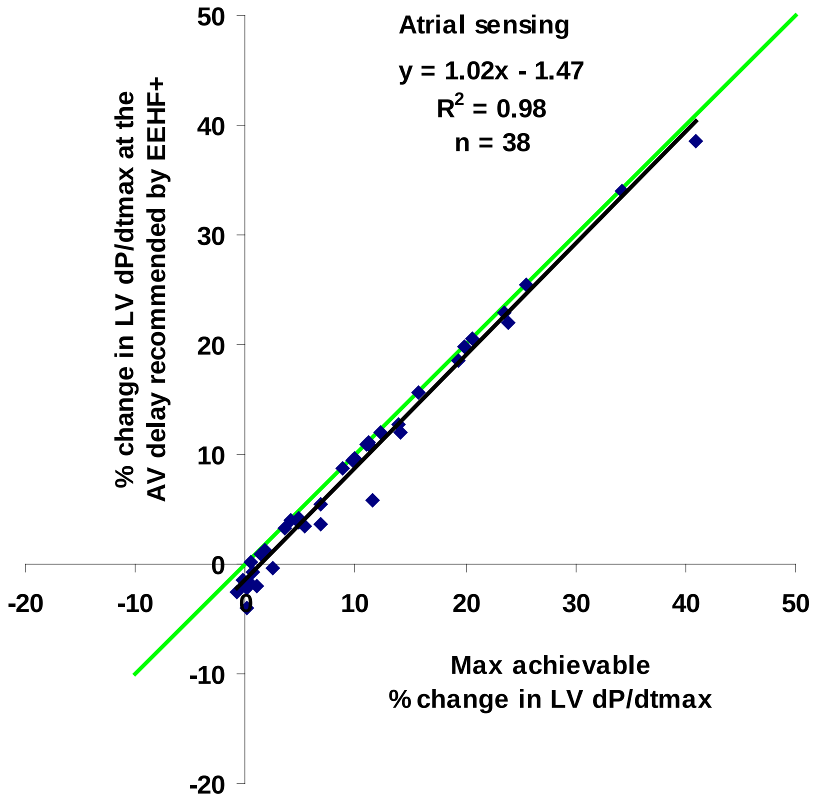
Boston Scientific conducted the CRTAVO study to evaluate SmartDelay and compare it to other AV optimization methods.

Using an invasive catheter to measure LV $(dP/dt)_{max}$, the CRTAVO study compared several AV delay optimization methods:

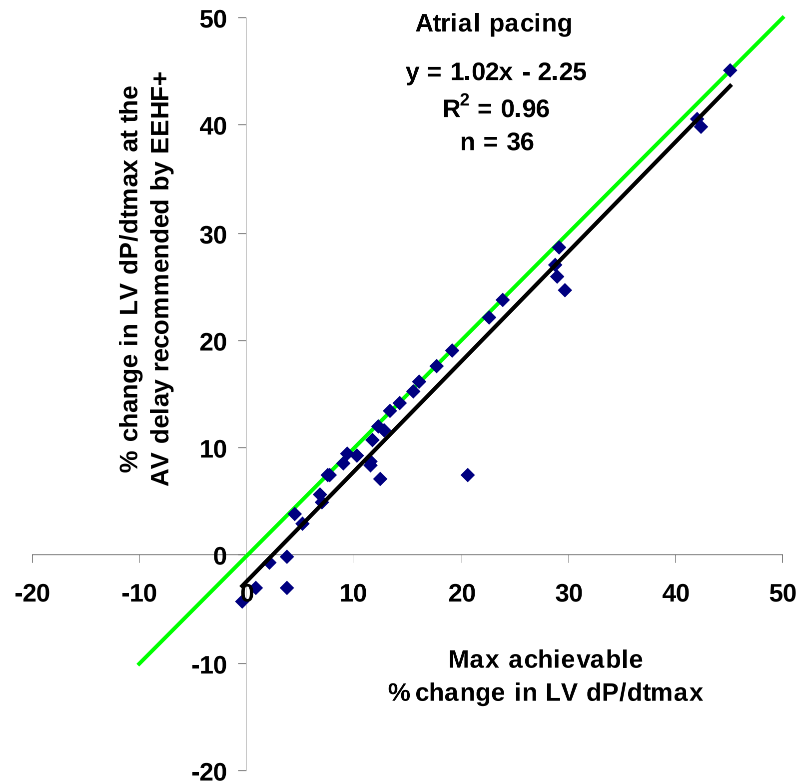
- SmartDelay optimization [manual mode]
- Echo optimization [stroke volume calculation by aortic VTI]
- Ritter method [echo-based technique]
- Fixed AV Delay values [100, 120, 140, and 160 ms]

(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]



Correlations between maximal achievable hemodynamic response (% change in LV dP/dt_{max}) and the response obtained at the AVD predicted by SmartDelay



Correlations between maximal achievable hemodynamic response (% change in LV dP/dt_{max}) and the response obtained at the AVD predicted by SmartDelay

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.

Device-based methods: SmartDelay (BSx)

- 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:

    $$AVD_{(p,s)} = 0.757 * AVI_{(p,s)} - 0.728 * QRS + 71.3 \text{ (ms)}$$

- Full test duration = **2.5 min** (pt @ rest, normal breathing, NO talking)

Clinical Support: SMART-AV

Overview of SMART-AV – 6 month data

- ***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**

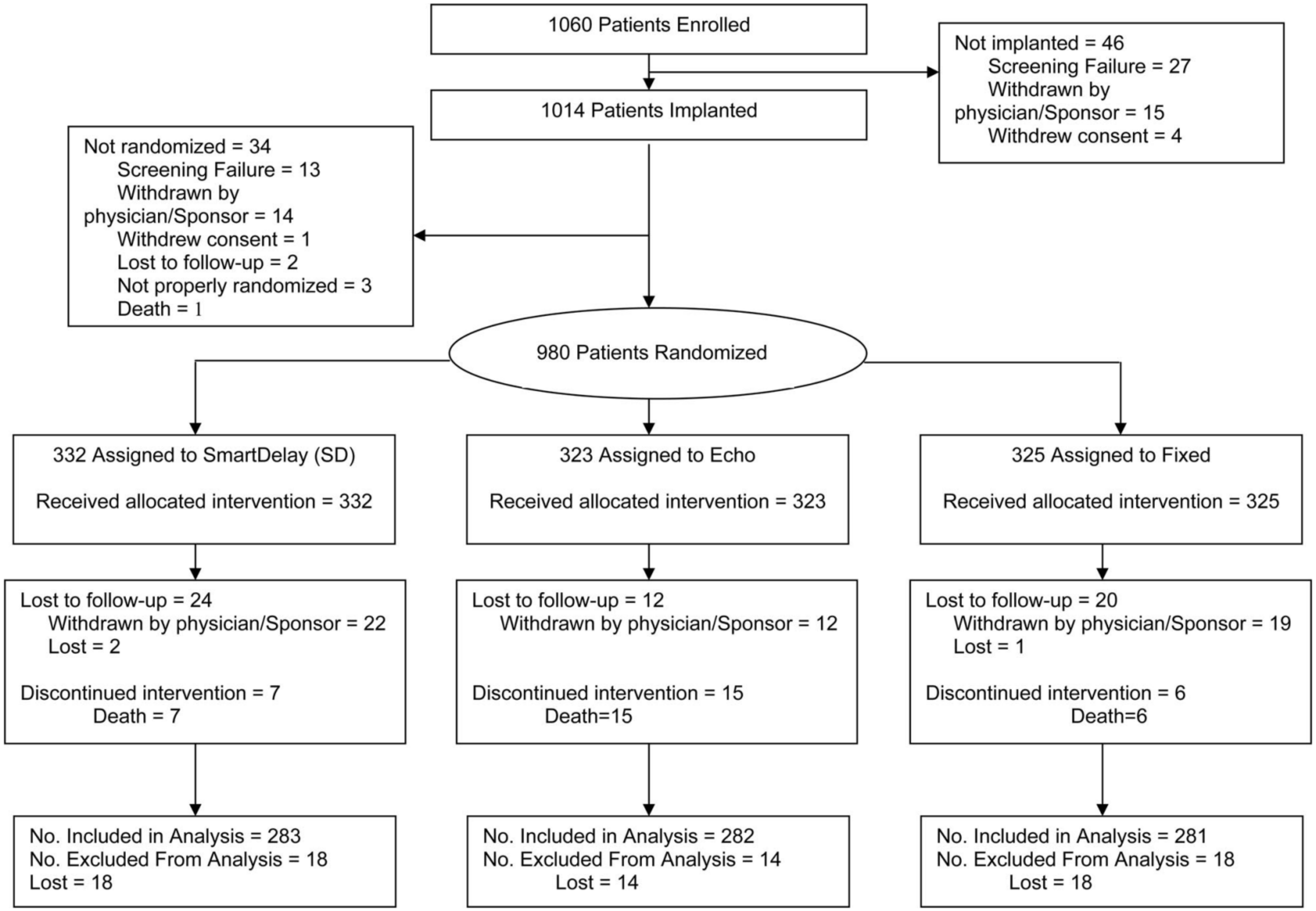
Randomization (1:1:1 SmartDelay: Echo: Fixed)
1 – 14 days post implant

- 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

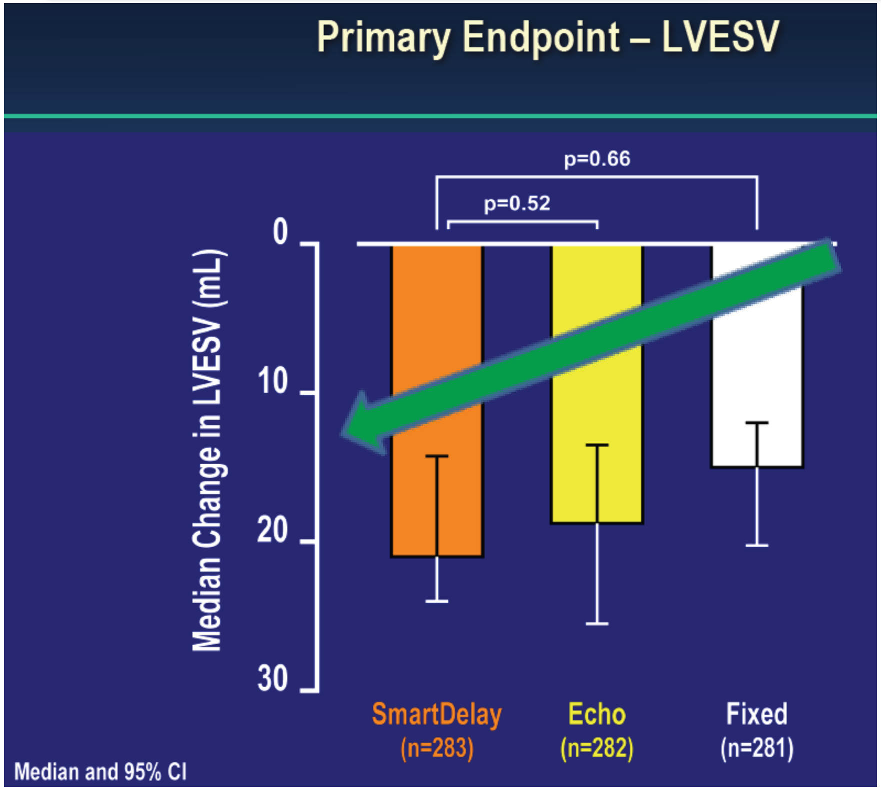
Clinical Support: SMART-AV

Study population



SMART-AV: LV remodeling (all p=ns)

SmartDelay (SD); BSx

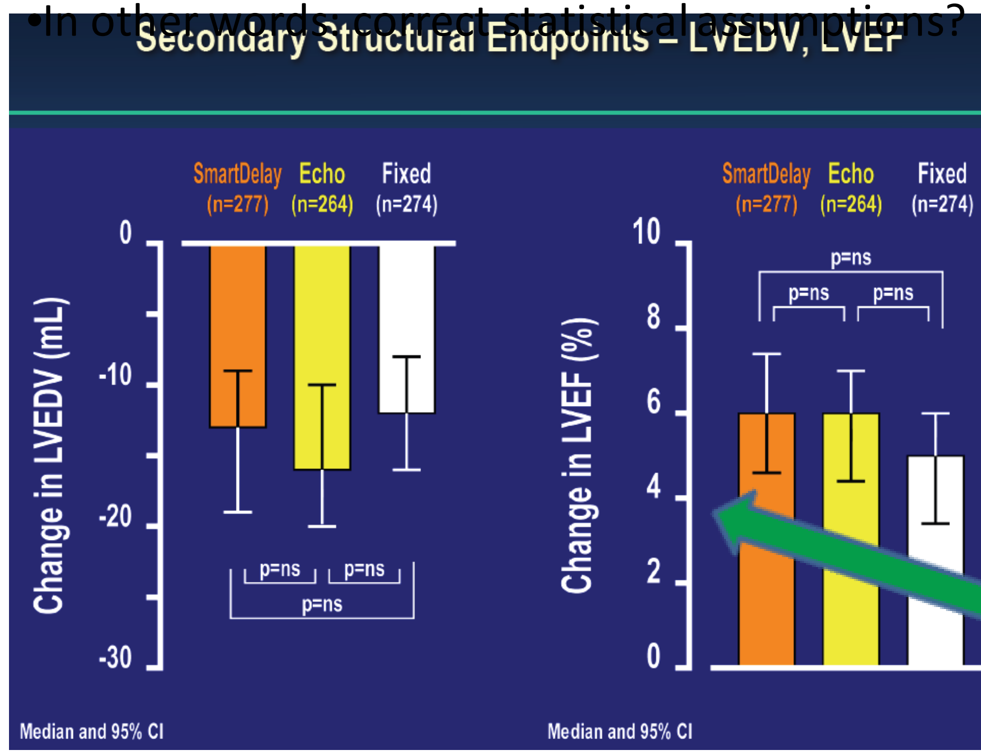


Some comments:

•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?



SMART-AV trial: summary / conclusions

SmartDelay (SD); BSx

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.

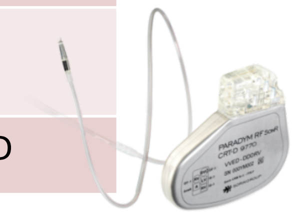
Subgroups: wide QRS duration, LBBB, non-ischemic CMP, and F gender responded more favorably to CRT (observed in general CRT registries)

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)*

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



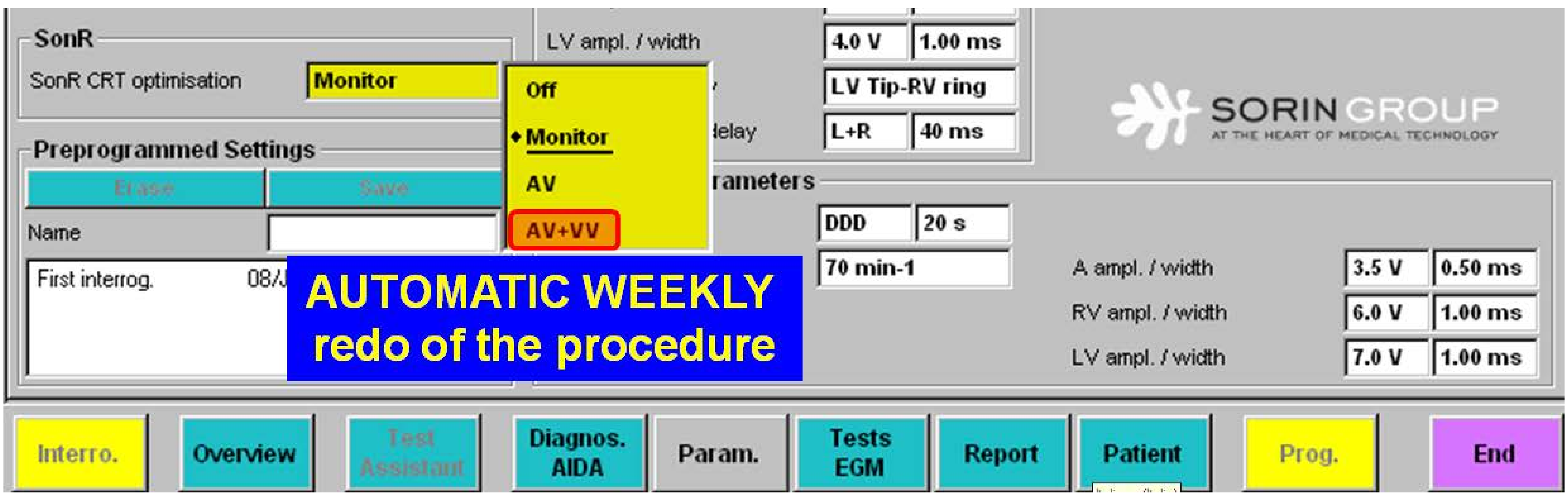
Endocardial acceleration sensor (correlated with LVdP/dt): combines LV contractility & LV filling to optimize CRT settings

Contractility ⟷ **LV filling**

SonR CRT optimization

AUTOMATIC methods: SonR technology *(SORIN Group)*

- 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



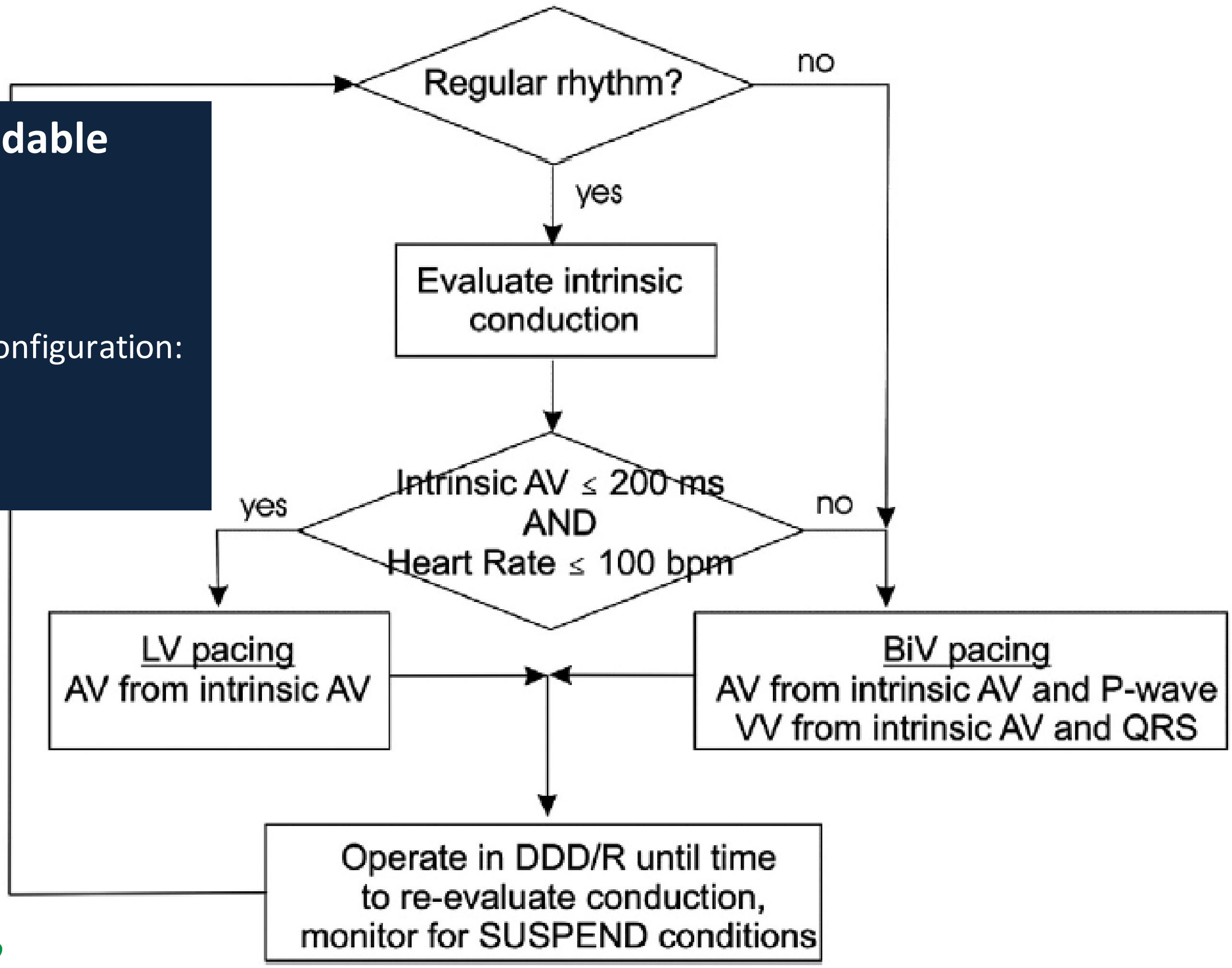
AUTOMATIC methods: Adaptive-CRT algo *(Mdt)*

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



Krum H & al. Am Heart J 2012

AUTOMATIC methods: “Adaptive-CRT” study *(Mdt)*


ARTICLE IN PRESS

Heart Rhythm 2012 Jul [Epub ahead of print]

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.

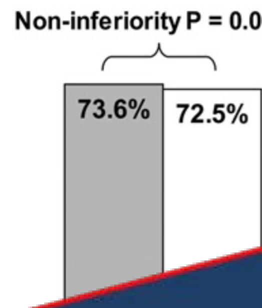
METHODS:

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.

Pittsburgh, Pennsylvania.

AUTOMATIC methods: “Adaptive-CRT” study *(Mdt)*

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



Safety

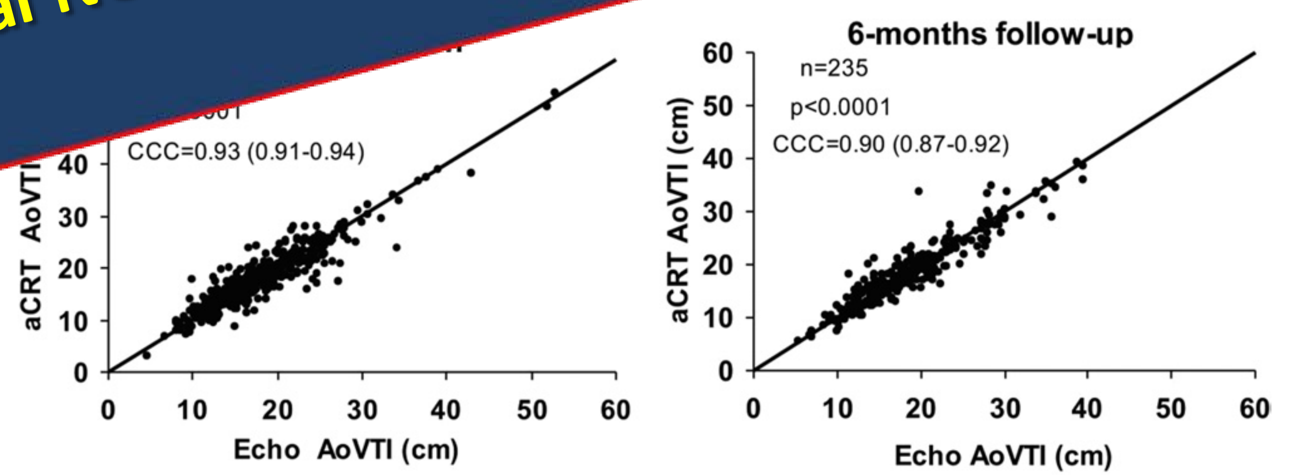
&

Clinical NON-INFERIORITY @ 6M

b) a-CRT and

high Conco

randomization & 6M after);



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

DEVICE-BASED methods @ a glance …

	QuickOpt (SJM)	SmartDelay (BSx)	AdaptivCRT (Mdt)	SonR (Sorin-G)
Based on	**IEGM** measures	**IEGM** measures	**IEGM** measures	**Hemodynamic (SonR)** sensor (contractility)
Programming	**1 parameter:** "Timing optimization"	**Paced HR + 1 parameter:** "CRT optimization"	**1 parameter** (dowloadable sw)	**1 parameter:** "SonR CRT optimization"
AVD optimiz.	Only **@ REST**; Paced & sensed	Only **@ REST**; Paced & sensed	Only **@ REST**; Paced & sensed	**@ REST & under EFFORT**; Paced & sensed
VVD optimiz.	OK	OK	OK (LV synchro or BiV)	OK
In-clinic (@ FU) vs Ambulatory (Automatic)	**In-clinic**	**In-clinic**	**Ambulatory** (dowloadable sw)	**In-clinic + Ambulatory (Weekly)**
Outcomes from trials: SAFETY	OK	OK	OK (dowloadable sw)	OK
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

CRT optimization a clinical must?

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

EXPERT REVIEWS

Optimizing atrioventricular and interventricular intervals following cardiac resynchronization therapy

Expert Rev. Cardiovasc. Ther. 9(2), 185–197 (2011)

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

CRT optimization a clinical must?

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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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:

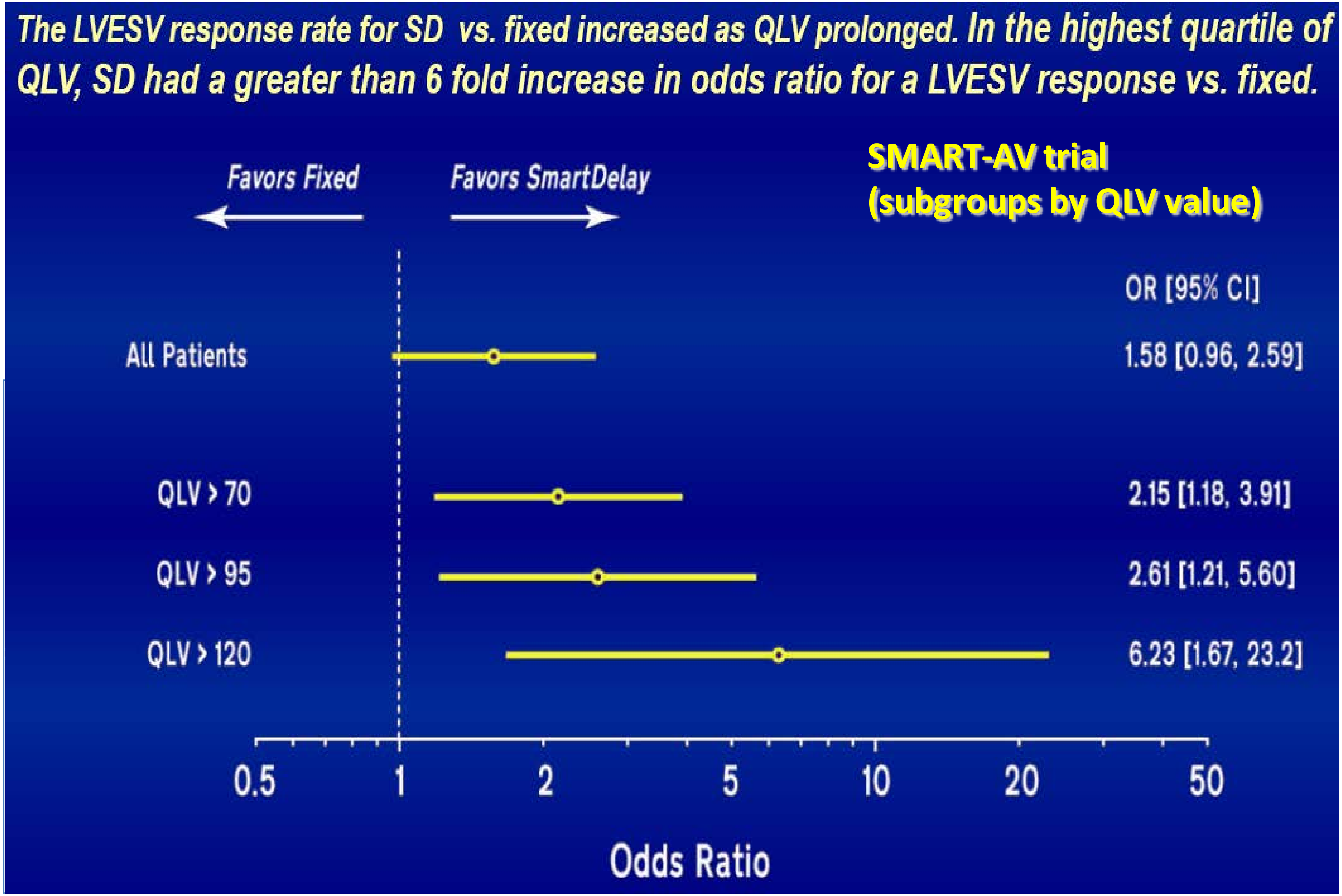
1. time from implant
2. effort vs resting phases
3. paced vs sensed atrial activity

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?



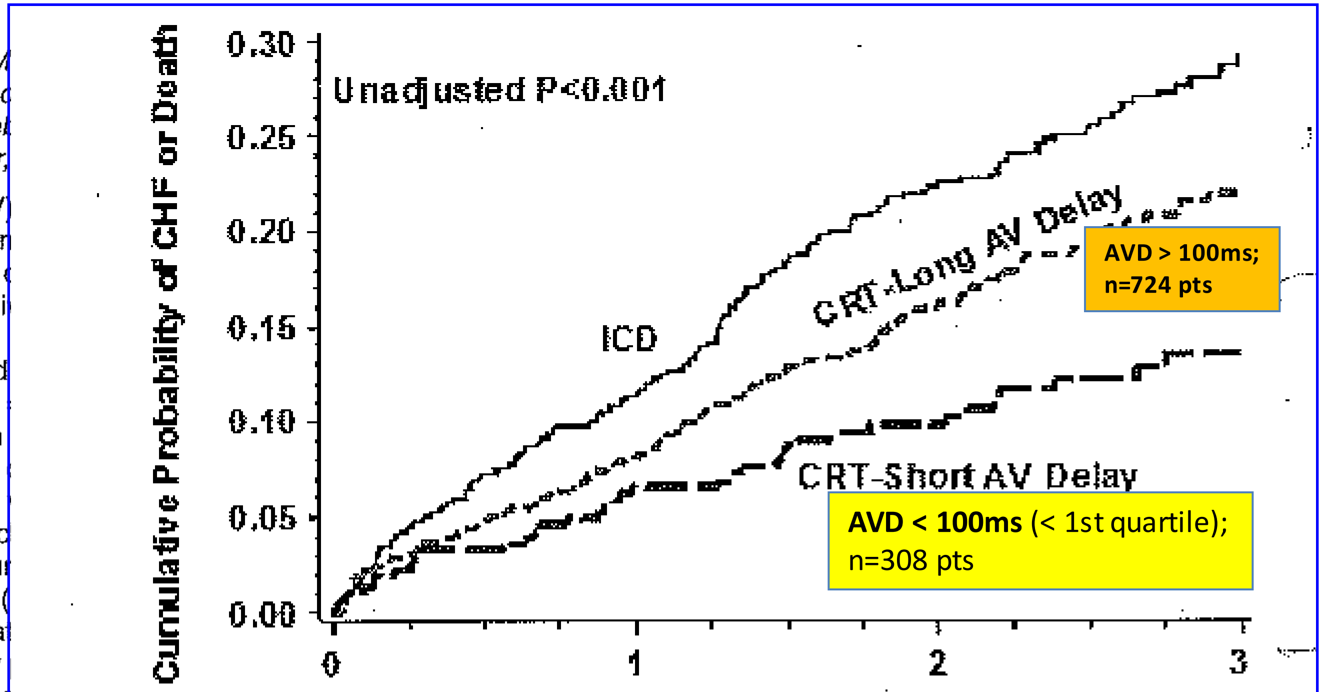
How do short (or very short) AVDs perform in clinical practice ?

AB29-03

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

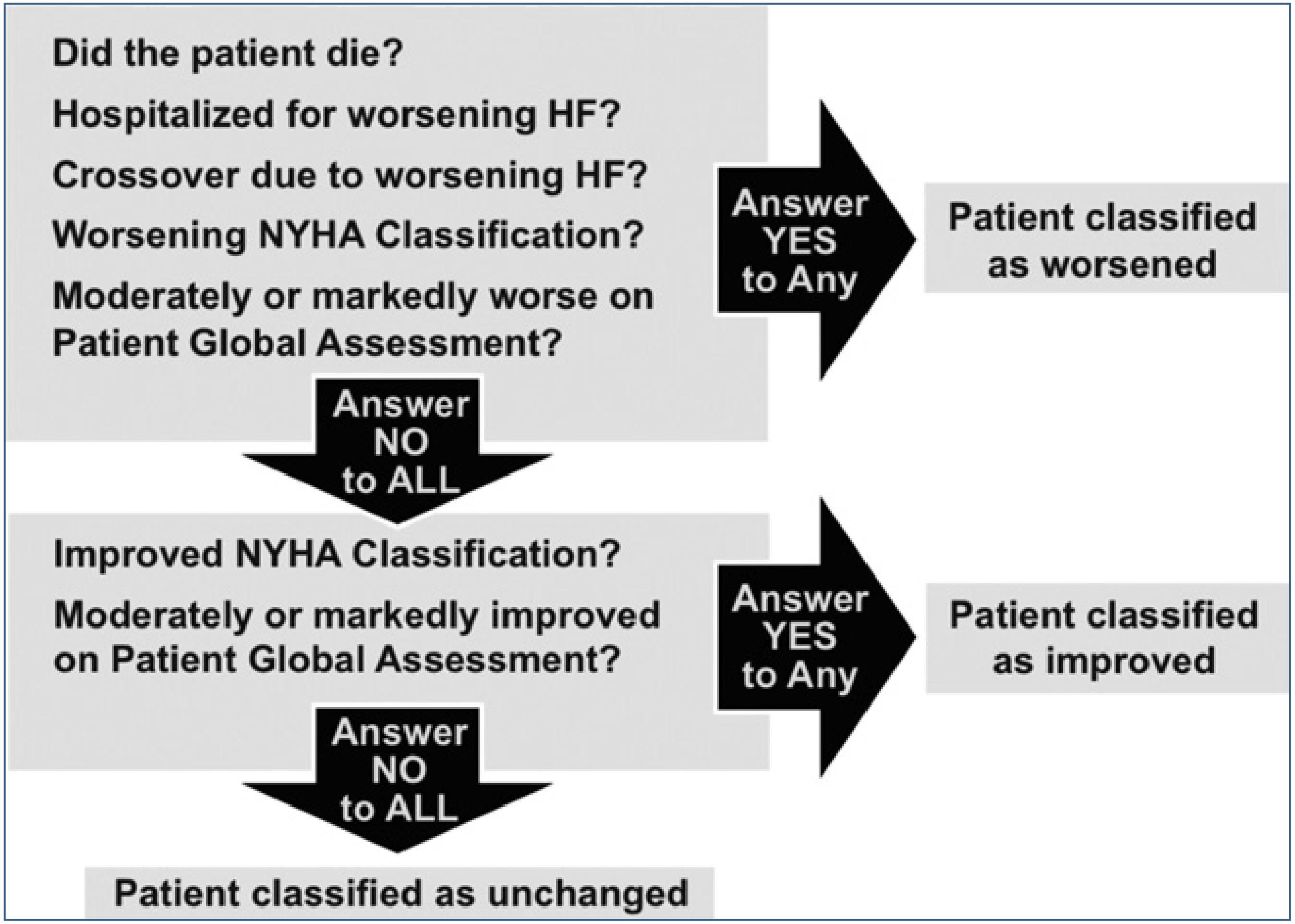
*Andrew J. Brenyo, MD, Christine Tompkins, M
MD, FHRS, Alon Barsheshet, MD, Mohan Rad
Huang, MD, Scott McNitt, MS, Wojciech Zare
Ilan Goldenberg, MD. University of Rochester,*

Introduction: The optimal atrioventricular (AV)
in cardiac resynchronization therapy (CRT) rer
determined. We hypothesized that shorter AV
the response to CRT through an increase in bi
and degree of resynchronization.
Methods: The effect of short AV delay defined
shorter than the lower quartile of 100 msec (n
delay (n = 724) was assessed in the CRT arm
The risk of HF or death and death alone were
ICD-only group (n = 711). Left ventricular (LV)
was analyzed comparing baseline to 1 year ec
Results: Kaplan-Meier survival analysis (Figu
the rate of HF or death at 3 years was lowest (
with a short AV delay (<100 msec); intermedia
with a long AV delay, and highest for ICD-only
p < 0.001 for the overall difference). Compared
CRT patients with both short and lon
significant reductions in the risk of H
0.42, p < 0.001; and 0.70, p = 0.001
in the CRT group a short AV delay w
significant 40% reduction in the risk
alone compared to long AV delay. At
AV delay was also associated with a
systolic volume (34%) compared to l
0.005) and ICD-only (10%, p < 0.00



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 Assessment?
Answer YES to Any
Patient classified as improved
Answer NO to ALL
Patient classified as unchanged