

## Friday 16 morning - Barbantini Room

12.30-14.00

Sorin Group satellite symposium

### Focus on: customizing CRT

Chairmen: L. Bonbempi / Brescia, Italy - B. Sassone / Cento, Italy

Automatic CRT optimization and follow up:

Clinical case 1 - monitoring

F. Zanon / Rovigo, Italy

Automatic CRT optimization and follow up:

Clinical case 2 - optimization

G. Mascioli / Bergamo, Italy

Multi-area pacing to enlarge CRT effect

Clinical case 1

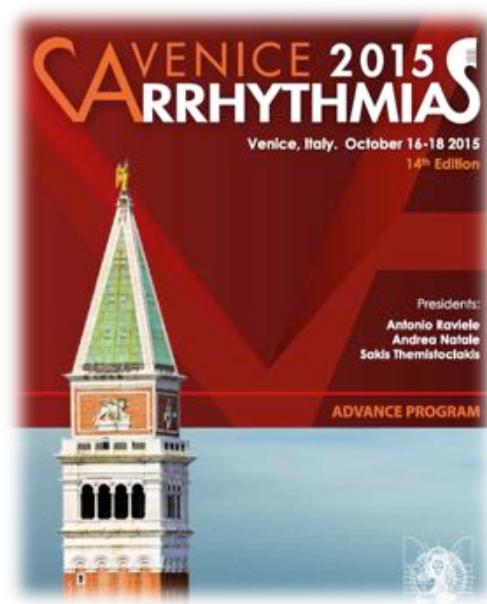
G. Zingarini / Perugia, Italy

Multi-area pacing to enlarge CRT effect

Clinical case 2

E. De Ruvo / Rome, Italy

Satellite symposium  
"Focus On: Customizing CRT"



# Automatic CRT Optimization and Follow-Up

## *Clinical Cases 2 - OPTIMIZATION*

**HUMANITAS**  
GAVAZZENI

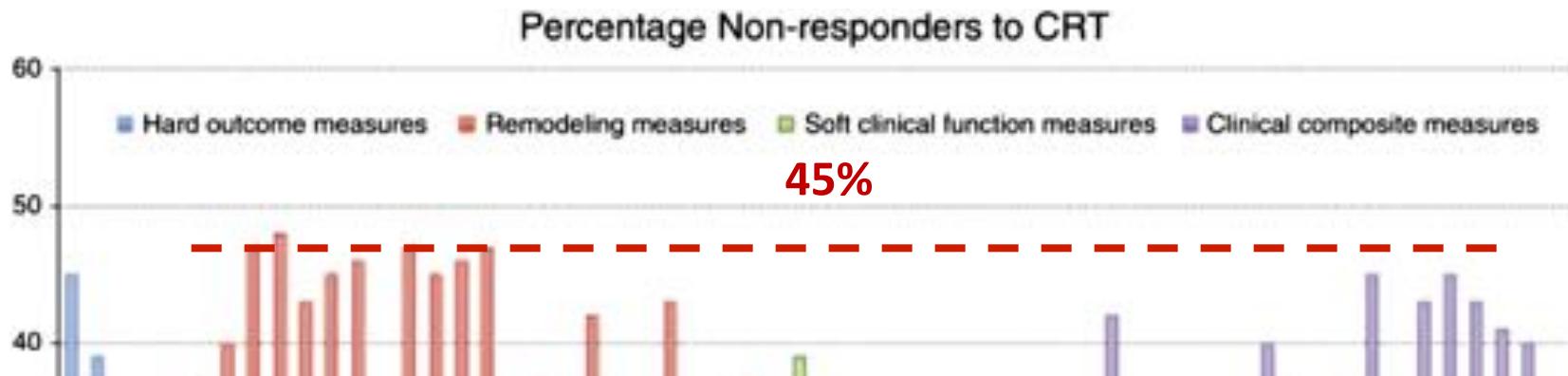
**MASCIOLI Giosuè, MD**  
*Cliniche Humanitas Gavazzeni*  
**BERGAMO (Italy)**



# DISCLOSURES

- Lecturer for Sorin
- Member of Advisory Boards for Biotronik

# CRT: “never-ending story” of NR pts ?



As CRT was more widely implemented, it became clear that even among pts with prolonged QRS, approx. 30% of pts (up to 40%-50% in some studies) do NOT achieve the expected clinical benefits.

Jaffe LM, Morin DP. **CRT: history, present status, and future directions.**  
Ochsner J. 2014 Winter;14(4):596-607.

# CRT response: not “black or white” ...

Super-responders  
↓ LVEF  $\geq 30\%$

Negative-responders

Long-Term Prognosis After  
Cardiac Resynchronization Therapy

Non-Responder → Non-Responder



(hopeless)

(fortun. small % of pts)

Non-Responder → Responder



(good job!)

Responder → Super-Responder



(great job!)



Absolute NR

Non-Responder

Responder

Super-Responder

# Likelihood to respond to CRT (big RCTs/registries)

Disease progression is so malignant to onset CRT benefit cannot be ruled out.

QRS > 150ms

LBBB morphology

F gender

Non-ischemic CMP

However, for most of the studies using MRI there is a lack of well conducted prospectively randomized controlled trials.

Most of the currently available evidence comes from single center series in which 1 single parameter has been investigated. Considering that location of the pacing lead with respect to the scar location might be of importance, it could be worthwhile to extend initiatives to merge preprocedural computed tomography or MRI scans with fluoroscopic imaging.<sup>37</sup> The discussion above is summarized in **Figure 2**.

**FAVOURABLE**

Besides the baseline criteria, also criteria regarding the post-CRT situation importantly predict CRT response. The most obvious criterion is the presence of electrical and eventually mechanical resynchronization. This can be determined by observing the reduction in QRS duration<sup>35</sup> and by a change in the shape of the QRS complex (indicating fusion of right ventricular and LV originating activation waves).<sup>27</sup> Proper

130ms < QRS < 150ms  
Co-morbidity +/-  
Persistently/Persistent AF



**UNKNOWN**  
**outcome**

fusion of these 2 wavefronts requires proper the pacing leads more or less opposite to each other (with the intrinsic conduction). The role of pacemoment in achieving the most perfect resynchronization is a matter of debate. Pre-clinical data are conflicting: are the clinical data. Helm et al showed that in canine hearts the position of the LV lead is not important. In contrast, Rademakers et al showed that the LV lead is very crucial in order to achieve a good response.<sup>35</sup> Both PATH-CHF I and II studies show that atrial or biventricular pacing at posterolateral wall achieves the best mechanical response to CRT.<sup>17,18</sup> In contrast, low-up data of both COMPANION and MADIT-III demonstrate a meaningful difference in outcome when paced at different ventricular sites. Singh et al reported worse outcome of CRT patients who were paced at the apical site; this observation is consistent with the hemodynamic benefit in the PATH-CHF I study.

Good resynchronization can also be assessed by cardiographic analysis, especially 2-dimensional echocardiography. Good resynchronization coincides with a better distribution of peak strain<sup>39</sup> and disappearance of

**Outcome generally**

**CRS < 130ms**  
**RBBB / IVCD morph**  
**Ischemic CMP**  
**Multiple co-morbidities**  
**NYHA class IV**



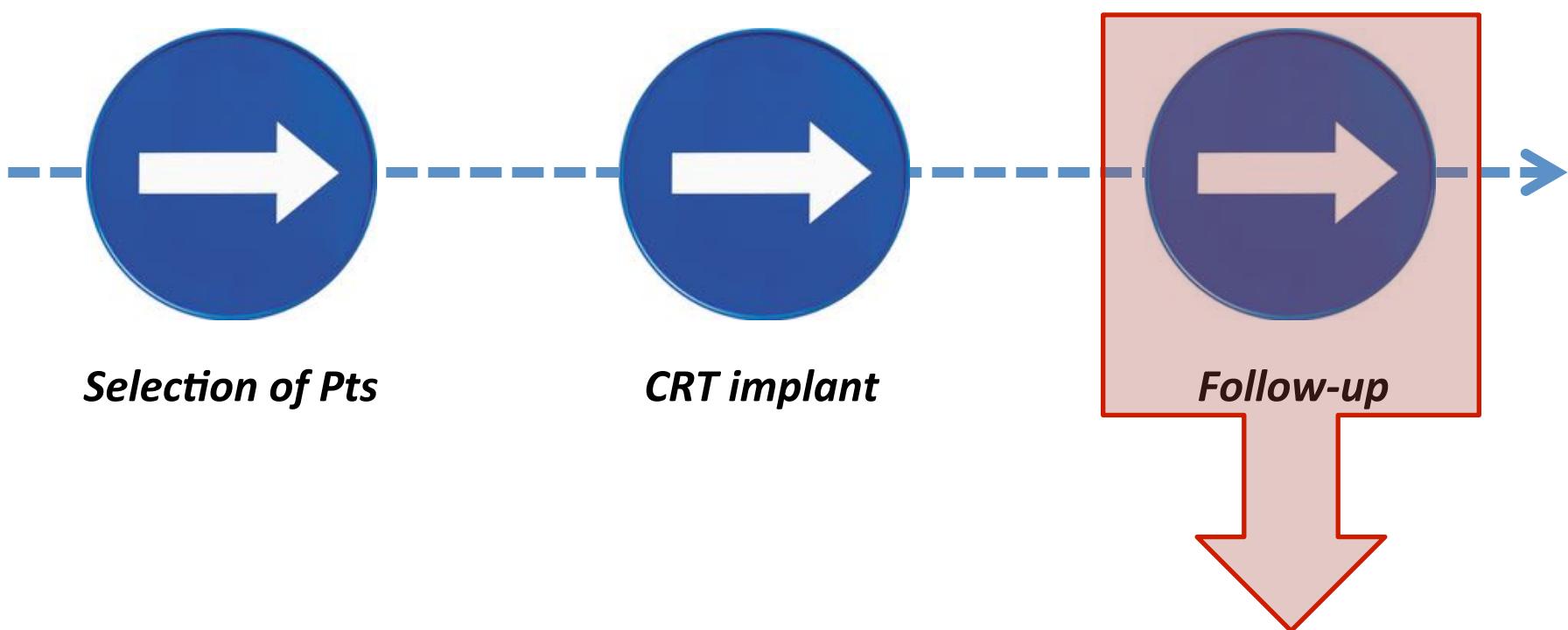
**Outcome generally**  
**UNFAVOURABLE**

# How to improve the profile of CRT response ?

MINIREVIEWS

## Cardiac resynchronization therapy: Dire need for targeted left ventricular lead placement and optimal device programming

Pastromas S, Manolis AS. World J Cardiol. 2014;6(12)



*Selection of Pts*

*CRT implant*

*Follow-up*

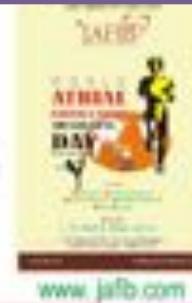
***Focus on pts' FU: a  
“DESPERATE” need for  
customization***

# FU of CRT pts: the effects of optimization



Featured Review

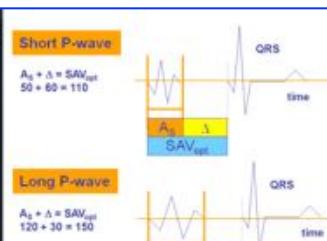
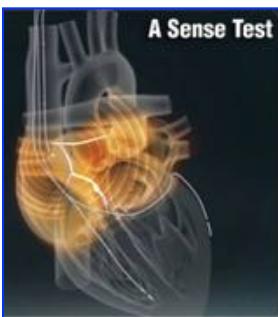
## Journal of Atrial Fibrillation



Lunati M, Magenta G & al.  
JAFIB 2014 Aug/Sep Vol. 7(2)

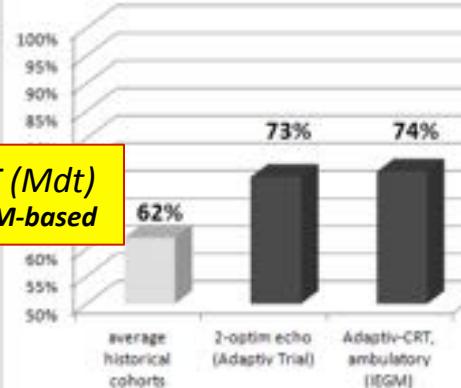
### Clinical Relevance Of Systematic CRT Device Optimization

Maurizio Lunati<sup>1</sup>, Giovanni Magenta<sup>1</sup>, Giuseppe Cattafani<sup>1</sup>, Antonella Moretti<sup>1</sup>, Giacomo Falascia<sup>1</sup>, Emanuela Locati<sup>1</sup>

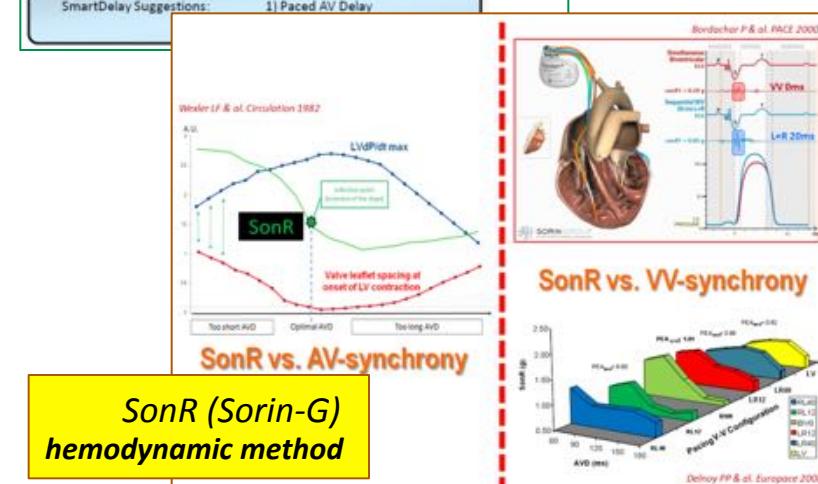
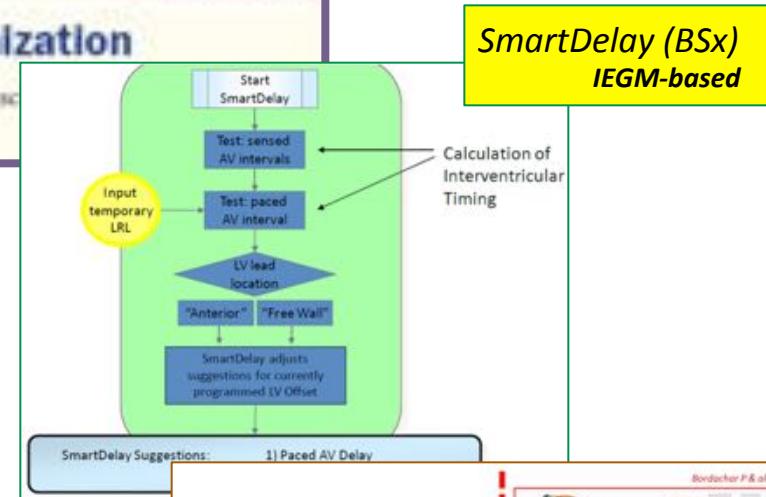


**QuickOpt (SJM)**  
IEGM-based

#### Clinical Combined Endpoint (6-month FU)

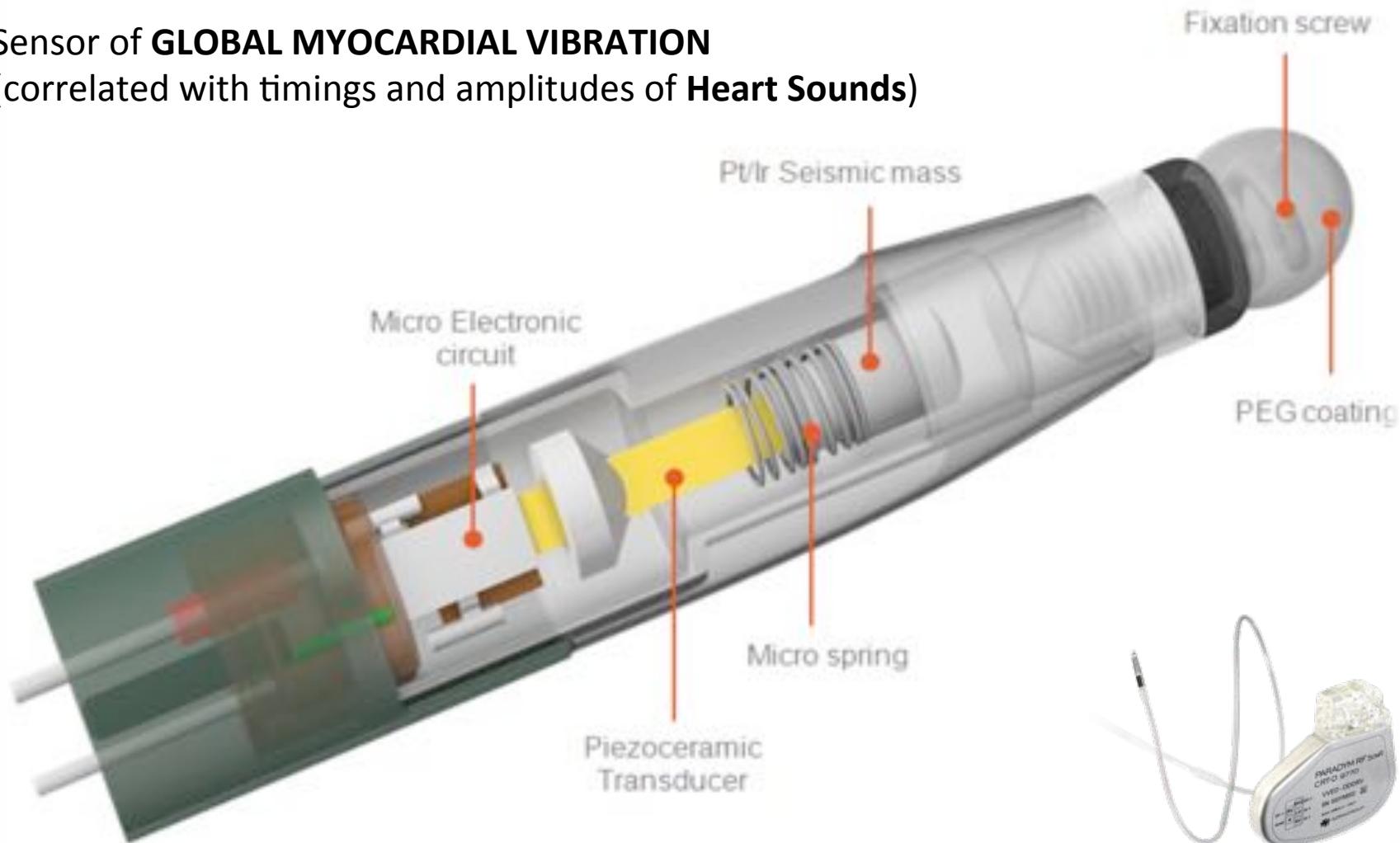


**Adaptive-CRT (Mdt)**  
IEGM-based

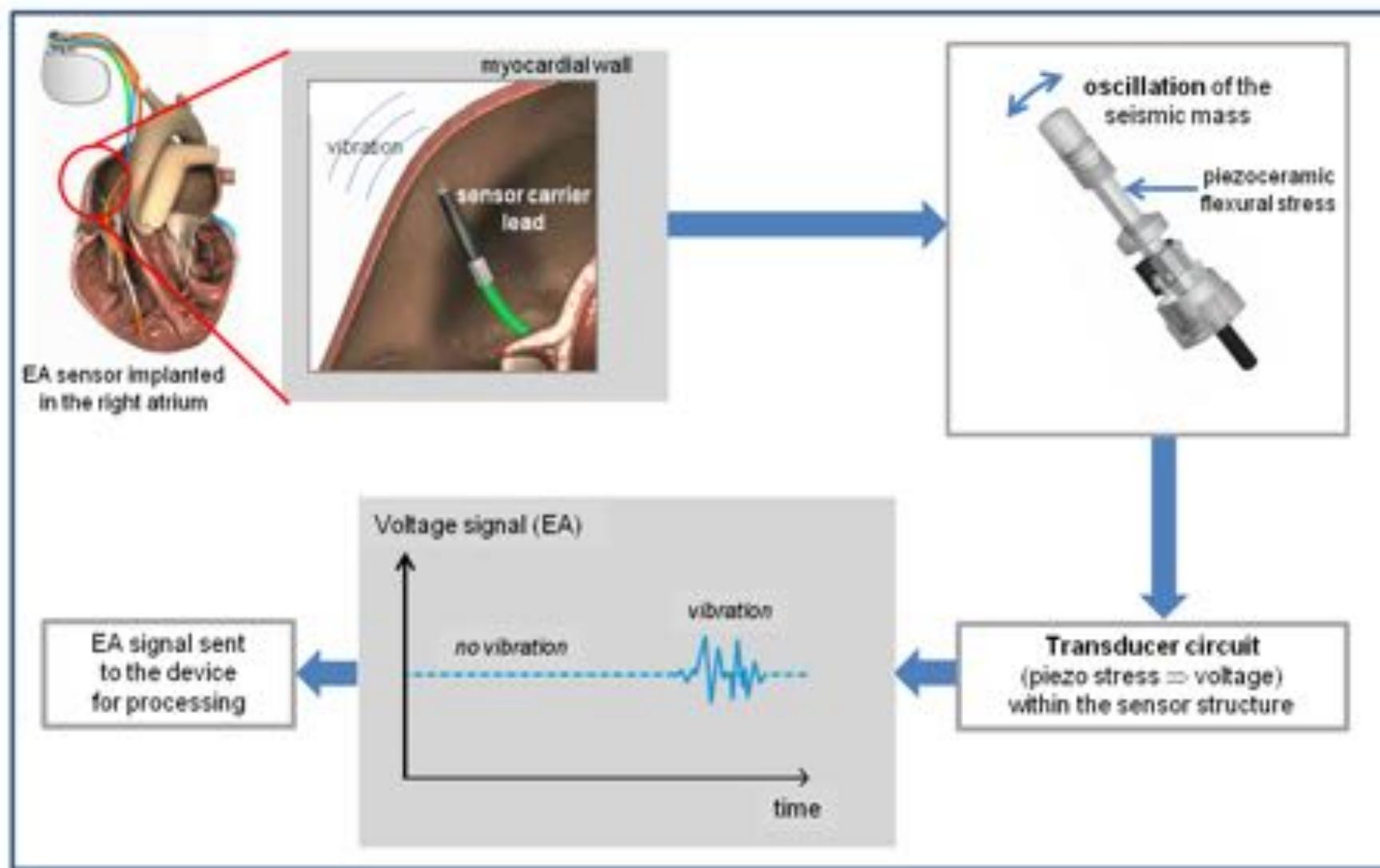


# Optimization based upon a hemodynamic sensor: the SonR technology (*atrial lead, SonRtip model, released Sept. 2011*)

Sensor of **GLOBAL MYOCARDIAL VIBRATION**  
(correlated with timings and amplitudes of **Heart Sounds**)

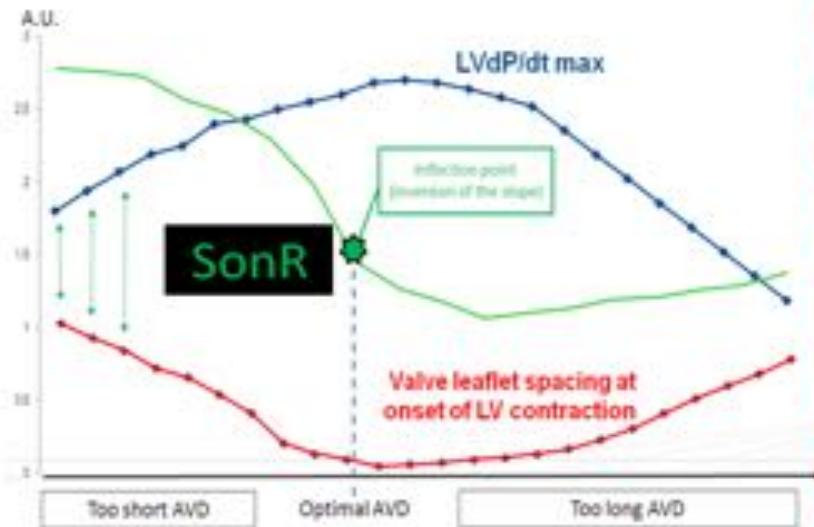


# Optimization based upon a hemodynamic sensor: the SonR technology (*atrial lead, SonRtip model, released Sept. 2011*)

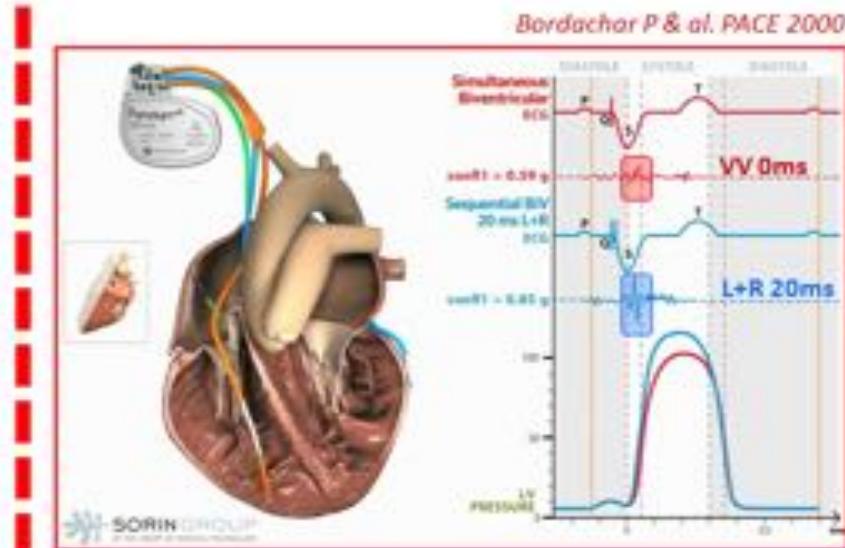


# SonR weekly automatic optimization of AVD/VVD (based upon contractility)

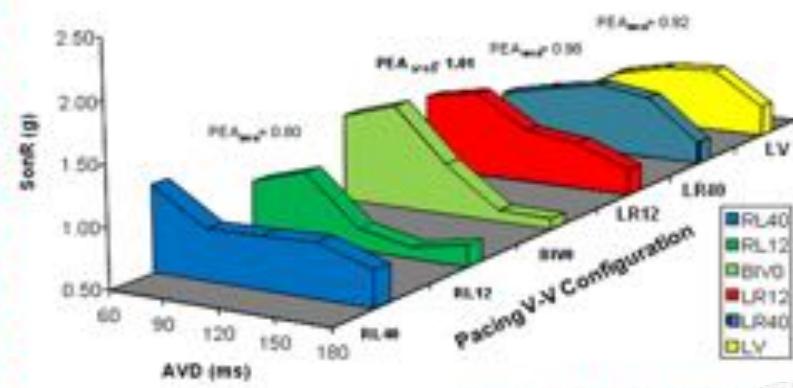
Wexler LF & al. Circulation 1982



## SonR vs. AV-synchrony



## SonR vs. VV-synchrony



Delnoy PP & al. Europace



# Clinical validation: safety of the SonR system



Parameters, n (%)	n = 99
Demographics:	
Age (mean $\pm$ SD, in years)	68.3 $\pm$ 9.2 years
Male gender	72 (72.7)
BMI (mean $\pm$ SD, in kg/m <sup>2</sup> )	27.1 $\pm$ 4.5 kg/m <sup>2</sup>
Implant indication:	
Primary prophylactic indication	91 (91.9)
Secondary prophylactic indication	8 (8.1)
NYHA functional class:	
I	3 (3.0)
II	42 (42.4)
III	49 (49.5)
IV	3 (3.0)
Left-ventricular ejection fraction:	26.2 $\pm$ 6.6
Heart failure aetiology:	
Ischaemic	54 (54.6)
Non-ischaemic	45 (45.5)
Valvular disease:	
Mitral	31 (31.0)
Aortic	8 (8.0)
Tricuspid	13 (13.0)
Conduction disorders:	
AVB—1st degree	13 (13.1)
AVB—2nd degree	6 (6.1)
AVB—3rd degree	5 (5.1)
Sinus dysfunction	6 (6.1)
Paroxysmal AA (flutter or fibrillation)	20 (20.2)
Persistent AA (flutter or fibrillation)	9 (9.1)
Associated conditions:	
Arterial hypertension	52 (52.5)
Diabetes mellitus	32 (32.3)
Renal failure	15 (15.2)

**99% complication-free rate @ 3M post-implant:**

- n = 1 atrial lead dislodgement 1-day after implant (repositioned, OK)
- n = 0 serious adverse events or adverse events related to the atrial lead

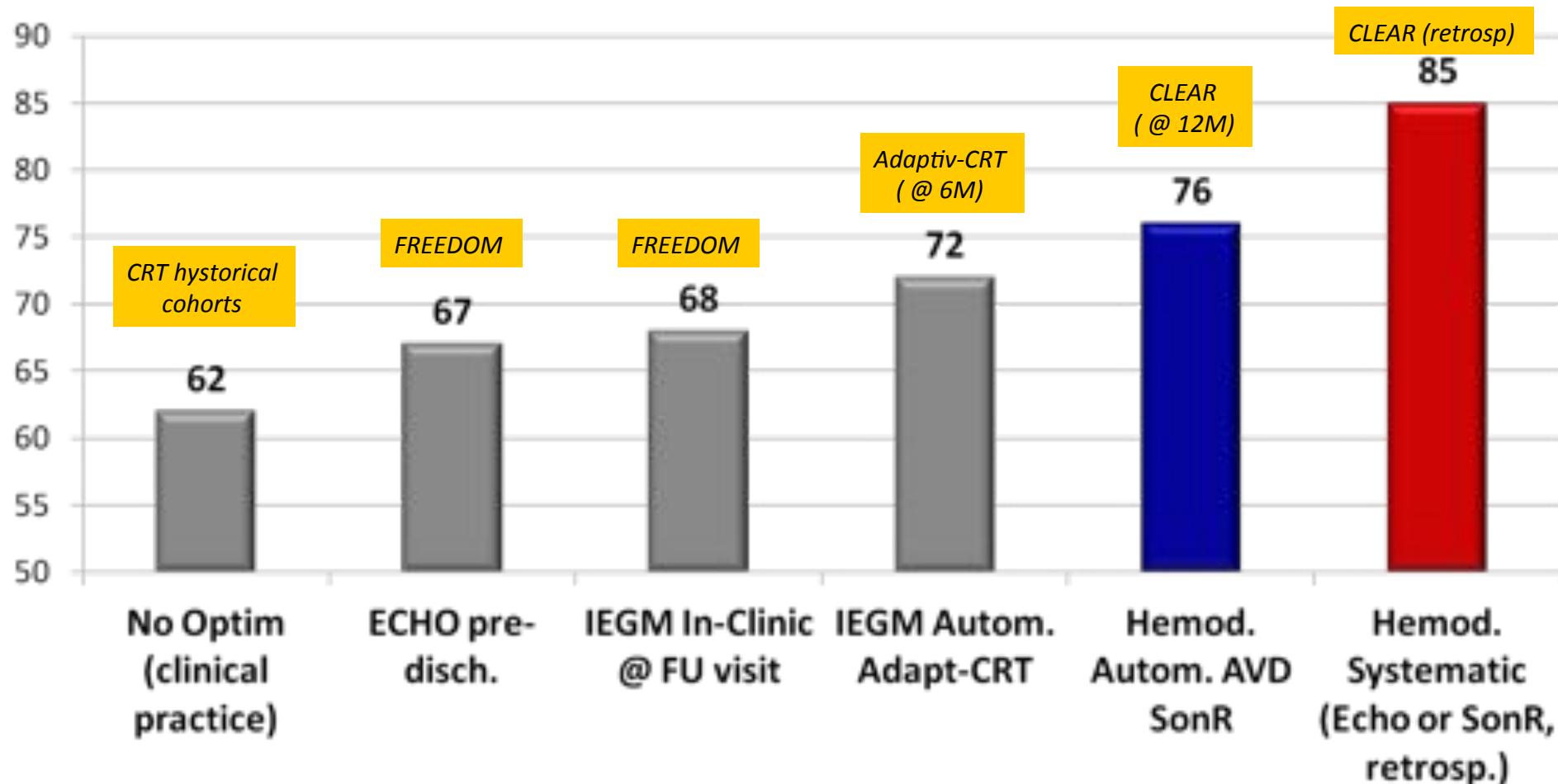
Over 1Y FU, SonR algo able to automatically reprogram  
AVD & VVD in **97% of pts** over **>75% of weeks**

## Conclusion

In conclusion, the implantation of the SonR tip atrial lead is easy and safe. Electrical performances are adequate and remain stable when implanted in different atrial target positions. The AV/VV optimization algorithm shows good performances for the majority of patients and therefore could offer a promising automatic tool to further improve response rates to CRT.

# FU of CRT pts: the effects of optimization

% Clinical Response Rate (Packer's combined endpoint)



*The combination of proper tools (**hemodynamic sensor**) together with a **frequent re-optimization** associates with a very high clinical response rate  
→ this relationship must be PROSPECTIVELY confirmed ...*

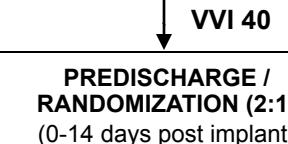
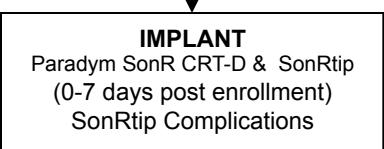
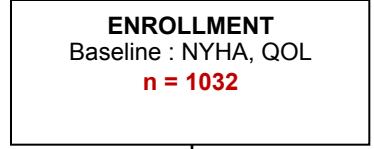
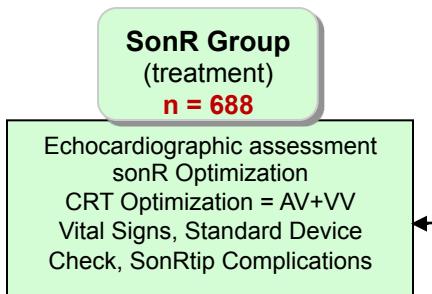
# RESPOND CRT

Clinical TRial of the SonRtiP Lead and Automatic AV-VV Optimization Algorithm in the ParaDym RF SonR CRT-D

**Study Design**  
(n = 1032 pts)

**2/3**

**1-ary endpoint:**  
Packer's Clinical  
Combined @ 12M



**1/3**

**Echo Group**  
(control)  
**n = 344**

Echocardiographic assessm  
Echocardiographic Optimiza  
CRT Optimization = OFF  
Vital Signs, Standard Device  
Check, SonRtip Complications

**SINGLE OPTIMIZATION**  
**AV & VV with ECHO**  
**@ PRE-DISCHARGE**

**WEEKLY OPTIMIZATION**  
(automatic, SonR-based,  
AV & VV delays)

**6W FOLLOW-UP**  
Vital Signs, Standard Device Check  
SonRtip Complications

**12M / 18M FOLLOW UP**  
Standard Device Check  
Mortality, HF-related  
Hospitalizations, NYHA, QOL  
SonRtip Complications

@ each FU visit:  
**BLINDED**  
assessment:  
NYHA class,  
QoL (KCCQ),

**6W FOLLOW-UP**  
Vital Signs, Standard Device Check  
SonRtip Complications

**3M / 6M / 12M / 18M FOLLOW**  
Standard Device Check  
Mortality, HF-related  
Hospitalizations, NYHA, QOL  
SonRtip Complications

**NO re-optimizations**  
**of AV & VV delays**  
**during FU allowed**

**SonR automatic function vs. Single-Echo in PHD**

**Inclusions termin. Oct 2014 (n=1039 pts; 125 Centers ww)**

**1-ary endpoint outcomes expected in May 2016**

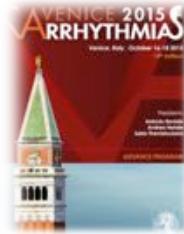
clinicaltrials.gov ID:  
NCT01534234  
(sponsor: SORIN Group)

(US only)  
Standard Device Check  
SonRtip Complications

(US on  
Standard Devi  
SonRtip Comp  
Brugada J & al (Steering Cmt)  
Am Heart J 2014

**Study End**

# CRT optimization with a hemodynamic sensor (SonR)



Automatic CRT Optimization and Follow-Up

*Clinical Cases*

HUMANITAS  
GAVAZZINI

MASCIOLI Giosuè, MD  
Cliniche Humanitas Gavazzeni  
BERGAMO (Italy)



- CASE 1: “*When a patient is perfect*”
- CASE 2: “*When CRT is not enough ...*”
- CASE 3: “*SonR chameleon*”

# CASE 1: when a pt is perfect ...

## ⦿ Female pt, 77 yrs old, SCD-HeFT ICD indication:

HF in NYHA class 3, OMT, LVEF 32%, Mitral Insufficiency,  
ISCHEMIC etiology (CNGF feb 2013: monovasal disease)  
ECG: QRS 145ms, **LBBB**, SR @ 77bpm

## ⦿ Clinical history / Co-morbidity:

Diabetes (Insulin-Dependant)  
Systemic arterial hypertension  
Poliomielitis in childhood

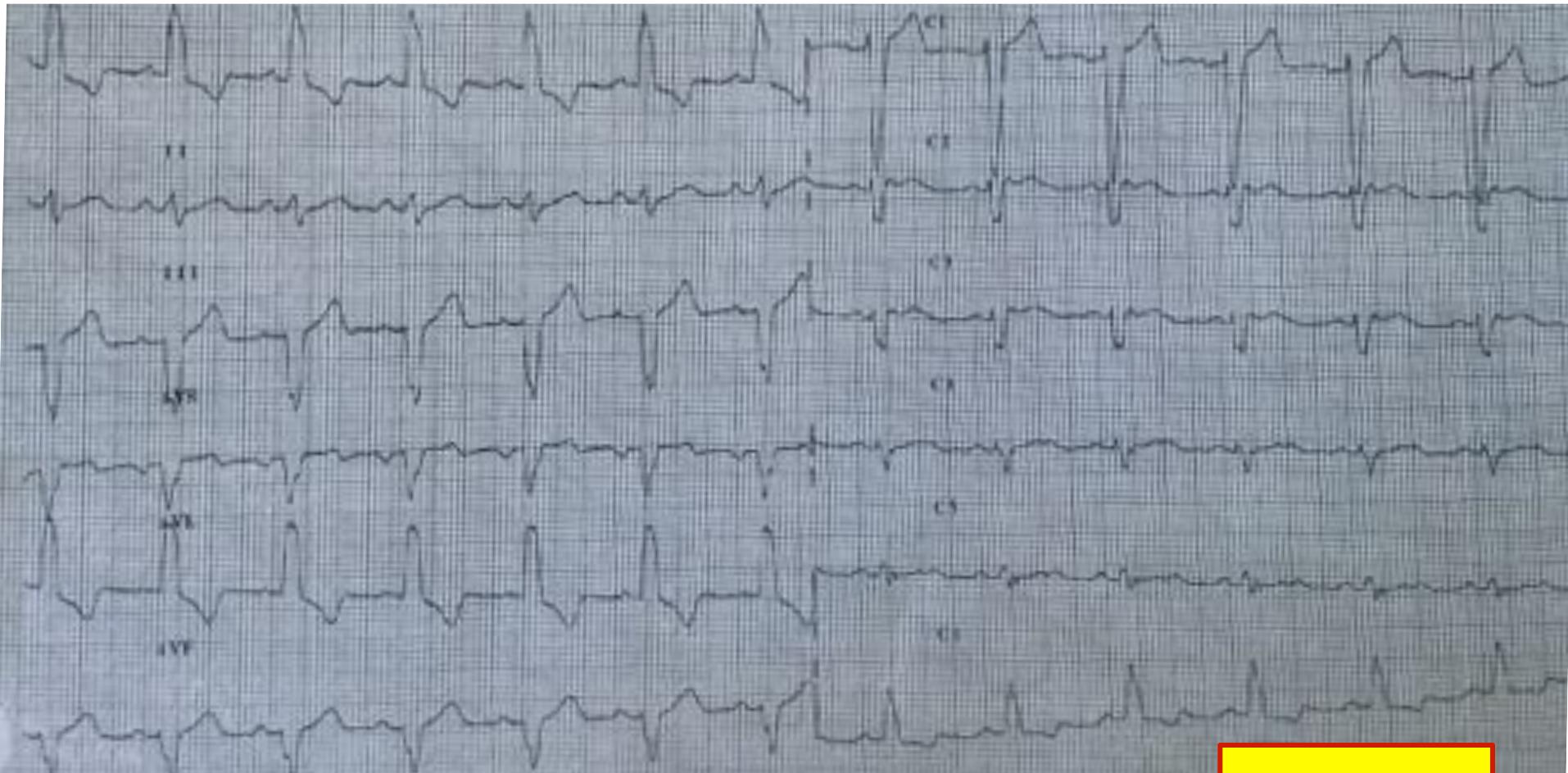
## ⦿ Basal ECHOCARDIO:

**LVEF 32%** (LVEDV 62ml; LVESV 42ml)  
**LPEI** 108ms  
**Jet-Area MR** 4.5cm<sup>2</sup>

## ⦿ Apr 2013: hospitalized for planned **CRT-D implant**

# CASE 1: when a pt is perfect ...

Pre-implant ECG (F, 77 yrs); SR @ 77 bpm, LBBB



QRS 145ms

# CASE 1: when a pt is perfect ...

LAO

**IMPLANT** (april 2013)

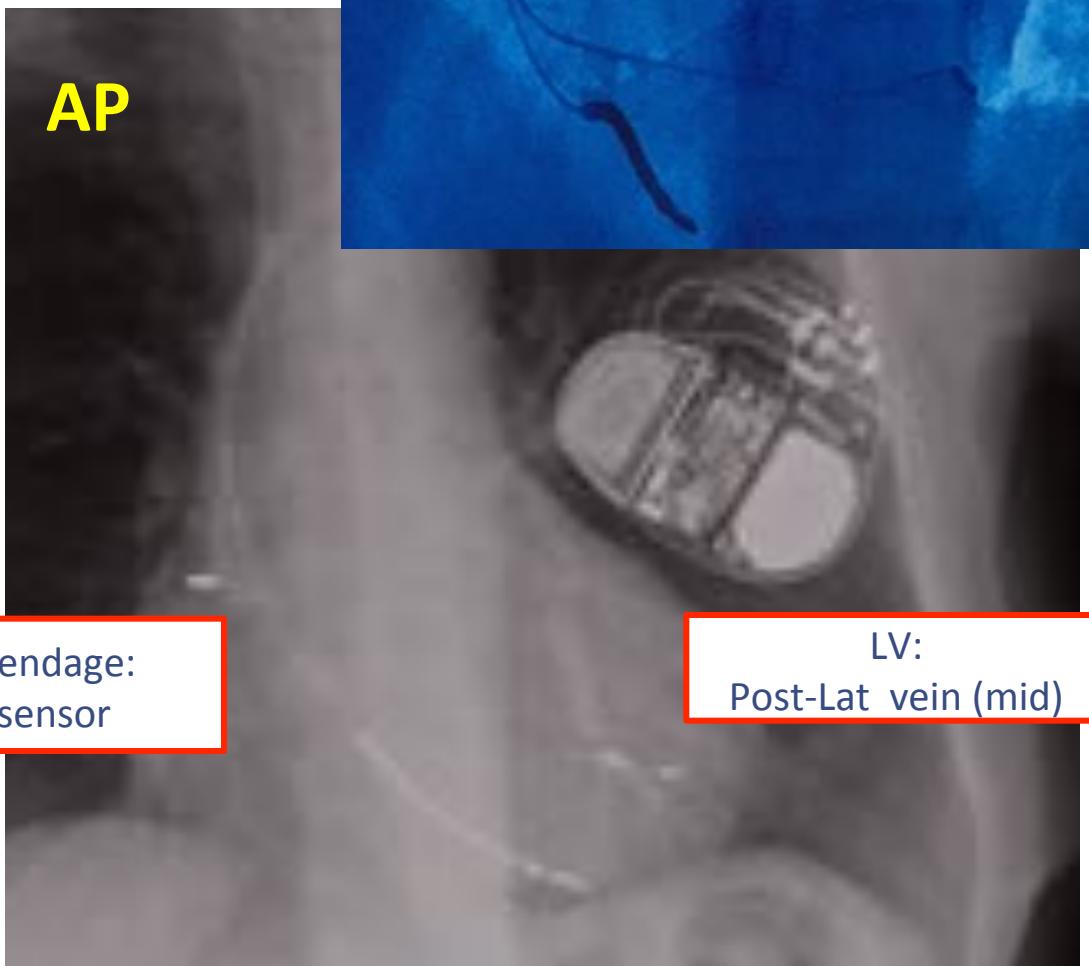
**CRT-D system equipped with SonR sensor**

Contractility sensor, correlated with LV dP/dt)

RA: *SonR tip in appendage*

RV: Apex

LV: Postero-Lateral vein (mid portion)



**SonR Weekly Automatic  
Optimization = ON  
(optimiz. AVD & VVD)**

RA appendage:  
SonR sensor

LV:  
Post-Lat vein (mid)

# CASE 1: when a pt is perfect ...

## Clinical variables during FU (2Y)

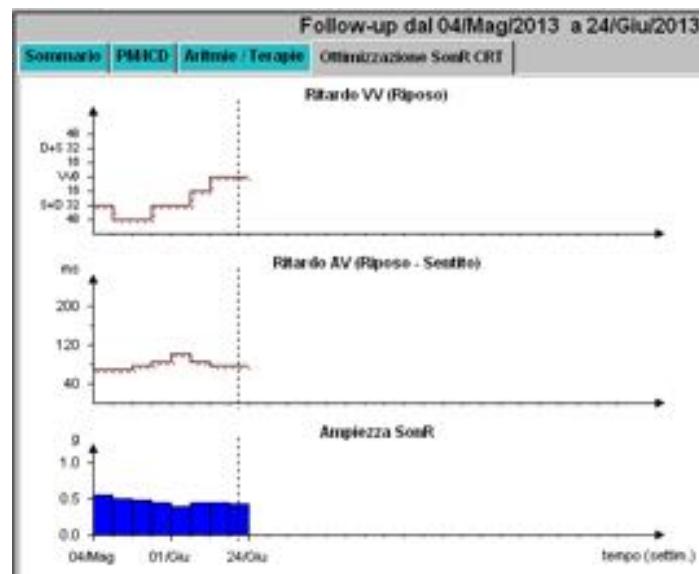
	NYHA	QRS (ms)	BiVp (%)	events	Med Thx	Arrhythmias	Notes
Pre-CRT	III	145	-	HFH	OMT	-	-
M1	II	125	100	No	-	No	-
M3	I	130	100	No	↑ Beta-Block	No	-
M6	I	125	100	No	-	No	-
M12	I	125	100	No	Thx optimization	1 ns-SVT	-
M18	I	120	100	No	-	1 ns-SVT	-
M24	I	120	100	No	-	No	-

## Hemodynamic variables during FU (1Y)

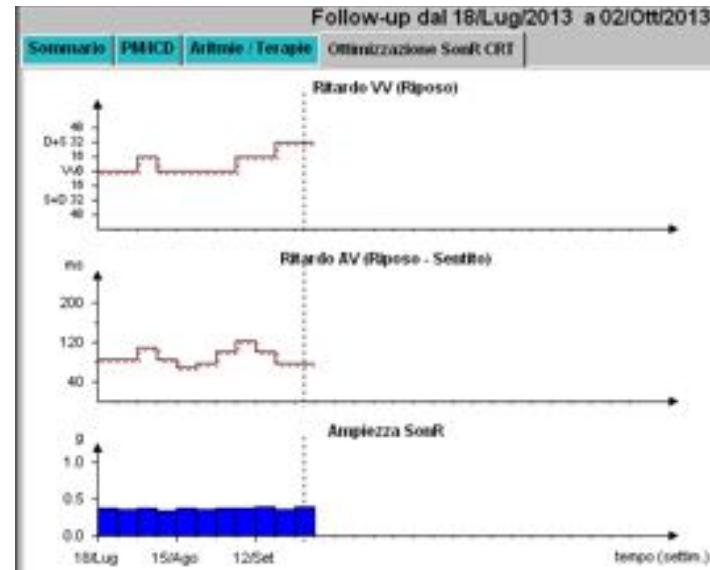
	LVEF (%)	LVEDV (ml)	LVESV (ml)	LPEI (ms)	Jet-A MR (cm <sup>2</sup> )	Notes
Pre-CRT	32	62	42	108	4.5	-
M12	66	51	17	104	1.6	-
	😊	😊	😊	😊	😊	

# CASE 1: when a pt is perfect ...

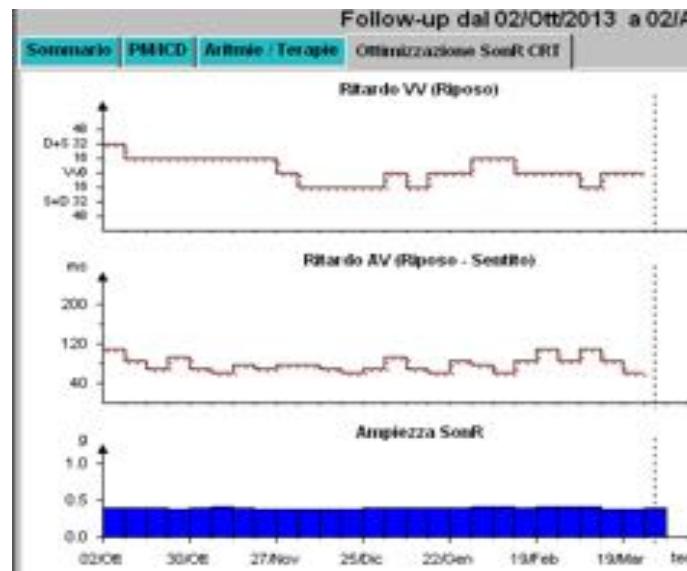
How much did the SonR sensor work ?



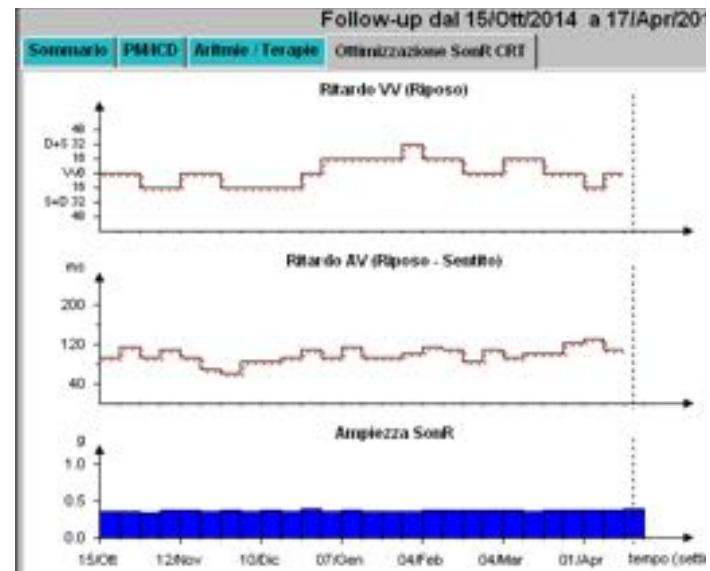
M3



M6



M12



M24

# CASE 2: when CRT is not enough ...

- ⦿ **Female pt, 69 yrs old, SCD-HeFT ICD indication:**

HF in NYHA class 3, OMT, LVEF 29%, SEVERE Mitral Insufficiency (grade: 3+),  
NON-ISCHEMIC etiology  
ECG: QRS 140ms, **LBBB**, SR @ 80bpm

- ⦿ **Clinical history / Co-morbidity:**

Istero-anneksiectomy  
Breast K (surgically treated)

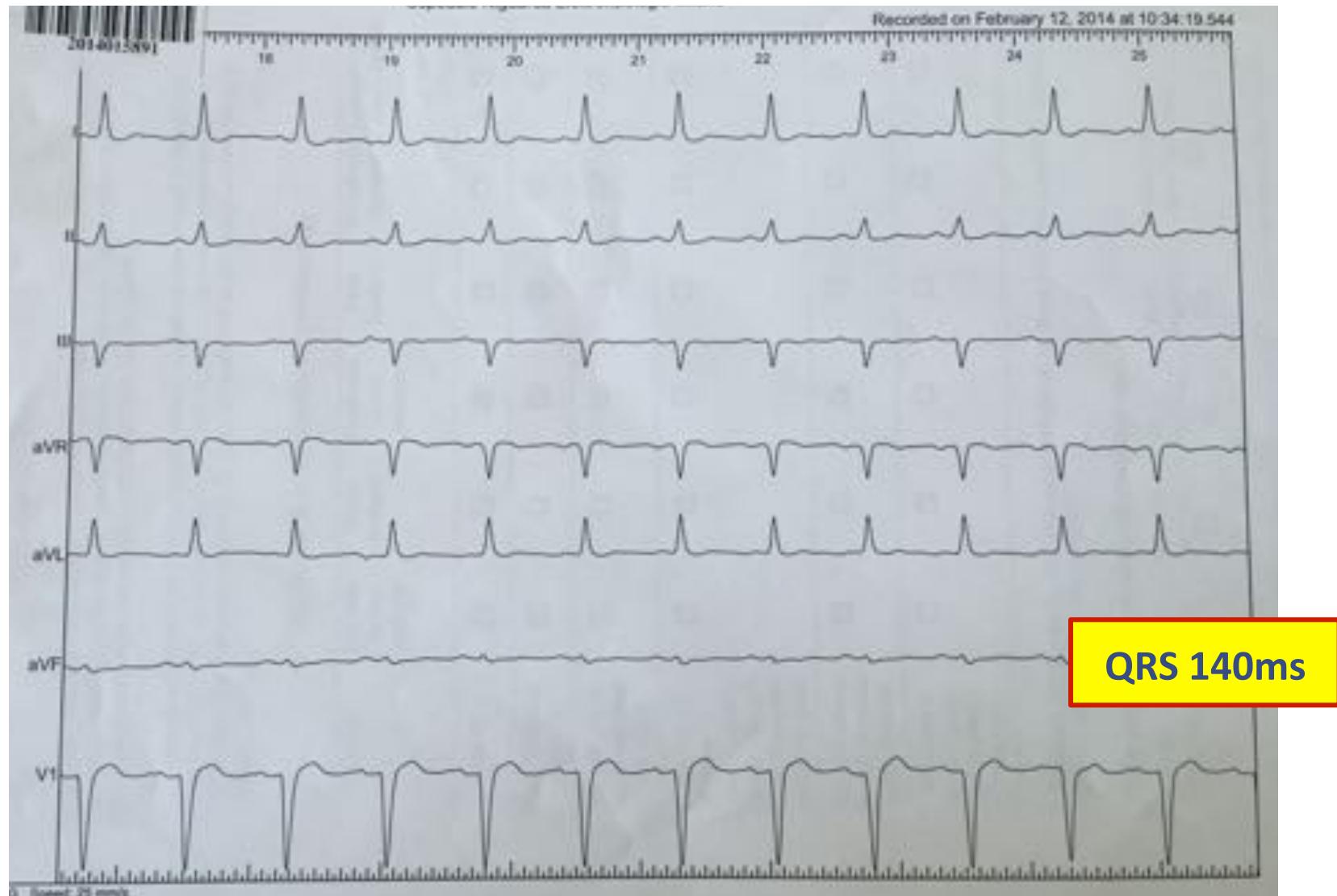
- ⦿ **Basal ECHOCARDIO:**

LVEF 29% (LVEDV 174ml; LVESV 124ml)  
**LPEI** 101ms  
**Jet-Area MR** 11.5cm<sup>2</sup>

- ⦿ **Feb 2014:** hospitalized for planned **CRT-D implant**

## CASE 2: when CRT is not enough ...

Pre-implant ECG (F, 69 yrs); SR @ 80 bpm, LBBB



# CASE 2: when CRT is not enough ...

IMPLANT

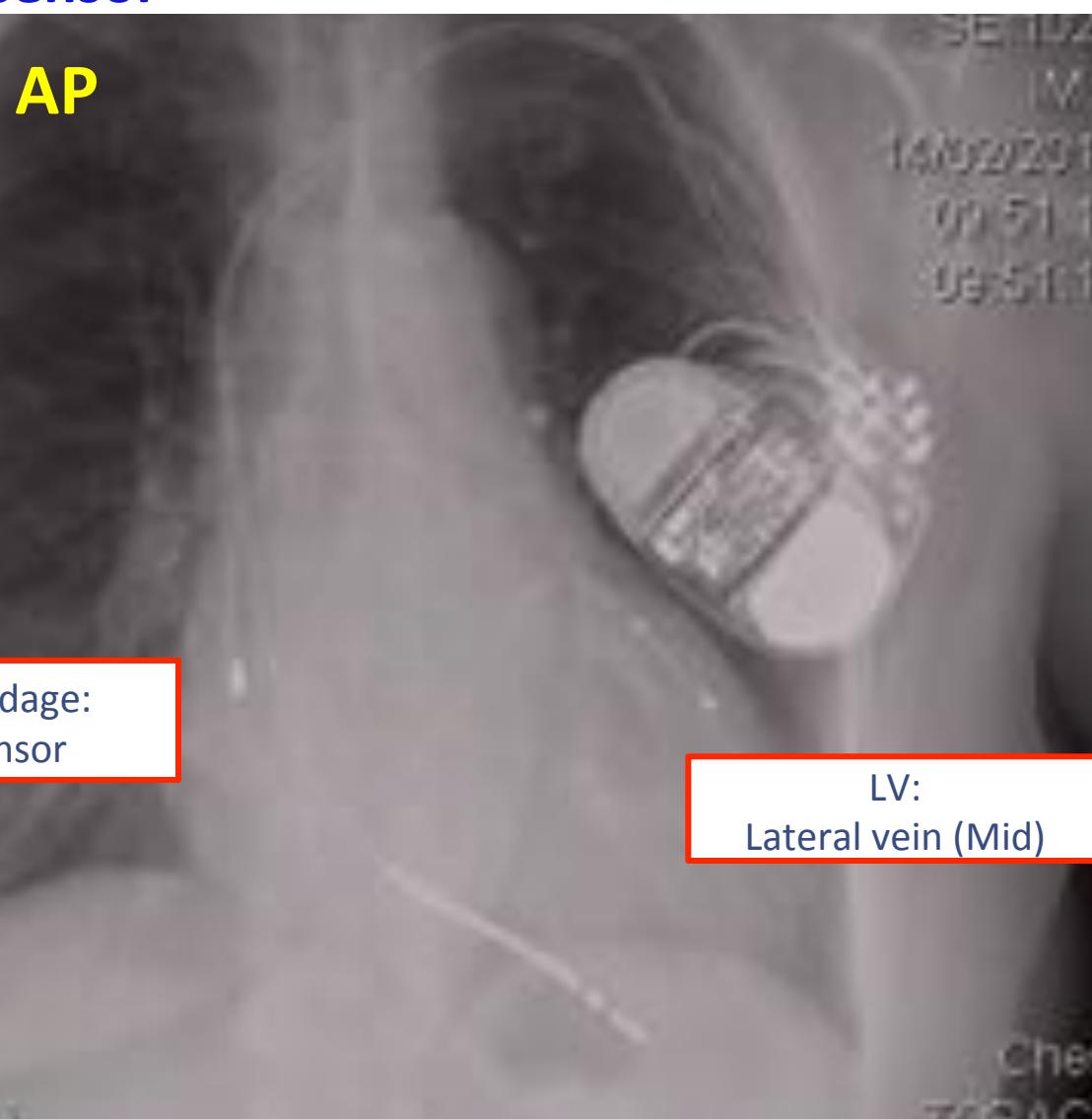
(feb 2014)

CRT-D equipped with SonR sensor

RA: *SonR tip in appendage*; RV: Apex;  
LV: *Lateral vein (mid portion)*

**QRS during BiV pacing: 140ms**

Weekly Automatic  
Optimization SonR = ON  
(optimiz.of AVD & VVD)



RA appendage:  
SonR sensor

LV:  
Lateral vein (Mid)

# CASE 2: when CRT is not enough ...

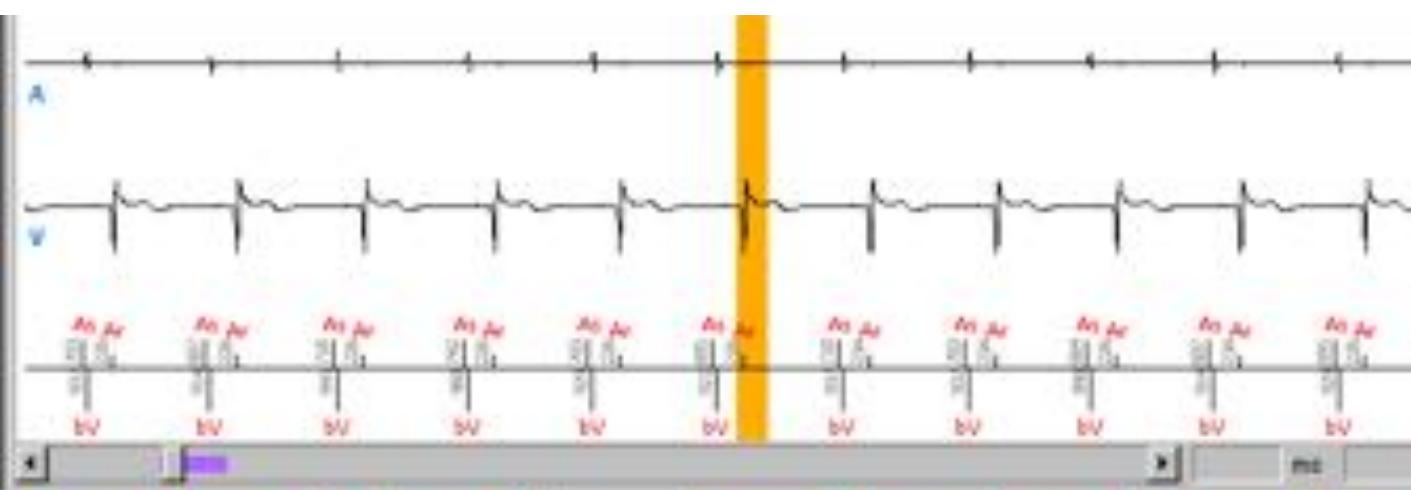
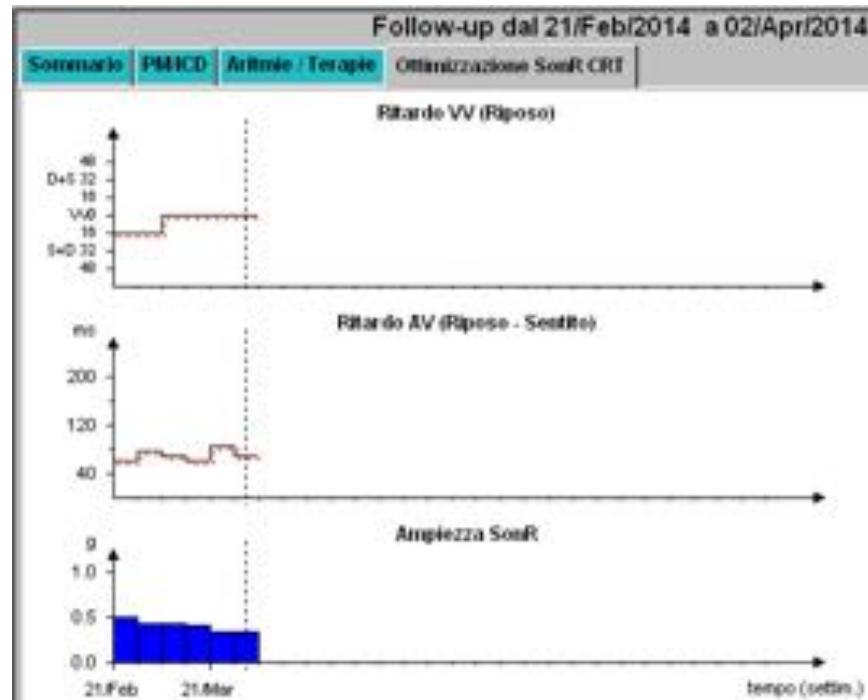
## Routine FU 1.5M (april 2014)

*Symptoms:* palpitations, astenia

BIV pacing 95%

VA Crosstalk → sensit. thresholds reprogrammed  
Slight reduction in the trend of contractility

*Clinically: no variations post-CRT vs. pre-CRT*



# CASE 2: when CRT is not enough ...

## Clinical variables during FU (1Y)

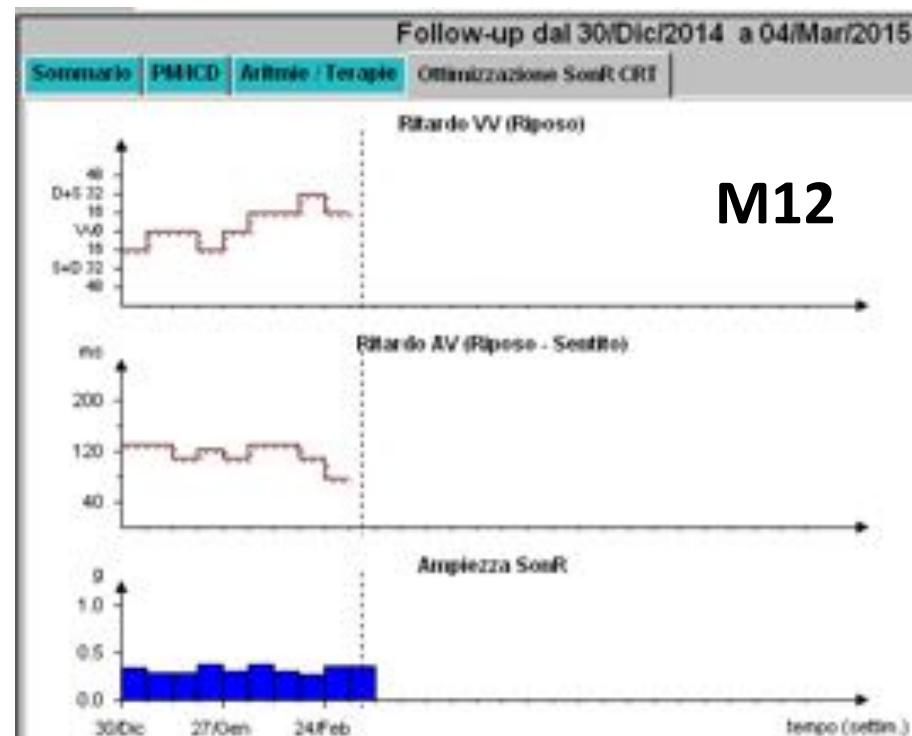
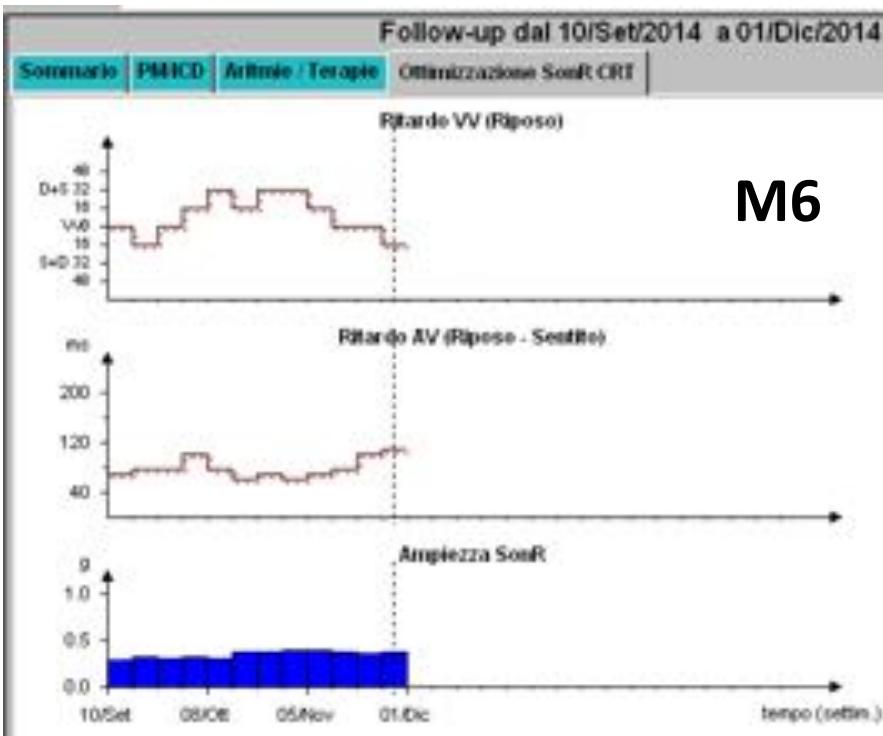
	NYHA	QRS (ms)	BiVp (%)	events	Med Thx	Arrhythmias	Notes
Pre-CRT	III	140	-	HFH	OMT	-	IM 3+
M1	II/III	140	95	No	-	No	Palpit., astenia
M3	II	120	99	No	-	No	Astenia, fatigue
M6	II	120	99	No	-	2h AF	Astenia
M8	II	120	99	No	Start Ivabradine	No	Astenia
M9	II/III	125	99	No	-	Chron. Incomp.	Rate Resp. ON
M12	II/III	125	100	No	-	No	Astenia, depress.

## Hemodynamic variables during FU (1Y)

	LVEF (%)	LVEDV (ml)	LVESV (ml)	LPEI (ms)	Jet-A MR (cm <sup>2</sup> )	Note
Pre-CRT	29	174	124	101	11.5	-
M12	31	177	122	101	10.8	-

# CASE 2: when CRT is not enough ...

How much did the SonR sensor work ?



“The guilty”: CRT does not impact on MI 3+ ...  
Pt hospitalized (apr 2015) for Mitraclip assessment

Pt in Warfarin due to presence of RA thrombi;  
Indication to Mitraclip to be re-assessed after 6M

# CASE 3: SonR chameleon ...

- ◎ **Male pt, 74 yrs old, SCD-HeFT ICD indication:**

HF in NYHA class 3, OMT, LVEF 32%,  
ISCHEMIC etiology (acute MI Y-1982)  
ECG: QRS 135ms, **LBBB**, SR @ 62bpm, AVB II d. (Mobitz-2)

- ◎ **Clinical history / Co-morbidity:**

abdominal aorta aneurysm;  
claudicatio (legs arteriopathy)

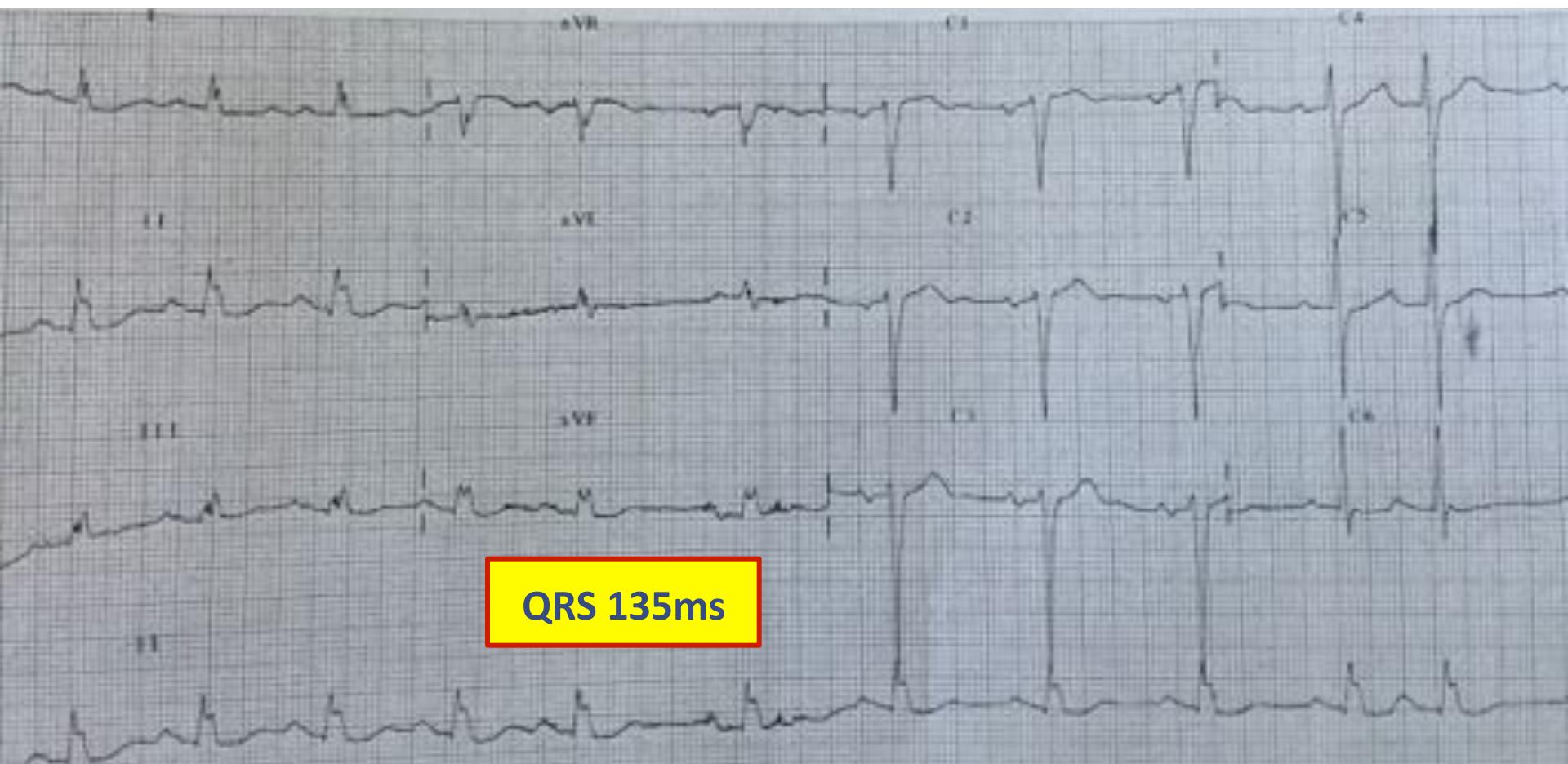
- ◎ **Basal ECHOCARDIO:**

**LVEF 32%** (LVEDV 193ml; LVESV 132ml)  
**LPEI** 104ms  
**Jet-Area MR** 1.6cm<sup>2</sup>

- ◎ **Apr 2013:** hospitalized for planned **CRT-D implant**

# CASE 3: SonR chameleon ...

Pre-implant ECG (M, 74 yrs); SR @ 62bpm, LBBB



QRS 135ms

# CASE 3: SonR chameleon ...

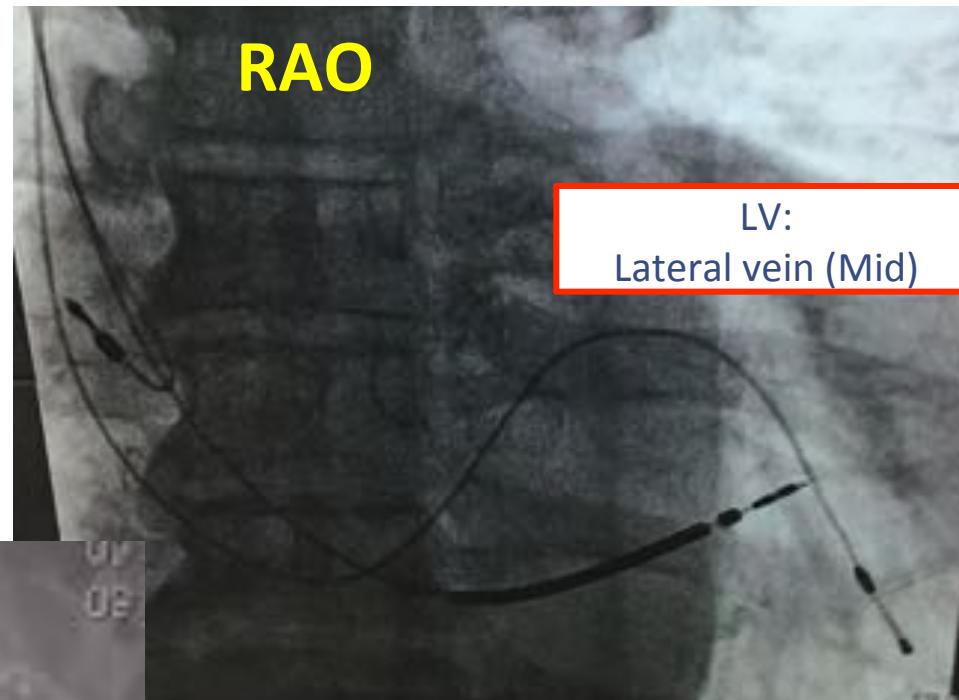
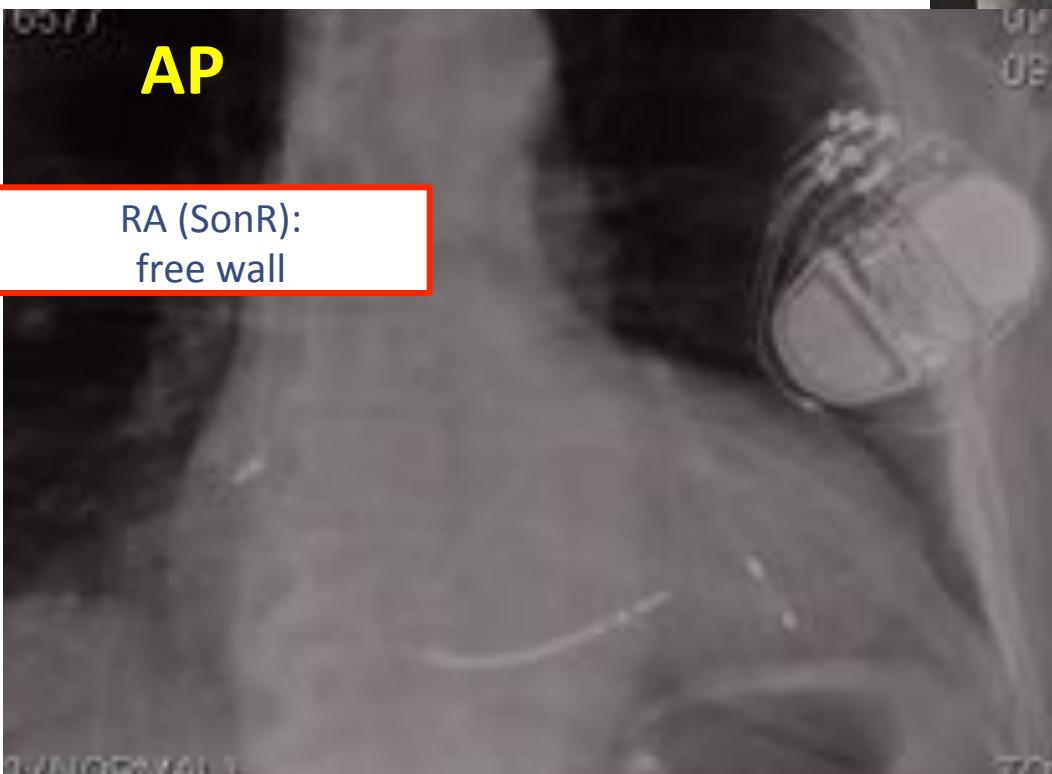
**IMPLANT** (april 2013)

**CRT-D system with SonR sensor**

(contractility, correlated with LV dP/dt)

*RA: SonR tip in free-wall; RV: medium-septal*

*LV: Postero-Lateral vein (mid portion)*



**Weekly Automatic  
Optimization SonR = ON  
(optimiz. AVD & VVD)**

# CASE 3: SonR chameleon ...

## Clinical variables during FU (2Y)

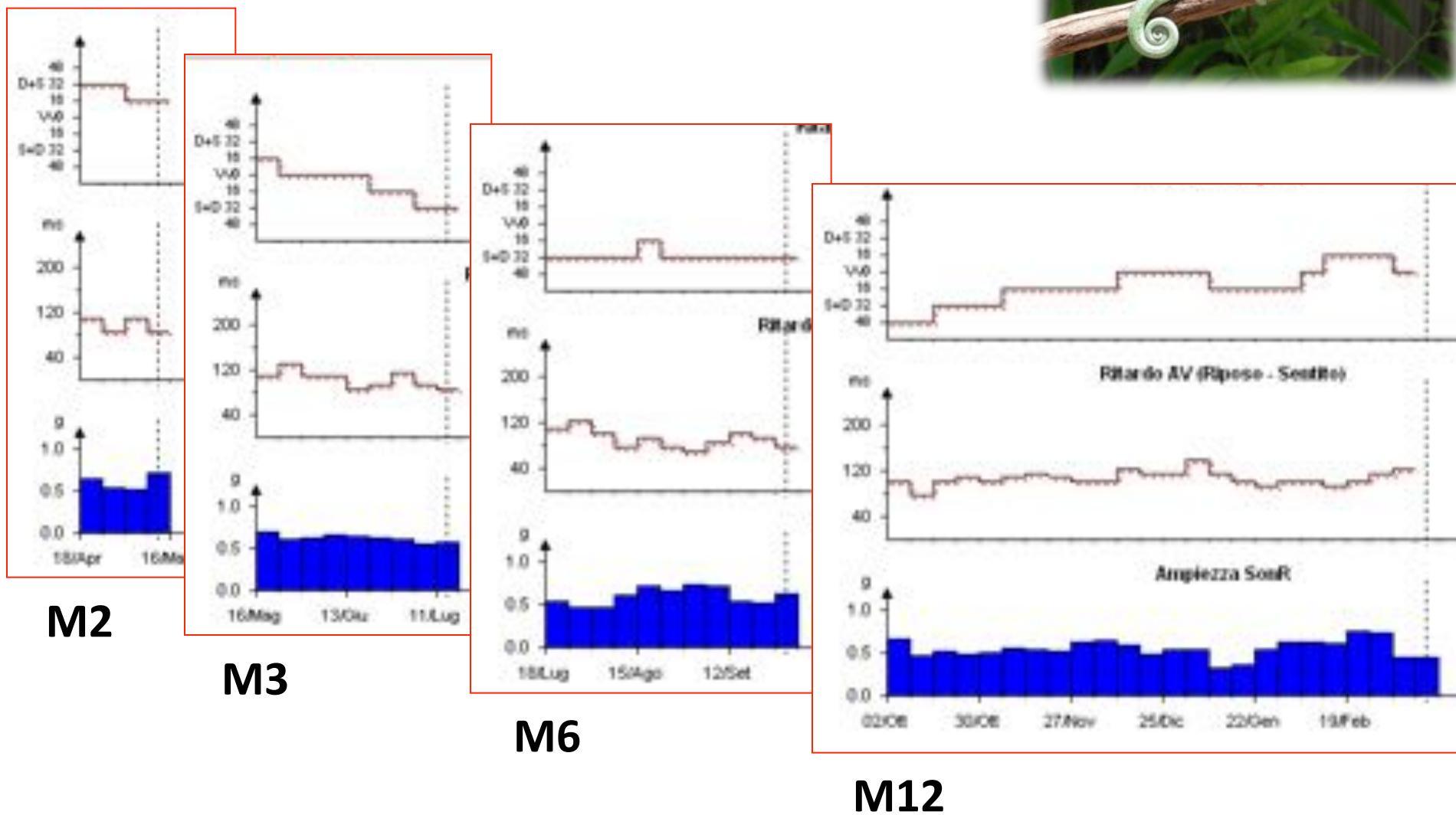
	NYHA	QRS (ms)	BiVp (%)	events	Med Thx	Arrhythmias	Notes
Pre-CRT	III	135	-	-	OMT	-	-
M1	II	120	97	No	Thx optimiz.	3% PVCs	-
M3	II	120	97	No	-	3% PVCs	-
M6	II	130	99	No	-	1% PVCs	-
M12	II	110	99	No	-	1% PVCs	-
M18	II	120	98	No	-	2 nsVT; 2% PVCs	-
M24	II	130	91	No	-	1 nsVT; 8% PVCs	-

## Hemodynamic variables during FU (1Y)

	LVEF (%)	LVEDV (ml)	LVESV (ml)	LPEI (ms)	Jet-A MR (cm <sup>2</sup> )	Notes
Pre-CRT	32	193	132	104	1.62	-
M12	44	123	69	122	0.0	-
	😊	😊	😊	☺	😊	

# CASE 3: SonR chameleon ...

How much did the SonR sensor work ?

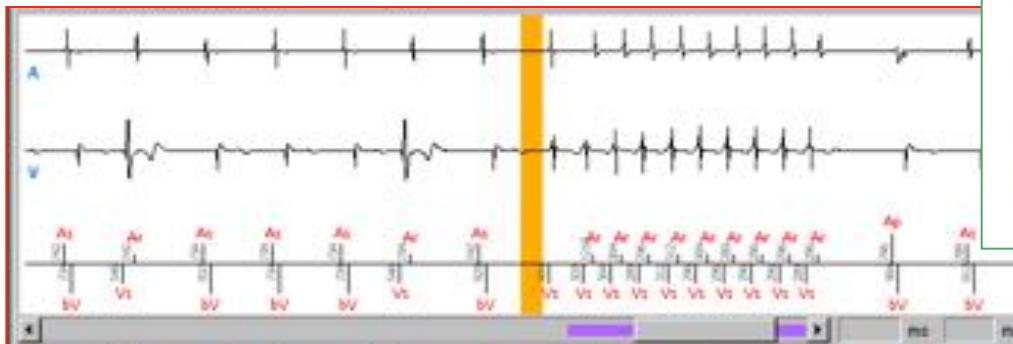


# CASE 3: SonR chameleon ...

How much did the SonR sensor work ?



M18





Automatic CRT Optimization and Follow-Up

Clinical Cases

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# Conclusions

- The SonR optimization algorithm **continuously works (weekly optim)** to achieve a satisfactory response (*in terms of contractility*)
- In selected pts the "**therapeutic target**" must be focused from the beginning: CRT has to impact on the "**primum movens**" of HF to be efficacious (*valvular disease, complex dyssynchrony, etc.*)
- Optimal CRT settings may significantly change over long-term FU after implant. **Automatic tools allow to track unexpected changes** in pts' individual needs