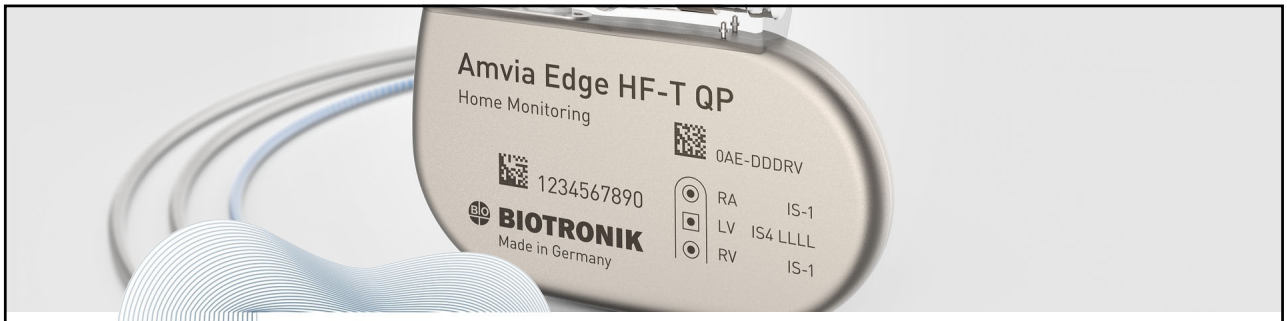

Rate Adaptive Sensors: Past & Present

David Hayes, M.D. – Chief Medical Officer
Doug Finch – Sr. Advanced Product Program Manager

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1

Characteristics of Ideal Sensor

- Appropriate speed of acceleration/deceleration
- Proportionality to workload
- Sensitive to exercise and non-exercise requirements, i.e. postural changes, emotional states, circadian variations
- Specificity, i.e. avoid false sensor activation by non-physiological needs

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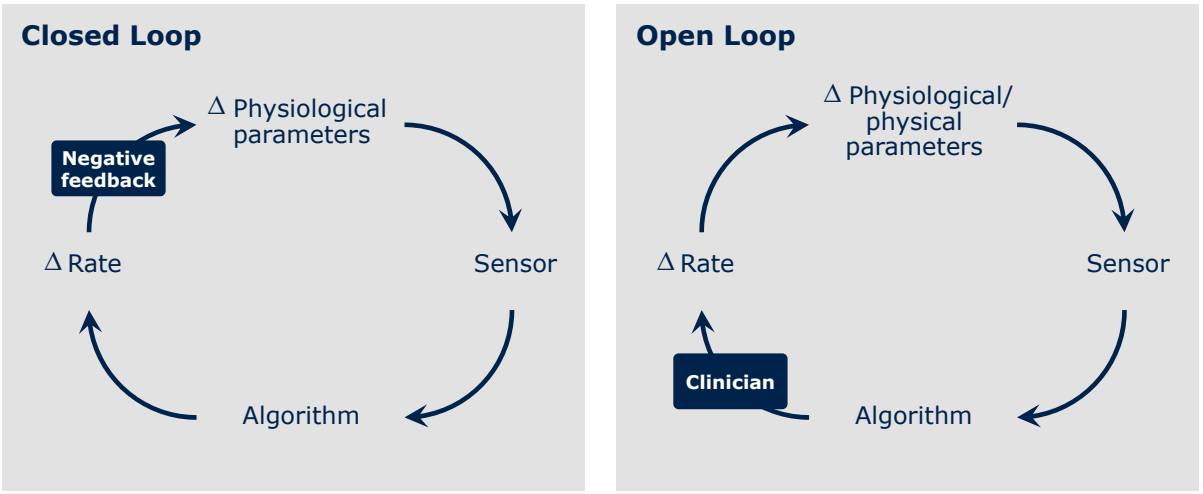
Open Loop vs. Closed Loop Sensors



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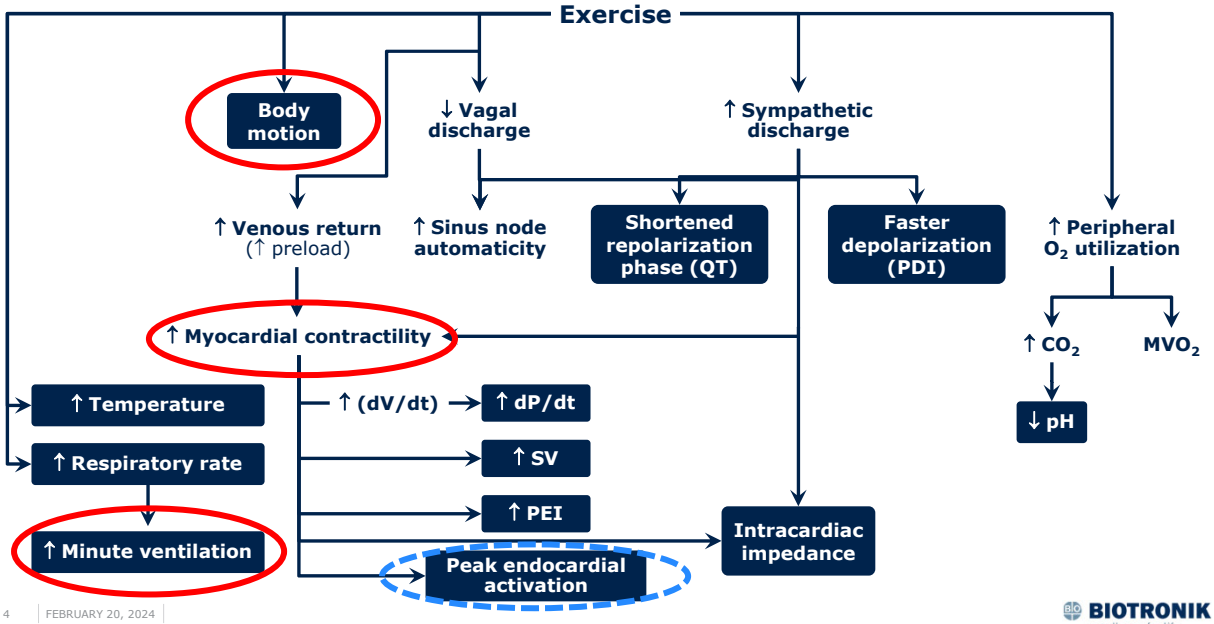
Schematic of Physiologic Drivers



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Sensors

Historical sensors

- *Piezoelectric crystal*
- Temperature
- QT interval
- O2 Saturation
- Pre-ejection interval
- Ventricular depolarization gradient
- *Peak endocardial acceleration*

Currently available

- Accelerometer
- Minute ventilation
- CLS (Myocardial Contractility Sensor)

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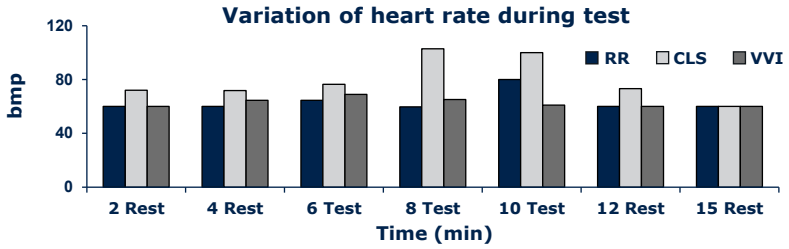
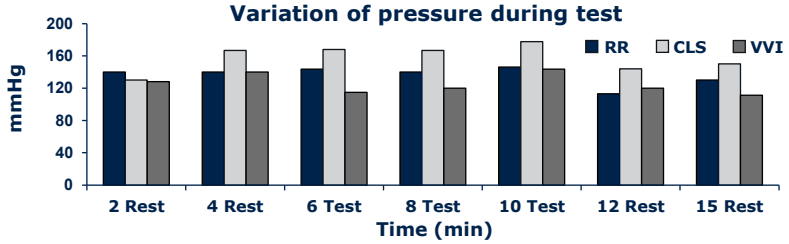
Mean Heart Rate Increase in CLS mode, VVIR mode, and VVI mode





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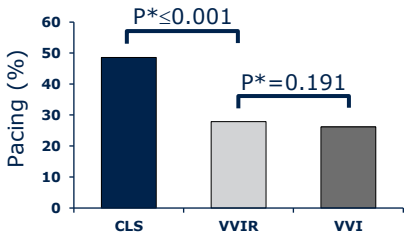
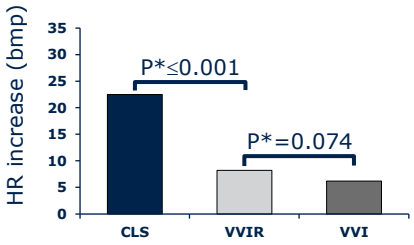
CLS vs. VVIR vs. VVI

Mean HR Increase



Mean Pacing (%)



***Tests of within-subject contrasts**

Proietti et al: PACE 2012;00:1-9

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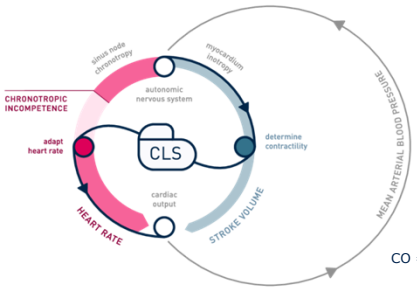
Closed Loop Stimulation (CLS)

Mimics normal heart rate

- CLS patients showed a 75% reduction in orthostatic hypotension events [1]
- Decreases in blood pressure can be modulated by CLS [1, 2, 3]
- CLS significantly reduces atrial burden [4, 5]
- CLS reduced frequency of AT episodes less than one hour [4]
- CLS responds to acute mental stress [6]
- CLS achieves a reduction in reoccurring syncope [7, 8]
- CLS achieves heart variability that is analogous to a healthy sinus node [9, 10]
- CLS precisely correlates heart rate and blood pressure [11]



CO = SV X HR

WHAT

CLS is the only rate adaptation algorithm that reacts to physiologic needs independent of body movement or respiratory rate.

HOW

CLS detects changes in myocardial contractility influenced by the autonomic nervous system.

SO WHAT

CLS appropriately manages cardiac output in response to physical activity, circadian rhythm, medication changes, disease progression and acute mental stress.[6,9,12,13,14]

1. Abi-Samra FM et al. *Europace.* 2013, 15(6).
2. Quaglione R et al. *Europace.* 2005, 7(4).
3. Palmisano P et al. *Europace.* 2017, Epub.
4. Puglisi A et al. *PACE.* 2008, 31(11).
5. Puglisi A et al. *Eur Heart J.* 2003, 24(21).
6. Chandiramani S et al. *PACE.* 2007, 30(8).
7. Baron-Esquivias, G *ACC* 2017,70(14).
8. Occhetta E et al. *Europace.* 2004, 6(6).
9. Quaglione R et al. PACE. 2009, 33(3).
10. Malinowski K. *PACE.* 1998, 21(11).
11. Zecchi P et al. *Prog Biomed Res.* 2000 5(2).
12. Tse HF et al., *JACC.* 2005, 46(12).
13. Wojciechowski D et al., *Prog Biomed Res.* 2001, 6.
14. Novak M et al. Prog in Biomed Res. 1998, June.

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Case Study 1

You are preforming a follow up on a 75-year-old patient implanted with an EDORA 8 DR-T pacemaker implanted 3 years ago. She is feeling well and is not expected to require any programming changes today. When asked, she notes that she is tired and really never has much energy but feels that is pretty normal for her.

She is Atrial paced 99% and Ventricular paced 100%. There is nothing remarkable from her previous follow-ups.

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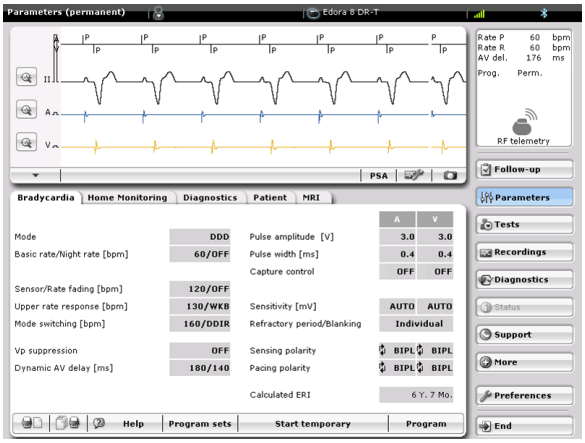
Case Study 1



Programmed:

- DDD 60 bpm /130 bpm
- AV Delay 180 ms-140ms (nominal)

Which of the following would be next most helpful in assessing her fatigue?

1. Ventricular pacing safety margin
2. A & V histograms
3. Atrial arrhythmia burden
4. Ventricular lead impedanc

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Case Study 1

Diagnostics:

- Atrial histogram - Blunted – 99% at Base Rate
- Ventricular histogram - Blunted – 100% V Paced

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Case Study 1

Sensing Test:

P & R waves within normal range

Which of the following parameters necessitates alternate programming?

1. Atrial sensitivity
2. Post-atrial ventricular blanking period
3. AV interval
4. Ventricular pulse-width

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Case Study 1

Final Programming

Two crucial programming changes were made for this patient considering her blunted rate histograms; 99% A & 100% V pacing; and intact intrinsic P & R waves.

1. Mode changed to DDDR (DDD-CLS)
   - Either CLS or accelerometer could be used but CLS was chosen given physiologic advantages of CLS
   - Consider the patient's age (220-age X 80%) when deciding Max sensor rate
2. AV Delay optimization: either I-OPT or AV Hysteresis

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Case Study 2

You are called to perform a routine follow-up on a 65-year-old patient with a dual chamber ICD. The patient's device has not been interrogated for over a year and the patient complains of increasing fatigue during normal daily activities despite optimal medical therapy and no apparent decompensation. No programming changes are expected to be made today.

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Case Study 2

What do we learn from the sensing test?

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Case Study 2

With a blunted histogram, what programming options should be considered?

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Case Study 2

Final programming options

- DDD-CLS to improve fatigue
- I-Opt to maintain low RV pacing percentage

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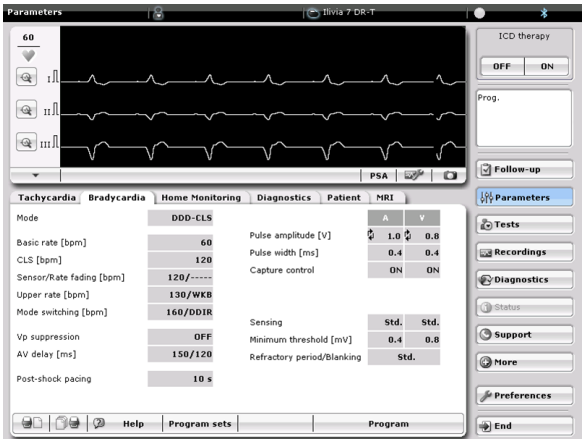
Case Study 2



- Turning CLS on by changing the mode to DDD-CLS
- Turn on I-Opt through the AV delay screen and choosing I-Opt from the AV hysteresis mode

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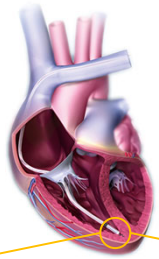
CLS – Impedance Principle

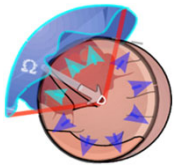
At rest baseline

Low inotropic state

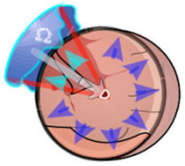


Physiologic demand

High inotropic state



Smaller fraction
of myocardium
=
Lower impedance
Slower contraction



Larger fraction
of myocardium
=
Higher impedance
Faster contraction

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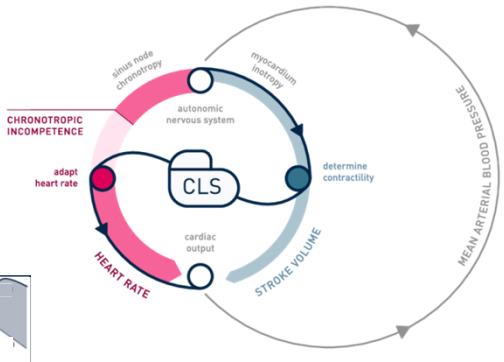
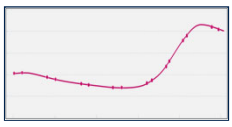
CLS Responds to Changes in the Autonomic Nervous System (ANS) on a Beat-To-Beat Basis

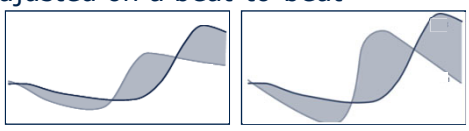
Closed Loop Stimulation (CLS)

- CLS is a myocardial contractility sensor and RV contractility correlates to ANS hemodynamic demands
- CLS uses impedance differentials to measure and respond to changes
- Heart rates are adjusted on a beat-to-beat





16 impedance measurements create reference waveform with patient at rest



Waveform changes compared to baseline and heart rate adjusted according to the measured differential

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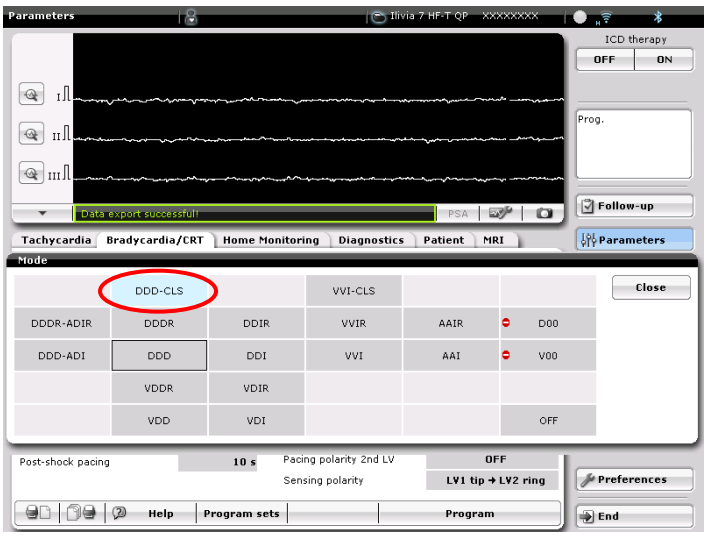
Simply Program CLS on by Selecting DDD-CLS Mode

Programming: One button to program CLS "On"



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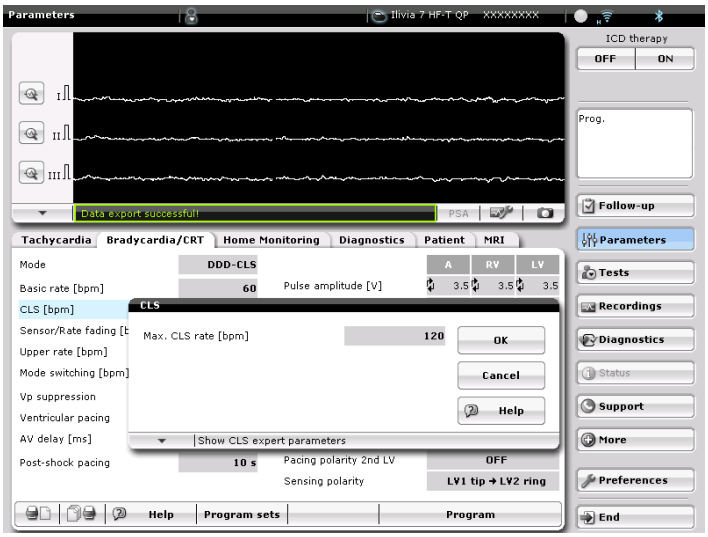
Set the Basic Rate and the Max CLS Rate, and CLS Will Automatically Optimize to the Patient

Programming: Easier to program than an accelerometer



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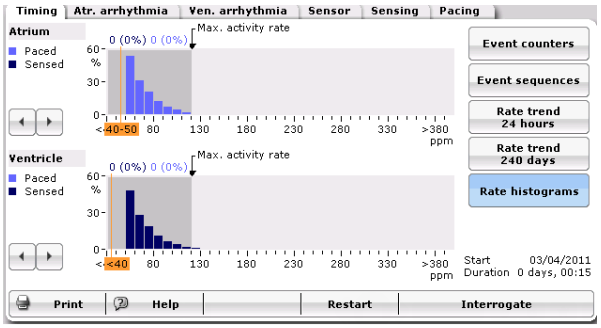
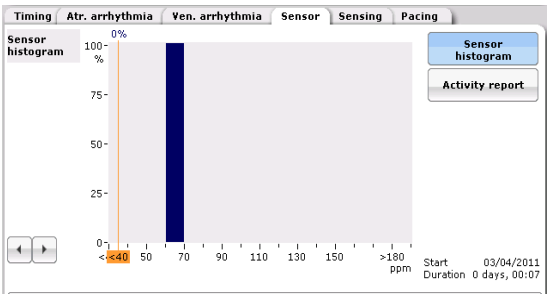
How Do I Know This Patient is Benefiting From CLS?

- Atrial rate histogram demonstrates patient was achieving pacing rates from 60 to 130, driven by CLS
- Sensor histogram shows the accelerometer would have paced at the lower rate limit of 60 bpm 100% of the time because no motion was detected
- A quick look at the activity report would verify that the patient is indeed sedentary





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DF0

Manipulating The HR Distribution with CLS

- There may be a desire to manipulate HR distribution to provide either elevated rates for pediatric patients or depress rates for symptomatic patients with elevated rates.
  - Can be done via CLS Response
- The device is set nominally to medium. CLS will always use an 80/20 algorithm to distribute 80% in the lower rate bins and 20% in the higher bins.
- CLS response provides the ability to move the 80/20 separation point or the Exertional Threshold Rate (ETR) allowing a greater distribution in the higher rate bins (Very High) or a greater distribution in the lower bins (Very Low). Nominal is Medium.

ETR Programmability Table

CLS Response	Range
Very low	ETR = (21% of rate range) + BR
Low	ETR = (26% of rate range) + BR
Medium	ETR = (33% of rate range) + BR
High	ETR = (41% of rate range) + BR
Very high	ETR = (51% of rate range) + BR

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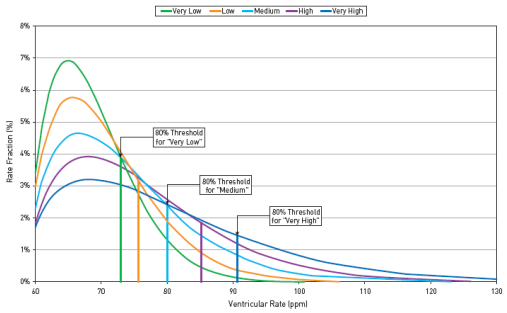
Slide 24

DF0 I added "or the Exertional Threshold Rate (ETR) " to slide 26 to clarify
Douglas Finch, 2024-02-19T20:33:22.538

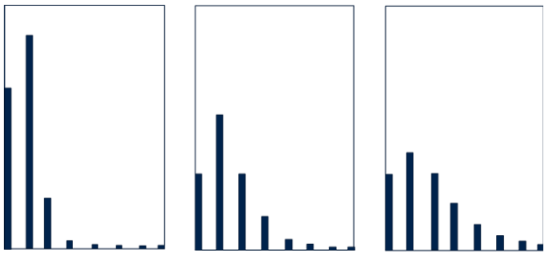
DF0

Understanding Rate Distribution

Rate Distributions for CLS Dynamics Settings



Atrial Rate Histograms at different CLS Response settings



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DF0

Expert Options

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Slide 25

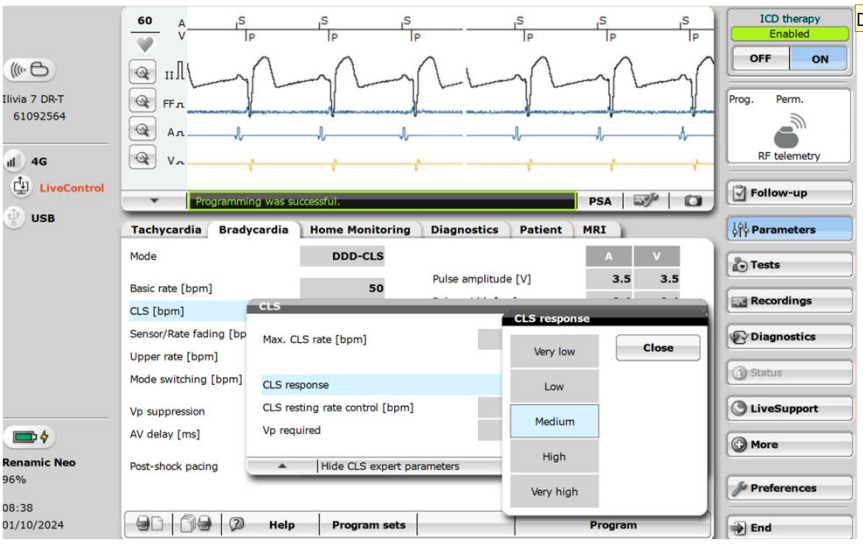
DF0 Added atrial rate histogram graphic
Douglas Finch, 2024-01-10T18:05:41.430

Slide 26

DF0 Changed screenshot with suggested basic rate
Douglas Finch, 2024-01-10T15:49:57.270

CLS Response Programming

Expert options



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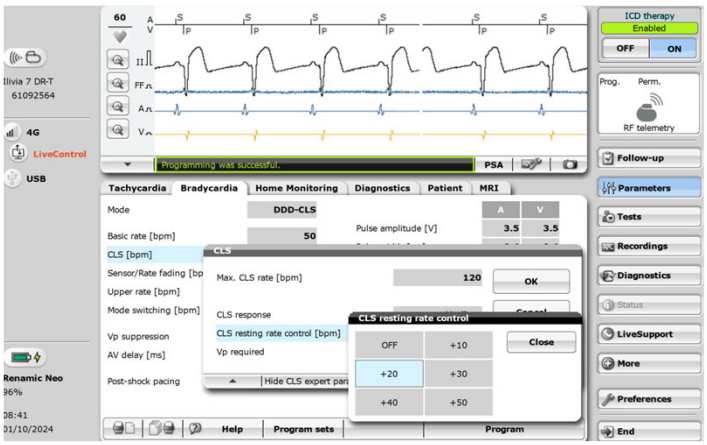
DF0

Suggested Programming Modifications for Syncope Patients

Resting rate control

- Resting rate control prevents inappropriate rate excursions during orthostatic changes or response to non-physical stimuli
- Resting rate control should be turned OFF only for dysautonomia patients:
  - Neurocardiogenic / cardio-inhibitory syncope
  - Vasovagal syncope
  - POTS
  - Autoimmune dysautonomia



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Slide 27

DF0 Added new screenshot to match previous slide no other changes to parameters
Douglas Finch, 2024-01-10T15:52:51.892

Slide 28

DF0 Added new screenshot to match previous slide no other changes to parameters
Douglas Finch, 2024-01-10T15:56:22.407

Rate-Adaptive Sensors: Past & Present

- Multiple sensors have been tried but only 3 are currently market available
- Sensors can be 'open-loop' or 'closed-loop' and clinically it is important to understand the difference
- CLS is the only 'closed loop' sensor available and has been shown to be advantageous for multiple clinical indications
- While programming CLS can be as simple as 'on' there are some more advanced programming options that can help optimize rate adaptation for an individual patient

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Questions

- Is CLS a dual or blended sensor? Answer Dual accelerometer only verifies rest and does not affect rate when mode is DDD-CLS

DF0

- Does CLS make rate calculations during a mode switch? No. The mode during a mode switch is DDIR so the accelerometer takes over during a mode switch

30

Slide 30

DF0 Requested questions added
Douglas Finch, 2024-01-10T18:10:42.058