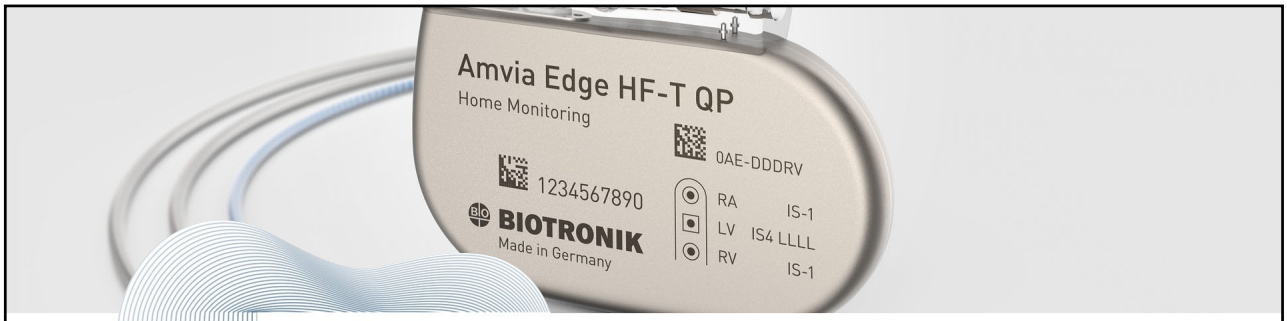


Rate Adaptive Sensors: Past & Present

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

BIOTRONIK excellence for life

1

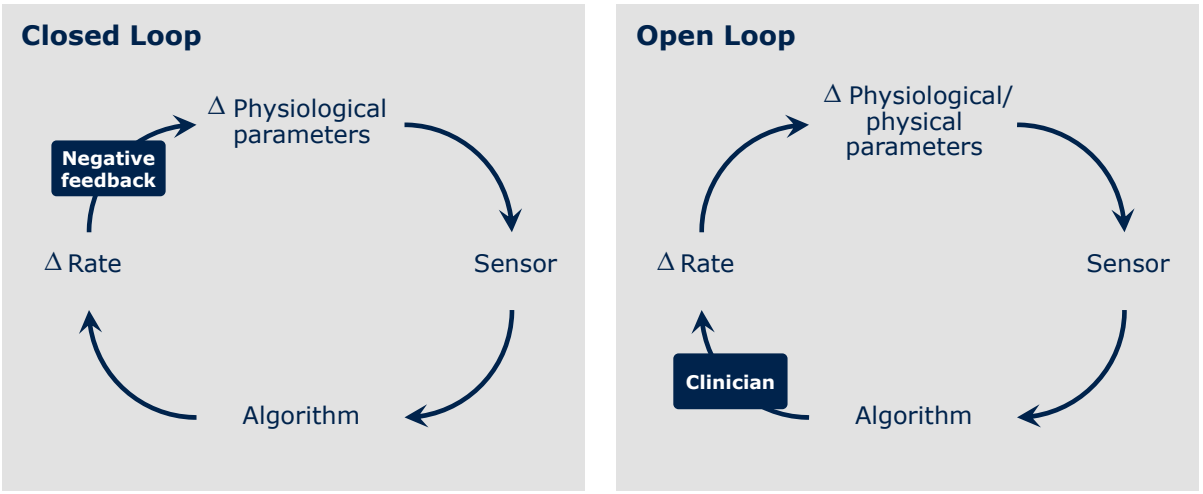
Characteristics of Ideal Sensor

- 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

BIOTRONIK excellence for life

2

Open Loop vs. Closed Loop Sensors

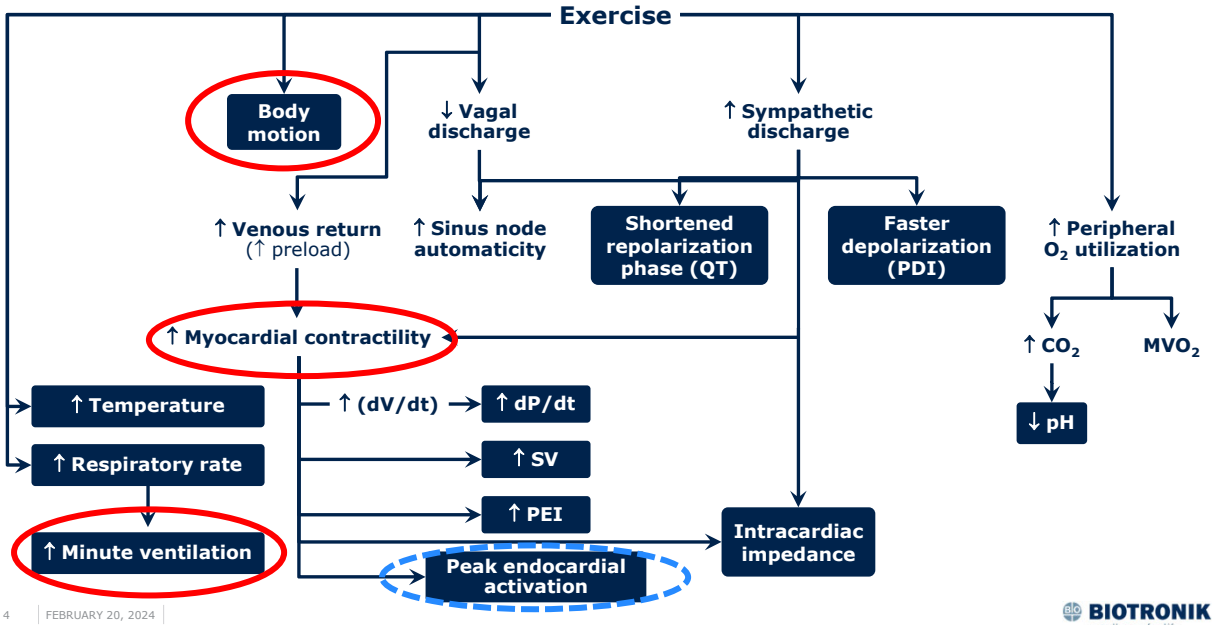


3 | FEBRUARY 20, 2024

BIOTRONIK excellence for life

3

Schematic of Physiologic Drivers



4 | FEBRUARY 20, 2024

BIOTRONIK excellence for life

4

Sensors

Historical sensors

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

Currently available

- Accelerometer
- Minute ventilation
- Myocardial Contractility (CLS)

BIOTRONIK excellence for life

5

Properties of a Normal Sinus Node

1. **Increases HR with exercise**
   - Proportionate and physiologically controlled
2. **Acute mental stress**
3. **P-P variability**
4. **Diurnal variability**
   - "normal" HR distribution/24 Hrs.
5. **Circadian variability**
   - "normal" HR distribution during sleep
6. **Compensatory response**
   - Changes in MABP due to vasodilation

6

Comparison of Sensor Ability to Mimic a Normal Sinus Node

	Accelerometer	MV	CLS
Increases HR with exercise	✓	✓	✓
Acute mental stress	✗	✓	✓
P-P variability	✗	✗	✓
Diurnal variability	✗	✗	✓
Circadian variability	✗	✗	✓
Compensatory response	✗	✗	✓

12-Feb-25

7

What is CLS & How Does It Work?

- **Primary Sensor**
  - Takes measurements directly from the myocardial tissue
- **Built on a beat-to-beat architecture**[1]
  - Rapidly evaluates every beat and is able to respond on the next beat
- **Automated with machine learning** [2]
  - Automatically learns the patient
  - Automatically recalibrates to systemic variations, e.g. changes in hydration, medication, etc.

Takes measurements of myocardial contractility (not motion or breathing). Why is this important? HR & BP should be correlated and are both managed by the autonomic nervous system

No sudden change criteria, resulting in immediate response to change. Why is this important? That's how the autonomic nervous system manages HR

No need for optimization, fully automated. Why is this important? CLS incorporates the device into the autonomic nervous system.

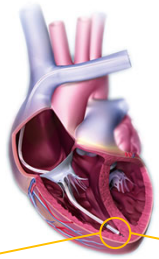
1, Malinowski et al. PACE 1998;21:11
2. Zechhi P et al. Prog Biomed Res 2000;5:2

12-Feb-25

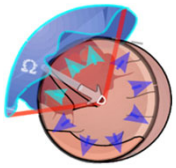
8

CLS – Impedance Principle

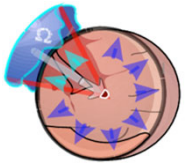
At rest baseline
Low inotropic state



Physiologic demand
High inotropic state



Smaller fraction
of myocardium
=
Lower impedance
Slower contraction



Larger fraction
of myocardium
=
Higher impedance
Faster contraction

9

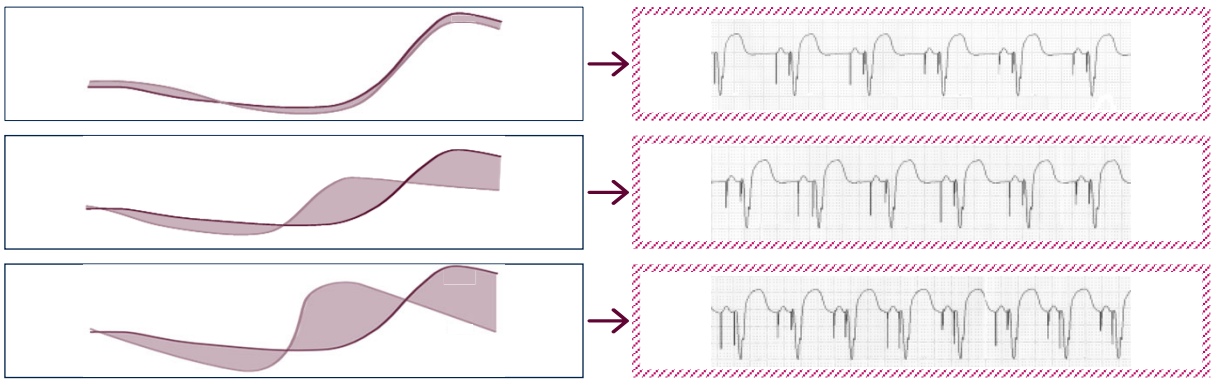
BIOTRONIK excellence for life

9

Impedance Changes into Rate

Increase in area differential

Physiologic increase in paced rate



10

BIOTRONIK excellence for life

10

Closed Loop Stimulation (CLS)

CLS patients showed a 75% reduction in orthostatic hypotension events [1]

Decreases in blood pressure can be modulated by CLS [1, 2, 3]

CLS achieves a reduction in reoccurring syncope [7, 8]

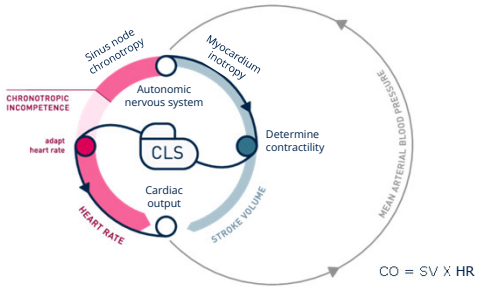
CLS precisely correlates heart rate and blood pressure [11]

CLS responds to acute mental stress [6]

CLS significantly reduces atrial burden [4, 5]

CLS reduced frequency of AT episodes less than one hour [4]

CLS achieves heart variability that is analogous to a healthy sinus node [9, 10]



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]

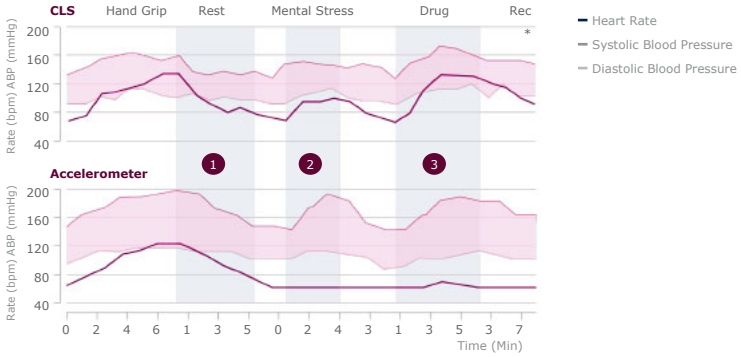
1. Abi-Samra FM et al. *Europace.* 2013, 15(6).
2. Quaglione R et al. *Europace.* 2005, 7(4).
3. Palmisano P et al. *Europace.* 2017, Epub.
4. Puglisi A et al. *PACE.* 2008, 31(11).
5. Puglisi A et al. *Eur Heart J.* 2003, 24(21).
6. Chandiramani S et al. *PACE.* 2007, 30(8).
7. Baron-Esquivias, G *ACC* 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.

Closed Loop Stimulation

VICRA Study

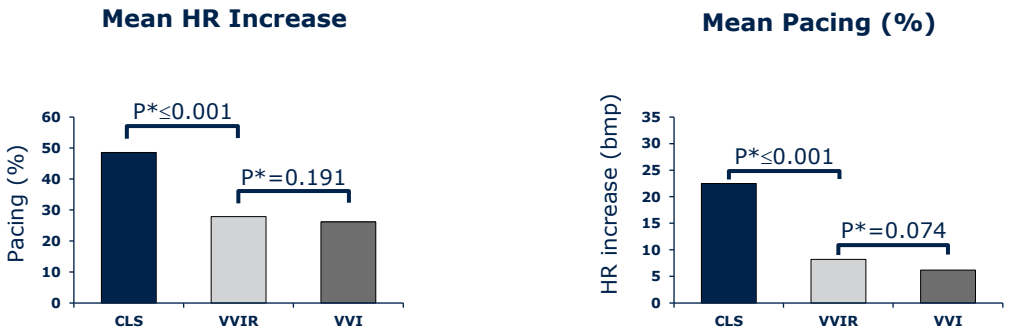
- CLS is the only pacemaker algorithm to respond to physiologic demands and acute mental stress on a beat-to-beat basis
- CLS precisely correlates heart rate and blood pressure

1. CLS delivers gradual rate decrease based on reduction of myocardial contractility.1
2. Only CLS provides physiological rate adaptation in response to acute mental stress.1
3. CLS provides rate adaptation during hemodynamic changes induced by Isoproterenol infusion.1



1. Zecchi P et al. *Prog Biomed Res.* 2000 5(2).

CLS vs. VVIR vs. VVI



*Tests of within-subject contrasts

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

BIOTRONIK excellence for life

13

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.

BIOTRONIK excellence for life

14

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

BIOTRONIK excellence for life

15

Case Study 1

Diagnostics:

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

BIOTRONIK excellence for life

16

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

BIOTRONIK excellence for life

17

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

BIOTRONIK excellence for life

18

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.

BIOTRONIK excellence for life

19

Case Study 2

What do we learn from the sensing test?

BIOTRONIK excellence for life

20

Case Study 2

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

BIOTRONIK excellence for life

21

Case Study 2

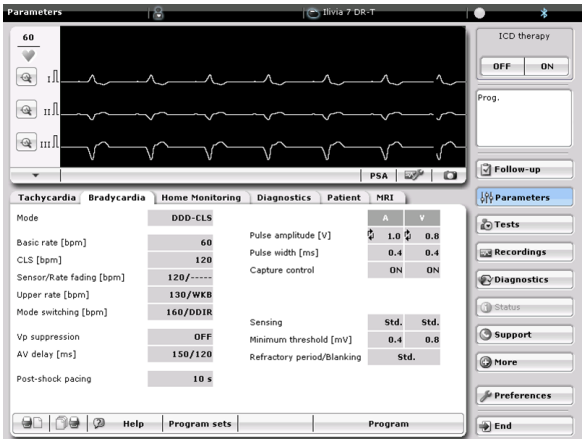
Final programming options

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

BIOTRONIK excellence for life

22

Case Study 2

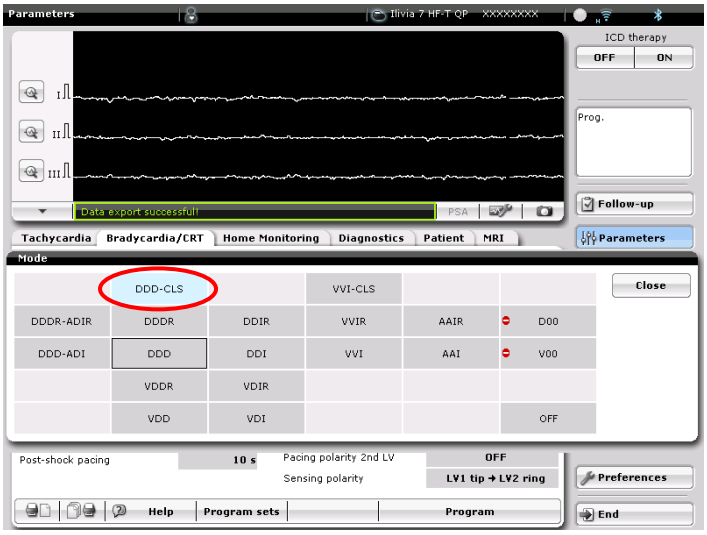


- Turning CLS on by changing the mode to DDD-CLS
- Turn on I-Opt through the AV delay screen and choosing I-Opt from the AV hysteresis mode

BIOTRONIK excellence for life

Simply Program CLS on by Selecting DDD-CLS Mode

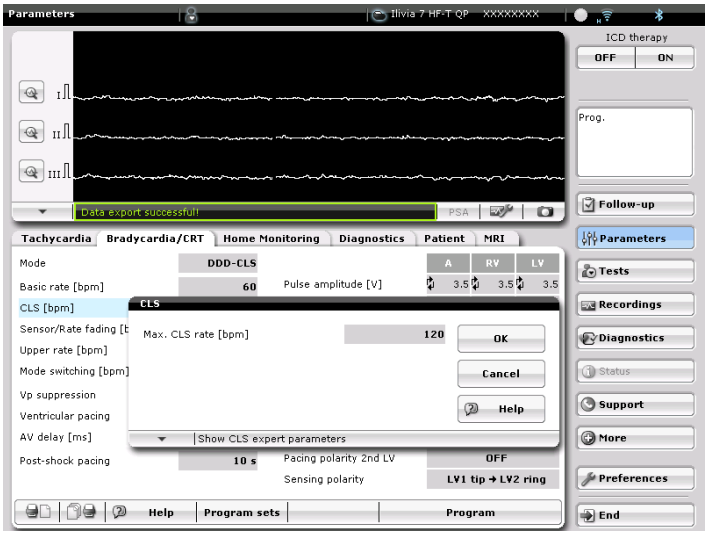
Programming: One button to program CLS "On"



BIOTRONIK excellence for life

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

Programming: Easier to program than an accelerometer

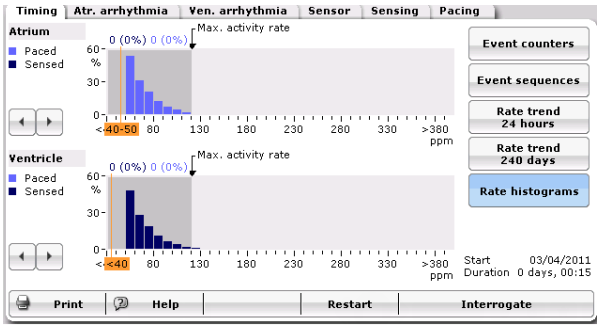


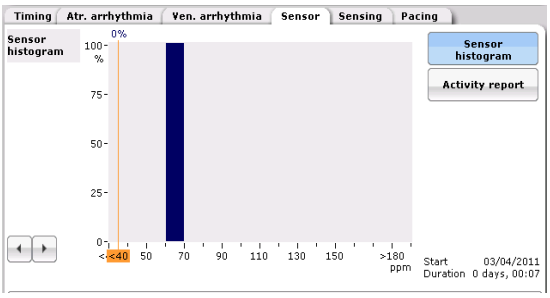
BIOTRONIK excellence for life

25

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



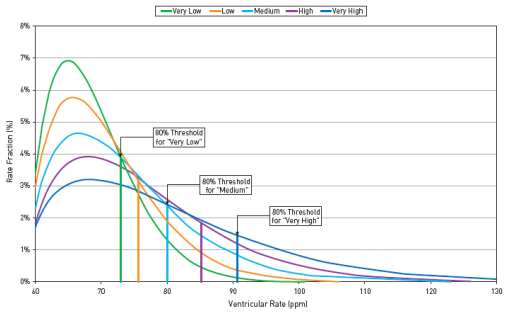


BIOTRONIK excellence for life

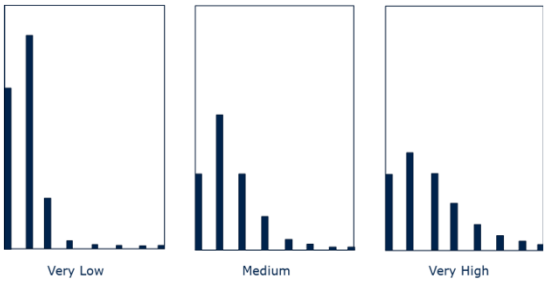
26

Understanding Rate Distribution

Rate Distributions for CLS Dynamics Settings



Atrial Rate Histograms at different CLS Response settings



BIOTRONIK excellence for life

27

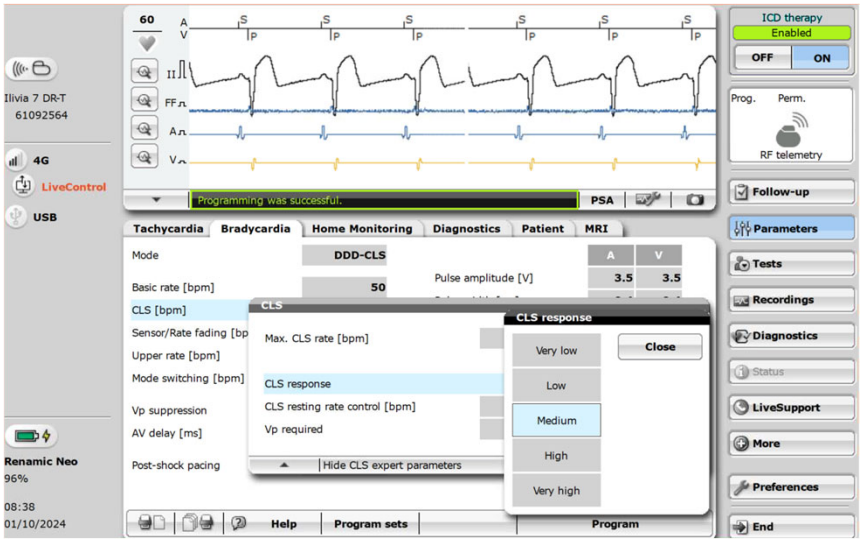
Expert Options

BIOTRONIK excellence for life

28

CLS Response Programming

Expert options



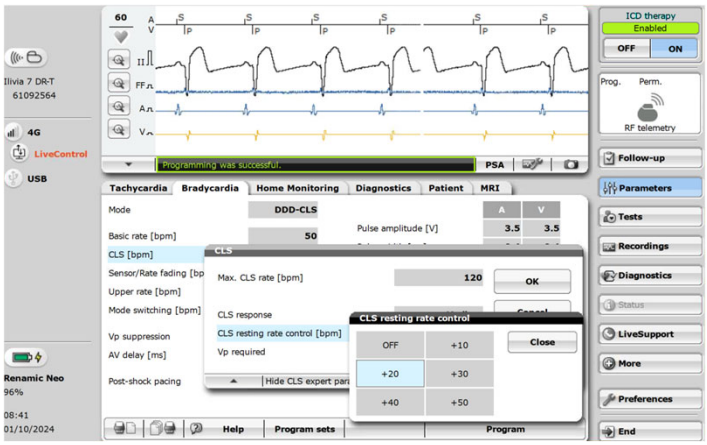
BIOTRONIK excellence for life

29

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



BIOTRONIK excellence for life

30

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

BIOTRONIK excellence for life