

ADVANCES IN CARDIAC ARRHYTHMIAS *and* GREAT INNOVATIONS IN CARDIOLOGY

XXVI Giornate Cardiologiche Torinesi

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Turin
October 23-25, 2014

Galleria D'Arte Moderna
Centro Congressi Unione Industriale di Torino



UNIVERSITÀ DEGLI STUDI DI TORINO



From Caliper to Catheter

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***“Closed loop” physiological stimulation: from
the pacemaker patient to the patient with an ICD***

Carlo Budano

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Physiological rate regulation

Sensor classification*

	Tertiary	Secondary	Primary
Sensor technology	Accelerometer	Minute ventilation, blended sensors	Closed Loop Stimulation
Definition	Detects parameters <i>resulting</i> from exercise	Detects parameters <i>resulting</i> from metabolic demand	Detects parameters <i>influencing</i> cardiac function

*Rickards et al., *Clin Prog Pacing Electrophysiol*, 1983, 1:12.

Physiological rate regulation

Closed Loop Stimulation - clinical rational

- Accelerometer and minute ventilation algorithms respond only during physical activity, independently of cardiac function.
- Effective response in all other mental situations is needed.
- A modulated response related to the cardiac function is more physiological and clinical appropriate.

Therefore, pacing modulation requires a natural mechanism of autonomic and contractility mediated control.

Physiological Rate Regulation

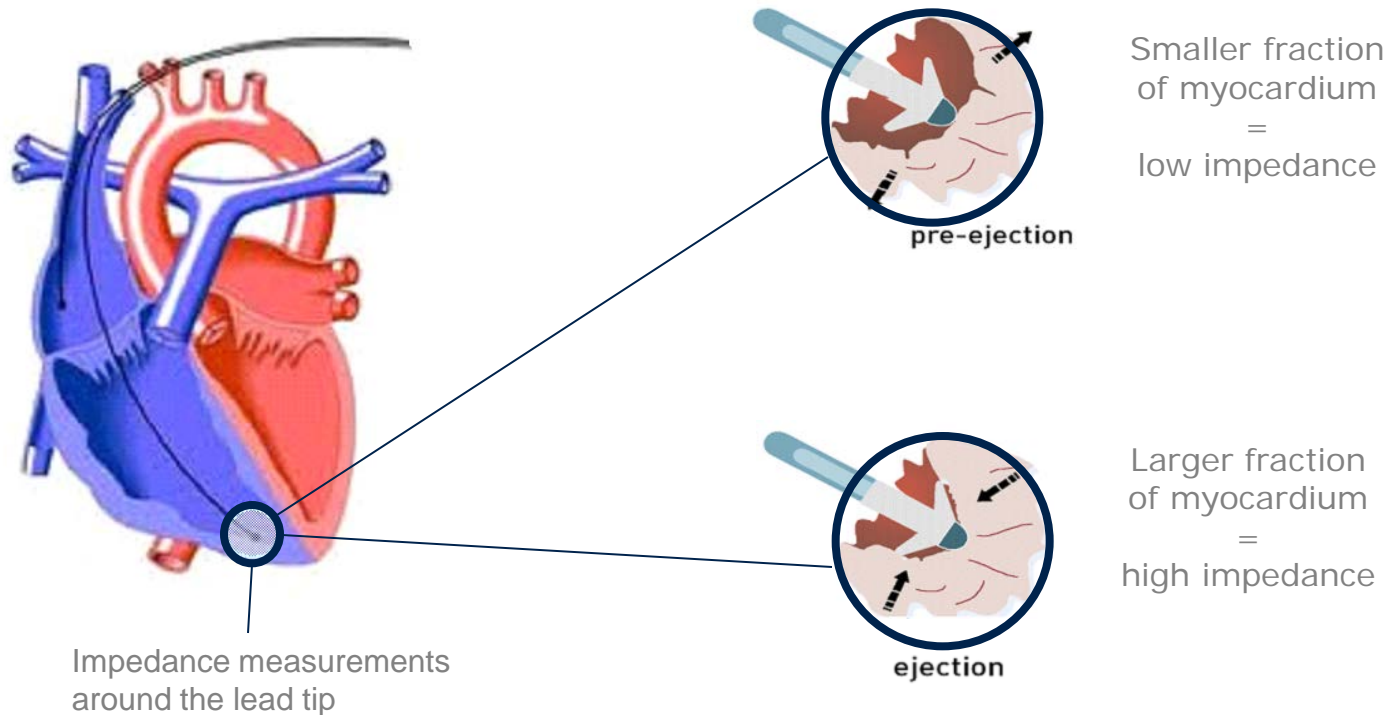
The autonomic nervous system (ANS), based on baroreceptor information, adjusts cardiac output by modifying:

- Rate (chronotropism)
- Contractility (inotropism)

Physiological Rate Regulation

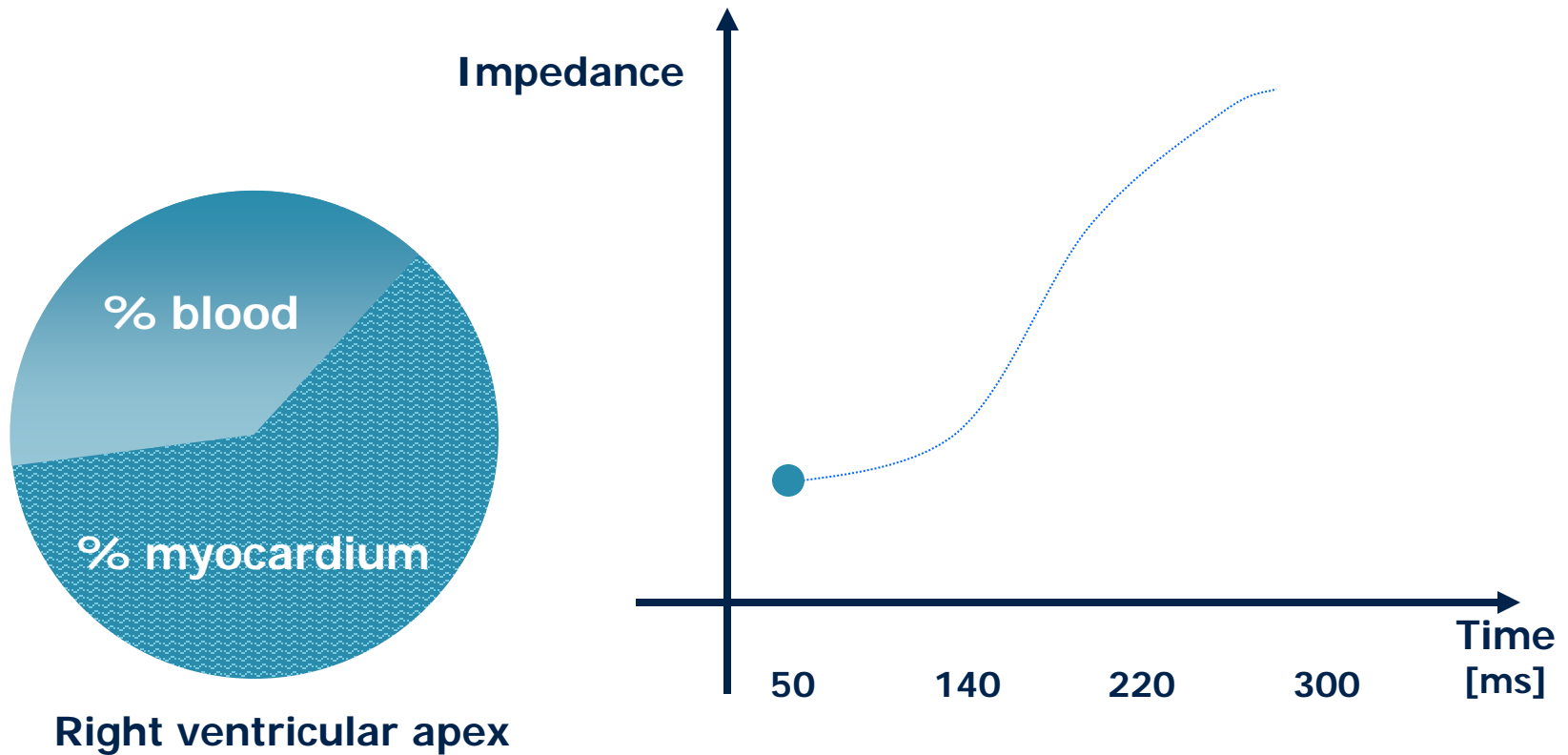
Closed Loop Stimulation - Measuring Impedance

- Impedance has a direct correlation with myocardial wall motion (inotropy).
- Changes in myocardial wall motion directly correlate to changes in autonomic tone.
- Increased inotropy compensates for the decreased heart rate.



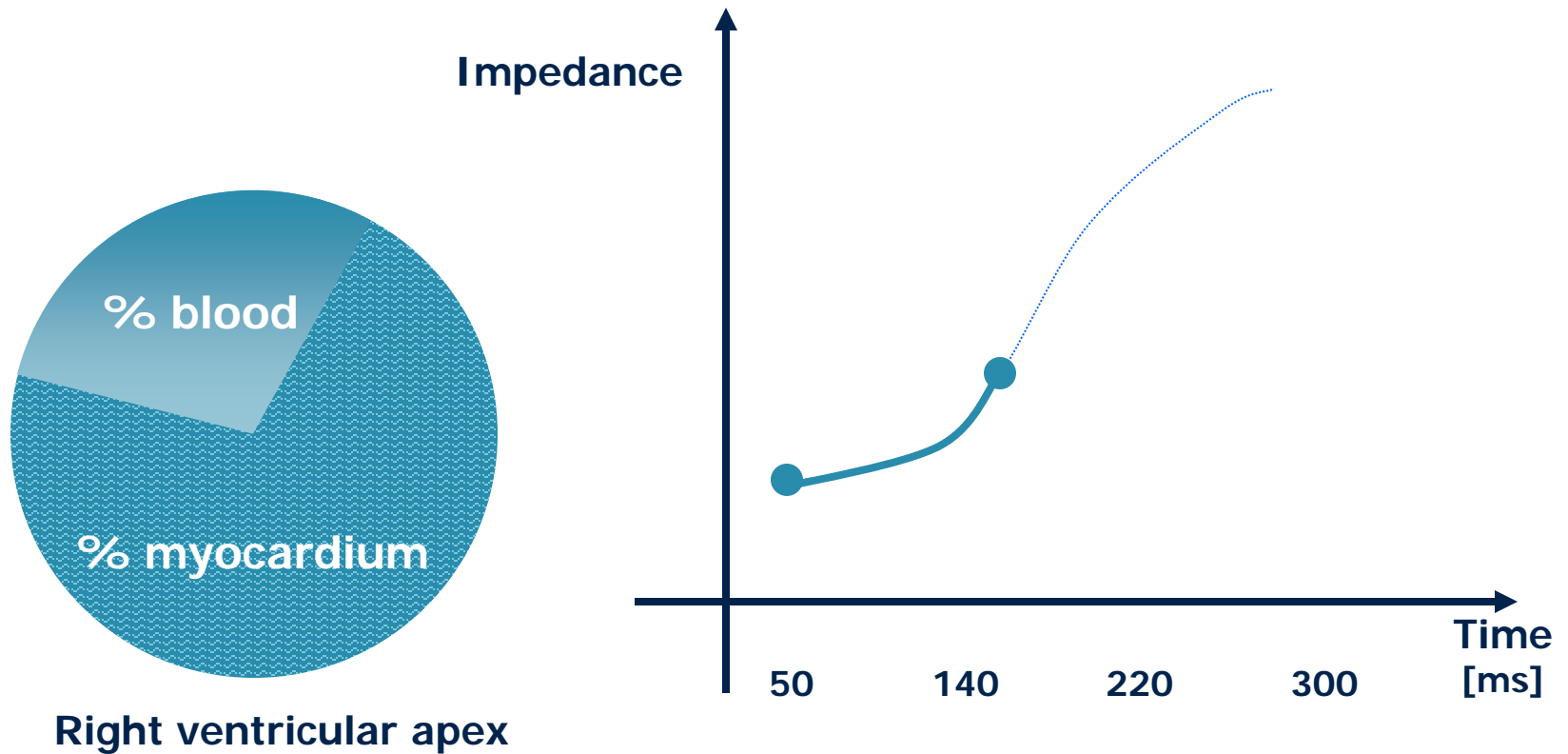
Contractile Dynamic and Impedance Curves

At the beginning of the systole, blood and muscle volumes define the impedance value.



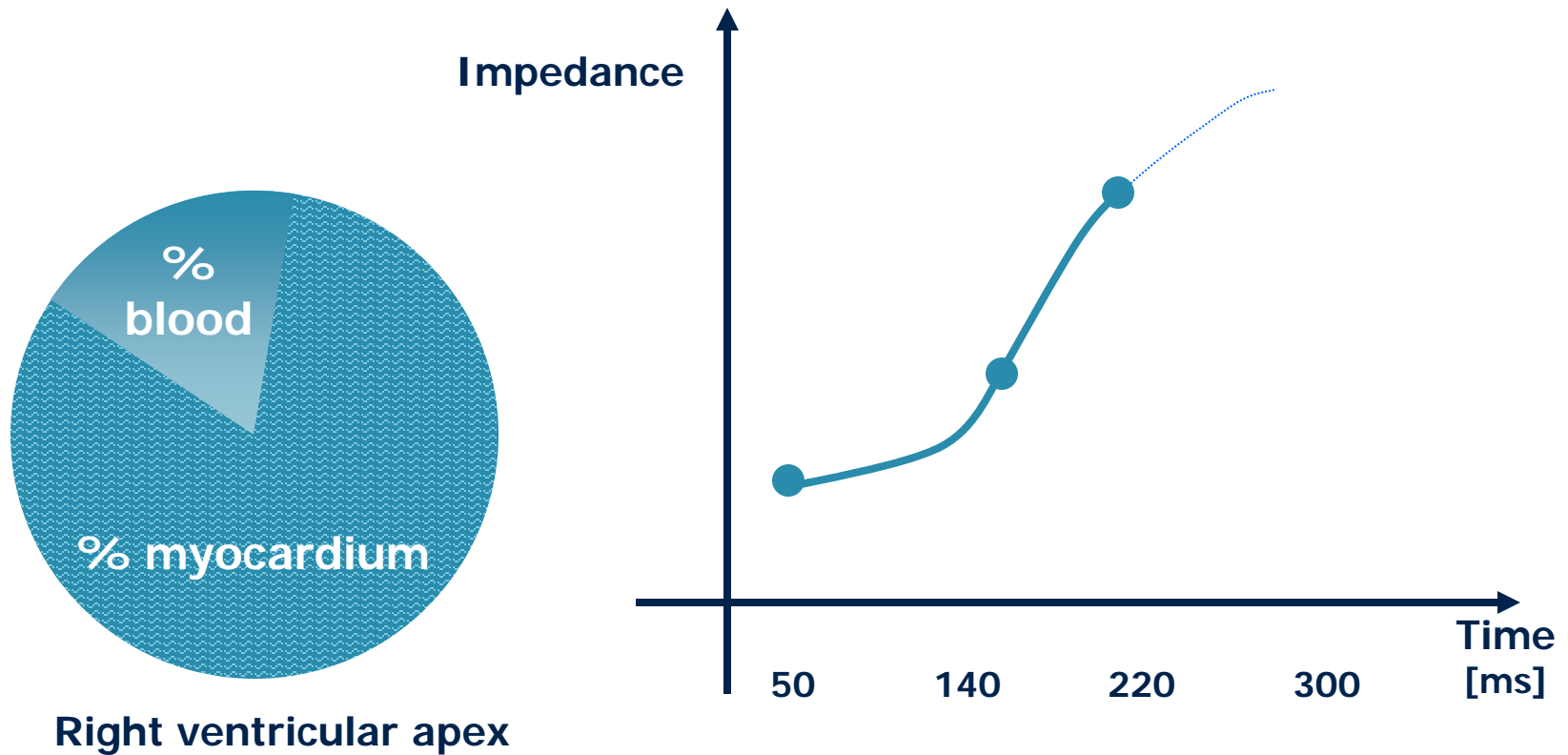
Contractile Dynamic and Impedance Curves

When the contraction starts, the percentage of muscle volume will increase—resulting in a higher impedance value.



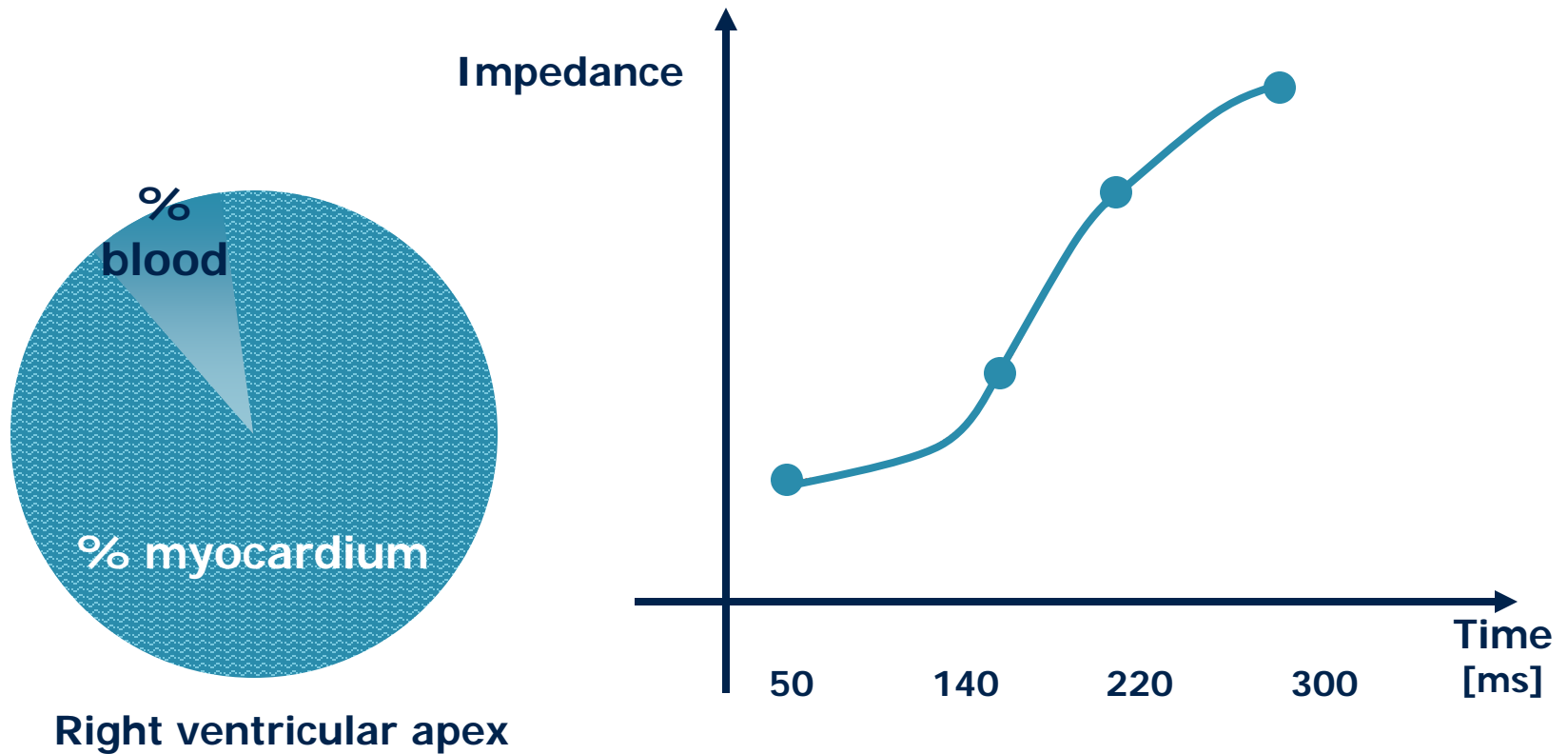
Contractile Dynamic and Impedance Curves

The contractility dynamics are represented by the impedance curve.



Contractile Dynamic and Impedance Curves

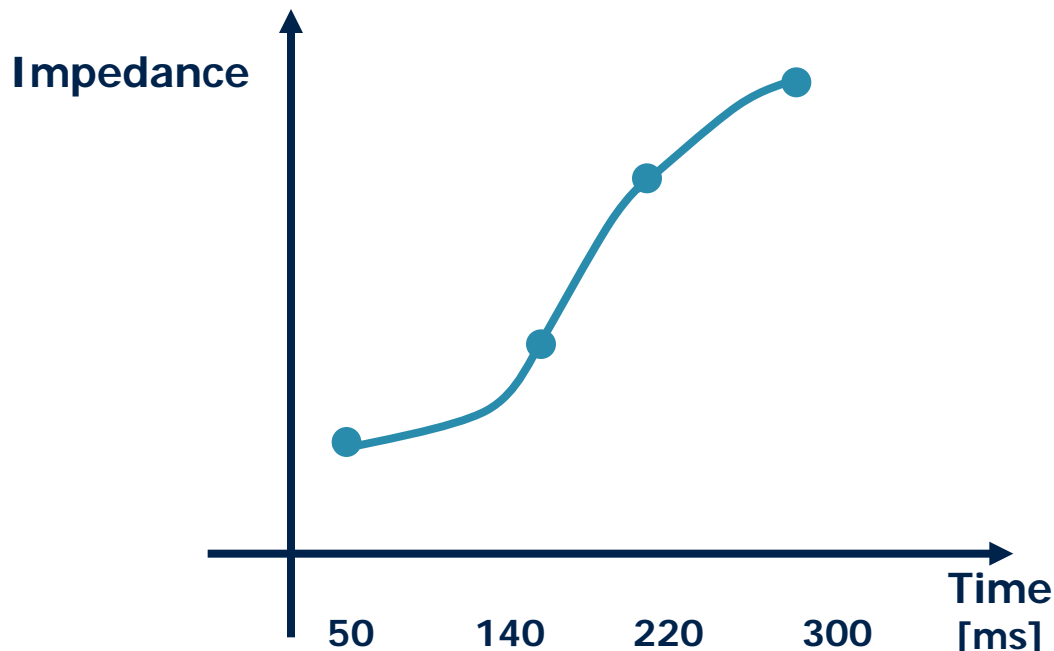
Closed Loop Stimulation (CLS) measures the impedance variation on a beat-to-beat basis.



Physiological Rate Regulation

Closed Loop Stimulation - the reference curve

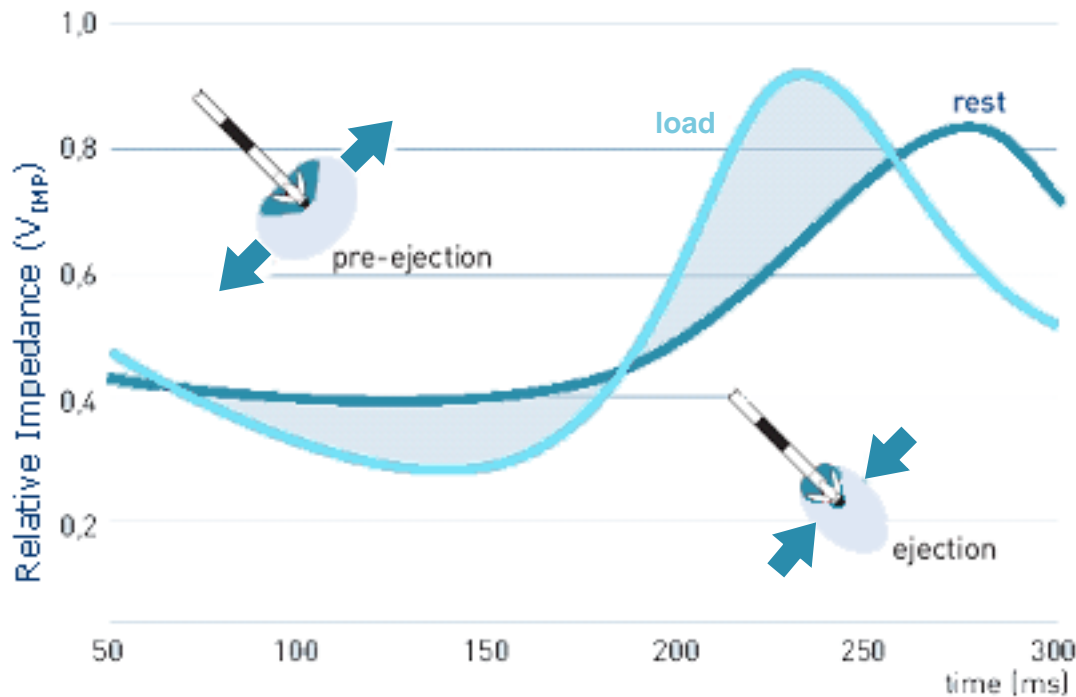
- During the “resting state,” the impedance values will establish a continuously updated reference curve (mean of 256 cycles).
- Changes in a patient’s drug therapy or cardiac remodeling do not affect the system, as it automatically updates the curves with the new data.



Physiological Rate Regulation

Closed Loop Stimulation - reference versus load curve

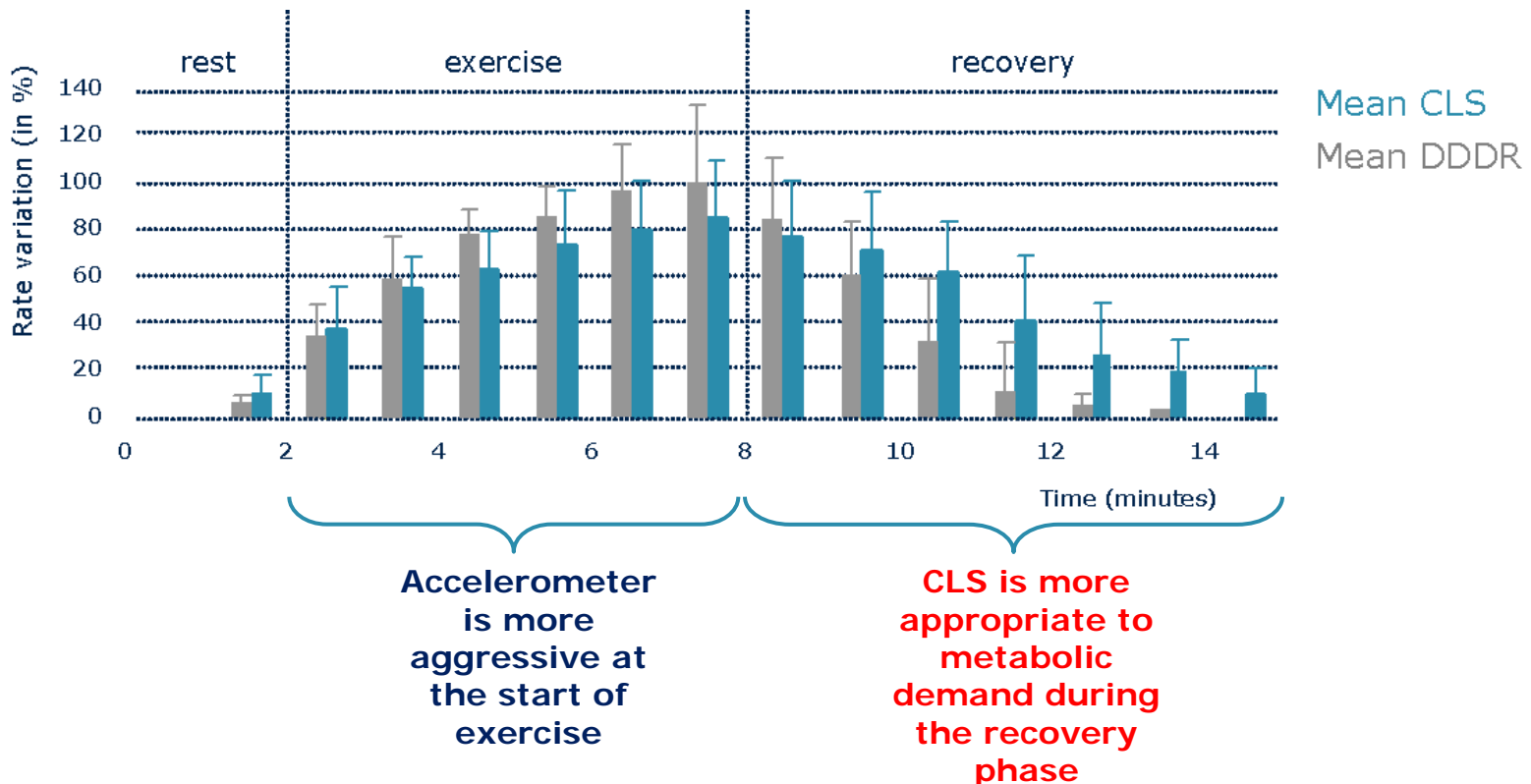
- With each heartbeat, CLS determines the impedance curve (V_{IMP}) during ventricular contraction (load curve) and compares it to its reference curve at rest (rest curve).



No particular lead needed

Closed Loop Stimulation - clinical examples*

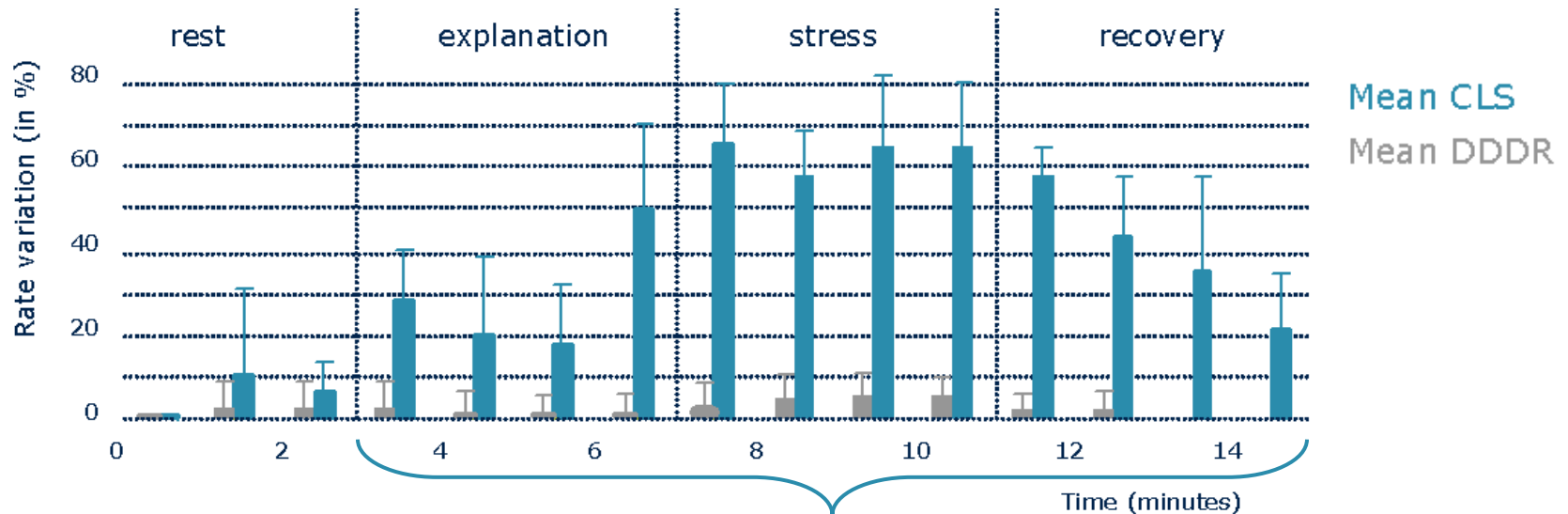
- Adequate heart rate adaptation during **physical activity**, even with differing levels (e.g., treadmill, cycling)



*Zecchi et al.; CLS vs. DDDR pacing: Benefits of hemodynamic pacing, *Prog Biomedical Res*, 2000, 5:292–296.

Closed Loop Stimulation - clinical examples*

- Restoration of ANS control enables patients to respond to daily activities that involve mental stress.



CLS clearly demonstrates superior rate adaptation compared with accelerometer

*Zecchi et al.; CLS vs. DDDR pacing: Benefits of hemodynamic pacing, *Prog Biomedical Res*, 2000, 5:292–296.

Clinical applications of **CLOSED LOOP STIMULATION - CLS**

- 1) Rate responsive pacing regulation**
- 2) Ventricular function related pacing rate control**
- 3) Hemodynamic cardiac function monitoring**
- 4) Vaso Vagal syncope prevention**

CLS and Atrial Fibrillation – The Burden I Study

Prevention of atrial fibrillation

European Heart Journal (2003) 24, 1952–1961



Clinical research

Impact of Closed-Loop Stimulation, overdrive pacing, DDDR pacing mode on atrial tachyarrhythmia burden in Brady-Tachy Syndrome

A randomized study

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Received 19 May 2003; received in revised form 21 July 2003; accepted 28 August 2003

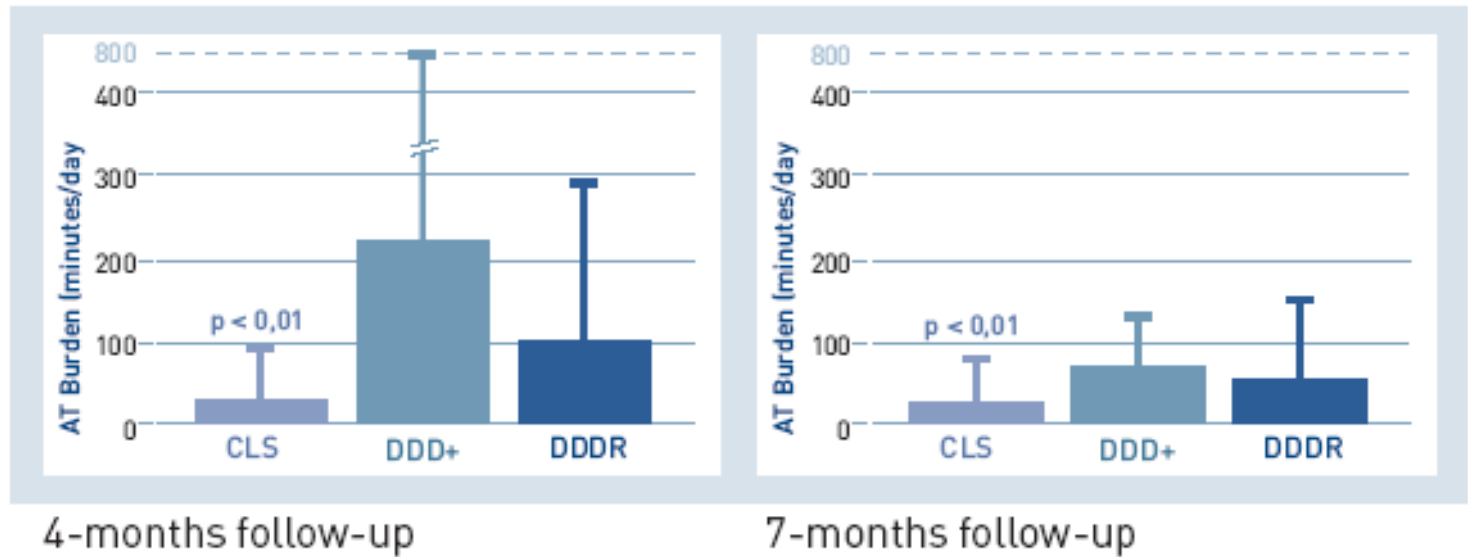
CLS and Atrial Fibrillation – The Burden I Study

General set-up

- Design: randomized; 3 arms
- Inclusion: Brady-Tachy Syndrome; at least one documented AT Episode within 6 months before implantation
- Patients: 149 included (98 with 7 months Follow Up)
- Randomisation: CLS 52; Overdrive 49; DDDR 48

CLS and Atrial Fibrillation – The Burden I Study

Results



Significant reduction of AT-Burden with CLS compared to the 2 other groups.

CLS and Atrial Fibrillation – The Burden II Study

Prevention of atrial fibrillation

Overdrive Versus Conventional or Closed-Loop Rate Modulation Pacing in the Prevention of Atrial Tachyarrhythmias in Brady-Tachy Syndrome: On Behalf of the Burden II Study Group

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(PACE 2008; 31:1443–1455)

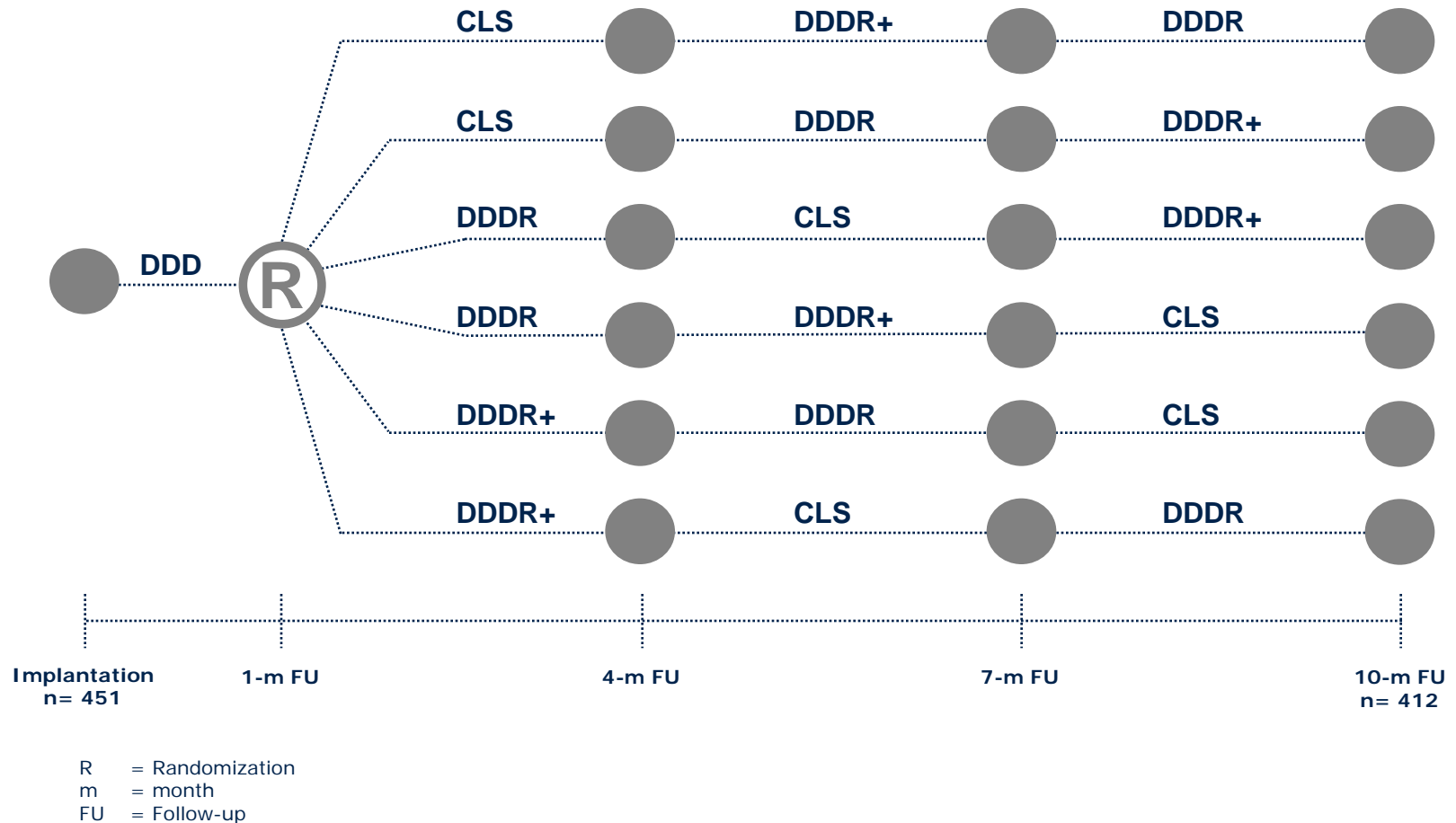
CLS and Atrial Fibrillation – The Burden II Study

General set-up

- Design: randomized; 6 arms with crossing over
- Inclusion: Patients with Brady-tachy syndrome and symptomatic bradycardia; at least one documented AT episode within 3 months before implantation
- Patients: 451 included
- Results: To exclude false-positive results
6658 IEGM recordings were analyzed

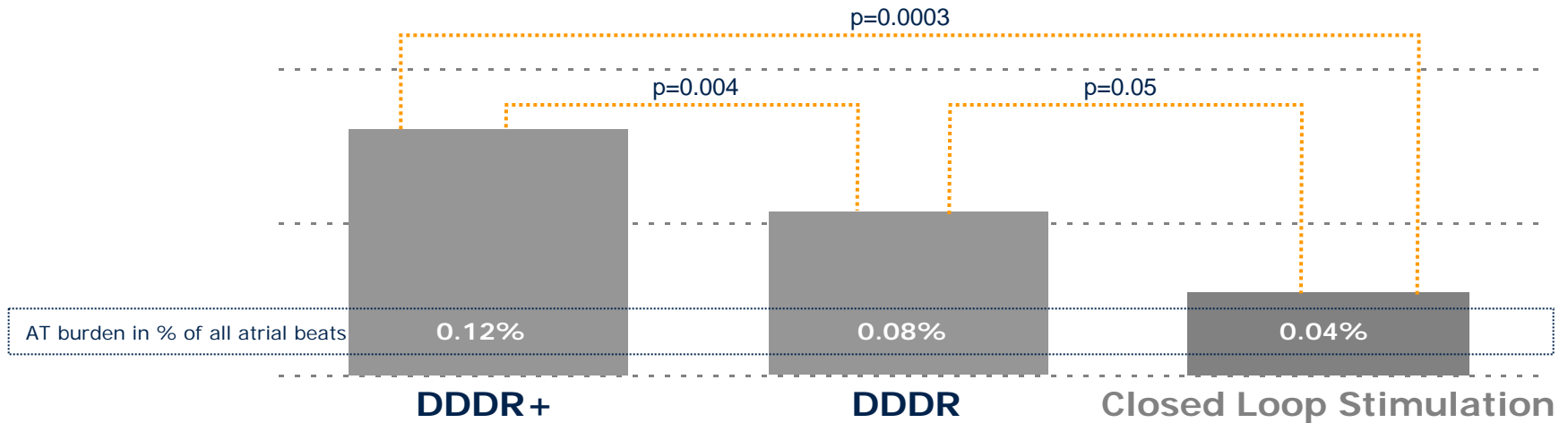
CLS and Atrial Fibrillation – The Burden II Study

Randomization



CLS and Atrial Fibrillation – The Burden II Study

Results: Mean AT burden*



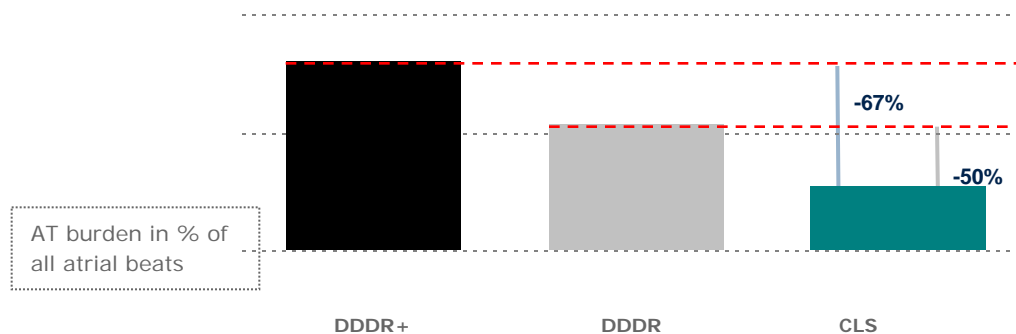
➤ Closed Loop Stimulation showed the lowest AT burden

* adjusted numbers; false-positive episodes were excluded

CLS and Atrial Fibrillation – The Burden II Study

Closed Loop Stimulation showed the lowest AT burden*

- CLS delivers physiological rate adaptation in AF patients providing optimal hemodynamic
- CLS demonstrated reduction of PACs, providing better heart rate modulation
- CLS and IRS+ can significantly reduce ventricular pacing to 6%, thus providing a better therapy for the patient

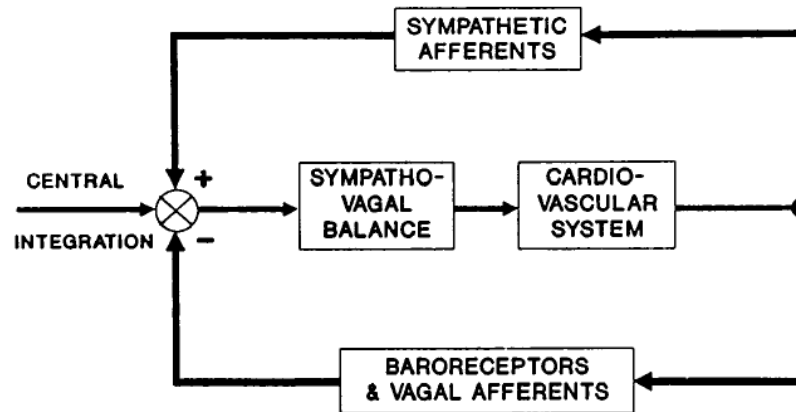


*Overdrive vs. Modulazione di frequenza convenzionale o Closed-Loop nella prevenzione della Tachiaritmia atriale nella sindrome Brady-Tachy. Puglisi A, et al.; PACE 2008; 31:1443-1455

How CLS works with Cardial Stimulation

Non physiological rate modulation may affects autonomic balance of sympathetic response¹⁻²

- The autonomic system is regulated by 2 components: the sympathetic activity and the vagal tone



In the frequency-domain analyses:

- The sympathetic activity or the sympathovagal balance is reflected by the low frequency (LF) components
- The vagal tone is reflected by the high frequency (HF) components

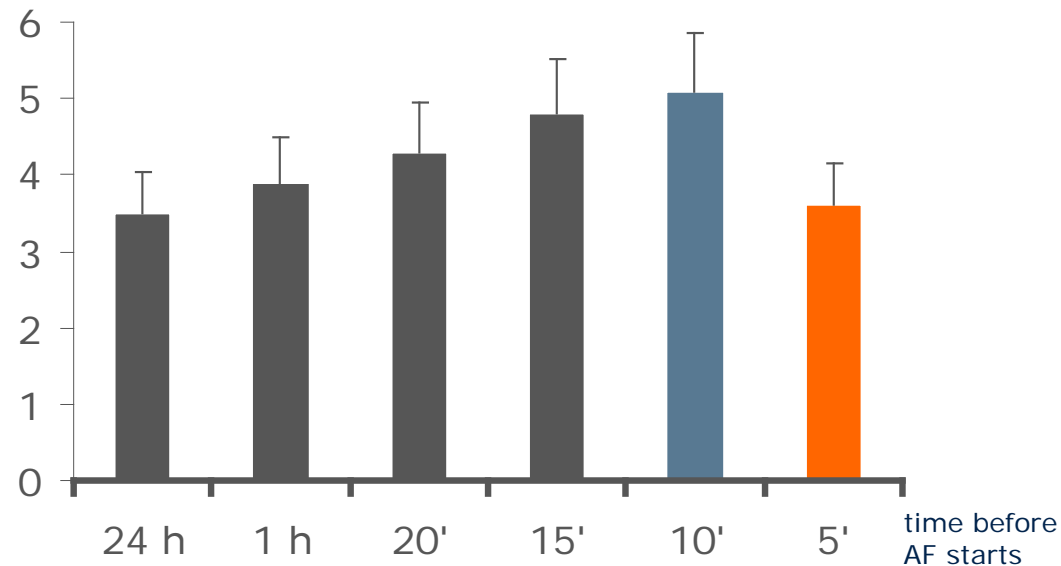
¹ Taylor, Morillo, Eckberg, Ellenbogen, Higher sympathetic nerve activity during ventricular (VVI) than during dual chamber (DDD) pacing, J. Am. Coll Cardiol 1996; 28:1753-58

² Chiladakis, Kalegeropoulos, Manolis, Autonomic response to single and dual chamber pacing. Am J Cardiol 2004; 93: 985-89

How CLS works with Atrial Fibrillation

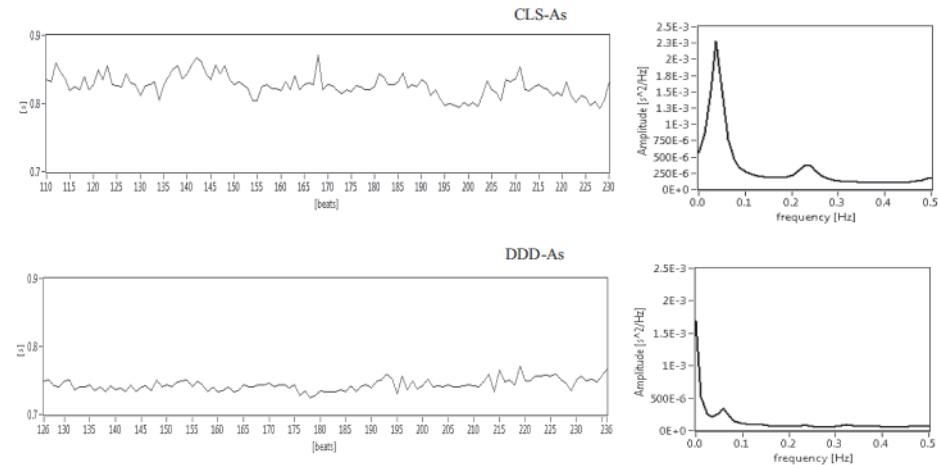
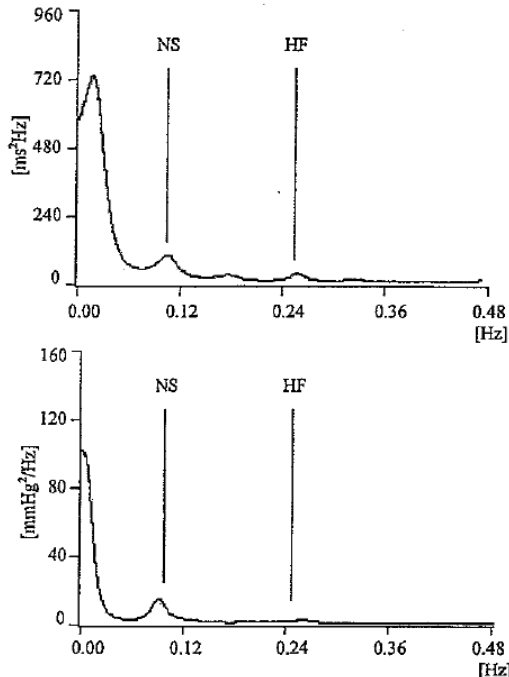
Mechanism

- Highest value of HF (vagal activity) observed during the 10 to 5 minutes preceding the onset of AF.
- An initial linear increase in LF (sympathetic activity) values was observed before the onset of AF, but it was present only until 15 minutes before the onset of AF and was then followed by a marked decrease



How CLS works with Atrial Fibrillation

- The CLS algorithm produces a heart rate variability with a “low/high frequency” ratio comparable to that of spontaneous beats.¹
- The HRV created by the CLS algorithm during patient daily life closely mimics the physiological one.¹



- CLS is the only algorithm showing a similar low frequency component in heart rate variability and systolic pressure spectra.²

1 Quaglione R et al., “Autonomic Function during Closed Loop Stimulation and Fixed Rate Pacing: Heart Rate Variability Analysis from 24-Hour Holter Recordings”, PACE 2009

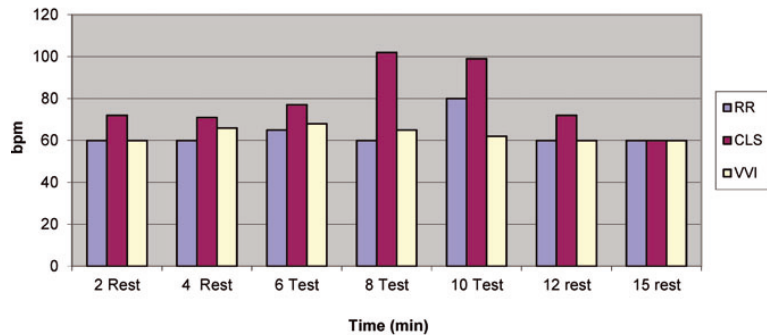
2 Santini, Ricci, Pignalberi, Biancalana, Censi, Calcagnini, Bartolini, Barbaro, Effect of autonomic stressors on rate control in pacemaker using ventricular impedance signal, Pace, January 2004, Vol 27

CLS and Atrial Fibrillation

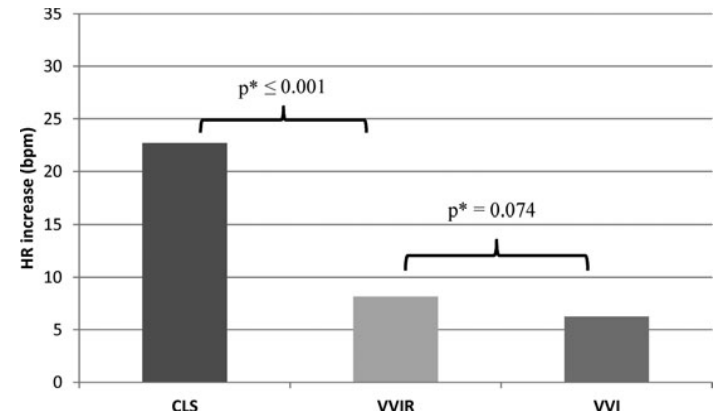
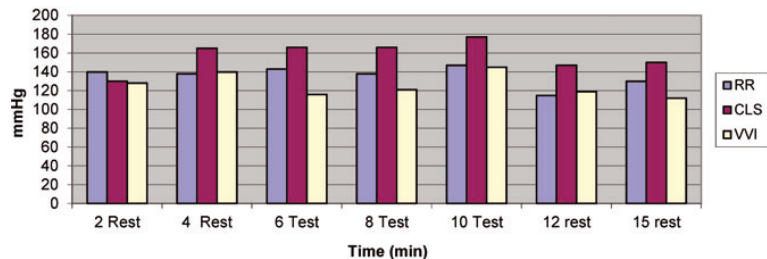
Closed Loop Stimulation is the best option even in VVI Mode

- Improvement in HR determines a better pressure profile during mental stress shown by a significant increase in systolic blood pressure from baseline.
- In the absence of a healthy sinus node, CLS in single-chamber device can bypass the sick atrium in rate-modulation through an adaptation of the pacemaker basic interval proportional to isotropic effort.

Variation of heart rate during test



Variation of pressure during test



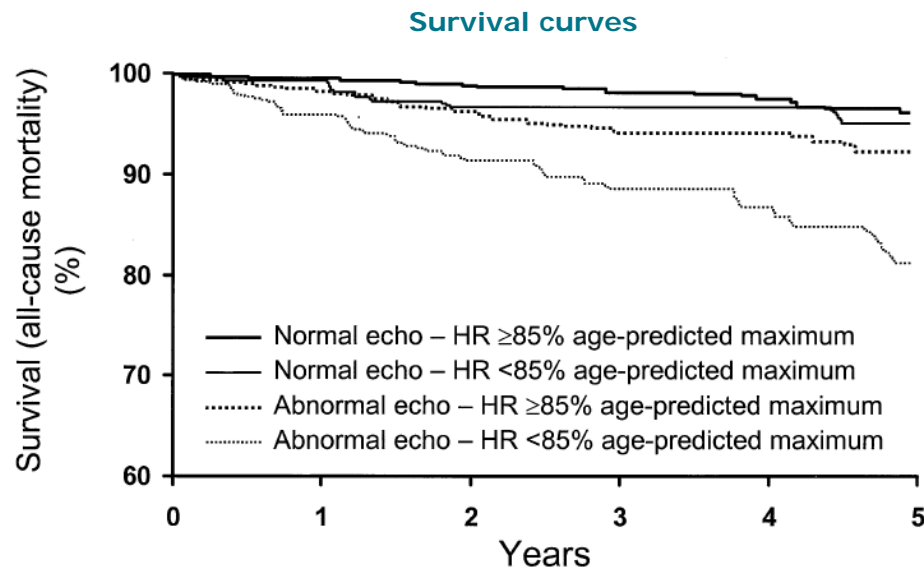
CLS and CHF



Prognostic Significance of
Impairment of Heart Rate Response to Exercise
Impact of Left Ventricular Function and Myocardial Ischemia
Abdou Elhendy, MD, PhD,* Douglas W. Mahoney, MSc,† Bijoy K. Khandheria, MD,

Rate regulation is a predictor of mortality

- Impaired chronotropic response to exercise is associated with increased mortality and cardiac events even after adjusting for LV function.
- Not only LV function has to be adjusted, but the rate regulation has to be adequate



Adequate rate response in **Heart Failure** patients

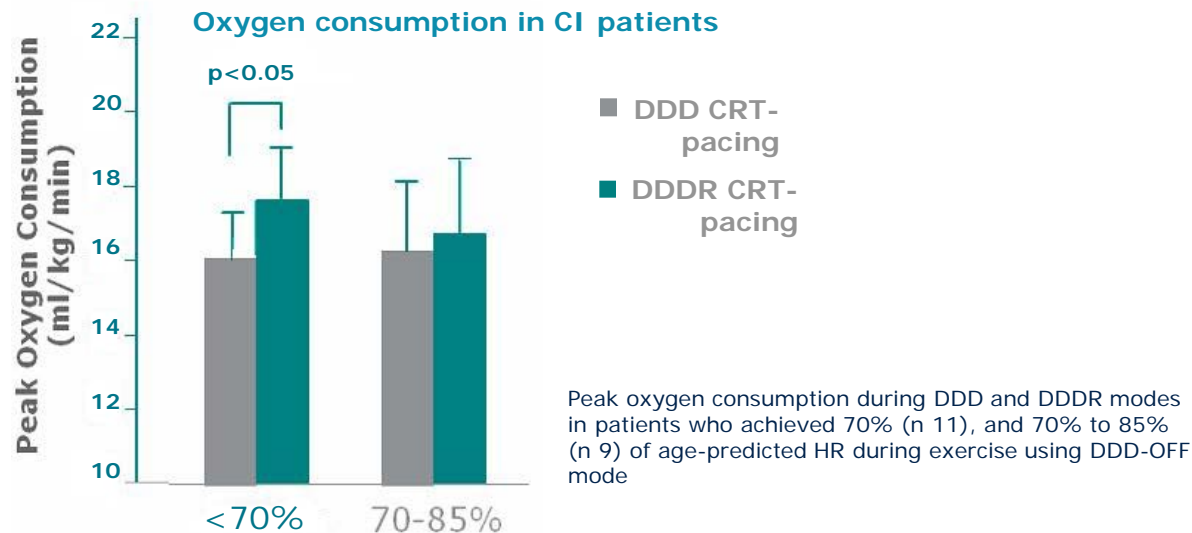


The Incremental Benefit of Rate-Adaptive Pacing on Exercise Performance During Cardiac Resynchronization Therapy

Hung-Fat Tse, MD, FACC,* Chung-Wah Siu, MBBS,* Kathy L. F. Lee,

Rate regulation is beneficial in severe CI

- In heart failure patients with severe CI, appropriate use of rate-adaptive pacing with CRT provides incremental benefit on exercise capacity during exercise.



CLS and CHF

Physiological rate regulation

- Blood pressure plays a critical role in the prognosis of acute heart failure.
- Lowering blood pressure in patients with hypertension is probably one of the most important population-based preventive measures for heart failure.

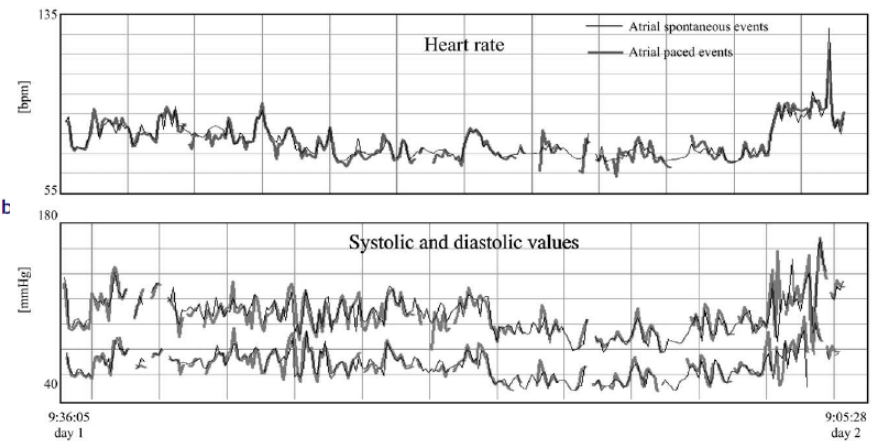
CLS is the only algorithm able not to modify systolic/diastolic pressure values, integrating spontaneous rhythm with paced one.

Effect of pacemaker rate-adaptation on 24h beat-to-beat heart rate and blood pressure profiles

Raffaele Quaglione ^a, Giovanni Calcagnini ^{b,*}, Federica Censi ^b

Table 2 Mean percentage differences of RR, SS and DD values during DDD-CLS and DDD pacing with respect to spontaneous beats

	Percentage differences with respect to spontaneous beats		
	DDD-CLS (%)	DDD (%)	P
Mean RR	+7.4	+20.1	0.0001
Mean SS	-1.7	-7.9	0.04
Mean DD	-3.7	-9.6	0.02



CI and HF

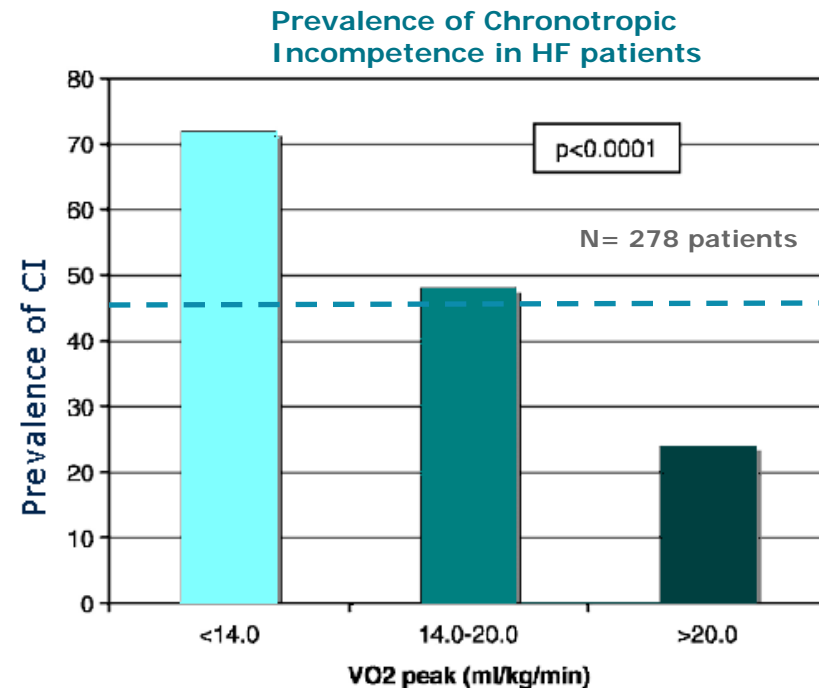
The
European Journal
of
Heart Failure

Chronotropic incompetence, beta-blockers, and functional capacity in advanced congestive heart failure: Time to pace?

Ulrich P. Jorde^{a,*}, Timothy J. Vittorio^b, Michael E. Kasper^b, Emma Arezzi^a,
Paolo C. Colombo^a, Rochelle L. Goldsmith^a, Kartikya Ahuja^b,
Chi-Hong Tseng^b, Francois Haas^b, David S. Hirsh^b

Up to 72% of patients with Heart Failure have CI

- The prevalence of CI is 72% in patients with most advanced CHF peak ($\text{VO}_2 < 14.0 \text{ ml/kg/min}$)
- The average prevalence of CI in CHF patients is 46%
- CI is equally prevalent in subjects receiving and not receiving chronic beta-blocker therapy



...“Modulation of CI using atrial pacing without induction of dyssynchrony should be further explored and may prove to be a worthy therapeutic intervention in a large proportion of patients with CHF.”...

General summary

- CLS delivers physiological rate adaptation in general population and in AF patients providing optimal hemodynamic
- CLS demonstrated reduction of PACs
- CLS seems to be very promising in a HF population.
- An adequate rate regularization could improve NYHA class and Ejection fraction.
- CRT treatment could be improved using a system able to integrate in the autonomic nervous system