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The role of rate modulation adapted to contractility through the closed loop stimulation: is there a role in CRT-D patient management?

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Background

In general population exercise capacity is determined by the LV stroke volume, heart rate and the arteriovenous oxygen difference.

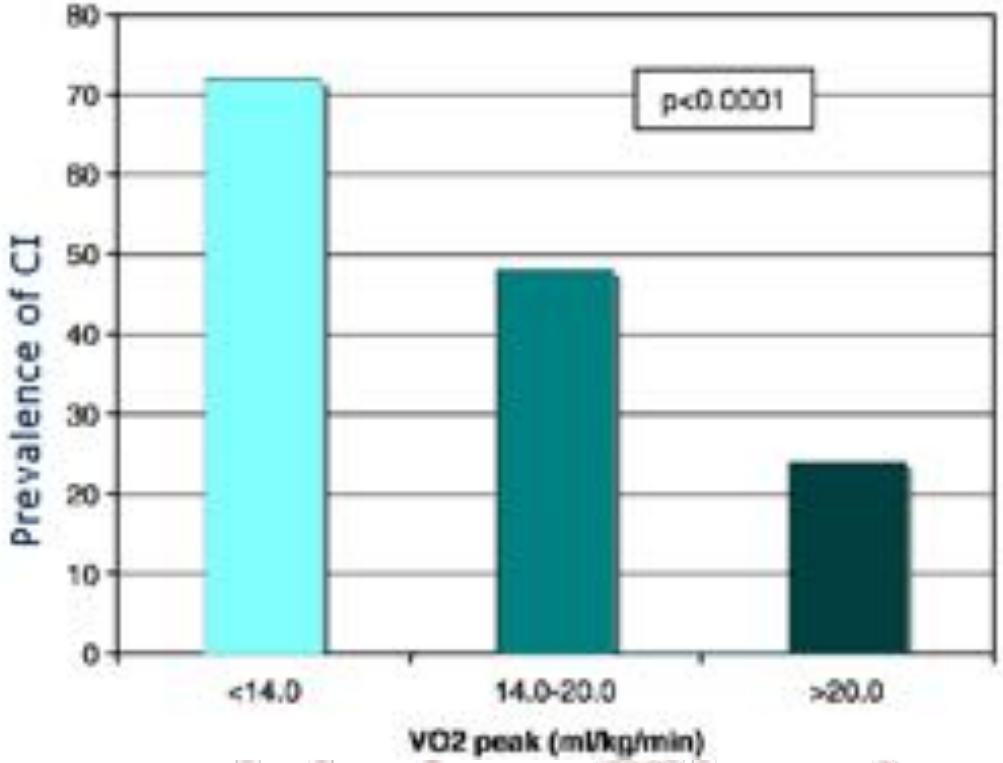
In heart failure patients during exercise the ability:

- to augment LV stroke volume without a concomitant increase in left atrial pressure is lost
- to maintain LV stroke volume by increasing myocardial contractility is markedly attenuated

As a result augmentation of heart rate is a major determinant of cardiac output and thus exercise capacity

Background

Chronotropic incompetence, the inability of the heart to increase its rate proportional to increased activity or demand, significantly reduce exercise capacity in HF patients



The average prevalence of CI in HF patients is 46% and increse to 72% in patients with most advanced HF

Jorde UP et al European Journal of Heart Failure 2008;10:96-101

Rate adaptive device in CRT patients with CI

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

All patients underwent a cardiopulmonary exercise treadmill test with their

CRT devices programmed in a randomized fashion to:

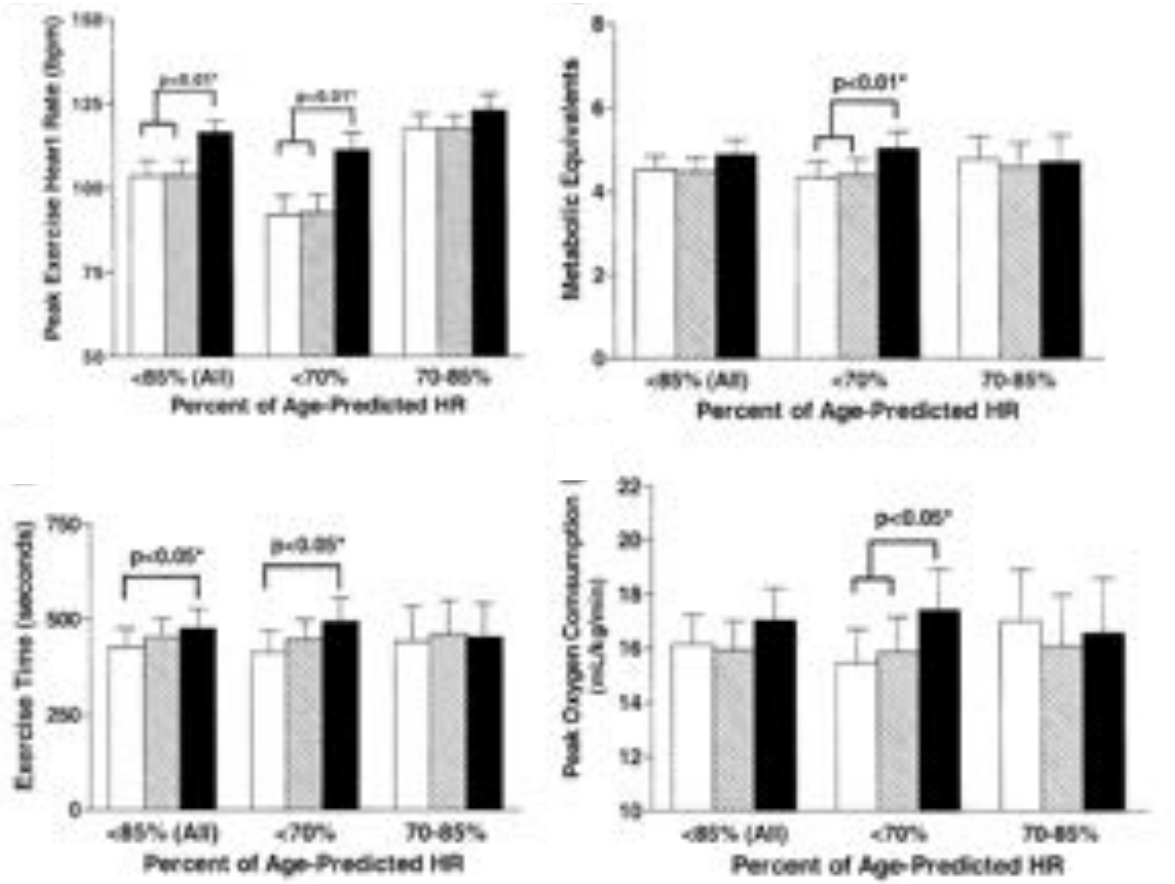
1) DDD mode with fixed AV interval (DDD-OFF);

2) DDD mode with adaptive AV interval (DDD-ON)

3) DDDR mode with adaptive AV interval (DDDR-ON)

Hung-Fat Tse et al J Am Coll Cardiol 2005;46:2292-7

Rate adaptive device in CRT patients with CI



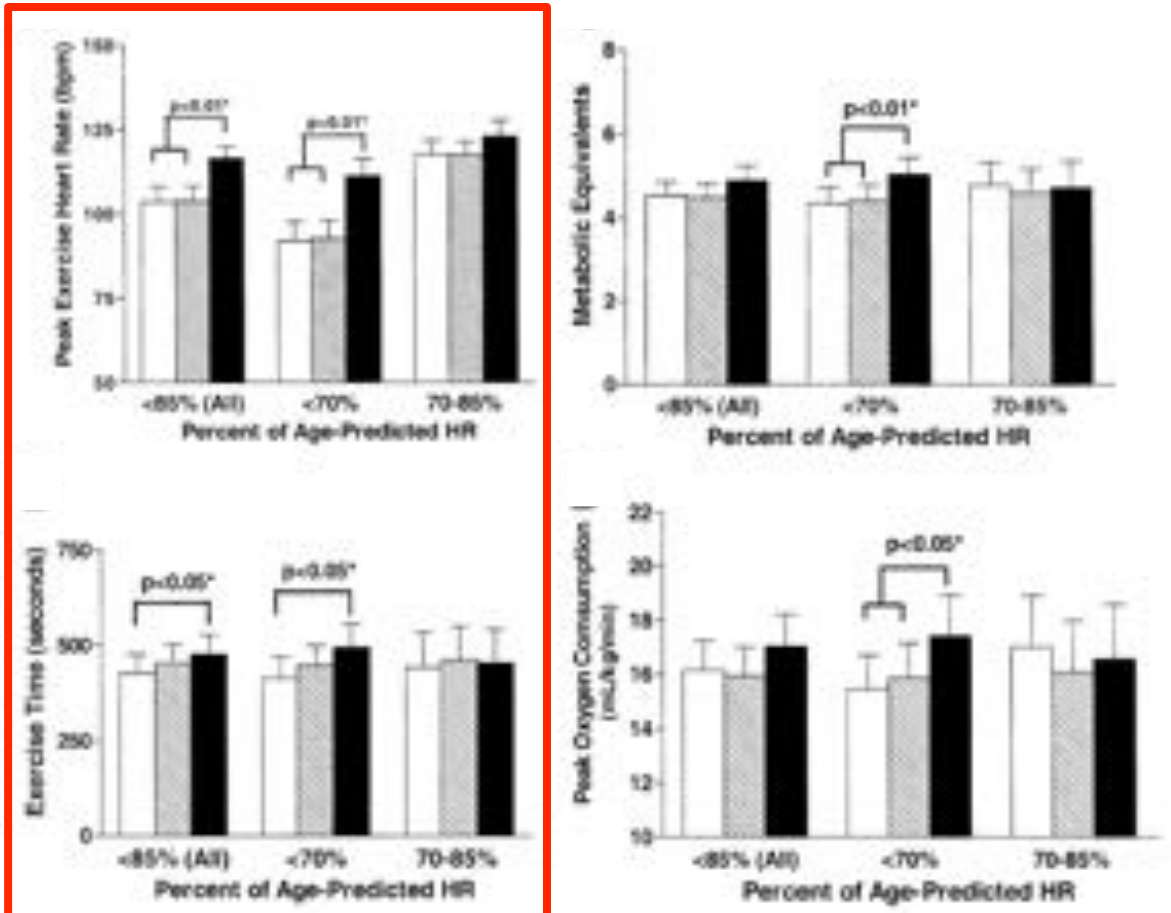
White bars = DDD-OFF; ruled bars = DDD-ON; black bars = DDDR-ON.

Adaptive AV interval alone did not have any significant effect.

This underline the importance of heart rate adaptation as the major determinant of cardiac output and thus exercise capacity in HF patients

Hung-Fat Tse et al J Am Coll Cardiol 2005;46:2292-7

Rate adaptive device in CRT patients with CI



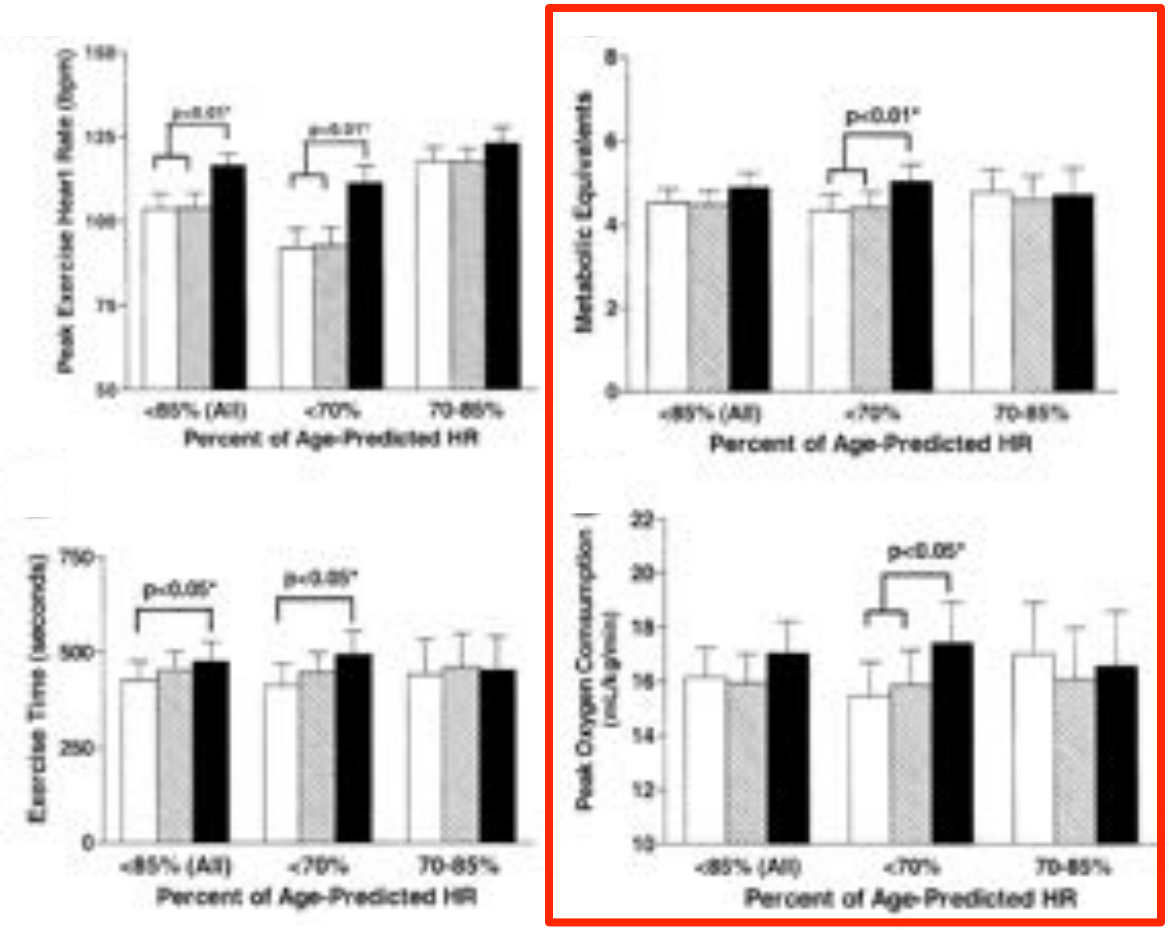
White bars = DDD-OFF; ruled bars = DDD-ON; black bars = DDDR-ON.

Rate-adaptive pacing increased:

- peak exercise heart rate
- exercise time

Hung-Fat Tse et al J Am Coll Cardiol 2005;46:2292-7

Rate adaptive device in CRT patients with CI



White bars = DDD-OFF; ruled bars = DDD-ON; black bars = DDDR-ON.

In patients with more severe chronotropic incompetence, rate adaptive pacing significantly increased exercise capacity

Hung-Fat Tse et al J Am Coll Cardiol 2005;46:2292-7

Rate adaptive device in CRT patients with & without CI

Atrial Support Pacing in Heart Failure: Results from the Multicenter PEGASUS CRT Trial

CRT programmation modality (randomized):

1) DDD 70 mode;

2) DDD 40 mode

3) DDDR 40 mode

The primary endpoint was a clinical composite score consisting of all-cause mortality, HF events, NYHA functional class

Martin DO et al J Cardiovasc Electrophysiol 2012;23: 1317-25

Rate adaptive device in CRT patients with & without CI

incidence of atrial arrhythmias.[28,29] Such arrhythmias, particularly atrial fibrillation, are a common and challenging problem among HF patients. However, there is also the potential risk of worsening HF status or outcomes with higher paced rates. Studies have shown that lowering heart rate is associated with better outcomes[27] and observational analyses show that mortality rate is inversely proportional to heart rate.[28-30]

Three previous studies[31–33] evaluated the effect of empirical atrial support pacing in patients receiving a dual chamber ICD who did not have a pacing indication. The INTRINSIC RV (Inhibition of Unnecessary RV Pacing with AVSH in ICDs) trial[31] compared DDDR-60 pacing mode to ventricular backup pacing (VVI-40), whereas the DAVID (Dual Chamber and VVI Implantable Defibrillator) II trial[32] compared AAI-70 to VVI-40 pacing. Both studies showed noninlack of differ
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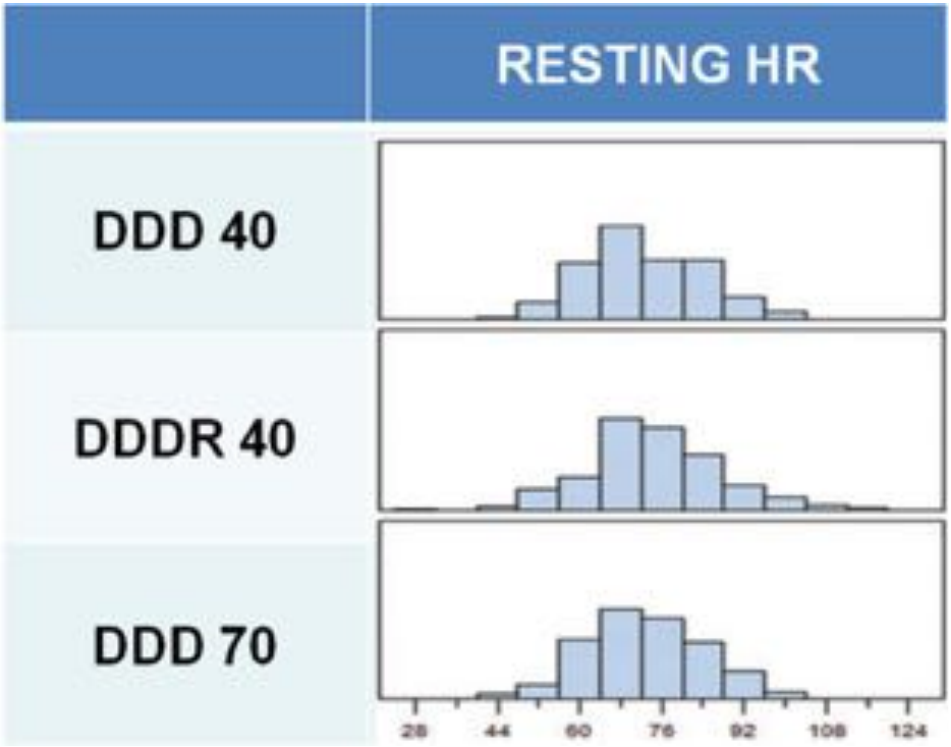
No significant differences were observed in the composite endpoint between either of the two atrial support treatment arms compared to the control arm

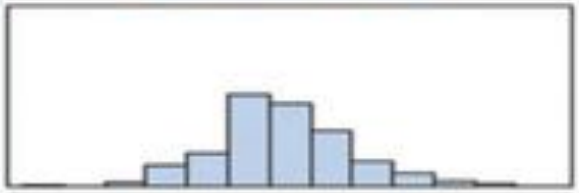
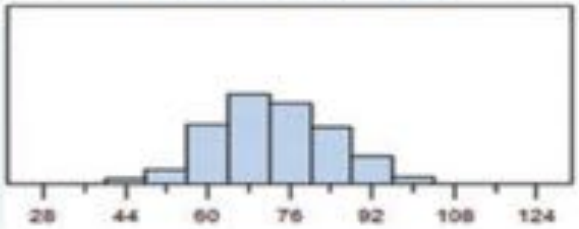
Martin DO et al J Cardiovasc Electrophysiol 2012;23: 1317-25

Rate adaptive device in CRT patients with & without CI



The majority of patients enrolled did not have chronotropic incompetence and therefore did not need atrial pacing support.

Rate adaptive device in CRT patients with & without CI

	RESTING HR	ATRIAL PACING (%)
DDD 40		3.7±13.7
DDDR 40		3.0±12.2
DDD 70		43.3±29.8

Accelerometer may not be the rate sensor of choice in HF patients as these patients are relatively inactive (92% of the day).

The amount of atrial pacing between the DDD 40 group and the DDDR 40 group was almost identical

Have we got other solutions for heart rate modulation?

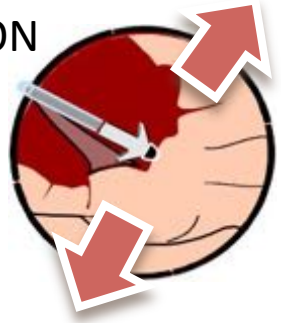
Have we got other solutions for heart rate modulation?

Closed loop stimulation

Closed loop stimulation - How it works?

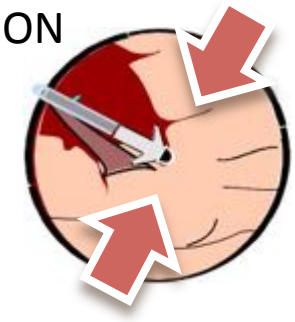
Based on impedance measurement

PRE-EJECTION



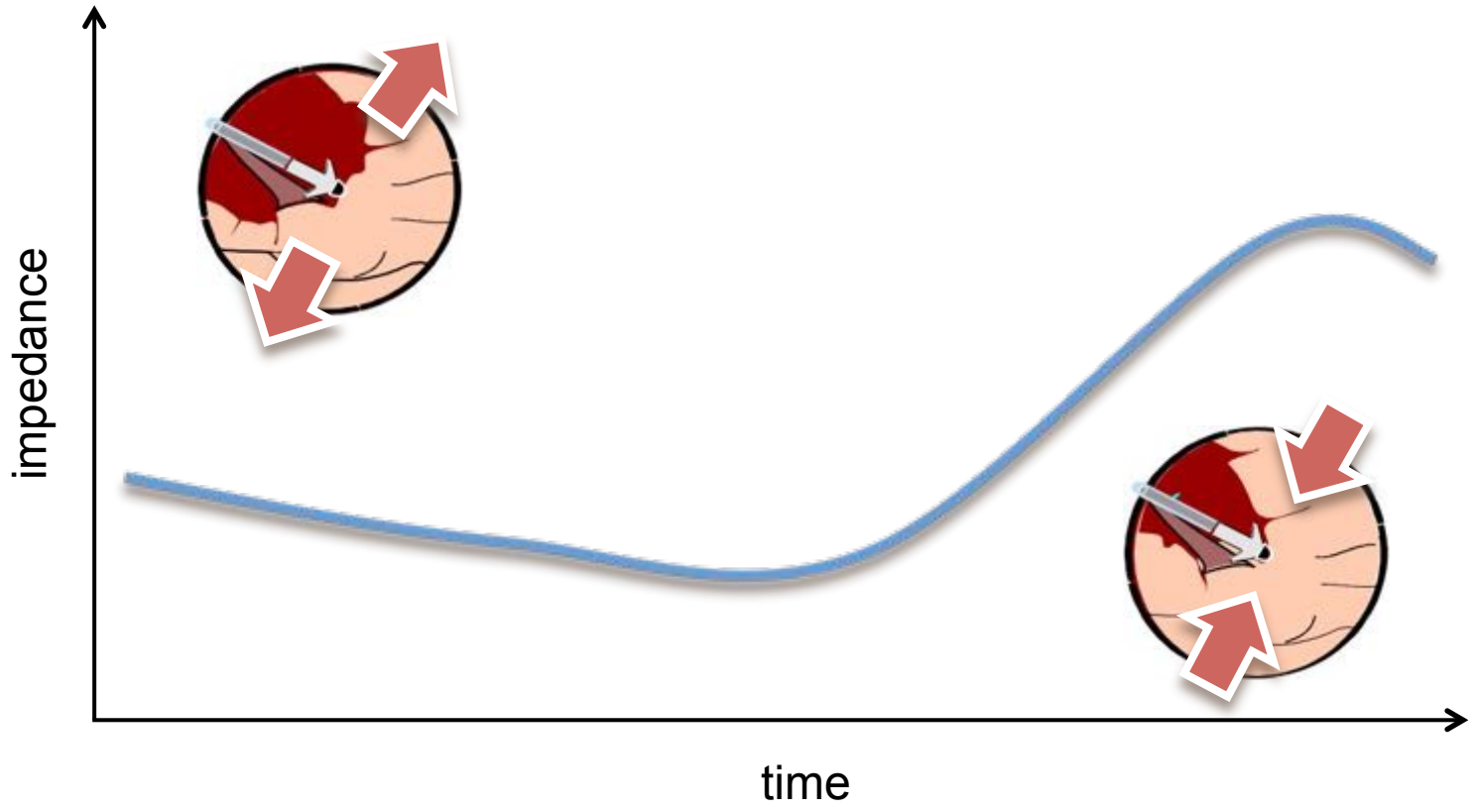
Smaller fraction of myocardium = low impedance

EJECTION



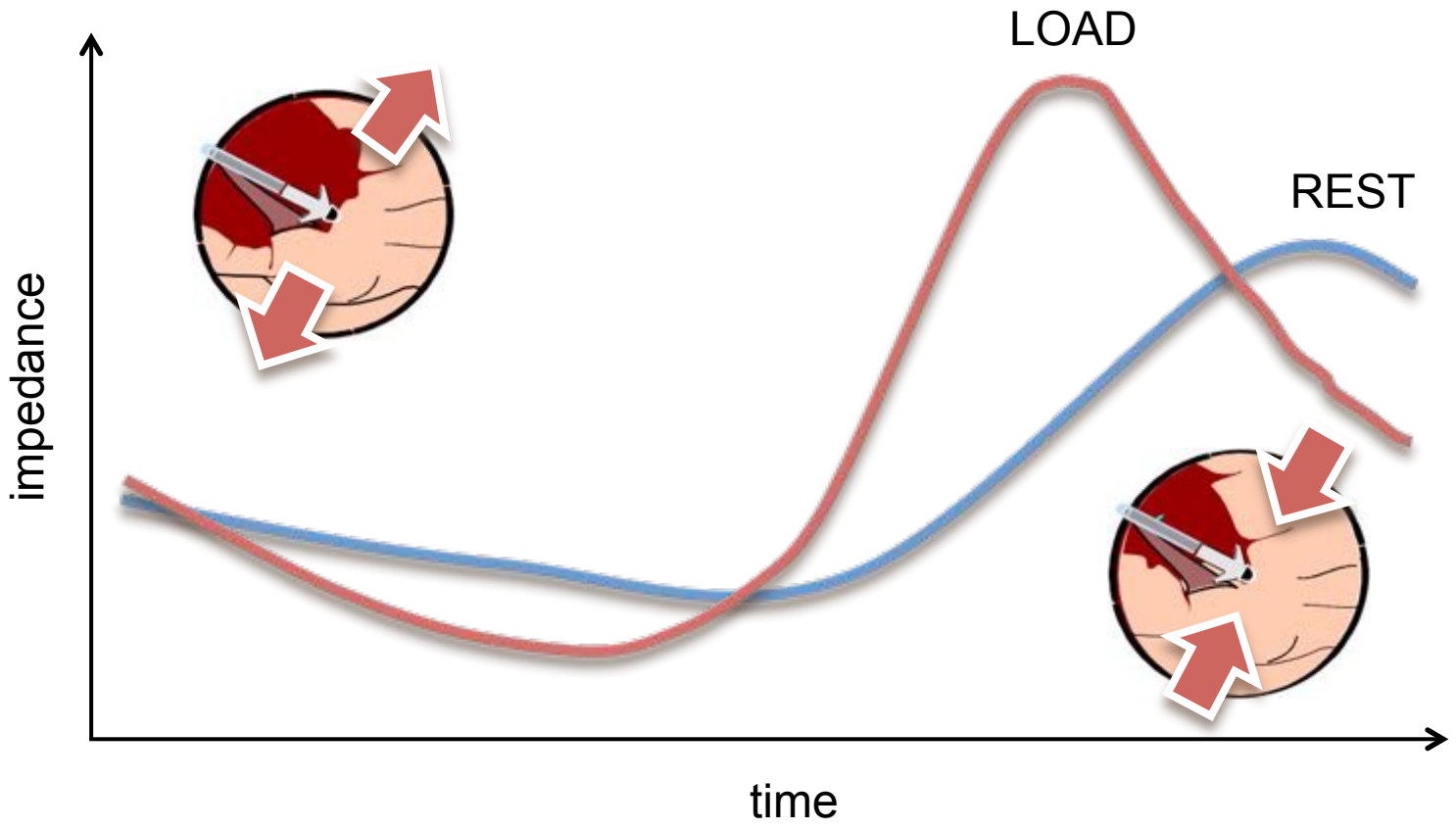
Larger fraction of myocardium = high impedance

Closed loop stimulation - How it works?



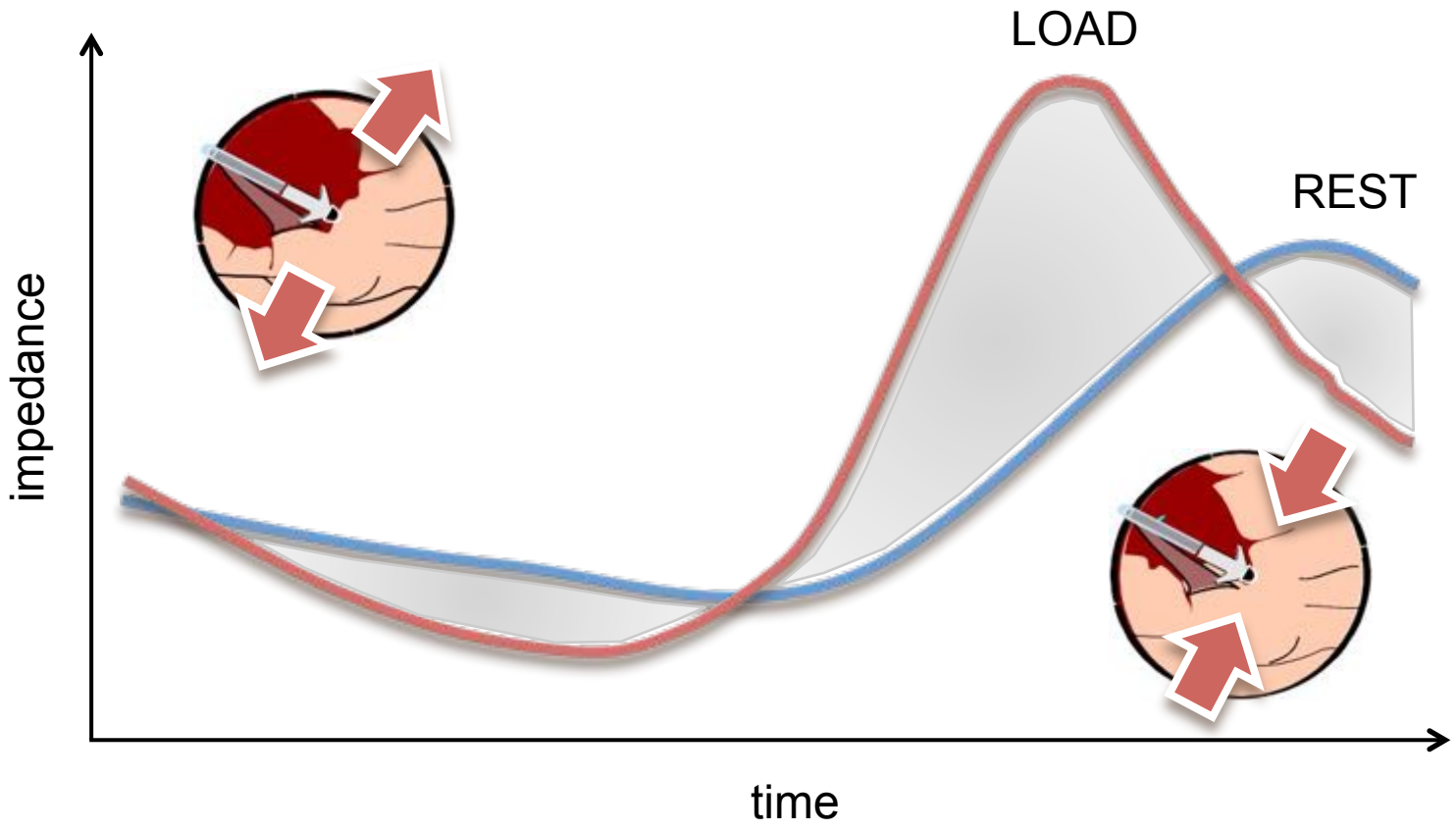
PM deliver subthreshold pulses every 15 ms (64 Hz) during the isovolumetric contraction and the beginning of the ejection phase. These pulses allow detection of the intracardiac impedance curve

Closed loop stimulation - How it works?



The impedence cuve collected during rest (reference) is beat to beat compared with the actualized curve (load).

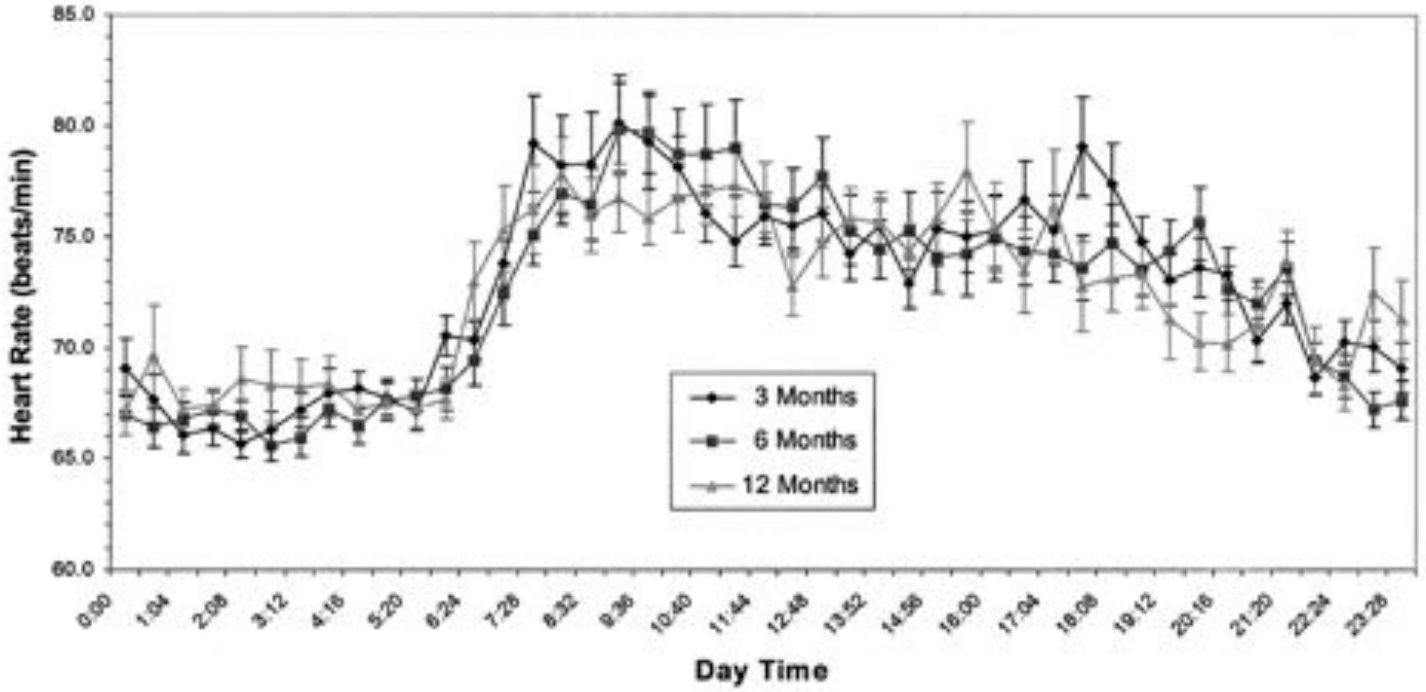
Closed loop stimulation - How it works?



CLS algorhitm provides an increase in pacing rate proportional to the detected difference.

Closed loop stimulation - Does it work?

Closed loop stimulation – Physiologic sensor



Circadian pattern of heart rates in closely matches with the behavior of healthy sinus rates.

The long-term stability of CLS systems was indicated by the absence of significant differences between the trend lines.

Griesbach L et al, *PACE 2003;26:1432-37*

Closed loop stimulation – Exercise activity

Activity	Peak Heart Rate* (beats/min)
Stair climbing	104 ± 18
Stair descending	95 ± 15
Slow walking	88 ± 11
Baseline (before exertion)	70 ± 10

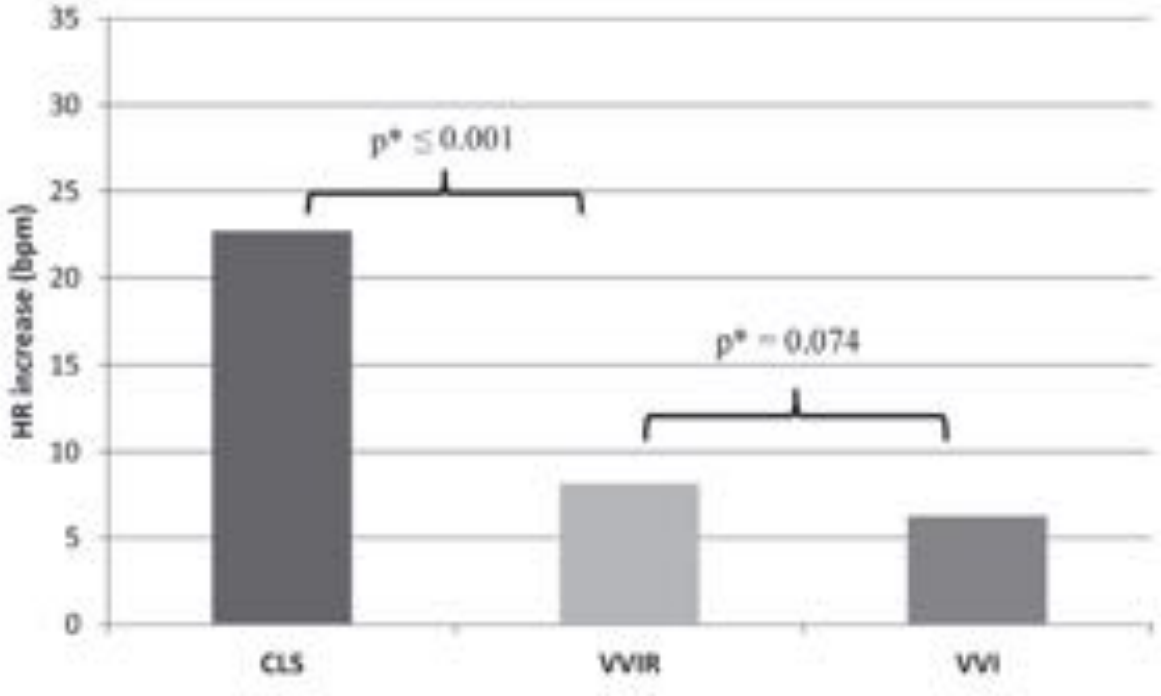
*Mean value ± SD. $P < 0.001$ for any pair of activities.

CLS clearly differentiated between stair climbing, stair descending, and slow walking.

Griesbach L et al, *PACE 2003;26:1432-37*

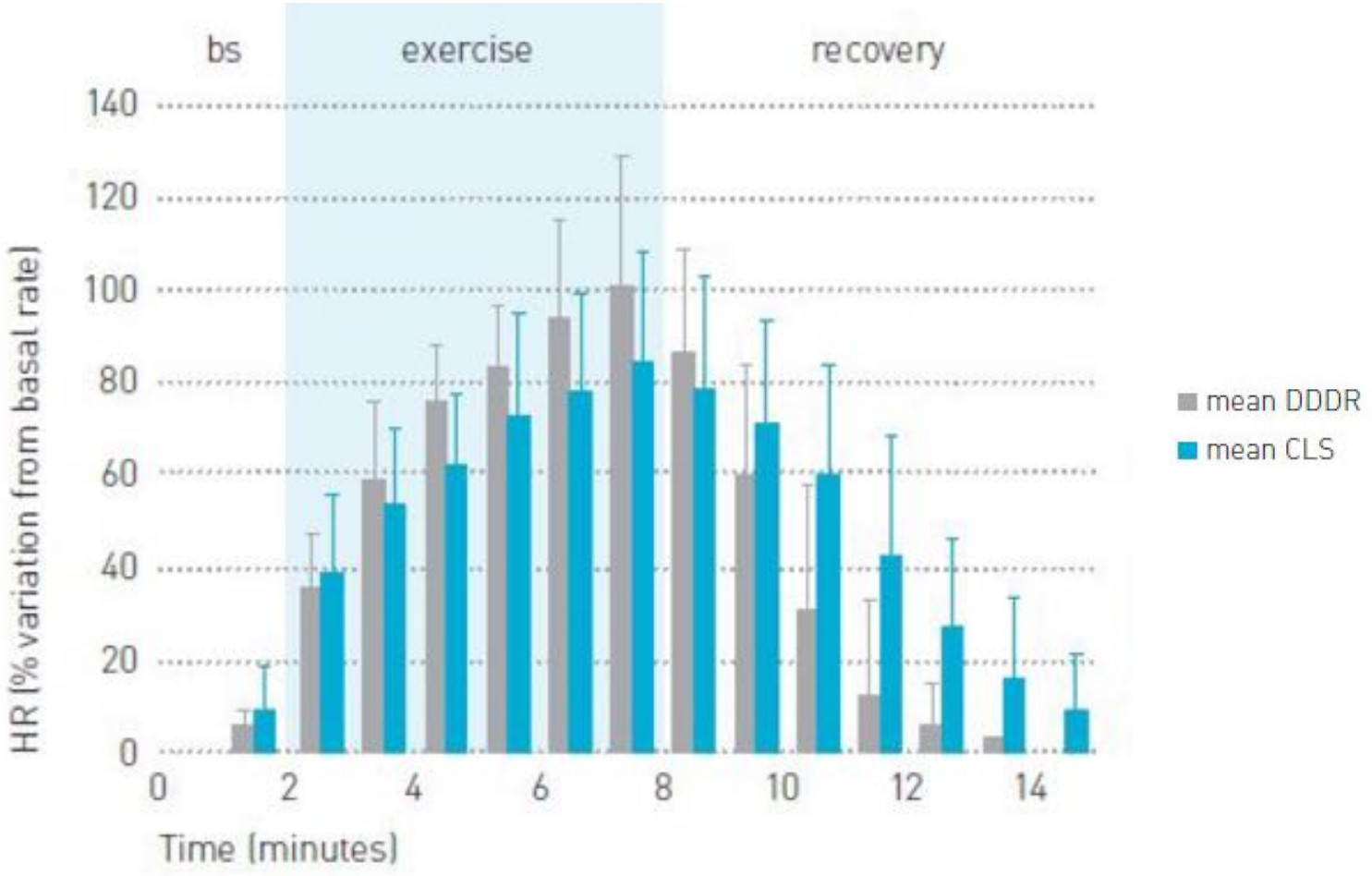
Closed loop stimulation – Mental stress

Closed Loop Stimulation is Effective in Improving Heart Rate and Blood Pressure Response to Mental Stress: Report of a Single-Chamber Pacemaker Study in Patients with Chronotropic Incompetent Atrial Fibrillation



Proietti R et al, PACE 2012; 35:990–998

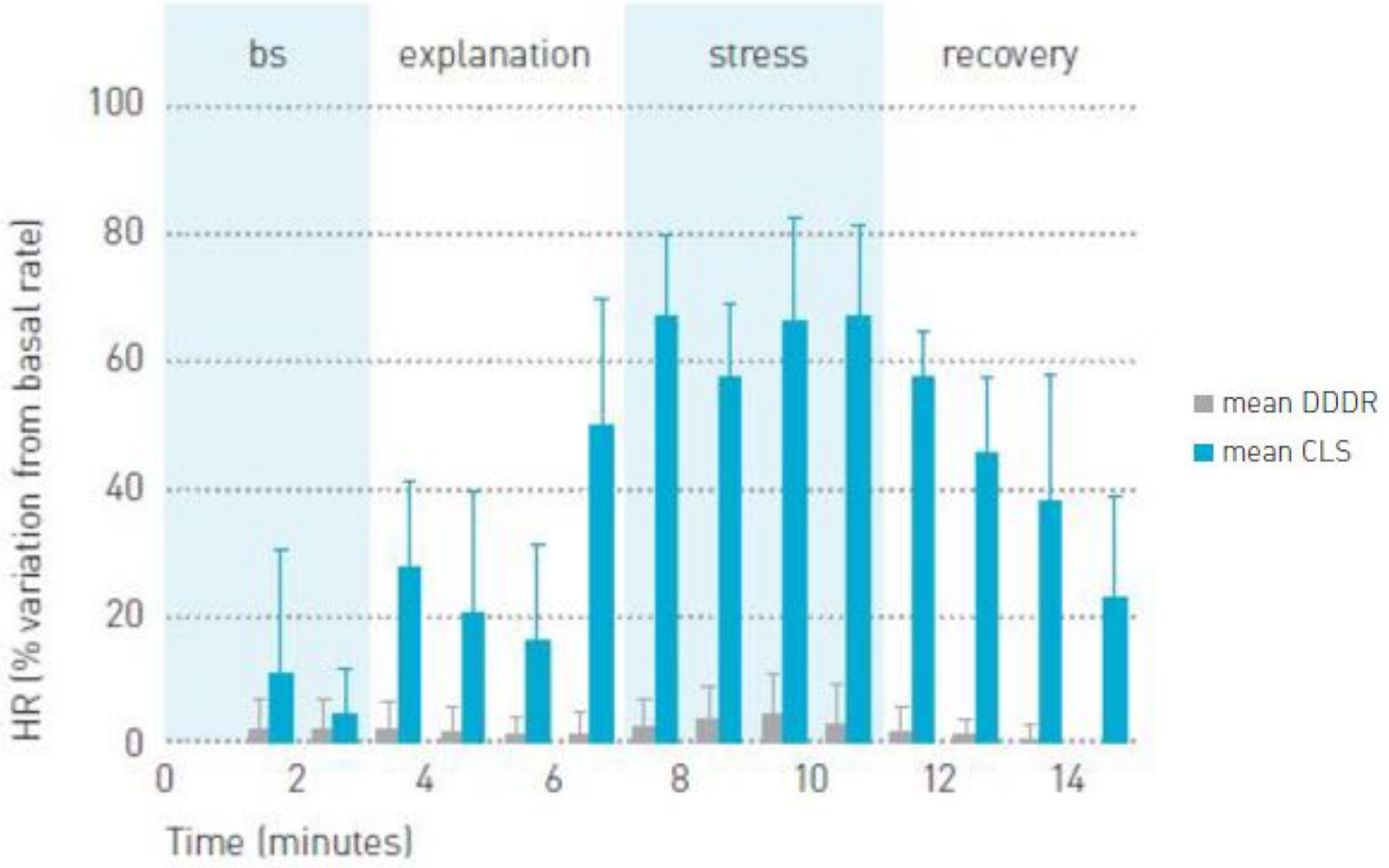
Closed loop vs Other Sensor - exercise



Different type of sensor allow a satisfactory heart rate modulation during exercise

Zecchi et al Progress in Biomedical Research 2000

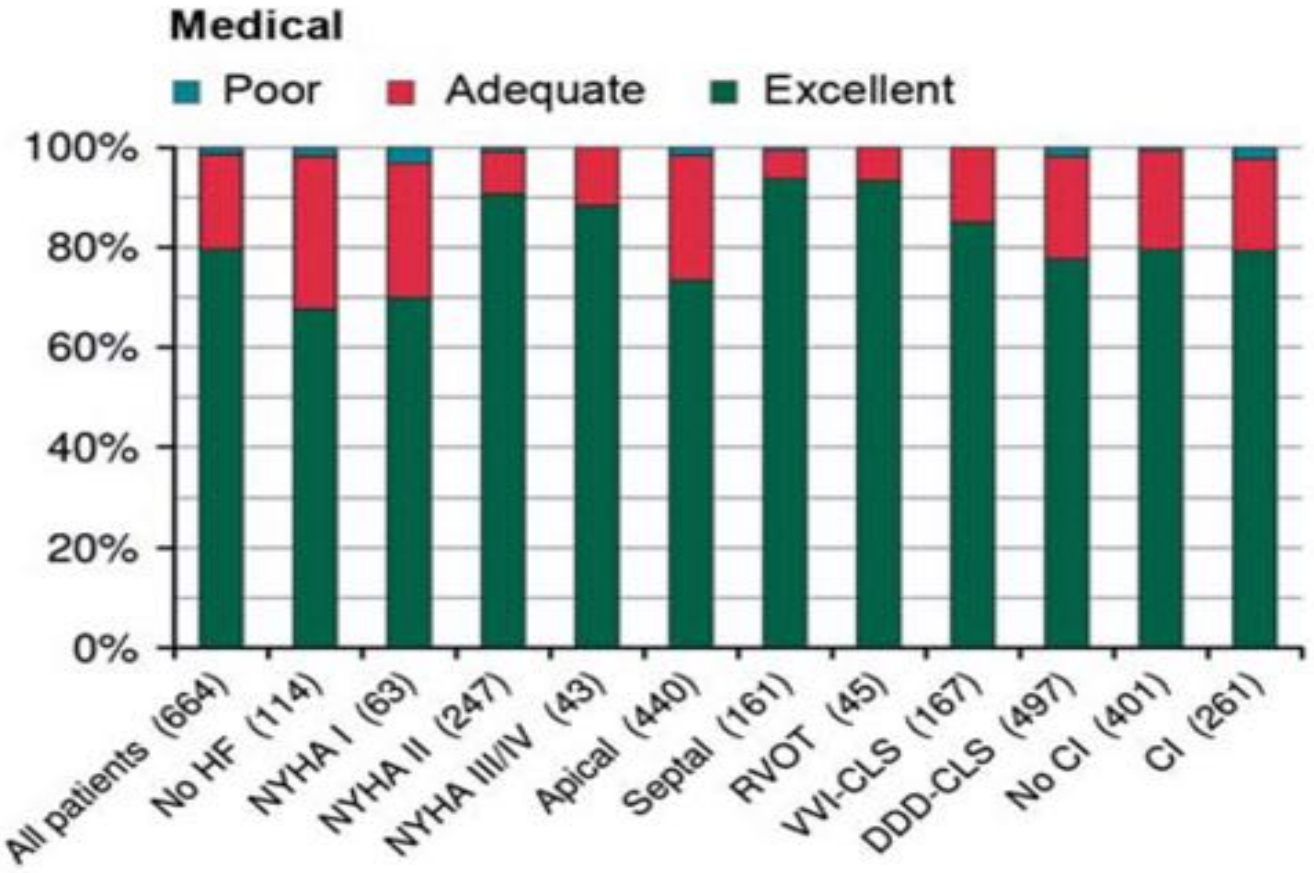
Closed loop vs Other Sensor – mental stress



CLS respond to mental stress

Zecchi et al Progress in Biomedical Research 2000

Closed loop in HF patients



RECORD registry showed a better satisfacion in terms of medical benefit in patients with heart failure symptoms than in patients without

Lindovska M et al, Europace 2012;14:1587-95

Conclusions

In heart failure patients prevalence of CI is high (45-70%).

In case of HF patients with CRT and severe CI rate-adaptive pacing provides incremental benefit on exercise capacity.

The CLS could have a role in all patients CRT with chronotropic incompetence where also traditional sensors showed an improvement.

Conclusions

Compared to traditional sensors CLS demostrates a better ability in detecting an hemodynamic demand due to both emotional stress and exercixe activity and supplying a proper rate modulation.

PEGASUS study underlines the inappropriateness of standard sensors in HF patients because they are relatively inactive with low physical stress level.

The CLS could be the rate sensor of choice in HF patients because it modulates the heart rate not only during a physical stress, but also during mental stress

Suggestions

What could be a benefit for patients with CRT or CRT-D indication?

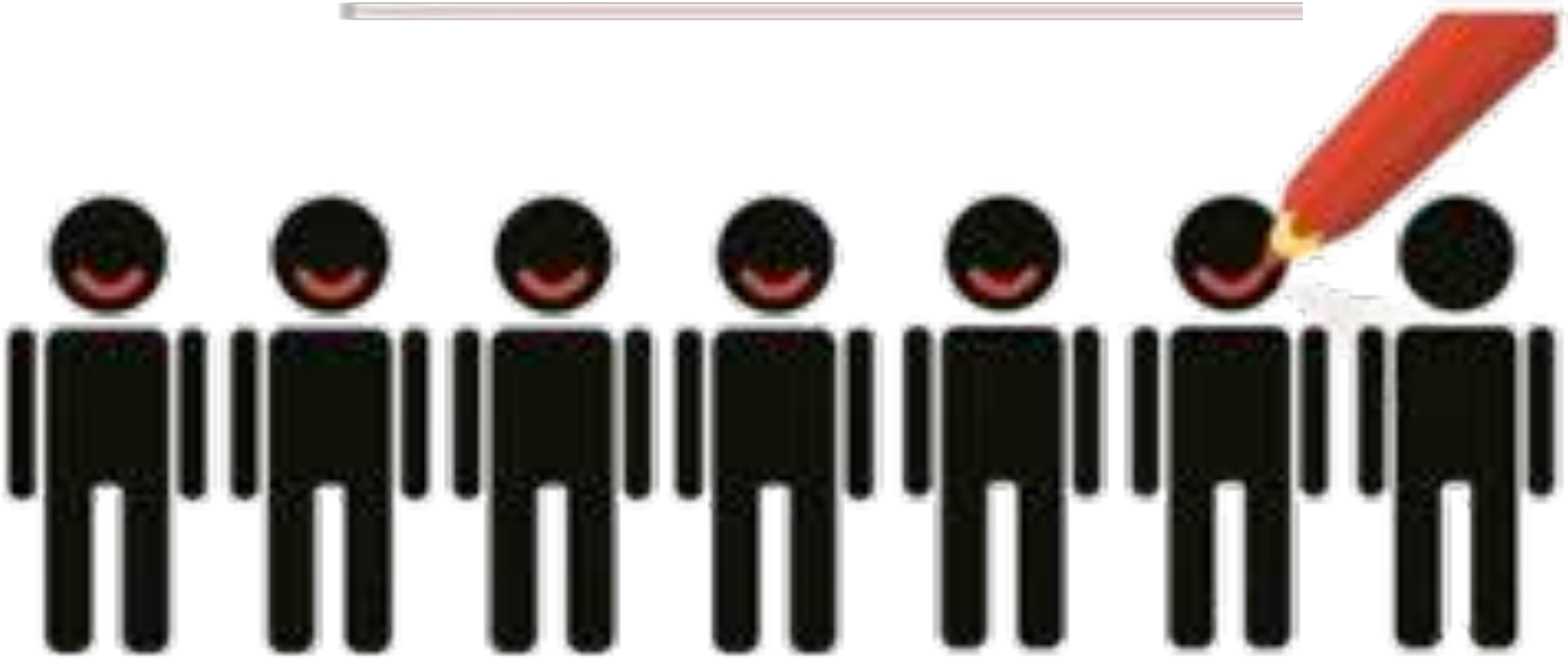
Battery with long expecting life

Quadripolar leads for LV pacing

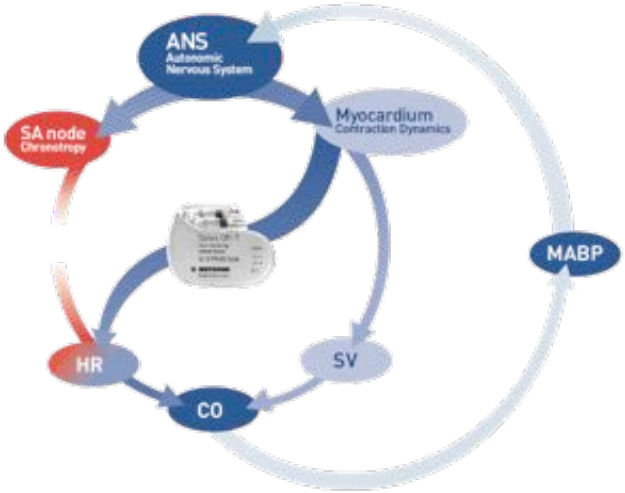
MRI conditional device

Device with also closed loop sensor

Thanks



Closed loop stimulation - How it works?



By measuring an intrinsic parameter that is directly affected by vagal and sympathetic output, CLS modify the pacing rate which, in turn, interacts with the autonomic nervous system via the negative feedback.

Should the heart rate be too low or too high, not matching current physiological requirements, a change in detected signal directs the pacemaker towards a more appropriate pacing rate. This principle allows continuous adjustment of the pacing rate to optimal values.