

## Heart Rate Variability in Patients with Closed Loop Stimulation

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### Summary

*Electrostimulation of the heart has been permanently developed into a very effective therapy for cardiac bradyarrhythmias, but, nevertheless, patients with implanted pacemakers can't be stressed in daily life as healthy subjects. Apparently, this reduction in the patient's quality of life is present as long as pacemaker therapy is not able to imitate the functions of the natural sinus node sufficiently. Just this is the concept of Closed Loop Stimulation (CLS) which is integrating the pacemaker into the cardiovascular control loop by monitoring the cardiac contractility. Under these conditions, CLS is not only sensitive to physical strain but, moreover, to mental stimulation by the autonomous nervous system. The interaction of CLS pacemakers with the autonomous nervous system can be deduced from measuring heart rate variabilities as a non-invasive cardiac diagnostic tool. Especially, parasympathetic and sympathetic activities cause characteristic fluctuations in heart rate occur which are related to special frequency ranges. By measuring heart rate variabilities in CLS patients with respect to other pacemaker patients and chronotropic competent subjects, sensitivity of CLS on the autonomous nervous system and, thus, the physiological nature of Closed Loop Stimulation was verified.*

### Key Words

Closed Loop Stimulation, quality of life, heart rate variability, autonomous nervous system

### Introduction

The basic idea of Closed Loop Stimulation (CLS) is to integrate the pacemaker in the cardiovascular system [1]. It has already been shown [2] that CLS is ensuring adequate pacing rates according to physical strain. On the other hand, it is more complicated to show the sensitivity of CLS on mental stress because of finding suitable standard diagnostic tools. Analysis of heart rate variability (HRV) has become such a suitable non-invasive diagnostic to the autonomous nervous system controlling the heart functions [3,4,5]. Heart rate variability as a risk factor for sudden cardiac death [6] or marker for further applications [7,8] base on small scale fluctuations of the heart rate caused by sympathetic or parasympathetic activities of the autonomous nervous system. In practise, from ECG curves normal to normal (NN) intervals are measured. Thereby, NN intervals are distinguished from common RR intervals

(time distance between two R points in ECG) by excluding ventricular extrasystols which are caused by different processes. Further study of heart rate variability is performed statistically, e.g. calculating standard deviation (SDNN), and performing spectrum analysis by Fast Fourier Transformation. The latter leads to power spectral density (PSD) which represents distribution of variance ( $SDNN^2$ ) on variability frequencies, i.e. integrating PSD over the complete frequency range yields ( $SDNN^2$ ). Because variability frequencies are defined as small scale fluctuations in heart rate, the frequency range less than 0.5 Hz is of interest. At least there are three specific frequency domains which are affected differently by parasympathetic and sympathetic activities of the autonomous nervous system. Oscillations inside the vasomotoric system including the baroreceptor reflex is in the order

of 0.1 Hz. At higher frequencies, respiratory sinus arrhythmia (RSA) is present which is caused by interaction of the respiratory and the cardiovascular system. Regulatory systems acting on low time scales, e.g. thermoregulation, cause fluctuations in the very low frequency range which is not of interest here. Of course, it is not useful to analyse single frequencies due to insufficient resolution and overlapping of the different mechanisms but, nevertheless, two frequency intervals are found to be suitable as indicators for sympathetic and parasympathetic activities [4]. The integral of the PSD carried out over the low frequency interval from 0.04 Hz to 0.15 Hz is defined as LF-power and the integral carried out over the high frequency interval from 0.15 Hz to 0.4 Hz as HF-power respectively. While the LF-power might be affected not only but mostly by sympathetic activity, the HF-power is predominantly parasympathetic influenced [5]. Thus, we will define relative indicators for the status of the autonomous nervous system  $LF_n = LF / (LF + HF)$  and  $HF_n = HF / (LF + HF)$ . Thereby, decreasing  $LF_n$  and increasing  $HF_n$  are associated with rise in sympathetic and reduction in parasympathetic activities. Hence, from measuring the heart rate variability in CLS patients and healthy subjects it can be clarified whether the autonomous nervous system has an impact on Closed Loop Stimulation.

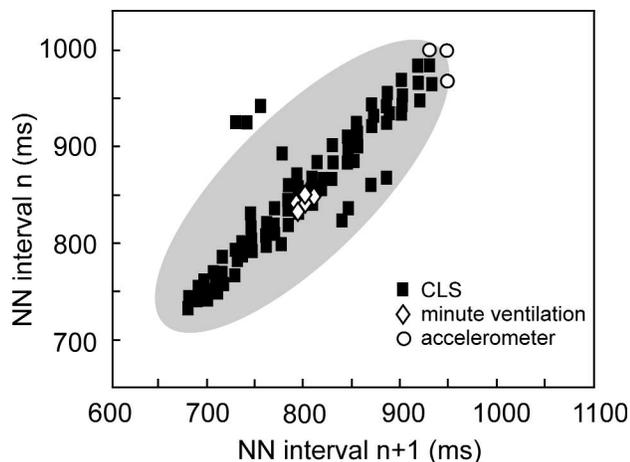


Figure 1. Plot of NN intervals (index  $n + 1$ ) versus the previous NN interval (index  $n$ ) for three different types of patients. The spread of points due to heart rate variability of the CLS patient (female, 61 years) is much more prolonged as of the accelerometer patient (male, 75 years) and the minute ventilation patient (male, 68 years).

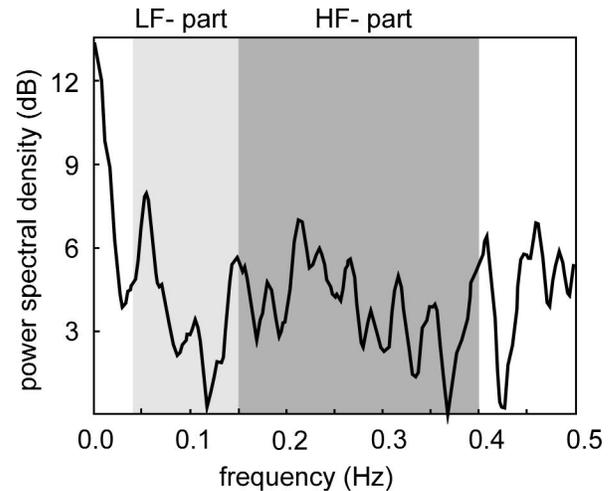


Figure 2. Power Spectral Density versus fluctuation frequency of the heart rate variability one week after automatic CLS initialization for a patient at rest.

## Methods

The investigations were performed in a group of 16 chronotropic incompetent patients with implanted CLS pacemakers (12 male, 4 female, average age  $68.1 \pm 7.4$  years) and a control group of 16 chronotropic competent subjects without pacemakers (13 male, 3 female, average age  $59.6 \pm 13.7$  years). Additionally, data of a patient (male, 75 years) with implanted accelerometer pacemaker system and a patient (male, 68 years) with implanted minute ventilation pacemaker system is included for comparison. In all the patients a high quality, 10 minute ECG was performed for the patients at rest, i.e. in horizontal position without any physical strain or mental stress due to conversation. Additionally, bicycle ergometry (10 minutes, constant load between 50-100 W according the constitution of the patient) was performed in those patients with sufficient constitution. The data regarding HRV was automatically deduced from ECG's by special software (Predictor, Dr. Kaiser Medizintechnik software), whereby VES events were excluded from the data afterwards.

## Results

Pacemakers which are not sensitive to the autonomous nervous system are expected to show negligible variations of the heart rate which is evident from Figure 1.

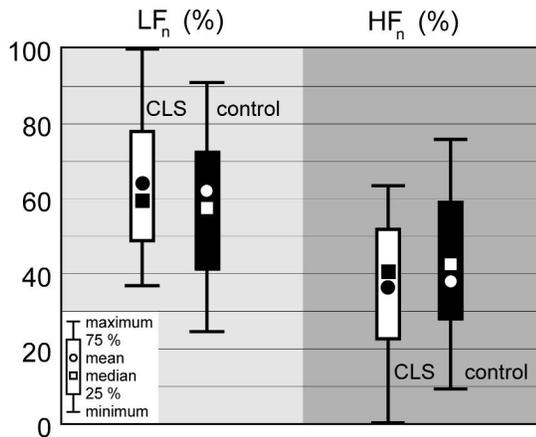


Figure 3. Statistics of normalized power spectral density HF<sub>n</sub>-part and LF<sub>n</sub>-part at rest for CLS patients (n = 16) compared with a control group (n = 16) of chronotropic competent patients without pacemakers. CLS group: mean heart rate = 68.1 ± 5.2 bpm, SDNN = 58.2 ± 43.6 ms. Control group: mean heart rate = 75.3 ± 7.2 bpm, SDNN = 31.2 ± 12.4 ms.

Closed Loop Stimulation leads to a wider spread of the heart rate variability in contrast to accelerometer or minute ventilation based pacing. Consequently, from ECG of CLS-patients the heart rate variability can be determined. Power spectral density one week after automatic CLS initialization consists of a well pronounced LF-part and HF-part (Figure 2) indicating parasympathetic and sympathetic response to the paced heart rate. Statistical analysis including all 16 CLS patients and 16 subjects from the control group are presented in Figure 3. No difference in the normalized power values was found, indicating a strong correlation of heart rate variability between Closed Loop Stimulation and sinus node functionality. In the following, measurements of 5 patients from the control group and 5 CLS patients are presented, who were able to perform the exercise ergometric test. A typical power spectrum of a patient from the control group is plotted in Figure 4a. At rest the LF-power and the HF-power are comparable whereas the main contribution comes from the LF-power when the proband is at exercise. From statistical analysis of 5 chronotropic competent patients (Figure 4b), increasing LF<sub>n</sub>-power and decreasing HF<sub>n</sub>-power from rest to exercise is obtained which is in order with sympathetic activity surmounts parasympathetic tone. The same behavior is observed in CLS-patients (Figure 5a, Figure 5b) too, whereby changes from rest to exercise are not as well pro-

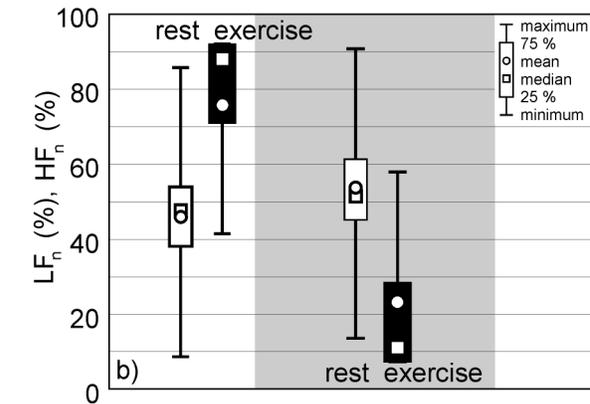
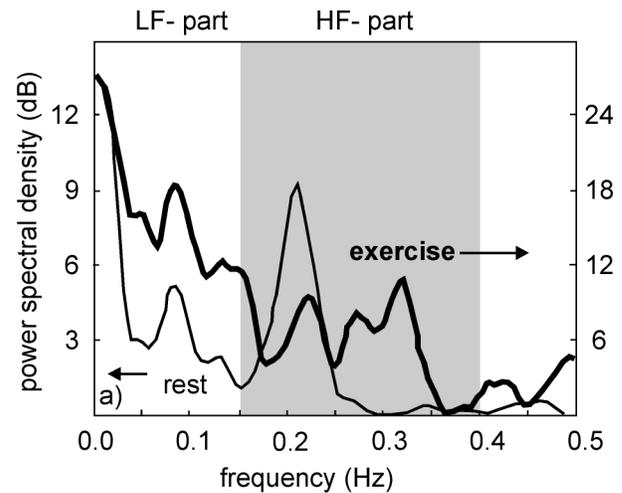


Figure 4a. Power Spectral Density versus fluctuation frequency of a control subject (male, 35 years) with intrinsic stimulation at rest and at exercise.

Figure 4b. Statistics of normalized power spectral density of 5 patients from the chronotropic competent control group at rest and at exercise.

nounced as for in the control group. This might be explained by different parasympathetic and sympathetic response to specific heart regions. Otherwise, it has to be taken into account that mean age of the control group differs from the CLS patients (Table 1), thus, lower response of the heart rate to the autonomous nervous system is expected in the older CLS-patients. At last, low statistics of n = 5 will affect the results as well. From this point of view, normalized power values, mean heart rates, and standard deviations from of CLS patients are in good agreement with patients from the control group.

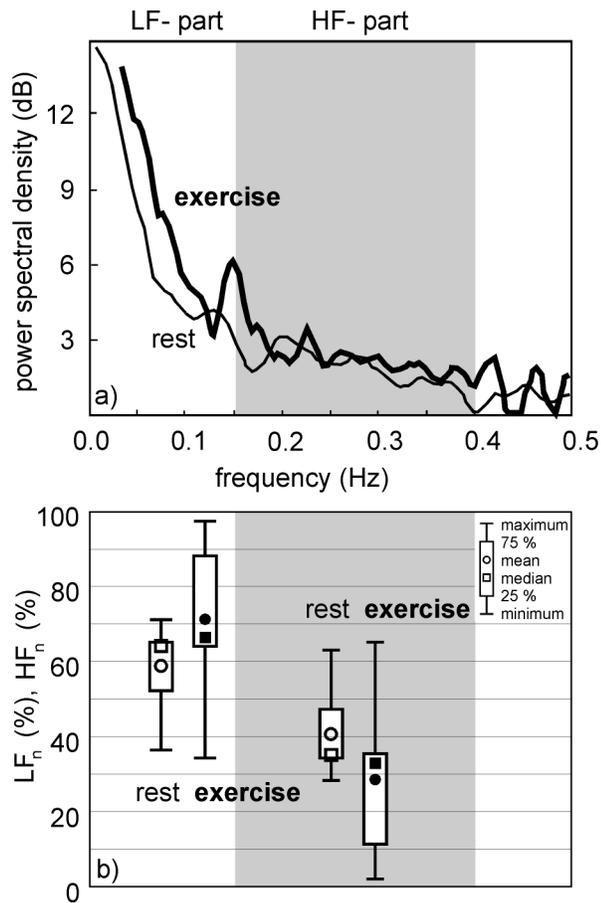


Figure 5a. Power Spectral Density versus fluctuation frequency of a CLS patient (female, 61 years) at rest and at exercise.

Figure 5b: Statistics of normalized power spectral density of 5 CLS patients at rest and at exercise.

## Conclusion

From measurements of the heart rate variability the advantage of CLS over other types of pacemakers was demonstrated. Only CLS pacing provides well pronounced variations of the heart rate due to interaction with the autonomous nervous system, which could be an indicator for a better prognosis of CLS-patients. It was shown as well that this variations are similar to those of the control group of patients without pacemakers. In both cases increasing  $LF_n$ -power and decreasing  $HF_n$ -power respectively is observed in case of physical strain due to more pronounced sympathetic than parasympathetic activity, demonstrating the strong consistency of CLS pacing to

		Control	CLS
<b>Data</b>	<b>n</b>	5	5
	<b>age (years)</b>	42.8 ± 13.3	65.5 ± 9.8
<b>Rest</b>	<b>HR (bpm)</b>	72.3 ± 5.1	66.2 ± 2.3
	<b>SDNN (ms)</b>	37.5 ± 6.2	40.2 ± 10.2
<b>Exercise</b>	<b>HR (bpm)</b>	107. ± 9.7	98.3 ± 8.7
	<b>SDNN (ms)</b>	35.1 ± 23.4	55.1 ± 12.6

Table 1. Mean values and standard deviations of CLS patients and probands in consideration at rest and at exercise.

intrinsic heart rate stimulation by the sinus node. Consequently, CLS pacemakers is shown to be part of the autonomous cardiovascular regulation of the heart and, therefore, sensitive to mental stress as well. From this result it is natural to assume that CLS pacemakers act comparably to the physiological sinus node which is the basic approach to increase the patients quality of life.

## References

- [1] Schaldach M. What is Closed Loop Stimulation? Prog Biomed Research. 1998; 3(2): 49-50.
- [2] Novak M, Hoffmann G, Schaldach M. Multi-Center Investigations with Automatically Initialized Closed Loop Stimulation - Rate Response during Daily Life and Physical Exercise Test. Prog Biomed Res. 1998; 3(3): 147-151.
- [3] Moser M, et al. Heart rate variability as a prognostic tool in cardiology. A contribution to the problem from a theoretical point of view. Circulation. 1994; 90(2): 1079-1082.
- [4] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Special Report: Heart Rate Variability. Circulation. 1996; 93(5): 1043-1061.
- [5] Löllgen H. Herzfrequenzvariabilität. Deutsches Ärzteblatt. 1999; 96(31-32): A-2029-A-2023.
- [6] Algra A, Tijssen JG, Roelandt J, Pool J, Lubsen J. Heart rate variability from 24-hour electrocardiography and the 2-year risk for sudden death. Circulation. 1993; 88: 180-185.
- [7] Malpas SC, Maling TJ. Heart-rate variability and cardiac autonomic functions in diabetes. Diabetes. 1990; 39(10):1177-81.
- [8] Baumer JH, Frey AW, Adt M. Analysis of heart rate variability. Background, method, and possible use in anesthesia. Anästhesist. 1995; 44(10): 677-687.
- [9] Berntson GG, Cacioppo JT, Quigley KS. Respiratory sinus arrhythmia: autonomic origins, physiological mechanisms, and psychophysiological implications. Psychophysiology. 1993; 30(2): 183-1969.