

Heart Rhythm Scanner Professional Edition

Comprehensive Health Assessment System

Practical Use Manual

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1. Introduction

For the past decades methods of the heart rate variability (HRV) analysis have become one of the most popular means of assessment of the autonomic nervous system (ANS) function because of their simple and very informative nature.

At this time there are well-defined standards and methodologies of using methods of HRV analysis, created special normative databases and criteria of assessment of various HRV parameters with regard to their comparison with normative ranges.

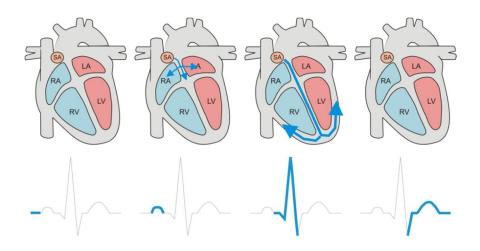
At the same time it is very important to point out that there is a tendency in specific cases to over-exaggerate diagnostic value of the assessment of results of HRV analysis when professionals attempt to use these results to make conclusions about presence or absence of certain diseases.

The above mentioned indicates that there is a need to better describe capabilities and limitations of the methods of HRV analysis.

This document is aimed to outline recommendation on how to practically use methods of HRV analysis with regard to the assessment of the autonomic nervous system function provided by Biocom Heart Rhythm Scanner Professional Edition.

2. Physiological Background

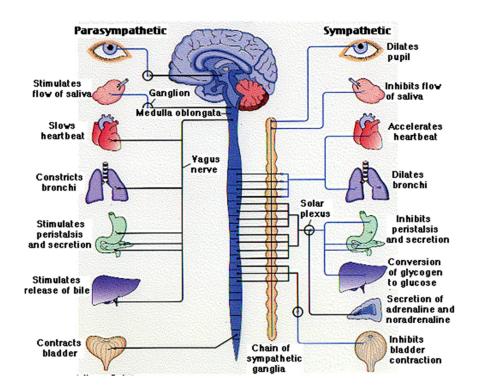
The origin of heartbeat is located in a right atrium wall of the heart, where a group of specialized cells forms so-called "sine node" that continuously generates electrical impulses spreading all over the heart muscle through specialized pathways and causing well-synchronized heart muscle contraction leading to its proper blood pumping.



The sine node generates around 100 - 120 heartbeats per minute at rest. However, healthy individuals have resting heart rate (HR) is usually much lower – around 60 - 70 beats per minute. This is due to continuous control of the autonomic nervous system (ANS) over the sine node activity.

The autonomic nervous system is a part of our nervous system responsible for non-voluntary control of our internal organs and systems like heart, lungs, intestines, glands, etc. ANS has its central (nuclei located in brain stem) and peripheral components (afferent and efferent fibers and peripheral ganglia) accessing all internal organs. There are two branches of the autonomic nervous system - sympathetic and parasympathetic (vagal) nervous systems that always work as antagonists in their effect on target organs.

For many organs increased stimulation of the sympathetic nervous system causes increase in their function, e.g. rising HR, increased heart stroke volume, adrenal secretion, etc. In contrast, increased stimulation of the parasympathetic nervous system inhibits their function. However for some other organs the effect of stimulation of the sympathetic and parasympathetic nervous system causes an opposed effect.



These specific effects serve our body as a very effective mechanism of survival by engaging in either stress ("fight or flight") or relaxation ("rest and digest") response.

Proper function of the autonomic nervous system is vital for maintaining the body in good health. Any factors affecting its function cause regulatory imbalance in the body. Repeated and prolonged negative influence of such factors may lead to persistent functional dysadaptation and development of various health conditions. This fact determines a high importance of having means to assess current body's autonomic function and degree of its failure when it occurs.

The simplest way to assess the autonomic function is to measure heart rate and perform its special analysis as described below.

A heart response time to the sympathetic stimulation is relatively slow. Upon stimulation of the sympathetic nervous system it takes about 5 seconds to start increasing HR and almost 30 seconds to reach its peak level.

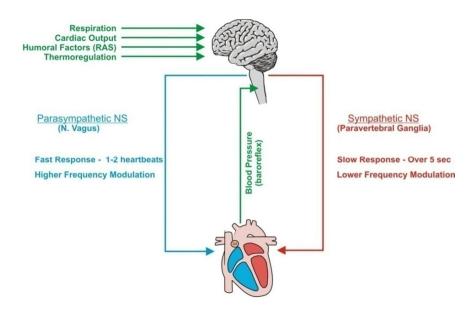
A heart response to the parasympathetic stimulation is almost instantaneous. Depending on actual phase of heart cycle, it takes just 1 or 2 heartbeats before heart slows down to its minimum level proportional to the level of stimulation.

At rest, both sympathetic and parasympathetic systems are active with moderate parasympathetic dominance. The actual balance between them is constantly changing maintaining an optimum body function.

There are various physiological factors affecting the autonomic regulation of heart rate: respiration, thermoregulation, hormonal regulation, blood pressure, cardiac output, etc. One of the most important factors is blood pressure. There are special cells in the heart and large blood vessels that sense blood pressure level and send afferent stimulation to the central structures of the ANS that control HR and blood vessel tonus forming a continuous feedback to maintain an optimal level of the blood pressure. This mechanism is also called baroreflex. It increases HR when blood pressure drops and vice versa and thus maintains a short-term stable blood supply to the vital organs.

One of the best ways to assess the autonomic function is to analyze minute changes in heart rate, which are caused by many factors including regulatory influence of the autonomic nervous system.

A special method of analysis can be applied to recorded heart rate readings. It is called Heart Rate Variability (HRV) analysis. The HRV analysis is a powerful, very accurate, reliable, reproducible, yet simple to do.



It is found that lowered HRV is associated with aging, decreased autonomic activity, hormonal tonus, specific types of autonomic neuropathies (e.g. diabetic neuropathy) and increased risk of sudden cardiac death after acute heart attack.

Other research indicated that depression, panic disorders and anxiety have negative impact on autonomic function, typically causing depletion of the parasympathetic tonus. On the other hand an increased sympathetic tonus is associated with lowered threshold of ventricular fibrillation. These two factors could explain why such autonomic imbalance caused by significant mental and emotional stress increases risk of heart attack followed by sudden cardiac death.

Aside from that, there are multiple studies indicating that HRV is quite useful as a way to quantitatively measure physiological changes caused by various interventions both pharmacological and non-

pharmacological during treatment of many pathological conditions having significant manifestation of lowered HRV.

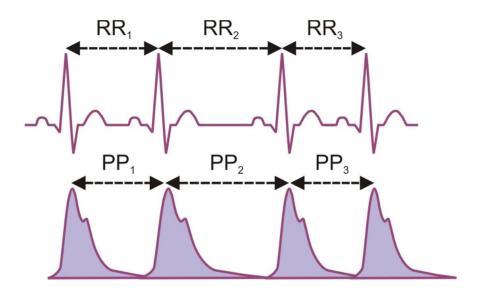
However it is important to realize that clinical implication of HRV analysis has been clearly recognized in only two medical conditions:

- 1. Predictor of risk of arrhythmic events or sudden cardiac death after acute heart attack
- 2. Clinical marker of diabetic neuropathy evolution

Nevertheless, as the number of clinical studies involving HRV in various clinical aspects and conditions grows, HRV remains one of the most promising methods of investigating general health in the future.

3. HRV Equipment

The source information for HRV analysis is continuous beat-by-beat (not averaged) recording of heartbeat intervals. There are many ways to measure and record those intervals. However two such methods are found to be the most appropriate for this.



Electrocardiograph (ECG or EKG) is considered as the best way to measure heartbeat intervals. ECG is an electrical signal reflecting minute changes in the electrical field generated by heart muscle cells. It is measured by a special electronic device with conductive electrodes placed on chest around heart area or limbs. ECG signal has a very specific and robust waveform simple to detect and analyze. Cardiac rhythm (sequence of heartbeat intervals) derived from ECG is the best way to detect normal heartbeats as well as all sorts of ectopic heartbeats, which must be excluded from the HRV analysis.

The Heart Rhythm Scanner utilizes Biocom 4000 USB and Biocom 5000 Bluetooth ECG recorders.



Biocom 4000 USB ECG Recorder



Biocom 5000 Bluetooth ECG Recorder

<u>Pulse wave</u> is another way of measuring heartbeat intervals. It is a simple and least invasive method of measurement based on photoplethysmograph (PPG). PPG is a signal reflecting changes in a blood flow in tiny blood vessels typically spotted in fingertips or earlobes. Typical PPG sensor emits infrared light towards the skin area of an earlobe or finger. The blood passing this area through numerous tiny vessels absorbs certain portion of that light while remaining light is detected by a special photocell. The amount of absorbed light is proportional to the amount of blood passing by. Since the blood flow is not constant due to pulsations caused by heartbeats the sensor generates a very specific waveform reflecting those changes in blood flow. This waveform is usually called as a pulse wave. This waveform can be processed by a special algorithm to derive beat-by-beat heartbeat intervals.

The Heart Rhythm Scanner utilizes Biocom 1200 and HRS-08WE pulse wave sensors.







HRS-08WE Pulse Wave Sensor

Refer to respective hardware setup guides for technical information and details on using these devices.

4. Assessment of the Autonomic Nervous System Function at Rest

4.1. Test Overview

The autonomic nervous system function can be evaluated with the Autonomic Balance Test.

This test is based on the short-term HRV analysis of resting heart rate recordings of 5 minutes long. Such recordings are assumed to be done at a steady-state physiological condition and should be properly standardized to produce comparable results.

According to the standards set forth by the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology in 1996, there are two methods of analysis of HRV data: time- and frequency-domain analysis. For both methods the heartbeat intervals should be properly calculated and any abnormal heartbeats found.

4.2. Cardiac Rhythm Data Recording

A new autonomic balance test should be done after fasting for at least 2 hours.

The recording must be performed in a comfortable relaxed sitting position with limiting body movements.

If patient feels physically tired due to coming to examination room, allow him/her to have a rest for 10-15 minutes before testing.

It is important to eliminate any factors which can cause emotional arousals. There is no need to specially train patients on how to be tested. However it is important to brief patient on what the test is and what to do during the test. This will help to lower patient's alertness and anxiety and establish good communication with technical personnel performing the test.

After placing a sensor (or electrodes) and starting the software (refer to the software User's Manual) the patient should be given the following instruction:

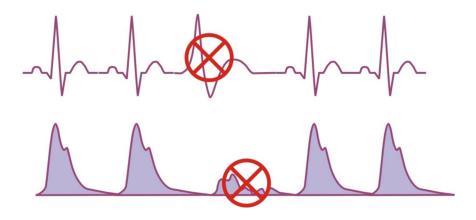
This test will last for 5 minutes. Please remain sitting relaxed and having idle thoughts. Limit your body movements. Try not to talk without a real need. If you need to swallow, do it but not very often.

4.3. Data Quality Check

It is very important to make sure that the quality of data recording is sufficient before it is interpreted.

One of the important issues when measuring either ECG or PPG is absence of any abnormal (irregular or dubious) heartbeats. Only heartbeats originated in a sine node are considered as normal (regular) heartbeats so the intervals measured between such heartbeats can be processed to obtain HRV data.

Whether there are irregular heartbeats or any signal distortions caused by movement or electrical noise which could be recognized as heartbeats, they must be excluded from analysis. There are various sophisticated statistical algorithms detecting such abnormal heartbeats filtering improper heartbeats out. Nevertheless, for the sake of accuracy of HRV analysis it is important to be able to visually verify all heartbeats that were automatically found by the software remove abnormal ones and include missing.



Use the software data verification procedure for final quality check as described in the software User's Manual.

4.4. Test Results

Once the test is recorded the following HRV parameters are calculated by the software.

4.4.1. Time-domain HRV Measures

Time-domain measures are the simplest parameters that can be calculated off 5-min recording. The following time-domain parameters are calculated:

Parameter	Unit	Description	Physiological Meaning
Mean HR	Mean HR bpm Mean heart rate value		Mean functional level of the cardiovascular system
Mean RR	ms	Mean heartbeat interval value	Same as above
SDNN	Ms	Standard deviation from the mean RR value	Net effect of the autonomic regulation on cardiovascular function
RMS-SD Ms Root mean square of the standard deviation		•	Activity level of the parasympathetic regulatory function
pNN50 % Percentage of heartbeat intervals differing more than 50 ms from previous intervals		1	Index of dominance of the parasympathetic regulatory function over the sympathetic function
TI a.u. Tension Index		Tension Index	Index of functional strain of the autonomic regulatory mechanisms primarily caused by mental stress factors
Mean BVP	a.u.	Mean blood volume pulse value	Indicator of arterial tonus caused by sympathetic regulatory influence
BVP SD a.u. Standard deviation from the mean blood volume pulse value			Indicator of baroreflex activity

4.4.2. Frequency-domain HRV Measures

A power spectrum analysis is applied to a 5-min sequence of normal heartbeat intervals. The following frequency-domain parameters are calculated:

Parameter	Unit	Description	Physiological Meaning
of RR intervals calculated fo		Total Power – a power spectrum of RR intervals calculated for a frequency range from 0.0033 Hz to 0.4 Hz.	Net effect of the autonomic regulation on cardiovascular function
VLF	ms^2/Hz	Very Low Frequency - a power spectrum of RR intervals calculated for a frequency range	The physiological meaning of this band is most disputable. With longer recordings, it is considered to represent sympathetic

Parameter	Unit	Description	Physiological Meaning
		from 0.0033 Hz to 0.04 Hz.	tone as well as slower hormonal and thermoregulatory effects. There are some findings indicating that in shorter recordings VLF has fair representation of various mental stress factors (negative emotions, worries, rumination etc.)
LF	ms^2/Hz	Low Frequency - a power spectrum of RR intervals calculated for a frequency range from 0.04 Hz to 0.15 Hz.	Sympathetic regulatory tone with some contribution of the parasympathetic tone.
HF	ms^2/Hz	High Frequency - a power spectrum of RR intervals calculated for a frequency range from 0.15 Hz to 0.4 Hz.	Parasympathetic (vagal) regulatory tone and fluctuations caused by spontaneous breathing (aka respiratory sinus arrhythmia)
LF/HF Ratio	a.u.	Low Frequency to High Frequency Ratio – a ratio between powers spectrums calculated for a low frequency and high frequency ranges.	Balance between sympathetic and parasympathetic tone. A decrease in this score might indicate either increase in parasympathetic or decrease in sympathetic tone. It must be considered together with absolute values of both LF and HF to determine what factor contributes in autonomic imbalance.
LF norm	%	Normalized Low Frequency - a percentage of the power spectrum of RR intervals calculated for a low frequency range to the total power spectrum less VLF: LF norm = LF / (TP – VLF) * 100%	Relative level of the sympathetic regulatory tone
HF norm	%	Normalized High Frequency - a percentage of the power spectrum of RR intervals calculated for a high frequency range to the total power spectrum less VLF:	Relative level of the parasympathetic regulatory tone

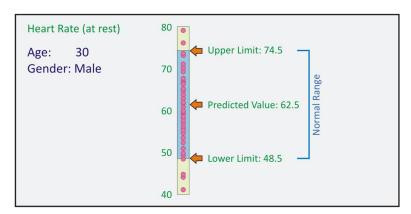
Parameter	Unit	Description	Physiological Meaning
		HF norm = HF / (TP – VLF) * 100%	

4.5. Evaluation of the Autonomic Balance Test Results

To make a conclusion on the test results actual readings of all HRV parameters are compared with their respective normal ranges specific to patient's age and gender. These normal ranges are taken from a normative database built in a special clinical study on a large pool of clinically validated healthy subjects.

Normal range is a range of values of certain HRV parameter representing statistical distribution of this parameter values in a large population of healthy individuals of selected age and gender. For instance, the logarithmic value of HF (ms^2/Hz) lies in range between 2.5 and 6.6 for males between 30 and 40 years old. Evidently comparing the actual value of evaluated parameter with its normative range gives only a ballpark assessment of its status.

The most appropriate way to assess the autonomic nervous system function is to use so-called predicted values defining normal values of specific HRV parameters, which we expect to obtain from a tested individual if we assume that this individual is healthy. Predicted value is a statistically most probable value of the parameter predicted based on correlation between this parameter values, age and gender of healthy individuals. Predicted values are calculated by the formulae created based on a special study obtained reading s from a large population of healthy subjects of different ages and gender.



The following example explains how to compare actual and predicted values of a specific HRV parameter and shows the problems which may arise when doing that.

Example. A 48 years old male was tested with an autonomic balance test. The test results showed an HF parameter value of 3.1 on logarithmic scale of ms²/Hz. A predicted value for 48 years old males is 4.03. Evidently the HF parameter is noticeably lower than its predicted value. But what does this mean? Is this

decrease significant and thus can be considered as abnormal or is it still normal? The answer to this could be given if we can find statistically significant boundaries of a certain range of values considered as a normal range for this parameter.

One of the widely used approaches is determining a normal range based on criteria of statistical distribution of measured parameter values in healthy subjects. Typically normal range is considered within 95% of the interval of confidence in both directions. This range would fit 95% of all readings obtained from healthy subjects of the selected population.

It is important to mention that there is a borderline zone (or conditional norm) in near proximity to the borders of the normal range. Actual readings falling into this zone have higher risk to be abnormal ones.

The above illustration shows how the predicted value and normal range are defined in the normative database. All test results of the healthy subjects tested in a special epidemiologic study were analyzed by separate gender and age groups. For example, all test results of all males of age 30 were put in one group. Predicted values for each HRV parameter were calculated as described above. Then all parameter values (in this example – mean heart rate) were grouped around the predicted values. 5% of the values most deviating from the predicted value are considered as outlying (outside of the normal range). The rest 95% of all values define the normal range.

The Heart Rhythm Scanner considers 15% of the most deviating values among those falling into 95% range as borderline range. Only remaining 80% of all values forms a true normal range used to form an interpretive Autonomic Balance diagram described below.

For the subject described in this example a lower borderline level of HF parameter is 2.64. Thus the value shown in the example above falls into a borderline zone.

When using the Heart Rhythm Scanner to monitor the dynamics of changes in the autonomic regulatory function or to evaluate the effects of specific factors on this function an important question is usually asked – if the changes in a measured parameter are considered significant or are result of normal variation of the random process. This question is answered based on assessment of the reproducibility and repeatability of the measured parameter.

Reproducibility is a variance of a parameter being repeatedly measured in the same subject within a limited time frame. Repeatability reflects natural variance of a specific parameter in the same subject observed during a long period of time (several weeks).

HRV parameters significantly depend on current condition of the subject at a time of testing. Thus it is virtually impossible to obtain absolutely identical readings measured at different moments. This means that the reproducibility and repeatability of the test cannot be 100%. High level of reproducibility and repeatability means only qualitative similarity of any two test results obtained from the same individual at substantially similar conditions of both subject and testing environment. When comparing test results, keep in mind that the autonomic nervous system is fairly sensitive to many internal and external factors including various genetically predetermined and transitory factors, health condition, etc.

4.6. Making an Assessment Conclusion on the Autonomic Balance Test

Based on the results of the autonomic balance test an assessment summary is generated consisting the following parts:

- 1. Prevailing Heart Rhythm
- 2. Heart Rhythm Disturbances
- 3. Autonomic Function Condition

4.6.1. Prevailing Heart Rhythm

A prevailing heart rhythm is determined based on comparing an actual mean heart rate to its predicted value.

Here is the list of possible heart rhythms:

	Result	Interpretation
1	HR is below normal range	Bradycardia – resting heart rate is lower than normal.
2	HR is within normal range	Normocardia – resting heart rate is within normal range.
3	HR is above normal range	Tachycardia – resting heart rate is higher than normal.

4.6.2. Heart Rhythm Disturbances

Heart rhythm disturbances are determined based on percentage of the number of ectopic heartbeats to the total number of all heartbeats recorded.

Here is the list of possible heart rhythm disturbances:

	Percentage of abnormal cardio intervals	Interpretation
1	0%	No heart rhythm disturbances detected

	Percentage of abnormal cardio intervals	Interpretation
2	Less than 5%, single episodes	Occasional ectopic heartbeats or other minor disturbances due to possible body movements. No significant effect on quality of assessment.
3	Less than 5%, contiguous series of abnormal intervals	Non-persistent series of ectopic heartbeats or other disturbances due to possible significant body movements. Quality of assessment maybe questionable.
4	Over 5%, single episodes	Persisting ectopic heartbeats or other disturbances due to possible body movements. Check signal waveform. Autonomic assessment cannot be completed in case of persistent ectopic heartbeats.
5	Over 5%, contiguous series of abnormal intervals	Major heart rhythm disturbances due to possible movement activity, poor quality of the signal or heart rhythm failure. Check signal waveform. Autonomic assessment cannot be completed in case of rhythm failures.

4.6.3. Autonomic Function Condition

The Heart Rhythm Scanner makes an assessment of the autonomic nervous system regulatory function condition based on two variables:

Autonomic Balance A ratio between levels of the sympathetic and parasympathetic activity.

Autonomic Tonus A net level of the sympathetic and parasympathetic activity.

There are three main types of the autonomic nervous system conditions:

- 1. **Predominant parasympathetic nervous system function** typical for a state of relaxation.
- 2. **Predominant sympathetic nervous system function** typical for a state of stress.
- 3. **Balanced autonomic nervous system function** typical for an idle calm state.

Each of these three categories may have three different levels of the autonomic tonus: **low**, **normal** or **high**.

The **Autonomic Balance** is calculated in points based on 80% of least deviated values of HRV parameters in the normative database. It ranges from -10 points to +10 points. The following chart describes interpretive meaning of specific point ranges of the Autonomic Balance:

Points	Autonomic Balance
-108	Significant predominance of parasympathetic regulation
-76	Moderate predominance of parasympathetic regulation
-54	Slight predominance of parasympathetic regulation
-32	In balance
-1 +1	In good balance
+2 +3	In balance
+4 +5	Slight predominance of sympathetic regulation
+6 +7	Moderate predominance of sympathetic regulation
+8 +10	Significant predominance of sympathetic regulation

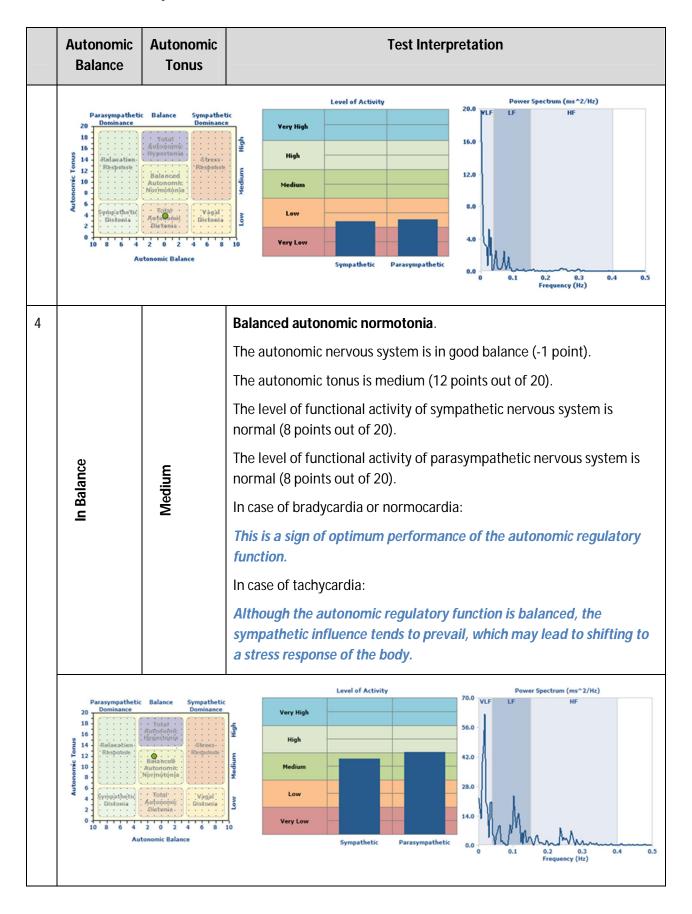
The **Autonomic Tonus** is calculated in points based on 80% of least deviated values of HRV parameters in the normative database. It ranges from 0 points to +20 points. The following chart describes interpretive meaning of specific point ranges of the Autonomic Tonus:

Points	Autonomic Tonus
0 3	Significantly low
4 6	Slightly low
7 13	Medium (Normal)
14 16	Slightly high
17 20	Significantly high

Below is a detailed description of all 7 possible combinations of these two variables:

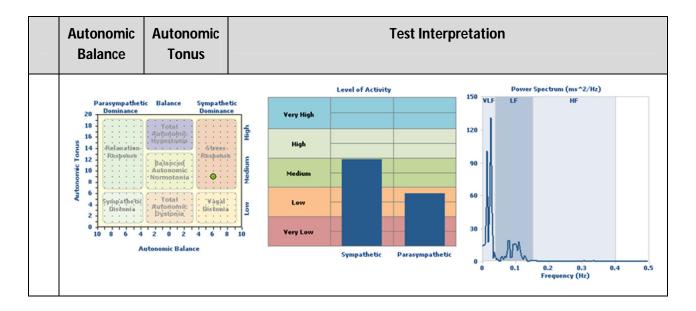
	Autonomic Balance	Autonomic Tonus	Test Interpretation
The level of functional activity than normal (4 points out of 20). This may be a sign of acceleration overwork, lack of sleep or positive.		Low	The autonomic nervous system is out of balance (-4 points) with slight predominance of parasympathetic regulation. The autonomic tonus is slightly low (4 points out of 20). The level of functional activity of sympathetic nervous system is lower than normal (4 points out of 20). The level of functional activity of parasympathetic nervous system is normal (8 points out of 20). This may be a sign of accelerated aging, chronic mental fatigue, overwork, lack of sleep or possible presence of any chronic health condition causing a decreased regulatory function of the sympathetic
	Parasympathetic Dominance 18 16 16 Relaxation 00 12 Response 00 8 Sympathetic Distonia 2 10 10 8 6 Au	Balance Sympather Dominance Total Autonomic Hypertonia Stress Raspools Autonomic Normotonia Total Autonomic Dystonia Dystonia Dystonia Balance 2 0 2 4 6 8	Yery High High Medium Low 2.00

_	Autonomic Balance	Autonomic Tonus	Test Interpretation
2	Responsible to the control of the co	Total Autonomic Hypestonia Stress Response Autonomic Normotonia Total Autonomic Normotonia Upstonia Distonia Distonia	Relaxation response. The autonomic nervous system is out of balance (-5 points) with slight predominance of parasympathetic regulation. The autonomic tonus is medium (13 points out of 20). The level of functional activity of sympathetic nervous system is normal (8 points out of 20). The level of functional activity of parasympathetic nervous system is higher than normal (15 points out of 20). This may be a sign of achieving mentally / physically restful condition and good relaxation. Power Spectrum (ms^2/Hz) Wery High High Hedium Description of Activity Parasympathetic Parasympathetic Parasympathetic Parasympathetic Parasympathetic Parasympathetic Parasympathetic Parasympathetic Parasympathetic Power Spectrum (ms^2/Hz) Power Spectrum (ms^2/Hz) Power Spectrum (ms^2/Hz) Parasympathetic Parasympathetic
3	In Balance	Low	Total autonomic dystonia. Although the autonomic nervous system is in good balance (0 points), the autonomic tonus is slightly low (4 points out of 20). The level of functional activity of sympathetic nervous system is lower than normal (2 points out of 20). The level of functional activity of parasympathetic nervous system is lower than normal (2 points out of 20). This may be a sign of accelerated aging process, physical or mental fatigue, chronic stress, possible presence of any chronic health condition associated with depressed regulatory function of the autonomic nervous system.



	Autonomic Balance	Autonomic Tonus	Test Interpretation
5	In Balance	High	Total autonomic hypertonia. The autonomic nervous system is in balance (-2 points). The autonomic tonus is slightly high (14 points out of 20). The level of functional activity of sympathetic nervous system is higher than normal (15 points out of 20). The level of functional activity of parasympathetic nervous system is higher than normal (15 points out of 20). In case of bradycardia or normocardia: This is a sign of high level of performance of the autonomic regulatory function, which is typical for active healthy individuals, athletes and other trained people. In case of tachycardia: Although the autonomic regulatory function is balanced at higher level, the sympathetic influence tends to prevail, which may lead to shifting to a stress response of the body.
	Parasympathetic Dominance 18 16 16 17 18 18 18 18 18 18 18 19 19 10 10 10 10 10 10 10 10 10 10 10 10 10	Total Autonomic Dystonia Total Autonomic Normotoria Total Autonomic Dystonia 2 0 2 4 6 8 utonomic Balance	Very High High High Low 100

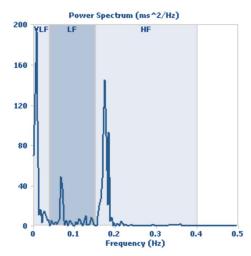
	Autonomic Balance	Autonomic Tonus	Test Interpretation
6	Sympathetic Dominance	Low	Vagal dystonia. The autonomic nervous system is out of balance (+4 points) with slight predominance of sympathetic regulation. The autonomic tonus is significantly low (2 points out of 20). The level of functional activity of parasympathetic nervous system is lower than normal (2 points out of 20). This may be a sign of physical or mental fatigue, chronic stress, possible presence of any chronic health condition causing a decreased regulatory function of the parasympathetic nervous system.
	Parasympathetic Dominance 18 16 18 16 14 Relacation Physics Control Physics C	C Balance Sympathe Dominance Total Autohomic Hypertonia Stress Balanced Autonomic Normotomia Vägal Autohomic Distonia Dystonia Dystonia Balance	Wedium Low 12.0 146H High 9.0 6.0
7	Sympathetic Dominance	Medium or High	Stress response. The autonomic nervous system is out of balance (+6 points) with moderate predominance of sympathetic regulation. The autonomic tonus is medium (9 points out of 20). The level of functional activity of sympathetic nervous system is higher than normal (15 points out of 20). The level of functional activity of parasympathetic nervous system is normal (8 points out of 20). This may be a sign of physical or mental stress or presence of any acute health issue causing the sympathetic nervous system function to increase.



There are typical patterns of the cardiac rhythm graph specific to each type of the autonomic nervous system function condition:

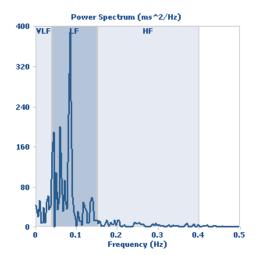
Parasympathetic dominance

Power spectrum graph of RR intervals shows prevailing energy distribution (most significant peaks) in the higher frequency range:



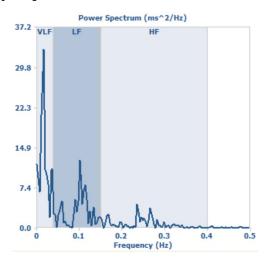
Sympathetic dominance

Power spectrum graph of RR intervals shows prevailing energy distribution (most significant peaks) in the lower frequency range:



Autonomic balance

Power spectrum graph of RR intervals shows equal energy distribution (most significant peaks) if both lower and higher frequency ranges:

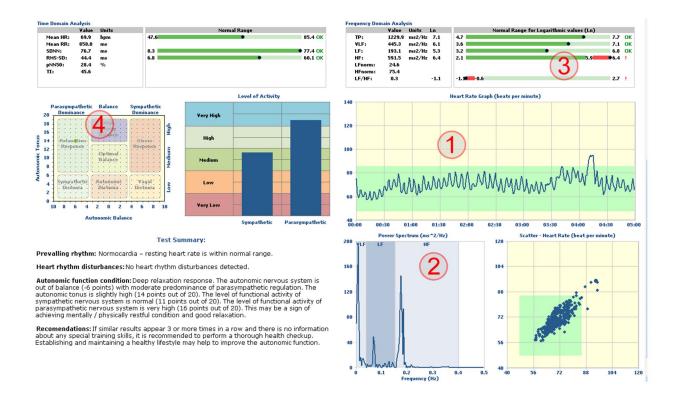


Below are a few typical samples of the autonomic assessments.

4.6.4. Typical Examples

Case 1: Relaxation Response

Patient – J.O., 48 years old male. The following picture shows his autonomic balance assessment report.



Pay attention to the following moments:

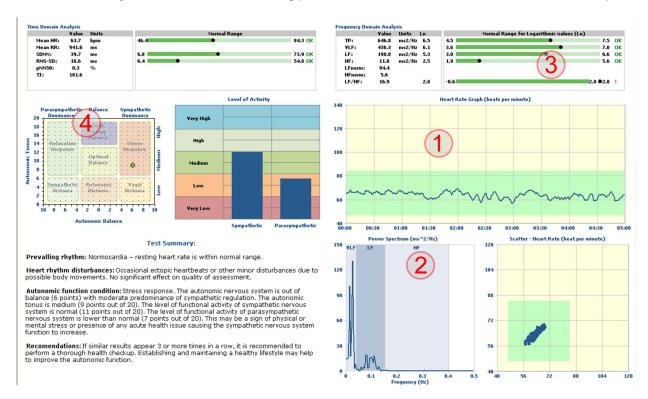
- 1) The heart rate graph (medium right segment of the report page) shows **a lot of distinctive high amplitude high-frequency waves** (aka respiratory sinus arrhythmia).
- 2) The power spectrum graph (bottom center segment of the report page) shows **prevailing spikes in the higher frequencies (HF) range** comparing to the lower frequencies (LF) range.
- 3) The numerical chart (top right segment of the report page) shows that **LF/HF Ratio parameter** value is very low (-1.1), which is below the lower boundary of its normal range (-0.6).
- 4) The autonomic balance diagram (medium left segment of the report page) shows that the resulting "dot" is located in the "Relaxation response" segment, which reflects parasympathetic dominance at the normal level of the autonomic tonus.

All these facts are typical signs of the parasympathetic dominance, which may be a sign of achieving mentally / physically restful condition and good relaxation.

Thus the assessment conclusion shown on this report page corresponds to the **Type 2** of the autonomic balance condition shown in the table above.

Case 2: Stress Response

Patient – M.F., 58 years old male. The following picture shows his autonomic balance assessment report.



Pay attention to the following moments:

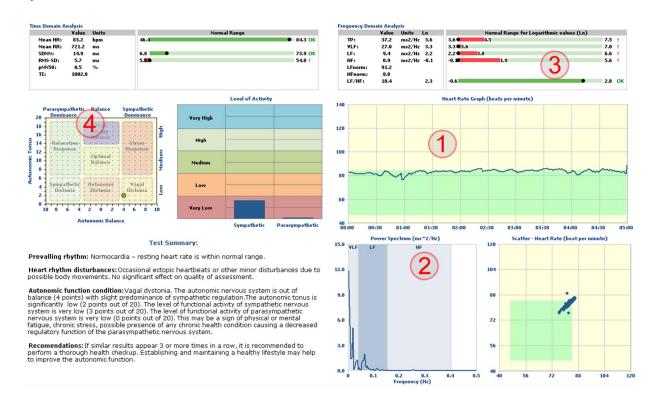
- 1) The heart rate graph (medium right segment of the report page) shows a **lot of distinctive low-frequency waves**, which are typical patterns of sympathetic arousals.
- 2) The power spectrum graph (bottom center segment of the report page) shows **prevailing spikes in the lower frequencies (LF) range** comparing to the higher frequencies (HF) range.
- 3) The numerical chart (top right segment of the report page) shows that **LF/HF Ratio parameter value is high** (+2.8), which is above the upper boundary of its normal range (+2.7).
- 4) The autonomic balance diagram (medium left segment of the report page) shows that the resulting "dot" is located in the "Stress response" segment, which reflects sympathetic dominance at the normal level of the autonomic tonus.

All these facts are typical signs of the sympathetic dominance, which may be a sign of physical or mental fatigue, chronic stress, possible presence of any chronic health condition causing a decreased regulatory function of the parasympathetic nervous system.

Thus the assessment conclusion shown on this report page corresponds to the **Type 8** of the autonomic balance condition shown in the table above.

Case 3: Vagal Dystonia

Patient – S.V., 54 years old female. The following picture shows her autonomic balance assessment report.



Pay attention to the following moments:

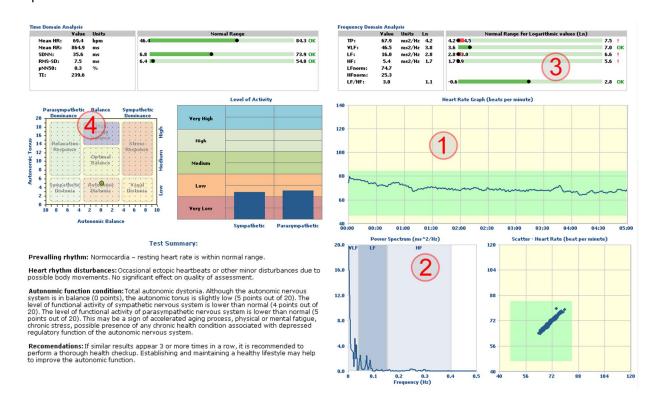
- 1) The heart rate graph (medium right segment of the report page) shows **very low amplitude high-frequency waves and higher amplitude low-frequency waves**, which is an indication of inhibited parasympathetic activity.
- 2) The power spectrum graph (bottom center segment of the report page) shows **prevailing spikes** in the lower frequencies (LF) range however their amplitude is rather low.
- 3) The numerical chart (top right segment of the report page) shows that **LF/HF Ratio parameter value is high** (+2.3), which is close the upper boundary of its normal range (+2.8). However the HF parameter value is extremely low (-0.1), which is far less than the lower boundary of its normal range (+1.9).
- 4) The autonomic balance diagram (medium left segment of the report page) shows that the resulting "dot" is located in the "Vagal Dystonia" segment, which reflects sympathetic dominance at the low level of the autonomic tonus primarily due to a significant decrease in parasympathetic function.

All these facts are typical signs of physical or mental fatigue, chronic stress, possible presence of any chronic health condition causing a decreased regulatory function of the parasympathetic nervous system.

Thus the assessment conclusion shown on this report page corresponds to the **Type 7** of the autonomic balance condition shown in the table above.

Case 4: Total Autonomic Dystonia

Patient – A.S., 49 years old female. The following picture shows her autonomic balance assessment report.



Pay attention to the following moments:

- 1) The heart rate graph (medium right segment of the report page) shows **extremely low amplitude in both high-frequency and low-frequency waves**, which is an indication of inhibited parasympathetic as well as sympathetic activity.
- 2) The power spectrum graph (bottom center segment of the report page) shows very low amplitude spikes in the lower frequencies (LF) range and no spikes in the higher frequencies (HF) range.

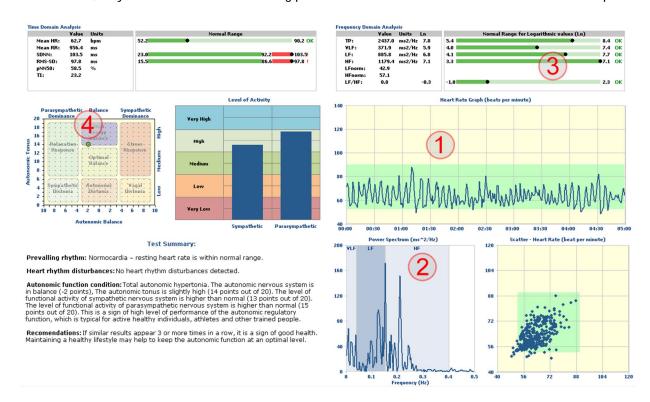
- 3) The numerical chart (top right segment of the report page) shows that **LF/HF Ratio parameter value is within normal ranges** (+1.1), which is an indication of a balance between sympathetic and parasympathetic nervous systems. However the HF parameter value (+1.7) is less than the lower boundary of its normal range (+1.9) and the LF parameter value (+2.8) is less than the lower boundary of its normal range (+3.0). This is an indication of inhibited activity of both sympathetic and parasympathetic nervous systems.
- 4) The autonomic balance diagram (medium left segment of the report page) shows that the resulting "dot" is located in the "Autonomic Dystonia" segment, which reflects total inhibition of the autonomic regulatory function.

All these facts are typical signs of accelerated aging process, physical or mental fatigue, chronic stress, possible presence of any chronic health condition associated with depressed regulatory function of the autonomic nervous system.

Thus the assessment conclusion shown on this report page corresponds to the **Type 4** of the autonomic balance condition shown in the table above.

Case 5: Total Autonomic Hypertonia

Patient – J.P., 20 years old male. The following picture shows his autonomic balance assessment report.



Pay attention to the following moments:

- 1) The heart rate graph (medium right segment of the report page) shows significantly high amplitudes in both high-frequency and low-frequency waves, which is an indication of a very high level of both parasympathetic and sympathetic activity.
- 2) The power spectrum graph (bottom center segment of the report page) shows many high amplitude spikes in the lower frequencies (LF) range as well as in the higher frequencies (HF) range.
- 3) The numerical chart (top right segment of the report page) shows that LF/HF Ratio parameter value is within normal ranges (-0.3), which is an indication of a balance between sympathetic and parasympathetic nervous systems. However the HF parameter value (+7.1) is at the higher boundary of its normal range (+7.1) and the LF parameter value (+6.8) is slightly below the higher boundary of its normal range (+7.1). This is an indication of increased activity of both sympathetic and parasympathetic nervous systems.
- 4) The autonomic balance diagram (medium left segment of the report page) shows that the resulting "dot" is located in the "High Energy Balance" (synonym to "Total Autonomic Hypertona") segment, which reflects significantly increased and balanced level of the autonomic regulatory function.

All these facts are typical signs of high level of performance of the autonomic regulatory function, which is typical for active healthy individuals, athletes and other trained people.

Thus the assessment conclusion shown on this report page corresponds to the **Type 6** of the autonomic balance condition shown in the table above.

These examples show that autonomic balance assessment reports include the following important data:

- 1. Absolute values of the assessed parameters
- 2. Their comparison with respective predicted values and normal ranges
- 3. Level of activity of the parasympathetic and sympathetic nervous systems on the scale:

VERY LOW significantly lower than normal LOW – lower than normal
MEDIUM – normal
HIGH – higher than normal
VERY HIGH – significantly higher t

significantly higher than normal

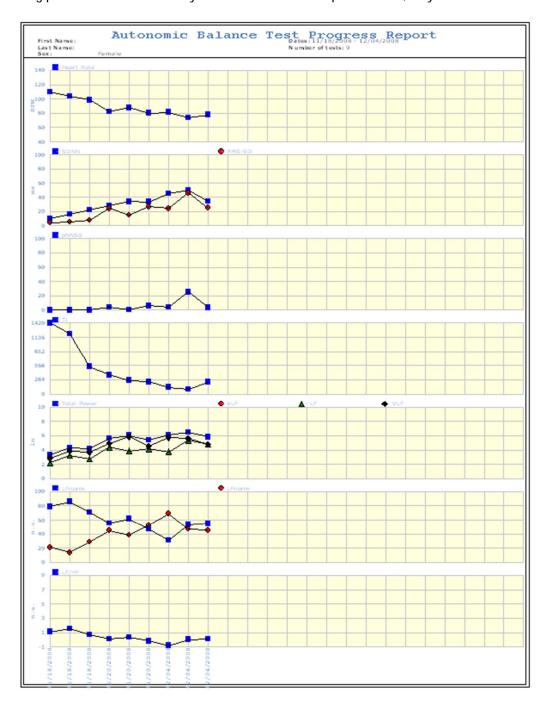
4. Visual and verbal interpretation of the status of the autonomic balance and its activity level.

In case of significant deviation of any parameters from their normal ranges the assessment reports gives recommendations to perform additional health checkup to discover potential health problems.

4.7. Assessment History

The Heart Rhythm Scanner system keeps records of all assessment of each kind and gives ability to review entire history of assessments of a patient and thus evaluate the effect of administered treatment.

The following picture shows the history of assessments of the patient N.P., 48 years old female.



This chart clearly shows positive effects of a special diet and exercise program prescribed to the patient as a part of her treatment of hypertension and obesity. Particularly the following tendencies can be seen:

- 1. Resting heart rate is decreasing.
- 2. Overall autonomic regulatory activity (SDNN, Total Power) is increasing.
- 3. Tension Index (TI) is decreasing.
- 4. Both sympathetic (LF) and parasympathetic activity (HF, RMS-SD) levels are increasing from their initial very low levels.
- 5. Shift from a significant autonomic imbalance (dominant sympathetic activity (LFnorm) over parasympathetic activity (HFnorm) at the beginning to a fairly well-balanced state at the end.

5. Assessment of Cardiovascular Functional Reserve and Adaptation Capacity

5.1. Test Overview

It is well-known that orthostatic challenge test is one of the most informative methods used to detect subtle changes in cardiovascular function and specifically its regulatory mechanisms. It helps to assess the ability of both sympathetic and parasympathetic nervous systems to adequately respond to regulatory challenge caused by gravitational shift in the body's blood mass. When body's position is changed from supine or sitting to standing, specific changes in heart rate and blood pressure happen as a compensatory reaction of the body. This standup maneuver as well as keeping a standing posture within several minutes does not cause any significant physical exertion to a healthy individual. However if body's regulatory mechanisms do not have adequate functional capacity or there is subtle cardiovascular deficiency then this maneuver becomes a significant stressor to the body.

5.2. Physiological Background

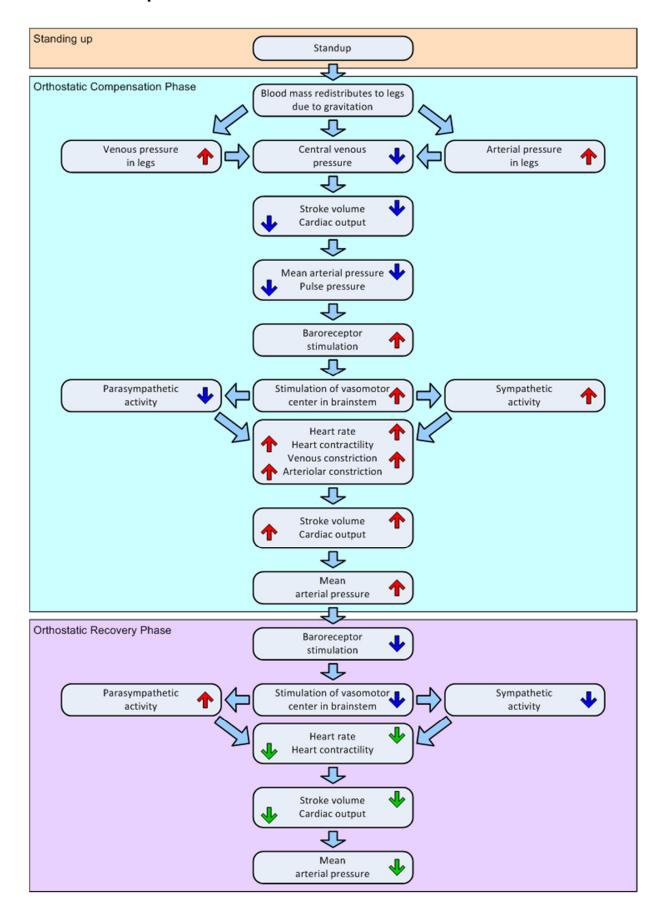
The diagram below describes a physiological process that occurs during the standup maneuver. This process includes two phases.

An Orthostatic Compensation Phase

Changing a body posture to standing causes blood mass to rush down to lower extremities due to gravitational pull. This causes an increase in arterial and venous pressure in the lower body and decrease in blood mass returned to the heart. Therefore the central venous pressure drops causing decrease in stroke volume and respectively cardiac output. Less blood is pumped into the large arteries so mean arterial pressure drops.

In response to decreased blood pressure in large arteries an internal regulatory mechanism turns on to avoid dizziness or even passing out due to a limited blood supply of the brain. The main goal of this mechanism is to bring mean blood pressure to normal as soon as possible and compensate blood supply of the vital organs.

A key part of this mechanism is called baroreflex. There are special baroreceptors located in the aortic arch wall and both carotid arteries, which continuously sense any changes in mean arterial pressure. Once mean pressure drops due to standing up, baroreceptors' stimulation increases so they begin sending signals to vasomotor center located in the brainstem. Increased stimulation of this center causes immediate drop in parasympathetic tonus and rapid increase in sympathetic tonus.



An increased sympathetic stimulation causes skeletal muscles to constrict and thus squeeze blood from over expanded veins and return it to the heart. At the same time a combination of decreased parasympathetic tonus and increased sympathetic tonus causes rapid increase in heart rate, contractility of the heart muscle and peripheral arterial vasoconstriction. This all leads to increasing of the stroke volume, cardiac output and mean arterial pressure. Thus the body achieves compensation of the cardiovascular deficiency caused by standup maneuver.

An Orthostatic Recovery Phase

Once the compensation has been achieved, the body begins a recovery process trying to find a balance in a new standing condition. The organism tries to gradually find a new equilibrium lowering heart rate, stroke volume and arterial blood pressure without compromising an adequate blood supply to the vital organs.

The increased level of mean arterial pressure lowers stimulation of baroreceptors, which reduces stimulation of vasomotor center in the brainstem and causes increase in parasympathetic activity and decrease in sympathetic activity. This finally leads to gradual decrease of heart rate and contractility, which reduces stroke volume, cardiac output and mean arterial pressure to the level adequate to new body condition.

The above said shows the complexity of the regulatory processes occurring in the body caused by standup maneuver. The efficiency of these regulatory mechanisms affects the ability of the body to adapt adequately to the demands of surrounding environment. Various types of pathologies cause negative impact on these regulatory mechanisms in first hand thus it is hard to overestimate the significance of assessing cardiovascular regulatory capability.

As stated above, the autonomic nervous system and specifically the sympathetic and parasympathetic nervous systems form the most essential part of this regulatory mechanism. Thus it is important to evaluate how both systems respond to a standup maneuver. There is a very accurate yet simple way to do that – the heart rate variability analysis (HRV). HRV is a powerful, very accurate, reliable, reproducible, yet simple method of assessment of the autonomic nervous system.

5.3. Recording Test Data

A new cardiovascular health test should be done after fasting for at least 2 hours.

The recording must be performed in a comfortable relaxed sitting position with limiting body movements.

If patient feels physically tired due to coming to an examination room, allow him/her to have a rest for 10-15 minutes before testing.

It is important to eliminate any factors which can cause emotional arousals. There is no need to specially train patients on how to be tested. However it is important to brief patient on what the test is and what

to do during the test. This will help to lower patient's alertness and anxiety and establish good communication with technical personnel performing the test.

After placing a sensor (or electrodes) and starting the software (refer to the software User's Manual) the patient should be given the following instruction:

The duration of this test is 11 minutes. For the first 5 minutes, please, remain sitting relaxed and having idle thoughts. Then upon a special command please slowly stand up and remain standing for another 6 minutes. Try to avoid any movements during the test when sitting or standing. Try not to talk without a real need. If you need to swallow, do it but not very often.

It is very important to make sure that the quality of data recording is sufficient before it is interpreted. Please refer to Section 4.3 for more details.

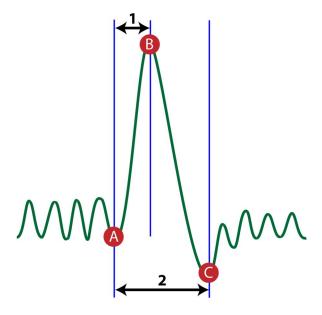
5.4. Test Results

Once the test is recorded the following HRV parameters are calculated by the software.

5.4.1. HRV Measures of a Standup Maneuver

The Standup Maneuver Analysis calculates specific HRV parameters describing physiological response of the cardiovascular system to the standup maneuver when body's position is being changed from sitting to standing position.

The following illustration will help to better understand the nature of HRV parameters calculated here:



The following parameters are calculated:

Parameter	Unit	Description	Physiological Meaning
30:15 Ratio	a.u.	Ratio between maximum heart rate within the first 15 seconds after standing up and minimum heart rate within the first 30 seconds after standing up (HR _B / HR _C).	One of the key indicators of the autonomic function showing regulatory capacity of the parasympathetic nervous system.
HR max	bpm	Maximum heart rate after standing up (HR_B).	When compared to resting HR (baseline), it reflects cardiovascular response to a standard physical exertion (standup maneuver) as a result of sympathetic stimulation.
HR min	bpm	Minimum heart rate after standing up (HR _c).	When compared to resting HR (baseline), it reflects cardiovascular reaction after a standard physical exertion (standup maneuver) as a result of compensatory parasympathetic stimulation.
Time HR max	Sec	Time to achieve maximum heart rate after standing up (time interval #1).	It reflects cardiovascular response time to a standard physical exertion (standup maneuver) as a result of sympathetic stimulation.
Time HR min	sec	Time to achieve minimum heart rate after standing up (time interval #2).	It reflects cardiovascular compensatory reaction time after a standard physical exertion (standup maneuver).

5.4.2. HRV Measures in Sitting and Standing Positions

Two sets of standard short-term HRV parameters are calculated for the first 5 minutes of data recorded in a sitting position and the last 5 minutes of data recorded in a standing position:

Parameter	Unit	Description	Physiological Meaning
Mean HR	bpm	Mean heart rate value	Mean functional level of the cardiovascular system

Mean RR	ms	Mean heartbeat interval value	Same as above
SDNN	ms	Standard deviation from the mean RR value	Net effect of the autonomic regulation on cardiovascular function
RMS-SD	ms	Root mean square of the standard deviation	Activity level of the parasympathetic regulatory function
ТР	ms^2/Hz	Total Power – a power spectrum of RR intervals calculated for a frequency range from 0.0033 Hz to 0.4 Hz.	Net effect of the autonomic regulation on cardiovascular function
VLF	ms^2/Hz	Very Low Frequency - a power spectrum of RR intervals calculated for a frequency range from 0.0033 Hz to 0.04 Hz.	The physiological meaning of this band is most disputable. With longer recordings, it is considered to represent sympathetic tone as well as slower hormonal and thermoregulatory effects. There are some findings indicating that in shorter recordings VLF has fair representation of various mental stress factors (negative emotions, worries, rumination etc.)
LF	ms^2/Hz	Low Frequency - a power spectrum of RR intervals calculated for a frequency range from 0.04 Hz to 0.15 Hz.	Sympathetic regulatory tone with some contribution of the parasympathetic tone.
HF	ms^2/Hz	High Frequency - a power spectrum of RR intervals calculated for a frequency range from 0.04 Hz to 0.15 Hz.	Parasympathetic (vagal) regulatory tone and fluctuations caused by spontaneous breathing (aka respiratory sinus arrhythmia)
LF/HF Ratio	a.u.	Low Frequency to High Frequency Ratio – a ratio between powers spectrums calculated for a low frequency and high frequency ranges.	Balance between sympathetic and parasympathetic tone. A decrease in this score might indicate either increase in parasympathetic or decrease in sympathetic tone. It must be considered together with absolute values of both LF and HF to determine what factor contributes in autonomic imbalance.

5.5. Evaluation of the Cardiovascular Health Test Results

To assess the results of the cardiovascular health test all HRV parameters described in section 5.4 are used.

Cardiovascular Tolerance is evaluated based on HRV parameters of standup maneuver (representing a physiological transitory process caused by this maneuver). It indicates dynamic regulatory reserves of the cardiovascular system. Its assessment is based on comparing an actual calculated value with its predicted value and normative range as described in section 4.5. The higher this parameter is the higher ability of the cardiovascular system to respond to physical or emotional challenges causing its adaptation response.

Cardiovascular Adaptation is evaluated based on HRV parameters derived off 5-minute data recorded in sitting and standing positions. It indicates the ability of the cardiovascular system to adapt to physiological changes caused by physical or emotional challenges causing its adaptation response. This assessment is based on changes occurred in the autonomic regulatory function under the influence of this challenge. The higher this parameter is the higher ability of the cardiovascular system to compensate changes in the body occurred due to this challenge and to achieve a new state of optimum performance.

Both cardiovascular tolerance and adaptation together help to assess the state of cardiovascular regulatory function. If these parameters remain lower than normal range for a prolonged period of time, this could be a sign of cardiovascular dysfunction, which typically occurs due to poor physical shape or onset of any type of cardiovascular disorder.

5.6. Making an Assessment Conclusion on the Cardiovascular Health Test

Based on the results of the cardiovascular health test an assessment summary is generated including the following parts:

- 1. Prevailing Heart Rhythm
- 2. Heart Rhythm Disturbances
- 3. Cardiovascular Function Condition

5.6.1. Prevailing Heart Rhythm

A prevailing heart rhythm is determined based on comparing an actual mean heart rate to its predicted value. This parameter is evaluated during the first 5 minutes while patient is in sitting position.

Here is the list of possible heart rhythms:

	Result	Interpretation
1	HR is below normal range	Bradycardia – resting heart rate is lower than normal.
2	HR is within normal range	Normocardia – resting heart rate is within normal range.
3	HR is above normal range	Tachycardia – resting heart rate is higher than normal.

5.6.2. Heart Rhythm Disturbances

Heart rhythm disturbances are determined based on percentage of the number of ectopic heartbeats to the total number of all heartbeats recorded. This parameter is evaluated during the first 5 minutes while patient is in sitting position.

Here is the list of possible heart rhythm disturbances:

	Percentage of abnormal cardio intervals	Interpretation
1	0%	No heart rhythm disturbances detected
2	Less than 5%, single episodes	Occasional ectopic heartbeats or other minor disturbances due to possible body movements. No significant effect on quality of assessment.
3	Less than 5%, contiguous series of abnormal intervals	Non-persistent series of ectopic heartbeats or other disturbances due to possible significant body movements. Quality of assessment maybe questionable.
4	Over 5%, single episodes	Persisting ectopic heartbeats or other minor disturbances due to possible body movements. Check signal waveform. Assessment cannot be completed in case of persistent ectopic heartbeats.

	Percentage of abnormal cardio intervals	Interpretation
5	Over 5%, contiguous series of abnormal intervals	Major heart rhythm disturbances due to possible movement activity, poor quality of the signal or heart rhythm failure. Check signal waveform. Assessment cannot be completed in case of rhythm failures.

5.6.3. Cardiovascular Function Condition

The Heart Rhythm Scanner makes an assessment of the cardiovascular function condition based on two variables:

Cardiovascular Tolerance Indicates dynamic regulatory reserve of the cardiovascular system

responsible for a quick reaction to rapid changes in the body's condition.

Cardiovascular Adaptation Indicates the ability of the cardiovascular system to adapt to physiological

changes in the body and establish a new stable regulatory state.

Each of these parameters may have three different levels of functioning: low, medium or high.

Below is a detailed description of all 9 possible combinations of these two variables:

	Cardiovascular Adaptation	Cardiovascular Tolerance	Conclusion
1	LOW	LOW	Total cardiovascular adaptive dysfunction.
			Cardiovascular adaptation (ability of the cardiovascular system to adapt to physiological changes in the body and establish a new stable regulatory state) is LOW (2 points out of 20).
			Cardiovascular tolerance (dynamic regulatory reserve of the cardiovascular system responsible for a quick reaction to rapid changes in the body's condition) is LOW (3 points out of 20).
			This may be a sign of accelerated aging, physical exhaustion, overtraining or possible presence of cardiovascular health problem causing a total deficit of the autonomic regulation of the cardiovascular function.

	Cardiovascular Adaptation	Cardiovascular Tolerance	Conclusion
2	LOW	MEDIUM	Prevailing cardiovascular disadaptation.
			Cardiovascular adaptation (ability of the cardiovascular system to adapt to physiological changes in the body and establish a new stable regulatory state) is LOW (2 points out of 20).
			Cardiovascular tolerance (dynamic regulatory reserve of the cardiovascular system responsible for a quick reaction to rapid changes in the body's condition) is MEDIUM (8 points out of 20).
			This may be a sign of accelerated aging, physical exhaustion, overtraining or possible presence of cardiovascular health problem causing a deficit of adaptation capabilities of the autonomic regulation of the cardiovascular function.
3	LOW	HIGH	Isolated cardiovascular disadaptation.
			Cardiovascular adaptation (ability of the cardiovascular system to adapt to physiological changes in the body and establish a new stable regulatory state) is LOW (2 points out of 20).
			Cardiovascular tolerance (dynamic regulatory reserve of the cardiovascular system responsible for a quick reaction to rapid changes in the body's condition) is HIGH (15 points out of 20).
			This may be a sign of physical exhaustion, overtraining or other condition causing a deficit of adaptation capabilities of the autonomic regulation of the cardiovascular function.

	Cardiovascular Adaptation	Cardiovascular Tolerance	Conclusion
4	MEDIUM	LOW	Prevailing cardiovascular intolerance.
			Cardiovascular adaptation (ability of the cardiovascular system to adapt to physiological changes in the body and establish a new stable regulatory state) is MEDIUM (8 points out of 20).
			Cardiovascular tolerance (dynamic regulatory reserve of the cardiovascular system responsible for a quick reaction to rapid changes in the body's condition) is LOW (2 points out of 20).
			This may be a sign of accelerated aging, physical exhaustion, overtraining or possible presence of cardiovascular health problem causing a deficit of cardiovascular tolerance to physical exertions.
5	MEDIUM	MEDIUM	Normal cardiovascular adaptive function.
			Cardiovascular adaptation (ability of the cardiovascular system to adapt to physiological changes in the body and establish a new stable regulatory state) is MEDIUM (8 points out of 20).
			Cardiovascular tolerance (dynamic regulatory reserve of the cardiovascular system responsible for a quick reaction to rapid changes in the body's condition) is MEDIUM (8 points out of 20).
			There are no evident signs of physical exhaustion, overtraining or other health conditions negatively affecting the autonomic regulation of the cardiovascular function.

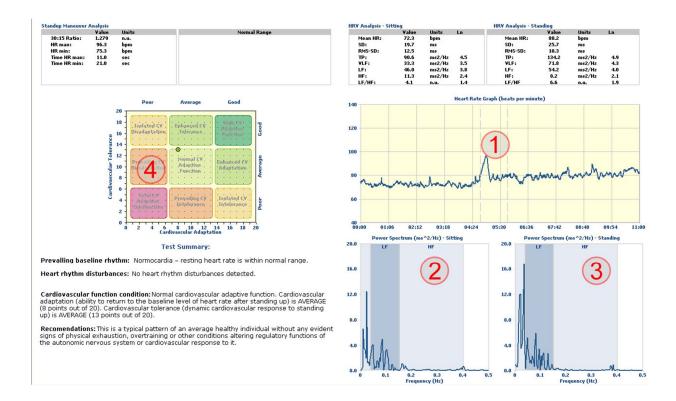
	Cardiovascular Adaptation	Cardiovascular Tolerance	Conclusion
6	MEDIUM	HIGH	Enhanced cardiovascular tolerance.
			Cardiovascular adaptation (ability of the cardiovascular system to adapt to physiological changes in the body and establish a new stable regulatory state) is MEDIUM (8 points out of 20).
			Cardiovascular tolerance (dynamic regulatory reserve of the cardiovascular system responsible for a quick reaction to rapid changes in the body's condition) is HIGH (15 points out of 20).
			The autonomic regulation of the cardiovascular function provides high ability to tolerate physical exertions and normal adaptation to their long-term effects. Typically this is a sign of absence of physical exhaustion, overtraining or any cardiovascular health conditions.
7	HIGH	LOW	Isolated cardiovascular intolerance.
			Cardiovascular adaptation (ability of the cardiovascular system to adapt to physiological changes in the body and establish a new stable regulatory state) is HIGH (15 points out of 20).
			Cardiovascular tolerance (dynamic regulatory reserve of the cardiovascular system responsible for a quick reaction to rapid changes in the body's condition) is LOW (15 points out of 20).
			This may be a sign of accelerated aging, physical exhaustion or other condition causing a deficit of cardiovascular tolerance to physical exertions.

	Cardiovascular Adaptation	Cardiovascular Tolerance	Conclusion
8	HIGH	MEDIUM	Enhanced cardiovascular adaptation.
			Cardiovascular adaptation (ability of the cardiovascular system to adapt to physiological changes in the body and establish a new stable regulatory state) is HIGH (15 points out of 20).
		Cardiovascular tolerance (dynamic regulatory reserve of the cardiovascular system responsible for a quick reaction to rapid changes in the body's condition) is MEDIUM (8 points out of 20).	
			The autonomic regulation of the cardiovascular function provides high ability for a long-term adaptation to physical exertions and to adequately tolerate them. Typically this is a sign of absence of physical exhaustion, overtraining or any cardiovascular health conditions.
9	HIGH	HIGH	High cardiovascular adaptive function.
			Cardiovascular adaptation (ability of the cardiovascular system to adapt to physiological changes in the body and establish a new stable regulatory state) is HIGH (15 points out of 20).
			Cardiovascular tolerance (dynamic regulatory reserve of the cardiovascular system responsible for a quick reaction to rapid changes in the body's condition) is HIGH (15 points out of 20).
			The autonomic regulation of the cardiovascular function provides high ability to tolerate physical exertions and high long-term adaptation capabilities. Typically this is a sign good physical shape and cardiovascular performance.

5.6.4. Typical Examples

Case 1: Normal Cardiovascular Adaptive Function

Patient – J.K., 48 years old male. The following picture shows his cardiovascular health report.



Pay attention to the following moments:

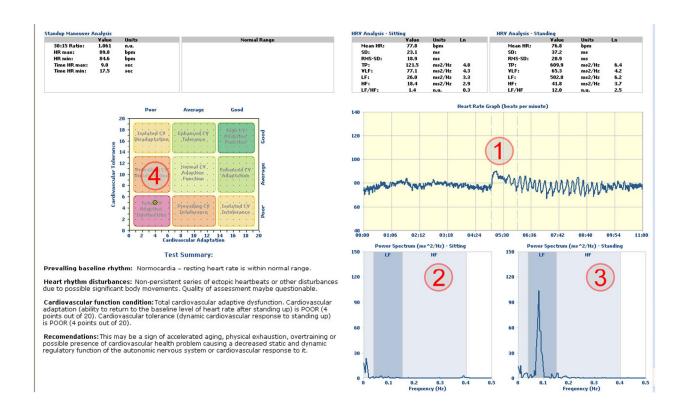
- The heart rate graph (medium right segment of the report page) shows a single high amplitude wave with a sharp fall. This indicates that patient's cardiovascular system adequately reacted to the standup maneuver and quickly recovered almost to the baseline level. This is a typical pattern indicating a normal cardiovascular tolerance.
- 2) The power spectrum graph (bottom center segment of the report page) shows prevailing spikes in the low frequencies (LF) range comparing to the high frequencies (HF) range. This is a sign of sympathetic dominance at rest.
- 3) The power spectrum graph (bottom right segment of the report page) shows **prevailing spikes in the low frequencies (LF) and very low frequencies (VLF) ranges** comparing to the high frequencies (HF) range. This is a sign of a slightly increased sympathetic dominance when standing comparing to sitting. This is a normal reaction of the cardiovascular system to the standup maneuver. So this is a typical pattern indicating a **normal cardiovascular adaptation**.
- 4) The cardiovascular health diagram (medium left segment of the report page) shows that the resulting "dot" is located in the "Normal CV Adaptive Function" segment, which indicates that both cardiovascular tolerance and adaptation are within normal range.

All these facts are typical signs of an adequate cardiovascular regulatory function observed in individuals without any signs of cardiovascular health problems.

Thus the assessment conclusion shown on this report page corresponds to the **Type 5** of the cardiovascular health condition shown in the table above.

Case 2: Total Cardiovascular Adaptive Dysfunction

Patient – N.P.,47 years old female. The following picture shows her cardiovascular health report.



Pay attention to the following moments:

- 1) The heart rate graph (medium right segment of the report page) shows a single low amplitude wave with a very gradual fall. This indicates that patient's cardiovascular system was not able to adequately react to the standup maneuver and recovered to the baseline level only after about two minutes. This is a typical pattern indicating a low cardiovascular tolerance.
- 2) The power spectrum graph (bottom center segment of the report page) shows **almost the absence of spikes in all frequencies**. This is a sign of the total autonomic dystonia at rest.
- 3) The power spectrum graph (bottom right segment of the report page) shows **prevailing spikes in the low frequencies (LF) range** comparing to the high frequencies (HF) range. This is a sign of an increased sympathetic dominance when standing comparing to sitting. This indicates that the **cardiovascular system is not able to adapt** in response to the standup maneuver.

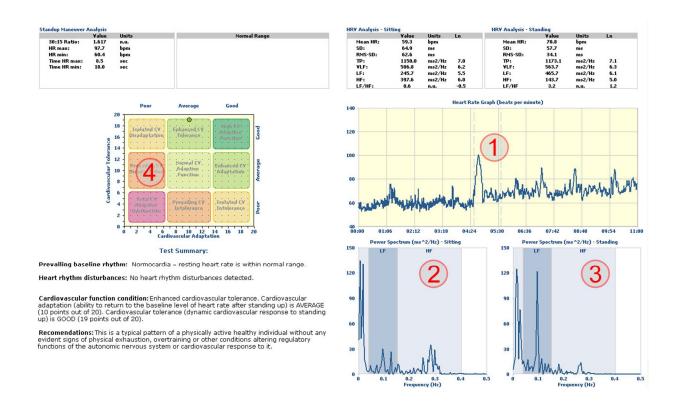
4) The cardiovascular health diagram (medium left segment of the report page) shows that the resulting "dot" is located in the "Total CV Adaptive Dysfunction" segment, which indicates that both cardiovascular tolerance and adaptation are very low.

All these facts are typical signs of an inadequate cardiovascular regulatory function observed in individuals very likely having cardiovascular health problems.

Thus the assessment conclusion shown on this report page corresponds to the **Type 1** of the cardiovascular health condition shown in the table above.

Case 3: Enhanced CV Tolerance

Patient – O.K., 41 years old female. The following picture shows her cardiovascular health report.



Pay attention to the following moments:

1) The heart rate graph (medium right segment of the report page) shows a distinctive single high amplitude wave with a sharp fall. This indicates that patient's cardiovascular system ideally reacted to the standup maneuver and quickly recovered to the baseline level. This is a typical pattern indicating a high cardiovascular tolerance.

- 2) The power spectrum graph (bottom center segment of the report page) shows fair amount of spikes in both low frequencies (LF) and high frequencies (HF) ranges. This is a sign of the autonomic balance.
- 3) The power spectrum graph (bottom right segment of the report page) shows **prevailing spikes in the low frequencies (LF) range** comparing to the high frequencies (HF) range. This is a sign of a moderately increased sympathetic dominance when standing comparing to sitting. This is a normal reaction of the cardiovascular system to the standup maneuver. So this is a typical pattern indicating a **normal cardiovascular adaptation**.
- 4) The cardiovascular health diagram (medium left segment of the report page) shows that the resulting "dot" is located in the "Enhanced CV Tolerance" segment, which indicates that patient has a high cardiovascular tolerance while cardiovascular adaptation is normal.

All these facts are typical signs of a good cardiovascular regulatory function observed in individuals without any signs of cardiovascular health problems.

Thus the assessment conclusion shown on this report page corresponds to the **Type 6** of the cardiovascular health condition shown in the table above.

6. Assessment of Baroreflex Function

6.1. Test Overview

An optimal level of the systemic arterial blood pressure is one of the vital physiological parameters determining adequate function of the cardiovascular system. If arterial pressure is too low then brain, heart and other vital organ do not receive an adequate blood supply so their functions may be affected, e.g. low blood supply to the brain would cause dizziness or even fainting. Alternatively too high arterial pressure causes unnecessary workload to the heart and negatively affects vascular system.

An arterial baroreflex is a key mechanism of short-term regulation of arterial blood pressure. Its whole purpose is to sense minute changes in blood pressure and adjust heart rate to compensate changes in blood supply to the vital organ caused by blood pressure changes.

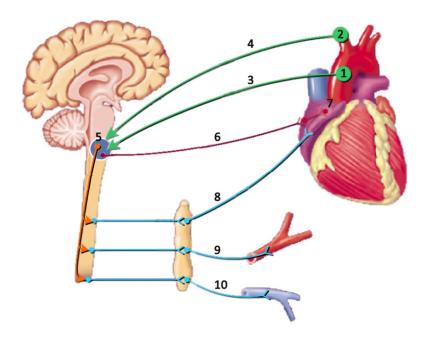
Baroreflex function significantly affects body's ability to adequately react to physical, emotional or mental stressors, which may cause significant changes in blood pressure.

Decreased baroreflex function may be an early sign of developing cardiovascular disorders such as arterial hypertension.

6.2. Physiological Background

Arterial baroreflex mechanism is a continuously functioning physiological regulatory system. Its goal is to maintain mean arterial blood pressure within normal range guarding its higher limit.

This illustration shows the structure and function of the baroreflex mechanism.



There are special baroreceptors located in the walls of aortic arch (1) and both carotid arteries (2). They continuously sense the level of arterial blood pressure. Increased blood pressure stretches these arteries causing baroreceptors to increase generation of electric impulses sent to cardioregulatory and vasomotor centers in the brainstem (5) via vagus (3) and glossopharyngeal (4) nerves respectively.

These baroreceptors are very sensitive to the speed of blood pressure changes. If even small changes in blood pressure occur very rapidly the receptors begin firing impulses at much higher rate causing faster response from the cardioregulatory and vasomotor centers.

The rate of generating impulses by baroreceptors depends on basal level of blood pressure. For example when blood pressure is increased from 130 to 140 mmHg baroreceptors increase their rate by 5 impulses per second. When blood pressure is increased from 180 to 190 mmHg the rate will be increased by 25 impulses per second.

Most of baroreceptors are sensitive to rapid changes of blood pressure. If blood pressure sustains high baroreceptors stop responding to elevated pressure and reset to its new level. This is an important adaptation mechanism ensuring an adequate blood supply in case of high demands like heavy physical labor.

As a result of increased neural stimulation coming form baroreceptors, the cardioregulatory center increases parasympathetic stimulation sent through the efferent fibers of the vagus nerve (6) to the sino-atrial node (7) located in the heart to quickly lower heart rate.

In addition to that the cardioregulatory center inhibits sympathetic stimulation sent to the heart via sympathetic efferent fibers (8) resulting in gradual decrease of heart rate and stroke volume.

In response to stimulation form baroreceptors the vasomotor center decreases sympathetic stimulation sent to peripheral arteries (9) and veins (10) causing their dilation, which facilitates lowering blood pressure as well.

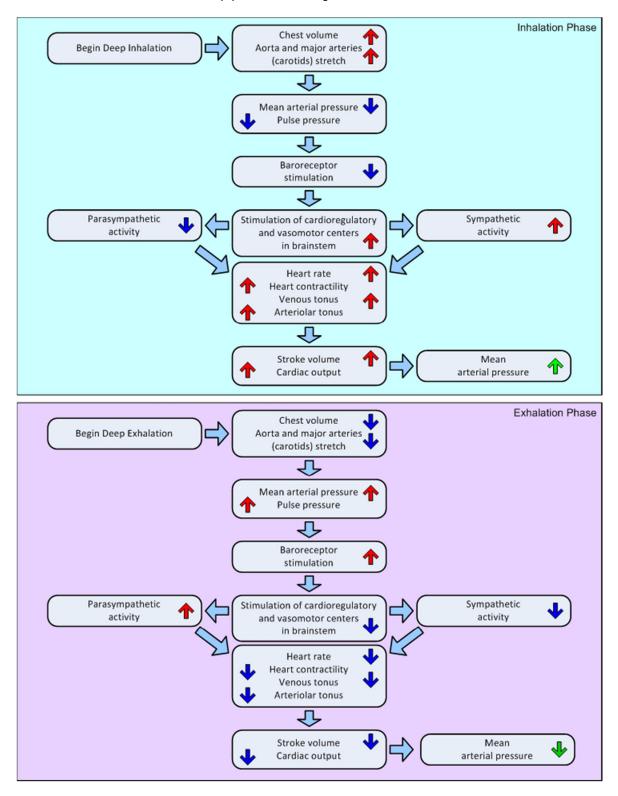
When blood pressure drops in major arteries (primarily in aorta and carotids) barorecepters sense it and trigger an opposite regulatory process. Lowered stimulation of the carioregulatory and vasomotor centers inhibit efferent stimulation of the vagus nerve and increase stimulation of the sympathetric nerves causing increase of heart rate, stroke volume and vasoconstriction of peripheral arteries and veins. This all leads to increase of blood pressure to its optimal level.

As stated above baroreflex mechanism is responsible for quick but short-term blood pressure regulation. If blood pressure needs to be maintained at higher level in longer term, other mechanisms of regulation take control of it.

Baroreflex function degrades with age because baroreceptors do not generate proper stimulation due to increased stiffness of arterial walls. This also happens in case of certain cardiovascular disorders like

arterial hypertension. Therefore baroreflex function is a very valuable indicator of cardiovascular health and aging process.

To measure baroreflex function a deep paced breathing maneuver is used.



During inhalation the chest is expanding and its internal pressure drops leading to a slight drop in blood pressure because large blood vessels inside the chest are stretched when chest is expanded. The baroreflex causes a quick increase in heart rate as described above.

During exhalation the chest contracts so its internal pressure rises causing blood pressure to rise as well due to shrinking large blood vessels in the chest. The baroreflex causes a quick decrease in heart rate as described above.

This phenomenon is also known as respiratory sinus arrhythmia.

Deep breathing causes maximum possible fluctuations in blood pressure, which helps measuring baroreflex function with larger stimuli.

It was found that the highest changes in heart rate induced by deep breathing happen when breathing at the rate of about 6 breaths per minute.

Measurement of heart rate oscillations when breathing deeply at 6 breaths per minute is a simple yet effective way to measure baroreflex function. The less sensitive baroreflex is the lesser heart rate oscillations occur.

6.3. Recording Test Data

A new baroreflex function test should be done after fasting for at least 2 hours.

The recording must be performed in a comfortable relaxed sitting position with limiting body movements.

If patient feels physically tired due to coming to examination room, allow him/her to have a rest for 10-15 minutes before testing.

It is important to eliminate any factors which can cause emotional arousals. There is no need to specially train patients on how to be tested. However it is important to brief patient on what the test is and what to do during the test. This will help to lower patient's alertness and anxiety and establish good communication with technical personnel performing the test.

After placing a sensor (or electrodes) and starting the software (refer to the software User's Manual) the patient should be given the following instruction:

The duration of this test is 1 minute. During the test breathe deeply and evenly closely following a visual metronome displayed on the screen. Breathe in when pacer goes up, hold breathing when pacer is still and breathe out when it goes down. Breathing should be deep but not forceful. During the test, try to avoid any movements, remain sitting relaxed and focused on breathing.

It is very important to make sure that the quality of data recording is sufficient before it is interpreted. Please refer to Section 4.3 for more details.

6.4. Test Results

Once the test is recorded the following HRV parameters are calculated by the software.

Parameter	Unit	Description	Physiological Meaning
Mean E/I Ratio	n.u	Mean ratio value between the longest heartbeat interval during expiration and the shortest interval during inspiration.	Can be used as an indicator of average baroreflex sensitivity.
Max E/I Ratio	a.u.	Maximum ratio value between the longest heartbeat interval during expiration and the shortest interval during inspiration.	Can be used as an indicator of maximum baroreflex sensitivity.
I		Resonant frequency of oscillations of heart rate.	Can be used as an indicator of test compliance. If it is very close to 0.1 Hz then the test was performed properly.
Standard bpm/ms Deviation HR/RR		Standard deviation of HR/RR values off their mean value.	Can be used as an indicator of average baroreflex sensitivity.
Max Variation bpm/ms HR/RR		Maximum variation of HR/RR within one breathing cycle.	Can be used as an indicator of maximum baroreflex sensitivity.
"		Mean variation of heart rate among all breathing cycles.	Can be used as an indicator of average baroreflex sensitivity.
'		Minimum HR/RR value during the test.	
Maximum HR/RR	bpm/ms	Maximum HR/RR value during the test.	

6.5. Evaluation of the Baroreflex Function Test Results

Baroreflex function is evaluated based on analysis of variation of the heart rate caused by deep breathing at 6 breaths/min rate. Its assessment is based on comparing an actual calculated value with its predicted value and normative range as described in section 4.5. The higher this parameter is the higher baroreflex function is.

High baroreflex function is a sign of good vascular elasticity and thus ability of the body to efficiently adapt to various physical, emotional and metal factors causing stress and raise of blood pressure.

Low baroreflex function typically is a sign of aging process or certain cardiovascular problem causing stiffness or arterial walls.

However before making conclusions about low baroreflex function it is important to make sure that patient followed specific test compliance rules:

- 1) Breathing must be deep and even without forceful attempts. Shallow breathing will cause lower test results.
- 2) Breathing must be strictly synchronized with a visual pacer. Lack of synchronization will prevent from getting accurate and valid test results.

6.6. Making an Assessment Conclusion on the Baroreflex Function Test

Based on the results of the baroreflex function test an assessment summary is generated consisting the following parts:

- 1. Heart Rhythm Disturbances
- 2. Baroreflex Ffunction Condition

6.6.1. Heart Rhythm Disturbances

Heart rhythm disturbances are determined based on percentage of the number of ectopic heartbeats to the total number of all heartbeats recorded.

Here is the list of possible heart rhythm disturbances:

	Percentage of abnormal cardio intervals	Interpretation
1	0%	No heart rhythm disturbances detected
2	Less than 5%, single episodes	Occasional ectopic heartbeats or other minor disturbances due to possible body movements. No significant effect on quality of assessment.
3	Less than 5%, contiguous series of abnormal intervals	Non-persistent series of ectopic heartbeats or other disturbances due to possible significant body movements. Quality of assessment maybe questionable.
4	Over 5%, single episodes	Persisting ectopic heartbeats or other minor disturbances due to possible body movements. Check signal waveform. Autonomic assessment cannot be completed in case of persistent ectopic heartbeats.
5	Over 5%, contiguous series of abnormal intervals	Major heart rhythm disturbances due to possible movement activity, poor quality of the signal or heart rhythm failure. Check signal waveform. Autonomic assessment cannot be completed in case of rhythm failures.

6.6.2. Baroreflex Function Condition

Here is the list of possible baroreflex function conditions:

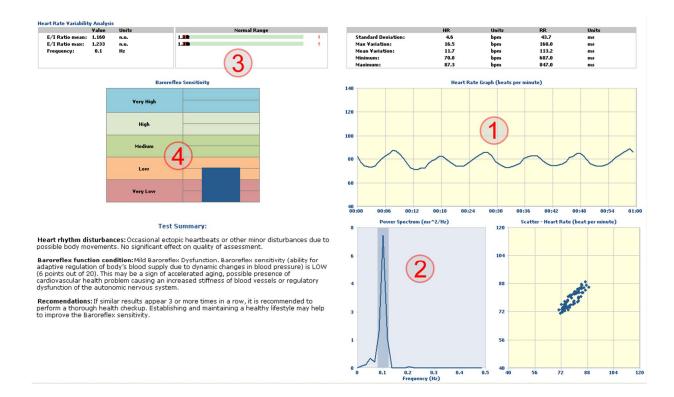
	Baroreflex Function	Conclusion
1	VERY LOW	Significant Baroreflex Dysfunction.
		Baroreflex sensitivity (ability for adaptive regulation of body's blood supply due to dynamic changes in blood pressure) is VERY LOW (2 points out of 20).
		This may be a sign of accelerated aging, possible presence of cardiovascular health problem causing a significant stiffness of blood vessels or regulatory dysfunction of the autonomic nervous system.
2	LOW	Mild Baroreflex Dysfunction.
		Baroreflex sensitivity (ability for adaptive regulation of body's blood supply

		due to dynamic changes in blood pressure) is LOW (6 points out of 20).
		This may be a sign of accelerated aging, possible presence of cardiovascular health problem causing an increased stiffness of blood vessels or regulatory dysfunction of the autonomic nervous system.
3	MEDIUM	Satisfactory Baroreflex Function.
		Baroreflex sensitivity (ability for adaptive regulation of body's blood supply due to dynamic changes in blood pressure) is MEDIUM (10 points out of 20).
		This may be a sign of natural aging process in blood vessels or regulatory function of the autonomic nervous system.
4	HIGH	Good Baroreflex Function.
		Baroreflex sensitivity (ability for adaptive regulation of body's blood supply due to dynamic changes in blood pressure) is HIGH (14 points out of 20).
		This may be a sign of a slow aging process resulting in good condition of blood vessels and regulatory function of the autonomic nervous system.
5	VERY HIGH	Very Good Baroreflex Function.
		Baroreflex sensitivity (ability for adaptive regulation of body's blood supply due to dynamic changes in blood pressure) is VERY HIGH (18 points out of 20).
		This may be a sign of a very slow aging process resulting in excellent condition of blood vessels and regulatory function of the autonomic nervous system.

6.6.3. Typical Examples

Case 1: Low Baroreflex Function

Patient – J.S., 48 years old male. The following picture shows his baroreflex function assessment report.



Pay attention to the following moments:

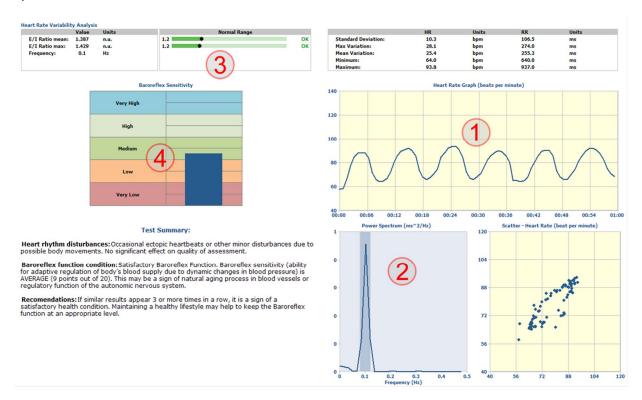
- 1) The heart rate graph (medium right segment of the report page) shows low amplitude waves synchronous to the slow breathing process. Assuming that patient breathed deeply enough, this indicates low baroreflex function.
- 2) The power spectrum graph (bottom center segment of the report page) shows one main peak at 0.1 Hz frequency. This indicates that patient was breathing synchronously with the pacer so test compliance requirements were followed.
- 3) The numerical chart (top left segment of the report page) shows that **E/I Ratio max parameter** value (1.233) is below the lower boundary of the normal range.
- 4) The baroreflex function diagram (left segment of the report page) shows that the resulting bar is in "Low" segment, which is not normal.

All these facts are typical signs of the low baroreflex function, which may be a sign of accelerated aging, possible presence of cardiovascular health problem causing an increased stiffness of blood vessels or regulatory dysfunction of the autonomic nervous system.

Thus the assessment conclusion shown on this report page corresponds to the **Type 2** of the baroreflex function condition shown in the table above.

Case 2: Normal Baroreflex Function

Patient – J.O., 49 years old female. The following picture shows her baroreflex function assessment report.



Pay attention to the following moments:

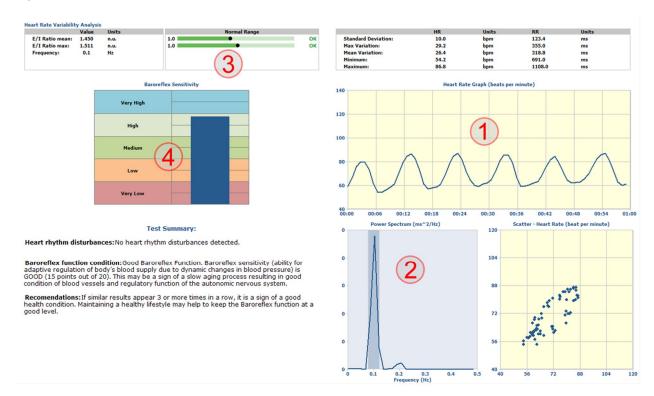
- 1) The heart rate graph (medium right segment of the report page) shows fairly high amplitude waves synchronous to the slow breathing process. Assuming that patient breathed deeply enough, this indicates normal baroreflex function.
- 2) The power spectrum graph (bottom center segment of the report page) shows one main peak at 0.1 Hz frequency. This indicates that patient was breathing synchronously with the pacer so test compliance requirements were followed.
- 3) The numerical chart (top left segment of the report page) shows that **E/I Ratio max parameter** value (1.429) is within the boundaries of the normal range.
- 4) The baroreflex function diagram (left segment of the report page) shows that the resulting bar is in "Medium" segment, which is normal.

All these facts are typical signs of natural aging process in blood vessels or regulatory function of the autonomic nervous system and absence of any serious cardiovascular health problems.

Thus the assessment conclusion shown on this report page corresponds to the **Type 3** of the baroreflex function condition shown in the table above.

Case 3: High Baroreflex Function

Patient – C.B., 61 years old female. The following picture shows her baroreflex function assessment report.



Pay attention to the following moments:

- 1) The heart rate graph (medium right segment of the report page) shows very high amplitude waves synchronous to the slow breathing process. Assuming that patient breathed deeply enough, this indicates high baroreflex function.
- 2) The power spectrum graph (bottom center segment of the report page) shows one main peak at 0.1 Hz frequency. This indicates that patient was breathing synchronously with the pacer so test compliance requirements were followed.
- 3) The numerical chart (top left segment of the report page) shows that **E/I Ratio max parameter value (1.511)** is slightly above the high boundary of the normal range.
- 4) The baroreflex function diagram (left segment of the report page) shows that the resulting bar is in "High" segment, which is normal for the patient's age group.

All these facts are typical signs of a slow aging process resulting in good condition of blood vessels and regulatory function of the autonomic nervous system and absence of any cardiovascular health problems.

Thus the assessment conclusion shown on this report page corresponds to the **Type 4** of the baroreflex function condition shown in the table above.