

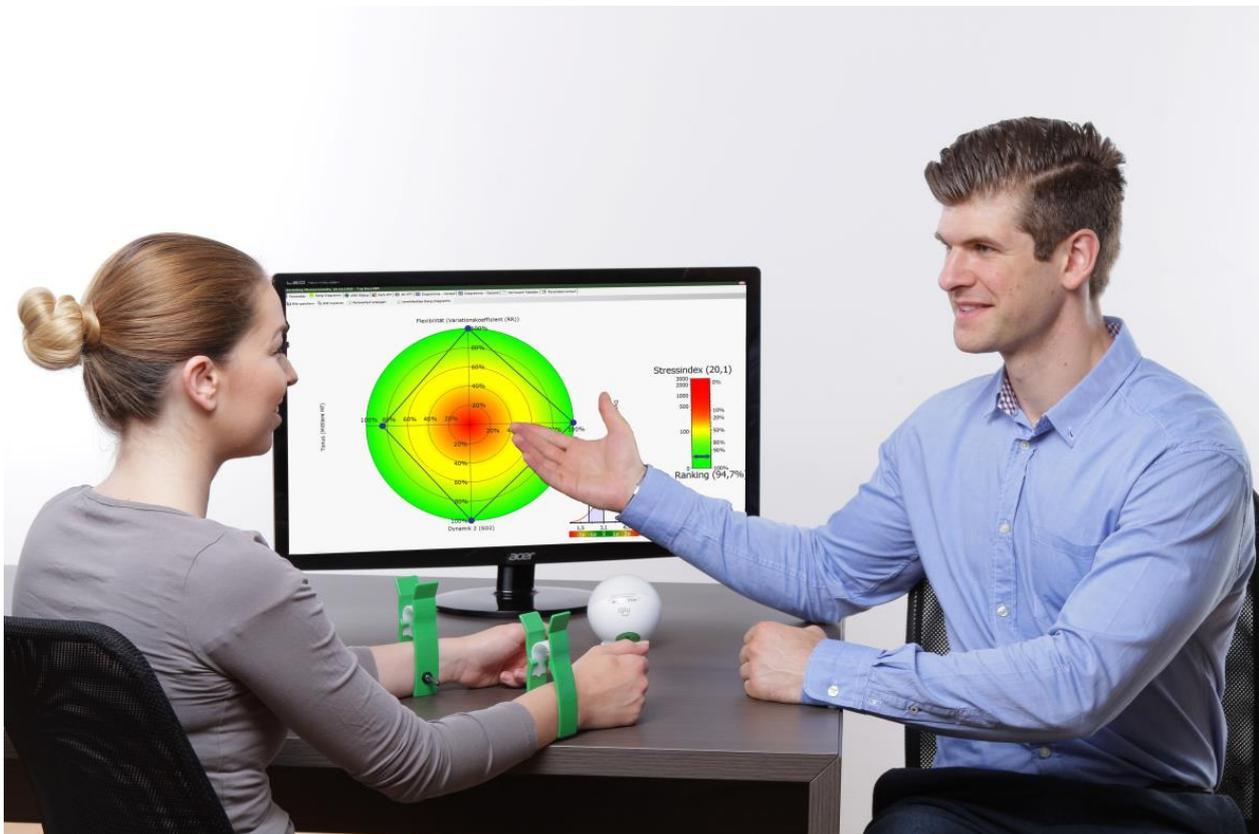
Documentation

for



Part 1:

**Basics, Deep Breathing Test, Short Term HRV,
HRV-Biofeedback / Qiu, Parameters,
FAQ, HRV and Respiration**



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SCIENCE FOR A BETTER LIFE

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Content

Foreword	7
Online training / support via TeamViewer	7
Questions about interpretation	7
Status of the documentation	7
Newsletters	7
Information for patients/clients	7
Our HRV concept	7
General	8
Setup of the HRV-Scanner software (HRV-Scanner and HRV-Scanner lite)	8
Uninstall the software	8
Licensing the software	8
Update license	8
Connecting the hardware	8
Start software	8
Append new examiner	8
Append new subject	9
The main window	9
Status display in the main window	9
Possible system configurations	9
Network mode	9
GDT Connection	9
Language selection	9
Your logo or information in the reports	9
Other important functions	10
Data backup	10
Import/Export	10
FAQ - common problems and questions	10
I made a measurement accidentally for the wrong subject	10
I forgot my access password	10
When I start the HRV-Scanner software, I am asked to enter a license code	10
I connected the hardware to the PC, but the status is "USB offline"	10
My HRV-Scanner hardware no longer shows ECG	10
Signal acquisition with the HRV-Scanner hardware during the measurement	11
Notes on improving data quality during analysis	15
Step 1: Visual control of heart rate curve and biosignal	15
Step 2: Optimal automatic determination of the heartbeat in the biosignal	16
Step 3: Manual editing in biosignal	17
Step 4: Graphic filtering	21
Step 5: Adjust plausibility check and heart rate filters	23
Limits of HRV determination	25
Example 1: many irregular heartbeats (marked in orange)	25
Example 2: Atrial fibrillation	26
HRV concept "Tone, Flexibility, Dynamics"	27
Tone	28
Flexibility	28

Dynamics.....	29
Understanding the rank chart	30
Basis HRV measurements	33
The Short-Term HRV	33
Target parameter in the rank diagram of the Short-Term HRV measurement ...	36
Flexibility (Coefficient of Variation RR)	36
Tone (mean HR)	37
Dynamics 1 (SD1)	37
Dynamics 2 (SD2)	37
SD2/SD1 ratio.....	38
Stress index.....	38
Respiration and HRV	39
Influence of breathing on the results of the short-term HRV	39
Distinguishing sympathetic - parasympathetic in the short-term HRV	40
Conclusion	41
Methods for measuring breathing	41
EDR - ECG Derived Respiration (HRV-Scanner standard and HRV-Scanner lite).....	41
Mechanical determination of respiration - breathing belt (HRV-Scanner plus)	42
The Deep Breathing Test.....	44
Target parameter in the rank diagram of the Short-Term HRV measurement ...	47
Flexibility (E-I)	47
Tone	47
Dynamics.....	48
Why two measurements as a basis HRV.....	49
What has a negative impact on HRV.....	50
Anticholinergic drugs.....	50
Drugs with anticholinergic action	50
Further diagrams in the analysis.....	51
Poincaré Plot	51
Histogram.....	52
Spectral analysis	53
Color-FFT.....	53
ANS status.....	55
Parameter History/Pre-measurements	56
Number of pre-measurements in the HRV-Scanner lite	57
Pre-measurements in the HRV-Scanner standard	57
Rank chart.....	58
Biofeedback History	58
Changes	60
Parameter.....	60
List of parameters.....	61
Calculate heart rate from []	61
Sampling rate [Hz]	61
Duration [hh:mm:ss]	61
Number of heartbeats [n]	61
Artefact ratio [%]	61
Well-being [%].....	61

DBT quality [%]	61
Test quality [%]	61
Biofeedback quality [%]	61
Subject age [years]	61
Subject height [cm]	61
Subject weight [kg] (initial)	61
Subject sex.....	61
Examiner	61
Mean HR [1/min.].....	62
Standard deviation (St.Dev.) [ms]	62
Coefficient of variation (HR) [%].....	62
Mean RR interval [ms].....	62
SDNN [ms]	62
PNN50 [%]	62
PNN20 [%]	62
Coefficient of variation (RR)	63
RMSSD [ms]	63
SD1 [ms].....	63
SD2 [ms].....	63
SD2/SD1 quotient.....	63
Normalized SD2/SD1 quotient [σ].....	64
Stress index [Pts.]	66
HF-Band [Hz]	67
LF-Band [Hz].....	67
VLF-Band [Hz].....	67
Power HF-band [ms^2].....	67
Power LF-band [ms^2]	67
Power VLF-band [ms^2]	67
Power total [ms^2]	67
rel. Power HF-band [%].....	67
rel. Power LF-band [%]	67
rel. Power VLF-band [%]	67
LF/HF ratio.....	67
Rhythmisation degree []	67
E-I [1/min.]	68
E/I []	68
MCR []	68
Ewing 30:15 value [].....	68
Biological HRV age [years].....	68
Valsalva-Ratio	69
Alpha 1 []	69
Respiration parameters	70
Impact breathing [%]	70
Respiratory rate [1min.]	70
Respiration stress[].....	70

Breathing variability []	70
Pulse wave latency [ms]	70
Guzik index.....	70
Parameter Guzik index	71
HRV biofeedback	73
HRV biofeedback	73
Online spectral analysis (Real time FFT).....	74
Rhythmisation	74
Fundamentals of HRV Biofeedback.....	75
From chaos to order.....	75
Breathing is the key to coherence	75
As you learn, breathing and heartbeat are rhythmic.....	76
How to improve coherence through biofeedback	76
What to do if coherence is always low?	76
What does the balloon mean in the center of the screen?	77
How often and how long should you practice HRV Biofeedback?	77
Important settings in HRV Biofeedback	78
Breathing rhythm	78
Exercise duration	78
Rhythmization degree target value (difficulty level of the exercise)	78
Evaluation of biofeedback sessions	79
Overview	79
Assessment of Biofeedback results.....	80
Explanation of the result diagram:	80
Typical examples of the result diagram.....	81
Qiu and HRV-Scanner.....	82
The Qiu	82
The Qiu-Modul in the HRV-Scanner-Software.....	82
Qiu-Configurator.....	82
Connecting the Qiu to the PC.....	82
Assigning a Qiu to a subject	82
Configuration of the breathing display on the Qiu.....	83
Determine the exercise difficulty.....	83
Set the exercise duration	83
Configuring the brightness of the biofeedback	83
Additional functions.....	83
Set the date / time of the Qiu.....	83
Clear the Qiu's measurement memory	83
Qiu Signal Check	83
Ear clip as an alternative	84
Qiu measurements.....	84
Defining the exercise plan by day of the week and time of day	84
Management of Qiu measurements	84
Rework the measurement	84
Overview of the exercise success with statistical evaluation	85
Statistical evaluation:	85
Filter settings	85

Overview of Exercise Compliance, Compliance Index.....	86
HRV-Monitoring with the Qiu	87
Instruction	87
How do you turn the Qiu on / off?	87
How can I leave the setting mode if it was accidentally activated when switching on?.....	87
Which holding position is suitable?	87
Which sensor position is suitable?	87
How do I recognize an inappropriate sensor position?.....	87
The optical biofeedback stays permanently on red or green, no matter what I do?	87
What does the wandering blue LED light at the equator of the Qiu mean?	88
Why does the Qiu light up brightly when it turns on?.....	88
After the bright light when switching on the Qiu flashes recently red once again, why?.....	88
After the light comes on, the Qiu flashes red three times and then turns off, why?.....	88
Does the time and date in the Qiu have to be reset after changing the battery?.....	88
How can the subject change the batteries?	88
Possibilities of ECG derivation	89
Derivation of a 1-channel ECG with clamp electrodes	89
Derivation of a 1-channel ECG with adhesive electrodes	90
Derivation of a 3-channel ECG (only HRV scanner hardware plus)	90
Technical Manual	91
PC Hardware PC Requirements	91
Maintenance and Servicing.....	91
Copyright.....	91
Liability	91
Warranty	91
Technical details	91
Appendix - Literature	92
Literature SD2/SD1 ratio	92

Foreword

Thank you for your interest in our HRV-Scanner system. BioSign has been active in the area of heart rate variability (HRV) and the analysis of the vegetative nervous system for over 20 years. The HRV-Scanner software as a major part of our HRV concept reflects our know-how gained over the years and is therefore quite extensive in some areas. We would be happy to answer any questions you may have and we would be pleased to assist you with our product.

Online training / support via TeamViewer

When purchasing an HRV-Scanner, or when using our free demos, we offer you online support or training via TeamViewer®. All you need is a PC with internet access on which the HRV-Scanner software is installed and a telephone. If you are interested, make an appointment with us. In addition, we offer seminars and full-day trainings. You can find more information on our homepage at www.biosign.de

Questions about interpretation

You have questions about the technical quality of your HRV measurement, or how to interpret the results? Please contact our free support by e-mail (support@biosign.de). For a fast and competent support, we have installed an export possibility of measurements in the HRV-Scanner. So, we can look at the measurements and give you tips and interpretation aids.

Status of the documentation

This documentation represents the status of the HRV-Scanner software when printing the copy in your hands. However, since we also do some scientific research and always make an effort to integrate the current state of science into our products, there are always changes and innovations in the software. All of our new features are fully accessible via our online software update system. Changes in the software also lead to a need to update this documentation from time to time. Therefore, you will always find a current version of this documentation as a PDF file together with the updates in your software under "Help".

Newsletters

Would you like to be kept up-to-date? We would be glad to send you our newsletter. This usually happens automatically when you buy one of our systems. You will receive our newsletter without obligation. You can unsubscribe at any time. The newsletter provides information about new software features or other important innovations for HRV-Scanner users.

Information for patients/clients

Do you need information material for your patients/clients? We offer flyers, posters, info brochures, info maps and much more. You can find more information in our online shop at www.biosign.de

Our HRV concept

In addition to the HRV-Scanner, we also offer HRV biofeedback devices for your patients/clients. This enables us to provide you an HRV monitoring concept for objective monitoring your therapy or intervention. The measurement data are accessible in the terminals or via an Internet cloud and trends can be calculated.

Please note that not all features listed in this documentation are available in the HRV-Scanner lite software.

General

Setup of the HRV-Scanner software (HRV-Scanner and HRV-Scanner **lite**)

Please download the current setup from our homepage (www.biosign.com). The setup can be found under: **HRV-Scanner -> Downloads ->**

<p>Download – Setup für HRV-Scanner und HRV-Scanner lite</p>  <p>aktuelles Setup HRV-Scanner/HRV-Scanner lite als EXE-Datei für Windows 7/8/10</p>	<p>Run the HS_Setup.exe program. To avoid problems with Windows user administration, we recommend an installation in a directory as proposed in the setup (C: \HRVScanner)</p>
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Uninstall the software

Uninstall the HRV-Scanner software by using the Windows Control Panel.

Licensing the software

The software license is located on the blue HRV-Scanner dongle, which must be connected to USB to run the software. Alternatively, there is the option of an online license via the Internet. *Note: You can install the software on any number of PCs. The software runs where the blue HRV-Scanner dongle (license) is attached.*

Update license

The HRV-Scanner software runs without time-limits. When you buy a system, you get 365 days of update license. This allows you to benefit from all further developments of the HRV-Scanner software free of charge. The software checks, at intervals (to be defined in the system control of the HRV-Scanner software), whether new updates are available and then downloads them from the BioSign server and installs them.

An extension of the update license after expiration is possible at any time. Use the order option in the HRV-Scanner software.

Connecting the hardware

Connect the HRV-Scanner hardware to your PC using delivered the USB cable. The HRV-Scanner software should not be started. Wait for the drivers of Windows to be installed and until Windows says, that the device can be used now.

Start software

First plug your HRV-Scanner dongle into a free USB port. If you do not have a free USB port, we recommend using a USB hub (included with the HRV-Scanner). Start the HRV-Scanner software by double clicking with the mouse on the HRV-Scanner symbol. Depending on which version you have received you can either run only the HRV-Scanner **lite** software or the HRV-Scanner and the HRV-Scanner **lite** software.

HRV-Scanner software

Full version with all features



HRV-Scanner **lite** software

Starter version for Windows Tablet and PC



Tip: At the beginning, the **lite** version can make the entry much easier since the user is guided by the software through measurements.

Append new examiner

When you first start the HRV-Scanner software, you must first create a new examiner. Enter the data for the new examiner. The password is optional and should be entered if a data record is to be protected against unauthorized access. After recording a new examiner, it appears in the login window. Press "OK" to log in to the system.

Append new subject

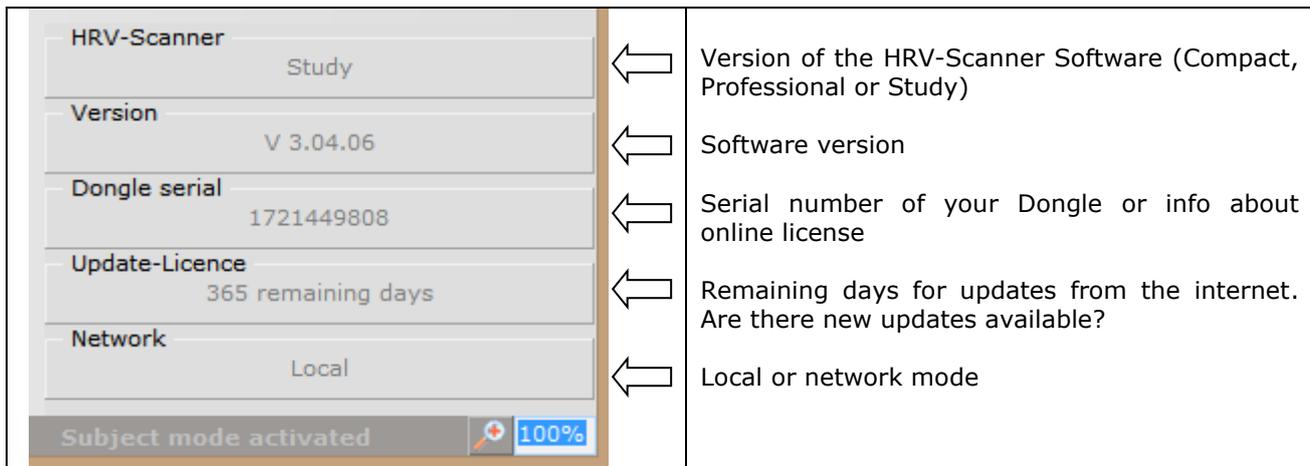
Before a measurement can be performed, the subject data must first be entered. To do this, go to the main menu and press "Subject" and then "Append new subject". After recording a subject, you can perform the first measurement.

The main window

After logging in to the examiner, you enter the main window of the HRV-Scanner. From here you can reach all other program features.

Status display in the main window

The status display is shown in the main window at the bottom right



You will also see in the status line below which examiner is logged in, whether you are in the subject or study mode, and the current percentage size of the software scaling.

Possible system configurations

Network mode

It is possible to run the HRV-Scanner software in network mode. This allows data to be stored centrally and used by several clients (examination room, meeting room, ...)

GDT Connection

A transfer of the patient data from a doctor's office software is possible via GDT.

Language selection

The HRV-Scanner software is available in several languages. Select the desired language in the system settings.

Your logo or information in the reports

You can include your logo and other information in the header of the reports

Other important functions

Data backup

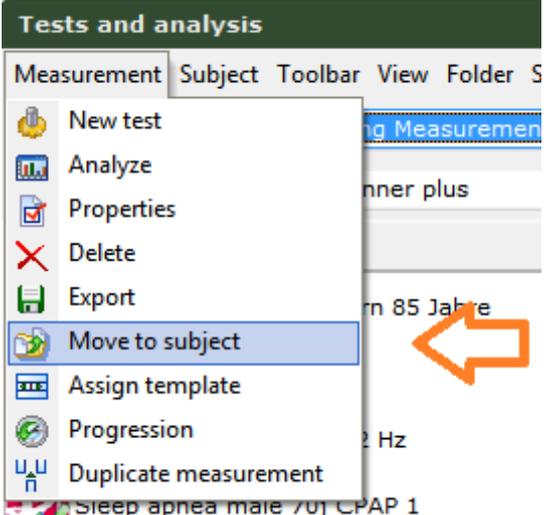
We recommend to regularly back up the data. There is a separate function in the HRV-Scanner software. Tip: we also recommend to save the entire HRV-Scanner directory, including all subdirectories, to an external data medium from time to time.

Import/Export

The HRV-Scanner software has an export/import system, which allows the export of measurements including all information on the subject. You can use this for data exchanged between several HRV-Scanner systems and also for the support. You can send measurements with anonymous test data by e-mail to us and write any questions.

FAQ - common problems and questions

I made a measurement accidentally for the wrong subject

	<p>Measurements can be moved to another subject. Use the function "Move to subject" in the title menu of the "Test and analysis" window.</p> <p>In the displayed window, select the subject to which the measurement should be moved.</p>
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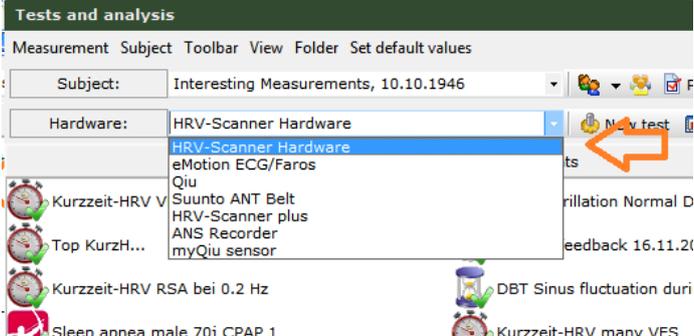
I forgot my access password

Please contact us by e-mail and send us the file "HRVScanner.mdb" from the HRV-Scanner directory by e-mail. We can read the encrypted file and give you your password.

When I start the HRV-Scanner software, I am asked to enter a license code

Is your USB dongle connected to the PC? Possibly the dongle is not recognized. This problem can often be solved by using the included USB hub.

I connected the hardware to the PC, but the status is "USB offline"

	<p>Did you select the right hardware before starting the measurement?</p>
---	---

My HRV-Scanner hardware no longer shows ECG

Do you still have a device from the first generation (battery compartment on the bottom). Then replace the batteries with new and charged batteries.

Signal acquisition with the HRV-Scanner hardware during the measurement

The HRV-Scanner software is compatible with several devices for signal acquisition. Devices are used via USB and Bluetooth. This chapter explains the acquisition of a 1-channel ECG and the pulse wave using the HRV-Scanner hardware.

Note: We recommend that you take care for a good biosignal while measuring. This avoids the post-processing during the analysis.



Connect the hardware elements, as shown in the picture. If the banana plugs cannot be inserted into the brackets, please turn the top wheel upwards. Plug the USB cable into an available USB port on your PC. If no free USB port is available, please use the included USB hub.

The drivers are installed when connecting the hardware to the PC for the first time. Please wait until this process is finished!

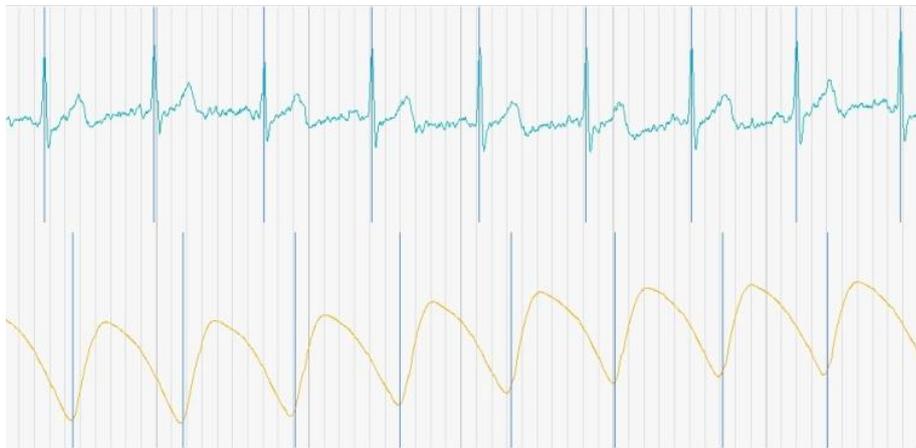


Apply the ECG clamp electrodes to the subject. In contrast to the picture above, in most cases the red cable should go on the right hand. Important is that the R-wave in the ECG points upwards. If the wave is pointing downwards, the ECG clamp electrodes should be replaced right/left. The ECG paper should be moistened with water and laid under the ECG clamp electrodes. Alternatively, electrode gel can also be used.

Note: If you do not get a sufficiently large R-wave with lead I (right wrist against left wrist), you should try lead III (right wrist against left wrist). To do this, place the clip from the left wrist to the left ankle. In most cases, one of the two leads brings a large R-wave and thus saves post-processing. (see also chapter: **Possibilities of ECG derivation**)



Place the ear clip as shown in the picture. Attach the silver holding clip of the cable at the shirt collar or neckline of the subject's clothes.



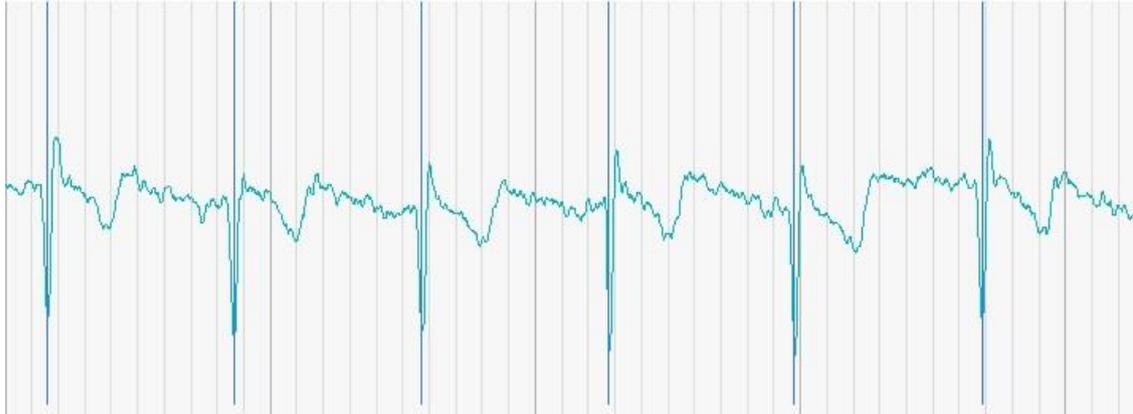
Two kinds of biosignals are basically recorded by the HRV-Scanner software. The ECG (taken off with clamps or electrodes) and the pulse wave (taken off with the ear clip). When using alternative hardware, depending on what hardware you are using, either both or only one of the two signal sources are available. E.g. the HRV-Scanner hardware records ECG and pulse wave, the Faros 180 only ECG, the Qiu and the myQiu hardware only pulse wave.



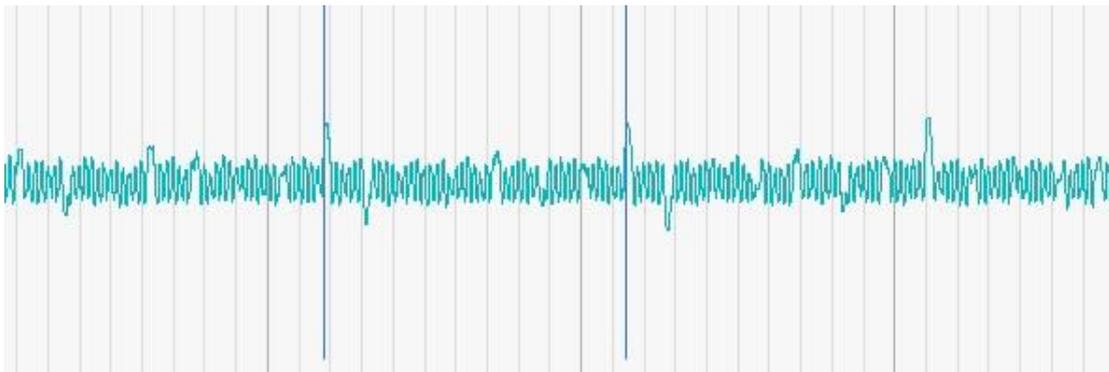
Here is an example of an optimal ECG signal. The sharp R-waves are clearly visible and directed upwards. The baseline of the ECG is slightly noisy and the R-waves are clearly distinguished in size from the rest of the signal. The vertical bar in the R-waves indicates that the software has detected and marked a heartbeat.

The shape of the ECG with its sharp R-wave makes it possible to set the time of a heartbeat very precisely. The pulse wave is a rather soft, vibrating signal. Here, setting the time of a heartbeat is more difficult and somewhat inaccurate. Furthermore, the pulse wave also is influenced by the regulation of the vessels, which may additionally increase the deviation compared to the accuracy of the ECG.

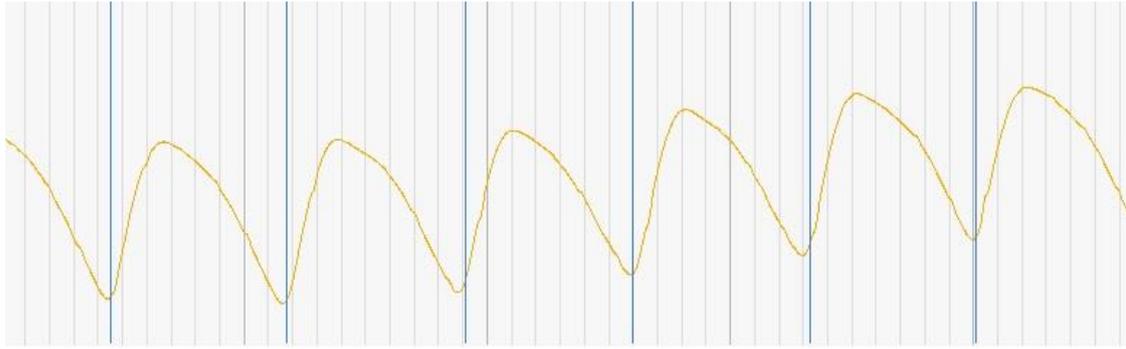
As a result, the ECG (and possibly in addition the pulse wave) should be used for HRV measurements (Deep Breathing Test, Short-Term HRV). The accuracy of the pulse wave alone is sufficient for the HRV biofeedback. Also because of the simpler application in practice one can use the pulse wave without hesitation to the HRV biofeedback.



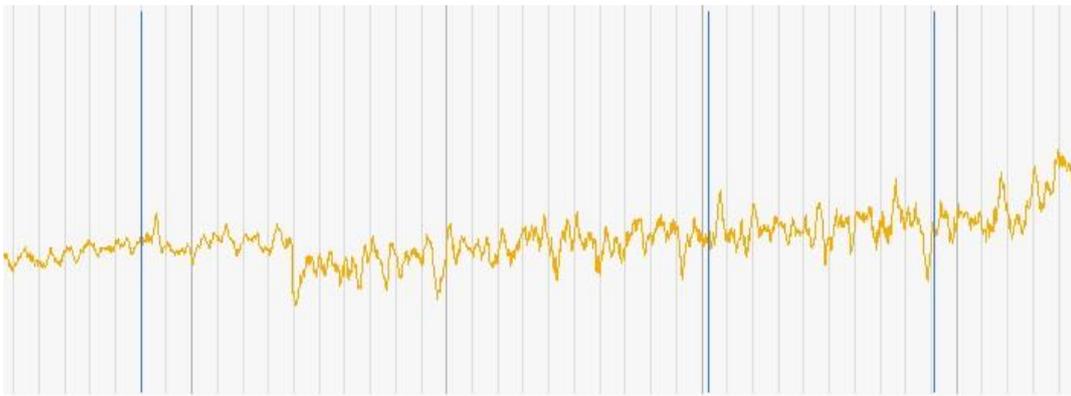
Here is an example of a non-optimal ECG signal. The high and sharp R-waves are clearly visible but directed downwards. This is called a wrong polarized ECG. This can be easily corrected by changing (left to right) the electrodes.



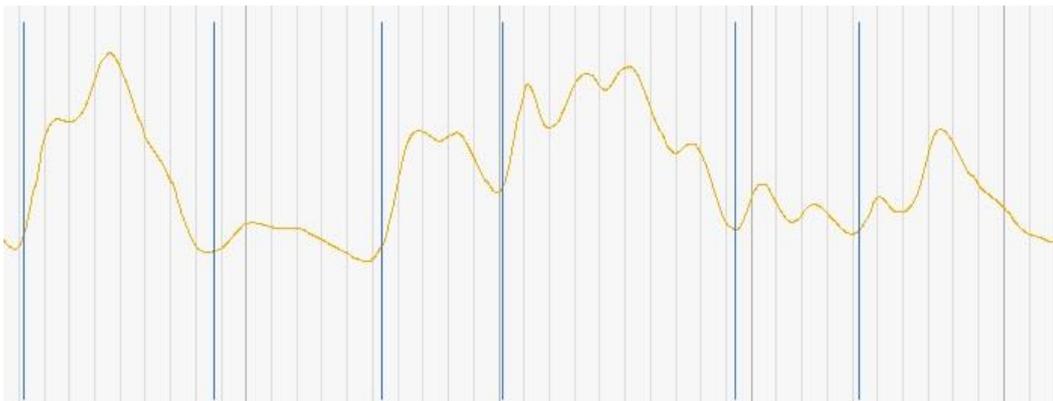
Here is an example of an unusable ECG signal. The R-waves are no longer clearly visible and their height is only slightly greater than the ground noise. One speaks here of a noisy ECG. The cause is either a source of interference (e.g., a fluorescent lamp, a defective charger on a notebook) or an insufficient electrical conductivity on the electrodes. To eliminate this, remove the source of interference (turn off the lamp, unplug the charger from the notebook) and place the moistened electrode paper under the clips or use electrodes contact gel.



A good pulse wave should look like this. The signal is similar to a sine wave. The zero line is clearly visible. The large vibrations correspond to the blood volume flow through the blood vessels. The blue vertical lines mark a detected heartbeat.



Here is an example of a bad pulse wave. The signal is very small and the individual volume pulses cannot be detected exactly. The ear clip should be positioned at a different location on the earlobe or to the other earlobe. It may also be helpful to rub the earlobe slightly before applying the ear clip to increase blood flow.



Here is an example of a pulse signal, which was shaken by movement of the subject. To avoid this, the subject should always keep the head calm during biofeedback/measurement. It also helps, when the cable with the silver clip is fixed at the shirt collar.

Notes on improving data quality during analysis

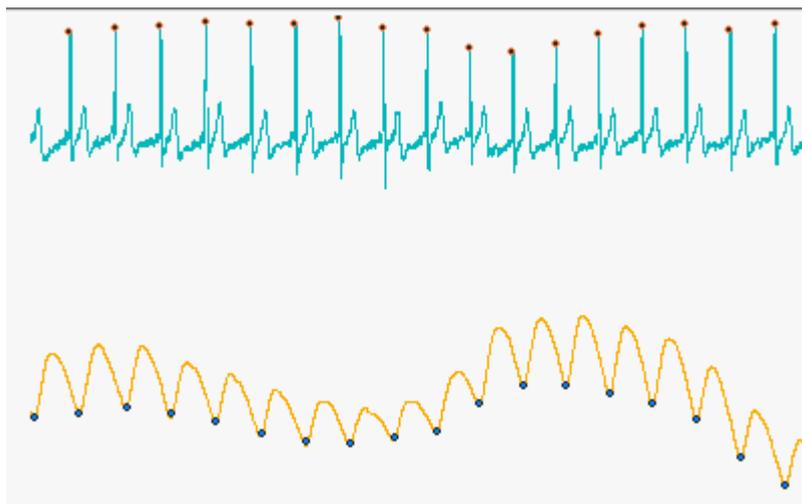
The registration of heart rate variability (HRV) provides valuable information about the state of the autonomous regulation. However, a requirement is a very high quality of the measurement, e.g. a very clean detection of the heart rate curve. There is hardly a medical method that is as sensitive to disturbances and artefacts as the HRV analysis. Even a single artefact in a 5-minute short term HRV may corrupt certain HRV parameters (e.g., RMSSD) by more than 100%.

For this reason, the accurate control of the heart rate curve and, if necessary, careful removal of all artefacts is the basis for a valid HRV evaluation. The following procedure has proved successful:

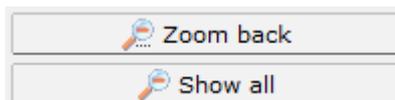
- **Step 1: Visual control of heart rate curve and biosignal**
- **Step 2: Optimal automatic determination of the heartbeat in the biosignal**
- **Step 3: Manual editing in biosignal**
- **Step 4: Graphic filtering**
- **Step 5: Adjust plausibility check and heart rate filters**

Step 1: Visual control of heart rate curve and biosignal

Both in the ECG and in the pulse wave signal, the heartbeat leads to characteristic signal fluctuations, which allow an accurate time determination of the heart activity. In the ECG, it is the R-wave, in the pulse wave the beginning of the steep rise



The HRV-Scanner indicates detected R-waves or detected pulse waves by a small orange (ECG) and blue (pulse wave) circle (see figure). It is recommended to scale some areas and confirm the correct position of the marks visually. You can scale by simply dragging a frame, with the left mouse button pressed, around the area of interest. The original scale can be restored by pressing the following buttons:

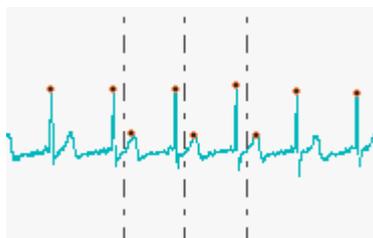


If the marks are incorrectly flagged, this leads to sudden jumps of the heart rate trace, which can be easily detected visually (see figure).

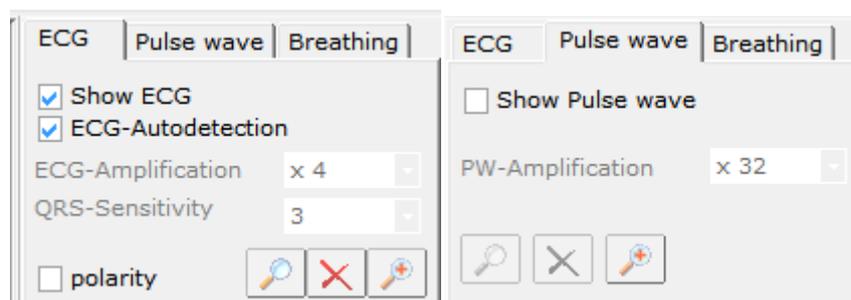


Step 2: Optimal automatic determination of the heartbeat in the biosignal

When the marks are systematically wrong or missing, re-running the automatic detection of heartbeats might fix the problem. Observe the lower figure: you will see that in addition to the correct detected R-wave, the T-waves have also been flagged.



This results in a wrong heart rate of over 200 beats per minute! Obviously, the sensitivity of automatic heartbeat detection is set too high. To change the sensitivity, you can adjust the settings for signal size and sensitivity (see picture).



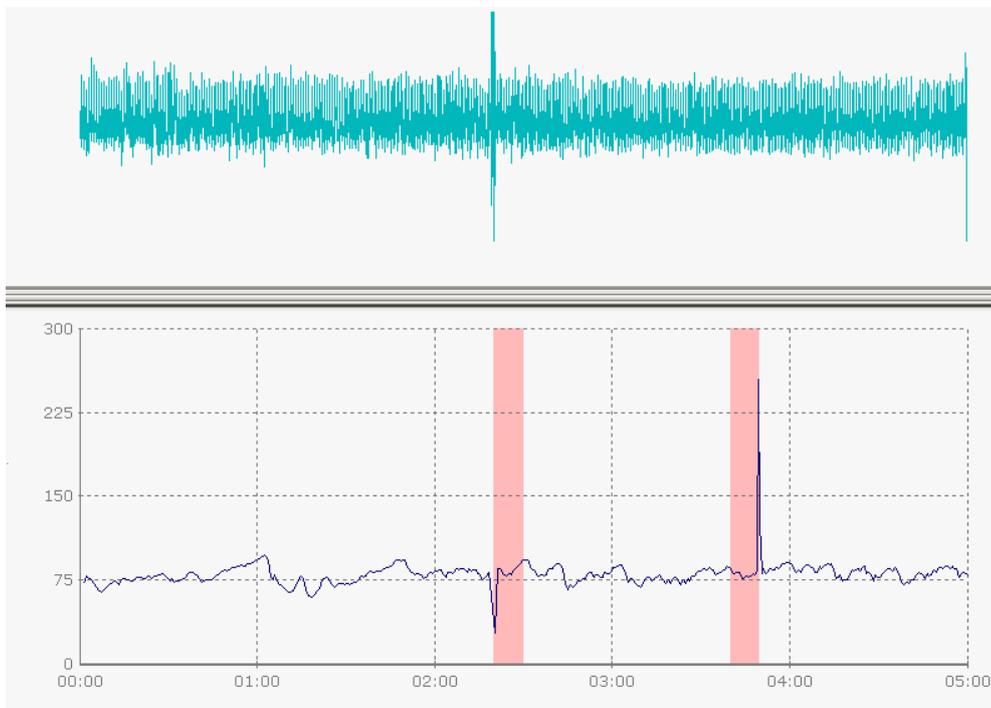
Change the settings for the biosignal you want to edit here. The ECG auto detection is activated by default. If this does not provide a satisfactory result, you should disable auto detection and manually adjust the amplification and QRS sensitivity settings.

Note: You must press the button with the magnifying glass symbol in order to run a complete re-analysis of the heartbeats with the changed settings!

Check the result visually and repeat the procedure, if necessary, until you cannot improve the quality of the data in this way. In this case, go to the next step and work out the remaining artefacts manually.

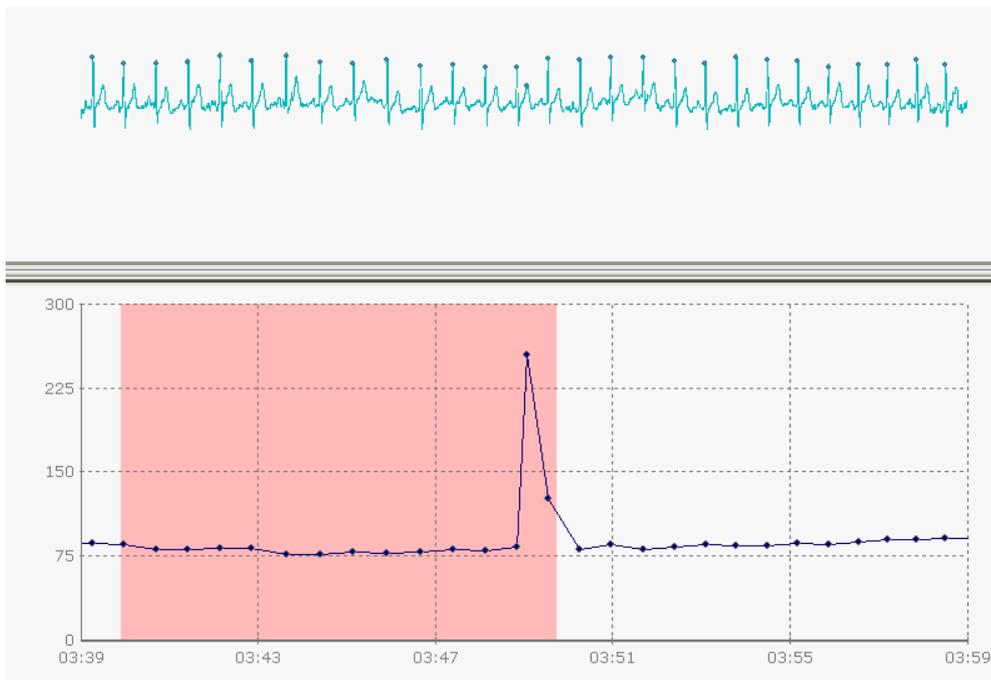
Step 3: Manual editing in biosignal

For shorter measurements (<10 minutes) and longer measurements with few artefacts, these should preferably be removed manually.

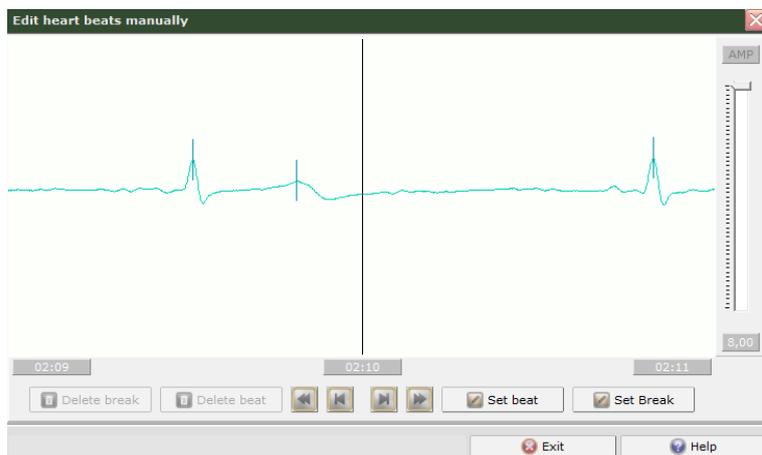


In the example shown, two artefacts were criticized by the Quality Wizard. A conspicuous deflection of the heart rate downwards, and a noticeable deflection of the heart rate upwards.

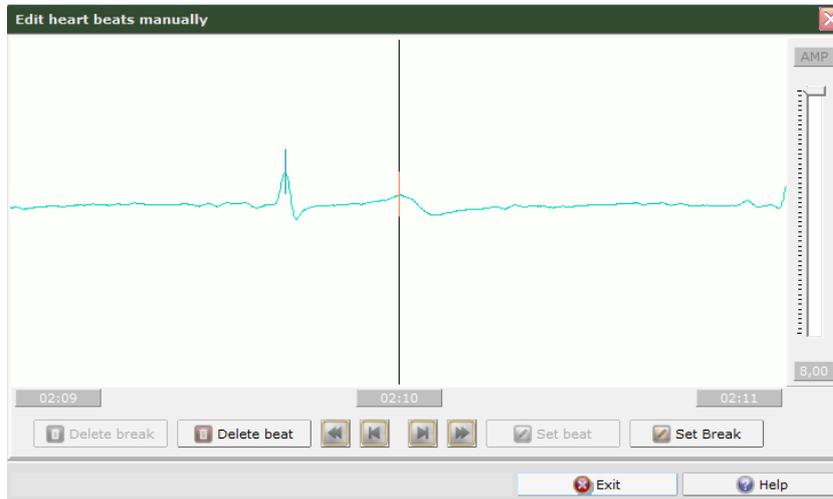
Such jumps should always be a reason to look more closely at the corresponding biosignal. Press the left mouse button and drag a frame around the jump in heart rate to scale the diagram (see figure).



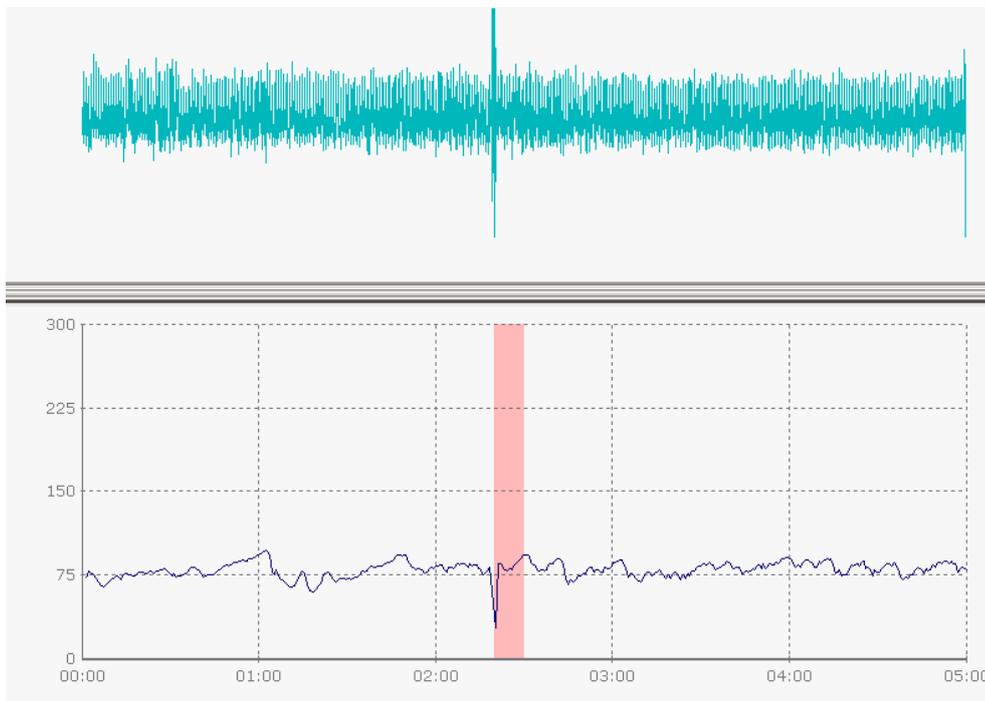
Now double-click on the point of interest. It doesn't matter whether you click in the biosignal diagram or in heart rate diagram. The double click starts the biosignal editor.



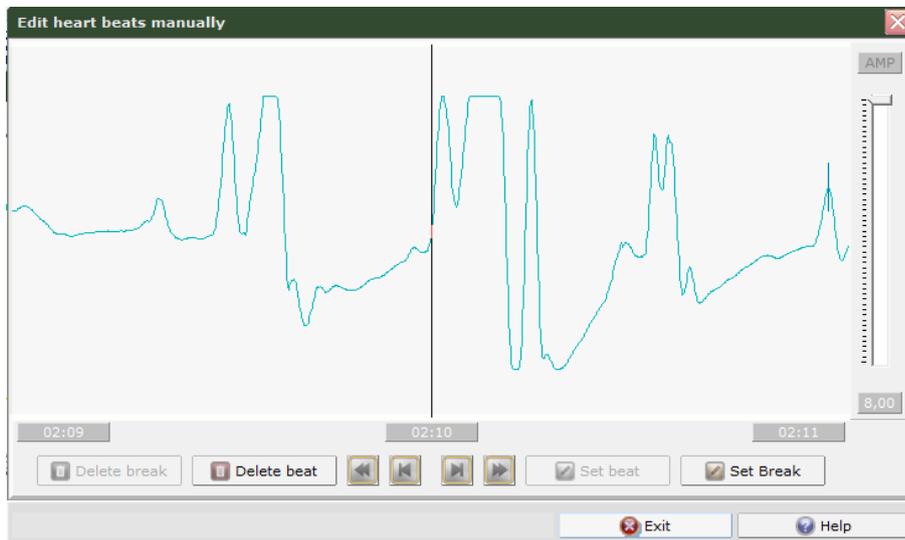
With the biosignal editor you can set and delete marks manually. Use the arrow buttons to move through the signal, until the vertical line in the middle is aligned with the point of interest. In the example above the T-wave is obviously marked as heartbeat. Here we have scrolled through the signal until we reached the incorrect mark (see figure).



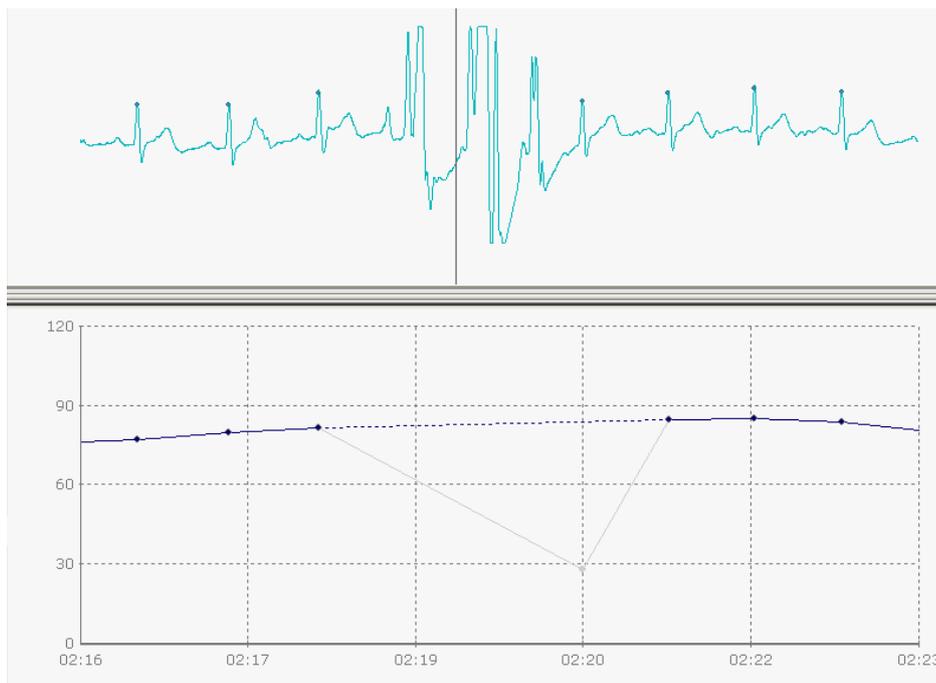
If the center line is over a marked beat the "Delete beat" button will be enabled. Press this button to remove the mark. The artefact is now cleared.



The second artefact, with the downward deflection, can be solved in the same manner. Scale the area of interest and start the editor (see figure).



Unlike the first example, we see here a more or less confused signal without any marks. It is impossible to detect the R-waves reliably. This explains the apparent downward jump: the time interval between the last detected R-wave before the disturbance and the first detected R-wave after it is several seconds long. This gap translates into a very low heart rate (remember: the heart rate of a single pair of heartbeats is computed by the formula 60 divided by the inter-beat interval, in seconds). In order to remove this kind of an artefact we insert a "break" somewhere inside the signal disturbance. A "break" instructs HRV-Scanner not to calculate a heart rate for this time interval.



Now look at the diagrams. You can see the break is marked by a vertical line in the signal diagram. In the heart rate trace a dotted line indicates the break area. There is also a fine grey line, which signals how the heart rate trace would have looked without correction.

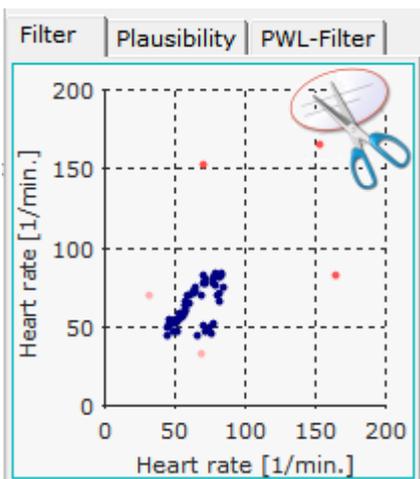
With these two manual editing steps of all of this measurement's quality problems can be corrected. The test is now ready for computing the HRV parameters.



Note: An artefact caused by a signal disturbance is not always the reason for sudden jumps of the heart rate. It might also be the case that the biosignal is correctly recorded, and the marks are all on the right positions. In this case the presence of the jumps may indicate an arrhythmia. It is not unusual to find occasional ectopic beats, which can be treated as artefacts. If the arrhythmia is too frequent, the HRV measurement becomes less reliable. In the case of atrial fibrillation, for instance, the HRV measurement is of no value.

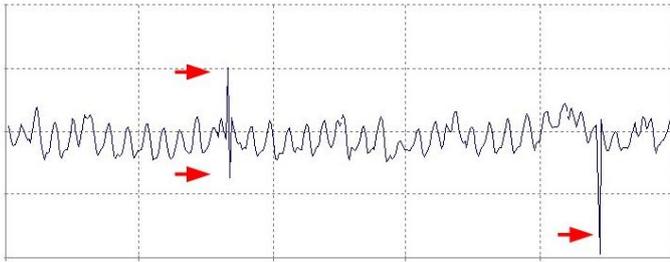
Step 4: Graphic filtering

Graphic filtering



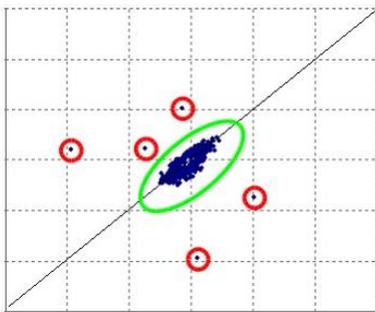
A HRV analysis should only include heartbeats that are under the control of the vegetative nervous system. Heartbeats that occur as a result of rhythmic disturbances distort HRV and usually lead to excessive HRV values, which can be mistakenly misinterpreted as a well-functioning neurovegetative regulation. A good way to separate "good" from "bad" heartbeats is to use the Poincare diagram. Neuroregulation-induced heartbeats are arranged along the bisector lines in the Poincare diagram, whereas heartbeats due to rhythm disturbances have an irregular pattern.

Example:



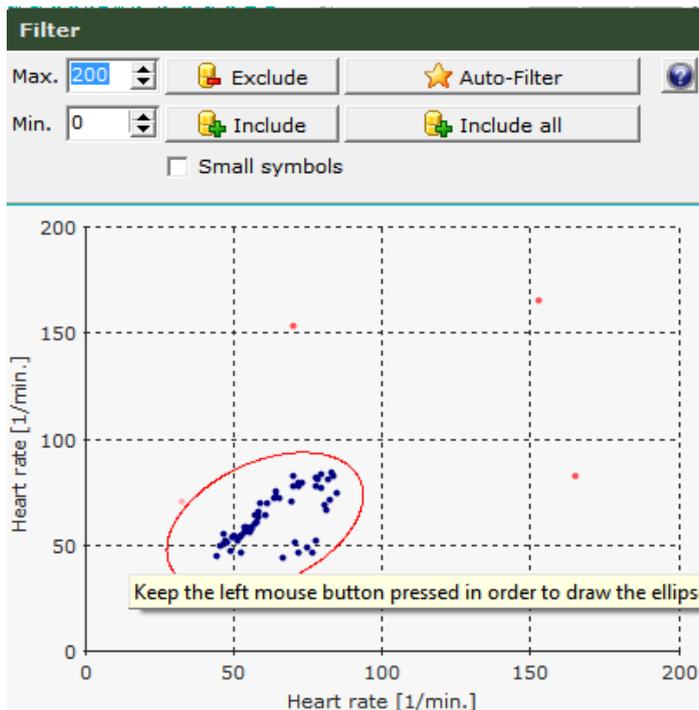
There have been some irregular heartbeats in the heart rate pattern, so-called extra-systoles, recognizable by the sudden changes in heart rate (red mark).

In the corresponding Poincare diagram, the irregular heartbeats can be seen even more clearly:



Heartbeats as a result of vegetative regulation arrange themselves as point cloud along the bisector (green ellipse). Irregular heartbeats differ from this distribution pattern and can easily be identified (red circles). The special feature of the Poincare diagram, to distinguish regular from irregular heartbeats, allows for optimal filtering of the heart rate.

Poincare based filtering



To remove the irregular heartbeats, simply drag an ellipse around the point cloud that is formed by the regular heartbeats.

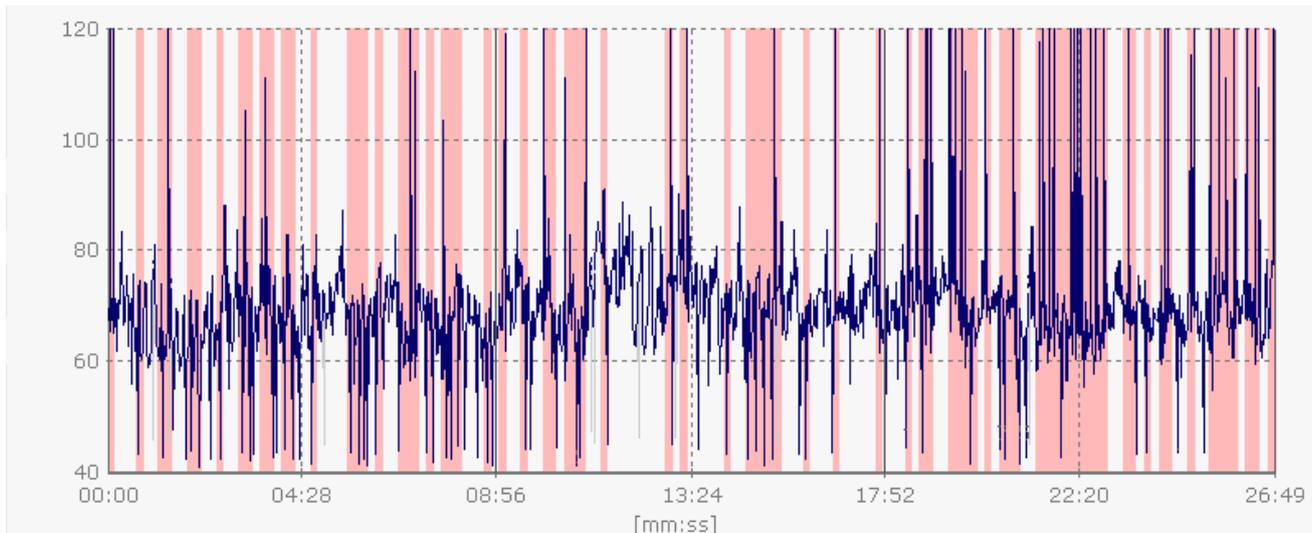
Click the "Exclude" button to remove all heartbeats outside the ellipse.

With the "Include" switch, you can record heartbeats back into the HRV analysis if accidentally excluded regular heartbeats.

Note: "Auto-Filter" takes the drawing of the ellipse and automatically calculates which heartbeats should be marked as artefacts and excluded during the evaluation. "Include All" causes an undoing of the graphic filter.

Step 5: Adjust plausibility check and heart rate filters

For longer measurements, it may be very time-consuming to process each individual artefact manually. For example, the following measurement contains numerous artefacts in approximately 30 minutes of measurement time.



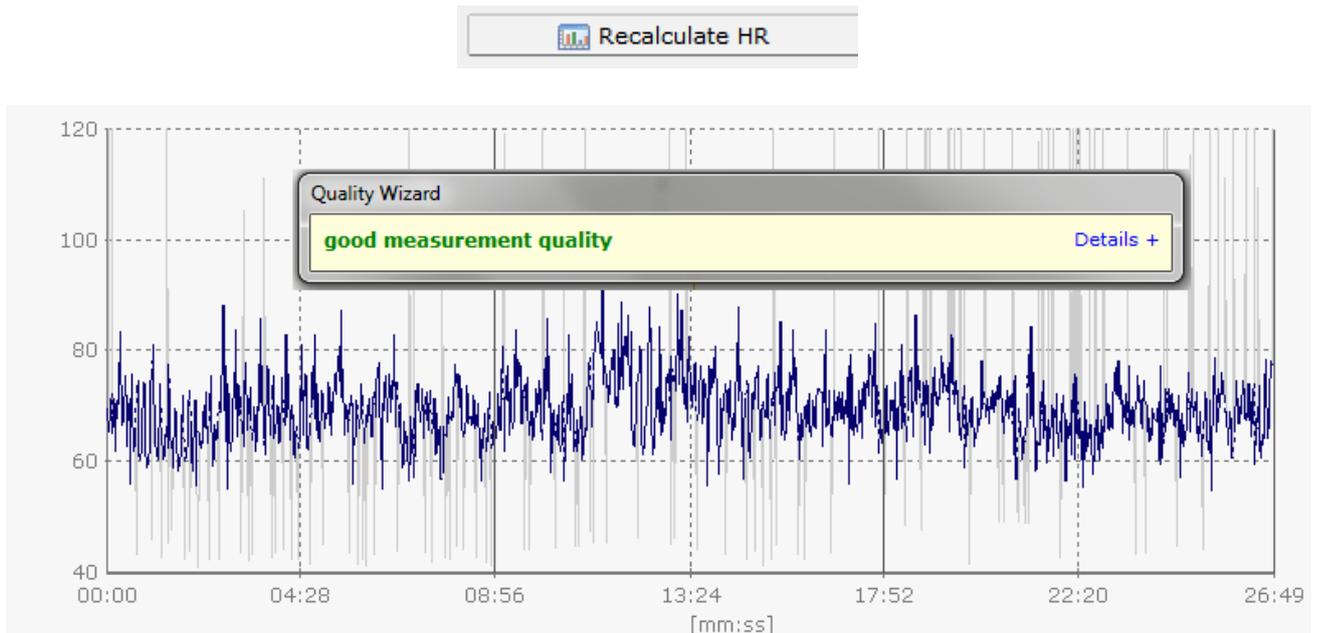
Since this is an import of a RR interval-based measurement, there is no biosignal in which the automatic heartbeat detection could be optimized (as described in step 1). In the case of shaky measurements with poor signal quality, such heart rate sequences can also be obtained, even with optimized heart rate detection.

It is recommended to adjust the plausibility check of the HRV-Scanner.

Filter	Plausibility	PWL-Filter
Min.	50	[/min.]
Max.	100	[/min.]
 Recalculate HR		

Because the heart rate fluctuates between 90 and 55 in the example, a very good result is already achieved with plausibility values of 50/100.

For the changed settings to take effect, press the Recalculate Heart Rate button.



As can be seen in the picture, the adaptation of the plausibility check has already been sufficient in the example in order to produce a good data quality.

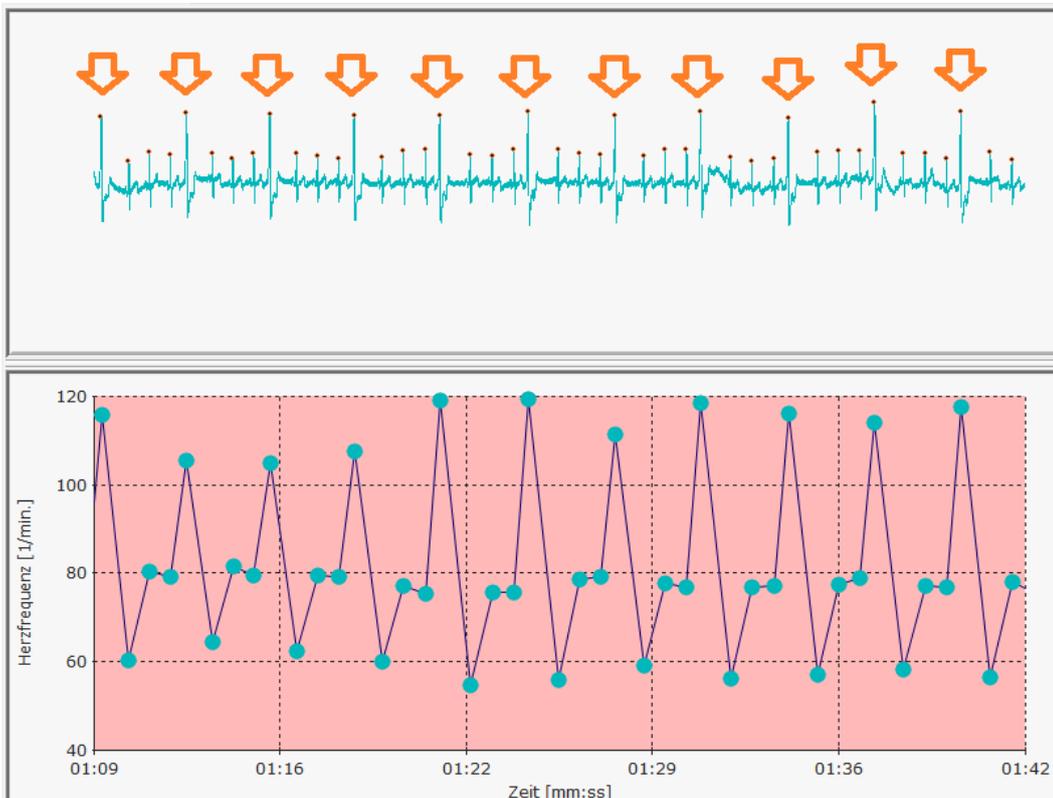
What happens during plausibility checks? In the plausibility check, the HRV-Scanner compares for each interval between two heartbeats whether the resulting heart rate is above or below the set limit values. If this is the case, the HRV-Scanner sets a "break" in this RR interval. "Breaks" we already know from step 2, they prevent the calculation of the heart rate from a RR interval provided with a "break".

Note: If artefacts persist despite the plausibility check, these can be corrected manually (see step 2).

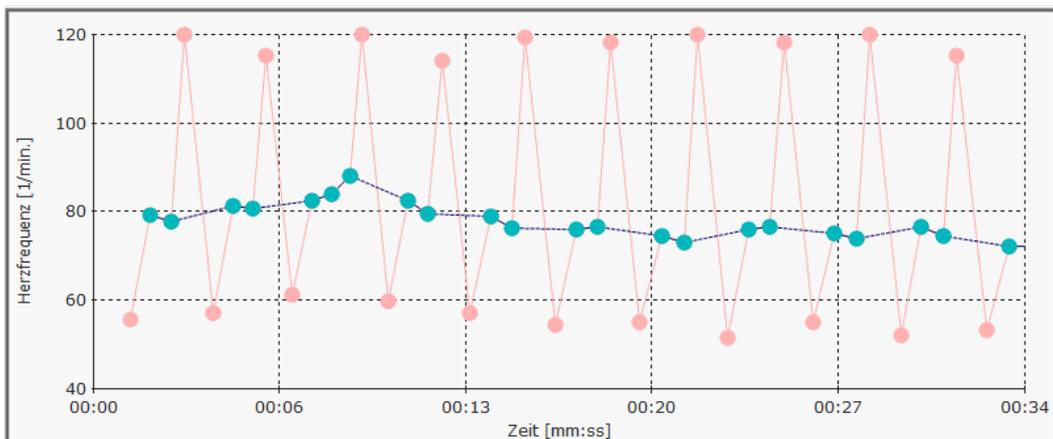
Limits of HRV determination

Heart rate variability, as the name implies, determines the variability of the heartbeat. This means that all kinds of artefacts (wobbling in the ECG due to movement, interference signals, ...) and heart rhythm disturbances (irregular heartbeats, atrial fibrillation, ...) lead to an increased HRV. However, since this regulation does not come from the sinus node innervated by the parasympathetic nervous system, we cannot evaluate such heart rate profiles without first removing all artefacts and all heartbeats not from the sinus rhythm (excitation from the sinus node and not from accessory pacemaker cells).

Example 1: many irregular heartbeats (marked in orange)

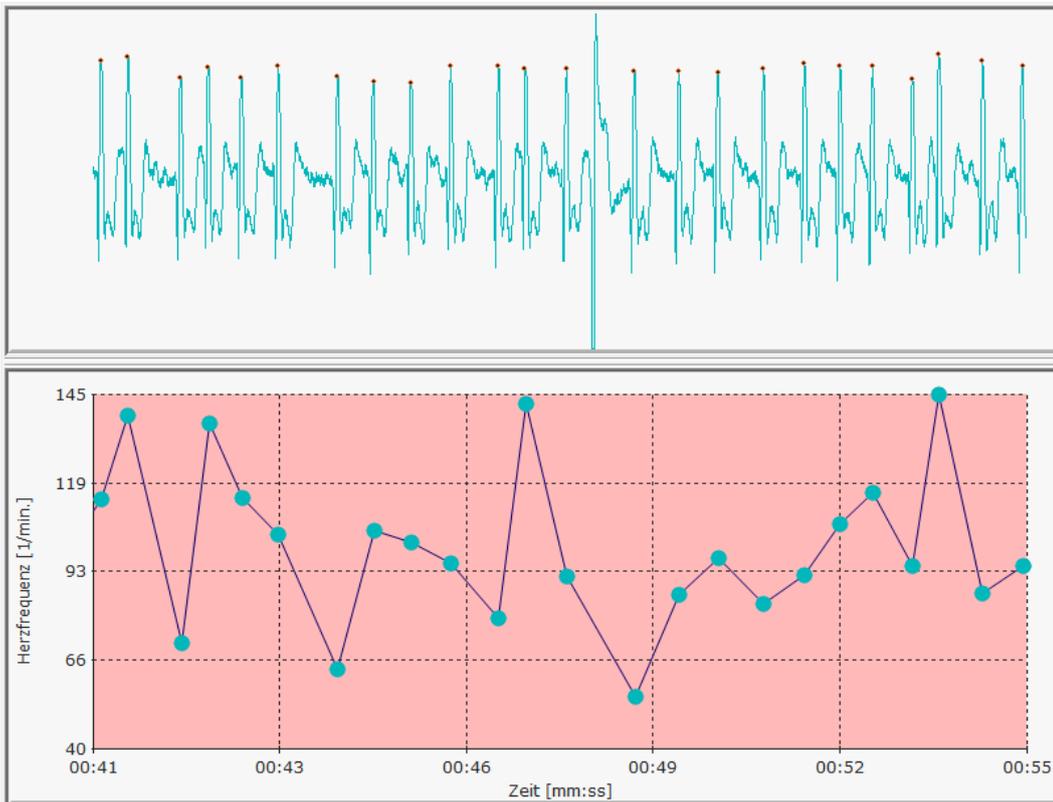


This shows the high variability in the heart rate curve due to the almost regularly occurring irregular heartbeats (3 normal QRS complexes as signs of excitation from the sinus node, then always an irregular heartbeat with compensatory pause afterwards).

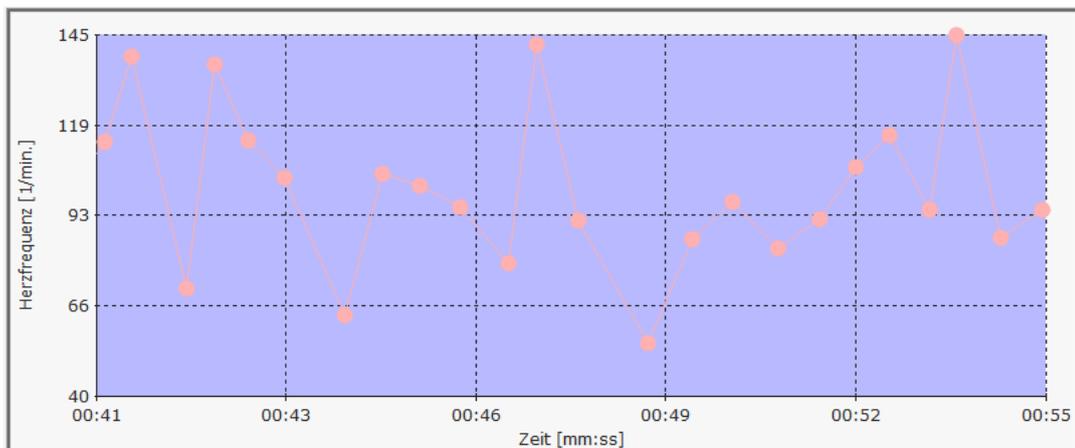


The heart rate after automatic filtering in the Poincaré filter. After exclusion of the irregular heartbeats (pink dyed), approximately 50% of the heart rate (green) remain for the evaluation. For a 5-minute Short-Term HRV measurement, this is just sufficient to determine the HRV.

Example 2: Atrial fibrillation



At first glance, a regular ECG is available. One would assume here only one extra heartbeat. However, a very disordered rhythm is observed when the heart rate curve is considered. This can be seen in the present atrial fibrillation. In the ECG, the missing P-waves are also seen as a sign of a non-regular atrial innervations.



The heart rate after automatic filtering in the Poincaré filter. After exclusion of the irregular heartbeats (pink dyed), nothing of the original heart rate curve remains for the evaluation. Thus, a determination of the HRV is not possible or useful in the case of present atrial fibrillation.

The detection of such rhythm disturbances often requires some experience. If you have any doubts, please feel free to use our support.

A good quality ECG is always important for a reliable analysis. Only with this it is possible to get a more detailed picture of the present rhythm disturbances. This is not possible either with the pulse wave or with an RR distance-based HRV measurement (chest belt without ECG).

HRV concept "Tone, Flexibility, Dynamics"

The concept in the HRV-Scanner "**Tone, Flexibility, Dynamics**" should help to structure the confusing amount of HRV parameters. It also facilitates evaluation and interpretation later on, and thus helps to better understand HRV measurements.

factor analysis extracts the principal components of heart rate variability

Variable	Faktorladungen Extraktion: Hauptkomponenten (Markierte Ladungen >,700000)		
	Faktor 1	Faktor 2	Faktor 3
CV_HR	0,959304	0,023655	0,023190
LF/HF Ratio	0,060667	0,592394	0,058098
Mean HR	-0,151470	0,208226	0,943346
Power HF	0,765579	-0,410370	0,102415
Power LF	0,846968	-0,087486	0,078846
Power Total	0,940370	-0,062544	-0,075956
Power VLF	0,615069	0,179412	-0,285452
SD1	0,808041	-0,511046	-0,195286
SD2	0,953021	0,025015	-0,219223
Sd2/SD1	-0,060707	0,897920	0,152777
SD2SD1norm	-0,079343	0,951984	0,151692
SDNN	0,956371	-0,061864	-0,221310
LN_SI	-0,821952	0,138351	0,386142
alpha1	-0,155677	0,835549	0,159377
Correl	-0,080564	0,894116	0,140807
Mean RR	0,163385	-0,196586	-0,946330
Erkl.Var	6,731791	4,140534	2,269172
Ant.Ges.	0,420737	0,258783	0,141823

If you are dealing with a large number of variables that give a rather confusing picture in their entirety, it makes sense to reduce the large number of variables to a few, which are the central components of the data set.

Such a data reduction can be achieved by means of factor analysis, which searches for the underlying factors in a pool of many variables and groups the individual variables according to their contribution to the respective main factor.

We applied such a factor analysis to the HRV measurements of more than 1000 people and found that the many HRV parameters can be reduced to essentially three main factors, which we will take a closer look at below.

Let's start with the factor on the right in the table. As you can see, it essentially describes the heart rate, since only the two parameters heart rate and mean RR distance, i.e. the distance between two heartbeats in milliseconds, contribute to this factor. We call this factor "**Tone**" because it describes, so to speak, the basic tone of the autonomic nervous system with which cardiovascular regulation takes place.

The second factor groups parameters that are primarily related to the rate of change, i.e. the dynamics of the heart rate curve. The ratio of slow heart rate changes to fast changes in heart rate, the SD2 to SD1 quotient, as well as the autocorrelation coefficient and the alpha1 value of the detrended fluctuation analysis, which also express how high the proportion of rapid changes in the Heart rate is. The SD1 value itself, that is, the mean change in heart rate from heartbeat to heartbeat, also has a comparatively high factor of 2. For short measurements, such as the one-minute determination of respiratory sinus arrhythmia, the RMSSD value is often used instead of SD1. However, RMSSD and SD1 both express the same thing, namely how the heart rate changes from one beat to the next and differ only in their amount. They can also be easily converted into one another.

Similar to SD1 and SD2, the power values are calculated using a spectral analysis. The Power HF is comparable to the SD1 and RMSSD, and the LF / HF ratio, similar to the SD2 to SD1 quotient, expresses whether the heart rate curve is composed of slow or fast changes in the heart rate. Overall, our second main component obviously has a lot to do with dynamics, which is why we gave the underlying factor the name "**Dynamics**".

Now let's look at the first factor. We see that those parameters have a high impact on this factor, which express the amplitude of the heart rate changes, such as the standard deviation SDNN, the coefficient of variation or the total power. The parameters that primarily quantify slow changes in heart rate, such as SD2 and low frequency power, can also be assigned to factor 1. So, factor 1 obviously evaluates the amplitude of the heart rate change. We have therefore chosen the term "**Flexibility**" for this factor. The flexibility expresses the adaptability of our cardiovascular system and describes the actual range of heart rate changes when disturbances to the inner homeostasis occur.

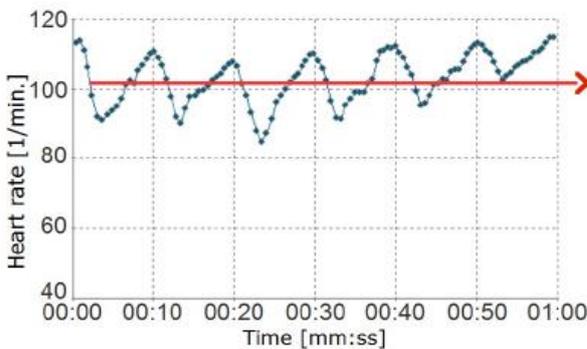
For each of these main components "**Tone, Flexibility and Dynamics**", clinical studies have shown that an unfavorable change is accompanied by a significant increase in mortality. For example, mortality increases threefold when the resting heart rate is > 90 beats per minute compared to a resting heart rate < 60 beats per minute. Each of these factors "**Tone, Flexibility and Dynamics**" therefore contains clinically relevant information that should not be missing in any HRV analysis.

So, there are essentially three questions that we ask in an HRV analysis:

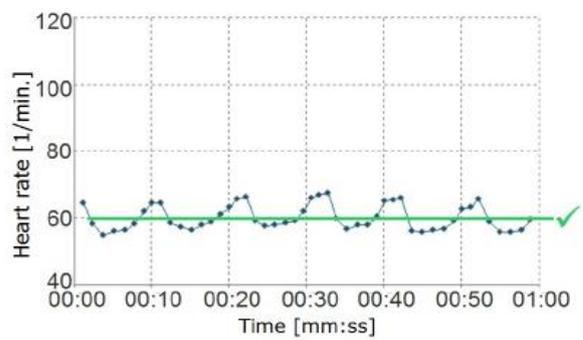
- What is the tone of the heart rate curve?
- How high is the flexibility of the heart rate curve?
- And how high is the dynamics of the heart rate curve?

Tone

When we speak of a high or good tone, we mean that the mean heart rate is comparatively low. A poor or low tone shows an excessive heart rate.



Example of low parasympathetic tone (high mean heart rate)

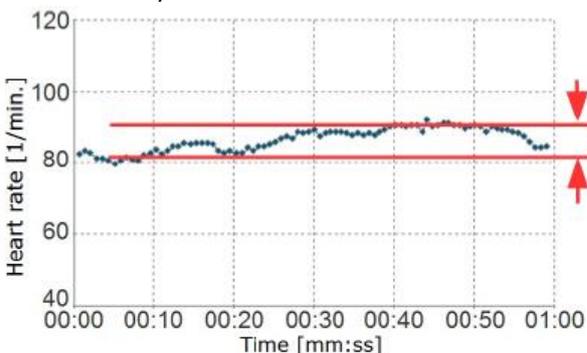


Example of high parasympathetic tone (low mean heart rate)

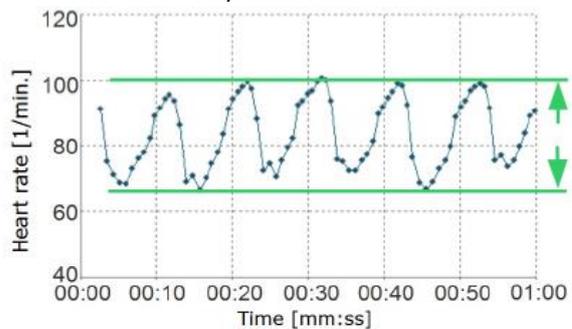
Flexibility

In terms of flexibility, we look at how much the heart rate fluctuates. For example: The deep breathing test determines the respiratory sinus arrhythmia by means of deep cycle breathing with 6 breaths per minute. We take the maximum of the heart rate when inhaling and subtract the minimum of the heart rate when exhaling. This gives us the amplitude of the sinus arrhythmia, the E-I value, where E stands for expiration and I for inspiration. When determining short-term HRV, in contrast to determining respiratory sinus arrhythmia, we do not prescribe a fix breathing pattern and therefore do not always see respiratory sinus arrhythmia. We therefore take another suitable parameter to assess flexibility, e.g. the standard deviation SDNN, the coefficient of variation or the total power.

A high degree of flexibility can be recognized by the fact that the heart rate changes extend over a larger area, whereas there is only a small fluctuation in the heart rate when the flexibility is low.



Example of a very low flexibility (heart rate oscillation substantially reduced)



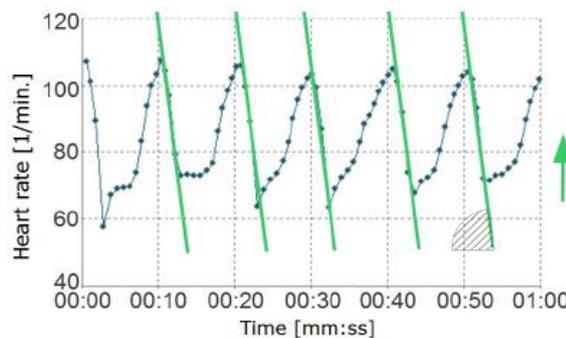
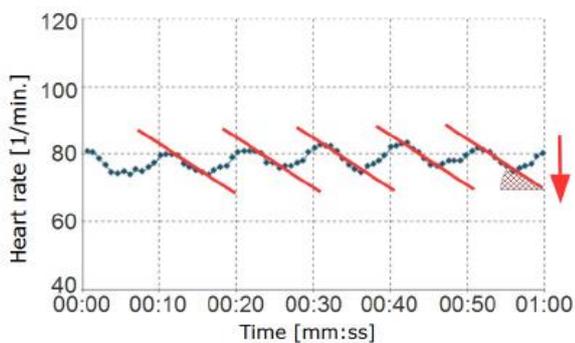
Example of high flexibility (large amplitude of the heart rate oscillation)

Dynamics

For the assessment of the dynamics, we analyze how fast the changes in the heart rate take place. So, we are interested in the speed of regulation. Interestingly, the speed of the heart rate adjustment is achieved by the parasympathetic nervous system (PNS), i.e. by our brake, not by our accelerator pedal (sympathetic nervous system, SNS). The SNS is comparatively slow and takes about 10 times longer to react than the parasympathetic nervous system. That is why the dynamics tell us primarily something about the functional state of the parasympathetic nervous system.

Good dynamics can be seen with the naked eye, for example, in Deep Breathing Tests. When you exhale, the heart rate usually drops much faster than it increases when you inhale. A top-trained competitive athlete, for example, often only needs a single heartbeat to drop the heart rate from the maximum when inhaling to the minimum when exhaling, as we can clearly see in this example of a measurement by a professional athlete, a multiple world champion.

If there is a marked weakness of the parasympathetic nervous system, there is a significant delay in the dynamics and it takes a lot more heartbeats to reach the minimum when exhaling, as can be seen in this example. The RMSSD or SD1 are parameters that primarily evaluate the speed of the heart rate change.



Example of a heart-brain axis that has little dynamic. The heart rate changes little from heartbeat to heartbeat.

Example of good dynamics. The heart rate changes very much during exhalation (decrease in heart rate).

In order to get an overall assessment of the HRV from flexibility, dynamics and tone, we still have to take into account that the respective age largely determines the performance of our neurovegetative regulation. The performance of the autonomic nervous system deteriorates with age. We lose about 1 to 1.5% per year of our original performance that we once had when we were young. The different components are affected differently by the aging process. The heart rate decreases slightly in old age, so the heart beats a little slower, which is fundamentally positive, whereas the flexibility and dynamics in old age are significantly lower than in young years. The respective measurement results for flexibility and dynamics must therefore be corrected for age, which the HRV-Scanner automatically does for you.

In the end, of course, you want to know whether the measurement result shows good flexibility or, for example, the dynamics are not sufficient. However, this cannot be seen from the mere numerical values of the HRV parameters. The HRV-Scanner therefore translates the results of the HRV calculations into rank values between 0 and 100%. These rankings show how many of 100 healthy and physically fit people of the same age have poorer HRV. For example, a 10% percent rank for flexibility means that only 10 out of 100 healthy and physically fit people have less flexibility and the vast majority of 90% achieve a better value. The same applies to dynamics. In terms of tone, a 10% result means that only 10 out of 100 healthy and physically fit people have an even higher heart rate and in 90% the heart beats slower. We remember that a high parasympathetic basic tone is characterized by a low heart rate.

In summary, it can be said that the concept "**Tone, Flexibility and Dynamics**" enables a meaningful structuring of the HRV parameters and takes into account all important main components of the HRV. With this concept, the focus is reduced to the essentials, the superfluous is left out and no longer obscures the view of potentially important changes in neurovegetative regulation. The concept of flexibility, dynamics and tone can also be communicated and explained to the measured people very easily and with comparatively little effort. This makes the HRV measurement more efficient.

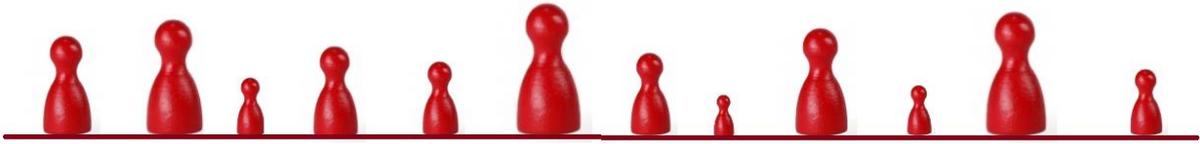
Understanding the rank chart

Rank diagrams show the most important measured values of the HRV analysis on a rank scale from 0 to 100%. Using this scale, we can evaluate the measurement result and make a statement as to whether it is a bad result (0%) or a good result (100%).

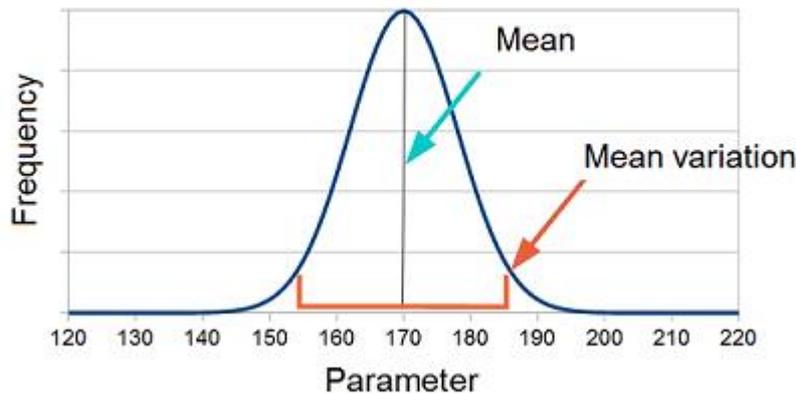
To do this, however, it is necessary to convert the individual HRV raw values to the corresponding rank values.

To understand how the HRV-Scanner does this, let's look at the following example:

In a group of people, we measure body size and, as expected, find that most people are different in height.



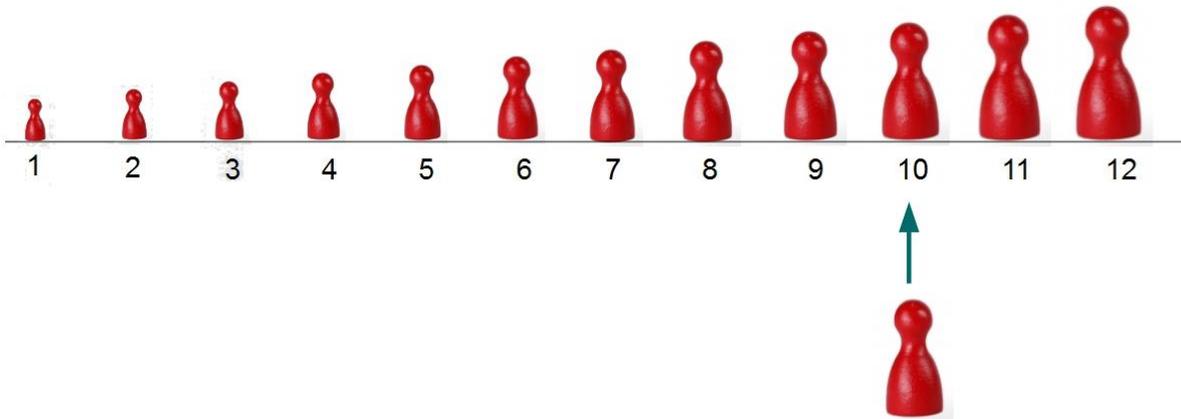
If we plot in a graphic how often individual body sizes occur, we get the associated distribution curve



A well-known example of a distribution curve is the Gaussian normal distribution. We can now take the mean value and the scatter range from the distribution curve. We immediately see that the measured values occur less frequently, the further they appear from the mean. In order to determine the rank of a single measured value, we arrange the individual measured values according to their size.

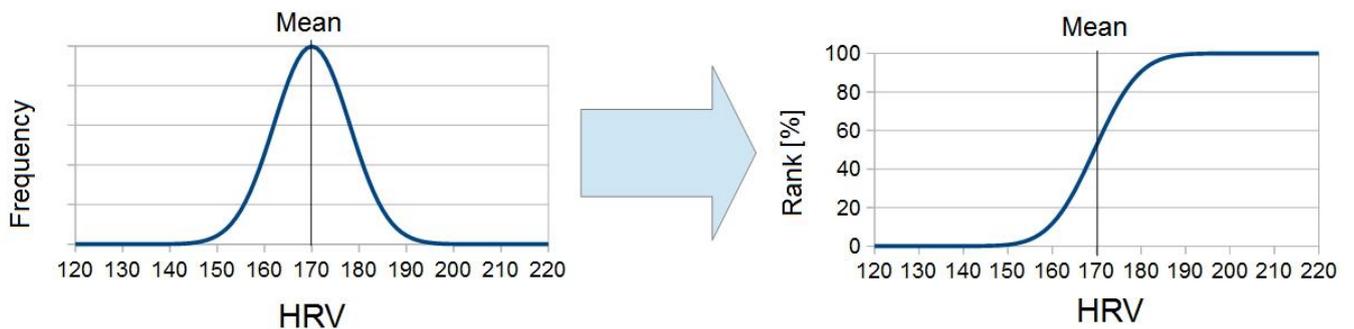


We then get the rank of each individual measured value in percent by determining the position of the measured value in the first step, i.e. at which point of our size-sorted sample the measured value is classified.

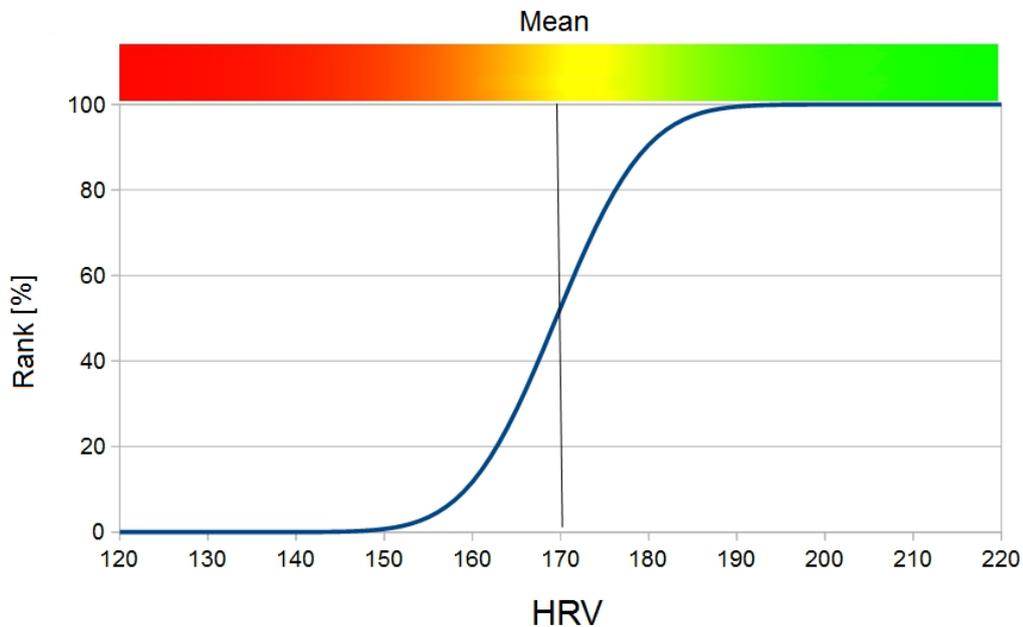


If we divide this location number of our measured value by the total number of measured values and multiply by 100, we get the percentile rank of the measured value.

The corresponding distribution function is now stored in the HRV-Scanner for each standard parameter, so that the associated percentile rank can be calculated for any measurement value.



For better illustration, the percentage range in the HRV-Scanner is colored according to the traffic light principle, so that it is clear at a glance whether the respective result is a good or bad result.



Rank values are practical because you can immediately see how an HRV value relates to a reference group. On the other hand, they have some special features that you have to take into account when interpreting them:

Let's take a look at the ranking curve, which gives us the corresponding percentile rank for each HRV value. We see an S-shaped curve, i.e. large changes in the HRV values in the low percentage range and in the high percentage range only lead to minor changes in the corresponding percentage rank.

In the middle area of the curve, it is exactly the opposite. Even small changes in HRV lead to large changes in percentile rank. In this area, the S-shaped curve acts like a lever that increases changes in HRV.

At the same time, due to the associated distribution function, the majority of the measured subjects are in this area. This means that the percentages of most people measured can fluctuate more or less strongly with repeated measurements, since HRV values, in contrast to other biological parameters such as body size, weight or bone density, change more from measurement to measurement. This change due to the leverage effect of the S curve is reinforced. Fluctuations in percentile ranks in repeated measurements in people with average HRV are therefore quite normal.

In contrast, people with severely restricted HRV experience significantly fewer fluctuations in percentile ranks. People with overt neurovegetative dysfunction generally retain their poor rankings even after repeated retests. Rank diagrams are therefore particularly well suited to determining a weakness of the neurovegetative regulation, since the percentile rank of the persons affected hardly changes even with fluctuations in the measured values.

If, on the other hand, we want to assess how the HRV changes over time and we have enough measurements, then we use a time series analysis instead, which is available to us in the Qiu module or in the measurement / parameter history.

This time series analysis can be applied to any HRV measurements and shows us not only whether and how strongly there is a trend in the development of HRV values, but also how much the HRV values vary. We do not use the percentile ranks here, instead we use the raw HRV data and therefore the leverage of the S-shaped distribution curve does not matter in the time series analysis.

Basis HRV measurements

The two basic HRV measurements are Short-Term HRV and Deep Breathing Test. By combining both measurements, the current state of the vegetative regulation can be reliably determined.

These two measurements are very suitable for initial and follow-up investigations.

Starting with the 5-minute Short-Term HRV for recording the actual HRV in rest. The subject should lie relaxed for 5 minutes or sit if not possible (please lift up the legs to minimize the orthostatic load).

After the Short-Term HRV, the Deep Breathing Test is performed. This is a 1-minute functional test of the parasympathetic.

The Short-Term HRV

The Short-Term HRV measurement is a trusted and clinically proven test for assessing heart rate variability at rest. The Short-Term HRV measurement should be performed with the ECG (and possibly additional pulse wave). Duration: pure measurement time 5 minutes, incl. preparation approx. 8-10 minutes

Prepare the measurement

As with any HRV measurement, the determination of the Short-Term HRV requires careful preparation of the subject. It should be ensured that all factors that could influence the neurovegetative balance are controlled or at least documented. These include: medication, current illness, strong physical exertion (sports) in recent days, or even coffee or nicotine just before the measurement. Before the measurement begins, the subject should be in the final lying position for a few minutes to allow vegetative resting.

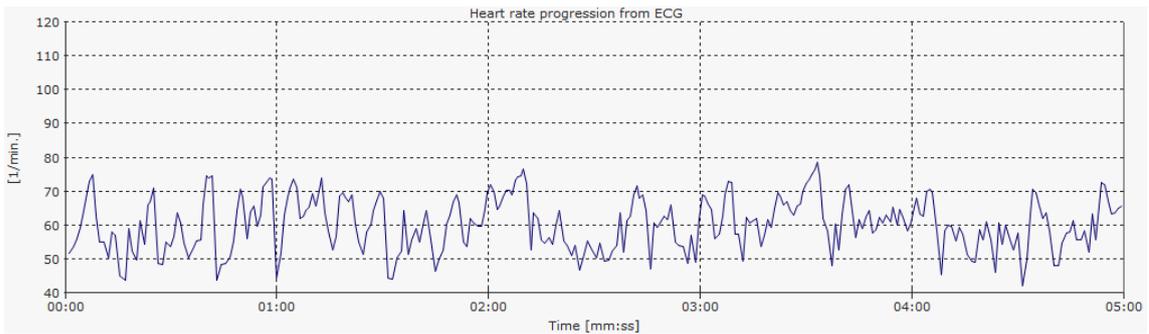
Perform the measurement

During the short-term measurement, ensure that the subject is quiet and breathes normally. The Short-Term HRV measurement should preferably be performed with the ECG. After the measurement time has elapsed, you will receive a message about the successful recording of the measurement. Close the measurement window. The measurement data are moved to an archive and an entry for the new measurement appears in the "Test and analysis" window.

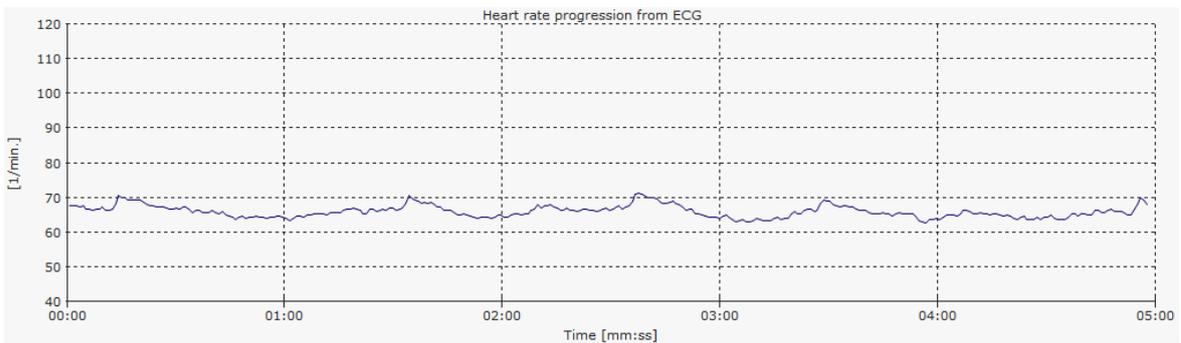
Evaluation

To do this, select the Short-Term HRV measurement in the " Test and analysis " window with the mouse and press "Analyze" or double-click on the measurement symbol. The course of the heart rate should show a steady up and down during the short-term HRV, in which the heart rate should be within the normal range (60-80 / min).

The lower picture shows a typical course of the heart rate during a Short-Term HRV measurement of a healthy subject.

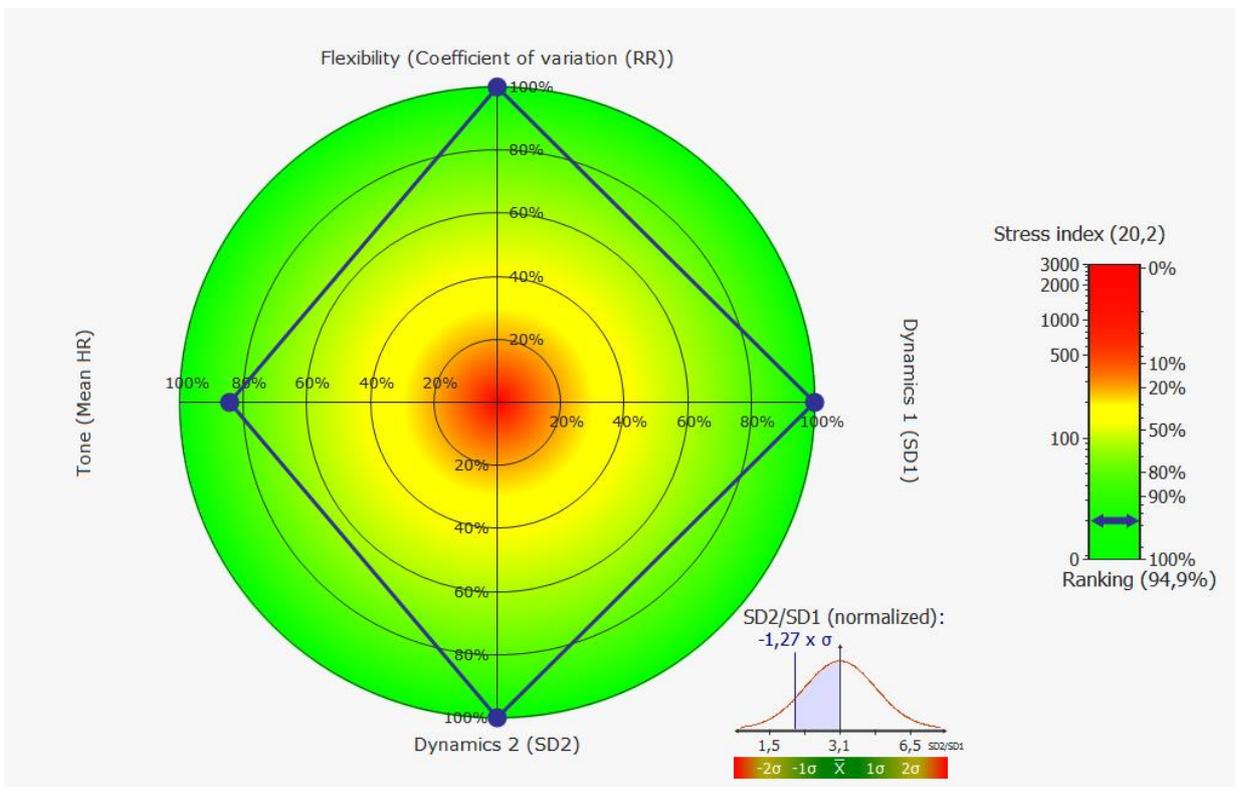


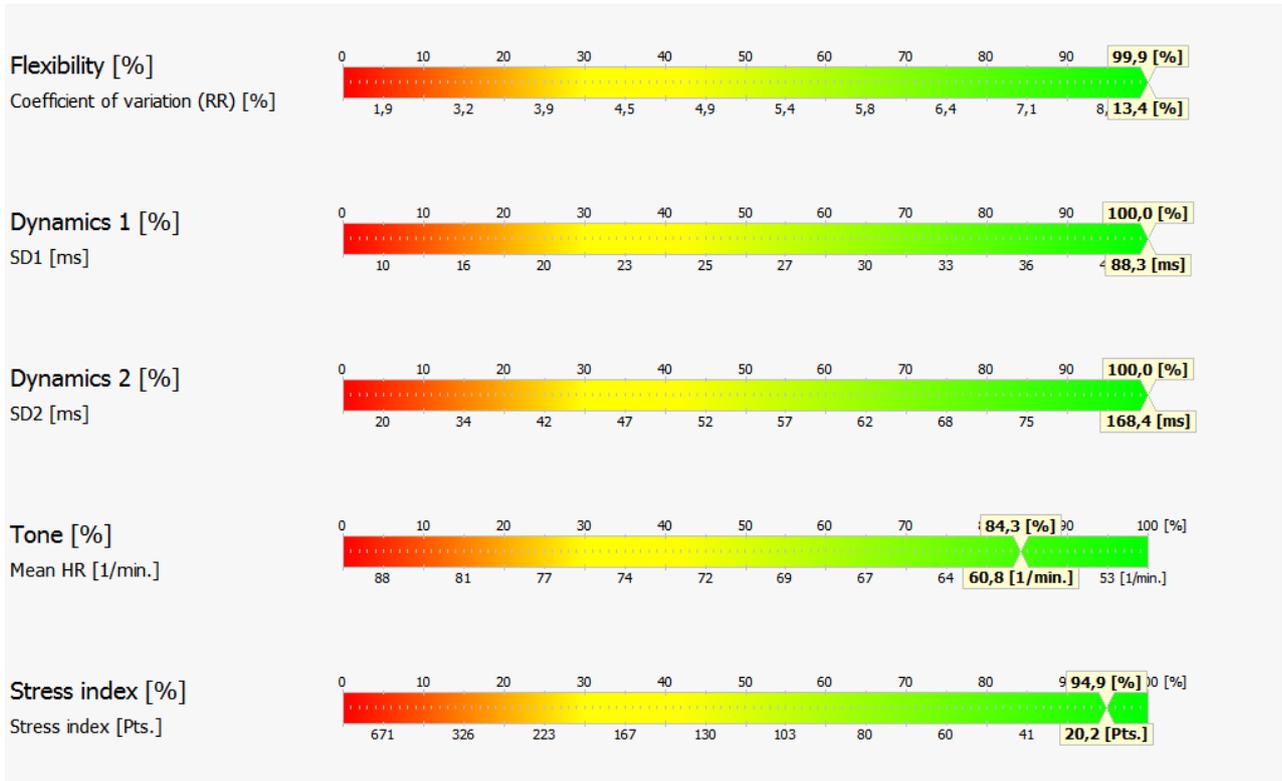
The lower picture shows a typical course of the heart rate during a Short-Term HRV measurement of a subject with markedly reduced heart rate variability.



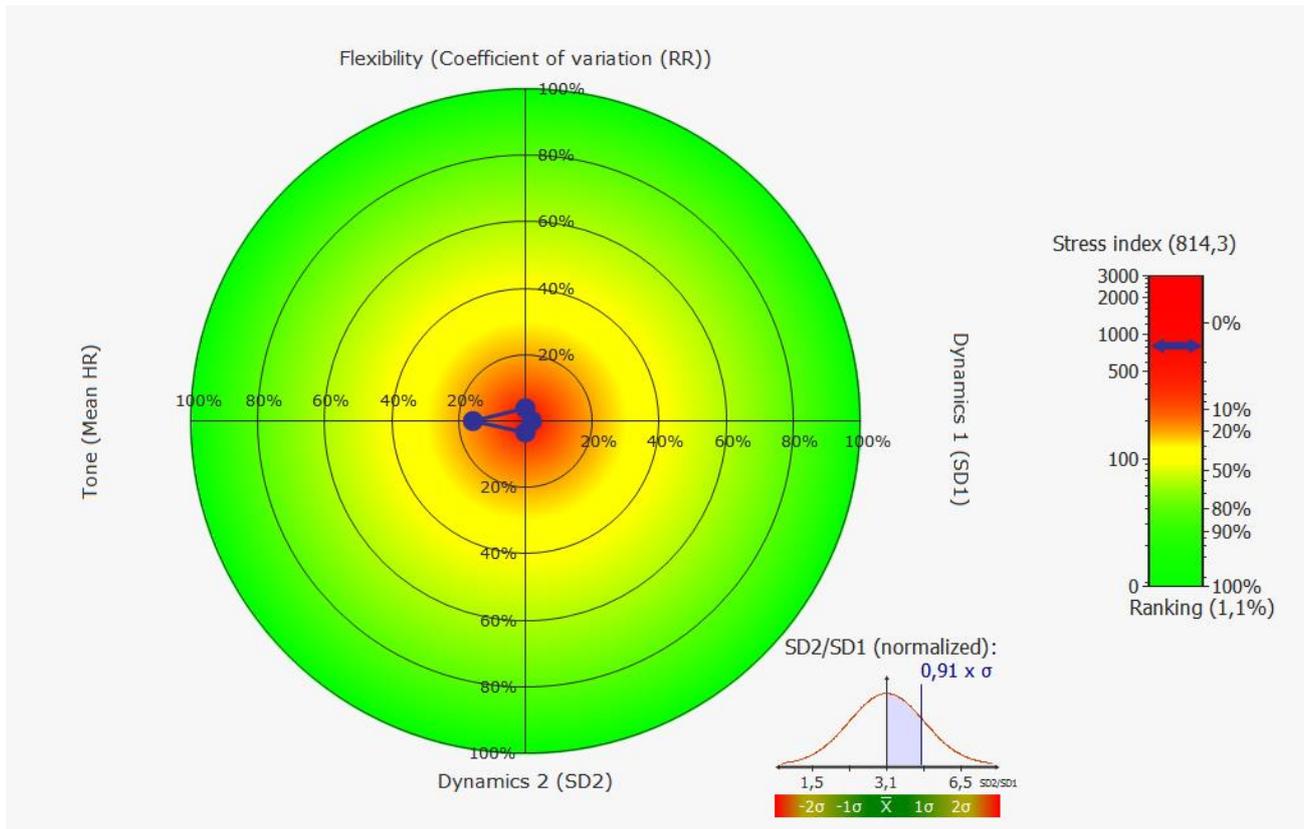
Standard values are stored for the most important parameters of the Short-Term HRV. This allows the comparison of the current measurement results with the results of healthy people of the same age.

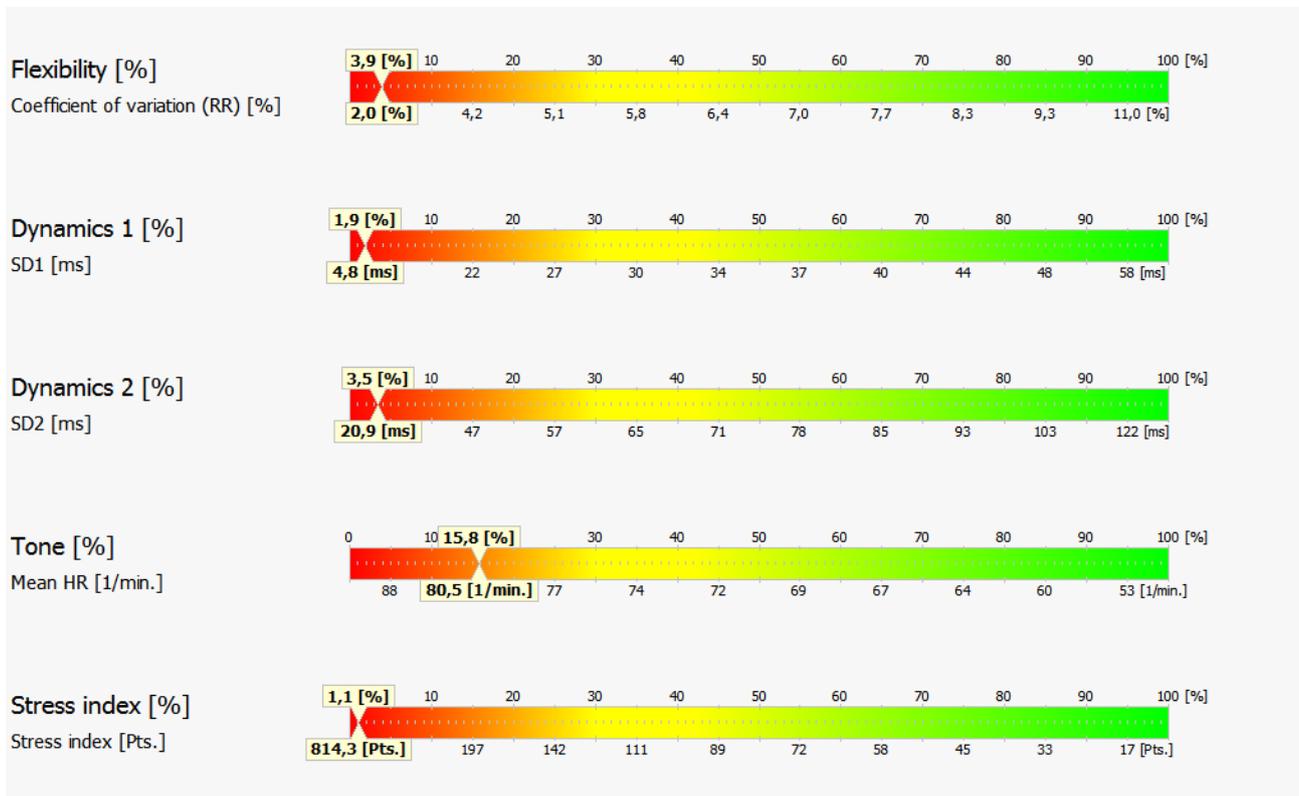
A typical result of a healthy subject could be as follows (spider web and bar graph):





The following pictures show a result of a subject with limited ability to regulate (spider web and bar graph).

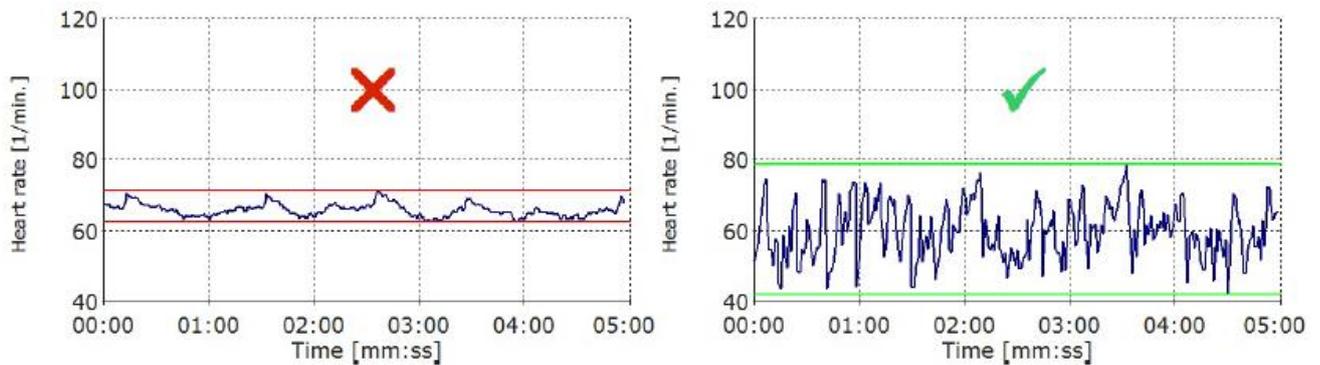




Target parameter in the rank diagram of the Short-Term HRV measurement

Flexibility (Coefficient of Variation RR)

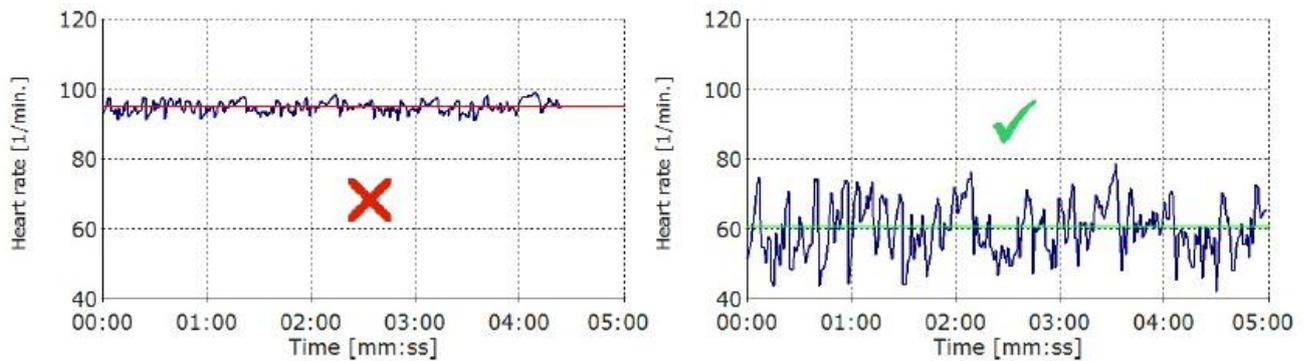
A sufficient adaptiveness is essential and is mainly achieved by a well-performing parasympathetic nervous system.



A high flexibility reflects a good adaptiveness of the cardiovascular system. Non-transient low values of flexibility indicate a weakness of the parasympathetic nervous system, which can affect your health adversely. Current events like infections, stress and strain can lower your flexibility temporarily.

Tone (mean HR)

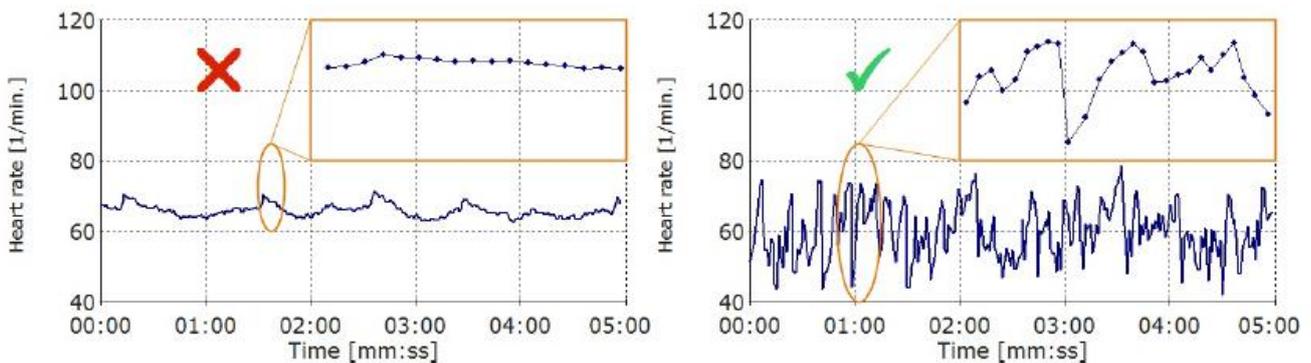
Only a powerful parasympathetic nervous system can ensure a good regulation and enables our vital adaptiveness.



A good parasympathetic tone corresponds to a low heart rate. For example, people with a heart rate > 90 bpm have a clearly higher health risk compared to people with a heart rate < 60 bpm. (HABIB, G.B. 1999. Reappraisal of heart rate as a risk factor in the general population. Eur. Heart J. Suppl. 1: H2-H10.)

Dynamics 1 (SD1)

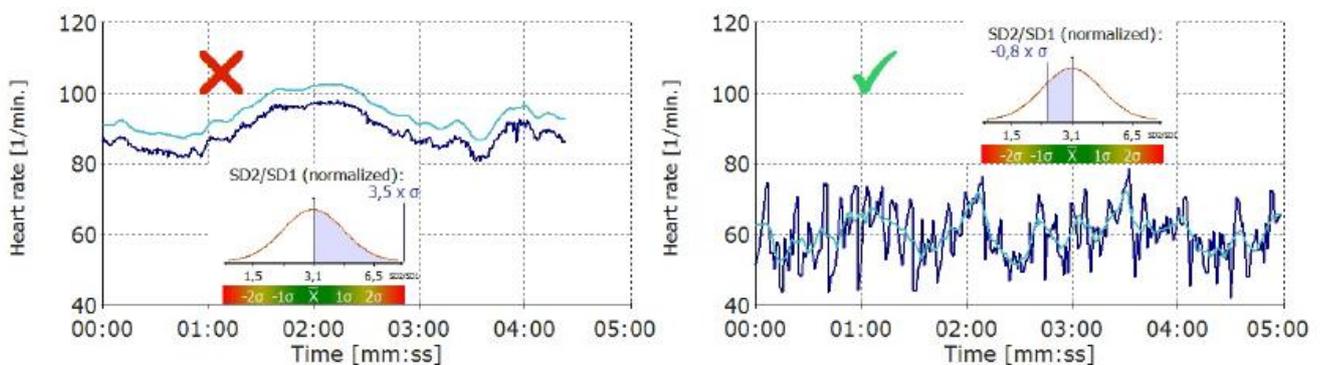
Fast fluctuations of the heart rate reflect a well-functioning 'inner brake'.



They are a sign of a fast information processing within the autonomous nervous system and indicate a good adaptability.

Dynamics 2 (SD2)

In addition to the fast heart rate oscillations there also occur slow heart rate fluctuations (light blue line).



Slow changes of the heart rate are caused both by the activity of the sympathetic 'accelerator' and the parasympathetic 'inner brake'. Their occurrence is therefore neither good nor bad. Nevertheless, slow and fast changes of the heart rate are normally in a certain relation, expressed by the SD2/SD1-ratio. If the slow dynamics (SD2) outweighs the fast dynamics markedly, the influence of the parasympathetic system is too low

for an optimal regulation. A disbalance between sympathetic and parasympathetic system cannot be excluded in this case.

SD2/SD1 ratio

The normalized SD2/SD1-ratio indicates, whether a favorable or more unfavorable relation of slow to fast fluctuations of the heart rate exists.



For this purpose, an individual SD2/SD1-ratio is compared to the mean value of a reference group. From this data a normalized SD2/SD1-ratio is calculated. High positive values indicate a predominance of slow heart rate oscillations. The higher the value, the less likely it is, that it is a normal finding. Negative values indicate higher proportions of fast heart rate fluctuations and are more favorable. Exceptions are extremely negative values ($< -2.0 \sigma$), which can indicate a missing sinus rhythm, irregular heartbeats or not removed artefacts. (The normalized SD2/SD1-ratio is the deviation of the SD2/SD1-ratio from the mean value of a reference group, expressed as multiples of its standard deviation, $n = 832$, normal distribution achieved after age correction and taking the logarithm, Kolmogorow-Smirnow-Test $p > 0.2$; Lilliefors $p > 0.2$)

More info about the SD2/SD1 ratio can be find at the explanation of the parameters.

Stress index

The stress index is especially sensitive to the unfavorable combination of a low heart rate variability with a high heart rate.



The stress index correlates significantly with accepted risk scores. Very high values can indicate an increased cardiovascular risk.

Respiration and HRV

Influence of breathing on the results of the short-term HRV

In interpreting the results of short-term HRV, respiration is usually not considered, although it represents a significant source of heart rate variance. Breathing has a major influence on heart rate regulation, especially in resting conditions.

In contrast to the RSA measurement, the short-term HRV does not guide the breathing. It is precisely the goal of the short-term HRV to observe how the parasympathetic nervous system adjusts to the supposed resting conditions. For example, stress, anxiety and depression patients often cannot calm down. These patients often breathe quickly and shallowly with a resulting low HRV.

The strong influence of respiratory rate and depth on neurovegetative cardiac regulation has long been known. In particular, a deep and slow breathing (4-6 breaths per minute) leads to a maximum of respiratory sinus arrhythmia. Increasing respiratory rates are associated with a reduction in respiratory sinus arrhythmia. The age of the patient also plays an important role: with increasing age, the respiratory sinus arrhythmia is reduced. The figure exemplifies the influence of respiratory rate and age on heart rate variability in short-term HRV.

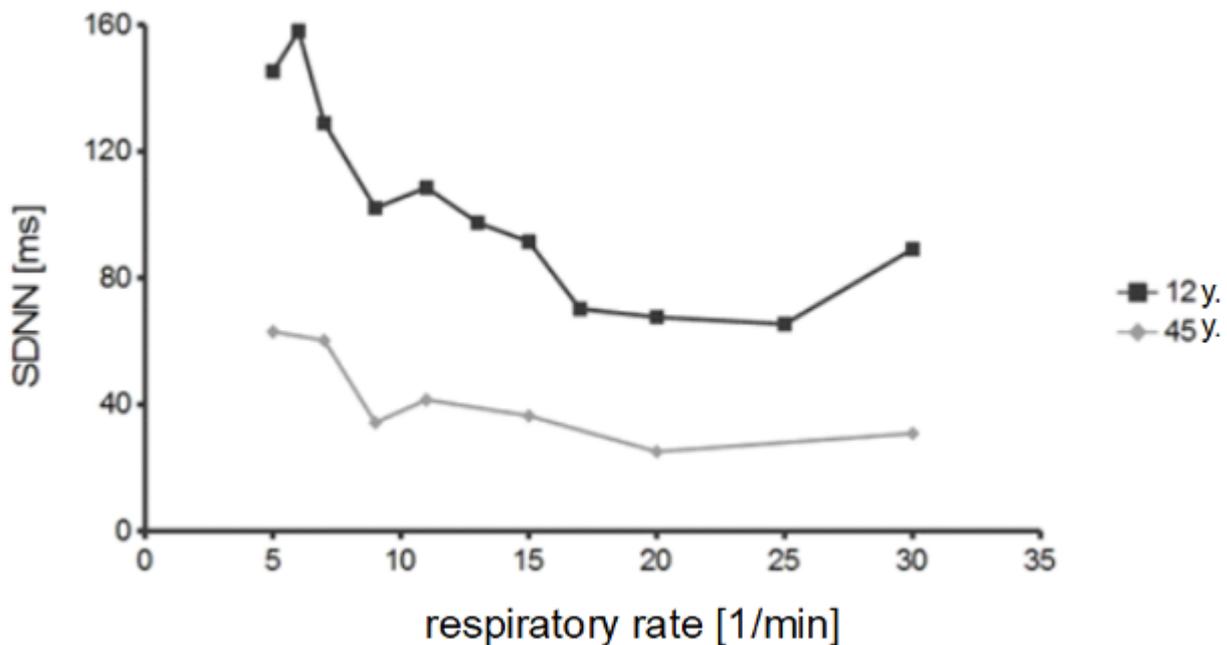


Fig. In both the child and the adult, the HRV increases with increasing Respiratory rate significantly.

We investigated in a study which respiratory rates occur during a short-term HRV and found a broad distribution of 4-23 breaths per minute. Due to the broad distribution, an influence of the respective respiratory situation on results of the short-term HRV must also be expected in everyday practice. For example, at high respiratory rates, especially in elderly patients, a low HRV result may occur. However, this does not necessarily imply an autonomic dysfunction; it can also be a physiological limitation of HRV due to rapid breathing. In the opposite case, a very low respiratory rate of 4-5 breaths per minute causes physiologically even higher amplitudes of the heart rate fluctuations but comparatively low RMSSD and SD1 values, because the coupled heart rate changes only slowly (RMSSD and SD1 measure rapid changes in the heart rate). It is therefore advisable to always consider the respiratory rate in the analysis of short-term HRV and to evaluate the HRV result in the context of respiration. In addition, it is recommended to always supplement the short-term HRV with an RSA measurement at 6 breaths per minute. Only with both tests a purely physiological restriction of HRV at high or very low respiratory rate can be differentiated from an actual parasympathetic dysfunction.

Our study has shown that mental stress leads to a significant increase in the respiratory rate in most subjects.

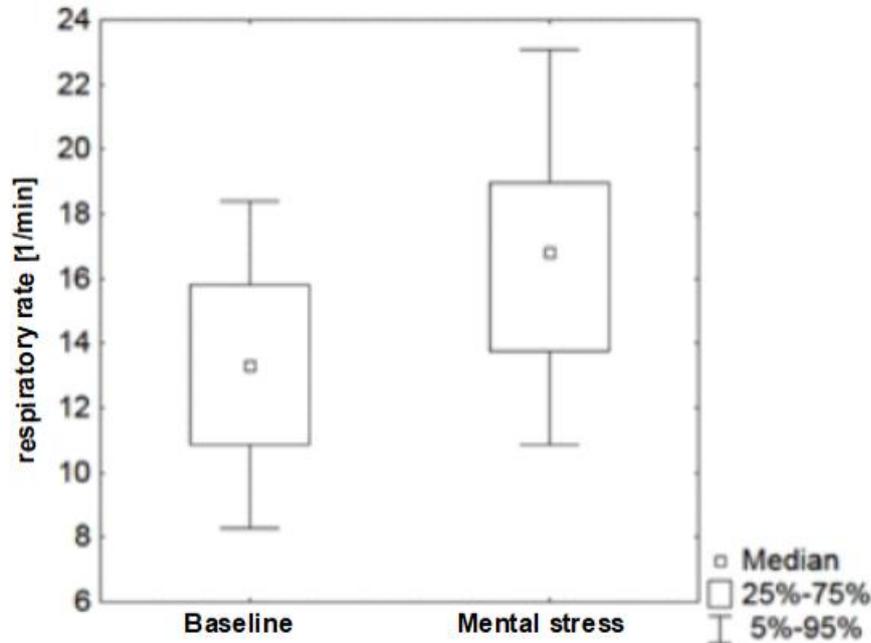


Fig. Respiratory rates at rest and under mental stress (stress by mental arithmetic)

It is also known that particularly anxious subjects respond to mental stress with an increase in the respiratory rate. The determination of the respiratory parameters during the short-term HRV can therefore be a diagnostic indication of the presence of a possible stress burden and should be recorded in addition to the HRV as a further physiological factor in stress and exercise examinations. If a stress and stress situation is present, the determination of the respiratory rate at rest would identify those patients who react to stress with a high respiratory rate. These patients would particularly benefit from breath-focused stress management training such as HRV biofeedback, meditation, and mindfulness-based stress reduction, as such training has a beneficial effect on respiratory rate at rest.

Distinguishing sympathetic - parasympathetic in the short-term HRV

The short-term HRV is primarily a parasympathetic functional test and does not provide diagnostically useful information about the sympathetic nervous system. At best, a detected parasympathetic dysfunction can be explained by an excessive sympathetic nervous system if signs of sympathetic activation such as high heart rate are present. Sometimes, however, an attempt is made to make a statement about the current activity of parasympathetic and sympathetic (vegetative balance). Previously used methods such as the LF / HF quotient and the SD2 / SD1 quotient cannot yet clarify this question satisfactorily. The regulation speed of the parasympathetic nervous system may be so high due to its physiology that its effect is on the regulation of the heart rate alone in the HF band of spectral analysis or a high SD1. However, with slow breathing, the parasympathetic nervous system can also regulate so slowly that its regulatory power, together with the sympathetic nervous system, lies in the LF band of spectral analysis or in a high SD2. So, we see, for example a pronounced RSA with respiration of 6 / min. at 0.1 Hz in spectral analysis and thus in the LF band. A clear separation between the two actors of the autonomic nervous system in the LF band or SD2 is not possible in this case without consideration of the respiration.

An aid here is the assessment of the influence of the respiration on the heart rate, expressed as a percentage 0% to 100% (= maximum match of heart rate and respiratory curve). If there is a high influence of the respiration on the heart rate, then it is an RSA (respiratory sinus arrhythmia) and thus a primary parasympathetic regulation performance - no matter whether the peak is in the spectral analysis in the LF or in the HF range.

Conclusion

The assessment of HRV especially in the short-term HRV is incomplete without consideration of respiration. That's why we've included the respiration rating in the HRV scanner. Breathing is measured either via the respiratory curve from the ECG (so-called **ECG Derived Respiration**, EDR) or directly mechanically via a chest belt (only HRV-Scanner plus). Both methods are able to allow a sufficiently good assessment of breathing under resting conditions. For the EDR, a good quality ECG is required.

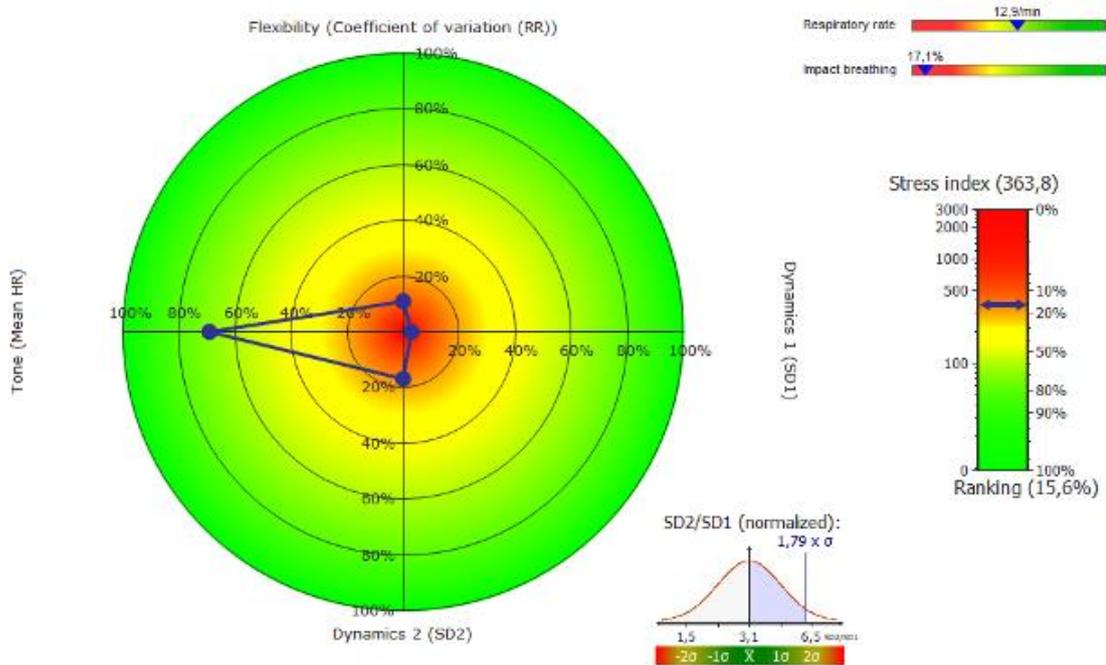


Fig. CAD patient with a pronounced parasympathetic dysfunction. Normal respiratory rate, yet hardly any respiratory sinus arrhythmia with severe limitation of the dynamic parts of the parasympathetic nervous system (SD1). Also, not stimuable by deep breathing in the RSA measurement.

The evaluation graph of the short-term HRV shows both the respiratory rate and the influence of the respiration on the heart rate (right upper corner). Both parameters allow a more differentiated assessment of HRV.

The following points should be noted:

- High respiratory rates are often an indication of stress and stress situations and may be an explanation for a decreased HRV.
- Low respiratory rates cause slow regulation in the parasympathetic nervous system and lead to comparatively low RMSSD / SD1 values at high amplitudes (high SDNN or coefficient of variation).
- A high influence of the respiration on the heart frequency indicates the existence of an RSA and thus for a high activity of the parasympathetic. This is also evident in the LF band of the spectral analysis and in the SD2 at low respiratory rate.
- A slight influence of the respiration on the heart rate speaks against the existence of an RSA. This may indicate a lack of parasympathetic activity (especially if signs of sympathetic activation such as high heart rates) or high respiratory rates and mental stress.

Methods for measuring breathing

EDR - ECG Derived Respiration (HRV-Scanner standard and HRV-Scanner lite)

An indirect method of registering respiration is the derivation of the ECG's breathing signal, called ECG Derived Respiration, abbreviated EDR. For the EDR, one makes use of the fact that the diaphragm movement causes a

slight change in the heart axis during breathing, which can be detected by the amplitude change of the R wave in the ECG (see Fig.).

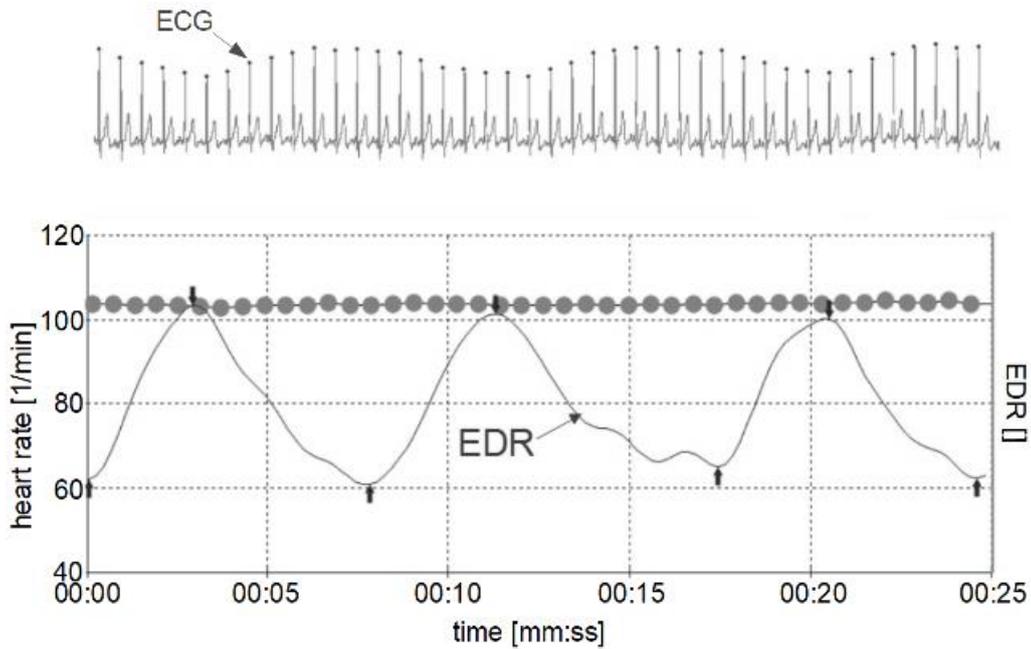
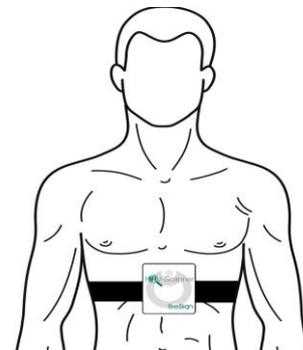


Fig. Breathing-synchronous changes of the heart axis occur due to the respiratory diaphragm movement, which lead to an alternating amplitude of the R-wave (upper curve). The lower image shows the corresponding heart rate curve and the breathing curve derived from the amplitude of the R-waves. (Note: The EDR curve was inverted in the HRV scanner in order to achieve an analogous course with the thorax movement.)

Mechanical determination of respiration - breathing belt (HRV-Scanner plus)

A chest strap measures the respiratory movement of the chest and determines breathing. The breathing belt is the gold standard for determining the respiratory rate in neuro-vegetative functional diagnostics.



EDR and mechanical sensors in the short-term HRV correlated with sufficient accuracy for an estimation of the respiratory rate using EDR ($r = 0.91$). For a precise analysis, however, a respiratory sensor is required because in individual subject's deviations in the respiratory rates of EDR and chest belt occurred up to 4 breaths per minute. Noticeable were non-respiratory fluctuations in the EDR signal, especially at lower respiratory rates, see figure below. Their origin is unclear. In addition to the diaphragmatic motion, there may also be other dynamic factors influencing the heart axis.

It is therefore recommended to visually inspect the EDR signal before interpreting the measurement result and to check for proper positioning of the inhalation and exhalation markers.

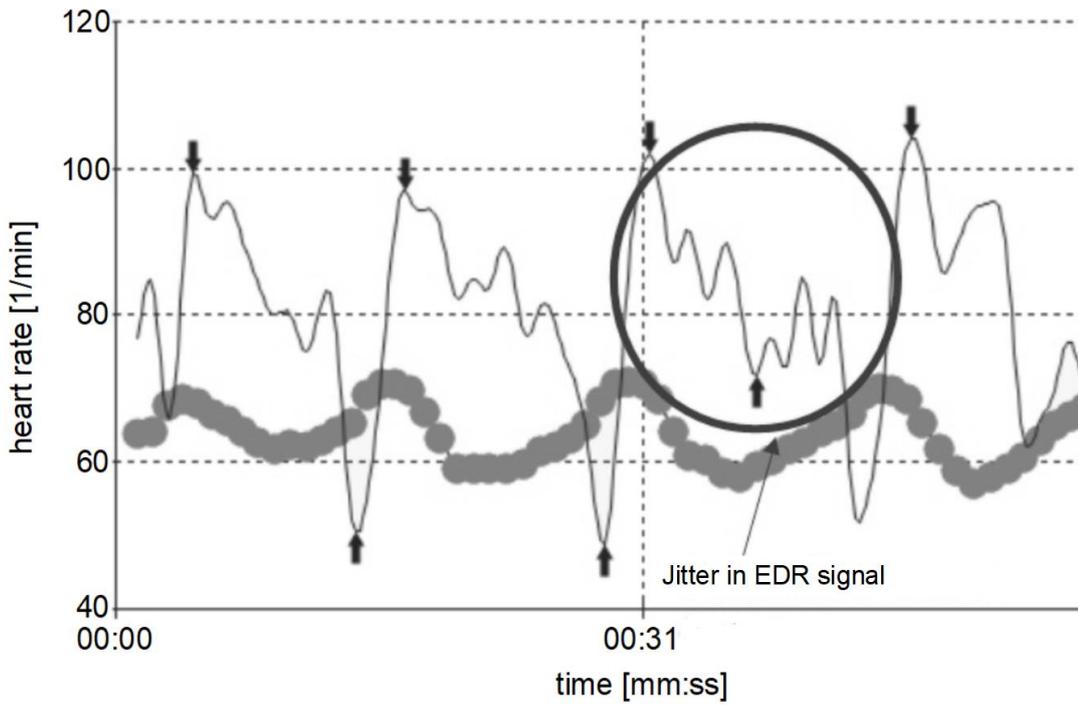


Fig. Errors in the EDR signal. It is not always possible to record a trouble-free EDR signal. Therefore, the EDR signal, and in particular the automatically set markings of the breathing cycles, should be checked for plausibility by the user.

The Deep Breathing Test

The Deep Breathing Test is a standard test in HRV diagnostics. The aim is the detection of the maximum available parasympathetic regulation (reserve). The Deep Breathing Test should be performed with the ECG (and possibly additional pulse wave). Duration: pure measurement duration 1 minute, incl. preparation approx. 5 minutes

The Deep Breathing Test (determination of respiratory sinus arrhythmia) reliably determines the current adaptability of our internal control system by means of a neurophysiologic test procedure, which has proven itself over the last four decades in medicine. A regularly performed measurement supports the identification of health risks, acute psychological and physical overloads and gives positive feedback in case of successful lifestyle changes. The properties "Flexibility", "Tone" and "Dynamics" describe the three components of the "internal brake".

Prepare the measurement

As with any HRV measurement, the determination of the Deep Breathing Test also requires careful preparation of the subject. It should be ensured that all factors that could influence the neurovegetative balance are controlled or at least documented. These include: medication, current illness, strong physical exertion (sports) in recent days, or even coffee or nicotine just before the measurement. This measurement usually takes place while sitting, so that the subjects can better follow the breathing pattern on the screen. The Deep Breathing Test is a function test. The subject must actively participate. Decisive is the maximum deep inhalation and exhalation of the subject according to the guidance of the respiration pattern. Breathing should be practiced before the start of the measurement together with the subject. The blood volume displacement caused by the breathing forces the body to regulate. As a result of the measurement, we see how well the vegetative nervous system is capable of doing so.

Perform the measurement

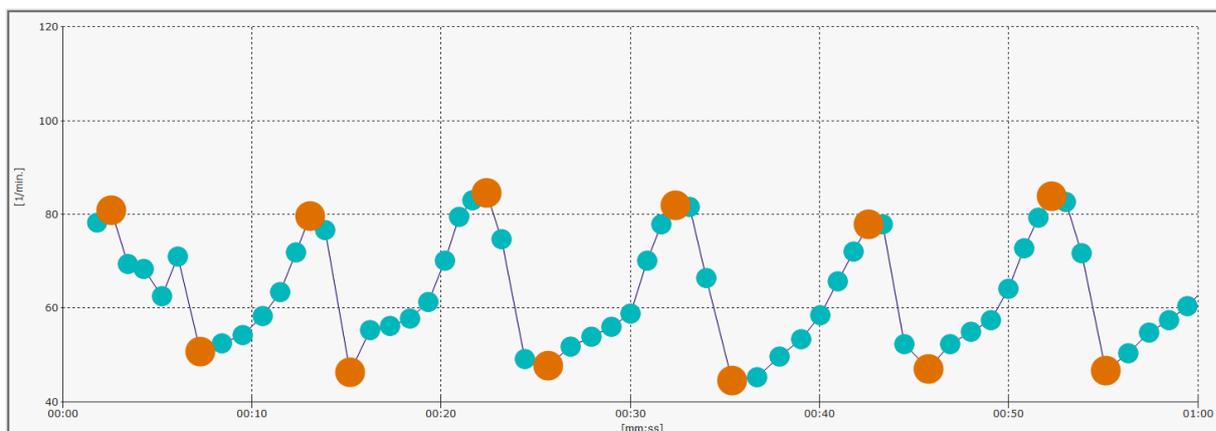
During the Deep Breathing Test, ensure that the subject breathes deeply and evenly. After the measurement time has elapsed, you will receive a message about the successful recording of the measurement. Close the measurement window. The measurement data are moved to an archive and an entry for the new measurement appears in the "Test and analysis" window.

Evaluation

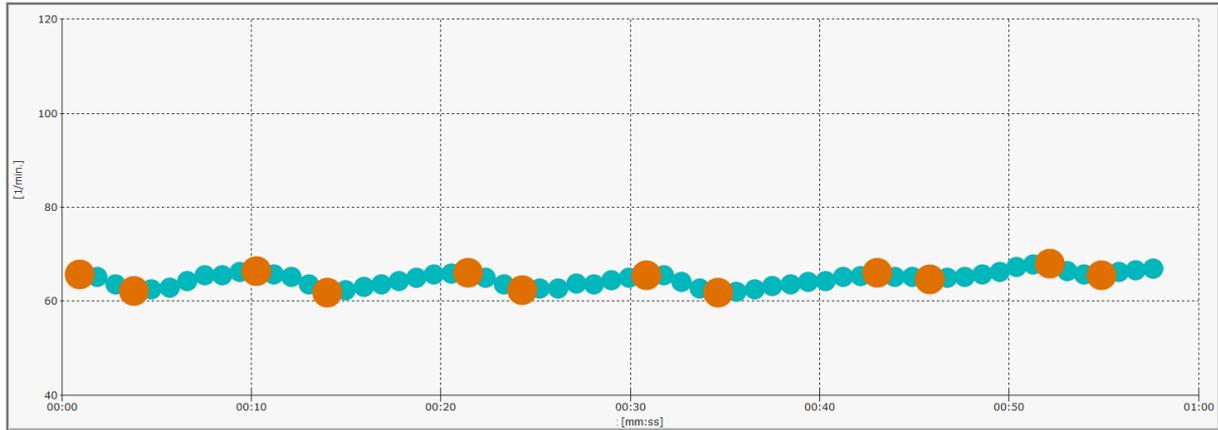
To do this, select the Deep Breathing Test carried out using the mouse in the "Test and analysis" window and press "Evaluate" or double-click on the measurement symbol.

The course of the heart rate during the Deep Breathing Test should show a steady breath-dependent up and down.

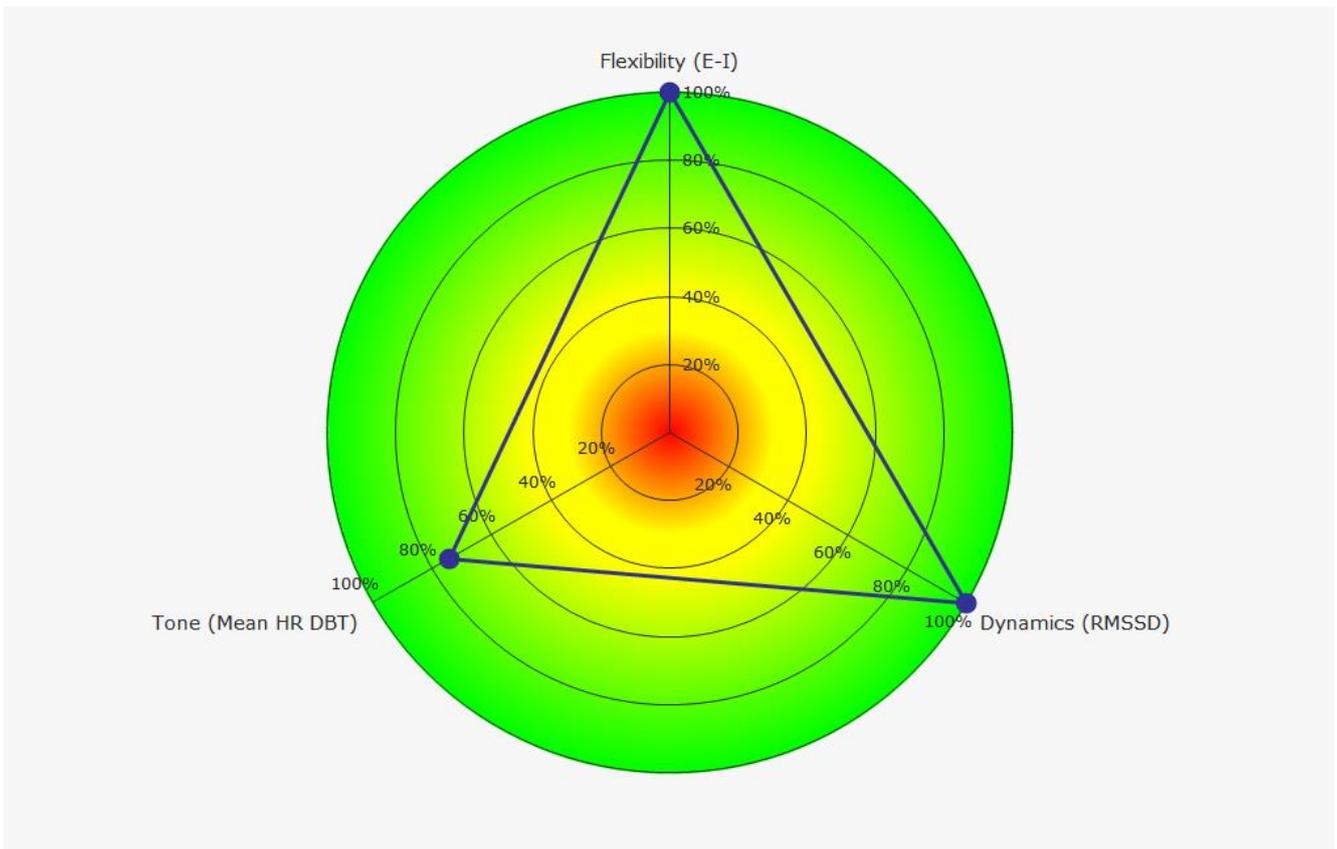
The lower picture shows a typical course of heart rate during a Deep Breathing Test of a healthy subject.

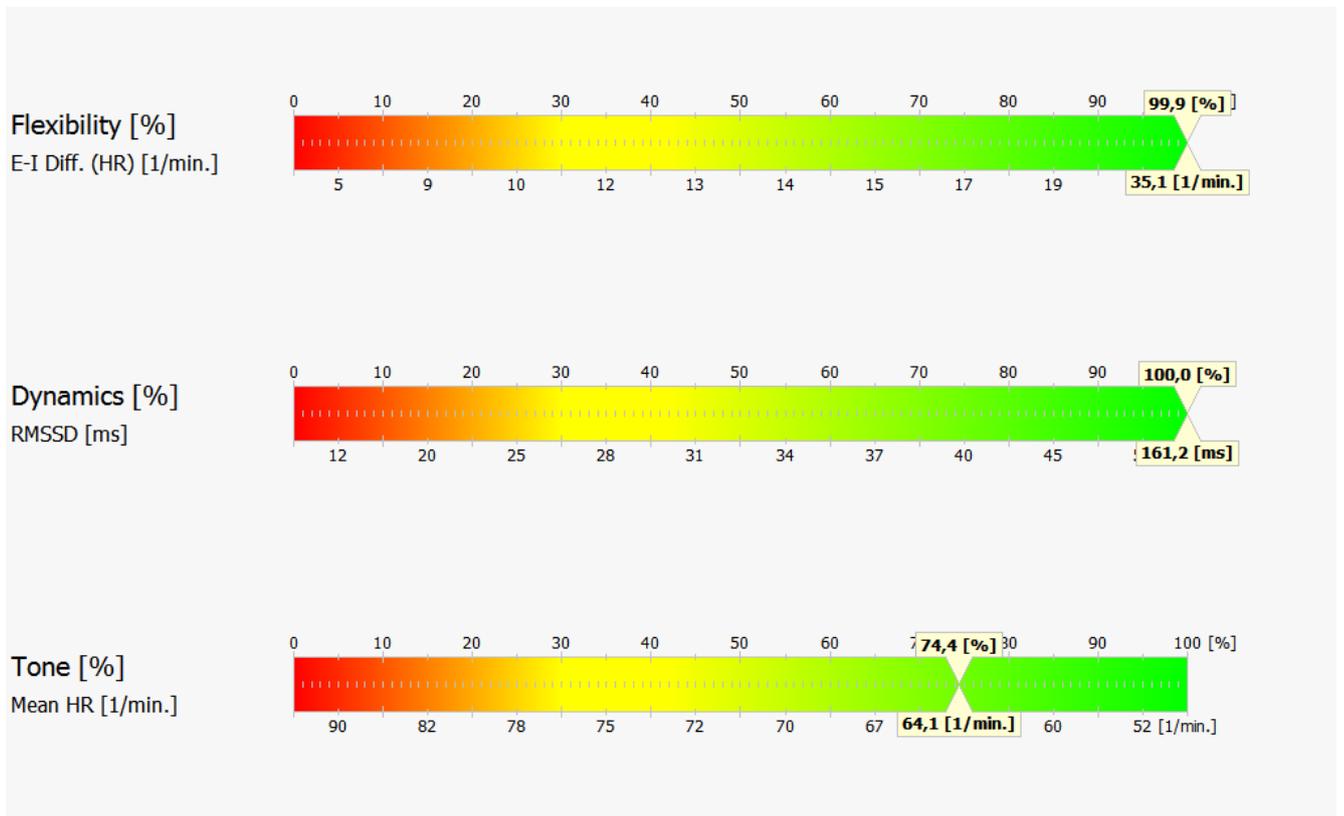


The lower picture shows a typical course of the heart rate during a Deep Breathing Test of a subject with significantly reduced heart rate variability.

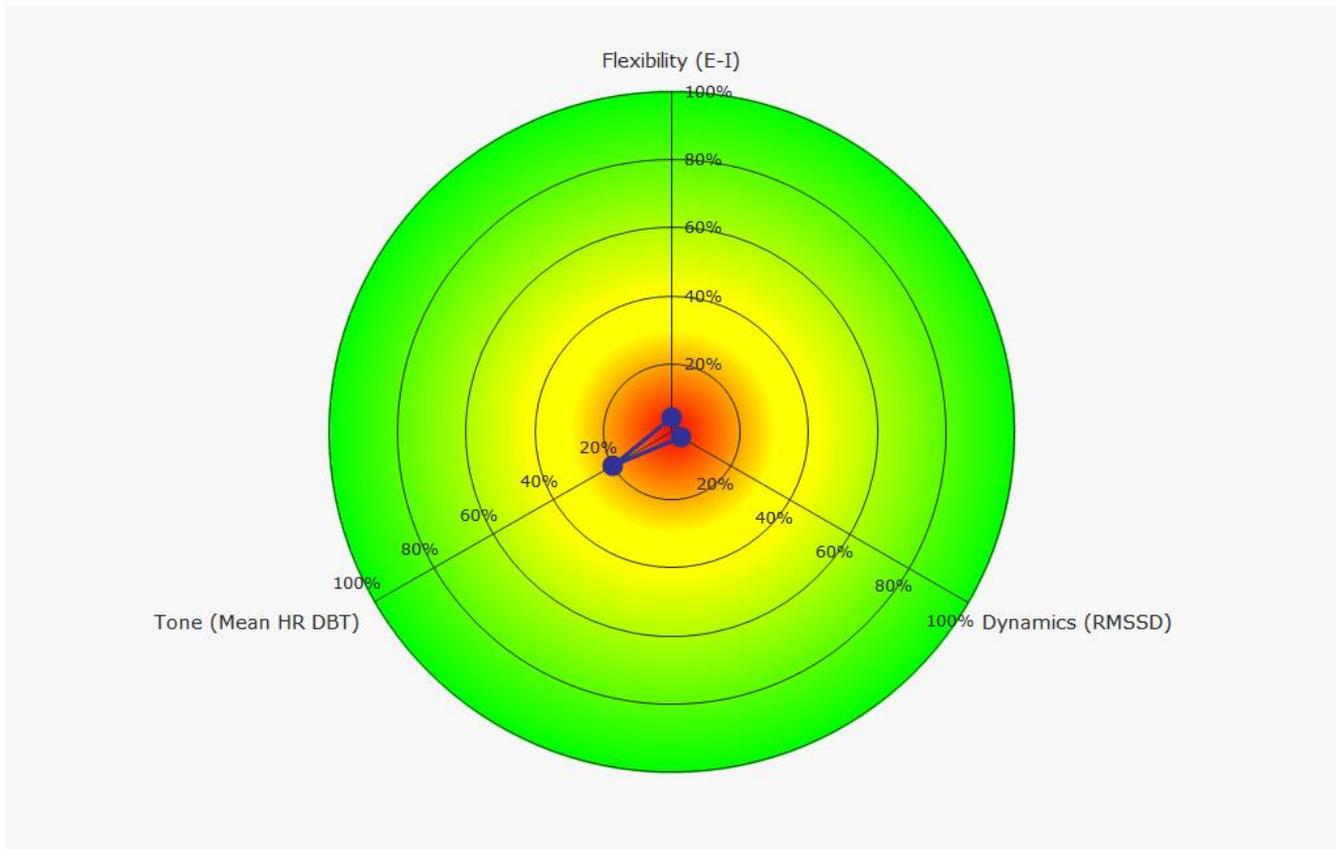


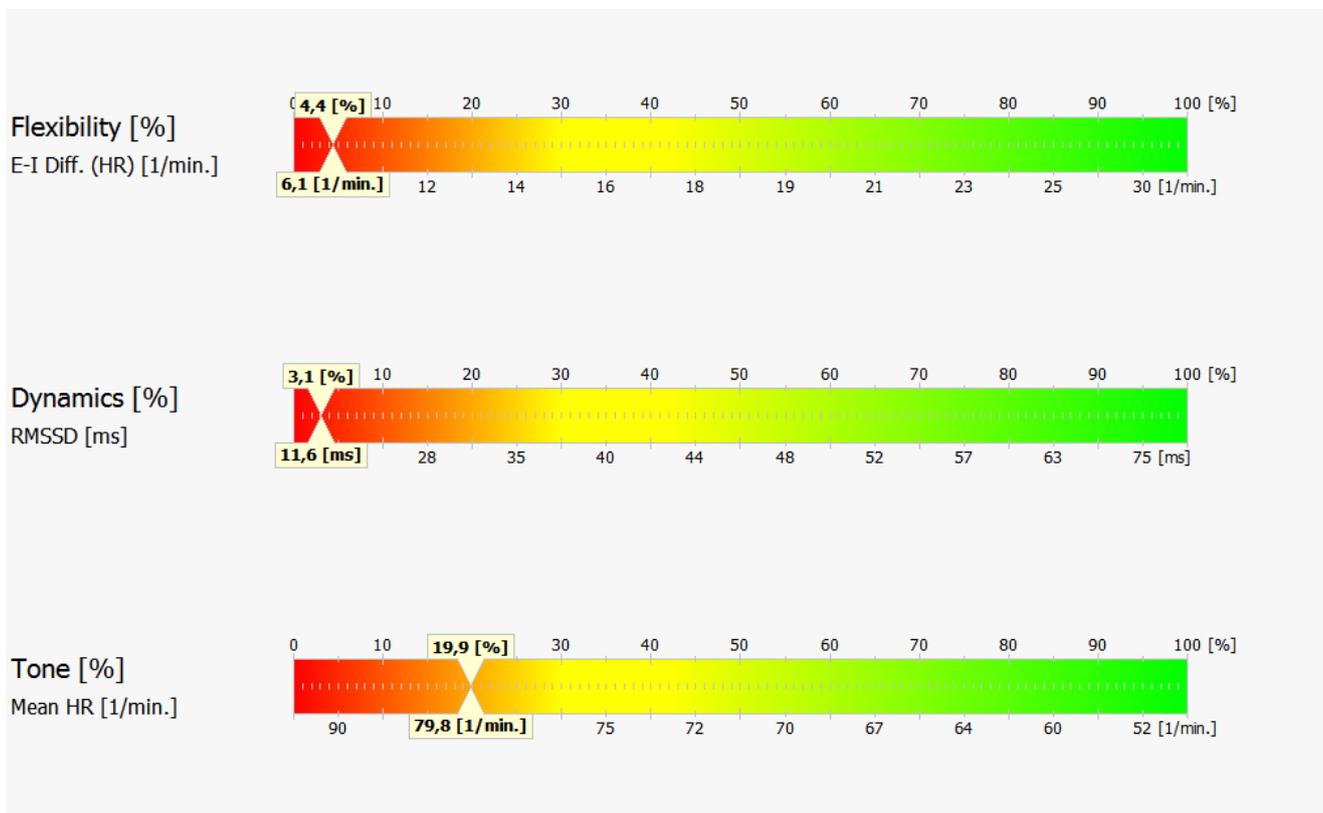
A typical result of a healthy subject could be as follows (spider web and bar graph):





The following pictures show a result of a subject with limited ability to regulate (spider web and bar graph).

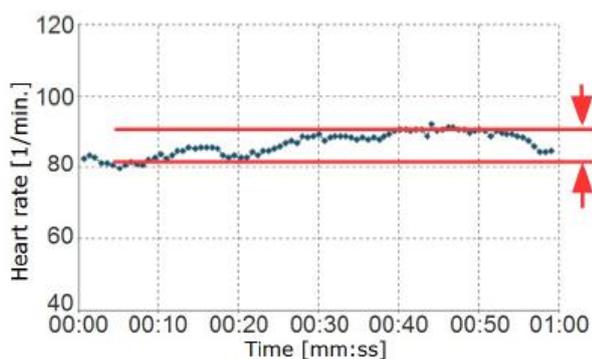




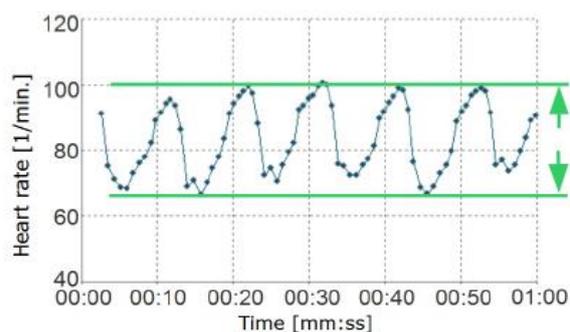
Target parameter in the rank diagram of the Short-Term HRV measurement

Flexibility (E-I)

„Survival of the fittest“. This often-misunderstood sentence in the context of the Darwinian theory of evolution literally means the "survival of the best adapted". This adaptability, which is necessary for survival, is already an absolute must at the level of body regulation and is ensured by a well-functioning heart-brain axis. A high flexibility value reflects a good adaptability of our cardiovascular system. On the other hand, long-term low flexibility is an expression of a lack of adaptability. For example, a low degree of flexibility is a prognostically unfavorable sign after myocardial infarction *.



Example of a very low flexibility (heart rate fluctuation not existent)

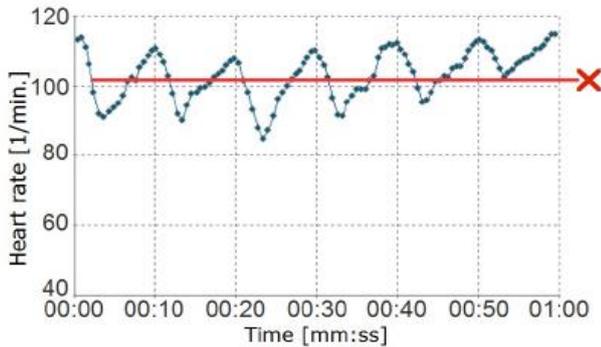


Example of a high flexibility (large amplitude of the heart rate fluctuation)

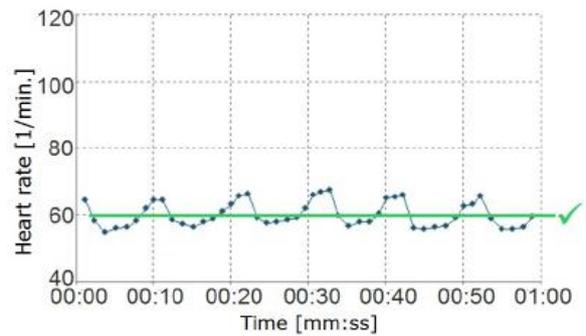
*A simple bedside test of 1-minute heart rate variability during deep breathing as a prognostic index after myocardial infarction. Katz A, Liberty IF, Porath A, Ovsyshcher I, Prystowsky EN. Am Heart J. 1999 Jul;138(1 Pt 1):32-8.

Tone

At rest our body-borne braking and regeneration system (parasympathetic nervous system) is the active part of our heart-brain axis. Only a powerful parasympathetic can control the body processes optimally and allows our life-long adaptability. A good parasympathetic root tone is expressed in a lower heart rate. For example, people with a heart rate > 90 / min have more than three times the risk of death than people with heart rate <60 / min *.



Example for a low parasympathetic tone (high mean heart rate)

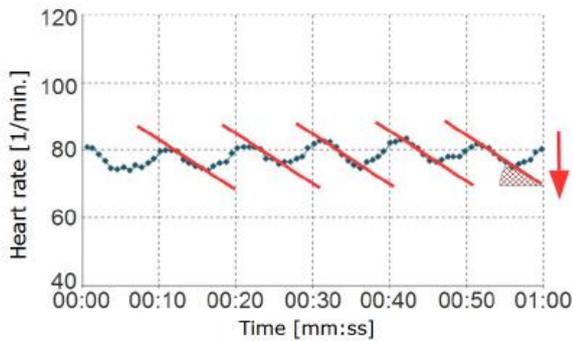


Example for a high parasympathetic tone (low mean heart rate)

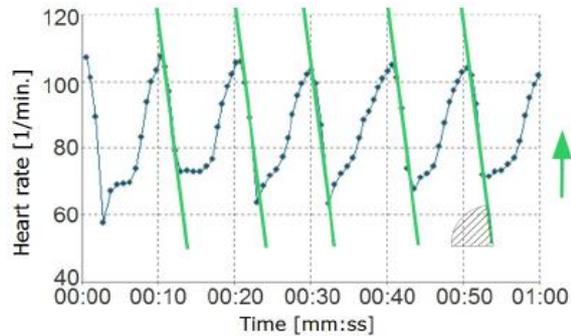
*HABIB, G.B. 1999. Reappraisal of heart rate as a risk factor in the general population. Eur. Heart J. Suppl. 1: H2-H10.

Dynamics

An essential feature of a powerful heart-brain axis is the speed with which the information processing and body regulation takes place. Similar to the braking test in the car, the faster the system comes to "standing", the more powerful is the built-in brake.



Example of a heart-brain axis, which has only a low dynamic. The heart rate changes only slightly from heartbeat to heartbeat.



Example of good dynamics. The heart rate changes very strongly during exhalation (decrease of heart rate)

Why two measurements as a basis HRV

Why do we recommend the combination of Short-Term HRV and Deep Breathing Test as the basis HRV measurement? What does the combined interpretation of the results of both measurements say?

Short-Term HRV	Deep-Breathing-Test	Description	Current HRV	Reserve HRV
+	+	<p>Good results in Short-Term HRV - and Deep Breathing Test</p> <p>The parasympathetic regulation works well under stimulation and at rest. The vegetative nervous system is in equilibrium. We usually find such results in people who are resting, healthy and athletic, and usually have a good work/life balance or a good stress resilience.</p>	+	+
-	-	<p>Bad results in Short-Term HRV - and Deep Breathing Test</p> <p>The parasympathetic regulation does not work well either under stimulation or at rest. In most cases a chronic damage to the parasympathetic is already present. The reason for this is often a chronic process. (diabetes, chronic stress, ...)</p>	-	-
-	+	<p>Bad results in Short-Term HRV, but good results in Deep Breathing Test</p> <p>The parasympathetic regulation works well under stimulation, but badly at rest. This gives us an indication that in principle there is still a good capacity/reserve of regulation, but this cannot be used under resting conditions. Possible causes are: rapid flat breathing as a sign of mental stress.</p> <p>Such results can usually be seen in younger subjects who have previously had a good regulation but are currently being influenced by stress. The prognosis for recovering a well-functioning vegetative regulation is positive, since the regulatory system has probably not suffered any structural damage.</p>	-	+

What has a negative impact on HRV

A markedly increased fasting blood glucose value leads to the assessment that a diabetes is present. In the case of HRV, the facts are unfortunately much more complex. How do we interpret poor results from our HRV measurements? Decisive is the knowledge about what can take effects on the HRV and the questionnaire (anamnesis). Combining both will quickly lead us to the cause of parasympathetic dysfunction, or the shifted vegetative balance.

Anticholinergic drugs

Anticholinergic drugs (antidepressants, ...) have a negative effect on HRV as they inhibit the transmission of information in the parasympathetic nervous system. These medicines can be identified with the following side effects (see leaflet): mouth dryness, slight visual disturbances, constipation, dry eyes, urinary retention.

Drugs with anticholinergic action

Drug group	Examples
Antiemetics, Antivertiginosa	Dimenhydrinat, Promethazine, Scopolamine
Drugs for Parkinson's disease	Benzatropine, Biperidene, Trihexyphenidyl, Metixen
gastrointestinal spasmolytics, inhibitors of secretion	Butylscopolamine, Pirenzepine
urological spasmolytics	Oxybutynine, Tolterodine, Fesoterodien, Darifenacine, Solifenacine
Intensive care, preoperative medication	Ipratropium, Tiotropium, Acridiniumbromid
Mydriatics	Atropine, Scopolamine, Homatropine, Tropicamid
Intensive care, preoperative medication	Atropine

Further information

You can find an overview under <http://www.hrv24.de/HRV-Medikamente.htm> (no guarantee).

Food / Drugs:

(e.g. caffeine, nicotine, alcohol)

Chronic diseases

(e.g. diabetes, Parkinson's disease, depression)

Acute diseases

(e.g. flu, heart attack)

Excessive sports, over training

Any kind of sporting overload will result in a temporary reduction of the individual HRV. For this reason, the HRV measurement can also be used to monitor exercise in sports.

Stress

Acute and chronic stress often has a marked negative impact on individual HRV. The extent depends on:

- individual sensitivity for stress
- quality of the stress
- duration of stress

Further diagrams in the analysis

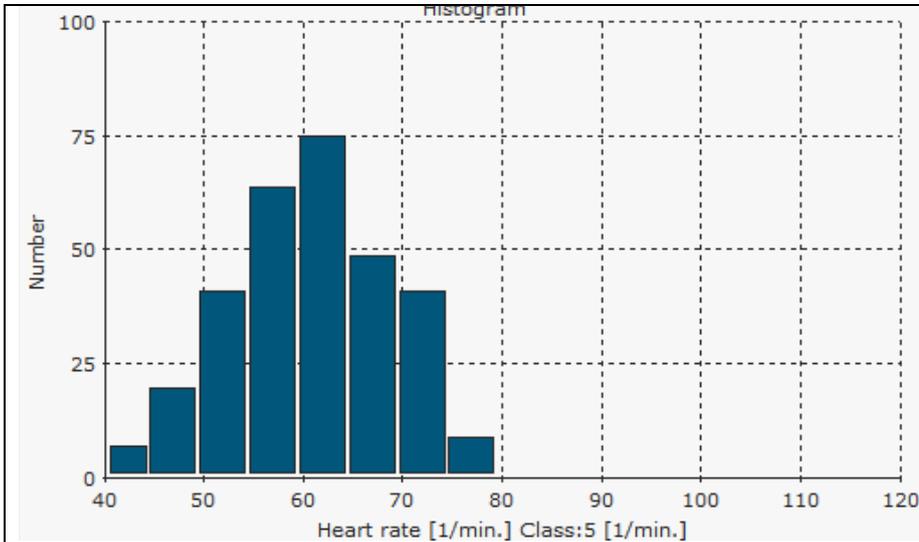
Poincaré Plot

The Poincaré Plot (Lorenz Diagram, Scatter Plot) was named after Henri Poincaré (1854-1912). Here, each RR interval (or heart rate) is plotted against its successor. This produces typical patterns that represent periodicity and similarity.

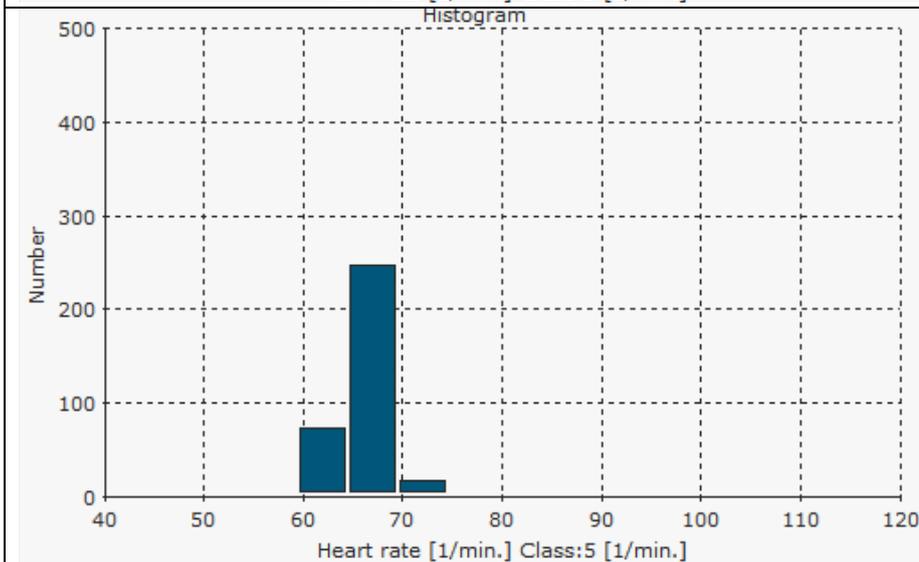
	<p>In the case of HRV, with good variability and periodicity, typically a point cloud is produced in the form of an ellipse on the bisector.</p>
	<p>A limited heart rate variability leads to a concentration of the point cloud</p>
	<p>Rhythm disturbances and artefacts typically form outside the elliptical point clouds. Therefore, we also use this diagram as a graphical filter for artefact detection and cleaning.</p>

Histogram

A histogram is a graphical representation of the frequency distribution of cardinal scaled features. It requires the classification of the data into classes. Rectangles that are directly adjacent to one another are drawn from the width of the respective class whose surface contents are the class frequencies. The heartbeats occurring in the measurement are distributed to the individual classes. The height of each rectangle then represents the number of heartbeats per class.



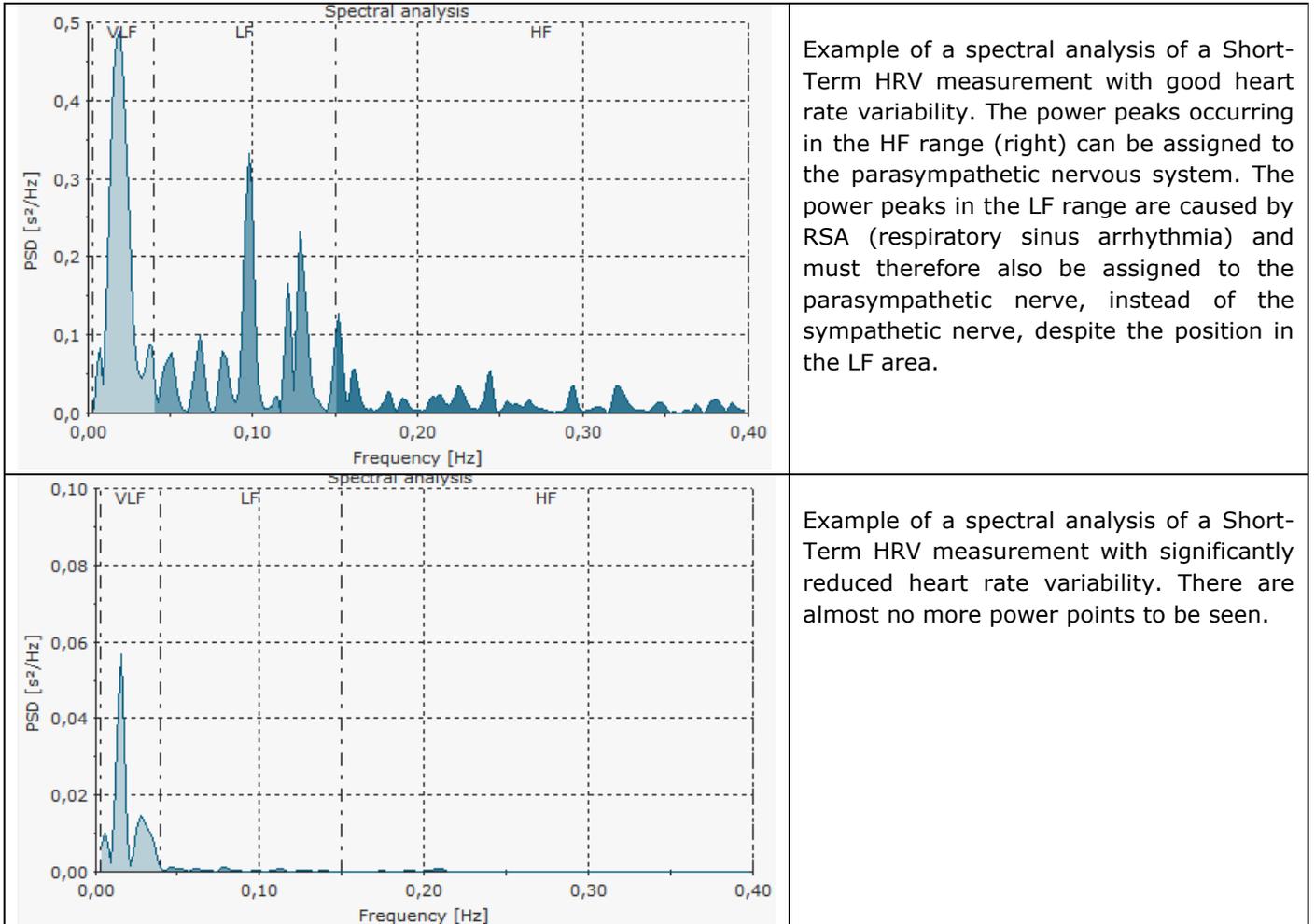
Histogram of a subject with good heart rate variability. The diagram appears wide and rather low (scaling of the Y-axis = pay attention to number!)



Histogram of a subject with restricted HRV. The diagram appears high and rather narrow (scaling of the Y-axis = pay attention to number!)

Spectral analysis

Spectral analysis describes the values obtained from the Fourier transformation in the signal and time series analysis. In this case, the heart rate profile of a measurement is examined with regard to occurring oscillation frequencies. The aim is to determine which branch of the VNS was involved in the regulation that took place, by determining the power values for the individual frequency bands. For this, one uses the fact that the parasympathetic can regulate faster than the sympathetic due to its physiology. All vibrations occurring in the high-frequency range (HF) can be unambiguously assigned to the parasympathetic nervous system. However, the sympathetic and parasympathetic nervous system is shared by the low-frequency region (LF). An estimation of the allocation is only possible with regard to breathing. The LF/HF quotient is therefore only very limited suitable for reproducing the balance between sympathetic and parasympathetic nervous system.



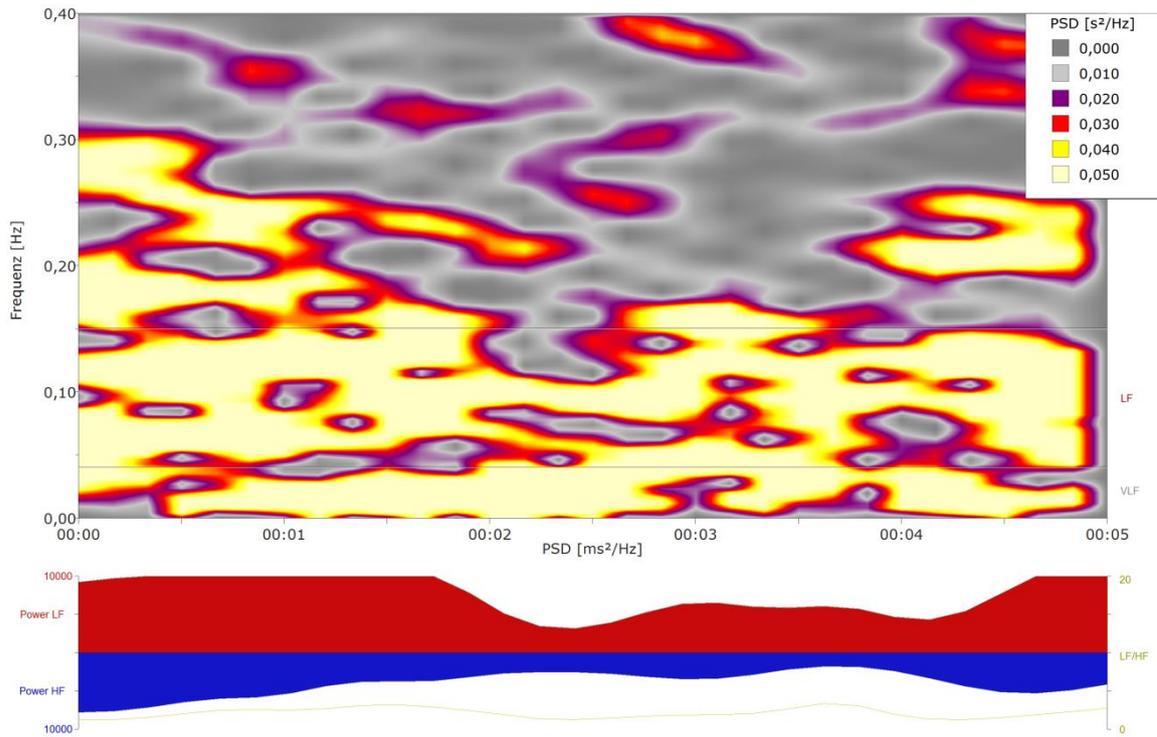
Color-FFT

Spectral analysis allows the determination of the frequency components in the heart rate curve. This can lead to the inhibition of parasympathetic and sympathetic activity within certain limits, since rapid changes in the heart rate (> 0.15 Hz) can only be triggered by parasympathetic regulation (see chapter "Parameters of heart rate variability, parameters of spectral analysis"). For longer measurements the spectral analysis can therefore be used to register the change in vegetative balance.

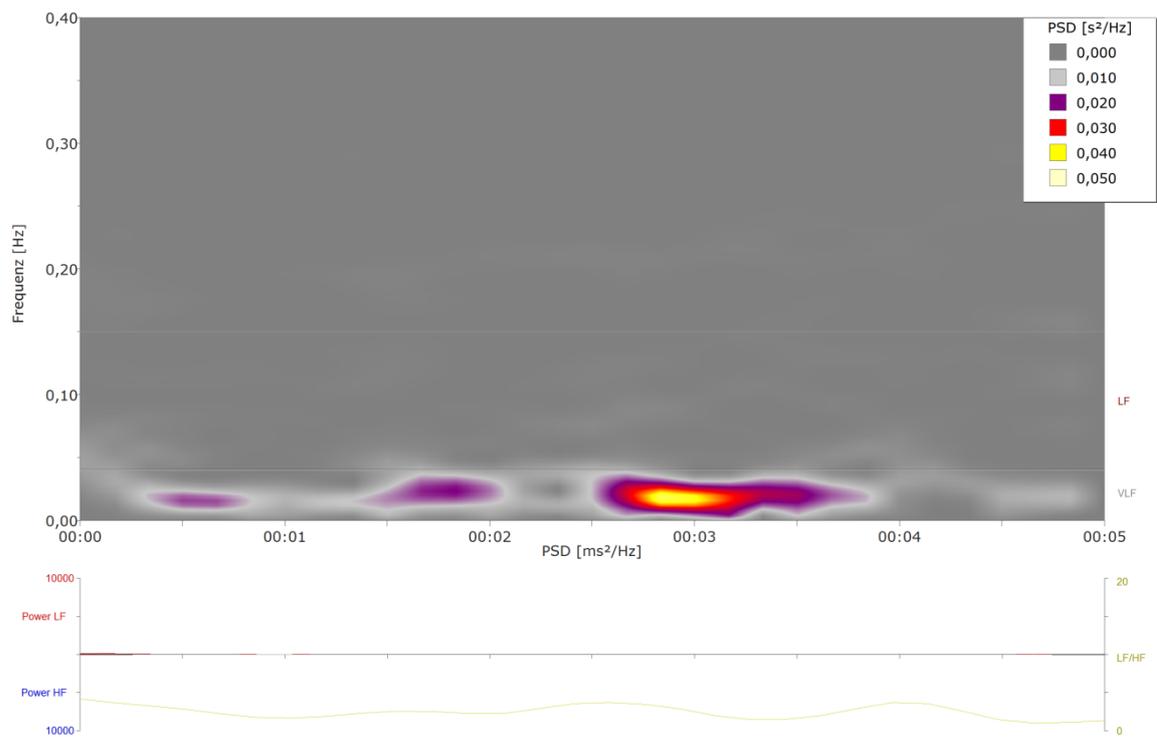
Two graphs visualize the changes in the spectral analysis during the measurement, the color FFT and the 3D FFT diagram. In the color FFT diagram, the activity in a particular frequency band is encoded by the color at a particular time.

In the lower section, the ratio LF/HF and Power LF/Power HF are displayed.

Example of a color FFT from a Short-Term HRV measurement with good HRV. The yellow bands are clearly visible as a representation of high PSD values (Power Spectral Density). High values indicate a frequent occurrence of regulation in the respective frequency range, here in the HF range as a sign of a clearly good parasympathetic function and in the LF range as a sign of a pronounced RSA and thus also a regulation from the parasympathetic nervous system.

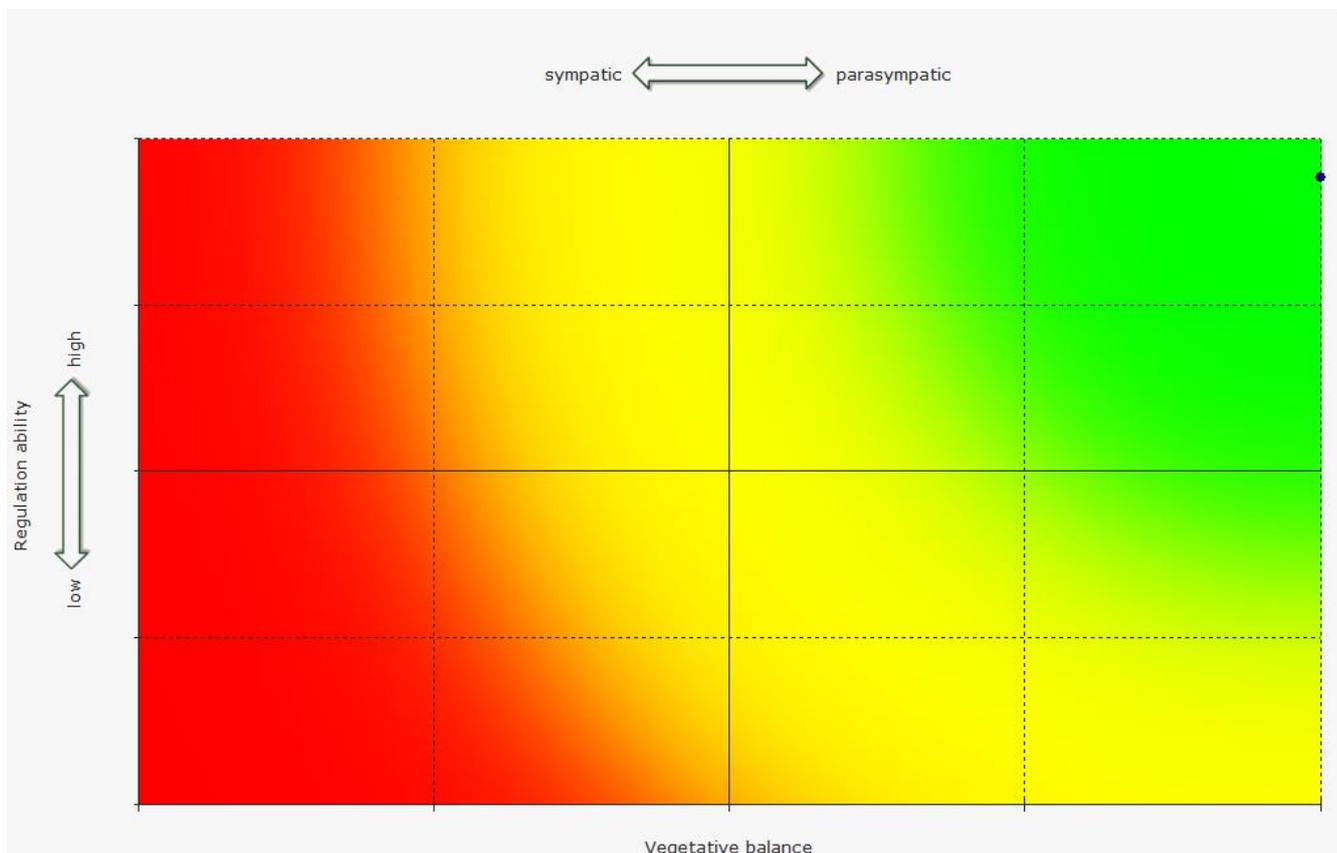


Example of a color FFT from a Short-Term HRV measurement with restricted HRV. Here, a complete absence of activity in the HF range is seen as a sign of a clear parasympathetic weakness. In the LF area only very discrete bands are visible, which also indicates a restricted regulation by the sympathetic. So overall, a very limited regulatory capacity.



ANS status

The ANS status diagram reflects the current state of the autonomic nervous system and the two opposing branches of the sympathetic and parasympathetic nervous system in two dimensions. The ratio of parasympathetic to sympathetic activity is plotted on the horizontal axis and the regulatory capacity of the vegetative nervous system on the vertical axis. Overcoming the parasympathetic is rated as "good", as is a high regulatory capacity. Therefore, in the optimal case, the blue marking is located in the right upper panel (green) and in the lower left panel (red) if the measurement results are unfavorable.



Based on heart rate variability, only a qualitative statement on an ordinal scale in the sense of "more parasympathetic than sympathetic" or "predominantly parasympathetic" can be attributed to the current state of the autonomic nervous system. An assessment in the sense of "twice as much parasympathetic as sympathetic activity" is not possible. For this reason, the diagram does not include scaling on the X axis and Y axis.

For the determination of the regulatory capacity, the age-corrected, achieved rank of the "total power" is used as the basis for both the sympathetic and the parasympathetic regulation power.

The assessment of the parasympathetic/sympathetic balance is made by means of a modified LF/HF-quotient. The LF/HF ratio is the ratio between the power in the low-frequency band (LF) of the spectrum analysis and the power in the high-frequency band (HF) and represents a measure for the vegetative balance accepted in international guidelines. However, only the HF is specific for the parasympathetic. Because only the parasympathetic can regulate in the high-frequency range due to its receptor morphology. The LF region contains both sympathetic and parasympathetic activity, which is mainly due to the influence of respiration. For this reason, the parasympathetic influence of the respiration is calculated out of the LF range in the HRV-Scanner and is attributed to the HF range. This clearly increases the separation severity of the quotient between sympathetic and parasympathetic activity.

Parameter History/Pre-measurements

HRV measurements enable the objective assessment of the success of therapies, coaching or training. Especially the comparison with pre-measurements can clarify the development of the neurovegetative regulation well. For this reason, the course of the pre-measurements or the change in the HRV parameters compared to the pre-measurements are given in many reports.

Diagrams of the HRV-history are available for Deep Breathing Test, Short-term HRV, Valsalva maneuvers, supine/standing HRV and for the biofeedback types (3D biofeedback, online spectrum, rhythmization and Qiu). For measurement types with normal values, the change can be shown for different HRV target parameters:

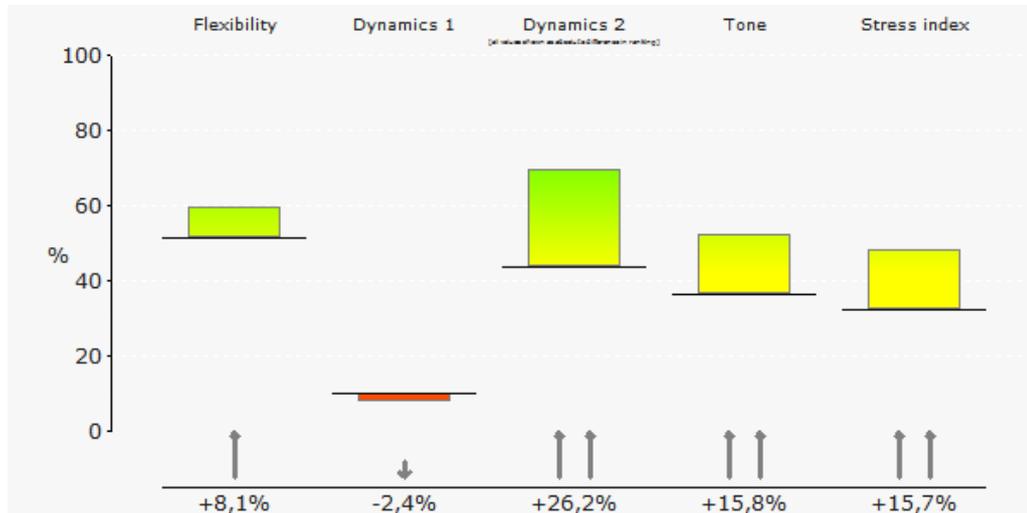


Fig. Change in the HRV parameters of Short-term HRV compared to the median from the last 25 pre-measurements

In some cases, e.g. in biofeedback, a certain HRV parameter (absolute degree of rhythmization in the example) is used. For the Short-term HRV for instance, the HRV parameter shown can be selected in the system settings.

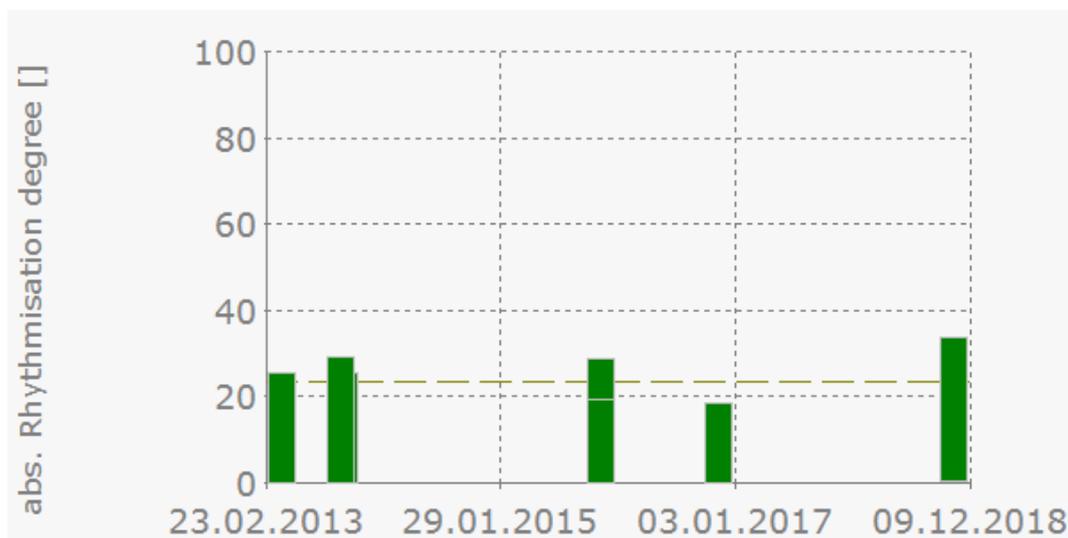


Fig. Course of the biofeedback pre-measurements with the target parameter "absolute degree of rhythmization". The median from the 8 pre measurements is shown as a dashed line.

How can it be determined which pre-measurements are to be taken into account in such a course? There are three options:

- Number of the last pre-measurements to be taken into account (n measurements before the currently evaluated measurement) (HRV-Scanner lite and HRV-Scanner standard)

- Period of the pre-measurements to be taken into account (n days before the currently evaluated measurement)
(standard HRV-Scanner only)
- Individual selection of the pre-measurements to be taken into account
(only HRV-Scanner standard)

In general, only pre-measurements can be taken into account in the course that have been previously evaluated and stored.

Number of pre-measurements in the HRV-Scanner lite

In the HRV-Scanner lite you will find the setting for the number of pre-measurements to be taken into account in the evaluation under the "Progression" tab:

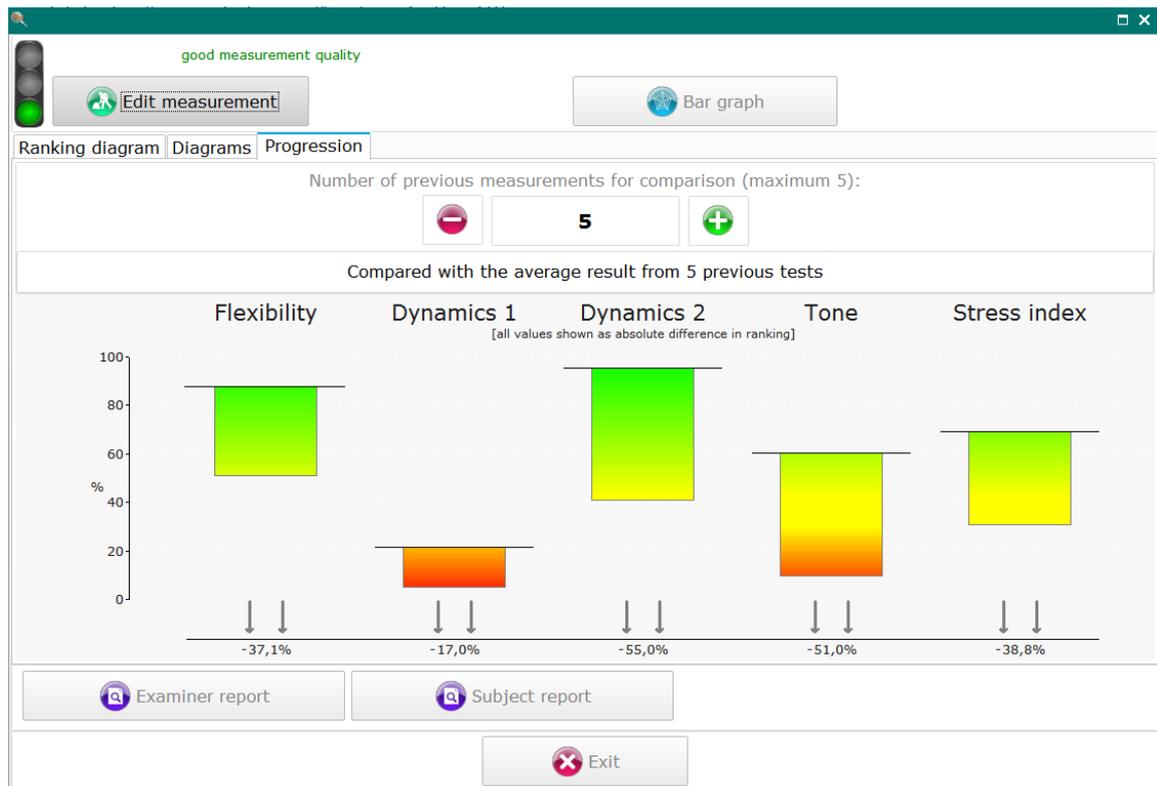


Fig. Course in the evaluation of the HRV-Scanner lite

Pre-measurements in the HRV-Scanner standard

In the HRV-Scanner standard, even more extensive settings for the pre-measurements can be made in the "Progression of parameters" tab.

Rank chart

In the "Previous tests" tab, you can see a ranking diagram for measurements with stored standard values, in which the currently evaluated measurement and the pre-measurements are drawn.

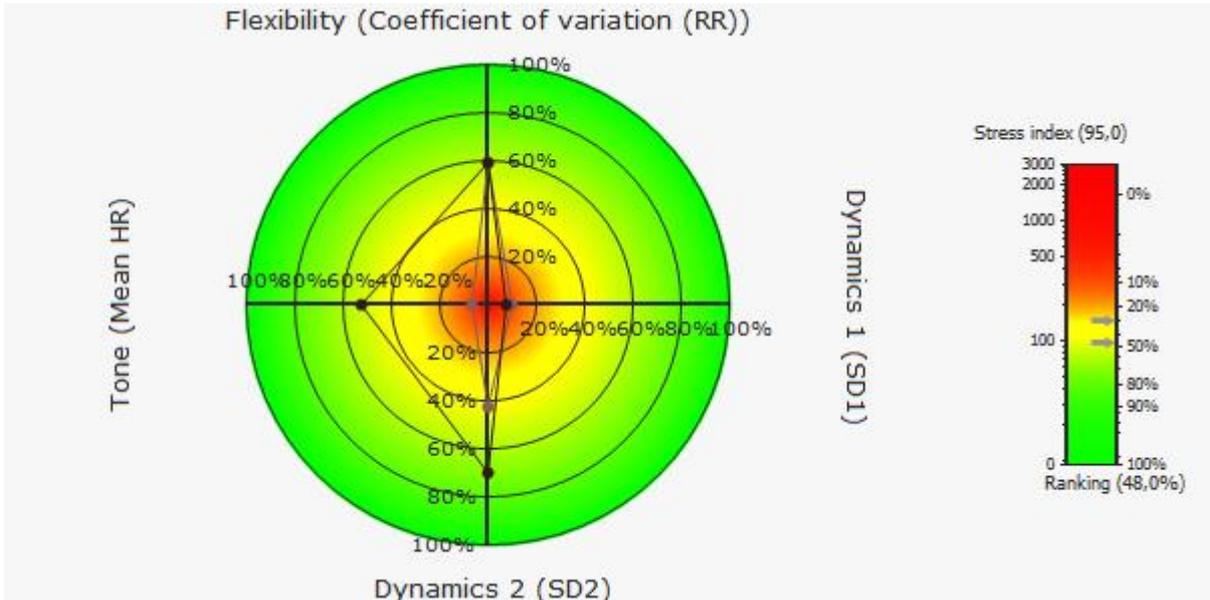


Fig. Rank diagram with the currently evaluated measurement and the pre-measurements

Biofeedback History

For biofeedback measurements, a history is displayed instead of the rank diagram:

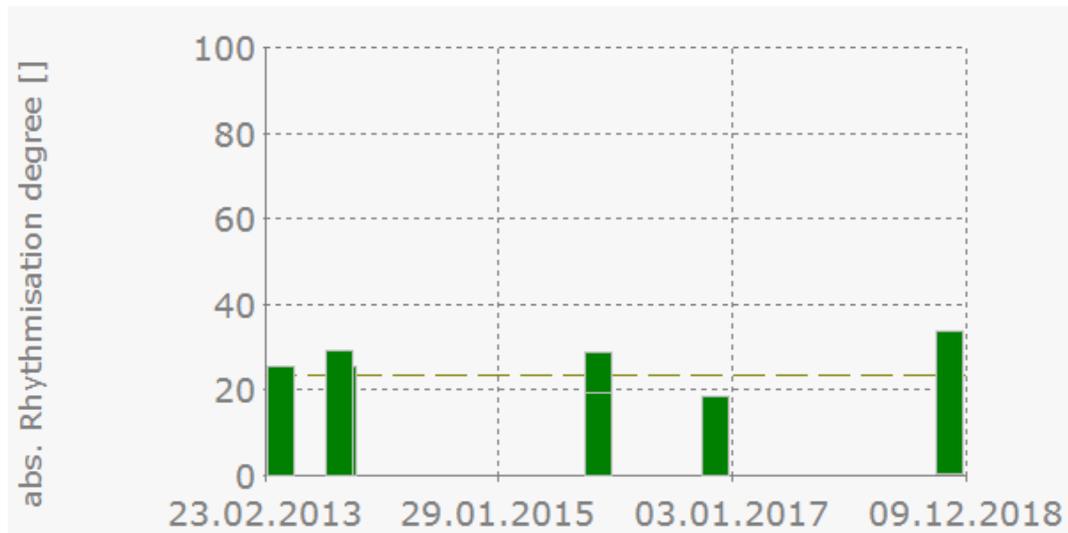


Fig. History of the biofeedback measurements

In the right-hand list "Reference tests", measurements can be activated or deactivated individually for display in the rank diagram or history.

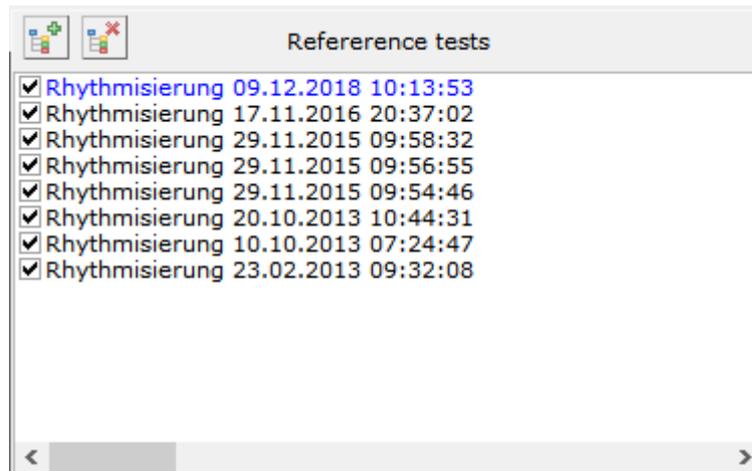


Fig. Individual selection of the preliminary measurements

Measurements that are checked in this window are also considered as pre-measurements in the history diagram and in the reports. With the two buttons above all measurements can be selected or deactivated.

To determine which measurements are displayed in the "Reference tests" window, please use the filter settings in the lower left part of the window:

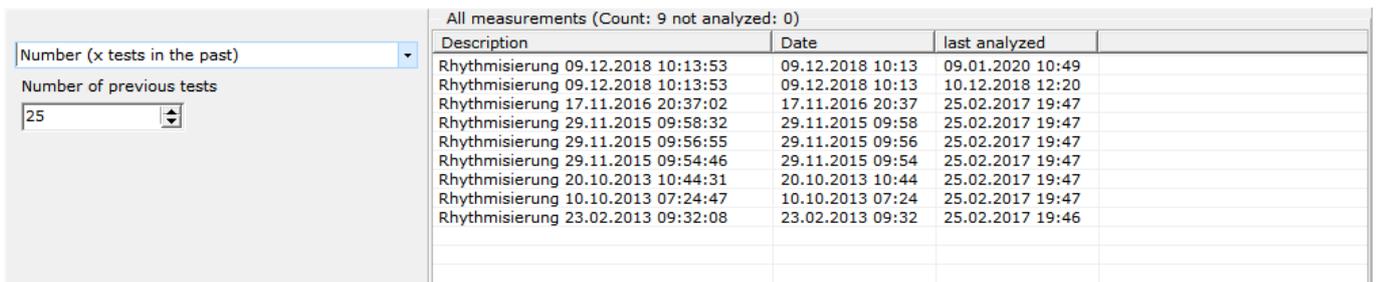


Fig. Filter settings for pre-measurements and list of all measurements

In the filter you can choose whether you want to display all pre-measurements, only a certain number of pre-measurements or only pre-measurements from a certain period.

Changes

For measurements with stored normal values, you also see the "Changes" diagram. The changes in the target parameters are shown here as the absolute difference between the current measurement and the medians from the pre measurements.

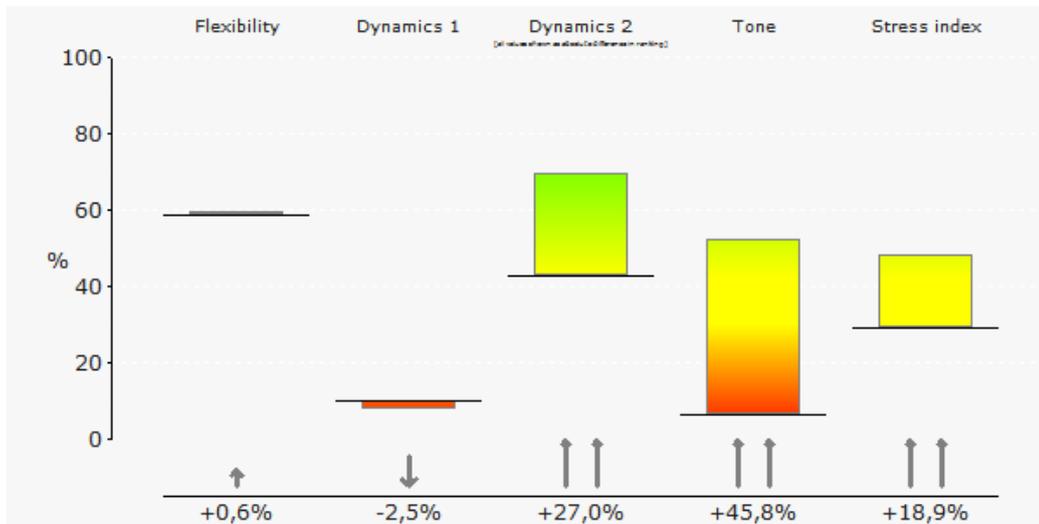


Fig. Changes in the HRV parameters

Parameter

Here you can display the course of individual parameters. The selection of the measurements to be shown is set at the bottom left using the filter. One or two diagrams can be displayed. The selection of the parameters can be selected for each diagram.



Fig. Parameter progression of certain parameters based on the selection of measurements

List of parameters

Calculate heart rate from []

Specifies whether the heart rate is calculated from the ECG or the pulse wave

Sampling rate [Hz]

Specifies the sampling rate for the biosignal (ECG, pulse wave) on which the measurement is based.

Duration [hh:mm:ss]

Duration of the measurement

Number of heartbeats [n]

Number of heartbeats detected in the measuring range, which have not been marked or filtered as an artefact

Artefact ratio [%]

Number of heartbeats marked or filtered as artefact in relation to all heart attacks detected in the measuring range. This parameter can be used very well to give an assessment of the evaluation of an HRV measurement. An artefact ratio of 0% means no artefacts or filtered heartbeats, an artefact ratio of 100% means that all heartbeats have been marked or filtered out of the measuring range as an artefact.

Well-being [%]

(only Deep Breathing Test and Short-Term HRV)

Value from the conditional assessment before Deep Breathing Test and Short-Term HRV measurement. This value is not included in the evaluation, but primarily serves to better interpret a measurement. Measurements with a rather subjectively tense condition suggest a worse result than measurements with a subjectively relaxed state of mind.

DBT quality [%]

(only Deep Breathing Test, instead of test quality)

Criterion about the quality of a Deep Breathing Test. Essentially, the uniformity of the heart rate matching resulting from the breathing is judged.

Test quality [%]

Criterion about the quality of a measurement. The measurement quality is adversely affected by sections with missing heartbeat (e.g., too many motion artefacts, ...) and sections with irregular rhythm.

Biofeedback quality [%]

(only biofeedback, instead of test quality)

Criterion about the quality of a biofeedback session on the basis of the measurement quality.

Subject age [years]

Age of the subject at the time of the measurement (calculation from the date of birth in the subject administration)

Subject height [cm]

Body size of the subject at the time of the measurement (transfer of the body size from the subjects management at the time of the measurement)

Subject weight [kg] (initial)

Weight of the subject at the time of the measurement (transfer of the weight value from the subjects management at the time of the measurement)

Subject sex

Sex at the time of the measurement (assumption of the sex from the subjects management at the time of the measurement)

Examiner

Which examiner did this measurement

Mean HR [1/min.]

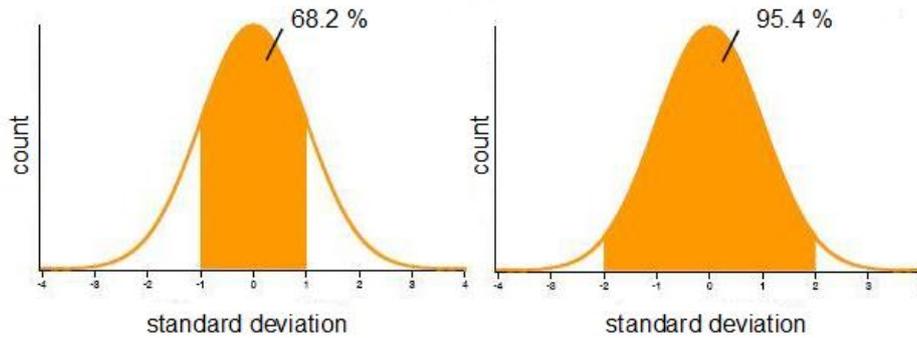
Average heart rate during the measurement.

Standard deviation (St.Dev.) [ms]

Coefficient of variation (HR) [%]

These parameters are derived from descriptive statistics. They express the width of the distribution of individual values around the mean value. It seems natural to use statistics as descriptors for HRV, because HRV itself can be interpreted as a statistical phenomenon: the individual heart rate values within a measurement vary around a mean heart rate, such that larger deviations are less frequent than values closer to the mean.

A classical distribution with these characteristics is the Gaussian (or "normal") curve:



In a Gaussian distribution, 68.2% of all heart rate values will fall within in the area corresponding to the first SD around the mean, and 95.4 % of the values will fall within 2 SDs of the mean. The coefficient of variation (cv) combines SD and mean into a single value. The cv is computed as follows:

Standard deviation

_____ X 100 = cv

Mean

The cv is expressed as a percentage. A cv of 10%, for instance, indicates that 68.2 % of the heartbeats are within a range of +/- 10% of the mean heart rate.

So: the higher the standard deviation or the VK, the greater the heart rate variability.

Mean RR interval [ms]

Analogous to the mean heart rate, the mean RR distance indicates the average RR interval of all heart attacks of the measurement.

SDNN [ms]

Standard deviation of the RR intervals. Analogous to the standard deviation of the heart frequencies, these statistical measures can also be expected over the RR intervals. The SDNN is a frequency - independent indicator of the overall variability (high SDNN - high HRV, low SDNN - low HRV)

PNN50 [%]

Percentage of successive RR intervals that deviate more than 50 milliseconds. A high pNN50 value means high spontaneous changes in heart rate

PNN20 [%]

Percentage of consecutive RR intervals that deviate more than 20 milliseconds.

Coefficient of variation (RR)

Similar to the coefficient of variation calculated from the heart frequencies, these statistical measures can also be calculated over the RR intervals.

RMSSD [ms]

(root mean square of successive differences - Meaning: root from the mean value of the squared differences of the RR intervals of successive heartbeats) The RMSSD is mathematically somewhat complicated, but it describes a simple fact: It expresses how much the heart rate changes from one heartbeat to the next.

$$RMSSD = \sqrt{\frac{1}{N} \times \sum_{i=1}^N (RR_{i+1} - RR_i)^2}$$

Artefacts are characterized by strong jumps of heart rate. In artefacts, therefore, the heart rate changes from one heart to the next. For this reason, the RMSSD is very sensitive to artefacts. A high RMSSD with a comparatively low standard deviation or a low coefficient of variation should be the reason to test the measurement for artefacts.

SD1 [ms]

SD2 [ms]

SD1 and SD2 describe the scattering of the heartbeats in the Poincaré diagram. SD1 expresses the width of the point clouds and is more sensitive to fast, higher frequency changes in the heart rate whereas SD2 describes the length of the point cloud and rather quantifies the long term HRV.

SD2/SD1 quotient

The SD2/SD1 quotient is the ratio of the already known parameters SD2 to SD1, which can be calculated from the Poincaré plot. SD2 reflects slow heart rate changes, whereas SD1 quantifies the rapid heart rate change from beat to beat. The ratio of the two parameters therefore expresses the ratio of slow changes in the heart rate as compared to rapid fluctuations in the heart rate.

The SD2/SD1 quotient is comparable to the LF/HF quotient, which is commonly used to quantify the autonomous equilibrium. One uses the characteristic of the parasympathetic to be able to change the heart rate relatively quickly - in contrast to the rather inert sympathetic. Vibrations in the high frequency band (HF) are therefore caused mainly by the parasympathetic activity, the sympathetic plays practically no role here. However, this clear separation between sympathetic and parasympathetic activity cannot be performed for the low frequency band (LF) because both branches of the autonomic nervous system (ANS) can cause slow fluctuations in the heart rate.

Due to the lack of discrimination in the LF range, the LF/HF quotient is at best a rough measure for the autonomous equilibrium. In addition, there is a second limitation on the practical usability resulting from its sensitivity to the influence of breathing. Breathing leads to sinusoidal oscillations of heart rate (respiratory sinus arrhythmia, RSA). Depending on the respiratory rate, the RSA is either in the LF band or in the HF band. The limit between HF and LF band is achieved with a breathing rate of 9 breaths. Higher breathing frequencies contribute to the HF band, lower breathing frequencies increase the LF performance. However, the RSA is always mediated by the parasympathetic system, independent of the respiratory rate. This causes a high LF/HF quotient in the presence of a high RSA and respiratory frequencies below 9 breaths per minute, which is often misinterpreted as overcoming the sympathetic. Small changes in respiratory rate, e.g. from 8 to 10 breaths per minute, can completely reverse the LF/HF quotients. Therefore, the LF/HF quotient is not a good measure to express the ratio of slow to fast heart rate changes.

Instead, we propose to use the SD2/SD1 ratio instead of the LF/HF quotient, since the SD2/SD1 quotient does not have frequency bands and has a continuous curve. (see figure 1).

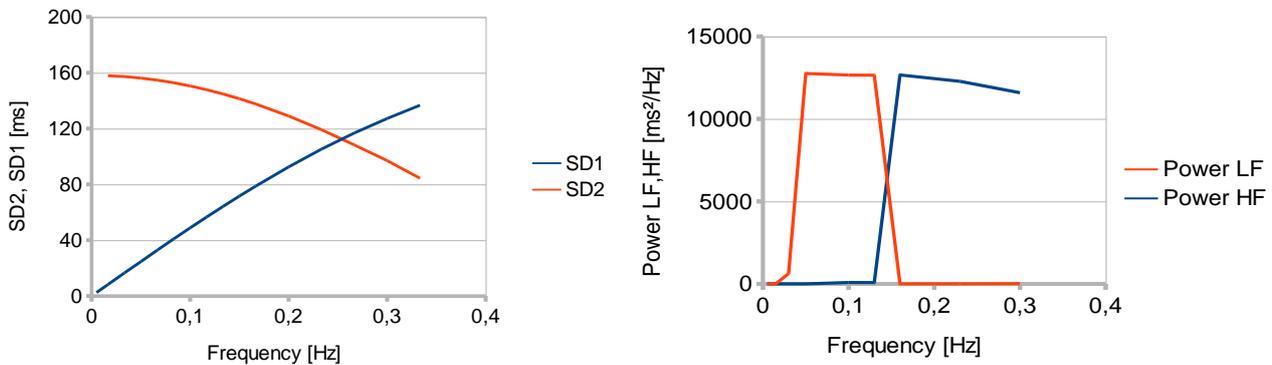


Figure 1

Individual heart rate oscillations of different frequencies from 0.005 Hz to 0.33 Hz, each with a constant amplitude of 20 beats / min, were analyzed one after the other in a computer simulation. The resulting values for SD2 and SD1 are shown (see left diagram). The right diagram shows the corresponding curves for the Power HF and Power LF.

As expected, SD1 decreases with increasing frequency while SD2 decreases. In contrast, the power values change with increasing frequency only when the oscillation changes the frequency band. The power values behave more like a binary on/off switch, but they are not able to display small changes in the dynamics.

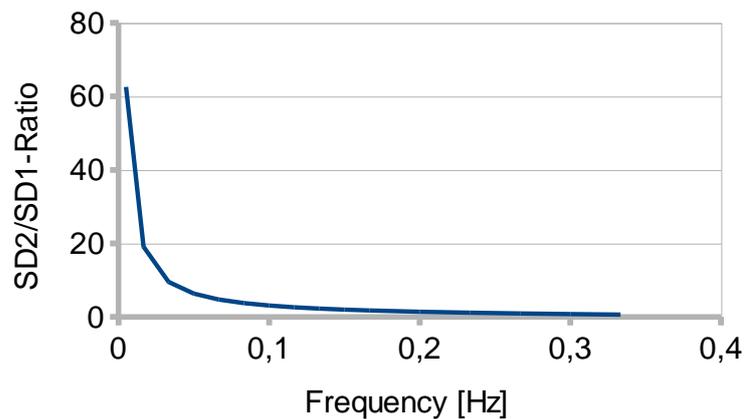


Figure 2 Course of the SD2/SD1 quotient for the corresponding SD values of Figure 1.

Normalized SD2/SD1 quotient [σ]

The calculation of the SD2/SD1 quotient leads almost automatically to the question, what is a "normal" SD2 /SD1 quotient and what is not. We therefore analyzed the distribution of the SD2/SD1 ratio in numerous Short-Term HRV measurements obtained in two different clinical trials. The first study was a standard value study, in the second study many people were subjected to a Short-Term HRV measurement. In this study, there were no strict exclusion criteria (cross-sectional study). In the first study (n = 204), an average SD2/SD1 ratio of 2.9 and the 95% interval of 1.37 to 5.97 resulted in a second study (n = 639) Similar distribution of the SD2/SD1 quotient: mean value: 3.1; 95% interval of 1.53 to 6.4.

For normalization, a Gaussian distribution was obtained by calculating the natural logarithm of the SD2/SD1 quotients (Kolmogorov Smirnov test > 0.2, Lilliefors > 0.2). The normalized SD2/SD1 quotient is then obtained as the difference of an SD2/SD1 quotient from the mean value of the Gaussian distribution, expressed as a multiple of the standard deviation.

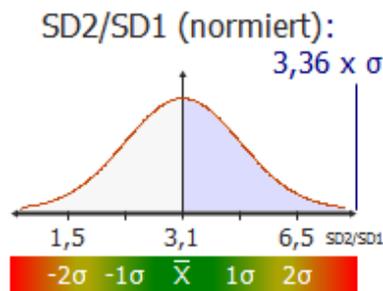


Figure 3

Gaussian distribution of the SD2/SD1 ratios of the two studies (n = 843). A normalized SD2/SD1 value of, for example, 2 σ means accordingly an SD2/SD1 quotient, which is two standard deviations to the right of the mean value. Because of the Gaussian distribution, only 2.3% of the people had an even higher SD / SD1 value.

Related to other HRV parameters

HRV parameters are usually highly correlated among each other. Thus, the correlation coefficient r in the Short-Term HRV measurements taken between Power HF and SD1 is 0.93. The relationship between Power LF and SD2 is also high with an r of 0.84. Other "classical" HRV parameters such as pnn50, SDNN and stress index are highly correlated among each other. Interestingly this is not so for the SD2/SD1 ratio - whether normalized or not. The correlation with the "classical" HRV parameters is comparatively low. If this were different and a high agreement would be found with one of the other usual HRV parameters, the additional benefit of the SD2/SD1 ratio would be low, the information would already be coded in another parameter. However, since this is not the case, the question arises whether information is contained in the SD2/SD1 quotient which is not reflected in the classical HRV parameters.

This seems to be because comparatively high correlations with two other clinically relevant HRV parameters are more likely to be attributed to the nonlinear HRV analysis: the alpha1 value of Detrended Fluctuation Analysis (DFA) and the auto-correlation coefficient (ICC). The correlation of the standard SD2/SD1 ratio with DFA-alpha1 was 0.71 in the examined measurements and even 0.93 with the autocorrelation coefficient ICC. The good correlation with DFA-alpha1 has already been confirmed by third parties in a recent study¹.

There are a number of studies that demonstrate that a reduced alpha1-DFA is associated with an increased mortality risk of ^{2,3,4,5,6}. In a study, the SD1/SD2 ratio, which is the reciprocal of our SD2/SD1 ratio, had the strongest association with mortality after heart attack ². The higher the SD1/SD2 quotient (= the lower the SD2/SD1 quotient), the higher the mortality risk. In another recent study of the relationship between coronary heart disease and HRV, it was interesting to see the opposite relationship between the SD2/SD1 ratio and the coronary heart disease. ⁷. The higher the SD2/SD1 ratio, the stronger the damage of the coronary arteries.

These seemingly contradictory results can be explained by the underlying physiology:

Physiological significance

High SD2/SD1 ratios show a dominance of slow heart rate fluctuations. This can result from an over activity of the sympathetic system and / or a weakness of the parasympathetic branch of the ANS, which can both adversely affect health. The higher the normalized SD2/SD1 quotient, the more unlikely it will reflect good parasympathetic activity. A lack of parasympathetic activity is correlated with the onset of inflammatory mediators in the blood, e.g. CRP, which is associated with inflammatory processes in the coronary arteries and the development of coronary heart disease.

In contrast, lower SD2/SD1 ratios indicate a sufficient occurrence of fast heart rate oscillations. Nevertheless, the low SD2/SD1 ratios were associated with higher mortality in several studies. This was due to the fact that such cases were no longer a "healthy" sinus rhythm, but either rhythmic disturbances or an "erratic" sinus rhythm, which is a prognostically rather unfavorable sign ⁶.

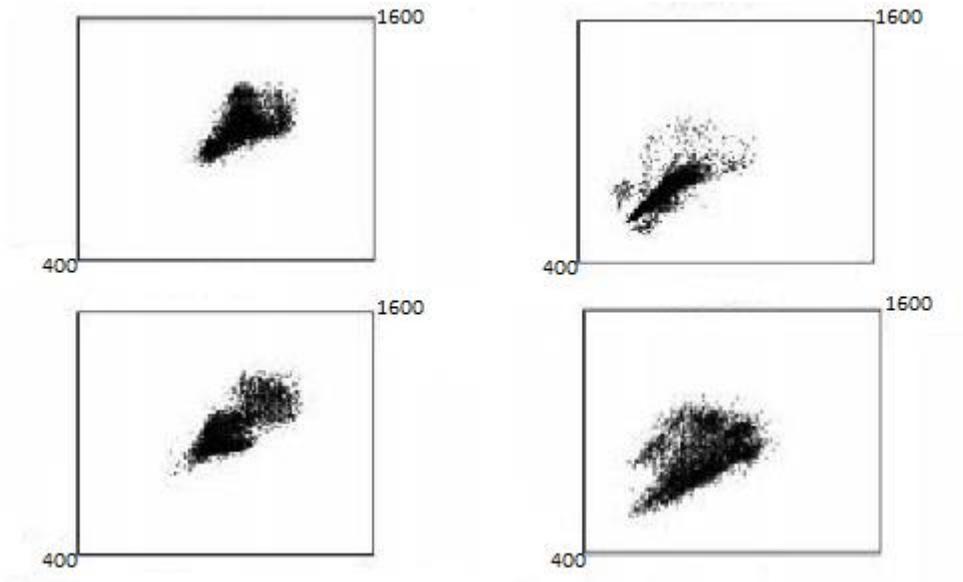


Figure 4 - Poincare plots of erratic sinus rhythms

Conclusion

Thus, an excessively high SD2/SD1 ratio would be unfavorable.



We therefore propose the following approach to interpretation:

Normalized SD2/SD1 quotient	Interpretation
< -1 σ	<p>Noticeable low result</p> <p>In the first step, check for artefacts and irregular heartbeats and remove them if necessary.</p> <p>In the second step, check whether there is a sinus rhythm (atrial fibrillation?). No meaningful HRV analysis can be performed without sinus rhythm.</p> <p>Age and medical history must be considered. Higher age and evidence of coronary heart disease or infarction suggest a more erratic sinus rhythm. In young athletes, very low SD2/SD1 ratios are indicative of a high dynamic regulation capacity of the parasympathetic nervous system.</p> <p>If a suspicious sinus rhythm is suspected, a 24-hour HRV measurement is recommended.</p>
-1 σ to 1 σ	Normal findings
> 1 σ	<p>Noticeable high result</p> <p>Significant overcoming of slow heart rate changes.</p> <p>Usually, other signs of parasympathetic dysfunction are present (low SD1, low power HF, high stress index)</p>

The corresponding literature for the SD2/SD1 parameter can be found in the appendix.

Stress index [Pts.]

The stress index is calculated based on Prof. Baevsky, who developed and validated this parameter within the framework of Russian space medicine. The stress index is becoming increasingly popular because it is sensitive to shifts in the vegetative balance between sympathetic and parasympathetic nervous system. It ultimately represents a mathematical description of the histogram:

$$\text{Stressindex} = \frac{A_{mo}}{2 \times M_o \times M_x D M_n}$$

M_o = modal value, most frequent value of the RR interval; A_{mo} = number of RR intervals corresponding to the modal value as a percentage of the total number of all measured values; $M_x D M_n$ = variability width, difference of the maximum and minimum RR intervals.

Because of its sensitivity, the stress index is a good measure to register changes within a subject over time. However, like all other HRV parameters, it is strongly influenced by the overall state of neurovegetative regulation. That is, an organically induced restriction of HRV (e.g., as a complication of long-term diabetes) is indicated by a high to very high stress index without stress loading.

HF-Band [Hz]

LF-Band [Hz]

VLF-Band [Hz]

Definition of the ranges for the separation of spectral analysis into different bands (High frequency, Low frequency, very low frequency)

Power HF-band [ms^2]

High Frequency Power, Power density spectrum in the frequency range of e.g. 0.15 to 0.40 Hz; Shows exclusively the parasympathetic part

Power LF-band [ms^2]

Low Frequency Power, Power density spectrum in the frequency range of e.g. 0.15 to 0.40 Hz; Both the sympathetic and the parasympathetic are involved, with the sympathetic being predominant.

Power VLF-band [ms^2]

Very Low Frequency Power, Power density spectrum in the frequency range of e.g. 0.15 to 0.40 Hz; Other central nervous sources of cardiac regulation are visible in the VLF band

Power total [ms^2]

The total power quantifies the total power over all frequency bands

rel. Power HF-band [%]

rel. Power LF-band [%]

rel. Power VLF-band [%]

The relative power of a frequency band indicates the percentage of the power of the frequency band as a percentage of the total power.

LF/HF ratio

The so-called LF / HF quotient indicates the ratio of the power in the LF band to the power in the HF band. It is often referred to as an expression of the vegetative balance of parasympathetic and sympathetic nervous system. This is, however, only partially true. Although the HF range is reliably assigned to the parasympathetic, the LF range contains both sympathetic and parasympathetically mediated regulation of heart rate. If, for example, pronounced respiratory sinus arrhythmia is present in slow and deep breathing, a very large LF / HF quotient is obtained, which, however, does not indicate strong sympathetic activity, but is an expression of well-functioning parasympathetic regulation.

Rhythmisation degree []

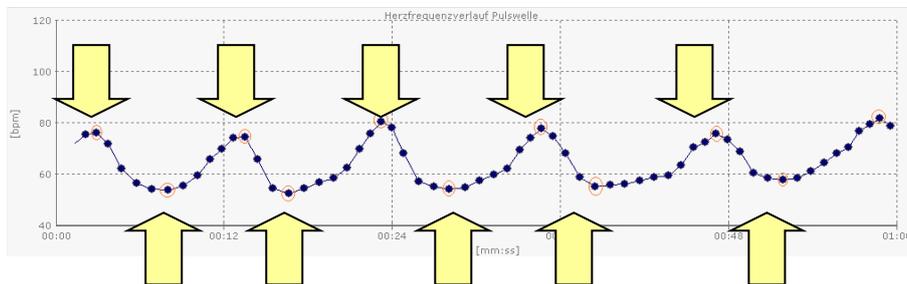
The degree of rhythmization quantifies "quality" and "quantity" of respiratory sinus arrhythmia. "Quantity" means the size (amplitude) of the resp. Sinus arrhythmia, "quality" expresses whether, in addition to the resp. Sinus arrhythmia, other regulatory processes in the heart rate are visible. Especially in the case of HRV biofeedback, the degree of rhythmicity plays an important role because a high degree of rhythmization (large resp. sinus arrhythmia, small other control processes) is here specifically trained.

E-I [1/min.]

E/I []

(Expiration-/Inspiration difference or quotient) - only Deep Breathing Test

The calculation of the E-I is the "classical" evaluation of a deep breathing test, as it is evaluated, for example, in hospitals that have an autonomous function laboratory. E-I and E / I are direct measures of respiratory sinus arrhythmia. The HRV-Scanner software calculates the highest and the lowest heart rate for each individual breathing cycle (see picture).



The E-I or E/I can now be calculated from the highest and lowest heart rate of each respiratory cycle. Because of the calculation basis using median values, E-I and E/I are relatively robust against artefacts. In the interpretation of the E-I, it should be noted that subjects with a very low mean heart rate (≤ 50 / min) have a low E-I as a subject with a normal or higher heart rate. The reason for this is the AV node (atrioventricular nodes, secondary pacemakers of the heart adjacent to the sinus node as a primary pacemaker), which limits the frequency drop down ($<40-50$ / min).

MCR []

(Mean Circular Resultant) - only Deep Breathing Test

The MCR represents a vector whose magnitude correlates well with the magnitude of respiratory sinus arrhythmia and is relatively insensitive to outliers and artefacts.

$$MCR = \sqrt{\left[\sum_{i=1}^n \cos\left(\frac{2\pi T_i}{\lambda}\right) \right]^2 + \left[\sum_{i=1}^n \sin\left(\frac{2\pi T_i}{\lambda}\right) \right]^2}$$

λ = cycle length; $T_1, T_2 \dots T_n$: time of the single heartbeats

(See also: Weinberg CR and Pfeifer MA, 1984, An improved method for measuring heart rate variability: assessment of cardiac autonomic function Biometrics 40: 855-61)

Ewing 30:15 value []

synonym. 30/15 ratio, 30/15 ratio (only lying / standing measurements)

The Ewing parameters quantify the change in heart rate after standing up. According to Ewing, the RR 15 indicates the RR interval of the 15th heartbeat after rising and the RR 30 the RR interval of the 30th heartbeat after rising. Since there are inter-individual differences in the response to standing up, the longest RR interval of the beats 5 to 25 and the shortest RR interval of the beats 20 to 40 are related in the HRV-Scanner. This has proven itself in practice, see Ziegler et al.

(Ziegler D., Laux G., Dannehl K., Spüler M., Mühlen H., Mayer P., Gries F.A., Assessment of Cardiovascular Autonomic Function: Age-related Normal Ranges and Reproducibility of Spectral Analysis, vector Analysis, and Standard Tests of Heart Rate Variation and Blood Pressure Responses, Diabetic Medicine, 1992, 9:166-175)

Biological HRV age [years]

(only Deep Breathing Test and Short-Term HRV)

The HRV is a strongly age-dependent variable. The older we become, the lower the HRV is usually. However, this is (in certain limits) a reversible effect. It can therefore be of interest to know the age of the HRV. To determine the biological HRV age, the age at which exactly 50% of the healthy subjects have better and 50% worse HRV values in the Deep Breathing Test is calculated. For the calculation in the Deep Breathing Test, E-I, E/I, MCR and RMSSD are used, for the Short-Term HRV SD1, SD2, Power HF, Power LF, Total Power and Stress index.

Valsalva-Ratio

(only Valsalva maneuver)

Quotient of the longest RR interval after the end of the press manoeuvre (reflexive bradycardia) and the shortest RR interval during the press maneuver.

Alpha 1 []

(detrended fluctuation analysis)

Calculation

In the theory, the "detrended fluctuation analysis" (DFA) quantifies the fractal properties (self-similarity) of a heart rate curve. For the calculation, the RR intervals are integrated and subdivided into sections of defined number of n RR intervals, where n increases with each run. In each section, the trend is removed and the resulting fluctuation of the RR intervals is calculated. The average fluctuation $F(n)$ is determined for all section variables n .

The resulting slope of the regression line in the $\log(F(n))$ to $\log(n)$ representation corresponds to the scalene exponent α . If the slope is calculated over short section sizes n (e.g., 4-16 heart rate per section), the resulting scale exponent expresses α short-term correlations (α_1 and DFA1, respectively). The slope over larger section sizes (e.g., n : 16-64) corresponds to correlations over a longer period of time (α_2 and DFA2, respectively). An α_1 of 0.5 indicates a completely random heart rate curve. A value of 1.5, on the other hand, would be a strongly autocorrected signal.

Physiological significance

There are several studies showing a good prognostic value of α_1 and α_2 in the 24-ECG, e.g. According to myocardial infarction (α_1) or mortality in the elderly (α_2).

Correlation to other HRV parameters

DFA1 is highly correlated with the parameter $LF / (LF + HF)$ and the $SD2 / SD1$ ratio. This relationship has already been described in the literature and is confirmed by BioSign in its own investigations. In a BioSign study with approximately 500 subjects, the correlation of α_1 and the $SD2 / SD1$ ratio was 0.71 and the $LF / (LF + HF)$ ratio was 0.72.

Thus, similar to the $SD2 / SD1$ ratio, DFA1 is a time domain equivalent of the spectral indices and therefore cannot distinguish linear from non-linear correlations. The most obvious difference between the DFA and the spectral analysis is that the DFA measures the examination sections in heart attacks, in contrast to the spectral analysis, which analyzes defined time sections.

Clinical benefit

Particularly in the case of short-term analyzes, the DFA must be interpreted with caution. The analyzes of BioSign show a strong correlation with the influence of respiration for DFA1. In the study already mentioned in 500 subjects, the correlation with the influence of breathing (cross-correlation of breathing signal and heart rate curve) was 0.53. A regression analysis with the independent variables $SD2 / SD1$, $LF / (LF + HF)$ and the influence of the respiration showed a correlation of 0.88.

Thus, it seems unlikely that the DFA can add significant additional information beyond the existing parameters of the time domain and frequency domain in the case of short-term HRV analyzes. The practical benefit of the DFA in the short-term HRV is also limited by the strong spread of the values. In the above study, the mean DFA1 was 1.03 and the standard deviation was 0.23. Due to the strong spread of the DFA1 values in the short-term HRV also in the normal population, no meaningful standard value limits can be specified.

Respiration parameters

(only Short-Term HRV)

Breathing is the primary trigger for the HRV at rest. It is therefore extremely helpful to take into account in evaluating a Short-Term HRV. A poor test result in the Short-Term HRV is not necessarily the expression of a parasympathetic regulatory disorder, but the subject may simply have breathed far too quickly and too flatly (e.g., high stress level). This can lead to seemingly contradictory findings in the Deep Breathing Test, where a good result is often obtained. It is therefore recommended to take a look at the breathing during the evaluation.

Impact breathing [%]

Influence of breathing on the change in heart rate. The larger the percentage, the more pronounced the respiratory sinus arrhythmia and the more relaxed is the measured person.

Respiratory rate [1min.]

Average breathing rate in the selected measuring section. High respiratory frequencies usually lead to a lower HRV. It is therefore advisable to check the respiratory frequency at low HRV values. However, even very slow breathing frequencies (<6 breaths per minute) can lead to low SD1 or RMSSD values because the parasympathetic is also slow to control with slow breathing.

Respiration stress[]

Estimation of stress from breathing. Similar to the stress index in the HRV, the respiratory stress value increases steeply (exponentially) if the respiratory rate is too high. Respiration stress and respiratory rate basically express the same thing (increase of the breathing frequency) and are therefore evaluated similarly in the corresponding normal value graphs. Note: strongly different assessments of respiratory rate and respiratory rate may occur when breathing is measured via EDR (ECG derivative respiration) and the EDR signal cannot be derived cleanly. In this case, the respiration parameters should not be included in the assessment.

Breathing variability []

Variability of breathing during measurement. A calm even breathing is characteristic of a relaxed state. High variability values can, for example, indicate mental stresses ("head kino").

Pulse wave latency [ms]

The pulse wave latency or pulse transit time (PTT) is a cardiovascular measurement value. It describes the time that a pulse wave requires to travel a certain distance in the vascular system. By measuring the pulse wave time, conclusions can be drawn about important vital parameters such as blood pressure and elasticity of the vessels. In the HRV-Scanner, the PTT is calculated from the temporal distance of the R-wave from the ECG and the pulse wave (e.g., ear clip at the ear).

Guzik index

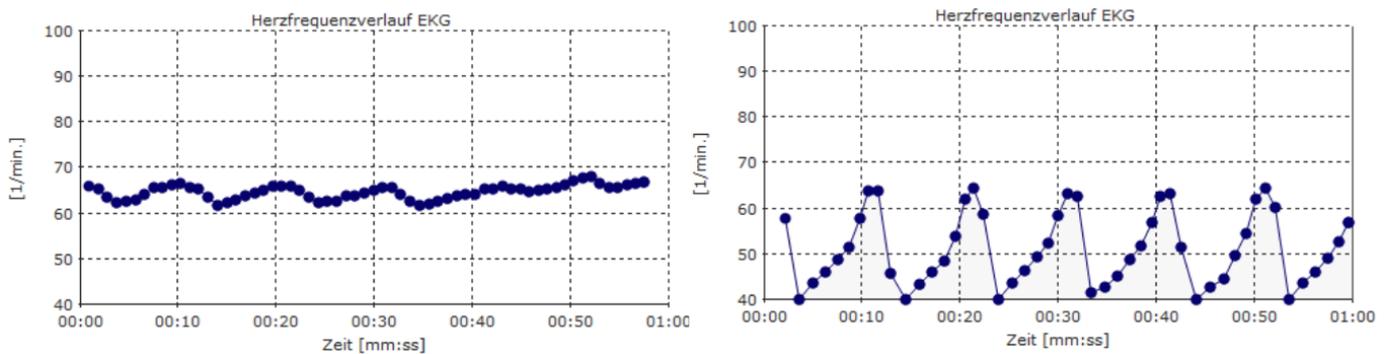
The determination of the respiratory sinus arrhythmia by means of paced breathing is the most important test of the vagus function. With the BioSign concept of flexibility, tone and dynamics, the individual aspects of vagus regulation can be recorded and assessed in a differentiated manner: A well-functioning vagus should ensure a sufficient basic tone (low heart rate) and be able to adapt over a wide control range (large oscillations of the heart rate = high flexibility) and regulate quickly (rapid drop in heart rate = high dynamics).

There are now indications that the drop in heart rate when breathing out is of particular importance. In a study published in 2016 on 941 heart attack patients, the sinus arrhythmia caused by exhalation proved to be a strong prognostic marker with regard to the survival rate (hazard ratio: 3.4).

Expiration-Triggered Sinus Arrhythmia Predicts Outcome in Survivors of Acute Myocardial Infarction. Sinnecker D, Dommasch M, Steger A, Berkefeld A, Hoppmann P, Müller A, Gebhardt J, Barthel P, Hnatkova K, Huster KM, Laugwitz KL, Malik M, Schmidt G. J Am Coll Cardiol. 2016 May 17;67(19):2213-2220

However, it was not only modern computer-aided medicine that was able to establish the connection between exhalation, HRV and importance for health. In fact, the first known description of the connection between a drop in heart rate during exhalation and health can already be found in the "The Yellow Emperor's Classic of Medicine", the standard work of the traditional Chinese medicine: "Counting four or more pulse beats per exhalation is a sign of death."

In the past 20 years we have seen countless deep breathing tests at BioSign. Our observations support the assumption that cardiac regulation during exhalation is a particularly good indicator of vagal function: the better the physical level of training, the faster the heart rate drop is usually during exhalation.



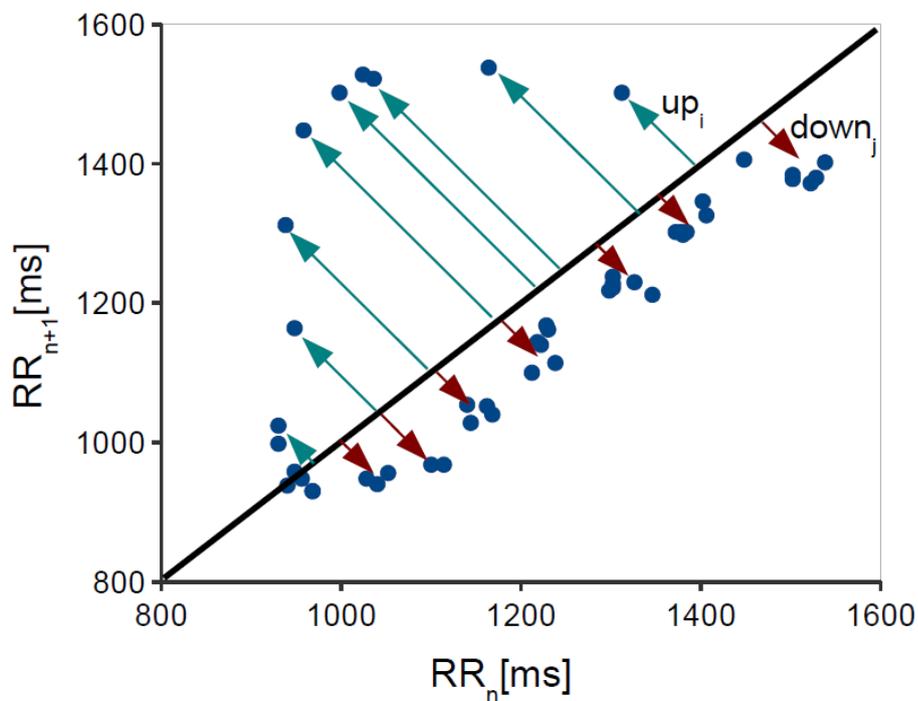
Heart rate curves during the deep breathing test with paced breathing. Left CHD patient, right competitive athlete. Characteristic is the very rapid and strong drop in heart rate when the athlete exhales compared to the slow and low drop in the CHD patient.

Reason enough to pay more attention to the heart rate regulation when exhaling in the latest version of the HRV scanner, especially since the publications by Guzik and Piskorski on "Heart Rate Asymmetry" provide a suitable framework and, above all, understandable and descriptive parameters.

Heart rate asymmetry by Poincaré plots of RR intervals. Guzik P, Piskorski J, Krauze T, Wykretowicz A, Wysocki H. Biomed Tech (Berl). 2006 Oct;51(4):272-5.

Parameter Guzik index

The heart rate increases when you breathe in and decreases when you breathe out. The RR intervals behave inversely: When the heart rate drops, the RR intervals lengthen. In the Poincare diagram, inhalation and exhalation can therefore be distinguished: All points above the bisector correspond to a slowing down of the heart rate (increase in RR intervals) and can be assigned to exhalation, all points below the bisector express an acceleration of the heart rate and fall in the inhalation phase.



Poincare diagram of a deep breathing test of a competitive athlete. Up (i) indicates the distance between the heartbeat (i) and the bisector during exhalation, down (j) the distance between the heartbeat (j) and the bisector during inhalation.

The average distance of all points from the bisector is the well-known SD1. According to Guzik, the SD1 can be represented as the sum of the SD1 values above (exhale) and below (inhale) the bisector:

$$SD1^2 = \frac{1}{n} \sum_{i=1}^n D_i^2 = \frac{1}{n} \sum_{j=1}^{n_{up}} u_j^2 + \frac{1}{n} \sum_{k=1}^{n_{down}} d_k^2$$

$$= SD1_{up}^2 + SD1_{down}^2$$

If you put the two amounts above and below the bisector in relation to each other, you get the Guzik index:

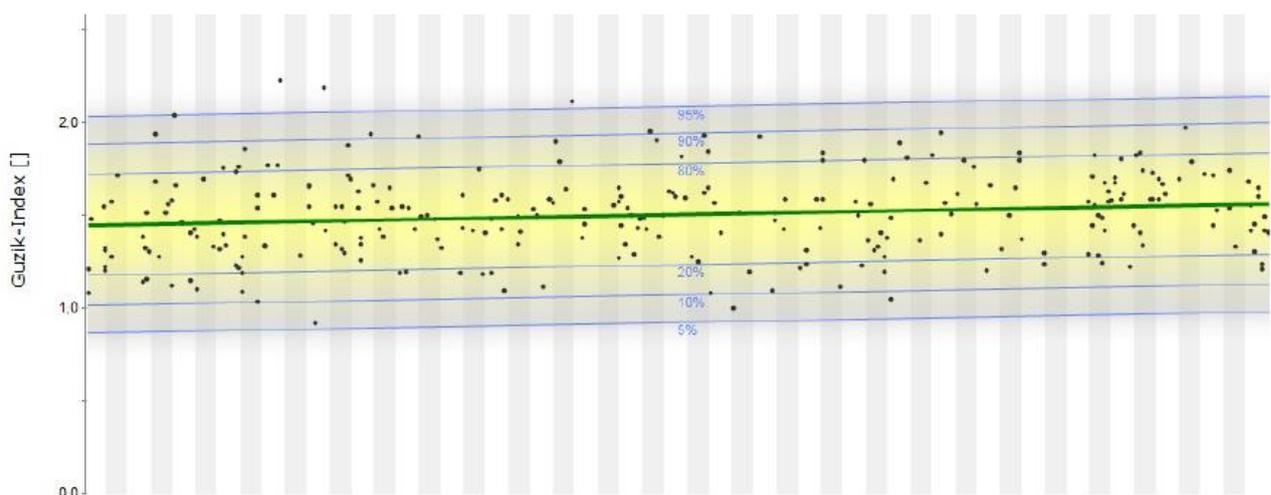
$$Guzik-Index = \frac{SD1_{up}^2}{SD1_{down}^2}$$

The Guzik index is the higher, the stronger and faster the heart rate drops during exhalation and, in our view, represents a useful addition to the generalized parameter SD1. With the help of the Guzik index, the dynamic component of vagal regulation can be viewed in a differentiated manner. The Guzik index is also helpful in assessing whether the dynamics are "healthy": In the case of arrhythmia or "erratic" sinus rhythm (heart rate fragmentation) that is unhealthier, SD1 and Guzik index change in opposite directions, see table.

Description	Parameter	Ranking (%)	Rank-Chart
Athlete	SD1: 134,58 ms Guzik-Index: 3,98	99,5 94,82	
Atrial fibrillation	SD1: 149,95 ms Guzik-Index: 1,05	99,8 7,2	
Erratic Sinus Rhythm	SD1: 94,45 ms Guzik-Index: 0,99	99,2 5,3	

We have analyzed approx. 800 RSA deep breathing test from our pool for the Guzik index and stored age-corrected reference values so that you can see at a glance whether there are abnormalities in the distribution of the dynamics between inhalation and exhalation.

We have also implemented the parameter in the analysis of the Qiu measurements. It is probably interesting for one or the other user to see whether and how much the dynamics can be trained during exhalation. The following example shows the course of the Guzik index over 12 months. The improvement is significant.



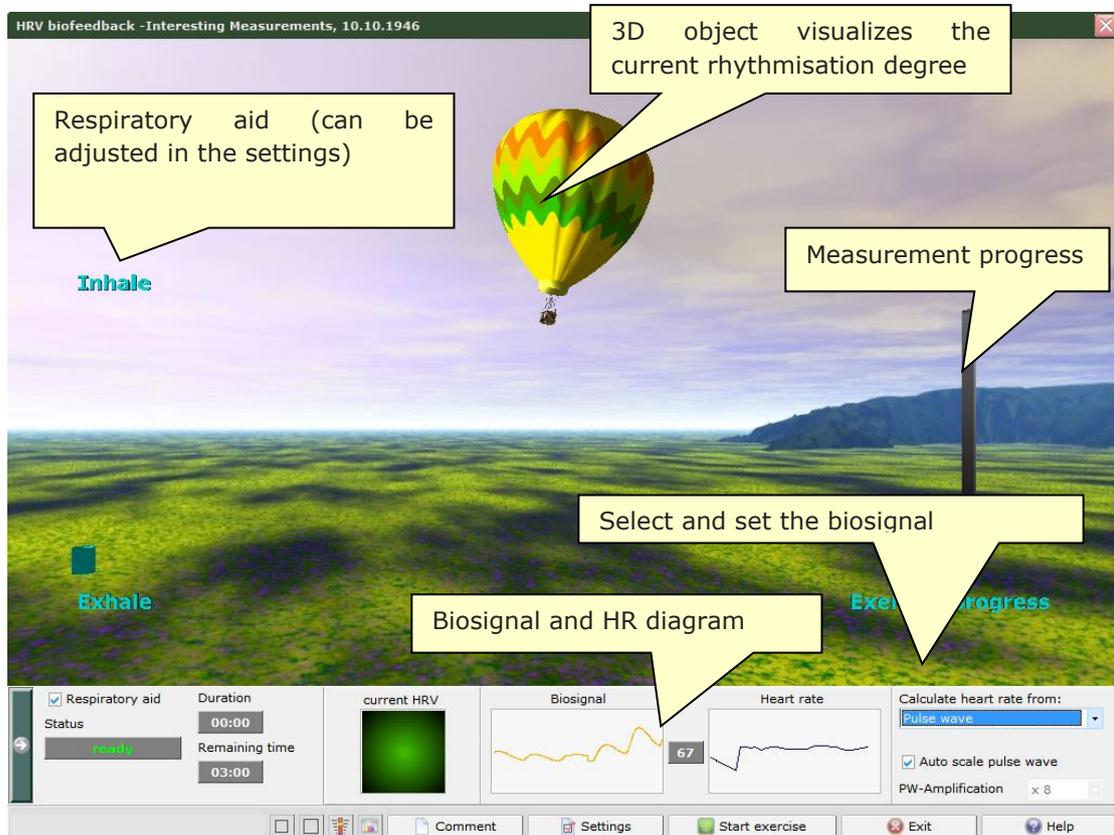
Significantly positive course of the Guzik index over 12 months of Qiu training (p <0.01)

HRV biofeedback

There are three modes of HRV biofeedback available in the HRV-Scanner:

HRV biofeedback

The biofeedback window shows in the basic setting a scene that has a relaxing effect on the subjects (different landscapes are available in the settings) and visualizes the calculated biofeedback parameters via an object (balloon, butterfly, ...). A pleasant background music and spoken instructions helps the subject to relax quickly and effectively.



Biofeedback window showing a scene with a balloon

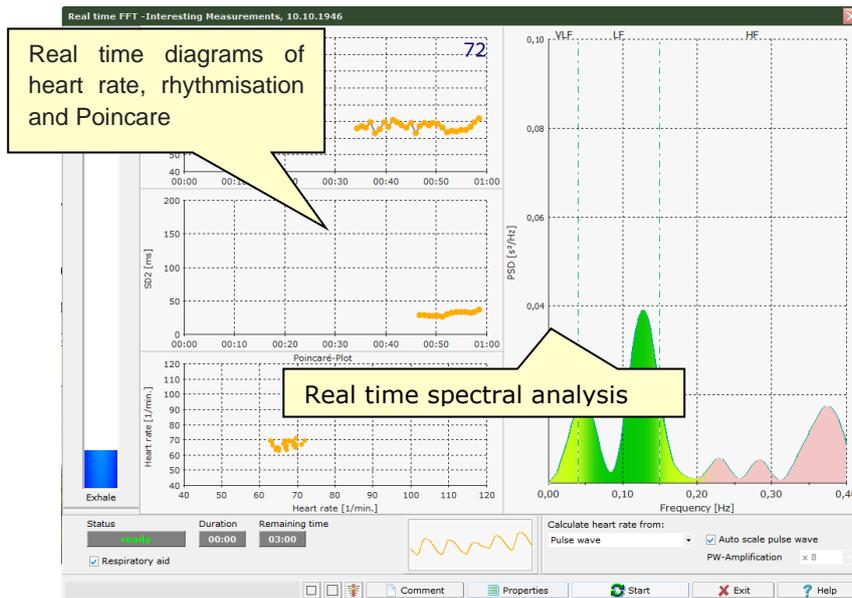
In the left part of the biofeedback window is the respiratory aid, which indicates the rhythm of the breathing. You can customize the breathing rhythm in the settings or hide it completely. The bar on the right represents the progress of the biofeedback exercise (the duration of the exercise can also be adjusted in the settings).

In the lower window there are further settings: the display for the current HRV, the biosignal, the current heart rate and the settings for the biosignal (gain, sensitivity) and heart rate detection.

The remaining measurement time and the elapsed time are shown in the status field. After the measurement time has expired, you will receive a message about the successful recording of the measurement. Close the biofeedback window. The measurement data is packed into an archive and an entry for the new measurement appears in the "Test and analysis" window.

Online spectral analysis (Real time FFT)

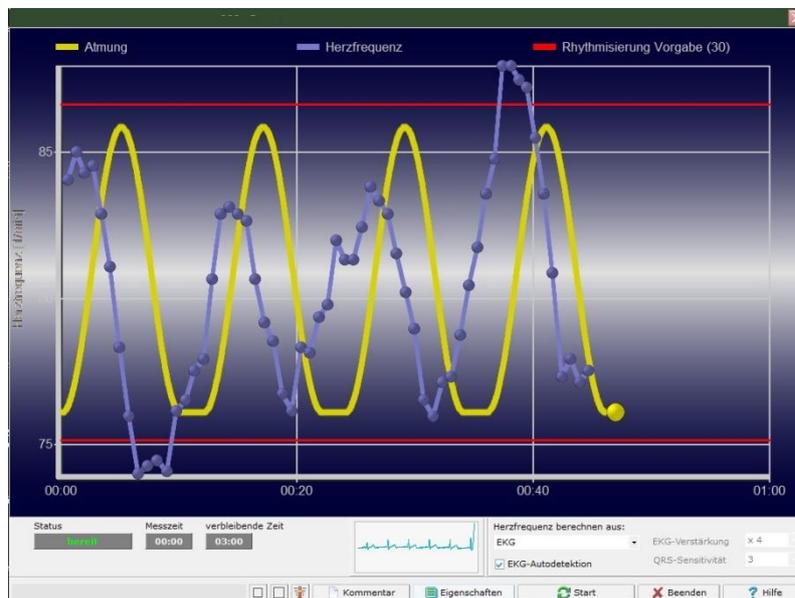
The online spectrum is similar to HRV biofeedback. Instead of an object, real time diagrams represent the current HRV. There is an online spectral analysis, a heart rate and Poincaré diagram and the current degree of rhythm.



Online spectrum window

Rhythmisation

The rhythmization is similar to the HRV biofeedback. The displayed respiratory curve (breathing pattern) and the heart rate progress should be synchronized.



Rhythmization - the breathing curve and heart rate should be synchronized

Fundamentals of HRV Biofeedback

From chaos to order

A variable heart rhythm is better than a too rigid rhythm. However, it is still much better to convert the disordered "chaotic" heart rate variability into an ordered, "rhythimized" heart rate variability (see figure).



"chaotic"



"rhythimized"

Rhythming occurs when the breathing and the heart rate are in a state of relaxation (coherence). With each inhalation, the heart rate increases, with each exhalation it falls off. When the state of the rhythm is reached, it has been possible to activate the "internal brake", the parasympathetic nerve. In many relaxation techniques (such as yoga, autogenous training), this coupling between breathing and heartbeat takes place in the state of relaxation. Using the HRV biofeedback, you can now train this process in a targeted way and get information on how well breathing and heartbeat are rhythmically.

How do we achieve a state of coherence or rhythm?

Breathing is the key to coherence



Respiratory aid

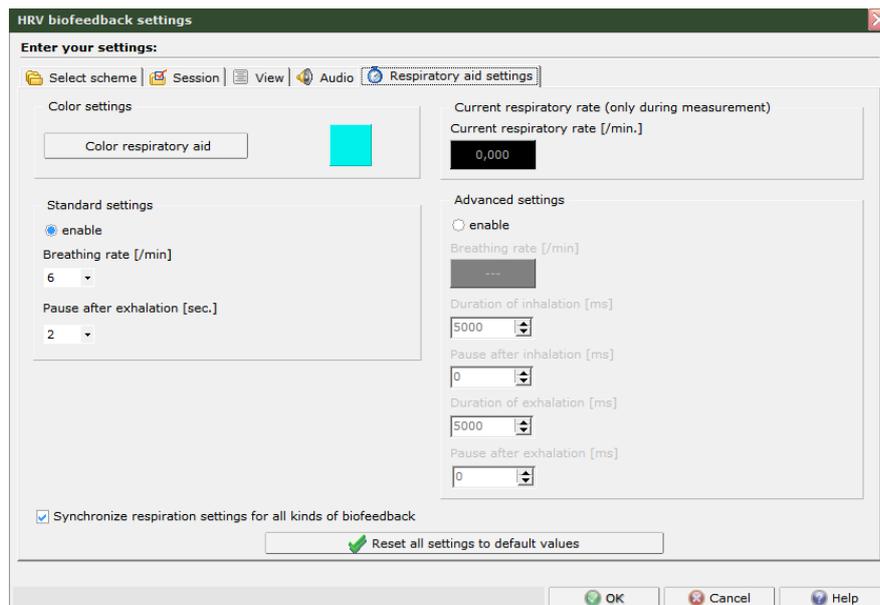
As it is said, coherence is the consistency of breathing and heartbeat. Proper breathing is therefore the central component of any successful HRV biofeedback. To assist in the proper breathing, the HRV-Scanner has a breathing aid:

The breathing aid is located on the left side of the screen. You see a colored bar, which moves rhythmically up and down. It is important to breathe in the rhythm of the beam. Inhale when the beam goes up, exhale when the beam moves down. The best breathing rate is 6 breaths per minute. At this breathing rate, HRV biofeedback is most effective.

If the subject does not get along with this breathing rhythm and the respiratory aid is disturbing, you can also hide it. To do this, deactivate the appropriate checkbox:

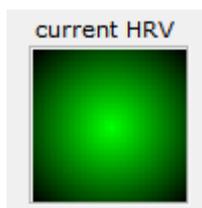


You can change and adjust the settings for the breath (e.g. frequency) in the "Settings" of the HRV biofeedback:

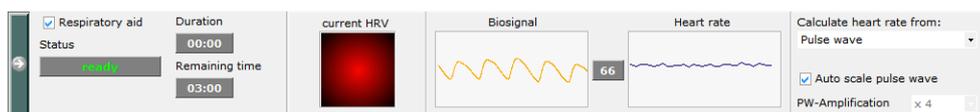


As you learn, breathing and heartbeat are rhythmic

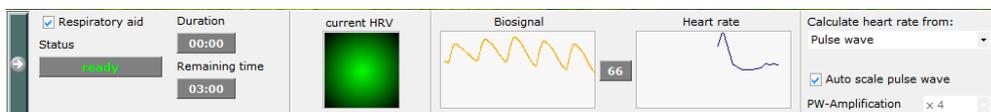
Focus your attention on the color chart at the bottom left:



The color chart shows you the current rhythm level (HRV).



If the color chart is red, the current rhythm level is low, respiration and heartbeat are separated. The heart rate runs irregularly and does not show the regular up and down of the breathing.



Very different here. You can already see the heart rate of how well its course is linked to breathing. Breathing and heartbeat are rhythmic. The parasympathetic, the "internal brake", is now active.

How to improve coherence through biofeedback

The color chart, the central object (balloon, butterfly, ...) the graphs in the online spectrum or the course of the curves in the rhythm are a very important part of the coherence training. We use them, as it were, as feedback, in order to improve the degree of rhythmization. This technique is also called biofeedback. Biofeedback is a method that is used successfully in many areas of medicine to influence the body's involuntary processes. We use biofeedback within the HRV biofeedback to activate the "inner brake" even more.

What to do if coherence is always low?

For example, the color chart is predominantly red, no matter how much the user tries to breathe properly while performing the biofeedback?

First check the pulse signal. Are you sure the pulse signal is OK?

If so, please note the following: The ability to achieve coherence varies from person to person. With age, for example, coherence is reduced. Likewise, hypertension, overweight, heart disease, chronic stress and various metabolic disorders lead to a loss of coherence. It is therefore advisable to measure the personal ability to coherence and compare it with others. This allows you to estimate whether the subject has low, normal, or even high coherence in comparison with others.

If personal coherence is low, the subject should not be discouraged. This is the best reason to do regular HRV Biofeedback. For this, however, you should adjust the HRV biofeedback to the personal level of the subject in the settings.

Click on the "Settings" button to access the settings window. Got to "Session". Set the default value for the Rhythmisation target degree value to a lower level and click OK. Now it should be easier for the subject to color the color chart. This makes biofeedback more effective.

What does the balloon mean in the center of the screen?

The HRV biofeedback is designed in such a way that it can be completed in a certain, preset time. The basic setting is three minutes. To set a different duration, enter the settings window and set the duration to your choice.

In the given period, a high degree of rhythmization should be maintained. The better this is achieved, the better the exercise is completed in the set duration. The HRV-Scanner calculates the current level of the rhythm and displays it by means of the object in the screen center.

For the individual objects, the following changes occur during the biofeedback as a function of the achieved rhythm:

Object	low rhythmization	high rhythmization
Balloon	balloon sinks	balloon rises
Butterfly	butterfly sinks, flutters restlessly	butterfly rises, flies calmly
Sphere	rotates fast	rotates little or not at all

How often and how long should you practice HRV Biofeedback?

"There is still no" scientifically verified "data on the" correct "exercise period. From the practical experience, however, one can deduce that the "correct" exercise period - that is, the probability that a positive effect is felt - is probably very different. However, since you hardly know how much a person is doing well or how much exercise you need, you should start with about three to five minutes HRV Biofeedback two to three times a day. If the subject is doing well, he can also practice 10 minutes two to three times a day.

Important settings in HRV Biofeedback

In addition to the settings for landscape, music, language, etc., there are a few settings which must be adapted individually to the subjects. These are:

Breathing rhythm

Set the breathing pattern so that the practitioner feels that breathing is relaxing. People with stress problems often have a fast and shallow breathing. Here it is not very helpful to press the practitioner into a very slow breathing. The frequency of breathing should be gradually adjusted. The goal is breathing by 6/min.

Exercise duration

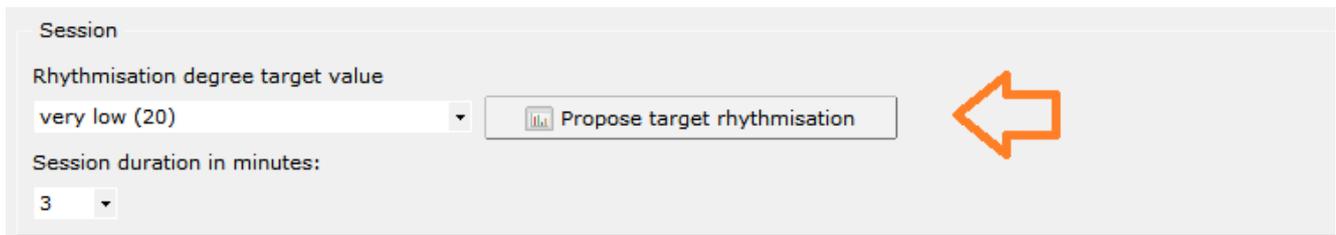
For the beginning, we recommend 3-5 minutes. Best 2 or 3 times daily. Over time, the duration can be increased (possibly also by lowering the daily exercise frequency).

Rhythmization degree target value (difficulty level of the exercise)

It is important to adjust the HRV biofeedback for each individual subject. A good dynamic should be seen in the reproduction of the current coherence (color chart, balloon rises and falls, Qiu glows green and red, ...). It makes little sense for the practitioner, when e.g. the color is constantly red, no matter how much he tries to breathe calmly and to relax mentally. Also e.g. a color chart, which is always green, no matter whether the practitioner breathes calm or rapid is senseless.

Therefore, the difficulty of the exercise has to be adapted to the subject's basic HRV. The best results are obtained from the results from the basic measurements (Short-Term HRV and Deep Breathing Test). Subjects with poor results should be set to a low level of difficulty.

You will find a function for calculating the suggested default value from the Deep Breathing Test in all biofeedback types.



Session

Rhythmisation degree target value

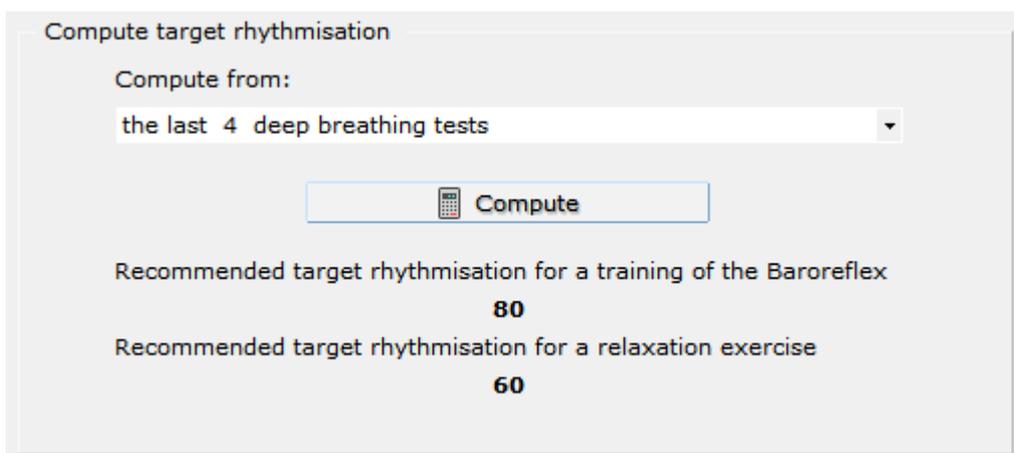
very low (20)

Propose target rhythmisation

Session duration in minutes:

3

Here, a value is calculated and suggested from the last or the few last Deep Breathing Tests.



Compute target rhythmisation

Compute from:

the last 4 deep breathing tests

Compute

Recommended target rhythmisation for a training of the Baroreflex

80

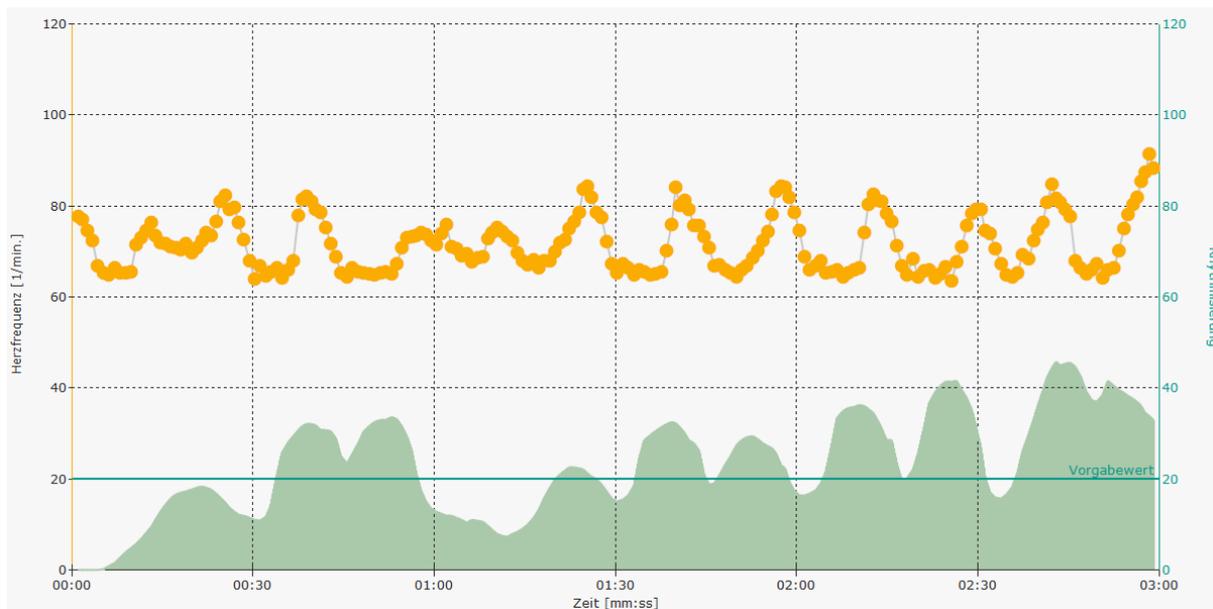
Recommended target rhythmisation for a relaxation exercise

60

A value for the relaxation training or the baroreflex training is calculated and proposed.

Evaluation of biofeedback sessions

Overview



In the overview you can see the heart rate (orange curve), the target rhythmization (green horizontal line, here at 20 target rhythmization) and the curve of the achieved rhythmization as a measure of rhythmization or health-promoting parasympathetic activity.

The example above clearly shows that the rhythmization decreases with a lower amplitude of the oscillation in the heart rate (coherence) (minute 1) and increases again with a higher oscillation of the heart rate (from minute 1:30).

You can also clearly see when the user has reached or even exceeded the target rhythmization. In the example above, this is often the case from minute 1:30 onwards.

The closer the current rhythmization comes to the target rhythmization, the "greener" the Qiu would become, or in 3D biofeedback, the higher the balloon would rise. When the degree of rhythmization reaches the target rhythmization, the Qiu is at its maximum green and the balloon is at the top of the screen. The user can therefore no longer experience a further increase in rhythmization. Tip: The target rhythmization can be increased for the next biofeedback exercise to make the exercise slightly more difficult and thus increase the training stimulus.

If the default value is set too high, the practitioner will not receive positive feedback as the Qiu will remain red or the balloon will "stick" to the bottom of the screen. They are then unable to achieve the specified goal. In the long run, this leads to demotivation. In this case, the target rhythmization should be reduced.

Assessment of Biofeedback results

The result diagram visualizes the three most important features of a biofeedback exercise (from outside to inside):

- Achieved rhythmization in relation to the target rhythmization (relative rhythmization)
- Absolute rhythmization achieved compared to the top 5% of the age group
- Proportions of time in the high, medium and low exercise success range

An explanatory text for the assessment is also displayed. Example:



Assessment text: *The exercise objective was to achieve an average rhythmization of 40 for 3:00 minutes. The average rhythmization was 30. 75% of the exercise target was therefore achieved. The highest rhythmization achieved was 56.*

Explanation of the result diagram:

Outer arc: relative rhythmization, the full circle corresponds to 100% of the target rhythmization.

Inner arc: absolute rhythmization - the full circle corresponds to the absolute rhythmization of the top 5% of the user's age group.

Note: The absolute rhythmization does not depend on the target rhythmization and is a measure of the absolute heart rate variability achieved. Similar to the RSA measurement, absolute rhythmization expresses how well the parasympathetic nervous system can regulate the heart rate. Absolute rhythmization is not a central parameter for biofeedback, as the immediate feedback results from the ratio of the actual rhythmization to the target rhythmization. This ensures that even users with a low HRV receive sufficiently positive biofeedback.

Inside: Time segments with low (red), medium (yellow) or high (green) exercise success (relative rhythmization).

The aim of the exercise is to achieve the largest possible green segment in the time slice, i.e. the rhythm should be in the upper third of the target value for more than 50% of the time during the exercise.

Typical examples of the result diagram



Optimal Target Rhythmization

Inside: The proportion of time spent in the green zone (high exercise success) is well over 50%. At the same time, there is still room for improvement.

Outer arc: The relative rhythmization is sufficiently high, but has also room for improvement.



Target Rhythmization too high

Inside: The proportion of time spent in the green zone (high exercise success) is well below 50%.

Outer arc: The relative rhythmization (achieved rhythmization in relation to the target value) is low.

The default value should be reduced. This will reduce the difficulty of the exercise and users will receive positive feedback more often.



Target Rhythmization too low

In principle, a successful biofeedback exercise, as positive feedback was achieved almost all the time. However, there is no more room for improvement.

Inside: Exercise success almost exclusively in the green zone.

Outer arc: The relative rhythmization is 100%.

If this result occurs regularly, we recommend increasing the target rhythmization by one level to ensure that there is still a sufficient training stimulus.

Qiu and HRV-Scanner

The Qiu

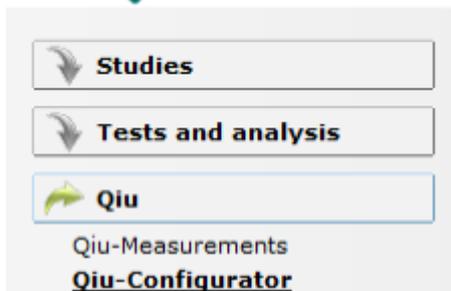


The Qiu is an easy-to-use, handy HRV biofeedback system with integrated memory for over 500 biofeedback exercises including date, time and heart rate curve. With the Qiu, your subjects can practice effectively and comfortably to their specifications at home or on the move, without having to rely on a PC or laptop.

The saved data will either be transferred to the Qiu module of your HRV scanner via the myQiu platform (cloud), via e-mail or the next practice visit via USB for further evaluation.

Each Qiu can be individually adjusted to the subject by means of the Qiu module of the HRV scanner. This allows you to optimally adapt the prescribed breathing, the difficulty and the duration of the biofeedback exercise to each subject.

The Qiu-Modul in the HRV-Scanner-Software



The Qiu module in the HRV scanner software allows the administration and evaluation of any number of Qiu measurements, as well as the individual configuration of the Qius for your subjects. The module is organized in two menu items:

- *Qiu-Configurator*
- *Qiu Measurements*

Qiu-Configurator

With the Qiu configurator, you can customize the Qiu for each of your subjects.

Connecting the Qiu to the PC

To activate the Qiu configurator, a Qiu must be connected to the PC.

Sometimes it can happen that the connection of the Qiu to the PC via USB does not work immediately. The following tips normally solve this problem:

- Use a different USB port
- Use a USB hub
- Reinstalling the USB drivers: please read this document
- **https://www.biosign.de/download_Qiu/Qiu-Treiber-Installation.pdf**

If the above tips do not solve your problem, please contact us (**support@biosign.de**).

Assigning a Qiu to a subject

A Qiu must necessarily be assigned to a subject, so that the stored measurements can be clearly assigned to the respective subject. A Qiu can only have one owner at a given time. However, a subject can be assigned several Qius. These assignments are stored in the subject master data in the "Qiu" tab and can be revoked there as well.

In a new assignment of a Qiu to a subject, the Qiu configurator checks if there are any measurements in the memory of the Qiu. These measurements should, unless they are from the subject to whom the Qiu is to be assigned, be deleted. Otherwise, there is an incorrect assignment of these measurements.

Configuration of the breathing display on the Qiu

The Qiu can display the desired breathing rhythm with its blue LEDs. You can program different respiratory rates or completely disable the breath indicator. If you want to define your own breathing rhythm, select "individual". You can then set the values for inhalation and exhalation yourself.

Determine the exercise difficulty

The difficulty of practicing determines which achieved degree of rhythmicity of the Qiu indicates a positive (green) feedback.

The exercise difficulty should be carefully selected and depends on the desired goal of the biofeedback. In biofeedback exercises where relaxation, improvement of body perception and emotional components are in the foreground, the exercise difficulty should be set so that even at submaximal depth of respiration, positive feedback is achieved.

Exercises to improve HRV and neurovegetative regulation require deeper stimulation of the underlying regulatory circuits and should therefore be performed with a higher exercise difficulty.

The standardized RSA measurement, which you can carry out with the HRV scanner under "Measure and evaluate", provides a clue for the correct default value. In the Qiu Configurator you will find under the menu item "Miscellaneous" the option "Suggest default value", where from the results of the last RSA measurements the optimal default value is estimated according to the purpose of the exercise.

As a safety precaution, after completing the configuration, subjects should conduct a biofeedback exercise with the newly programmed Qiu under supervision to ensure that the subject is able to reach the set target but may not be under-challenged.

Set the exercise duration

Here you can set the duration of the exercise between one minute and 20 minutes. The Qiu then automatically shuts off when the exercise time is reached. At the beginning we recommend an exercise time of 3-5 minutes.

Configuring the brightness of the biofeedback

The Qiu has two options for optical biofeedback, color-coded or intensity-coded biofeedback. Levels 1 through 7 set the brightness of the color-coded biofeedback, and Level 8 activates the intensity-coded biofeedback, which is primarily intended for users with red / green weakness. It is recommended to set the highest possible brightness levels so that the Qiu can also be used in daylight.

Note: All important settings of the Qiu can also be made directly on the device (see Qiu operating instructions)

Additional functions

Set the date / time of the Qiu

Before the subject begins to practice Qiu, the Qiu's date and time must be set correctly. This is the only way to correctly manage the Qiu measurements in the exercise plan later on and to calculate the compliance.

Clear the Qiu's measurement memory

When a Qiu is reassigned to a subject, it is necessary to clear the Qiu memory to avoid accidentally reading old measurements that are not from the current subject.

Qiu Signal Check

This feature allows you to see in real time the pulse signal and the derived heart rate and rhythmization curve. This feature is particularly useful for finding a suitable exercise and holding position for the Qiu in the subject's hand. For example, in subjects with low blood pressure or circulatory disorders, the pulse amplitudes in some parts of the hand (e.g., the ball of the thumb) are too low for reliable registration of the heart rate. With the aid of the display of the measured pulse wave in real time, different holding positions can be tried out and the most suitable one can be determined.

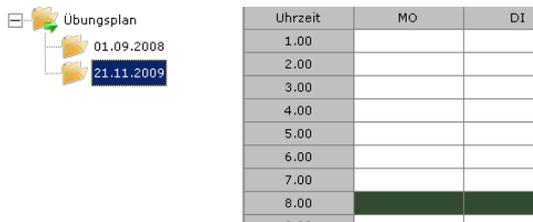
Ear clip as an alternative

If no good biosignal is found via the built-in sensor, we recommend using the ear clip as an alternative. Please note that the ear clip must always be inserted into the Qiu before switching on the Qiu. The Qiu searches for external sensors when it is switched on. If no external sensor connected is found, the integrated sensor will be used, even if subsequently an ear clip is plugged in.

If the Qiu cannot take a sufficiently good pulse signal with the ear clip, it helps to rub the earlobe a little with your fingers or to change the position of the ear clip on the ear a little.

Qiu measurements

Defining the exercise plan by day of the week and time of day



Übungsplan	Uhrzeit	MO	DI
01.09.2008	1.00		
21.11.2009	2.00		
	3.00		
	4.00		
	5.00		
	6.00		
	7.00		
	8.00		

To edit the exercise plan, click on "Qiu Measurements" in the Qiu module. From the subject list above, select the correct subject and then the "Exercise Planner" tab.

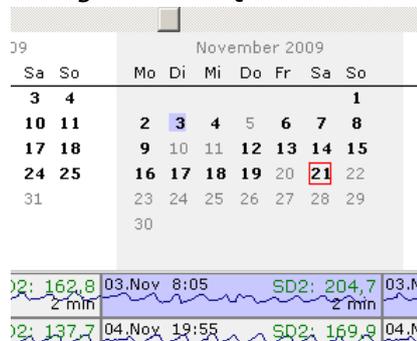
For each subject, a training plan with the exercise times can be created.

To schedule a biofeedback exercise for a particular day at a specific time, simply click on the appropriate cell in the table. Once you have set all practice times, click on "Assign the exercise plan to the subject from now on" to activate the new exercise plan.

Please note that there is a maximum of one exercise plan per day. The new exercise plan is valid from the day of creation until it is replaced by a new exercise plan. The exercise plan history to the left of the table shows you chronologically all previous exercise plans of the subject. By clicking on an entry in the list, the corresponding exercise scheme is shown in the table.

In the later compliance overview, the actual exercise times are compared with the exercise plan automatically, so that you can assess the test person's compliance at a glance.

Management of Qiu measurements



Click "Read Qiu Measurements" to transfer the Qiu data to the HRV scanner. All measurements in the connected Qiu that have not yet been transferred are now transferred to the HRV scanner software. Afterwards the exercise data will be evaluated automatically and entered in the calendar. Use the scroll bar above the calendar to move through the calendar.

Click on a calendar month to display all measurements of this month. Bold calendar days of a month indicate that exercises were performed that day.

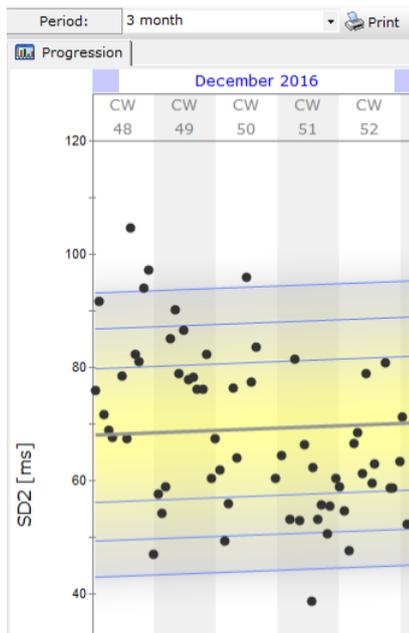
If you click on a single day with the mouse, all measurements of this day will be marked blue in the measurement overview.

Rework the measurement

To zoom in on a single measurement, click on the measurement in the measurement overview with the mouse. The selected measurement is now displayed in the large diagram below the measurement overview. You can now rework this measurement or remove it from the evaluation, if the exercise has cannot be evaluated due to too many artifacts. To edit, click "Edit", to remove, click "Do not use".

Note: Careful post-processing is important so that only artifact-free and high-quality measurements are used in the subsequent evaluation. If post-processing due to e.g. poor quality of data is not possible, the measurement should be marked as unusable (click on "Do not use")

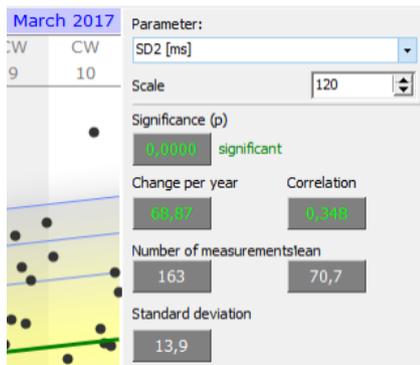
Overview of the exercise success with statistical evaluation



Due to the many HRV data collected with the Qiu when used regularly, changes in HRV are much better documented than with occasional HRV measurements. Statistical testing for linear (Pearson) correlation of HRV values over time enables reliable identification of systematic trends in the development of HRV.

Click on "Progression" in the bottom of the calendar to get the overview of the HRV value development. You can set a timeframe for viewing between 1 month and 2 years for "Period". With the scroll bar below the diagram, you can display and analyze any time window. To select from different HRV parameters, use the "Parameter" drop-down list.

Statistical evaluation:



For all displayed measurements in the diagram, a correlation analysis according to Pearson is performed. The correlation coefficient r (range $-1 < r < 1$) indicates the degree of correlation between HRV and time. The statistical significance p shows whether the trend found is coincidence or a systematic change. A p -value < 0.05 is considered statistically significant (green marked P -value). P -values greater than 0.05 indicate a random trend (red marked P -value). With a p -value < 0.05 , it can be assumed with a probability of error of 5% that there is a systematic influence on the HRV.

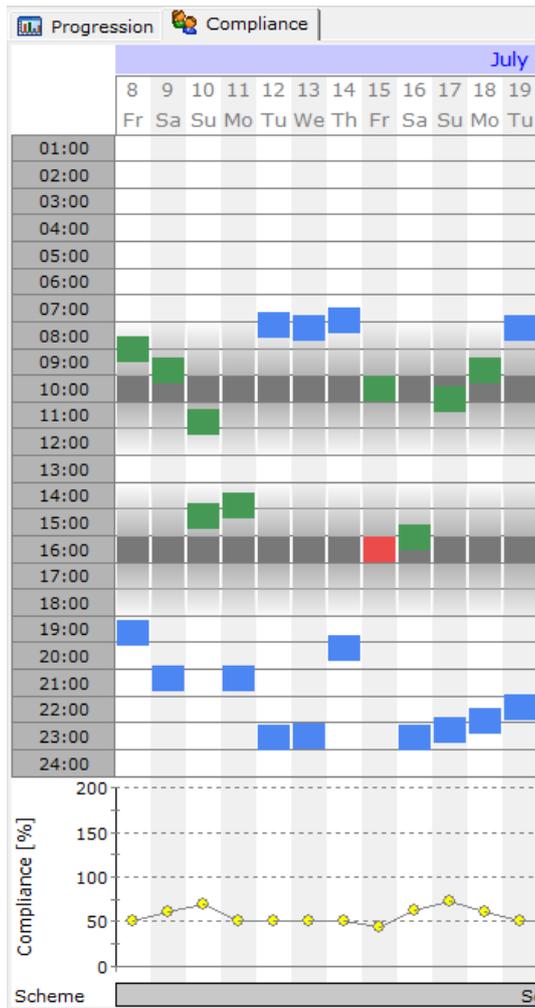
In order to estimate the size of the HRV change, the change in the HRV is extrapolated to one year and displayed ("change / year").

Note: There is a systematic, negative trend of HRV that affects all subjects equally, namely the age-related decline in HRV. Approx. 1-2% of the HRV is lost every year (based on the baseline of a 20-year-old). A negative trend in this size is therefore considered normal. (Cave! Stress Index (SI): The SI becomes larger with decreasing HRV = positive trend)

Filter settings

In the case of a large number of Qiu measurements, strongly deviating measurement results can occasionally occur due to artifacts, measurement errors or an acute illness. In order not to influence the trend analysis, it makes sense to remove these outliers from the analysis. To avoid having to search and manually exclude each of these measurements in the calendar, you can filter the data before analysis. Activate the checkbox "Filter active". By clever setting of the filter limits, all erroneous measurements can be excluded as a rule.

Overview of Exercise Compliance, Compliance Index

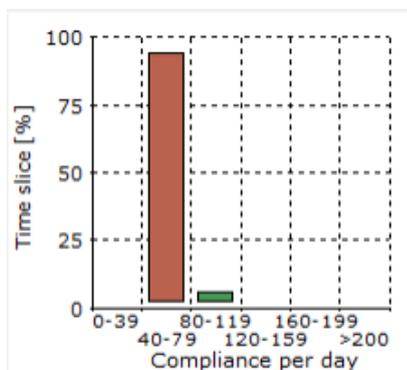


The compliance overview makes it clear how well your test person adheres to the given exercise plan. For this purpose, the times of the Qiu measurements are compared with the exercise plan and displayed graphically



For each day, the daily compliance is calculated. A compliance of 100% means an exact fulfillment of the exercise requirement on this day. Compliance greater than 100% means overfilling the constraint, i. the subject has done more than he should.

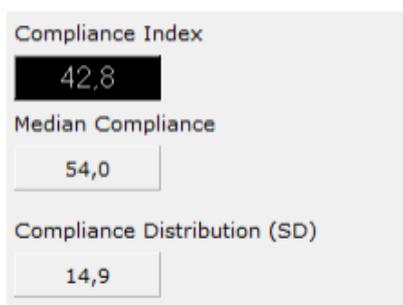
Correspondingly, compliance smaller than 100% means too little practice on the subject.



The compliance diagram below the compliance overview shows the compliance process in the selected time frame. A summary of compliance is provided by the histogram. The height of each column indicates the number of days (in percent) in the period displayed that daily compliance is equal to a value within the class boundaries of each pillar. In the histogram on the right is e.g. about 90% of the days the compliance between 40% -79%.

By means of the check box "Evaluate time deviation" you can specify whether deviations from the given time are included in the calculation of the compliance.

If the checkbox is activated, late or premature practice will reduce compliance. If the measurement time deviates from the time of specification by more than two hours, the compliance of this measurement is reduced to 50%. Within the range of two hours, the compliance adjustment is fluent, for example with a deviation of one hour, the compliance of the measurement is rated at 75%.



The compliance values of the days shown are used to calculate an index for compliance. Simply put, the Compliance Index is a mathematical description of the histogram. Relative to this is the proportion of the desired compliance (middle range of the histogram) to the width of the histogram (scattering). The Compliance Index can take values between 100 (consistently good compliance on all days) and 0 (no compliance).

HRV-Monitoring with the Qiu

Often, HRV is used as a parameter to objectify the success or progression of therapies aimed at improving parasympathetic function. For this purpose, a basic HRV examination (RSA measurement and short-term HRV) is usually performed at the beginning with the subject. This is followed by a measurement to start the treatment or, ideally still occasional measurements in the course of treatment, but due to the high cost, usually at longer intervals. Here, the risk that these few measurements do not reliably record the course of HRV is high.

Many things have a sometimes unfavorable, but short-term impact on the HRV. For example, mental stress states (quarrels, acute working stress), short infectious diseases or overstraining (sports) partly influence the results of the HRV measurements considerably. Such outliers can affect the course very unfavorably.

Therefore, it makes sense to give the subjects during a therapy a Qiu. On the one hand there is a training of the parasympathetic nervous system, on the other hand you get so a large number of measured values. Comparable to the blood pressure diary, the Qiu provides a valid documentation of the HRV.

Ideally, the volunteer's measurements are made available to the therapist via the cloud virtually in real time for inspection by the myQiu platform. Subject and therapist synchronize the measurement inventory via the myQiu platform. Using the HRV scanner, the therapist can view and evaluate all the subjects' measurements (Qiu, myQiu, PC biofeedback, ...).

An extension to smartphone apps and data transmission via Bluetooth, as well as the integration of external sensors (smartwatches, BT-Qiu) is in preparation.

Instruction

The success of the biofeedback exercise and the usability of the measurement data obtained depend strongly on the good preparation and instruction of the subject in the Qiu. The time you invest here saves you a lot of effort later on when reworking poor quality measurements.

The briefing should therefore answer at least the following questions from the subject if possible:

How do you turn the Qiu on / off?

Press and hold the button until the blue LEDs on the breath screen indicate the on / off cycle.

How can I leave the setting mode if it was accidentally activated when switching on?

Press the button until the Qiu shuts off.

Which holding position is suitable?

The Qiu should be kept in a sedentary position with the hand on a quiescent surface well below the level of the heart (for example, a hand rest on the thigh).

Which sensor position is suitable?

Preferably, the fingertips of index, middle finger or thumb should be used. A suitable sensor position can also be found by means of the "Qiu Signal Check" function in the Qiu configurator of the HRV scanner.

How do I recognize an inappropriate sensor position?

At the beginning of each biofeedback exercise, the Qiu seeks the pulse for about 10 seconds. During this time, he reflects the amplitude of the pulse optically in the form of blue pulsations. If these pulsations are absent, and the Qiu does not switch to biofeedback mode, or if the Qiu often interrupts the exercise to seek the pulse again, the pulse sensor is not optimally placed. In this case, it is recommended to stop the exercise, turn the Qiu off and on again, and select a different sensor position.

The optical biofeedback stays permanently on red or green, no matter what I do?

The subject may have set a wrong level of difficulty in the setting. If the subject is familiar with configuring the Qius with the button on the Qiu, he can control this himself, if not, the setting would have to be checked by you.

What does the wandering blue LED light at the equator of the Qiu mean?

The row of blue LEDs indicates the direction and speed of inhalation and exhalation of the volunteer during HRV biofeedback. Conveniently, the subject has exercised this under supervision for a few breaths to ensure safe execution.

Why does the Qiu light up brightly when it turns on?

During power up, the battery level is checked under load, so the Qiu is switched to maximum brightness for one second.

After the bright light when switching on the Qiu flashes recently red once again, why?

The charge of the battery is approaching the end. There are still a few exercises that can be done, but spare batteries should be provided.

After the light comes on, the Qiu flashes red three times and then turns off, why?

The batteries / resp. Batteries are empty and should be changed quickly. Important: The current less state during the change of the batteries should be as short as possible, because the clock in the Qiu stops during this time.

Does the time and date in the Qiu have to be reset after changing the battery?

It is not necessary to set the watch by the subject if the test person has changed the batteries quickly. The clock will continue to run at the point where it has stopped, with full batteries installed. The short runtime difference of usually a few minutes is of no practical importance for the assignment of the measurements in the HRV scanner.

How can the subject change the batteries?

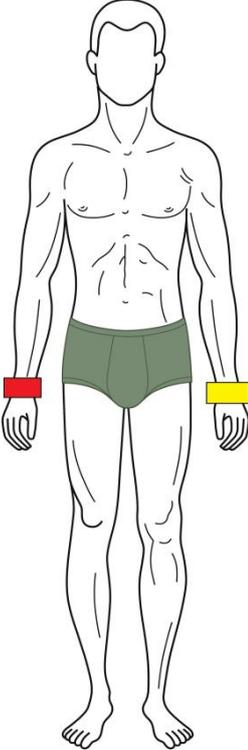
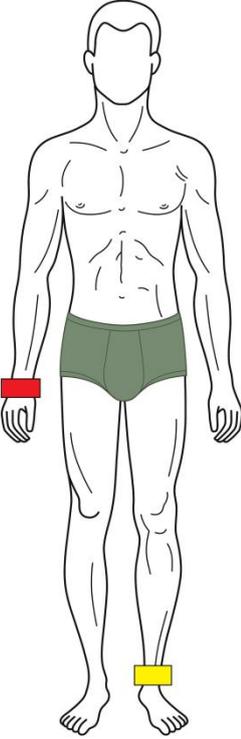
To open the Qiu, the transparent upper shell can be unlocked and lifted by turning it counterclockwise. The battery compartment can then be opened and the batteries removed. After inserting the batteries, closing the battery compartment and placing the upper shell, the latter is locked by a short clockwise rotation.

Note: Pay attention to the correct polarity of the new batteries.

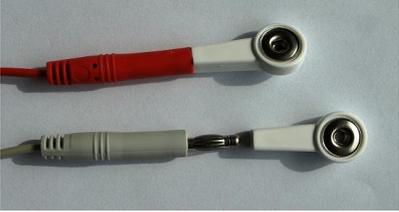
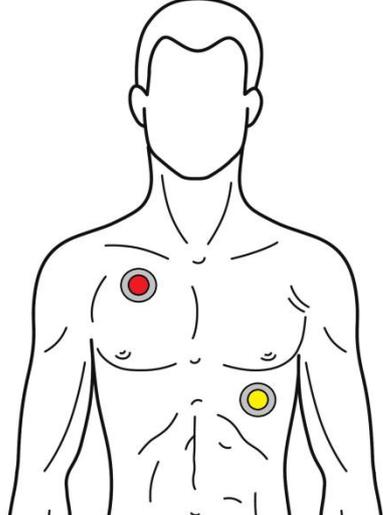
Possibilities of ECG derivation

Derivation of a 1-channel ECG with clamp electrodes

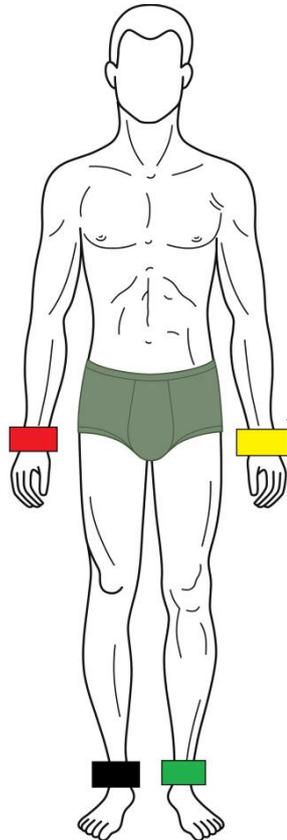
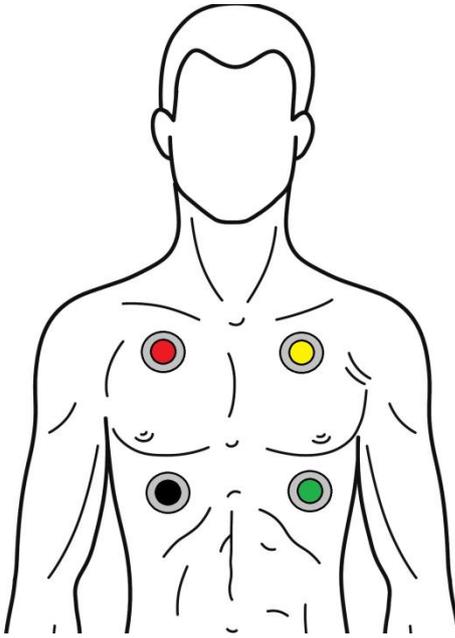
Preparation: connect the clamp electrodes with the ecg cable

<p>Hardware standard (2-wire ECG cable, banana plug)</p>	<p>Hardware plus (4-wire ECG cable, electrode clip)</p>
	
<p>1) Derivation of right arm against left arm</p>	<p>2) Derivation of right arm against left foot</p>
	
<p>This type of derivation works in 98% of cases. Exception would be e.g. an ECG in which the R-wave and the T-wave are approximately the same, and the T-wave in the ECG is larger than the R-wave.</p>	<p>Alternative derivation</p>

Derivation of a 1-channel ECG with adhesive electrodes

<p>Preparation at the hardware standard (2-wire ECG cable, banana plug)</p>	<p>Glue the adhesive electrodes as shown in the figure and connect the electrode clips of the ECG cable to the electrodes</p>
<p>Plug the adapters onto the two banana plugs.</p> 	

Derivation of a 3-channel ECG (only HRV scanner hardware plus)

<p>Derivation of a 3-channel ECG with clamps</p>	<p>Derivation of a 3-channel ECG with adhesive electrodes</p>
	

Technical Manual

PC Hardware PC Requirements

- Operating system Windows 7/8/8.1/10
- USB slot \geq V 1.0
- minimum 300 MB free disk space
- 3D graphic card (\geq 32 MB)
- DirectX 9.0 or higher

Maintenance and Servicing

The HRV is not subject to a mandatory maintenance schedule. The user simply has to ensure that the device is only ever operated under the conditions stated in the Technical Data manual. In case of damage the device should be switched off immediately and sent for repair. Please note that opening the device will void any warranty claim.

Copyright

The software is protected by copyright and may only be used for private purposes. In particular leasing, swapping, transmitting, duplication, copying, distribution and editing in electronic systems in any form whatsoever are fundamentally prohibited.

Liability

The HRV is in no way intended to replace or act as a substitute for a medical diagnosis or therapy by a qualified medical professional. Neither BioSign nor their agents accept any liability for slightly negligent breaches of duty, as long as no essential contractual obligations, damages resulting in loss of life, physical injury or damage to health or warranties are involved or claims under the German Product Liability Act are affected.

In case of violations of essential contractual obligations BioSign shall only be liable for contract-typical, foreseeable damages. The statutory period of limitation for damage claims not due intentional behavior for which BioSign is answerable is one year. This excludes damage claims from consumers resulting from faults in things supplied as new by BioSign as well as claims of compensation from suppliers in accordance with § 478 BGB (German Civil Code).

Warranty

The warranty period for HRV-Scanners is two years from the date of purchase (please retain your proof of purchase).

Technical details

Power Supply

Operating voltages	+5 V
Current consumptions	100 mA
Safety fuses	None

Pulse Wave

Sensor current for IR LED	c. 16 mA
Frequency range	c. 0.5 ...10 Hz
Sensor	M3405, connectible by plug
Scan rate	500 Hz

ECG

Type	an earth discharge L-R
Time constant	app. 3 s
Sensor	2 ECG clips, adhesive electrodes, connectible by plug
Scan rate	500 Hz

PC-Interface

Type	USB 1.1
Device class	HID (Human Interface Device)

Additional Data:

Safety	ECG part: power supply via insulated DC / DC converter. Signal isolation via optocouplers (Double insulation according to EN 60335-1, when connected to a PC) The device may only be connected to a PC provided with European certification mark!
Dimension (WHD)	app. 92 mm x 150 mm x 32 mm
Weight	app. 0.15 kg (without sensors)

Environmental Operating Conditions:

Temperature range	10 °C ... 40 °C
Rel. humidity	25% ... 95 %
Air pressure	700 ... 1200 hPa
No mechanical shocks or vibrations	

Environmental Conditions During Storage and Transportation

Temperature	-20 °C ... 60 °C
Rel. humidity	30 % ... 95% (non condensing)
Air pressure	700 ... 1200 hPa

The device must not be used on humans for the purpose of producing a medical diagnosis.

The HRV-Scanner is a protection class III device, compliant with EN 60335-1. The device conforms to the relevant EC ordinances. This is confirmed by the EC declaration of conformity.

Appendix - Literature

Literature SD2/SD1 ratio

- 1) Hoshi RA, Pastre CM, Vanderlei LC, Godoy MF. Poincaré plot indexes of heart rate variability: relationships with other nonlinear variables. *Auton Neurosci*. 2013 Oct;177(2):271-4. Epub 2013 Jun 5.
- 2) Stein PK, Domitrovich PP, Huikuri HV, Kleiger RE; CAST Investigators. Traditional and nonlinear heart rate variability are each independently associated with mortality after myocardial infarction. *J Cardiovasc Electrophysiol*. 2005;113-20
- 3) Makikallio TH, Hoiber S, Kober L, Torp-Pedersen C, Peng CK, Goldberger AL, Huikuri HV. Fractal analysis of heart rate dynamics as a predictor of mortality in patients with depressed left ventricular function after acute myocardial infarction. *Am J Cardiol*. 1999;83:836.
- 4) Laitio TT, Huikuri HV, Makikallio TH, Jalonen J, Kentala ES, Helenius H, Pullisaar O, Hartiala J, Scheinin H. The breakdown of fractal heart rate dynamics predicts prolonged postoperative myocardial ischemia. *Anesth Analg*. 2004; 98:1239-44.
- 5) Stein PK, Barzilay JI, Chaves PH, Mistretta SQ, Domitrovich PP, Gottdiener JS, Rich MW, Kleiger RE. Novel measures of heart rate variability predict cardiovascular mortality in older adults independent of traditional cardiovascular risk factors: the Cardiovascular Health Study (CHS). *J Cardiovasc Electrophysiol*. 2008 Nov;19(11):1169-74.
- 6) Stein PK, Domitrovich PP, Hui N, Rautaharju P, Gottdiener J. Sometimes higher heart rate variability is not better heart rate variability: results of graphical and non-linear analyses. *J. Cardiovasc Electrophysiol* . 2005 ; 16 : 954 – 959
- 7) Simula S, Vanninen E, Lehto S, Hedman A, Pajunen P, Syväne M, Hartikainen J. Heart rate variability associates with asymptomatic coronary atherosclerosis. *Clin Auton Res*. 2013 Nov 30.