IntelleWave

A Non-Invasive Quantitative assessment of the Autonomic Nervous System

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IntelleWave is a fully automated cardiac monitoring device that provides quantitative assessment of the Autonomic Nervous System (ANS) on the basis of R-R interval variability and blood pressure analysis. The system is used to objectively confirm or exclude a Cardiovascular Autonomic Neuropathy (CAN), a Diabetic Autonomic Neuropathy (DAN), syncope, dizziness and other dysautonomia problems.
It is able to distinguish between the early and late stages of autonomic neuropathy.

IntelleWave is distinguished by its accuracy and speed, high reliability and ease of operation.

In addition, IntelleWave can provide up to 24 hours of "real-time" quantitative ANS assessment .

ANS status can be monitored in a variety of settings, i.e.:

INTELLEWAVE helps to evaluate a patient's ANS state before and after treatment, which can provide an accurate and reproducible assessment of treatment effectiveness.

– during anesthesia.
– in intensive care to see effectiveness of medication.
– using implantable devices.
– using ambulatory Holter – ANS status can be monitored during sleep studies to see the difference between "sleep time" and "awake time".

The system provides instant assessment of QT-interval and ST-segment of the ECG data registered during the test (consisting of 448 QRS complexes), as well as complete interpretation of 2 tests – Orthostatic test and Valsalva maneuver combined with deep breathing. A variety of data collected during the test (R-R interval variability, blood pressure and ECG readings) enables clinicians to evaluate a patient's ANS status.

Our system's proprietary sophisticated algorithm based on artificial intelligence approach evaluates all components of the spectral analysis including shifting of these components during the test. The unique representation of results provided by IntelleWave allows physicians to recognize up to 81 different variations in the relationship between Sympathetic and Parasympathetic activities. The system uses Cartesian system of coordinates with high-frequency (HF) Parasympathetic intensity on the horizontal axis and low-frequency (LF) Sympathetic intensity on the vertical axis. The point of intersection is interpreted as the point of Autonomic Balance. The graphical image of this method is presented on the next page.

Please note that clinical decision about autonomic function can be made by combined analysis of HF(Parasympathetic) and LF(Sympathetic) relationship with blood pressure data.

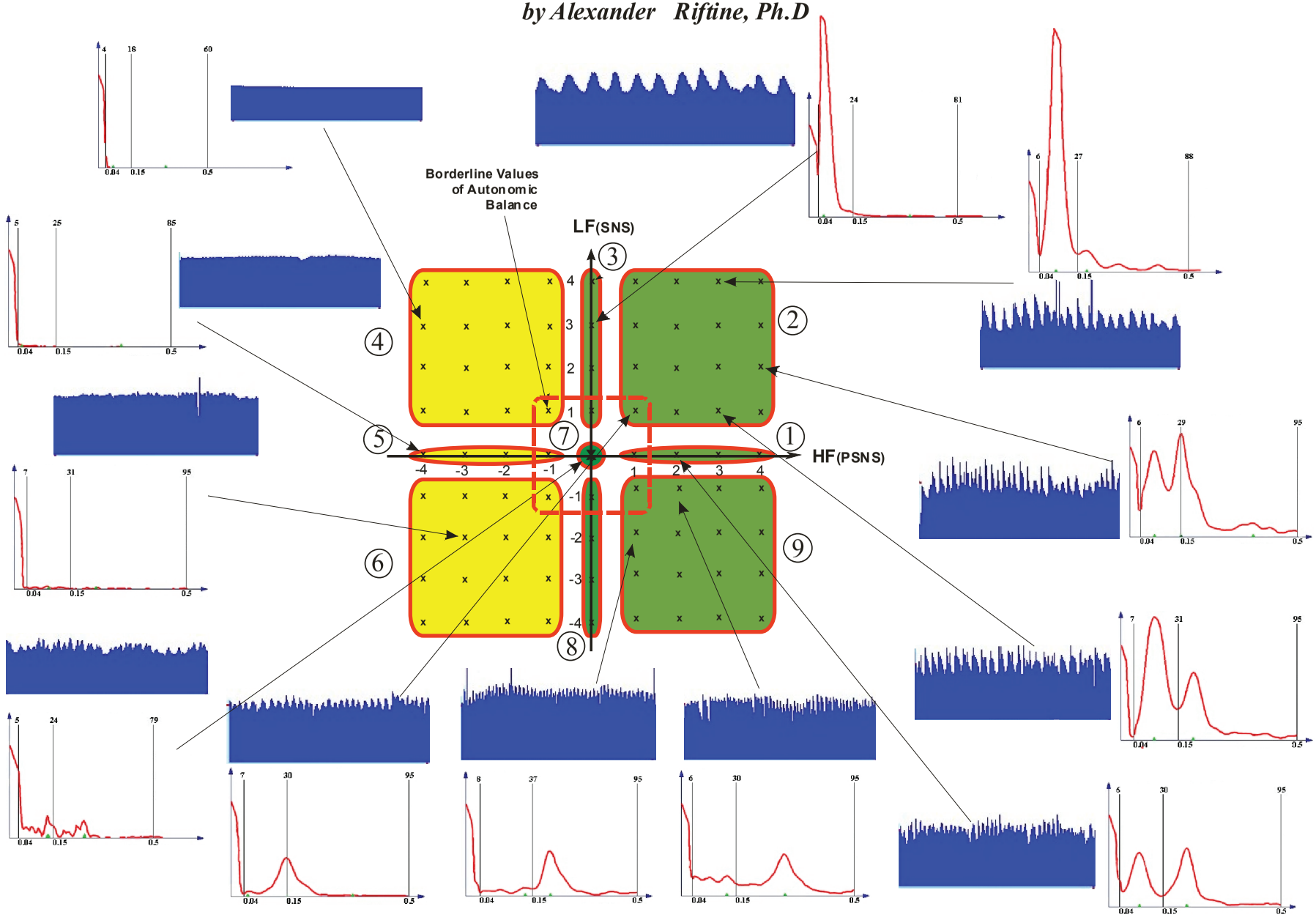
An earlier version of the system was validated with excellent results by Columbia University.

System Components

- PC-ECG wireless Acquisition Device or PC-ECG wire device.
- Automatic blood pressure-measuring device.
- Finger Pulse Oximeter.
- Mini notebook computer with integrated bluetooth and portable printer.
- ECG and R-R interval variability Analyzer Software for display, measurement and interpretation of test results.

Clusterization of the Autonomic Nervous System's states

by Alexander Riftine, Ph.D



Common Reasons for Administering the ANS Test defined by American Medical Association

1. Presense of symptoms of Cardiovascular Autonomic Neuropathy (CAN) and/or Diabetic Autonomic Neuropathy (DAN).
2. Assessment and/or recognition of *syncope*.
3. Optimization of *beta-blocker therapy.*
4. Risk stratification of sudden cardiac death.

On the following pages please find samples of the test results and interpretations for the above mentioned cases and diagnoses.

Cardiovascular Autonomic Neuropathy (CAN) and Diabetic Autonomic Neuropathy (DAN)

The test is prescribed to a patient if symptoms of CAN or DAN are present.

The goal of administering the test in this case is to get objective data to confirm or exclude CAN or DAN diagnosis. Treatment protocol wiill depend on the stage of CAN.

The process of administering the test shall include the following steps:

- Prescribe the test only in the presence of CAN or DAN symptoms
- Use test results in clinical decision making
- Conduct a follow-up test to evaluate effectiveness of the prescribed treatment and make adjustments if necessary.

Guidelines for excluding CAN or DAN diagnosis

- The Parasympathetic level during Deep breathing in the *Valsalva Maneuver Combined with Deep Breathing test* is greater than +1 on the clusterization chart *(see page 6).*
- The Valsalva Ratio is more than 1.7.
- The 30/15 Ratio is less than 0.75.

Note: The Valsalva Ratio and the 30/15 Ratio are calculated as a ratio of the minimum heart rate to the maximum heart rate during the Valsalva Maneuver and Orthostatic intervention.

Guidelines for Recognizing the CAN or DAN status

Guidelines for recognition of the early stage of CAN or DAN *(see page 7):*

- In the *Orthostatic test and Valsalva Maneuver Combined with Deep Breathing test* the PSNS level is -1 or -2 on the clusterization chart.
- The Valsalva Ratio is less than 1.7.
- The 30/15 Ratio is between 0.65 and 0.80.

Guidelines for recognition of the chronic stage of CAN or DAN *(see pages 8-9):*

- In the *Orthostatic test and Valsalva Maneuver Combined with Deep Breathing test* the PSNS level must be -3 or -4 on the clusterization chart.
- The Valsalva Ratio is less than 1.3.
- The 30/15 Ratio is more than 0.80.

Treatment protocol will depend on the test results. A follow-up test is administered upon completion of the course of treatment. Corrections in the treatment protocol can then be made based on results of the follow-up test.

Optimization of beta-blockers therapy

Side effects during use of beta-blockers are well known in medicine and described in the pharmaceutical guides. Therefore, the main problem related to beta-blockers therapy is optimization of use of different types of beta-blockers and their dosages.

While prescribing beta-blockers, physician is aiming to achieve not only clinical outcome, such as normalization of blood pressure and heart rate, but also take care of physiological aspect by optimizing the dose of beta-blockers in order to avoid side effects. Intellewave technology provides simple solution to help physicians to achieve such goals and avoid beta-blockers overdose.

To determine the optimal dose of beta-blockers, heart rate data is not sufficient, since it only indirectly provides information about the level of sympathetic activity. In order to confirm the case of overdose, it is essential for a physician to know not only the level of sympathetic activity, but also the level of parasympathetic activity.

Beta-blockers overdose exists only in case when the patient has low level of both sympathetic and parasympathetic activity (please refer to page 11 of the enclosed brochure to see the case of the patient with beta-blockers overdose). For instance, when a beta-blockers patient has low sympathetic activity (heart rate 45-50), but his parasympathetic activity is not lower than -1 (slight decrease of parasympathetic activity), such case cannot be qualified as overdose case. However, when a beta-blockers patient has sympathetic activity level from -2 to -4 and parasympathetic activity from -3 to -4, can be certainly confirmed as an overdose.

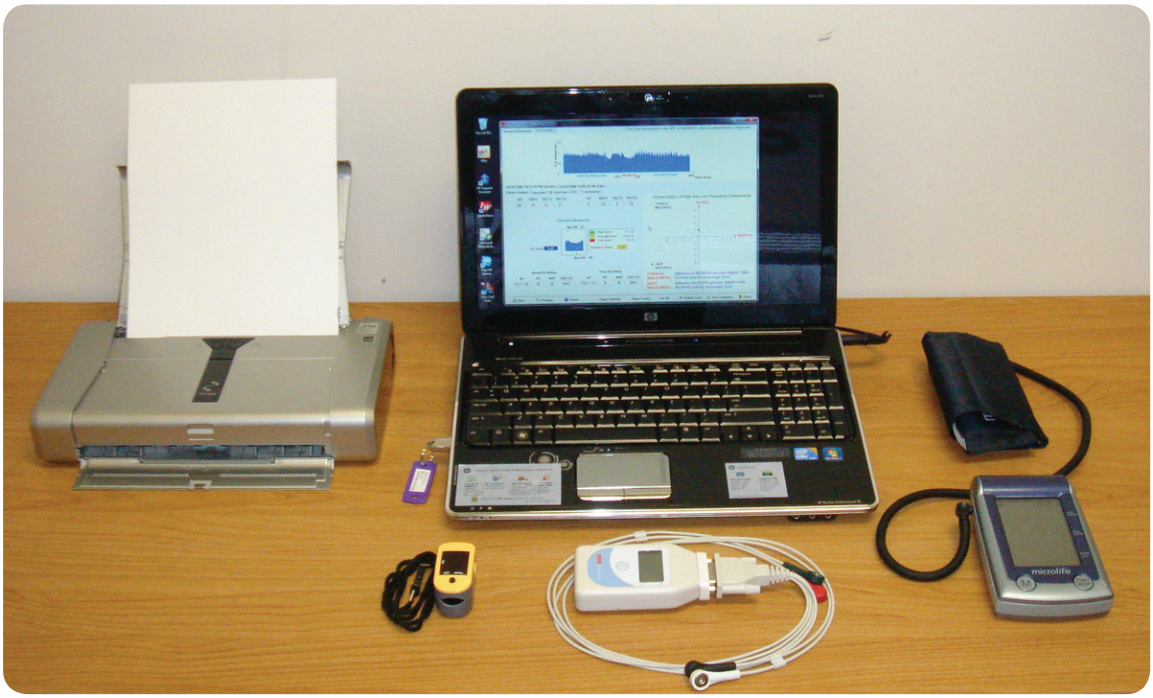
Intellewave system provides physician with objective quantitative information to confirm or exclude beta-blockers overdose case.

DEVICE CONFIGURATIONS

Intellewave system 1.3 is available in two configurations:

1. Intellewave Wireless

   This option includes wireless BT3/6 bluetooth device produced by Corscience GMBX.



2. Intellewave USB Connection

   This option includes PC ECG device produced by Pulse Biomedical Inc.