



The Vagus ECG smartwatch to monitor changes in cardiac-respiratory synchronization and QRST amplitude during the progress of Cardiac-Respiratory infection.

Case: Global Coronavirus COVID-19 Open Crowdsourced Data Study

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The Vagus ECG smartwatch enable hand-to-hand ECG (Electrocardiogram) with 30- and 90-seconds long tests. The 90 seconds 'Vagus ECG Test' (pat.pend) is designed to detect cardiac/respiratory synchronization and it provides novel analytics of changes in this synchronization. The test contains two parts - a 30 seconds base phase and 60 seconds controlled breathing when the user is doing taking longer inhales and exhales according to instructions displayed on the watch. These tests have their own applications in the watch and the ECG data is the downloaded to the 'Vagus App' and from there to the 'Vagus User Interface Cloud'. The user can then self-monitor and/or send the ECG graphics and Vagus Health analytics results to her/his doctor or other medical professional for clinical evaluations. By using the Vagus Watch, users do not need to physically visit a health service provider to do an ECG test and the user can do a test promptly if she or he is experiencing cardiac and/or respiratory issues.*

Viral illness is a well-known destabilizing factor in chronic cardiovascular disease, a general consequence of the imbalance between infection-induced increased metabolic demand and reduced cardiac reserve. The viral infection along with superimposed pneumonia will directly and indirectly affect the cardiovascular system. Both coronary artery disease and heart failure patients are at increased risk of acute events or exacerbation; viral illness can potentially destabilize coronary plaques through several mechanisms including systemic inflammatory responses which have been recently documented with COVID-19.

SARS/MERS analog: Although published literature on cardiovascular implications of SARS/MERS is limited, in the absence of more detailed reporting on COVID-19, it may prove instructive:

- 60% of MERS cases had one or more pre-existing comorbidity, resulting in a poorer prognosis; expert guidance suggests patients with diabetes, CVD, or renal disease should be prioritized for treatment.

- Both SARS and MERS have been linked to acute myocarditis, acute myocardial infarction, and rapid-onset heart failure. In one early published report, 2 out of the 5 deaths were attributed to myocardial infarction. (American College of Cardiologist ACC, Clinical Bulletin of Cardiac Implications of Novel Coronavirus – COVID-19, published February 28th 2020, <https://www.acc.org/~media/665AFA1E710B4B3293138D14BE8D1213.pdf>)

The vagus nerve

The vagus nerve is the longest and most complex of the 12 pairs of cranial nerves. It transmits information to and from the brain to organs in the body such as the gut and heart. The Vagus nerve is the main component of the parasympathetic nervous system which is also known as the 'rest and digest' system. The 'opposite' of this system is the sympathetic nervous system which is known as the 'fight and flight' system. It is activated when the body is in stress such as during disease progress. One very important part of the vagus nerve is that it is synchronizing the heart beats to breathing in order to optimise oxygen delivery to body tissues. This function is more active when the body is relaxed. When the body is stressed from mental issues or disease, this heart/breathing synchronization is altered. The word 'vagal' is here used according to the definition 'relating to the vagus nerve'.



Cardiac-, respiration- and immune homeostasis

Human life requires that many of the body's interior parameters maintain a 'magic' interval known as the homeostatic range. The process of achieving this balanced state is called homeostasis ⁽²⁹⁾ In its broadest sense, homeostasis is considered a description of when the body is self-sustaining and enable to uphold optimum balance for continued longer life. There are also many narrow definitions of homeostasis limiting themselves to certain control centres that for instance enable healthy balance in fluids, temperature, gut-, gene-, immune-, mental-, molecular- and internal cell activities. Traditionally it is considered that the vagus nerve is an essential part of cardiac-, respiratory-, digestion-, organ- and autonomic nervous system homeostasis. Lately it has been found that it is also a very important part of the mental- and immune homeostasis ^(18, 24).

Science Background

Much research has been done on heart rate variability (HRV) which is considered a fundamental indicator of vagal tone (the level of activation of the vagus nerve influence on the heart). Measures of HRV have been strongly correlated to morbidity and mortality from diverse diseases. Early clinical findings, first observed more than 50 years ago, revealed that variability in RR intervals predict the onset of foetal distress before any measurable changes in absolute heart rate. There is now extensive experience using HRV measures in diverse disease syndromes and these data indicate that decreased vagus nerve activity is associated with increased morbidity and mortality. ^(24.)

Prior to knowledge of the inflammatory reflex, it was thought that decreased vagus nerve activity in these cases resulted from neural damage associated with the underlying diseases. It is now possible to consider an alternative explanation that decreased vagus nerve activity and the associated loss of the tonic inhibitory influence of the cholinergic anti-inflammatory pathway on innate immune responses and cytokine release, may enable significantly enhanced cytokine responses to stimuli that would have been otherwise harmless in the presence of a functioning neural circuit. ⁽²⁴⁾

Most of the studies report HRV analyses to diagnose sepsis 12 to 24 hours prior to traditional clinical methods and markers (for example, fever or tachycardia). In fact, one study reported observable changes in HRC as early as 3 to 4 days before the onset of sepsis. Ample evidence indicates that HRV monitoring may enhance the diagnosis and prognosis of infection. ⁽²⁶⁾ The vagus nerve is a very important part of the immune system and its homeostasis. As body stress arises due to rising levels of infections or viral disease – the pattern of heart rate / breathing synchronization is changed. ^(3, 18, 19)

Short timespan HRV measurements and tests (< 5min) are often unreliable and they should not exclusively be used for instance in homeostasis analytics ⁽³⁾. By combining Respiratory Sinus Arrhythmia (RSA), Cardiac/Respiratory Synchronization (RSAsync), heart rate variability (HRV), resting pulse and other bio-signal measurements from the Vagus ECG smartwatch – it is possible to make better and more comprehensive vagus nerve activity analysis than with traditional HRV analytics. Immune system changes affect multiple vagus nerve activities and can be measured by doing a resting state and controlled breathing test with the Vagus ECG Smartwatch ⁽³⁾.

In the the study 'ECG changes after rabbit coronavirus infection' the author's found systematic QRS and T-wave voltage reductions and pattern changes as the disease progressed. The first changes were detected a few days after contraction of the corona virus without reporting other non-invasively measurable changes. *'T-wave voltages were reduced throughout the acute phase in 45% of the*



rabbits, with the lowest mean voltage (0.11 ± 0.12 mV) recorded on day 5 postinfection, ($P < .001$ vs baseline). The ECG and pathologic findings associated with RbCV infection are consistent with changes seen in humans and are similar in many respects to other animal models of viral myocarditis. (31, Alexander et al)

Fig 1. Baseline Electrocardiograms of rabbit, days 0–49 from infection (31, Alexander et al.)

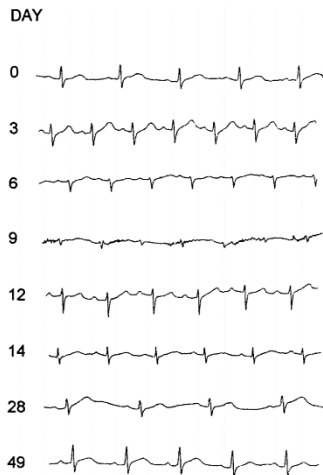
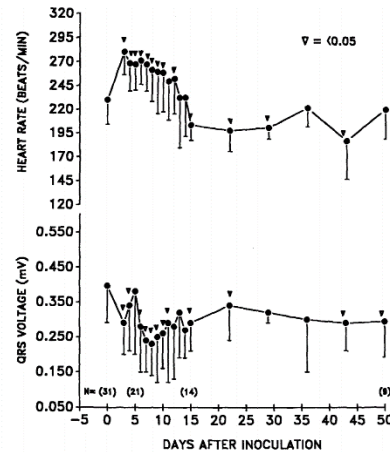


Fig 2. Mean QRS voltage and heart rate versus days from infection (31, Alexander et al.)



Vagus ECG Smartwatch ‘Vagus test’ for viral contraction risk assessments – hypothesis

Gustaf Kranck and Vagus Health Ltd has been studying and developing diagnostics systems for vagus nerve heart/breathing synchronization with hand-to-hand electrocardiogram devices since 2012. The recently launched Vagus ECG Smartwatch has a built-in ‘Vagus Test’ which enable the detection and diagnostics of heart/breathing synchronization failure. The ‘Vagus Test’ has an application in the smartwatch which instructs the user of how to do the 90 seconds test. The first 30 seconds is a base ECG recording when the person sits still and does normal breathing. During the next 60 seconds, the person does controlled breathing where each deep inhale and exhale lasts 5 seconds. Instructions for this is shown on the watch-screen and it is very easy and quick for users to do. After doing this test, the watch transmits the data via Bluetooth to the smartphone Vagus App which then transmit the data to the Vagus Cloud for diagnostics. The analytics results are transmitted back to the phone within a few seconds.

I hypothesize that it is possible to determine immune system changes with the Vagus ECG Test results. I think that this risk-assessment can be used for instance to detect cardiac/respiratory changes prior to when the person is showing visible signs of contracting a disease such as fever or coughing in respiratory diseases. There are other causes for ‘very low or low’ results such as mental stress, chronic low-grade inflammations or digestion reactions from for instance alcohol intake. With personalized health tracking and longer-term data collection, I hope to improve the distinction between different causes to changes in the analysis results.

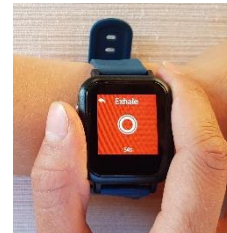


Method and examples

Measurement Position



Vagus Test and Breathing Instructions

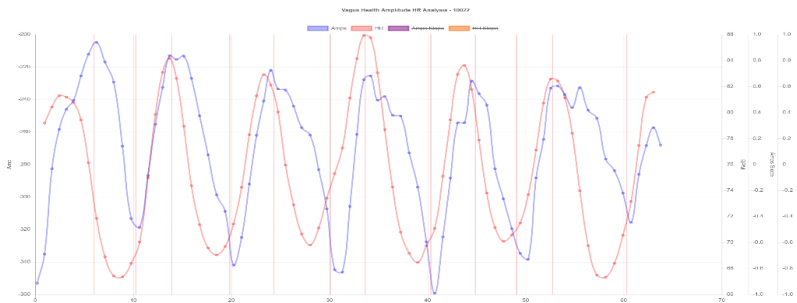


Example 1: Healthy Person

Cardiac/ Respiratory synchronization, RSAync: *good*

Graph 1: Heart/Breathing synchronization graph

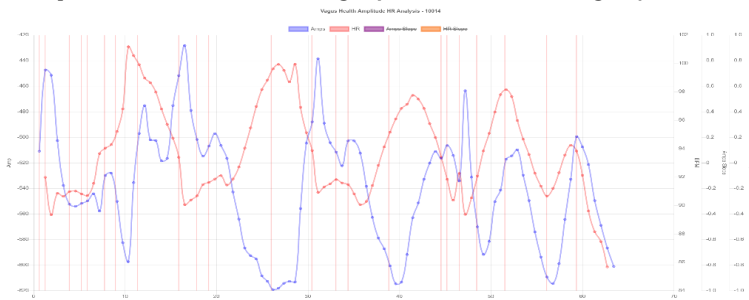
(The blue line shows each breath and red line its corresponding heart rate.)



Example 2: A person in bad health due to longterm inflammation

Cardiac/ Respiratory synchronization, RSAync: *low*

Graph 2: Heart/Breathing synchronization graph





Summary

Respiratory virus diseases such as the Coronavirus can spread from person-person before the person gets sick. Therefore, there is an urgent need for various types of early-detection methods. The here hypothesized additional risk assessment method has the potential to detect the Coronavirus earlier in the disease progress than some traditional screening methods and it provides an additional tool for the user to determine the need to visit a healthcare provider or hospital.

The *Vagus Test* risk assessment is done in the cloud and it is shown on the phone app within seconds from finishing the test. Even though there will be some false positives and all subjects will not have cardiac/respiratory symptoms - this assessment combined with traditional screening methods, provides an additional screening process to what is now used worldwide.

It is the authors hope that this hypothesis can either be used for crowdsourced data-collection or that relevant authorities or medical institutions urgently conduct further testing in guaranteed groups in order to independently verify this proposed screening method.

****Medical disclaimer:*** *The Vagus ECG smartwatch and the Vagus ECG Test analytics are NOT medical-devices or diagnostics tools. They are currently in beta-testing phase. There are no medical trials to yet confirm the here stated hypotheses. Any of the analytics or here mentioned risk-assessments should NOT be used a medical diagnostic. They should not be used to decide alternations or additions to medical treatments without consulting a medical doctor or certified professional. I recommend always to do blood tests for infection levels before any medical- or essential health altering actions are taken.*



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