shimmer
DISCOVERY IN MOTION

COVID-19:

Wearable Sensors and Continuous Data

To Improve Outcome

Concept Paper

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1. Introduction

COVID 19 virus is now a global pandemic. The COVID 19 virus causes an illness which is asymptomatic or mild in most cases, serious in a small minority and fatal in between 2 and 3%.

The priorities for public health now are to ***limit the spread of the disease***, and to ***use finite available resources optimally*** - which (among other things) are *clearly predicated on identifying infected individuals, testing them, isolating and treating them in the appropriate setting.*

- Symptomatic disease from COVID 19 can occur 3 – 13 days after exposure. This interval is critically important to identifying individuals who need testing, and to detecting symptomatic cases
- COVID 19 infections have few, and quite non-specific, symptoms that include fever, cough, fatigue and anorexia. Muscle and joint aches are sometimes part of the constellation. In severe cases dyspnea (respiratory distress) develops.
- Based on the experience in China, greater than 80% can be expected to have asymptomatic, mild or moderate disease. Approximately 16% will require hospitalization and 5% will need intensive care.
- Certain patient groups have an increased risk after exposure and a propensity to have more severe disease. These include the elderly, patients with chronic disease such as diabetes, heart disease, COPD, asthma, CKD, and immunocompromised patients. These patients should receive special consideration for monitoring after a possible exposure.

Thoracic Bioimpedance

Thoracic Bioimpedance, as an indicator of total fluid in the chest, has long been studied in Chronic Heart Failure (CHF) and the Acute Respiratory Distress Syndrome (ARDS). In these settings, thoracic bioimpedance monitors can provide a number of useful indicators including respiration rate, respiratory [tidal] volume, and bioimpedance which is inversely proportional to the amount of fluid in the thoracic cavity. Tomographic applications of bioimpedance have been able to assess the distribution of fluid within the chest. An abbreviated bibliography is listed in the appendix.

Shimmer Sensors are capable of monitoring thoracic bioimpedance continuously through use of a wearable sensor. The sensor produces continuous breath to breath data and can be deployed in the home, the clinic, or the hospital to monitor subjects who test positive for the disease.

Because COVID-19 most significantly affects the lungs, and can induce ARDS, these measurements can be useful in following the course of COVID 19 infected patients and provide clear indications of the progression of the disease. Initial applications:

- Monitoring patients remotely at home to determine, if and when, they will need to be admitted to the hospital
- Monitoring patients in hospital to determine when they need more aggressive treatment (e.g. intensive care, ventilatory assistance)
- Enabling the earlier release of stable patients to be monitored at home

- Adjusting treatment based on the rate of progression of disease

Shimmer has an off the shelf product (the Shimmer3 EBio) that can be used to monitor bioimpedance, ECG, posture, and activity. Because COVID-19 is a new disease, baseline information needs to be obtained to develop thresholds and protocols for patient management. Shimmer is actively pursuing research to develop these digital biomarkers but, because of the urgency, we are encouraging additional researchers to use the Shimmer 3 to pursue this goal in parallel with the Company's efforts.

2. Equipment

The Shimmer3 EBio sensor was introduced in 2014 and has been used successfully in literally thousands of studies in over 70 countries. It is CE marked for safety but is not a registered medical device. However, Shimmer is a registered ISO 13485:2016 medical device manufacturer and will seek regulatory approval as appropriate.

Figure 1 shows a photo of the sensor *in situ* on a subject. Figure 2 shows the recommended placement of electrodes when used in the bioimpedance mode. Only three electrodes are required for bioimpedance measurements. The LL and Vx electrodes are used to capture ECG signals. The raw sensor data from all the sensors are available to the researcher.

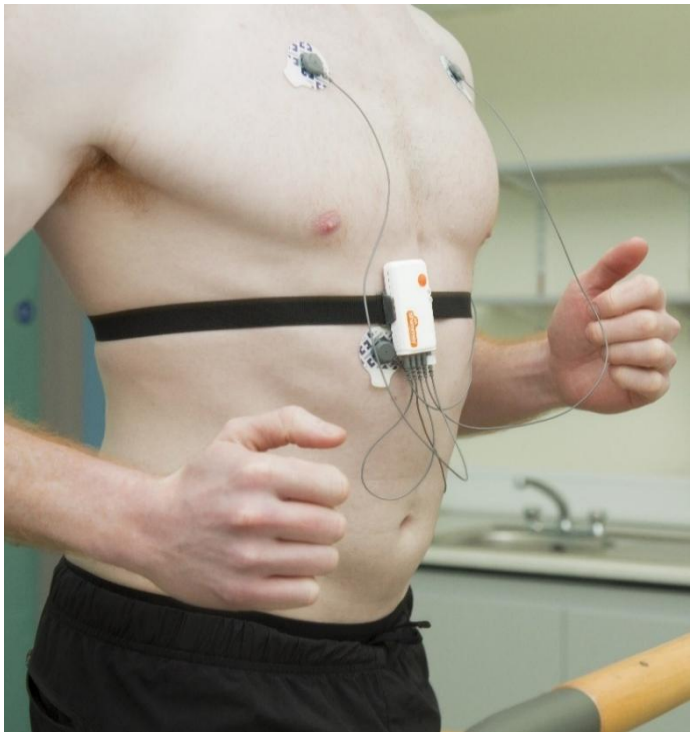

Figure 1: *Shimmer3 ECG/Bioimpedance Sensor*

Data can be collected at a variety of sampling rates, from 1Hz to over 1kHz. We recommend a minimum 200Hz data rate for bioimpedance. Data can be either stored on board or else wirelessly transmitted via Bluetooth. At 200Hz, the sensor has onboard storage that will last 29 days. For the remote monitoring application, data can be stored on the device and uploaded upon return to the site.

The Shimmer3 EBio system uses any standard ECG electrode to capture the ECG and/or bioimpedance signal. We will work with the Sites to select the most appropriate for this study.

In addition to ECG and bioimpedance data, the sensor can simultaneously collect 9 degrees of freedom IMU data (3-axis accelerometer, 3-axis gyro, and 3-axis magnetometer). This provides important contextual information, such as the posture of the patient (supine or upright) as well as activity levels. These signals are also important in identifying periods of motion artefact.

The battery will provide the needed energy to run the equipment for 2+ days without recharging in the local data storage mode. In the streaming mode, the battery life is 8+ hours.

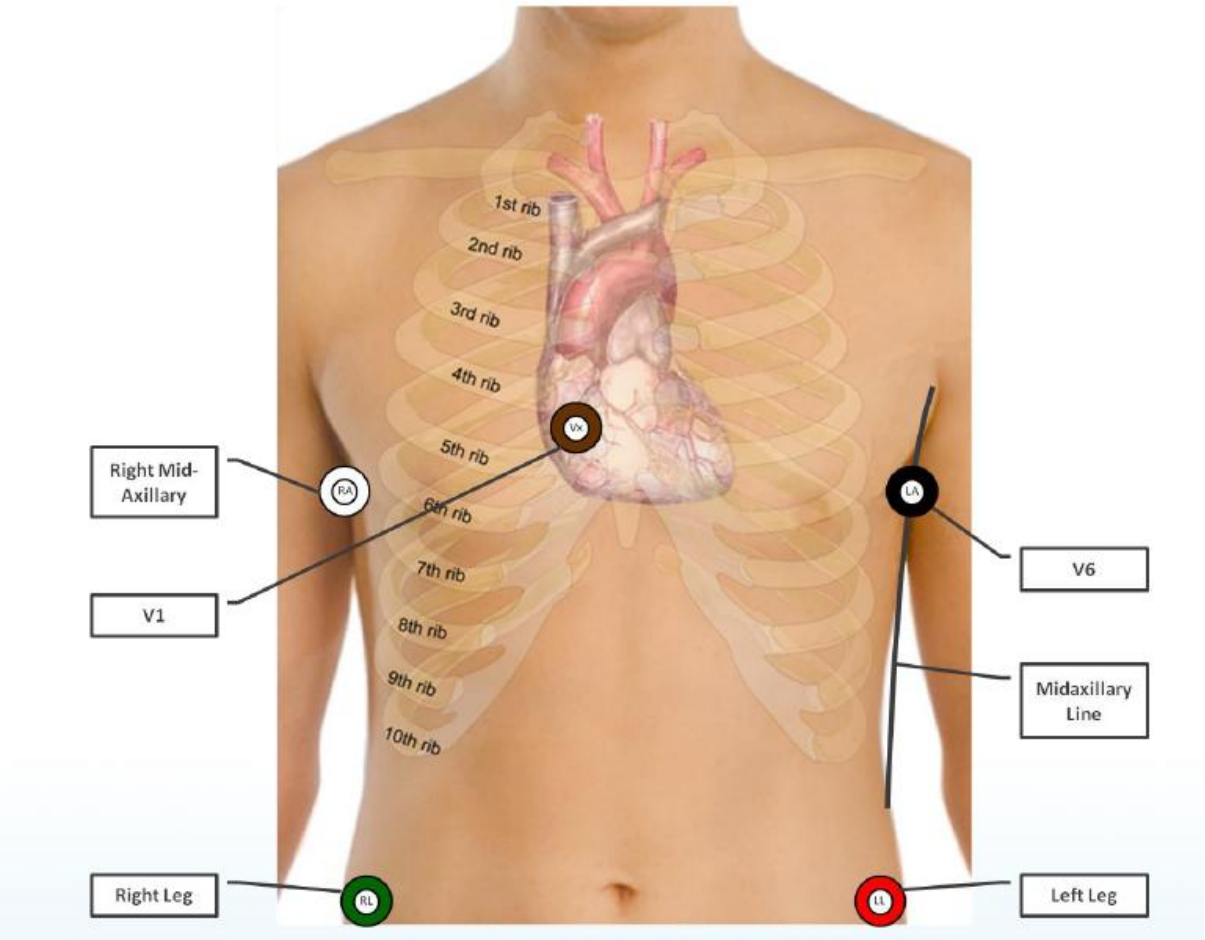

Figure 2 *Recommended Bioimpedance Electrode Placement*

3. The Signals

As indicated before, the ECG-Bioimpedance monitor captures ECG, Bioimpedance, and a 9 degree-of-freedom inertial measurement unit (IMU, containing a 3-axis accelerometer, a 3-axis gyroscope, and a 3-axis magnetometer) data.

Because the electrodes are in non-standard locations for ECG and the bioimpedance signals generate high frequency noise that must be filtered out, the shape of the ECG wave may be affected somewhat. However, the signal is more than adequate to capture accurate heart rate, especially after filtering. Figure 3 below shows the ECG and bioimpedance signals before and after filtering.

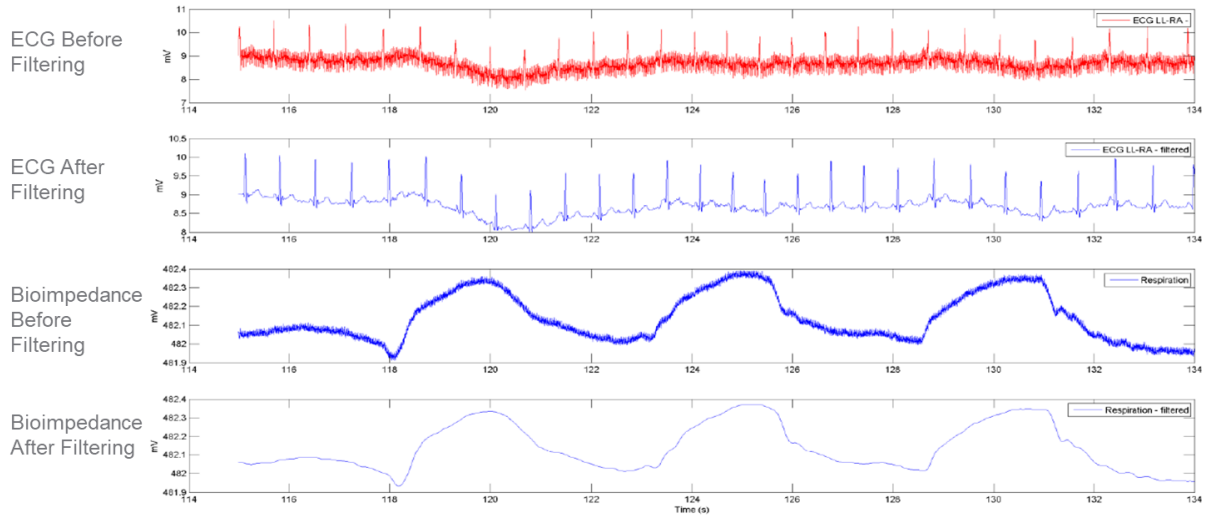

Figure 3 *ECG and Bioimpedance before and after filtering*

As can easily be seen in the ECG signal, the R waves stand out very clearly even before filtering. The change in the bioimpedance signals are driven by the lungs tidal exchange of air. Since air is less conductive than bodily fluids, when the lungs fill with air or other gases, the impedance increases. When the subject exhales, the impedance returns to baseline at FRC (functional residual capacity). The rate of the peaks is equivalent to the respiration rate (RR) and the width of the peaks indicates time and can thus yield an I:E (inspiration to exhalation) ratio.

Furthermore, the height of the peaks is related to the depth of breath. Figure 4 below shows some different breathing patterns and how they registered on bioimpedance. There is clearly a relationship between the depth breathing (tidal volume) and the height of the peaks. This relationship may not be linear.

Lastly, there is likely a relationship between the average bioimpedance and the amount of fluid in the thoracic cavity – the most dynamic component of which is lung water – since an increase in fluid will affect electrical impedance. This is unlikely to be a linear relation because the fluid will likely not be homogeneously distributed. In addition, there will be confounding factors (like the change in impedance in the skin/electrode interface over time). However, it may be possible to track relative change in lung fluid status over time with analytic techniques that account for the confounding factors and recognize pattern signatures.

In addition to the electrical signals, the IMU can provide measurements of activity, body position, posture, and sleep. These algorithms are well known but are not integrated into the system at this time.

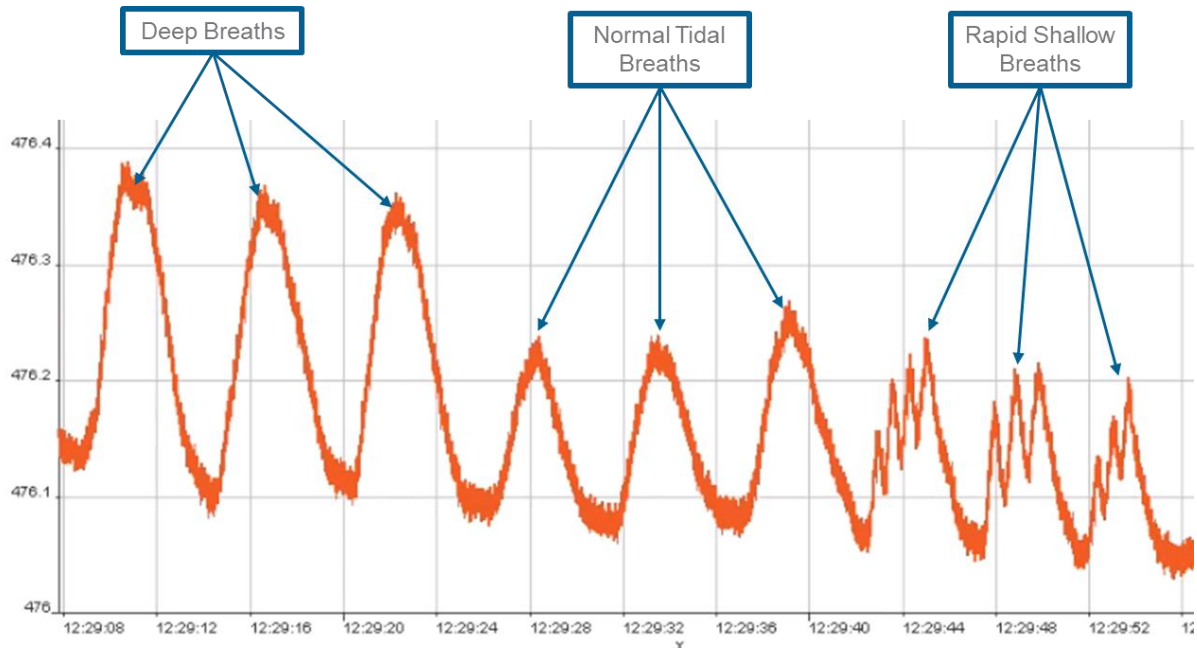

Figure 4 *Bioimpedance with different breath modalities*

4. Monitoring COVID-19

With these sensors, the Shimmer3 ECG-Bioimpedance monitor can assess a very wide range of COVID-19 symptoms. The table below outlines the systems and sensing modalities of the system.

Symptom	Digital Biomarker	Sensing Modality with Shimmer3 ECG-Bioimpedance Sensor
Fever	Elevated HR Elevated RR Δ HRV	ECG Thoracic Bioimpedance ECG
Cough	Thoracic Cage Movement Thoracic Volume Pattern	Accelerometer Thoracic Bioimpedance
Fatigue	Body Position and Posture Active Time and Intensity Δ Sedentary Time	Accelerometer Accelerometer Accelerometer
Respiratory Distress	Rapid Shallow Breathing Elevated RR Elevated HR Disrupted sleep	Thoracic Bioimpedance Thoracic Bioimpedance ECG Accelerometer

5. Deploying the Shimmer3 ECG-Bioimpedance Monitor

As mentioned in the introduction, Shimmer is actively pursuing a research program to translate these signals into actionable insights. Our goal is to use the best possible approaches, even if not developed in-house. We are confident that we will be able to come to a business understanding with whomever develops the best approach.

To be actionable, these insights need to be put into a system that can be made available to healthcare professionals and patients. For that reason, Shimmer is working to integrate the Shimmer 3 into one or more remote patient monitoring systems, in parallel with conducting the research program. Our goal is to have end-to-end systems ready by the time the algorithms are ready to convert the data into actionable insights. We will be happy to support the integration of our sensor into any system that may provide value to the COVID 19 challenge. Please contact us if you wish to learn about how to integrate the Shimmer3 EBio into your platform.

6. Summary

The Shimmer3 EBio sensor is an off-the-shelf product that offers the opportunity to measure critical indicators of lung health, a primary concern for COVID-19 patients. With this knowledge, healthcare systems can optimize the treatment of individuals and utilization of healthcare resources.

Shimmer has initiated research into to establish the digital biomarkers to predict the course and outcome of COVID-19, but we are inviting other researchers to join in this effort to accelerate it and provide independent validation.

7. Appendix: Sample of References using Bioimpedance to Monitor Fluid in the Lungs

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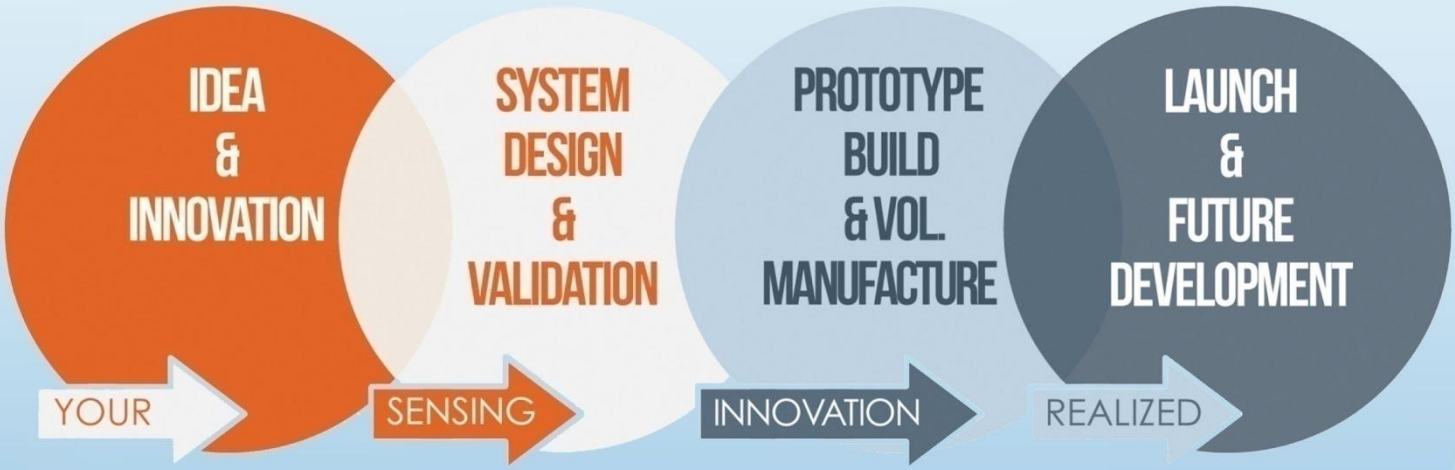

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