**Abstract**

As of today, more than 3 million individuals worldwide have been confirmed with COVID-19, and >200,000 were killed by the disease. COVID-19 acute respiratory distress syndrome (ARDS) is often the symptomatic culprit of this high mortality rate, and it requires hospital-based imaging (e.g., CT scan) to gauge the extent of ARDS. Because the pulmonary edema associated with ARDS increases the local fluid buildup at the level of the lung (i.e., pulmonary edema), we propose to develop a handheld and wearable pulmonary edema sensor to quantify the severity of ARDS. The proposed device can operate in two modes. The first is a manual scanning mode that allows the scan of the whole chest for edema distribution diagnostics, as demonstrated in our earlier work on brain hemorrhage scanner for stroke detection. The second mode is to wear the device on chest for continuous monitoring of the lung edema, breathing (including breathing rate and quantification of inhaled air volume) and the progression of ARDS. This continuous monitoring mode provides early warning of a deteriorating patient. Coincidentally, this is the device an UCSF doctor was calling for in a recent (April 20, 2020) Caltech-UCSF COVID Zoom Workshop.

The proposed device is based on the principle of an eddy current sensor. If a lung is with edema or mucus-like alveolar coating and under an ac magnetic field, it will induce much larger eddy currents that are proportional to the size and the volumetric occupancy of the edema and/or mucus. The induced eddy currents (i.e., the signals) can then be clearly detected by a coil and an electronic circuit. Tai lab has already developed such circuits before so we only need to design and optimize the right coil combination (Figure1) for the sensor and it will be ready for human trials. The proposed device uses only available electronic parts so it can be mass-produced with low cost (total parts <$100). We believe such a device would greatly help in fast triaging such as at drive-thru checkpoints or screening patients at hospitals with moderate to severe symptoms of COVID-19 for timely treatment.
An Unmet Need

As of April 29, 2020, >3 million people worldwide have been confirmed with the SARS-CoV-2 infection, resulting in symptomatic Coronavirus Disease 2019 (COVID-19) [1]. Of these individuals, >200,000 have died because of complications from the disease [1]. Pulmonary complications associated with the disease are clinically characterized as COVID-19 acute respiratory distress syndrome (ARDS) and have been shown to cause interstitial pulmonary edema and fibrosis, which both make it hard for patients to breathe [2]. As a result, many patients are relying on invasive ventilation devices that use pressure differences to force oxygen deep into the patients’ lungs, facilitating breathing. CARDS, among others, is the major cause of death of COVID-19. Diagnosis and screening of CARDS often involves a chest x-ray or computed tomography (CT) scans and, in many patients with CARDS, it is possible to see a ground-glass pattern on CT imaging, signifying interstitial edema in the lungs [2]. The degree of CARDS seen on imaging may then be used to guide clinical assessment of the severity of COVID-19 in the patients. It is often patients with moderate to severe ARDS that progress to pulmonary failure requiring invasive mechanical ventilatory support. A recent Lancet paper [3] further provided strong biopsic evidence of lung inflammation, alveolar damage, lung edema and even alveolar mucus-like coating (e.g., hyaline membrane formation).

For many reasons, CT scanning is not a convenient and high-throughput tool for infectious and severe COVID-19 patients in the context of the ongoing epidemic. In addition, there is limited availability of CT scanning devices, limiting imaging to patients admitted to a hospital who are already suspected of being infected with COVID-19. Coincidentally in an UCSF-Caltech mini-COVID-19 zoom workshop (April 20), an emergency doctor was calling for an easy (e.g., wearable) sensor that can continuously monitor the lung alveolar permeability of COVID-19 patients that he would like to use on his patients. Tai’s lab has since looked into this unmet need and sadly found nothing in the public domain; although one may suggest an ultrasonic approach but it is well known that ultrasound is inherently difficult for this usage because of air in the lung. As a result, we propose an easy-to-use imaging and wearable device here such that it can be used to provide whole-chest scanning images of pulmonary edema, help to quickly triage patients in light of the COVID-19 epidemic, and monitor continuously the progression of CARDS.

Proposed Sensor and its Risk/Benefits

The basic principle of our proposed edema sensor is similar to that of a metal detector. A metal detector uses a magnetic coil to generate alternative (i.e., ac) magnetic field to look for induced “eddy currents” inside the field and mathematically the whole system of a coil and eddy-current-generating materials in a 3D space can be accurately calculated by Maxwell’s equations. In theory, any conductive material (e.g., as piece of metal or in our case edema or mucus in the lung) will induce eddy currents except that edema induces much “smaller” eddy currents due to its small conductivity (~1.6S/m) compared to that of metals (~10^7S/m). Unlike traditional eddy current sensors used for metal detection, we need a much more sensitive circuit so we designed our circuit with the sensor coil paired with a capacitor to form a high-quality-factor resonant circuit. In a real electronic setup, the eddy current flows in the direction such that it increases the coil resistance and decreases the coil inductance, both of which can be detected by an electronic circuit. When edema or mucus in front of the coil, the induced counteracting magnetic field causes a decrease in the coil inductance, or equivalently, a rise in the coil resonant frequency that can be measured by a precise frequency counter. Our device measures the total eddy currents from all tissues including chest wall, normal lung tissues and edema/mucus inside the lung, although we
are targeting at the changes from normal tissues. One should note here that the conductivity of an edema fluid is still much higher than normal lung tissues so the main signals of a lung scan can come from the lung edema. To elaborate, the composition of the fluid that constitutes pulmonary edema is comparable to that of saline, in which is it extremely conductive (1.6 S/m) [4]. Lung normally has little fluid of similar conductivities located within, and pulmonary edema drastically increases the local concentration of saline-like fluid and as a result, increases the local conductivity at the level of the lung. With a set of concentric planar magnetic coils, it can probe the conductivities and concentrations of biological fluids deep within the body. Figure 1 then shows our first proposed scanning device with three combinational coils and electronics. Note that this design has a handle part for the easy of scanning but the handle can be removed so as to flatten out like a hockey plug to facilitate its usage in wearable mode.

We believe such a sensor can benefit patient care on several different levels. Rapid bedside diagnostics make it possible to triage high-risk COVID-19 patients in minutes and offers the possibility of wearable edema sensors. Thus, patients with severe disease may be able to achieve supportive care faster thus lowering the risk for significant morbidity and mortality. We do not see any major risk in the development of the proposed device in terms of feasibility since we already have promising preliminary data (see Related Preliminary Data). In addition, we believe that we can use it to minimize costs to the patient/healthcare system. The materials used to create our COVID-19 pulmonary edema sensor cost <$100, which is negligible compared to prices of CT scanners which run in the multi-million-dollar range. Imaging machines also have operating costs and are limited within the hospital systems due to their large size and cost, and our device bypasses both pitfalls. Further, the novel sensor we have developed does not emit any ionizing radiation, thereby providing safety to patients. Lastly, our device is small, non-invasive, scalable, and portable, and it would be possible to scan for pulmonary edema while in an ambulance, the field (at home), or a rural clinic.

“Related” Preliminary Data
Our proposed lung edema sensor can operate in two modes: the scanning mode and the continuous monitoring mode. The continuous monitoring mode detects the change of lung conductivity over time. The scanning mode creates an edema distribution image inside the lungs. The image-processing algorithm we have developed highlights regions with extraordinary high conductivity.

Figure 1: the proposed lung edema-scanning sensor with three different sizes of coils to cover the whole chest space in thickness.

Figure 2: (left) Prototype device used to scan the simulating hemorrhage. (right) Scanning Mode: composite image of bleeds with various volume embedded at different locations (red circles) in a gelatin brain model.
conductivity. We have not built a lung edema sensor yet but we have built a brain hemorrhage-scanning device that is similar to an edema sensor so some of the related data we obtained from our brain hemorrhage sensor are presented here. For example, the scanning mode is demonstrated with our hemorrhage sensor on a head model embedded with bleeds (30mL to 50 mL of physiological saline) is scanned with our device (Figure 2). The bright white regions showing higher conductivity match well with their actual locations marked by red circles. Both modes suggest the feasibility of applying our device to diagnose and image pulmonary edema related to COVID-19.

The second mode is to wear the device on chest for continuous monitoring of breathing (i.e., rate and quantification of inhaled air volume) and the progression of lung edema and, hence, ARDS. This mode can provide early warning of a deteriorating patient. Coincidentally, this is the kind of device an UCSF doctor was calling for in a recent (April 20) Caltech-UCSF COVID Zoom Workshop. Preliminary data of this mode of monitoring breathing is showing in Figure 3, where the periodic inhale/exhale from regular breathing causes rises and falls in averaged lung conductivity, which is detected as the sensor signal. The magnitude difference between the inhale peak and the exhale valley is proportional to the amount of air going into the lung, which is an important parameter to monitor.

**Proposed work and Milestones**

We propose to first develop and improve our current technology into a complete lung edema sensor. This include the engineering completion of a new device capable of both scanning mode and continuously wearable mode. The sensor turns our conductivity readings into images that can better “localize” the pulmonary edema and then the wearable mode to provide clinicians with continuous information to diagnose and treat COVID-19 patients. The final device will consist of multiple coils to noninvasively probe different depths into the lung and be used manually to scan across the chest. The device will be able to locate the center of the edema and estimate the fluidic volume of the edema if there is a pulmonary edema. As a result, the 6-month milestones are given in Figure 4.

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Figure 4: Continuous Monitoring of breathing using our prototype device: normal breathing signals with two consecutive breaths; peak = inhale, valley = exhale.
Divisional Project Exception and Institutional IRB for “Lung” Diagnostics

We have obtained words from the EAS Division that, if granted, this COVID grant will get Project Exception. As or IRB approval for human study, we have previously obtained an IRB with a human subject protocol at Caltech for our wearable “heart” sensor (Caltech IRB No. 19-0952). As of the time of submission of this proposal, we have already submitted a separate IRB approval for the proposed “lung” sensor. Since the two sensors share the same operating principles and similar physical dimensions and are equally safe, we expect to obtain the IRB approval for our new lung sensor soon.

Human Trials with healthy subjects

For this project, however, we only plan to use it for healthy human subjects to establish the baseline of our sensors to prove its feasibility. The scanning mode will be verified by manual scanning across the chest, and the data collected at different locations will be processed to form a conductivity distribution image inside the chest. The continuous monitoring mode will be tested by wearing the device on the chest at a fixed location. The device readout will be continuously recorded over time and sent to a computer for analysis.

Summary and Future Plan

In response to an unmet need from a COVID emergency doctor, we propose here to develop a lung edema sensor that can operate in both a scanning mode and a wearable mode. As so, such devices should benefit the triage of the epidemics, screening of moderate/severe patients and in-bed monitoring of CARDS progression. For 6 months, we will develop and demonstrate the devices on healthy human subjects. Afterwards we plan team up with USC and UCLA to move forward with clinical trials on COVID-19 patients. We have already identified collaborators at USC and UCLA (see the next Team section). Our USC and UCLA collaborators will arrange simple feasibility study with one or two human subjects with their internal resource. In addition, we also plan to reach out to other institutes such as UCSF, Huntington Memorial Hospital and Cedars Sinai Hospital. With real COVID patient data done, we plan to go for major human trial project from NIH or other COVID funds. If necessary, we are ready to spin off a company with the help of Caltech OTT.

Team Members

(Caltech members) Dr. Yu-Chong Tai is the Anna L. Rosen Professor and the Executive Officer (i.e., Chairman) of the Department of Medical Engineering. For the last 20 years, his research has been focusing on building medical devices. Mr. Shane Shahrestani is a MedE graduate student in Dr. Tai’s lab and is finishing his 4th year in the interdisciplinary USC-Caltech MD/PhD program. Mr. Tzu-Chieh Chou, is a senior EE graduate student in Dr. Tai’s lab. Both students will be helping to develop this novel device.

(Non-Caltech members) Dr. Tzung Hsiai (MD/PhD, UCLA) is the Professor of Medicine (Cardiology) and Bioengineering at UCLA. His broad transdisciplinary research has included collaboration with UCLA Wireless Health Institute, Medical Imaging Informatics, Atherosclerosis Research Unit, Cardiovascular Research Lab, Cellular, Molecular and Developmental Biology, and UCLA Center for Human Nutrition. Dr. Gabriel Zada (MD, USC) is an Associate Professor of Neurological Surgery in the USC Keck School of Medicine. He is a board-certified neurosurgeon and internationally recognized expert in brain, skull base and pituitary tumor surgery, as well as a variety of endoscopic and minimally invasive neurosurgical techniques.
References