Beren Semiz | Research Summary

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Research Goals and Broader Impact

The age of **digital biomarkers** is imminently on the horizon: with recent advances in **wearable technology** and **machine learning**, engineered devices and algorithms may soon transform healthcare delivery from phone calls and intermittent clinic visits to feed-back controlled **continuous health monitoring**. To meet the compelling need for quantitative schemes for assessing disease or injury state, my research (1) proposes wearable sensor modalities to enable **continuous and non-invasive** health and treatment monitoring regardless of time and environmental settings, (2) develops algorithms to extract clinically useful information from the **acoustical and vibrational signals** captured through these sensors, and (3) uses this information to derive digital biomarkers for **quantifying human health**.

Digital Biomarker Discovery using Acoustic and Vibration Signals

The diagnosis and treatment titration for any disease or injury are mostly achieved with conventional biomarkers; however, their derivation requires frequent hospital visits and expensive laboratory tests. Thus, there is a compelling need for novel modalities which can digitize the derivation of such indicators, and employ continuous and non-invasive health monitoring outside the physical confines of the clinic.

Acoustic and vibration signals carry information that is in many cases complementary to electrophysiology, biomechanics and movement. As they originate from the body, they have direct relationships to the underlying physiological events. Acoustic and vibration analysis can potentially be leveraged in the design of wearable sensing modalities since they can provide a non-invasive method to assist in acquiring useful physiological information from the body. Such modalities can provide continuous monitoring during daily life regardless of time, environmental setting and stressors, and thus are of great importance for the digitization of healthcare and transformation towards personalized treatment.

Below, I summarize the novel frameworks I have developed which leverage wearable vibration and acoustic measurements for knee joint and cardiovascular health assessment. Additionally, I discuss the potential effectiveness of such modalities, how they could be leveraged in real world solutions and future directions to consider.

Using Knee Acoustical Emissions for Knee-Health Assessment: There are both invasive and non-invasive procedures for knee health evaluation; however, they fail to provide early diagnosis, are cost-ineffective and inconvenient to perform for continuous monitoring. Motivated by the need for a quantitative, unobtrusive, and affordable method for assessing knee joint health, I designed and implemented a novel framework for extracting a clinically relevant and actionable joint health score from acoustical emission signals measured with miniature sensors that can be embedded into a wearable system, such as a knee brace, for home use.

In this project, I collaborated with Emory University School of Medicine, and my target population was children with Juvenile Idiopathic Arthritis (JIA) — which is the most common rheumatic condition in children. In the knee, vibrations are emitted from the mid-patellar region during active movements, which can be measured on the surface of the skin as sound. When I compared the signals acquired from the healthy subjects and subjects with JIA, I discovered that the acoustical emissions acquired from the healthy and affected knees have different representations in the time and frequency domains. Leveraging this fact, I developed a novel framework consisting of an automated, end-to-end pipeline for the analysis of knee acoustical emissions via feature exploration and machine learning. The output of my framework is a **knee audio score**: an interpretable metric for assessing knee health, which places the recorded joint along a gradient from healthy to an involved joint with JIA, i.e., the derived knee audio score is close to 0 for healthy joints and close to 1 for joints affected with JIA.

In addition to accurately **distinguishing between healthy and affected joints**, my framework is also able to **monitor the treatment effectiveness** via continuous monitoring of subjects with affected joints. Through follow-up studies, I observed improvement in knee audio score in correlation with successful treatment. The proposed framework constitutes a novel biomarker, and it can potentially be generalized and extended beyond JIA to assist in rehabilitation following muscoskeletal injury. Especially after achieving biomarker phenotyping through quantification of the range of motion, swelling, and structure of the joints individually, different diseases or injuries could be distinguished from each other, which could potentially assist in personalized treatment.

Acoustical Analysis of Left Ventricular Assist Devices for Thrombosis Detection: The number of patients awaiting a heart transplant has increased over the past years while the worldwide availability of donor hearts has decreased. Therefore, the use of mechanical assist devices, such as left ventricular assist devices (LVADs), emerged as a solution. However, many patients are readmitted to clinics due to development of pump thrombosis (occurrence of blood clotting within the pump). Unfortunately, there is no technology currently available to characterize and monitor hemodynamics and pump functionality of LVAD recipients at home.

I hypothesized that the operating sounds of LVADs, i.e., their acoustical signatures, may provide substantial information regarding pump thrombosis. I collaborated with University of California San Francisco, where the pump sounds of LVAD recipients were recorded using a digital stethoscope. Each recording belonged to one of the following three classes: "normal", "thrombosis" or "post-thrombosis" (post-treatment). I developed a new feature selection algorithm for extracting and selecting the most relevant acoustical features based on their correlation with actual blood biomarkers. I built a machine learning pipeline to distinguish between normal versus thrombosis recordings, and showed that using my **proposed acoustical features yields higher accuracy and sensitivity in thrombosis detection**, compared to using only LVAD pump parameters. Even more interestingly, I showed that my proposed machine learning model is able to **detect recurrent thrombosis episodes among post-thrombosis recordings, before the pump parameters and blood biomarkers started to change**. This finding is significant in the sense that it can be used to detect and prevent recurrent thrombosis episodes before it starts to change hemodynamic parameters and pump performance, especially in home settings.

Wearable Seismocardiography for Non-Invasive and Continuous Stroke Volume Monitoring: Proper fluid management is critical in every stage of surgery and can greatly impact the clinical outcomes. Fluid management requires accurate measurement of the stroke volume (SV), which is commonly monitored with transesophageal Doppler (TED). Unfortunately, TED is invasive, limited to intra-operative settings when the patient is anesthetized, and requires constant supervision. Currently, there is no device regularly used in clinics that can track patient's SV continuously and non-invasively both during and after surgery.

In this project, we proposed the use of a wearable patch mounted on a patient's mid-sternum, which captures the seismocardiogram (SCG) and electrocardiogram (ECG) signals continuously to predict SV in patients undergoing major surgery. While the ECG waveform measures the *electrical* activity of the heart, the SCG waveform assesses the *mechanical* motions and corresponds to the local chest vibrations originating from the contraction of the heart and ejection of blood. In collaboration with Northwestern University, I presented an end-to-end signal processing and regression-based prediction algorithm using features extracted from the patch signals. I used TED as a reference standard against which the estimates from the wearable patch could be compared. Results from my algorithm showed that the **SCG contains substantial information regarding SV**. This project provides, **for the first time, a system to monitor SV continuously and non-invasively inside and outside the operation room**. Additionally, when I analyzed the acoustic ($>$ 20 Hz, also known as phonocardiogram) and vibration ($<$ 20 Hz) parts of the SCG signals individually, I found out that the stroke volume estimation benefits from both the acoustic and vibrational characteristics of the cardiovascular system.

With this proposed method, the wearable patch can be mounted on the conscious and ambulatory patients, and used to monitor SV without requiring anesthesia or any invasive intervention. In addition, given the recent success of fluid management protocols based on monitoring intra-operative SV, this wearable technology can also be used to **guide peri-operative fluid management**. As a continuation of this project, a unique wearable device acquiring cardiogenic and pulmonary data (vibrations, acoustics, pressure, etc.) could be designed to track the clinical status of the heart, lung and blood simultaneously through quantifying pulmonary activity (edema, respiratory rate, etc.), cardiovascular performance (atrial and ventricular performance, etc.), and blood pressure and oxygen saturation. Such a system could potentially assist in achieving large-scale health monitoring, especially in cases like the current COVID-19 pandemic.

Final Remarks

Wearable technology is in its early stages today and the projects presented in this dissertation are only some examples of how wearable technology can be used to quantify human health. This dissertation paved the way for leveraging wearable acoustic and vibration measurements for remote health monitoring. Once verified and validated through large studies, such systems can potentially assist in clinical decisions and improve the management of various diseases and injuries outside the physical confines of the clinic.