

Development of a Non-Invasive Device for Detection of Troponin-I as a Predictive Biomarker for Heart Failure

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Abstract—Heart attacks are a leading cause of mortality worldwide. Acute Myocardial infarction (AMI) - commonly known as a silent heart attack, is a fatal cardiovascular disease with symptoms such as chest pain, fatigue, arrhythmia, etc. Improving early detection can significantly reduce the mortality rates and enhance the overall health and well-being of the community. Thus, there is an urgent need for a portable device that provides real-time results, making it a point-of-care solution that eliminates the need for patients to visit hospitals for prior diagnosis. The proposed minimally invasive and non-invasive device operates on the principles of photoplethysmography, where a specific wavelength light-emitting diode (LEDs) is used to emit light. The development of the proposed benchtop non-invasive device that estimates Troponin-I levels in the bloodstream has different phases involved: (i) Ex-vivo exploratory research, (ii) Development of a minimally invasive benchtop model, and (iii) Development of a Non-invasive finger model. In the first phase, an investigational study is conducted to determine the spectral features of Troponin-I with the optical characterization using the pure form of Troponin-I. In the second phase, a minimally invasive benchtop model is developed and tested for estimating the accuracy of detecting the Troponin-I. Other proteins, which are considered reference proteins in the body, are procured and tested to study the spectral overlapping. Three subjects are randomly recruited, and whole blood is collected to detect the Troponin-I in the blood. In the last phase, a non-invasive finger model is proposed and developed that can detect Circulatory Troponin-I levels in the blood.

Keywords—Cardiac biomarkers, Myocardial Infarction, Troponin-I, Minimally Invasive, Non-Invasive Detection.

I. INTRODUCTION

Acute Myocardial infarction (AMI) - commonly known as silent heart attack, is a fatal cardiovascular disease with symptoms such as chest pain, fatigue, shortness of breath, nausea, and arrhythmia [1]. Myocarditis is a heart condition that mimics AMI with similar symptoms. Myocarditis is often caused by infectious agents such as viruses, bacteria, or other pathogens. The heart muscle's inflammatory response to the virus can lead to instability in atherosclerotic plaques, causing disruption and superimposed thrombosis, which can result in heart attacks [2].

Heart attacks are a leading cause of mortality worldwide. According to WHO, heart attacks account for nearly 17.9 million global deaths annually [3]. In India, there has been a significant increase in deaths due to cardiovascular diseases over the past decade, and studies indicate a concerning trend among younger people [4].

The root causes of the high mortality rate due to heart attacks in India are multifaceted, including delayed

detection, inaccessible, and unaffordable healthcare facilities. Up to 80% of premature heart attacks and strokes can be prevented if they are detected early [5].

Improving early detection can significantly reduce the mortality rates and enhance the overall health and well-being of the community. Focusing on these areas is essential to provide a more inclusive healthcare system to ensure timely and effective care for all individuals. Thus, there is an urgent need for a portable device that provides real-time results, making it a point-of-care solution that eliminates the need for patients to visit hospitals for prior diagnosis.

Myocarditis is detected by various methods, including electrocardiograms (ECGs), imaging techniques, cardiac biomarkers, etc. Traditional methods like ECGs performed in hospitals are inconvenient and require specialized expertise. Moreover, the lack of real-time results is a significant drawback, as it hinders the early detection of heart attacks, delaying crucial medical intervention [6]. Techniques involving biomarkers primarily involve minimally invasive techniques that require blood samples from patients.

Cardiac Circulatory Biomarkers are released into the bloodstream when the heart muscle is damaged. Troponins are a group of proteins that are produced during heart muscle damage. They are of three types of Troponin-I, Troponin-T, and Troponin-C. While Troponin T and C can also be found in any skeletal muscle damage in the body, Circulatory Troponin-I is considered the gold standard cardiac biomarker due to its superior sensitivity and specificity in detecting myocardial injury. The elevated levels of circulatory Troponin-I help in faster diagnosis and intervention [7].

The proposed solution revolutionizes the diagnosis of the risk of heart attacks by using a wearable, non-invasive, portable, accessible, cost-effective, and point-of-care device for Circulatory Troponin-I detection. The device is wearable, allowing patients to monitor their troponin levels continuously and receive immediate feedback on their condition. By overcoming the limitations of traditional diagnostic methods, this device ensures timely intervention, accessibility, and affordability, ultimately saving lives and improving outcomes for individuals worldwide.

Currently, wearable devices that are used for monitoring SpO₂ and glucose levels operate on the photoplethysmography technique, which is what the proposed solution is based on, where a specific wavelength LED is used to emit light. Beer-Lambert's law relates the attenuation of light to the properties of the molecule through which the light is travelling. The emitted light passes through the skin and tissues. Depending on the properties of the

molecule, it absorbs the light. A photodetector placed on the other side measures the change in the light intensity. The device uses an LED specific to Circulatory Troponin-I. This provides real-time results without the need for invasive procedures.

This idea differs from existing solutions by offering a non-invasive, portable, point-of-care, user-friendly device that provides real-time results, making it easily scalable. The presently available methods to detect Circulatory Troponin-I, such as reverse iontophoresis [8], needle patches, biosensors [9], and rapid kits, are minimally invasive. Researchers also used Nanotechnology to detect Circulatory Troponin-I using gold nanoparticle-based methods and surface plasmon resistance sensors [10], [11]. Devices utilizing near-infrared spectroscopy are non-invasive; however, they are larger in size and thus cannot be used as wearable devices [12].

The aim of this paper is to develop a non-invasive device that can detect levels of Circulatory Troponin-I in the blood. The proposed solution presents a groundbreaking approach to tackling heart health, prioritizing the reduction of heart attack fatalities through early detection, essential for prompt intervention and effective treatment of this critical condition.

II. METHODOLOGY

The development of the proposed benchtop non-invasive device that estimates Troponin-I levels in the bloodstream has different phases involved: (i) Ex-vivo exploratory research, (ii) Development of a minimally invasive benchtop model, and (iii) Development of a non-invasive finger model.

A. Ex-vivo exploratory research:

In the first phase, an investigational study is conducted to determine the spectral features of Troponin-I with optical characterization using the pure form. The pure form of Troponin-I (VIDAS® Highly sensitive Troponin-I) is procured from Breach Candy Hospital, Mumbai. A spectrophotometer (UV-1900 series, UV-002) is used to identify the spectral absorbance for Troponin-I. This helps to detect the presence of Troponin-I in the body using the developed minimally invasive and non-invasive devices.

To determine if there will be any overlaps of absorbance peaks by other circulating molecules in the body, two proteins are identified and checked for their absorbance at 200 nm. Total protein (Total protein kit, Meril Life Sciences) and Heat Shock Protein (HSP70 - Human HSP70, Ray Biotech) proteins, usually considered as reference proteins in the body, are procured from ZOI Hospital, Hyderabad. To achieve this, a minimally invasive benchtop cuvette ex-vivo device model is built using the specific wavelength obtained from the pure form.

B. Development of minimally invasive benchtop model:

An ultraviolet (UV) LED of the required wavelength as determined in the ex-vivo exploratory research, a UV sensor, a crystal quartz cuvette suitable for light in the wavelength range of 190-2500 nm, and a liquid crystal display (LCD) are procured. Fig. 1 illustrates the block diagram of the developed benchtop model.

A UV-LED is positioned opposite to the UV sensor, and a hole is created in the box to accommodate the quartz cuvette (UV non-responsive). The entire assembly is fixed to a board with the LCD display screen and the power supply. The

experimental procedure is initiated by establishing a baseline voltage measurement.

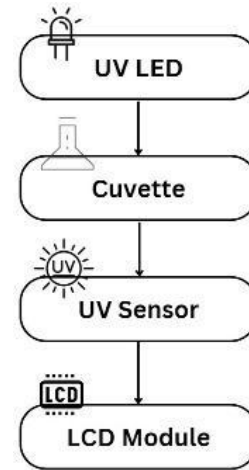


Fig. 1. Block diagram of the developed minimally invasive benchtop model.

The quartz cuvette is filled with 1 ml of the pure form of the Troponin-I sample, and the voltage change is measured. Next, the cuvette is filled with 1 ml of distilled water, and the voltage change is recorded. Similar measurements are conducted with the Total Protein, and HSP70 samples to compare their absorbance profiles with that of Troponin-I. The experiment is repeated several times to measure the variation in the signal procured and for obtaining statistical measurements.

C. Development of a Non-invasive finger model:

A non-invasive finger model is developed as the final prototype. This model incorporates two points of contact for 2 fingers: the first point of contact contains IR and UV sections. Fig. 2 illustrates the block diagram of the instrumentation of non-invasive devices developed from the exploratory phase.

The IR section contains an IR LED and associated IR Sensor, while the UV section consists of a UV-LED and UV-Sensor, which are placed on the same side of the finger, so that the reflective properties are considered. The IR section functions as a reference, and the UV section forms the Troponin-I dependent. The second point of contact is equipped with a heartbeat sensor, providing physiological context to the readings.

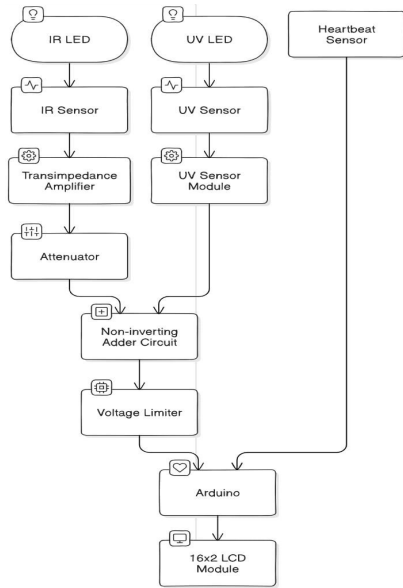


Fig. 2. Block diagram of the instrumentation of the non-invasive device finger model.

The signals from the IR and UV sensors are then transmitted to an Arduino Uno, which processes the data and displays the result. An operational amplifier is used to combine IR and UV signals. The IR signal is amplified, and the UV signal from the sensor is attenuated and provided to the adder circuit built around the operational amplifier (TL 084). The results from the UV and IR sensors after the adder circuit, which are analog in nature, are provided to the analog input of the Arduino board. The signal from the heartbeat sensor is processed during which each heartbeat is identified by the processor as a pulse. The number of pulses per 30 seconds is counted and the quantity thus obtained is doubled and is subsequently displayed on an LCD screen, with voltage values for the UV sensor and numerical values for the heartbeat sensor.

D. Data Collection:

Three subjects are randomly recruited, and 2 ml of whole blood is collected. The inclusion and exclusion criteria are not considered. Subject 1 is a cardiac male patient aged 65 years. Subject 2 is a non-cardiac male patient aged 62 years. Subject 3 is a non-cardiac female patient aged 33 years. 1 ml of whole blood is filled in the cuvette for testing the presence of Troponin-I and subsequent voltage changes are recorded for all the three subjects.

III. RESULTS

To determine the precise absorbance properties of pure Troponin-I, a spectral analysis is employed during the first research step i.e. ex-vivo exploration phase. This phase involved the testing of a pure form of Troponin-I using a spectrometer. The optical readouts representing the signature Troponin-I absorbance peaks are investigated. As shown in Fig. 3, the maximum absorbance peak for Troponin-I is observed at 200 nm.

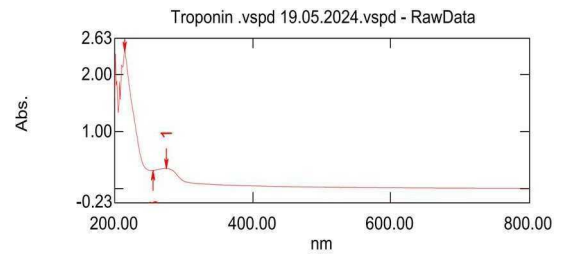


Fig. 3. Spectral features of Troponin-I.

As the next step, to verify whether other proteins in the bloodstream exhibit overlapping absorbance with Troponin-I, a benchtop model is developed using the wavelength identified during the ex-vivo phase. Fig. 4 shows the developed minimally invasive benchtop cuvette model.



Fig. 4. Developed Minimally Invasive Benchtop Cuvette Model.

UV LED with 200 nm as the specific wavelength of light is focused on the cuvette. Initially, without any sample, the voltage observed is 56 mV. Fig. 5 shows that when water is loaded in the cuvette and tested voltage observed is 60mV. Later, the Troponin-I sample is loaded in the cuvette, and the voltage noted is 5 mv.

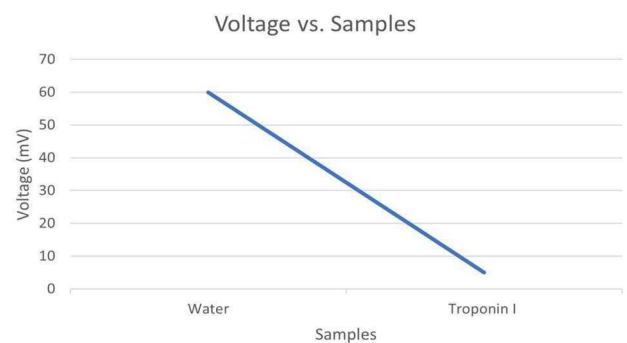


Fig. 5. Voltages of Water and Troponin-I.

The benchtop model measured voltage changes corresponding to the absorbance of UV light by different protein samples. As shown in Fig. 6, the voltage alterations obtained from the other proteins are observed. Total Protein showed 48 mV and HSP70 showed 53mV.

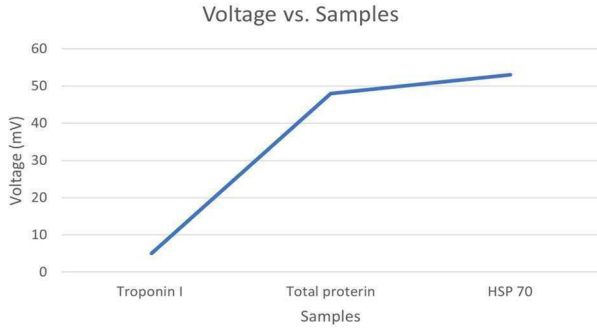


Fig. 6. Voltages of Troponin-I, Total Protein, and HSP70.

As the next step, the whole blood collected from the three volunteer subjects is tested for the alteration of Troponin-I, and the subsequent voltages observed are noted. As shown in Fig. 7 the voltage values for subjects 1, 2 and 3 are 20mV, 32mV, and 25mV respectively.

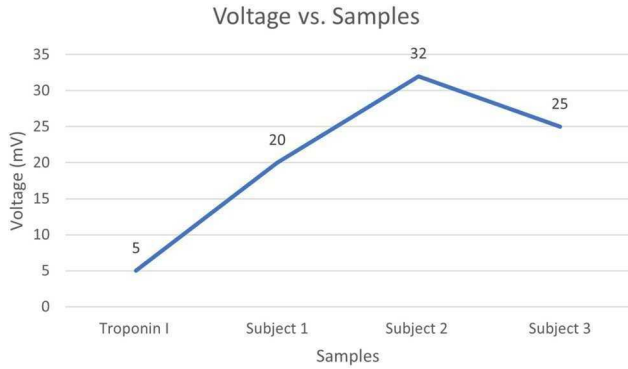


Fig. 7. Voltages of the pure form of Troponin-I and whole blood of subjects.

As the next step, the drift in voltage is measured for pure Troponin-I protein for 5 mins. Fig 8. Illustrates the measured drift in voltage when the pure form of Troponin-I is loaded for 5 minutes. The samples are checked multiple times, and the mean and standard deviation are calculated as shown in Fig. 9. The standard deviation is found to be very low, indicating that the device has high precision. This shows the accuracy of the benchtop model.

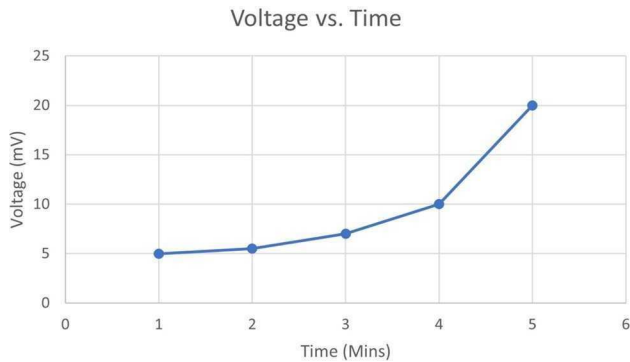


Fig. 8. Drift in voltage of the pure form of Troponin-I.

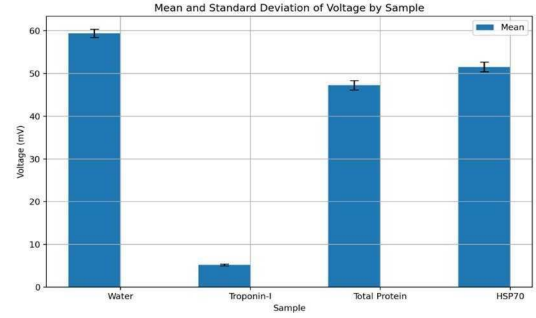


Fig. 9. Mean and Standard Deviation for the samples.

As the next step, considering the results obtained from the minimally invasive benchtop model, the project is extended and a Non-invasive finger model for the detection of Troponin-I is proposed and developed. Fig. 10 shows the developed non-invasive device. The device consists of a heartbeat sensor and a UV and IR LED setup that detects Troponin-I.

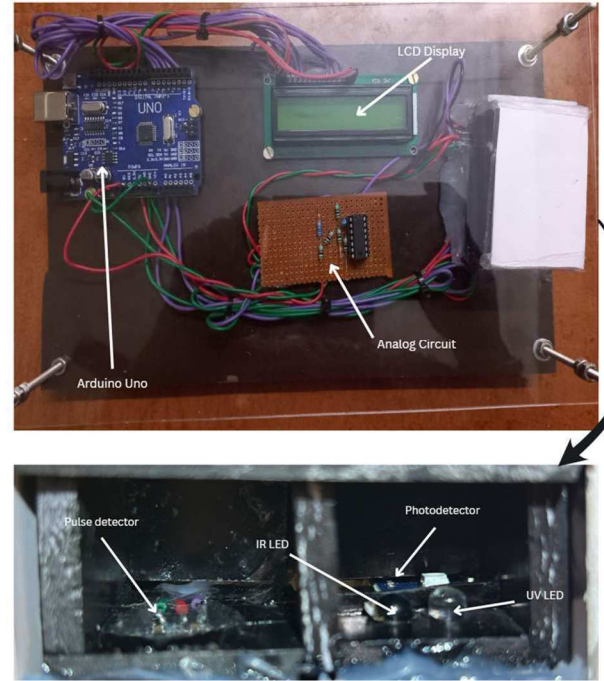


Fig. 10. Developed non-invasive device from the exploratory prototype phase.

IV. DISCUSSION

For the diagnosis of AMI, circulating Troponin levels are often needed in addition to electrocardiograms. Current standard-of-care (i.e. blood draw method) for identifying Troponin-I restricts the number of measurements depending on the patient's clinical history. In this study, the investigators focused on finding the spectral features of Troponin-I, developing and testing a minimally invasive benchtop device for its detection, and finally developing a non-invasive finger model that identifies the levels of Troponin-I protein.

The main purpose of the present investigation is to develop a device that detects the early onset of AMI based on the elevated levels of Circulating Troponin-I. Further, the paper checks the feasibility of the proposed and developed model. Absorption spectroscopy is a technique commonly used to study the spectral features of the molecule of interest in its native state. When a certain wavelength of spectral light is incident on the molecule equivalent to its vibrational mode [12], light is absorbed leading to an active vibrational mode that is unique to the molecule. Therefore, by measuring the light before and after it travels through the molecules, the composition of the material may be determined. In the first research step, that is the ex-vivo exploratory phase, the spectral features of Troponin-I are detected. As of the current literature, a wide range of absorbance spectra of Troponin-I is noted [12], [13], [14], [15]. Analyzing the data obtained from the spectrometer when tested, the absorbance peak of Troponin-I is observed at approximately 200 nm. Few investigators noted that Troponin-I had a good spectral features graph in the UV-range [14]. UV light emitted from a UV LED is focused on the finger, and the intensity is set such that it is harmless to the skin [16].

The second phase involved the testing of a pure form of Troponin-I using the developed minimally invasive benchtop model. The spectral features obtained when other samples i.e. Water, Total protein, and HSP70 were tested for any variations compared with the values obtained from the pure form of Troponin-I. Water is used as a blank and compared with the voltage changes when using Troponin-I. When water is tested, no voltage drop is observed. The substantial voltage-drop for Troponin-I compared to other proteins underscores its distinct spectral profile, supporting the potential of our method for specific detection in a minimally invasive device. The obtained results confirm that the benchtop model is sensitive to detecting the presence of Troponin-I.

The next step involved the detection of Troponin-I in blood samples of volunteers using a benchtop model. Subject 1, previously operated with bypass surgery, is observed to have the least absorbance value. The non-cardiac subjects (i.e. 2, 3) are observed to have more absorbance values. This might be because of the low Troponin-I values. However, more cardiac tests need to be performed for the subjects to verify and validate the obtained results.

In the present study, voltage drift is observed for a period. Less output voltage over time is considered to avoid results after protein degradation. Usually, any protein should be stored in cold temperatures to avoid protein degradation. A peak increase in the voltage is observed after 5 minutes of testing. This might be because of the initiation of the protein denaturation at 35 degrees of room temperature [17].

Initial tests demonstrated the basic functionality of the device. The findings of the ex-vivo exploratory phase and the minimally invasive benchtop model confirmed the feasibility of detecting Troponin-I through UV absorbance and provided a clear direction for future work. As an extended study for detecting Troponin-I, a non-invasive finger model prototype is proposed and developed. The specific wavelength used for the IR LED will deal with skin tone, tissue, and blood flow in the path. The UV signal is responsive to the Troponin-I levels in the blood, apart from the skin tone, tissue, and blood. Thus, the difference between the IR and UV signals is responsive

only to the Troponin level. The ambient light interference can be avoided by providing a concealed casing that protects the IR and UV LEDs from the surrounding light. Other studies showed that non-invasive detection of troponin-I is possible [12], [18]. Recently, a point-of-care device was developed by Abbott iSTAT [19], [20]. Other research teams worked on photoplethysmography techniques using infrared LED sources [12], [18]. Both studies lacked large sample validation.

V. CONCLUSION

First and foremost, a more thorough feasibility study needs to be carried out to determine the most practical and dependable approach for Troponin-I detection before conducting any additional research. To identify the distinct feature of the protein from its spectrum and to differentiate the Troponin-I protein from other proteins that contain amino acids with conjugated characteristics, a unique algorithm is necessary. The results obtained from the developed non-invasive device need to be analyzed and validated. Sample validation requires ethical clearance, marking the next phase of our research, including extended testing and refinement of the prototype to ensure accuracy and reliability in clinical settings. After obtaining ethical clearance for the study, the research will be conducted on the patient and normal groups to minimize the correlation of troponin-I with optical absorbance from other optical confounders in the measurand. This will help to determine a standard cut-off value for circulatory Troponin-I levels, distinguishing between normal and elevated levels. The data will be collected after the patient's consent. As the instrument gathers data optically, external light and environmental factors might affect the output. This can be greatly reduced by using dark backgrounds when collecting the data. Future studies with larger sample sizes should address the diagnostic performance of the algorithm in detecting the early occurrence of heart attacks with elevated levels of Troponin-I. As a future scope, the project can be extended with an integrated artificial intelligence (AI) model for predictive analysis. The AI model will assess the severity and likelihood of cardiac events based on how far a patient's Troponin-I levels deviate from the established threshold. This predictive capability will provide valuable insights into patient prognosis and enable timely interventions. Furthermore, the project envisions the development of an Internet of Things (IoT)-enabled device, capable of functioning in remote or resource-limited settings. This device will be designed to transmit test results to a cloud platform, where healthcare professionals can remotely access the data, provide expert opinions, and recommend further action.

In conclusion, the paper outlines the development of a non-invasive, accessible, and cost-effective point-of-care device for detecting Circulatory Troponin-I. Utilizing the principles of photoplethysmography, the proof of concept is proposed for real-time monitoring of Troponin-I levels without invasive procedures. Initial studies confirm the distinct absorbance characteristics of Troponin-I at 200 nm, and the benchtop model has demonstrated promising specificity. The developed non-invasive finger model should be analyzed and validated.

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