Clotime
Impedance-based point of care blood coagulation monitoring device

Product Concept

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Approvals

Title/Function	Signature	Scope of Approval	Date
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Abbreviations

IC - integrated circuit
INR - international normalized ratio
LCD - liquid crystal display
PCB - printed circuit board
Z - impedance response

1. General Information

1.1. Device name

The device and its components are named as follows:

- The Device: Referred to as “Clotime”, derived from the combination and truncation of the words Clot and time, or “the device”.
- The Strips: Referred to as “Clotime strips”, “test strips”, and “strips”

1.2. Introduction

Blood coagulation is a complex, dynamic physiological process which enables clots to be formed to end bleeding at an injury site. There are however several health conditions and medications that either inhibit or overstimulate clotting. This can lead to deadly outcomes such as hemorrhaging or vascular blockages. Clotime serves as a point of care device for at-risk individuals to monitor their blood clotting time from the comfort of their own home or even when travelling. While there are other coagulation time measuring devices available in the market which fulfill a similar criteria, the distinguishing factor of the Clotime device is its mechanical simplicity and service life due to new low power and high accuracy electronics that enable impedance based measurements to determine coagulation time.

1.3. Scope

This document is intended to describe the system concept as a whole, including the basic functionality and known constraints of the device. The device in question is a point of care blood coagulation time measuring medical instrument. The requirements outlined in this document are intended to be accessible and practical, and will serve as a starting point for developing more detailed requirement specifications.

This document is part of a series of documents on CarePoint’s device Clotime. Please see **P04D02a** [1] for the architectural design of the device, **P04D02b** [2] for requirement specifications, and **P04D03** [3] for the risk management plan..

1.4. Indications for use

The Clotime device is indicated for measuring blood coagulation time in patients with health conditions such as liver disease, hemophilia and thrombophilia [4]. These individuals are often at high risk of internal clotting or excessive blood loss.

1.5. Intended use

The device is intended for use in monitoring of coagulation time of blood in patients. The user is any adult including medical professionals, patients, or patient's caregivers. The system is intended for home use.

2. The Clotime point of care system concept

2.1. Principle of Operation

The device operates on two key principles, microfluidics and impedance response (Z) of blood as it coagulates. A drop of blood from the patient is placed onto a microfluidics strip with embedded electrodes. The strip then wicks the blood into channels where the blood comes into contact with the exposed electrodes. On inserting the strip firmly into the appropriate port on Clotime, electrical contact is made with the electrodes. To begin testing a potential (voltage) is applied across the electrodes which lead to current passing through the blood plasma and cells. The transition of the plasma from a liquid into an electrically insulating solid gel (when clotted) drastically changes the conductivity of the blood sample, which is recorded through the impedance measurements [8]. The results of the impedance data can then be used to determine the clotting time as seen in **Figure 2.1** [5] where the impedance is normalized to the maximum and its change is plotted over time. Clotting is evident by the change of the shape of the curve and is complete at the point marked by the arrow in **Figure 2.1** [5]. This data can be presented to the patient and healthcare individuals on the device's display while also being capable of transmission via USB C to any computer device.

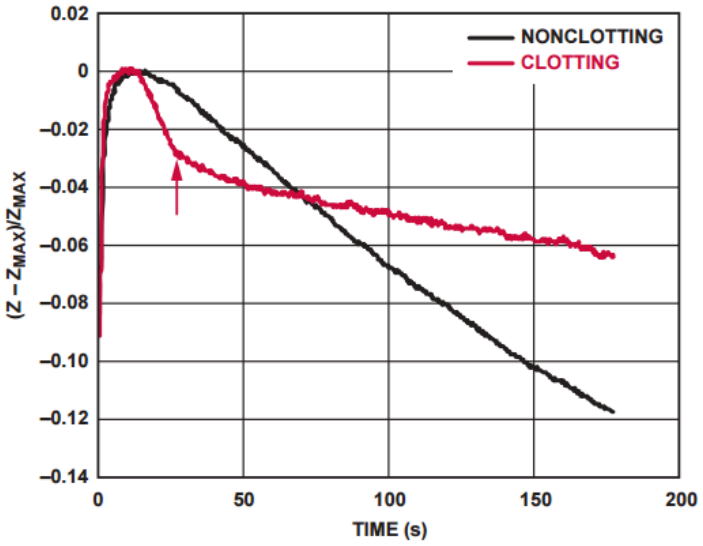

Figure 2.1 Indication of clotting time with respect to the impedance of the blood

2.2. Device Components

This document partitions the components of the Clotime into electrical hardware, mechanical hardware and the user interface. They are all outlined as follows:

2.2.1 Electrical design

The Design includes a printed circuit board (PCB) that includes all the related processing electronics such as:

- Power supply and management circuitry
- Memory and memory management circuitry
- Communications blocks
- Analog devices AD59338 (key technology)
- Microcontroller
- a 160x420 pixel screen with driver IC (Integrated circuit)
- Lithium ion battery and smart charging IC

2.2.2 Mechanical design

Figure 2.2 illustrates the microfluidic strip and the device. Strip (50*20mm) has four parts: 1- plastic substrate, 2- a microfluidic channel (1.5 * 40mm) that draws blood from the reservoir onto the electrodes, 3- three copper electrodes for reference, positive and negative electrodes for impedance measurement, and 4- a thin plastic cover to avoid contamination from outside to the blood.

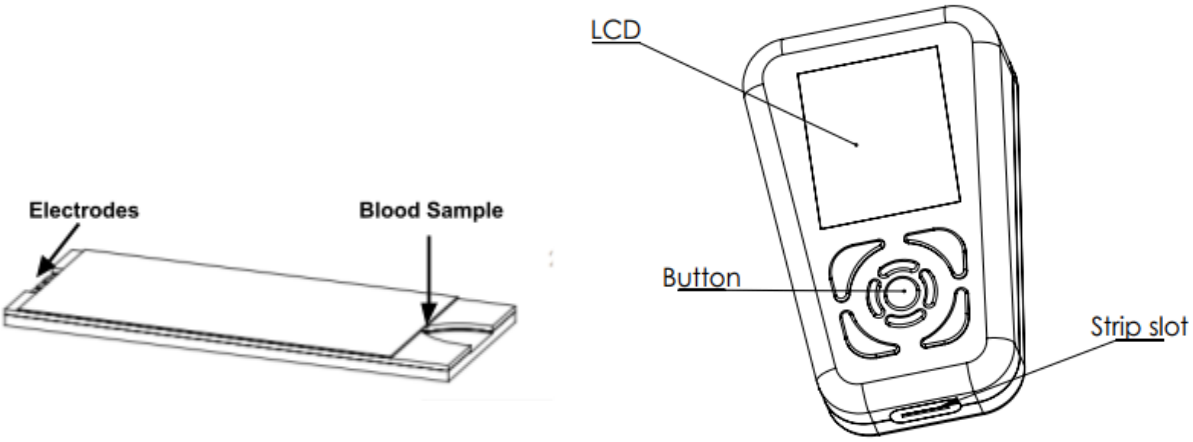

Figure 2.2. 3D sketch of the microfluidic strip with electrodes (left) and the Clotime device.

The Clotime device contains a liquid crystal display (LCD) to display results and other user interface features. Physical buttons are integrated to interact with the user (navigation buttons, and power button) and a USB-C port is implemented for charging and data transmission. The dimensions of the device are 170*110 mm and the trapezoidal shape is designed for an ergonomic grip in the hand of the user. The microfluidic strip is to be inserted into the Clotime through the strip slot.

Figure 2.3. coagulation measurement device currently on the marketCoag-Sense.

There are other coagulation time measuring devices available in the market such as the Coag-Sense [6] shown in **Figure 2.3** which relies on the blood stopping micro gears from turning to determine coagulation state. Clotime is mechanically simpler with potentially better reliability compared to similar devices with complex micromechanical systems in place for testing. This may enable Clotime to have an increased service life and a lower manufacturing cost.

2.2.3. User Machine Interface and software

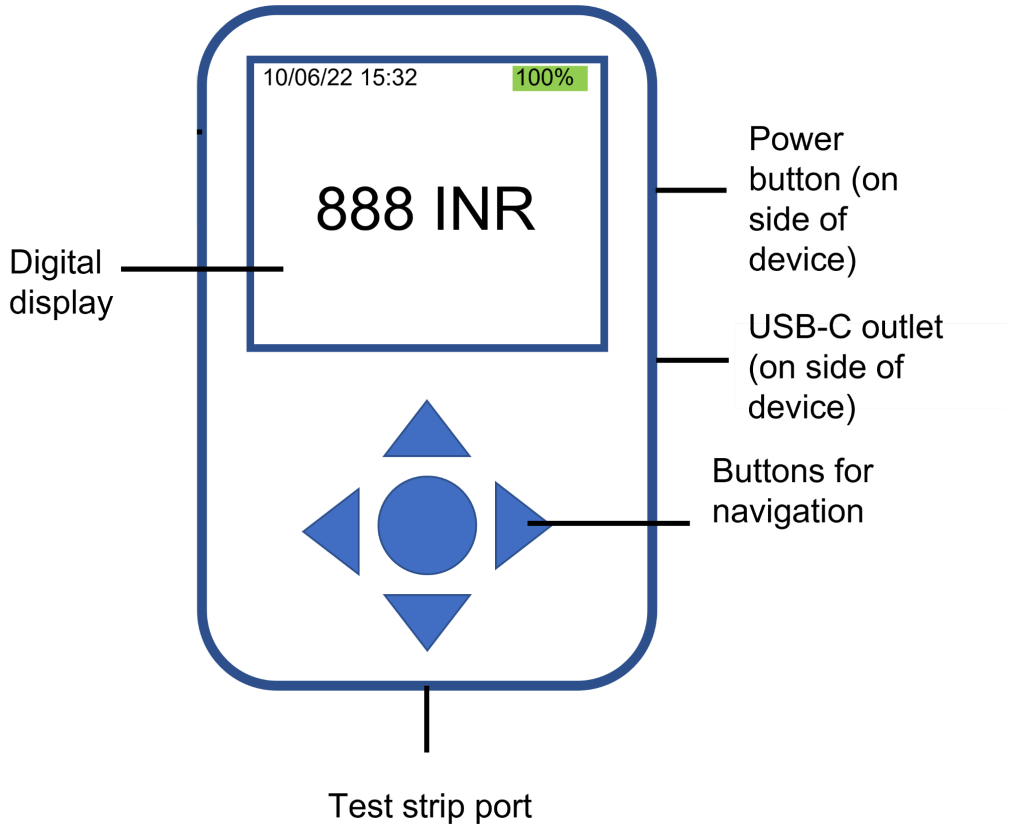

Figure 2.4. Illustration of user-machine interface.

Display screen: Upon starting the device, the user will be presented with a menu screen with the following options: “Test”; “My Results”; “Reminders”; “Settings”; and “Other”. The time is also shown on the screen, as well as a battery percentage.These details can be seen in **Figure 2.4**.

- **Test**: to conduct a measurement test, the user can select “Test” and follow the directions on the screen. When the device is in the process of measuring blood coagulation time, the test “Please wait. Measurement in progress.” will show. The blood coagulation time will then be shown in units INR, and the user will be presented with the option to return to the menu when they are ready.

- **My Results**: The user can view up to 50 previous measurements on the device in tabular and graphical format. Selecting this option will also present the user with the option to transfer their data to an external device via the type C port or Bluetooth.

- **Reminders**: The user can choose to set reminders for measurements.

- **Settings**: The user can choose to change the date and time shown on the device to their current time. The user can also choose between French and English. The user can also be presented with the option to connect to a device through Bluetooth. When the Bluetooth

option is selected, instructions along with a verification code are presented for the user to input on the secondary device.

- **Other**: Information about the device and manufacturer can be found here.

Power button: press to turn on or off

Navigation buttons: Use the directional buttons for navigation and the central button to select an option. Long pressing the button pointing left will take the user back.

Type C port: For both data transfer and charging. When plugged into another device, users are prompted to select whether they want to transfer data.

Blood sample input: Users can follow device instructions to insert the test strip through the port here.

2.2.4. Accessories

The device may come packaged with accessories that could also be purchased separately from external sources.
The two primary accessories are the :

- USB C cable - The cable is used to charge the battery of the device and for data transmission to compatible computing equipment
- Lancing device - The blood drop required and absorbed by the strip will most likely be acquired through a commercial lancing device. There are several popular and regulated lancing devices from companies such as Accu-Chek [7] which may be used in conjunction with the proposed product

2.3. Key Technologies

The key technologie at the heart of the Clotime device is the AD59338, a fully integrated single-chip impedance analyzer. This IC is an impedance-converter system that combines an on-board frequency generator with a 12-bit, analog-to-digital converter (ADC). Using these components, the magnitude and relative phase of the impedance at each frequency point along the sweep can be easily calculated. The AD5933 can measure impedance values between 100 Ω and 10 MΩ to a system accuracy of 0.5% for excitation frequencies from 1 kHz to 100 kHz [5]. These characteristics, along with significant advantages in terms of power savings, portability, final instrument footprint, and reduced system complexity allow the Clotime to be a competitive alternative to other such devices available on the market.

2.4. Design effort

The design effort is to be focused on electrical, mechanical, software features, their components and assemblies. The electrical design involves electrode design, AD59338 signal interpolation, human machine interface, power management and microprocessor integration. The mechanical design incorporates the device body, Physical buttons, ports, display, physical buttons and the strip. The firmware of the device is minimalist with inbuilt safety precautions as well as an intuitive user interface for individuals from a wide range of age groups and education level. Additionally the firmware incorporates usb communication protocols to enable data transfer to computers.

2.5. Feasibility

Feasibility analysis of Clotime as a point of care product is encouraging. Firstly, other compact point of care devices for blood clot time measurement are readily available on the market such as the Coag-Sense [6]. While such devices are competitors their existence and usage is a strong indicator of market size. The main differentiating factor is the mechanism by which the coagulation time is calculated. Moreover the key technology of Clotime, the AD59338 has been shown to reliably measure clotting time in test subjects in studies at the Biomedical Diagnostics Institute Ireland in critical care settings as seen in **Figure 2.5** [5].

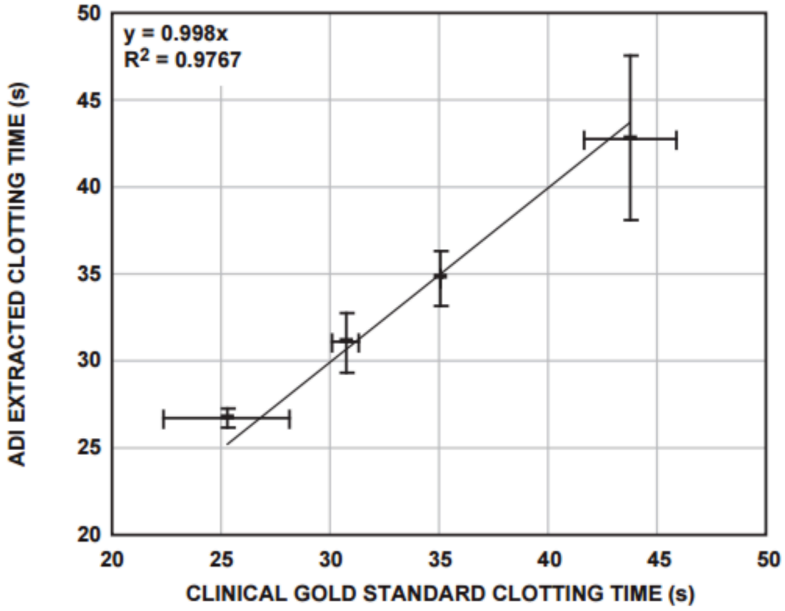

Figure 2.5. Correlation of extracted clotting time measured using the AD5933 measurement system vs. the clinical gold-standard measurement of clotting time, n = 6 for each sample.

3. Design constraints

- The device must comply with all applicable standards and regulations, including ISO 13485:2016, ISO 14971:2019, and IEC 60601-1.
- All components of the device must be compliant with the Restrictions of Hazardous Substances (RoHS) directive.
- Power delivery and data transmission protocols must comply and be compatible with USB C standards.

4. Preliminary system requirements

Note: The following requirements are intended as high-level guidelines for the device for reference only. For lower level, verifiable requirements refer to the separate high level design document: **P04D02b** [2].

Table 4.1. Preliminary system requirements for Clotime.

IR#	**Requirement**	**Source**
IR01	The device shall comply with the ergonomics of human-system interaction standards ISO 9241-11	Usability/functionality
IR02	The device shall be portable	Market
IR04	The device shall be capable of measuring blood coagulation time accurately and in a timely manner.	Functional
IR05	The device shall comply with portability requirements of the IEC 62366-1:2015	Safety
IR06	The device shall comply with medical data transfer standards of the IEC 62304.	Compatibility
IR07	Labelling of the device should be in English and French	Regulatory
IR08	Stand alone platform	Usability/functionality

References

[1] S. Wani *et al.*, *P04D01 "Clotime" Product Concept*, CarePoint, 2022.

[2] A. Bahari *et al.*, *P04D02a "Clotime" Architectural Design*, CarePoint, 2022.

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[4] A. Pietrangelo, *Coagulation tests: Types, procedure, and results*, Healthline, 2018. Accessed: Oct. 14, 2022. [Online]. Available: https://www.healthline.com/health/coagulation-tests

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