PROJECT IMPACT

19017 The technology development of wearable sweat sensing devices. Including affiliated control electronics, clinical use cases, and clinical studies.

March 2024

Despite hospital early warning tools many upcoming disorders are not detected in a timely fashion and frequently requiring costly none-reimbursed resuscitation interventions. An example of such disorder is delirium. Despite current early warning tools, admitted patients have a 24% chance of obtaining a delirium. According to healthcare professionals, monitoring chemical biomarkers will improve these tools substantially. The Sentinel project developed wearable sweat-sensing patches for frequent measurement of these biomarkers.

Background, objectives of the project and challenges

The National Institute for Health and Care Excellence recommends that all patients should be monitored to help identify those whose clinical condition is deteriorating or is at risk of deterioration . Adverse events are estimated to affect up to 12% of hospitalized patients and to cause up to 95,000 patient deaths per year in the European Union alone. Early Warning Systems capture deterioration[1] using physiological vital signs (blood pressure, respiration rate, etc). To obtain a clinically relevant scoring methodology to quantify the severity of these phenomena in a timely manner, two issues have to be developed: (1) a technology that simultaneously can measure relevant factors in a semi-continuous manner including chemical biomarkers and (2) provide signal analysis and data analytics to discover clinically relevant relationships between the measured parameters and disorders. Especially chemical biomarkers will improve the specificity of the relationships.

The Sentinel objective was to develop and de-risk technologies thereby enabling future product development of a wearable that integrates semicontinuous quantitative hybrid sensing of physiological, contextual, and biomolecule markers. Graphically depicted in figure 1.

In the Sentinel project various challenges have been addressed:

1. A wearable format
2. Design & realization of a functional wearable, demonstrating sweat sampling, sweat transport & sensing sweat rate
3. Construction of a functional module that can measure a biomarker (glucose) in sweat
4. Development of affiliated algorithms that translates raw data into clinically relevant data
5. Design & set-up of manufacturing technology for device-prototypes.
6. In the domain of Patient Monitoring analyse use cases in clinical setting for Sepsis, Delirium and Kidney failure.
7. Showcase new developments in micro-nano technology, with a major development in miniature electrowetting on large area, required i.e. to interface with the person's bio-liquids and allow for (semi)continuous measurements for one week.

Figure 1: Patient monitored by wearable sweat sensing patch. Monitoring of biomarkers in patch[2] format, in concert with vital signs and contextual information, is a unique solution to decrease the substantial number of complications in the hospital.

Technological achievements

Why are autonomous tests in need:

Current point of care (POC) tests for in-vitro diagnostics (IVD) take 10-15 minutes, an unacceptable impact on the nurse's workflow when used for patient monitoring. Here monitoring reflects to measurements repeated typically every 30 to 60 minutes to follow patient's health status while in-vitro diagnostics is typically conducted once

to determine the cause of an illness. Using diagnostic tools for monitoring is in the current state-of-affairs not suitable due to expenses and negative impact on nurse's workflow. Monitoring of chemical biomarkers means frequent measurement and is only acceptable for a patient if sampling is done non-obtrusively and for a nurse if execution is autonomous.

The autonomous operating device:

A wearable sweat sensing device has been developed that samples sweat non-obtrusively, without needle piercing and operates autonomously. Sweat is rich in biomarkers, but patients in sedentary state sweat very little. A major breakthrough has been accomplished by developing a device capable of collecting small sweat volumes in a discretized manner and actively transporting sweat droplets in fast pace to the sensors, conceptualized in figure 2.

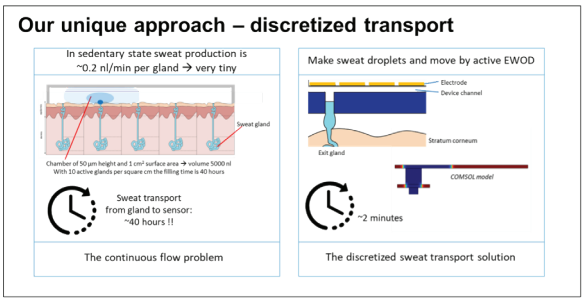


Figure 2. Difference between applying natural sweat flow and using an active transport within a wearable device[3]. Left picture depicts long sampling times by use of patient's natural sweat rate. Right picture shows discretized sampling & transport, capable of sampling & transporting minute amounts of sweat from gland to sensor in minutes.

Hundred prototypes have been manufactured for testing. Active transport of minute sweat droplets ~100 picolitres) is accomplished by Electrowetting on Dielectrics; electrically charged electrodes in sequence attract aqueous droplets as shown in figure 3. In the thesis of Emma Moonen[4] a barcode can be scanned showing a movie of the droplet being transported.

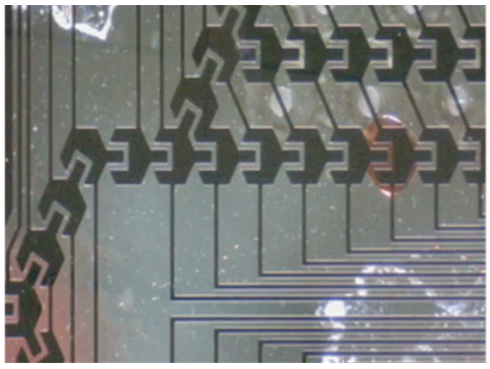


Figure 3. Droplet transport by electrowetting[5] . Part of device is depicted and for demonstration purposes the droplet is coloured red. The droplet is visible above one of the electrowetting electrodes. By sequential charging and decharging of electrodes the droplet is transported in seconds to the left towards the sensors.

Below the full device is presented in figure 4. The device is build up from three frames, the PCB with connectors, the glass substrate with the electrowetting structures and the black coloured housing. Configured such that the glass substrate is in touch with the skin. The connectors on the PCB allow electrical connections to the acquisition/control system as depicted in figure 5.

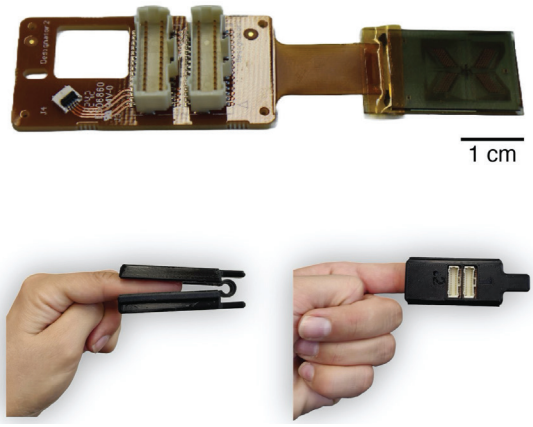


Figure 4. The wearable sweat sensing device[6] . The upper part at the left shows frame 1 being the PCB. The upper part at the right shows frame 2 being the electrowetting structure with 200+ electrodes (too tiny to observe) connected to the PCB. The lower part shows frame 3, constituting the housing and clamping hinge; containing the frame1-2 combo.

The affiliated electronic acquisition & control system is depicted below.

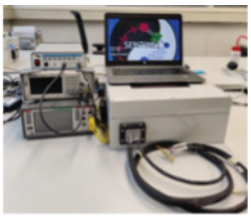


Figure 5. Acquisition/actuation electronics[7]. Contains actuation-electronics charging the electrowetting electrodes in sequence & an acquisition system that digitizes sensor data.

Two clinical studies were conducted and evaluated: (i) dialysis monitoring - urea & (ii) delirium - cortisol. As illustration the workflow for the delirium clinical study is shown in figure 6.

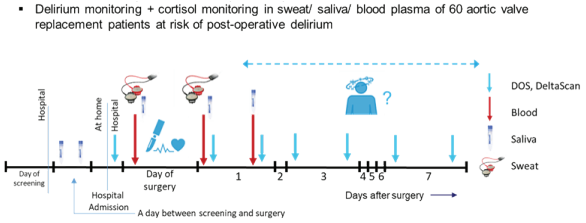


Figure 6. Summary of clinical study monitoring cortisol, stress hormone, before and after aorta valve replacement surgery[8]. Three biofluids where sampled before and after surgery.

Market Potential

In the new market field "Semi-continuous monitoring" there are currently two players that offer patches for measuring glucose relying on invasive needle piercing through the skin sensing the interstitial fluid. The market segments and size for the Sentinel fully non-invasive wearable sweat-sensing device, denoted in figure 7.

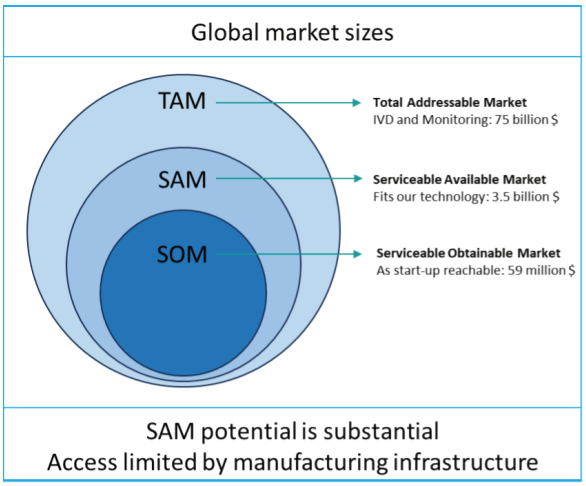


Figure 7. Summary of market potential. From our market study (ref 10) we obtained the potential in the market (upper part) and identified market segments whereof the most promising are denoted (lower part). Glucose sensing is an important marker in the hospital i.e. for infections and for diabetics at home. Delirium is a frequent occurring life threatening complica-tion in the hospital, 24% of all hospital patients will have a delirium and offering urea-monitoring will improve quality of life for kidney failure patients[9].

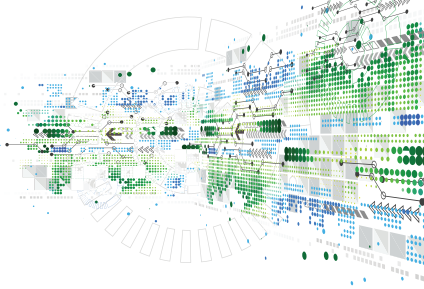
Since project's intended product is based on a platform, with interchangeable biosensors, various biomarkers can be assessed each related to a market segment. Progressing insights showed that not only the hospital can use the developed solution, but also chronic patients at home, which have the same essential requirements of non-obtrusive biofluid collection and autonomous operation. Project partners play an important role in the eco-system that supports a spin-out initiative with vice versa benefits.

Societal & Economic Impact

Before Sentinel, the US scientific community dominated the research in the field of sweat sensing for patients. The discretized concept of sweat sensing as derisked by the European Sentinel project has introduced a superior technology for sweat sensing. Thereby claiming an European stronghold in the field of sweat sensing research. In addition an economic impact is expected by the next phase of product development. The emerging field of Semi Continuous monitoring will claim a substantial position within assessing Patients health status. From market research[10], we estimate that for wearable sweat sensing at least an annual sales of 3.5 billion dollar is accessible.

Figure 8. Overview of the markers with respect to measuring health indicators[11]. To the left the existing market of continuous monitoring (Patient monitoring) of physiological markers like ECG etc. To the right the well-established market of spot checks (one time In-Vitro Diagnostic tests) of biomarkers like biomolecules, bacteria and viruses. Finally in the middle the relative new market field of semi-continuous monitoring of biomolecules as biomarkers.

Patients with complications require substantial effort of hospitals affiliated with huge waste of medical materials. The use of sweat sensing is expected to reduce the number of patients with serious complication by enabling early intervention, reducing the number of crash interventions and thereby substantially lowering the environmental footprint of hospitals. At least equally important is the societal impact; by improving early warning, patients will experience less serious complications and experience much less residual chronic effects after being discharged by the hospital. Especially acquiring less mental permanent disorders will mean a better life after hospital release. In the last decades hospitals made large progress in curing patients, however less attention has been paid to care, addressing the quality of life after discharge. Sentinel's sweat sensing technology is adding to a balanced focus between cure and care.



KEY APPLICATION AREAS

Health & Well-Being

ESSENTIAL CAPABILITIES

Systems and Components Architecture, Design & Integration

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KEY PROJECT DATES

01 April 2020 to 30 September 2023

Patents, Standardisation, Publications

A substantial IP portfolio has been generated on sweat sensing prior to Sentinel and via the Project Contract Agreement key patents were brought in as background being available for the consortium. The developed technology is rather new and when going forward with product development the need for standardisation will become in focus. At the final review, 22 publications have been presented. At least 5 more will follow.

Future Developments

Currently a start-up is being set-up called Dxcrete and an initial team of six persons is working in a trajectory towards the establishment of a start-up company. The basis for this journey is the Sentinel exploitation plan, see ref 10. High tech XL provides the guidance for this journey, warranting that all information is readily available for potential investors. Philips is instrumental in providing licences of relevant IP and the BOM, a local development company, provides seed money. After this journey DXcrete will formally be founded and ready for acquiring investments.

[1] *European Resuscitation Council and European Society of Intensive Care Medicine Guidelines for Post-resuscitation Care 2015 Section 5 of the European Resuscitation Council Guidelines for Resuscitation 2015*

[2] *Source & copyright: Philips. This picture is released for use in public Sentinel deliverables.*

[3] *Source & copyright: Philips. This picture is released for use in public Sentinel deliverables.*

[4] *Emma Moonen, Thesis Discretised microfluidics for non-invasive health monitoring (2024), page 137 (ISBN 978-90-386-5956-5).*

[5,6,7] *Source & copyright: Eindhoven University of Technology, released for use in public Sentinel deliverables.*

[8] *Source & copyright: Catharina hospital Eindhoven, released for use in public Sentinel deliverables.*

[9] *Source & copyright: Philips. This picture is released for use in public Sentinel deliverables.*

[10] *Sentinel deliverable 7.3. Exploitation plan_v1, 17-07-2023. Consortium confidential.*

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