The importance of biomarker stability and sampling procedures of saliva for the design of Point-Of-Care and Lab-On-Chip devices

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***Abstract*— This work highlights the importance of sampling procedure and sample storage of saliva for the development of portable Point-of-care (POC) including disposable Lab-on-a-Chip (LOC).**

I. INTRODUCTION

Early detection plays a crucial role for the prognosis and treatment of diseases. The possibility to obtain clinical information using non-invasive and low risk procedures and devices represents one of the most important goal of health monitoring [1]. Although sampling of blood or tissues is the standard method to assess the health status, drawbacks such as invasiveness, psychologic stress, risks of infection, creation of hazardous waste and need of specialized personnel suggest looking for alternatives.

Saliva is a promising specimen that can be easily and unobtrusively collected, even from non-collaborative subjects (e.g. disabled people) [2, 3]. Point-of-care (POC) and Lab-on-a-Chip (LOC) are innovative devices for the rapid and accurate assessment of biomarkers [4]. Saliva analysis by POCs and LOCs can thus be a breakthrough for patients' screening and monitoring, especially if these devices are equipped with remote communication capabilities. Nevertheless, sampling procedures and sample storage can affect saliva composition, so their effect on the concentration of biomarkers has to be investigated before translating LOCs/POCs from the lab to clinical practice.

This work shows how the design of a LOC/POC for monitoring patients suffering from heart failure (HF) can benefit from knowledge of the stability of biomarkers in saliva samples and the effect of sampling procedures.

II. METHODS

Two different saliva-sampling devices were compared: the SalivaBio Oral Swab (SOS, from Salimetrics) and Salivette® (Sarstedt). A long-term stability study of HF salivary biomarkers included N-terminal pro-brain natriuretic peptide (NT–proBNP), tumour necrosis factor-α (TNF–α), Interleukin-10 (IL–10) and cortisol. Enzyme-Linked ImmunoSorbent Assays (ELISAs) were used to determine the first three molecules in saliva samples, whereas ultra-high performance chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS) was used to measure salivary cortisol. Saliva samples were collected and immediately analyzed (time T_0), and then stored at –20 and –80 °C up to two months. Variations in the initial concentrations were determined after one month (T_1) and two months (T_2).

III. RESULTS

Salivette® led to a quantitative recovery of Cortisol, whereas the others analytes were recovered less than 65%. An almost quantitative recovery of TNF-α and NT-proBNP was observed using SOS. The stability of the biomarkers largely depended on time with the exception of cortisol, which remained stable throughout the observation period in both conditions.

IV. DISCUSSION & CONCLUSION

Saliva-sampling devices are not yet fully suitable to be used straightly in a POC because the loss from the initial concentrations of analytes could lead to poor reproducible results. The low quantitative recovery can also affect the dilution process, which is usually integrated in the POC or in LOC. The tests of stability of saliva samples suggest that the biosensors integrated in a LOC should be wisely tuned when using stored samples because the protein structure could be not well preserved after a long time.

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