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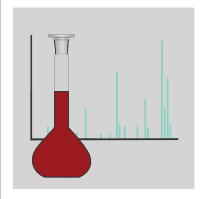

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Biomarker-based Diagnostics for Mild Traumatic Brain Injury (mTBI) at POC – Rising to the Challenges

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Every year 56 million people worldwide experience mild traumatic brain injuries (mTBI, concussion), and there are plenty of unreported cases. Contrary to moderate or severe forms of head injuries, mTBI is difficult to detect with imaging techniques (CT, MRI) and patients often have only unspecific or no apparent symptoms. Repetitive mTBI from multiple head impact events (*cf.* sports accidents) has been associated with greater severity of symptoms, longer recovery times, and with early onset of neurodegenerative diseases.

A laboratory *in vitro* diagnostic (IVD) test for mTBI developed by Banyan Biomarkers was approved by the FDA in 2018. The test is based on a chemiluminescent ELISA for determining two biomarkers, glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase isozyme L1 (UCH-L1) in blood samples. Early 2021 Abbott pioneered the first handheld POC diagnostic test based on their i-STAT™ Alinity™ device to measure these two biomarkers amperometrically. Other companies, such as Medicortex, NanoDx, and ABCDx followed the same path, developing POC diagnostic tests based on other analytical techniques and (partially) different biomarkers. However, all these approaches are limited by the number of biomarkers that can be measured simultaneously.

Aiming to develop a 'next-generation' POC multiplex IVD device for mTBI, our group established both a demonstrator device and a sensitive 3-plex assay to simultaneously quantify the biomarkers GFAP, human fatty acid-binding protein (h-FABP), and S100 calcium-binding protein B (S100β). The test is based on a spatially resolved electrochemiluminescence immunoassay (SR-ECLIA), supported by a low-cost screen-printed carbon electrode (SPCE) that can be integrated into a disposable cartridge. Signal generation occurs at distinct areas of the electrode functionalized with capture antibodies, via a tripropylamine-mediated redox process with $Ru(bpy)_3^{2+}$-luminophores attached to detection antibodies. At the current development stage, the demonstrator is a compact tabletop device that includes a specifically designed light collection module and an sCMOS detector. The three mTBI biomarkers can reproducibly be quantified in 50% diluted serum in the pg mL^{-1} range.

The demonstrator device and assay signify milestone achievements towards a future high-sensitivity multiplex IVD system for mTBI testing at the POC.

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Fig. 1. Simulated use case scenario with a person having suffered a TBI and first responders providing *ad hoc* patient care at the site of an accident. At the bottom right, on the foldable patient stretcher, a model of the envisioned POC diagnostic device for multi-biomarker detection with inserted sample preparation cartridge is depicted. The five bars on the display represent results from a putative 5-plex SR-ECLIA. Device designed by MADI comunicazione and Marc E. Pfeifer. Copyright HES-SO Valais-Wallis (based on Shutterstock photo).

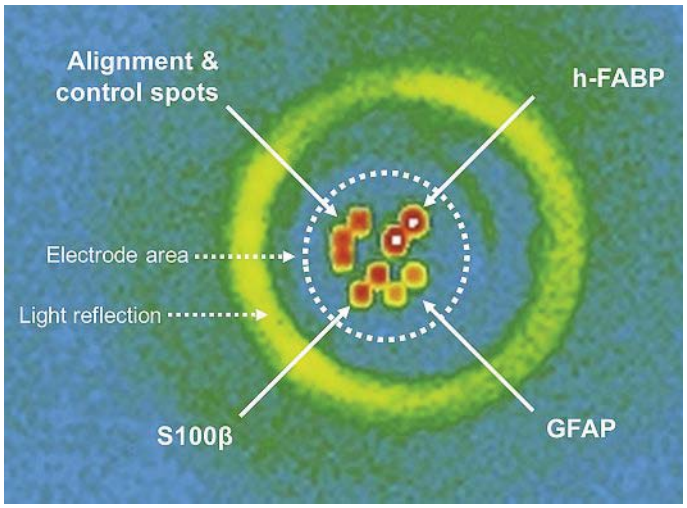

Fig. 2. Early proof-of-principle of the spatially resolved electrochemiluminescence immunoassay (SR-ECLIA) experiment for the concurrent detection of the mTBI biomarkers h-FABP, GFAP and S100β in duplicate spots.

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