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Impedimetric Microanalysis System for Deep Vein Thrombosis Point-of-Care Testing

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Deep Vein Thrombosis (DVT) and the associated condition of Pulmonary Embolism (PE) are the most common cause of unexpected death in developed nations. DVT is an internal clot formed in one of the body's deep veins, typically in the leg. If a part of the clot breaks free and moves into the lung, it can lead to pulmonary embolism (PE) which is often fatal.
D-dimer is a recognised marker for the diagnosis of thrombus and is routinely used by skilled technical staff as part of an ELISA technique in hospital laboratories. Current D-dimer point-of-care tests are not sufficiently quantitative to allow them to be used to exclude DVT/PE. As a consequence, clinicians need to rely on the use of expensive Doppler ultrasound imaging (DUS), creating additional pressure on national health services[1]. The DUS examination can take several days, during which time heparin is required to be administered to the patient. There is increasing in the development of low cost Lab-on-a-chip systems that will allow chemical and biological processing by non-specialist staff. A low cost, easy to use, portable and quantitative device for DVT/PE would be highly desirable since it would provide reliable diagnosis and aid faster treatment and recovery as well as lower healthcare provider costs.

We report on the development of a portable system for the quantification of D-dimer in whole blood through the use of a label-free impedimetric approach for monitoring ligand-receptor (antigen-antibody) immunoassay. The system, comprises a disposable cartridge, carrying receptor ontop electrochemical transducer and allowing sample transport, and a reusable portable hand-held reader. The electrochemical transducers being developed include three-point and inter-digitated electrodes (IDEs). The IDEs have a higher surface interface than 3-point electrodes and consequently the higher surface area will result in higher measurement sensitivity. Further in the case of IDEs, simulation shows that 80% of the current is found to flow in a layer not higher than 2L/3 above the surface (where L = inter-electrode distance). As a consequence, all of the electric field will be concentrated close to surface of the electrodes where the immobilised D-dimer ligand binding occurs. Immobilisation of the His-tag and Avitag model antibody has been carried out by electrodeposition of polypyrrole. We have also demonstrated contact printing immobilization approach using amine terminated D-dimer antibody onto gold substrates as a precursor for printing directly onto the electrodes. A tagged D-dimer antibody immobilized to a three-point electrode structure for D-dimer detection in buffer and plasma has respectively dynamic ranges of 100pg/ml – 500ng/ml (standard deviation with four electrodes of 9.3%) and 100pg/ml – 100ng/ml.

The disposable cartridge system is developed as two separate pieces for subsequent joining. The bottom piece comprises the electrochemical transducer structure, with the bioreceptor as well as electrical connectivity test electrodes and temperature sensors. The cartridge lid carries the necessary elements to transport blood over the electrochemical transducer. The cartridge system is being prototyped using hot embossing and micro-injection moulding but will allow roll-to-roll mass manufacturing technologies to reduce costs.

References

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