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### Advanced Handheld Spectroscopic Portable Technologies for Point-of-Care Neurodiagnostics

Traumatic Brain Injury (TBI) is a major cause of morbidity and mortality, with increasing incidence worldwide, causing long-term disability. After head trauma, critical decisions affecting patients' treatment and outcomes must be made rapidly. However, TBI is hard to diagnose at the point-of-care with many patients often exhibiting no specific clinical symptoms and remaining undiagnosed. The current lack of point-of-care diagnostics often results in incorrect patient management and causes avoidable cognitive, emotional, or physical morbidity. There is a clear urgent need for rapid portable point-of-care diagnostics technologies to enable timely intervention. We have developed a technology for rapid data acquisition of molecular Raman fingerprints of TBI biochemistry to safely measure proxies for cerebral injury through the eye, providing a tangible path towards non-invasive point-of-care neurological diagnostics using simultaneous Raman spectroscopy and fundus imaging, packaged as a low-cost, hand-held device, analysing the neuroretina and optic nerve, as a projection of the central nervous system. This device exploits the optical properties of the eye to focus a harmless collimated sensory beam onto the optic nerve and retina to instantaneously detect TBI-related biochemical changes. To demonstrate the capability to detect endogenous neuromarkers in murine and porcine neuro-retina, our portable and eye-safe device was optimised and tested on an eye phantom, which mimics the optical and spectral characteristics of the eye. Subsequently, testing on the porcine eye posterior detected an enhancement of high-wavenumber bands via the 633nm excitation laser, whilst in the murine eyes, the most intense peaks detected suffered little interference exhibiting a clear separation between TBI and healthy cohorts, further classified using our advanced artificial neural network (ANN) algorithm, which enabled an automated interpretation of Raman data. Clinically, this ANN decision support translates into reduced reliance on specialist support, dramatically improving the speed and cost of diagnosis. Designed as a handheld cost-effective platform, the developed technology can allow clinicians to rapidly assess TBI at the point-of-care including, at the roadside, or pitch-side and can also be used to quantify long-term brain injury, identify changes in brain biochemistry or function due to acute or chronic neurological diseases.

