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Editorial

Biosensors: from personalised medicine to population health

Want to know your blood glucose level? Check the colour changes of your tattoo. Combining tattoos with biosensors for rapid measurement of glucose levels in the user's sweat might sound like science fiction, but this scenario is closer to becoming a reality thanks to recent advances in biosensor technology. Since the first biosensor was invented in 1962, a wide range of biosensors, specifically miniaturised and non-invasive forms, are fast developing and will soon be widely available to the public. These sensor-based technologies will allow individuals to track their health-related data, such as heart rate, sleep or physical activity, thereby moving analytical services closer to the patients, with the potential for a wide range of health-care applications not limited to blood glucose monitoring.

Biosensors are often used to detect specific biomarkers in biofluids, but some gadgets can analyse gas samples to predict a patient's response to a treatment or disease. Michel van den Heuvel and colleagues from Radboud University Medical Centre (Nijmegen, Netherlands) used an electronic nose (eNose) with sensors to predict immunotherapy responses in patients who have non-small cell lung cancer (NSCLC). Immune checkpoint inhibition is an effective treatment strategy for these patients, but only a small subset of patients benefits from this treatment. The team did a prospective observational study in 143 patients with advanced NSCLC to collect and analyse volatile organic compounds in breath and found that eNose can predict responses to immunotherapies with 85% accuracy. Their findings, published in the *Annals of Oncology* on September 17, 2019, indicated that eNose has better predictive accuracy than immunohistochemistry, which is the gold standard for predicting responses to anti- programmed cell death-1 immunotherapies. Although these findings need to be validated in a larger cohort, eNose could eventually be implemented as a useful, non-invasive tool for predicting immunotherapy responses at the point of care. iKnife is another interesting device that can detect tumours during surgery. By connecting an electrosurgical knife to a mass spectrometer, iKnife almost instantly distinguishes between cancerous and healthy tissue by analysing the smoke when tissue is vaporized during incision. The iKnife is now under pilot clinical trials in breast cancer (NCT03432429) and endometrial cancer (NCT03207074) in several research groups at Imperial College London (London, UK).

Microneedles were initially developed for use in transdermal drug delivery. Recent developments in biomaterials, as well as in the bioengineering field, have expanded the applications of this device. A small-scale clinical trial published in the *Lancet Digital Health* on September 30, 2019, led by Timothy Rawson from Imperial College London (London, UK), showed that microneedle biosensors can be used to evaluate antibiotic responses in real-time in healthy individuals, and produced similar results to the ones obtained from blood samples. It is the first in-human study to monitor drug concentration changes using microneedles. Some smart microneedles are not just measuring the physiological changes but are also able to respond to those measurements. A research group led by Zhen Gu from University of California, Los Angeles (CA, USA) developed a glucose-responsive microneedle patch for monitoring and treatment of diabetes and tested it in animal models. Microneedles in the patch were made up of glucose-sensing polymer encapsulated with insulin. In a hyperglycaemic state, increasing negative charges in the polymeric matrix causes the microneedle to swell and release the pre-loaded insulin into the skin. This preclinical study was published in *Nature Biomedical Engineering* on February 3, 2020, and showed that the coin-sized patch can effectively control glucose levels in diabetic mini-pigs for over 20 hours. Early research, which has indicated the potential of integrating the microneedle in a closed-loop system for automated drug delivery or treatment, shows that this application might bring this innovation into consumer use sooner than expected. On December 13, 2019, the US Food and Drug Administration approved the use of a closed-loop system, the Control-IQ Hybrid Closed Loop System from Tandem Diabetes Care (CA, USA), for patients who have type I diabetes. This closed-loop system, also referred to as the artificial pancreas, uses a computer algorithm for monitoring blood glucose levels using data fed by the glucose monitor sensor, which can automatically deliver insulin on-demand with an insulin pump, whereas other closed-loop systems on the market are limited to adjustment of the basal rate and cannot automatically deliver the correct dose of insulin. This type of smart system frees people from fingerstick testing and avoids daily injections to maintain a steady blood glucose level. According to the 6 month International Diabetes Closed Loop trial, published in the *New England Journal of Medicine* on October 31, 2019, patients with type I diabetes who use this new system have increased time in the target glycemic range (3·9 to 10·0 mmol per litre) compared with the control group.

Other than directly assessing an individual's health conditions, the combination of biosensors with mobile health care, like wearable devices, enable individuals to track their physical activities and is being used to generate population health data. This strategy is especially useful for predicting the outbreak of infectious diseases, which requires early surveillance to limit the spread of infection. As described in an article published in the *Lancet Digital Health* on January 16, 2020, Jennifer Radin and colleagues from Scripps Research Translational Institute (CA, USA) used wearable biosensors to collect longitudinal physiological data from individuals with acute infection for predicting influenza outbreaks in the USA. They obtained 2 years of anonymous data on resting heart rate and sleep activity from

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47 249 wearable device users in five US states. Compared with the state level influenza-like illness (ILI) incidence reporting from the US Centers for Disease Control and Prevention, which relies on reporting from outpatient health-care providers and often has 1 to 3 weeks lag, biosensor data improved ILI prediction in all five states.

There are multiple ways in which biosensors can be applied to personalised and predictive health-care treatments. Currently, the number of preclinical studies done in this field far outweighs the number of devices that eventually could be developed for clinical use. Many reasons lay behind the lack of clinical translation; one big challenge for biosensors is to display accurate and stable responses in physiological conditions. Concerted efforts involving multi-disciplinary teams including, but not limited to, biomedicine, bioengineering, and biomaterials, will facilitate the successful translation of biosensors from the research laboratory to clinical practice. *EBioMedicine* welcomes translational studies on new devices that could accelerate disease diagnosis, management, and treatment.

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