Non-Invasive Intelligent Nanosensors for Monitoring Pandemics

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The emergence of the COVID-19 pandemics has once again hit headlines over the urgent need for rapid and non-invasive diagnostic tools for various pandemics, including Tuberculosis. Harnessing nanosensors for the detection of volatile organic compounds (VOCs) emitted from viral and bacterial agents and/or their microenvironment poses a great potential for detecting infections at early stages. VOCs can be emitted into the exhaled breath as well as the skin headspace – easy sources for non-invasive collection. We have completed successfully an exploratory clinical study in Wuhan, China, on 140 participants in detecting and following-up individuals who are at-risk or have an existing COVID-19 infection.[1] The study cohort included confirmed COVID-19 patients, healthy controls, and non-COVID lung infection controls. When applicable, positive COVID-19 patients were sampled twice: during the active disease and after recovery. Exhaled breath samples were collected by a handheld analyzer, by blowing into the device for 2-3 seconds from a distance of 2-3 cm. Discriminant analysis of the obtained signals from, cross-reactive, capped gold nanoparticles-based sensors achieved very good test discriminations between the different groups. The training and test set data exhibited respectively 94% and 76% accuracy in differentiating patients from controls as well as 90% and 95% accuracy in differentiating between patients with COVID-19 and patients with other lung infections.[1] The same approach, based on exhaled breath sampling, was also tested for detection of active pulmonary Tuberculosis (N=198) in Cape Town, South Africa, resulting in above 90% accuracy, specificity, and sensitivity in the test set data.[2] In both studies, the influence of confounding factors, such as smoking, was evaluated and found to be negligible.[1][2] A skin-based approach that relies on non-invasive wearable sensing patches was also demonstrated successfully to collecting Tuberculosis-related biomarkers that appear in the headspace of the inner arm area. The studies were conducted in South Africa, India and Latvia, resulting in identifying VOC profiles related to Tuberculosis and creation of a global classifier based on analysis of nanomaterial-based sensor array resulted in 90.1% sensitivity, 91.3% specificity and 90.1% global accuracy. As a pilot, an online sampling device, including the nanomaterial-based sensors was tested in Latvia, yielding 82.76% specificity, 100% sensitivity, and 89.36% accuracy. While further validation studies are needed, the results may serve as a base for technology that would lead to a reduction in the number of unneeded confirmatory tests and lower the burden on hospitals, while allowing individuals a screening solution that can be performed in PoC facilities. The proposed method can be considered as a platform that could be applied for any other disease infection with proper modifications to the artificial intelligence and would therefore be available to serve as a diagnostic tool in case of a new disease outbreak.

[1] Shan, B.; Broza, Y. Y.; *et al.* Haick, H.; *ACS Nano* **14**, 12125-12132 (2020).
[2] *Nakhleh, M. K.; et al.; Haick, H.; Europ. Resp. J.* **43**, 1522-1525 (2014).

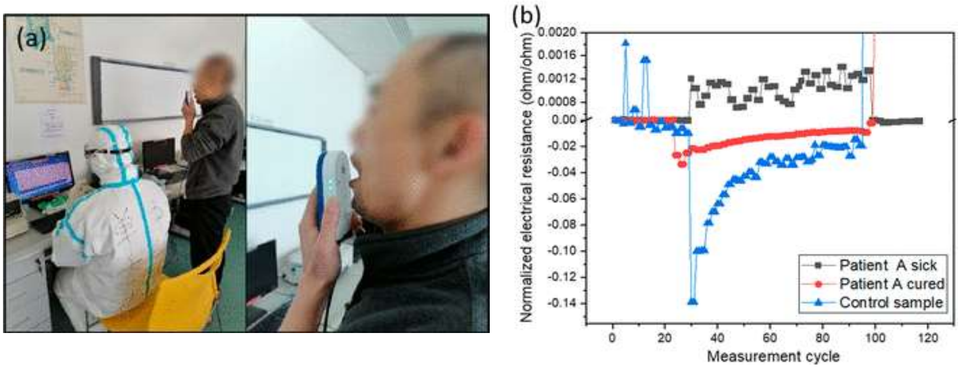

Figure 1: (a) Example of breath collection with breathalyzer system from a patient in Wuhan, China. (b) Representative response of a sensor to three different breath samples: patient A, COVID-19, first sample while infected; patient A, second sample after determined as recovered; and a healthy control. The x-axis represents the cycle measurement; each unit is one cycle of the sensor.[1]