Volatile organic compound sensors – the future of cancer detection?

Professor Han Jin from Ningbo University focuses on developing novel diagnostic technologies based on profiling volatile organic compounds (VOCs) in breath samples. VOC patterns can be used to identify different diseases and distinguish between different types of cancer. To achieve his goal of developing a novel VOC breath sensor for early stage disease diagnosis, Professor Jin must create a highly sensitive and accurate sensor that can be used in clinical environments. The team and cooperators must also develop a detailed database that associates specific VOC biomarkers with certain diseases.

Volatile organic compounds are present in cigarettes, as well as paints, air fresheners and other everyday items.

Cancer is the second leading cause of death globally. According to the World Health Organization, one in six deaths is due to cancer. Survival rates can vary drastically depending on the type of cancer, its severity and how early it is detected. Testicular cancer, prostate cancer and malignant melanoma all have survival rates in excess of 80%. However, other cancer types, such as lung, stomach, brain and pancreatic, are much more difficult to diagnose and treat and survival is often less than 20%.

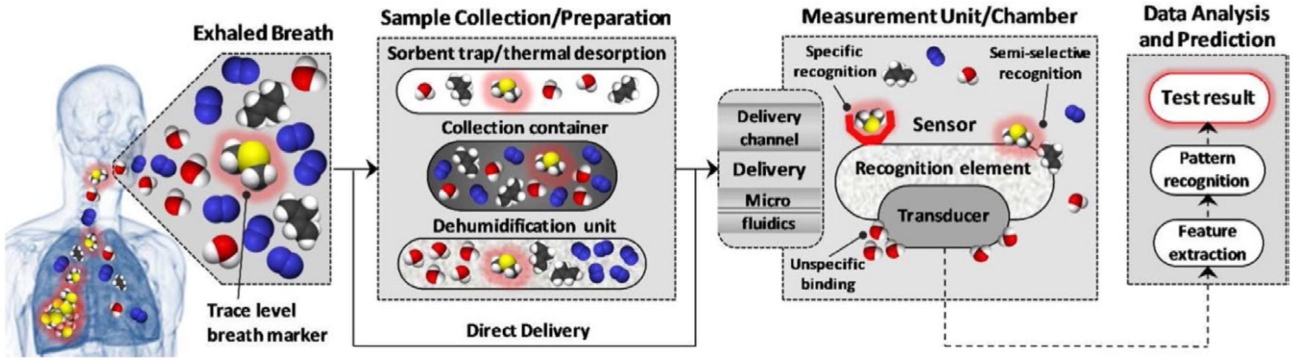
Early diagnosis significantly enhances treatment success and survival rate. Indeed, disease prevention is a much more cost-effective approach compared to treatment of the cancer. However, some available diagnostic methods lack enough sensitivity and specificity to be truly effective at detecting cancer in its earliest stages. This inspired Professor Jin and his team to develop novel, inexpensive and non-invasive technologies to improve cancer detection, increasing the chance of survival. These pioneering diagnostic tools are based on the analysis of volatile organic compounds (VOCs) which originate from diseased cells.

VOLATILE ORGANIC COMPOUNDS

VOCs are compounds that become vapours at room temperature. They can occur both naturally and artificially in consumer products such as cigarettes, air fresheners and paints. In terms of biochemistry, VOCs offer an insight into the physiological and pathophysiological processes occurring in both healthy and diseased humans.

Breath analysis can identify the specific VOCs released from cells and their surrounding micro-environment. Interestingly, it has been shown that VOCs derived from cancer patients exhibit specific patterns that are significantly different from healthy individuals. This exciting finding suggests that breath testing has the potential to diagnose some early-stage cancers. To further advance this as a suitable screening tool, Professor Jin and his team need to overcome two key challenges: i) the development of an informative database that contains all the VOC profiles that correspond to specific cancers and ii) the development of highly sensitive VOC sensors. In collaboration with Qi Diagnostics Ltd (a pioneering biotechnology company based in Hong Kong that designs innovative tools for detecting early-stage diseases), Professor Jin and his team are co-developing a tailor-made artificial intelligence sensor array based on volatolomics (the study of VOCs). With the help of Qi Diagnostics Ltd, the team are also collating a highly detailed VOC database and creating an artificial intelligence algorithm for data analysis.

THE PROCESSES INVOLVED IN BREATH TESTING



There are many processes involved in breath testing. This image gives an overview of them.

DEVELOPING A VOC DATABASE

A thoroughly detailed database which can match VOC biomarkers to a specific disease is essential for the success of the screening. For instance, five kinds of VOCs have been verified as lung cancer diagnostic biomarkers including ethylbenzene, styrene and hexanal. However, despite the potential of VOC profiling as a diagnostic tool, only a few VOC databases have been developed by the scientific community. Of those that exist, the majority are focused on the structural information of scent or microbial emitted VOCs, rather than specifically focussing on VOCs as biomarkers for disease. Therefore, more profiling needs to be done to be able to effectively identify a wide range of diseases, including different types of cancer.

The team (including Qi Diagnostics Ltd) are currently working on establishing this database which will include both detailed qualitative and quantitative information on the VOC profile. To do this, Professor Jin and his colleagues will use gas chromatography-mass spectrometry (GC/MS) which is an effective tool to identify VOC biomarkers in exhaled breath. However, it is important to note that confounding factors such as the patient's age, gender and clinical history may affect the VOC profile. The accuracy of the test must therefore be interrogated. The team will begin by establishing a lung-cancer specific database with breath samples collected from Hong Kong hospitals and will then create a database for lung cancer, colorectal cancer and heart failure.

VOC SENSORS

Currently, there are a wide range of gas sensors and sensor arrays used for the detection of VOCs. For example, colorectal sensors, quartz microbalance sensors, surface acoustic wave sensors and chemiresistors or chemicapacitors. However, these methods used for VOC detection are limited by humidity which can interfere with their performance. Furthermore, these sensors are not effective at classifying complex VOC mixtures. Therefore, Professor Jin and his team are focused on developing an inexpensive, portable and highly sensitive VOC detector.

Electrochemical sensors using yttria-stabilised zirconia (YSZ) electrolytes have the potential to be a candidate for VOC detection. Currently these gas sensors are used to monitor exhaust gases due to their high selectivity and reliable performance under harsh conditions e.g.

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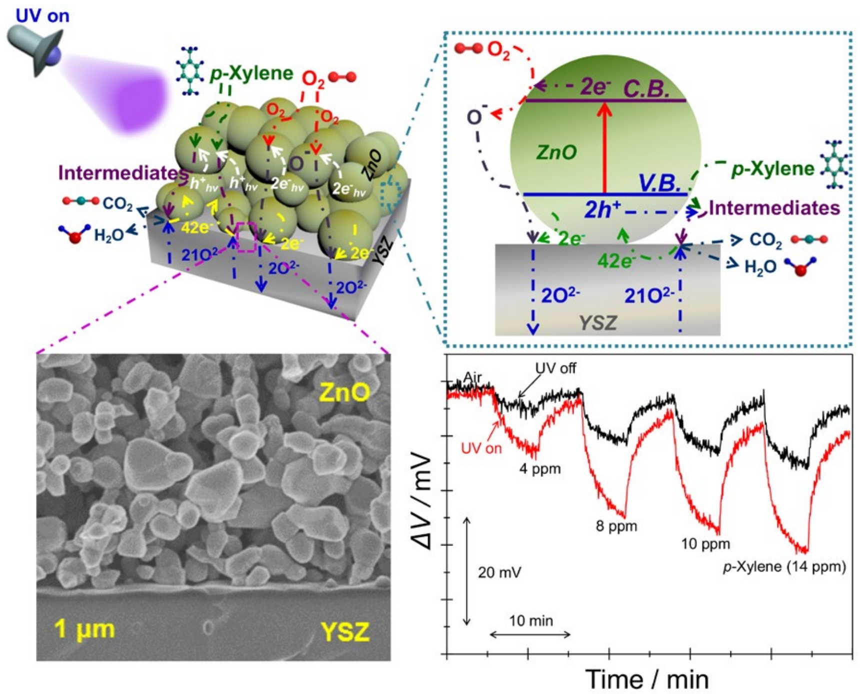
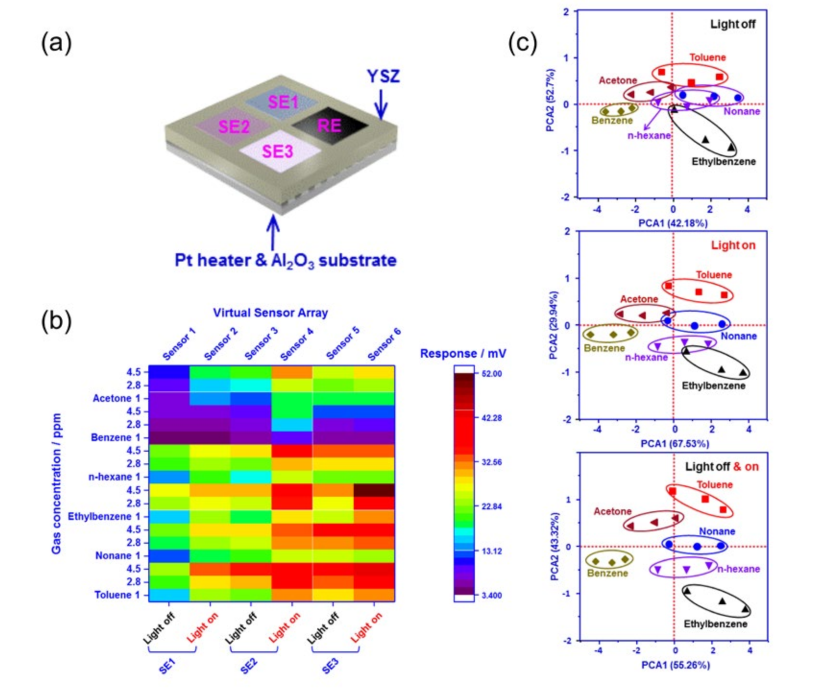


Schema of the light-regulated electrochemical reaction in sensing of volatile compounds.

high humidity and temperature. However, these electrochemical sensors have a detection limit of dozens of parts per million (ppm), whereas the concentration of VOC markers from human breath is typically tens of parts per billion (ppb): therefore, a higher sensitivity is required.

Recently, Professor Jin and his colleagues investigated ways in which to improve the sensitivity of electrochemical sensors. One way in which this was achieved was by using UV illumination to enhance the electrochemical reaction. Interestingly, the performance of the illuminated sensor was not affected by low operating temperatures and humidity changes. Furthermore, illumination regulation of the electrochemical reaction resulted in a two-fold increase in the sensing magnitude and sensitivity and these sensors were able to identify more gases (e.g. six VOCs by using three sensors) compared to non-illuminated sensors. These exciting findings suggest that the light-regulated electrochemical reaction used in these studies could be used for designing compact and highly effective VOC sensing devices for clinical applications.



(a) a light-regulated YSZ-based sensor array composed of three kinds of sensing electrodes (SE) and Mn-based reference electrode (RE); (b) response patterns of the sensor array (operated at light off and/ or on) towards six kinds of VOCs plotted in the form of a heat map; (c) principle component analysis (PCA) scheme obtained with the sensor array operated at light off and/or on.

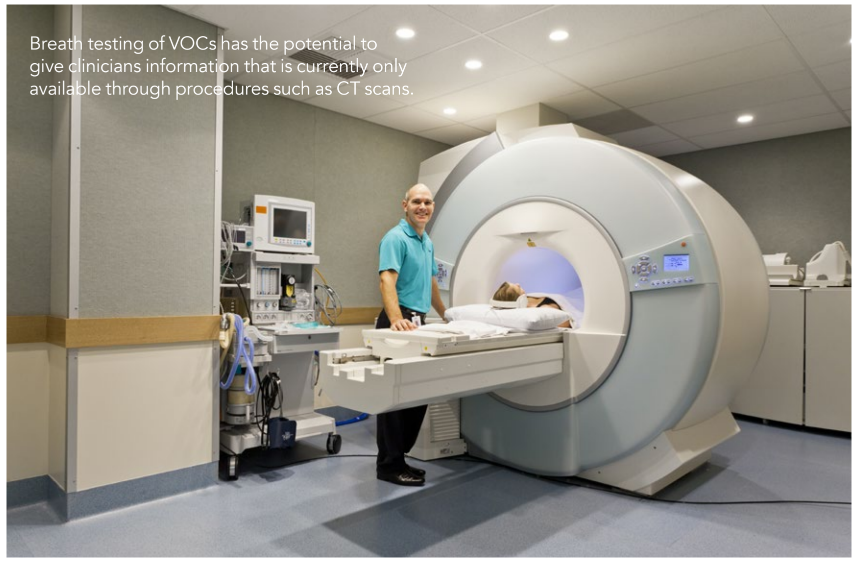
Tools based on VOCs have the potential to identify cancers early on.

FUTURE CHALLENGES

Invested in by Qi Diagnostics Ltd, Professor Jin and his team have designed revolutionary diagnostic tools based on VOCs that have the potential to identify cancers early on, increasing the chance of survival. However, there are many challenges that must be overcome before these VOC sensors can be clinically used. Currently, many scientists focus on materials science and investigating novel algorithms. However, it is of vital importance that more researchers focus their efforts on developing novel sensing devices and improve their knowledge of the complex relationship between VOC biomarkers and the disease in question.

Perhaps the most significant challenge that Professor Jin and his team must overcome is the lack of informative and detailed databases. Although Professor Jin and Qi Diagnostics Ltd are devoting more effort to this research, creating such a database will be extremely time-consuming, expensive and complex as confounding factors such as gender, age and living habits may affect the accuracy of the breath test. Therefore, these databases must consider these variables. However, in the future it may be easier to determine how these variables affect VOC composition in breath samples, improving the accuracy of the results. For example, using a combination of Artificial Intelligence, big data analysis, descriptive analytics (measuring what has happened), predictive analytics (using the descriptive data to predict likely outcomes) and prescriptive analytics could help.

Overall, it is essential that different researchers, specialising in different disciplines, collaborate to design effective diagnostic tools that can accurately diagnose early-stage diseases, saving countless lives.



Breath testing of VOCs has the potential to give clinicians information that is currently only available through procedures such as CT scans.

Behind the Research

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Research Objectives

Professor Jin aims to develop a novel technology that can identify concerned diseases, including cancer, based on the profiling of volatile organic compounds (VOCs) found in patients' breath.

Detail

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Bio

Han Jin received his PhD from Kyushu University (Japan) and furthered his postdoctoral research in Technion (Israel). Currently, he is an Associate Professor in Ningbo University and Ningbo Institute of Material Technology and Engineering (Chinese Academy of Science) as well as the key member of "3315 Plan on Innovation Team" (Ningbo).

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Collaborators

- Hong Kong Qi Diagnostic Limited Company
- Shanghai No. 6 People's Hospital, Department of respiration
- Ningbo Institute of Material Technology and Engineering (Chinese Academy of Science), Prof. Weijie Song's Group
- Tongji University, Prof. Yao Qing's Group
- Gungxi University, Prof. Yinghui Wang's Group
- Wuhan University of Technology, Prof. Yueli Liu's Group
- Shanghai Jiaotong University, Prof. Daxiang Cui's Group
- Technion-Israel Institute of Technology, Prof. Hossam Haick's Group

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Personal Response

What is the benefit of using volatile organic compound detection devices over current diagnostic tools?

" Studies have shown that volatile organic compounds (VOCs) exhaled from cancerous patients exhibit specific distinguishable patterns. Therefore, profiling VOCs by breath testing has the potential of diagnosing cancer at a very early stage. Besides, breath testing with portable devices is comparably simple, and its results may be interpreted rapidly and automatically, making it suitable for cost-effective screening of large populations in a non-invasive way. Our design of light-regulated electrochemical sensors means breath testing could become more accurate and cheaper, particularly suitable for household healthcare. "