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Editorial

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Exhaled gas detection for medical diagnosis: can it be made a tool for self-screening?

Abstract

Exhaled gases and volatile compounds have relation with health status of the human body. Detection of these compounds can be used as a non-invasive tool for early diagnosis of diseases such as cancer. If reliable low cost point-of-care devices that can selectively respond to these gases and organic compounds are developed, normal people can use them for routine self-examinations and get an early warning on the occurrence of fatal diseases. This editorial gives an overview of the relevance of exhaled gas detection in medical diagnosis.

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Abbreviations: VOCs, Volatile Organic Compounds; NO, Nitric Oxide; ROS, Reactive Oxygen Species; PUFA, Polyunsaturated Fatty Acids; PPM, Parts Per Million; PPB, Parts Per Billion; GCMS, Gas Chromatography Mass Spectrometry

Editorial

"A 44-year-old woman was referred to our pigmented lesion clinic with a lesion on her left thigh. This was excised and histological examination confirmed malignant melanoma……. The patient first became aware of the lesion because her dog would constantly sniff at it", wrote Williams and Pembroke in their letter to the Editor of 'The Lancet' in 1989 .[1] Having been excited by this experience, the authors suggested the use of dogs in cancer diagnosis. A few other incidents were also reported thereafter. It was apparent that the dogs sensed the presence of malignant tissues through odor. The dogs are attracted either by a change in the strength of the odor or a new odor that the disease creates within the body and then releases. A number of studies relate volatile organic compounds (VOCs) released from the human body to the presence of different kinds to cancers .[2,3] There are now companies that train dogs to sniff out certain specific types of cancers .[4]

A short while before the letter from Williams and Pembroke was published, nitric oxide (NO) had been identified as an endothelial cell derived relaxing factor produced and released from arteries and veins.[5] Later studies linked nitric oxide in breath gas to airway diseases like allergic asthma .[6] An exhaled nitric oxide test (eNO) is often used in clinics for asthma diagnosis. It is now known that concentrations of various gases including VOCs, NO, hydrogen, methane etc. in the exhaled gas can be used to differentiate the healthy functioning of the human body from abnormal activities caused by cancer, digestive problems, cardiovascular diseases, diabetes, tuberculosis etc. .[7,8]

Different gases and volatile compounds in the body may have different causes or origination. For example, the VOC concentrations in the body are altered, or new VOCs are generated, to adjust the body's chemistry when it has metabolic diseases like cancer.[2] Oxidative stress and induction of cytochrome p-450 are considered two vital risk factors for cancer development. The oxidative stress in the body is related to the general equilibrium between formation and deactivation of reactive oxygen species (ROS) and free radicals. As part of the cellular process in the mitochondria, the cell produces ROS that can attack different molecules in the body like polyunsaturated fatty acids (PUFA) and proteins. During oxidative stress, ROS and free radicals are excreted from the mitochondria in the cell, generating volatile alkanes. Alternate hypotheses were also proposed to explain the biochemical origin of exhaled breath VOCs and their link with cancer.[2,9] More than 3000 VOCs have been reported to be related to different types of cancers .[2,10]

We, thus, have ample information about many of the exhaled compounds and their connections to various diseases. How can we use this knowledge to improve the lives of people? Let's take the case of cancer. Per the American Cancer Society statistics, more than five hundred thousand deaths from different types of cancers were predicted in the United States for the year 2015 alone. One reason for the high mortality rate is the detection after cancer becomes metastatic. In many cases cancer does not give any noticeable symptoms at the early stages and by the time it is diagnosed it might have spread to vital organs. For example, the breast cancer can be considered harmless if the lump is confined within the breast. However, lumps cannot be detected by mammography till the size reaches as a few millimeters. Lack of routine medical examinations often leaves these lumps undetected and the disease spreads to vital organs. Socio-economic, cultural and religious factors could make people reluctant to having routine medical examinations or to consulting a doctor when initial symptoms appear. Studies showed that the VOCs appear in breath in the early stages of malignant cell growth. Thus, the detection of endogenously produced VOC could be used for early diagnosis of cancer. Availability of non-invasive point of care (POC) devices could change the perception of people and perhaps motivate them to consult the doctors when indications appear from VOC detectors.

Although the gases and volatile compounds could be released through skin, urine, blood, saliva etc. also, breath analysis is the most widely used methodology. Breath contains ~5 vol. % CO2, ~ 5 vol. % water vapor and traces of volatile organics and other gases such as hydrogen, nitric oxide and carbon monoxide. The concentrations of these trace gases/organic compounds are generally in the range of parts per million (ppm) or parts per billion (ppb) level. Analytical methods such as gas chromatography mass spectrometry (GCMS) are used to identify them and determine their concentrations. These analytical methods are expensive and it requires experts to analyze the results. Furthermore, people have to make visits to clinics/labs to have such measurements done. For the average person to use exhaled gas detection as a self-screening method for assessing their health status, the device should be simple to use and affordable.

Chemical sensors are such simple devices that could be used to detect permanent gases and volatiles released from the body through

breath or skin and give indications when the body changes from a healthy state to a diseased state. Efforts are being made by various research groups to develop such devices working on different principles for non-invasive early detection as well as monitoring of various diseases and health problems.[11-14] For example, clinical tests done using titania nanotube array ultrahigh sensitivity chemiresistive hydrogen sensors on patients having lactase deficiency indicated correlation between lactose intolerance and transcutaneous and breath hydrogen gas concentrations.[13,14] The chemical sensors do not offer the accuracy or precision that a GCMS provides. Lack of specificity (or selectivity) is a problem in many such devices. Nevertheless, these devices can still be used for an early indication to prompt people to consult a doctor and discuss the issue. Increased hospital visits as a result of inaccurate information from these devices can be a potential problem. Such concerns can be minimized upon developing reliable sensors or multifunctional sensor arrays. Although low cost chemical sensors can be developed, the technology has not yet been successful in yielding such reliable devices commercially. Let us hope that the new generation devices based on nanotechnology will enable the development of such highly reliable devices and help reduce the casualties from lethal diseases.

Acknowledgments

None.

Conflicts of interest

None.

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