

EDITORIAL

BREATH BIOPSY: A PROMISING DIAGNOSTIC TOOL

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Breath biopsy or breath analysis is a relatively recent field of research with much promise in scientific and clinical studies. Breath contains endogenously produced volatile organic compounds (VOCs) resulting from metabolites. The principle behind breath biopsy lies in the fact that many diseases produce specific metabolic changes in the body that result in the release of unique VOCs. These compounds can be detected and quantified by using advanced analytical techniques, such as gas chromatography-mass spectrometry (GC-MS) and selected ion flow tube mass spectrometry (SIFT-MS) etc. More than 2000 VOCs have been detected in the exhaled breath. These VOCs may be related to hydrocarbons, alcohols, aldehydes, ketones, esters, ethers, carboxylic acids, heterocyclic hydrocarbons, aromatic compounds, nitriles, sulfides and terpenoids. VOCs in exhaled breath may be endogenous or exogenous. Endogenous VOCs can diagnose about twenty-five diseases including lung cancer, breast cancer, diabetes, COPD, and even COVID-19 by analysing the breath of patients.

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Bad smelling breath or halitosis can result from several causes. While poor oral hygiene is the most common cause of halitosis, it is not the only one. Smoking, alcoholic drinks, diabetes, infections in nose, throat or lungs, sinusitis, tonsil stones, liver or kidney disease or head and neck cancers, may cause bad breath.¹ Exhaled breath is tested for many conditions. The police used to smell the mouth of a suspected drunkard driver and then the breath alcohol test is used to measure the amount of alcohol in the blood by testing exhaled air by an electronic device.² Another well known breath test is called '*H. pylori* breath test or urea breath test' that is still used to detect *H. pylori* infection which causes peptic ulcer.³ Acetone breath of liver disease is well known to physicians and residents and interns since long.

Breath biopsy or breath analysis is a relatively recent field of research with much promise in scientific and clinical studies. Breath contains endogenously produced volatile organic compounds (VOCs) resulting from metabolites of ingested precursors, gut and air-passage bacteria or environmental contacts, etc. Numerous recent studies have suggested changes in breath composition during the course of many diseases, and breath analysis may lead to the diagnosis of such diseases. Identifying specific VOCs and applying them as disease-specific biomarkers to obtain accurate, reproducible, and fast disease diagnosis could serve as an alternative to traditional invasive diagnostic methods.⁴ Breath biopsy or breath analysis is a non-invasive method that has gained significant attention in recent years due to its potential for early disease detection, including various types of cancers and respiratory conditions.

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by using advanced analytical techniques, such as gas chromatography-mass spectrometry (GC-MS) and selected ion flow tube mass spectrometry (SIFT-MS). GC-MS combines the separation capabilities of gas chromatography with the identification power of mass spectrometry. In this method, a sample is vaporized and carried through a column where different compounds are separated based on their volatility and interaction with the column material. As compounds exit the column, they are detected and analysed by mass spectrometry, allowing for the determination of their molecular weights and structures. This technique is highly sensitive and can detect trace levels of VOCs, making it valuable in clinical diagnostics and environmental monitoring.⁵

On the other hand, SIFT-MS is a more recent technique that enables real-time analysis of VOCs. SIFT-MS utilises an extremely soft ionisation process which greatly simplifies the resulting spectra and thereby facilitates the analysis of complex mixtures of gases, such as human breath.⁶ Many commercially available instruments analyse gas-phase samples. Samples need no pre-treatment. Results are in real time to pptv (parts per trillion by volume) level. Diverse chemical species are quantified simultaneously. It utilizes a flow tube where ions are generated and selected based on their mass-to-charge ratio. These ions interact with the VOCs present in the sample, leading to the production of characteristic product ions that can be quantified. SIFT-MS is particularly advantageous for its rapid analysis and the ability to provide quantitative results without extensive sample preparation. Both techniques, GC-MS and SIFT-MS, are crucial in advancing our understanding of VOCs and their implications in health and environmental science.

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hydrocarbons, alcohols, aldehydes, ketones, esters, ethers, carboxylic acids, heterocyclic hydrocarbons, aromatic compounds, nitriles, sulfides and terpenoids. VOCs in exhaled breath may be endogenous or exogenous. Endogenously created VOCs comprise high vapor pressure byproducts of normal or pathophysiological metabolic pathways, as well as of microbiome metabolism. Exogenously originated VOCs are correlated with the environment and the habits of the person. Exogenous VOCs are related with cleaning fluids, personal care products, plastic-related VOCs, blazes, or air pollution due to industrial/transport gas emissions and they enter human organism through extended inhalation and are excreted via exhaled breath. Concentration differences for some exhaled VOCs could potentially be associated with an abnormal condition of the body, as the metabolic processes producing the VOCs are altered in a distinctive way by different diseases. In fact, VOC pattern or ‘breathprint’, consists of the signature of a specific disease, correlating with the underlying pathophysiology; this pattern should therefore be recognized so as to achieve disease diagnosis.⁷

Various volatile organic compounds (VOCs) have been identified as potential biomarkers. In breast cancer, compounds such as 2-butanone, isoprene, and toluene have been linked to malignant processes in breast tissue. Key VOCs associated with lung cancer include acetone, isoprene, and benzene. In tuberculosis, notable VOCs include 2-pentanone, isoprene, and various aldehydes. In diabetes, VOCs detected include acetone and isoprene. Acetaldehyde, isoprene, and various aldehydes are major VOCs detected in Chronic Obstructive Pulmonary Disease. A FeNO test measures the amount of nitric oxide, a byproduct of inflammation, in the breath. About twenty-five diseases including lung cancer, breast cancer, diabetes, COPD, kidney and liver

diseases and even COVID-19 can be diagnosed by analysing the breath of patients.⁸

Breath biopsy is a rapid, non-invasive diagnostic tool that detects volatile organic compounds (VOCs) present in exhaled breath, which are biomarkers for various diseases. With the ongoing developments in the field and real-data analysis, breath biopsy or breath analysis holds promise to become a useful screening tool that will not only aid but also improve existing diagnoses for several diseases and disorders. Large studies in real-world screening settings, with a focus on standardizing the breath collection protocol and validation in different and independent population samples, should be carried out to accelerate the use of breath analysis for disease diagnosis.

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