Finding aroma clues in the human breath to diagnose diseases

History of human odor analysis in disease diagnosis

The use of the sense of smell as an indicator of human disease probably originated with Hippocrates (circa 400 BC). Early medical practitioners recognized that the presence of human diseases changed the odors released from the body and breath. Physicians once relied heavily on their sense of smell to provide useful clues for identifying the causes of human ailments. Descriptive terms were used to describe odors (or aromas) associated with specific human diseases and disorders (Fig. 1). This odor information was a valuable tool for physicians to assess patients' conditions and help diagnose diseases centuries before modern analytical instruments became available for this purpose. Odor recognition by human smell was used by doctors (with diminishing emphasis) up until the early 1980's, just before electronic noses (e-noses) came on the scene.

Disease type	Body source	Descriptive aroma (odors)
Diabetes	Breath	Fingernail polish remover
Fetor hepaticus	Breath	Newly-mown clover
Hyperaminoaciduria	Infant's skin	Dried malt or hops
Hypermethioninemia	Infant's breath	Boiled cabbage
Isovaleric acidemia	Skin, sweat, breath	Sweaty feet
Liver failure	Breath	Musty fish
Maple syrup urine disease	Sweat, urine, ear wax	Maple syrup
Pseudomonas infection	Skin, sweat	Grape juice
Rubella	Sweat	Freshly plucked feathers
Smallpox	Skin	Pox stench
Trimethylaminuria	Skin, urine	Fishy
Tuberculosis lymphadenitis	Skin	Stale beer
Typhoid	Skin	Freshly-baked brown bread
Yellow fever	Skin	Butcher's shop

Fig. 1. Aroma descriptions for diagnoses of specific diseases.

Analysis of disease biomarkers in human breath

Analysis of expired human breath is particularly valuable because it can be monitored noninvasively. Diseases of the human body arise from different mechanisms, such as from metabolic disorders, exposure to toxins, and through microbial disease-causing agents that alter normal physiological processes of the human body. These mechanisms of disease result in the production of unique mixtures of abnormal chemicals (biomarker metabolites) in the body that are characteristic of specific diseases. Regardless of where these abnormal chemicals are produced or originate in the body, they are picked up by the circulatory system and eventually expelled out through the lungs. Consequently, analysis of the complex gaseous mixtures of volatile organic compounds (VOCs) released from the lungs through the breath provide very useful diagnostic

clues to the presence of disease processes occurring in the body (Fig. 2).

Early disease diagnoses using e-noses

Electronic nose (e-nose) devices are relatively new gas-detection technologies adapted for use as medical tools for various clinical applications. These small, simple and portable devices are particularly useful for the noninvasive early detection of human diseases. A major advantage of using e-noses, such as for disease diagnoses by human breath analysis, is that they provide quicker, more efficient diagnostic results and cause less stress, anxiety, and no pain to patients.

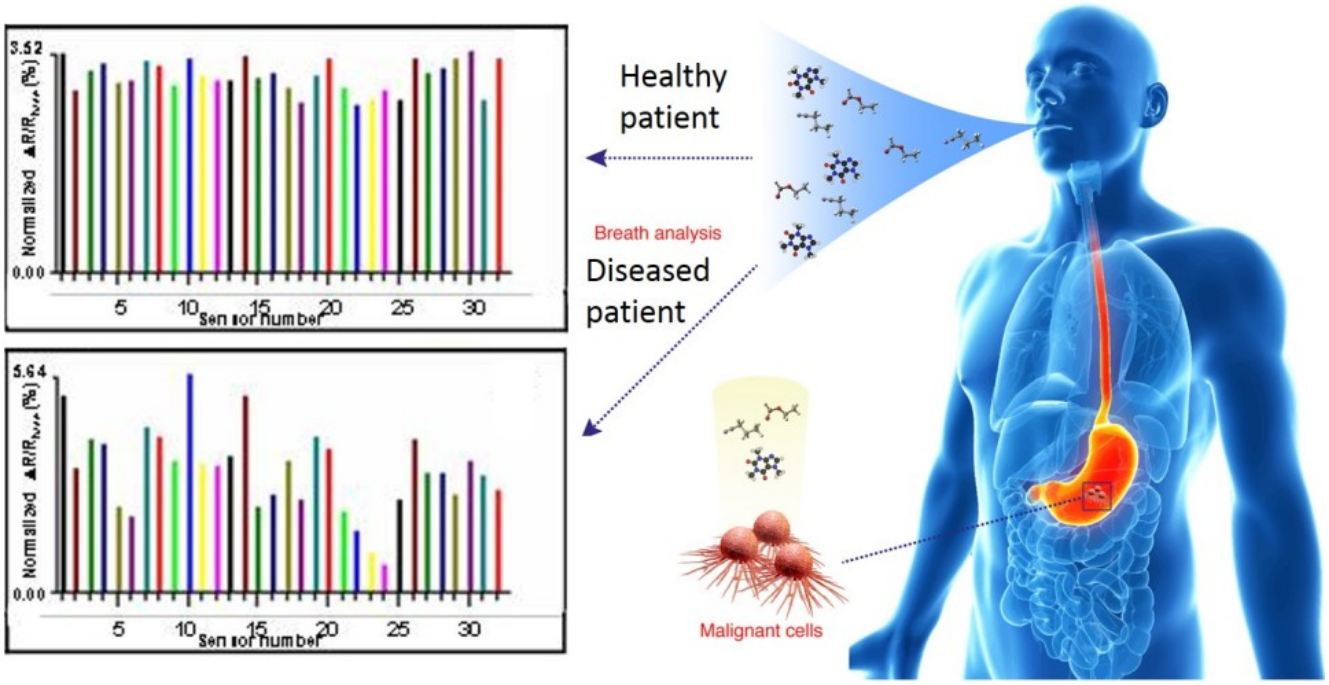

Fig. 2. E-nose analysis of volatile biomarker metabolites in the human breath

Importance of this review: why use e-noses and biomarkers in early disease detection?

Conventional methods utilized for clinical diagnostics are very expensive, time-consuming, and often result in delays in diagnoses and treatments for human diseases. Electronic-nose devices are not yet widely used in clinical practice, but significant progress is currently underway. The benefits of early detection using e-noses, allowing early treatments of diseases, are obvious as prognoses are greatly improved. Many patients often avoid regular prophylactic checkups and early disease screenings because many current methods (e.g., colonoscopies, X-ray mammographies, tissue biopsies, etc.) still involve invasive, painful, or expensive procedures. Many of these methods also present risks of significant negative side effects and often are sufficiently painful to discourage patients from participating in preemptive, prophylactic disease-screening procedures. Recent advancements in the use of e-nose devices to analyze human breath profiles for the presence of

specific volatile metabolites (unique biomarkers of specific human diseases), is providing the potential for these new noninvasive tools to facilitate point-of-care clinical disease diagnoses. This exciting new area of e-nose disease detection and diagnosis promises to yield much faster and earlier detection of human diseases, allowing earlier and more effective treatments with more rapid patient recovery. This review article provides a brief summary of recent progress in the development of e-nose applications and technologies for clinical examinations through human breath analysis.

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