



## Electronic-nose Devices – Potential for Noninvasive Early Disease-Detection Applications

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### Editorial

Significant progress in the development of portable electronic devices is showing considerable promise to facilitate clinical diagnostic processes. The increasing global trend of shifts in healthcare policies and priorities toward shortening and improving the effectiveness of diagnostic procedures by utilizing non-invasive methods should provide multiple benefits of increasing treatment efficiency and lowering healthcare costs while accelerating the speed and accuracy of diagnoses. The results of this improved approach will lead to earlier treatments that ultimately result in more favorable prognoses, more rapid patient recovery, and shorter hospital stays. Electronic-nose (e-nose) and similar devices have been at the forefront of recent clinical research focused on the development of new potential diagnostic tools to aid in disease detection and etiology for point-of-care testing (POCT). E-noses are artificial gas-sensing systems, usually containing chemical cross-reactive multi-sensor arrays capable of characterizing the aroma patterns of volatile organic compounds (VOCs), which utilize pattern-recognition algorithms for aroma classification [1]. The most useful e-nose devices are lightweight, portable handheld tools that provide real-time data. These low-cost instruments have the potential to revolutionize many diagnostic, clinical procedures used to detect a multitude of human diseases with diverse etiologies. Numerous types of e-nose devices have been developed, based on different operational mechanisms, offering varying capabilities, sensitivities, response times, and advantages for different clinical applications [2]. Currently available e-nose technologies most commonly used for clinical practice include carbon nanofiber (CNF), conducting polymer (CP), metal oxide semiconductor (MOS), polymer carbon black composite (PCBC), quartz crystal microbalance (QCM), and surface acoustic wave (SAW) devices.

Many conventional diagnostic tests involve invasive or painful procedures that often discourage patients from seeking preemptive early disease-detection screenings. Other tests require time-consuming or expensive and sophisticated laboratory chemical tests that often delay the availability of results for diagnostic evaluation and preclude early disease treatments, potentially putting patients at greater risk with less favorable prognoses [3-5]. This is particularly true for acute infectious diseases, caused by systemic infections (sepsis) by virulent moribund pathogens with short incubation periods which produce rapid onset of tissue damage, organ degeneration, and critical life-threatening conditions.

E-nose devices are particularly useful for noninvasive early detection of diseases by sensing specific mixtures of VOCs that serve as effective chemical biomarkers of disease. Multi-sensor arrays of portable e-nose instruments provide unique VOC-metabolite signatures for specific diseases, allowing simpler diagnoses than by nuclear magnetic resonance (NMR) metabolomics, selected ion flow tube-mass spectrometry (SIFT-MS), proton transfer reaction-mass spectrometry (PTR-MS) or gas chromatography-mass spectrometry (GC-MS) methods that often require extensive data manipulations, intensive analyses and complex modeling before diagnostic interpretations are possible. E-noses often yield faster results and provide earlier detections of human diseases, allowing earlier, more effective treatments and consequently more rapid patient recovery [6].

Electronic-nose devices offer many additional advantages over conventional diagnostic tools such as low operating costs, ease of operation without extensive training required, rapid results and response times, good precision, greater portability and flexibility for clinical or field use, and high adaptability for specialized applications [7,8]. These versatile gas-sensing devices also provide a means for rapidly checking patient identity and confirming physiological status prior to administering drugs, invasive surgical procedures, or other irreversible treatments [2].

E-nose analysis of headspace volatiles from diagnostic air samples, including expired breath, body fluids, and skin, provides effective means for detecting many diseases noninvasively [7,9].

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Through e-nose breath analysis, the overall health of a patient may be monitored continuously to determine changes in physiological (healthy or diseased) states based on the presence of unique breath VOC-mixtures, corresponding to diagnostic e-nose smellprint-signatures (in reference libraries), previously associated with specific diseases or conditions. Breath monitoring of patients by e-nose analyses following treatments also may provide indications of the effectiveness of treatments, recovery from disease conditions, wound and graft healing, and indications of prognoses going forward.

The range of types and categories of diseases detectable with e-nose instruments include various respiratory diseases, numerous types of cancers, metabolic disorders, urinary- and intestinal-tract infections, and related physiological monitoring of diseases (progress and recovery) [7,10]. Some more recent advances include e-nose detection of patient's drug use, exposure to hazardous gases and toxins, organ dysfunctions and failures, and physiological abnormalities [2]. E-nose devices also have been used in forensic medicine to determine postmortem cause and time of death [11].

Metabolic fingerprinting of many major diseases has been accomplished through the identification of key VOC biomarker metabolites. A large number of different specific types and classes of chemical disease biomarkers have been identified. Different categories of chemical biomarkers, associated with e-nose smellprint signatures, provide indicators of different types of diseases. Disease biomarker signatures may be categorized as indicators of abiotic diseases (including genetic and metabolic diseases), infectious diseases, and non-infectious diseases. Additional disease biomarker signatures have been classified into subcategories such as disease-predisposition biomarkers, pathogen-specific biomarkers, and location or organ-specific biomarkers (e.g. gut-microflora) that may be the basis of application-specific or disease-specific e-nose detection [12-16].

The rapidity and accuracy of diagnoses based e-nose detection of disease biomarker mixtures are greatly improved by the use of application-specific e-nose databases, containing breathprints or smellprints (VOC biomarker disease-signatures) for specific sets of closely related diseases. This approach greatly reduces the possibility of false positive, false negative and unknown diagnostic determinations. The e-nose can be programmed to utilize a wide range of application-specific reference databases, depending on the diagnostic applications required.

The improved universal standardization of portable e-nose instruments and protocols for different disease-detection applications should speed up the development and implementation of these devices for routine clinical diagnostic use. The eventual increased use of e-nose instruments for clinical diagnostic applications will not necessarily preclude the use or replacement of conventional diagnostic methods, but they will likely provide additional tools for improving efficiency and earlier indications of probable diagnoses. New-generation dual-technology e-nose instruments are now being developed that provide headspace aroma signatures from an e-nose sensor array as well as chemical analysis data for component identifications [2]. These new advanced e-noses may be used in combination with other physiological sensor devices to aid in disease diagnosis and classification [17].

## Conclusion

Current clinical research with e-nose devices is achieving significant progress in the development of new biomedical

applications that should help accelerate many clinical operations and procedures. Emerging electronic-nose technologies offer great potential for numerous POCT diagnostic applications in early disease detection with many advantages over conventional invasive, painful and time-consuming tests that discourage patients from seeking preemptive disease-screening procedures. Ongoing research and clinical trials are providing application-specific protocols and efficacy data that should eventually allow e-nose devices to be integrated as effective tools to enhance disease-diagnostic procedures in routine clinical practice. The greater potential cost-effectiveness of e-nose based early clinical disease diagnosis, by means of real-time detection of VOC-disease signatures, offers new alternative approaches to cutting diagnostic costs and facilitate clinical decision-making. E-nose devices ultimately may play a role in offering a more personalized approach to disease detection and therapy in the future when used in combination with other early disease-screening procedures for patients with predispositions to specific diseases.

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