

Review

The Screening and Diagnosis Technologies Towards Pneumoconiosis: From Imaging Analysis to E-Noses

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Abstract: Pneumoconiosis, as the most widely distributed occupational disease globally, poses serious health and social hazards. Its diagnostic techniques have evolved from conventional imaging and computer-assisted analysis to emerging sensor strategies covering biomarker analysis, routine breath sensing, integrated electronic nose (E-nose), etc. All of them both have special advantages and face shortcomings or challenges in practical application. In recent years, the emergence of advanced data analysis technologies, including artificial intelligence (AI), has provided opportunities for large-scale screening of pneumoconiosis. On the basis of a deep analysis of the characteristics of the technologies for screening and diagnosis of pneumoconiosis, this paper comprehensively and systematically reviews the current development of these technologies, especially focusing on the research progress of emerging sensor technologies, and provides a forecast for their future development.

Keywords: occupational disease; pneumoconiosis; diagnostic technique; early screening; imaging; breath analysis; E-nose



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1. Introduction

As one of the most common occupational diseases worldwide, pneumoconiosis has an extremely wide range of occupational exposures. In various types of dust-filled workplaces, workers may suffer from more than 10 types of pneumoconiosis, including coal workers' pneumoconiosis and silicosis. It is a chronic preventable but currently incurable interstitial occupational lung disease that can lead to serious and long-term health and social problems [1–3]. The situation is particularly concerning because the disease can continue to develop even after exposure to dust has stopped. Moreover, it can trigger or worsen other comorbidities or complications, particularly chronic obstructive pulmonary disease (COPD) and tuberculosis (TB) [4,5]. Regarding COPD, individuals with pneumoconiosis are at higher risk of developing this condition compared to the general population due to occupational exposure and subsequent recurrent respiratory infections. The lung damage caused by pneumoconiosis further impairs the normal structure and function of airways and alveoli, exacerbating the characteristic airflow limitation in COPD. The coexistence of pneumoconiosis and COPD often leads to more severe respiratory symptoms, accelerated decline in lung function, and increased risk

of respiratory failure. TB represents another significant comorbidity because the immunological changes in the lungs induced by pneumoconiosis increase susceptibility to Mycobacterium TB infection. The compromised lung tissue and reduced immunity create a favorable environment for the growth and spread of TB bacilli. This coexistence creates a vicious cycle: pneumoconiosis increases the risk of TB infection, while TB exacerbates the existing lung damage caused by pneumoconiosis.

In addition, as the middle-aged and elderly male labor force is the main affected group, and there is a trend of younger onset, the burden and harm to families and society are even more severe. The currently widely accepted pathogenesis is mainly that after the inhalable dust enters the lungs and is phagocytosed by macrophages, it cannot be expelled and digested, leading to retention and causing lesions mainly characterized by inflammation and diffuse fibrosis of lung tissue [6]. Due to the high morbidity and disability rate, and the lack of effective treatment and cure methods, as well as the diverse and complex manifestations of the lesions, early screening and diagnosis have long been the focus and difficulty of occupational disease research and are also the key to early detection and complete control of the patient's condition. The World Health Organization (WHO) and the International Labour Organization (ILO) jointly established the Joint Commission on Occupational Health. In 1995, this commission launched the "International Plan for the Global Elimination of Silicosis". The aim of this plan was to significantly reduce the incidence rate of pneumoconiosis by 2010 and completely eliminate pneumoconiosis by 2030 [7]. However, the achievement of this ultimate goal may now need to be postponed considerably, especially given the different stages of development in different countries.

As an occupational disease, pneumoconiosis is diagnosed based on both medical and policy considerations, making it an attribution diagnosis. Over the past several decades, considerable advancements have been achieved in this area, but many challenges persist. Previously, there have been some reviews focusing on the progress of imaging technologies used in this field [8–10]. Unlike them, this paper offers a systematic evaluation of the development situation of existing technologies from traditional imaging to pulmonary function tests (PFTs), tissue invasion, etc., as well as of advanced sensing technologies for pneumoconiosis markers (from biomarking to routine breath sensing and integrated E-noses) (Figure 1). Lastly, this paper provides a forward-looking perspective, including the optimization direction of existing technologies, the great value of artificial intelligence (AI)-assisted analysis and diagnosis, etc.

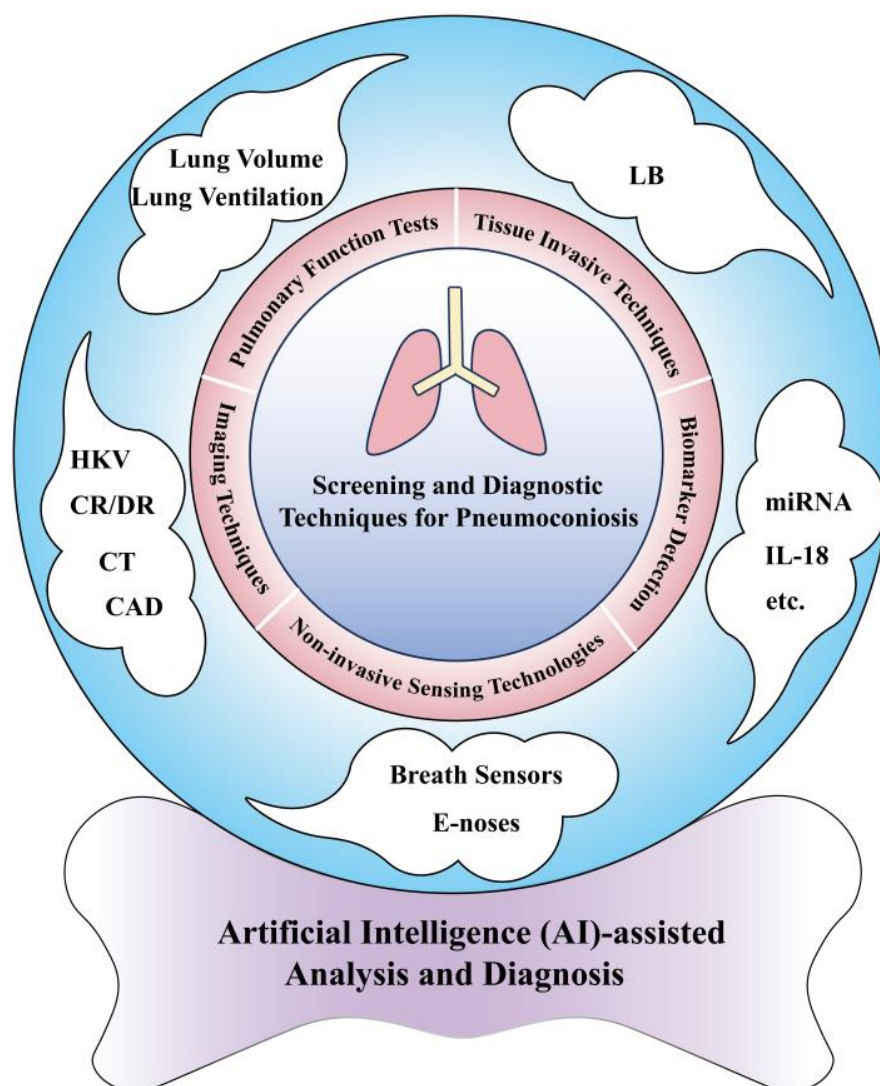


Figure 1. Screening and diagnostic techniques for pneumoconiosis include imaging techniques (high-kV (HKV) X-ray imaging, computed radiography (CR), direct digital radiography (DR), computed tomography (CT), computer-aided diagnosis (CAD)), PFT, tissue-invasive techniques (lung biopsy (LB)), biomarker detection (miRNA, IL-18, etc.), and non-invasive sensing technologies (breath sensors and E-noses).

2. Established Techniques for Screening and Diagnosis of Pneumoconiosis

2.1. Imaging Techniques

2.1.1. HKV X-Ray Imaging

Chest X-ray films utilize the different absorption amounts of X-rays during the process of penetrating the human body, forming grayscale images of lung tissues due to differences in density [11,12]. Then, indicators such as the profusion of small opacities and the distribution in lung regions are used to indirectly display pathological differences. Conventional low-kilovolt chest X-ray films adopt a tube voltage of 60 to 70 kilovolts (kV). Although they can be used for diagnosis, they have relatively low sensitivity to the early manifestations of pneumoconiosis. There are deficiencies, such as the overlap of anterior and posterior chest images, low image density resolution, and unclear display of the internal structures of small and large opacities, which easily lead to misdiagnosis and missed diagnosis [13]. However, HKV chest X-ray films adopt a tube voltage of ≥ 120 kV with an exposure of 5 mAs to 7 mAs. The load on the X-ray tube is low. As the absorption coefficient of substances for X-rays

decreases with the increase in tube voltage, the exposure time is significantly shortened [14]. This results in advantages, such as a reduced radiation dose for the examinees, rich image layers, high image quality, and higher resolution for small opacities and fine tissues. Currently, the chest X-ray of HKV is an authoritative diagnostic method in the national diagnostic standards for pneumoconiosis in China (such as GBZ 70-2015). While HKV chest X-rays optimize lung visualization by reducing bone artifacts and enhancing penetration through thick tissues, the image contrast can be influenced by several factors. These include technical parameters (such as tube current and exposure time), patient-specific conditions (e.g., body habitus), equipment performance, and post-processing techniques [15,16]. These variables may alter the final image quality and contrast, potentially affecting diagnostic accuracy. However, in the differentiation of inflammatory masses, pulmonary tuberculosis, lung abscesses, lung cancer, and so on, it still has an advantage over chest CT [8,17,18].

2.1.2. CR and DR

Compared with HKV, both CR and DR are digital imaging techniques, which combine computer digital image processing technology with traditional X-ray imaging technology and have many similarities and differences in image quality and post-processing [19–22]. CR is an indirect digital imaging method. It requires an imaging plate as an information intermediary and goes through steps such as recording, reading, processing, and displaying image information before an image can be formed. On the other hand, DR is a direct digital imaging method [23–25]. It relies on amorphous selenium flat-panel detectors and analog-to-digital converters to directly convert X-ray information into digital images. Compared with CR, DR has a faster imaging speed, higher image contrast and clarity, richer image layers, and higher density resolution, thus ensuring image quality. Moreover, it exposes the examinees to less radiation, has a faster photography speed, is convenient for quality control, can display images instantly, and is more efficient. Therefore, the DR technique is used for the screening and staging diagnosis of pneumoconiosis [9,26]. However, it is required that image post-processing techniques, such as noise reduction and edge enhancement, are not used because they will lead to problems such as insufficiently clear display of small opacities on chest X-ray films and the loss of some detailed image information. In addition, DR equipment has a high cost and requires a high level of technical expertise. It needs to be operated and maintained by professional technicians to ensure image quality and the normal operation of the equipment [27].

Both CR and DR digital imaging possess powerful post-processing functions. They can change the grayscale by adjusting the window width and window level, which increases the tolerance of the instrument's technical parameter settings, reduces the noise caused by inaccurate selection of exposure conditions, enables the acquisition of more information about different tissues, and allows for direct annotation on the computer. Moreover, they can be remotely transmitted to realize remote expert consultations. However, digital radiography requires different program controls in all aspects, such as photographic imaging, image display, processing, and printing. And the technical differences between the equipment of different manufacturers must also be taken into account [28,29]. Therefore, at present, their application in the diagnosis of pneumoconiosis is still greatly restricted. There is still no unified diagnostic standard formulated, and there is a lack of standard films for imaging classification. Nevertheless, with the continuous improvement of relevant technologies and the continuous reduction in the cost of equipment and its use, it is believed that they will completely replace analog imaging techniques in the future and become the main tools for clinical diagnosis and remote consultations.

2.1.3. CT

CT is a widely used imaging technique that converts X-rays passing through the body into digital signals, which are then processed to generate detailed chest images for lung examination. Compared to traditional X-ray imaging, CT offers higher accuracy and resolution, enabling the detection of subtle pathological changes in the lungs, such as characteristic small opacities, which are critical for early pneumoconiosis diagnosis [30,31]. However, CT has limitations, including exposure to ionizing radiation, the potential toxicity of iodinated contrast agents, increased diagnostic costs, and the lack of standardized evaluation protocols.

High-resolution CT (HRCT) further enhances diagnostic capabilities by providing sub-millimeter slice reconstruction and finer morphological details of lung parenchyma. Despite its improved sensitivity and specificity, HRCT remains an auxiliary tool for early screening and staging due to the non-specificity of imaging changes and clinical symptoms in pneumoconiosis [32,33]. When combined with advanced image post-processing techniques, such as 3D reconstruction and multiplanar reconstruction (MPR), HRCT can improve diagnostic accuracy and aid in the identification of complications. HRCT scanning risks inducing other diseases from radiation exposure. Thus, low-dose CT (LDCT) scanning for pneumoconiosis CT examinations has drawn special attention and is widely used, aiming to balance radiation dose and diagnostic image quality [33]. However, LDCT image quality is lower than routine CT and HRCT, with higher noise and unclear fine structures, potentially affecting lesion detail observation and analysis [34,35]. Dual-energy spectrum CT, another advanced technique, quantifies dust content in lung tissues, improving staging accuracy, though its high technical requirements limit widespread adoption [36]. Thin-section CT with multiplanar reconstruction can clearly show bronchial conditions, local masses, and tissue invasion, helping distinguish stage III pneumoconiosis large opacities from lung cancer masses [37]. But its thin slice thickness and limited range mean more slices, longer scan time, and higher radiation dose when scanning a larger area. Multislice spiral CT (MSCT) scans and acquires data fast, has high temporal and spatial resolution, better image quality, and obvious 3D effects. It is advantageous in observing lung small opacities, overcoming respiratory interference, and detecting other diseases [38]. However, its radiation dose is relatively high, especially in large-range or multiple scans. As CT technology becomes more accessible and affordable, it is expected to play an increasingly routine role in pneumoconiosis diagnosis. Table 1 shows the advantages and limitations of diagnostic techniques such as HKV X-ray imaging, CR, DR, HRCT, LDCT, dual-energy spectrum CT, thin-section CT, and MSCT.

Table 1. Advantages and limitations of different diagnostic techniques.

Diagnostic Techniques	Advantages	Limitations
HKV X-ray Imaging	Short exposure time; less radiation dose	Multifactorial
CR	Indirect digital imaging; reduces the exposure dose	Low image resolution and clarity, slow imaging process vs. DR
DR	Direct digital imaging; high image resolution and clarity, fast imaging process vs. CR	High cost; complex lesions inferior to CT; specialized technical staff required
HRCT	High spatial resolution	Risk of radiation exposure
LDCT	Low radiation dose; universal adoption	Increased image noise vs. HRCT
Dual Energy Spectrum CT	High accuracy	Complicated operation
Thin-Section CT	High clarity	Limited scanning range
MSCT	Fast scanning and data acquisition speed; high temporal and spatial resolution; higher image quality; obvious 3D effects	High radiation dose

2.1.4. CAD

CAD, a technology that assists physicians in interpreting medical data, plays a crucial role in processing and analyzing diverse medical data, particularly in the diagnosis of pneumoconiosis [39]. In recent years, AI, especially deep learning (DL)—a subset of AI that enables autonomous feature learning through computer algorithms—has seen significant advancements in medical imaging research. Since 2012, DL has been increasingly applied to analyze complex medical data, offering improved accuracy over traditional machine learning models that rely on manual feature extraction [40]. Chest X-ray examination is a common preliminary screening method for pneumoconiosis. DL models, trained on large datasets of chest X-ray images (including normal lungs and pneumoconiosis cases at various stages), can automatically identify disease-related features, such as changes in lung texture and the appearance and distribution of nodules. By integrating their expertise with CAD-generated reports, physicians can make more accurate diagnostic decisions. This collaborative approach enhances diagnostic accuracy and efficiency and alleviates the workload on physicians while lowering healthcare costs [41]. In addition to DL, models constructed using algorithms such as decision trees, support vector machines (SVM), and artificial neural networks (ANN) have achieved relatively satisfactory results in the diagnosis of lung diseases [42,43]. For instance, SVM models incorporating multiple biomarkers (e.g., TGF- β 1, CTGF, and PDGF) have shown clinical value in pneumoconiosis screening [44,45]. However, these models face challenges, including limited specificity and small sample sizes.

Despite these advancements, the application of AI in pneumoconiosis diagnosis faces several challenges. The need for large-scale, high-quality datasets and lengthy training cycles limits the widespread adoption of AI technologies [46]. Additionally, the lack of standardized evaluation criteria for CT diagnosis of pneumoconiosis hinders the application of AI in CT image analysis. While AI cannot yet replace manual diagnosis entirely, the “AI + physician” dual-reading mechanism reduces diagnostic errors, alleviates physician workload, and bridges gaps in expertise, particularly benefiting primary hospitals and less experienced physicians [47,48]. However, this approach requires careful validation to avoid over-reliance on AI-generated results.

Recently, the integration of large language models (LLMs) with visual encoders, as demonstrated by PnuemoLLM, has enabled feature extraction and accurate classification of pneumoconiosis from chest X-ray images [49]. Unlike traditional DL methods, LLMs combined with visual encoders can leverage natural language processing capabilities to enhance feature extraction and classification. This approach not only improves diagnostic accuracy but also reduces reliance on extensive training data, offering new perspectives and methods for medical imaging analysis (Figure 2).

2.2. PFT

Since imaging and biomarker techniques cannot assess the functional status of patients, PFT methods, such as lung volume and lung ventilation, have been used as important supplementary approaches to evaluate the disease severity of patients with pneumoconiosis [50,51]. PFT is a universal method for diagnosing airflow limitation, as it can assess a patient’s respiratory function and help physicians understand the lung’s ventilation capacity and the elasticity of lung tissue. Patients with pneumoconiosis may experience symptoms such as dyspnea, shortness of breath, and chest tightness. Therefore, PFTs are used as important supplementary methods for evaluating the severity of pneumoconiosis. They are also important bases for identifying the labor capacity, judging the prognosis, and thus confirming the disability grade [52]. The study by Huang et al. indicates that pulmonary function abnormalities in patients with pneumoconiosis are closely related

to occupational dust exposure, and obstructive and mixed ventilatory dysfunction have been observed in patients [53]. PFT has been used in occupational health examinations for decades and is an important auxiliary diagnostic technique for pneumoconiosis. For dust-exposed workers, a significant decline in pulmonary function test results within the normal range should raise concerns. A limitation of this technique is the lack of a direct and specific correlation between the decline in pulmonary function and the pathological changes of pneumoconiosis, as changes in pulmonary function can be influenced by various factors, such as age, lifestyle habits (e.g., smoking), other pulmonary diseases, and the individual's overall health status.

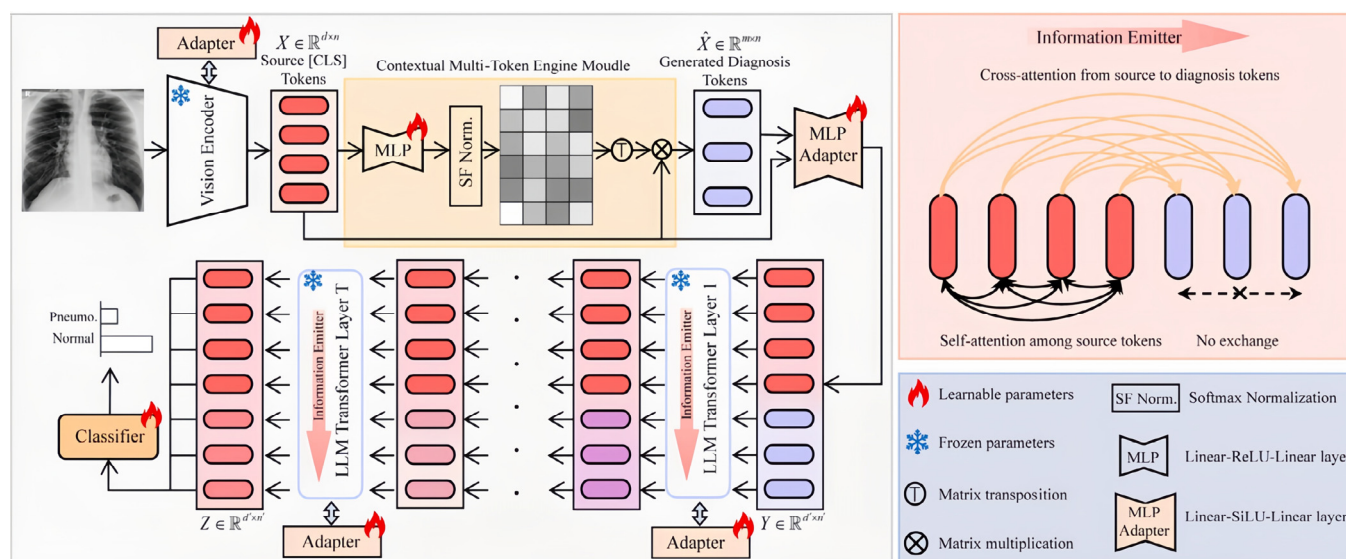


Figure 2. Schematic diagram of the proposed PnuemoLLM for pneumoconiosis diagnosis [49].

2.3. Tissue-Invasive Techniques

LB is a technique to obtain lung tissue samples for pathological examination. When the imaging manifestations are atypical or in the early stage of the development of pneumoconiosis, LB techniques can detect and provide evidence of early pathological changes caused by dust in lung tissue specimens, improving diagnostic accuracy and reducing the rates of misdiagnosis and missed diagnosis [54,55]. Currently, the main LB techniques include surgical lung biopsy (SLB), transbronchial lung biopsy (TBLB), percutaneous lung biopsy (PCLB), transbronchial cryobiopsy (TBCB), etc. Among them, TBCB is the safest and most effective, and it can obtain high-quality large-area tissue specimens, which is suitable for diagnosing diffuse lung diseases [56,57]. LB can provide direct evidence of dust exposure and pathological changes in the lung tissue, thereby assisting in the diagnostic process of pneumoconiosis [58]. However, as lung tissue biopsy is an invasive procedure, it can cause certain degrees of physical trauma [59,60]. Additionally, due to the stringent technical requirements and medical conditions necessary for its performance, it is currently less frequently used in the diagnosis of pneumoconiosis and is not suitable as a routine or population-based screening method for detecting pathological changes.

3. Advanced Sensing Technologies for Screening and Diagnosis of Pneumoconiosis

3.1. Biomarker Detection

Biomarkers, encompassing proteins, genes, metabolites, and other molecular indicators, are critical for identifying structural or functional changes in systems, organs, tissues, cells, and subcellular components [61–63]. In pneumoconiosis, various biomarkers are

associated with its pathogenesis, including inflammatory responses, pulmonary fibrosis, oxidative stress, and immune dysfunction. For instance, neopterin (NPT), an oxidative stress marker released by activated mononuclear macrophages, has been extensively studied. Research shows that serum NPT levels are significantly elevated in silicosis patients compared to healthy controls, highlighting its diagnostic potential [64]. However, biomarkers in serum proteins, cytokines, and apoptosis-related factors may suffer from limited sensitivity and specificity.

Epigenetic mechanisms, such as DNA methylation, histone modification, and miRNA regulation, have also gained attention for their role in maintaining genetic stability while responding to environmental stimuli [65]. Serum-specific miRNAs, which are stable, detectable, and resistant to freeze-thaw cycles, are particularly promising for clinical applications. Studies have linked the expression levels of certain miRNAs (e.g., miR-155 and miR-4516) to the severity of pneumoconiosis, suggesting their utility in early diagnosis [66–68]. However, these studies are often limited by small sample sizes and a lack of exploration into metabolic pathways, necessitating further validation [69]. Additionally, the complexity, cost, and time-intensive nature of current detection technologies hinder their widespread clinical adoption. miRNAs, which serve as early biomarkers for pneumoconiosis, are traditionally detected using methods that suffer from high temperature requirements, contamination risks, fluorescence bleaching, and primer design challenges. To overcome these limitations, surface-enhanced Raman spectroscopy (SERS) has emerged as a groundbreaking alternative. SERS offers advantages such as room-temperature detection, non-contact operation, label-free analysis, and no need for RNA primers, making it an ideal tool for rapid and ultrasensitive miRNA detection. Cui et al. [70] utilized the label-free SERS technique to conduct detection and analysis on miRNA biomarkers related to pneumoconiosis based on 3D gold-coated zinc oxide nanorod arrays (Au-ZnO NRA) (Figure 3a). The miRNA biomarkers (miR-19a, miR-149, miR-146a, and miR-155) used in the study are associated with the occurrence of pneumoconiosis. The presence of these miRNAs in blood and bronchoalveolar lavage fluid has been screened as biomarkers for early pneumoconiosis. Detecting these miRNAs through the label-free SERS method can provide a rapid, reliable, and ultrasensitive alternative approach for the early diagnosis of pneumoconiosis.

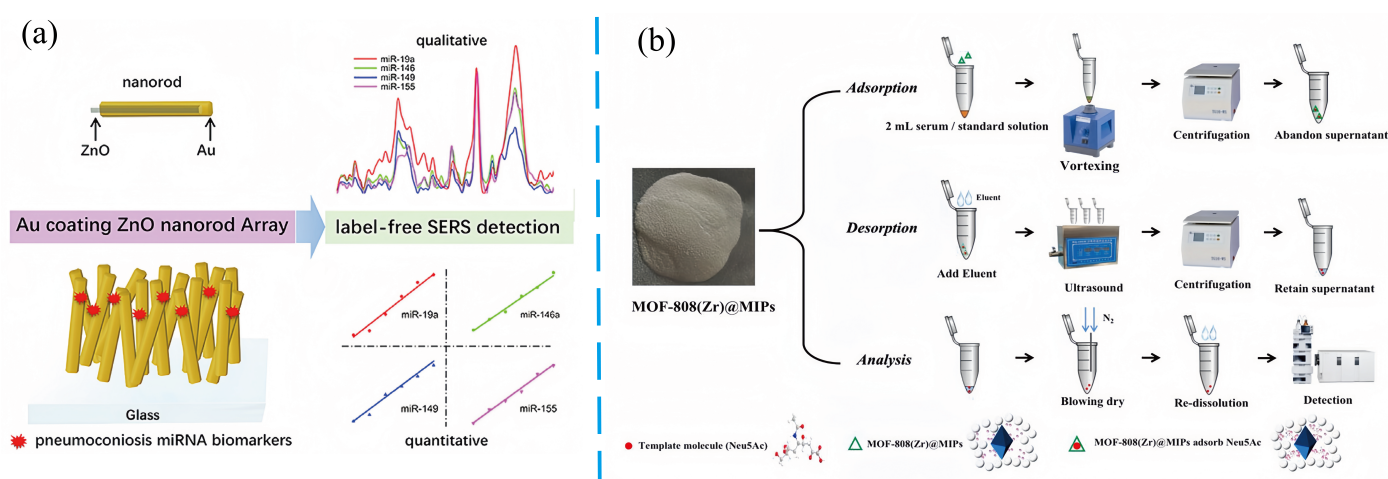


Figure 3. (a) Label-free SERS detection of miRNA [70]. (b) Technical route for Neu5Ac determination [71].

In addition to miRNAs, free N-acetylneuraminic acid (Neu5Ac) in serum can also serve as a biomarker for the early diagnosis of pneumoconiosis (Figure 3b). Lin et al. [71] took metal-organic frameworks (MOFs) as carriers and synthesized a type of molecularly

imprinted polymer (MIPs), which was used for the specific adsorption of free Neu5Ac in human serum. And they adopted liquid chromatography-tandem mass spectrometry (LC-MS/MS) to determine the free Neu5Ac in serum samples. The linear range of this detection system is 50–10,000 ng mL⁻¹. The limit of detection (LOD) and the limit of quantification (LOQ) are 3 and 10 ng mL⁻¹, respectively. Under these conditions, the recovery rates of serum samples are between 83.54% and 92.21%. This method has been successfully applied to the analysis of free Neu5Ac in the serum of pneumoconiosis patients without protein precipitation. Furthermore, Wang et al. [72] applied non-targeted metabolomics and lipidomics techniques to conduct characterization and analysis on the serum of patients with pneumoconiosis and silicosis. Four metabolites were discovered, namely 1,2-dioctanoyl-sn-glycero-3-phosphocholine, phosphatidylcholine (O-18:1/20:1), indole-3-acetamide, and L-homoarginine. In addition, kynurenine, N-tetracosanoylsphingosine 1-phosphate, 5-methoxyethanol, and phosphatidylethanolamine (22:6/18:1) can be used to predict the staging of pneumoconiosis.

Beyond epigenetic markers, other biomarkers, such as pulmonary surfactants, cytokines (e.g., IL-18, TGF-β1), and long non-coding RNAs (e.g., lncRNA-ATB) have been explored. The upregulation of plasma lncRNA-ATB is closely related to the genetic targets in pneumoconiosis. lncRNA-ATB can be activated by TGF-β and is significantly upregulated in patients with pneumoconiosis, closely correlating with the expression levels of TGF-β1 [73]. TGF-β1 plays a key role in the fibrosis process of pneumoconiosis, and its genetic polymorphisms (such as +869T/C) are associated with susceptibility to pneumoconiosis and the degree of fibrosis [74]. As pneumoconiosis progresses, the degree of fibrosis in lung tissues increases, and the expression levels of TGF-β1 usually rise accordingly. Therefore, the upregulation of lncRNA-ATB may be a result of the activation of the TGF-β1 signaling pathway, further promoting the fibrosis process in pneumoconiosis and increasing the disease risk for patients [75]. Similarly, dysregulation of the respiratory microbiome, characterized by altered abundances of specific bacterial genera (e.g., Prevotella, Actinobacillus, Leptotrichia), has been linked to inflammatory and fibrotic indicators in pneumoconiosis. These microbial shifts, alongside elevated levels of inflammatory markers such as TNF-α and hydroxyproline (HYP), provide insights into the dynamic progression of pulmonary lesions and offer potential avenues for microbial-based diagnostic approaches [76,77].

B cell-derived immunoglobulins are routinely used in clinical practice for the diagnosis of coal workers' pneumoconiosis, as they provide crucial information on the humoral immune status. Previous studies have shown that the concentrations of IgA and IgG increase in patients with coal workers' pneumoconiosis, but little is known about the role of serum IgG subclasses in the diagnosis of coal workers' pneumoconiosis [6]. Li et al. [6] found that compared with dust-exposed workers without pneumoconiosis and healthy controls (HCs), the levels of serum IgG1, IgG2, IgM, and IgA were elevated in patients with coal workers' pneumoconiosis. In particular, the IgG2/IgG3 ratio provides a feasible alternative approach for the diagnosis of coal workers' pneumoconiosis. The study involved the biomarkers IgG1, IgG2, IgG3, IgG4, IgA, and IgM (Figure 4a). It analyzed the ROC curves of immunoglobulins in coal workers' pneumoconiosis and dust-exposed workers (Figure 4b), as well as the ratios of IgG1/IgG3 and IgG2/IgG3 (Figure 4c). Additionally, ROC analysis was performed on pulmonary function parameters and the IgG2/IgG3 ratio to distinguish coal workers' pneumoconiosis from workers exposed to dust (Figure 4d). In coal workers' pneumoconiosis patients, the serum concentrations of IgG1, IgG2, IgA, and IgM are increased, while the concentration of IgG3 is decreased. The IgG2/IgG3 ratio shows a certain value in distinguishing between coal workers' pneumoconiosis and dust-exposed workers, with a relatively large area under the curve. Its diagnostic performance is better

than that of IgG1 or IgG2 alone, and there is no significant difference compared with the lung function index FEV1/FVC, suggesting that it can be regarded as a potential biomarker for the diagnosis of coal workers' pneumoconiosis.

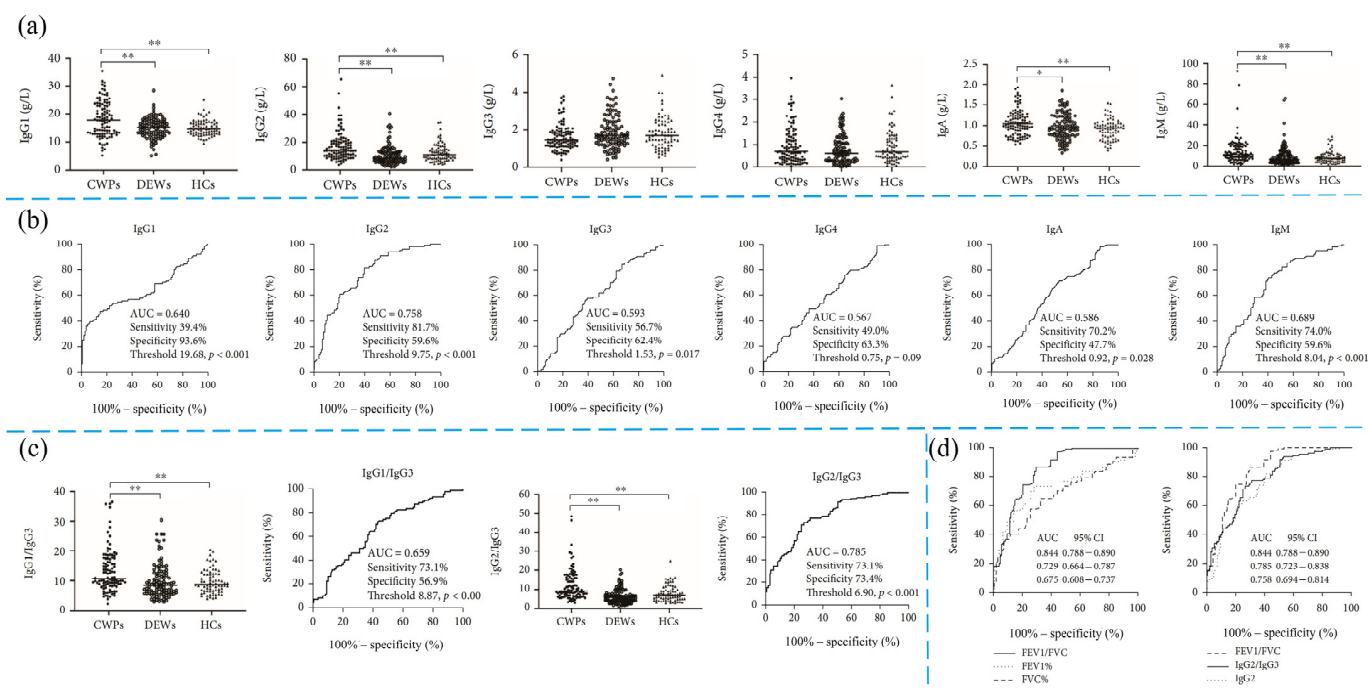


Figure 4. (a) Comparison of serum concentrations of IgG1, IgG2, IgG3, IgG4, IgA, and IgM among the study groups, * $p < 0.05$, ** $p < 0.01$. (b) The ROC curve analysis of immunoglobulin test results between coal workers' pneumoconiosis and dust-exposed workers. (c) Comparison of the IgG1/IgG3 ratio and IgG2/IgG3 ratio among the study groups. (d) ROC analysis of the spirometry parameters and the IgG2/IgG3 ratio for distinguishing coal workers' pneumoconiosis and dust-exposed workers [6].

In summary, the exploration of biomarkers for pneumoconiosis diagnosis has yielded promising yet incomplete results. While oxidative stress markers (e.g., NPT), epigenetic regulators (e.g., miRNAs, DNA methylation), B cell-derived immunoglobulins, and inflammatory cytokines (e.g., TNF- α , IL-1 β) provide valuable insights, challenges related to sensitivity, specificity, and technological limitations persist. Future research should focus on multi-omics approaches, combining multiple biomarkers and advanced detection technologies to enhance diagnostic accuracy and facilitate early intervention in pneumoconiosis.

3.2. Breath Analysis

3.2.1. Monitoring of Exhaled Components

For early pneumoconiosis screening, both sensitivity and accuracy are indispensable. However, the convenience and non-invasiveness of the tests are also of great importance. Existing technologies based on large-scale instruments and equipment, such as X-ray, CT, MRI, and so on, are all costly, invasive, or may have side effects related to radiation exposure that can affect health, be time-consuming, or require well-trained personnel. All these factors are not conducive to the popularization of the equipment and the implementation of extensive population screening.

Thousands of volatile organic compounds (VOCs) have been found in exhaled breath, and they are related to the internal biochemical processes of the human body, either directly or indirectly [78–80]. For example, lipid peroxidation plays an important role in the pathogenesis of pneumoconiosis. Pentane and methylated alkanes such as C5–C7, as

metabolites of lipid peroxides, constitute the main VOCs in the breath of patients with pneumoconiosis [81]. Compared with the technologies based on high-end instruments and professional operators mentioned above, breath sensors and their arrays (electronic noses) are cutting-edge and hot sensing technologies that have attracted extensive attention in recent years. They also represent a kind of diagnostic technology that is rapid, simple, non-contact, safe, non-invasive, capable of continuous sampling, and easy to repeat [81–87]. Some patients may not have obvious organic lesions in the early stage, but their exhaled breath already contains specific VOCs with disease characteristics [88]. Breath analysis technology, leveraging VOCs as disease biomarkers, demonstrates significant potential for non-invasive diagnostics. While current applications in pulmonary disorders (e.g., lung cancer, tuberculosis), infectious diseases, and urological conditions have advanced, their clinical adoption remains limited due to unresolved pathophysiological mechanisms governing VOC metabolic alterations. Research limitations include small sample sizes, confounding variables from environmental exposures (e.g., smoking) and host metabolic processes, and nascent exploration in pneumoconiosis detection. As an adjunctive tool, breath analysis could prioritize high-risk individuals for confirmatory imaging studies, thereby optimizing resource allocation and transforming disease management paradigms. Its non-invasive nature and capacity for continuous monitoring position it as a revolutionary approach in early disease detection and personalized healthcare, particularly for occupational lung diseases like pneumoconiosis.

Respiratory sampling may not require advanced and specialized techniques and knowledge, but it still needs to utilize high-end technologies such as spectroscopy to detect and analyze the VOCs exhaled in diseases [89]. Commonly used techniques include gas chromatography, gas chromatography-mass spectrometry, proton transfer reaction mass spectrometry, selected ion flow tube-mass spectrometry, ion mobility spectrometry, and laser spectroscopy [90,91]. These devices are powerful, yet they have relatively high requirements in terms of instrument cost and size, operational professionalism and proficiency, data analysis level, sample pretreatment, etc., and they are also relatively time-consuming. Therefore, it is quite necessary to develop miniaturized and direct respiratory sensor analysis platforms. However, the real market-oriented application of this technology still depends on the improvement of material technology, sensor technology, machine learning methods, and disease-specific reference libraries and databases, especially the search and identification of potential biomarkers for specific respiratory diseases.

3.2.2. Respiratory Physiological Parameters

Pneumoconiosis poses life-threatening risks through respiratory failure and other severe complications, necessitating comprehensive respiratory physiological parameter monitoring throughout diagnosis and treatment. Real-time continuous breath sensor-based surveillance plays a critical role in the early detection of pathophysiological deteriorations, including respiratory arrhythmias and hypoxemic exacerbations, particularly given the compromised pulmonary parenchyma and fragile respiratory function in affected patients. Such monitoring enables dynamic risk stratification for complication prevention. Furthermore, the heterogeneous nature of pneumoconiosis (variable disease severity, comorbidities, and treatment responses) mandates precision medicine approaches, where sensor-derived physiologic data support evidence-based adjustments to individualized therapeutic regimens. The detailed information provided by breath sensors gives doctors a basis for accurately evaluating patients' responses to existing treatment measures [82]. For example, by analyzing the data recorded by breath sensors, doctors can determine whether drug treatment has achieved the expected results and whether oxygen therapy meets the actual needs of patients. Based on these accurate evaluation results, doctors can make targeted

fine adjustments to drug dosages and reasonably adjust key treatment parameters such as the duration and intensity of oxygen therapy. This not only improves the precision and effectiveness of treatment but also significantly enhances patients' treatment experience, making them more comfortable during the treatment process. Meanwhile, it helps to improve the prognosis and brings greater hope for patients' recovery.

In the field of early diagnosis of the disease, breath sensors also have a unique value. They can continuously monitor key parameters such as patients' breathing patterns, respiratory frequencies, and depths of breathing. In the early stage of pneumoconiosis, patients' bodies often undergo some subtle changes, and these slight alterations in these parameters may be important signals in the early stage of the disease [92]. Thanks to their high sensitivity, breath sensors can detect these early changes in a timely manner, providing doctors with valuable diagnostic clues and thus enabling the early diagnosis of pneumoconiosis. Early diagnosis is crucial for the treatment of pneumoconiosis, as it can buy more treatment time for patients and increase the success rate of treatment. Although imaging examinations, such as X-rays and CT scans, are important means for the diagnosis of pneumoconiosis, breath sensors can provide additional physiological information and serve as a powerful supplement to imaging examinations. For example, by monitoring the gas exchange efficiency during breathing, doctors can indirectly infer the degree of pulmonary fibrosis. Pulmonary fibrosis is an important pathological feature of pneumoconiosis, and understanding its degree is of great significance for accurately assessing patients' lung conditions and formulating reasonable treatment plans [93]. The combination of breath sensors and imaging examinations is like providing doctors with a pair of "X-ray eyes" that can comprehensively and accurately understand patients' conditions, enabling them to provide higher-quality medical services for patients.

3.2.3. Key Factors and Strategies for Enhancing Breath Analysis Performance

High-quality breath analysis samples also rely on the control of individual breathing patterns, breathing depths, sampling time methods, working temperatures, etc., as well as the progress of gas sample storage technologies. In addition, the lack of selectivity and the reliability of working in high-humidity environments (the exhaled breath of a normal human body has a high relative humidity of 90%) remain the key factors limiting the use of most sensors. Moreover, when the concentration of a single VOC component is relatively high, problems such as sensor drift and the inability to accurately calibrate the sensors may also occur [90]. It is also necessary to establish standardized methods to utilize different datasets and consider the reproducibility of instruments and classification models among different sensors, that is, repeatability. The responses of sensors to VOCs can be analyzed by pattern recognition algorithms to classify different situations separately. Among them, principal component reduction and subsequent discriminant analysis pattern recognition are the most commonly used types of raw data analysis in their responses. Other AI technologies can also be used for data analysis, such as machine learning algorithms and ANN [94], but the diversity of analysis techniques may hinder the standardization of sensor array technologies.

Therefore, by selecting materials with high specific surface area, unique crystal structures, and favorable electronic properties—such as metal oxide semiconductors, graphene and its derivatives, and metal-organic frameworks (MOFs)—high-performance breath sensors can be developed [95–98]. By employing chemical methods to introduce specific functional groups or active sites on the surface of the sensing material, it can interact specifically with target volatile organic compound (VOC) molecules, thereby significantly enhancing the sensor's selectivity [99]. Furthermore, constructing an array of sensors with different sensitivities and combining it with pattern recognition algorithms (such

as principal component analysis and artificial neural networks) to process and analyze the response signals enables accurate identification and concentration measurement of various VOCs, thus greatly improving the sensor's selectivity and anti-interference capability [100]. Choosing appropriate packaging materials is also crucial. Materials such as polydimethylsiloxane (PDMS) and cellulose nanocrystals (CNC), which have good gas permeability and chemical stability, can effectively isolate the sensor's sensitive elements from the external environment, preventing interference from moisture, dust, and other impurities while ensuring that target VOCs gases can reach the sensing surface [101,102]. Integrating environmental compensation components within the sensor package allows for real-time monitoring of changes in environmental parameters, such as temperature and humidity, and compensating the sensor's response through circuitry or algorithms, thereby enhancing the measurement accuracy of the sensor under different environmental conditions [103].

3.3. E-Noses Technology

Compared with breath sensors that have a single structure and lack practicality, E-noses utilize gas sensor arrays to achieve sensing and data analysis directly after sampling and realize pattern recognition of diseases, food, pharmaceuticals, explosives, drugs, etc. on site. The E-nose is an advanced device that simulates the human olfactory system. Its working principle is based on the precise detection of gas chemical components by an array of sensors. These sensors can sensitively identify and respond to various VOCs, efficiently converting the captured chemical signals into electrical signals that are easy to analyze. The VOCs in the exhaled breath of patients with pneumoconiosis are significantly different from those of healthy individuals. The electronic nose leverages this characteristic by analyzing the unique patterns of VOCs in exhaled breath to identify biomarkers associated with pneumoconiosis, thereby providing a strong basis for its diagnosis [104,105]. The detection using the electronic nose has many advantages. First, the detection process only requires the collection of exhaled breath, eliminating the need for invasive procedures. This greatly enhances the patient experience, making it more comfortable and convenient. This feature also makes the electronic nose suitable for large-scale screening. Second, the detection is rapid and capable of being completed in a short time, meeting the need for efficient testing. Moreover, the electronic nose has excellent detection capabilities for low-concentration VOCs, which is beneficial for the early diagnosis of pneumoconiosis, providing patients with valuable treatment time [106].

However, the application of the electronic nose in the detection of pneumoconiosis still faces some challenges. On the one hand, research on VOC biomarkers related to pneumoconiosis is still ongoing and not yet fully clarified, which, to some extent, limits the accuracy and reliability of electronic nose detection. On the other hand, VOCs in exhaled breath are easily influenced by factors such as diet and environment. Effective measures need to be taken during the detection process to exclude these interferences and ensure the validity of the detection results. The application of the electronic nose in pneumoconiosis detection is still in the developmental stage. More research is needed to fully validate its clinical value and promote its widespread use in the diagnosis of pneumoconiosis [107]. The research on E-noses involves many interdisciplinary fields and generally includes three structural units, namely the sensor unit array, the signal processing unit, and the pattern recognition unit. The sensor and its array technology, as well as the pattern recognition system (mathematical and statistical algorithms such as discriminant factor analysis and partial least squares method) and AI technologies, such as ANNs, are the two construction bases of electronic noses. Electronic and computer technologies are the preparation bases, while neurophysiology and mathematics are the theoretical bases and

point out the direction for their development [108]. It not only means real-time monitoring to help doctors achieve the detection and treatment of patients but also can be combined with in-vehicle analysis, wearable analysis, and so on.

The sensing array units of the E-noses also rely on the development of sensing materials and technologies. Currently, the gas-sensitive sensing units are still mainly based on several relatively mature types, such as metal oxide semiconductors [109], field-effect transistors [110], quartz oscillators [111], optical methods [112], and surface acoustic waves [113]. They involve materials like metal oxides, conductive polymers, carbon-based materials such as carbon nanotubes (CNTs), and two-dimensional (2D) materials [114–116]. Each of these materials has its own advantages and disadvantages, and the selectivity of a single material is limited. For example, the E-nose based on the CNT-TiO₂ composite structure developed by Shooshtari et al. can distinguish acetone, ethanol, butanol, and propanol vapors with an accuracy rate of 97.5%, which can be used for rapid and efficient monitoring of VOCs [117]. With the development of sensing technologies, microfabrication technologies, nanotechnologies, advanced signal processing algorithms, etc., and the development of sensor arrays with strong selectivity and high sensitivity, together with the significant optimization of data processing algorithms, it is believed that the E-nose technology will eventually play a significant role in the screening, diagnosis, and treatment of pneumoconiosis [85,115,118].

As an endeavor, Xuan et al. [87] developed an E-nose based on an array of 16 organic nanofiber sensors (Figure 5a). It combines machine learning, pattern recognition algorithms, big data analysis techniques, etc. They constructed an exhaled breath screening and diagnosis model for pneumoconiosis and an early warning model for pulmonary fibrosis lesions, with an accuracy rate of over 85%. The organic nanofiber sensors in the E-nose system can respond to VOCs present in exhaled breath. When people suffer from diseases such as silicosis, the concentrations of these VOCs may change. Metabolites generated by lesions in the alveolar-capillary membrane are directly released into the alveolar space and can be detected in the breath. The sensor array is directly exposed to the breath mixture, and the composite profile (breath fingerprint) generated by the responses of all 16 nanofibers can distinguish between diseased and healthy control groups, reflecting metabolic changes in the breath components. This method is similar to the olfactory system of mammals, where a large number of olfactory receptors (sensors) work as a cooperative array to generate specific patterns for different odors or mixtures without the need to know the detailed information of individual components. In this way, the E-nose can quickly and non-invasively detect diseases, providing an ideal technology for large-scale disease screening (Figure 5b).

In addition to detecting pneumoconiosis, E-noses can also detect lung cancer. For example, Tirzite et al. [119] applied the E-nose combined with logistic regression analysis (LRA) in the detection of lung cancer. The study involved 252 lung cancer patients and 223 non-lung cancer patients. Exhaled breath samples were collected and analyzed through the Cyranose 320 sensor device, and LRA was used for data analysis to distinguish between lung cancer patients, patients with other lung diseases, and healthy individuals. The sensitivities for cancer detection among smokers and non-smokers were 95.8% and 96.2%, respectively, and the specificities were 92.3% and 90.6%, respectively. This indicates that the combination of E-nose and LRA can effectively identify lung cancer patients, thus assisting doctors in diagnosing lung cancer at an early stage and providing more timely treatment for patients. Of course, in the medical field, a single detection method often has limitations, while multimodal detection can improve the diagnostic accuracy of diseases by integrating the advantages of multiple detection means. For example, combining breath analysis, imaging examinations, and blood tests can evaluate patients' health conditions more

comprehensively, especially for complex diseases such as lung cancer, chronic obstructive pulmonary disease (COPD), and pneumoconiosis [120].

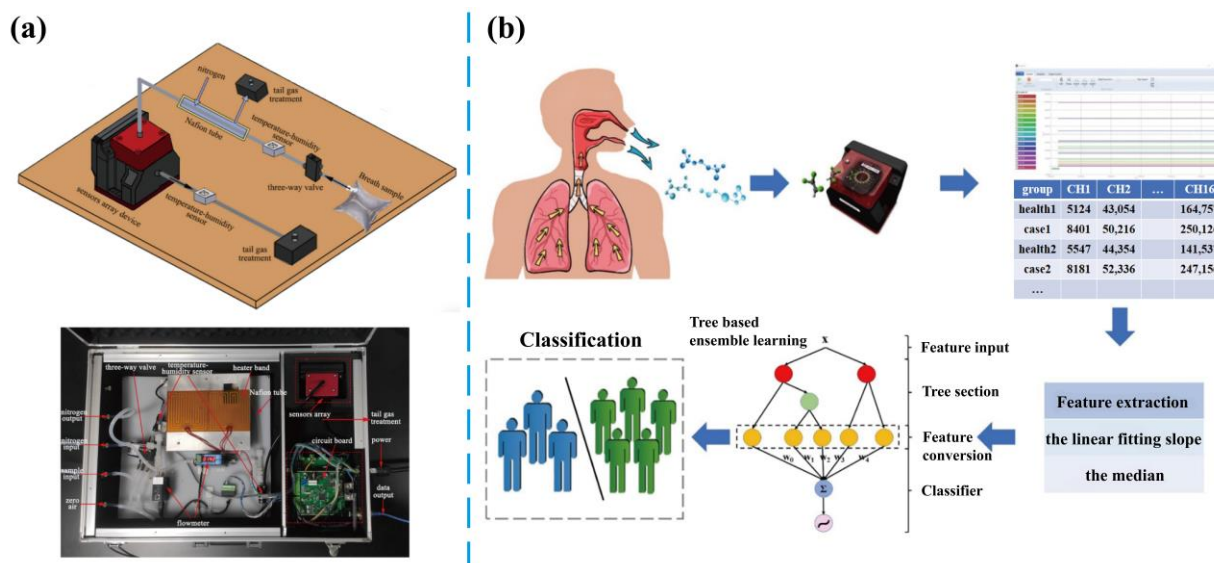


Figure 5. (a) E-nose system. (b) Schematic diagram of the process of screening for pneumoconiosis with an E-nose system [87].

4. Conclusions and Outlook

In summary, this paper provides a comprehensive overview of various screening and diagnostic technologies for pneumoconiosis, ranging from the dominant and most widely used clinical imaging analysis, PFT, tissue-invasive techniques, and biomarker detection to E-nose technology. When these technologies are used in combination, their strengths are fully realized. Imaging analysis offers macroscopic structural information about the lungs. PFT provides quantitative assessment information on lung function, while tissue-invasive techniques provide precise pathological diagnoses and biomarker technologies offer diagnostic evidence at the biomolecular level. The E-nose, on the other hand, provides an ideal non-invasive chemical sensing technology by analyzing the chemical composition of exhaled breath. Together, these technologies complement and validate each other, allowing for a comprehensive assessment of the patient's condition from multiple dimensions. This significantly improves the accuracy and reliability of pneumoconiosis diagnosis.

However, currently, the situation of preventing and controlling pneumoconiosis remains extremely severe. Early prevention and control are still crucial tasks in this work, which still demand the coordinated cooperation and long-term efforts of the government, enterprises, workers, and researchers. They should not only consider the sensitivity, specificity, and the employed technology itself but also take into account factors like convenience, cost-effectiveness, and safety. There is still a long way to go to optimize mainstream imaging technologies, especially considering their reliance on the doctors' experience and the non-negligible misdiagnosis rate. Thus, the development of other technologies, such as biomarkers and respiratory sensing, are given great expectations, combined with the rapid progress in technologies like mobile devices, remote consultations, and digital imaging. The continuous reduction in the costs of equipment and usage will further offer more opportunities for their widespread implementation, especially in developing countries and specific industries with high pneumoconiosis incidence. However, the development of biomarker technology is still restricted by issues such as high technical barriers, a relatively small sample size in clinical studies, and the complexity of excluding interfering factors, so its future promotion will be greatly limited. Currently, although some potential biomarkers

(such as inflammatory factors) may be of significant importance for the early diagnosis and assessment of disease progression in pneumoconiosis, their clinical application value has not yet been verified through large-scale clinical trials. In the future, with a deeper understanding of the pathogenesis of pneumoconiosis and continuous advancements in detection technologies, new biomarkers are expected to play an important role in clinical diagnosis and treatment. However, before large-scale clinical application, their sensitivity, specificity, and clinical utility must be rigorously validated through clinical trials.

In contrast, as a type of chemosensor for gaseous analytes detection, non-invasive diagnosis of pneumoconiosis through expiratory VOC sensing is quite ideal and suitable for large-scale, low-cost, and easily accepted screening. It can safely and frequently collect a wide range of samples and is expected to become the best option for screening the whole population and for daily monitoring. However, developing high-performance breath sensors or even E-nose devices remains a complex challenge that awaits persistent endeavors and in-depth research. For example, the production of VOCs is associated with a variety of pathophysiological processes, including inflammation, oxidative stress, and microbial infections. Due to the complex pathological mechanisms of pneumoconiosis, changes in VOCs may overlap with other pulmonary diseases, thus greatly limiting their specificity and sensitivity. The strong interference of the moisture co-existing with VOCs in the expiratory air with their detection also needs to be taken seriously, compared with other detection scenarios. To address these challenges, existing experience with general VOC sensors should be actively used: (a) enhancing selectivity through material innovation and sensor array design, etc.; (b) realizing humidity interference through constructing hydrophobic surfaces, using humidity-resistant materials (e.g., porous silicon), employing AI-based humidity compensation algorithms, etc.; (c) enhancing sensitivity through material innovation and functional design, etc.; (d) AI-driven data processing and pattern recognition, etc. These will help address the challenges and drive breakthroughs in the field of pneumoconiosis detection using breath analysis and E-noses. In addition, significant progress may be made to produce wearable devices, which could lay a solid foundation for the application of pneumoconiosis-related pathogenic environmental monitoring simultaneously. Combining sensors with the Internet of Things (IoT) and communication technologies can also minimize the possibility of workplace accidents to the greatest extent. This will help to reduce the incidence or severity of pneumoconiosis at the source.

Moreover, animal models and related methods, as powerful scientific research tools, deserve more attention. Their establishment and application can not only provide a basis for clinical treatment but also lay a solid foundation for research on the occurrence, development, and mechanism of pneumoconiosis. But there are ethical and other limitations to real animals; in contrast, *in vitro* biomimetic architectures like that using microfluidic chips have shown great application prospects as a model for the study of pneumoconiosis pathophysiology.

No matter which strategy is used, the explosive development of big data, AI, and other technical principles has greatly promoted the progress of this field [41]. In particular, the explosive development of AI-generated content (AIGC) technology is making the “AI doctor” a reality. It not only fills the technical gap caused by the difference in medical conditions and doctor experience but also makes remote diagnosis and larger population screening possible and will greatly improve the efficiency and accuracy of diagnosis. It also may partially eliminate the diagnostic errors caused by a single technology and enable collaboration across territories, disciplines, and industries so as to better benefit pneumoconiosis patients or potential populations in the future. Most importantly, it could make up for the imbalance between different countries and regions, ultimately, for the benefit of all mankind.

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