Chapter 8
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Fourier Transform Infrared (FTIR) Spectroscopy in Breath Analysis

Andrei A. Bunaciu [a*] and Hassan Y. Aboul-Enein [b++*]

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ABSTRACT

There are several potential medicinal and scientific uses for breath analysis, a relatively new field of inquiry. The environment, microorganisms in the gut and airways, and metabolites of ingested precursors all contribute to the body's internal production of volatile organic compounds (VOCs) that are detected in breath. Several recent studies suggest that breath analysis may aid in the diagnosis of illnesses associated with alterations in breath composition. Infrared spectroscopy is a promising analytical method for the metabolic analysis of breath. There are substances in human breath that can be used to assess environmental exposure, diagnose diseases, and monitor physiological conditions. Exhaled breath promotes collaboration and is the ideal biological fluid because it is nearly limitless and causes little to no discomfort for the patient. Breath analysis is a suitable technique for certain applications, as exhaled breath can be captured without the need for medical personnel or privacy, and it typically doesn't produce infectious waste (although airborne infections may be present). Breath analysis is a non-invasive technique that reveals the overall health and condition of the body's metabolism by describing the volatile content of the bloodstream and airways using the volatile composition of exhaled breath (EB). However, because exhaled breath includes relatively little of the metabolites, the absorption strength of the metabolites is still quite moderate. This chapter presents recent applications of the infrared spectroscopic technique published between 2020 and 2025.

Keywords: FT-IR analysis; breath analysis; infrared spectroscopy; non-volatile compounds; biomarkers; early disease diagnosis applications.

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[a] *S.C. AAB_IR Research S.R.L., 9-11A Gloriei Street, Bragadiru – Ilfov District, 077025, Romania.*
[b] *Pharmaceutical and Medicinal Chemistry Department, Pharmaceutical and Drug Industries Research Division, National Research Center, Cairo 12622, Egypt.*
[++] *Professor;*
**Corresponding authors: E-mail: aabunaciu@gmail.com, haboulenein@yahoo.com;*

1. INTRODUCTION

Breath analysis presents a great potential for scientific and clinical research, being one of the oldest medical diagnostic techniques, utilising specific odours to identify diseases (Huh, 1613). Each person has a unique "breath print" that can reveal a lot about their health. Thousands of molecules are released with every breath we exhale (Bunaciu & Aboul-Enein, 2025).

The field of breath analysis is as old as medicine itself. Doctors have known since the time of Hippocrates (460–370 BC) that a person's breath can provide accurate information about health problems and, in some cases, help with evaluation. Hippocrates described fetor oris and fetor hepaticus in his treatise on breath aroma and disease (Sharma et al., 2023, Phillips, 1992). Later, Lavoisier and Laplace studied guinea pigs' CO_2 breath for the first time between 1782 and 1783 and showed that the body's combustion produces the exhaled breath, the respiration consumes oxygen, and expels carbon dioxide (Duveen & Klickstein, 1955). Nebelthau demonstrated that diabetics release breath acetone (Hubbard, 1920), while Anstie separated ethanol from breath (the basis for modern breath alcohol testing) (Baldwin, 1977).

In the 1970s, Linus Pauling, using gas-liquid partition chromatography, made a significant contribution to the scientific study of breath by proving that exhaled breath contains more than the traditional gases of carbon dioxide, nitrogen, oxygen, and water vapour (Pauling et al., 1971). At that time, 250 compounds were found, but now it is possible to identify over 1000 distinct chemicals using contemporary technologies (Bunaciu & Aboul-Enein, 2025). A wide range of volatile organic molecules and elemental gases, such as carbon monoxide and nitric oxide, are examples of these substances. Exhaled breath also comprises droplets of aerosols, which have been identified as "exhaled breath condensate" and incorporate proteins that are dissolved in it, as well as other non-volatile compounds. For example, an experienced medical practitioner may easily recognise the musty and fishy smell of advanced liver disease, the urine-like smell of kidney failure, the vile smell of a lung abscess, and the distinctive fruity smell of acetone in diabetes. Breath analysis is therefore a desirable biochemical monitoring method to detect the emergence of other diseases and physical abnormalities.

This technique can also help predict such illnesses because it is non-invasive and applicable to different substances (Bunaciu & Aboul-Enein, 2025). The first review to address VOCs in exhaled breath was published by (Manolis, 1983). The discovery of numerous VOCs in physiological fluids and healthy human breath was demonstrated in a recent review by (Drabińska et al., 2021). By better understanding the metabolic pathways involved in the synthesis of VOCs, this information may aid in the identification of illnesses.

The human body is among the universe's most complex living entities. For a complex metabolism to continue functioning, a wide range of metabolic events must occur. During these metabolic activities, a variety of chemical and biological

components are produced or changed. Monitoring the concentration of the molecules of interest over time allows one to follow the emergence (or recurrence) of a disease and the effectiveness of a treatment (Kim et al., 2009). Thus, a technique to do breath analysis with high-resolution, broad-spectrum coverage, high specificity, and high sensitivity will be more widely available and adopted (Kim et al., 2009).

Due to the numerous metabolic processes involved in the induction, progression, or regression of conditions such as shock, injuries, or diseases, many of these molecular species will enter the blood medium and be carried over to the lungs, where the volatile species among them will be exhaled. Since the processes leading to the production of these molecules will depend on the specific disease and its various stages, they will be "Fingerprints" of such disease conditions. Thus, the study of exhaled air can provide information regarding a person's physiological state and overall health. As a result, it can be used to diagnose many diseases early on, even when they are just starting (Nakhleh et al., 2017). Detection of diseases from exhaled breath has been shown in different fields of medicine, particularly infectiology (Bunaciu & Aboul-Enein, 2025, Shokouhmand et al., 2025) and oncology (Wang & Wu, 2025, Capuano et al., 2025, Ren et al., 2025).

Blood, plasma, faeces, urine, cells, herbal extracts, exhaled breath (EB), and exhaled breath condensate (EBC) represent some of the biological elements used in the most recent health investigation (Khoubnasabjafari et al., 2022). EBC is typically a sample obtained by capturing exhaled aerosols that come from the fluid that lines the lungs (Bunaciu & Aboul-Enein, 2025). It primarily consists of nonvolatile analytes, particularly those that dissolve in aqueous solutions (Hunt, 2007). The term "EB" describes gaseous samples drawn from exhaled breath and primarily comprises volatile analytes with trace amounts of nonvolatile analytes, particularly those with lower boiling temperatures (Dweik & Amann, 2008). Breath is a crucial matrix for VOCs' analysis and non-volatile compounds produced by the body. After passing through the body's bloodstream and arriving at the alveolar interface, these substances are eventually exhaled. Analysing exhaled breath to find VOCs may reveal if a person is healthy or ill. Similar to blood testing in clinical medicine, but quicker and less invasive, identifying the type and concentration of molecules in breath is an effective method of evaluating a person's general health (Bunaciu & Aboul-Enein, 2025). A diagnosis can be made easier if a certain molecule (or combination of molecules) has been detected and is indicative of the existence of an illness or infection (Liang et al., 2021).

With the appearance of new technologies (such as infrared, electrochemical, chemiluminescence, e-nose, and others) and the development of highly sensitive mass spectrometers, breath analysis has advanced significantly in the twenty-first century, and several techniques are currently in clinical use or on the verge of entering that field (Li et al., 2023, Su et al., 2023, Smith et al., 2023, Pu et al., 2023, Stewart et al., 2024, Arachchige & Muller, 2024, Xie et al., 2023, Uthra et al., 2024, Zhang et al., 2025, Dumitras et al., 2020).

Investigating molecular vibrations is a crucial component of vibrational spectroscopy methods, such as Fourier transform infrared (FTIR) spectroscopy. An overview of the vibrational spectroscopic techniques used in breath analysis during the past few years is presented here. There will also be an emphasis on future applications of the advanced spectroscopic techniques. FTIR spectroscopy is a promising alternative to conventional diagnostic methods since it provides label-free, non-invasive bacterial detection, identification, and antibiotic susceptibility testing in a single step, according to the review's conclusions. To minimise the overall burden of outbreaks, prevent resistant germs, decrease the use of needless antimicrobial medications, and enhance patient care and diagnostics, rapid, accurate, and reasonably priced tests are important.

One of the main disadvantages of diagnostic breath analysis is the difficulty of proving the connection between identified marker molecules and pathology, since precise metabolic pathways are frequently unknown. Sampling is a crucial step because the levels of chemicals in exhaled air vary depending on the circumstances and are frequently at a trace level (Di Francesco et al., 2005). Mid-infrared (MIR) spectroscopy is an excellent substitute method for identifying compounds at the trace level with good sensitivity and molecular selectivity. For near real-time analysis evaluating highly discriminative vibrational and rotational chemical fingerprints, MIR spectroscopy appears to be more adapted to integration and downsizing than GC-MS. These are two significant benefits for typical clinical applications (Mansfield et al., 2002, Pebay-Peyroula & Nicaise, 1970).

In human breath, nitrogen, oxygen, water, and carbon dioxide are the most prevalent matrix components (Lide, 2004, Buszewski et al., 2007, Fenske & Paulson, 1999). At this, we can add about 3500 distinct VOCs identified using gas chromatography and mass spectrometry in a study of breath samples from fifty healthy people (Phillips et al., 1999). More than 1000 components are present in exhaled breath at trace levels, at ppm or ppt levels, and several of these substances may be biomarkers for particular illnesses, physiological states, or the effectiveness of treatment (Bunaciu & Aboul-Enein, 2025). Some substances found in exhaled breath (EB) have been thoroughly investigated, and their connections to various disease pathologies have been identified. However, because these biomarkers are often found at low levels below the ppb (v/v) range of EB, molecularly precise identification of these biomarkers in EB at clinically significant levels remains a practical and analytical problem. MIR spectroscopy and sensing techniques need to be significantly improved to be a viable option for breath analysers that may be used in clinical settings. Thus, when a person transitions from a healthy to a diseased condition, a slight but significant change in the VOC spectrum (in concentration and composition) is seen; this phenomenon is called breath metabolomics (breathomics) (Beale et al., 2016). This change can be recognised and used for diagnosis and monitoring.

Infrared spectroscopy's biggest challenge for analysing biological samples is the high concentration of water vapour in gaseous biofluids. For instance, a healthy

person's breath sample normally comprises 5–7% water vapour (Phillips et al., 1999). There are several methods for breath analysis, but this chapter will cover only some of the most recent applications of infrared spectroscopy published between 2020 and 2025.

2. BREATH ANALYSIS SELECTED APPLICATIONS

Two significant obstacles must be overcome to create breath diagnostic instruments based on infrared spectroscopy (Bunaciu & Aboul-Enein, 2025). First, a major barrier to using infrared spectroscopy in breath is the high water (Zieliński & Przybylski, 2012) content of an exhaled breath sample. A significant (factor of 2500) decrease in water vapour from the exhaled breath sample at -60^{0}C has been made possible by the recent development of a water suppression approach from gaseous biofluids (Apolonski et al., 2019). A hierarchical correction process was suggested to carry out the baseline corrections (Selvaraj et al., 2020).

There are some other reviews related to breath analysis using infrared spectroscopy, published during this period (Dumitras et al., 2020, Selvaraj et al., 2020, Xia et al., 2024, Khoubnasabjafari et al., 2022, Mortazavi et al., 2023).

Water removal from the sample without altering the constituent molecules is the primary benefit of breath analysis utilising infrared spectroscopy over tissue or liquid-phase biological samples. Recently, a very effective method for removing water was proposed (Maiti et al., 2018).

A typical water-suppressed breath spectrum of a healthy volunteer is presented in Fig. 1a.

The spectra display a wide range of spectral properties. Except for CO_2, most of them are obscured by water spectra when water suppression is not present. Although our bodies use it for a variety of biological processes, it is not sufficiently informative because it is difficult to quantify the amount produced by each activity (Bunaciu & Aboul-Enein, 2025). However, many of the tiny VOCs in our breath are produced by a single biological process, particularly when we are ill. Breath analysis's main objective is to identify those particular VOCs and establish their bodily origins.

Generally speaking, C-H stretch vibrational absorptions are present in the spectral range (2800–3200 cm^{-1}) (Roy & Maiti, 2018). Since the CH bond is a property of biological molecules, all biological compounds exhibit a high concentration of CH absorption peaks in this spectral region, making them appear as highly crowded spectral features. Consequently, it is almost impossible to use fingerprints to identify individual molecules in the CH stretch vibrational range. But a distinct spectral characteristic at about 3100 cm^{-1} is recognised as the **R** branch of methane. While methane's **P** branch is obscured by other molecules' large C-H absorption spectra, a very strong **Q** branch is visible at 3020 cm^{-1}.

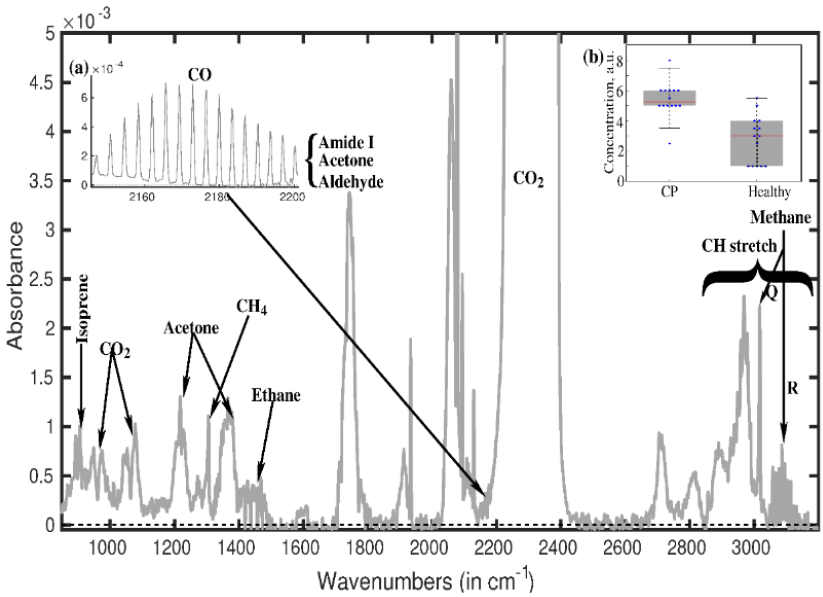

Fig. 1. A typical water-suppressed breath spectrum (Apolonski et al., 2019)

Between two groups of volunteers, two distinct spectral characteristics have been identified at 1189 cm^{-1} (**I**) and 1203 cm^{-1} (**II**). The spectral widths of the two features are comparable at 10 cm^{-1}. Without any specific exception, the signatures present for 92% (I) and 83% (II) of healthy people and discovered for 100% (I) and 86% (II) of CP patients are, on average, around a factor of two higher in concentration for the former cohort (Bunaciu & Aboul-Enein, 2025). In the inset of Fig. 1(b), the peak's strength at 1189 cm^{-1} is displayed for both volunteer groups. Through statistical analysis using the two spectral features indicated above, we were able to discriminate between the individuals in the groups with an accuracy of over 90%.

Evidence of detectable VOCs in breath linked to lung and breast cancer has been established. Finding every factor affecting the number of VOCs in exhaled air has piqued the curiosity of the scientific community. It has concentrated on standardising the breath sample and analysis methodology in this context. Rapid and non-invasive diagnosis of several illnesses, including diabetes and cancer, may be possible with breath analysis (Pereira et al., 2015).

Normal human subjects' breath has been found to include a variety of chemicals, although it is typically unknown what metabolic pathways these molecules originate from. Certain chemicals have been linked to increased amounts of ovulation, diabetes, cirrhosis, renal disease, and cancer. Yet, many other illnesses have not yet been investigated in this light.

VOC analysis can reveal important details about a person's health, particularly concerning several illnesses. As a result, it can be applied to the early detection of numerous illnesses, even at the initiation (Nakhleh et al., 2017). The primary benefits of breath analysis over other tests currently used to investigate diseases are that it is completely non-invasive, sampling is simple, there are essentially no restrictions on sample size or source, results are available quickly, objective diagnoses can be made using AI/ML (Artificial Intelligence/Machine Learning) methods, requires only reasonably priced equipment, and can be performed by trained technicians without the need for medical professionals (Bunaciu & Aboul-Enein, 2025).

Fig. 2 presents the human body pathways for VOCs (a) and the schematic of the liver's mitochondrial matrix (b), where acetoacetate, beta-hydroxybutyrate, and acetone are formed (Zheng et al., 2024).

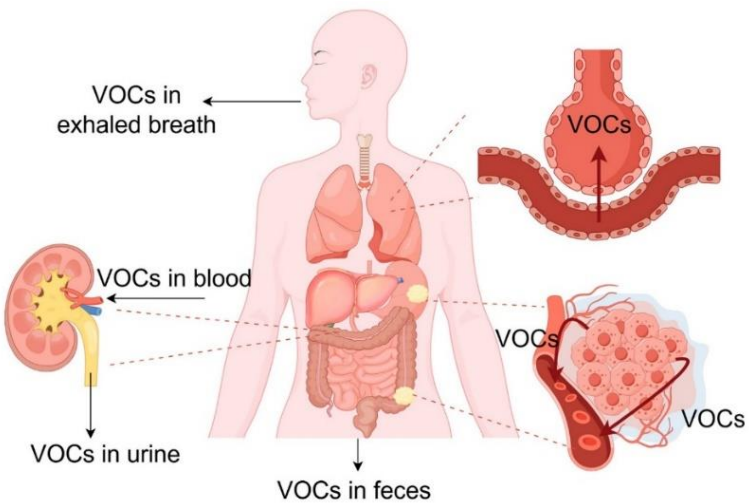

Fig. 2. Human body pathways for VOCs (Zheng et al., 2024)

Although there have been some successful attempts to separate cancer samples from healthy controls by analysing blood and tissue VOCs (Mezmale et al., 2023, Astolfi et al., 2023). These techniques serve primarily in research scenarios rather than therapeutic ones. Sample preparation is the first step in VOC analysis. A system's capacity to handle samples easily affects its generalizability, and the quality of the samples determines how accurate the results are. In addition to highlighting their use in medical practice and analysing their advantages and disadvantages, this study focuses on sample preparation methods found in human VOC studies. The cancer-related volatile organic compounds, produced as a result of metabolic alteration in cancer tissues, diffuse into the blood and are carried by the bloodstream to other parts of the body. They cross the alveolocapillary barrier and enter exhaled breath.

A higher degree of physical, emotional, and financial well-being for society is achieved through early diagnosis of diseases like various cancers, resulting in more effective therapy and quicker recovery (Bunaciu & Aboul-Enein, 2025). This allows for significant cost savings in medical care and prevents the loss of human resources. Internal organ cancers (ovarian, liver, pancreatic, etc.), cardiovascular diseases, and communicable diseases of pathogenic origins (like COVID-19) are examples of non-communicable diseases that make up the majority of the health care burden. These diseases require dependable techniques that can detect them early through cost-effective, noninvasive, universally applicable - that is, affordable, acceptable, and accessible - diagnostic methods (V. R et al., 2021).

For neonates' long-term development, it is essential to monitor their health status to provide early therapeutic intervention if physiological circumstances deviate (Batra et al., 2023, Yoo et al., 2024). Preterm newborns require extra caution in physical and neurological diagnostic procedures because of their immaturity. These should ideally be radiation-free, noninvasive, and noncontact. As a noninvasive, noncontact, and radiation-free diagnostic method, exhaled breath from 71 neonates, with a focus on preterm infants, was analysed using infrared spectroscopy (Feddahi et al., 2024). For instance, the risk of cerebral palsy (CP) or other neurological problems is negatively correlated with gestational age (GA); the earlier a child is born, the greater the chance of neurological impairment (Marlow et al., 2005). It was hypothesised that infrared spectroscopy for breath biomarker analysis could contribute to neonatal health monitoring, providing a feasible means of collecting an adequate quantity of exhaled breath.

In Fig. 3, the infrared absorption spectra of ambient air, incubator air (containing a neonate), exhaled air from a neonate with spontaneous (S) respiration, and input and outlet air of a CPAP (Continuous Positive Airway Pressure) system are displayed. Spectra are focused on the carbon dioxide absorption spectra.

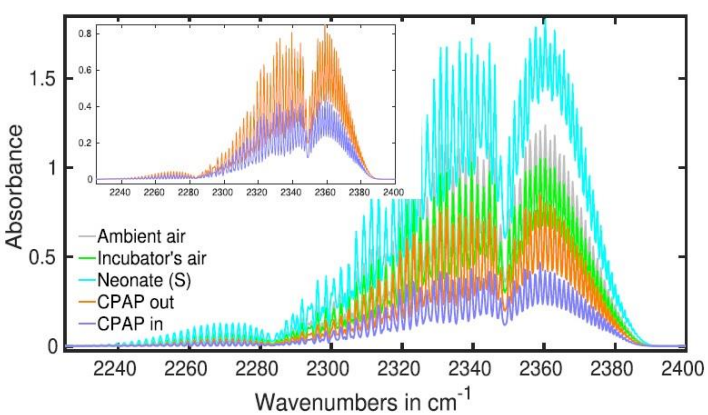

Fig. 3. FTIR spectra for neonates exhaled breath analysis (Feddahi et al., 2024)

Studying the obtained spectra, it was concluded that the most prominent CO_2 infrared absorption peak is usually seen at about 2350 cm^{-1}, whereas the CO peak is found at 2170 cm^{-1}. The atmosphere contains several greenhouse gases, including methane. Each person inhales methane from the surrounding air during inhalation, and an equivalent amount is anticipated in exhaled breath (Bunaciu & Aboul-Enein, 2025).

The main cause of periodontitis is the Gram-negative anaerobic bacillus *Porphyromonas gingivalis*. The infrared absorption spectra of the gases released by the cultured bacteria were recorded at a resolution of 0.5 cm^{-1} within the wavenumber range of 500–7500 cm^{-1} using strains of oral bacteria that were cultivated, such as P. gingivalis and the oral commensal bacteria *Actinomyces viscosus* and *Streptococcus mutans (Kaneda et al., 2024)*. A decision tree-based machine learning technique was used to extract the infrared wavenumbers from these spectra, corresponding to distinctive absorptions in the gases that P. gingivalis emitted. Lastly, peaks at comparable locations in the P. gingivalis gases, NH_3, and CO spectra were found when the resulting absorbance spectra of ammonia (NH_3) and carbon monoxide (CO) were compared using the HITRAN (High-Resolution Transmission Molecular Absorption) database. This technique offers an efficient way to identify P. gingivalis in oral bacteria by differentiating its gases from those of other oral bacteria. The suggested approach may prove useful as a straightforward, noninvasive pathogen diagnosis method in clinical settings.

Alcohol enters the small intestine and stomach when it is consumed. After being absorbed into the blood, it travels throughout the body and into the lungs and brain. Breathing causes it to be exhaled.

For quantitative analysis and ethanol identification are several reviews have been published in this period (Su et al., 2023, Jones, 2022, Gandhi et al., 2024, Mitsubayashi et al., 2022, Paleczek & Rydosz, 2024), and the majority of breath-alcohol instruments currently in use for evidence use infrared (IR) spectrometry as the analytical principle (Harding & Zettl, 2008).

A common quick test for excessive alcohol use in forensic science and legal medicine is the measurement of ethanol in exhaled breath. To maintain sobriety in individuals suspected of driving while intoxicated, police officers employ breath analysers (Bunaciu & Aboul-Enein, 2025). A recent paper discusses the physiological underpinnings, historical evolution, and real-world uses of breathalysers in legal medicine and forensic research (Jones, 2016).

However, several nations chose to employ different BBRs (blood-breath ratio), which varied from 2000:1 to 2400:1, when calculating statutory BrAC (breath-alcohol concentration) limitations (Jones, 2011).

Because of the global pandemic caused by COVID-19, early detection techniques are desperately needed. Breath analysis has demonstrated

significant promise as a quick and non-invasive method of COVID-19 detection (Laird et al., 2023, Sharma et al., 2023, Liang et al., 2023).

Fourier transform infrared spectroscopy (FTIR) (Ruszkiewicz et al., 2020) was one of the techniques utilised recently to analyse exhaled air or exhaled breath condensate to detect COVID-19.

Fig. 4 presents the FTIR spectra for a breath infrared analysis of patients with COVID-19 virus infection.

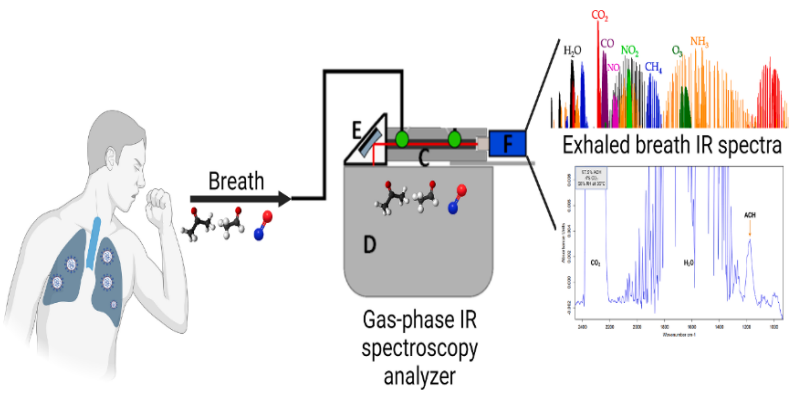

Fig. 4. The FTIR spectra for a breath infrared analysis of patients with COVID-19 virus infection (Glockler et al., 2023)

It was demonstrated that a unique approach of using a panel of thirty-four carbonyl compounds detected in all exhaled breath samples for the detection of COVID-19 can be used for the differentiation of the Alpha from the Delta variant and the detection of asymptomatic COVID-19 infection (Xie et al., 2024). Carbonyls are an organic molecule class derived from lipid oxidation (Ratcliffe et al., 2020) and are essential for many biological processes, including oxidative stress and inflammation, which are dramatically triggered by SARS-CoV-2 infection (Fu et al., 2020).

The most often detected VOCs in the exhaled breath of people infected with COVID-19 include nitric oxide, alcohols, aldehydes, and ketones (Glockler et al., 2023). As for acetaldehyde, a recent investigation using GC-MS found that patients with COVID-19 had simultaneous increases in acetaldehyde and acetone in their exhaled breath (Török et al., 2022). Additionally, acetaldehyde, propanal, and n-propyl acetate abundances in the exhaled breath of children infected with COVID-19 were found to rise during acute infection and fall as the illness subsided, according to another study (Berna et al., 2021).

Infection with *Helicobacter pylori (H. pylori)* has been widely linked to gastrointestinal disorders, including gastritis, peptic ulcers, and gastric cancer. Therefore, a precise diagnosis of H. pylori infection is necessary to stop the condition from getting worse and to direct treatment, especially for patients who have had ulcer disease in the past, when immediate eradication therapy (Cho et al., 2021, Magalhães Queiroz & Luzza, 2006) is crucial.

A recent study examines the potential value of MIR exhaled breath sensors using substrate-integrated hollow waveguide (iHWG) technology for the accurate measurement of the isotopic ratio of $^{13}CO_2$ vs. $^{12}CO_2$, simulating conditions pertinent to the exhaled breath analysis method of detecting Helicobacter pylori in the upper gastrointestinal tract. Optimised light-gas interaction and adequate sensitivity are necessary for future integration of such a sensing module, for example, into a cell phone attachment, since the diagnosis relies on detecting the presence of $^{13}CO_2$ 30 minutes after the administration of ^{13}C-labeled urea via a gel or pill, which is metabolised by H. pyl. (Flores Rangel et al., 2025).

The system's ability to distinguish and measure this isotopologue in simulated breath gas mixtures is confirmed by the linear calibration curve based on the $^{13}CO_2$ peak in the right panel of Fig. 5 (left panel), which shows how the peaks corresponding to both isotopologues change with changing $^{13}CO_2$ concentrations. The spectrum of $^{13}CO_2$ at increasing concentrations of the latter has at least a minor impact on the $^{12}CO_2$ signature, even though a threshold evaluation for an H. pylori infection is undoubtedly achievable.

Identifying chemical components in exhaled human breath offers a chance to evaluate environmental exposure, diagnose illness, or ascertain physiological conditions. Metabolic profiles can be obtained from a range of biological sample types, which can be collected non-invasively (such as faeces, urine, sputum, or breath) or invasively (such as blood, serum, or tissue biopsies) (Pham & Beauchamp, 2021).

Exhaled breath is the perfect biological fluid because it is nearly limitless and causes little discomfort for the patient, promoting collaboration (Bunaciu & Aboul-Enein, 2025). Breath analysis is a desirable method for a variety of applications since exhaled breath can be sampled without requiring privacy or medical professionals, and it usually does not produce infectious waste (despite airborne pathogens) (Pleil et al., 2020).

Early cancer detection is one of the most important factors in saving many lives. In this way, there are several reviews related to cancer screening using breath analysis (Grooms et al., 2024, Le & Priefer, 2023, Chaudhary et al., 2024). Tragically, it might be challenging to identify urogenital malignancies early on. Even at advanced stages, the accuracy of current noninvasive prostate cancer (PCa) diagnoses is limited (less than 70%) (Maiti et al., 2021).

Fig. 6 presents the spectral range, centred at 1005 cm^{-1}, that differentiates healthy patients from different cancer groups, including kidney (KC), prostate (PCa), and bladder cancer (BC), due to the presence of acetic anhydride (AA) in exhaled breath.

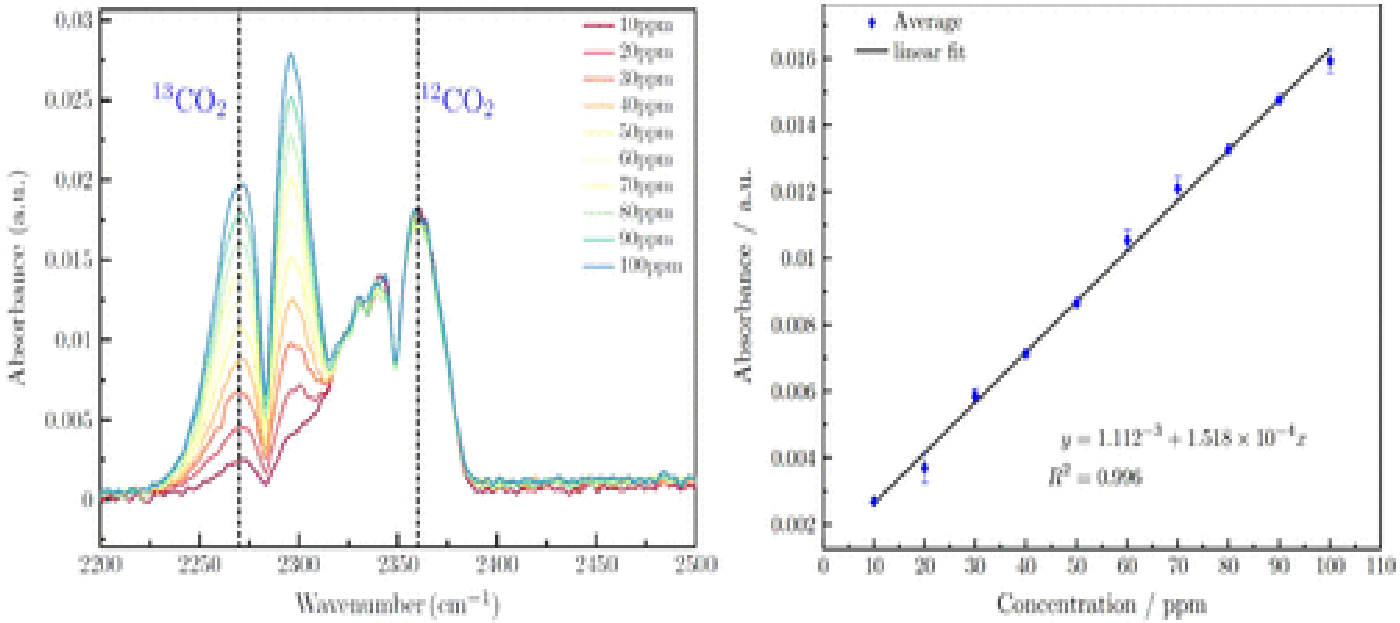

Fig. 5. Exemplary IR spectra show the $^{13}CO_2/^{12}CO_2$ ratios in 10-cm iHWGs, with $^{12}CO_2$ fixed at 200 ppm and varying $^{13}CO_2$ concentrations from 10 to 100 ppm (Left). The calibration curve was derived from the mixture as a function of $^{13}CO_2$ concentration (Right) (Flores Rangel et al., 2025)

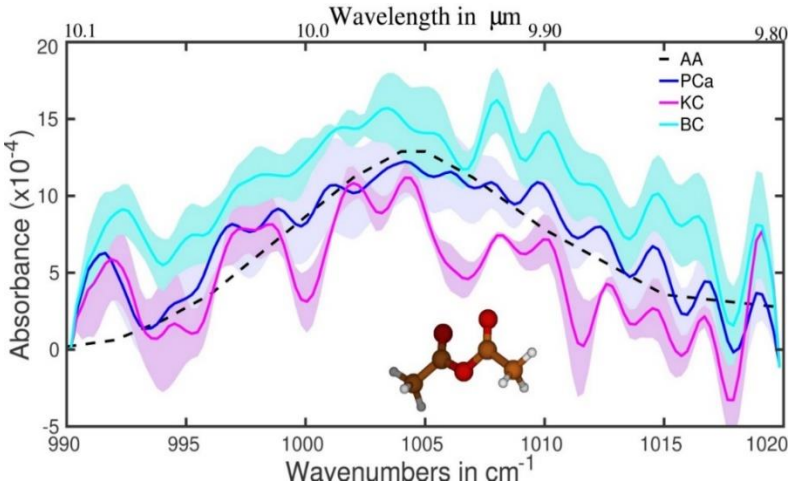

Fig. 6. The average absorption spectra for healthy and different cancer groups (Maiti, 2023)

Oscillations visible for the range >1010 cm^{-1} (especially at 1015, 1019 and 992 cm^{-1}) are due to the contribution of CO_2 (Rothman et al., 2013).

Although AA is not an end product, it can only remain in the body for a few minutes before converting to acetic acid through a reaction with water or other products through acetylation.

Now, let's note that mass spectrometry, the most practical approach for analysing metabolites in gas and liquid phases, was not previously used to detect AA in patient biofluids. First, ten molecules with a molecular mass of 102.09 amu and the formula $C_4H_6O_3$ are identical. These chemicals can be easily distinguished using mid-infrared spectroscopy, which we used in the fingerprint region, but they are difficult to differentiate using GC-MS. The identification process is further complicated by the fact that, in addition to those 10, there are several molecules whose molecular mass differences are less than 0.1%. The FTIR method is better suited for light volatile metabolites in gaseous and liquid phases than the GC method, which is better suited for heavier ones.

The sensitivity and specificity of > 95% offer an excellent scenario for early cancer detection (Bunaciu & Aboul-Enein, 2025). A further reason in favour of this confidence is the patient who was diagnosed with cancer but did not have the original tumour (i.e., T0; following resection during the biopsy, with additional surgery). The methods used here must be changed to show early (pre-symptomatic) cancer detection.

The prognosis is very bad for lung cancer patients who have malignant pleural effusions (MPE). Making the distinction between MPE and benign pleural

effusion (BPE) is essential. Based on FTIR near-infrared spectroscopy (NIRS) in conjunction with a machine learning approach, a recent study attempts to create a quick, practical, and affordable diagnostic tool for classifying clinical pleural effusions (Chen et al., 2021).

Fig. 7 presents the average NIR spectra for MPE (red) and BPE (blue) samples.

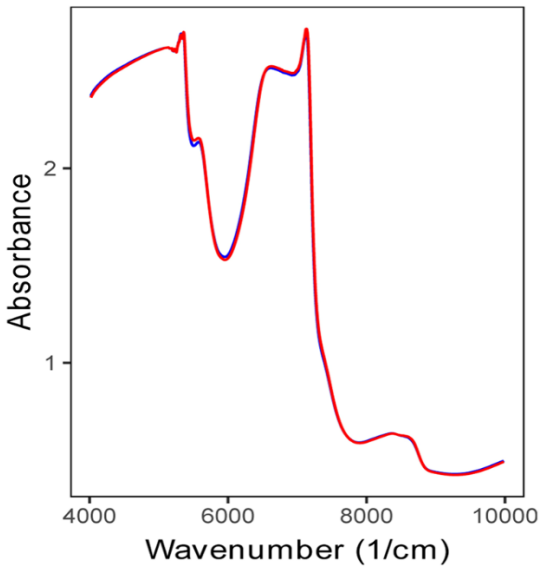

Fig. 7. Average NIR spectra for MPE (red) and BPE (blue) samples (Chen et al., 2021)

Even so, the NIR spectra provide a wealth of information about the chemical makeup of the pleural effusion, even in the absence of feature peaks (Bunaciu & Aboul-Enein, 2025). The first overtone of CH is indicated by wavenumbers between 4200 and 5500 cm^{-1}, the first overtone of OH, NH, and CH is indicated by wavenumbers between 5400 and 6100 cm^{-1}, wavenumbers between 6200 and 7600 cm^{-1} indicate the first overtone of CH, and wavelengths between 7900 and 9000 cm^{-1} indicate the second overtone of CH. Wavelengths of 6200 to 7600 cm^{-1} were used to indicate NH and CH combinations, whereas wavelengths of 7900 to 9000 cm^{-1} were used to indicate the second overtone of CH (Chen et al., 2015, Li et al., 2016).

This is the first study to use NIRS for pleural effusion categorisation. MPE typically denotes advanced cancer growth, which helps create a distinct malignant microenvironment that differs greatly from the surrounding healthy tissues and has different metabolites, such as proteins and lipids (Chen et al., 2015, Li et al., 2016, Zhou et al., 2012).

According to some other results, the IR-CRDS (infrared cavity ring-down spectroscopy) classification of alveolar breath is a potentially effective method for breast cancer screening (Naz et al., 2022).

3. CONCLUSIONS

The primary benefits of breath analysis over other tests currently used to investigate diseases are that it is non-invasive, sampling is relatively simple, results are available quickly, objective diagnoses can be made using AI/ML (Artificial Intelligence/Machine Learning) methods that require only relatively inexpensive equipment, and trained technicians can perform the test without the assistance of medical professionals such as radiologists, pathologists, oncologists, etc., particularly for preliminary screening of susceptible subjects (smokers, females over a certain age group, etc.).

Early disease identification, such as that of many types of cancer, results in more effective treatment and quicker recovery, which allows for significant cost savings in healthcare and prevents the loss of human resources. It also raises the standard of physical, emotional, and financial well-being in society (Bunaciu & Aboul-Enein, 2025). Non-communicable diseases, which make up the majority of healthcare costs, such as cancers of the internal organs (ovarian, liver, pancreatic, etc.), cardiovascular conditions, and communicable diseases of pathogenic origin (like COVID-19), require dependable methods that can identify them early using noninvasive, cost-effective, and universally applicable - that is, accessible, affordable, and acceptable - diagnostic techniques.

Breath analysis is not yet a diagnostic tool that clinicians may use, despite several VOC-based detection methods being available and considerable efforts. Given the tens of VOCs found in breath, infrared absorption spectroscopy is a promising method to close this gap.

AUTHORS' CONTRIBUTIONS

Author AAB contributed to conceptualisation, methodology, sampling and sample analysis, and wrote the first draft of the manuscript. Author HYAE contributed to data curation, supervision and wrote, review and edited the manuscript.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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