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Review Article

# FTIR Spectroscopy Used in Disease Treatment Monitoring

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## Abstract

Many acute and chronic illnesses are becoming more prevalent as the world's population ages and the medical field undergoes rapid change. As a result, there is a growing need for "point-of-care" (POC) identification/detection and real-time management of health issues that have been necessary for a long time. The human body develops many deadly illnesses in silence, with symptoms only showing up after the disease is far advanced. Vibrational spectroscopic (infrared and Raman) techniques in biofluids have advanced clinical diagnosis and prognosis; this review aims to demonstrate this development through a thorough literature assessment. IR (infrared) technology offers a suitable limit of detection for real-time, non-invasive, and non-destructive examination of organic substances. This review aims to compile the most relevant applications of infrared spectroscopy published between 2020 and 2026 that assess gait characteristics and related algorithms, demonstrating potential for assisting in disease diagnosis and symptom monitoring.

**Keywords**: Infrared Spectroscopy; Biomedical Analysis; Monitoring Disease Treatment

## Introduction

The goal of medical science is to determine the primary root of a disease, because pathology at the gross cellular level and morphological level is no longer sufficient. Targeting molecular events is the key to curing many severe diseases, which has led scientists to shift their focus to the molecular level. But until now, conventional imaging technologies, including magnetic resonance imaging (MRI), computed tomography (CT), and ultrasound (US), have been used to measure any modifications in a tumor's anatomical size to evaluate the response to treatment. However, with the advent of cytostatic medications, cancer vaccines, immunotherapy, cytokines, and so-called tailor-made drug therapy for individual patients, it is now crucial to assess the tumors' response to treatment at an extremely early stage, even before the anatomical size and clinical symptoms change [1].

One of the most significant concerns in clinical studies is treatment compliance. Study sponsors are now focusing on ways to engage patients and maximize drug adherence because chronic disease patients' non-adherence is associated with higher healthcare expenses, increased patient and society burden, and generally lower quality of life.

The human body develops many deadly illnesses in silence, with symptoms only showing up after the disease is far advanced, such as cancer [2], heart diseases [3], diabetes [4], etc.

Monitoring disease represents a periodic measurement that guides the treatment of a chronic or recurrent illness. Patients, clinicians, or both may carry out this task. Monitoring to determine whether the disease is progressing or regressing and whether complications are developing is typically part of the routine visitation ritual for most chronic diseases. Choosing what to monitor, when to monitor it, and how to modify treatment are all necessary for such inspections. Poor decisions in each can result in unsafe treatment modifications, poor time management, and poor control.

A cutting-edge technique in clinical research, biofluid spectroscopy provides researchers with a simple way to gather diagnostic and observational data from frequently collected samples. Because of its high sensitivity to minute biological changes and versatile sampling options, infrared spectroscopy is well-suited to analyze a wide variety of biofluid samples, including blood and its derivatives, as can be seen in Figure 1 [5].

**Figure 1:** Workflow of infrared spectroscopy in biological fluids (reproduced with permission from ref [5]).



For liquid biofluid analysis, ATR-FTIR spectroscopy should be given preference over conventional FTIR techniques because of its shorter sample pathlength and exponentially declining evanescent waves, which lessen interaction with the water molecules' strong dipole potential [6].

The goal of therapeutic monitoring, whether through functional or anatomical imaging, is to measure any or all of the aforementioned parameters before and after treatment. The World Health Organization (WHO) has set criteria for assessing how well a tumor responds to therapy. These standardized standards for evaluating therapy response state that the tumor's size should be assessed in two diameters that are perpendicular to each other. A reduction of at least 50% in the product of these two diameters resulting from therapy is referred to as a tumor response. A reaction is deemed complete if, following therapy, no lesion is still visible. The reaction is categorized as partial otherwise. These standards are derived from a 1976 X-ray investigation conducted by Moertel and Hanley [7].

By investigating the papers published from 2020 to 2026 on biological products, this study seeks to highlight additional important uses of infrared spectroscopy, in addition to those recently reported [8-17] to assess patients' health following a course of therapy. "Monitoring treatment disease using infrared spectroscopy" was used as a keyword, and over 9000 papers were found on the ScienceDirect, Wiley, Taylor & Francis, and SpringerLink websites.

## Infrared spectroscopy applications

To update the survival prognosis, get precise information on the tumor's response to therapy, and make prompt decisions about the next course of treatment, cancer treatment should be closely monitored. Magnetic resonance imaging (MRI), computer tomography (CT), positron emission tomography (PET), and other imaging methods are frequently used for monitoring cancer treatment [18,19], as well as specific blood tests. For many cancer types, however, determining response or prognosis is still difficult [20,21]. It is essential to have a rapid, easy, painless process that produces clinically significant data without upsetting the patient.

A new study turned the main disadvantage of NIR spectra - high water absorption - into an advantage by proposing an alternate technique for processing and analyzing them [22]. A conceptually different approach was applied - aquaphotomics, which studies the aqueous medium in biological samples.

## Viruses

The more research is done on viruses, the more data appear about new diseases caused by them.

Since its discovery in 1983, *Helicobacter pylori* (Hp), a type of stomach bacteria, has attracted a lot of interest [23] due to its potential to cause gastric issues, including peptic ulcer disease [24]. A quadruple treatment (QAC) of broad-spectrum antibiotics is a popular eradication strategy. QAC achieved 95% eradication success in 2011 [25]. It should be mentioned that Hp's adaptability to the antibiotics causes the course's success rate to decline with time [23,26]. After *Helicobacter pylori* was eradicated with an antibiotic course, a proof-of-principle spectroscopic analysis of one volunteer's breath was conducted to improve it. Treatment-sensitive absorption spectral patterns in the mid-infrared spectrum were identified using Fourier transform spectroscopy.

Two spectral bands were observed, with the associated structures closely linked to the beginning and conclusion of the treatment [27]. It turned out that the spectra correspond to two VOCs, namely methyl butyrate (1170 $cm^{-1}$ and 2972 $cm^{-1}$) and ethyl pyruvate (1130 $cm^{-1}$). Digital elimination of the above-lying carbon dioxide and aldehyde-related structures revealed structures at 1130 $cm^{-1}$ and 1170 $cm^{-1}$ [28].

Another virus of interest is COVID-19. Post-COVID Condition (PCC), a chronic health condition caused by the COVID-19 pandemic, manifests at least three months after the initial SARS-CoV-2 infection and can persist for years. Several studies have demonstrated the viability of infrared spectroscopy for diagnosis in the specific context of COVID-19 [15,16,29,30]. The spectroscopic workflow and optimization framework for PCC diagnosis and severity assessment are illustrated schematically in Figure 2. The picture illustrates the way the patient cohort is separated and blood samples are collected and processed into pellet fractions and supernatant, with 65 patients from previous proteomics and lipidomics research (Omics group) and 65 new patients (Extended group). Both fractions are subjected to UV-VIS-NIR-MIR spectroscopy, and various spectral preprocessing methods are employed, emphasizing the optimal spectral range of 297–600 nm. These methods include trimming, scatter correction, and second-order derivation. The optimization method is directed by the highest Jaccard score [17] and ensures the best alignment between spectral clustering and clinical categorization (symptomatic vs. asymptomatic). The two clusters (CL0 and CL1) that illustrate the patient clustering procedure and the iterative optimization cycle that selects the spectral parameters most closely linked to clinical severity are also shown in the workflow. Finally, it should be mentioned that the diagnostic model was validated using a larger sample size.

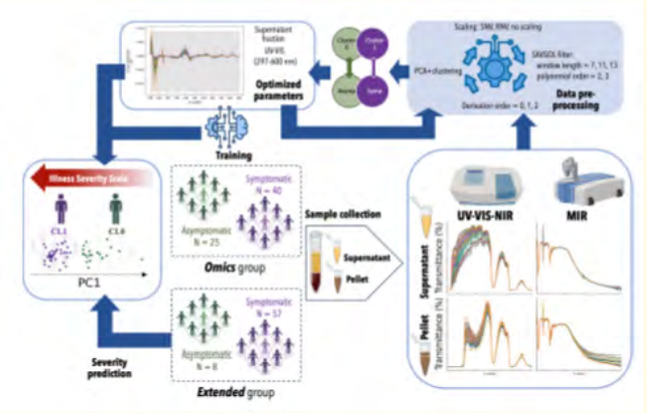


**Figure 2:** The spectroscopic workflow and optimization framework for PCC diagnosis and severity assessment (Reproduced with permission from ref [17]).


Rapid diagnosis and severity scale of post-COVID condition using advanced spectroscopy

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The potential utility of UV-VIS-NIR-MIR spectroscopy for the quick diagnosis and evaluation of PCC severity was examined. The identification of spectral regions is strongly associated with patient symptomatology and clinical outcomes, and was obtained by analyzing blood samples from 130 patients, 65 of whom had previously undergone lipidomic and proteomic investigations. These blood samples were evaluated, and spectral regions that were significantly associated with patient symptomatology and clinical outcomes were found.

While the MIR region provides rich information on vibrational modes, allowing a comprehensive study of molecular structures and interactions, the UV–VIS–NIR region is very sensitive to electronic transitions in biomolecules, making it excellent for detecting changes in electronic states. Because supernatant and pellet fractions include complementary information, studying both helps gain a thorough understanding of the molecular makeup and interactions of blood. Insights into soluble proteins, lipids, and other circulating biomolecules can be gained from the supernatant fraction, which mostly contains plasma. On the other hand, the pellet fraction, composed of cellular components and other luteal materials, provides information about the intracellular milieu and substances linked with cells. While the MIR region provides precise information on vibrational modes, allowing a comprehensive study of

molecular structures and interactions, the region is very sensitive to electronic transitions in biomolecules, making it excellent for detecting changes in electronic states. Studying both supernatant and pellet fractions is useful for a thorough knowledge of blood's molecular makeup and interactions, as they include complementary information. Soluble proteins, lipids, and other circulating macromolecules are revealed by the supernatant fraction, which mostly contains plasma. In contrast, the pellet portion, comprising cellular components and other particulate matter, offers information about the intracellular milieu and cell-associated chemicals. Distinctive patterns and absorptive characteristics that may point to particular biochemical alterations or ease states can be found by examining the spectra of both fractions. The potential application of UV-VIS-NIR-MIR spectroscopy for the quick diagnosis and severity evaluation of post-COVID condition (PCC) was examined in this work.

Given the circumstances of the pandemic of novel coronavirus disease 2019 (COVID-19), which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and has resulted in a significant loss of human life and economic damage, studies for the development of respiratory virus detection methods, particularly those with low cost, rapid ease of use, and high accuracy, are urgently needed.

The literature has rarely reported the use of portable NIR spectrometers to identify SARS-CoV-2 or the impact of the viral infection, in part due to the devices' comparatively poor quality and insufficient specificity and accuracy. This study's main goal was to investigate the viability of using a portable NIR spectrometer in conjunction with machine learning to detect the presence or absence of a respiratory virus, such as the Sendai virus (SEV) or respiratory syncytial virus (RSV), in an in vitro aqueous sample [31].

Two of the most popular medications for bacterial infections are ampicillin (AMP) and amoxicillin (AMX). While accuracy and analysis speed are two issues that traditional drug monitoring systems frequently confront, optical-based techniques present a possible substitute. An established method that works well for this is Fourier Transform Infrared Spectroscopy (FTIR). They may be challenging to distinguish using FTIR spectroscopy due to their similar chemical structures and distinctive infrared absorption characteristics. Chemometric analysis is therefore crucial to overcoming this obstacle.

By utilizing vibrational spectroscopy's capabilities, a study presents a fresh approach to the conventional techniques of antibiotic detection and monitoring, supporting antimicrobial stewardship [32].

The ATR-FTIR spectra of amoxicillin and ampicillin under heat and acidic conditions, and the non-degraded control group, are compared in the graphs in Figure 3.

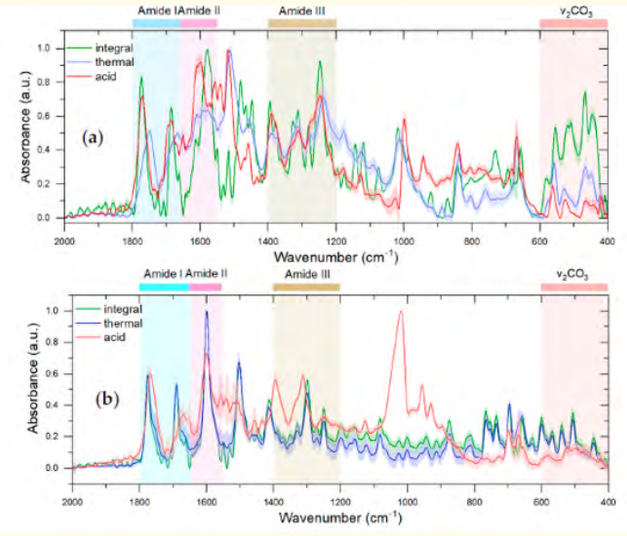



**Figure 3:** FTIR spectra of (a)AMX and (b)AMP under integral, thermal, and acidic degradation conditions.

(reproduced with permission from ref [32]).

There is a linear relationship between AMX concentration and peak intensity at 1313 $cm^{-1}$. The 1398 $cm^{-1}$ peak was used similarly for AMP

## Diabetes mellitus (DM)

Hyperglycemia is a signature of this metabolic disease, which is brought on by either insufficient secretion or decreased insulin action in peripheral tissues, and/or a diminished impact of insulin on glucose uptake in peripheral organs like the liver, adipose tissue, and skeletal muscle [33-36]. The International Diabetes Federation (IDF) estimates that 425 million people globally have diabetes, with an additional 212 million likely to go undiagnosed [37]. Diabetes mellitus (DM) can be accurately diagnosed with blood, but the process is intrusive, expensive, and painful. In this respect, the integration of ATR-FTIR spectroscopy and machine learning algorithms across diverse biological samples has been employed as an alternative approach to establish a non-invasive, rapid, inexpensive, and label-free diagnostic or screening platform for numerous disorders, including DM.

Despite being thought of as potentially fatal, diabetes mellitus (DM) is an incurable metabolic disease that is hypoglycemic due to the destruction of insulin-secreting pancreatic β-cells, which causes the body to metabolize glucose inefficiently and elevate blood glucose levels [38]. Both macrovascular and microvascular consequences, such as neuropathy [39], cardiovascular disease [40], diabetic kidney disease [41], are linked to diabetes mellitus (DM). For those with diabetes, these consequences can result in a lower quality of life, blindness, renal failure, and an increased risk of death [42,43].

Generally speaking, blood glucose monitoring for diabetes is an intrusive, uncomfortable, and expensive procedure. Although applications in the monitoring of diabetes treatment are still in their infancy, ATR-FTIR spectroscopy has been utilized to diagnose several diseases [44]. Potential salivary biomarkers linked to glucose monitoring were identified by evaluating the saliva of non-diabetic (ND), diabetic (D), and insulin-treated diabetic (D+I) mice using a novel technique called ATR-FTIR spectroscopy [45]. Representative average ATR-FTIR spectra (3000–400 cm-1) in the saliva of rats with diabetes (D), non-diabetic rats (ND), and diabetic rats receiving insulin treatment (D+I) are shown in Figure 4.

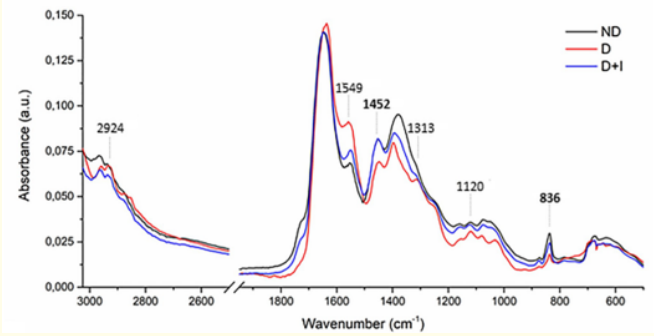



**Figure 4:** Representative average ATR-FTIR spectra (3000–400 $cm^{-1}$) in the saliva of rats with diabetes (D), non-diabetic rats (ND), and diabetic rats receiving insulin treatment (D+I) (reproduced with permission from ref [44]).



The ability of ATR-FTIR spectroscopy in saliva to distinguish between diabetic and non-diabetic rats, as well as insulin-treated diabetic rats, was demonstrated in the conclusion. In univariate analysis, these findings point to certain fingerprint regions (two salivary spectral modes, 1452 $cm^{-1}$ and 836 $cm^{-1}$) that can distinguish between hyperglycemic and normoglycemic circumstances (whether or not insulin has been administered). The PCA-LDA (principal component analysis followed by linear discriminant analysis) and HCA (Hierarchical Cluster Analysis) multivariate models also achieved a very high discriminatory accuracy of 95.2% for separating the infrared spectra of saliva between rats with diabetes, rats without diabetes, and rats receiving insulin. All things considered, these salivary findings imply that ATR-FTIR spectroscopy may provide a novel non-invasive diabetes monitoring technique that supports medical decision-making to avoid insulin overtreatment or undertreatment when combined with univariate or multivariate chemometric analysis.

These results suggest that two salivary band regions, at 1452 $cm^{-1}$ and 836 $cm^{-1}$, may be considered non-invasive spectral biomarkers for monitoring diabetes treated with insulin, which could have clinical implications. It should ideally be possible to distin-

guish between various pharmacological treatments and glycemic levels; thus, more research is required.

The benefits, drawbacks, and other details of the non-invasive optical techniques under discussion were compared in some reviews [8,16,46]. These techniques have a lot of promise, but they also have drawbacks, such as problems with sensitivity, stability, specificity, biological influences, and calibration. To overcome these drawbacks and, ideally, replace the current conventional approaches, these non-invasive optical techniques must be improved.

According to recent recommendations, people suffering from type 2 diabetes mellitus (T2DM) should control their glycated hemoglobin (HbA1c) level to lower their risk of macrovascular disease [47,48]. However, glycemic excursion and hypoglycemia, both of which have an impact on cardiovascular outcomes in T2DM patients, are not addressed by HbA1c, which represents the approximate average plasma glucose level during the preceding 8–12 weeks [49,50].

A recent study [51] used serial intravascular ultrasound (IVUS) and near-infrared spectroscopy (NIRS) imaging, both of which have been demonstrated to predict the future risk of cardiovascular events, to compare the effects of GCM (continuous glucose monitoring) and HbA1c (glycated hemoglobin) guided glucose control on coronary atherosclerosis in T2DM patients with CAD (coronary artery disease) [52,53].

Urine can be analyzed using a variety of techniques, and ATR-FTIR spectroscopy can be a good choice because it is sensitive and non-destructive. When applied to liquid matrices, ATR-FTIR spectroscopy may extract complex biochemical information from the vibrational energy present in chemical bonds found within biomolecules, including lipids, proteins, carbohydrates, and nucleic acids. By adjusting components absorbed at specific wavenumbers using the infrared (IR) spectrum, ATR_FTIR may assess several urine components, including creatinine, urea, uric acid, phosphate and sulfate, and cystinuria [54].

Through the use of infrared (IR) spectrum manipulation, ATR-FTIR, in particular, can assess a variety of urine components, including creatinine [55], urea [56], and cystinuria [57]. ATR-FTIR spectroscopy is employed in a recent study as a unique method to track changes in urine chemicals altered by diabetes [58], and to demonstrate how ATR-FTIR spectroscopy combined with machine learning modeling can distinguish between the urine components of rats that are diabetic and those that are not.

In Figure 5, the FTIR-ATR spectra of raw (a) and average (b) spectra acquired within the bio-fingerprint region, spanning the wavenumber range of 1800–900 $cm^{-1}$, extracted from samples belonging to individuals with diabetes and those from controls [58].

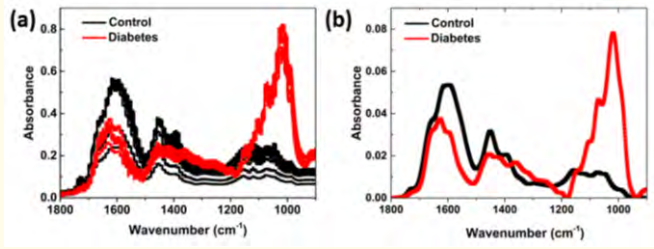



**Figure 5:** FTIR-ATR spectra of raw (a) and average (b) spectra (reproduced with permission from ref [58].



The accuracy of machine learning models for distinguishing individuals with diabetes, diabetes and periodontitis, and those without systemic disorders (control group) was assessed in a recent study [59]. The FT-IR spectra of these patients' saliva samples were analyzed to construct these models. Additionally, it was determined that the primary molecular components of each study group's saliva samples produced data to possibly assess the viability of using real-time saliva analysis to non-invasively diagnose periodontitis and diabetes in future FT-IR clinic implementations.

The accuracy of machine learning models for distinguishing between individuals with diabetes, diabetes and periodontitis, and those without systemic disorders (control group) has been assessed in this work. The FT-IR spectra of these patients' saliva samples were analyzed to construct these models. Furthermore, we have determined the primary molecular components of each study group's saliva samples and produced data that may be used

to assess the viability of using real-time saliva analysis in future FT-IR clinical implementations to non-invasively diagnose diabetes and periodontitis.

The mean FT-IR spectra of control patients, patients with diabetes alone (no periodontitis), and patients with diabetes + periodontitis are displayed in Figure 6. The fingerprint region between 600 and 1300 $cm^{-1}$ may differ between control and diabetic patients, according to the mean FT-IR spectra. This includes the peak at the band centered at 1076 $cm^{-1}$ that corresponds to the vibrational mode of the skeletal cis conformation of DNA, a band of symmetric $CH_3$ bending modes of protein methyl groups and collagen's $\delta sCH_3$, and a band of asymmetric $CH_3$ bending modes of protein methyl groups at 1403 $cm^{-1}$. It may be necessary to combine data from multiple spectral regions to distinguish between patients with diabetes and those with diabetes and periodontitis.

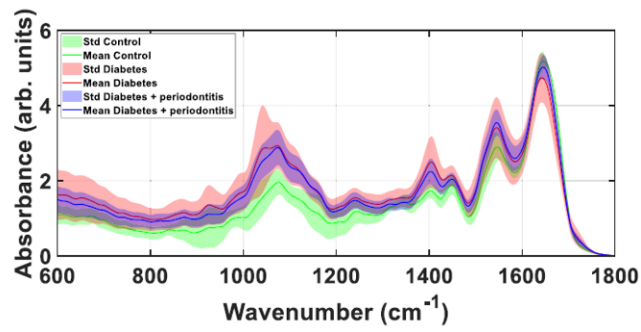



**Figure 6:** Mean and standard deviation (Std) of FT-IR spectra of saliva samples of each study group.



(reproduced with permission from ref [59].

Cancer is a complex disease linked to cancer cell division, metastasis-associated tumor characteristics, and organs associated with the main tumor. Prolonged, unchecked cell proliferation can lead to cancer. Cancer is linked to about 10 million deaths annually, making it the second most deadly disease in the world, according to the World Health Organization [60]. In 2040, there will likely be over 30 million cases worldwide, a 47% increase from 2020.

The microscopic examination of stained tissue samples by pathologists, which is carried out when malignant or precancerous tumors are visible and already contain notable genetic alterations, remains the gold standard for the majority of cancer diagnoses. Furthermore, because the histological diagnosis mostly relies on the subjective assessment of pathologists, which causes variances both within and between observers, it is intrusive, time-consuming, and has low sensitivity.

As a result, tissue assessment frequently involves misdiagnosis with high rates of false positives and false negatives [61]. In actuality, 10% of pathologic evaluations were unable to produce a definitive diagnosis due to either histologically identical tumors or poorly differentiated cells that made it difficult to identify the tissue of origin [62]. Finding new biomarkers linked to a disease may result from FTIR spectroscopy's sensitivity to chemical changes that occur during the change from a normal to a diseased state or during therapy [63]. Therefore, FTIR spectroscopy is a powerful tool with enormous potential for clinical use that extends beyond cancer screening, diagnosis, and prognosis to monitoring ongoing therapy responses and disease progression or regression in personalized medicine.

In the present day, the most popular cancer therapies are chemotherapy, radiation, and surgery, with surgery serving as the foundation for solid tumor treatment. During surgery, a visible tumor is removed with a fringe of normal tissue to guarantee total tumor removal. Since the range of surgical removal is strongly related to patients' long-term survival and post-operative recovery, adequate resection margins during surgery are crucial to preventing under- or over-treatment.

The primary objective of FTIR spectroscopy was to find the absorption characteristics in the mid-infrared (4000–600 $cm^{-1}$) range. The various vibrations of biomolecules, including proteins, nucleic acids, lipids, and carbohydrates, are the main source of the sharp bands in this region. As a result, each sample has a very different spectral profile and absorption pattern (Figure 7). Sample preparation, spectrum acquisition, and data interpretation are the primary processes. The type of sample determines how the samples are pretreated. After that, the sample is put on a substrate for infrared spectroscopy, like $BaF_2$ slides. The A2780 ovarian cancer cell line's representative infrared spectrum is displayed. Asymmetric and symmetric phosphodiester vibrations of nucleic acids ($\nu_{as}PO_2^-$ and $\nu sPO_2^-$), ester C=O stretching of phospholipids, pro-

tein absorption bands (Amide I and Amide II), asymmetric and symmetric vibrations of fatty acyl moieties ($v_{asym}$ $CH_3$ and $CH_2$), and C–O–C vibrations for sugars are the primary absorption bands that identify cellular components. According to a recent research [64], spectral characteristics were collected, and the data analysis was intricate, as presented in earlier studies [64-66].

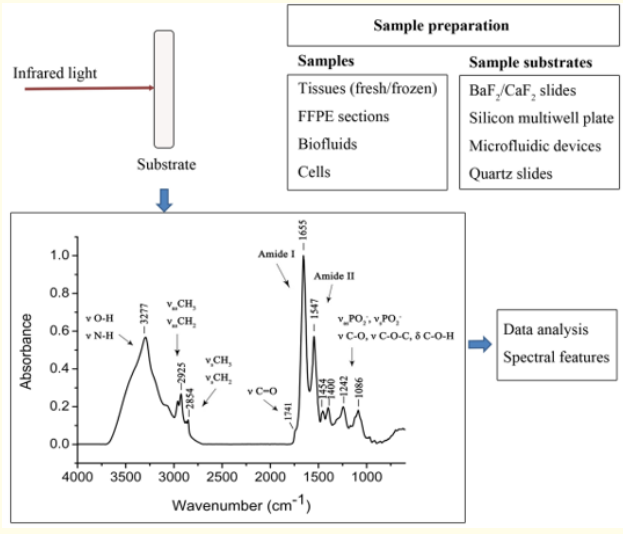



**Figure 7:** Schematic illustration of the FTIR spectroscopy measurement flow.

(reproduced with permission from ref [67]).



When used on blood serum or plasma samples [67] it produces an infrared molecular fingerprint (IMF) that represents the molecular blood phenotype of the individual, or the chemical makeup of the sample [68,69]. It offers a platform for discovery that offers chances to find more biomarkers for lung cancer detection [70].

The substantial correlation between IMFs and the advancement of lung cancer is depicted in Figure 8b. In Figure 8a, the infrared spectra of blood samples are presented. In particular, we plot the differential fingerprint for several matched lung cancer case-control groups (controls are healthy volunteers who do not exhibit any symptoms) according to the TNM (Tumor, Node, Metastasis) stage in Fig. 8b. It was noted that patterns associated with disease cover a wide spectrum. Specifically, the 1000 $cm^{-1}$–1700 $cm^{-1}$ range offers informative patterns associated with many possible biomolecules. The absorbance of proteins and carbohydrates, particularly glycosylated proteins, has historically been associated with this area. Changes in their concentration, structure, or glycosylation pattern may therefore be the cause of changes in this area.

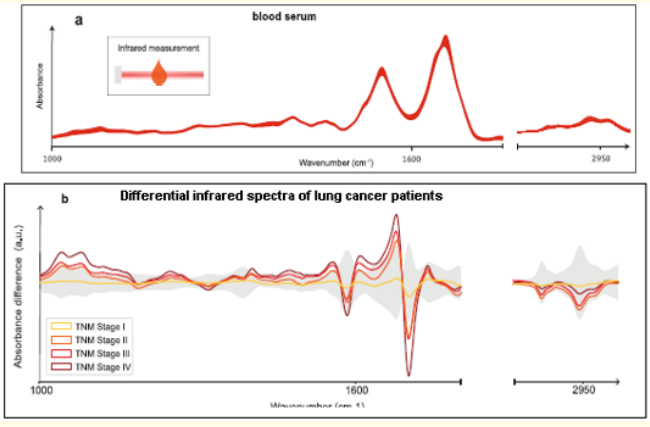



**Figure 8:** Infrared spectra of blood samples (a) and lung cancer patients (reproduced with permission from ref [67]).



The hemodynamic and metabolic status of the tumor can be changed by cancer treatment, which impacts the effectiveness of later treatments [71]. In the presence of high hemoglobin and low oxygen saturation, tumors are visible for NIR spectroscopy due to their high metabolic requirement and/or occasionally poor perfusion. The monitoring of tumor hemodynamic alterations and tissue oxygen are key factor in the selection of anticancer medications and the best dosage [72].

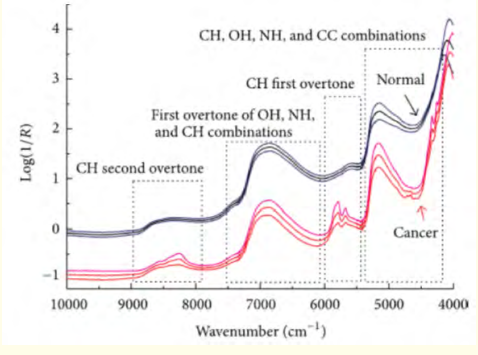



**Figure 9:** Mean NIR spectra of healthy control and cancerous samples, with an indication of the major NIR-absorbing components (oxy -, deoxy -, and total-hemoglobin, water, and lipids), (Reproduced with permission from ref [73]).

Cancer serum diagnostics using ATR-FTIR is a promising analytical method for a variety of malignancies, such as brain [74], lung [75], ovarian [76,77] and others [78]. Clinical translation is still a challenge. Several significant technological obstacles have been encountered throughout the shift from research to normal clinical testing. These obstacles include those posed by the current patient pathway and the acceptability of a new diagnostic test by clinicians.

ATR-FTIR spectroscopy and machine learning models in liquid biopsies are used to detect solid tumors, as can be seen in Figure 10 [76].

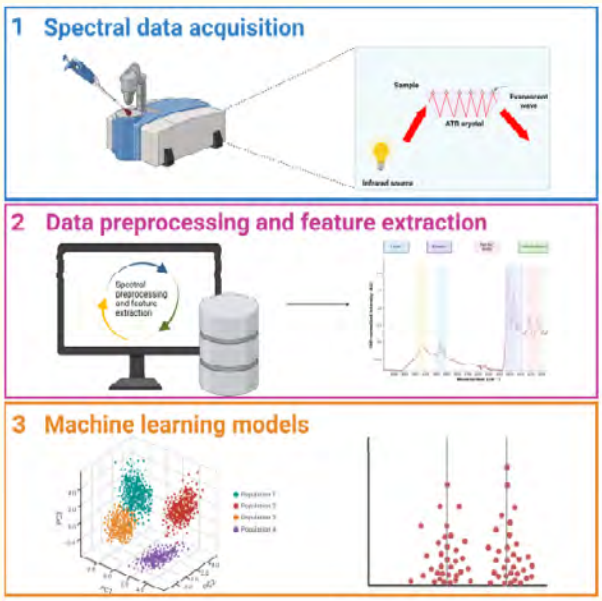



**Figure 10:** ATR-FTIR spectroscopy and machine learning in liquid biopsies are applied in this workflow for solid cancer identification. (Reproduced with permission from ref [76]).



Liquid biofluid samples, like serum or plasma, are applied to the spectrometer's ATR crystal in the first step, known as spectral data acquisition. An evanescent wave created at the crystal–sample contact allows infrared light to interact with the sample, creating a distinct spectral fingerprint that indicates the chemical composition of the biofluid. The obtained spectra are processed to lower noise, fix baseline variations, and normalize the data in the second stage, which also involves feature extraction and data processing. Proteins, carbohydrates, lipids, and nucleic acids are among the components whose important biochemical characteristics are isolated for additional study. Principal component analysis (PCA) and supervised models like support vector machines (SVMs) are used to analyze the processed spectral data during the machine learning stage.

In China, lung cancer is the most prevalent type of cancer and the main cause of death. Histopathological analysis of tumors is the current gold standard for clinical lung cancer detection; nevertheless, its ease of use and practical applicability are limited. As a result, scientists are still working to create new instruments and techniques for quick and non-invasive evaluation of lung cancer patients' health. Human health concerns are directly linked to hair, which is a reflection of the body's metabolism. Fourier-transform infrared (FTIR) spectroscopy has the potential to investigate the primary chemical compositions found in hair [79]. Additionally, it was shown that FTIR spectroscopy could be used to track the hair of patients with lung cancer receiving chemotherapy, and it was verified that the FTIR spectra of the hair might represent the chemotherapy's side effects. Accordingly, this study supports the use of FTIR spectroscopy in hair analysis to help with lung cancer medical diagnosis and to track the health of patients receiving therapy.

Figure 11 presents a comparative workflow for hair analysis for healthy or lung cancer patients [79].

With a focus on HCC (hepatocellular carcinoma), a recent study attempts to explore the utilization of circulating EVs' (extracellular vesicles) mid-IR spectral response as a possible source of novel cancer biomarkers [80]. The study comprised 10 HCC patients with underlying cirrhosis and 16 cirrhotic individuals without liver cancer symptoms (control group) to accomplish this goal. ATR-FTIR spectroscopy was used to characterize the EVs that were extracted from these individuals on a dry deposit. Significant spectral differences between the two patient groups were found by this analysis,

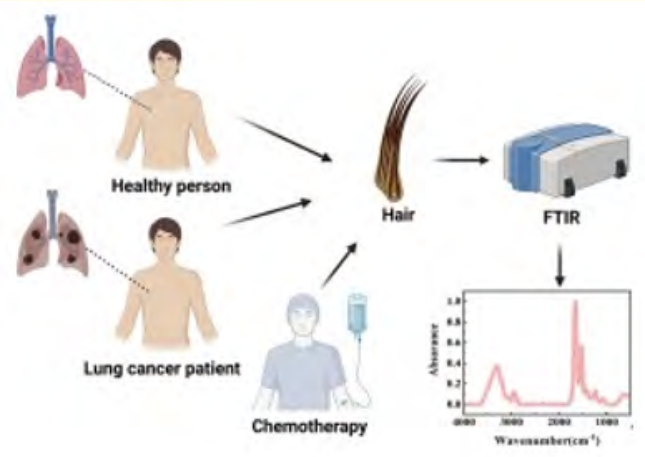
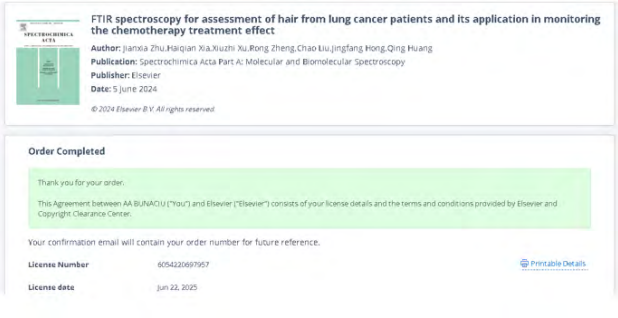



**Figure 11:** Comparative workflow for hair analysis for healthy or lung cancer patients (Reproduced with permission from ref [79]).


FTIR spectroscopy for assessment of hair from lung cancer patients and its application in monitoring the chemotherapy treatment effect

Author: Jianxia Zhu,Haiqian Xia,Xiuzhi Xu,Rong Zheng,Chao Liu,Jingfang Hong,Qing Huang

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and these differences could potentially improve AFP's (alpha-fetoprotein) diagnostic effectiveness if they are confirmed in subsequent research.

The average mid-infrared (mid-IR) spectra of HP samples taken from individuals with cirrhosis (blue solid line) and HCC (red solid line) are shown in Figure 12a. The 95 percent confidence bands that correspond to the mean spectra are displayed as shaded regions. The mid-IR spectral response of EV-enriched samples taken from cirrhotic patients (shown by the cyan continuous line) and HCC patients (shown by the red continuous line) is compared in Figure 12b.

X-ray radiation treatments are widely used in radiotherapy. FTIR spectroscopy, even when we are talking about classical or microspectroscopy techniques, proved to be useful for monitoring radiotherapy effects [81].

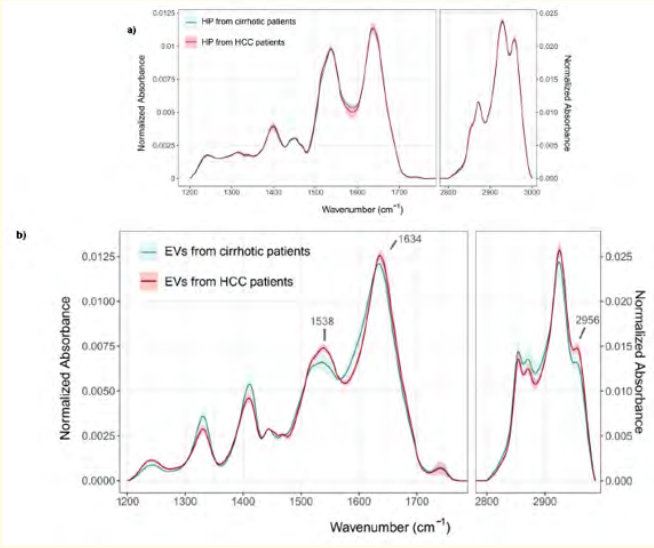


**Figure 12:** Comparison of average mid-IR spectra a). between cirrhotic (blue solid line) and HCC (red solid line) patient samples b). between EV-enriched samples from cirrhotic patients without signs of liver cancer (cyan) and HCC patients with underlying cirrhosis (red). (reproduced with permission from ref [80].



Figure 13 shows the average spectra of cells subjected to various X-ray doses (0, 2, and 4 Gy) and fixed right away after two and four hours of irradiation. When comparing the spectra of the irradiated and control samples, X-ray exposure causes wavenumber shifts as well as changes in the intensity and shape of the absorbance bands associated with the lipid, protein, DNA, and carbohydrate cell components.

## Conclusions

Clinical FTIR spectroscopy's primary goal is to develop new and enhanced techniques for identifying illnesses that are currently challenging or costly to diagnose using current techniques. By looking for global changes in the spectra that may be connected to the disease but do not necessarily have a known cause, or by examining the spectrum of samples for particular spectral markers, spectroscopy can be used to diagnose diseases.

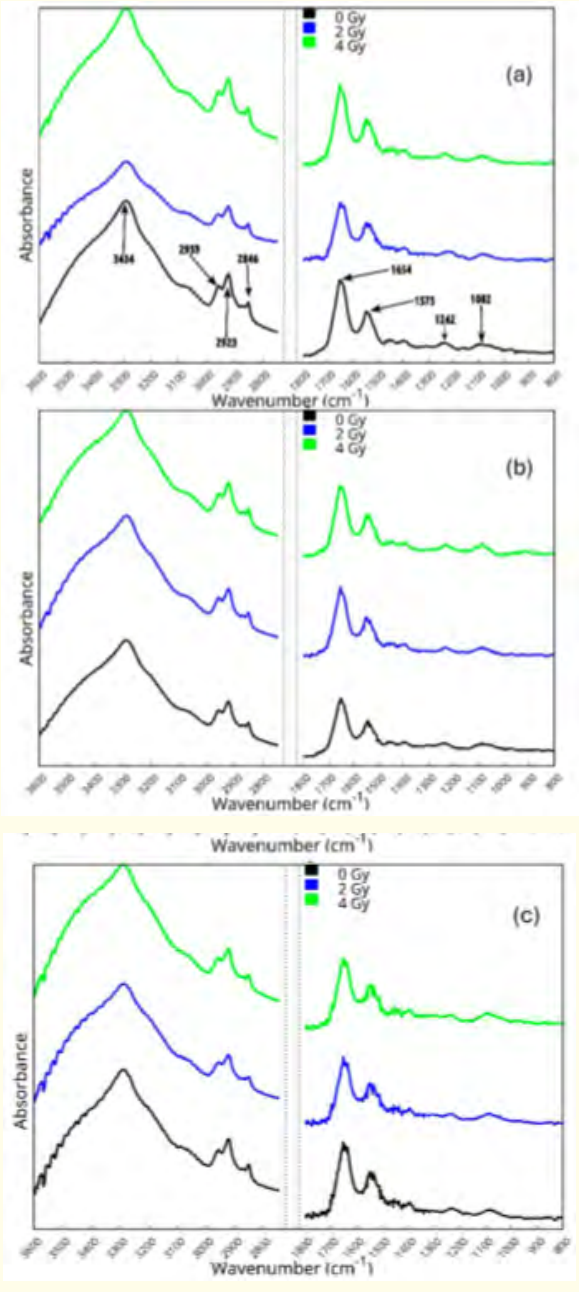


**Figure 13:** Average spectra for control and irradiated cells in the wavenumber region from 3600 to 800 cm−1 at different X-ray doses (0, 2, and 4 Gy) and fixed at different times after irradiation ((a) immediately after (t = 0), (b) 2 h after, and (c) 4 h after irradiation]. The spectra are vertically shifted to avoid overlapping. (reproduced with permission from ref [81]).



The promise of infrared spectroscopy as a quick, affordable, and clinically useful diagnostic tool that can be used for several diagnostic paths in our contemporary healthcare system has been well demonstrated. On the road to clinical translation, infrared spectroscopy is still in its early stages, and several obstacles need to be overcome before infrared spectroscopic technologies may be clinically used in the healthcare industry.

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