



Ftir Spectroscopy Used in Cancer Diagnostics

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Abstract

Although infrared spectroscopy has long been used to describe chemical molecules, its applicability to the analysis of biological materials containing very complex chemical components is questionable. Recent advancements have significantly increased infrared spectroscopy's capacity to examine various biological materials. As a result, more research is being done with infrared spectroscopy for disease screening and diagnosis. By identifying biochemical alterations in cancer patients, Fourier transform infrared spectroscopy has the potential to enhance clinical decision-making and patient outcomes because it is more straightforward, quick, accurate, affordable, non-destructive, and automated than current screening, diagnosis, management, and monitoring techniques. By accurately identifying the molecular conformations, bonding types, functional groups, and intermolecular interactions that make up the specimen, FTIR spectroscopy can determine biochemical compositions inside biological materials, such as nucleic acids, proteins, lipids, and carbohydrates. IR spectroscopy creates a distinctive spectral fingerprint of absorbance peaks for various characteristics of the genome, lipidome, proteome, and metabolome in the sample under study, since every molecule has a different spectrum based on the wavelength and amount of infrared light being absorbed.

Keywords: Infrared Spectroscopy; Biomedical Analysis; Cancer Diagnostic; Treatment Monitoring

Introduction

Cancer is a broad range of diseases that can start in almost any organ or tissue of the body when abnormal cells multiply uncontrollably, travel beyond normal limits to infect adjacent body parts, and/or spread to other organs. One of the main causes of cancer-related death is the latter phase, known as metastasis. Other synonyms for cancer include malignant tumor and neoplasm.

Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2024, or nearly one in six deaths [1]. The most common cancers are lung, breast, colon and rectum, and prostate cancers. Nearly a quarter of deaths from cancer are due to

tobacco use, alcohol consumption, high body mass index, low fruit and vegetable intake, and lack of physical activity. In addition, air pollution is an important risk factor for lung cancer.

The term "cancer" describes a collection of diseases associated with uncontrolled cell changes caused by tumor growth. Organs that frequently form tumors include the skin, lungs, prostate, breast, and pancreas. The majority of specialists agree that some of the most prevalent causes of tumor growth are age, genetic predisposition, alcohol intake, smoking, UV radiation, unhealthy lifestyles, and toxins, even though there are no specific factors that affect the disease's spread.

A major tactic to lower death rates from cancer is early diagnosis because therapy is more successful at this stage. Additionally, ongoing advancements in cancer development research and molecular biology have led to more precise and efficient treatments for a variety of tumors) [2].

Numerous scientific fields and techniques have been studied to enhance early cancer detection. Research was performed on the identification of circulating tumor DNA (ctDNA), but this approach has not yet been successfully incorporated into clinical practice due to technological challenges and economic limitations [3]. However, numerous proof-of-principle studies have shown that a range of biofluids can be analyzed using infrared (IR) spectroscopy [4]. It has the potential to be a very useful clinical tool for the early detection of a variety of malignancies because of its low cost, non-invasive nature, speed, high sensitivity, and specificity.

A significant strategy for decreasing death rates from cancer is early diagnosis, since therapy is more successful at this stage. Furthermore, current developments in cancer progression research and molecular biology have led to more precise and efficient treatments for a variety of tumors [2]. Screening is based on the identification of tumor-specific biomarkers present in various body tissues or biofluids. It is an essential method for the early detection of numerous malignancies. These same biomarkers can also be used for diagnosis, staging, and illness monitoring [3].

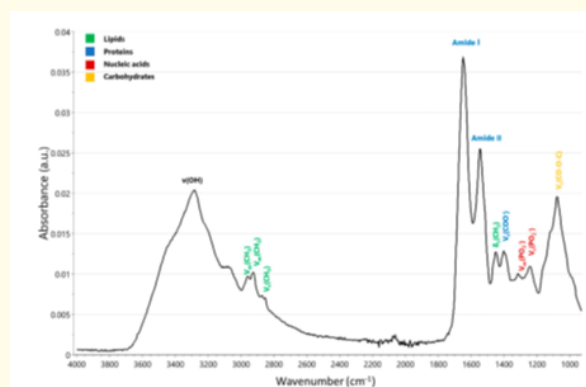
Modern clinical testing, such as cytological examination, immunohistochemistry, and imaging techniques, has demonstrated exceptional efficacy in disease diagnosis. However, several of them still have only mediocre diagnostic accuracy. Moreover, they require costly and time-consuming procedures. They might also involve several tests, be non-automated, or need user interpretation. To satisfy these needs, infrared spectroscopy has been suggested as a technique for identifying and diagnosing a wide range of disorders. By providing information on several biological molecules at once, these technologies create a biochemical “fingerprint” that can be used to identify whether a disease is present and the stage at which it is progressing.

The accuracy of the test must always be considered when assessing the usefulness of screening. Sensitivity is the test’s ability to correctly identify people with cancer among those with cancer (true positives/true positives + false negatives), while specificity is the test’s ability to correctly identify people without cancer among the population without cancer (true negatives/true negatives + false positives). The majority of cancer tests have a sensitivity of 70% to 80% and a somewhat lower specificity of 60% to 70%, although no diagnostic test may achieve both.

It is feasible to investigate the molecular structure of both organic and inorganic materials using vibrational spectroscopy. However, interest in vibrational spectroscopy in the medical field has just recently grown. Even though histology is still the gold standard for diagnosing cancer, numerous studies have looked into using infrared (IR) spectroscopy to analyze cells, tissues, and biofluids because of the technique’s ease of use, speed, and affordability, which could pave the way for early cancer detection and clinical implementation [4-9].

The ability of infrared spectroscopy to detect even the smallest metabolic changes at the molecular level allows for the identification of spectral variations that correlate to the onset of disease.

Conventional techniques for obtaining diagnostic samples, such as tissue or blood biopsies, are time-consuming, intrusive, and uncomfortable. For gathering and analysis, they might also require specialized tools and skilled workers. Patient outcomes may suffer as a result of these restrictions, which delay diagnosis and treatment. As a result, quick, non-invasive diagnostic techniques that yield precise and trustworthy results are required. Saliva is the sample type for illness detection and monitoring because it is a fluid that is easily accessible for non-invasive collection. It includes a variety of biomolecules that can reveal important details about a person’s health [10].



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Figure 1: A typical MIR spectrum measured with attenuated total reflection-Fourier transform infrared (ATR-FTIR) spectroscopy of a saliva sample (Reproduced with permission from ref [10]).

The characteristic IR spectrum of saliva, presented in Figure 1, reveals the presence of lipids (3000–2800 cm^{-1}), proteins (1700–1600 and 1560–1500 cm^{-1}), and nucleic acids (1250–1000 cm^{-1}). The amide A band, characterized by a broad peak at 3273 cm^{-1} and a medium-intensity narrow peak at 2057 cm^{-1} , corresponds to thiocyanate (SCN^{-1}) anions and is characteristic of saliva. The bands located at 1649 and 1543 cm^{-1} are assigned to amide I and II, respectively, while the band at 1075 cm^{-1} is attributed to sugar fragments.

We have already discussed some significant uses of FT-IR spectroscopy in biomedical research [4,5,11]. This study aims to showcase recent applications of FT-IR spectroscopy for differentiating malignant and normal cells with varying degrees of dysplasia and to monitor the impact of treatment on the affected tissue. Using biological materials ranging from the most commonly used blood and tissue specimens to the less frequently used urine and sputum samples, I discussed the clinical applications of FTIR spectroscopy for cancer in this review. The justification and benefits of employing EVs for FTIR spectroscopic analysis in cancer screening and diagnosis are also covered. It also discusses the difficulties and potential paths for practical application of the method for cancer.

Applications of infrared spectroscopy in cancer analysis

Effective cancer management requires accurate staging and grading of disease to determine appropriate treatments, predict the clinical behavior of malignancies, and facilitate the exchange of precise information among clinicians. Cancer staging denotes the anatomic extent of the disease spread. The internationally accepted staging criteria for cancer, the tumor-node-metastasis (TNM) system, comprises: (i) tumor size and local growth (T); (ii) extent of lymph node metastases (N); and (iii) occurrence of distant metastases (M) [12].

Next, I will present some results that come from several studies published between 2020 and 2026 on the use of FTIR spectroscopy for analysis of various cancer types.

Bladder cancer is increasing by 1 % annually, and it is more common in men than in women. The American Cancer Society's estimates for bladder cancer in the United States for 2026 are: about 84,530 new cases (64,730 in men and 19,800 in women),

and about 17,870 deaths (about 12,640 in men and 5,230 in women) [13].

Urinary cytology and cystoscopy are two examples of current diagnostic techniques that have serious drawbacks. Despite being the gold standard, cystoscopy is invasive, has a 5.5% risk of urinary tract infections, and can be traumatizing for patients because it must be repeated frequently for monitoring [14]. Urinary cytology, which has a 90% sensitivity for high-grade tumors, is still ineffective for low-grade tumors [15]. Additionally, there is a lot of individual variation in urinary cytology, which influences how it is interpreted [16].

There are several reviews published in this period of time related to the analysis of bladder cancer using FTIR spectroscopy [17-22].

To prevent spectral alteration from freezing [23], a study intends to assess the potential of mid-infrared absorption spectroscopy on entire, fresh urine samples as a diagnostic method for bladder urothelial cancer [15].

Four cancer stages can be used to classify the “tumor” group: Tis (CIS): Non-invasive carcinoma, also known as carcinoma in situ (CIS), in which the tumor stays contained to the deepest layer of the bladder without entering the muscle or connective tissues. Ta: Non-invasive papillary carcinoma that penetrates the core of the bladder but has not yet spread to the layers of muscle or connective tissue. T1: The tumor has not yet penetrated the muscle layer but has penetrated the connective tissue beneath the bladder lining layer. T2: The bladder's muscular layer is invaded by the tumor, but it hasn't completely penetrated the muscle to reach the surrounding adipose tissue.

Figure 2 presents the FTIR spectrum comparison of the control and tumor stages.

In a different investigation, benign and malignant bladder diseases, including the grade and stage of malignancy, were distinguished ex vivo right after resection using near-infrared (NIR) spectroscopy [24]. They showed that each diseased group can have clearly distinct spectra obtained with a portable NIR spectrometer. The fluctuating concentration of tissue constituents such as water, lipids, DNA, and proteins is responsible for the peaks

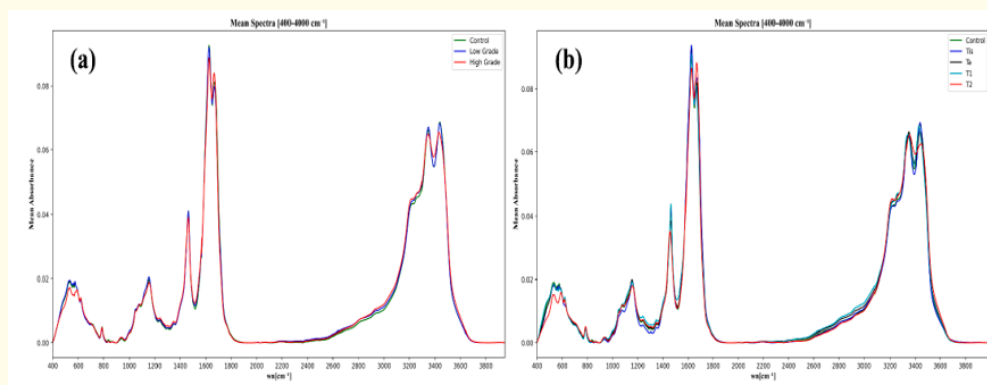


Figure 2: Mean FTIR spectrum comparison (Reproduced with permission from ref [15]).

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and troughs at particular wavelengths (Figure 3). The spectral dataset validated the scientific foundation of our methods by

showing a good correlation with wavelengths reported in prior NIR investigations [25].

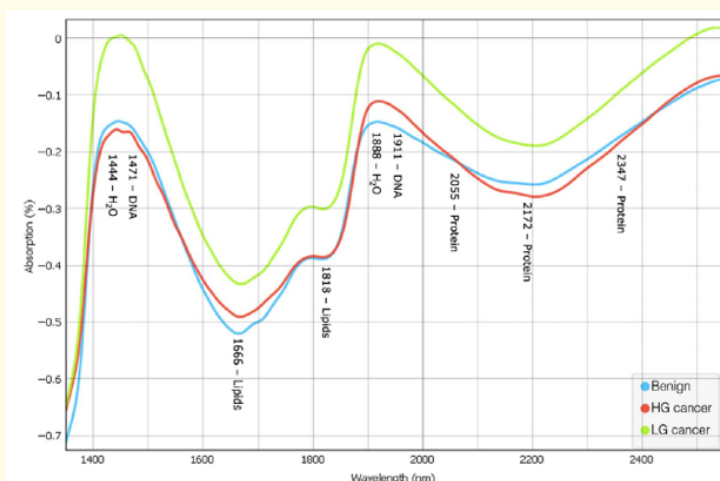


Figure 3: The mean NIR spectra for each of the three pathological groups (Reproduced with permission from ref [25]).

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The capacity of NIR spectroscopy to quickly extract spectra from tissues is one of its important features. The spectrum capture time in this trial was 5 s, which allowed for real-time diagnosis and input to the operating urologist about the degree of additional resection needed.

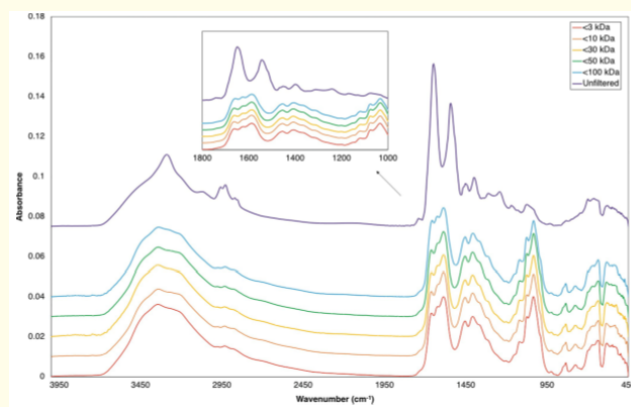
Furthermore, it is possible to get this spectral information without causing any harm to the tissue under analysis. This stands in sharp contrast to frozen section or traditional histological evaluation, where a professional uropathologist evaluates the material after it has undergone lengthy processing, embedding,

cutting, and staining. Diagnosing *brain cancer* is difficult. The most prevalent symptoms are non-specific (such as headaches) and are more likely to be linked to a diagnosis that is not related to a tumor. Six distinct regions of serum (five fractions plus unfiltered whole serum) were examined using a serum-based ATR-FTIR technique to stratify brain cancer patients against non-cancer controls [26] previously reported sensitivity of 92.8% and specificity of 91.5%) [27].

The patient's serum was analyzed using supervised machine learning techniques, such as random forest (RF) and partial least

squares discriminant analysis (PLS-DA), after an unsupervised exploratory principal component analysis (PCA) in accordance with previously published work.

The spectral discrepancies between unfiltered serum from the same GBM patient (glioblastoma multiforme) sample and each of the five molecular weight cut-off locations are shown in Figure 4. A 100 kDa filter was used to separate each patient's serum first, then a 50 kDa filter, a 30 kDa filter, a 10 kDa filter, and finally a 3 kDa filter. The filtrate, or the area that passed through the filter, was then analyzed.



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Figure 4: Example of patient serum spectra including unfiltered whole serum and each molecular weight region (Reproduced with permission from ref [27]).

After molecular weight components (>100 kDa) were eliminated, the serum spectra showed a significant difference. In the higher wavenumber range between 3700 and 2700 cm^{-1} , this is noteworthy. More significantly, there are a lot of variations between 1800 cm^{-1} and 1000 cm^{-1} ; hence, this was chosen as the area of interest for additional research.

There are several reviews published during this period of time related to the analysis of brain cancer using FTIR spectroscopy [28-33].

The most common malignancy among women is still *breast cancer*. For women between the ages of 50 and 74, biennial mammography has been strongly recommended to detect this disease early. When paired with magnetic resonance imaging (MRI), mammography's sensitivity is about 92.7%. However, sensitivity may be 52% when combined with ultrasound (US). Consequently, for women who are at high risk and for whom additional screening is recommended [34].

Artificial neural networks (ANN) have the potential to accurately diagnose breast cancer using infrared spectroscopy,

according to a study [35]. In particular, it created several ANNs to use ATR-FTIR data to identify cancer from breast tissues. This suggested approach might be used as a starting point for spectral data analysis and, more significantly, offer pathologists and other medical professionals' fresh perspectives and guidance.

The median absorbance spectra of benign ($n = 78$) and malignant ($n = 88$) breast tissue samples are shown in Figure 5.

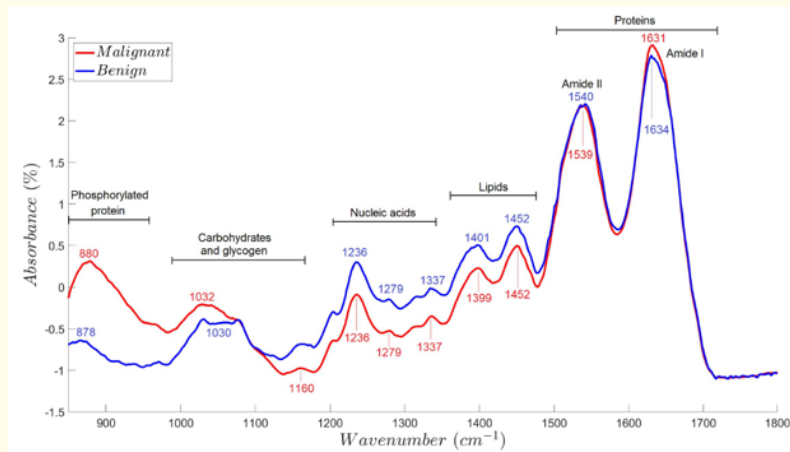


Figure 5: Median ATR-FTIR absorbance spectra of malignant and benign breast tissue samples (Reproduced with permission from ref [35]).

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The absorbance spectra of the benign and malignant tissues were clearly different from one another in the fingerprint spectral region (1800 cm^{-1} to 850 cm^{-1}), particularly at bands $1452\text{ cm}^{-1}/1452\text{ cm}^{-1}$, $1399\text{ cm}^{-1}/1401\text{ cm}^{-1}$, $1337\text{ cm}^{-1}/1337\text{ cm}^{-1}$, $1279\text{ cm}^{-1}/1279\text{ cm}^{-1}$, and $1236\text{ cm}^{-1}/1236\text{ cm}^{-1}$, which stand for lipids, DNA, RNA, and phospholipids. Other investigated peaks were not distinct among samples. These bands correspond to phosphorylated proteins, carbohydrates, glycogen, amide I proteins, and amide II proteins.

Another study investigates the potential of Attenuated Total Reflection Infrared Spectroscopy (ATR-FTIR) to detect various biochemical components in bodily fluids like serum and saliva from people with BC, people with benign breast disease (BBD), and people in good health [36].

Figure 6 presents a comparison of serum and saliva fluids in samples from breast cancer patients.

Infrared with attenuated total reflection Fourier transform infrared (ATR FT-IR) spectroscopy emerges as a non-destructive sample tool, which is non-invasive, label-free, has a low operating cost, and requires only a small amount of sample, including liquid plasma samples, for the determination of breast cancer [37]. The control group's band at 1511 cm^{-1} and the cancer group's bands at 1502 and 1515 cm^{-1} , which are the peaks of the bands corresponding to proteins and amide II, showed the greatest variation between the groups. ATR FT-IR spectroscopy has shown promise as a breast cancer screening technique due to its strong

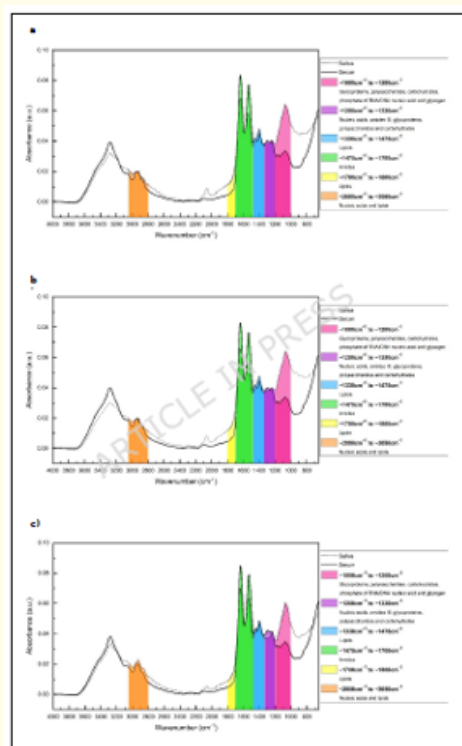


Figure 6: FTIR spectra comparison for serum and saliva (Reproduced with permission from ref [36].

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capacity to differentiate between the liquid plasma samples of breast cancer patients and healthy controls, as well as its time efficiency and cost-effectiveness.

There are several reviews published during this period related to the analysis of breast cancer using FTIR spectroscopy [38-43].

About 25–30% of malignancies in children under the age of 15 are *acute lymphoblastic leukemia* (ALL), the most prevalent pediatric cancer [44]. It is characterized by clonal growth of immature lymphoblasts in the bone marrow and peripheral blood and results from malignant transformation of lymphoid progenitors, most commonly of B-lineage.

FT-IR spectroscopy on serum is a promising addition to existing hematology diagnostics. To assess its potential as a screening

tool in pediatric oncology, it was investigated whether blood FT-IR spectra can distinguish pediatric ALL from healthy and non-ALL hematological controls [45]. Spectra were analyzed in the 800–1800 cm^{-1} and 2800–3500 cm^{-1} areas, which include the main biological bands in serum, for chemometric and diagnostic purposes.

Visual inspection of the group-averaged spectra revealed systematic differences between LEUK-PD and CONTROLS (combined HC and HEMC groups), most pronounced in protein- and lipid-associated regions. Specifically, LEUK-PD samples exhibited increased absorption in the amide I ($\sim 1640 \text{ cm}^{-1}$) and amide II ($\sim 1545 \text{ cm}^{-1}$) bands, whereas lipid-associated CH_2 vibrations at 1450 cm^{-1} and 2920 cm^{-1} showed reduced intensity.

Figure 7 presents the averaged vector-normalized FTIR spectra of serum samples.

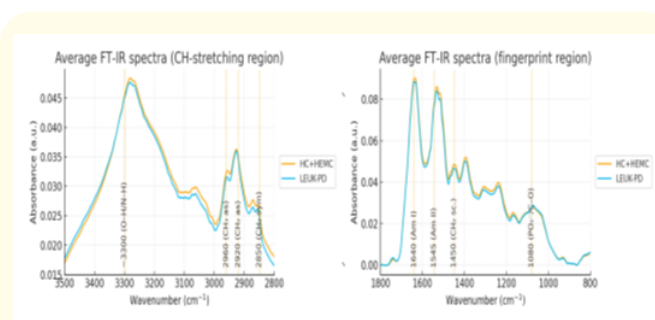


Figure 7: The averaged vector-normalized spectra of serum samples (Reproduced with permission from ref [45]).

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There are several reviews published during this period of time related to the analysis of leukemia cancer using FTIR spectroscopy [46-48].

The incidence and mortality of *ovarian cancer* are expected to rise significantly over the next 20 years, making it the eighth most prevalent cancer-related cause of death for women worldwide [49].

After encouraging results in preliminary investigations [50,51], spectroscopic analyses of blood and urine samples from a large patient cohort were investigated to assess the possibility of ATR-FTIR spectroscopy in ovarian cancer diagnosis [52]. Additionally, the impacts on acquired spectra were investigated because a portion of the recruited ovarian cancer patients had received NACT.

Figure 8 presents the PLS-DA regression coefficients for identification of spectral biomarkers in plasma, serum, and urine. Key wavenumber regions have been marked with different colors. Top graphs: non-chemotherapy ovarian cancers (OC no chemo) versus all benign controls (controls). Bottom graphs: NACT ovarian cancers (OC chemo) versus all benign controls (controls). OC, ovarian cancers; chemo, chemotherapy; NACT, neoadjuvant chemotherapy.

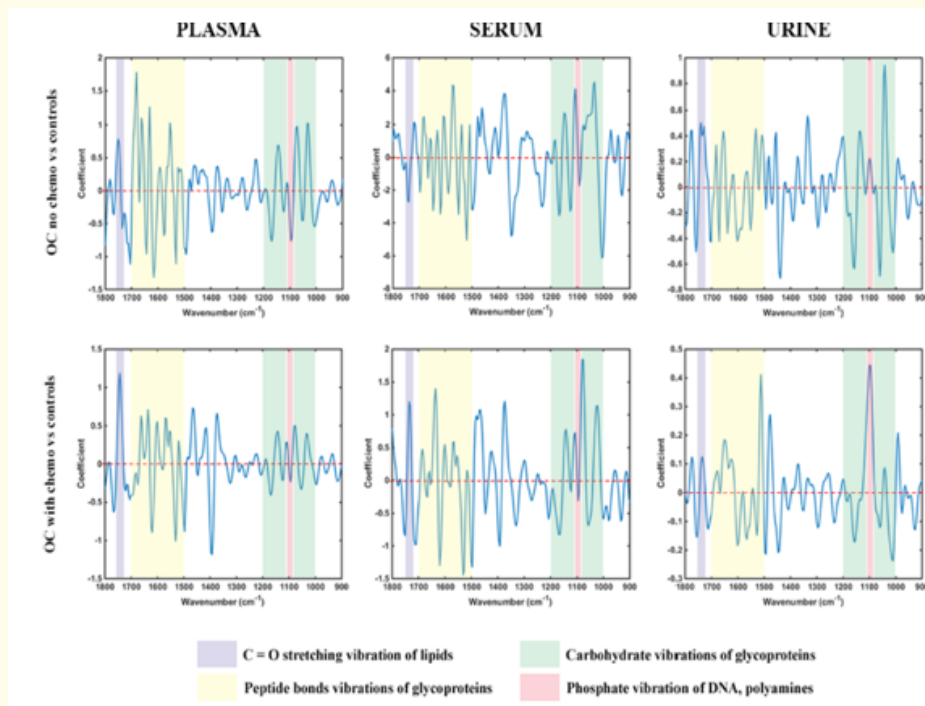


Figure 8: Regression coefficients for identification of spectral biomarkers in plasma, serum, and urine (Reproduced with permission from ref [52]).

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In summary, this work demonstrated that whereas urine has unsatisfactory findings, ATR-FTIR spectroscopy of blood-derived biofluids (mostly serum) compares favorably with currently utilized diagnostic modalities in ovarian cancer. Chemotherapy

effects can be evaluated and benign gynecological disorders can be classified using spectrochemical changes that can be linked to circulating CA125 levels and structural abnormalities.

There are several reviews published during this period of time related to the analysis of ovarian cancer using FTIR spectroscopy [53-57].

The signs of digestive tract cancer (DTC) are typically non-specific and often manifest as typical symptoms of a benign non-tumor illness, such as fever, sour eructation, diarrhea, and abdominal pain [58]. The majority of general practitioners frequently diagnose them as emergency presentations. Even though some are actually connected to a specific early DTC, it's frequently challenging to make a correct diagnosis using standard medical screening methods in regular clinics and health check-ups.

To identify DTC triages in 252 blood serum samples classified into the following groups: liver cancer (LC), gastric cancer (GC), colorectal cancer (CC), and their three stages, respectively, an in-situ blood-based ATR-FTIR spectroscopic data mining pathway was developed as part of a proposed diagnostic protocol for DTC [59].

Figure 9 presents the ATR-FTIR spectra for different liquid DTCs, including three types of LC, GC, CC, and control serum samples, and their signature analysis of DTCs.

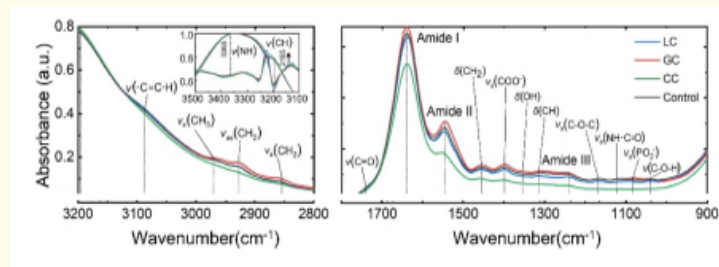


Figure 9: ATR-FTIR profiles for different liquid DTCs (Reproduced with permission from ref [59]).

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The potential use of attenuated total reflection Fourier-transform infrared (ATR-FTIR) spectroscopy to more thoroughly examine extracellular vesicles (EVs) extracted from urine samples was investigated [60]. Although the method has been used since the 1990s to distinguish prostate cancer biopsies from normal benign biopsies [61], its accuracy remains a major concern because complex tissue does not provide sufficient evidence for diagnosis.

Figure 10 presents average raw FTIR spectra of urinary EVs: (a) cancerous vs. non-cancerous EVs; (b) Gleason score groups (GS < 7, GS = 7, and GS > 7).

The absorbance spectrum of the malignant EVs showed higher values at a few peaks than that of the non-cancerous EVs, suggesting a distinction between the two groups (Figure 10a). There was a difference between the early and later stages of the malignancies, as shown by the larger spectrum of absorbance for GS < 7 EVs compared to GS = 7 and GS > 7 groups (Figure 10b).

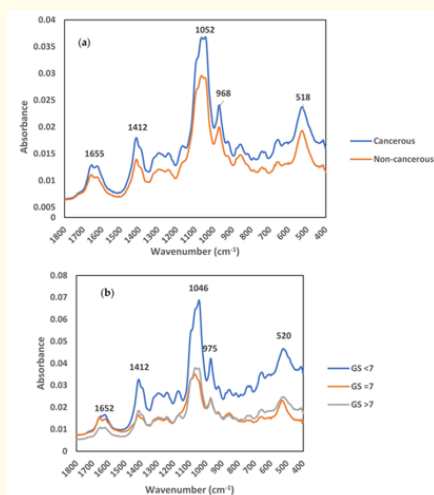


Figure 10: Average raw FTIR spectra of urinary EVs: (a) cancerous vs. non-cancerous EVs; (b) Gleason score groups (GS < 7, GS = 7, and GS > 7) (Reproduced with permission from ref [60].

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Conclusions

The vibrational spectroscopic methods, FTIR and Raman spectroscopy, have the advantages of ease of use, speed, low cost, and little or no sample preparation. IR spectroscopy has enormous potential in biomedical research since it may provide molecularly detailed biochemical information without requiring external labeling and without being invasive to the system being studied. This work showed that FT-IR spectroscopy in combination with chemometric approaches can be used to identify the biomarkers (proteins, lipids, collagen, esters, etc.) of healthy and malignant samples. The results showed that both malignant and healthy

By analyzing Fourier-transform infrared spectroscopy (FTIR) spectra from urinary extracellular vesicles (EVs) and patient clinical data to create a predictive model, a related study investigates a non-invasive approach for prostate cancer screening [62]. The goal of the study was to determine the best machine learning model for precise and trustworthy prostate cancer prediction.

Urinary EV spectra from prostate cancer patients and healthy controls are qualitatively comparable in Figure 11a, showing minute spectral changes such as changes in relative intensity, shape, and band location across several important spectral regions. To improve the variance between the sample groups and show more pronounced changes in spectral features, the IR spectra were converted into their first derivatives (Figure 11b).

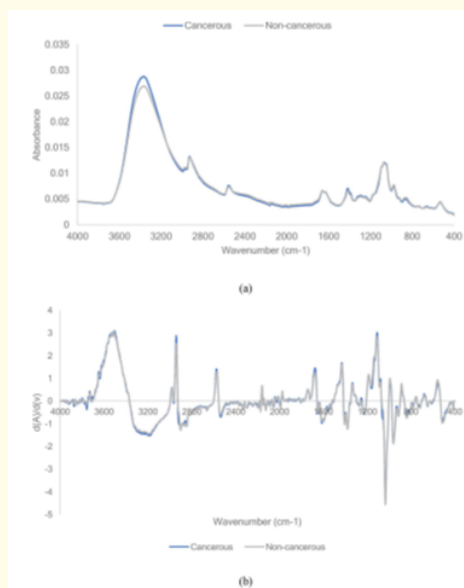


Figure 11: Mean infrared spectra of extracellular vesicles in prostate cancer analysis (Reproduced with permission from ref. [62].

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samples had unique spectra and spectral features. The proposed techniques solve the issues with the harmful, costly, and time-consuming biochemical approaches currently in use. The main objective of clinical FTIR spectroscopy is to provide new and improved methods for diagnosing diseases that are now difficult or expensive to diagnose with existing methods. Spectroscopy can be used to diagnose diseases by searching the spectrum of samples for specific spectral markers or by searching for global changes in the spectra that may be related to the disease but do not necessarily have a recognized cause. Further studies are needed to properly evaluate the role of FTIR spectroscopy as a diagnostic tool in carcinogenesis.

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