REVIEW

Fourier Transform Infrared Spectroscopy: An Innovative Method for the Diagnosis of Ovarian Cancer

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Abstract: Ovarian cancer is the most lethal gynecologic malignancy due to the late diagnoses at advanced stages, drug resistance and the high recurrence rate. Thus, there is an urgent need to develop new techniques to diagnose and monitor ovarian cancer patients. Fourier transform infrared (FTIR) spectroscopy has great potential in the diagnosis of this disease, as well as the real-time monitoring of cancer development and chemoresistance. As a noninvasive, simple and convenient technique, it can not only distinguish the molecular differences between normal and malignant tissues, but also be used to identify the characteristics of different types of ovarian cancer. FTIR spectroscopy is also widely used in monitoring cancer cells in response to antitumor drugs, distinguishing cells in different growth states, and identifying new synthetic drugs. In this paper, the applications of FTIR spectroscopy for ovarian cancer diagnosis and other works carried out so far are described in detail.

Keywords: diagnosis, Fourier transform infrared spectroscopy, ovarian cancer, spectral feature, tumor monitoring

Introduction

The incidence of ovarian cancer is lower than that of cervical cancer and endometrial cancer of the gynecologic malignancies, but its mortality rate is the highest, accounting for 295,414 new diagnoses and 184,799 new deaths worldwide in 2018.[1,2] In developed regions, the number of new cases of ovarian cancer is more than that of cervical cancer.[3–5] One of the main reasons for the high mortality rate is that there are no symptoms or the symptoms are mild and atypical for early-stage ovarian cancer, leading to difficulty in early detection and treatment;[6,7] other reasons include drug resistance and difficulty with controlling and monitoring cancer metastasis and recurrence.[8–10] Most of the patients are at advanced stages at the time of diagnosis, and the established treatment strategy is cytoreductive surgery followed by neoadjuvant platinum chemotherapy.[11] Although the combination of poly(ADP-ribose) polymerase (PARP) inhibitors and/or drugs targeting homologous recombination deficiency improves the efficacy of platinum chemotherapy, up to 80% of patients relapse, and the median progression-free survival is estimated to be approximately 12–18 months.[12] Therefore, it is necessary to develop new methods for diagnosing and monitoring ovarian cancer patients.

Fourier transform infrared (FTIR) spectroscopy is widely applied to the biomedical sample analysis.[13,14] This technique is dependent on the absorption of infrared light

through vibrational transitions in covalent bonds, in which the intensities offer quantitative data and the frequencies indicate the properties and structure of the bonds. Here, FTIR spectroscopy was mainly used to detect the absorption modes in the mid-infrared region (4000–600 cm^{-1}). The sharp bands in this region primarily come from the specific vibrations from biomolecules, such as proteins, nuclear acids, lipids and carbohydrates, which result in a highly distinct absorption pattern and spectral profile for each sample (Figure 1).[15–17] FTIR spectroscopy is a simple, rapid and noninvasive measuring technique in which clear characteristic wavebands can be used as spectral makers for a sample.

During the early stage of tumor occurrence or in the process of tumor deterioration, tissues and blood or other liquids from the body undergo changes in metabolism and in the composition and content of the main biomolecules that make up tissues and cells.[18,19] However, these changes have not yet led to specific clinical symptoms or imaging changes. FTIR technology enables the capture of these tiny changes in precancerous lesions or during cancer progression through the biochemical and molecular information they provide.[20] Molecular structure changes, particularly the secondary structure of proteins, are also available from the FTIR spectral analysis.[21] Thus, these changes can be identified as cancer markers, enabling sensitive and specific distinction between normal and tumor tissues and the real-time monitoring of tumor progression. Other potential uses of FTIR spectroscopy for biomedical detection have been demonstrated in multiple areas, including distinguishing cell apoptosis from necrosis,[22] monitoring cell growth and differentiation,[23] identifying stem cell differentiation phenotypes,[24] and detecting and imaging cell organelles.[25] The purpose of this review is to provide a description of the work carried out so far in the application of FTIR spectroscopy in ovarian cancer, the most lethal cancer in women.
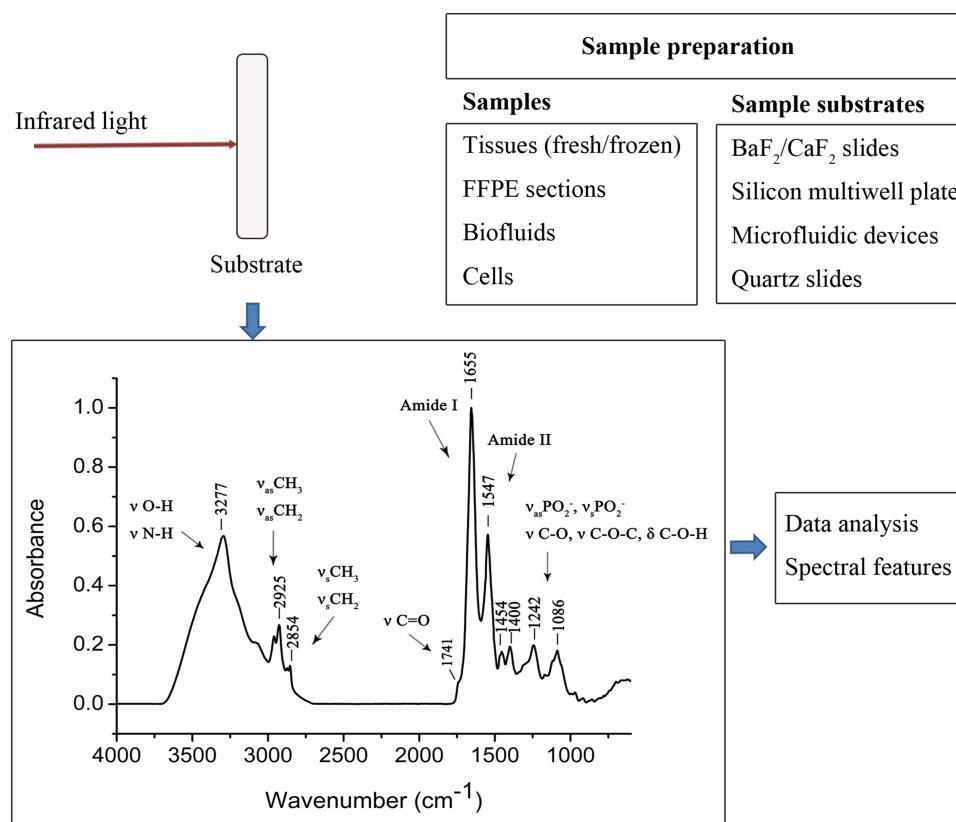

Figure I Schematic illustration for the FTIR spectroscopy measurement flow. The main procedures include sample preparation, spectral acquisition and data analysis. Pretreatment of the samples depends on the sample type. The sample is then placed on a substrate, such as BaF2 slides, for IR spectroscopy. The representative IR spectrum is presented from an A2780 ovarian cancer cell line. The main absorption bands indicating cellular components are the asymmetric and symmetric vibrations (ν_{asym} CH$_3$ and CH$_2$) of fatty acyl moieties, ester C=O stretching of phospholipids, protein absorption bands (Amide I and Amide II), asymmetric and symmetric phosphodiester vibrations of nucleic acids (ν_{as}PO$_2^-$ and ν_sPO$_2^-$), and C–O–C vibrations for sugars. Spectral features were extracted and the data analysis was complex according to the aim of the research. The schematic refers to previous studies.[15–17]

The Application of FTIR Spectroscopy in the Diagnosis of Ovarian Cancer

Ovarian cancer is the third most common cancer in women with malignant tumors, and the incidence of ovarian cancer exceeds that of cervical cancer in developed populations.[3] Current diagnostic methods for ovarian cancer include histopathological diagnosis, the measurement of biomarkers such as cancer antigen 125 (CA-125), and imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI).[26,27] However, histopathological examination has limitations, including complicated operation, time-consumption, and reliance on subjective judgment.[28] CA-125 detection shows low specificity and sensitivity, and CA-125 levels also increase in other types of cancer, such as breast, endometrial and lung cancer, and fluctuate during the menstrual cycle of premenopausal women.[29,30] CT and MRI are expensive and difficult to use in the diagnosis of early-stage ovarian cancer.[31] New methods for early detection and prevention by molecular genomics are being rapidly developed. With the development of the personalized medicine era, next-generation sequencing has become more widely used to determine the precise genetic map of patients and to identify new mutations for new drug targets. For example, ovarian cancer patients with *BRCA* mutations or homologous recombination deficiency acquire therapeutic benefits from platinum drugs and PARP inhibitors, while immune checkpoint inhibitors are available for tumors with microsatellite instability.[32] As a convenient, sensitive and rapid technique, FTIR spectroscopy has also been indicated to be valuable and widely used in multiple tumors, such as in the diagnosis of lung,[33] breast,[34] colorectal,[35,36] cervical,[37] gastric,[38] liver[39] and thyroid tumors.[40]

The Diagnosis of Ovarian Cancer Using Tissue Samples

The study of the infrared spectrum in ovarian cancer diagnosis has been developed in recent years (Table 1). In 2007, Krishna et al[41] used FTIR and Raman spectroscopy to analyze paraffin-embedded tissue samples of normal ovaries, benign ovarian tumors and malignant ovarian neoplasms. They demonstrated that normal tissues showed significantly higher levels of protein and lower levels of DNA and lipids than cancer tissues, and benign tissues had higher levels of protein and lower levels of DNA and lipids than malignant tissues. Subsequently, Mehrotra et al[42]

reported higher lipid and DNA content in frozen sections of cancer tissues than in normal tissues. Changes in the secondary structure of proteins in cancer tissues have also been observed. When identifying the heterogeneous subtypes of 35 benign ovarian tumors, 30 borderline ovarian tumors and 106 cases of ovarian epithelial cancer (including serous, mucinous, clear cell and endometrioid ovarian cancers), Theophilou et al[43] reported that the relative content of lipid/protein and nucleic acid/carbohydrate were higher in paraffin-fixed malignant tissues than in borderline and benign tissues. The ratio of the RNA/DNA absorption peaks was lower in malignant tissues than in normal and benign tissues. In 2018, Grzelak et al[44] used synchrotron radiation-based FTIR spectroscopy (SR-FTIR) from 8 frozen tissue samples of ovarian cancer patients and revealed increased content of lipids and DNA in the malignant cases. In addition, the protein content was also increased in malignant tumors compared to borderline ovarian tumors. Our previous work investigated five ovarian cancer cell lines versus a normal epithelial cell line and was validated by 12 frozen tissues from epithelial ovarian cancer patients.[45] We observed an increased amount of protein in ovarian cancer cell lines and an altered secondary structure of protein. We also found that the ratio of 1454/1400 was lower in malignant cells/tissues than in normal cells/tissues. Although the use of infrared spectroscopy technology for ovarian cancer diagnosis has not been widely studied, these results suggest that infrared spectroscopy can distinguish normal ovaries from benign, borderline and malignant tumors via the analysis of protein, nucleic acid and lipid content, as well as protein conformation. However, some of the results are diverse and controversial. This may be partially due to the different preparation processes for the samples (fresh, frozen or paraffin-fixed samples), the small sample size, and the complex characteristics of ovarian cancer tissues in these studies.

The Diagnosis of Ovarian Cancer Using Blood and Urine Samples

In addition to the infrared imaging of cancer cells and tissues, the spectral analysis of serum or plasma from patients can also be used to diagnose ovarian cancer. Gajjar et al[46] demonstrated a 96.7% accuracy in diagnosing ovarian cancer (30 ovarian cancer patients vs 30 normal controls) and an 81.7% accuracy in diagnosing endometrial cancer (30 endometrial cancer patients vs 30 normal controls) using serum or plasma samples by

Table 1 Diagnosis of Ovarian Cancer Using Tissue Samples Included in the Review

Author	Year	Sample	Preparation	No. of Patients	Method	Spectral Significance
Krishna et al[41]	2007	Normal, benign, and malignant ovarian tissues	Paraffin-fixed	24	FTIR and Raman spectroscopy	Normal vs malignant: higher protein content and lower DNA and lipid content
				8 normal, 10 benign, 6 malignant		Benign vs malignant: higher protein content and lower DNA and lipid content
Mehrotra et al[42]	2010	Normal and ovarian cancer tissues	Frozen sections	12	FTIR spectroscopy	Malignant vs normal: higher content of DNA and lipids
						Variations in protein secondary structures
Theophilou et al[43]	2015	Normal, borderline and malignant ovarian tissues	Paraffin-fixed sections	171	ATR-FTIR spectroscopy	Normal vs malignant: lower lipid/protein ratio, lower phosphate/carbohydrate ratio and higher RNA/DNA ratio
				35 benign, 30 borderline, 106 malignant		Normal vs borderline: lower phosphate/carbohydrate ratio and higher RNA/DNA ratio
						Borderline vs malignant: lower lipid/protein ratio and lower phosphate/carbohydrate ratio
						Normal and benign: similar
Grzelak et al[44]	2018	Borderline and malignant ovarian tissues	Frozen sections	8	SR-FTIR spectroscopy	Malignant vs borderline: higher content of proteins, DNA and lipids
				1 borderline, 7 malignant		
Li et al[45]	2018	Normal and ovarian cancer cells/tissues	Frozen sections	12	FTIR spectroscopy	Malignant vs normal cell lines: higher content of proteins, variations in protein secondary structures
				6 cell lines		Malignant vs normal tissues: lower content of DNA and lipids

attenuated total reflection FTIR (ATR-FTIR) spectra coupled with a proposed classification method. Owens et al[47] explored the spectral characteristics of serum and plasma in patients with ovarian cancer using both ATR-FTIR and Raman spectroscopy. The diagnostic accuracy of the Raman spectrum was 74%, and that of the ATR-FTIR spectrum was 93.3%. Lima et al[48] further confirmed a 100% sensitivity and specificity for differentiating stage I from stages II–IV in ovarian cancer, a 94.0% sensitivity and specificity for diagnosing serous and non-serous ovarian cancers, and a 100% sensitivity and specificity for distinguishing between patients under 60 years of age and those over 60 years of age using plasma samples; the diagnostic accuracies for these categories were 91.6%, 93.0%

and 96.0%, respectively, when the spectra from patients' serum samples were used.

In a recent study, Paraskevaidi et al[49] used ATR-FTIR spectroscopy to assess urine samples from patients with endometrial cancer (n = 10), patients with ovarian cancer (n = 10) and normal subjects (n = 10). The diagnostic accuracy was high for both cancers (endometrial: 95%; ovarian: 100%). These findings provide preliminary evidences that infrared spectroscopy from blood and urine samples can potentially be a powerful tool for screening and diagnosing ovarian cancer. Another advantage is that as a non-destructive, label-free and sensitive technique, FTIR imaging, which relies on a minimal amount of blood and urine samples, shows no harm to ovarian cancer patients.

The Diagnosis of Ovarian Cancer Using Distinctive Marker Groups

FTIR spectroscopy is powerful for analyzing functional groups within molecules. The methylation of cytokines in CpG islands has been demonstrated to induce ovarian cancer. FTIR spectroscopy can distinguish cells with high methylation levels from those with low methylation levels, an ability that may lead to the early diagnosis of ovarian cancer and the identification of demethylating anticancer drugs.[50] This result also provides new insights for potential ovarian cancer diagnosis by detecting the known molecular biomarkers screened by previous studies.

Comparison of FTIR Spectroscopy with Other Diagnostic Methods

As an assistive diagnostic technique, FTIR spectroscopy has been used in multiple cancers, including ovarian cancer, showing high specificity and accuracy. Thus, the efficacy of the FTIR technique has been compared with widely used methods. Sindhuphak et al[51] compared FTIR results with histological examinations on cervical cell samples from 108 abnormal and 167 normal cases of Thai women undergoing hysterectomy. According to the histological results, the FTIR results showed up to a 96.3% sensitivity and 96.4% specificity. When high definition (HD) and ultra-high definition (UHD) FTIR spectral data were compared with histopathological examination in a breast cancer mouse model, the two methods showed good consistency with respect to the localization of metastases smaller than 1 mm. In addition, the infrared spectra can differentiate the types of malignant cells.[52] These results show that spectral histopathology is in good agreement with the histopathological diagnosis, and can provide more specific and in-depth interpretation.

Smolina et al[53] demonstrated that FTIR data were in strong correlation with the gene expression mode in diverse breast cancer cell lines, indicating that the two methods exhibited consistent patterns of cell variations. Rymsza et al[54] also observed that ATR-FTIR spectroscopy analysis was consistent with the results of PCR testing that amplified the L1 gene for human papillomavirus (HPV) detection in 41 patients undergoing gynecological examination. These results show that spectral detection and molecular detection have the same effectiveness in some aspects.

The Real-Time Monitoring of Tumor Development and Treatment Progress by FTIR Spectroscopy
FTIR Detection of Response to Chemotherapy

Real-time monitoring of ovarian cancer development and treatment process is still in the laboratory stage using cell lines. For example, infrared spectroscopy has preliminarily shown potential for the identification of chemoresistance. Zendehdel et al[55] used FTIR spectroscopy to study two cisplatin-resistant ovarian cancer cell lines (OV2008-DDP (C13) and A2780-CP) and a cisplatin-sensitive cell line (A2780). They demonstrated that changes in the secondary structure of proteins and a transition to high wavenumbers related to CH_2 stretching vibrations were the spectral characteristics of cisplatin resistance. The data provided primary evidence and research direction for the potential identification of resistance to cisplatin in the clinic.

Besides ovarian cancer, the application of FTIR for evaluating the response to chemotherapy in other cancers, such as breast cancer, using tissue samples has been described by Depciuch et al.[56] They observed that the infrared spectra of breast tissues after chemotherapy were similar to those of healthy breast tissues, indicating a good treatment effect. The chemotherapy was ineffective when the spectra of breast tissues after chemotherapy were similar to those of cancerous tissues, indicating a useful approach for the detection of chemotherapy efficacy.[57] The same conclusion was seen in colorectal cancer.[58]

Further mechanisms underlying the chemotherapeutic drugs and DNA interaction can be studied using multiple experimental techniques, including FTIR spectroscopy. For example, after exposure to two cisplatin-like Pt/Pd-drugs, DNA was extracted from a human triple-negative breast cancer cell line and detected by ATR-FTIR. Batista et al found the main pharmacological targets and the DNA conformation changes after treatment with these drugs.[59] This may provide new insights into the mechanism of the chemotherapy drugs.

FTIR Detection of Response to Other Drugs

As for monitoring the responses to other antitumor drugs in ovarian cancer, Al-Jorani et al[60] used ATR-FTIR to detect the effects of organoamidoplatinum (ii) complexes

on cellular metabolism in cisplatin-sensitive and cisplatin-resistant cell lines. Our previous work also used FTIR to monitor the dihydroartemisinin-induced growth inhibition effect in ovarian cancer cells and normal cells, showing an increase in the amount of lipids and nucleic acids in the growth inhibition cells (data unpublished).

Drug treatment can lead to molecular changes in tumor cells, resulting in the corresponding changes in molecular vibrations captured by FTIR. Gasparri et al[61] monitored the cell apoptosis induced by camptothecin, a cytotoxic drug, in HL60 leukemia cells by ATR-FTIR and observed that the apoptotic maker was correlated with the absorption of nucleic acids (1200–900 cm^{-1}). Plaimee et al[62] investigated the apoptotic effects of melatonin in a human lung cancer cell line SK-LU-1 by FTIR spectroscopy and revealed an increase in lipids and a decrease in nucleic acid/DNA. The secondary structure of protein was also changed in content and in the position of peaks. Zelig et al[22] used FTIR to distinguish and characterize the different modes of cell death, such as apoptosis and necrosis, after exposure to different drugs. Therefore, these studies demonstrate FTIR spectroscopy as a useful tool for studying drug responses.

FTIR Monitoring of Tumor Development

Besides capturing the responses to agents, spectral biomarkers can also monitor cancer progression in real time, including changes in the intensities and positions of the specific bands of proteins, lipids and nucleic acids during tumor metastasis.[63] Although FTIR imaging has not been studied in monitoring ovarian cancer development to date, it has been used in other cancers that can be seen as a reference.

Yang et al[64] established an in vitro 3D model exploring the mechanism of lung cancer cell metastasis. Cell invasion was detected by FTIR technique. The authors found that compared with the spectra of non-invading cells, the band position assigned to amide A, I and II of the spectra of the invading cells changed. The band 1080 cm^{-1} can be an indicator for the invading cells. Tian et al[65] used FTIR spectroscopy for the identification of lymph node metastasis during surgery, and the sensitivity, specificity and accuracy were 94.7%, 90.1% and 91.3%, respectively. These studies provide new evidences for the evaluation of tumor metastasis, which might facilitate the stratification of patients and adjustment of treatment strategies in time.

Applications of FTIR Spectroscopy in Other Areas

In addition to ovarian cancer, IR spectroscopy has been widely implemented in other biomedical and biological areas (Table 2). Multiple studies have focused on cancer investigation, such as brain,[66] lung,[67] and prostate cancer,[68] as well as non-cancerous diseases; for example, neurodegenerative disorders,[69] nephropathy,[70] malaria,[71] and osteoarthritis.[72] Microbiology is also a major field that uses this technology for detecting and classifying microbes[73–75] and identifying microbial colony heterogeneity.[76] This technique has also been applied in other fields, such as food safety[77] and environmental pollution.[78] Implementation in other fields is helpful to the further understanding and development of IR spectroscopy in the diagnosis and monitoring of ovarian cancer.

Future Challenges and Considerations

Standardization of Spectral Detection and Analysis in Cancer Diagnosis

As mentioned above, various biological samples, including tissues, cellular materials and biological fluids, can be spectral analyzed. Although still in the experimental stage, due to the sensitivity of spectral detections, it is also essential to have repeatability and reliability of the spectral data in large-scale studies or from different research groups, which will make the technology more convenient for clinical applications. For example, to reduce differences in personal operation, instruments, laboratories, and the environment (eg, temperature and humidity), it is not negligible to normalize the sample preparation procedure and develop a standardized spectrum analysis model.[79]

The preparation of these samples varies according to the type of samples. Fresh and snap-frozen tissues are preferred, as they have no contaminants. Formalin-fixed, paraffin-embedded (FFPE) treatment contributes to characteristic peaks and hinders biological information. FFPE samples need to be thoroughly deparaffinized before analyzing.[80] As water can interfere and cover the biological information in the spectra, the internal instrument should be dried to lower the humidity, and samples should also be dried to avoid water interference.[79] The biofluids can be centrifuged and the supernatant can be retained for further analysis if the cells in these fluids are not the focus

Table 2 Examples of Applications of FTIR Spectroscopy in Other Areas

Sample	Method	Main Points	Ref.
Cancer			
Brain cancer	ATR-FTIR spectroscopy	Using 1 µL serum per person, 3897 spectra from 433 patients, to discriminate cancer vs non-cancer, cancer severity and metastasis with high sensitivity and specificity	[66]
Lung cancer	Infrared spectral histopathology	Classification of cancer vs non-cancer, cancerous vs necrotic tissue, lung cancer subtypes with high accuracy using FFPE tissue sections	[67]
Prostate cancer	ATR-FTIR or Raman spectroscopy	Discriminating 156 prostate tissues from different years to indicate a trans-generational phenotypic change	[68]
Non-cancerous disease			
Neurodegenerative disorders	ATR-FTIR spectroscopy	Using blood plasma samples from 347 patients and 202 controls to diagnosis various neurodegenerative diseases with high sensitivity and specificity	[69]
Nephropathy	FTIR spectroscopy	Prediction of nephropathy using FFPE tissue sections	[70]
Malaria	ATR-FTIR spectroscopy	Quantification of malaria parasitemia, glucose and urea using whole dried blood samples	[71]
Osteoarthritis	Near infrared spectroscopy	Distinguishing mild and advanced cartilage degeneration with high sensitivity	[72]
Microbiology			
Scrapie	FTIR spectroscopy	Distinguishing normal and scrapie-infected animals and their clinical stage	[73]
Enterococci	ATR-FTIR spectroscopy	Phenotypic identification and discrimination of clinically relevant enterococcal species using 60 clinical isolated samples	[75]
Other areas			
Food safety	Near infrared spectroscopy	Food safety surveillance and control	[77]
Environmental pollution	ATR-FTIR spectroscopy	Detecting levels of organochlorine pesticides in the brain of wild birds	[78]

of the research. Anticoagulant (EDTA, citrate or heparin) should also be taken into account, as it may form unexpected peaks.[81,82] It is also worth noting that repeated freezing and thawing should be avoided, as well as long-term storage, since these may lead to confounding factors for the spectral analysis.[83] Thus, stable samples and a consistent preparation are crucial for obtaining reliable results. Additionally, five or more spectra should be collected for each sample, and for heterogeneous samples, spectra should be collected to cover the whole sample as uniformly as possible. It is also recommended to collect three sample replicas.[17,84] In addition to the investment of the instrument, spectral detection has the advantages of low cost and convenient preparation with a small sample amount.[79]

Before acquiring a high-quality spectrum, some of the instrument parameters, such as resolution, spectral range, aperture size, interferometer mirror velocity and co-additions should be adjusted to increase the signal-to-noise ratio.[79] Each spectrum may be acquired within 2–5 min under the instrument. A background spectrum should be acquired before each sample to reflect atmospheric changes. The spectra are subjected to a primary system to undergo a standardization model in which all the spectra data are first preprocessed in the same steps, followed by exploratory analysis, outlier detection, classification techniques and data standardization; after these processes, the final model would be constructed.[17,79] It may take a technician to perform the experimental procedures and an analytical chemist to construct the model. Thus, the

spectra collected from different conditions can be standardized into a chemometric model using this computational-based analysis, making a practical spectral analysis model available for routine detection and clinical application in the future, especially in cancer diagnosis.

Application in Ovarian Cancer Diagnosis

Currently, few studies have screened ovarian cancer by FTIR spectral profile. Although there are some common insights in the above-mentioned studies, some results are conflicting; for example, regarding the differences in protein content between cancer tissues and normal tissues. Another limitation of the previous studies is the relatively small sample size. Therefore, more work needs to be done to support the diagnosis of ovarian cancer by FTIR spectroscopy.

1. It is necessary to perform more comprehensive studies by FTIR spectroscopy in larger cohorts in order to establish a data bank of spectral features and summarize the accurate cancer markers for the possible discrimination of ovarian cancer.
2. The data bank may include diversified samples: blood, urine and ascitic fluid samples; tissue samples from healthy and tumor tissues with heterogeneous subtypes of ovarian cancer and different developmental and treatment stages.[85] Of course, standardized operating procedures should be followed.
3. The notable spectral features include the band positions and intensities at 3000–2800 cm^{-1} (lipids), 1800–1700 cm^{-1} (phospholipids), 1700–1500 cm^{-1} (amide I and amide II groups in proteins) and 1200–900 cm^{-1} (nucleic acids)[17] or their relative intensity ratios; the secondary structure of protein; and specific intensity ratios, such as the ratios of 2925/2958 (lipid saturation level), 3013/2958 (lipid unsaturation level)[86] and 1454/1400. Our previous study demonstrated a higher 1454/1400 band intensity ratio in normal cells than in ovarian cancer cells.[45] We also revealed a higher 1454/1400 ratio in cells exhibiting drug-induced growth inhibition,[87] indicating that this ratio may be a spectral marker for detecting the effects of drugs or identifying cells with different growth characteristics. However, this conclusion needs further verification.
4. An understanding of the combination of various diagnostic methods will be critical for the development of early detection and therapeutic interventions for ovarian cancer patients. For example, the employment of other/multiple techniques, such as conventional biochemical assays or 3D models for suspected changes in the biomolecules, could supplement the findings of the FTIR detection, leading to a more accurate diagnosis or real-time monitoring during treatment.

Other Applications of FTIR Spectroscopy

The advantage of FTIR imaging is its capability of capturing tiny differences in detailed cell signatures.[84] FTIR can be used in a wide range of biomedical fields. In addition to monitoring cell growth and drug responses as mentioned above, subcellular differentiation and organelle localization can also be performed using spectral features; for example, in MCF-7 breast cancer cells.[25] Further work using FTIR is required for multiple studies on the biomolecular changes of cancer cells in response to different drugs in different conditions and the biodistribution and discrimination of subcellular organelles.

Conclusion

Currently, FTIR imaging has specifically attracted substantial attention as a tool for cancer diagnosis and real-time monitoring of tumor development and therapy. In addition, new studies are expected, including those on cell growth and differentiation, subcellular processes, cell responses to drugs, and the assessment and identification of synthetic drugs. Overall, FTIR spectroscopy has great potential in ovarian cancer diagnosis and other clinical aspects of ovarian cancer in the future.

Abbreviations

FTIR, Fourier Transform Infrared; PARP, poly(ADP-ribose) polymerase; CA-125, serum Cancer Antigen 125; MRI, Magnetic Resonance Imaging; CT, Computed Tomography; BRCA1/BRCA2, breast cancer susceptibility gene 1/2; ATR-FTIR, attenuated total reflection Fourier-transform infrared; SR-FTIR, synchrotron radiation-based FTIR spectroscopy; HD, high definition; UHD, ultra-high definition; HPV, human papillomavirus; MET, metformin; FFPE, formalin-fixed, paraffin-embedded.

Data Sharing Statement

All data generated or analyzed during this study are included in this article.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Funding

Disclosure

The authors have no conflicts of interest.

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