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Use of Vibration Spectroscopy in the Diagnosis of Gynaecological Tumours and Determination of Treatment Efficacy

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Highlights:
- Gynaecological tumors
- Radiotherapy efficacy
- Vibration spectroscopy

Keywords:
- Gynaecological tumours
- Radiotherapy
- Treatment efficacy
- Vibration spectoscopy

ABSTRACT:

The aim of this study was to investigate the efficacy of radiotherapy in patients with gynecologic diagnosis and radiotherapy indications using vibrational spectroscopy as an alternative method to standard methods. Vibration spectroscopy is a non-invasive and sensitive technique for the diagnosis of gynecologic tumors and determination of treatment efficacy. This method analyzes biochemical components by examining the characteristic vibrational frequencies of molecules and includes techniques such as Raman spectroscopy and infrared (IR) spectroscopy. Raman spectroscopy analyzes protein, lipid and nucleic acid contents, with the capacity to identify biomolecular changes in cancerous tissues, while FTIR spectroscopy detects changes at the cellular level. Raman spectroscopy clearly revealed biochemical differences between cancerous and normal tissues. Significant changes in protein and lipid content were observed in cancerous tissues. CA-125 and HE-4 biomarker levels showed significant differences between before and after treatment. There was a strong correlation between spectroscopic data and biomarker levels. FTIR spectra were effective in identifying changes at the cellular level. Changes were detected in the FTIR spectra of cancer cells, especially in phospholipid and nucleic acid content.In conclusion, vibrational spectroscopy plays an important role as an alternative method to standard methods in the diagnosis of gynecologic tumors and determination of treatment efficacy, and its widespread use in clinical practice contributes significantly to successful outcomes in the management of gynecologic cancers.

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INTRODUCTION

Gynecological tumors are a significant health problem affecting women's health, and early diagnosis and treatment can significantly improve patient outcomes. In addition to traditional diagnostic methods, their potential role in the diagnosis and treatment of gynecological tumors has gained importance with the development of innovative approaches such as molecular spectroscopy techniques in recent years. In gynecological tumors, when determining the treatment method, it is necessary to know the characteristics of the tumor as well as the form and routes of spread. The International Federation of Gynecology and Obstetrics (FIGO) staging system is used, which is a clinical pathological staging system based mainly on the size of the tumor and its spread within the pelvis (GÜL et al. 2024). Vibrational spectroscopy is also a technique that has recently become widely used in biomedical sample analysis (Chan and Kazarian 2016). Due to various factors, diagnosing gynecological tumors and determining treatment efficacy are pretty complicated. These difficulties arise from the biological diversity of tumors, the vagueness of symptoms, the limitations of diagnostic methods, and the challenges in monitoring response to treatment. Biological diversity is assessed in terms of different histopathological types and genetic and molecular heterogeneity. Different Histopathological Types: Gynecological tumors include a wide variety of histopathological subtypes. For example, cervical, ovarian, and endometrial cancers each exhibit different biological behaviors and require different treatment approaches (Siegel RL, Miller KD 2016). This diversity complicates the diagnostic process, as specific diagnostic tests and protocols are required for each tumor type. Genetic and Molecular Heterogeneity: Even within the same tumor type, there can be significant differences in different patients at the genetic and molecular levels. This heterogeneity makes it difficult to predict treatment responses and develop individualized treatment approaches. Late development of apparent symptoms Gynecological cancers, especially ovarian cancer, often progresses without showing obvious symptoms. Therefore, most cases are diagnosed in advanced stages, making diagnosis and treatment planning difficult (Siegel, Naishadham, and Jemal 2012). In conditions such as ovarian cancer, symptoms are often vague and can be confused with gastrointestinal disorders, preventing early diagnosis (Goff et al. n.d.). The late onset and vagueness of symptoms can lead to patients delaying their visit to the doctor, increasing the likelihood that the cancer will be advanced when diagnosed and limiting treatment options (Siegel et al. 2011). On the other hand, imaging methods (ultrasound, CT, MRI) used in the diagnosis of gynecological tumors may sometimes be insufficient to detect small sizes or tumor spread. In particular, small tumors or metastases may be difficult to identify (Timmerman et al. 2010). In the treatment response phase, gynecological tumors may develop resistance to treatments such as chemotherapy and radiotherapy. This resistance may be due to changes in the tumor's genetic structure or mutations that occur during treatment. When resistance develops, monitoring treatment effectiveness and identifying new treatment strategies becomes difficult. For all these reasons, Raman spectroscopy and FTIR can be used as an alternative to traditional methods to monitor changes in the biochemical composition of tumors during treatment due to their advantages, such as noninvasiveness, short response time, no radiation exposure, high accuracy rate, and the ability to work with small-scale samples.

Vibrational Spectroscopy and Techniques

Vibrational spectroscopy is a powerful tool for enabling molecular-level analyses of biological samples. Fourier transform infrared (FTIR) and Raman spectroscopy are among the techniques used to characterize gynecological tumors and detect pathological changes (Jones et al. 2019; Smith, Wright,

and Ashton 2016). Vibration spectroscopy is a non-invasive method that causes minimal patient discomfort and provides early diagnosis due to its high sensitivity. The study by Wilson et al. demonstrated the effectiveness of non-invasive Raman spectroscopy in diagnosing endometrial cancer (Wilson, Jermyn, and Leblond 2018). Therefore, vibrational spectroscopy, especially in clinical applications, saves time with its rapid data acquisition capacity and contributes to more effective treatment process management. At this stage, FTIR and Raman spectroscopy are the most critical spectroscopic techniques used in this field.

FTIR spectroscopy and clinical applications

FTIR spectroscopy is a method used to understand the biochemical content of tumor tissue. For example, it may provide potential for early diagnosis of gynecologic malignancies such as cervical cancer and determination of the risk of recurrence after surgery. We evaluated the sensitivity and specificity of FTIR spectroscopy in diagnosing endometrial cancer and showed that spectral signatures obtained with this technique can be used as disease markers (Baker et al. 2008). Raman Spectroscopy and Clinical Applications.

A study by Raman spectroscopy has significant potential for characterizing gynecological tumors at the cellular level revealed that Raman spectroscopy is an effective tool to study the molecular structure of cervical cancer cells and monitor disease progression after treatment (Birtoiu et al. 2016). This method can be used in clinical applications such as evaluating surgical margins and determining the risk of recurrence after surgery. Smith et al. distinguished cancerous from healthy tissues by examining protein and lipid profiles in ovarian cancer cells (Hage et al. 2019).

MATERIALS AND METHODS

Before the study, biopsies are taken from tumor tissues of patients diagnosed with gynecological cancer before and after radiotherapy. In addition, healthy control tissues can be collected. Afterward, the tissue samples are stored appropriately and prepared for analysis. This usually involves preparing tissue slices and drying the samples. In the second stage, Raman and FT-IR spectroscopy analyses are performed on the tissue samples taken as spectroscopic analysis and the obtained spectra are recorded. The obtained spectra are then analyzed to determine biochemical changes. Changes in protein, lipid and DNA molecules after radiotherapy are examined. After these procedures, the spectra obtained before and after radiotherapy are compared. Biomarkers that respond to treatment are identified. The obtained data are analyzed using statistical methods, and the effectiveness of radiotherapy is evaluated. What we have said is visualized in Figure 1.

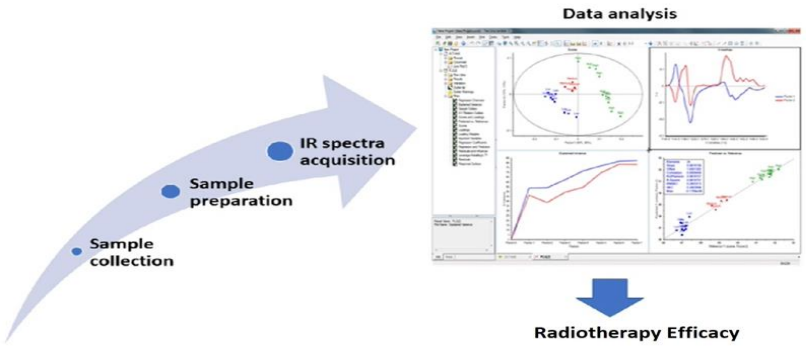

Figure 1. Schematic Representation of the Stages of Determining Treatment Effectiveness
Treatment Efficacy in Gynecological Tumors

Determining the effectiveness of treatment for gynecological tumors is a complex process for various reasons and requires a multidisciplinary approach. This process includes choosing the proper treatment methods, monitoring the response to treatment, and making necessary adjustments. Surgery, chemotherapy, radiotherapy, and immunotherapy play a significant role in monitoring these responses. In addition, imaging techniques, biomarker monitoring, and genetic testing are other methods used in treatment effectiveness. Imaging, especially Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), evaluates tumor size and spread before and after treatment. Imaging results allow direct observation of treatment response (Sala et al. 2010). On the other hand, CA-125 and HE-4, which we know as cancer markers, are biochemical tests used in both diagnosis and treatment effectiveness in ovarian cancer. CA-125, especially CA-125 used in ovarian cancer, is a common biomarker for monitoring treatment response. A decrease in CA-125 levels during treatment indicates a response to treatment (Bast, Hennessy, and Mills 2009). HE4 is another biomarker used in ovarian cancer and provides higher accuracy in diagnosis and treatment monitoring when used in conjunction with CA-125 (Moore et al. 2008). These have disadvantages as they involve both radiation exposure and invasive techniques.

RESULTS AND DISCUSSION

IR spectroscopy's non-invasive nature and rapid data generation capacity can potentially improve early diagnosis tactics. Ferguson et al. conducted a comparative study of IR spectroscopy for the classification of malignant tissues, including gynecological malignancies (Ferguson et al. 2022). Yang and colleagues created an in vitro 3D model to investigate the mechanism of lung cancer cell metastasis. They detected cell invasion by FTIR technique (Yang et al. 2005). In addition to ovarian cancer, the application of FTIR using tissue samples to assess response to chemotherapy in other cancers, such as breast cancer, has been described by Depciuch et al. (Depciuch et al. 2016). In addition to monitoring cell growth and drug responses in MCF-7 breast cancer cells through FTIR spectroscopy, subcellular differentiation and organelle localization can also be performed using spectral features (Clède, Policar, and Sandt 2014). Tian et al. used FTIR spectroscopy to identify lymph node metastasis during surgery and found the sensitivity, specificity, and accuracy to be 94.7%, 90.1%, and 91.3%, respectively (Tian et al. 2015). Smolina et al. showed in their study by FTIR spectroscopy that there is a strong correlation with the gene expression mode in various breast cancer cell lines (Smolina and Goormaghtigh 2018). All these studies have shown that Raman and FTIR spectroscopy are effective tools in the diagnosis of gynecological tumors and in monitoring the effectiveness of treatment. Raman Spectroscopy revealed the biochemical differences between cancerous and normal tissues. Significant changes were observed in protein and lipid contents in cancerous tissues. FTIR spectra were influential in determining changes at the cellular level. Changes were detected in the FTIR spectra of cancerous cells, especially in phospholipid and nucleic acid contents. Regarding biomarker changes, CA-125 and HE-4 biomarker levels showed significant differences between pre-and post-treatment. A strong correlation was found between spectroscopic data and biomarker levels. In the Treatment Response Monitoring phase, Raman spectroscopy allowed real-time monitoring of biochemical changes during the treatment process. FTIR spectroscopy was influential in determining residual disease after treatment.

CONCLUSION

Vibrational spectroscopy, especially Raman and FTIR, plays a vital role in examining the chemical changes and structural properties of biomolecules in cancer diagnosis and determining the

effectiveness of radiotherapy. It can detect molecular changes occurring in cancerous tissues with high sensitivity. It is minimally invasive compared to traditional invasive methods such as biopsy. Raman spectroscopy, in particular, can collect data from living tissue without contact. This is a less traumatic diagnostic method for patients. It allows results to be obtained quickly, allowing rapid diagnosis and treatment. When determining treatment efficacy in radiotherapy, vibrational spectroscopy can monitor biochemical changes caused by radiotherapy and evaluate cellular responses to show the treatment's effectiveness. This method can also help create personalized treatment plans by examining each patient's biochemical profile. This can increase the effectiveness of treatments, especially radiotherapy. In conclusion, vibrational spectroscopy will contribute significantly to the literature due to the following alternatives; Development of early diagnosis methods, monitoring of treatment efficacy, understanding of tissue and tumor heterogeneity, increasing interest in non-invasive and rapid diagnosis technologies, biomarker discovery and tumor classification.

Conflict of Interest

The article authors declare that there is no conflict of interest between them.

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