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Investigation of Fourier Transform Infrared (FT-IR) Spectroscopy and Chemometric Analysis Method as an Alternative Method in the Diagnosis of Prostate Cancer

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Abstract: Prostate cancer is one of the most common types of cancer in men. It usually grows slowly and may not show obvious symptoms at first. Prostate cancer can be diagnosed by symptoms or by a doctor performing certain tests during routine health checkups. These tests include physical examination, PSA (Prostate Specific Antigen) Test, biopsy, imaging techniques, and Gleason score. In addition, Fourier transform infrared spectroscopy (FT-IR) is an analysis method used for prostate cancer diagnosis. This study aims to demonstrate FT-IR spectroscopy as an alternative method to other diagnostic methods in the diagnosis of prostate cancer. The FT-IR spectroscopy method is used to examine the molecular structure of samples. For prostate cancer diagnosis, FT-IR spectroscopy can be used to identify molecular changes in prostate tissue and identify characteristics by which cancerous cells differ from healthy cells. FT-IR spectroscopy is based on spectral data obtained by exposing samples to infrared radiation. These spectral data are based on properties associated with the movements of the molecules contained in the samples, such as vibration, rotation and bending. Molecular changes caused by diseases such as prostate cancer may be evident in these spectral data. These changes can provide information about the presence or stage of cancerous cells. Data obtained using FT-IR spectroscopy is processed with statistical analysis methods. These analyses are used to identify molecular differences between cancerous and healthy prostate tissues. In this way, FTIR spectroscopy can help obtain sensitive and accurate results in the diagnosis of prostate cancer.

Prostat Kanseri Tanısında Alternatif Bir Yöntem Olarak Fourier Dönüşümlü Kızılötesi (FT-IR) Spektroskopisi ve Kemometrik Analiz Yönteminin İncelenmesi

Anahtar Kelimeler
FT-IR Spektroskopisi, Prostat kanseri, Teşhis yöntemleri, Kemometrik Analiz

Öz: Prostat kanseri, erkeklerde en sık görülen kanser türlerinden biridir. Genellikle yavaş büyür ve ilk başlarda belirgin belirtiler göstermeyebilir. Prostat kanseri teşhisi, belirtiler veya rutin sağlık kontrolleri sırasında doktorun belirli testler yapmasıyla konulabilir. Bu testler; Fiziki muayene, PSA (Prostat Spesifik Antijen) Testi, biyopsi, görüntüleme teknikleri, gleason skorudur. Bunların yanısıra, Fourier dönüşümlü kızılötesi spektroskopisi (FT-IR), prostat kanseri teşhisi için kullanılan bir analiz yöntemidir. Bu çalışma da prostat kanseri teşhisinde diğer teşhis yöntemlerinde alternatif bir yöntem olarak FT-IR spektroskopisini göstermektir. FT-IR spektroskopi yöntemi, örneklerin moleküler yapısını incelemek için kullanılır. Prostat kanseri teşhisi için FT-IR spektroskopisi, prostat dokusundaki moleküler değişiklikleri belirlemek ve kanserli hücrelerin sağlıklı hücrelerden farklı olduğu özellikleri tespit etmek amacıyla kullanılabilir. FT-IR spektroskopisi, örneklerin infrared radyasyona maruz bırakılmasıyla elde edilen spektral verilere dayanır. Bu spektral veriler, örneklerin içerdiği moleküllerin vibrasyon, rotasyon ve bükülme gibi hareketleriyle ilişkilendirilmiş özelliklere dayanır. Prostat kanseri gibi hastalıkların neden olduğu moleküler değişiklikler, bu spektral verilerde belirgin olabilir. Bu değişiklikler, kanserli hücrelerin varlığı veya evresi hakkında bilgi verebilir. FT-IR spektroskopisi kullanılarak elde edilen veriler, istatistiksel analiz yöntemleriyle işlenir. Bu analizler, kanserli ve sağlıklı prostat dokuları arasındaki moleküler farkları belirlemek için kullanılır. Bu şekilde, prostat kanserinin teşhisinde FTIR spektroskopisi hassas ve doğru sonuçlar elde etmeye yardımcı olabilir.

1. INTRODUCTION

Prostate cancer is the second most common type of cancer among men in the world and is estimated to be the sixth most common cause of cancer-related deaths. Although imaging techniques are advancing today, digital rectal examination (DRM), prostate-specific antigen (PSA) and biopsy indication remain the basic methods for diagnosing prostate cancer [1]. Prostate cancer usually does not cause symptoms in the early stages. Still, in later stages, it may cause symptoms such as frequent urination, pain in the pelvis, difficulty urinating, and blood in the urine. Imaging methods such as positron emission tomography (PET), computed tomography (CT) and magnetic resonance imaging (MRI) are essential methods used today for the advanced diagnosis of prostate cancer [2]. With these imaging methods, it may be difficult to precisely determine the location and boundaries of prostate cancer due to the limitations of a single imaging method, such as insufficient resolution and sensitivity. For this reason, combining more than one imaging method for accurate and definitive diagnosis may sometimes be necessary [3], [4]. FTIR spectroscopy is an essential alternative for many clinical applications, from cancer screening, diagnosis and evaluation of response to treatment to continuous monitoring of disease progression or regression [5]. As with other types of cancer, it is essential to diagnose prostate cancer quickly, cheaply and accurately. Therefore, FT-IR spectroscopy is used as an auxiliary diagnostic method in the diagnosis of prostate cancer, showing high specificity and accuracy. This study aims to show that FT-IR spectroscopy can be used as an alternative method to existing imaging methods in the diagnosis of prostate cancer.

2. MATERIAL AND METHOD

2.1. Fourier Transform Infrared (FT-IR) Spectroscopy

Accurate classification and staging of cancer is one of the most essential uses of FTIR spectroscopy [5]. FTIR spectroscopy is a technique that has been used for many years to analyze chemical components. This infrared spectroscopy has significantly increased its capacity to analyze residual types of biological samples in recent years. Figure 1 shows the FT-IR spectroscopy device. The reason for such approaches is the lack of methods with high sensitivity and specificity for early cancer diagnosis. FT-IR spectroscopy is a technique that examines vibrations at the molecular level. Here, functional groups are associated with characteristic infrared absorption bands corresponding to the fundamental vibration bands of these functional groups [6]. This spectroscopic method allows us to investigate the vibrational properties of amino acids and cofactors sensitive to minimal structural changes. The spectrum of each molecule varies depending on the wavelength and amount of infrared radiation it absorbs. Therefore, the studied sample's absorbance peaks for the multiplex parameters of the lipidome, proteome, metabolome, and genome produce a signature fingerprint. These biochemical fingerprints are specific to the molecular changes of different diseases and contain essential information in diagnosing each disease. Since biological materials absorb in the mid-IR region (400-4000 cm-1), amide I is the spectral fingerprint region measured to examine these samples (1700-1500 cm-1). The higher wavelength region (3500–2550 cm−1) is associated with stretching vibrations, including C–H, O–H, N–H, and S–H. Low wavelength regions are generally associated with bending and carbon skeleton fingerprint vibrations [7]. Figure 2 shows typical FT-IR spectra of biomolecules and relevant functional groups in biofluids at 3000–800 cm−1 wavelengths. In summary, the vibrational frequencies of a particular chemical group are expected to be in certain regions depending on the type of atoms involved and the type of chemical bonds. Tables are available for amino acid side chains and the main chemical groups. One of the most essential advantages of IR spectroscopy is that it offers the opportunity to study solid, liquid, gas, powder and fiber materials with appropriate preparation. With IR spectroscopy, successful results have been obtained by examining proteins, peptides, lipids, biomembranes, carbohydrates, pharmaceuticals, foodstuffs, and plant and animal tissues. One of the most essential advantages of IR spectroscopy is that it offers the opportunity to study solid, liquid, gas, powder and fiber materials with appropriate preparation. With IR spectroscopy, successful results have been obtained by examining proteins, peptides, lipids, biomembranes, carbohydrates, pharmaceuticals, foodstuffs, and plant and animal tissues [8].

Figure 1. FTIR Spectroscopy Device

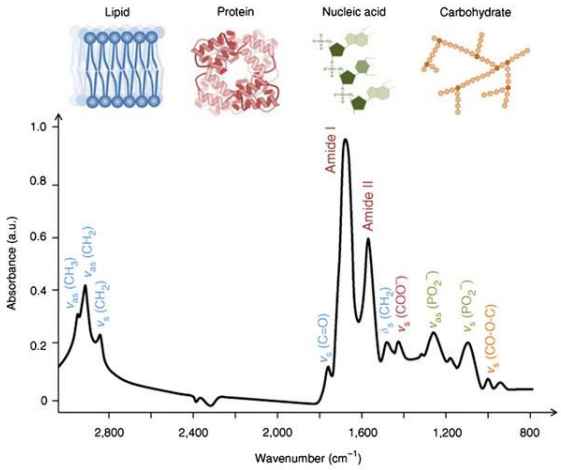

Figure 2. Typical FT-IR spectra of biomolecules and relevant functional groups in biofluids at wavelengths of 3000–800 cm−1 [7]

2.2. Chemometric Analysis

As in many fields, multivariate statistical clustering and classification methods are used to analyze spectroscopic data. Multivariate statistical methods try to optimize the use of studies involving more than one measured variable [9]. Since large-scale data generated by spectroscopy-based methods sometimes make it challenging to perform practical analysis with known spectral analysis methods, multivariate chemometric analyses are needed, especially in distinguishing between groups and determining specific spectral biomarkers. One chemometric analysis technique is Principal Component Analysis (PCA). This transformation technique reduces the dimensions of a data set containing many interrelated variables to fewer dimensions while preserving the variance in the data as much as possible. This technique has been combined with portable FT-IR spectroscopy for cancer diagnosis [10] and many cancers as its yield [11] has been noted. PCA can also be used for clustering. Another chemometric analysis technique is hierarchical cluster analysis (HCA). When deciding which clusters should be combined in studies, there must be a similarity measure between data sets. PCA can distinguish these similar variables, but it may not always make a good distinction. This analysis technique mainly aims to group groups based on their characteristic features [11], [12]. This critical analysis technique, developed to improve the noninvasive diagnosis of brain tumors, can provide information from which the relative position and distribution in feature space of selected tumor classes can be calculated from magnetic resonance imaging and spectroscopy data. For example, Figure 3 displays the information obtained with the help of chemometric analysis using magnetic resonance images and spectroscopy in brain tumor classification [12]. In another study where chemometric analysis methods were applied, serum samples taken from nearly 100 prostate cancer patients were examined. The infrared spectrum of serum from these samples, as seen in Figure 4, provided valuable information about biomolecules such as structure, functional groups, bond types and their interactions. Prostate volume, density, etc. Another method used to diagnose prostate cancer early using features is the Support Vector Machine (SVM) algorithm [13]. SVM is used in pre-processing the Prostate cancer dataset to reduce inhomogeneous distributions in the dataset [14]. Rustam et al. In a study conducted by SVM, it was concluded that SVM was better at classifying prostate cancer data, especially in terms of accuracy. It has also been stated that this method shows promise in allowing healthcare personnel to classify diseases or other medical conditions easily [15].

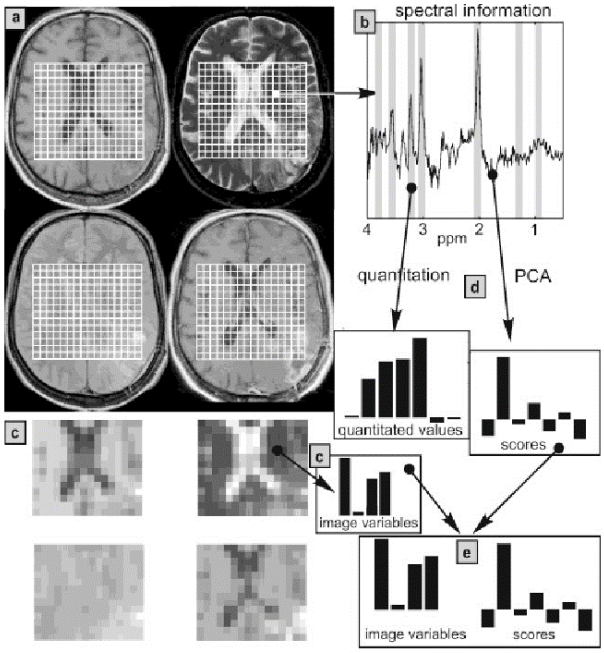

Figure 3. Data processing and data analysis on magnetic resonance images [16].

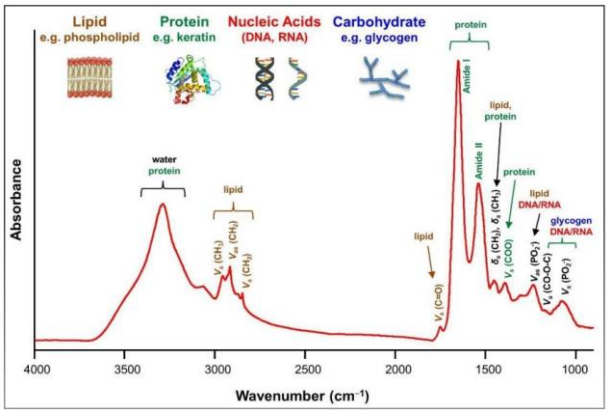

Figure 4. Bond structures corresponding to infrared (FTIR) bands and spectral regions obtained from blood sera from prostate cancer patients [17]

3. RESULTS

In cancer diagnosis, the sensitivity and specificity of biomarkers currently used to detect the disease are generally low. For example, the prostate-specific antigen (PSA) test detects prostate cancer. Although the specificity of this test is as high as approximately 87-95%, its sensitivity is much lower, ranging from 33-59% [14]. FT-IR spectroscopy can distinguish cancer samples from non-cancers with high sensitivity, specificity, and accuracy. Therefore, it can be used as a prospective new

diagnostic method for many different types of cancer. In his study on ten prostate cancer tissues and ten healthy tissues, Albayrak used orthogonal partial minimum analysis, an advanced form of principal component analysis (PCA), to determine the behavior of these 20 samples against infrared light between 50-4000 cm-1 applied squares analysis (Orthogonal Partial Least Square, O-PLS) algorithm. He performed O-PLS analysis to distinguish cancerous and healthy cells. The sensitivity and specificity of the proposed method were found to be very high with the help of the Orthogonal Signal Correction (OSC) pre-processing way, thus showing that the FT-IR method could be an alternative method for prostate cancer diagnosis from paraffin blocks [15]. Baker et al. They used 40 prostate cancer tissue biopsy samples obtained as paraffin-embedded blocks from 39 male patient [16]. Serial sections of 10-micron thickness were collected from each sample. Infrared rays were applied to malignant samples of hematoxylin and eosin (H&E) sections. As a result, overall sensitivity and specificity rates of 92.3% and 98.9%, respectively, were recorded [18]. Their results also show that, for the first time, a system based on two-band criteria identifies features that distinguish tumors that are clinically confined to the prostate from those that are clinically invasive. These findings are essential in developing better prostate cancer diagnosis, prognosis, and treatment planning techniques [19]. For example, when defining the tumor volume in patients receiving radiotherapy treatment, determining the border of the clinical target volume (CTV) in the tissue is also crucial regarding possible reactions [20]. FTIR spectroscopy appears promising as an alternative clinical tool to other diagnostic tools in cancer diagnosis. It is a label-free, non-invasive, non-destructive, fast and objective technology for prostate cancer diagnosis and beyond. FTIR spectroscopy provides essential information about the origin and progression of the disease based on biochemical changes in the preliminary diagnosis of the disease. FTIR analysis of urine samples combined with a multivariate (PCA) model (Figure 5) of a simple, rapid, accurate, inexpensive, noninvasive method may be a potential noninvasive alternative for cases where the results of PSA testing are unstable.

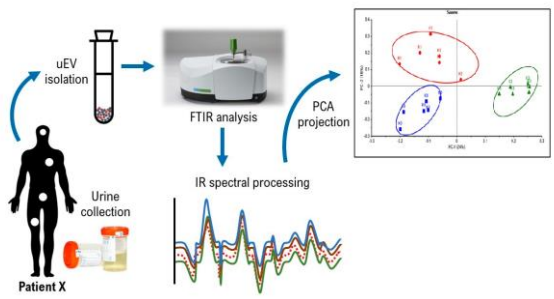

Figure 5. Propose workflow for FTIR analysis and derivation of diagnostic classifier for prostate cancer detection using PCA score plot [21].

Variability from patient to patient, tissue to tissue, and even cell to cell must also be taken into account. Therefore, it isn't easy to access relevant information. This situation has been implemented and adapted in many techniques.

4. DISCUSSION AND CONCLUSION

The importance of spectral analysis is becoming more important day by day. Especially considering the impact of the results obtained in medical diagnoses, the combination of spectral analysis and data processing must give the "right answer". However, sometimes it can be impossible to find the right answer in real life. Therefore, complex simulated data sets containing measurement artifacts, sample-to-sample variability, and instrumental variability can be critical in validating and optimizing data analysis techniques. Optimized spectroscopic technologies and analysis techniques are essential for disease diagnosis and beyond.

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