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A decade (2004 – 2014) of FTIR prostate cancer spectroscopy studies: An overview of recent advancements

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ABSTRACT

This paper presents a retrospective study from 2004 to 2014 of FTIR prostate cancer spectroscopy related to tissues and cell biology. Since vibrational spectroscopy is delicately sensitive to the biochemical composition of the sample and variations therein, it is possible to monitor metabolic processes in tissue and cells, and to construct spectral maps based on thousands of collected IR spectra. These reveal information on tissue structure, distribution of cellular components, metabolic activity and the health condition of cells and tissues. In addition, rapid collection, reliable data, a powerful ability to structure elucidation about IR spectroscopy, and the need for a rapid diagnosis of traditional biopsy (subject to sampling and inter-observer) have potentiated infrared as a way for a new type of analysis based on optical examination and being more objective than conventional colour methods.

Contents

Abbreviations: ANN, Artificial Neural Networks; ATR, Attenuated Total Reflection; BPH, Benign Prostatic Hyperplasia; PCa, Prostate Cancer; EMSC, Extended Multiplicative Signal Correction; FCM, Fuzzy C-means; FSD, Fourier Self-Deconvolution; FPA, Focal Plane Array; FTIR, Fourier-Transform Infrared Spectroscopy; GA, Genetic Algorithm; GS, Gleason Score; HCA, Hierarchical Cluster Analysis; IR, Infrared; LDA, Linear Discriminant Analysis; MIR, Mid-Infrared Region; MCT, Mercury–Cadmium–Telluride; MS, Mass Spectrometry; MSC, Multiplicative Scatter Correction; NIRS, Near-infrared Spectroscopy; PCA, Principal Components Analysis; QCL, Quantum-Cascade Laser; SNR, Signal-To-Noise Ratio; SNV, Standard Normal Variate; SPA, Successive Projection Algorithm; TNM, Tumour/Node/Metastases.

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1. Introduction

This paper presents a review of vibrational micro-spectral imaging classification of prostate tissue and cancer diagnosis from 2004 to 2014. Historically, the beginning of increasing interest in IR as a potential technique in various areas dates back over 60 years, with studies by Blout and Mellots (1950) and Woernley (1952), who investigated IR spectra of tissue homogenates in search of disease indicators. They were carried out using single beam, manually scanned instruments, which required milligram quantities of the sample, and exhibited poor sensitivity and reproducibility. Furthermore, since the framework for interpreting the observed spectra had not yet been developed, the field was abandoned [1]. In the 1980's, research of living systems started again with many advances in instrumentation, interpretation methods and structure elucidation. In this period, the focus was investigations on the identification of bacterial and fungal pathogens [2]. In the 1990's, the focus was investigations on human cell and tissue diseases, with the first being Wong in 1991 which did not overcome the issue of tissue heterogeneity. Only when microspectroscopic methods were used did a detailed histopathological correlation between spectra and disease stage become possible [1].

Well known rapid collection, reliable data and a powerful ability to structure elucidation of Fourier-transform infrared (FTIR) spectroscopy technology [3] added to the need for a rapid diagnosis versus the traditional biopsy has potentiated infrared imaging as a way for a new type of analysis based on optical examination. In addition, it is more objective than conventional colour methods, since it is possible "to read" the biochemical changes instead of an approach based on morphological changes.

In the 1990's, Malins D.C et al. [4] provided a virtually perfect separation of clusters points representing DNA from normal prostate tissue, benign prostatic hyperplasia, and adenocarcinoma in prostate cancer using exploratory analysis (PCA) coupled with FTIR. The findings suggested that the progression of normal prostate tissue to benign prostatic hyperplasia and to prostate cancer involves structural alterations in DNA that are distinctly different. A few years after, Malins D.C. et al. [5] investigated prostate glands of certain healthy men over 55 years of age, showing that the same DNA signature exists in normal tissues adjacent to tumours.

Prostate tissue is structurally complex, primarily consisting of glandular ducts lined by epithelial cells and supported by heterogeneous stroma. The tissue also contains blood vessels, blood, nerves, ganglion cells, lymphocytes and stones (which are comprised of luminal secretions and cellular debris) that are organized into structures, measuring from tens to hundreds of microns, and that are readily observable within stained tissue using bright-field microscopy at low to medium magnifications [6].

Histopathological typing using the Gleason grading system is the standard approach for grading prostate cancer and provides an indication as to the aggressiveness of a tumour. However, this system is based upon a visual criterion of pattern recognition that is operator-dependent and subject to intra- and inter-observer variability. Thus, there is a need for molecular based techniques to grade tissue samples in a reliable and reproducible manner. FTIR imaging of microarrays was coupled with statistical pattern recognition techniques in order to demonstrate histopathologic characterization of prostatic tissue and to differentiate benign from malignant prostatic epithelium [6–10].

The transition of a normal cell to a diseased cell is accompanied by a change in a variety of biomolecules that can be simultaneously and indiscriminately probed by FTIR microspectroscopy, yielding spectral signatures that enable differentiation between normal and cancerous cells and tissues [6,11–13].Therefore, this demonstrates that histopathologic changes can now be defined by biochemistry-based, objective spectroscopic criteria that do not require a pathologist's interpretation. Spectroscopic imaging represents a new avenue for the chemical interpretation of tissue and offers additional capabilities for automated, statistically controlled and reproducible subtype recognition.

All of these aspects have allowed IR biospectroscopy applications to be applied to diagnosing many types of cancer over the years. In this paper, the diagnosis and classification of prostate cancer is specifically emphasized.

2. FTIR spectroscopy in prostate cancer diagnosis, classification and imaging

Within vibrational spectroscopy in the last few years, FTIR has been applied to metabolomics and to diagnose diseases of interest far more than either Raman (which predominantly measures non-polar bonds, as opposed to the polar bonds that FTIR measures) or NIRS. In the case of NIRS, it is predominantly overtones and combination vibrations that are measured, while the FTIR spectra that are collected in the MIR are much more information-rich in terms of chemical content, as it is the fundamental vibrations that are being measured [6].

FTIR is based on the principle that when a sample is investigated with an infrared (IR) beam, the functional groups within the sample will absorb the infrared radiation and vibrate in one of a number of ways; either stretching, bending, deforming or combining vibrations. These absorptions/vibrations can then be directly correlated to (bio)chemical species, and the resultant infrared absorption spectrum can be described as an infrared 'fingerprint' characteristic of any chemical or biochemical substance [14].

Infrared (IR) spectroscopy exploits the ability of cellular biomolecules to be absorbed in the MIR region through vibrational transitions of chemical bonds. For most disease diagnoses, researchers have concentrated on this MIR part of the spectrum (from 4000–600 cm^{-1}), because in contrast to Near Infrared Spectroscopy (NIRS) (14000–4000 cm^{-1}) the fundamental vibration is seen rather than being overtone or harmonic. Thus, the MIR spectra contain many sharp peaks and is very information rich. In biological terms, the vibrations in the 1500–1750 cm^{-1} wavenumber region (the amide I and II bands) are ascribable to CLO, NH and C–N from proteins and peptides, for example. Due to its rapidity, reproducibility, holistic nature and ability to analyse carbohydrates, amino acids, fatty acids, lipids, proteins and simultaneous polysaccharides of FTIR, it has been recognized as a valuable tool for metabolic fingerprinting/footprinting [14–16].

Some cellular biomolecules (or biochemicals) of interest that absorb at different wavenumbers are amide I (≈1.650 cm^{-1}), amide II (≈1.550 cm^{-1}), protein (≈1.425 cm^{-1}), Amide III (≈1.260 cm^{-1}), asymmetric phosphate stretching vibrations ($\nu_{as}PO_2^{-}$ ≈1.225 cm^{-1}), carbohydrates (≈1.155 cm^{-1}), symmetric phosphate stretching vibrations ($\nu_s PO_2^{-}$ ≈ 1.080 cm^{-1}) and protein phosphorylation (≈970 cm^{-1}) [17–19].

After the progress in research about IR spectroscopy being used in biological material and for diagnosing diseases in the last decade (1994 – 2004) as indicated by Diem et al. [1], many other studies and papers using FTIR spectroscopy as an imaging tool or in classifying spectral categories and determining the distinction between benign and malignant tumours in tissue samples of prostates have been reported by Lasch et al. [20], Gazi et al. [11,21,22], Harvey et al. [11,23], Baker et al. [24–26], Bassan et al. [27–30], Hughes et al. [31] and Malins et al. [4,5]. More particularities of FTIR application in prostate cancer diagnoses and classification are described further in this review.