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A REVIEW ON THE APPLICATION OF ELASTIC SCATTERING SPECTROSCOPY FOR DIAGNOSIS OF EPITHELIAL CANCERS

Physics

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ABSTRACT

Optical techniques such as elastic scattering spectroscopy (ESS), Raman spectroscopy and fluorescence spectroscopy have potential for non-invasive cancer detection. Particularly, ESS is a relatively sensitive technique for the morphological changes that occurs with the progression of cancer. The combination of ESS with appropriate analysis algorithms can provide the results with high sensitivity and specificity. In this review article, the development of ESS for the detection of different type of epithelial cancers is discussed. The results of the studies show that ESS can be an alternative for real time diagnosis of cancers at an early stage with more accuracy.

KEYWORDS

Elastic scattering spectroscopy, epithelial cancer, optical devices

INTRODUCTION

Cancer, is a group of diseases in which abnormal cells start growing in an uncontrolled manner. Globally, cancer is the second leading cause of the death with around 10 million deaths, in 2019 [1,2]. Most of the cancers such as cervical cancer, skin cancer, breast cancer, lung cancer, prostate cancer, colorectal cancer, esophagus cancer etc. start from epithelial layer of the tissue which are also known as carcinoma [1,2]. The conventional techniques for diagnosis of these epithelial cancer are invasive, time consuming and do not give real time results, need surgical environment, and limited by sensitivity and specificity. These limitations increase the mortality rate and hence, new techniques are needed for early detection which can become a life savior if treated properly [1,2].

Recently in the past few decades, significant efforts have been made for developing optically measurement-based systems [3]. These techniques are non-invasive, more accurate, doesn't need a surgical environment, cost effective, and provide real time diagnosis results [3]. The high sensitivity and specificity of these techniques in measuring the morphological and biochemical changes with the progression of the disease encouraged researchers to develop optical devices for in-vivo detection of different type of cancers [3-5]. A range of optical spectroscopies such as elastic scattering spectroscopy (ESS), fluorescence spectroscopy, and Raman spectroscopy have been investigated for the diagnosis of different cancers [5]. Elastic scattering spectroscopy is a sensitive technique and detects the morphological aspects like shape, size and density of tissue molecules [6]. Irving J. Bigio and his group at Los Alamos National Laboratory developed the idea of using the ESS to detect abnormalities due to pathologies including a majority of cancer forms and reported a significant architectural change which are shown at the cellular and subcellular level [7,8]. They have claimed that the ESS is able to detect the morphological changes in biological tissues with significant sensitivity and specificity [7]. Later various research groups have studied the potential to detect morphological changes with more specificity and sensitivity using ESS and polarized ESS [9-14,17,19,21-23].

Polarized ESS helps to detect any abnormality in epithelial layer due to the property of changes in degree of polarization in few scattering steps which occurs from uppermost layer and depolarization in highly scattering media [14]. The changes in the size and concentration of cells with cancer progression can be differentiated using polarized elastic scattering spectroscopy measurements [14]. Growing interest has shown in the propagation of polarized light in randomly scattered media, particularly for use in the medical field. Alfano and his group suggested the use of polarized light for the separation of ballistic pictures from the hazy background [15]. Jacques his group studied the backscattered polarization light for use in imaging beneath the surface [16]. Backman described an in-situ approach for examining the structure of live epithelial cells based on polarized light scattering spectroscopy [17]. Studies have shown that in spite of the substantial tissue background, the polarization scattering spectroscopy can retrieve morphological information from living cells [14,17-20].

In this review article, the development of elastic scattering spectroscopy for the detection of epithelial cancers using its efficacy of measuring the morphological changes taking place with cancer progression has been discussed.

ELASTIC SCATTERING SPECTROSCOPY

A typical ESS system consists of a xenon arc lamp, an optical fiber probe, a UV-VIS spectrometer, and a computer to record the elastic scattering spectra. To collect the spectroscopic signal the white light from the xenon arc lamp is directed towards tissue sample through optical fiber probe such that the tip of the fiber probe is touching the surface of the sample. As shown in figure 1, usually the probe consists of one or more than one source fibers and detector fibers [9-13].

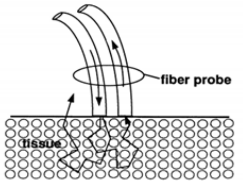

Figure 1. A typical schematic diagram of an ESS system [11].

To minimize the variations due to instrumental and external factors, the ESS system is calibrated using a standard method. The background corrected measured spectra from the sample are normalized with standard reference spectrum [9-13]. The absorption effects of the hemoglobin and oxyhemoglobin can be seen in the ESS spectra [9]. The spectral variations due to morphological changes with disease progression can be seen in the ESS spectra taken from normal and cancer samples. Studies show that multivariate discrimination algorithms can be performed and samples of different grades of the cancer can be discriminated from normal sample with high sensitivity and specificity [10-13,]. Based on ESS several groups have developed portable optical devices for the detection of different type of cancers [11-13,21-23]. Table 1 shows the list of some of the selected optical probes based on optical techniques developed by various research groups for the detection of different types of cancers.

TABLE-1 LIST OF DIFFERENT PROBES BASED ON ESS TECHNIQUES DEVELOPED BY VARIOUS GROUPS FOR DETECTION OF DIFFERENT TYPES OF CANCERS

Probe	Specifications/Findings
Diagnosis of breast cancer using elastic-scattering spectroscopy: preliminary clinical results [11]	Sensitivity: 67% and 91% and specificity: 85% and 93% for breast tissue and sentinel nodes respectively using different classification methods.

Assessment of oral premalignancy using elastic scattering spectroscopy [21]	Sensitivity: 72% and specificity: 75% using LDA classification algorithms.
Elastic scattering spectroscopy for detection of cancer risk in Barrett's esophagus: experimental and clinical validation of error removal by orthogonal subtraction for increasing accuracy [13]	Sensitivity: 82% and specificity: 90% using error removal by orthogonal subtraction (EROS) statistical method
The Safety and Effectiveness of Elastic Scattering Spectroscopy and Machine Learning in the Evaluation of Skin Lesions for Cancer [22]	The overall sensitivity: 92.3% (95% CI: 87.1 to 95.5%). The sensitivity for subgroups of lesions was 95% (95% CI 75.1% to 99.9%) for melanomas, 94.4% (95% CI 86.3% to 98.4%) for BCCs, and 92.5% (95% CI 83.4% to 97.5%) for SCCs. The overall device specificity was 36.6% (95% CI 29.3% to 44.6%).
Elastic scattering spectroscopy for early detection of breast cancer: partially supervised Bayesian image classification of scanned sentinel lymph nodes. [23]	Sensitivity and specificity of 85% and 94%, respectively.

CONCLUSIONS

Elastic scattering spectroscopy is a relatively sensitive technique for the morphological changes that occurs with progression of cancer. Detection of these subtle changes can be a key to identify the disease at an early stage and control the mortality rate due to cancer. The combination of ESS with an effective analysis method can provide the results with high sensitivity and specificity. The results of the studies show that ESS can be an alternative for real time diagnosis of cancers at an early stage with more accuracy.

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