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# Differentiation of Cancerous Prostate tissue from Non-Cancerous Prostate tissue by using Elastic Light Single-Scattering Spectroscopy: A Feasibility Study

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***Abstract*—**Elastic light single-scattering spectroscopy system with a single optical fiber probe was employed to differentiate cancerous prostate tissue from non-cancerous prostate tissue ex-vivo just after radical prostatectomy. First, ELSSS spectra were acquired from cancerous prostate tissue to define its spectral features. Then, spectra were acquired from normal prostate tissue to define difference in spectral features between the cancerous and normal prostate tissues. Of the total 66 tissue samples were evaluated from nine patients by ELSSS system. Comparing of histopathology results and ELSSS measurements revealed that sign of the spectral slopes of cancerous prostate tissue is negative and non-cancerous tissue is positive in the wavelength range from 450 to 750 nm. Based on the correlation between histopathology results and sign of the spectral slopes, ELSSS system differentiates cancerous prostate tissue from non- cancerous with a sensitivity of 0.95 and a specificity of 0.94.

***Keywords*—**Diagnosis, prostatic neoplasm, prostatectomy, spectrum analysis

## I. Introduction

PROSTATE cancer is the most common cancer among American men. It causes death of men more than any other type of cancer apart from lung cancer. In the European Union, estimated prostate cancer incidence is 237,800 and mortality is 85,200 in 2004 [1]. Early prostate cancer usually causes no symptoms. Often, it is diagnosed during the workup for an elevated prostate- specific antigen (PSA) noticed during a routine checkup. Locally advanced prostate cancer disease has a low-cure rate compared to organ confined disease.

Biochemical composition of cancerous tissue is different than non-cancerous tissue. Therefore, reflectance and autofluorescence spectrum of cancerous tissue is different than non-cancerous tissues [2],[3]. Elastic light scattering spectroscopy has been used by several research groups for diagnostic proposes of cancerous tissues [4],[5]. Diagnosis of the tissues by spectroscopy is based on variation of either scattering or absorption properties of the tissues. In the application of the reflectance spectroscopy in diagnosis of pathologic tissues, light travel from a source to a detector within a tissue and detected light reflect absorption and scattering properties of the tissues. Extracting absorption and scattering coefficient of the tissues from the reflectance spectra is desirable for the diagnostic proposes. One way of minimizing of the tissue absorption on the reflectance spectra is using a single optical fiber optical probe for both delivery and detection of light to and from the tissue [6]. Most of the detected light is singly-scattered. Therefore, it is called elastic light single-scattering spectroscopy (ELSSS) and it is sensitive to size of scatters rather than absorption and scattering properties of tissues due to small optical path length of the detected photons [6],[7]. ELSSS system has been used for diagnosis of malignant skin lesions on human [8] and demarcation of brain tumors from surrounded normal brain tissue [9]. ELSSS system has been successfully used in demarcation of melanoma tissues from non-melanoma skin tissue on an animal model [10].

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## II. Material And Method

### *A. Study Design*

The clinical study was conducted at Akdeniz University Hospital with the approval of the Akdeniz University Institutional Review Board. Patients undergoing open radical prostatectomy at Akdeniz University Urology Department were recruited. Of the total 66 fresh prostate specimens were removed from nine patients undergoing radical prostatectomy, and then transported to the histopathology cutup room. Where, the prostate tissues were inked and serially sectioned at 3 mm intervals in a plane perpendicular to the prostatic urethra, and each is placed in separate labeled small cassettes to determine surgical margins.

### *B. Instrumentation*

Elastic light single-scattering spectra of prostate tissue were acquired using a system consisting of a spectrometer (USB2000 with OOIBase32TM Platinum Spectrometer Operating Software, Ocean Optics, Tampa, Florida), a tungsten halogen white-light source, a single fiber optical probe, and a laptop computer. The single fiber optical probe

was used for both delivery and detection of white light to and from the tissue as illustrated in Fig. 1.

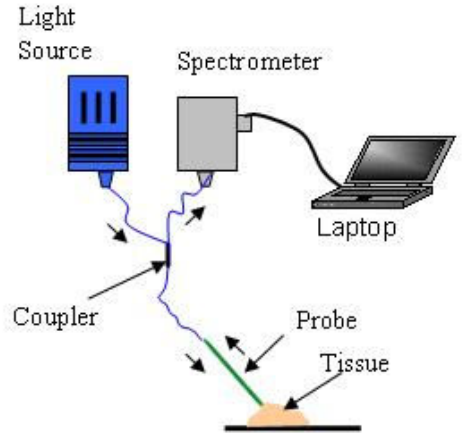


Fig. 1 Elastic light single scattering system

The single fiber optical probe was a 1x2 fiber optical coupler with a splitting ratio of 50%. One proximal end of the coupler was connected to the light source, and the other was connected to the spectrometer. The diameter of the distal end of the probe's fiber was 100 µm with a numerical aperture of 0.22.

*C. Optical Measurements and Data Analyses*

Before acquiring the data from each tissue specimen, three spectra were measured for system calibration. The first one was a background spectrum measured from pure water by inserting the tip of the probe into water in a black container. The second spectrum was taken to define the spectral distribution of the light source, where the probe was placed nearly 1 mm above a white-light reflectance standard (Spectralon, Labsphere, Inc.) in water and the spectral distribution of the light source was measured. The last spectrum was measured from 10% aqueous suspension of monodisperse polystyrene microspheres with a diameter of 2 ± 0.5 µm to test the performance of the single fiber optical probe.

The single fiber optical probe with a fiber core diameter of 100 µm was gently placed on the prostate tissue specimen in a cassette with a surface area of 9.8 $mm^2$ (2.8 mm x 3.5 mm) and at least 16 ELSSS measurements were taken by a random sampling within 3 to 5 minutes. This is not a systematic scan of the tissue surface and always there is a possibility of missing small tumor islands on the tissue surface.

The spectral measurements were performed on total 66 prostate tissue specimens from nine patients by the collaborating pathology. ELSSS spectra were obtained in the wavelength range of 350–800 nm, and the spectra were corrected in the wavelength range of 450–750 nm to calculate spectral slopes of the prostate tissue specimens for each cassette. The measured spectra were corrected for the wavelength dependence of system components and specular reflection. The corrected spectrum [6] is

$$R(\lambda) = \frac{R(\lambda)_s - R(\lambda)_{bg}}{R(\lambda)_c - R(\lambda)_{bg}} \quad (1)$$

Where, $R(\lambda)_s$ is a spectrum of the a tissue, $R(\lambda)_c$ is a spectrum of Spectralon (Labsphere, Inc.) in water and $R(\lambda)_{bg}$ is a background spectrum taken from pure water in a black container. Spectral data were processed in real time, and the corrected spectra are visualized on the computer screen. The single fiber optical probe was tested taking spectrum from %10 polystyrene microspheres with a diameter of 2 ± 0.5 µm dispersed in pure water to test whether the probe is detecting singly-scattered photons from the tissue phantom. As seen in Fig. 2, observing Mie oscillation from the spectrum of monodispersed microspheres confirm that the ELSSS system detects single scattered photons from turbid media rather than diffused photons.

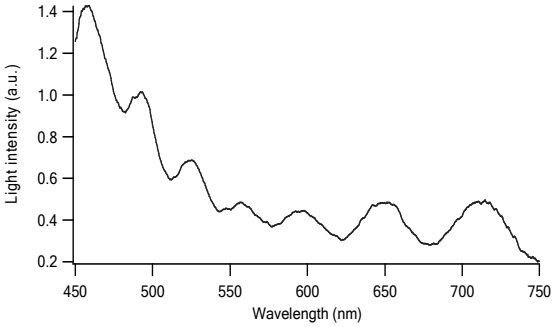


Fig. 2 Corrected spectrum of tissue phantom was acquaes dispersion of polystyrene microspheres with a diameter of 2 µm.

## III. Results

Total 66 prostate tissues of nine patients underwent spectroscopic analysis. All spectra of the tissues were corrected using Eq. 1. In the first section of the study results of the histopathology of all 47 prostate cancer tissues were positive. There were spectra with negative spectral slopes from the tissues in 45 cassettes out of 47. Negative and positive spectral slopes of ELSSS spectra are an indication of cancerous and non-cancerous tissues respectively [5]-[7]. Cancerous prostate tissues from the two cassettes were missed. In the second section of the study, the spectral data acquired from 19 normal prostate tissues. There was no any ELSSS spectra with negative spectral slopes acquired from the tissues in 18 cassettes out of 19. ELSSS system correctly identified normal prostate tissue of 18 out of 19 and one specimens were misidentified as positive cancerous tissues.

As seen in Fig. 3. corrected spectra of the tumor tissue has a negative slope, and the benign tissue has a positive slope.

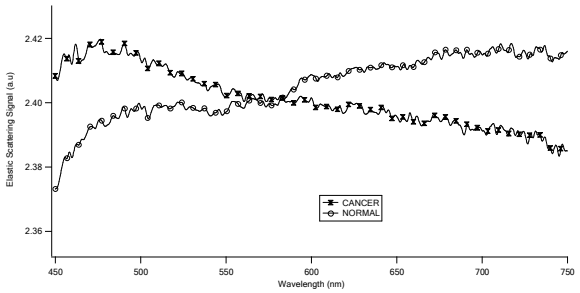


Fig. 3 Corrected spectra of the tumor and the benign prostate tissues

Since tumor cells spread out as small clusters in prostate tissue only one spectrum among all others with a negative slope accepted as an indication of tumor in the region of the interested tissue. If there was no longer any spectrum with a negative slope, the tissue is accepted as non-cancerous based on the spectral analysis.

## IV. Discussion and Conclusions

In this study, we employed a new technology to differentiate between non-cancerous and cancerous prostate tissues. We demonstrated that ELSSS system could differentiate prostate cancer from benign tissue with a sensitivity of 0.95 and a specificity of 0.94 in a consecutive nine case with prostate cancer.

In the application of ELSSS in tissue light scatters due to heterogeneity in the index of refraction. The index of refraction for cell membranes is greater than the index of refraction for extracellular liquid, which cause scattering of light at the cell membrane. Similarly, light scatters inside a cell at the nucleus, mitochondria, and other organelles due to a difference in the index of refraction between intracellular compartments and the surrounding cytoplasm. It has been shown that most of the scattering from the cells takes place within the cells due to its structure [11]. The average refractive indices of cytoplasm and membranes of the cells and organelles are 1.38 and 1.48, respectively [12]. ELSSS spectrum is sensitive to size of the scatterers rather than scattering and absorption coefficient of medium [6].

Optical reflection spectroscopy has been used to differentiate renal tumor from normal parenchyma using an optical fiber probe [2]. Spectral slopes of the spectra in the wavelength range from 630 to 880 nm were used as a discrimination parameter to differentiate between renal tumor and normal parenchyma tissue. In another study, reflection spectroscopy in the wavelength range of 450 nm to 900 nm has been used for diagnosis of prostate cancer. A classification procedure was developed to discriminate cancerous prostate tissue from benign prostate tissue. Sensitivity and specificity of the reflection spectroscopy in diagnose of cancerous prostate tissue [13] are 0.94 and 0.64 respectively.

The ELSSS system cannot provide detailed information about tissue and cannot replace histopathology. It can provide information in real time and in-vivo whether the tissue is cancerous or non-cancerous. Only one single optical fiber probe with a diameter of 100 μm was used to deliver and detect light to and from tissues in this study. Therefore, interrogating positive tissue margins with the single optical fiber probe is time consuming.

*Abbreviations*

ELSSS = Elastic light single-scattering spectroscopy

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