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Noninvasive In-Vivo Optical Properties of Skin Tumors

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ABSTRACT

This paper presents a study for in-vivo estimation of optical properties of pigmented skin tumor by oblique incidence diffuse reflectance spectroscopy. The developed system has been tested in clinical conditions to compare the optical properties of melanomas, dysplastic nevi and common nevi. The spatio-spectral data are collected in the wavelength range of 455 to 765 nm from 96 pigmented skin lesions including 10 histopathologically diagnosed as melanoma, 67 as dysplastic nevi and 19 lesions as common nevi. The preliminary results indicate significantly larger average reduced scattering coefficient spectra for malignant and dysplastic lesions than for benign common nevi.

Keywords: Absorption coefficient, scattering coefficient, spectroscopy, skin cancer, melanoma.

1. INTRODUCTION

Skin cancer is the most common form of cancer, with about a million new cases estimated in the U.S. each year.¹ Melanoma is the most dangerous type of skin cancer and is the leading cause of death among the skin diseases. The American Cancer Society estimates that there are more than 62,000 new cases of melanoma in the United States every year. About 8,000 people are expected to die of this disease each year. Several researchers have studied the potential use of optical spectroscopy for early detection of cutaneous malignant tumors.²⁻⁶ Early detection and treatment of skin cancer can significantly improve patient outcomes. Our previous studies have shown that Oblique Incidence Diffuse Reflectance Spectrometry (OIDRS) as an effective tool to separate carcinoma skin cancer lesions from benign keratoses.⁷ In clinical practice, dermatologists use the ABCD rule (asymmetry, border, color and diameter) and change in the appearance of a mole or pigmented area, to spot suspicious skin lesions. After the skin check a skin biopsy is preformed for assessing whether the pigmented lesion is benign or malignant. For early stage melanoma the treatment is usually a surgery to remove the tumor and a small amount of normal tissue around it. Dysplastic nevi are atypical moles with architectural disorder. Depending of the degree of atypia, dysplastic nevi are mild moderate or severe. Researchers believe that dysplastic nevi are more likely than ordinary moles to develop into a melanoma.⁸ For this reason severe dysplastic nevi are commonly surgically removed in the same way than melanoma.

2. EXPERIMENTAL SETUP

The design of the OIRDS probe consists of three source fibers and two linear arrays of twelve collection fibers within an area $2 \times 2 \text{ mm}^2$ (Fig. 1). The small effective area can provide the needed spatial resolution for the detection of early-stage cancer lesions. Three micro-machined positioning devices are fabricated for accurate placement of the source and collection fibers. The position device for the source fibers consists of silicon substrate with lithographically patterned SU-8 guiding structures (100 μm thick). Each position device for the collection fibers consist of bulk etched channels on a silicon substrate.⁹ After assembling both source and collection fibers into the guiding structures, all the positioning chips are stacked and glued together with epoxy. The probe is then assembled into an aluminum holder to facilitate its clinical use.

Fig. 1. Probe description.

The schematic of the experimental setup is illustrated in Fig. 2. White light from a halogen lamp is coupled to an optical fiber (200 μm diameter). The probe was placed gently on the skin area of interest without significant compression. An optical multiplexer allows delivering light through only one source fiber at a time to the area of interest. Once the light is delivered to the skin, it interacts with the medium and the diffuse reflectance is collected by another set of optical fibers. The collection fibers are coupled with an imaging spectrograph that generates an optical spectrum for each fiber. A CCD camera collects the spectral-images from the wavelength range 455 to 765 nm. This information is stored on a computer for future data analysis.

Fig. 2. System setup.

3. OPTICAL PROPERTIES

The spatially resolved steady-state diffuse reflectance for oblique incidence can be calculated using a modified two-source diffusion theory approximation with one positive source located below the sample surface and one negative

located above the sample surface.^{10, 11} The resolved steady-state diffuse reflectance at a particular wavelength is described by

$$R(x) = \frac{1}{4\pi} \left[\frac{\Delta z(1 + \mu_{eff} \rho_1) \exp(-\mu_{eff} \rho_1)}{\rho_1^3} + \frac{(\Delta z + 2z_b)(1 + \mu_{eff} \rho_2) \exp(-\mu_{eff} \rho_2)}{\rho_2^3} \right] \quad (1)$$

where ρ_1 and ρ_2 are the distances between the point of observation on the sample surface and the point of incidence. Δz is the distance between the virtual boundary and the tissue depth and z_b is the distance between the virtual boundary and the sample surface. The effective attenuation coefficient (μ_{eff}) is defined by

$$\mu_{eff} = \sqrt{\frac{\mu_a}{D}} \quad (2)$$

where D is the diffusion coefficient, μ_a is the absorption coefficient and μ_s' is the reduced scattering coefficient. The diffusion coefficient can be calculated by

$$D = \frac{1}{3(0.35\mu_a + \mu_s')} \quad (3)$$

The distance from the point of incidence to the positive point source $d_s = 3D$. The shift of the point sources in the x direction (Δx) is

$$\Delta x = d_s \sin(\alpha_t) = \frac{\sin(\alpha_t)}{0.35\mu_a + \mu_s'} \quad (4)$$

where α_t is the angle of refraction (Fig. 3). Using simple transformations the absorption and reduced scattering coefficients can be calculated by

$$\mu_a = \frac{\mu_{eff}^2 \Delta x}{3 \sin(\alpha_t)} \quad (5)$$

$$\mu_s' = \frac{\sin(\alpha_t)}{\Delta x} - 0.35\mu_a \quad (6)$$

Fig 3. Oblique incidence diffuse reflectance for a single wavelength.

The OIDRS system was calibrated and validated using liquid phantoms made with polystyrene micro-spheres as scattering elements and trypan blue as absorber.

4. EXPERIMENTAL RESULTS

The data acquisition from skin abnormalities was performed at The University of Texas M.D. Anderson Cancer Center (Melanoma and Skin Center). The OIRDS probe was used to collect spatio-spectral images from skin lesions and adjacent healthy skin. The diffuse reflectance spectra were collected from 96 pigmented skin lesion including 10 histopathologically diagnosed as malignant melanoma. Each spectral image from a lesion was normalized by a spectral image collected from the surrounding healthy tissue. An example of a spectral image is shown in Fig. 4.

Fig. 4. In-vivo spatially resolved diffused reflectance.

The biopsy determined that the pigmented lesions in data set consists of benign common nevi (CN), mildly dysplastic nevi (DN1), moderately dysplastic nevi (DN2), severely dysplastic nevi (DN3), melanoma (M). The number of lesions is described in Table 1.

Table 1. Data description.

Melanoma	10
Severe Dysplastic Nevi	5
Mild Dysplastic Nevi	21
Moderate Dysplastic Nevi	41
Common Nevi	19

After the measurements were completed, a biopsy was performed for each sample and submitted for histopathological diagnosis. The biopsy determined that the pigmented lesions in the data set consists of 10 melanomas, 67 dysplastic nevi and 19 common nevi. The scattering and absorption coefficient were estimated in for each skin lesion. The average scattering properties for malignant and dysplastic cases is larger than for the benign common nevi. The size of the scattering centers in cells is on the order of 100–1000's of nm, which is very similar to the wavelengths of light used in the OIRDS system. Mitochondria, other cytoplasmic organelles and structures within the cell nuclei, are expected to be significant light scatterers and the average effective size of the scattering centers is on the order of a few hundred nm.^{12,13} The absorption coefficient spectra for melanoma and dysplastic cases are generally higher than for the benign ones. The melanoma cases have similar average absorption spectra with that of the dysplastic cases.

5. SUMMARY AND DISCUSSION

The presented system can estimate the in-vivo optical properties of skin tumors. This information can potentially be used to assist the photodynamic therapy, and in-vivo and non-invasive diagnosis of human skin pathologies. This higher scattering coefficient for the melanoma cases could be explained by larger average effective size of the scattering centers. Melanoma has a higher absorption coefficient for the melanoma cases can be related to higher volume-averaged concentration of hemoglobin, which could be indicative of angiogenesis cancerous lesions.

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