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High-Efficiency and Side-Viewing Micro Fiber Optic Probe for In-Vivo Diffuse Reflectance Measurements of Human Epithelial Tissues

Alejandro Garcia-Uribe[1,2], Karthik C. Balareddy[1], Cheng-Chung Chang[1], Murat K. Yapici[1], Jun Zou[1] and Lihong V. Wang[2]

[1]Department of Electrical and Computer Engineering, Texas A&M University, College Station TX, USA
[2]Department of Biomedical Engineering, Washington University in St. Louis, St. Louis MO, USA

***Abstract*— In this paper, we present a new micro fiber optic probe for in-vivo diffuse reflectance measurents of human epithelial tissues. The probe consists of seven, 120x120 μm collection fibers and one 200 μm incidence source fiber, arranged into a side-viewing configuration by using curved air-core waveguides with high optical transmittance. The outer dimension of the probe is 2x8mm^2. The extremely small size, high transmission efficiency and side-viewing capability of the new probe make it suitable for endoscopic spectroscopic applications inside the human body.**

I. Introduction

Recent advancement in biomedical optics has revealed that the optical properties (e.g. absorption, scattering, fluorescence, etc) of human epithelial tissues (e.g. skin and mucosa) are closely linked to certain critical physiological parameters of their cancer states [1-5]. Therefore, developing and applying novel optical sensing or imaging techniques to capture and process these optical parameters is expected to have profound medical significance in the diagnosis and even treatment of various epithelial cancers.

Oblique incidence diffuse reflectance spectroscopy (OIDRS) is an optical sensing method, which utilizes a special fiber optic sensor probe to robustly and accurately measure the diffuse reflectance of inhomogeneous media (e.g. biological tissues) in contact [6]. In our previous studies, a remarkably high accuracy of 95% was obtained in differentiating (pre)cancerous skin lesions from benign ones through processing of OIDRS data [7]. These results indicate that OIDRS could provide a n

ovel approach for early detection of skin cancers and potentially other epithelial cancers. To extend the application of OIDRS from skin to other organ systems inside the human body, miniaturized fiber optic probes for inner-body diagnoses will be needed.

In this paper, we report the development of a new micro fiber optic probe for OIDRS. The extremely small size, high optical transmission efficiency, and also side-viewing configuration make it well suitable for various endoscopic applications for the in-vivo diffuse reflectance measurements on epithelial tissues both outside and more importantly inside the human body.

II. Principle Of Oblique Incidence Diffuse Reflectance Spectroscopy

As shown in Fig. 1, when light is incident on the surface of an inhomogeneous media (e.g. biological tissue), part of the incident light will be directly reflected (specular reflectance) and the remaining will transmit into and interacts with the media. After undergoing multiple times of scattering and absorption, part of the transmitted light will be "turned" back and escape from the surface the media, which forms the diffuse reflectance. The spatially resolved steady-state diffuse reflectance for particular wavelength and oblique incidence can be calculated by [8].

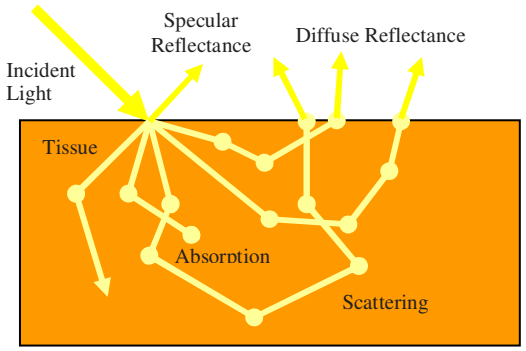

Fig. 1. Light interaction in a scattering and absorbing media

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

where ρ_1 and ρ_2 are the distances between the source point and the observation point on the skin surface. Δz is the distance between the virtual boundary and the tissue depth, and z_b is the distance between the virtual boundary and the surface of the sample (Fig. 2). The distance from the point of incidence to the positive point source $d_s = 3D$. For oblique incidence the diffusion coefficient is $D=(3(0.35\mu_a+\mu_s'))^{-1}$, where μ_a is the absorption coefficient and μ_s' is the reduced scattering coefficient.

The effective attenuation coefficient $\mu_{eff} = (\mu_a / D)^{1/2}$. The shift of the point sources in the x direction $\Delta x = \sin(\alpha_t)/(3(0.35\mu_a+\mu_s'))$, and α_t is the angle of light transmission into the tissue. The absorption and reduced scattering coefficients can be calculated by

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

$$\mu_s' = \frac{\sin(\alpha_t)}{\Delta x} - 0.35\mu_a \quad (3)$$

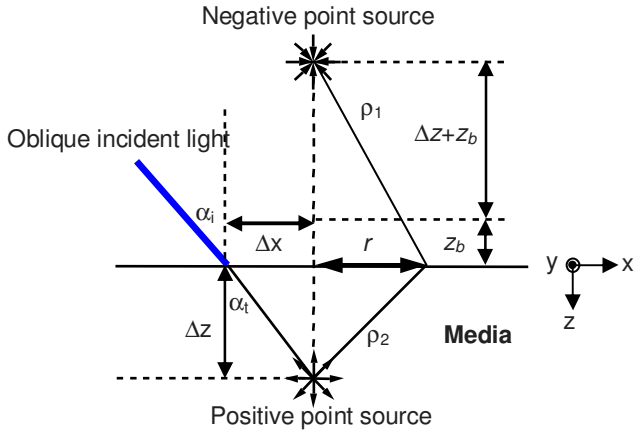

Fig. 2: Schematic of the diffusion theory model for oblique incidence.

The diffusion equation assumes that the reduced scattering coefficient is much larger than the absorption. The source and detector must also be separated in space so that the light is diffuse when it reaches the detector. When the distance between the source and the detectors is comparable to the transport mean free path (~1 mm), diffusion theory does not apply. In this case, Monte Carlo simulation can be applied for the extraction of optical properties from the measured diffuse reflectance [9].

III. Probe Design & Fabrication

To conduct OIDRS measurement, it is necessary to accurately deliver light of particular wavelength at a desirable oblique incidence angle on the tissue surface and also collect the one-dimensional linear distribution of the diffuse reflectance $R(x)$. The measurements from tissue inside human body, such as esophagus, require a side-viewing configuration that facilitates the in-vivo measurement in the narrow places like the esophagus (Fig. 3).

To develop an OIDRS probe capable of in-vivo measurements inside the human body, several size constraints have to be met. Currently the smallest endoscopes can hold attachments no bigger than 2.4x 2.4 mm^2. To overcome these issues, we have investigated the feasibility of designing and microfabricating probes that are small, reliable and cost effective. The probe uses one source fiber which provides light at an oblique angle to the tissue are of interest, and 7 collection fibers that collect the diffuse reflected light from the tissue. A 230 µm diameter fiber is used as the source while 115 µm diameter fibers are used for collection. In addition to the size constraints, the entire probe must have a side viewing configuration to fit and collect measurements in the narrow cavities present like the esophagus.

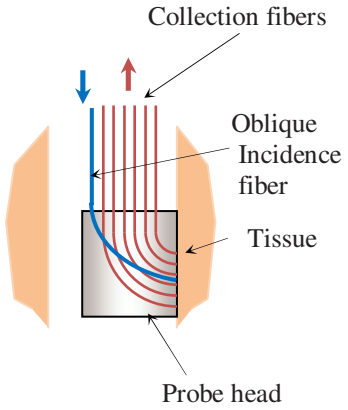

Fig. 3 Schematic of OIDRS probes: (a) side viewing configuration. (b) Source fiber guides; (c) Collection waveguide substrates

The probe consists of four pieces of substrates as shown in Fig. 4. Two pieces are used to hold and position the source fiber, while the other two pieces are used to interface the collection fibers with the air waveguides and a top cover with interlocking patterns to maximize efficiency. Each substrate is fabricated using a silicon substrate and photolithography patterned SU-8.

The fabrication of the probe consists of two step 1) microfabrication and 2) assembly of the 4 pieces of substrates to make the final device. We chose SU-8 as the structural material as it can be easily used to form very thick layers (100µm to 500µm) and can be easily patterned using photolithography to form high aspect ratio structures. Using SU-8 100 as the structural material eliminates the need of expensive microfabrication equipment and complex process steps (e.g. deposition and etching), which results in a straightforward and low-cost fabrication process. The substrates used to align the 230 µm source fiber are fabricated by spin coating a 120 to 130 µm thick layer of SU-8, which is subsequently patterned using near UV light and developed according to the process recipe recommended by Microchem Inc. This process was repeated to fabricate the substrates used to interface the air waveguides and optical fibers. Care needs to be taken during fabrication to ramp the temperature progressively

to avoid accumulating too much stress between the SU-8 layer and silicon substrate, which could cause a loss of adhesion between the two layers or cracks in the thick SU-8 layer.

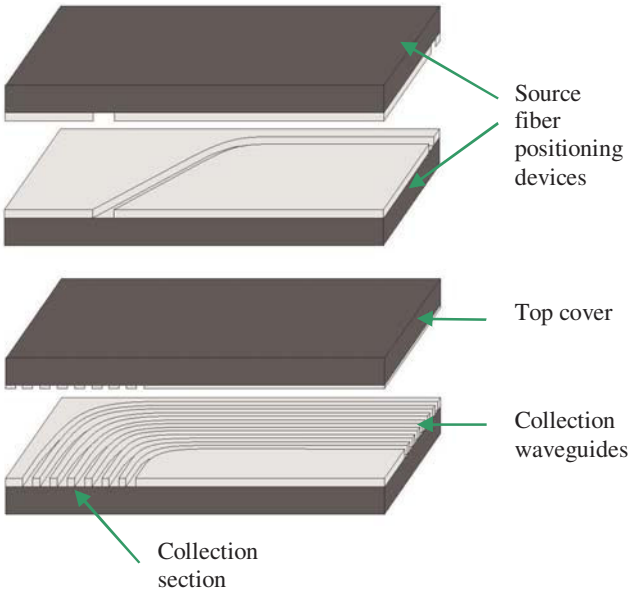

Fig. 4. Probe schematic.

To create the interlocking structures that cover the air waveguides SU-8 2005 is used to produce a 5 micron think layer which is processed using the recipe provided by the company to achieve the desired results. All these pieces are then coated with a thin (10 nm) layer of titanium which acts as an adhesion promoter between SU-8 and the thick layer (300 nm) of silver. During deposition by E-beam sputtering the substrate are placed at a $\pm$ 45° with respect to the source. This ensures a good deposition on the side walls as well as the top surface, increasing reflectivity of the waveguides and decreasing crosstalk between waveguide channels.

After fabrication the pieces can be assembled to complete the probe. First the source fiber is carefully placed in the source fiber guide and bonded in place using clear glue. Then the 7 collection fibers are similarly bonded in their respective channels using the same glue.

The clear glue is used to bond the top covers for the source and collection fibers in place and the two pieces are then stacked and bonded together by usinzg clear black epoxy. The proximal end of the fibers are placed in SMA connectors to enable interfacing with the OIDRS system (Fig. 5).

IV. OIDRS System

The OIDRS system is shown in Fig. 6. It consists of white light source (halogen lamp), multiplexer, imaging spectrograph, a CCD camera, and a personal computer to automatically record the spectra of the collected light. Before an OIDRS measurement is conducted, the source fiber of the sensor probe is connected to the output of the light source via SMA connectors. The proximal end of each collection fiber is fitted with SMA 905 connectors and then connected to the input bundle of the spectrograph. After the sensor probe comes into contact with the sample, white light is delivered through the source fiber and the diffuse reflectance is then captured by the collection fibers.

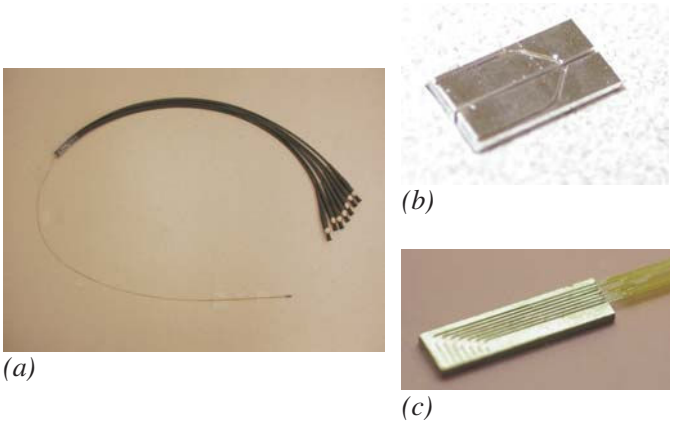

Fig. 5. (a) Complete OIDRS probe; (b) Source fiber guides; (c) Collection waveguide substrates

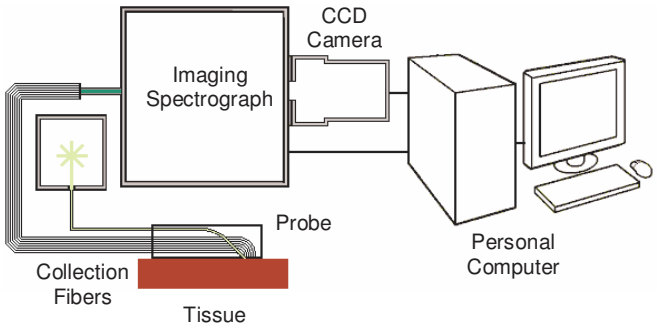

Fig. 6. Schematic of the OIDRS system.

The collection fibers are coupled with the imaging spectrograph that generates an optical spectrum for each fiber. The CCD camera collects the spectral-images from the wavelength range of 455 to 765 nm. The spectral images represent the steady-state diffuse reflectance spectra from each collection fiber, which are stored in the computer for further analysis. This system is capable of capturing one frame of spectral image in a fraction of a second.

V. Measurement Results

The OIDRS system is used to collect the steady-state spatially resolved diffuse reflectance spectra $R_d(x)$ from human skin. The main absorbers of human skin

are oxy-hemoglobin, deoxy-hemoglobin and melanin. The absorption picks of oxy-hemoglobin around 540 and 576 nm are clearly visible in the diffuse reflectance spectra from each collection waveguide (Fig. 7).

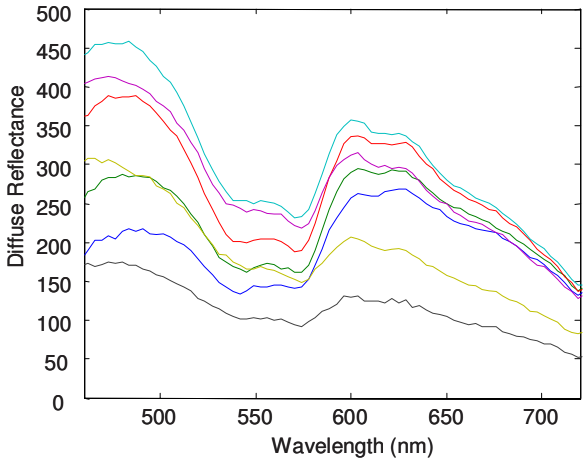

Fig. 7. Diffuse reflectance collected in-vivo from human skin.

CONCLUSIONS

In summary, we have successfully developed a new micro OIDRS probe for in-vivo diffuse reflectance measurents of human epithelial tissues. The use of an innovative curved air-core waveguide structure allows the 90^{o} light bending with minimum loss and crosstalk. It enables a much transmission efficiency and wider wavelength range than the curved polymer waveguide we previously demonstrated. The extremely small size, high transmission efficiency and side-viewing capability of the new probe make it suitable for endoscopic OIDRS, but also many other endoscopic spectroscopic applications as well.

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