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Evaluating and improving the quality of time-dependent, diffuse reflectance spectroscopic signals measured from *in vivo* brain during craniotomy

Nitin Yadav[a,*], Sanjiv Bhatia[b], John Ragheb[b], Yinchen Song[a], Adrian Romero[a], Sanghoon Oh[c], Wei-Chiang Lin[a,b]

[a] *Department of Biomedical Engineering, Florida International University, Miami, FL, USA*
[b] *The Brain Institute, Miami Children's Hospital, Miami, FL, USA*
[c] *Memorial Sloan-Kettering Cancer Center, New York, NY, USA*

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ABSTRACT

Background: Optical spectroscopy can be used to assess the pathophysiological characteristics of diseased and injured biological tissue *in vivo* in a non-destructive way. It is often used in conjunction with a contact optical probe for the purposes of operating and sensing in a sterile field. Since the probe is often held by the hand of an investigator during data acquisition, any hand instability can affect the quality of acquired data and, hence, degrade the accuracy of diagnosis. This study was designed to quantitatively characterize these artifacts, and then propose an effective engineering solution to remove them.
Methods: Time-dependent diffuse reflectance spectra ($Rd(\lambda,t)$) were acquired from the normal cortex region of pediatric patients undergoing epilepsy surgery. They were acquired at a rate of 33 Hz, and their range was 400 and 900 nm. Two distinct ways of collecting data were tested: one with the fiber optical probe held by the surgeon's hand during data acquisition, and the other with the probe held by a specially designed probe holder. The probe holder was designed and constructed to minimize the variations in probe contact pressure and contact point for the full duration of any given investigation. Spectral data acquired using *versus* not using the probe holder were characterized and compared in the time, wavelength, and frequency domains, using both descriptive and inferential statistics.
Results: Hand motion manifested as strong random variations in $Rd(\lambda,t)$ which impacted temporal and frequency characteristics of $Rd(\lambda,t)$. The percentage standard deviation %STD of $Rd(\lambda,t)$ acquired without probe holder could be as high as 60%, and they are significantly higher than those with probe holder at all wavelengths. This difference is especially prominent between 400 and 600 nm. $Rd(\lambda,t)$ acquired without the probe holder also processed a higher spectral power energy in the frequency domain than those with the probe holder. The correlation analysis revealed that the hand motions induced synchronistic variations in $Rd(\lambda,t)$ between 600 and 800 nm, but this synchronicity is not obvious between 400 and 600 nm.
Conclusion: The results of this investigation demonstrate the nature and the magnitude of hand motion induced artifacts in *in vivo* diffuse reflectance spectra and propose one potential solution (*i.e.*, a probe holder) to remove them. These findings allow us to improve the quality of time-dependent, diffuse reflectance signals acquired to study the dynamic characteristics of biological tissues, like brain, *in vivo*.

1. Introduction

Spectroscopy-based optical diagnostic technologies have been investigated and evaluated widely over the past two decades; they are primarily used to detect pre-cancer in various tissue organs [1–6] and guide tumor resection intraoperatively [7–10]. These technologies are built upon the principle of light-tissue interactions: light absorption and scattering inside a biological tissue are governed by the tissue's structural and compositional characteristics and these intrinsic characteristics are altered by disease and/or injury [4,11–15]. These technologies hold several advantages over existing diagnostic technologies, in that they are relatively inexpensive, highly portable, and can be used real-time. To make these technologies applicable within an *in vivo* or intraoperative environment, a sterilized contact probe often is employed to achieve remote sensing from *in vivo* tissue. The probe usually is held by

* Corresponding author. Tel.: +1 7863031767.
E-mail address: nyada001@fiu.edu (N. Yadav).

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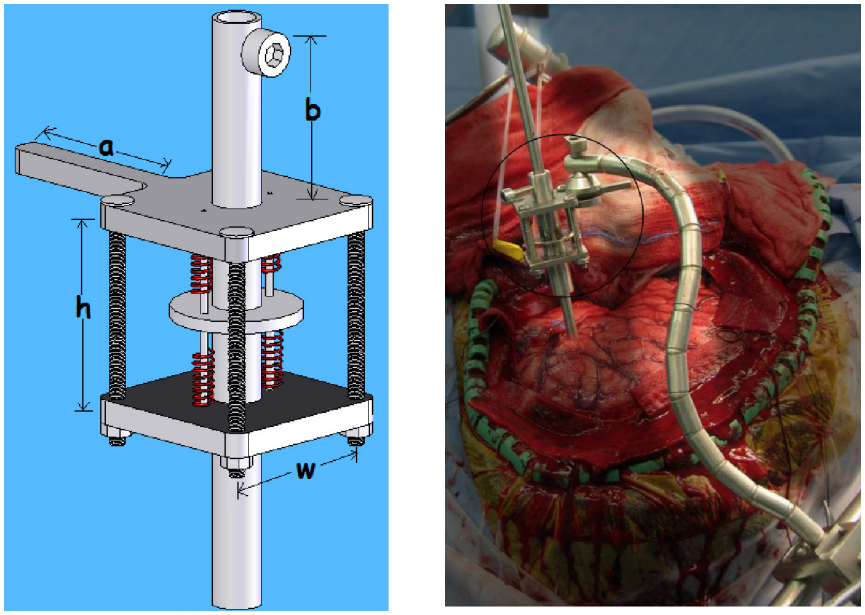

Fig. 1. (a) Schematic of the mechanical holder for the fiber optic probe. Here $h = w = 1$ in. (b) The probe holder is attached to a Greenberg retractor system during *in vivo* data acquisition.

the hand of an operator. One common problem with such a practice is motion artifacts in the acquired data; unintentional hand movements or tremors alter the pressure of the probe against the target tissue (*i.e.*, probe contact pressure) or shift the site of investigation. Consequently, these movements induce additional noise or artifacts in the *in vivo* spectra acquired. This phenomenon is especially pronounced in studies involving time dependent measurements. A couple of earlier reports have suggested that probe contact pressure does not significantly affect fluorescence intensity of the cervix [17,18]. A similar finding was noted in a study in which Raman spectroscopy was used to detect pre-cancerous lesions within the gastrointestinal tract [19]. However, several other studies have shown that excessive probe contact pressure, resulting from hand movements, can lead to strong alterations in the hemodynamic and metabolic characteristics of local tissue [20–26]. In addition, the effect of varying probe contact pressure on acquired optical spectral data is tissue type dependent: the softer the tissue, the greater the effect [16]. Despite this recognition, the intrinsic characteristics of the spectral artifacts induced by hand motions have not yet been thoroughly investigated, and no systematic approach to combat this obstacle has been proposed.

In this paper, we report the results of an *in vivo* study of the brains of pediatric patients undergoing epilepsy surgery, so as to quantify the spectral and temporal artifacts induced by hand motions. Specifically, time-dependent diffuse reflectance spectra were acquired from the normal cortex of patients during epilepsy surgery using a fiber-optic spectroscopy system. Two distinct methods of spectral data acquisition were compared: one with the fiber-optic probe held by the surgeon's hand during data acquisition, and the other with the probe held by a mechanical probe holder. The probe holder was devised to eliminate hand-motion artifacts in the recording and to counteract any spontaneous movements of the *in vivo* brain. Recordings from the two data-acquisition methods were compared in the time, frequency, and wavelength domains, using both descriptive and inferential statistics. From these results, the characteristics of spectral artifacts induced by hand movements were determined and characterized.

2. Materials and methods

2.1. Instrumentation

The instrumentation for *in vivo* diffuse reflectance spectral acquisition consisted of a fiber-optical probe and a portable spectroscopic system. It was calibrated using a calibrated tungsten halogen light source (LS-1-CAL, Ocean Optics, Dunedin, FL) in order to remove any spectral alterations induced by the instrument. Details of this system can be found in a previous publication by our group [7].

2.2. Design of the probe holder

A mechanical probe holder was designed and engineered to eliminate the need for a surgeon to hold the optical probe throughout a single data acquisition procedure. The introduction of this holder enabled us to identify and, hence, quantify the spectral alterations induced by hand movements. The three critical design criteria of the probe holder were: (1) it had to be able to withstand the ethylene oxide gas sterilization procedure; (2) it should limit the lateral movement of the probe and hence maintain a constant site of investigation; and (3) it should maintain constant probe-contact pressure, if feasible, against the *in vivo* brain tissue. The final design of the probe holder is depicted in Fig. 1. To meet the sterilization criterion, medical grade Stainless Steel 361 was used to construct the entire holder. To meet the stability criterion, the probe holder was designed to be used in conjunction with the Greenberg self-retaining retractor system. This approach reduced the susceptibility of the probe holder to movements of the patient during data acquisition, as the Greenberg system [26] was attached directly to the Mayfield head clamp (Integra LifeSciences Corp., Cincinnati, OH) which was attached to the surgical bed. The center of the probe holder was a stainless-steel tube with an inner diameter slightly larger than the diameter of the optical probe. The optical probe was inserted through the tube and secured using a side thumbscrew. To enable movement of the optical probe along its primary axis, the center tube was attached to the frame of the holder *via* a two-bar track system (Fig. 1). The range of the axial