Noninvasive optical method of measuring tissue and arterial saturation: an application to absolute pulse oximetry of the brain

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We present a frequency-domain optical method for real-time noninvasive measurement of absolute tissue and arterial saturation. This method is based on quantitative measurement of the tissue absorption spectrum (for tissue saturation) and of the amplitude of the arterial-pulsation-induced absorption oscillations (for arterial saturation) at eight wavelengths in the range 633–841 nm. We report results obtained from readings taken from the forehead of a healthy volunteer, showing baseline saturation values of 74.7 ± 0.2% (tissue) and 96.9 ± 0.5% (arterial). These values dropped to minimum values of 71.6 ± 0.2% and 90.0 ± 0.2%, respectively, after 1 min of reduced inspired oxygen concentration [10% (by volume) O_2 from a baseline value of 21% O_2].

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Optical spectroscopy in the wavelength range from 600 to 900 nm achieves sufficient photon penetration depth for noninvasive probing of macroscopic tissue volumes, and it is sensitive to the oxygen saturation of hemoglobin. These two features have been exploited since the 1940's for performing optical tissue oximetry.[1] Recently the introduction of time-resolved spectroscopy in conjunction with diffusion theory has led to quantitative tissue spectroscopy and absolute tissue oximetry.[2,3] Optical tissue oximetry measures the hemoglobin saturation in tissue (Y), and it is most sensitive to the blood in the capillaries,[4] where oxygen exchange with tissue occurs.

Optical spectroscopy can also be used to measure the saturation of arterial blood (SaO_2). The hemoglobin concentration in tissue oscillates with time as a result of the arterial pulsation associated with the systolic–diastolic pressure variation.[5] Consequently the detected oscillations in the optical signal can be attributed to the arterial blood, whose saturation is then related to the oscillatory components of the optical densities at two or more wavelengths. On the basis of this principle, pulse oximetry was introduced in 1974[6] and entered clinical practice in the 1980's. The pulse oximeter, which is usually applied to a finger, toe, nose, or earlobe, gives an SaO_2 reading on the basis of an empirical scaling based on a preliminary calibration on a population of reference subjects.[7] Such empirical scaling causes inaccurate readings in the low (<80%) and the high (>97%) saturation limits.[8] Furthermore, the SaO_2 saturation measured in a finger or a toe may not be representative of the systemic arterial saturation.

In this Letter we present a novel approach to absolute oximetry that yields simultaneous absolute measurements of Y and SaO_2, noninvasively and in real time. We have applied this novel technique to absolute measurements of local saturation in the brain, even though it can be applied to other tissues as well. Our approach does not require any preliminary calibration (not even an instrument calibration), nor does it use an empirical lookup table based on data from a reference subject population.

Our frequency-domain tissue spectrometer (see Fig. 1) operates at a modulation frequency of 110 MHz and at eight discrete wavelengths (633, 670, 751, 776, 786, 814, 830, and 841 nm). This spectrometer is a modified version of a two-wavelength frequency-domain tissue oximeter[9] (Model 96208, ISS, Inc., Champaign, Ill.). The 16 light sources (2 laser diodes per wavelength) are electronically multiplexed at a rate of 71.4 Hz, so that each light source is on for 14 ms. The total acquisition time for a full cycle of the 16 light

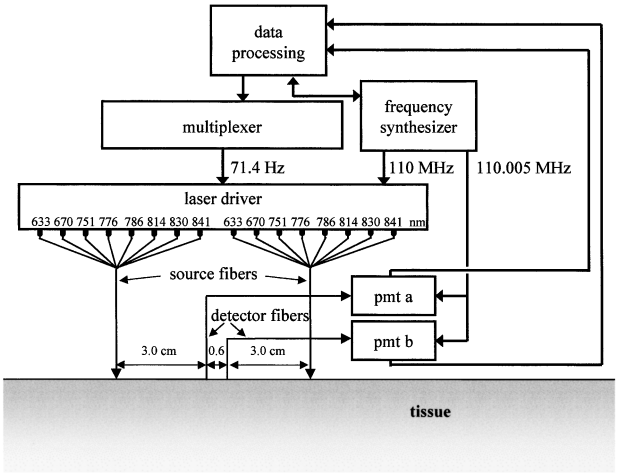

Fig. 1. Block diagram of the frequency-domain tissue spectrometer and geometric arrangement of the source and detector fibers on the forehead. The frequency synthesizer modulates the intensity of the laser diodes at a frequency of 110 MHz; the second dynode of the two photomultiplier tube detectors (pmt a and pmt b), at a frequency of 110.005 MHz. The 16 laser diodes (2 per wavelength) are multiplexed at a rate of 71.4 Hz to time share the two parallel detectors.

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sources is therefore 224 ms. We group the two sets of eight fibers (each 400 μm in core diameter) that guide the light at the eight wavelengths into two fiber bundles (source fibers). The optical signal detected at the tissue surface is guided to the two parallel detector channels of the spectrometer by two optical fiber bundles, each 3 mm in internal diameter (detector fibers). The source and the detector fibers are placed on the same side of the examined tissue (the forehead in this case) in the symmetrical configuration shown in Fig. 1. This geometric arrangement, first described by Hueber *et al.*, features two distinct source–detector separations (3.0 and 3.6 cm) and provides quantitative spectroscopy that is independent of source, detector, and optical-coupling terms, i.e., without requiring any sort of instrumental calibration.[10]

Absolute tissue oximetry requires measurement of the absolute absorption spectrum of the tissue. We performed absolute tissue spectroscopy, using the multidistance frequency-domain method, assuming a homogeneous and semi-infinite geometry.[11] The absolute values of the absorption (μ_a) and the reduced scattering (μ_s') coefficients of the tissue are given in terms of the dc and the phase slopes versus source-detector separation (S_{dc} and S_{Φ}, respectively).[11] To maximize the signal-to-noise ratio we updated the calculation of μ_s' every 10 s. In this fashion we significantly reduced the contribution of the phase noise to the measurement of μ_a, while keeping the 224-ms acquisition time for the absorption spectrum.

Absolute pulse oximetry requires quantitative measurement of the amplitude of arterial-pulsation-induced absorption oscillations. The absorption oscillations ($\Delta\mu_a$) can be effectively measured from the variations in the average intensity at each source–detector pair, by use of the differential path-length factor (DPF) method.[12] The DPF method requires knowledge of the average photon path length in the tissue and, most importantly, of its wavelength dependence. Since assuming a wrong wavelength dependence of the DPF can lead to significant errors in the value of SaO_2, we have taken advantage of the frequency-domain data to measure the DPF spectrum, rather than relying on DPF spectra reported in the literature. We evaluated the amplitude of the arterial-pulsation-induced absorption variations by taking the sum of the amplitudes of the fast Fourier transform of $\Delta\mu_a$ over the heartbeat band. We evaluated the fast Fourier transform of $\Delta\mu_a$ over 64 points, corresponding to a time trace 14.3 s long, to achieve reliable and reproducible spectra from a number of heartbeat periods. We verified that the absorption oscillations at the eight wavelengths were in phase.

We stress that frequency-domain data are of crucial importance in our approach to absolute tissue and pulse oximetry. In fact, we used both the intensity and the phase data to measure the reduced scattering coefficient of the tissue (in the determination of Y) and the spectrum of the DPF (in the determination of SaO_2). To measure the hemoglobin saturation we fitted the absorption spectra with a linear combination of the extinction spectra of oxy-hemoglobin ($\epsilon_{\mathrm{HbO_2}}$) and deoxy-hemoglobin ($\epsilon_{\mathrm{Hb}}$). The fitted parameters are the concentrations of oxy-hemoglobin ([HbO_2]) and deoxy-hemoglobin ([Hb]). The hemoglobin saturation is then given by the expression [HbO_2]/([HbO_2] + [Hb]).

To achieve a variation in the arterial and the cerebral saturation we performed a measurement protocol involving a change in the oxygen concentration inspired by the subject. A healthy volunteer breathed a 21% oxygen concentration (by volume; room air) for 1 min; then the inspired oxygen concentration was lowered to 10% (by volume) for 1 min, and finally it was brought back to 21%. This protocol was approved by the Institutional Review Board of the University of Illinois at Urbana–Champaign. Simultaneously with the measurement from the forehead with our frequency-domain spectrometer, we monitored SaO_2 with a commercial pulse oximeter (Nellcor N-200) attached to the index finger of the subject.

The absolute absorption spectra and the spectra of the amplitude of the absorption oscillations at the heartbeat frequency are shown in Fig. 2 under baseline conditions (21% inspired oxygen) and at maximal desaturation induced by 1 min of 10% inspired oxygen concentration. In Table 1 we report the values of Y and SaO_2 obtained from the fits of Fig. 2, and we compare them with the corresponding values of SaO_2 provided by the commercial pulse oximeter. In Fig. 3 we show the time traces of Y and SaO_2 recorded on line during the experiment. The values of SaO_2 measured with our absolute spectroscopic method and with the commercial pulse oximeter were in excellent agreement throughout the experiment.

We have presented a frequency-domain approach to noninvasive measurement of the absolute values of

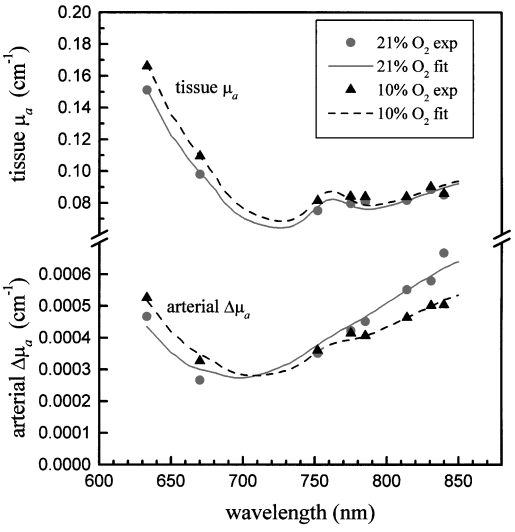

Fig. 2. Effect of the reduced inspired oxygen concentration [1 min of 10% (by volume) O_2 from a baseline value of 21%] on the tissue absorption spectrum (tissue μ_a) and on the spectrum of the amplitude of the pulsed absorption component at the heartbeat frequency (arterial $\Delta\mu_a$). The symbols are the experimental data measured from the forehead, and the curves are the best fits of the data with a linear combination of the extinction spectra of HbO_2 and Hb. The saturation values corresponding to the four fitted spectra are reported in Table 1.

Table 1. Tissue Saturation (Y) and Arterial Saturation (SaO_2) in the Forehead as Measured by Frequency-Domain Tissue Spectroscopy (FDTS) and Arterial Saturation Measured from the Index Finger by a Commercial Pulse Oximeter (Pulse Ox.)[a]

	FDTS		
Condition	Y(%)	SaO_2(%)	SaO_2(%)−Pulse Ox.
Baseline	74.7 ± 0.2	96.9 ± 0.5	97
Maximal desaturation	71.6 ± 0.2	90.0 ± 0.5	91

[a]The first row refers to a baseline condition of 21% (by volume) inspired oxygen concentration, whereas the second row refers to the maximal desaturation condition after the inspired oxygen concentration was decreased to 10% for 1 min.

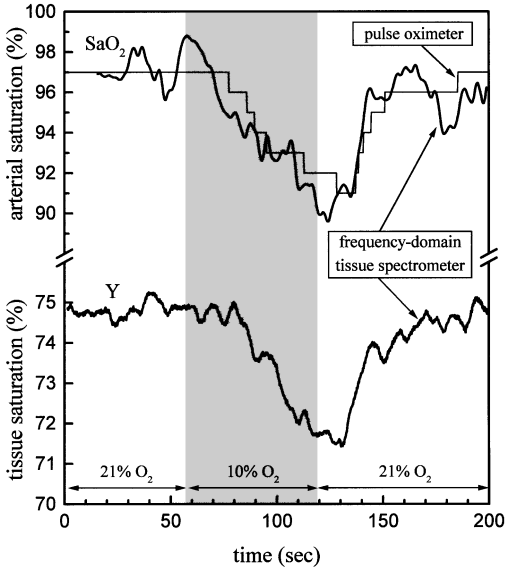

Fig. 3. Time traces of Y (measured with frequency-domain tissue spectroscopy) and SaO_2 (measured with frequency-domain tissue spectroscopy from the forehead and with a commercial pulse oximeter on the subject's finger) during the protocol involving a change in the concentration of inspired oxygen. The shaded area indicates the period of reduced inspired oxygen concentration (10% by volume from a baseline value of 21%).

local Y and SaO_2 simultaneously and in real time. The good fits obtained with the eight wavelengths that were used (Fig. 2) confirm that Hb and HbO_2 are the major species that contribute to the absorption spectra. Therefore two wavelengths may be sufficient for measuring absolute Y and SaO_2. With respect to conventional pulse oximetry, our approach provides more-comprehensive information about the tissue oxygenation level, it can provide the local SaO_2 of the brain, and it can be applied over the full range of SaO_2 values.

At a recent conference (BiOS '99 Biomedical Optics Symposium, San Jose, California, January 23–29, 1999) we presented part of this work, and W. Colier's group showed a method for absolute pulse oximetry based on cw measurements. We thank John Maier for his assistance during the measurements on the human subject and Dennis Hueber for his help in the configuration of the 16-bit acquisition card of the tissue spectrometer. This research was supported by U.S. National Institutes of Health (NIH) grant CA57032 and by Whitaker-NIH grant RR10966. M. A. Franceschini's e-mail address is mari@physics.uiuc.edu.

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