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Application of near-infrared tissue oxymetry to the diagnosis of peripheral vascular disease

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Abstract. Near-infrared spectroscopy (NIRS) is a noninvasive technique to measure the tissue oxygenation in real time. This optical method has many advantages over the invasive analysis currently used for clinical tests. Among the possible applications of near-infrared oxymetry, we report three protocols (exercise, venous occlusion and tilting table) in conjunction with NIRS, and discuss their applicability in the diagnosis of peripheral vascular disease (PVD).

1. Introduction

The oxymetry techniques currently in use rely on the physical–chemical analysis of a blood sample, being therefore invasive. Among the physical–chemical analysis, the only exception is gas transcutaneous oxymetry, which uses a Clark electrode to measure the weak current which is related to the partial pressure (pO_2) of oxygen in the underlying capillaries. This method presents many disadvantages: the measurement is indirect, it is limited to the subclavicular or dorsalis pedis area, where perfusion is more consistent, and the result of the analysis is strongly affected by numerous parameters difficult to control, such as the room temperature and humidity.

Near-infrared spectroscopy provides a non-invasive, real time measurement of the tissue optical parameters (the absorption coefficient and the reduced scattering coefficient) which allows to calculate the concentrations of oxy-, deoxy- and total hemoglobin in tissues. The measurement of these parameters, and especially the study of their dynamics during certain physiological processes, finds application in many medical fields, such as sports medicine, surgery, neonatal intensive care, and in the diagnosis of peripheral vascular disease.

The advantages brought by near-infrared oxymetry compared with the conventional techniques are numerous: it allows a non invasive, real time measurement of the concentrations of interest, the observation time is unlimited, it can be used to monitor the time evolution of the tissue oxygenation during physiological or metabolic processes, it uses instrumentation of relatively small dimensions and it is cost effective. All these characteristics are fundamental for clinical use. To show some possible applications of near-infrared oxymetry, we report on three protocols (exercise, venous occlusion and tilting table) associated with near-infrared spectroscopy, which have been used in an effort to discriminate control subjects and patients affected by peripheral vascular disease.

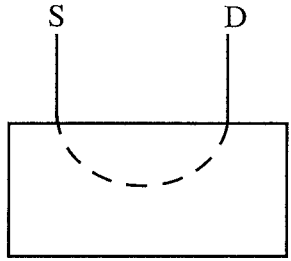


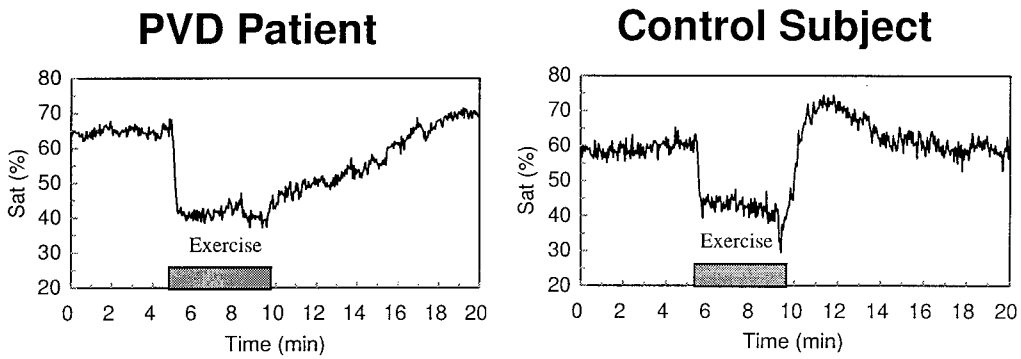
Fig. 1. Scheme of noninvasive near-infrared tissue oxymetry: the source (S) and the detector (D) optical fibers are placed on the skin, few centimeters apart, and the detector fiber picks up the light which, after having traveled through the tissue, is diffusely reflected from the skin.

2. Theory

In near-infrared spectroscopy, the light emitted by appropriate sources (typically laser diodes), at wavelengths in the range 650–900 nm, is conveyed to the skin of the subject, in correspondence to the tissue to be investigated. The light intensity on the skin is typically of a few mW/mm^2, so that the measurement is innocuous. While propagating through the tissue, the light undergoes two physical processes: scattering and absorption [5,6]. Scattering is due to the discontinuities in the refractive index, which typically take place at the cellular membranes and organelles. The diffusion process is anisotropic, so that in a single scattering photons are scattered preferentially in the forward direction. The randomization of the direction of propagation of photons after multiple scattering events is described by the reduced scattering coefficient (μ_s'), which is defined as the inverse of the average distance traveled by a photon before loosing memory of its initial direction of propagation. The optical absorption is generally due to a large number of substances present in tissues. In the near-infrared, the dominant absorbing species are water, cytochromes a and a_3, myoglobin and hemoglobin in its oxygenated and reduced forms. In the wavelength range between 700 and 850 nm, the absorption is mostly due to oxy- and deoxy-hemoglobin. Part of the light emitted by the source, after having traveled through the tissue, is diffusely reflected from the skin, and can be detected at a certain distance (typically a few centimeters) from the source (Fig. 1). Since the absorption coefficient (μ_a) depends on the concentrations of the absorbing substances in the tissue, by measuring the absorption coefficient at two wavelengths in the above mentioned range, it is possible to calculate the concentrations of both oxy- and deoxy-hemoglobin. In frequency domain near-infrared spectroscopy, the light intensity is sinusoidally modulated, and the measured parameters are the alternate component (AC), direct component (DC), and phase (ϕ) of the diffusely reflected, modulated signal [2,3].

3. Materials and methods

All the measurements reported in this paper were performed using a frequency-domain, near-infrared tissue spectrometer (ISS Inc., Champaign, IL) [2]. This instrument has two optical probes, thus allowing the simultaneous measurement of the hemoglobin parameters of interest at two distinct tissue locations. We placed the two probes on the right and left calf muscles, respectively, on the posterolateral aspect of the gastrocnemius. The light emitted by this instrument is delivered to the tissue by optical fibers, so that the electronics of the instrument is isolated from the subject. The two wavelengths used are 750 and 830 nm. The instrument exploits the dependance of the AC, DC and phase from the interoptode distance to measure the tissue absorption and reduced scattering coefficients on the basis of diffusion theory. The



	Baseline (%)	Exercise (%)	Delta Sat (%)	Rec Time (min)
PVD	64.67	40.75	23.92	1.60
Control	60.49	43.85	16.65	0.69

Fig. 2. Typical traces for the oxygen saturation during the exercise protocol for a subject affected by peripheral vascular disease and for a control subject. The table reports the baseline value for the saturation before exercise, the new baseline during exercise, the variation in the saturation and the recovery time, in the two cases.

absorption coefficients at two wavelengths are used to calculate the concentrations of oxy-, deoxy-, total hemoglobin, as well as the hemoglobin saturation [3]. The sampling time was 0.64 s, so that we could monitor in real time the dynamics of the concentrations in the tissue.

In the *exercise protocol*, the subject is sitting on a stationary bicycle with the optical probes positioned on the right and left calf muscles. After a couple of minutes of baseline, the subject starts pedaling for a few minutes, and then stops. When the exercise starts, a decrease in hemoglobin saturation is observed, and a new steady value, lower than at baseline, is kept throughout the exercise. When the exercise is interrupted, the saturation recovers the initial rest value after a certain time (recovery time) (Fig. 2).

In the *venous occlusion* protocol, the optical probes of the near-infrared (NIR) oxymeter are positioned on the right and left calf muscle of the subject. A pressure cuff is positioned on each thigh, and inflated to a pressure of 60 mmHg, causing the interruption of the venous flow, while arterial flow is not affected. The resulting accumulation of blood in the calf produces an increase of oxy-, deoxy- and total hemoglobin. It has been proposed that the rate of increase of the deoxy- and total hemoglobin concentration can be used to calculate the blood flow and the oxygen consumption.

In the *tilting table protocol*, the subject lies on a bed, and the oxymeter probes are again positioned on the right and left calf muscles. After two minutes of baseline, the bed is tilted by 10 degrees to the horizontal, with the head up and the legs down. This position is kept for 1 min, and then the subject is brought back to the horizontal position. The effect of the tilting on the traces of hemoglobin concentration has shown to be analogous to the one observed during the venous occlusion protocol. The values of local blood flow and oxygen consumption can be therefore calculated in the same way as in the venous occlusion protocol.

4. Results and discussion

A typical trace of the hemoglobin saturation during the exercise protocol, for a peripheral vascular disease patient and a control subject, is reported in Fig. 2. It is clear that the recovery time, defined as

the time needed by the saturation to recover half way to the baseline value, is different in the two cases. We measured the recovery time on both legs on four subjects, recruited by the V.A. Medical Center of Dallas, TX, and we found that in healthy legs the recovery time is of the order of few seconds, while it is of the order of minutes in legs affected by peripheral vascular disease. In conclusion, the recovery time calculated from the exercise protocol is a parameter which allows to discriminate between control subjects and peripheral vascular disease patiens. Of course, a much more detailed study is needed to establish a threshold which separates the two categories. A wide population, of 90 subjects, has been studied, and the preliminary results are published in a work by D. Wallace et al. [7].

Blood flow and oxygen consumption can be calculated from the rate of increase in the concentrations of total and deoxyhemoglobin during the venous occlusion and tilting table protocol. In an extensive study that we carried out at the V.A. Medical Center of Danville, IL, we found very similar results with both techniques, which will then be reported together [1,4]. The values of blood flow and oxygen consumption measured with the two protocols in conjunction with near-infrared spectroscopy are in agreement with those reported in the literature (average values measured on 28 subjects: BF = 1.51 ml (100 ml)$^{-1}$ min^{-1}, OC = 6.10 μmol (100 ml)$^{-1}$ min^{-1}). We did not find a significant correleation between the values of blood flow and oxygen consumption measured at rest and the presence of vascular disease. This is because during the exercise protocol, the requirement of oxygen for muscle metabolism strongly challenges the oxygen delivery, so that a control subject and a patient affected by peripheral vascular disease will react differently. On the other hand, the values of blood flow and oxygen consumption measured at rest during the venous occlusion or the tilting table protocols, do not vary between a control and a diseased subject: in fact, even in the presence of an occlusion, collateral circulation can balance the circulatory insufficiency.

5. Conclusions

In this paper we reported three examples of applications of near-infrared tissue oxymetry. This method presents numerous advantages over conventional physical–chemical analysis, providing a noninvasive, real time measurement of tissue oxygenation, whith no discomfort for the subject. In regard to the diagnosis of peripheral vascular disease, while the rest blood flow and oxygen consumption have proven to be unable to differentiate control and diseased subjects, the exercise protocol has demonstrated to be effective. It should be mentioned that not all of the patients are able to exercise. In order to overcome this limitation, other protocols have been proposed and tested, which do not require physical activity. In this respect, an interesting example is the modulation of the fraction of inspired oxygen.

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