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Validation of time domain near infrared spectroscopy in muscle measurements: effect of a superficial layer

Rebecca Re[a], Davide Contini[a], Lucia Zucchelli[a], Lorenzo Spinelli[b], Alessandro Torricelli[a]
[a] Dipartimento di Fisica, Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133 Milano, Italy;
[b] Istituto di Fotonica e Nanotecnologie, Consiglio Nazionale delle Ricerche, Piazza Leonardo da Vinci 32, 20133 Milano, Italy;

ABSTRACT

In reflectance spectroscopy, a major concern is the possibility to discriminate signals coming from different layers of the investigated medium. In this work, the case of time-domain near infrared spectroscopy of muscle is studied with particular attention in the estimation of the pathlength in the different tissue's layers and its impact in the calculation of chromophores concentration.

Keywords: Time Resolved Diffuse Optics, Photon Migration, Bilayer model, Muscle measurement

1. INTRODUCTION

In near infrared spectroscopy (NIRS), a major concern is the possibility to discriminate signals coming from different layers of the investigated medium. In the time domain (TD) approach to NIRS, picosecond pulsed lasers and fast photodetectors are used to acquire the photon distribution of time-of-flights (TOF) in the tissue. There is a direct and intuitive link between the time spent by photons inside the tissue and the mean partial pathlength (MPP) traveled within the probed tissue itself: the longer the TOF the larger the penetration depth. Thus, by exploiting the information encoded in the photon TOF, it is possible to discriminate signals coming from different depths[1, 2]. This holds for each acquisition channel (i.e. for each source-detector pair), without the need of implementing a multi-channel or a multi-distance approach like in CW measurements. However, the accurate quantification of the hemodynamic changes in the different compartments of tissues is still an open issue. In particular, there is still the need to understand the best model to employ for a given tissue and then the best way to analyze the data acquired. In this work, we applied a recent analysis method based on refined computation of the pathlength[3] traveled by photons within each layer the tissue is composed of, by taking into account the non-idealities of the system set-up and the heterogeneous structure of the tissue. In particular, we will focus on the validation of this method in TD NIRS measurements of the muscle and of the surrounding tissues where the thickness variability of the adipose layer can be a problem. In the first part of the work we simulate a realistic situation where the concentrations of oxy- , deoxy-, and total-hemoglobin and tissue oxygen saturation vary as during an arterial occlusion. We implemented different conditions in terms of geometry (layer thickness) and instrument set-up (instrument response function, IRF) and investigated different ways to analyze data (homogenous or bi-layered model). In the second part, we validate the results of the previous section on data acquired during an in vivo measurement.

2. SIMULATIONS

We created a synthetic dataset, which aims to numerically simulate the TD NIRS curves obtained during a real in-vivo measurement on muscle of an adult arm. We modeled the arm as a bi-layer structure composed of a superficial layer (UP, not involved in muscle activity: skin, lipid and surface capillary bed) and a deeper layer (DW, muscle tissue). The thickness of the upper layer was varied in the range 2-10 mm, in 2 mm step. The deeper layer was kept at a fixed thickness: 100 mm. As reference dataset we simulated a TD NIRS measurement at two wavelengths (690 and 821 nm), with interfiber distance of 20 mm and for an ideal δ-like IRF set-up. Then we introduced an IRF with full width at half maximum (FWHM) around 160 ps and a decay time constant (τ) around 100 ps in order to simulate a real case study. The baseline absorption coefficients of the two layers were calculated, at the two wavelengths, starting from the concentration of the main tissue's constituents, shown in Table 1, with the Lambert Beer Law[4], where the extinction coefficients were assumed as known. We considered as main arm chromophores: oxy-hemoglobin (O_2Hb), deoxy-hemoglobin (HHb), lipid and water. From HHb and O_2Hb, total-hemoglobin (tHb = HHb + O_2Hb) and tissue oxygen

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saturation ($SO_2 = O_2Hb/tHb$) can be derived. The reduced scattering coefficients were set for the upper (deeper) layers at 11.19 (10.43) cm^{-1} @690 nm and 10.26 (8.77) cm^{-1} @821 nm respectively. These values were obtained applying a simple approximation of the Mie theory[5]. The baseline values were kept for six points (simulated time) followed by 12 points with varying parameters and six recovery points to return to the same baseline values, simulating a 24 second measurement. The resultant TD NIRS curves were obtained by computing the solution of the diffusion equation in the bi-layer geometry[6] by means of a home-made software. A Poisson noise was added in order to simulate a real result measurement and the count rate was set at 10^8 photons/s. The 12 experiment points were thought in order to mimic an arterial occlusion (Table 1). We consider at first variation of the hemodynamics parameters of two layers at the same time, as usually happens during real measurements. Thereafter we considered separately hemodynamics variations of the UP layer, keeping fixed the ones in the DW, and vice versa in order to decouple the two effects. The reflectance curves obtained from the numerical simulations were at first divided in 10 temporal time-window (or time gates). With a custom made software, the mean partial pathlengths (MPPs) were calculated for all layers, all wavelengths and for the different UP layer thicknesses. Once the MPPs are calculated, we can estimate for each wavelength the absorption changes ($\Delta\mu_a$) with respect to the baseline, occurring in the following 18 simulated points, as explained in Zucchelli et al.[3]. Knowing from the simulations' settings the lipid and water concentration in both the muscle layers, it is then possible, with the Lambert Beer's law, to calculate O_2Hb, HHb, tHb and SO_2 concentration in the UP and DW layer.

Table 1. Simulated variations of the hemodynamic parameters during an arterial occlusion for the UP and the DW layer.

		Baseline	**Arterial Occlusion**						**Cuff Release**						**Recovery**
	Time [s]	1-6	7	8	9	10	11	12	13	14	15	16	17	18	19-24
UP	O_2Hb [μM]	30	28	26	24	22	20	18	20	28	32	30	30	30	30
	HHb [μM]	10	12	14	16	18	20	22	20	12	8	10	10	10	10
	SO_2 [%]	40	40	40	40	40	40	40	40	40	40	40	40	40	40
	tHB [μM]	75	70	65	60	55	50	45	50	70	80	75	75	75	75
DW	O_2Hb [μM]	150	140	130	120	110	100	90	100	140	160	150	150	150	150
	HHb [μM]	50	60	70	80	90	100	110	100	60	40	50	50	50	50
	SO_2 [%]	200	200	200	200	200	200	200	200	200	200	200	200	200	200
	tHB [μM]	75	70	65	60	55	50	45	50	70	80	75	75	75	75

3. RESULTS AND DISCUSSION

As reference dataset we kept the one calculated for an ideal δ-like time-resolved instrument and a setup with 20 mm interfiber distance during an arterial occlusion when changes in both layers are simulated. In figure 1 and 2 the hemodynamic parameters' changes for UP and DW layers are respectively represented at the biggest (10 mm) and smallest (2 mm) UP layer thickness. In these figures, the initial simulated values are also plotted to be used as reference values. In both the figures, we can first of all notice that the calculated baseline values fit well with the nominal ones. If gradually we look at the following points, when the variation starts to grow, it is possible to observe that for small variations the simulated and nominal points are well aligned, while with the increasing of the absolute value variations, their gap increases. This is in accordance with the fact that the model works better for small variations[1,2]. In figure 1, we observe that if the concentrations of the UP layer are growing (decreasing) we have an underestimation (overestimation) in the determination of the correct value which is bigger is the layer is smaller. In figure 2, we can see for the DW layer an underestimation (overestimation) for HHb (O_2Hb) of the nominal values, which is bigger if the layer is bigger as well. The absolute values of the percentage errors, calculated with respect to the baseline period, were also estimated for both the UP and DW layer. The biggest error (6.92% for O_2Hb) in the UP layer is found when the UP layer thickness is small (2 mm). In this case the UP layer is so thin that the path traveled by photons inside it is much smaller than the total pathlength, causing an error in the estimation of the optical properties and then of the hemodynamic parameters. Looking at thicker UP layers (6-8-10 mm) the error decrease till the 0.56% and can be then considered as negligible. Similarly in the DW layer: when the UP layer is thicker (10 mm) the error is bigger (maximum: 12.34% for SO_2) because the path traveled by photons in the DW layer is much smaller than the one traveled in the UP layer. When the layer is thinner (2 mm) the error is much smaller (minimum: 0.75% for tHb).

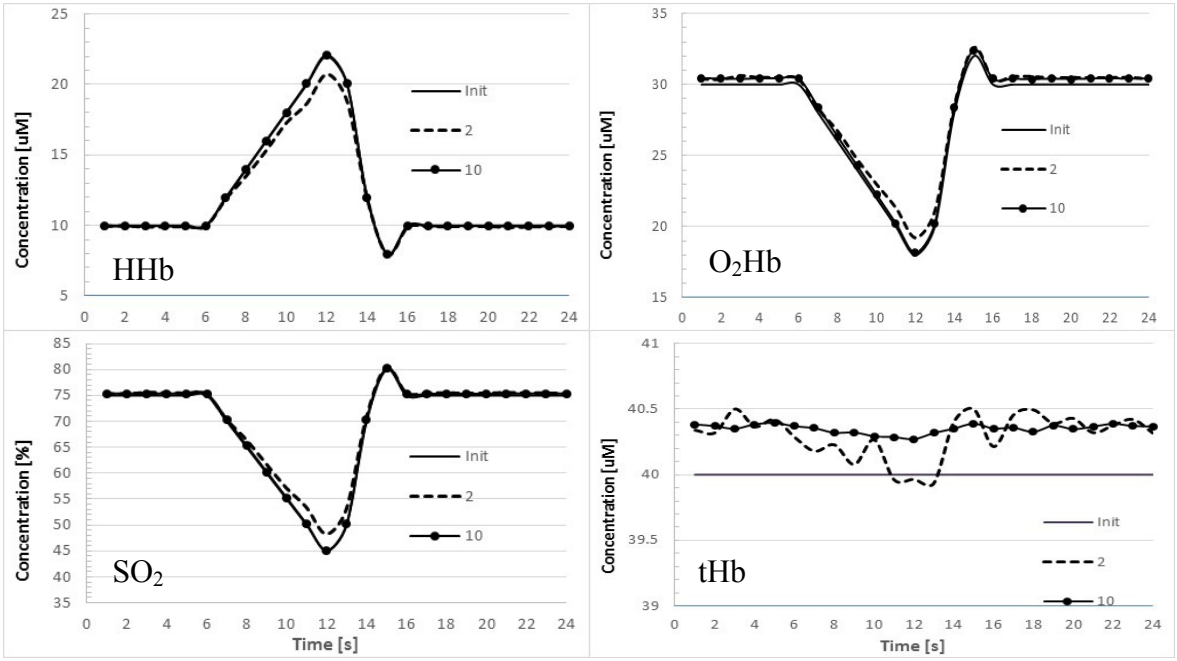

Figure 1. UP hemodynamics variations when variations in both layers are simulated. The different lines represent the biggest (10) and smallest (2) UP thickness and the initial simulated values (Init).

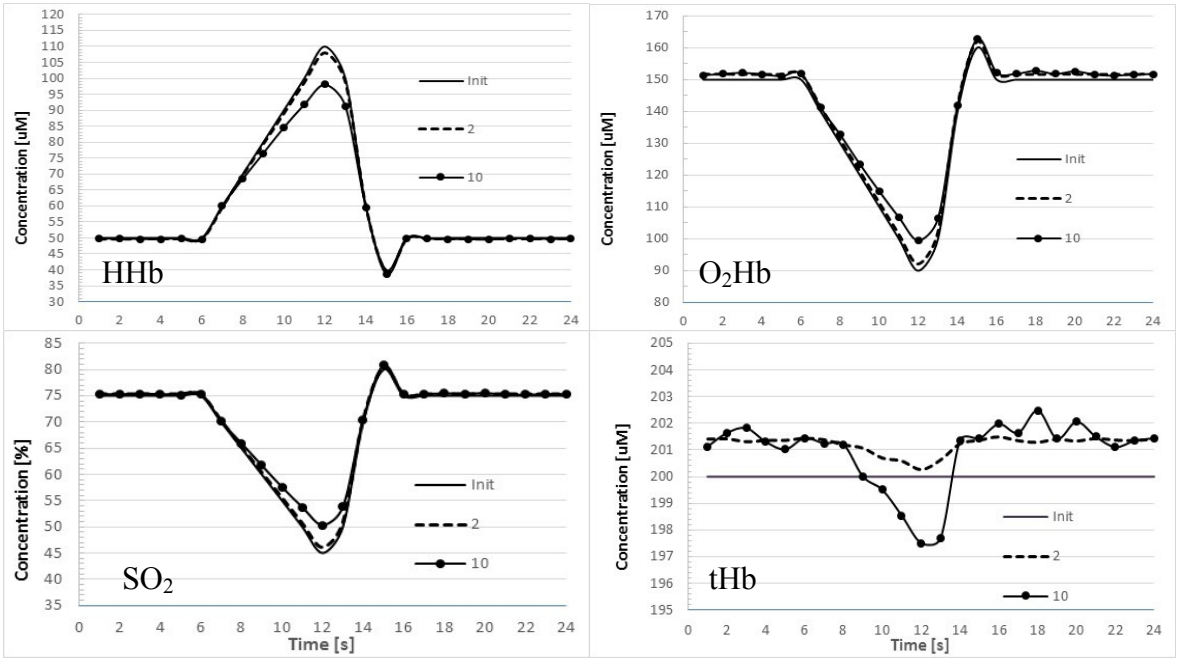

Figure 2. DW hemodynamics variations when variations in both layers are simulated. The different lines represent the biggest (10) and smallest (2) UP thickness and the initial simulated values (Init).

When the arterial occlusion effects are simulated only in the UP layer and baseline values are kept constant in the DW layer for the whole experiment, the percentage relative error is always smaller than 2% in both the layers. This

happens for all the UP layer thicknesses. This means that the variations in the UP layer can be determined with a negligible error and that they have no significant influences in the estimation of the DW layer parameters. Conversely, when changes occurs only in the DW layer, the percentage relative errors in the two layers are not always negligible. In particular, we can affirm that the hemodynamic parameters in the DW layer can be calculated with errors, which are bigger if the UP layer is thicker (around 3% for the 2 mm UP layer, and 15% for the 10 mm one) for all the hemodynamic parameters. The DW variations influence also the capability of calculating the UP layer hemodynamic parameters in particular if the UP layer is thinner (maximum error around 15%). Anyway, the errors found in this particular case are higher than the ones found when both the layers are varying.

The previous dataset was simulated considering a δ-like temporal response. If we now consider the effect of the IRF in the MPPs calculation, when we simulate variations in both the layers, we have to consider an additional error in the calculation of the hemodynamic parameters' variations, since the introduction of the instrument contribution cause a decreasing in the contrast. In particular, if the UP layer is thin (2 mm) and the variations small (<20%) we can affirm, for the DW layer, that the relative error is so small (<5%) that we can neglect it and the IRF doesn't differ significantly from the δ –like for the whole hemodynamic parameters.

Finally, we investigated the error when the muscle is modeled as a bi-layer medium and it is analyzed as a homogeneous one. In this case, the error is too high (the values are extensively underestimated), so that is not possible to consider the muscle as a homogeneous medium also if the UP layer is very thin.

4. IN VIVO MEASUREMENT

We perform an in-vivo arterial cuff occlusion (180 mm Hg) on the left arm of one male volunteer in order to test our method. The measurement protocol consisted of an initial baseline period of 1 min, 2 min of arterial occlusion and 3 min of recovery, for a total duration of the acquisition of 6 min. The measurements were performed in a reflectance geometry, with an interfiber distance of 20 mm. During the in vivo data analysis, we have to take into account two aspects which differ from the simulations: at first we have to know the thickness of the UP layer. In this case, it was measured with a skinfold caliper and the value found was 1.7 mm. The other problem is that we don't know the baseline optical properties of the subject. For this reason, before the calculation of the MPPs, we have to fit the baseline with a bi-layered model in order to find the baseline optical properties. In figure 3 the time courses for the variations of O_2Hb, HHb, SO_2 and tHb, for the DW layer of the left arm, are presented. Once the chromophores are calculated as explained in the previous sections, we calculated the difference (Δ) between their time courses and the average values over the first 30 s of the baseline period. During the arterial occlusion, the deoxygenated (oxygenated) blood through the veins (arteries) cannot go outside (inside) the occluded part, so that we have an increase of the HHb and a decrease of O_2Hb during the entire occlusion task. When the cuff is deflated we observe the typical reactive hyperemia peak and then a slow return to the baseline values. We notice a delay in the response of HHb compared to O_2Hb, as expected, since the veins are released after the arteries, this effect is enhanced by the slow release of the cuff.

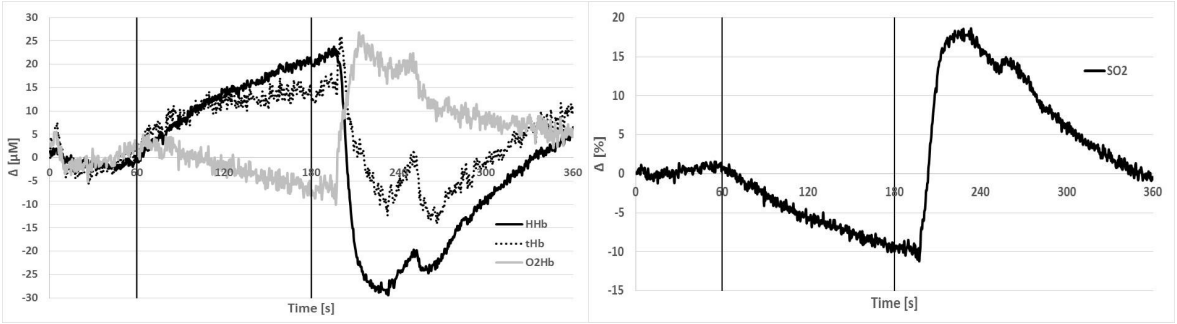

Figure 3. DW hemodynamics variations during an arterial cuff occlusion of the left arm: an in vivo application.

5. CONCLUSION

In this work, we have validated the use of TD NIRS in the study of the hemodynamic changes in muscles using an analysis method based on the estimation of the MPPs in the different layers. Limits and applicability of the technique were studied and tested in particular with reference on the thickness of the superficial adipose layer, which can be used as a priori information in order to tailor the strategy of data analysis. Finally, the proposed method was test on a subject during an in vivo arterial cuff occlusion.

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