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## Sensitivity of TD-NIRS in Estimating Neonatal Cerebral Hemodynamics with Homogenous Models of Analysis

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**Abstract:** We assessed the sensitivity of 1D and 2D homogeneous photon diffusion models for Time Domain NIRS in estimating preterm and term neonates' cerebral hemodynamic parameters simulated by Monte Carlo methods on realistic 3D anatomical meshes.

#### 1. Introduction

Near Infrared Spectroscopy (NIRS) techniques are widely used in neonatology, for monitoring neonates' cerebral hemodynamics and autoregulation [1]. Compared to other commonly used techniques, such as Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI), Xe-clearance, which are bulky, need patient transport and immobility (and some of them are invasive), NIRS is an advantageous alternative for non-invasively continuous monitoring cerebral health in neonates, at bed-side [2]. Time Domain NIRS (TD-NIRS) exploits picosecond laser pulses, and measure the time distribution of the reemitted pulse. Absolute values of the optical properties, absorption ( $\mu_a$ ) and reduced scattering ( $\mu'_s$ ) coefficients, can be retrieved, and absolute concentration of oxygenated hemoglobin (O<sub>2</sub>Hb), deoxygenated hemoglobin (HHb), total hemoglobin (tHb) and oxygen tissue saturation (S<sub>1</sub>O<sub>2</sub>) can be estimated. NIRS techniques are influenced by the shallow tissues of the head, i.e. scalp, skull, and by the cerebrospinal fluid (CSF). Thus, it is extremely important to determine the sensitivity of NIRS in retrieving hemodynamics of deeper head tissues (i.e. brain cortex). To our knowledge no systematic study has been done to determine the accuracy of TD-NIRS in estimating brain hemodynamic parameters in neonates. In this work we simulated photon propagation in preterm and term neonates' head structures through Monte Carlo method and considered in the inversion problem the solution of the Diffuse Equation for two homogeneous geometries: semi-infinite and spherical. We observed a good accuracy in retrieving brain StO<sub>2</sub>, and an underestimation of tHb, probably due to the presence of CSF. These results highlight the need of more complex model of analysis to retrieve accurate values of brain tHb.

#### 2. Methods

We considered the mesh of two head structures: 29 and 44 weeks post menstrual age (PMA) neonates [3] (Fig. 1). The two meshes were divided in three domains: extracerebral tissue (ECT, comprehensive of scalp and skull), CSF and brain. We simulated photon propagation in the two head structures at two wavelengths (690 nm and 830 nm) though a Mesh-based Monte Carlo tool [4]. We reported in Table 1 the optical properties, selected from literature [5], assigned to each tissue type, at the two wavelengths, in baseline condition ( $S_1O_2 = 70\%$  and tHb=53  $\mu$ M).

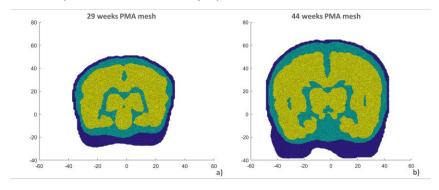


Fig. 1. 29 (panel a)) and 44 (panel b)) weeks PMA meshes, from coronal view in the plane defined by C<sub>z</sub> of the 10-20 International EEG system of electrodes placement. The head structures are divided in three domains: ECT (blue), CSF (green), brain (yellow)

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Table 1. Optical properties used for each tissue type in baseline condition at the two wavelengths (690nm and 830nm). n is the refractive index, and g the anisotropy coefficient.

| Head region | $\mu_a^{690nm}[cm^{-1}]$ | μ' <sub>s</sub> <sup>690nm</sup> [cm <sup>-1</sup> ] | $\mu_a^{830nm}[cm^{-1}]$ | $\mu'_{s}^{830nm}[cm^{-1}]$ | n[a.u.] | g[a.u.] |
|-------------|--------------------------|--|--------------------------|-----------------------------|---------|---------|
| ECT         | 0.206                    | 23.7   | 0.122                    | 18.1                        | 1.45    | 0.89    |
| CSF         | 0.004                    | 0.1  | 0.02                     | 0.1                         | 1.33    | 0.89    |
| Brain       | 0.122                    | 14.4   | 0.137                    | 10.7                        | 1.45    | 0.89    |

The absorption coefficient of the brain tissue was varied from its baseline value, according to the Beer's law, to simulate three common scenarios in neonates: ischemia (reduction of brain  $S_tO_2$  from 70% to 40%); hyperoxygenation (increase of brain  $S_tO_2$  from 70% to 100%), and hypoventilation (simultaneous reduction of brain  $S_tO_2$  from 70% to 40% and increase of tHb from 53  $\mu$ M to 93 $\mu$ M). Monte Carlo simulations were performed assuming  $\mu_a$ =0cm<sup>-1</sup> in all the domains, and the absorption effects were added *a posteriori* [6]. Source and detection were placed in the frontal region: the detector in the AFp7 position of the 10-20 EEG system of electrodes placement, and the source 15 mm away along the scalp surface. All the simulations in each scenario were repeated 10 times to reduce the statistical noise. Moreover, to be as realistic as possible, we convolved the simulated Distribution Time of Flight (DTOF) with the IRF of the BabyLux device, a TD-NIRS system optimized to perform measurements on neonates [7]. The obtained time-resolved curves were analyzed considering the solution of the Diffuse Equation for a homogeneous medium, in semi-infinite and spherical geometries. In the latter case, the head structures were approximated to spheres of diameter the distance between Inion and Nasion (82 mm in case of 29 weeks PMA mesh, and 118 mm for 44 weeks PMA mesh).

#### 3. Results

In Fig.2 we reported the results obtained for tHb and S<sub>t</sub>O<sub>2</sub>.

The strong underestimation of tHb is probably caused by the presence of the CSF. Indeed, due to the lower values for  $\mu'_s$  and  $\mu_a$  compared to the brain, it generates a reduction in retrieved optical properties [8]. On the contrary, the presence of ECT cause an overestimation of the optical properties (due to the higher  $\mu'_s$  and  $\mu_a$  compared to the brain). These two opposite effects better compensate in 44 weeks PMA mesh, where the thickness of ECT, measured in the region of the optode, is higher (3.5 mm) compared to 29 weeks PMA mesh (2.7 mm), and lead to better results in case of 44 weeks PMA mesh. These results suggest that the thinner is the ECT, the stronger is the CSF influence; thus the younger is the neonate, the larger is the underestimation of tHb.

Concerning the two models of analysis, the tHb estimated with semi-infinite geometry is higher, in accordance with previous findings [9]. Comparing the results obtained for semi-infinite and spherical analysis, the differences are larger in 29 weeks' mesh, due to the smaller radius of the sphere used to approximate the head structure.

 $S_tO_2$  values estimated in the two meshes are very close to the one simulated in the brain, suggesting that HHb and  $O_2Hb$  underestimation compensate when  $S_tO_2$  is computed. Moreover, the angular coefficient of the linear regression curve that better fits the estimated  $S_tO_2$ , is always higher when spherical geometry is applied, thus variations of brain  $S_tO_2$ , are better retrieved with spherical model.

Finally, comparing  $S_tO_2$  in scenario 1 (Fig. 2 b) and scenario 3 (Fig. 2 f) it can be noticed that the simulated values in the brain (black lines) are the same, but the slopes of the estimated  $S_tO_2$  curves are lower for scenario 3. The only difference between the two scenarios is the value of tHb, which is constant in case of scenario 1 (53  $\mu$ M), while increases (from 53  $\mu$ M to 93  $\mu$ M) in scenario 3, suggesting that an increase of tHb in the brain reduces TD-NIRS ability in retrieving variations of  $S_tO_2$ .

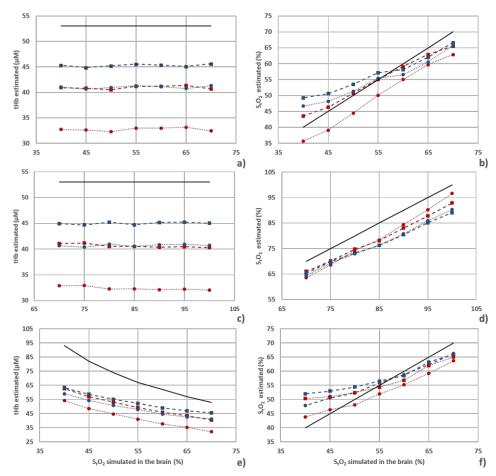


Fig. 2. tHb (left panels, a, c, e) and S<sub>1</sub>O<sub>2</sub> (right panels b, d, f) estimated in case of 29 (red) and 44 (blue) weeks PMA meshes. The squares are the results obtained with semi-infinite geometry, the circle with spherical geometry. The three rows are the three scenarios of ischemia (panels a and b), hyperoxygenation (panels c and d), and hypoventilation (panels e and f). Black continuous lines are the values simulated in the brain.

#### 4. Conclusions

In this work, we determined the accuracy of TD-NIRS in estimating neonatal brain hemodynamics when a homogeneous model for diffuse media, both in semi-infinite and spherical geometries, is considered in the inverse problem. Head structures of neonates with different gestational age were considered (29 and 44 weeks PMA) to maximize the influence of head geometry. In both meshes and for both geometries an underestimation of tHb was observed, probably due to the influence of CSF. On the contrary, values of  $S_tO_2$  estimated were very close to the ones simulated in the brain. These results suggest that a homogeneous model is suitable for brain  $S_tO_2$  estimation, but more complex, i.e. heterogeneous, models of analysis are necessary for a precise monitoring of other vital parameters as brain tHb.

#### 5. References

- [1] L. M. Dix et al., "Monitoring cerebral oxygenation in neonates: An update," Front. Pediatr., 4, 46, (2017).
- [2] A. Torricelli et al., "Time domain functional NIRS imaging for human brain mapping," Neuroimage, 85, 28–50 (2014).
- [3] S. Brigadoi, et al., "A 4D neonatal head model for diffuse optical imaging of pre-term to term infants," Neuroimage, 100, 385–94 (2014).
- [4] Q. Fang and D. R. Kaeli, "Accelerating mesh-based Monte Carlo method on modern CPU architectures," Biomed. Opt. Express, 3 (12), 3223–3230 (2012).
- [5] J. W. Barker, et al., "Accuracy of oxygen saturation and total hemoglobin estimates in the neonatal brain using the semi-infinite slab model for FD-NIRS data analysis," Biomed. Opt. Express, 5 (12), 4300–4312 (2014).
- [6] D. A. Boas, et al., "Three dimensional Monte Carlo code for photon migration through complex heterogeneous media including the adult human head," Opt. Express, 10(3), 159–170 (2002).
- [7] M. Giovannella, et al., "BabyLux device: a diffuse optical system integrating diffuse correlation spectroscopy and time-resolved near-infrared spectroscopy for the neuromonitoring of the premature newborn brain," Neurophoton. 6 (2), 025007 (2019)
- [8] D. Ancora, et al., "Noninvasive optical estimation of CSF thickness for brain-atrophy monitoring," Biomed. Opt. Express, 9 (9), 4094–4112 (2018).
- [9] A. Sassaroli, et al., "Performance of fitting procedures in curved geometry for retrieval of the optical properties of tissue from time-resolved measurements," Appl. Opt., 40 (1), 185–197 (2001).