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Time domain NIRS sensitivity to neonatal brain haemodynamics

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Summary. — Impairment of cerebral autoregulation and haemodynamics is an important cause of morbidity and mortality in neonates, making a continuous monitoring of brain health extremely important in Neonatal Intensive Care Unit. Time Domain NIRS (TD-NIRS) is an advantageous technique for non-invasively continuous monitoring of brain hemoglobin concentration at bed side. However, NIRS measurements are influenced by superficial tissues (*i.e.*, scalp, skull and cerebrospinal fluid) and head geometry, which could affect the estimation of brain haemodynamic parameters. In this work we evaluated the accuracy of TD-NIRS in estimating neonatal cerebral haemodynamics through Monte Carlo simulations. In particular, we simulated photon propagation inside two realistic meshes of preterm (29 weeks post-menstrual age (PMA)), and term (44 weeks PMA) neonates' head. The obtained results were analyzed with semi-infinite and spherical homogeneous model for photon migration, and showed an underestimation of hemoglobin concentration, and good accuracy for brain saturation, empowering the ability of TD-NIRS technique in estimating brain tissue saturation.

1. – Introduction

Brain injuries are an important cause of morbidity and mortality in neonates, this is why a continuous monitoring of cerebral perfusion and oxygenation in Neonatal Intensive Care Units (NICU) is extremely important. In this scenario Near Infrared Spectroscopy (NIRS) techniques are the perfect candidates, allowing a continuous non-invasive monitoring of brain haemodynamics at bed side [1]. NIRS techniques exploit differences in absorption spectra of the main biological tissue's constituents to retrieve their concentration. Three different NIRS techniques can be distinguished: continuous wave NIRS [2] (CW-NIRS) employs light of constant intensity and, by measuring backscattered light amplitude variations (due to interaction with tissues, at different wavelengths), changes of hemoglobin concentration in the probed tissue are retrieved; frequency domain NIRS (FD-NIRS) [3] exploits variations, in amplitude and phase of modulated light, due to the interaction of light with biological tissues; and time domain NIRS (TD-NIRS) [4] profits

from variations in shape and amplitude of injected light pulses with short (*i.e.*, picosecond) duration. FD-NIRS and TD-NIRS are more complex techniques as compared to CW-NIRS, but allow to non-invasively estimate absolute concentrations of oxygenated (O_2Hb) and deoxygenated (HHb) hemoglobin, therefore providing estimates also for total hemoglobin ($tHb = O_2Hb + HHb$) and tissue oxygen saturation ($S_tO_2 = O_2Hb/tHb$). NIRS techniques are influenced by superficial tissues [5,6], scalp, skull and cerebrospinal fluid (CSF), thus it is extremely important to measure their accuracy in retrieving brain haemodynamics. Barker *et al.* [7], measured accuracy of FD-NIRS in measuring neonatal brain haemodynamics, but to our knowledge no systematic study has been done for TD-NIRS. In this work we assessed the sensitivity of TD-NIRS technique in measuring haemodynamic parameters in preterm and term neonates head through Monte Carlo simulations. We analyzed the obtained results with two homogeneous model for photon migration: semi-infinite and spherical model, to appreciate the effects of finite head domain.

2. – Methods

We used a meshed-based Monte Carlo tool [8] to simulate photon propagation inside realistic head structures at 690 and 830 nm wavelengths. The head meshes were selected from an online data set where neonates' head structures from 29 to 44 weeks PMA were collected [9]. We choose the two extreme cases to maximize the influence of head structures on TD-NIRS signal. We distinguished three different tissue types (fig. 1): extra-cerebral tissue (ECT, comprehensive of scalp and skull), CSF and brain.

The optical properties of baseline condition for each tissue types were selected from the literature [7] and are summarized in table I.

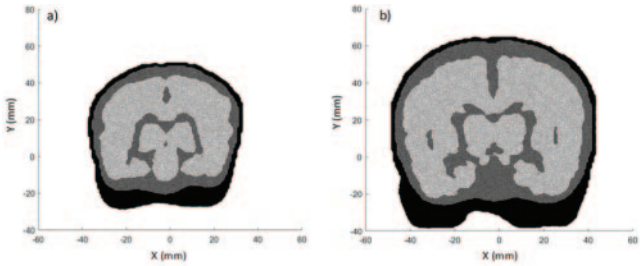

Fig. 1. – 29 (a) and 44 (b) weeks PMA mesh shown from the coronal view in the plane defined by the C_z position of the 10–20 International EEG system of electrodes placement. Black region is ECT, dark gray the CSF, and light gray brain.

TABLE I. – *Optical properties used for different tissues' types at the two wavelengths of 690 nm and 830 nm. n is the refractive index of the medium and g the anisotropy coefficient.*

Tissues	$\mu_{a,690}$ [cm^{-1}]	$\mu'_{s,690}$ [cm^{-1}]	$\mu_{a,830}$ [cm^{-1}]	$\mu'_{s,830}$ [cm^{-1}]	n [-]	g [-]
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

Starting from these baseline values we modified the absorption coefficient of the whole brain tissue (according to the Beer law [7]), to simulate realistic haemodynamic scenarios in neonates: scenario 1, reduction of brain S_tO_2 from 70% (baseline condition) to 40% (ischemia); scenario 2, increase of brain S_tO_2 from 70% to 100% (hyperoxygenation); scenario 3, reduction of brain S_tO_2 from 70% to 40% with simultaneous increase of tHb from 53 μM to 93 μM (hypoventilation). In this simulations, no variations of hemodynamic parameters were modelled in ECT and CSF, thus their absorption coefficients were not modified and they were kept constant to the ones reported in table I . In our simulations μ_a was set to 0 cm^{-1} in all tissue types, and the absorption effect was added *a posteriori* [10]. Each simulation was repeated ten times to reduce the statistical noise.

For both meshes photons were injected in the AFp7 position of 10–20 EEG International System of electrode placement, and the detection 15 mm away along the scalp surface. Finally, the Distributions of Time of Flight (DTOF) obtained from the simulations were analyzed with two homogeneous models for photon migration: semi-infinite (most widespread model, due to its low level of complexity) and spherical model (to evaluate the effects of finite head dimensions). In the second case, we approximate the neonates' head to a sphere of diameter equal to the distance between inion and nasion, which resulted to be 41 mm and 59 mm for 29 and 44 weeks PMA meshes, respectively.

3. – Results and discussion

Results for tHb and S_tO_2 are summarized for the two head structures in fig. 2.
tHb was underestimated for both meshes and model of analysis, and it is more evident

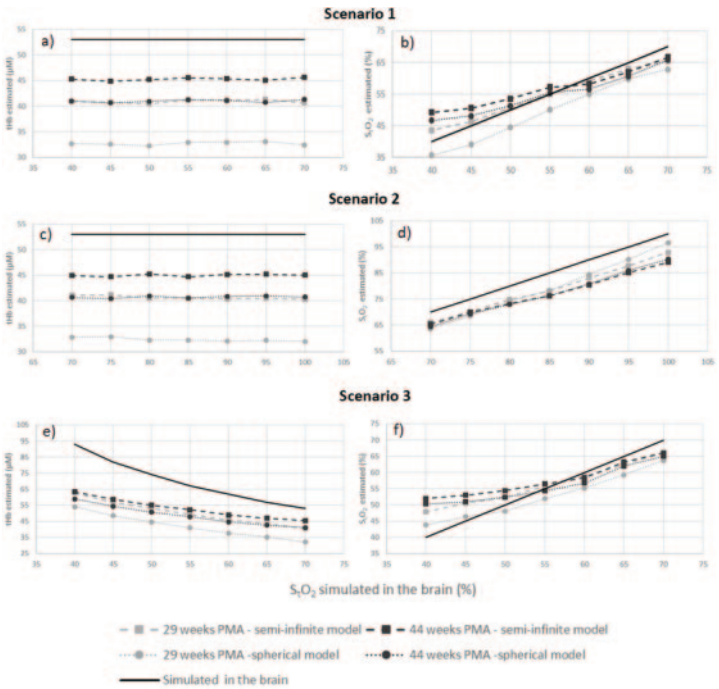

Fig. 2. – Estimated tHb (left column) and S_tO_2 (right column) for 29 (gray) and 44 (black) PMA meshes with semi-infinite (squares) and spherical (circles) model of analysis. Black continuous lines represent the values simulated in the brain.

for 29 weeks PMA mesh and spherical model. This underestimation could be related to the presence of CSF (as suggested by previous work from Ancora *et al.* [6]) that causes a reduction in retrieved μ_a when homogeneous models of analysis are used. Layered model could be employed to reduce the influence of CSF on tHb estimation.

Higher values of tHb were estimated with semi-infinite model as compared to spherical one. This result is in accordance with previous work of Sassaroli *et al.* [11], where an overestimation of μ_a was observed when semi-infinite homogeneous model was used to analyze data simulated with cylindrical and spherical geometries.

Concerning S_tO_2, estimated values are very close to the one simulated in the brain, suggesting that underestimations of O_2Hb and HHb compensate when S_tO_2 is computed. In all the reported scenarios, data obtained with spherical model present an higher slope, closer to the nominal values in the brain. Differences between the two models of analysis are more evident for 29 weeks PMA mesh, since the higher is the radius the more appropriate is the semi-infinite approximation.

Finally, it can be noticed that there are no differences in S_tO_2 simulated in scenario 1 and 3, the only difference between the two simulations is the value of tHb, which is constant ($53\,\mu$M) for scenario 1, and increases (from $53\,\mu$M to $93\,\mu$M) in scenario 3. However, comparing S_tO_2 estimated in these two scenarios (fig. 2(b) and (f)) a reduction of the curves' slopes in scenario 3 can be observed, suggesting that an increase of tHb reduces the ability of TD-NIRS in retrieving S_tO_2 variations.

4. – Conclusions

In this work we estimated the accuracy of TD-NIRS technique in measuring neonatal cerebral haemodynamics. We simulated photon propagation in preterm and term neonates' head structures, and we analyzed the results with two homogeneous models for photon migration (semi-infinite and spherical). The presented results empower the ability of TD-NIRS in measuring brain saturation, and pave the way for a new model of analysis to reduce tHb underestimation.

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