Chapter 24
The Effect of Basic Assumptions on the Tissue Oxygen Saturation Value of Near Infrared Spectroscopy

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Abstract Tissue oxygen saturation (StO_2), a potentially important parameter in clinical practice, can be measured by near infrared spectroscopy (NIRS). Various devices use the multi-distance approach based on the diffusion approximation of the radiative transport equation [1, 2]. When determining the absorption coefficient (μ_a) by the slope over multiple distances a common assumption is to neglect μ_a in the diffusion constant, or to assume the scattering coefficient (μ_s') to be constant over the wavelength. Also the water influence can be modeled by simply subtracting a water term from the absorption. This gives five approaches A1–A5. The aim was to test how these different methods influence the StO_2 values. One data set of 30 newborn infants measured on the head and another of eight adults measured on the nondominant forearm were analyzed. The calculated average StO_2 values measured on the head were (mean ± SD): A1: 79.99 ± 4.47%, A2: 81.44 ± 4.08%, A3: 84.77 ± 4.87%, A4: 85.69 ± 4.38%, and A5: 72.85 ± 4.81%. The StO_2 values for the adult forearms are: A1: 58.14 ± 5.69%, A2: 73.85 ± 4.77%, A3: 58.99 ± 5.67%, A4: 74.21 ± 4.76%, and A5: 63.49 ± 5.11%. Our results indicate that StO_2 depends strongly on the assumptions. Since StO_2 is an absolute value, comparability between different studies is reduced if the assumptions of the algorithms are not published.

Keywords Absorption coefficient • Methodology • Near-infrared spectroscopy • Tissue oxygen saturation

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1 Introduction

Tissue oxygen saturation (StO_2) has a great potential to become an important clinical parameter, especially in neonatology [3, 4]. It is related to the oxygen metabolism in the tissue on an absolute scale. Slightly different approaches are used to calculate StO_2, depending on the manufacturer. This is reflected in different naming, e.g., tissue oxygenation index for the NIRO (Hamamatsu Photonics, Japan) [5] or regional oxygen saturation for the INVOS (Somanetics Corp., USA) or Critikon (Johnson & Johnson, UK). Studies have been published, which compared the values obtained from the three different devices and found differences between INVOS and Critikon [6] and agreement between the NIRO and INVOS [7, 8]. However, both found *unacceptable* baseline differences. Several reasons were given as explanation: Differences in the technical setup, the effect of extracranial blood flow and differences in the algorithm.

However, the influence of the algorithm itself has to our knowledge not been evaluated. Our aim was to test the influence of basic assumptions of the multi-distance approach [1], which is similar to spatially resolved spectroscopy [2]. Using the different approaches on the same data sets excludes the instrumentation or extracranial blood flow as a source of differences.

2 Methods

2.1 Subjects

Data sets from two different studies have been evaluated. First, 30 newborn infants have been studied previously in our group with the aim to identify precision of NIRS [9]. Second, eight adult subjects (all male, age range 26–45, median 29.5) were investigated within a still ongoing study. Both studies were approved by the ethical committee of the Kanton of Zurich and informed consent was obtained prior to the study.

2.2 Protocol

Neonatal group. The frontal and temporal cerebral region was measured four times for approximately 1 min. The sensor was repositioned between the measurements [9].

Adult group. Five repeated measurements per subject were taken from the non-dominant forearm, near to musculus brachioradialis. The sensor was fixated with an elastic bandage around the forearm. Each measurement took 1 min, in between measurements the bandage was completely removed and the sensor was repositioned to approximately the same place as before.

2.3 NIRS Measurement

The neonatal group was measured with the MCPII, which is described in detail elsewhere [10]. It uses three wavelengths (750, 800, and 875 nm) at distances of 1.25 and 2.5 cm.

The adult group was assessed by a novel continuous wave NIRS device, the *OxyPrem*, which is similar to previous wireless sensors [11]. It measures light attenuation at 760 and 870 nm, at distances of 1.5 and 2.5 cm.

2.4 Theory

Tissue oxygen saturation was calculated by a self-calibrating multi-distance approach [1] based on the diffusion approximation of the radiative transport equation and using two sources and two detectors. The light intensity decreases with the distance. This relation is linear (semi-infinite boundary condition).

$$\ln(dc(r)r^2) = r\mathrm{Sl}_{dc}(\mu_a, \mu_s') + \mathrm{In}_{dc}'(D, K_{dc}), \tag{24.1}$$

$dc(r)$ is the average light intensity as a function of distance r, Sl_{dc} the slope of the intensity loss and In_{dc}' the intercept. μ_a and μ_s' are the absorption and the reduced scattering coefficient, respectively. K_{dc} is a constant. The diffusion constant D equals

$$D = \frac{1}{3\mu_a + 3\mu_s'} \cong \frac{1}{3\mu_s'}. \tag{24.2}$$

μ_a is often neglected because tissue scattering is much larger than absorption (μ_s'). However, here we distinguish between simplified and exact diffusion constant (as seen below).

When evaluating (24.1) at two distances r_L and r_S and subtracting them, the slope can be calculated from the ratio of the measured intensities.

$$\mathrm{Sl}_{dc} = \frac{\frac{1}{2}\ln\left(\frac{dc_1(r_L)dc_2(r_L)}{dc_1(r_S)dc_2(r_S)}\right) + 2\ln\left(\frac{r_L}{r_S}\right)}{r_L - r_S}, \tag{24.3}$$

where r_L is the longer source–detector distance and r_S the shorter one, respectively. Equation (24.3) is a special self-calibrating form, whereby the use of two source–detector pairs [giving the four intensity values $dc_{1,2}(r_L, r_S)$] the coupling factors between the tissue and source/detector cancel out [1]. Then μ_a can be calculated as

$$\mu_a = \mathrm{Sl}_{dc}^2 D. \tag{24.4}$$

When the absorption is determined at least at two wavelengths, concentrations of oxygenated ([O_2Hb]) and deoxygenated hemoglobin ([HHb]) and the tissue oxygen

saturation can be calculated. We used the absorption coefficients from Matcher et al. [12], averaged over the measured intensity spectrum of each light source. Coefficients for scattering were taken from Matcher et al. [13] for the adult arm and from ISS OxyPlex measurements on 36 term infants [14] for the neonates, extrapolated to 750, 800, and 875 nm (3.81, 3.49, and 3.01[cm^{-1}]).

$$\begin{bmatrix} [\mathrm{HHb}] \\ [\mathrm{O_2Hb}] \end{bmatrix} = \mathbf{A}^{-1} \begin{bmatrix} \mu_a(\lambda_1) \\ \mu_a(\lambda_2) \end{bmatrix}, \quad \mathbf{A} = \begin{bmatrix} a_{\mathrm{HHb},\lambda_1} & a_{\mathrm{O_2Hb},\lambda_1} \\ a_{\mathrm{HHb},\lambda_2} & a_{\mathrm{O_2Hb},\lambda_2} \end{bmatrix} \tag{24.5}$$

where $a_{i,j}$ is the absorption coefficient for i=([HHb], [O_2Hb]) at the wavelength j. StO_2 is calculated as [O_2Hb]/([O_2Hb]+[HHb]). We examine five different assumptions A1–A5 for the determination of the absorption:

A1. $$\mu_a = -\frac{\mu_s'}{2} + \sqrt{\frac{1}{4}\mu_s'^2 + \frac{1}{3}\mathrm{SI}_{dc}^2} - a_{\mathrm{H_2O},\lambda}\, 55.5\ \mathrm{M}\, \frac{p_{\mathrm{H_2O}}}{100\%}, \tag{24.6}$$

A2. $$\mu_a = -\frac{\mu_s'}{2} + \sqrt{\frac{1}{4}\mu_s''2 + \frac{1}{3}\mathrm{SI}_{dc}^2}, \tag{24.7}$$

A3. $$\mu_a = \frac{\mathrm{SI}_{dc}^2}{3\mu_s'} - a_{\mathrm{H_2O},\lambda}\, 55.5\ \mathrm{M}\, \frac{p_{\mathrm{H_2O}}}{100\%}, \tag{24.8}$$

A4. $$\mu_a = \frac{\mathrm{SI}_{dc}{}^2}{3\mu_s'}, \tag{24.9}$$

A5. $$\mathrm{StO_2} = \frac{a_{\mathrm{HHb},\lambda_1} - a_{\mathrm{HHb},\lambda 2}\left(\frac{\mathrm{SI}_{dc}(\lambda_1)}{\mathrm{SI}_{dc}(\lambda_2)}\right)^2}{(a_{\mathrm{HHb},\lambda_1} - a_{\mathrm{O_2Hb},\lambda_1}) - (a_{\mathrm{HHb},\lambda_2} - a_{\mathrm{O_2Hb},\lambda_2})\left(\frac{\mathrm{SI}_{dc}(\lambda_1)}{\mathrm{SI}_{dc}(\lambda_2)}\right)^2}, \tag{24.10}$$

Equations (24.6) and (24.7) use the exact diffusion constant, while (24.8)–(24.10) use the simplified one. In (24.10), μ_s' is assumed to be constant over the wavelength. Hence, it cancels out in StO_2 calculation as shown. Equations (24.6) and (24.8) are accounting for water in tissue. Here $a_{\mathrm{H2O},\lambda}$ is the absorption of water at the wavelength λ in 1/(M*cm) and p_{H2O} is the amount of water in the tissue. We used 70% for the adult forearm and 90% for the neonatal head. Water contains approximately 55.5 mol atoms/l.

2.5 Statistics

Between-subject variability and within-subject variability were determined using *R* (version 2.6.1, *R* Development Core Team, Austria) with its linear mixed effects function LME. StO_2 was the random variable and subject the factor.

Table 24.1 StO_2, within-subject variability and between-subject variability for 30 newborn infants measured on the head for the five different assumptions A1–A5

	A1	A2	A3	A4	A5
$StO_2 \pm SD$ [%]	79.99 ± 4.47	81.44 ± 4.08	84.77 ± 4.87	85.69 ± 4.38	72.85 ± 4.81
Var_{bet} [%]	4.2	3.84	4.64	4.16	4.56
Var_{within} [%]	2.76	2.55	2.73	2.51	2.83

Table 24.2 StO_2, within-subject variability and between-subject variability for eight adults measured on the forearm for the five different assumptions A1–A5

	A1	A2	A3	A4	A5
$StO_2 \pm SD$ [%]	58.14 ± 5.69	73.85 ± 4.77	58.99 ± 5.67	74.21 ± 4.76	63.49 ± 5.11
Var_{bet} [%]	5.54	4.65	5.52	4.64	4.98
Var_{within} [%]	2.96	2.43	2.95	2.42	2.60

3 Results

For the neonatal head measurements the mean $StO_2 \pm$ standard deviation (SD), the within-subject variability (Var_{within}) and the between-subject variability (Var_{bet}) are given in Table 24.1. In Table 24.2 the values for the adult group are shown.

In both adults and the neonates assumption A5 deviates in value ~10%. In neonates including a water term (A1 vs. A2, A3 vs. A4) has a minor effect on StO_2, but the use of the exact or simplified diffusion constant (A1 vs. A3, A2 vs. A4) induces a change in StO_2 by 5%. In contrast, on the adult arm, the water term makes a large difference of ~15%, while the diffusion constant assumption does induce smaller changes. For both groups, between-subject variability and within-subject variability are smaller when not including the water term (A2 and A4). Both variables are ~0.3% larger when additionally assuming μ_s' to be constant (A5 against A2, A4).

4 Discussion and Conclusion

Our results show, that slight differences in the assumptions have a relevant influence on the final StO_2 value. This difference is also dependent on the measured tissue. The water term seems to have a smaller influence in neonates than the tissue homogeneity ($\mu_a \ll \mu_s'$). This may reflect the influence of the cerebral spinal fluid in the brain [15]. Since the water term only induces a small correction of StO_2 we believe that the water correction is more or less correct. However, the variability within and in between subjects is smaller when not including the water term, although only by ~0.2%.

Regarding the arm tissue of the adults, the concentration of lipid is higher and the water concentration is lower than for the neonatal head. While the diffusion constant assumption does not affect the StO_2 value, the water term makes a difference of ~15%. Since no real reference value exists for StO_2, it is not possible to state if

one assumption is more valid than another. From a mathematical point of view, the water term has no relevant influence if the slope (24.3) is much larger than the water term. Hence, the ratio between the long and short distances is much smaller than 1. If the ratio is close to 1, the slope will be small and the water term (usually in the order of 10^{-2}) dominates. This means the ratio is closer to 1 when measuring the adult arm. This may be due to the lipid concentration in the arm, which has not been taken into account, or due to the 70% water assumption, which may be too high, or both. We calculated the body mass index (BMI) for the subjects, which correlated with the change in StO_2 (data not shown), i.e., the higher the BMI and hence the lipid concentration, the higher the change of StO_2 when taking water into account. The latter is supported by the fact that not subtracting the water lowers the variability. The additional assumption A5 lowers the StO_2 values, compared to A2 and A4. This suggests that this assumption is not valid, neither in the neonatal head nor in the adult arm.

In conclusion, we investigated the effect of the assumptions $\mu_s' , \mu_a \ll \mu_s' = \text{constant}$ over the wavelengths and the water contribution and their combinations when using the multi-distance approach of StO_2 calculation. We found significant differences in StO_2 and its variability, depending on the assumptions made and the tissue investigated.

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