Chapter 52
Comparison of Near-Infrared Oximeters in a Liquid Optical Phantom with Varying Intralipid and Blood Content

S. Kleiser, S. Hyttel-Sorensen, G. Greisen, and M. Wolf

Abstract The interpretation of cerebral tissue oxygen saturation values (StO_2) in clinical settings is currently complicated by the use of different near-infrared spectrophotometry (NIRS) devices producing different StO_2 values for the same oxygenation due to differences in the algorithms and technical aspects. The aim was to investigate the effect of changes in scattering and absorption on the StO_2 of different NIRS devices in a liquid optical phantom. We compared three continuous-wave (CW) with a frequency domain (FD) NIRS device. Responsiveness to oxygenation changes was only slightly altered by different intralipid (IL) concentrations. However, alterations in haematocrit (htc) showed a strong effect: increased htc led to a 20–35 % increased response of all CW devices compared to the FD device, probably due to differences in algorithms regarding the water concentration.

Keywords Near-infrared spectroscopy • Instrumentation • Comparison • Water correction • Liquid phantom

1 Introduction

In the last decades, NIRS has evolved to a valuable tool to measure and monitor StO_2 in research and various clinical applications [1]. StO_2 gives insight into the local balance of oxygen supply and demand. This new information could be clinically useful. Especially for critically ill patients such as preterm children who are often suffering from unstable cerebral oxygen supply and lack of cerebral auto-regulation, this information may be of value for tailoring clinical management [2].

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Despite this potential, routine use is being hampered by the fact, that different devices give different readings [3]. It is necessary to quantify these differences in order to transfer findings from one device to another. Testing devices on human subjects is problematic due to a lack of a reference method, inter-subject variations, poor precision, and physiological fluctuations in oxygenation [4–6]. Furthermore, analysis of dynamic response is limited because large variations of oxygenation can only be induced non-invasively and safely by cuff occlusion in limbs, but not in the brain.

Recently, we compared multiple NIRS devices under controlled conditions in a liquid phantom with scattering and absorption similar to neonatal brain tissue [7]. Oxygenation was changed by a membrane oxygenator, which allowed a comparison over the whole saturation range. The aim of the present study was to improve the experimental procedure and to additionally investigate mixtures with different blood and IL content to examine how NIRS devices compare under variable conditions.

2 Methods

Three CW NIRS devices (Somanetics INVOS 5100 adult sensor, Hamamatsu NIRO 300 and OxyPrem, an in-house built prototype) and one FD NIRS device (ISS OxiplexTS) were compared. The OxiplexTS was calibrated on a solid phantom with known optical properties before the first experiment. The sensors were fixed to the rim of a black bucket (see Fig. 52.1a). The NIRO 300 sensor was wrapped in thin plastic foil for moisture protection, whereas all other sensors were directly immersed into the liquid. The top of the bucket was covered with thin plastic foil and dark cloth to reduce entrance of room air and ambient light.

The main ingredients of the phantom were 6 l of phosphate buffered saline (pH 7.4, pre-heated to 37 °C), 4 g of baker's yeast, a variable amount of Fresenius Kabi Intralipid (IL) 200 mg/ml and human whole blood. The liquid was permanently mixed with a magnetic stirrer. Temperature of the phantom was stabilized and monitored by a MTRE Criticool temperature controller with its heat exchange mat wrapped around the bucket. Oxygenation was changed similarly to a previous experiment [8]: yeast continuously metabolized glucose and O_2, thus caused a steady decrease of phantom oxygenation. Reoxygenation was achieved by bubbling pure O_2. Important events were marked on all devices within a few seconds.

Two experiments were conducted, both with the same initial composition. In the first experiment, starting from 0.5 %, IL content was increased to 1.5 % in two steps while haematocrit (htc) was kept constant at 1 %. This resulted in changes of the scattering coefficient, which is essentially determined by the IL concentration [9]. In a second experiment, htc was raised from 1 to 2 % by adding blood while IL concentration was kept at 0.5 %. This mainly changed absorption and not scattering.

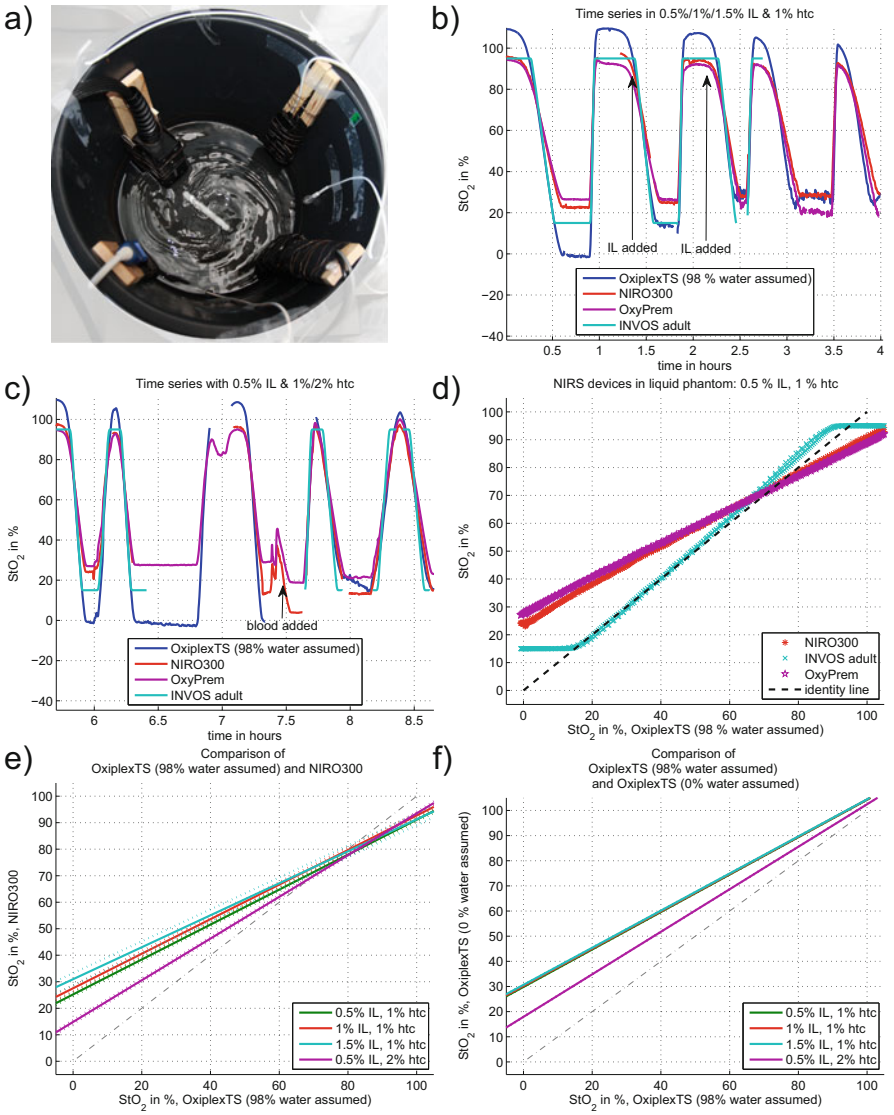

Fig. 52.1 (**a**) Bucket with sensors mounted. Clock-wise from the *top left*: ISS OxiplexTS, OxyPrem, Hamamatsu NIRO300, Somanetics INVOS adult sensor. (**b**) Time series showing readings from all instruments during experiment 1 with constant htc and increasing IL concentration. (**c**) Time series showing readings from all instruments during experiment 2 with constant IL and increasing htc. (**d**) Data points of NIRO 300, INVOS adult sensor and OxyPrem in 0.5 % IL and 1 % htc compared to ISS OxiplexTS with 98 % water assumption. (**e**) Relationship of NIRO 300 and ISS OxiplexTS with 98 % water assumption for different IL concentrations and htc. (**f**) Relationship of ISS OxiplexTS with 0 and 98 % water assumption for different IL concentrations and htc. For (**e**) and (**f**) *dotted lines* show the 95 % confidence interval of the linear fits

OxyPrem StO_2 was computed from raw data using a self-calibrating algorithm [10] assuming 0 % water, scattering of 0.5 % IL (interpolated from [9]) and applying absorption coefficients from [11] (weighted with LED emission spectra). OxiplexTS StO_2 was computed from raw data using the ISS Software OxiTS (version 3.1.1.0). Absorption coefficients were applied from the manual (version 3.1) and as suggested by the manufacturer, 0.01 cm^{-1} were subtracted at 692 nm as background absorption. All light paths were included in the analysis. Two StO_2 datasets were calculated: one accounting for the presumably true water content of 98 % (ISS98) and another without water correction (ISS0).

StO_2, timestamps and events from all devices were imported into Matlab. Time shifts between device clocks were determined and removed by searching the maximum of the event cross-correlation. Subsequently, data were interpolated (piecewise cubic) to a common time base and down-sampled to the slowest sampling rate of any of the devices (~0.2 Hz). For all comparisons and linear fits between the values of any two devices, only data during periods of decreasing oxygenation were used and only if both devices were in the StO_2 range of 40–85 %.

3 Results

The yeast induced a steady decline in oxygenation until all devices abruptly reached a lower steady state at the same time. Adding oxygen similarly led to an upper steady state quite synchronized repeatedly in all devices (Fig. 52.1b and c).

During repeated desaturations in mixtures of 0.5 % IL and 1 % htc the INVOS adult sensor was in good agreement with the ISS98 between 15 and 95 %, whereas both OxyPrem and NIRO 300 were much less responsive to the change in oxygenation with similar values at 70 %, but an overreading of as much as 25 % at the lowest StO_2 (Fig. 52.1d).

The stepwise increase in IL led to a stepwise increase in the StO_2 at lower steady state by the ISS98 and to a much smaller degree by the NIRO 300 (Fig. 52.1b). This response was not visible for the OxyPrem. The INVOS signal was at all times clipped at <15 and >95 %.

Increasing IL did not impact the association between ISS98 and NIRO 300, but doubling the htc increased the steepness of the curve by a factor of 1.19 and reduced the overreading at the lowest StO_2 to approximately 15 % (Fig. 52.1e). For the OxyPrem and the INVOS adult sensor, the steepness increased by a factor of 1.25 and 1.35, respectively. ISS98 vs. ISS0 showed an overreading at the lowest StO_2 of 30 % in the mixture with 0.5 % IL and 1 % htc which reduced to 19 % StO_2 when doubling htc, whereas steepness increased by a factor of 1.14 (Fig. 52.1f). The linear correlation coefficient between ISS98 and all CW devices was $R^2 > 0.99$ in the StO_2 range 40–85 % for all mixtures.

4 Discussion and Conclusion

In the present liquid phantom study changes in IL concentration only had minor impact on the pair-wise device relations, whereas an increase in htc resulted in a 'steeper' response of all CW devices compared to the FD device (ISS98).

The absolute value of scattering theoretically cancels out when calculating StO_2 and only the wavelength dependence remains, which was shown to be quite stable across different human tissues [12]. Consequently, it is not surprising that the responsiveness of the StO_2 was independent of changes in IL concentration.

NIRO 300 and ISS0 behaved remarkably similarly to the increase in htc, which seems related to both [8] not taking water absorption into account. The overreading by 25–30 % by OxyPrem, NIRO 300 and ISS0 at 1 % htc compared to ISS98 StO_2 at 0 % could be caused by water absorption at longer wavelengths (>800 nm). This contributes more significantly to the total absorption when htc is low, thus causing an overestimation of mainly oxyhemoglobin concentration. This effect is dependent on wavelengths employed by the device. This can explain the observed overreading at the lowest levels of StO_2 as well as the lowered responsiveness to oxygenation changes. Metz et al. [13] reported only a small influence of water assumption on absolute StO_2 values measured on the neonatal head (high StO_2) and a high influence on the adult forearm (low StO_2), which agrees well with our findings (Fig. 52.1f); they observed higher variability when accounting for water, which can be explained by the increased responsiveness also observed in this study.

Although the design of the phantom aimed at reducing the possibilities of inhomogeneity in the phantom by eliminating the distinct outlet tube in [7], the presence of oxygenation gradients from top to bottom as well as a gradient in yeast concentration cannot be entirely excluded. Sensors were placed at slightly different heights in the phantom. Therefore, all absolute results have to be treated with care, as sensors could potentially have 'seen' different true oxygenations and changes thereof. However, in the two experiments shown here, sensor positions were unchanged, thus the relative changes caused by changing mixtures should not be affected by these possible gradients.

In mixtures with increased IL or htc, the lower steady-state StO_2 for ISS98 did not reach 0 %. Also, the ISS98 reached maximum StO_2 well above 100 %. An O_2 gradient could explain these observations. However, we do not expect a possible gradient to affect the current analysis which is looking only at relative changes of pair-wise relations, because we only considered values in the range 40–85 % showing linear relations ($R^2 > 0.99$) and it seems unlikely that a potential gradient was different at different phantom compositions.

In comparison with [7], the OxyPrem vs INVOS adult sensor relation was different in the present experiments. Possibly different sensor heights in combination with an O_2 gradient could explain both changes in relative sensitivity as well as absolute numbers. Furthermore, OxyPrem measured horizontally whereas all other sensors measured vertically in the direction of the gradient, which could also lead to a difference. Responsiveness of NIRO 300 vs INVOS adult sensor was approximately

0.59 at 1 % htc and 0.51 at 2 % htc, which is in line with 0.53 at 1.5 % htc reported in [7]. This would be reasonable even if there was a saturation gradient, as they were mounted at the same height.

In conclusion, we have employed an optical phantom with variable scattering and blood content to investigate the effect of such changes on the steepness of the pair-wise relation of three CW NIRS oximeters and one FD NIRS oximeter which measured scattering and allowed to make user-defined corrections for water content of the phantom. Findings were that scattering changes had a minor influence on the devices, but changes in htc led to different responsiveness to oxygenation changes presumably due to the water assumption made in the algorithms.

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