

## The clinical validity of the absolute value of near infrared spectroscopy

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### Introduction

Cerebral oxygen saturation ( $Sc_{O_2}$ ) measured by near infrared spectroscopy (NIRS) has been used clinically as a noninvasive and continuous monitor. In evaluating cerebral vasomotor reactivity, there was a good correlation between NIRS values and cerebral blood flow velocity determined by transcranial Doppler [1–3]. Two commercially available devices, NIRO (Hamamatsu Photonics, Hamamatsu, Shizuoka, Japan) and INVOS (Somanetics, Troy, Michigan, IL, USA) demonstrated that  $Sc_{O_2}$  measured by NIRS reflected the change of cerebral oxygen balance under  $CO_2$  challenge [4]. Further NIRS measurements have demonstrated its usefulness for evaluating the cerebral oxygen balance during cardiopulmonary bypass, as an index of cerebral

injury [5,6]. In spite of such great advantages, there has been no gold standard in regard to its absolute value [7]. NIRS measurement could only report changes from a baseline [8,9].

Near infrared light can penetrate skull and soft tissue to some degree. In contrast to the infant brain, in the adult brain there are some difficulties for accurate NIRS measurement. In adult brain tissue, near infrared light cannot travel in a straightforward way, due to the large amount of myelin sheath. In addition, the thickness of the skull and the area of the cerebrospinal fluid layer had an effect on NIRS values [10]. Further, the hemoglobin concentration affected NIRS measurement and there was a significant correlation between the hemoglobin concentration and  $Sc_{O_2}$  measured by NIRS [11,12]. Here, we discuss how previous studies have clarified the difficulties in performing accurate NIRS measurements, and we examine the possible future of NIRS measurement.

### Contamination of NIRS measurement by extracranial blood flow

Near infrared light travels through brain tissue and returns to the light detector a few centimeters apart. Changes in near infrared light intensity should reflect the changes in oxyhemoglobin ( $HbO_2$ ) or deoxyhemoglobin (Hb) concentration only in the brain tissue. However, changes in  $HbO_2$  or Hb in the extracranial blood flow can be confusing in the calculation of  $Sc_{O_2}$ . Gurmon et al. [13,14] demonstrated the contamination of NIRS measurement by extracranial blood flow by using a tourniquet on the forehead in an early NIRS model. The study was then repeated with a pneumatic tourniquet inflated to a pressure of 200 mmHg at the level of the supraorbital ridge for 3 min. NIRS included extracranial blood flow. This would be a noise in  $Sc_{O_2}$  measurements.

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## Optical pathlength

When near infrared light at specific wavelengths in the window of 600 to 950 nm is shone through tissue, information about the amounts of HbO<sub>2</sub> and Hb can be obtained. To calculate the HbO<sub>2</sub> and Hb concentrations, a modified Beer Lambert law (MBL) has been used, in which the optical pathlength is included in the formula. In brain tissue, near infrared light travels by scattering and attenuating like an arch. Changes in HbO<sub>2</sub> and Hb concentrations can be calculated by the following formula:

$$\Delta A = \epsilon L * \Delta C$$

where “ $\Delta A$ ” is the change in light absorbance, “ $\epsilon$ ” is the mol absorbance coefficient, “ $L$ ” is the pathlength, and “ $\Delta C$ ” is the change in HbO<sub>2</sub> or Hb concentration. To simplify the calculation with the MBL, the optical pathlength has been assumed to be constant. However, previous experimental and human studies demonstrated that a reduction in the hemoglobin concentration changed the optical pathlength [15,16]. If  $L$  increases 1.5 times as a result of hemodilution, but  $L$  is assumed to be constant,  $\Delta C$  could be 1.5 times the actual  $\Delta C$ .

The thickness of the skull and the area of the cerebrospinal fluid layer had an association with the optical pathlength [17,18]. The skull seemed to have a role as a channel of near infrared light. We tried to reveal whether the thickness of the skull and the area of the cerebrospinal fluid layer, and the hemoglobin concentration had an effect on  $Sc_{O_2}$  measured by INVOS or NIRO [15]. We used slices of computed tomography (CT) images of the head corresponding to the position of the emitter and detector of near infrared light. In the CT scan image, the skull thickness and the area of the cerebrospinal fluid layer were calculated. Regional cerebral oxygen saturation ( $rS_{O_2}$ ) values measured by INVOS 4100 had a significant association with the hemoglobin concentration, area of the cerebrospinal fluid layer, and skull thickness, but the tissue oxygen index (TOI) values measured by NIRO 100 were not affected by these factors, because the algorithm used by the NIRO 100 is different from that used by the INVOS 4100. NIRO uses space-resolved spectroscopy, which is free from the optical pathlength [19].

## Various algorithms of NIRS

To remove the noise related to the optical pathlength for more validated and sophisticated NIRS measurement, algorithms of NIRS measurement have been developed. In contrast to the algorithm free from the optical pathlength, another trial, to calculate optical pathlength, has been done, and this yielded a frequency-

domain methodology, which combined phase-resolved spectroscopy and spatial-resolved spectroscopy. This algorithm enables us to calculate the optical pathlength by a modulated near infrared wave. The ISS oximeter (ISS, Champaign, IL, USA) is a commercially available device using frequency domain methodology. Vernieri et al. [3] reported that  $Sc_{O_2}$  measured by the ISS oximeter had a significant association with cerebral blood flow velocity during a balloon occlusion test of the carotid artery, but these authors did not validate the absolute values of NIRS measurement [3]. Further studies are still needed to validate the NIRS measurement of the ISS oximeter.

There is another algorithm which can calculate the optical pathlength, the absorption coefficient, and the scatter coefficient, with the photon diffusion theory. Hamamatsu Photonics have developed time-resolved spectroscopy (TRS); however, there have been few human studies of this method for evaluating cerebral oxygen balance [20,21]. We have preliminary data for investigating the relationship between  $Sc_{O_2}$  values measured by TRS and jugular venous bulb oxygen saturation ( $S_{j_{O_2}}$ ) during carotid endarterectomy ( $n = 23$ ). There was a significant association between  $Sc_{O_2}$  and  $S_{j_{O_2}}$  ( $r = 0.60$ ;  $P = 0.02$ ). We also evaluated the association between estimated  $Sc_{O_2}$  ( $e_{-}Sc_{O_2}$ ) and  $Sc_{O_2}$ .  $Sc_{O_2}$  measured by NIRS included arterial and venous components. The proportions of the arterial and venous blood components were approximately 25% and 75%, respectively [9]. Therefore, we calculated  $e_{-}Sc_{O_2}$  according to the following formula:  $e_{-}Sc_{O_2} = 0.75 * S_{j_{O_2}} + 0.25 * Sa_{O_2}$ . There was also a significant correlation between  $Sc_{O_2}$  and  $e_{-}Sc_{O_2}$  ( $r = 0.60$ ;  $P = 0.01$ ) Bland and Altman analysis demonstrated the narrow limit of agreement between  $e_{-}Sc_{O_2}$  and  $Sc_{O_2}$  (bias, 9.6; precision, 4.9). The result indicated the possibility that the absolute value of  $Sc_{O_2}$  measured by TRS would be reliable clinically.

## Conclusion

Previous studies have been trying to establish the validity of  $Sc_{O_2}$  measured by NIRS. Some limitations in NIRS measurement still remain to be resolved. However, the developed algorithm—TRS—enables the calculation of absolute values of  $Sc_{O_2}$ . In the near future, although further studies are still needed, the safety limit of  $Sc_{O_2}$  could be validated and applied for clinical use at the bedside.

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