

Accuracy of a Cerebral Oximeter in Healthy Volunteers under Conditions of Isocapnic Hypoxia

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Background: A cerebral oximeter measures oxygen saturation of brain tissue noninvasively by near infrared spectroscopy. The accuracy of a commercially available oximeter was tested in healthy volunteers by precisely controlling end-tidal oxygen ($P_{ET}O_2$) and carbon dioxide ($P_{ET}CO_2$) tensions to alter global cerebral oxygen saturation.

Methods: In 30 healthy volunteers, dynamic end-tidal forcing was used to produce step changes in $P_{ET}O_2$ resulting in arterial saturation ranging from ~70% to 100% under conditions of controlled normocapnia (each person's resting $P_{ET}CO_2$) or hypercapnia (resting plus 7–10 mmHg). Blood arterial (SAO_2) and jugular bulb venous ($S_{jv}O_2$) saturations during each $P_{ET}O_2$ interval were determined by co-oximetry. The cerebral oximeter reading (rSO_2) and an estimated jugular venous saturation ($\hat{S}_{jv}O_2$), derived from a combination of SAO_2 and rSO_2 , were compared with the measured $S_{jv}O_2$.

Results: The $S_{jv}O_2$ was significantly higher with hypercapnia than with normocapnia for the same SAO_2 . The rSO_2 and $\hat{S}_{jv}O_2$ were both highly correlated with $S_{jv}O_2$ for individual volunteers (mean $r^2 = 0.91$ for each relation); however, the slopes and intercepts varied widely among volunteers. In three of them, the cerebral oximeter substantially underestimated the measured $S_{jv}O_2$.

Conclusions: During isocapnic hypoxia in healthy persons, cerebral oxygenation as estimated by near infrared spectroscopy precisely tracks changes in measured $S_{jv}O_2$ within individuals, but the relation exhibits a wide range of slopes and intercepts. Therefore the clinical utility of the device is limited to situations in which tracking trends in cerebral oxygenation would be acceptable. (Key words: Cerebral blood flow; cerebral oxygenation; hypercapnia; jugular bulb saturation; jugular venous bulb saturation.)

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CEREBRAL oximetry is a method of measuring brain tissue oxygen saturation noninvasively by near infrared spectroscopy. This technique is conceptually similar to that of pulse oximetry. Hemoglobin has characteristic infrared absorption spectra that shift with oxygenation. Because near infrared light at these wavelengths penetrates the scalp, skull, and cranial contents by several centimeters,¹⁻³ relative changes in the concentrations of reduced and oxygenated hemoglobin in these tissues can be detected.⁴⁻⁶ Research has suggested that cerebral oximetry may provide a way to monitor cerebral oxygenation and guide therapy during surgical procedures⁷⁻¹⁰ or in critically ill patients.^{11,12} It has also been used to estimate cerebral blood flow and volume.¹³⁻¹⁵

Because cerebral venous hemoglobin oxygen saturation reflects the balance between oxygen delivery and oxygen uptake, a practical way to determine the accuracy of a cerebral oximeter is to alter oxygen delivery by increasing or decreasing arterial oxygen content, cerebral blood flow, or both and comparing measurements made by the device to jugular venous bulb oxygen saturation. The assumption is made that cerebral oxygen uptake does not change. Changes in cerebral oxygen delivery can be accomplished by controlling the end-tidal tensions of oxygen (O_2) and carbon dioxide (CO_2). In healthy persons, control of end-tidal O_2 ($P_{ET}O_2$) and CO_2 ($P_{ET}CO_2$) reflects similar control of arterial concentrations.

Previous studies of the accuracy of cerebral oximetry in healthy volunteers have not precisely controlled $P_{ET}O_2$ and $P_{ET}CO_2$ tensions^{16,17}; as a result, readings from the device, blood samples, or both may have been obtained when cerebral O_2 saturation was unstable. The purpose of these experiments was to test the accuracy of a cerebral oximeter (model INVOS 3100A; Somanetics Corp., Troy, MI) in healthy volunteers, using precise regulation of end-tidal gas tensions to achieve the same range of arterial O_2 saturation at two different levels of

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arterial CO₂ pressure (P_{CO₂}; *i.e.*, two different levels of cerebral blood flow).

Materials and Methods

Volunteers and the Protocol

Thirty healthy volunteers (11 women, 19 men; aged 19–40 yr) were paid for their participation in these experiments. The study protocol was approved by the institutional review board. Volunteers gave written informed consent before undergoing preliminary testing, which included a medical history, physical examination, resting electrocardiogram, and measurement of hematocrit concentration. Pregnancy in women was excluded by medical history. Subjects were studied after a minimum 4-h fast.

The electrocardiogram and finger pulse oximeter (Siemens Sirecust 404, Danvers, MA) were monitored continuously for volunteer safety; blood pressure was measured noninvasively before and after placement of intravascular catheters, at the end of each experiment, after removal of the catheters, and as indicated throughout the experiments. Each volunteer was placed in the supine position and, after local anesthesia with 1% lidocaine, a 20-gauge or 22-gauge catheter was placed in either the right or left radial artery. Each volunteer was then placed in the Trendelenburg position and a 20-gauge, 5-inch catheter (Arrow International, Reading, PA) was placed retrograde in the right internal jugular vein, using routine sterile techniques, local anesthesia with 1% lidocaine, and ultrasound guidance (Site Rite, Dymax, Pittsburgh, PA) to identify the vein. The catheter was advanced until the volunteer noted a sensation in the jaw, indicating that the tip of the catheter was in the jugular bulb. The straight, retrograde course of the catheter to the mastoid process was confirmed using ultrasound. The volunteer was positioned supine for the remaining experiments. The cerebral oximeter probe (model INVOS 3100-SD, Somanetics Corp.) was placed on the right forehead, with the caudad border approximately 1 cm above the eyebrow with the medial edge at the midline. This position places the light source and sensors away from the frontal sinus. The oximeter algorithm averages data over 4-s intervals and the device displays a running 20-s average (*i.e.*, an average of five 4-s values).

Volunteers breathed from a high-flow gas mixing chamber through a low dead-space face mask (Vital Signs, Totawa, NJ). Inhaled and exhaled gas volumes (Sensor Medics VMM 11, Laguna Hills, CA) and gas con-

centrations (model MGA 1100 mass spectrometer; Perkin-Elmer, Pomona, CA) were recorded breath by breath by computer using the TIDAL software package.¹⁸ The flow meter and mass spectrometer were calibrated before each volunteer's experiments with volume and gas reference standards. The calibration of the cerebral oximeter was set at the factory and was not altered for any of the experiments.

The technique of dynamic end-tidal forcing was used to control P_{ET}O₂ and P_{ET}CO₂ tensions.¹⁹ With this technique, a computer-driven gas mixing system adjusts the inspired concentrations of carbon dioxide and oxygen on a breath-by-breath basis. As ventilation changes, the system alters the composition of the inspired gas to maintain end-tidal gas tensions at constant values. A combination of predictive and adaptive control algorithms in the computer software allows precise regulation of end-tidal gas tension over prolonged periods and can also accomplish abrupt transitions in P_{ET}O₂ or P_{ET}CO₂.

Volunteers first completed an experiment in which they breathed room air through the face mask for 10 min; P_{ET}CO₂ was averaged by the computer and the mean P_{ET}CO₂ for the last min was designated as that volunteer's resting P_{ET}CO₂. No blood samples were drawn during this 10-min period. Volunteers then completed two experiments with at least 30 min of rest between them. The first 30 s of each experiment was used to initialize the control algorithm; volunteers breathed room air from the gas mixing system. Then P_{ET}O₂ was controlled in the same sequence for all experiments: 80 mmHg for 6 min, followed by 4-min intervals at 45 mmHg, 60 mmHg, 51 mmHg, and 41 mmHg. For the final 4 min FiO₂ was controlled to 0.50. The O₂ tensions for these six test stages were designed to produce arterial saturation ranging from ~70% to 100%. After the first 30 s of room air breathing, P_{ET}CO₂ was controlled to ~2 mmHg greater than resting (experiment 1, normocapnia) or to 7–10 mmHg greater than the P_{ET}CO₂ used during the first experiment (experiment 2, hypercapnia).

During the last 30 s of each test stage of controlled O₂ tension, arterial and jugular venous blood samples were drawn over 10 s into syringes prepared with heparin and the cerebral oximeter reading (rSO₂) was recorded simultaneously. Blood samples were immediately stored on ice and within 2 h were analyzed in duplicate by co-oximetry (model IL282; Instrumentation Laboratories, Lexington, MA). The co-oximeter was calibrated at the beginning of each day and as needed during the experiments.

Data Analysis

There is no "gold standard" to use in assessing the accuracy of this device; *i.e.*, there is no actual measurement of brain tissue oxygen saturation within the field of the sensor to compare with readings made by the cerebral oximeter. There are, of course, multiple sources for differences between the jugular venous saturation and the actual brain tissue oxygen saturation, including regional inhomogeneity of cerebral oxygenation, inaccuracy in the co-oximeter, and contamination of the jugular bulb sample with extracranial blood. There are also sources of error between the oximeter's reading and the actual tissue saturation in the field of the sensor, including contamination of the signal with extracranial absorption, intracranial arterial blood in the field, and inaccuracies in the signal processing and algorithms in the oximeter. Previous studies^{16,17,20} have compared the oxygen saturation measured by the device (rSO_2) to a calculated "field saturation" (S_{fO_2}). The S_{fO_2} is derived from the arterial and the jugular venous saturations (equation 1), based on the assumption that the distribution of blood in the cerebral vasculature is three quarters in the venous bed and one quarter in the arterial bed, the same as in the rest of the body.²¹⁻²³ This assumption introduces a source of error in addition to those listed above.

$$S_{fO_2} = 0.75 \cdot S_{jvO_2} + 0.25 \cdot SaO_2$$

By substituting rSO_2 (from the cerebral oximeter) for S_{fO_2} and using the measured SaO_2 , this equation can also be used to estimate the jugular venous O_2 saturation (\hat{S}_{jvO_2}) (equation 2).

$$\hat{S}_{jvO_2} = [rSO_2 - 0.25 \cdot SaO_2] / 0.75$$

We compared the cerebral oximeter reading, rSO_2 , and the derived \hat{S}_{jvO_2} (equation 2), with the directly measured blood S_{jvO_2} . We also compared S_{jvO_2} with SaO_2 because, under conditions of constant cerebral oxygen consumption and cerebral blood flow, S_{jvO_2} tracks changes in SaO_2 . Use of the measured jugular bulb blood saturation as the standard assigns most of the error to the cerebral oximeter reading and thus should provide a conservative evaluation of the accuracy of the device.

The cerebral oximeter with two wavelengths estimates only oxy- and deoxyhemoglobin, whereas the co-oximeter with four wavelengths also measures methemoglobin and carboxyhemoglobin. Therefore, to compare the readings made by the cerebral oximeter with

co-oximeter measurements of blood samples, percentage O_2 hemoglobin ($\%O_2Hb$) readings from the co-oximeter were corrected for methemoglobin and carboxyhemoglobin ($\%O_2Hb/[100 - \%COHb - \%MetHb]$). This correction was used for arterial and jugular bulb samples; *i.e.*, for SaO_2 and S_{jvO_2} . The average of the duplicate analyses of each blood sample was used in all calculations.

Statistical Analysis

The relations of SaO_2 , rSO_2 , or \hat{S}_{jvO_2} to S_{jvO_2} were determined by simple linear regression for each volunteer and for all volunteers combined (*i.e.*, the pooled data for both experiments). The comparison of rSO_2 or \hat{S}_{jvO_2} to S_{jvO_2} for the pooled data was also made by examining the difference plotted against the average of the two values, as described by Bland and Altman.²⁴ The error was expressed as bias and precision, where bias was calculated as the mean difference between rSO_2 or \hat{S}_{jvO_2} and S_{jvO_2} and precision was calculated as 2 SDs of this difference. The significance of differences between mean values for different test stages or experiments was determined using paired *t* tests; for repeated *t* tests, the Bonferroni method was used to correct the accepted level of significance. A *P* value of 0.05 was considered significant.

Results

All 30 volunteers completed the experiments without complications. No measurements were made from the cerebral oximeter for 2 of 360 test stages due to an inability of the device to capture a signal; both of these missing readings occurred in the same volunteer during the hypercapnic experiment. All arterial and jugular venous samples were obtained and analyzed. Samples representing the two cerebral oximeter readings that were not obtained were not used in subsequent analyses.

Figure 1 shows a breath-by-breath record of the control of $P_{ET}O_2$ and $P_{ET}CO_2$ and the resulting pulse oximeter and cerebral oximeter readings for experiment 2 (hypercapnia) for a representative volunteer. With the exception of brief periods at the transients from one level of $P_{ET}O_2$ to another, $P_{ET}O_2$ and $P_{ET}CO_2$ were tightly controlled and were stable when readings from the cerebral oximeter and blood samples were obtained (the last 30 s of each test stage). Note that the finger pulse oximeter reading (SpO_2) exhibited the expected delay of ~60 s after each transition in end-tidal (and therefore

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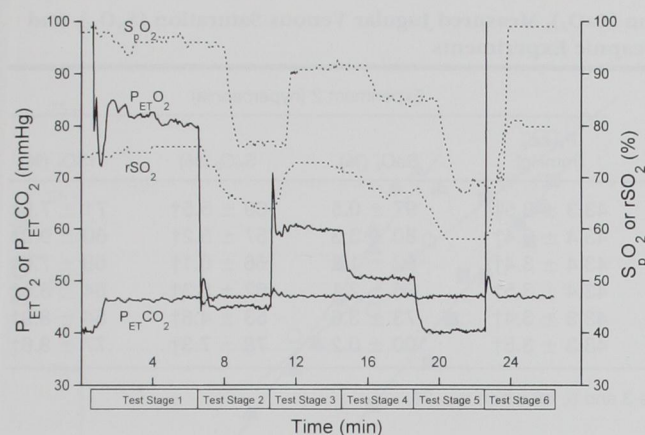


Fig. 1. End-tidal concentrations of oxygen ($P_{ET}O_2$) and carbon dioxide ($P_{ET}CO_2$) (solid lines) and resulting finger pulse oximeter reading (rSO_2) and cerebral oximeter reading (rSO_2) (dotted lines) for experiment 2 (hypercapnia) for a representative volunteer. Target $P_{ET}O_2$ = 80 mmHg for test stage 1, 45 mmHg for test stage 2, 60 mmHg for test stage 3, 51 mmHg for test stage 4, and 40 mmHg for test stage 5. $P_{ET}CO_2$ was controlled to 0.50 for test stage 6.

arterial) saturation.²⁵ The rSO_2 value from the cerebral oximeter also changed as predicted in response to changes in SaO_2 . Although the transitions in rSO_2 were slower than the SpO_2 transitions, the cerebral oximeter had reached a stable reading by the end of each 4-min step in $P_{ET}O_2$.

The $P_{ET}CO_2$ averaged 36.4 ± 3.5 mmHg (mean \pm SD) for experiment 1 (normocapnia) and 43.1 ± 4.7 mmHg for experiment 2 (hypercapnia). There were no significant differences among $P_{ET}CO_2$ values for the different test stages within either experiment. There were no significant differences in blood SaO_2 between the normocapnic and hypercapnic experiments for any test stage. The purpose of our protocol was achieved, in that blood $S_{jv}O_2$ was significantly higher in hypercapnia than in normocapnia at every SaO_2 (test stage). The rSO_2 tracked the changes in $S_{jv}O_2$ and was significantly higher in hypercapnia than in normocapnia. Although rSO_2 and $S_{jv}O_2$ did not differ during hypercapnia, rSO_2 was significantly higher than measured $S_{jv}O_2$ during normocapnia for all test stages except hyperoxia. Table 1 summarizes these data.

Table 2 gives statistics for the linear regressions between measured $S_{jv}O_2$ and SaO_2 , rSO_2 , or $\hat{S}_{jv}O_2$ (from equation 2) for individual volunteers. When data for both levels of $P_{ET}CO_2$ were combined, the mean r^2 for the SaO_2 relation was 0.71. Mean r^2 was much higher (0.91) for rSO_2 and $\hat{S}_{jv}O_2$ (*i.e.*, for the data based on

the cerebral spectroscopy measurement). However, the slopes and intercepts for all three relations varied widely among volunteers. For some, there were large differences between estimated and measured saturation, whereas for the other volunteers the values corresponded closely. As a result, for the pooled data on all volunteers, $S_{jv}O_2$ was only loosely correlated with any of the other measures ($S_{jv}O_2 = 0.81 SaO_2 - 10.5\%$, $r^2 = 0.55$; $S_{jv}O_2 = 0.63 rSO_2 + 20\%$, $r^2 = 0.44$; $S_{jv}O_2 = 0.45 \hat{S}_{jv}O_2 + 34.7\%$, $r^2 = 0.30$). Figure 2 illustrates the error that can be introduced by this range of slopes and intercepts. This figure shows the data from three individual volunteers; as can be seen, an rSO_2 reading of 65% corresponds to a jugular venous saturation of 48%, 58%, or 66%, depending on the volunteer.

A Bland-Altman plot of the error of the cerebral oximeter reading, rSO_2 , revealed two "populations" of data (fig. 3). Most of the data clustered within ± 2 SDs of the bias (the mean error), and for this subset of the data the error did not vary systematically with the mean of the two measurements. However, there was a smaller subset of data with very large negative error (*i.e.*, the cerebral oximeter grossly underestimated the measured $S_{jv}O_2$). Most of these data were obtained in three volunteers for whom the cerebral oximeter underestimated $S_{jv}O_2$ at all levels of SaO_2 and both levels of CO_2 (indicated by the triangles in fig. 3). For individual volunteers, bias ranged from -40% to $+10\%$ and precision ranged from 3% to 64%. For all, the data bias was 3.8%, and the precision was 17.8%. When the comparison was made with $\hat{S}_{jv}O_2$, the bias was -4.4% with a precision of 22%. The error was not correlated with either $P_{ET}CO_2$ ($r^2 = 0.05$) or arterial saturation ($r^2 = 0.02$).

Discussion

The cerebral oximeter assessed in this study (model INVOS 3100A, Somanetics Corp.) was recently approved by the US Food and Drug Administration for clinical use. Ours is the first validation study of this device in healthy volunteers to tightly control end-tidal (and therefore arterial) tensions of O_2 and CO_2 . The dynamic end-tidal forcing technique allowed us to step rapidly from one level of $P_{ET}O_2$ to another and maintain a constant level of saturation for 4–6 min while also controlling $P_{ET}CO_2$. By regulating end-tidal gas tensions, we have tried to ensure that the degree of cerebral vasodilatation secondary to Pa_{CO_2} and the arterial oxygen saturation were constant at the time of measure-

Table 1. End-tidal CO₂ (P_{ET}CO₂), Measured Arterial Oxygen Saturation (SaO₂), Measured Jugular Venous Saturation (S_{JV}O₂), and Cerebral Oximeter Reading (rSO₂) for the Normocapnic and Hypercapnic Experiments

Test Stage	Experiment 1 (normocapnia)				Experiment 2 (hypercapnia)			
	P _{ET} CO ₂ (mmHg)	SaO ₂ (%)	S _{JV} O ₂ (%)	rSO ₂ (%)	P _{ET} CO ₂ (mmHg)	SaO ₂ (%)	S _{JV} O ₂ (%)	rSO ₂ (%)
1	36.5 ± 3.8	97 ± 0.8	61 ± 4.5	67 ± 8.3*	43.3 ± 3.5†	97 ± 0.5	69 ± 5.5†	71 ± 7.6†
2	36.2 ± 3.3	81 ± 2.9	49 ± 4.4	57 ± 8.0*	43.4 ± 3.4†	80 ± 3.3	57 ± 5.2†	60 ± 9.0†
3	36.5 ± 3.6	91 ± 1.8	57 ± 4.4	63 ± 7.0*	43.4 ± 3.4†	92 ± 1.2	66 ± 6.1†	68 ± 7.6†
4	36.2 ± 3.4	85 ± 3.0	52 ± 4.4	59 ± 7.8*	43.4 ± 3.5†	86 ± 2.1	62 ± 5.3†	64 ± 8.5†
5	36.2 ± 3.3	74 ± 4.6	45 ± 4.8	51 ± 9.0*	43.3 ± 3.4†	73 ± 3.6	53 ± 4.8†	54 ± 8.9†
6	36.8 ± 3.6	100 ± 0.2	68 ± 4.9	70 ± 6.7	43.3 ± 3.5†	100 ± 0.2	78 ± 7.3†	77 ± 8.6†

Values are mean ± SD. N = 30 except for hypercapnic experiments for test Stages 3 and 6, for which n = 29.

* $P < 0.05$ versus measured S_{JV}O₂.

† $P < 0.05$ versus normocapnia for the same measurement at the same test stage.

ment. Previous studies have used fixed inspired concentrations of O₂ without control of CO₂¹⁷; fixed FiO₂ with voluntary hyperventilation, CO₂ rebreathing, or both¹⁶; or have used a constant low FiO₂ resulting in "ramp" changes in SaO₂.²⁰ Consequently, cerebral oximeter readings and blood sampling may have occurred in a changing cerebral oxygenation "environment."

Validation of the cerebral oximeter is difficult because there is no way to directly measure regional brain oxygenation in the field of oximeter probe. Previous studies have compared readings from the cerebral oximeter to a "field" or "combined" saturation calculated from a combination of arterial and ipsilateral jugular venous bulb saturation.^{16,17,20} This calculated value ($0.25 \cdot \text{SaO}_2 + 0.75 \cdot \text{S}_{\text{JV}}\text{O}_2$) is based on the assumption that the distribution of blood in the cerebral vasculature is the same as that in the rest of the body²² and the fact that approximately three-quarters of the peripheral blood volume is usually stored in the peripheral venous bed.²¹

Because few data support this stated proportional distribution of arterial and venous blood, we compared the measured jugular venous saturation to both the adjusted and unadjusted oximeter readings. The correction did not significantly improve either the accuracy or the correlation of the measurement. In interpreting the data, it should be remembered that the jugular bulb receives some venous blood from the contralateral brain but almost none from the posterior fossa²⁶ and may reflect the middle cerebral artery more than the anterior cerebral artery. Therefore, whereas jugular venous bulb saturation may reflect global cerebral oxygen delivery in relation to demand, it may not accurately reflect regional saturation in the cortical tissue of the frontal lobe of the brain (*i.e.*, the region underlying the oximeter probe).

If we assume that global cerebral oxygen consumption does not change during the period of measurement, jugular bulb saturation should decrease with de-

Table 2. Relationship between the Measured Arterial Saturation (SaO₂), the Cerebral Oximeter Reading (rSO₂), or the Calculated S_{JV}O₂ (Derived from Cerebral Oximeter Reading and Measured Arterial Saturation, Equation 2) and Measured S_{JV}O₂ (from Jugular Venous Bulb Blood Samples) for Individual Subjects

		Both Levels of P _{ET} CO ₂		
		Slope	Intercept (%)	r ²
S _{JV} O ₂ vs. SaO ₂	Mean ± SD	0.806 ± 0.116	-11.3 ± 9.2	0.71 ± 0.14
	Range	0.518 to 1.064	-30.3 to 6.3	0.24 to 0.96
S _{JV} O ₂ vs. rSO ₂	Mean ± SD	1.219 ± 0.323	-17.9 ± 23.1	0.91 ± 0.06
	Range	0.550 to 1.847	-58.3 to 39.9	0.72 to 0.99
S _{JV} O ₂ vs. S _{JV} O ₂	Mean ± SD	1.357 ± 0.486	-15.5 ± 30.3	0.91 ± 0.06
	Range	0.388 to 1.651	-79.5 to 42.8	0.75 to 0.98

* Significant difference between normocapnic and hypercapnic experiments ($P < 0.05$).

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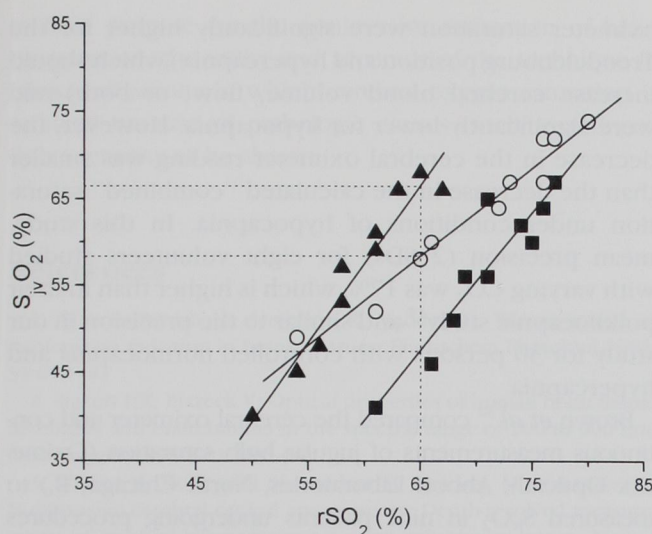


Fig. 2. The relation between measured jugular bulb venous ($S_{jv}O_2$) saturation and rSO_2 (the cerebral oximeter reading) for three volunteers, with lines of best fit by simple linear regression. $\blacktriangle y = 1.79 \times -50.4$, $r^2 = 0.94$; $\circ y = 1.02 \times -8.0$, $r^2 = 0.96$; $\blacksquare y = 1.59 \times -56.1$, $r^2 = 0.86$. Note that an rSO_2 reading of 65% corresponds to a measured $S_{jv}O_2$ of 66.6%, 58.4%, or 47.6% depending on the slope and intercept of the relation.

creased arterial saturation or decreased Pa_{CO_2} due to decreased oxygen delivery. In 1942 Nims *et al.*²⁷ reported that a 1 vol% change in CO_2 content of the arterial blood produced a 0.5 vol% change in O_2 content of jugular venous blood in three healthy persons; the relation was approximately linear over a wide range of hypo- and hypercapnia. As expected, we found that measured $S_{jv}O_2$ was lower with lower SaO_2 for the same $P_{ET}CO_2$ and higher with hypercapnia than with normocapnia for the same SaO_2 .

Because the saturation of hemoglobin in extracranial tissue in the light path of the oximeter probe is expected to be one of the major contaminants producing errors in the measurement, it is important to carefully examine the errors at a constant SaO_2 for different $P_{ET}CO_2$. Changes in $P_{ET}CO_2$ at constant arterial saturation would be expected to change $S_{jv}O_2$ without changing the hemoglobin saturation in extracranial tissue. We obtained the same target SaO_2 for all test stages (table 1). The oximeter reading increased with hypercapnia, indicating that the cerebral oximeter is responding to changes in intracranial hemoglobin oxygen saturation. However, the cerebral oximeter reading was significantly higher than blood $S_{jv}O_2$ for normocapnia for all P_{O_2} values except hyperoxia, whereas the cerebral ox-

imeter reading did not differ from $S_{jv}O_2$ during hypercapnia. These observations could indicate either that not all the contamination from extracranial tissue has been eliminated or that the ratio of arterial to venous blood in the light path is altered by hypercapnia. Because hypercapnia is a potent cerebral vasodilator, the latter is a likely possibility. Interestingly, Pollard *et al.*¹⁶ found that the decrease in the cerebral oximeter reading was smaller than the decrease in the calculated "combined" saturation under conditions of hypocapnia in a small number of healthy volunteers.

Several case reports and small clinical series have indicated that cerebral oximetry tracks expected changes in cerebral oxygen saturation with changes in arterial blood pressure or oxygen saturation,⁹ hypothermic circulatory arrest,¹⁰ carotid artery compression,²⁸ and subsequent morbid clinical events.^{11,29} It has therefore been suggested that cerebral oximetry may be useful for clinical monitoring of brain oxygen supply during various procedures.^{7,8,12,30} However, few published studies have addressed the accuracy of the newly approved device in humans and only two previous reports have considered its accuracy under conditions of controlled cere-

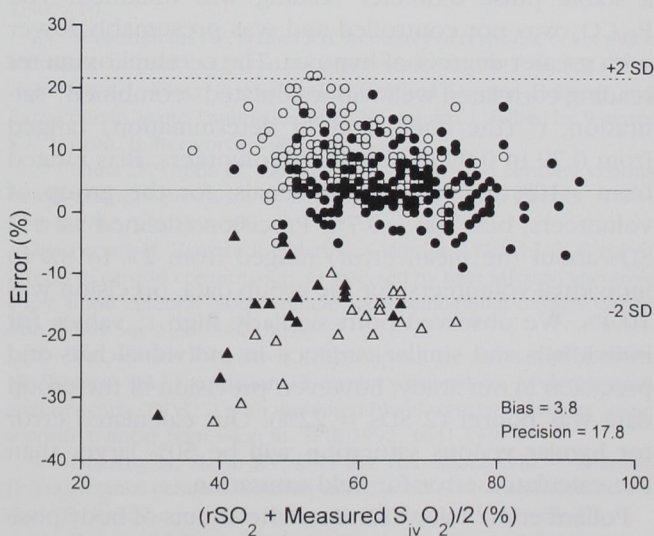


Fig. 3. Plot of the error (cerebral oximeter reading [rSO_2] – measured jugular bulb venous saturation [$S_{jv}O_2$]) versus the mean of rSO_2 and measured $S_{jv}O_2$ using the method of Bland and Altman²⁴ for both experiments and all test stages for all 30 volunteers. The plot indicates that the cerebral oximeter reading and the standard measure are not closely associated because the limits of agreement are wide. Precision was defined as 2 SDs about the mean error (the bias). Open symbols = data for normocapnic experiments. Closed symbols = data for hypercapnic experiments. Triangles = data for three volunteers with large negative error for all measurements.

bral metabolism and oxygen delivery in healthy human volunteers.^{16,17}

Dujovny *et al.*,³¹ using a prototype of the current device that had a shorter emitter-detector spacing, reported no relation between the baseline reading and age in 100 persons studied. McCormick *et al.*²⁰ compared readings from that same device with measured arterial and jugular venous bulb saturations in nine patients in the neurologic intensive care unit. Oximeter readings correlated poorly ($r^2 = 0.55$, $n = 68$) with "field" saturation calculated from two models of cerebral blood distribution (arterial:venous = 0.18:0.82 or 0.28:0.72). McCormick *et al.*²⁰ also tested the device in seven healthy persons with ramp changes in SaO_2 induced by breathing 7% O_2 but did not collect jugular venous blood samples and therefore could not perform the correlation analysis for the healthy persons. The short emitter-detector distance was subsequently lengthened to the current 30 mm and 40 mm in an attempt to reduce extracranial contamination of the saturation reading.

Pollard *et al.*¹⁷ studied the response of the newly improved device (model INVOS 3100A) to arterial hypoxemia in 22 healthy persons. Hypoxemia was induced by having volunteers breathe hypoxic gas mixtures until a stable pulse oximeter reading was obtained. The $\text{P}_{\text{ET}}\text{CO}_2$ was not controlled and was presumably lower with greater degrees of hypoxia. The cerebral oximeter reading correlated well with calculated "combined" saturation; r^2 (the coefficient of determination) ranged from 0.79 to 0.99 in individual volunteers. Bias ranged from -10% to +8% in individuals; for the group of volunteers, bias was -0.7%. Precision (defined as ± 2 SDs about the mean error) ranged from 2% to 8% in individual volunteers; for the group data, precision was 10.4%. We observed both similarly high r^2 values for individuals and similar variance in individual bias and precision in our study; however, precision of the group data was poorer (2 SDs = 22%). Our calculated error for jugular venous saturation will be 50% larger than the calculated error for field saturation.

Pollard *et al.*¹⁶ also examined the effects of body position (20% Trendelenburg, supine, or 20% reverse Trendelenburg) with and without varying $\text{P}_{\text{ET}}\text{CO}_2$ on the accuracy of the INVOS 3100A cerebral oximeter during arterial hypoxemia. Carbon dioxide was designated "normal" (*i.e.*, $\text{P}_{\text{ET}}\text{CO}_2$ not controlled, as in the previous study), "high" (volunteers inhaled CO_2 to increase $\text{P}_{\text{ET}}\text{CO}_2$ to > 55 mmHg), or "low" (volunteers voluntarily hyperventilated to $\text{P}_{\text{ET}}\text{CO}_2 < 15$ mmHg). Jugular venous saturation, "combined" saturation, and cerebral

oximeter saturation were significantly higher for the Trendelenburg position and hypercapnia (which should increase cerebral blood volume, flow, or both) and were significantly lower for hypocapnia. However, the decrease in the cerebral oximeter reading was smaller than the decrease in the calculated "combined" saturation under conditions of hypocapnia. In this study, mean precision (2 SDs) for eight volunteers studied with varying CO_2 was 17%, which is higher than in their poikilocapnic study¹⁷ and similar to the precision in our study for 30 persons with controlled normocapnia and hypercapnia.

Brown *et al.*³² compared the cerebral oximeter and continuous measurements of jugular bulb saturation (Oximetrix Opticath, Abbott Laboratories, North Chicago, IL) to measured S_{vO_2} in nine patients undergoing procedures involving cardiopulmonary bypass; data were collected throughout surgery, including before and after bypass. The cerebral oximeter was much less precise (2 SDs = 28.2%) than the Opticath (2 SDs = 5.4%), and error of the cerebral oximeter varied systematically over the range of measured S_{vO_2} (~40% to ~95%). This difference was attributed to changes in partitioning of arterial, capillary, and venous blood in the brain during nonpulsatile flow, which would presumably affect the cerebral oximeter but not the saturation of jugular venous blood. In individual healthy volunteers, the cerebral oximeter reading correlates well with measured "combined" or "field" saturation and does not exhibit systematic bias^{16,17} (this study). Interestingly, Trubiano *et al.*³³ recently reported poor precision (2 SDs = ~42%) of the Opticath in a similar clinical situation. It is unclear why the accuracy of the Opticath was so vastly different between these two studies.

Our major finding is that S_{vO_2} can be estimated by the INVOS 3100A using the uncorrected direct measurement rSO_2 or by correcting the measurement using the measured SaO_2 (equation 2) under conditions of hypoxic exposure with controlled normocapnia and hypercapnia. This implies that the device detects changes in cerebral oxygen saturation, due to changes in cerebral blood flow induced by changes in $\text{P}_{\text{ET}}\text{CO}_2$, which are not apparent from the arterial saturation. However, the wide variability among volunteers of the slope and intercept of the relation between the actual jugular venous saturation and the estimate from the device, as well as the occurrence of three clear outliers (fig. 2), limits the clinical use of the device to situations in which tracking trends in cerebral oxygenation would be acceptable. An improved algorithm in the device has eliminated the problem with outliers (Henson LC, Ward DS. Unpublished data). Although cerebral oximetry appears

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to hold promise for the noninvasive estimation of brain oxygenation, the utility and accuracy of the technique in clinical situations in which cerebral oxygen saturation is reduced because of pathologic causes (such as reduced flow) remains to be shown.

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