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Differences of cerebral oxygen saturation in dialysis patients: a comparison of three
principals of near infrared spectroscopy

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Abstract

Purpose

It has been reported that cerebral oxygen saturation (rSO₂) measured by near infrared spectroscopy is low in dialysis patients. We compared the rSO₂ values of dialysis patients before living donor kidney transplantation and their donors as controls by using three spectroscopes that utilize different principals, the INVOS 5100C (spatially resolved spectroscopy), FORE-SIGHT ELITE (modified Beer-Lambert law) and tNIRS-1 (time-resolved spectroscopy).

Methods

Before induction of anesthesia, the sensors of one of the three spectroscopes were placed on the forehead and rSO₂ values were recorded followed by the same measurement using the other 2 spectroscopes. The primary objective was to compare the rSO₂ values of the dialysis patients and controls using the three spectroscopes by the unpaired t-test. Then we compared the rSO₂ values among the spectroscopes in both dialysis patients and controls by one-way ANOVA. Finally, we examined the relations between the rSO₂ values and the physiological values by using the Pearson correlation coefficient.

Results

Fifteen pairs of dialysis patients and controls were studied. With the INVOS 5100C, the values of the dialysis patients ($59.7 \pm 9.7\%$ (mean $\pm$ standard deviation) were 13% lower than those of the controls ($73.3 \pm 6.9\%$) ($P < 0.01$). With the tNIRS-1, the values were $57.8 \pm 4.8\%$ in the dialysis patients and $63.3 \pm 3.5\%$ in the controls ($P < 0.01$). Almost no differences were observed with the FORE-SIGHT ELITE ($71.6 \pm 4.9\%$ [dialysis patients] vs. $70.8 \pm 4.3\%$ [Controls]) ($P = 0.62$). Among the spectroscopes, the values were significantly different in both dialysis patients and controls. For the INVOS 5100C and tNIRS-1, correlation coefficients between rSO₂ values and blood Hb and serum Alb were more than 0.5.

Conclusions

The rSO₂ values for comparisons between the dialysis patients and the controls were different according to differences of the principles of the near infrared spectroscopes. In the INVOS 5100C and tNIRS-1, rSO₂ values may be related to blood Hb and serum Alb.

Introduction

It has been reported that the cerebral oxygen saturation (rSO_2) measured by near infrared spectroscopy is lower in dialysis patients than in healthy controls [1-4]. In addition, impairment of cognitive function is related to lower rSO_2 values in dialysis patients [5, 6] and in patients with chronic kidney disease [7]. Accordingly, it is important to clarify the cause of this low rSO_2 in dialysis patients. However, the causes of it seem not to have been elucidated yet.

As far as we know, all previous studies comparing rSO_2 values of dialysis patients and healthy controls used series of the INVOS (Somanetics, Troy, MI, USA), one of the representative near infrared spectrometers used to estimate rSO_2 [1-4]. Recently, it was reported that in hemodialysis patients the rSO_2 values measured by the INVOS 5100C were significantly lower than the jugular venous oxygen saturation (SjO_2) values, which are another index of cerebral oxygenation, although the bias between rSO_2 and SjO_2 was almost zero in non-hemodialysis patients [8]. Thus, there is a possibility that rSO_2 values measured by the INVOS 5100C may underestimate cerebral oxygenation in dialysis patients.

There are several principals of measurement in near infrared spectroscopy: the modified Beer-Lambert (MBL) law, spatially resolved spectroscopy (SRS), time-resolved spectroscopy (TRS) and so on [9]. The INVOS series utilizes SRS. As mentioned above, there seem to be no studies comparing rSO_2 values of dialysis patients and controls by using other spectrometers that utilize MBL or TRS.

Accordingly, in this study we compared the rSO_2 values of dialysis patients before living donor kidney transplantation and their donors as controls by using three spectrometers which utilize different principals: the INVOS 5100C, FORE-

SIGHT ELITE (CAS Medical Systems Branford, CT, USA), which uses MBL, and the tNIRS-1 (Hamamatsu Photonics, Hamamatsu, Japan), which utilizes TRS.

Materials and Methods

This study was a prospective observational study of living donor kidney transplantation performed from July 2021 to November 2022. It was approved by the ethics committee of the Hokkaido University Hospital (No. 017-0490) in accordance with the ethical principles outlined in the Declaration of Helsinki and Good Clinical Practice. Written informed consent was obtained from all patients. It was registered in the UMIN Clinical Trials Registry prior to patient enrollment (UMIN000044279). Adult recipients with ASA physical status classification 3, whose history of dialysis was more than 1 year were enrolled. Exclusion criteria were: 1) cardiovascular diseases of NYHA classification 3 or above and 2) cerebral diseases. As controls, their donors with ASA physical status classification 1 or 2 were enrolled. The donors with cerebral diseases were excluded.

After the recipients (dialysis patients) and donors (controls) became stable in the supine position under room air in the operating room and an electrocardiograph, blood pressure measurement cuff, and percutaneous arterial blood oxygen saturation (SpO₂) monitor were employed. Before induction of anesthesia, the sensors of one of the three spectroscopes were placed on both sides

of the forehead and the rSO₂ values in both sides were simultaneously recorded after the values became stable. Then the same measurement was performed using the other 2 spectroscopes. The order in which the spectroscopes were used was rotated in the order of patients, beginning with 1) the INVOS 5100C, 2) FORE-SIGHT ELITE and 3) tNIRS-1 for the first patient, followed by 2, 3, 1 for the second patient, 3, 1, 2 for the third patient, etc. Left and right values in each spectroscope were averaged. After the measurement of rSO₂, blood pressure, SpO₂ and the temperature of the forehead were recorded. Then general anesthesia was induced, and the arterial line was secured.

Statistical Analysis

The primary objective was to compare the rSO₂ values of the dialysis patients and controls obtained using the three spectroscopes. In our institute, there are about 30-40 cases of adult living donor kidney transplantation during one and half years. Assuming that the recipients whose history of dialysis is more than 1 year account for half of all the cases, we set the number of cases as 15 that could be treated within the study period. In a previous study using the INVOS 5100C, the rSO₂ values in dialysis patients were $49.5 \pm 12.5\%$ (mean $\pm$ standard deviation) while those in healthy controls were $68.9 \pm 8.5\%$ [2]. By using

G*Power 3.1.9.7 (Heinrich Heine University Dusseldorf Germany), the effect size of the unpaired t test was calculated to be 1.82 and 15 samples per group would provide 99.8 % power at a two-tailed α of 0.05. For the primary objective, the unpaired t-test was used.

The secondary objective was to compare the rSO₂ values among the spectroscopes in both dialysis patients and controls. For this, one way ANOVA was used. The third objective was to examine the relations between rSO₂ values and the physiological values. It is reported that rSO₂ can be expressed as a function of arterial oxygen saturation (SaO₂), the blood hemoglobin concentration (Hb), cerebral blood flow, and the cerebral metabolic rate for oxygen [10]. Previous studies also reported that the rSO₂ in dialysis patients was associated with the serum albumin concentration (Alb), duration of dialysis, mean blood pressure, and presence of diabetes mellitus (DM) [1, 2, 11]. Accordingly, the correlations between rSO₂ values and serum Alb, blood Hb, SpO₂, mean blood pressure and the temperature of the forehead were evaluated using the Pearson correlation coefficient in 30 patients, including dialysis patients and controls, using each spectroscope. We assumed that rSO₂ values were directly influenced by the changes of these physiological factors regardless of whether the subjects were under dialysis or not. Serum Alb was measured one day before the surgery.

Blood Hb values were obtained from the arterial blood gas data after the induction of anesthesia. Next, the correlation between rSO₂ and the duration of dialysis was evaluated in the dialysis patients by using the Pearson correlation coefficient. Finally, rSO₂ values of the dialysis patients with DM and without DM were compared by the unpaired t-test.

Physiological data of the dialysis patients and controls were compared by the unpaired t test. Statistical analysis was performed using SPSS ver. 25.0 (Armonk, USA). A P-value of <0.05 was considered statistically significant.

Results

Measurement was done in 17 pairs of the dialysis patients and controls. For one patient, rSO₂ data were insufficient due to contact failure of the sensors. For another dialysis patient, the dialysis was done one day before surgery, while it was performed 2 days before surgery in other dialysis patients. A recent report demonstrated that intervals between hemodialysis and surgery were significantly associated with postoperative mortality, possibly due to weight gain and extracellular volume overload, electrolyte disequilibrium and accumulation of uremic toxins [12]. Therefore, the difference of dialysis timing may affect the results. After excluding the 2 pairs including these patients, 15 pairs were studied.

Demographic and physiological data are shown in Table 1. The relations between dialysis patients (recipients) and controls (donors) were 12 couples of husband and wife, and 3 couples of mother and child. The causes of renal failure in the dialysis patients were 4 cases of IgA nephropathy, 4 cases of diabetic nephropathy, 4 cases of nephrosclerosis and the others were one case each of membranoproliferative glomerulonephritis, polycystic kidney, and interstitial nephritis. Physiological data demonstrated that the blood Hb values were significantly lower in the dialysis patients than in the controls.

Table 2 and Figure 1 show the differences of rSO₂ values between dialysis patients and controls for each spectroscope. In the dialysis patients, the rSO₂ values were 13% lower with the INVOS 5100C and they were 5% lower with the tNIRS-1, whereas there were almost no differences with the FORE-SIGHT ELITE. With the INVOS 5100C, the values were distributed over a broad range of 40% in the dialysis patients and 25% in the controls. On the other hand, the distribution range was within 20% with the FORE-SIGHT ELITE and tNIRS-1. Comparison among the spectroscopes is also shown in Table 2. In both dialysis patients and controls, significant differences were observed by one-way ANOVA.

Table 3 shows the Pearson correlation coefficients between rSO₂ values and various patient factors. In the INVOS 5100C and tNIRS-1, correlation coefficients for blood Hb and serum Alb were more than 0.5. In Figure 2, scatter plots comparing rSO₂ and blood Hb or serum Alb are shown. There were no significant differences in rSO₂ values between DM and non-DM dialysis patients (Table 4).

Discussion

In this study, rSO₂ values were measured in dialysis patients before the induction of anesthesia for living donor kidney transplantation and their donors as controls by using three spectroscopes that utilize different principals. With the INVOS 5100C, the values in the dialysis patients were more than 10% lower than those in the controls, as was reported in previous studies [1-4]. With the tNIRS-1, the degree of decrease was about 5% and almost no changes were observed with the FORE-SIGHT ELITE. Among the spectroscopes, the values were significantly different in both dialysis patients and controls. With the INVOS 5100C and tNIRS-1, correlation coefficients between rSO₂ values and blood Hb and serum Alb were more than 0.5.

As far as we know, all previous studies that compared rSO₂ values in dialysis patients and healthy controls used series of the INVOS [1-4]. In 2007, Prohovnik et al. reported that when using the INVOS 4100, rSO₂ was extremely low before dialysis in hemodialysis patients compared with healthy controls (41% vs. 70%) [4]. In 2014, Hoshino et al. reported that when using the INVOS 5100C before hemodialysis, patients had significantly lower rSO₂ values than controls (56% vs. 70%) [3]. The same group reported in 2015 that the rSO₂ values measured with

the INVOS 5100C were significantly lower in hemodialysis patients than in healthy controls (50% vs. 69%) [2]. In peritoneal dialysis patients, rSO₂ values measured using the INVOS 5100C were significantly low compared with healthy controls (57% vs. 69%). Thus, regardless of whether hemo- or peritoneal dialysis was performed, the rSO₂ values measured using the INVOS series were more than 10% lower in dialysis patients than in controls, as was seen in our study.

The FORE-SIGHT ELITE employs MBL and uses five wavelengths (680, 730, 770, 805, and 870 nm) of light that may enhance accuracy and reduce extracranial contamination [13]. The tNIRS-1 utilizes TRS, one of the most reliable algorithms based on the photon diffusion theory, which enables good correctness and reproducibility [14]. In previous reports that compared the effects of posture and extracranial contamination among the INVOS 5100C, FORE-SIGHT ELITE and NIRO-TRS (Hamamatsu Photonics, Hamamatsu, Japan), which is the prototype of the TRS spectroscope, the rSO₂ values in healthy controls were 74%, 72% and 63% for the INVOS 5100C, FORE-SIGHT ELITE and NIRO-TRS, respectively [15]. These results were compatible with those for the controls in our study. In that study, the changes in rSO₂ values against the changes in posture were different among the spectroscopes, and the effect of extracranial contamination was lowest for the NIRO-TRS. In addition, studies

that examined the effects of hypoxia among several spectroscopes, including the INVOS 5100C and FORE-SIGHT ELITE showed that the changes were different according to the spectroscopes [16, 17]. Thus, there may be a risk when applying evidence generated with one spectroscope to other ones [16].

With the INVOS 5100C and tNIRS-1, the correlation coefficients for blood Hb were more than 0.5. As mentioned above, rSO_2 can be expressed as a function of SaO_2 , blood Hb cerebral blood flow, and the cerebral metabolic rate for oxygen [10]. Accordingly, these findings are reasonable. Indeed, a study that evaluated the rSO_2 values measured using the INVOS 5100C twice in hemodialysis patients showed that rSO_2 was low in the presence of low blood Hb at the initiation of hemodialysis and improved in response to blood Hb increase [18]. In addition, it was reported that following intradialytic blood transfusion in hemodialysis patients with severe anemia, blood Hb levels significantly increased and rSO_2 values measured by the INVOS 5100C also significantly improved [19]. In our study, blood Hb was lower in the dialysis patients than in the controls. This low blood Hb level may be related to the low rSO_2 values in the dialysis patients obtained using the INVOS 5100C and tNIRS-1. Moreover, in a study that compared the rSO_2 values of the INVOS 4100 and NIRO-100, which utilizes SRS, in patients with brain or heart disease, the range of values was 1.5 times

wider for the INVOS 4100 [20]. In that study, the values obtained using the INVOS 4100, but not the NIRO-100, were significantly related to blood Hb. Therefore, the INVOS series may overestimate the changes in the cerebral hemoglobin concentration [15], as was seen in our study.

With the INVOS 5100C and tNIRS-1, correlation coefficients for serum Alb were also more than 0.5. Some studies using the INVOS 5100C also indicated a relationship between low serum Alb levels and low rSO₂ values in dialysis patients [1, 2, 11]. The serum albumin concentration contributes to the formation of colloid osmotic pressure in vessels, which may increase circulatory blood volume and cardiac output. Cardiac output is related to cerebral blood flow [21]. Indeed, it was reported that serum Alb was positively correlated with the regional cerebral blood flow in patients with liver cirrhosis [2]. Accordingly, low serum Alb may contribute to low rSO₂. Alternatively, anemia and hypoalbuminemia are representative symptoms in patients with chronic kidney disease [22]. In our study, the correlation coefficient between serum Alb and blood Hb was 0.48 (data are not shown). Therefore, serum Alb and blood Hb may not be independent factors. In addition, in our study, there was no clinical difference between dialysis patients and controls (4.0g/dL vs 4.2g/dL). Therefore, the serum Alb level may not be related to the difference of rSO₂ values so much in the INVOS 5100C and

tNIRS-1.

There are some limitations in this study. First, there is no gold standard of cerebral oxygenation. Accordingly, we do not know which spectroscopy provides the right results. Considering the low blood Hb in the dialysis patients, it is plausible that the rSO₂ was low in these patients. However, considering previous reports [8, 15, 20], the results obtained using the INVOS 5100C may be overestimated. Second, a previous study demonstrated that cerebral atrophy and a higher amount of cerebrospinal fluid are observed in dialysis patients [4]. It was also reported that rSO₂ values measured with the INVOS 4100 were affected by the cerebrospinal layer and skull thickness in addition to blood Hb compared to the NIRO-100 [20]. Thus, the rSO₂ values measured with the INVOS series may be more affected by extra-brain components in dialysis patients. However, in this study, we did not estimate the effect of extra-brain components such as the cerebrospinal layer and skull thickness. In addition, the timing of the measurement of blood Hb and serum Alb was not the same as that of the rSO₂ measurement because we did not do blood collection for study due to this being an observational study.

In conclusion, this study compared the rSO₂ values of three spectroscopies in dialysis patients before the induction of anesthesia for living donor kidney transplantation and donors as controls. For the INVOS 5100C, the values in the dialysis patients were more than 10% lower than those in controls. With the tNIRS-1, the degree of the decrease was about 5% and almost no changes were observed with the FORE-SIGHT ELITE. Thus, the rSO₂ values for comparisons between the dialysis patients and the controls were different according to differences of the principles of the near infrared spectroscopies. In the INVOS 5100C and tNIRS-1, rSO₂ values may be related to blood Hb and serum Alb.

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Conflicts of Interest:

The authors have no conflicts of interest to declare.

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Figure Legends

Figure 1 Differences of rSO_2 values between dialysis patients and controls for each spectroscopy.

Round red dots indicate values of controls and square blue dots indicate those of dialysis patients.

Horizontal lines indicate mean values.

Figure 2 Scatter plots comparing rSO_2 and blood Hb or serum Alb for each spectroscopy.

The data of 30 patients, including dialysis patients and controls, were used.

Table 1

	Controls	Dialysis patients	P values
Number	15	15	
Demographic data			
Age (years old)	59.9±8.8	55.1±13.4	
Sex (male/female)	5/10	8/7	
Height (cm)	162.4±6.	162.2±9.1	
Body weight (kg)	59.5±7.9	58.4±14.2	
ASA (1/2/3)	8/7/0	0/0/15	
Hemodialysis/peritoneal dialysis		14/1	
Duration of dialysis (months)		44.7±30.7	
Comorbidities			
Diabetes mellitus	4	4	
Hypertension	3	8	
Cardiac disease	0	5	
Lung disease	1	2	
Liver disease	2	0	
Endocrine disease	2	3	
Mental disease	0	1	
Physiological data			
Serum Alb (g/dL)	4.2±0.3	4.0±0.4	0.05
Mean blood pressure (mmHg)	100±9	108±18	0.13
SpO ₂ (%)	98±2	98±1	0.15
Temperature of forehead (°C)	36.6±0.2	36.7±0.2	0.64
Blood Hb (g/dL)	12.2±1.0	9.7±1.2	<0.01
Numeric data are expressed as mean ± standard deviation.			

Table 2 Comparison of rSO₂ values (%)

	Controls	Dialysis patients	P values (unpaired t-test)
INVOS 5100C	73.3±6.9	59.7±9.7	<0.01
(range)	61.5-86.5	40.5-78	
FORE-SIGHT ELITE	70.8±4.3	71.6±4.9	0.62
(range)	65-80	66.5-80	
tNIRS-1	63.3±3.5	57.8±4.8	<0.01
(range)	58.5-69.5	51-66.5	
P values (one-way ANOVA)	<0.01	<0.01	

The rSO₂ values are expressed as mean ± standard deviation.

Table 3 Correlation coefficients between rSO₂ and various factors

	Blood Hb	Serum Alb	Mean blood pressure	SpO ₂	Temperature of forehead	Duration of dialysis
INVOS 5100C	0.69	0.55	-0.14	-0.28	-0.15	0.16
FORE-SIGHT ELITE	0.04	0.31	-0.38	-0.38	-0.19	0.04
tNIRS-1	0.56	0.6	-0.28	-0.34	-0.01	0.22

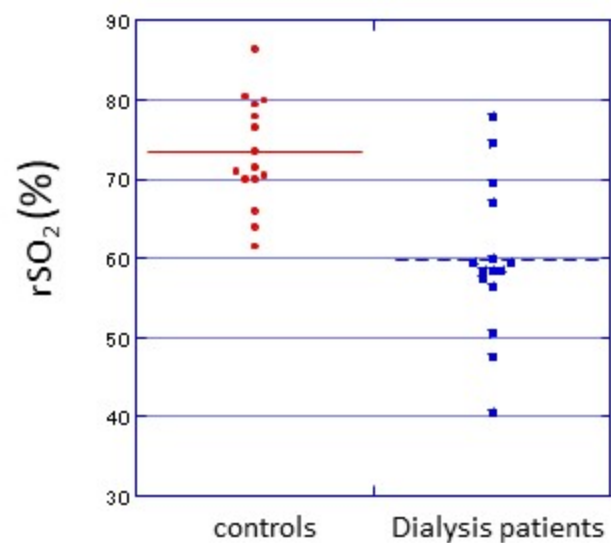
Correlation coefficients between rSO₂ and duration of dialysis were obtained for the 15 dialysis patients.

Correlation coefficients for other factors were obtained for 30 patients, including both dialysis patients and controls.

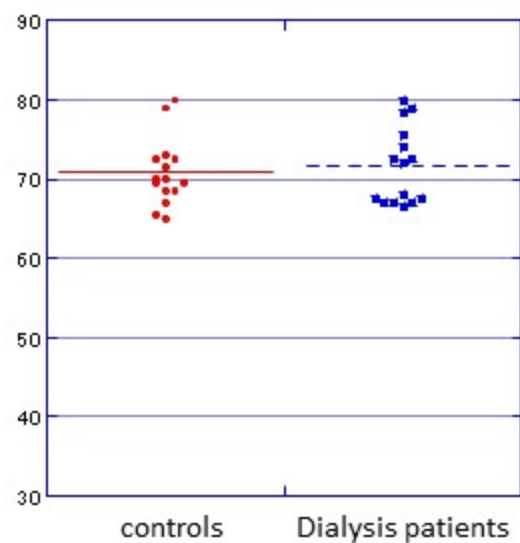
Table 4 Comparison of rSO₂ values of DM (DM+) and non-DM (DM-) dialysis patients

	DM+	DM-	P values
Number	4	11	
INVOS 5100C	58.1±1.5	60.3±11.4	0.55
FORE-SIGHT ELITE	70.5±3.2	72.1±5.4	0.61
tNIRS-1	55.3±5.0	59.0±4.8	0.21

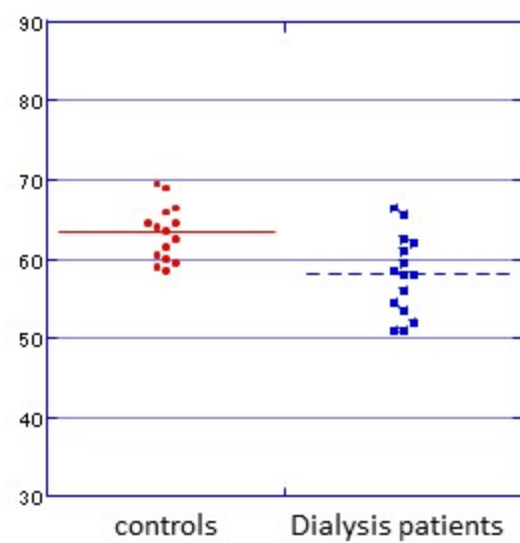
The rSO₂ values are expressed as mean ± standard deviation



INVOS 5100C

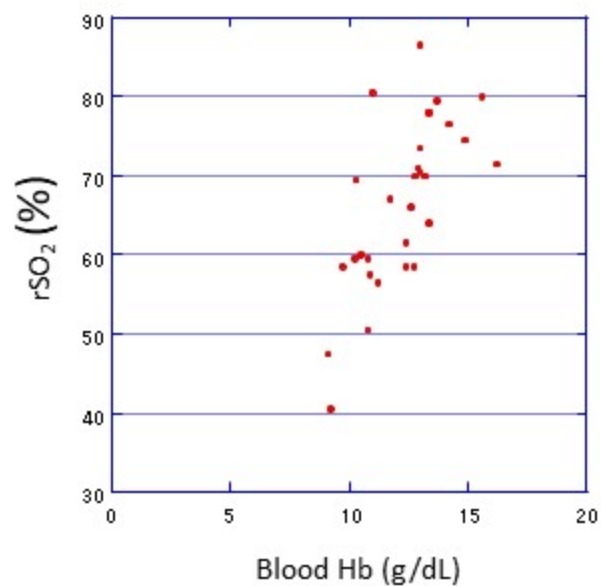


FORE-SIGHT ELITE

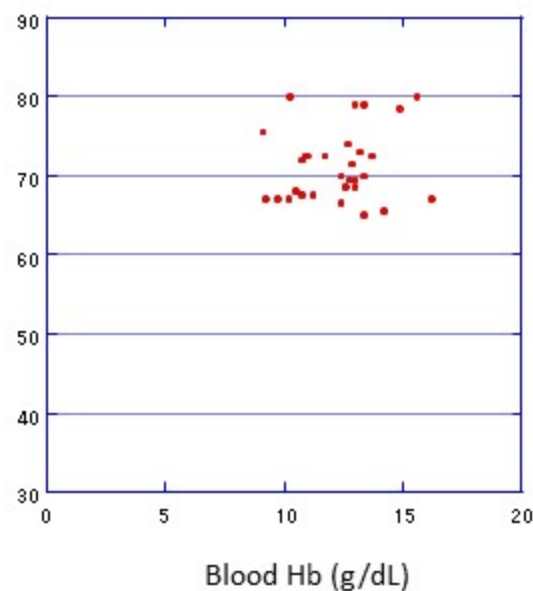


tNIRS-1

INVOS 5100C



FORE-SIGHT ELITE



tNIRS-1

