

## A comparison of non-invasive versus invasive methods of haemoglobin estimation in patients undergoing intracranial surgery

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**Background:** Until recently, invasive monitoring techniques were the only ones available for the estimation of haemoglobin (Hb) in the blood. However, following the introduction of a new non-invasive monitor, Hb concentration could be non-invasively and continuously monitored. It allows immediate and ongoing Hb changes to be displayed during surgery, which may aid in the rapid detection of clinically significant blood loss. To test the accuracy of this non-invasive monitor, we compared Hb levels obtained using standard invasive techniques (laboratory and arterial blood gas machine analysis) with those derived from a non-invasive monitor.

**Method:** Thirty patients undergoing various intracranial surgeries were enrolled in the study. Blood samples were withdrawn for Hb estimation from the laboratory [total haemoglobin mass (tHb)] and arterial blood gas (ABG) machine (aHb), using automated Hb analyser techniques randomly at any point during the surgery. At the same time, the Hb values displayed on the non-invasive monitor [Radical-7<sup>®</sup> Pulse Co-oximeter (SpHb<sup>®</sup>)], together with the perfusion index (PI), were also noted.

**Results:** The perfusion index (PI) was less than 1.4 in eight patients. The obtained Hb values were unreliable, as per the manufacturer's recommendations. Statistical analysis showed poor correlation between the invasive and non-invasive techniques of Hb estimation in the remaining 22 patients.

**Conclusion:** Non-invasive Hb monitoring (SpHb<sup>®</sup>) may not have sufficient accuracy to minimise the need for invasive Hb monitoring. However, it may allow continuous monitoring of Hb and could guide clinicians as to the need for invasive monitoring.

**Keywords:** comparison, haemoglobin estimation, intracranial, invasive, monitoring, non-invasive, surgery

### Introduction

Neurosurgical procedures, such as resection of meningiomas or aneurysm clipping, might involve rapid and massive blood loss. The decision to measure the haemoglobin (Hb) level, and on the basis of the results obtained, when to transfuse blood, is important and crucial. A sample of the patient's blood may be sent to the laboratory which allows Hb to be measured using various methods, or the Hb value may be obtained by arterial blood gas (ABG) analysis (aHb) in the operating room. Until recently, these invasive monitoring methods were the only ones available to assess Hb levels at intermittent intervals. This required clinicians to make a decision about the timing of sampling on the basis of clinical conditions. However, a new device, Radical-7<sup>®</sup> Pulse Co-oximeter (SpHb<sup>®</sup>), (Masimo, Irvine, USA), is now available that not only allows Hb concentrations to be monitored continuously, but also non-invasively.<sup>1</sup> This device displays immediate and ongoing changing Hb levels, and may help the clinician to determine when a patient's Hb needs to be measured invasively. In our study, we aimed to compare Hb levels obtained using non-invasive techniques (SpHb<sup>®</sup>), with those derived using invasive methods.

### Method

This study was conducted after approval from our institutional ethics committee (Ref: IEC/NP-250/2011, 2 November 2011). American Society Anesthesiologists physical status grade I and II adult patients of either sex, undergoing general anaesthesia for neurosurgical procedures, were included in the study. Patients were excluded if they refused to provide consent to participate in the study, or if they had peripheral vascular disease, haemoglobinopathy and sickle cell disease. Informed

written consent was obtained from participants, who then underwent a detailed pre-anaesthetic examination.

Patients fasted for eight hours before the scheduled surgery, and received premedication with glycopyrrolate 0.2 mg intramuscularly, one hour prior to surgery. Anaesthesia was induced with fentanyl 2 mg/kg and propofol 1.5–2 µg/kg. Tracheal intubation was facilitated with rocuronium 1 mg/kg. Isoflurane (0.8–1.2 minimum alveolar concentrations) in a mixture of O<sub>2</sub> and N<sub>2</sub>O (1:2) was used for the maintenance of anaesthesia, together with fentanyl 1 µg/kg, as an intermittent bolus to maintain analgesia. Vecuronium 0.15 mg/kg was used intermittently to provide neuromuscular blockade. All of the patients received mannitol 1 g/kg 30 minutes before opening the duramater. Intravenous fluids (crystalloid and/or colloids) were administered to replace the estimated fluid deficit. Randomly, at any point of time during the surgery, blood samples were collected for Hb estimation from the arterial blood gas (ABG) machine (aHb), and laboratory (tHb), using an automated Hb analyser. Simultaneously, the Hb reading from the SpHb<sup>®</sup> was recorded. Other values displayed on the monitor, such as the perfusion index (PI) and methaemoglobin (metHb), were also recorded. PI is a calculated value that is displayed with the SpHb<sup>®</sup> because obtaining SpHb<sup>®</sup> values with a PI < 1.4 is not recommended by the manufacturer. Also, the blood oxygen saturation values from the standard used pulse oximeter (SpO<sub>2</sub>), SpHb<sup>®</sup> (SpO<sub>2</sub>) and arterial blood gas (SO<sub>2</sub>) were noted at the same point of time.

Data analysis was performed using SPSS<sup>®</sup> 17. Statistical analysis summarised the distribution of observed differences

using means, medians and ranges. Following the approach recommended by Bland and Altman,<sup>2</sup> owing to the possibility of within-individual correlation between successive measurements, standard deviation (SD) was estimated using mixed-effect, linear regression models.<sup>2</sup> Statistical significance was achieved when the *p*-value was less than 0.05. The Bland-Altman plot shows the relationship between observed differences (between values obtained from two different methods) and the mean of two measures. Horizontal lines correspond to the limits of agreement, and each dot represents individual values. The limits of agreement between the two methods were calculated as the mean  $\pm$  2 SD of the differences between the results obtained. If the differences are normally distributed, 95% of the differences between the methods lie between these limits, and the two methods can be used interchangeably if these differences are not clinically important.<sup>3</sup>

## Results

Thirty patients participated in the study. However, the data for only 22 patients was analysed, the PI was less than 1.4 in eight patients (values of Hb obtained with a PI of less than 1.4 are not recommended by the manufacturer). Our primary outcome variables were the SpHb<sup>®</sup>-tHb and SpHb<sup>®</sup>-aHb differences. Table 1 shows the patient characteristics. Table 2 shows the PI, methHb, Hb values (SpHb<sup>®</sup>, laboratory and ABG) and blood oxygen saturation (pulse oximeter, SpHb<sup>®</sup> and ABG) for individual patients. The mean Hb concentration was 11.4 g/dl, 10.59 g/dl and 10.4 g/dl, using the SpHb<sup>®</sup>, laboratory and ABG, respectively. MethHb values were also measured, which were in

the range of (1.4–3.3%), and the PI varied between 1.5 and 9.8. Table 3 shows the correlation between the paired samples.

Figure 1 displays the Bland-Altman plot of the relationship between the observed differences between aHb and SpHb<sup>®</sup> (ABG-SpHb<sup>®</sup>) and the mean of the two measures. Limits of agreement (horizontal lines) indicate that 21 of the 22 estimates of SpHb<sup>®</sup> were within the limits. The limits of agreement are defined as the mean difference  $\pm$  2 SD, and the calculated lower and upper limits for aHb-SpHb<sup>®</sup> are between  $-3.7$  to  $+3.6$ . Figure 2 displays the Bland-Altman plot of the relationship between observed differences between tHb and SpHb<sup>®</sup> (laboratory-Radical-7<sup>®</sup> Pulse Co-oximeter) and the mean of the two measures. Limits of agreement (horizontal lines) indicate that 21 of the 22 estimates of SpHb<sup>®</sup> were within the limits ( $-4.7$  to  $+3$ ). Figure 3 displays the Bland-Altman plot of

**Table 1:** Patient characteristics

Weight in kg*	67.3 (10.26)
Age in years*	30.19 (11.63)
Male to female ( <i>n</i> )	12:10
<b>Diagnosis (<i>n</i>)</b>	
Pituitary adenoma	2
Meningioma	8
Glioma	4
Acoustic schwannoma	2
Basal ganglia bleed	4
Aneurysm	2

\* mean (standard deviation)

**Table 2:** Data of individual patients obtained from the Radical-7<sup>®</sup> Pulse Co-oximeter, the laboratory, arterial blood gas and the pulse oximeter

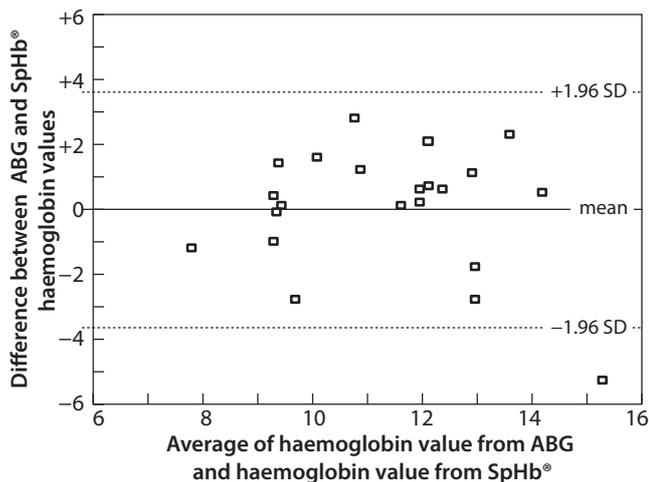
Patient	PI	MetHb	SpHB <sup>®</sup> (g/dl)	tHb (g/dl)	aHb (g/dl) (%)	SpO <sub>2</sub> (%)	SpO <sub>2</sub> SpHB <sup>®</sup> (%)	SO <sub>2</sub>
1	2.8	2.8	10.3	11.2	11.5	100	99	97.9
2	2.1	1.8	11.1	8.1	8.3	100	100	100
3	2.3	3.3	8.7	9.5	10.1	99	97	97.9
4	1.6	2.3	11.8	11.6	12.5	100	100	100
5	1.6	1.5	9.1	9.1	9.5	100	100	100
6	1.7	2	9.4	11.3	12.2	100	100	100
7	3.9	2	11.9	11.3	12.1	100	100	99.9
8	1.5	1.8	13.9	11	12.1	100	100	100
9	4.6	2.3	11.6	10.5	11.7	99	100	100
10	3.9	1.8	9.4	9.2	9.5	99	98	100
11	1.6	1.6	9.8	8.3	8.8	98	100	99.9
12	3.2	2.8	12.1	12.6	12.7	100	100	100
13	8.4	1.5	14	12.7	14.5	99	100	100
14	4.6	2.4	12.5	13	14.8	99	98	100
15	1.6	2.1	12.4	12.6	13.5	98	97	98
16	4.1	2.6	18	11.2	12.7	99	100	100
17	1.4	1.4	11.7	11	12.3	100	100	100
18	5.2	2	14.4	10.4	11.6	100	100	100
19	2.2	2.2	9.3	10.1	10.9	100	100	100
20	2.5	2.1	8.4	7	7.2	99	100	100
21	9.8	1.6	9.4	8.7	9.3	100	100	100
22	8.1	1.6	11.8	12.6	12.5	100	100	100

aHb: haemoglobin estimation (arterial blood gas), MetHb: methaemoglobin, PI: perfusion index, SO<sub>2</sub>: oxygen saturation (arterial blood gas), SpHb<sup>®</sup>: haemoglobin estimation using the Radical-7<sup>®</sup> Pulse Co-oximeter, SpO<sub>2</sub>: oxygen saturation (pulse oximeter), SpO<sub>2</sub> SpHb<sup>®</sup>: oxygen saturation (SpHb<sup>®</sup>), tHb: haemoglobin estimation (laboratory)

**Table 3:** Paired sample correlation between the various methods of haemoglobin estimation

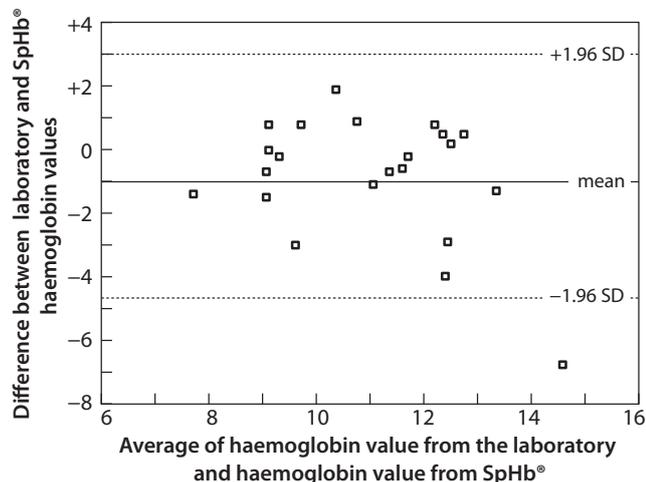
Pairs	<i>n</i>	Correlation	Significance
Pair 1: Haemoglobin estimation (SpHb <sup>®</sup> ) and haemoglobin estimation (tHb)	22	0.553	0.008
Pair 2: Haemoglobin estimation (SpHb <sup>®</sup> ) and haemoglobin estimation (ABG)	22	0.634	0.002
Pair 3: Haemoglobin estimation (tHb) and haemoglobin estimation (ABG)	22	0.970	0.000

ABG: arterial blood gas, *n*: number of patients, SpHb<sup>®</sup>: Radical-7<sup>®</sup> Pulse Co-oximeter, tHb: laboratory



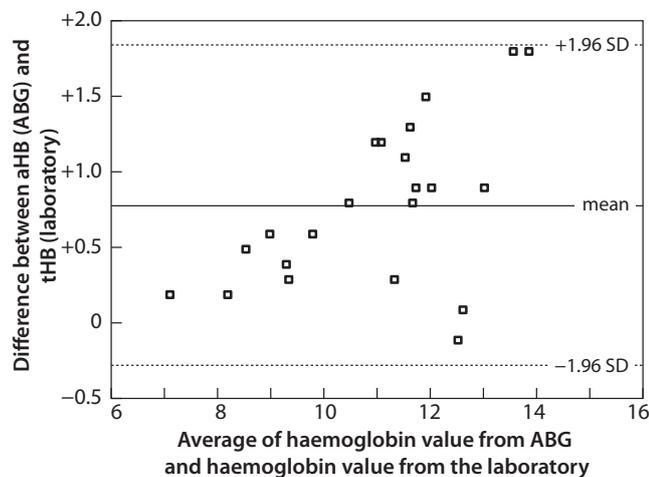
ABG: arterial blood gas, aHb: haemoglobin estimation by the ABG method, SD: standard deviation, SpHb<sup>®</sup>: Radical-7<sup>®</sup> Pulse Co-oximeter

**Figure 1:** Bland-Altman plot of relationship between observed differences between aHb-SpHb<sup>®</sup> (ABG-Radical-7<sup>®</sup> Pulse Co-oximeter) and the mean of two measures



SD: standard deviation, SpHb<sup>®</sup>: Radical-7<sup>®</sup> Pulse Co-oximeter, tHb: haemoglobin estimation from the laboratory

**Figure 2:** Bland-Altman plot of relationship between observed differences between tHb-SpHb<sup>®</sup> (laboratory-Radical-7<sup>®</sup> Pulse Co-oximeter) and the mean of two measures



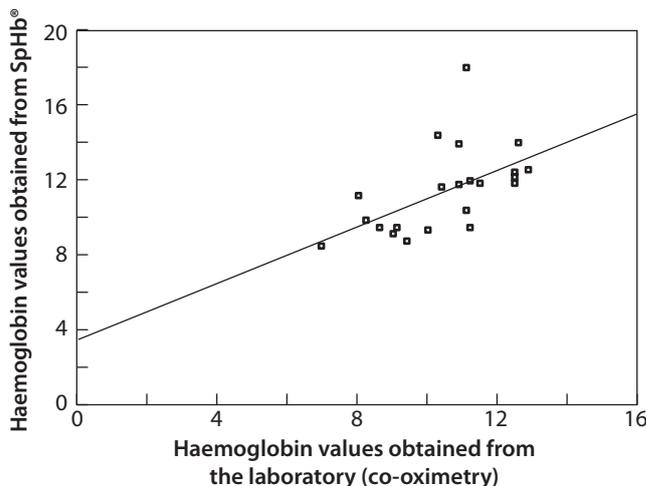
ABG: arterial blood gas, aHb (ABG): aHb: haemoglobin estimation by the ABG method (arterial blood gas), SD: standard deviation, tHb: haemoglobin estimation from the laboratory

**Figure 3:** Bland-Altman plot of relationship between observed differences between aHb-tHb (ABG-laboratory) and the mean of two measures

the relationship between observed differences between aHb and tHb (ABG-laboratory) and the mean of the two measures. Limits of agreement (horizontal lines) indicate that 22 of the 22 estimates were within the limits (-0.26 to +1.84). In Figures 4 and 5, the regression lines show the relation between the SpHb<sup>®</sup> and tHb (laboratory) trends and SpHb<sup>®</sup> and aHb (ABG) trends, respectively.

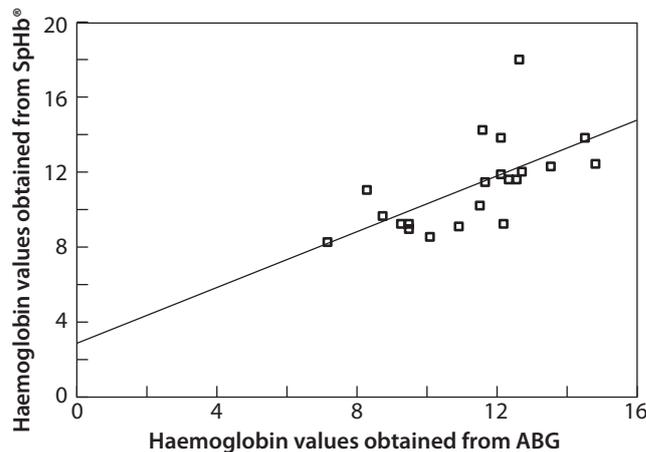
**Discussion**

The findings of our study suggest that, although the non-invasive monitor provided continuous and immediate Hb values, currently, it is unable to replace invasive Hb monitoring techniques. Based on the results of the Bland-Altman plots, the two methods can be used interchangeably if the differences fall between the 95% confidence interval (CI) of the difference, and if the differences are not clinically important. In this study, the calculated 95% CI for the difference calculated on the sample (ABG analysis and SpHb<sup>®</sup>) was -3.7 to 3.6. Therefore, a measurement might really be 10 mg/dl, but could be reported to be low as 6.3 mg/dl or as high as 13.6 mg/dl. This is undoubtedly a clinically important difference, and hence making decisions for blood transfusions based on these results would not be acceptable. The same is true for the difference between SpHb<sup>®</sup> and the laboratory Hb values. This wide variation may be either owing to the small sample size of the study, or to a variation in the accuracy of the non-invasive



SpHb<sup>®</sup>: Radical-7<sup>®</sup> Pulse Co-oximeter; R<sup>2</sup> = 0.3

**Figure 4:** Relationship between Radical-7<sup>®</sup> Pulse Co-oximeter (SpHb<sup>®</sup>) and laboratory (tHb) trends



ABG: arterial blood gas, SpHb<sup>®</sup>: Radical-7<sup>®</sup> Pulse Co-oximeter; R<sup>2</sup> = 0.4014

**Figure 5:** Relationship between SpHb<sup>®</sup> and aHb (ABG) trends

monitor. However, the inaccuracy of SpHb<sup>®</sup> was the most likely explanation as the Hb values obtained from ABG analysis demonstrated good correlation with the laboratory values in same patients.

Moreover, in 8 out of 30 patients enrolled in the study, the Hb values were not obtained using the non-invasive monitor, a major limitation thereof. This further questions the clinical utility of this device. There are several variables that could have influenced the differences found between the non-invasive SpHb<sup>®</sup> and tHb (laboratory) measurements. Peripheral perfusion at the site of the measurement of SpHb<sup>®</sup> might have influenced the detection of Hb levels. The function of the SpHb<sup>®</sup> sensor depends on adequate blood flow to the finger, as indirectly reflected by the PI. The PI is a calculated value that is displayed together with the SpHb<sup>®</sup>, because obtaining SpHb<sup>®</sup> values with a PI < 1.4 is not recommended by the manufacturer.<sup>1</sup> When perfusion diminishes, SpHb<sup>®</sup> underestimates true Hb, so it should not be used to determine the need for blood transfusions without validation using a direct (invasive) measurement method.<sup>1</sup> As perfusion improves, the SpHb<sup>®</sup> becomes a more accurate measurement methodology. Therefore, the PI is as useful a clinical guide, as is the actual SpHb<sup>®</sup> measurement.<sup>1</sup> In our study, we excluded patients who had a PI less than 1.4. In this study, we found poor correlation (Table 3 and Figures 4 and 5) between the non-invasive (SpHb<sup>®</sup>) and invasive methods (laboratory and ABG). The correlation coefficient between the SpHb<sup>®</sup> and laboratory values was 0.553, and that between the SpHb<sup>®</sup> and arterial blood gas analysis values was 0.634, as against the laboratory and arterial blood gas analysis values, which had good correlation (a correlation co-efficient of 0.97). The correlation value close to 0.5 showed virtually no correlation. Nelson's syndrome was detected in one sample in which Hb determination by SpHb<sup>®</sup> was fairly high (18 g/dl) in comparison to the Hb values from the laboratory and ABG method. The SpHb<sup>®</sup> values in this sample did not lie within the limits of correlation. However, the laboratory and arterial gas blood analysis values correlated well in this patient. This might partly explain the poor correlation between the non-invasive and invasive techniques.

Hahn et al<sup>4</sup> recently published the results of a study using the SpHb<sup>®</sup> (version 7.4.0.9), with a repeated-use probe that lasts for 60 hours. The authors concluded that non-invasive continuous Hb monitoring (SpHb<sup>®</sup>) could not provide useful kinetic data in individuals during volume loading. In addition, two other recent works that assessed the same device reported controversial results on the accuracy of this device.<sup>4,5</sup> Specifically, an inverse relationship was found between the pulse-oximeter saturation (SpO<sub>2</sub>) value and bias in the SpHb<sup>®</sup> measurement in one study.<sup>6</sup>

A recent pilot study assessed the relationship between the fraction-of-inspired oxygen (FiO<sub>2</sub>) and SpHb<sup>®</sup>, as indicated by the SpHb<sup>®</sup>.<sup>7</sup> While patients received 100% oxygen via a facemask, FiO<sub>2</sub>, SpO<sub>2</sub> and SpHb<sup>®</sup> were continuously recorded until the end-expiratory oxygen fraction was > 90%. Thereafter, anaesthesia was initiated. The mean SpHb<sup>®</sup> between FiO<sub>2</sub> at 21%, and FiO<sub>2</sub> at 100%, increased in four patients, decreased in two and remained stable in two, resulting in an overall significant increase of SpHb<sup>®</sup> during pre-oxygenation (non-linear, mixed-effect model). There was no change in volume or blood mass.<sup>7</sup>

Preliminary evidence from studies in non-obstetric surgical patients indicates that the mean difference in SpHb<sup>®</sup> to aHb is approximately 1 g/dl.<sup>5,8,9</sup> Butwick et al<sup>10</sup> reported that SpHb<sup>®</sup> values from the SpHb<sup>®</sup> were higher than laboratory Hb concentrations in 16/17 venous and arterial blood samples. Despite a significant correlation between SpHb<sup>®</sup> and laboratory Hb values ( $r = 0.90$ ), they suspected that this device overestimated SpHb<sup>®</sup> values as median SpHb<sup>®</sup> values were significantly higher than laboratory Hb values. With further improvements in technology, we may be able to gain better insight into the relationship between perfusion, acute changes in Hb and intravascular volume through the performance of this non-invasive monitor, and in future, non-invasive Hb monitor (SpHb<sup>®</sup>) may become the standard monitor of care for assessing patients at risk of bleeding, and also to guide transfusion therapy.<sup>1</sup>

On the basis of the findings in this study, we propose that the SpHb<sup>®</sup> does not have sufficient accuracy to minimise the need for invasive Hb monitoring, and could not be used effectively in eight out of 30 (27%) patients because of low PI due to poor perfusion.

*Conflict of interest* — The authors declare that they have no financial or personal relationships which may have inappropriately influenced them in writing this paper.

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