Heart, Lung and Vessels. 2014; 6(3): 197-203

Direct comparison between cerebral oximetry by INVOS™ and EQUANOX™ during cardiac surgery: a pilot study

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Heart, Lung and Vessels. 2014; 6(3): 197-203

ABSTRACT

Introduction: Several near-infrared spectroscopy oximeters are commercially available for clinical use, with lack of standardization among them. Accordingly, cerebral oxygen saturation thresholds for hypoxia/ischemia identified in studies conducted with INVOS™ models do not necessarily apply to other devices. In this study, the measurements made with both INVOS™ and EQUANOX™ oximeters on the forehead of 10 patients during conventional cardiac surgery are directly compared, in order to evaluate the interchangeability of these two devices in clinical practice.
Methods: Cerebral oxygen saturation measurements were collected from both INVOS™ 5100C and EQUANOX™ 7600 before anesthetic induction (baseline), two minutes after tracheal intubation, at cardiopulmonary bypass onset/offset, at aortic cross-clamping/unclamping, at the end of surgery and whenever at least one of the two devices measured a reduction in cerebral oxygen saturation equal to or greater than 20% of the baseline value. Bland-Altman analysis was used to compare the bias and limits of agreement between the two devices.
Results: A total of 140 paired measurements were recorded. The mean bias between INVOS™ and EQUANOX™ was -5.1%, and limits of agreement were ± 16.37%. Considering the values as percent of baseline, the mean bias was -1.43% and limits of agreement were ± 16.47. A proportional bias was observed for both absolute values and changes from baseline.
Conclusions: INVOS™ and EQUANOX™ do not seem to be interchangeable in measuring both absolute values and dynamic changes of cerebral oxygen saturation during cardiac surgery. Large investigations, with appropriate design, are needed in order to identify any device-specific threshold.

Keywords: *near-infrared spectroscopy, cerebral oximetry, cardiac surgery.*

INTRODUCTION

In recent years, near-infrared spectroscopy (NIRS) is increasingly used to monitor regional cerebral oxygen saturation (rSO_2) during cardiac surgery (1-4). In fact, neurologic injury is still a common complication after cardiac surgery, with rates of postoperative neurocognitive decline (PONCD) and stroke of up to 50% and 1-3%, respectively (5). Moreover, stroke after cardiac surgery results in a 10-fold increase in mortality and in a 3-fold increase in hospital stay (6). In an attempt to reduce these potentially disastrous complications, NIRS has been therefore advocated as a routine monitor to prevent or minimize brain injury by detecting cerebral oxygen supply-demand imbalances (7-9). Actually, several experimental

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data are gradually accumulating to show that both preoperative values and intraoperative changes of rSO_2 can predict important complications and long-term outcomes after cardiac surgery, including stroke (10), delirium (11), neurocognitive decline (12), organ dysfunction (13, 14), length of hospital stay (12, 13, 15) and mortality (14).
Nevertheless, not everyone considers these evidences sufficient to justify the routine use of NIRS monitoring in cardiac surgery (4, 16), that remains debated (7, 17) and poorly defined, with little consensus for its appropriate use (3). Probably, one of the reasons for this is the poor agreement among different devices (3, 7, 17-19), that has been also confirmed by two recent investigations (2, 20).
Currently, several NIRS devices are commercially available for clinical use, with lack of standardization among them (2, 16, 19, 21). In fact, although the various models are mostly based on spatial resolution spectroscopy (16, 22), they differ in numerous important aspects related to the acquisition of their cerebral oxygen saturation measurements, including the algorithms adopted, the type of light source, the wavelengths of light emitted and the distance between the various light emitters and detectors (19). This makes comparisons between clinical studies using different devices difficult and, therefore, rSO_2 thresholds for the development of hypoxia/ischemia remain elusive (23, 24). Particularly, since the majority of clinical data currently available have been generated using various INVOS™ devices (the first to be approved by the U.S.A. Food and Drug Administration) (16), it is not clear whether the thresholds identified in studies conducted with these models (11, 12-14, 25) may also apply to devices from other companies.
In the present study, for the first time far as the authors know, the measurements made by both INVOS™ and EQUANOX™ NIRS oximeters on the forehead of adult patients during different moments of cardiac surgical procedures are directly compared, with the objectives of evaluating both the feasibility of such simultaneous measurements and the interchangeability of the two devices in clinical practice.

METHODS

The study protocol was approved by the local Ethical Committee. After informed consent, 10 patients (6 males, 4 females), mean age 65.1 ± 15.84, scheduled for conventional cardiac surgery with or without cardiopulmonary bypass (CPB) were enrolled in the study (*Table 1*).
Two different NIRS monitors were applied to patients: the 2-wavelength INVOS™ 5100C (Somanetics, Troy, MI) and the 3-wavelength EQUANOX™ 7600 (Nonin Medical, Inc, Plymouth, MN).
After rubbing and cleaning the skin with an alcohol swab, 2 sensors (one left and one right) Adult SomaSensor SAFB-SM (Covidien, Mansfield, MA) and 2 sensors (one left and one right) EQUANOX™ ADVANCE™ Sensor-Adult model 8004 CA (Nonin Medical, Inc, Plymouth, MN) were placed over the forehead of the patients, as close as possible, being careful not to overlap light emitters and detectors. INVOS™ sensors were placed lower than EQUANOX™ ones in five patients, and higher than EQUANOX™ ones in the other five (*Figure 1*). All sensors where then connected to the respective devices via their proprietary cables.
Regional cerebral oxygen saturation (rSO_2) measurements were collected before anesthetic induction with patients breathing ambient air (baseline values), two minutes after tracheal intubation, two minutes after CPB onset, at aortic cross-clamping, at aortic unclamping, at CPB offset (when appli-

Table 1 - *Age, sex, type of surgery, number of measurements recorded (from each device) and number of desaturations ≥20% from baseline (displayed by one or both of the two devices) of the patients investigated.*

Patient N.	Sex	Age (years)	Type of surgery	N. of measurements (L + R)	N. of desaturations ≥20% from baseline		
					INVOS™	EQUANOX™	Both
1	M	63	AVR	14	0	0	0
2	M	60	CABG	20	**5**	**3**	**3**
3	F	79	OPCAB	12	**5**	0	0
4	M	79	MVR + CABG	20	**6**	0	0
5	M	75	CABG	14	0	0	0
6	M	44	AVR	14	0	0	0
7	M	75	MVR	14	0	0	0
8	F	70	OPCAB	6	0	0	0
9	F	74	OPCAB	12	**4**	0	0
10	F	32	MVR	14	0	0	0

M = male; F = female; L = left; R = right; AVR = aortic valve replacement; CABG = coronary artery bypass graft; OPCAB = off-pump coronary artery bypass; MVR = mitral valve replacement.

cable), at the end of surgery and whenever at least one of the two devices measured a bilateral or monolateral reduction in cerebral oxygen saturation equal to or greater than 20% of the baseline value. Each measurement, as well as an absolute value, was also recorded as a percentage of the respective baseline value according to the formula:

% of baseline=absolute valuex100/baseline value.

In all patients, whilst the EQUANOX™ monitor seemed not significantly influenced by the presence of the operating INVOS™ sensors, no rSO2 values were displayed (and a "poor signal quality" error message appeared) on the INVOS™

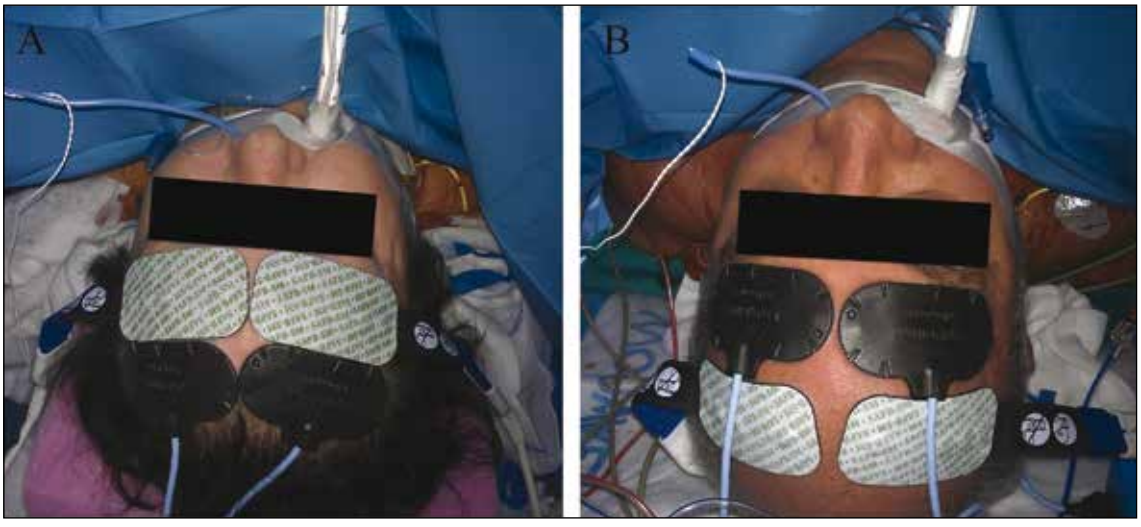

Figure 1 - *Relative positioning of NIRS sensors on the forehead of patients 1, 3, 5, 7 and 9 (panel A) and 2, 4, 6, 8 and 10 (panel B). NIRS = near-infrared spectroscopy.*

oximeter when the EQUANOX™ device was switched on. For this reason, it was not possible to record the rSO_2 values from the two devices simultaneously. Therefore, immediately after collecting INVOS™ data, it was turned off and, simultaneously, the EQUANOX™ device was turned on and its data were recorded.

Bland-Altman analysis was used to compare the bias and limits of agreement (bias ± standard deviation x 1.96) between the two devices. Moreover, linear regression was applied to the Bland-Altman plots in order to test the presence of a proportional bias. IBM SPSS Statistics software v 19.0 (IBM, Armonk, New York) was used for statistical analysis. A 2-tailed value of $p < 0.05$ was considered significant.

RESULTS

A total of 140 measurements (70 left, 70 right) were collected from both devices in the 10 patients (*Table 1*). The mean bias between INVOS™ and EQUANOX™ was -5.1 %, and limits of agreement were ± 16.37 %. (*Figure 2A*) The Bland-Altman plot showed the presence of a statistically significant proportional bias (n = 140; R = 0.541; $R^2 = 0.293$; p = 0.000).

When considering the dynamic changes of rSO_2 (expressed as percent of baseline) showed by the two devices (120 measurements), the mean bias was -1.43 % and limits of agreement were ± 16.47 (*Figure 2B*). Also in this case, there was a significant proportional bias (n = 120; R = 0.680; $R^2 = 0.462$; p = 0.000).

Interestingly, of the 20 total episodes (considering each individual sensor) of significant (or "threshold") cerebral desaturation (i.e., a reduction equal to or greater than 20 % from baseline) (25, 26) reported by INVOS™ in four patients, mostly during heart displacement for coronary artery exposure or during episodes of hypotension over CPB, only 3 (in one patient) were also reported by EQUANOX™. No other "threshold" desaturation was reported by EQUANOX™ (*Table 1*).

All significant desaturations were prompt-

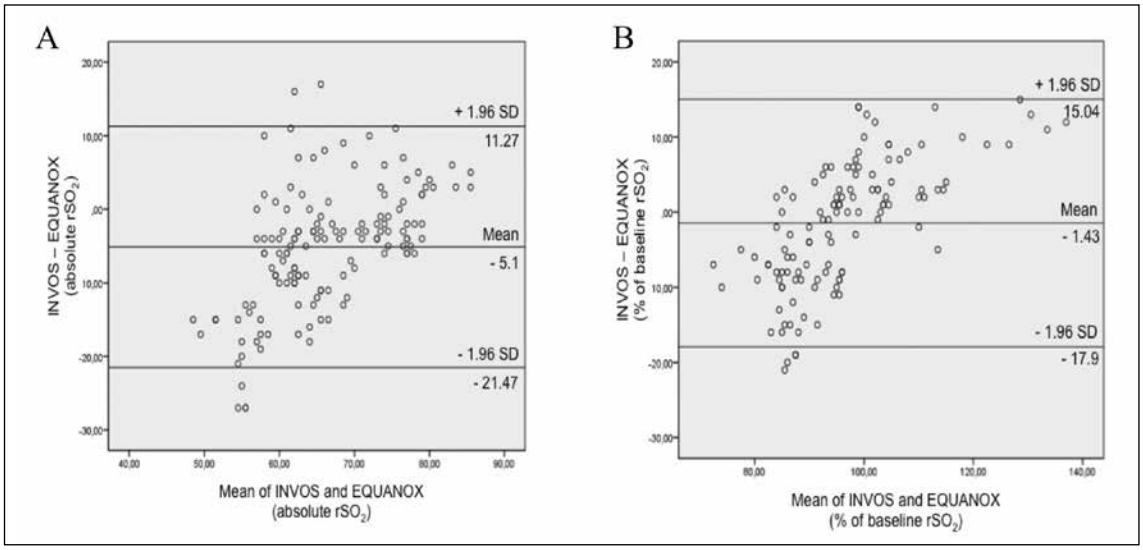

Figure 2 - *Bland-Altman analysis between absolute values (panel A) and changes from baseline (panel B) of rSO2 measured by INVOSTM and EQUANOXTM in the 10 patients.*

ly corrected with conventional strategies (such as administer fluids or vasopressors or raise pump flow) (13) and no patients had complications.

DISCUSSION

The results of this investigation suggest a clinically important difference between INVOS™ and EQUANOX™ in measuring cerebral oxygen saturation as well as its variations during cardiac surgery, probably due to some of the characteristics in which they differ (such as the number of light emitters and detectors, the different distance between them and, consequently, a different tissue penetration of light, the number of wavelengths adopted, and a different built-in proprietary algorithm to assess oxygen saturation) (20).

In particular, in our series the bias between INVOS™ and EQUANOX™ in measuring absolute values of rSO_2 showed a moderate correlation with the mean values from the two devices, with a tendency of INVOS™ to underestimation (or a tendency of EQUANOX™ to overestimation) for the lower values. Of course, it is rather difficult to determine which of the two devices provide the "more true" absolute values.

Most importantly, the limits of agreement were very wide. Accordingly, the two devices do not seem to be interchangeable in routine clinical practice. Therefore, the results of previous investigations that identified threshold absolute values of rSO_2 able to predict outcomes such as postoperative delirium (11) and mortality (14) using INVOS™ may not to be applicable to EQUANOX™.

While these results are not particularly surprising, given that a poor reliability of absolute values of rSO_2 measured by INVOS™ had already been showed (27, 28), the similar differences observed also in changes from baseline given by the two devices require caution in interpreting trends given by EQUANOX™ according to thresholds previously identified in studies using INVOS™ (1, 12-14, 25, 26). In fact, although the mean inter-device bias for dynamic changes of rSO_2 was lower than that for the absolute values, the limits of agreement were, also in this case, wide. Moreover, an even stronger proportional bias was observed, meaning that the two devices may display a different magnitude of desaturation in similar clinical situations. Accordingly, we observed much more "threshold" desaturations from INVOS™ than from EQUANOX™, although the number of episodes is not sufficient for confident statistical analysis.

Of course, these results do not exclude that both devices may adequately describe the variations in cerebral oxygen supply-demand balance, although device-specific thresholds are probably needed to interpret correctly these variations in clinical practice.

Our findings are consistent with the results of other recent investigations. In fact, even if this is the first report of a direct comparison between INVOS™ and EQUANOX™ measurements at cerebral level and in a clinical context, the agreement between the two devices has been previously evaluated, both directly (2, 20) and indirectly (2, 19, 29), in healthy volunteers. Davie et al. (19) reported variable sensitivity to extracranial tissue contamination among INVOS™, EQUANOX™, and FORE-SIGHT® (CAS Medical Systems, Inc, Brandford, CT) devices. This may partly explain the inter-device differences in absolute values of rSO_2, but should not significantly affect the variations from baseline. However, Fellahi et al. (20) and Hyttel-Sorensen et al. (29) demonstrated that INVOS™ and EQUANOX™, positioned simultaneously on calves or one at the time on forearms of healthy

volunteers, respectively, are not comparable in measuring both absolute values and dynamic changes of peripheral rSO_2 after vascular occlusion tests. Finally, Bickler et al. (2) evaluated the performance of five commercially available cerebral oximeters (including INVOS™ and EQUANOX™), applied two at the time per subject in 23 adult healthy volunteers, and found a large variation in reading bias (calculated as the difference between the instrument's reading with the weighted saturation of venous and arterial blood) between subjects, especially during hypoxia. Similar differences were also found when comparing INVOS™ with other devices (18, 30).

This study has several limitations, the most important being the small number of patients enrolled. However, the number of paired measurements, that can be considered independent among themselves, allows us to give some significance to our findings. One of the reasons why we limited our observations to a few patients is the convinction, gained during the collection of these initial data, that different study designs may be preferable in order to investigate the differences among the various devices. In fact, direct comparison of two NIRS devices seems to be somewhat difficult, since the sampled areas, though close, are not the same and interferences between the two sensors can not be excluded (20, 30). Regarding the latter, we report for the first time an important interference, due to which the paired measurements were not simultaneous but spaced each other by a few seconds, that is another important limitation of the present study. Maybe, in other investigations not reporting such interference, the distances between sensors were greater: in fact, Fellahi et al. (20) placed the sensors on calves, while Bickler et al. (2) applied only two sensors (one for each device) on the forehead, instead of four as in this report. A plausible explanation for INVOS™ but not EQUANOX™ being markedly disturbed by the other device is the use of three wavelengths (730, 810 and 880 nm) by EQUANOX™ and two wavelengths by INVOS™, in particular two of the three used by EQUANOX™ (730 and 810 nm).

CONCLUSION

The present study suggests that INVOS™ and EQUANOX™ are not interchangeable in measuring both absolute values and dynamic changes of cerebral rSO_2 during cardiac surgery. Accordingly, device-specific thresholds are probably needed to guide interventions aimed to prevent postoperative brain injury as well as other adverse outcomes. Since direct comparison of NIRS devices in such clinical context seems to be of poor feasibility and difficult interpretation, large investigations on each device are needed in order to identify any of such specific thresholds and to allow a more extensive and better-defined use of this promising technology.

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Cite this article as: Pisano A, Galdieri N, Iovino TP, Angelone M, Corcione A. Direct comparison between cerebral oximetry by INVOS™ and EQUANOX™ during cardiac surgery: a pilot study. Heart, Lung and Vessels. 2014; 6(3): 197-203.

Source of Support: Nil. **Disclosures:** Dr. Galdieri and Dr. Pisano have lectured in a course entitled "INVOS monitoring in cardiac and vascular surgery". Dr. Galdieri received a grant from Covidien for this.