

TRANSLATIONAL RESEARCH

Feasibility and accuracy of nasal alar pulse oximetry

T. E. Morey^{1*}, M. J. Rice¹, T. Vasilopoulos², D. M. Dennis^{1,3} and R. J. Melker^{1,3}

¹ Department of Anesthesiology, University of Florida, PO 100254, 1600 SW Archer Road, Gainesville, FL 32601-0254, USA

² Department of Psychiatry and Behavioral Neuroscience, University of Chicago, 5841 S. Maryland Ave., MC 3077, CNPRU, Room L-603, Chicago, IL 60637, USA

³ Xhale, Inc., 3630 SW 47th Ave., Suite 100, Gainesville, FL 32608, USA

* Corresponding author. E-mail: morey@ufl.edu

Editor's key points

- Nasal pulse oximetry is an attractive alternative when digital perfusion is poor or inaccessible.
- Use of monitoring devices outside of their intended use requires specific validation.
- Results obtained from volunteer studies may not translate to the clinical environment.
- The performance of monitoring devices is most crucial at the margins of the normal range.

Background. The nasal ala is an attractive site for pulse oximetry because of perfusion by branches of the external and internal carotid arteries. We evaluated the accuracy of a novel pulse oximetry sensor custom designed for the nasal ala.

Methods. After IRB approval, healthy non-smoking subjects [$n=12$; aged 28 (23–41) yr; 6M/6F] breathed hypoxic mixtures of fresh gas by a facemask to achieve oxyhaemoglobin saturations of 70–100% measured by traditional co-oximetry from radial artery samples. Concurrent alar and finger pulse oximetry values were measured using probes designed for these sites. Data were analysed using the Bland–Altman method for multiple observations per subject.

Results. Bias, precision, and accuracy root mean square error (A_{RMS}) over a range of 70–100% were significantly better for the alar probe compared with a standard finger probe. The mean bias for the alar and finger probes was 0.73% and 1.90% ($P<0.001$), respectively, with corresponding precision values of 1.65 and 1.83 ($P=0.015$) and A_{RMS} values of 1.78% and 2.72% ($P=0.047$). The coefficients of determination were 0.96 and 0.96 for the alar and finger probes, respectively. The within/between-subject variation for the alar and finger probes were 1.14/1.57% and 1.87/1.47%, respectively. The limits of agreement were 3.96/–2.50% and 5.48/–1.68% for the alar and finger probes, respectively.

Conclusions. Nasal alar pulse oximetry is feasible and demonstrates accurate pulse oximetry values over a range of 70–100%. The alar probe demonstrated greater accuracy compared with a conventional finger pulse oximeter.

Keywords: alar nasal cartilages; lateral nasal cartilages; nasal cartilages; oximetry; pulse oximetry

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Pulse oximetry remains a vital tool in healthcare facilities and a standard monitor to measure the oxygenation of patients receiving anaesthesia. Fingers are a commonly used site for probe placement, but may be suboptimal because diminished perfusion from numerous causes may result in loss of sufficient pulse signal to provide an accurate pulse oximetry oxygen saturation (Sp_{O_2}).^{1–3} Additionally, finger use may be limited by injury, presence on the surgical field, non-invasive arterial pressure cuff interruption, arm tucking, and shivering.^{4–6} Finally, digital pulse oximetry produces an unacceptably high incidence of failure (79%) during emergency pre-hospital airway management.⁷ Therefore, application to sites other than fingers may be useful. Several alternative probe sites on the head have been suggested (e.g. earlobe, forehead, cheek, tongue) because perfusion to these structures may provide adequate pulsatile signal even in the presence of significant pathophysiology and because the time to detect desaturation

is less when measured from a site on the head, compared with a finger or toe.^{8–12}

Recently, Saban and colleagues¹³ demonstrated that branches of both the facial and ophthalmic arteries perfuse the nasal alae, the lateral walls of the nares (Fig. 1).¹³ The ophthalmic artery, which is a branch of the internal carotid artery, has been shown to autoregulate during experimental hypotension to preserve blood flow.^{14 15} Integrating these anatomical and physiological data, we hypothesize that the nasal ala should be a suitable pulse oximetry location. As a first step, the primary aim of this investigation was to validate the performance characteristics of alar pulse oximetry probes similar to the seminal pulse oximeter evaluations of Yelderian and New¹⁶ in 1983. In healthy subjects receiving hypoxic mixtures of gas to generate oxygen saturations of 70–100%, we compared novel alar pulse oximetry and conventional finger pulse oximetry with the reference standard, co-oximetry measurement of radial artery blood specimens

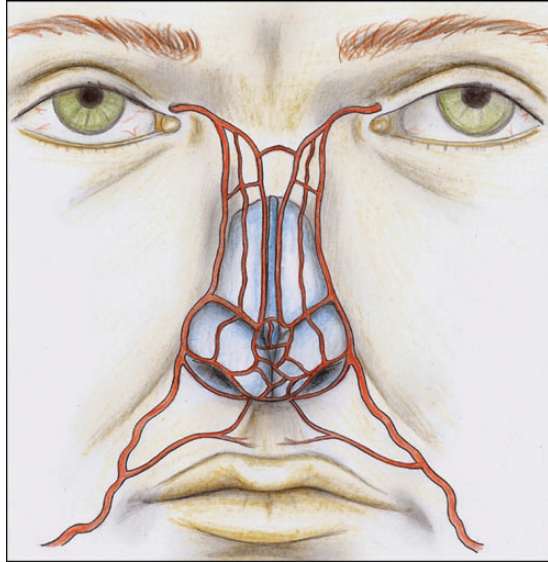


Fig 1 Reproduction of the anastomotic polygonal system forming the arterial supply of the nose that includes the facial artery from the external carotid artery and the nasal branch of the ophthalmic artery from the internal carotid artery. Note the anastomosis of the external and internal carotid arterial system at the right and left ala. Reproduced from Saban and colleagues¹³ with permission. ©(2012) American Medical Association. All rights reserved.

Methods

Subject recruitment

This non-treatment investigation was approved by the University of California at San Francisco Committee on Human Research under protocol H6301-01706-24 and was conducted at the HYPO₂XIALAB at that institution (San Francisco, CA, USA). Written, informed consent was obtained from all recruited subjects, who were aged 18–50 yr. Subjects self-identified their own ethnic and racial categories as defined by the National Institutes of Health. Exclusionary criteria were history of tobacco smoking, hypertension, respiratory disease, or haemoglobin ≤ 10 g dl⁻¹.

Protocol

On the day of study, a catheter was inserted using aseptic technique into a radial artery of each subject in order to aspirate blood for determination of arterial oxyhaemoglobin saturation (Sa_{O_2}). Values for Sa_{O_2} were measured using a multi-wavelength oximeter (OSM3[®] Hemoximeter, Radiometer Medical A/S, Copenhagen, Denmark), which served as the reference standard for subsequent comparisons with Sp_{O_2} readings. An alar pulse oximeter sensor (Assurance BioSense, Inc., Glastonbury, CT, USA) was placed on the right ala to measure Sp_{O_2} . An additional, conventional pulse oximeter probe and monitor was placed on the index finger for reference purposes (N-595 Pulse Oximeter, Mallinckrodt Inc., St Louis, MO, USA). Date- and

time-stamped data (Sp_{O_2} , heart rate) were collected from the probes at a rate of 1 Hz and automatically logged onto a spreadsheet supported by a personal computer for later analysis.

After instrumentation, subjects began the experimental protocol for desaturation similar to that previously conducted in this laboratory.¹⁷ In brief, subjects were in a 30–45° head-up position. Two arterial blood samples were obtained <30 s apart while each subject breathed room air. After aspiration of blood (2 ml), the samples were immediately processed and analysed to measure the Sa_{O_2} . Investigators placed a tight-fitting full facemask to prevent entrainment of room air. Thereafter, hypoxia was induced by supplying a fresh gas mixture of nitrogen, room air, and carbon dioxide. Each plateau level of oxyhaemoglobin saturation was maintained for at least 30 s until pulse oximeter readings stabilized. Then, two arterial blood samples were obtained ~30 s apart. Each stable plateau was therefore maintained for at least 60 s defined by Sp_{O_2} variation $\leq 3\%$. The different plateaus were nominally at 98–100% (room air saturation), 93%, 90%, 87%, 85%, 82%, 80%, 77%, 75%, and 70%. This procedure was performed twice with the second epoch completing any saturation values missed during the first run. Approximately 25 samples were obtained across this anticipated range of saturation (70–100%) for each subject that completed the protocol.

Statistical analysis

Descriptive data are reported as mean (sd). Data were analysed to calculate bias, precision, and the accuracy root mean square error (A_{RMS}). A_{RMS} is a composite value determined by both bias and precision and is used as an overall index of uncertainty of the Sp_{O_2} value by regulatory authorities such as the US National Institute of Standards in Technology with values <2–3% considered to be acceptable.¹⁸ A_{RMS} was calculated as $\sqrt{\text{bias}^2 + \text{precision}^2}$. These values were calculated for oxyhaemoglobin saturation bands of 70–80%, 80–90%, and 90–100%, and 70–100% (all data).¹⁸ Differences in bias between the nasal alar probe and finger probe were assessed using a paired Student's *t*-test, utilizing the full sample of subject measurements across all saturation bands and within each band. A folded *F*-test for homogeneity of variances was similarly used to determine significant differences in precision between the probes.

In review of the medical literature, we did not discover a method to statistically evaluate A_{RMS} values. We did learn, however, of a potential approach for similar metrics that have been utilized in other fields by Nilsson and colleagues.¹⁹ We adapted these methods to evaluate statistical differences in A_{RMS} between probes. A_{RMS} values were calculated for each subject ($n=12$). Specifically, subject-level bias and precision were first calculated using the multiple measurements obtained from each subject. Then, these bias and precision values were combined to determine A_{RMS} for each subject. This resulted in two sets of A_{RMS} values, with one set for each type of probe. The average A_{RMS} values for each probe were then compared using a paired Student's *t*-test. To the best of our knowledge, this is the first study to adapt this type of approach to examine statistical differences in A_{RMS} .

Additionally, method comparisons were performed using revised Bland–Altman analysis using Sa_{O_2} as the reference standard. In the original Bland–Altman technique, only one measurement per subject was described under constant conditions.²⁰ Some investigators, however, measure subject variables (e.g. Sp_{O_2} , Sa_{O_2}) repeatedly under different conditions such as variable inspired concentrations of oxygen. Measurement of the subject more than once and under changing conditions violates assumptions of independent sampling. Therefore, they proposed a newer method that we have used herein.²¹ In the technique described in section 3 of their publication [a required statistical analysis by the US Food and Drug Administration for 510(k) medical device clearance], Bland and Altman provide a way to determine within-subject variance using analysis of variance (SigmaPlot 12.2, Systat Software, Inc., San Jose, CA, USA), between-subject variance, total variance, bias, and limits of agreement for subjects providing multiple samples under changing physiological conditions that would normally violate assumptions of independent sampling.²¹ Additionally, we pooled data for each subject

to calculate the bias and limits of agreement as suggested by Myles and Cui.²² $P < 0.05$ was considered significant.

Results

Patient characteristics data

Subjects ($n=12$) aged 28 (23–41) yr were divided evenly between males ($n=6$) and females ($n=6$). The ethnic and racial categories were as follows: six Asians, four non-Hispanic whites, one Hispanic white, and one African-American. Skin tone was variable and characterized as light ($n=3$), light-medium ($n=2$), medium ($n=3$), medium-dark ($n=2$), and dark ($n=2$). Eleven subjects completed the entire protocol of the study with 25 or more saturation observations. One subject complained of anxiety during the first episode of desaturation and self-terminated participation after collection of eight saturation observations. All subjects' data were included in this analysis.

Oximetry data

A representative study (Subject 1) of the alar Sp_{O_2} values and heart rate over time are shown in an illustrative example (Fig. 2). A number of co-oximetry oxyhaemoglobin saturations were episodically collected as well. Using these data from Figure 2 and from all other subjects ($n=12$ for all subjects), analysis was performed to determine the bias, precision, and A_{RMS} for oxyhaemoglobin saturation bands of 70–80%, 80–90%, and 90–100% (Table 1). The bias from the alar probe was significantly less than that from the finger probe for all bands of saturation. However, across the separate bands, there were not consistent significant differences in precision and A_{RMS} between probes. Using the method comparison technique for multiple measurements, no magnitude effect on bias was evident. Further, the Bland–Altman method comparison analysis was also performed with all saturation results (70–100%) as noted in Table 2.

Revised Bland–Altman analysis of pooled data for repeated measurements showing bias plots for the alar (Fig. 3) and finger (Fig. 4) probes are shown.^{21 22} Overall, less bias across all saturations was noted with the alar probe compared with the finger probe ($P < 0.001$). Additionally, the nasal alar probe

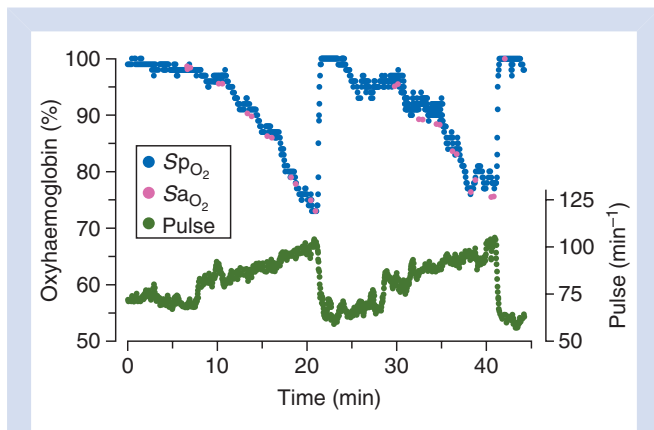


Fig 2 Representative study of oxyhaemoglobin saturation and heart rate over time in a human subject receiving variable concentrations of inspired oxygen by a facemask. Shown is the oxyhaemoglobin concentration measured by alar pulse oximetry ($n=2620$) with some points also measured concurrently by co-oximetry ($n=25$).

Table 1 Bias and A_{RMS} for alar and finger pulse oximetry data stratified by co-oximeter oxygen saturation bands from human subjects ($n=12$) receiving variable fresh gas flow concentrations of inspired oxygen by a facemask. Oxygen saturation band grouping was determined by co-oximetry measurement

Saturation (%)	Observations	Parameter	Alar	Finger	P-value
70–80	85	Bias	0.82	2.93	<0.001
		Precision	1.77	1.98	0.305
		A_{RMS}	1.95	3.53	0.023
80–90	97	Bias	1.13	2.06	<0.001
		Precision	1.49	1.52	0.862
		A_{RMS}	1.87	2.56	0.155
90–100	93	Bias	0.22	0.82	<0.001
		Precision	1.51	1.24	0.063
		A_{RMS}	1.53	1.49	0.396

Table 2 Bland–Altman analysis of oxyhaemoglobin saturation for alar and finger oximetry probes with comparison with co-oximetry saturations as the reference standard method in human subjects ($n=12$) receiving variable concentrations of inspired oxygen by a facemask

Parameter	Alar	Finger
n	275	275
Regression	$y=0.96x+3.92$	$y=0.89x+10.97$
Coefficient of determination (r^2)	0.96	0.96
Within-subject variation	1.14	1.87
Between-subject variation	1.57	1.47
Total variation	2.71	3.34
Standard deviation	1.65	1.83
Bias	0.73	1.90
Upper limits of agreement	3.96	5.48
Lower limit of agreement	-2.50	-1.68
Overall A_{RMS}	1.78	2.72

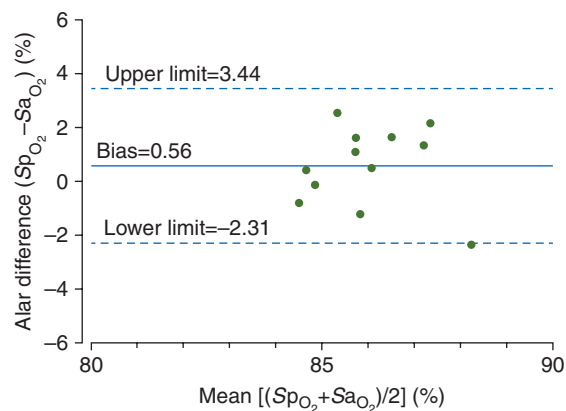


Fig 3 Revised Bland–Altman analysis for multiple measurements of oxyhaemoglobin concentrations measured by alar pulse oximetry (Sp_{O_2}) and co-oximetry (Sa_{O_2}) for human subjects ($n=12$) receiving variable concentrations of inspired oxygen by a facemask. Shown are individual subjects' pooled observations, bias (solid blue line), and upper and lower limits of agreement (dashed blue line).

was overall more precise than the finger probe ($P=0.017$). For both Figures 3 and 4, the outlying point originates from the subject that completed only eight saturation values at the greater end of the desaturation protocol before withdrawing from the investigation. After calculating A_{RMS} for each subject for each probe, the average A_{RMS} for the alar probe (1.76%) and finger probe (2.54%) using this approach closely matched the overall A_{RMS} values that were calculated using each subject measurement separately (Table 2). Using this approach, the average A_{RMS} for the alar probe was significantly less than that for the finger probe ($P=0.047$). (Note: The

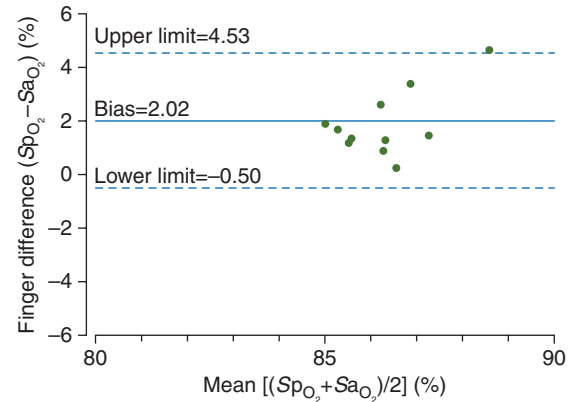


Fig 4 Revised Bland–Altman analysis for multiple measurements of oxyhaemoglobin concentrations measured by finger pulse oximetry (Sp_{O_2}) and co-oximetry (Sa_{O_2}) for human subjects ($n=12$) receiving variable concentrations of inspired oxygen by a facemask. Shown are individual subjects' pooled observations, bias (solid blue line), and upper and lower limits of agreement (dashed blue line).

Bland–Altman analysis using non-pooled data is shown in Supplementary Figs S1–S4.)

Discussion

We designed and tested the accuracy of a novel, alar pulse oximeter sensor in healthy volunteers during both normal (room air) and hypoxic conditions, using a standard method for testing pulse oximeters and sensors. The A_{RMS} of the alar data set compares favourably with the accepted instrument specifications of a $\leq 4\%$ A_{RMS} for functional oxygen saturation promulgated by the International Organization for Standardization (IOS), $\leq 3\%$ for the US Food and Drug Administration, and $\leq 2\%$ A_{RMS} for most other regulatory agencies.¹⁸ Moreover, the sensor demonstrated acceptable accuracy not only for all aggregated data (70–100%), but also at all incremental saturation bands tested. An A_{RMS} of 2% does not mean that all points are within 2% of the reference standard co-oximetry, but rather that most points ($\sim 67\%$) are within this range. Furthermore, a sensor could theoretically have a relatively poor bias or low precision, but not both, and meet the ambiguity target of $\leq 4\%$ A_{RMS} . Manufacturers of pulse oximeters generally claim an accuracy of 2–3% over the saturation range of 70–100%, which would roughly correspond to an A_{RMS} of 2%, but the International Standard Organization reminds us that ‘...only about two-thirds...’ of measurements will fall within the stated twice the A_{RMS} .^{1–3 23} Likewise, Batchelder and Raley¹⁸ point out that the A_{RMS} represents a group of values and does not allow for consideration of temporary ‘pop-ups’ or assess dynamic performance conditions. Notwithstanding, the present alar probe possessed acceptable characteristics as currently assessed by various agencies. Furthermore, via several significance testing approaches, the nasal alar probe demonstrated significantly less bias, better precision, and lower A_{RMS} .

when compared with a finger probe when all saturations (70–100%) were analysed. These differences in bias were also evident when analyses were performed across oxyhaemoglobin saturation bands of 70–80%, 80–90%, and 90–100%. However, the significant differences in precision and A_{RMS} were not similarly consistent across each saturation band. These inconsistent results could be due to the reduced sample sizes of the analyses using the separate bands, which would reduce power to detect group differences.

We specifically selected the nasal ala as a potential new site for pulse oximetry because of its unique arterial perfusion characteristics. Recently, Saban and colleagues¹³ used ultrasonography on 40 living subjects and anatomical dissection on 20 cadavers to demonstrate that the nose is perfused by a four component, multidirectional, arterial arcade to form a polygonal system of vessels that anastomose the external and internal carotid arteries (Fig. 1). In contrast, the arterial supply of the ear, pharynx/cheek, and tongue originates solely from the external carotid artery. During periods of severe pathophysiology (e.g. shock, hypothermia, stress) that potentially require vasopressor therapy, pulse oximeter sensors on the fingers may cease to function because of reduction in systemic blood flow, particularly to the periphery. During these conditions, however, cerebral perfusion may be maintained via the internal carotid artery with autoregulation of blood flow to the central nervous system. Although not answered in the present feasibility investigation, we hypothesize that alar pulse oximetry will be a superior site for pulse oximetry during periods of low systemic blood flow because of preserved arterial perfusion to the central nervous system. Since the nasal branch of the ophthalmic artery provides a sample of internal carotid artery flow and partially perfuses the ala, an adequate pulse oximetry signal could be preserved to provide accurate Sp_{O_2} values.

The only other region of the head with a blood supply originating from the internal carotid artery and assessable non-invasively for oximetry is the forehead which is perfused by a branch of the internal carotid artery (supraorbital artery). This oximetry site has been demonstrated to have acceptable bias and limits of agreement for patients undergoing vascular surgery, is more accurate than finger Sp_{O_2} measurement in critically ill patients receiving high-dose vasopressor therapy, and responds more rapidly than a finger Sp_{O_2} monitor.^{8–12 24–26} Monitoring at this site requires reflectance oximetry, however, wherein precise localization of the sensor and the presence of a corresponding vein in close proximity may cause erroneously decreased Sp_{O_2} values.^{13 27} To prevent erroneous values, the use of a circumferential headband is suggested to dampen venous pulsations.^{14 15 28} Because these data demonstrate that monitoring from the nasal ala is feasible, accurate Sp_{O_2} monitoring using transmittance oximetry may be useful for patients where traditional finger placement fails and is an alternative approach to the supraorbital artery.

The major limitation of this study was subject selection. That is, only healthy adult volunteers were observed over a short time period. In this initial investigation, no paediatric or neonatal subjects were included that would have required a smaller alar pulse oximetry probe. Moreover, the subject

population was entirely healthy with a normal perfusion state. Specific testing is required with subjects in a low perfusion state and subjects with impaired circulation to determine if alar pulse oximetry is accurate in these subjects when digital pulse oximetry fails. Finally, the long-term effects of continuous alar oximetry over days and weeks at this anatomical location are not known.

In summary, we have demonstrated acceptable accuracy of a novel nasal alar pulse oximetry sensor in subjects both with normal and low oxygen saturations and also have provided evidence that nasal alar pulse oximetry may be less biased, more precise, and more accurate than conventional finger pulse oximetry. Future studies should focus on the use and accuracy of this sensor in subjects under a variety of pathophysiological conditions such as trauma, cardiopulmonary bypass, and in subjects in critical care units.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

Authors' contributions

The authors individually contributed to the study design and data acquisition (R.J.M., T.E.M.), data analysis (T.E.M., D.M.D., T.V.), and early drafts of the manuscript (T.E.M., M.J.R., R.J.M.) and critical revisions (T.E.M., M.J.R., T.V., R.J.M., D.M.D.). All authors have approved the final version of the manuscript.

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Declaration of interest

R.J.M. and D.M.D. are employees of Xhale, Inc., the company that sponsored the study. T.E.M. is a consultant for Xhale, Inc. R.J.M., D.M.D., and T.E.M. also own equity in Xhale, Inc. In addition, the University of Florida owns equity in Xhale, Inc. If a device is sold commercially, then the authors listed above and the University of Florida could benefit financially.

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