Comparison of use of an infrared anesthetic gas monitor and refractometry for measurement of anesthetic agent concentrations

Tamas D. Ambrisko, DVM, PhD, and Alan M. Klide, VMD

Objective—To assess agreement between anesthetic agent concentrations measured by use of an infrared anesthetic gas monitor (IAGM) and refractometry.

Sample—4 IAGMs of the same type and 1 refractometer.

Procedures—Mixtures of oxygen and isoflurane, sevoflurane, desflurane, or N_2O were used. Agent volume percent was measured simultaneously with 4 IAGMs and a refractometer at the common gas outlet. Measurements obtained with each of the 4 IAGMs were compared with the corresponding refractometer measurements via the Bland-Altman method. Similarly, Bland-Altman plots were also created with either IAGM or refractometer measurements and desflurane vaporizer dial settings.

Results—Bias ± 2 SD for comparisons of IAGM and refractometer measurements was as follows: isoflurane, –0.03 ± 0.18 volume percent; sevoflurane, –0.19 ± 0.23 volume percent; desflurane, 0.43 ± 1.22 volume percent; and N_2O, –0.21 ± 1.88 volume percent. Bland-Altman plots comparing IAGM and refractometer measurements revealed nonlinear relationships for sevoflurane, desflurane, and N_2O. Desflurane measurements were notably affected; bias ± limits of agreement (2 SD) were small (0.1 ± 0.22 volume percent) at < 12 volume percent, but both bias and limits of agreement increased at higher concentrations. Because IAGM measurements did not but refractometer measurements did agree with the desflurane vaporizer dial settings, infrared measurement technology was a suspected cause of the nonlinear relationships.

Conclusions and Clinical Relevance—Given that the assumption of linearity is a cornerstone of anesthetic monitor calibration, this assumption should be confirmed before anesthetic monitors are used in experiments. (*Am J Vet Res* 2011;72:1299–1304)

Infrared absorption spectroscopy is commonly used during routine anesthesia of veterinary patients to measure concentrations of inhaled anesthetic agents. There may also be a need to use these monitors for measuring anesthetic agent concentrations during clinical research projects (eg, minimum alveolar concentration–related studies) or for testing the accuracy of vaporizers. The accuracy of IR absorption spectroscopy may be adversely affected by multiple factors, such as the presence of other molecules in the sample with overlapping IR absorption spectra (eg, methane or propellant of medical aerosols),[1,2] pressure-broadening effect,[3] calibration problems,[4,5] and artifacts.[6]

Refractometry, gas chromatography, and mass spectrometry are commonly used as reference methods with which the accuracy of other instruments is compared. The superior accuracy of refractometry is established, and it has been recommended to be used as the gold standard for testing vaporizers and anesthetic gas monitors.[7,8] The accuracy of an IAGM (similar to the monitor used in the study of this report) has been determined for halothane and isoflurane but not for sevoflurane and desflurane.[9] The purpose of the study reported here was to assess agreement between anesthetic agent concentrations measured by use of an IAGM and refractometry. The IAGM was a commercially available device used in our veterinary hospital, and its accuracy for measurement of isoflurane, sevoflurane, desflurane, and N_2O concentrations was compared with that of a portable refractometer.

ABBREVIATIONS

IAGM	Infrared anesthetic gas monitor
IR	Infrared

Materials and Methods

IAGMs—Four identical side-stream anesthetic gas monitors[a] were tested in the study. These IR analyzers use multiple wavelengths of light between

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From the Department of Clinical Studies, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19104. Dr. Ambrisko's present address is Division of Anaesthesia and perioperative Intensive Care, Department for Companion Animals and Horses, University of Veterinary Medicine, 1210 Vienna, Austria.

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Address correspondence to Dr. Ambrisko (tamas.ambrisko@vetmeduni.ac.at).

3 and 20 μm to identify and quantify as many as 5 halogenated anesthetic agents (isoflurane, halothane, enflurane, desflurane, and sevoflurane). Carbon dioxide and N_2O are also measured by use of the principles of IR absorption spectroscopy but with a single wavelength. The IAGMs were calibrated by hospital staff every month using the calibration gas supplied by the manufacturer. The monitors were also regularly inspected and maintained by a professional service to ensure that they were in good condition. The manufacturer's original 2.4-m-long polyvinyl chloride sampling tubes and water traps were used in the study. Before measurements were obtained, the IAGMs were allowed a period of at least 10 minutes, which is more than the recommended minimal warming up time (90 seconds), to reach full specifications.[a] Anesthetic gas sampling rate was set at 0.15 L/min. The measurement results were displayed on the monitors' screens at a resolution of 0.1 volume percent for the halogenated agents and 1 volume percent for N_2O.

Refractometry—The measurements obtained by use of the IAGMs were compared with those from a handheld refractometer.[b] This was a Jamin-type refractometer that used a double optical path.[7,10] The scale in this refractometer unit allowed direct reading of desflurane from 0 to 20 volume percent. The concentration of other agents can also be measured with this refractometer if appropriate conversion factors are applied (agent volume percent = desflurane volume percent reading × conversion factor). The following conversion factors were used in this study: 0.78 for isoflurane, 0.81 for sevoflurane, and 4.29 for N_2O.[b] The scale of this refractometer was suitable for measuring agent concentrations across the clinically applicable ranges: isoflurane, 0 to 15 volume percent; sevoflurane, 0 to 16 volume percent; and N_2O, 0 to 85 volume percent. The refractometer was calibrated before each experiment by use of 100% oxygen and air. Both gases have an indicated point on the refractometer's scale. The unit is supplied with a T-piece adapter and polytetrafluoroethylene tubing to facilitate sampling of anesthetic gas. A handheld suction bulb was used (squeezed 3 times) for suctioning a gas sample into the refractometer. The accuracy of this refractometer was claimed to be within 3% of the scale reading.[b]

Experimental protocol—For testing of the IAGMs, 4 anesthetic agents were used: isoflurane,[c] sevoflurane,[d] desflurane,[e] and N_2O.[f] Oxygen was the carrier gas. One anesthetic agent was used at a time, and all measurements with a single agent were completed in 1 experiment. The order of agent concentrations was randomized with a random number generator.[g] Sampling lines of the 4 IAGMs were attached to plastic endotracheal tube adapters. These adapters and the sampling T-piece of the refractometer were combined and attached to the common gas outlet of an anesthesia machine[h] in an airtight fashion. The free end of the adapters was connected to a long corrugated hose leading to an open scavenging interface of the hospital's active scavenging system. The measurements were completed with all of the instruments quasisimultaneously with each gas mixture. Commercially available anesthetic vaporizers[i–k] were used to deliver halogenated anesthetic agents by use of the following dial settings: 0.6%, 1%, 2%, 3%, 4%, and 5% for isoflurane; 0.6%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, and 8% for sevoflurane; and 36 dial settings between 0.5% and 18% for desflurane. Thirty different N_2O and O_2 mixtures were generated with the flow meters of the anesthesia machine to achieve N_2O volume percents distributed evenly across a range of 0% to 85%. A carrier gas flow of 4 L/min was used with the halogenated agents, and a flow of ≥ 2 L/min was used with N_2O. At least 1 minute was allowed for the measurements to stabilize after each change in vaporizer dial or gas flow setting. The results were manually recorded. During the study, the ambient temperature was approximately 21° to 22°C and the ambient pressure was approximately 765 mm Hg.

Data analysis—Agreement between the IAGM and refractometer data was determined via Bland-Altman analysis.[11] Five measurements (4 with the IAGM and 1 with the refractometer) were performed for each gas mixture. Differences between and means of each of the 4 IAGM measurements and the corresponding measurements obtained by use of the refractometer were separately calculated for each gas mixture and plotted. Bias was defined as the mean difference between the IAGM and refractometer measurements, and the limits of agreement were bias ± 2 SD. To examine agreement between IAGM or refractometer measurements and desflurane vaporizer dial settings, Bland-Altman plots (plots of differences in values derived with each device and the dial setting vs means) were also created. Relationships between variables were evaluated by observing the scatterplots and the difference-versus-mean plots. Statistical tests such as regression analysis and confidence interval calculations could not be performed in this study because these tests would require that the data be independent from each other. The data in this study are not independent because only a single anesthesia machine was used with each agent and multiple measurements were obtained from each measuring device. This is a limitation of the study.

Results

For isoflurane, sevoflurane, desflurane, and N_2O concentrations, measurements were obtained by use of the single type of IAGM and refractometer (**Table 1**). Agent volume percent data were analyzed by use of the Bland-Altman method (**Figure 1**), and scatterplots of the original measurements were created (**Figure 2**). For sevoflurane, desflurane, and N_2O, nonlinear relationships between concentrations determined by use of the 2 devices were evident on the scatterplots. The bias of isoflurane measurements was near zero, and the limits of agreement (plus or minus) were < 0.2 volume percent. Most of the sevoflurane measurements obtained by use of the IAGMs were lower than the measurements obtained by use of the refractometer, but the limits of agreement were narrow, similar to those for the isoflurane measurements. However, the limits of agreement for desflurane and

N_2O measurements were much wider. The difference-versus-mean plots for IAGM and refractometer measurements revealed nonlinear relationships for sevoflurane, desflurane, and N_2O. When desflurane mea-

Table 1—Descriptive statistical data of isoflurane, sevoflurane, desflurane, and N_2O concentration measurements (volume percent) determined by use of a single type of IAGM and a refractometer.

	Isoflurane		**Sevoflurane**		**Desflurane**		**N_2O**	
Variable	**Refractometer (n = 6)**	**IAGM (n = 24)**	**Refractometer (n = 9)**	**IAGM (n = 36)**	**Refractometer (n = 36)**	**IAGM (n = 144)**	**Refractometer (n = 26)**	**IAGM (n = 104)**
Mean	2.9	2.9	4.2	4.0	9.3	9.7	46.8	46.6
SD	1.9	1.8	2.7	2.5	5.2	5.6	22.9	21.9
Minimum	0.7	0.6	0.5	0.4	0.4	0.4	10.1	11.0
Maximum	5.6	5.6	8.3	8.3	17.8	19.9	83.6	85.0

Commercially available anesthetic vaporizers were used to deliver halogenated anesthetic agents at various dial settings. Five measurements (4 obtained by use of 4 IAGMs and 1 obtained by use of a refractometer) were obtained for each gas mixture. Each of the 4 IAGM measurements and the corresponding refractometer measurement were subsequently compared and analyzed for each gas mixture.

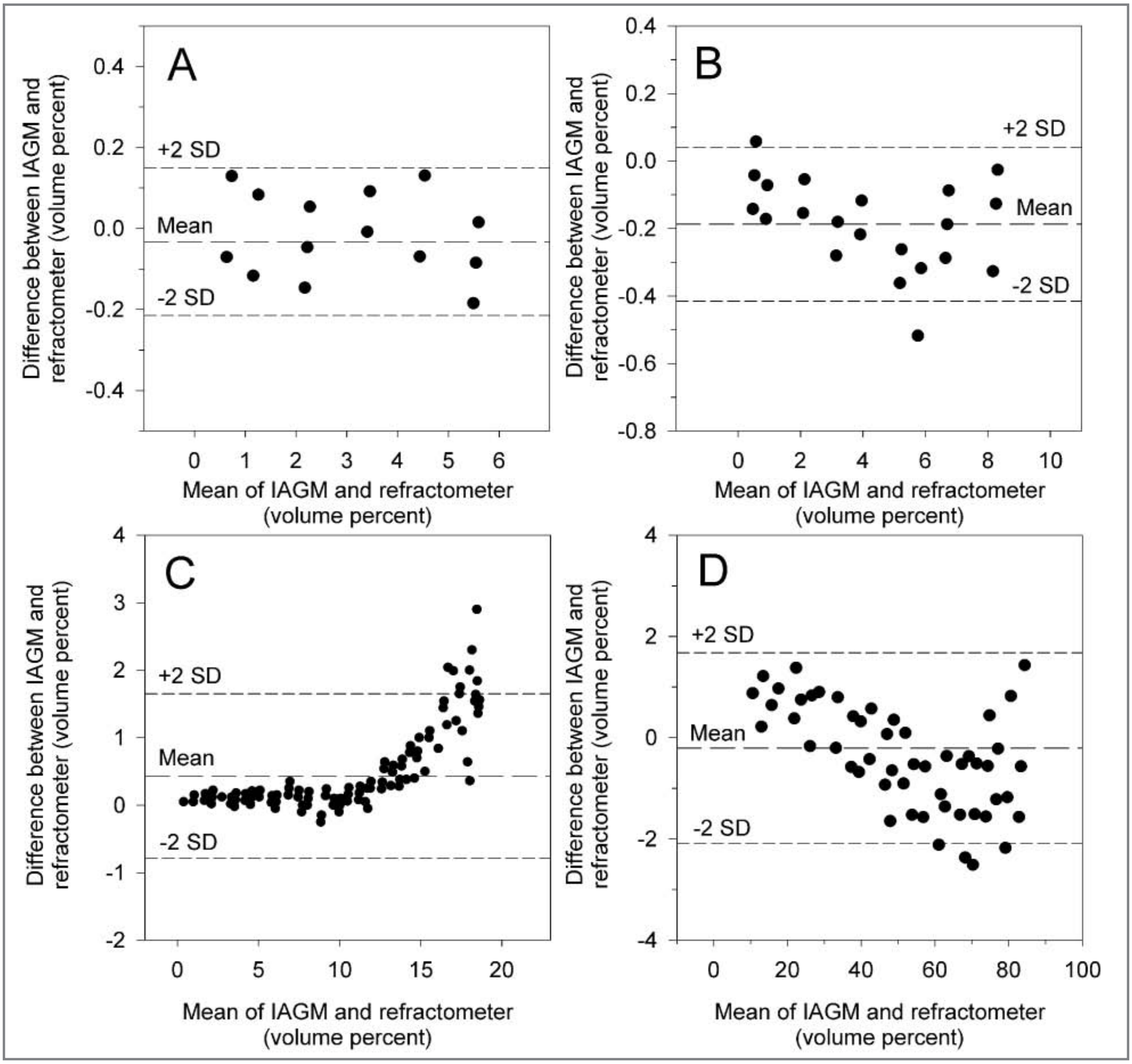

Figure 1—Plots of differences between concentration measurements obtained by use of a single type of IAGM and a refractometer versus the mean value of those measurements for isoflurane (A), sevoflurane (B), desflurane (C), and N_2O (D). Five measurements (4 obtained by use of 4 IAGMs and 1 obtained by use of a refractometer) were obtained for each gas mixture. Long-dashed lines indicate the bias (mean difference between device measurements), and short-dashed lines indicate the limits of agreement (mean ± 2 SD). Nonlinear relationships are evident for sevoflurane, desflurane, and N_2O.

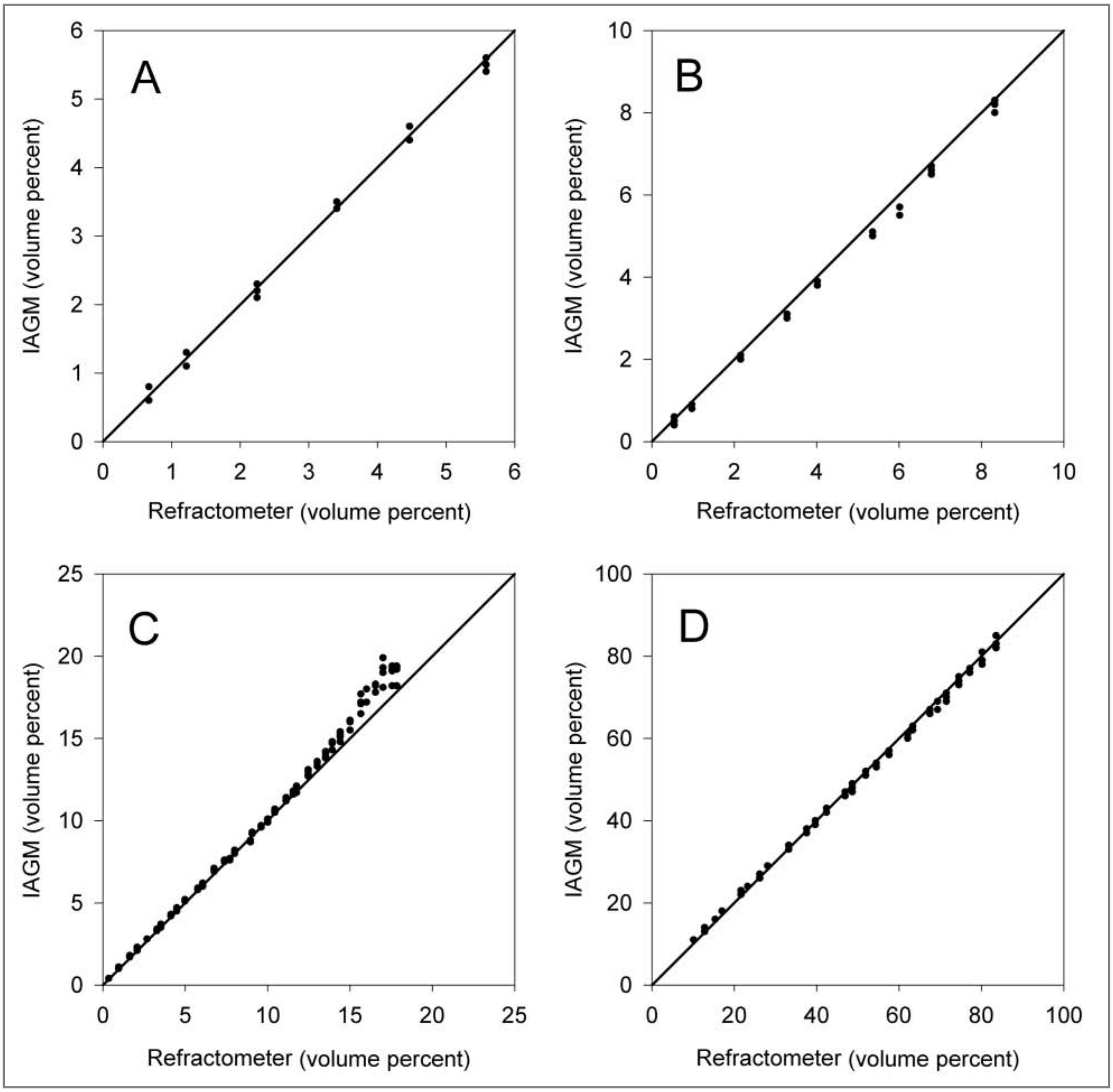

Figure 2—Scatterplots of concentration measurements (volume percent) obtained by use of a single type of IAGM and a refractometer for isoflurane (A), sevoflurane (B), desflurane (C), and N_2O (D). Five measurements (4 obtained by use of 4 IAGMs and 1 obtained by use of a refractometer) were obtained for each gas mixture. Solid lines indicate the line of ideal agreement (y = x). Nonlinear relationships between measurements are evident for sevoflurane, desflurane, and N_2O.

surements of 0.5 to 12 volume percent were analyzed separately, the agreement between the devices was good (bias ± limits of agreement, 0.1 ± 0.22 volume percent) and there was no correlation between differences and means of the 2 device measurements (data not shown). However, at higher desflurane concentrations, the differences between IAGM and refractometer measurements increased in a nonlinear pattern and the variance of the differences also increased. The IAGMs were unable to measure N_2O at < 10 volume percent because they displayed a zero value in situations when the refractometer measurements and the settings of the flow meters suggested that N_2O concentrations were between 0 and 10 volume percent. These N_2O data were excluded from Bland-Altman analysis and not otherwise reported.

Desflurane measurements obtained with the refractometer agreed with the vaporizer dial settings (0.06 ± 0.29 volume percent), and correlation between differences in values and means of the values derived via the device and the dial settings could not be observed (**Figure 3**). However, desflurane measurements obtained with IAGMs did not agree with the dial settings (0.49 ± 1.18 volume percent) and there was a nonlinear relationship between differences and means. The agreement between IAGM measurements and dial settings for desflurane was better at < 12 volume percent desflurane, and correlation could not be identified within this range.

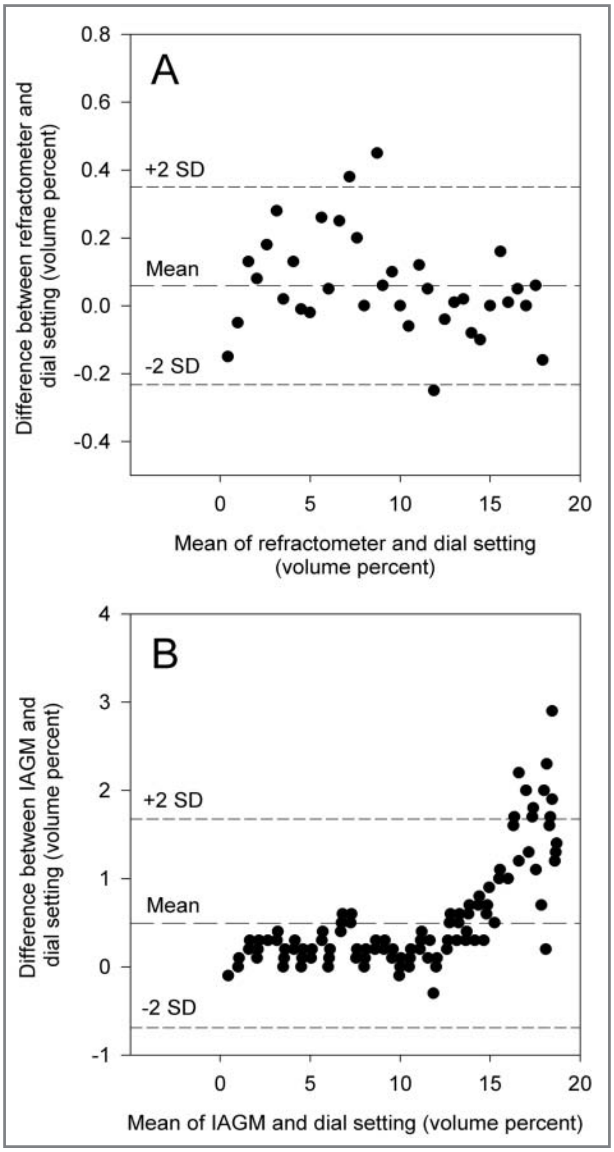

Figure 3—Plots of differences between desflurane concentration measurements (volume percent) obtained by use of a refractometer (A) or a single type of IAGM (B) and the concentration indicated by the desflurane vaporizer dial setting versus the mean of the values derived with each device and the dial setting. Five measurements (4 obtained by use of 4 IAGMs and 1 obtained by use of a refractometer) were obtained at each vaporizer dial setting. Long-dashed lines indicate the bias (mean difference between the device measurement and dial setting), and short-dashed lines indicate the limits of agreement (mean ± 2 SD). A nonlinear relationship between the differences and means of IAGM measurements and dial settings is evident.

Discussion

The primary aim of the present study was to compare the use of a certain type of IAGM with refractometry for measurement of commonly used anesthetic agent concentrations. Surprisingly, Bland-Altman plots of the differences between and means of IAGM and refractometer measurements revealed nonlinear relationships for sevoflurane, desflurane, and N_2O. Nonlinear response is an undesirable quality for any measurement device, and in this instance, it could have been attributed to either the IAGM or the refractometer or to both devices. The relevance of these nonlinear responses depends on whether the limits of agreements are considered important for a certain clinical or research purpose. With regard to isoflurane measurements, this type of IAGM is suitable, when this range of error is acceptable, for clinical monitoring of isoflurane concentrations and for research purposes. The agreement between devices was similar for sevoflurane, but the IAGM generally underestimated the refractometer measurements. This may lead to the delivery of slightly higher sevoflurane concentrations to patients when anesthetic agent dosing relies on this IAGM, and it is also undesirable for research purposes. The most important finding of the present study concerned desflurane measurements; at < 12 volume percent, the agreement between devices was good with narrow limits; however, at higher concentrations, IAGM measurements overestimated refractometer measurements. This type of IAGM monitor can be useful for measuring desflurane concentrations between 0 and 12 volume percent, which is the range of concentrations most often used in clinically and in research studies. Although it is not common practice, higher desflurane concentrations are sometimes used in research, such as in animal experiments,[12] in vitro studies,[13] and studies involving children.[14] If the IAGM was the source of poor agreement in the present study, this monitor would not be able to accurately measure such high desflurane concentrations. The pattern of N_2O measurements was also nonlinear, but this is probably less important because the bias was close to zero and the limits of agreement were narrow, compared with the high minimum alveolar concentration of N_2O in animals.[15]

One of the limitations of the present study was that the accuracy of the refractometer was not verified with self-made calibration standards. Two-point calibration of the refractometer was undertaken (by use of 100% oxygen and air), but both points were low on the desflurane measurement scale (< 3 volume percent) and accuracy and linearity at higher concentrations (up to 20 volume percent) had not been evaluated by the authors. In this regard, the authors relied on the calibration of the refractometer by the manufacturer and the established physical principles of refractometry.[7,8] Theoretically, inaccuracy of conversion factors might have caused some bias when different agents (other than desflurane) were measured with the refractometer, but it did not influence linearity of measurements because the use of conversion factors implies linear function (measurement = scale reading X conversion factor). Nevertheless, the accuracy of correction factors is independent of possible errors of the particular refractometer unit because they are defined by the refractive indices of desflurane and the other agents in question. The fact that the refractometer measurements agreed with desflurane vaporizer dial settings but the IAGM measurements did not reinforces the assumption that the IAGM was responsible for the nonlinearity observed in this study. Theoretically, refractometry uses a straightforward physical principle and its measurements change strictly linearly with concentrations of each component of a binary gas mixture when the temperature and pressure are constant,[7] as in the present study. On the other hand, IR spectroscopy is based on the Beer-Lambert law, which is subject to many assumptions,[16] some of which may not always be fulfilled, and is influenced by interactions between molecules and therefore may provide nonlinear responses.

Another limitation of the study was that only a single anesthesia machine was used for generating gas mixtures with each agent. Theoretically, the characteristics of this machine might have influenced the results of the study. However, it is unlikely because the anesthesia machine was only used to generate a stabile flow of gas mixtures and the measurement processes occurred entirely within the IAGMs and the refractometer. This situation is different from that in which clinical measurements are obtained; clinical measurements are also influenced by the subjects in which the assessment is performed.

The reason for decreased accuracy when measuring high desflurane concentrations with the IAGM is difficult to explain without in-depth knowledge of the construction and function of this type of monitor. One possible explanation may be the pressure (or collision)-broadening effect. Pressure broadening in anesthesia commonly refers to the fact that the presence of certain molecules changes the IR absorption spectra of other molecules. Typical examples would be the effect of N_2O or desflurane on CO_2 measurements.[3,17] However, pressure broadening has other forms, such as resonance broadening (or self-broadening), which means that a substance may affect its own spectral lines at higher pressures.[18] This phenomenon may also result in spectral line broadening and shift. If resonance broadening occurred at higher desflurane concentrations in the present study, it may explain the decreased accuracy of desflurane measurements with this type of unit. Other types of IAGMs may use different wavelengths of light for detection of anesthetic agents and may perform differently from the one used in this study.

The main finding of the present study was that the IAGM tested did not respond linearly. It is possible that the nonlinearity was caused by the inherent properties of IR absorption technology used in this unit; therefore, other anesthetic agent monitors that function with similar technology may also be affected. The assumption of linearity is important because manufacturers typically recommend a 2-point calibration, including 0 and (usually) a fairly low agent concentration, and they assume linearity at higher (and lower) agent concentrations. This mode of calibration is commonly used in clinical and sometimes in laboratory studies. The results of the present study have indicated that this method may not always be acceptable for anesthetic agent concentrations higher than the calibration points. Based on the findings of this study, it may be prudent to confirm the assumption of linearity before use of IAGMs in research studies. The best policy for use of IAGMs in research would be to calibrate them against known standards or against a reference measurement method involving multiple agent concentrations and encompassing the concentration range of interest.

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[a] POET IQ, model 602-6B, Criticare Systems Inc, Waukesha, Wis.
[b] Riken 1802D, Riken Keiki Co Ltd, Tokyo, Japan.
[c] Attane, Minrad Inc, Bethlehem, Pa.
[d] SevoFlo, Abbott Laboratories, North Chicago, Ill.
[e] Suprane, Baxter International Inc, Deerfield, Ill.
[f] Nitrous oxide USP, Airgas East Inc, Salem, NJ.
[g] Microsoft Excel 2002, Microsoft Corp, Redmond, Wash.
[h] Narkovet Deluxe, North American Dräger, Telford, Pa.
[i] Vapor 19.1, North American Dräger, Telford, Pa.
[j] Sigma Delta, Penlon Ltd, Abingdon, Oxfordshire, England.
[k] TEC-6, Datex-Ohmeda Inc, Madison, Wis.

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