Clinical Performance of an In-Line, ex Vivo Point-of-Care Monitor: A Multicenter Study

GLENN F. BILLMAN,1 AMY B. HUGHES,2 GOLDE G. DUDELL,3 ELIZABETH WALDMAN,1 LISA M. ADCOCK,4 DAN M. HALL,5 EDMUND N. ORSINI, JR.,6 ADOLPH J. KOSKA,7 LINDA J. VAN MARTER,8 NEIL N. FINER,9 JEFF C. KULHAVY,10 RONALD D. FELD,10 and JOHN A. WIDNESS2*

Background: The management of critically ill infants and neonates includes frequent determination of arterial blood gas, electrolyte, and hematocrit values. An objective of attached point-of-care patient monitoring is to provide clinically relevant data without the adverse consequences associated with serial phlebotomy.

Methods: We prospectively determined the mean difference (and SD of the difference) from laboratory methods of an in-line, ex vivo monitor, the VIA LVM Blood Gas and Chemistry Monitoring System® (VIA LVM Monitor; Metracor Technologies, Inc.), in 100 critically ill neonates and infants at seven children’s hospitals. In doing so, we examined monitor stability with continuous use. In vivo patient test results from laboratory benchtop analyzers were compared with those from the VIA LVM Monitor on paired samples. In a separate in vitro comparison, benchtop analyzer and monitor test results were compared on whole-blood split samples.

Results: A total of 1414 concurrent, paired-sample measurements were obtained. The mean differences (SD of differences) from laboratory methods and r values for the combined data for the VIA LVM Monitor from the seven sites were 0.001 (0.026) and 0.97 for pH, 0.7 (3.6) mmHg and 0.94 for PCO2, 4.2 (9.6) mmHg and 0.98 for PO2, 0.0 (2.9) mmol/L and 0.87 for sodium, 0.1 (0.2) mmol/L and 0.96 for potassium, and 0.3% (2.9%) and 0.90 for hematocrit. Performance results were similar among the study sites with increasing time of monitor use and between in vivo paired-sample and in vitro split-sample test results.

Conclusion: The VIA LVM Monitor can be used to assess critically ill neonates and infants.

© 2002 American Association for Clinical Chemistry

Technologic innovations in the development and fabrication of biosensors and microprocessors have led to the development and patient bedside use of small, highly accurate point-of-care (POC)¹¹ devices. These devices include “analyzers”, which require permanent removal of blood specimens from patients, and “monitors”, which do not. POC devices have the potential for promoting improved patient outcomes through their ability to shorten the therapeutic turnaround time of diagnostic tests and to increase accuracy by reducing or eliminating preanalytic error and specimen preparation (1, 2). Because monitors are designed to operate as closed systems with insignificant blood loss, the need for erythrocyte transfusions to neonates and the risk of nosocomial infections may also be reduced. These advantages have motivated the development and introduction of continuous and near-continuous patient-attached POC monitors.

Despite numerous reports describing the clinical per-

¹¹ Nonstandard abbreviations: POC, point-of-care; Hct, hematocrit; and NICU, neonatal intensive care unit.
formance characteristics of near-patient POC devices, few studies have included infants and children (3–7), and none of the reports on infants and children have included sufficient numbers of individuals drawn from multiple settings to allow generalization about the bedside performance of POC monitoring in this population. In this study, we prospectively evaluated the performance of a recently introduced in-line, ex vivo monitor specifically designed for use in critically ill neonates, infants, and other volume-restricted patients. This monitor, the VIA Low Volume Mode Blood Gas and Chemistry Monitoring System® (VIA LVM Monitor; Metracor Technologies, Inc., San Diego, CA), measures pH, \(P_{\text{O}_2}\), \(P_{\text{CO}_2}\), Na\(^+\), K\(^+\), and hematocrit (Hct) by automatically drawing blood from a patient’s arterial catheter, analyzing it, and reinfusing the blood sample back into the patient. The monitor’s fluid circuitry design and its proprietary stopcock prevent excessive amounts of sterile calibration solution from being infused into the patient.

In the present study, we hypothesized that acceptable VIA LVM Monitor comparative mean differences, SD of differences, stability, and trouble-free use would be observed in the context of a prospective in vivo multicenter clinical trial in which different makes and models of instruments in use at different study sites functioned as comparison analyzers and in a single-site in vitro split-sample comparison of the VIA LVM Monitor with a single comparison analyzer.

Materials and Methods

ROLE OF SPONSOR

The present study was investigator-initiated. Although the authors had complete responsibility for study design, data analysis, and reporting, the sponsor was provided with the opportunity to provide comments and criticisms for all of these. The authors were free to publish and comment on any and all data without restriction by the sponsor.

PATIENT SELECTION

Institutional Review Board approval was a prerequisite for study site participation. Informed written consent was obtained from one or both parents. Study enrollment was limited to 100 neonates or infants younger than 8 months of age with umbilical or peripheral arterial catheters inserted for clinical indications and an anticipated need for at least 10 blood gas determinations during the subsequent 72 h. Admission into the trial was offered irrespective of whether a patient was receiving medical or surgical treatment. Similarly, the composition of a patient’s primary arterial line fluid was not restricted, but instead varied according to site preference. Monitors were discontinued if the arterial catheter was no longer required for patient care, persistent waveform dampening occurred, or the VIA LVM Monitor or its sensor failed.

INSTRUMENT COMPARISON

Consecutive, clinically ordered tests for blood gases, Na\(^+\), K\(^+\), and Hct were analyzed by both a central laboratory instrument and the in-line monitor. The study did not restrict which laboratory instruments were used or their location within the hospital. Similarly, the method of specimen handling and delivery to the reference laboratory occurred in each facility’s usual fashion.

The VIA LVM Monitor evaluated in the present study is a Food and Drug Administration-approved, patient-attached, closed-system monitor designed for use in critically ill neonates, infants, and other volume-restricted patients. Operation of the VIA LVM Monitor was performed as recommended by the manufacturer. Like the monitor’s adult predecessor (8), the in-line neonatal/infant monitor uses conventional electrochemical detection methods for measuring pH, \(P_{\text{O}_2}\), \(P_{\text{CO}_2}\), K\(^+\), Na\(^+\), and Hct. Specifically, ion-selective electrodes are used to measure pH, \(P_{\text{CO}_2}\), K\(^+\), and Na\(^+\). A Clark \(P_{\text{O}_2}\) electrode is used to measure \(P_{\text{O}_2}\). Hct values are determined indirectly by measuring the electrical conductance. The six sensors are organized in an array that is entirely contained in a fluid-filled, thermostatically controlled flow cell. All measurements are performed at 37 °C.

Before each patient attachment, the VIA LVM Monitor and sensor undergo an in vitro two-point calibration. Subsequently, one-point calibrations are automatically performed every 30 min (or more frequently if directed by the operator) using a sterile, isotonic, heparinized calibration solution continuously bathing the sensor array. This solution is composed of 500 mL of Normosol R (Abbott Laboratories), 10 mL of 84 g/L NaHCO\(_3\) (Abbott Laboratories), and 5 mL of sodium heparin (100 units/mL). The addition of heparin was optional, depending on each site’s preference. Fluid circuitry design restricts the volume of fluid administered to the patient before, during, and after each measurement cycle and permits the same catheter to be used clinically for pressure waveform monitoring and fluid administration.

When the instrument operator triggers a sample analysis, the VIA LVM Monitor aspirates ~1.5 mL of arterial blood through microbore tubing into the sensor array over ~1 min. The volume withdrawn is sufficient to present an undiluted blood sample to the sensor array. Specimen equilibration and analysis take an additional 70 s during which the blood sample is warmed to 37 °C. As soon as the analysis phase is completed, the results are displayed on the monitor screen. After analysis, all but ~25 μL of blood is automatically returned to the patient along with a 0.5-mL flush of calibration solution fluid (7). When not in sample mode, the sensor array is cleansed by calibration fluid set at a flow rate of 5 mL/h and diverted into a collection bag. The minimum interval between blood sampling for the monitor is ~5 min. To ensure the accuracy of measurements, fresh calibration fluid is prepared each day of use. In accordance with hospital-
dictated infection control guidelines, sensors are replaced every 72 h.

**IN VIVO PAIRED-SAMPLE TESTING**
The VIA LVM Monitor and the comparison laboratory instrument analyzed consecutive, physician-ordered blood samples. The samples submitted to the laboratory were drawn from a stopcock located between the patient and the in-line sensor array. This was done during the monitor’s 70-s analysis period. The transportation and analysis of the paired sample for laboratory analysis occurred according to the usual practice of each site. Duration of sensor use for individual study participants was defined as the time interval between when the first and the last blood samples were drawn.

**IN VITRO SPLIT-SAMPLE TESTING**
Fresh (<8 h old) fetal umbilical cord and adult blood samples were analyzed in duplicate at one study site by a split-sample method using two analytic instruments (ABL625; Radiometer) and two in-line monitors. To encompass the range of values to include those encountered in the clinical trial, individual blood samples were modified by gas tonometry, hemoconcentration, hemodilution, or addition of electrolytes. Blood samples (5 mL) were tonometered for 5–10 min with an IL 237 Tonometer (Instrumentation Laboratory, Inc.), drawn into a syringe, and analyzed within 3 min in random sequence by each of the four measuring instruments.

**DATA INCLUSION/EXCLUSION CRITERIA**
VIA LVM Monitor data points were compared with those obtained from reference laboratory instruments if (a) the most recent one-point calibrations were within limits for both the monitor and analyzer, (b) the monitor and laboratory instruments both successfully performed the requested analyses, and (c) the laboratory specimen was free of air contamination or clots. In addition, the data sets for each of the six analytes were screened for outliers by use of NCCLS outlier exclusion criteria (9). With this procedure, outliers are identified as data points in which the difference between the two methods exceeds four times the absolute mean difference for all of the data points. Up to 2.5% of the data points for each analyte may be excluded. For split-sample, in vitro paired comparisons, comparison instrument values falling within 3 SD of the paired-sample clinical data were included.

**STATISTICAL ANALYSIS AND DATA HANDLING**
Deming regression was used to assess the agreement between the results obtained with the comparison methods and the VIA LVM Monitor for all of the analytes except Hct (for which quality-control calibrators are unavailable). For Hct, Pearson correlation and simple linear regression were used to assess agreement between the two methods. Error analysis was performed by the method of Bland and Altman (10). The mean difference of the results of the two assay methods and SD of the differences between the two methods were calculated after the exclusion of NCCLS outliers. Statistical data are presented as the mean ± SD. Only two-tailed testing was done. P <0.05 was considered statistically significant.

**Results**

**IN VIVO PAIRED-SAMPLE STUDY**

**Patient and site characteristics.** One hundred critically ill newborns and infants with umbilical or peripheral arterial catheters already in use were enrolled at the seven clinical sites (Table 1). Infant weight at enrollment ranged from 3100 to 5500 g. The duration of VIA LVM Monitor use in individual patients differed significantly by site (P <0.0001), with usage time ranging from 4 to 72 h with a mean of 49 h. The different sites also varied with respect to the composition of the parenteral solutions infused through the arterial line, the location of the reference laboratory in relation to the intensive care unit, the method for getting the sample to the reference laboratory (e.g., by hand or by pneumatic tube), and the preanalytic period of the reference sample. Four sites used the Chiron Model 865 (Bayer, Inc.); one site used Chiron Models 855, 860, and 865; and two used the Radiometer Model ABL625. During the course of the study, no patient complications related to the use of the VIA LVM Monitor were reported, and no events necessitating monitor discontinuation occurred.

**Clinical study data characteristics.** From the 100 study participants there were 1433 paired-sample results available for comparison. Of these, 19 were excluded for technical reasons, including microbubbles in the sensor array (n = 8), parenteral fluid contamination (n = 7), and improper collection (n = 4). Among the remaining 1414 paired data sets, differences were observed in the number of individual paired analyte measurements. These differences were the result of analysis of blood samples for selected analytes at some study sites rather than the complete panel of six analytes assessed by the monitor.

The application of NCCLS outlier exclusion criteria led to the exclusion of a small number (and percentage) of the total number of paired samples analyzed (9). These included 20 for pH (1.4%), 3 for \( PCO_2 \) (0.2%), 9 for \( PO_2 \) (0.7%), 7 for \( Na^+ \) (0.6%), 14 for \( K^+ \) (1.3%), and 7 for Hct (0.7%). Only 2 of the 1414 paired-sample data sets had more than one analyte that was a NCCLS outlier.

The ranges of values encountered for the six laboratory variables were as follows: 6.94–7.74 for pH; 17–170 mmHg for \( PCO_2 \); 22–215 mmHg for \( PO_2 \); 121–158 mmol/L for \( Na^+ \); 2.0–8.4 mmol/L for \( K^+ \); and 27.5–64.1% for Hct. For the paired \( PO_2 \) data sets, values for the laboratory instruments that exceeded 217 mmHg (i.e., >3 SD above the mean; n = 25) were excluded from analyses. The exclusion of values above this threshold was done to avoid the potential of confounding preanalytic error caused by gas diffusion and aspirated air. This \( PO_2 \)
Clinical performance correlation, mean difference, and SD of differences. All six study analytes showed highly significant agreement between the results obtained with the laboratory instrument and the VIA LVM Monitor (Fig. 1). The correlation coefficients (r) for five of the six analytes were \( \geq 0.90 \), whereas the correlation coefficient for \( \text{Na}^+ \) was 0.87 (\( P < 0.0001 \) for all comparisons). The Bland–Altman plots of all six study analytes had mean differences that approximated zero (Fig. 2). The vertical scatter of the paired patient data samples about the mean differences in the Bland–Altman plots showed that the majority of data points fell within CLIA criteria limits used for proficiency testing accreditation of clinical laboratories (11).

SECONDARY OUTCOMES
Comparison of results among study sites. A key objective in conducting this multicenter trial was to assess how monitor performance was impacted by the differences in patient care that distinguish one site from another. Accordingly, the seven participating sites were asked to incorporate the VIA LVM Monitor into their existing practices and processes. Standardization across the sites was limited to the manufacturer’s training syllabus and the data collection protocol. It was anticipated that results from each site would reflect the influence of factors and variables present at that site.

Comparison of the monitor’s mean difference and SD of differences across the seven participating sites demonstrated close agreement (Table 2). Site F had the least operational experience with the monitor and recorded one-third to one-fifth as many paired samples as the other sites. Study sites E and F had too few \( \text{Na}^+ \), \( \text{K}^+ \), and Hct values for meaningful comparison and thus were excluded from analysis of individual study sites. Most of the performance variability noted among sites was evident as subtle differences in the mean difference. Site C had the greatest mean pH difference offset, i.e., 0.024. For \( \text{PCO}_2 \), sites A, B, and C had mean differences that were larger than those of the other sites. Except for sites D and E, which showed a slightly lower mean \( \text{PO}_2 \) difference, mean \( \text{PO}_2 \) differences were similar among the other sites. For \( \text{Na}^+ \), study site G showed a greater mean difference relative to the other sites. For \( \text{K}^+ \), minimal variability in mean differences and the SD of differences were observed at all sites. For Hct, although site A showed a negative mean difference relative to the other sites, the Hct SDs of these differences were comparable among all sites.

Influence of duration of sensor use on results. Across the 72-h period of study, the number of patients, their medical conditions, the instrument operators, and the arterial line infusates all differed. Despite these differences, variability in the mean difference and the SD of the differences
among the six analytes throughout the entire study period were modest and thus unlikely to impact clinical decision-making (Fig. 3). Approximately one-fourth of the patients enrolled in the study completed 72 h of continuous monitoring with the VIA LVM Monitor. Results of paired samples generated at startup and after each cycle of calibration and/or patient monitoring included the time and date of the analysis. The monitor printouts were used to determine the corresponding duration of in-line sensor array use for each patient. To test for sensor drift, paired
Data sets were sorted according to the duration of in-line sensor array use, and monitor mean difference and SD of differences were determined. With the exception of $P_{CO_2}$, the data demonstrated no clinically significant sensor instability throughout the 72-h period of investigation. A slight increase in the SD of differences, but not in the mean difference was noted for $P_{CO_2}$ determinations beginning at 48–60 h of sensor use.

**In vitro split-sample study**

In vitro split-sample comparisons were performed at study site D. One hundred four blood samples were analyzed for each of the six study analytes by four instruments: the two in-line monitors and the two laboratory instruments.

NCCLS guidelines were applied to the 104 split-sample in vitro data sets to identify outliers. This procedure
identified 5 outliers for pH (n = 90), 6 for Pco2 (n = 87), 2 for Po2 (n = 91), 5 for Hct (n = 87), 4 for Na+ (n = 89), and 6 for K+ (n = 88). After the range of values was restricted to ± 3 SD of the mean in vivo paired-sample data, the final numbers of in vitro samples used in the mean difference and SD of differences calculations were as follows: pH (n = 59), Pco2 (n = 61), Po2 (n = 102), Na+ (n = 69), K+ (n = 44), and Hct (n = 89). The resulting in vitro split-sample data ranges were as follows: 7.128–7.728 for pH, 10.8–72.7 mmHg for Pco2, 11–217 mmHg for Po2, 122–155 mmol/L for Na+, 1.60–5.69 mmol/L for K+, and 24.2–65.1% for Hct.

**IN VITRO PERFORMANCE RESULTS**

All six study analytes showed highly significant agreement between results obtained with the comparison instrument and the VIA LVM Monitor (Fig. 4). Correlation coefficients for five of the six analytes were ≥0.98, whereas the r value for Hct was 0.95 (P < 0.0001 for all comparisons). Bland–Altman plots of five of the six study analytes revealed mean differences that approximated zero (Fig. 5). The mean difference for Pco2 was 3.46 mmHg. The vertical scatter of the paired patient data samples about the mean differences in the Bland–Altman plots showed that the majority of data points fell within CLIA criteria limits (11). No clinically significant differences emerged between adult blood samples and fetal cord blood samples for mean difference or SD of differences.

**COMPARISON OF IN VIVO AND IN VITRO RESULTS**

For pH, Na+, K+, and Hct, the multicenter mean difference and SD of differences were consistent between the aggregate in vivo paired-sample clinical data and the range-limited in vitro split-sample results (Table 2). For Pco2, the mean difference identified by in vitro testing was substantially larger than that of the composite in vivo mean difference (3.46 vs 0.68 mmHg). Furthermore, for Pco2, the mean difference for in vitro testing was larger than the individual in vivo mean Pco2 difference at study site D, the site where the in vitro test was performed (i.e., 3.46 vs 0.01 mmHg). The Po2 mean difference and SD of the Po2 differences predicted by in vitro testing at site D were comparable to the observed in vivo mean difference and SD of differences data measured at this same site (–0.15 and 4.61 mmHg vs –0.20 and 6.7 mmHg, respectively), but were better than the aggregated Po2 mean difference and SD of difference data for the aggregate of all seven sites (4.17 and 9.58 mmHg, respectively).

The r values derived from in vitro split-sample testing for all six of the analytes were equal to or greater than the r values measured from in vivo paired-sample testing.
Specifically, for pH, $r$ was 0.99 vs 0.97; for $P_{CO_2}$, it was 0.98 vs 0.94; for $P_{O_2}$, it was 1.00 vs 0.98; for $Na^+$, it was 0.98 vs 0.87; for $K^+$, it was 0.99 vs 0.97; and for Hct, it was 0.95 vs 0.90.

**Discussion**

This multicenter clinical study was conducted to assess the analytic performance and stability of an in-line, ex vivo monitor, the VIA LVM Monitor, which is capable of near-continuous measurement of arterial blood gases, electrolytes, and Hct. The performance of the monitor was comparable to that of conventional benchtop blood gas analyzers and to other continuous and near-continuous in-line in vivo and ex vivo monitoring devices.

Widness et al. (7) previously characterized the in vivo performance of the VIA LVM Monitor in 16 neonatal patients at one site. The current study extends and more broadly characterizes the performance of the VIA LVM Monitor among critically ill infants and neonates with various medical and surgical disorders being cared for in freestanding children’s and university-based hospitals in the US. To better approximate “real-world usage” of the monitor, no attempt was made to restrict the study to a specific comparison instrument, catheter location, arterial line infusate, or location of the comparison instrument. Instead, preexisting blood gas and electrolyte analyzers along with established methods of specimen collection, transport, and analysis were used. During the 72-h study period, parenteral fluids infused through the arterial catheters used to obtain blood samples varied from site to site. In addition, at each site monitors were set up and operated by a variety of clinical personnel, i.e., nurses, respiratory therapists, laboratory technologists, and physicians.

These diverse practice patterns were included to more thoroughly characterize vulnerabilities and strengths of the VIA LVM Monitor in a variety of clinical venues. Despite considerable differences among the seven sites, the analytic performance of the VIA LVM Monitor, i.e., its mean difference and SD of differences, for five of the six analytes was similar to those of other POC monitors and analyzers (Table 3). The analytic performance of Hct was the least desirable of the six analytes based on the relatively greater SD of the differences relative to the comparison instruments. The monitor’s less than desirable performance in the analysis of Hct is likely attributable to differences in the methodologies of the two measuring devices, i.e., the monitor measures Hct by electrical conductance whereas the laboratory instruments measure hemoglobin spectrophotometrically and indirectly derive Hct values based on an empiric correction factor.

Not unexpectedly, the analytic performance of both the in vivo paired and the in vitro split whole-blood samples was not better than that of the laboratory instruments using quality-control materials (Fig. 6). This notwithstanding, the data derived from the present study document that the VIA LVM Monitor functioned in an equivalent manner at the seven sites when operated by a spectrum of medical personnel, in a variety of busy critical care environments, and during the entire 72-h period of sensor use. Although our study did not address cost comparisons of the monitor with standard blood gas analysis systems, a report on neonates weighing 500-1000 g at birth indicates that use of the monitor can be cost-effective (12).

The similarity in the analytic performance of the in-line VIA LVM monitor utilized in the present study relative to reports of other POC analyzers and monitors (Table 3) is noteworthy for several reasons. (a) The existing NCCLS methods comparison protocol (9) is based on split-sample analysis. This manner of comparison is not possible for in vivo or ex vivo devices being tested in the clinical setting with patient samples. Sequential (nonidentical) paired samples must be used when conducting these types of comparison studies with attached patient monitors. (b) The VIA LVM Monitor was operated by a variety of
nonlaboratorians at the seven sites, under different environmental conditions, and with four different benchtop analyzers as comparison instruments. (c) The blood samples analyzed were clinical specimens obtained from patients with a broad range of medical and surgical disorders whose physiologic conditions varied widely. (d) The clinical specimens submitted for traditional laboratory analysis were subject to preanalytic error during collection, transport, and analysis. Because the monitor withdraws blood samples into a closed system and does

Fig. 4. Comparison of results obtained with the VIA LVM Monitor and the laboratory instruments for the in vitro laboratory split samples. The diagonal dashed line in each panel indicates the line of identity. The solid line represents the best-fit regression line for the range of values included. The equation for the regression line, the $r$ value, the SD of the residuals ($S_y$), and the number of data points for each analyte are as follows: for pH (A), $y = 0.873x + 0.94$ ($r = 0.99$; $S_y = 0.019$; $n = 59$); for $P_{CO_2}$ (B), $y = 0.842x + 2.44$ mmHg ($r = 0.98$; $S_y = 2.7$ mmHg; $n = 61$); for $P_{O_2}$ (C), $y = 0.949x + 3.8$ mmHg ($r = 1.00$; $S_y = 3.7$ mmHg; $n = 102$); for Na$^+$ (D), $y = 0.898x + 13.7$ mmol/L ($r = 0.98$; $S_y = 2.7$ mmol/L; $n = 61$); for K$^+$ (E), $y = 1.008x + 0.03$ mmol/L ($y = 0.99$; $S_y = 0.073$ mmol/L; $n = 44$); for Hct (F), $y = 0.851x + 6.49$% ($r = 0.95$; $S_y$ not applicable; $n = 89$).
not require specimen transport, preanalytic errors are greatly reduced or eliminated.

The ability of the VIA LVM Monitor to reliably and reproducibly measure pH, $P_{CO_2}$, $P_{O_2}$, $Na^+$, $K^+$, and Hct is further supported by the results of the split-sample in vitro study. The in vitro data provide a useful benchmark of the potential analytic performance of the VIA LVM Monitor in a controlled laboratory environment. With the exception of $P_{CO_2}$, the in vitro $r$ values were improved relative to the in vivo $r$ values. The generally close agreement of the paired-sample in vivo and split-sample in vitro data suggests that the instrument’s analytic performance is effectively buffered from the less-controlled operating conditions found in the neonatal intensive care unit (NICU) environment. The regimen of periodic self-calibration and the temperature-controlled flow cell are
Table 3. Comparison of estimated bias and imprecision values among POC devices.

<table>
<thead>
<tr>
<th>Category of POC device</th>
<th>pH</th>
<th>PO2, mmHg</th>
<th>Na, mmol/L</th>
<th>K, mmol/L</th>
<th>Hct, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Near-patient analyzers</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Near-patient monitors</td>
<td>-0.00</td>
<td>0.02</td>
<td>0.14</td>
<td>0.22</td>
<td>0.38</td>
</tr>
<tr>
<td>In-line/in vivo monitors</td>
<td>0.00</td>
<td>0.03</td>
<td>0.08</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td>In-line/ex vivo monitors</td>
<td>-0.00</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Neotrend (Diametrics)</td>
<td>0.00</td>
<td>0.03</td>
<td>0.03</td>
<td>0.03</td>
<td>0.03</td>
</tr>
<tr>
<td>Paratrend (Diametrics)</td>
<td>-0.00</td>
<td>0.02</td>
<td>0.03</td>
<td>0.03</td>
<td>0.03</td>
</tr>
<tr>
<td>Monitors: i-Stat Portable Clinical Analyzer (4); SenDx 100® (SenDx Medical Inc.) (24); OPTI 1 (AVL) (25); Scientific Corp. IRMA® (Diametrics Inc.) (26, 27).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VIA LVM (present study)</td>
<td>0.00</td>
<td>0.02</td>
<td>0.03</td>
<td>0.03</td>
<td>0.03</td>
</tr>
</tbody>
</table>

The SDs of the differences of the quality-control standards for five of the six analytes include the mean imprecision of the comparison method for the seven participating sites, i.e., pH, PO2, Na, and K, as well as the SD of the differences for the analyte of interest. Because quality-control samples for Hct are not available, this analyte was not included. Note the similarity of these data with the 1999 College of American Pathologists data shown in Fig. 6.

The value of monitoring devices rests on their ability to reliably provide timely, accurate, and precise laboratory information. The evaluation of laboratory results from patients in the clinical setting is traditionally based on sporadic or scheduled sample collection and analysis. Although suitable for the management of most patients, this manner of testing provides insufficient detail to assess or intervene in dynamic clinical situations. For unstable, critically ill patients in the hospital setting, the availability of frequent patient data is more likely to identify unrecognized or evolving events with sufficient advance time to permit correction before adverse events occur or before emergent corrective action becomes necessary. Similarly, the frequent measurement of laboratory data may permit medical personnel to more appropriately adjust treatment for maximum benefit.

The selection of groups of patients who will benefit from the intensive scrutiny provided by POC devices such as the VIA LVM Monitor remains to be defined. For some patients, the availability of near-instantaneous test results offers the potential for more efficient, cost-effective, and appropriate adjustment of pharmacologic agents and ventilatory support. For example, within the NICU, it is well documented that cerebral blood flow and long-term neurodevelopmental outcomes are significantly impacted by marked increases and decreases in PCO2, e.g., those associated with intraventricular hemorrhage and periventricular leukomalacia (3). Thus, for preterm infants, maintaining PCO2 concentrations within defined boundaries and avoiding the extremes of hypoxia and hyperoxia that are also associated with adverse long-term outcomes are desirable goals. The VIA LVM Monitor offers the potential for addressing these problems by providing timely and accurate laboratory information with little laboratory blood loss.

The focus of our study was limited to critically ill neonates and infants. The instrument may benefit and be useful in the care of other patient populations, especially those vulnerable to fluid overload because of cardiac, hepatic, or renal pathology. Patients with highly dynamic and unstable disorders are those most likely to benefit from the availability and use of patient-attached monitors. As a group, critically ill neonates and infants possess additional vulnerabilities that may allow them to derive other benefits from monitoring devices. Specifically, neo-
nates and infants have reduced blood volumes that predispose them to anemia as a consequence of frequent laboratory testing. Iatrogenic blood loss has been estimated to be responsible for up to 90% of the transfusions administered in the NICU (13–16). In a preliminary report, the use of the VIA LVM Monitor in extremely low birth-weight infants produced a dramatic decrease in red blood cell transfusions in the first 2 weeks of life (17).

Other potential advantages of the use of a near-continuous blood gas and electrolyte monitor include reduced blood exposure of healthcare personnel and reduced rates of nosocomial infections.

The safe and appropriate duration of sensor use remains to be defined. Although the present study was limited to sensor use of 72 h, no significant deterioration in sensor performance was identified during this period. The current 72-h period of use was dictated by existing hospital infection control practice standards. The highly stable sensor performance observed across the period of study supports inquiry into whether this period might safely be increased in a more cost-efficient manner. Finally, the 72-h sensor stability data support inquiry as to whether it is necessary to repeat the comparison of paired VIA LVM Monitor and benchtop reference samples as

Fig. 6. Mean differences and the SD of the mean differences relative to the comparison methods for the multicenter patient split-sample (left) and the in vitro laboratory split-sample (right) analyses of the six analytes.

The mean difference and the SD of the differences are indicated by the filled circles and error bars, respectively. The two horizontal dashed lines indicate the CLIA performance criteria limits referenced to a zero difference. The numbers in brackets indicate the number of data points for each analyte. The shaded areas indicate the reported SDs of proficiency test results from the College of American Pathologists 1999 Aqueous Blood Gas Survey for all types of instruments and thus include other sources of variation (36). Note that there are no College of American Pathologists aqueous proficiency test results for Hct.
long as the initial paired-sample comparison has met quality-control criteria.

The results of this multicenter study are encouraging from the standpoint of the performance of the monitor tested. Particularly noteworthy was the robust performance of the VIA LVM Monitor when used in a variety of locations and operated by staff with diverse backgrounds. The monitor compared favorably with the conventional blood gas analyzers used at the seven study sites. We conclude that this in-line, ex vivo monitor can be reliably used in the management of critically ill neonates and infants when arterial catheters are in use. The optimal time period of sensor use, the required frequency for paired-sample quality-control testing, the manner and extent to which the near-continuous availability of data provided by POC monitoring impact patient care, and the cost-effectiveness of providing near-continuous monitoring are fundamental issues requiring additional study (18, 19).

We thank Michele Richardson, Sabrina Sood, and Cathy Butterfield for data entry assistance, and Mark A. Hart for technical assistance. For the in vitro study, we acknowledge Brian Hicks, Erin McGuire, David Buse, and the NICU laboratory staffs for technical support, and Karen J. Johnson, Gretchen A. Cress, and Laura K. Knosp for obtaining blood samples for the split-sample in vitro study. Statistical help with the Deming regression analysis was provided by M. Bridget Zimmerman, PhD. This study was supported in part by funding provided by the NIH General Clinical Research Centers Program (Grant RR00059), by the Child Health Corporation of America, and by Metracor Technologies Inc. (San Diego, CA). We had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analyses. None of us serves on any of the advisory or governing boards of either the Child Health Corporation of America or Metracor Technologies, Inc. Child Health Corporation of America and Dr. Billman hold equity in Metracor Technologies Inc.

References