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Assessment of a Whole Blood Neonatal Bilirubin Method on the RAPIDPoint 405 Instrument versus a Plasma Method on the VITROS 950 Chemistry System

White Paper

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Abstract

Background: In the neonate, bilirubin is measured as an aid for assessing jaundice and the risk of kernicterus. A fast turnaround time on minimal sample volume is often required. We present an initial hospital evaluation of a new whole blood neonatal bilirubin (nBili) method for the point-of-care, cartridge-based Siemens Healthcare Diagnostics RAPIDPoint® 405 (RP405) blood gas analyzer compared to plasma nBili analysis on the Ortho-Clinical Diagnostics VITROS® 950 chemistry system.

Method: Heparinized whole blood specimens from neonates (0–14 days old) were obtained over an 8-day research study. Samples from each specimen were spun and measured as plasma on the VITROS system; remnant volume was measured as whole blood on up to two RP405 instruments (n = 218). Imprecision was monitored daily on the RP405s using aqueous controls. No adjustments to the RP405 bias to reference correction algorithms were applied at this time.

Results: The RP405 total imprecision (%CV) of controls was 3.1%, 2.9%, and 2.9% at 19.8, 9.6, and 5.1 mg/dL (n = 26), respectively. Least squares regression comparing the RP405 (without final bias to reference correction) versus the VITROS system yielded a slope of 0.89 and intercept of -0.43, with $r = 0.973$ across the nBili range of 2.1–19.2 mg/dL (see figure 4). No significant change in RP405 nBili bias was observed as a function of specimen total hemoglobin (tHb; range of 11.6–22.0 g/dL). RP405 nBili bias to reference was also not significantly affected by specimen pH (range of 7.31–7.76). The RP405 system reports results in approximately 1 minute from sample introduction.

Conclusions: The RAPIDPoint 405 whole blood neonatal bilirubin method gives analytical values comparable to those of the VITROS plasma chemistry method without the need for preanalytical centrifugation. It presents a quick time-to-patient-result alternative for monitoring neonatal bilirubin.



Introduction

Newborns normally excrete bilirubin in the bile a few days after birth, a consequence of immature hepatic function and the breakdown of fetal hemoglobin as it is replaced with adult hemoglobin. An increased level of bilirubin in the blood (hyperbilirubinemia) causes jaundice. Jaundice is usually harmless in newborns; however, high levels of bilirubin in infants may cause bilirubin encephalopathy (i.e., kernicterus), a form of brain damage, or may indicate disease conditions.

The neonatal bilirubin test is intended for use on the Siemens Healthcare Diagnostics RAPIDPoint® 405 blood gas system as an in vitro diagnostic test for the determination of the total neonatal bilirubin (nBili) concentration for the laboratory or point-of-care setting. The RAPIDPoint 405 nBili whole blood measurement is by direct photometry utilizing the optical technology currently used on the RAPIDPoint 405 for CO-oximetry determination. The performance of the RAPIDPoint 405 whole blood nBili method using hospital neonatal patient specimens was evaluated against the VITROS 950 plasma neonatal bilirubin (NBIL) assay.

Materials and Methods

Two RAPIDPoint 405 systems (Siemens, Deerfield, IL, US) were installed near two VITROS 950 chemistry analyzers (Ortho-Clinical Diagnostics, Raritan, NJ, US) resident in the core lab at Northwest Community Hospital (Arlington Heights, IL, US). Whole blood neonate samples were collected in lithium heparin microtainers (Becton Dickinson, Franklin Lakes, NJ, US; p/n 22254823) and transported to the lab. On samples with excess volume, capillary aliquots of whole blood were removed and set aside, covered to reduce light exposure. The blood specimens in the microtainers were spun in a microcentrifuge. When the resulting plasma aliquot was assayed for bilirubin on either of the standard laboratory instruments (using the NBIL method), the retained whole blood counterpart was measured on one of the two RAPIDPoint 405 systems (or both, if sufficient volume was available). The RAPIDPoint 405 results were obtained in approximately 1 minute; the VITROS 950 method requires a 5-minute chemistry incubation period. For analysis of precision, three levels of aqueous quality controls (RapidQC® Complete, Siemens) were analyzed daily on the RAPIDPoint 405 systems.



Note: The original abstract included a figure displaying a graphical analysis of the comparison of the RAPIDPoint 405 whole blood nBili method against the VITROS 950 plasma method. The figure appears in this white paper as Figure 4.

Results

Over an 8-day period, 218 paired specimens were used to compare the results of a whole blood nBili assay on the RAPIDPoint 405 blood gas system with the VITROS 950 plasma NBIL assay. As the bilirubin reportable range on the RAPIDPoint 405 analyzer is 2.0–30.0 mg/dL, samples with nBili levels of <2 mg/dL were not included in this data set. The demographics of the specimens are summarized in Table 1. The patient values for pH, total hemoglobin (tHb), carboxyhemoglobin (COHb), and hemoglobin oxygen saturation (sO₂) were determined simultaneously on the RAPIDPoint 405 instruments.

Distribution of the neonatal patient age (Figure 1) indicates that the majority of the specimens were from patients less than 2 days old. Approximately 33 percent of the patients were 3 to 7 days old, the age range in which neonatal bilirubin typically spikes.

The frequency distribution of the bilirubin levels for the clinical specimens shows that the data set covered a wide range of bilirubin values; roughly half of the specimens had bilirubin levels greater than 12.0 mg/dL (Figure 2).

Table 1. Demographics of the neonatal specimens.

Patient Demographics	Range
Age	<1–14 days
Gender	F, 44%; M, 56%
tHb	11.6–22.0 g/dL
sO ₂	76.6%–100.0%
pH	7.314–7.765
COHb	0.0%–3.4%

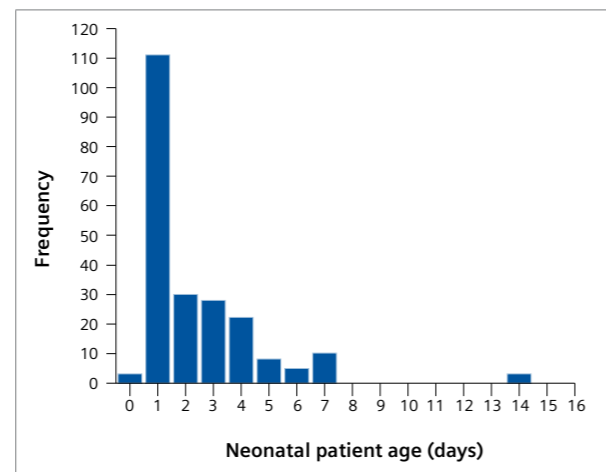


Figure 1. Neonatal age frequency distribution.

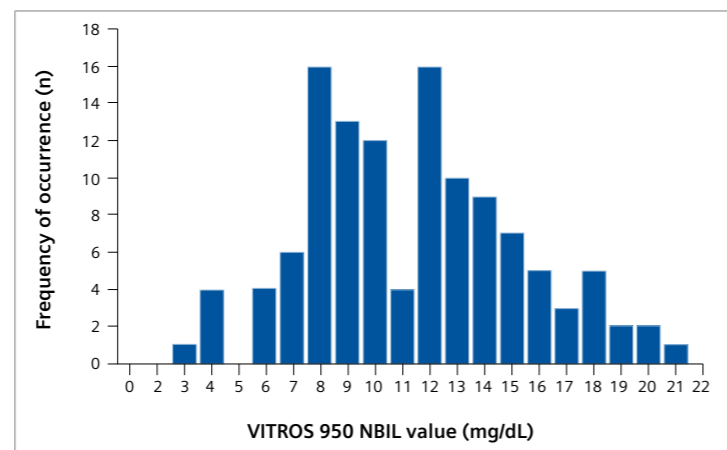


Figure 2. Bilirubin level frequency distribution for hospital neonatal specimens.

The relationship of patient age to plasma neonatal bilirubin concentration is shown in Figure 3. Twelve of the specimens exhibited bilirubin levels ≥ 15 mg/dL as measured on the VITROS 950 instruments, with the highest level (19.2 mg/dL) from a 7-day-old.

The whole blood results for the clinical specimens run on the RAPIDPoint 405 system were compared to the plasma results for the same specimens run on the VITROS 950 system. Ordinary least squares regression comparing the combined paired data yielded the following linear equation: RAPIDPoint 405 = $-0.43 + 0.887$ (VITROS 950); $r = 0.973$. Both RAPIDPoint 405 instruments performed similarly, as the estimates of slope and intercept for the two RAPIDPoint 405 analyzers vs. the VITROS 950 systems were not significantly different ($P < 0.05$). Figure 4 displays the graphical analysis of the comparison of the RAPIDPoint 405 whole blood nBili method against the VITROS plasma NBIL method.

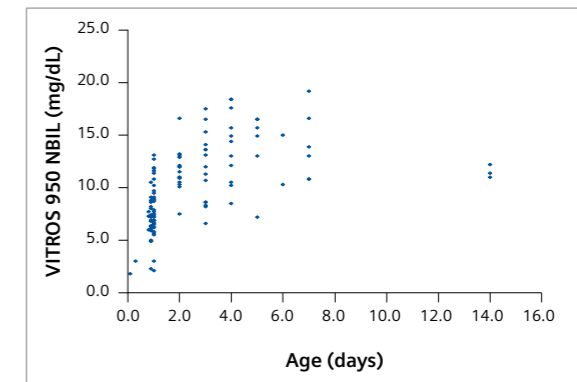


Figure 3. Neonatal bilirubin levels graphed by age.

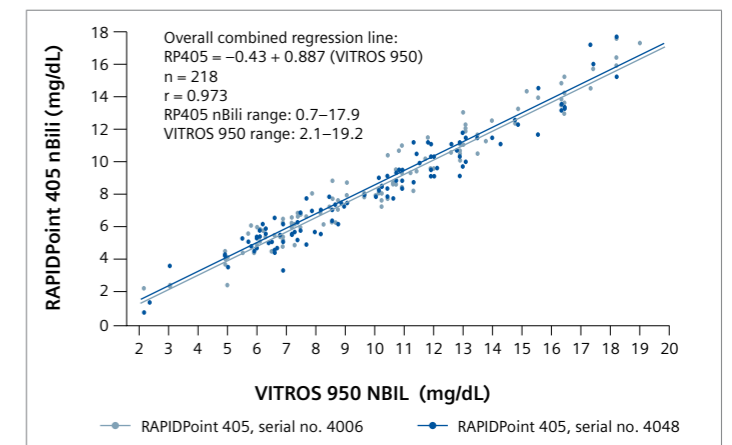


Figure 4. Regression of RAPIDPoint 405 nBili vs. VITROS 950, by RAPIDPoint 405 system.



In the following figures, dots of two colors indicate values from the two RAPIDPoint 405 analyzers.

The bias of each pair of data points (RAPIDPoint 405 nBili minus VITROS 950 NBIL) was calculated and plotted in Figures 5 and 6. The bias plot along with the linear regression slope < 1.00 and negative y-intercept indicates an underrecovery for RAPIDPoint 405 nBili relative to the VITROS 950 system. Without applying any corrections, the RAPIDPoint 405 nBili assay was on average 2 mg/dL lower than the VITROS assay. Although not used in this study, the ability to enter slope and intercept correlation coefficients is available if matching reference method or current comparative assay method is desired.

Neither of the two RAPIDPoint 405 analyzers showed a significant change in bias as a function of tHb, pH, or sO₂ concentration. Figure 6, for example, indicates no significant relationship between tHb level and the bias of RAPIDPoint 405 nBili results relative to VITROS 950 results.

Unpartitioned estimates of total imprecision were obtained by pooling all the results for three control lots and calculating the simple standard deviation. Results are summarized in Table 2.

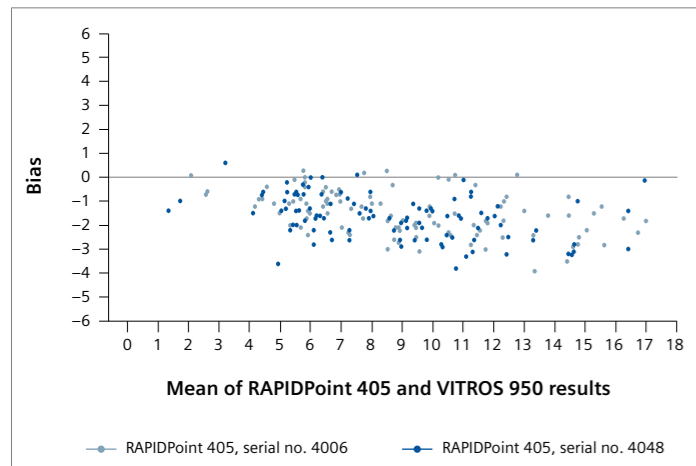


Figure 5. Bland–Altman (bias) plot of RAPIDPoint 405 nBili vs. VITROS 950 results.

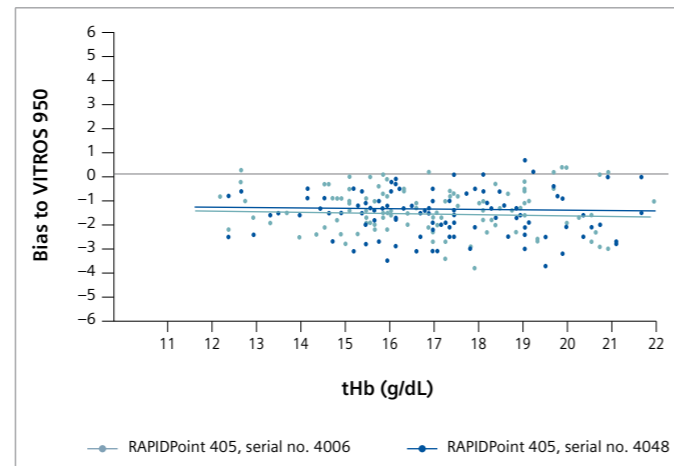


Figure 6. Bias to the VITROS 950 method as a function of tHb level by RAPIDPoint 405 instrument.

Table 2. Precision results (mg/dL) for control materials.

QC Level	n	nBili Grand Mean	Total SD	Min.	Max.
1	26	20.25	0.62	19	21.4
2	28	10.52	0.31	9.8	11.1
3	26	4.89	0.14	4.7	5.1

Conclusions

The whole blood neonatal bilirubin method available on the RAPIDPoint 405 system provides analytical results similar to those of the VITROS plasma chemistry method. With no need for sample preanalytical centrifugation, the RAPIDPoint 405 nBili assay provides a fast method for monitoring bilirubin levels and assessing the risk of kernicterus of newborns in the point-of-care or laboratory setting.

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