



카트리지 형태의 현장 검사 혈액 가스 장비 i-Smart 300의 성능 평가

Performance Evaluation of Cartridge-Type Blood Gas Analyzer: i-Smart 300

이아람 · 김한아 · 문희원 · 허미나 · 윤여민

Ahram Yi, M.D., Hanah Kim, M.D., Hee-Won Moon, M.D., Mina Hur, M.D., Yeo-Min Yun, M.D.

건국대학교 의학전문대학원 진단검사의학교실

Department of Laboratory Medicine, Konkuk University School of Medicine, Seoul, Korea

Background: Blood gas analysis plays a crucial role in critical care settings, and immediate and precise analysis improves clinical outcomes through prompt treatment. We evaluated the performance of a cartridge-type blood gas analyzer, i-Smart 300 (i-SENS, Korea), according to the Clinical and Laboratory Standard Institute (CLSI) guidelines and compared it to a conventional blood gas analyzer.

Methods: The precision was evaluated according to CLSI EP5-A3. The i-Smart 300 was compared to the Stat Profile Critical Care Xpress (STP CCX) (Nova CCX; Nova Biomedical, USA) according to CLSI EP9-A3 using the following eight parameters: pH, partial carbon dioxide pressure, partial oxygen pressure, sodium, potassium, chloride, ionized calcium, and hematocrit. Linearity was determined using five levels of control materials according to CLSI EP6-A.

Results: Within-run precision and total precision, demonstrated as coefficients of variation, ranged from 0.02 to 2.50% and from 0.05 to 3.46%, respectively. Correlation analysis yielded a correlation coefficient from 0.966 to 0.996 between the i-Smart 300 and the conventional analyzer (Nova CCX). The i-Smart 300 showed excellent linearity at eight parameters with acceptable percent recovery.

Conclusions: The i-Smart 300, a portable cartridge-type blood gas analyzer, showed high precision and good correlation with a traditional bench-top blood gas analyzer. It could be useful in critical care settings.

Key Words: i-Smart, Blood gas analyzer, Point-of-care systems, Performance

INTRODUCTION

Blood gas analysis is a critical tool in assessing a clinical diagnosis and in therapeutic monitoring of severely ill patients in the emergency department and intensive care unit (ICU) [1, 2]. Most blood gas analyzers measure the whole blood pH, partial carbon

dioxide pressure ($p\text{CO}_2$), and partial oxygen pressure ($p\text{O}_2$). Moreover, the simultaneous measurement of electrolytes such as sodium (Na^+), potassium (K^+), chloride (Cl), and ionized calcium (Ca^{2+}) is available with hematocrit (Hct). Integration and immediate therapeutic response using these results allows for prompt treatment and improvement of prognosis. Therefore, blood gas analyzers are being demanded for both their rapid turn-around of test results and sophisticated result accuracy. While most of the blood gas analyzers are used on-site, such as in emergency departments and ICUs for point of care (POC) testing, even bench-top models are currently in use at most clinical laboratories.

In the use of POC analyzers, quality control is a big issue. The users of POC analyzers are often unfamiliar with laboratory instruments and unacquainted with the maintenance and quality control of the instrument. Therefore, cartridge-type instruments are welcomed for most POC instruments, not only blood gas analyzers, but also molecular diagnostic analyzers [3]. If, however,

Corresponding author: Yeo-Min Yun

Department of Laboratory Medicine, Konkuk University School of Medicine Konkuk University Hospital, 120-1 Neungdong-ro, Gwangjin-gu, Seoul 05030, Korea

Tel: +82-2-2030-5582, Fax: +82-2-2030-5587, E-mail: ymyun@kuh.ac.kr

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there are discrepant results between a POC analyzer and central bench-top analyzer, this can confuse physicians and makes it more difficult to treat patients properly. Therefore, the performance evaluation of blood gas analyzers and determination of analyzer-specific differences in bias and precision are important to reduce the conflicting results between different instruments [4].

Recently, a brand new blood gas analyzer, i-Smart 300 (i-SENS, Seoul, Korea) was launched and is a cartridge-type blood gas analyzer, which is preferred in the clinical field. This study aims to evaluate the analytical performance of this new cartridge-type blood gas analyzer in comparison with the Stat Profile Critical Care Xpress (Nova CCX; Nova Biomedical, Waltham, MA, USA) as a reference method according to the Clinical and Laboratory Standard Institute (CLSI) guidelines.

MATERIALS AND METHODS

1. Analyzer

The i-Smart 300 blood gas analyzer consists of an operating instrument and a disposable cartridge containing all sensors, a reagents waste bag, tubing, and sample probe for analysis. The stand-alone disposable cartridge is a self-contained miniature analyzer, a functioning analyzing unit that contains all necessary parts: reagents, calibrators, reference solution, sample probe, valves, tubing, and sensors. Therefore, equipment maintenance is very convenient involving only replacing a cartridge. The i-Smart uses three levels of aqueous quality control (QC) material, RNA QC 623 Blood Gas-Electrolyte Control (RNA Medical, Devens, MA, USA), and two levels of RNA QC 900 Hematocrit Control (RNA Medical, Devens, MA, USA). This analyzer measures the whole blood pH, $p\text{CO}_2$, $p\text{O}_2$, Na^+ , K^+ , Cl^- , Ca^{2+} , and Hct using 80 μL heparinized whole blood.

2. Specimens

In March 2015, a total of 40 heparinized whole blood specimens were prospectively and consecutively collected. The specimens were anaerobically drawn from arterial vessels using heparinized blood sample kits, Becton Dickinson's Preset (BD Becton Dickinson Co., Plymouth, UK), according to the CLSI guideline [5]. The remaining specimens were used in anonymous way, and this study was approved by the Institutional Review Board of the Konkuk University Medical Center (KUH1200047).

To determine the imprecision of i-Smart for eight analytes, aqueous QC materials were used. For seven analytes, except Hct, three levels of aqueous QC material, RNA QC 623 Blood Gas-Electrolyte Control (RNA Medical, Devens, MA, USA) were used, and two levels of RNA QC 900 Hematocrit Control (RNA Medical, Devens, MA, USA) were used for Hct. For carry-over analysis, two levels of QC materials were tested. Five calibration verification materials [RNA CVC 123 Calibration Verification Controls and RNA CVC 9005 Hematocrit Calibration Verification Controls (RNA Medical, Devens, MA, USA)] were used for linearity assessment.

3. Study Design

The total run imprecision was determined using within-laboratory precision with the CLSI EP5-A3. It uses a design with 20 testing days, two runs per testing day, and two replicate measurements per run ($20 \times 2 \times 2$) for each samples using a single reagent and single calibrator lot. Carry-over was estimated with replicate measurements of the high-low sequences and was calculated by the equation: $\% \text{ carry-over} = \{L1 - (L3 + L4) / 2\} \times 100 / \{(H2 + H3) / 2 - (L3 + L4) / 2\}$. An acceptability criterion was $\% \text{ carry-over}$ of less than 1% [6, 7].

Linearity analysis was performed with five levels of commercially available linearity material with two repetitions of each level according to the CLSI EP6-A. Acceptability criteria were a slope between 0.9 and 1.1 and a recovery of between 90% and 110% [8].

Method comparison and difference estimation were assessed using a Nova CCX in the core laboratory. Forty heparinized whole blood specimens were analyzed on the i-Smart and the Nova CCX according to the CLSI EP9-A3 [9].

4. Statistical Analysis

Before statistical analysis, all data were processed to detect and reject outliers according to the CLSI EP9-A3 [9]. To compare the results of the i-Smart and Nova CCX, Pearson correlation coefficient and Passing-Bablok regression analysis were used. Each estimated slope and intercept, as well as 95% confidence intervals (CI), was calculated. The Nova CCX is the laboratory's current method and not a recognized reference method, so the trueness of the test methods could not be determined. The differences (absolute and relative) by the Bland-Altman difference plot were calculated. We used percent difference between the two methods, so bias from difference of scale or units could be excluded.

Statistical analysis was performed using Analyse-it Software

(version 3.905; Analyse-it Software, Ltd., Leeds, UK) and MedCalc Software (version 14.12.0; MedCalc Software, Mariakerke, Belgium). *P* values of less than 0.05 were considered statistically significant.

RESULTS

1. Precision and Carry-over

Total precision (percent coefficients of variation, CV) of eight parameters was determined by analyzing three levels of QC material on 20 consecutive days according to the CLSI guidelines (Table 1). Within-run CV ranged from 0.02 to 2.50%, and the total-run CV ranged from 0.05 to 3.46%. The %CV of Na⁺ at low level, Ca²⁺ at low level, Cl⁻ at high level, and Hct at low level were: 0.52, 1.61, 0.73, and 1.83%, respectively, and narrowly escaped the desirable precision criteria [10]. However, the other measured values

were within the allowable total error [11]. Carry-over ranged from -0.04 to 0.05% and was acceptable within 5% [7].

2. Linearity

Linearity was demonstrated according to the CLSI guidelines for all eight measurable parameters. Overall correlation coefficients (*r*) ranged from 0.9994 to 0.9998. The range of recovery was 94.3 – 120.6%. The slope and intercept of the regression equation are shown in Table 2. The recovery of *p*O₂ at low levels was 120.6%, and narrowly escaped the acceptable criteria, while the other values lay within the criteria.

3. Method Comparison

The results of Passing-Bablok regression analysis and mean difference estimations are summarized in Table 3. Pearson correla-

Table 1. Evaluation of total precision for blood gas and electrolytes using three levels of control materials on the i-Smart 300 blood gas analyzer, with allowable precision, difference, and total error

Parameter	Level	Mean	Between-run		Between-day		Within-run		Total-run		CV _w *	Desirable precision criteria (%)*
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)		
pH	Low	7.1604	0.0020	0.03	0.0033	0.05	0.0027	0.04	0.0047	0.07	0.2	0.1
	Medium	7.4094	0.0036	0.005	0.0000	0.00	0.0014	0.02	0.0039	0.05		
	High	7.6433	0.0040	0.05	0.0042	0.05	0.0020	0.03	0.0061	0.08		
<i>p</i> CO ₂ (mmHg)	Low	18.77	0.23	1.24	0.05	0.25	0.12	0.61	0.26	1.40	4.0	2.0
	Medium	39.23	0.45	1.14	0.00	0.00	0.16	0.40	0.47	1.20		
	High	66.21	0.50	0.76	0.24	0.36	0.45	0.67	0.71	1.08		
<i>p</i> O ₂ (mmHg)	Low	70.6	1.49	2.11	0.80	1.13	1.77	2.50	2.45	3.46	N/A	N/A
	Medium	90.5	2.13	2.24	0.70	0.73	1.02	1.08	2.46	2.60		
	High	126.5	2.40	1.90	0.00	0.00	1.20	0.95	2.68	2.12		
Na ⁺ (mmol/L)	Low	113.7	0.00	0.00	0.36	0.32	0.46	0.41	0.59	0.52	0.6	0.3
	Medium	132.4	0.40	0.30	0.00	0.00	0.46	0.35	0.61	0.46		
	High	154.8	0.37	0.24	0.41	0.26	0.46	0.30	0.72	0.46		
K ⁺ (mmol/L)	Low	2.02	0.02	0.78	0.03	1.61	0.02	1.11	0.04	2.10	4.6	2.3
	Medium	4.28	0.02	0.37	0.04	0.83	0.02	0.45	0.04	1.02		
	High	5.98	0.02	0.26	0.05	0.78	0.04	0.67	0.06	1.07		
Cl ⁻ (mmol/L)	Low	74.9	0.32	0.42	0.14	0.19	0.35	0.47	0.50	0.66	1.2	0.6
	Medium	94.4	0.37	0.39	0.14	0.15	0.46	0.49	0.61	0.64		
	High	126.0	0.58	0.46	0.58	0.46	0.40	0.32	0.92	0.73		
Ca ²⁺ (mmol/L)	Low	0.577	0.004	0.07	0.007	1.26	0.004	0.73	0.009	1.61	1.7	0.9
	Medium	1.163	0.009	0.79	0.004	0.35	0.006	0.48	0.011	0.99		
	High	1.474	0.006	0.39	0.014	0.97	0.008	0.53	0.017	1.17		
Hematocrit (%)	Low	27.0	0.32	1.17	0.23	0.87	0.30	1.10	0.49	1.83	2.7	1.35
	High	51.6	0.39	0.75	0.23	0.44	0.37	0.72	0.58	1.13		

It uses a design with 20 testing days, two runs per testing day, and two replicate measurements per run (*n* = 20 × 2 × 2 = 80) for each sample using a single reagent and single calibrator lot, according to the CLSI EP5-A3. Three levels of aqueous quality control (QC) material were used, RNA QC 623 Blood Gas-Electrolyte Control (RNA Medical, Devens, MA, USA), and two levels of RNA QC 900 Hematocrit Control (RNA Medical, Devens, MA, USA) were used.

*Within-subject variation and desirable analytical precision criteria are referenced from Ricos et al. [10], and the biological variation database specification on Westgard's website (<https://www.westgard.com/biodatabase1.htm>) [11].

Abbreviations: CV, coefficient variation; CV_w, within-subject biological variation; NA, not available.

Table 2. Evaluation of linearity from eight parameters using five levels of control materials with the i-Smart 300 blood gas analyzer

Parameter (unit)	Test range	Observed linear range	Manufacturer claimed AMR		Correlation (r)	Regression	% Recovery	P value
			i-Smart 300	Nova CCX				
pH (pH unit)	6.867-7.802	6.867-7.802	6.500-8.000	6.500-8.000	0.9994	$y = 0.9992x + 0.0175$	100.0-100.4	< 0.0001
pCO ₂ (mmHg)	12.7-83.7	12.7-83.7	5.0-150.0	3.0-200	0.9994	$y = 0.9726x + 0.3973$	96.1-99.8	< 0.0001
pO ₂ (mmHg)	41.0-462.5	69.0-462.5	5-700	0-800	0.9998	$y = 0.9959x + 2.8820$	98.6-120.6*	< 0.0001
Na ⁺ (mmol/L)	86.0-160.5	86.0-160.5	80-200	80-200	0.9998	$y = 0.9879x + 0.1835$	98.5-99.4	< 0.0001
K ⁺ (mmol/L)	1.60-11.30	1.60-11.30	1.0-20.0	1.0-20.0	0.9998	$y = 1.0150x - 0.1078$	95.0-100.9	< 0.0001
Cl ⁻ (mmol/L)	67.5-130.0	67.5-130.0	50-150	50-200	0.9998	$y = 1.0200x - 1.0100$	94.3-101.9	< 0.0001
Ca ²⁺ (mmol/L)	0.265-3.345	0.265-3.345	0.25-5.00	0.1-2.7	0.9998	$y = 1.0190x - 0.0292$	100.0-101.6	< 0.0001
Hematocrit (%)	21.5-69.0	21.5-69.0	10-70	12-70	0.9998	$y = 0.9934x + 0.3701$	100.0-102.4	< 0.0001

*The % recovery of pO₂ ranged from 98.6% to 120.6%. Except for the coded concentration 34, the % recovery of pO₂ ranged from 98.6% to 101.5%. Abbreviation: AMR, analytical measurement range.

Table 3. Comparison of results obtained using the i-Smart 300 and Nova CCX (n=40)

Parameter	Test range	Correlation (r) (95% CI)	Slope* (95% CI)	Intercept* (95% CI)	Mean difference [†] (95% CI)
pH (pH unit)	7.067-7.540	0.982 (0.967-0.991)	1.33 (1.25 to 1.40)	-2.36 (-2.94 to -1.79)	0.0424 (0.0330 to 0.0518)
pCO ₂ (mmHg)	19.9-77.9	0.979 (0.958-0.988)	0.95 (0.85 to 1.05)	-3.38 (-7.44 to 0.68)	-5.41 (-6.053 to -4.762)
pO ₂ (mmHg)	37.2-225.8	0.993 (0.987-0.996)	1.08 (1.03 to 1.12)	-3.00 (-8.97 to 2.97)	5.73 (3.10 to 8.36)
Na ⁺ (mmol/L)	124.5-144.8	0.966 (0.936-0.982)	1.02 (0.93 to 1.10)	-3.09 (-14.24 to 8.06)	-1.01 (-1.36 to 0.66)
K ⁺ (mmol/L)	2.67-6.59	0.996 (0.993-0.998)	0.88 (0.86 to 0.91)	0.34 (0.23 to 0.45)	-0.128 (-0.161 to -0.095)
Cl ⁻ (mmol/L)	88.8-116.7	0.970 (0.943-0.984)	1.05 (0.95 to 1.14)	-4.17 (-14.22 to 5.88)	0.86 (0.49 to 1.23)
Ca ²⁺ (mmol/L)	0.78-1.51	0.975 (0.952-0.987)	1.05 (0.95 to 1.15)	-0.15 (-0.27 to -0.03)	-0.091 (-0.100 to -0.082)
Hematocrit (%)	24-53	0.974 (0.951-0.986)	1.07 (0.99 to 1.15)	-5.08 (-8.08 to -2.08)	-2.6 (-3.0 to -2.1)

*Determined using Deming fit; [†]Mean difference is defined as measured values of the i-Smart 300 minus Nova CCX. Abbreviation: CI, confidence interval.

tion analysis yielded generally very high correlation coefficients ranging from 0.966 to 0.996 for all parameters being evaluated. The slopes of the regression equations ranged from 0.88 to 1.29 for all analytes.

Bland-Altman plots showed the means of the paired difference in the concentrations of eight analytes obtained using the i-Smart 300 and Nova CCX, which are shown in Fig. 1(B, D, F, H, J, L, N, P). Comparison of the two blood gas analyzers showed acceptable comparability for all analytes. According to the Bland-Altman plots, most paired data lay within ± 1.96 standard deviation (SD).

DISCUSSION

It is well known that results of blood gas and electrolyte analysis are crucial in managing the ICU and emergency department [12]. Furthermore, emergency conditions in the operating room, ICU, and emergency department require immediate and precise analysis to treat patients promptly. The i-Smart 300, a portable cartridge-type blood gas analyzer, can eliminate the time needed to deliver samples to central laboratory and help physicians to as-

sess disease and treat patients promptly. Unlike a conventional blood gas analyzer, the i-Smart 300 can be stored with the cartridges and reagents at room temperature, without occupying space in a refrigerator. Disposable cartridges include internal quality control materials and reagents, so it is easy to operate and use internal quality controls and, thus, the results could be reliable even when users are inexperienced.

In this study, we evaluated the i-Smart 300 by comparing precision, carry-over, linearity, and correlation with a conventional blood gas analyzer. For precision evaluation, various judgment parameters were applicable. Generally, the desirable analytical precision criteria are used according to intra-individual biologic variation [13]. Typically, if precision is within 50% of the intra-individual biologic variation, it is regarded as suitable clinical test. Also, in a specific patient, when followed by serial tests, it means the analytical errors allow for distinguishing between normal biologic variation and clinically significant changes [10, 14, 15]. For the precision performance analysis of the i-Smart 300 using quality control materials, each parameter's within-run precision and total precision were demonstrated as coefficients of variation and ranged

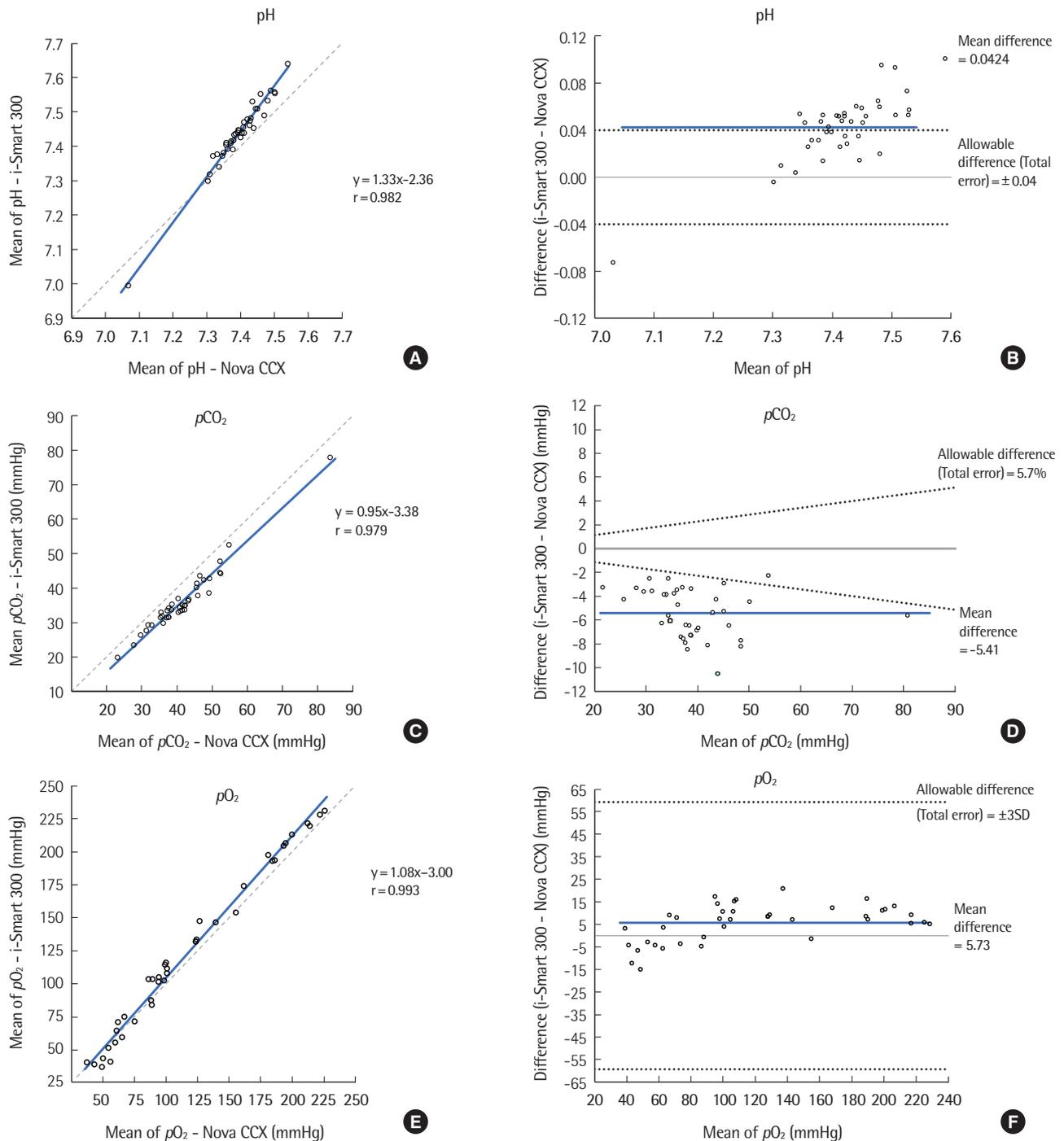


Fig. 1. Comparison of pH, $p\text{CO}_2$, $p\text{O}_2$, Na^+ , K^+ , Cl^- , Ca^{2+} , and Hematocrit results tested by the i-Smart 300 and STP CCX for 40 samples. (A, C, E, G, I, K, M, O) Correlation between the i-Smart 300 and Nova CCX. Solid line, Passing-Bablok regression; dashed line, identity line. (B, D, F, H, J, L, N, P) Difference between the i-Smart 300 and Nova CCX. Bold line, mean difference between values; dotted lines, desirable specification for allowable total error. (continued to the next page)

from 0.02 to 2.50% and from 0.05 to 3.46%, respectively. All parameters except Na^+ , Cl^- , Ca^{2+} , and Hct fit the total desirable precision criteria. Therefore, pH, $p\text{CO}_2$, $p\text{O}_2$, and K^+ can be used for as a patient follow-up purposes [11]. Cl^- and Hct were among the four

parameters that did not meet the precision criteria, however, they met the minimum precision criteria, which is 75% of biological variation [16].

The i-Smart 300 showed excellent carry-over, all of the param-

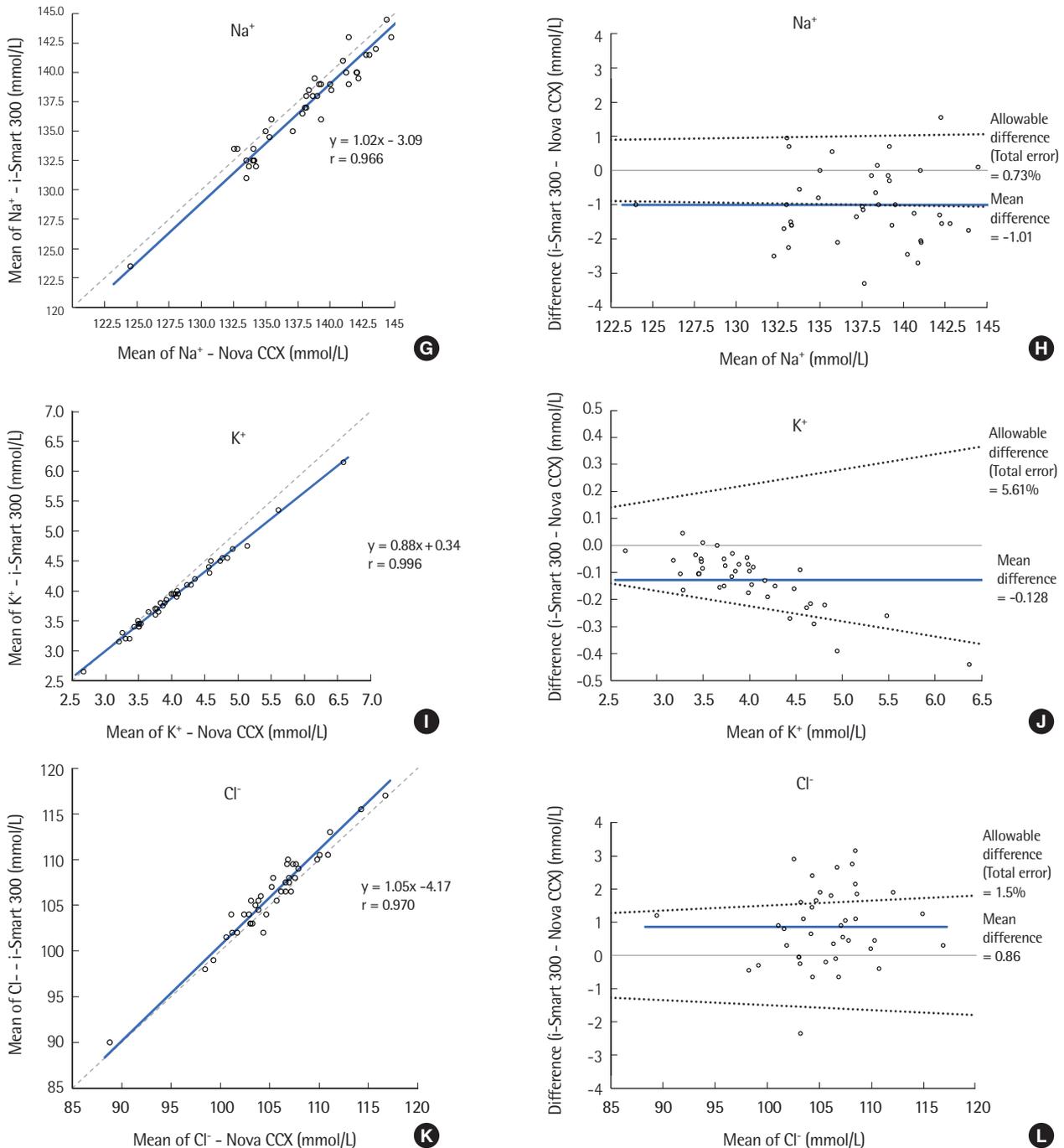


Fig. 1. Continued.

ters' carry-over were within 1.0%, and values were similar to a conventional blood gas analyzer. The specific carry-over ranged between -0.04% and 0.05%. Typically, the goal is within 1%, therefore, the carry-over of the i-Smart 300 is excellent [17]. All eight analytes showed excellent linearity within the acceptable recovery range. Moreover, correlation statistics between the i-Smart 300 and Nova CCX using Pearson's correlation coefficients all were greater than 0.96, meaning high correlation.

ter than 0.96, meaning high correlation.

According to the Bland-Altman plots, most analytes of the i-Smart 300 such as $p\text{CO}_2$, Na^+ , K^+ , Ca^{2+} , and Hct showed lower values compared to those measured by the Nova CCX.

Some of the limitations of our study are that the results of the Nova CCX, which we use as the standard, have not been verified as the true value.

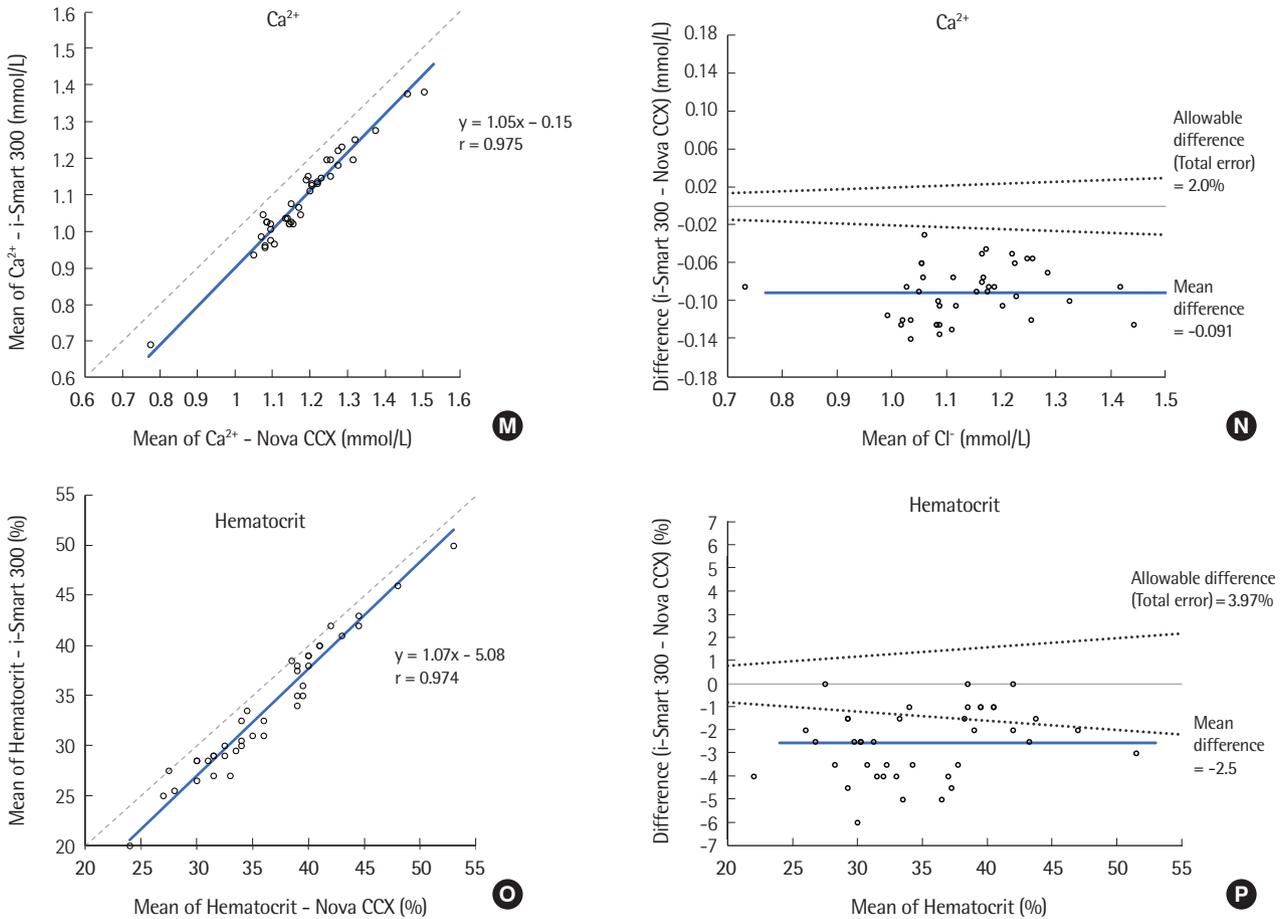


Fig. 1. Continued.

We also used samplers, which contain lyophilized heparin, so that we could avoid the dilution effect.

In conclusion, this study is the first evaluation of the newly launched i-Smart 300 according to the CLSI guidelines. The i-Smart 300 showed excellent precision, linearity, carry-over, and inter-analyzer correlation, even though it is a portable, cartridge-type blood gas analyzer. There are advantages in terms of the convenience to users and the stability of the analyzer, so the i-Smart 300 can be utilized in various clinical settings, such as ICU, operating room, and emergency department as a blood gas analyzer.

요약

배경: 혈액가스 분석은 의료 분야에 있어서 중요한 역할을 하고 있고, 즉각적이고 정확한 분석은 즉각적인 치료를 통해 임상적 결과를 향상시킨다. 우리는 카트리지 형태의 혈액가스 분석 장비인 i-Smart 300의 분석능을 기존 혈액가스 분석 장비와 비교하여, Clinical and

Laboratory Standard Institute (CLSI) 지침에 따라 평가하였다.

방법: 정밀도는 CLSI EP5-A3에 따라 검증하였다. i-Smart 300은 다음과 같은 8가지 지표에 대하여 Stat Profile Critical Care Xpress (STP CCX) (Nova CCX; Nova Biomedical, USA)와 비교 평가를 시행하였다. : pH, partial carbon dioxide pressure (pCO_2), partial oxygen pressure (pO_2), sodium (Na^+), potassium (K^+), chloride (Cl^-), ionized calcium (Ca^{2+}), and hematocrit (Hct). 직선성은 CLSI EP6-A에 근거하여 5가지 농도의 control 물질을 이용하여 판정하였다.

결과: 검사차례내 정밀도는 0.02-2.50%, 총 정밀도는 0.05-3.46%로 낮은 변이계수를 보였다. 장비 간 비교에서 상관계수는 0.966-0.996의 값을 보였다. 8가지 측정항목에서 우수한 직선성과 수용할 수 있는 범위내의 기대값 대비 회수율을 보였다.

결론: 본 연구는 i-Smart 300의 CLSI 가이드라인에 근거한 최초의 분석능 평가라는 의미를 갖는다. i-Smart 300은 이동식 카트리지 형태의 혈액가스 분석 장비로서, 높은 정밀도와 기존 장비와의 좋은 상관관계를 보였다. 그러므로 의료 환경 내에서 유용하게 쓰일 수 있을 것으로 생각된다.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTERESTS

No potential conflicts of interest relevant to this article were reported.

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