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Title	Evaluation of a miniaturized clinical laboratory system for lipid analysis
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Abstract

Objectives: The aim of this study was to evaluate the analytical performance of a miniaturized clinical laboratory system for lipid analysis, including direct measurement of low density lipoprotein cholesterol. Design and methods: To demonstrate analytical performance of the Theranos miniLab system we evaluated precision (2 levels, 5 replicates per day for 5 days over 3 miniLabs), analytical sensitivity (limit of detection and limit of blank), linearity (11 levels, 4 replicates), and interferences (standard interferents and lipid-lowering medications) for total cholesterol, high density lipoprotein cholesterol (HDL), direct low density lipoprotein cholesterol (LDL) and triglycerides. The miniLab lipid analysis was also compared to two FDA-approved methods for each analyte: Siemens Advia (total cholesterol, HDL, direct LDL, triglycerides), Roche Cobas (total cholesterol, HDL, triglycerides), and the Sekisui direct LDL assay run on the Cobas. All studies were done with fresh, residual, de-identified serum samples collected for lipid analysis. Results: The miniLab met standard precision goals for lipids with all measures of imprecision being less than 3%. Analytical sensitivity was sufficient to detect low physiologically relevant concentrations for all analytes. All assay components were deemed linear over the concentration range tested. There was no significant interference detected with any of the interferents tested for all lipid analytes. Compared to two FDA-approved methods the miniLab showed a strong correlation and no significant bias for all analytes except for LDL cholesterol when compared to the Advia (-7% bias), but not compared to the Sekisui assay run on the Cobas (-1% bias). Conclusions: This is the first independent evaluation of the miniLab system and confirms that this miniaturized clinical laboratory system is capable of measuring lipids, including a direct measure of LDL, with comparable performance to two different Federal Drug Administration (FDA) approved methods for each analyte.

Keywords	Lipid analysis; cholesterol screening; point-of-care lipids; dyslipidemia; cardiovascular disease; direct low-density lipoprotein.
Taxonomy	Laboratory Diagnosis, Bioanalysis, Laboratory Medicine
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December 20, 2017

Loralie Langman, PhD
Editor-in-Chief
Clinical Biochemistry

Dear Dr. Langman,

I am submitting an original contribution, Evaluation of a miniaturized clinical laboratory system for lipid analysis, for consideration for publication as an article in *Clinical Biochemistry*.

The objective of this study was to evaluate the analytical performance of lipid analysis on a miniaturized clinical laboratory system, including direct measurement of low density lipoprotein cholesterol. Cardiovascular disease accounts for 1 of every 3 deaths in the United States and can be attributed to modifiable risk factors such as dyslipidemia. Early detection and treatment of dyslipidemia has significant public health implications since risk for cardiovascular disease can be lowered through a modified diet and lipid-lowering therapies. Lipid panels are predominately run on automated analyzers in central laboratories using venous blood samples, however, point-of-care (POC) capillary whole blood lipid analyzers have also been used for screening in a variety of settings. There are currently no POC analyzers capable of measuring LDL directly. Given the limitations with calculated LDL and the need to be fasting for accurate measurements, these requirements result in decreased compliance in fulfilling laboratory test orders and is not conducive to screening in a public health or outreach settings. The lipid assays on the miniaturized clinical laboratory system under evaluation were tested for sensitivity, precision, linearity, interferences, and compared to two FDA-approved methods for each analyte in the lipid panel.

This is the first independent evaluation of the miniLab system and confirms that this miniaturized clinical laboratory system is capable of measuring lipids, including a direct measure of LDL, with comparable performance to two different Federal Drug Administration (FDA) approved methods for each analyte. Thank you for your consideration.

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Evaluation of a miniaturized clinical laboratory system for lipid analysis

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Abstract

Objectives: The aim of this study was to evaluate the analytical performance of a miniaturized clinical laboratory system for lipid analysis, including direct measurement of low density lipoprotein cholesterol.

Design and methods: To demonstrate analytical performance of the Theranos miniLab system we evaluated precision (2 levels, 5 replicates per day for 5 days over 3 miniLabs), analytical sensitivity (limit of detection and limit of blank), linearity (11 levels, 4 replicates), and interferences (standard interferents and lipid-lowering medications) for total cholesterol, high density lipoprotein cholesterol (HDL), direct low density lipoprotein cholesterol (LDL) and triglycerides. The miniLab lipid analysis was also compared to two FDA-approved methods for each analyte: Siemens Advia (total cholesterol, HDL, direct LDL, triglycerides), Roche Cobas (total cholesterol, HDL, triglycerides), and the Sekisui direct LDL assay run on the Cobas. All studies were done with fresh, residual, de-identified serum samples collected for lipid analysis.

Results: The miniLab met standard precision goals for lipids with all measures of imprecision being less than 3%. Analytical sensitivity was sufficient to detect low physiologically relevant concentrations for all analytes. All assay components were deemed linear over the concentration range tested. There was no significant interference detected with any of the interferents tested for all lipid analytes. Compared to two FDA-approved methods the miniLab showed a strong correlation and no significant bias for all analytes except for LDL cholesterol when compared to the Advia (-7% bias), but not compared to the Sekisui assay run on the Cobas (-1% bias).

Conclusions: This is the first independent evaluation of the miniLab system and confirms that this miniaturized clinical laboratory system is capable of measuring lipids, including a direct measure of LDL, with comparable performance to two different Federal Drug Administration (FDA) approved methods for each analyte.

Keywords: Lipid analysis, cholesterol screening, point-of-care lipids, dyslipidemia, cardiovascular disease, direct low-density lipoprotein

Abbreviations: high density lipoprotein, HDL; low density lipoprotein, LDL; Federal Drug Administration, FDA; total cholesterol, TC; point-of-care, POC; limit of blank, LoB; limit of detection, LoD; dLDL, direct low density lipoprotein.

1. Introduction

Cardiovascular disease accounts for 1 of every 3 deaths in the United States and can be attributed to modifiable risk factors such as dyslipidemia [1]. An estimated 37.5% of Americans have total cholesterol (TC) of 200 mg/dL or higher and 1 of every 3 have high levels of low-density lipoprotein (LDL) cholesterol, the most common atherosclerotic risk marker [1]. Early detection and treatment of dyslipidemia has significant public health implications since risk for cardiovascular disease can be lowered through a modified diet and lipid-lowering therapies.

Dyslipidemia is diagnosed through a standard lipid panel which includes the measurement of total cholesterol, high-density lipoprotein cholesterol (HDL) and triglycerides. These measures are typically used to calculate an estimate of LDL using the Friedewald equation [2]. This estimation is inaccurate when there are high levels of triglycerides and thus most screening protocols require a fasting specimen. A fasting requirement typically results in decreased compliance in fulfilling laboratory test orders and is not conducive to screening in a public health or outreach settings. Methods that directly analyze LDL are available and used in some laboratories, however, calculated LDL is still the standard measure despite the limitations associated with its use. Lipid panels are predominately run on automated analyzers in central laboratories using venous blood samples, however, point-of-care (POC) capillary whole blood lipid analyzers have also been used for screening in a variety of settings [3-6]. There are currently no POC analyzers capable of measuring LDL directly.

Centralized laboratory testing using various technologies on large-scale automated analyzers has been the long-standing foundation for diagnostic testing. Currently there are also POC analyzers available that can multiplex the detection of multiple analytes; however, they are typically engineered with one type of detection method limiting the possible panel of tests. Also, POC analyzers typically suffer from performance limitations compared to centralized laboratories. The purpose of this study was to evaluate a new miniaturized clinical laboratory system designed to test a diverse range of analytes in decentralized settings. The miniLab is a bench top modular hardware platform with a small footprint (56 cm x 41 cm x 33 cm; up to 43 kg) that is designed to perform immunoassays, general chemistry, nucleic acid, and cellular characterization assays on a variety of sample types [7]. It is engineered with a centrifuge, sonicator, and 4 miniaturized detector modules: thermal cycling and isothermal fluorescence detection system, photodetector, spectrophotometer, and fluorescence microscope. The system has been shown to be able to measure a diverse array of analytes [7]; however, it has yet to be operated and evaluated by an independent laboratory and is not FDA-approved. The objective was to evaluate the analytical performance of the miniLab for lipid analysis, including measurement of direct LDL. To demonstrate analytical performance we evaluated precision, analytical sensitivity, linearity, interferences, and method comparison with two FDA-approved methods operating routinely in two CLIA-certified laboratories.

2. Materials and methods

2.1 Study samples

Residual, de-identified serum samples from ambulatory and hospitalized patients collected between July 15, 2017 to October 12, 2017 for routine lipid testing were used for all studies. This study was approved by the University of California Institutional Review Board who determined that patient consent was not necessary for the use of remnant de-identified samples for method evaluation.

2.2 Lipid panel measurements

Unless noted, all experiments were performed on the Theranos miniLab system (Newark, CA), in the author's laboratory, using a Theranos mulitplexed lipid panel. The panel includes TC, HDL, direct LDL-cholesterol (dLDL), and triglycerides in one cartridge using one protocol on the miniLab. The details of the methods are previously described [7]. In short, the assay used a series of coupled enzyme peroxidase-based Trinder reactions in which a quinonimine dye is produced and measured at 500 nm (total cholesterol) or 545 nm (HDL, dLDL, triglycerides). Assay consumables and test cartridges were obtained from Theranos (Newark, CA). Two levels of quality control (liquid assayed multiqual, levels 1 and 3, Bio-Rad Laboratories, Hercules, CA) were assayed daily on the miniLab instruments prior to operation and were required to be within pre-established QC ranges.

For the method comparison studies (described below), multiple assay platforms that are in routine operation in CLIA-certified laboratories were used. The Siemens (Erlangen, Germany) Cholesterol_2, Direct HDL Cholesterol, LDL Cholesterol Direct, and Triglycerides_2 assays were performed on the ADVIA Chemistry Systems (1800 and/or XPT) in the author's CLIA-certified laboratory. The Roche Diagnostics (Indianapolis, IN) Cholesterol Gen.2, HDL 3rd Gen, and TRIGL assays were performed on the Roche Cobas c502 at a national clinical reference laboratory. The Sekisui Diagnostics (Lexington, MA) N-geneous LDL assay was performed on the Roche Cobas c702 at a national clinical reference laboratory. All comparator assays (Siemens, Roche, Sekisui) used are FDA-approved and were performed according to the manufacturers' instructions in a CLIA-certified laboratory.

2.3 Precision

Remnant serum samples were pooled to generate two precision sample pools at concentrations near medical decision points. Precision experiments were performed on the miniLab for each measurand with 5 replicates per day over 5 days across 3 miniLabs in accordance with the multisite precision

guidelines CLSI EP05-A3 [8]. All results for each lipid analyte were analyzed using a two-way nested ANOVA analysis, with "day" nested within "device". Within-day (repeatability), within-device, between-day, between-device, and total imprecision (reproducibility) and associated 95% confidence intervals were determined. Potential outliers were identified using Grubbs' test, with up to one outlier allowed per miniLab for each level and for each measurand.

2.4 Analytical Sensitivity

Limit of blank (LoB) and four limit of detection samples (LoD) were generated from SeraCon II Lipid Depleted Negative Diluent (SeraCare, Milford, MA) and remnant serum samples. The limit of blank sample was tested over 5 days with 12 replicates per day for a total of 60 measurements. Each limit of detection sample (N=4) was tested over 5 days with 3 replicates per day for a total of 60 measurements. All results were analyzed following the guidelines for Classical Approach analysis in CLSI EP17-A2 [9]. The limit of blank was calculated using the following equation: $LoB = M_B + 1.645(SD_B)$, where M_B is the mean of all blank measurements and SD_B is the standard deviation for all blank results. The limit of detection was calculated using the following equation: $LoD = LoB + 1.645(SD_L)$, where SD_L is the pooled standard deviation for all limit of detection samples.

2.5 Linearity

Linearity was assessed for all lipid analytes using high and low remnant serum sample pools. SeraCon II Lipid Depleted Negative Diluent (SeraCare, Milford, MA) was mixed with the low remnant serum sample pool to generate lower lipid levels in the low pool. Commercial concentrated fractions of triglycerides and lipoproteins were used to spike into the high remnant sample pool to generate higher lipid levels for the high pool. These reagents included, Human Cholesterol Concentrate LDL and Human Cholesterol Concentrate HDL from Lee Biosolutions, Inc. (Maryland Heights, MO) and Intralipid (triglycerides) from Sigma-Aldrich (Saint Louis, MO). The final high pool was serially diluted into the final low pool to

generate 11 linearity samples that were analyzed with 4 replicates each. Data were analyzed in accordance with CLSI EP06-A [10].

2.6 Interference Testing

The following interferents were evaluated for all analytes in two different (low and high) remnant serum sample pools: conjugated bilirubin (20 mg/dL), hemolysate (500 mg/dL), triglycerides (800 mg/dL), ascorbic acid (6 mg/dL), acetylsalicylic acid (65.2 mg/dL), atorvastatin (0.06 mg/dL), colestipol (1.8 mg/dL), ezetimibe (0.60 mg/dL), fenofibrate (4.50 mg/dL), alpha-linolenic acid (50 mg/dL), niacin (120 mg/dL), and simvastatin (2.40 mg/dL). Interferents were purchased from Sigma-Aldrich (Saint Louis, MO), Bio-Rad Laboratories (Hercules, CA), Cerilliant (Round Rock, TX), and Cayman Chemicals (Ann Arbor, MI). Data analysis was performed in accordance with CSLI EP07-A2 [11]. The percent interference (d_{obs}) and associated 95% confidence intervals were calculated. The following equation was used to calculate the percent interference for each interferent at each level (low and high): $d_{obs} = (mean_{control} - mean_{test}) \div mean_{control}$. A percentage effect $\geq$ 10% effect was considered a significant interference.

2.7 Method comparison

Inter-assay variability was evaluated using 133 fresh (never frozen) remnant serum samples spanning the analytical range for all four lipid analytes. Testing on all platforms (miniLab, ADVIA, Cobas) was conducted within 48 hours of receipt in the laboratory for each sample. The Siemens, Roche and Sekisui assays were used as the comparator methods to evaluate the miniLab assays. Data analysis was performed in accordance with CLSI EP09-A3 [12]. Deming regression was calculated along with associated slope, intercept, 95% confidence intervals, and correlation coefficient. Bland-Altman analysis was conducted, and graphs generated to show the distribution of mean bias across each measurand's analytical range. Potential outliers were identified using Grubbs' test, with up to one outlier allowed per miniLab for each level and for each measurand.

2.8 Data analysis and statistics

All data analysis and statistics were completed using a combination of EP Evaluator (Data Innovations, Burlington, VT), Microsoft Excel (Microsoft Corporation, Redmond, WA), Analyse-it Software (Analyse-it, Software, Ltd, Leeds, UK), and cp-R, a graphical interface to the R statistical programming (http://sourceforge.net/projects/cprchempath/).

3. Results and Discussion

3.1 Precision

Within-day (repeatability), within-device, between-day, between-device, and total imprecision (reproducibility) results are summarized in Table 1 for total cholesterol, HDL, dLDL, and triglycerides. The precision CVs ranged from 0 – 2.1% for total cholesterol, 0.8 – 2.7% for HDL, 0.2 – 2.3% for dLDL, and 0.1 – 2.8% for triglycerides. For each of the measurands at both levels tested, most of the variability was captured in the repeatability component, with minimal day-to-day and device-to-device variability across the 3 miniLabs evaluated. The miniLabs operated consistently across devices and days and the results are all within established precision goals for lipid analysis.

3.2 Analytical Sensitivity

The limit of blank (LoB) was determined to be 10 mg/dL for cholesterol, 0 mg/dL for HDL, 6 mg/dL for dLDL, and 3 mg/dL for triglycerides (Table 1). The limit of detection (LoD) was determined to be 15 for cholesterol, 3 mg/dL for HDL, 9 mg/dL for dLDL, and 9 mg/dL for triglycerides (Table 1). These values are all well below the low end of typical physiological concentrations.

3.3 Linearity

All assay components were deemed linear over the concentration range tested (Table 1). The linear range was determined to be 54 – 691 mg/dL for total cholesterol (slope = 0.997, intercept = 0.2 mg/dL),

17 – 132 mg/dL for HDL (slope = 1.002, intercept = 0.11 mg/dL), 25 – 420 mg/dL for dLDL (slope = 0.995, intercept = -0.06 mg/dL), and 17 – 949 for triglycerides (slope = 0.992, intercept = 0.2 mg/dL). These analytical measurement ranges meet clinical testing needs and are consistent with other FDA-approved methods.

3.4 Interference Testing

There was no significant interference (±10%) detected with any of the interferents tested for all lipid analytes in both sample pools (Table 2). The calculated percent bias was less than ±5% for all interferents except, conjugated bilirubin in pool 1 (-5.33%) and triglycerides in pool 2 (-5.17%). The interferents tested included common analytical interferents and common medications prescribed to patients with heart disease.

3.5 Method comparison

Each lipid analyte in the miniLab multiplexed lipid panel was compared to two assay platforms. Method comparison results are summarized in Table 3. Deming linear regression analysis and Bland-Altman plots for each comparison are shown in Figure 1. For total cholesterol the miniLab showed good correlation with the Advia (R=0.997, slope=0.98) and Cobas (R=0.995, slope=0.99). No significant bias was detected (Advia, -3.5% and Cobas, -0.9%). For HDL, the miniLab showed good correlation with the Advia (R=0.969, slope=0.79) and a small negative bias (-4.03%) was observed. The correlation between the miniLab and Cobas for HDL was also good (R=0.936, slope=0.75), and no significant bias (-2.30%) was observed across the range evaluated. For dLDL, the miniLab showed good correlation with both the Advia (R=0.978, slope=0.88) and Sekisui (R=0.981, slope=0.95), however a negative bias was observed when compared to the Advia (-7.14%) but not compared to the Sekisui method on the Cobas (-0.96%). For triglycerides, the miniLab showed a strong correlation with the Advia (R=0.999, slope=0.99) and Cobas (R=0.999, slope=0.99) and a slight negative bias was observed for the miniLab compared to the Cobas (-2.5%), but

not compared to the Advia (0.0%). The miniLab provides lipid results comparable to these FDA-approved methods across the physiologic range.

4. Conclusions

In this study we performed an independent evaluation of a miniaturized clinical laboratory system for the evaluation of total cholesterol, HDL, LDL (measured directly), and triglycerides. The miniLab met standard precision goals for lipids with all measures of imprecision being less than 3%. Analytical sensitivity was sufficient to detect low physiologically relevant concentrations for all analytes. In addition to standard interferents such as bilirubin, triglycerides, and hemolysate, we evaluated the assay for interference from commonly prescribed lipid-lowering drugs such as HMG-CoA reductase inhibitors (atorvastatin), bile acid sequestrants (cholestipol), and cholesterol absorption inhibitors (ezetimide). There was no significant interference detected with any of the interferents tested for all lipid analytes. The National Cholesterol Education Program defines performance measures for percent bias for lipid parameters to be: TC $\leq$ 3%, HDL $\leq$ 5%, LDL $\leq$ 4%, triglycerides $\leq$ 5%, when compared to a reference measurement procedure [13-16]. Compared to two FDA-approved methods, which are not reference measurement procedures, the miniLab lipid performance met these specifications for all analytes except for LDL cholesterol when compared to the Advia (-7%). This bias was not seen when comparing LDL on the miniLab to the Sekisui assay run on the Cobas (-1%). As a reference it is important to note that the bias was also seen when comparing the two FDA-approved methods. LDL on the Advia had a positive bias (7%) when compared to the Sekisui assay, suggesting that the Siemens assay was the outlier.

This is the first independent evaluation of the miniLab and confirms that this miniaturized clinical laboratory system is capable of measuring lipids, including a direct measure of LDL, with comparable performance to two different FDA-approved methods for each analyte. These assays on the miniLab system are not currently approved or cleared by FDA and are not available for clinical

diagnostics. Future studies are needed to evaluate the other detection modules and assay systems available on the miniLab and FDA-approval or clearance will be required prior to diagnostic use. Additionally, only venous samples were evaluated in this study. Future work will need to determine if lipid measures on capillary blood is comparable to the performance observed for venous samples.

Figure Legend

Figure 1. Inter-instrument variability between the miniLab and comparator FDA approved methods for total cholesterol, high density lipoprotein cholesterol (HDL), direct measurement of low density lipoprotein cholesterol (dLDL), and triglycerides. For each comparison the Deming linear regression plot is shown followed by the Bland Altman bias plot.

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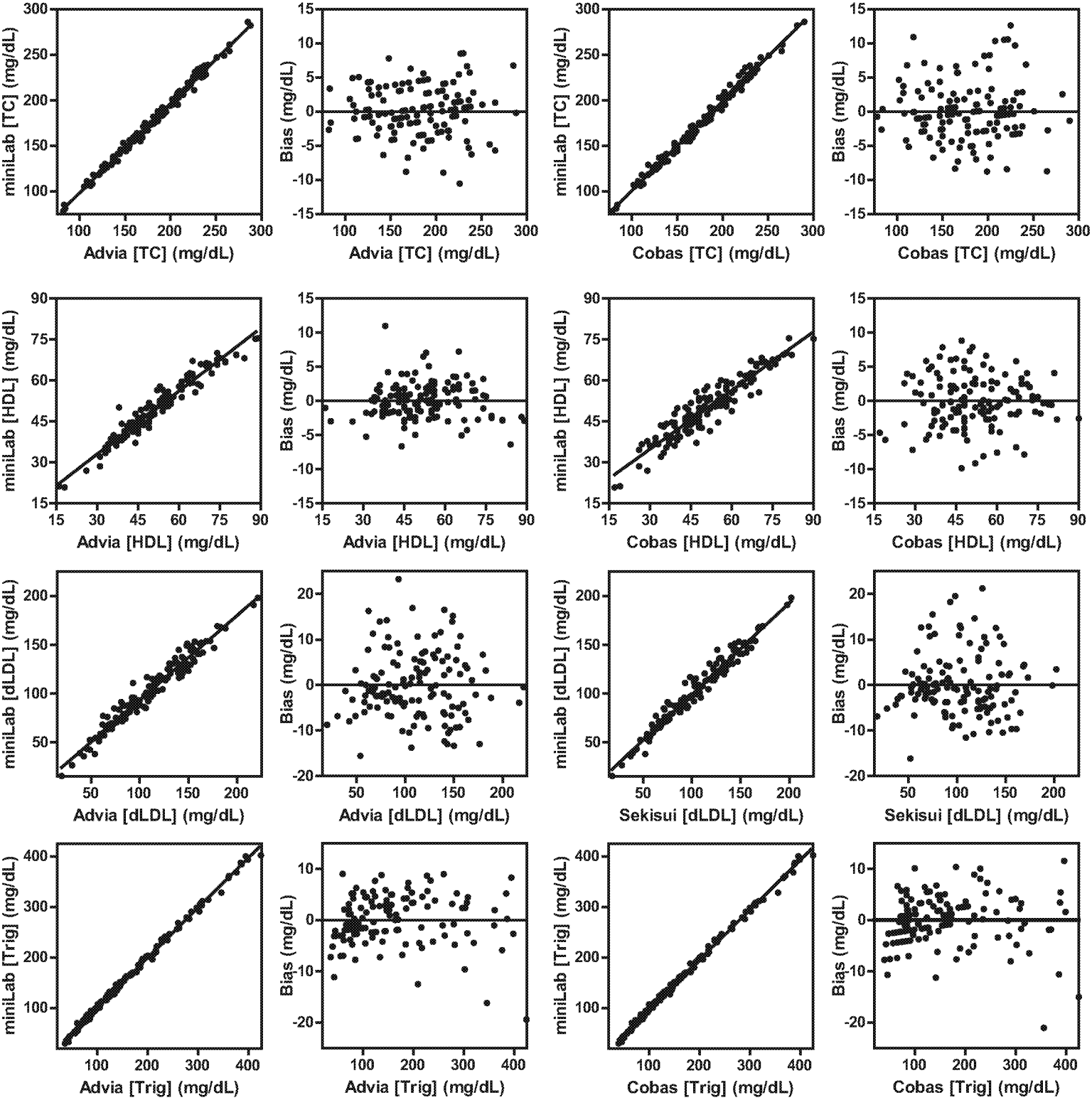

Fig 1. Inter-instrument variability between the miniLab and comparator FDA approved methods for total cholesterol, high density lipoprotein cholesterol (HDL), direct measurement of low density lipoprotein cholesterol (dLDL), and triglycerides. For each comparison the Deming linear regression plot is shown followed by the Bland Altman bias plot.

Table 1. Precision, sensitivity, and linearity results for the miniLab

Analyte	Precision						Sensitivity (mg/dL)		Linearity		
	Mean (mg/dL)	Within-day	Within-miniLab	Between-day	Between-minilab	Reproducibility	LOB*	LOD*	Range (mg/dL)	Slope	Intercept
Total Cholesterol	151	1.6%	1.6%	0.0%	1.3%	2.1%	10	15	54 - 691	0.997	0.20
	245	1.2%	1.3%	0.4%	0.7%	1.4%					
HDL Cholesterol	57	2.1%	2.3%	0.9%	1.1%	2.6%	0	3	17 - 132	1.002	0.11
	50	2.5%	2.6%	0.8%	0.8%	2.7%					
LDL Cholesterol	71	2.1%	2.2%	0.6%	0.6%	2.3%	6	9	25 - 420	0.995	-0.06
	158	1.3%	1.3%	0.2%	0.3%	1.3%					
Triglycerides	120	1.7%	1.7%	0.2%	2.2%	2.8%	3	9	17 - 949	0.992	0.20
	243	1.7%	1.7%	0.1%	0.1%	1.7%					

*LOB = limit of blank, LOD = limit of detection

Table 2. Interference testing for the miniLab

	Total Cholesterol		HDL		dLDL		Triglycerides	
Interferent	Pool 1 (187 mg/dL)	Pool 2 (265 mg/dL)	Pool 1 (47 mg/dL)	Pool 2 (55 mg/dL)	Pool 1 (100 mg/dL)	Pool 2 (145 mg/dL)	Pool 1 (152 mg/dL)	Pool 2 (423 mg/dL)
Conjugated bilirubin	-5.33 (-5.25, -5.40)	-4.06 (-4.00, -4.11)	-1.3 (-1.30, -1.30)	-4.38 (-4.36, -4.39)	-1.12 (-1.11, -1.12)	-2.56 (-2.55, -2.57)	-8.2 (-8.1, -8.3)	-4.89 (-4.76, -5.03)
Hemolysate	4.39 (4.34, 4.45)	3.87 (3.82, 3.92)	-0.42 (-0.42, -0.42)	-1.06 (-1.06, -1.06)	3.68 (3.65, 3.70)	1.60 (1.59, 1.60)	-1.64 (-1.63, -1.65)	-0.88 (-0.87, -0.89)
Triglycerides	-1.6 (-1.58, -1.61)	0 (0, 0)	1.15 (1.15, 1.15)	-5.17 (-5.15, -5.19)	-1.29 (-12.9, -1.30)	-0.57 (-0.57, -0.57)	ND**	ND**
Ascorbic acid	-1.74 (-1.73, -1.76)	-2.36 (-2.34, -2.38)	3.20 (3.19, 3.21)	-2.87 (-2.86, -2.88)	1.23 (1.22, 1.23)	-0.89 (-0.89, -0.90)	-0.67 (-0.66, -0.67)	-1.89 (-1.86, -1.91)
Acetylsalicylic acid	-1.61 (-1.59, -1.62)	-1.42 (-1.40, -1.43)	0.01 (0.01, 0.01)	-2.11 (-2.10, -2.11)	-0.63 (-0.62, -0.63)	0.40 (0.40, 0.40)	.033 (0.33, 0.33)	-0.65 (-0.65, -0.66)
Atorvastatin	-2.13 (-2.11, -2.16)	-0.95 (-0.94, -0.95)	-2.76 (-2.75, -2.77)	-1.82 (-1.82, -1.82)	0.32 (0.32, 0.32)	1.03 (1.02, 1.03)	-3.57 (-3.55, -3.60)	1.78 (1.74, 1.82)
Colestipol	-1.46 (-1.45, -1.48)	0.19 (0.19, 0.19)	-0.10 (-0.10, -0.10)	-2.87 (-2.86, -2.88)	0.77 (0.77, 0.77)	0.24 (0.24, 0.24)	-0.33 (-0.33, -0.33)	-0.59 (-0.58, -0.60)
Ezetimibe	-2.53 (-2.51, -2.56)	0.28 (0.28, 0.29)	3.02 (3.01, 3.02)	3.50 (3.48, 3.52)	1.77 (1.78, 1.78)	0.48 (0.48, 0.48)	-1.14 (-1.13, -1.14)	0.24 (0.23, 0.24)
Fenofibrate	0 (0, 0)	-0.57 (-0.56, -0.58)	3.12 (3.11, 3.13)	1.09 (1.09, 1.09)	2.35 (2.34, 2.36)	0.51 (0.51, 0.52)	0.32 (0.32, 0.32)	-0.41 (-0.41, -0.42)
Alpha-linolenic acid	0 (0, 0)	0 (0, 0)	0.94 (0.93, 0.94)	-0.64 (-0.64, -0.64)	1.87 (1.87, 1.88)	0.58 (0.58, 0.59)	1.46 (1.46, 1.47)	0.89 (0.88, 0.90)
Niacin	-1.46 (-1.45, -1.48)	-1.42 (-1.40, -1.43)	-4.54 (-4.52, -4.56)	-2.43 (-2.42, -2.44)	-1.12 (-1.11, -1.12)	0.89 (0.89, 0.90)	-2.3 (-2.28, -2.31)	-0.47 (-0.47, -0.48)
Simvastatin	-1.60 (-1.59, -1.61)	-0.57 (-0.57, -0.57)	1.14 (1.14, 1.15)	0.32 (0.32, 0.32)	-0.52 (-0.52, -0.53)	-0.21 (-0.21, -0.21)	-1.62 (-1.62, -1.63)	0.06 (0.06, 0.06)

*first number represents percent interference, while numbers in parentheses represent the 95% confidence intervals

**not determined

Table 3. Method comparison results

	Slope	y-Intercept	R	Bias (%)
Total Cholesterol				
miniLab vs. ADVIA	0.98 (0.97, 1.00)	-0.2 (-2.8, 2.5)	0.997	-3.5 (-1.9%)
miniLab vs. Cobas	0.99 (0.97, 1.01)	1.1 (-2.1, 4.2)	0.995	-0.9 (-0.5%)
HDL Cholesterol				
miniLab vs. ADVIA	0.79 (0.75, 0.82)	8.98 (7.16, 10.80)	0.969	-2.09 (-4.03%)
miniLab vs. Cobas	0.75 (0.71, 0.80)	11.50 (9.02, 13.99)	0.936	-1.18 (-2.30%)
LDL Cholesterol				
miniLab vs. ADVIA	0.88 (0.85, 0.91)	5.65 (1.86, 9.43)	0.978	-7.90 (-7.14%)
miniLab vs. Sekisui/Cobas	0.95 (0.92, 0.98)	4.34 (0.84, 7.84)	0.981	-0.99 (-0.96%)
Triglycerides				
miniLab vs. ADVIA	0.99 (0.98, 1.00)	1.4 (-0.3, 3.0)	0.999	0.0 (0.0%)
miniLab vs. Cobas	0.99 (0.98, 1.00)	-1.9 (-3.6, -0.1)	0.999	-4.1 (-2.5%)