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Rapid evaluation of fibrinogen levels using the CG02N whole blood coagulation analyzer**Short title:** Rapid evaluation of fibrinogen levels**Authors:**

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Conflict of interest

S.G. obtained research funds from A&T Corporation, Kanagawa, Japan. All other authors declare no conflicts of interest.

Abstract

Rapid evaluation of fibrinogen levels is essential for maintaining homeostasis in patients with massive bleeding during severe trauma and major surgery. This study evaluated the accuracy of fibrinogen levels measured by the CG02N whole blood coagulation analyzer (whole blood-Fbg) using heparinized blood drawn for blood gas analysis. A total of 100 matched pairs of heparinized blood samples and citrated blood samples were simultaneously collected from patients in the intensive care unit. Whole blood-Fbg results were compared with those of citrated plasma (standard-Fbg). The whole blood coagulation analyzer measured fibrinogen levels within 2 minutes. Strong correlations between standard-Fbg and whole blood-Fbg were observed ($\rho = 0.91$, $P < 0.001$). Error grid analysis showed that 88% of the values were clinically acceptable, and 12% were in a range with possible effects on clinical decision-making; none were in a clinically dangerous range without appropriate treatment. Using a fibrinogen cutoff value of 1.5 g/L for standard-Fbg, the area under the receiver operating characteristic curve of whole blood-Fbg was 0.980 (95% confidence interval 0.951–1.000, $P < 0.001$). The whole blood coagulation analyzer can rapidly measure fibrinogen levels in heparinized blood and could be useful in critical care settings where excessive bleeding is a concern.

KEYWORDS: Fibrinogen; point of care; coagulopathy; massive transfusion

ABBREVIATIONS:

Whole blood-Fbg, fibrinogen levels measured from whole blood drawn for arterial blood gas measurements by dry reagent methods.

Standard-Fbg, fibrinogen levels measured from citrated blood samples by Clauss method.

BACKGROUND

Fibrinogen plays an important role in clot formation. Low fibrinogen levels are associated with hemostatic impairment, thus increasing a tendency toward bleeding.^{1,2} Furthermore, during massive bleeding, fibrinogen levels decrease before the development of other hemostatic abnormalities.³⁻⁷ Previous studies have indicated that low fibrinogen levels are a strong risk factor for poor outcomes in trauma patients⁸⁻¹⁴ and in those undergoing major surgery.¹⁵⁻¹⁷

The Clauss method and the prothrombin time-derived method are widely used to measure plasma fibrinogen levels.^{18,19} Although knowledge of plasma fibrinogen levels is required for the prompt treatment of patients with a propensity for bleeding, the measurement of fibrinogen levels by these two methods usually takes more than 30 minutes. Recently, a compact whole blood coagulation analyzer (CG02N; A&T Corporation, Kanagawa, Japan) with the ability to analyze citrated whole blood and plasma has been developed in Japan and is commercially available in East Asia (Fig. 1). This analyzer uses dry reagent methods (dry hematology) that measure thrombin-induced clot formation, a functional assay, in an oscillating magnetic field.^{20,21} The analyzer does not require the preparation of a solution reagent or calibrator, and a dry card-type single-use reagent in an aluminum-packed form is used for each measurement (Fig. 2). The instrument can measure prothrombin time, activated partial thromboplastin time, thrombotest, heparin test, and fibrinogen levels within 1 to 2 minutes. The Ministry of Health, Labour, and Welfare in Japan has approved both the instrument and its reagents as a high-precision method of measuring fibrinogen levels in citrated whole blood and plasma. Furthermore, a recent study reported that the results of fibrinogen measurements in

citrated whole blood and plasma with the CG02N blood coagulation analyzer were in agreement with the results of the Clauss and prothrombin time-derived methods.²¹

However, in the emergency department and operating room, heparinized blood is frequently drawn for arterial blood gas analysis. Use of this blood for measurement of fibrinogen levels would be highly convenient for point-of-care use in patients with massive bleeding. To help evaluate this possibility, this study evaluated the accuracy of fibrinogen measurements in heparinized whole blood samples drawn for arterial blood gas analysis, using the CG02N blood coagulation analyzer.

MATERIALS AND METHODS

The present study was approved by the Institutional Review Board of Hokkaido University Hospital (study number: 012-0389).

Collection of Blood Samples

All samples were drawn directly from the arterial catheter used for blood pressure monitoring. Samples for arterial blood gas analysis were drawn using an arterial blood sampling kit (Line Draw Plus[®] 1 mL; Smiths Medical Japan Ltd, Tokyo, Japan). The arterial blood-sampling syringe contains 23.5 IU of dry lithium heparin; the heparin concentration in these samples is dependent on the volume collected (0.5–1.0 mL). Samples for the coagulation test were drawn using a vacuum blood collection tube (Venoject II; Terumo Corp, Tokyo, Japan), wherein 1.8 mL of blood was collected with 0.2 mL of 3.2% sodium citrate. To prepare samples

with a low level of fibrinogen, some samples were diluted two- or threefold with Owren's Veronal Buffer (OV-30; Sysmex Co, Kobe, Japan).

Measurement of Fibrinogen Levels

Fibrinogen levels in citrated plasma (standard-Fbg) were measured by the Clauss method using Thrombocheck Fib(L) (Sysmex Co.) and CS-1000i (Sysmex Co.) as the standard. Arterial blood gas and hematocrit in heparinized whole blood samples were analyzed using an ABL 800 FLEX (Radiometer Co., Tokyo, Japan). Fibrinogen levels in the heparinized whole blood (whole blood-Fbg) were measured with the CG02N instrument. Measurements were performed as follows. (1) A dry card-type reagent for fibrinogen measurement was placed in the analyzer and pre-warmed to 37°C. (2) Whole blood from a sampling syringe was transferred to a microtube. (3) Whole blood from the microtube (25 µL) was withdrawn and placed in a new microtube containing 100 µL of diluent and mixed using a micropipette. (4) Subsequently, 25 µL of the mixture of whole blood and diluent was applied to the dry card-type reagent. The dry card-type reagent contained bovine thrombin activator (final concentration: 33 IU/mL), which was able to overcome effects of heparin, and paramagnetic iron oxide particles that move in response to an oscillating magnetic field. Furthermore, heparin neutralizer also was contained in the dry card-type reagent. (More information was non-disclosure.) The applied sample moves via capillary action and mixes with paramagnetic iron oxide particles and reagents within the testing chamber. As the thrombus is formed, particle movement decreases. The light (870 nm) illuminates the inner reaction cell, and the signal movements of particles are quantified as changes in scattered light. Clotting time was determined as a 30% decrease in maximal amplitude and was correlated to fibrinogen concentrations determined by the reference

laboratory method. (5) The results of the fibrinogen measurement were available within 2 minutes after application to the dry card-type reagent (30 ± 2 seconds for measurement of 1 g/L fibrinogen and 72 ± 4 seconds for measurement of 0.4 g/L fibrinogen; data provided by A&T Corporation). (6) The resulting fibrinogen concentration presupposes that the hematocrit of the sample was 50%. Therefore, the result was corrected according to the measured hematocrit of the sample based on the following calculation formula:

$$\text{Fibrinogen concentration} = \text{the result value} \times 50 / (100 - \text{hematocrit}).$$

Statistical Analysis

Correlations between two measurements were investigated by simple regression analysis. A Bland-Altman plot was used to check the bias and limits of agreement between the results. Bias was defined as the mean difference between standard-Fbg and whole blood-Fbg. The 95% limits of agreement were calculated as the bias $\pm$ ($1.96 \times \text{SD}$).

Error grid analysis was used to evaluate the clinical relevance of differences between standard-Fbg and whole blood-Fbg. A fibrinogen level >2.0 g/L was considered normal, whereas fibrinogen levels <1.5 g/L were defined as coagulopathic, requiring supplementation with fibrinogen concentrates and/or fresh-frozen plasma.^{22–26} Furthermore, fibrinogen levels <1.0 g/L were defined as severely coagulopathic.^{22–26} The error grid analysis scatterplot is divided into three zones. Zone A indicates the clinically acceptable measurement area, with an acceptance level of 20% deviation between the two measurements. Zone B shows an error $>20\%$, with fibrinogen deficiency being overestimated or underestimated with possible effects on clinical

decision-making. Zone C presents a clinically dangerous situation, leading to inadequate or unnecessary treatment.

Fibrinogen deficiency was defined as fibrinogen levels <1.5 g/L, based on recent guidelines for the management of massive bleeding.^{22–26} The receiver operating characteristic (ROC) curves for fibrinogen deficiency measured by whole blood-Fbg were constructed for fibrinogen deficiency and compared with the results of standard-Fbg. The areas under the curve (AUCs) were examined by a significance test for AUC.

The statistical software package SPSS version 20.0 (Japan IBM Co, Ltd, Tokyo, Japan) was used for all statistical analyses. $P < 0.05$ was considered statistically significant.

RESULTS

Forty-two pairs of samples for standard-Fbg and whole blood-Fbg analysis were simultaneously drawn from 26 consecutive patients admitted to the intensive care unit. Thirty sample pairs were diluted two- and three-fold to prepare 60 diluted samples. Two pairs of samples were excluded from the analyses since they exceeded 4.0 g/L, which is the upper limit of measurement for the CG02N instrument. Therefore, 100 pairs of matched heparinized whole blood and citrated plasma samples were analyzed.

Correlations are presented in Figure 3. Simple regression analysis revealed a strong correlation between the results of standard-Fbg and whole blood-Fbg ($\rho = 0.91$, $P < 0.001$). The error grid analysis is also shown in Figure 3. Overall, 88% of the values were located in zone A

(clinically acceptable), 12% in zone B (with possible effects on clinical decision-making), and 0% in zone C (clinically dangerous situation with possible inappropriate treatment).

The Bland-Altman plot is presented in Figure 4. The bias of the 2 measurements was -0.10 g/L (solid line in Fig. 4), and the SD of the differences in the two measurements was 0.36 g/L. Therefore, the 95% limits of agreement were taken as -0.81 to $+0.61$ g/L (dashed line in Fig. 4).

Using a cutoff value of 1.5 g/L to indicate fibrinogen deficiency, the fitted ROC curve with the results of standard-Fbg and whole blood-Fbg is presented in Figure 5. The AUC was 0.980 (95% confidence interval $0.951-1.000$, $P < 0.001$). These results indicate that the CG02N instrument can identify fibrinogen deficiency with high accuracy.

DISCUSSION

Measurement of fibrinogen in heparinized whole blood using the CG02N analyzer demonstrated strong correlations with standard fibrinogen measurements performed in the central laboratory. Furthermore, the whole blood coagulation analyzer detected fibrinogen deficiency rapidly and accurately.

Whole blood thromboelastometry has been widely used for early diagnosis of coagulation abnormalities.²⁷⁻³⁰ With this method, clot amplitude is clinically correlated with fibrinogen levels, permitting detection of fibrinogen deficiency.²⁷⁻²⁹ However, one limitation of thromboelastometry is that it requires 10 to 15 minutes to measure fibrinogen levels,²⁷⁻²⁹ which is an unacceptable length of time for patients at high risk for massive bleeding. The timely

diagnosis of fibrinogen deficiency and supplementation with fibrinogen are crucial in patients with massive bleeding and/or coagulopathies. The whole blood coagulation analyzer tested in this study rapidly and accurately measured fibrinogen concentrations in heparinized blood within 2 min, allowing for a rapid and accurate diagnosis of fibrinogen deficiency.

The results of thromboelastometry, including fibrinogen-specific parameters, are affected by both hematocrit levels and platelet counts,^{31–35} and high hematocrit levels can lead to underestimation of fibrinogen deficiency.^{31–33} For example, in samples with identical plasma fibrinogen levels, those with high hematocrit values show lower whole blood fibrinogen concentrations than those with low hematocrit values.³¹ Furthermore, high platelet counts increase clot firmness, which leads to the underestimation of fibrinogen deficiency when measured by thromboelastometry.³³ In the present study, the whole blood coagulation analyzer directly measured fibrinogen levels in whole blood, and fibrinogen levels in whole blood were then manually corrected to fibrinogen levels in plasma based on the hematocrit value.

The CG02N analyzer can measure prothrombin time, activated partial thromboplastin time, thrombotest, and heparin test, including fibrinogen levels, in citrated whole blood and plasma. For hemostatic control, appropriate monitoring of not only fibrinogen, but also prothrombin time and activated partial thromboplastin time, is important. Recent transfusion guidelines recommended prothrombin time and activated partial thromboplastin time measurements to evaluate the need for fresh frozen plasma transfusion.^{36, 37} However, coagulation tests in a central laboratory usually take more than 30 minutes. This delay is a critical issue for appropriate hemostatic control during massive bleeding, such as in patients undergoing major surgery or experiencing severe trauma. Thus, the CG02N analyzer may be useful for rapid assessment of hemostatic ability, including prothrombin time, activated partial

thromboplastin time, and fibrinogen in patients with bleeding tendency, such as during major surgery, severe trauma, gastrointestinal bleeding, postpartum hemorrhage, and infectious disease-associated coagulopathy/fibrinogen depletion/consumption. Disappointingly, heparinized whole blood was not able to use for measurement of prothrombin time and activated partial thromboplastin time.

The main limitations of the present study are that the study was limited to an assessment of fibrinogen, and that some of the samples included diluted samples from patients without fibrinogen deficiency. Thus, to confirm these findings, clinical evaluation of rapid fibrinogen measurements using heparinized whole blood in patients with massive bleeding and/or known fibrinogen deficiency may be necessary.

In conclusion, fibrinogen measurements using the CG02N instrument for heparinized whole blood samples drawn for arterial blood gas analysis show strong correlations with standard fibrinogen measurements. Importantly, the whole blood coagulation analyzer can rapidly detect dysfibrinogenemia, and is hence suitable for all healthcare settings where core laboratory measurement may be unavailable in a very short time. It may also be useful for patient monitoring during infectious outbreaks leading to massive bleeding or severe coagulopathy, such as Ebola virus infection outbreaks.

ABBREVIATIONS:

Whole blood-Fbg, fibrinogen levels measured from whole blood drawn for arterial blood gas measurements by dry reagent methods.

Standard-Fbg, fibrinogen levels measured from citrated blood samples by Clauss method.

AUTHORSHIP

M.H. contributed to the study design, data acquisition and interpretation, statistical analysis, and drafting of the manuscript. S.G. contributed to data interpretation and drafting of the manuscript. Y.O., A.M., K.K., K.M., D.M., T.W., Y.Y., and A.S. contributed to data acquisition and interpretation.

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References

1. Levy JH, Szlam F, Tanaka KA, Sniecinski RM. Fibrinogen and hemostasis: a primary hemostatic target for the management of acquired bleeding. *Anesth Analg* 2012;114:261–274
2. Schlimp CJ, Schochl H. The role of fibrinogen in trauma-induced coagulopathy. *Hamostaseologie* 2013;34:29–39
3. Hiippala ST, Myllylä GJ, Vahtera EM. Hemostatic factors and replacement of major blood loss with plasma-poor red cell concentrates. *Anesth Analg* 1995;81:360–365
4. McLoughlin TM, Fontana JL, Alving B, Mongan PD, Bünger R. Profound normovolemic hemodilution: hemostatic effects in patients and in a porcine model. *Anesth Analg* 1996;83:459–465
5. White NJ, Martin EJ, Brophy DF, Ward KR. Coagulopathy and traumatic shock: characterizing hemostatic function during the critical period prior to fluid resuscitation. *Resuscitation* 2010;81:111–116
6. Hayakawa M, Gando S, Ono Y, Wada T, Yanagida Y, Sawamura A. Fibrinogen level deteriorates before other haemostatic variables and massive transfusion in the early phase of severe trauma: a retrospective observational study. *Semin Thromb Hemost*. In press
7. Lippi G, Favaloro EJ, Cervellin G. Massive posttraumatic bleeding: epidemiology, causes, clinical features, and therapeutic management. *Semin Thromb Hemost* 2013;39:83–93
8. Schöchl H, Cotton B, Inaba K, et al. FIBTEM provides early prediction of massive transfusion in trauma. *Crit Care* 2011;15:R265
9. Chambers LA, Chow SJ, Shaffer LE. Frequency and characteristics of coagulopathy in trauma patients treated with a low- or high-plasma-content massive transfusion protocol. *Am*

- J Clin Pathol 2011;136:364–370
10. Inaba K, Karamanos E, Lustenberger T, et al. Impact of fibrinogen levels on outcomes after acute injury in patients requiring a massive transfusion. J Am Coll Surg 2013;216:290–297
 11. Schöchl H, Solomon C, Traintinger S, et al. Thromboelastometric (ROTEM) findings in patients suffering from isolated severe traumatic brain injury. J Neurotrauma 2011;28:2033–2041
 12. Goodnight SH, Kenoyer G, Rapaport SI, Patch MJ, Lee JA, Kurze T. Defibrination after brain-tissue destruction: a serious complication of head injury. N Engl J Med 1974;290:1043–1047
 13. Kushimoto S, Shibata Y, Yamamoto Y. Implications of fibrinogenolysis in patients with closed head injury. J Neurotrauma 2003;20:357–363
 14. Sawamura A, Hayakawa M, Gando S, et al. Disseminated intravascular coagulation with a fibrinolytic phenotype at an early phase of trauma predicts mortality. Thromb Res 2009;124:608–613
 15. Karkouti K, Callum J, Crowther MA, et al. The relationship between fibrinogen levels after cardiopulmonary bypass and large volume red cell transfusion in cardiac surgery: an observational study. Anesth Analg 2013;117:14–22
 16. Rahe-Meyer N, Solomon C, Hanke A, et al. Effects of fibrinogen concentrate as first-line therapy during major aortic replacement surgery: a randomized, placebo-controlled trial. Anesthesiology 2013;118:40–50
 17. Weber CF, Görlinger K, Meininger D, et al. Point-of-care testing: a prospective, randomized clinical trial of efficacy in coagulopathic cardiac surgery patients. Anesthesiology 2012;117:531–547

18. Clauss A. Rapid physiological coagulation method in determination of fibrinogen [in German]. *Acta Haematol* 1957;17:237–246
19. Miesbach W, Schenk J, Alesci S, Lindhoff-Last E. Comparison of the fibrinogen Clauss assay and the fibrinogen PT derived method in patients with dysfibrinogenemia. *Thromb Res* 2010;126:e428–e433
20. Oberhardt BJ, Dermott SC, Taylor M, Alkadi ZY, Abruzzini AF, Gresalfi NJ. Dry reagent technology for rapid, convenient measurements of blood coagulation and fibrinolysis. *Clin Chem* 1991;37:520–526
21. Ogawa S, Tanaka KA, Nakajima Y, et al. Fibrinogen measurements in plasma and whole blood: a performance evaluation study of the dry-hematology system. *Anesth Analg*. Epub 2014 Sep 15
22. O'Shaughnessy DF, Atterbury C, Bolton Maggs P, et al. British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. *Br J Haematol* 2004;126:11–28
23. British Committee for Standards in Haematology, Stainsby D, MacLennan S, et al. Guidelines on the management of massive blood loss. *Br J Haematol* 2006;135:634–641
24. Spahn DR, Cerny V, Coats TJ, et al. Management of bleeding following major trauma: a European guideline [published erratum appears in *Crit Care*. 2007 11:414]. *Crit Care* 2007;11:R17
25. Gaarder C, Naess PA, Frischknecht Christensen E, et al. Scandinavian Guidelines--“The massively bleeding patient”. *Scand J Surg* 2008;97:15–36
26. Spahn DR, Bouillon B, Cerny V, et al. Management of bleeding and coagulopathy following major trauma: an updated European guideline. *Crit Care* 2013;17:R76

27. Rugeri L, Levrat A, David JS, et al. Diagnosis of early coagulation abnormalities in trauma patients by rotation thrombelastography. *J Thromb Haemost* 2007;5:289–295
28. Rouillet S, Pillot J, Freyburger G, et al. Rotation thromboelastometry detects thrombocytopenia and hypofibrinogenaemia during orthotopic liver transplantation. *Br J Anaesth* 2010;104:422–428
29. Ogawa S, Szlam F, Chen EP, et al. A comparative evaluation of rotation thromboelastometry and standard coagulation tests in hemodilution-induced coagulation changes after cardiac surgery. *Transfusion* 2012;52:14–22
30. Solomon C, Cadamuro J, Ziegler B, et al. A comparison of fibrinogen measurement methods with fibrin clot elasticity assessed by thromboelastometry, before and after administration of fibrinogen concentrate in cardiac surgery patients. *Transfusion* 2011;51:1695–1706
31. Ogawa S, Szlam F, Bolliger D, Nishimura T, Chen EP, Tanaka KA. The impact of hematocrit on fibrin clot formation assessed by rotational thromboelastometry. *Anesth Analg* 2012;115:16–21
32. Spiezia L, Radu C, Marchioro P, et al. Peculiar whole blood rotation thromboelastometry (Rotem) profile in 40 sideropenic anaemia patients. *Thromb Haemost* 2008;100:1106–1110
33. Nagler M, Kathriner S, Bachmann LM, Wuillemin WA. Impact of changes in haematocrit level and platelet count on thromboelastometry parameters. *Thromb Res* 2013;131:249–253.
34. Jensen AS, Johansson PI, Idorn L, et al. The haematocrit—an important factor causing impaired haemostasis in patients with cyanotic congenital heart disease. *Int J Cardiol* 2013;167:1317–1321
35. Smith SA, McMichael MA, Gilor S, Galligan AJ, Hoh CM. Correlation of hematocrit, platelet concentration, and plasma coagulation factors with results of thromboelastometry in

- canine whole blood samples. *Am J Vet Res* 2012;73:789–798
36. O'Shaughnessy DF, Atterbury C, Bolton Maggs P, et al. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. *Br J Haematol* 2004;126:11–28.
37. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. *Anesthesiology* 2006;105:198–208.

Figure Legends

Figure 1. The CG02N rapid coagulation analyzer.

Figure 2. Dry card-type reagent used with the CG02N instrument. Magnetic materials are mixed with the reagent and filled in the reaction cell present on the card. The card is composed of three layers: base (card), a spacer that forms a reaction cell on the substrate (medium layer), and cover (upper layer).

Figure 3. Correlation and error grid analysis of the results of fibrinogen levels measured in citrated plasma (standard-Fbg) and in heparinized whole blood (whole blood-Fbg). Simple regression analysis revealed a strong correlation between standard-Fbg and whole blood-Fbg ($\rho = 0.91$, $P < 0.001$). Overall, 88% of the values were located in zone A (white), which indicates clinically acceptable results; 12% were located in zone B (light gray), which represents possible overestimated or underestimated coagulopathy with possible effects on clinical decision-making; and no values were located in zone C (dark gray), which indicates a clinically dangerous situation, with possible inappropriate treatment.

Figure 4. Bland-Altman plot of fibrinogen levels measured in citrated plasma (standard-Fbg) and in heparinized whole blood (whole blood-Fbg). The solid line indicates the mean of the difference between the results of standard-Fbg and whole blood-Fbg. The dashed line shows the 95% limits of agreement.

Figure 5. The fitted ROC curve with fibrinogen levels measured in citrated plasma (standard-Fbg) and in heparinized whole blood (whole blood-Fbg). CI, confidence interval.

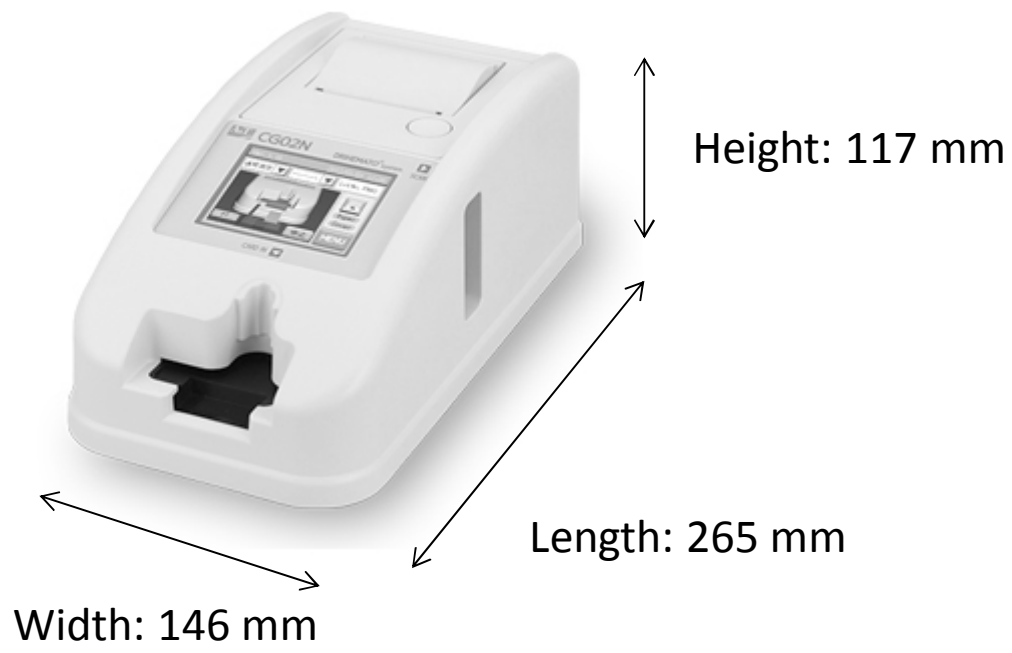


Figure 1

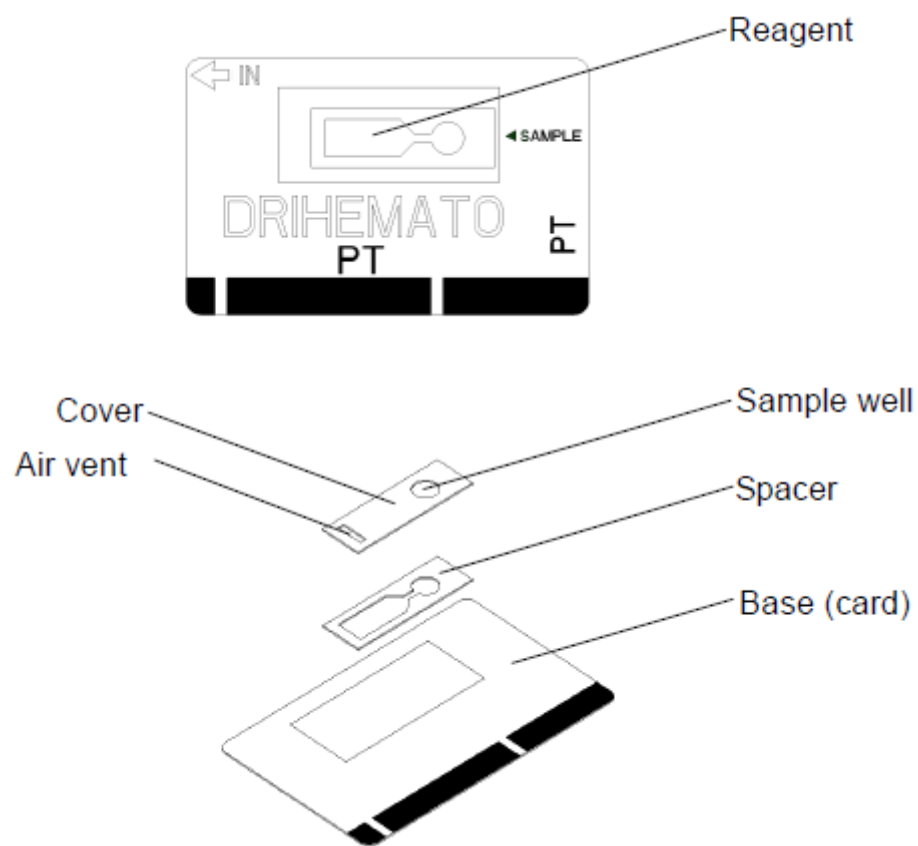


Figure 2

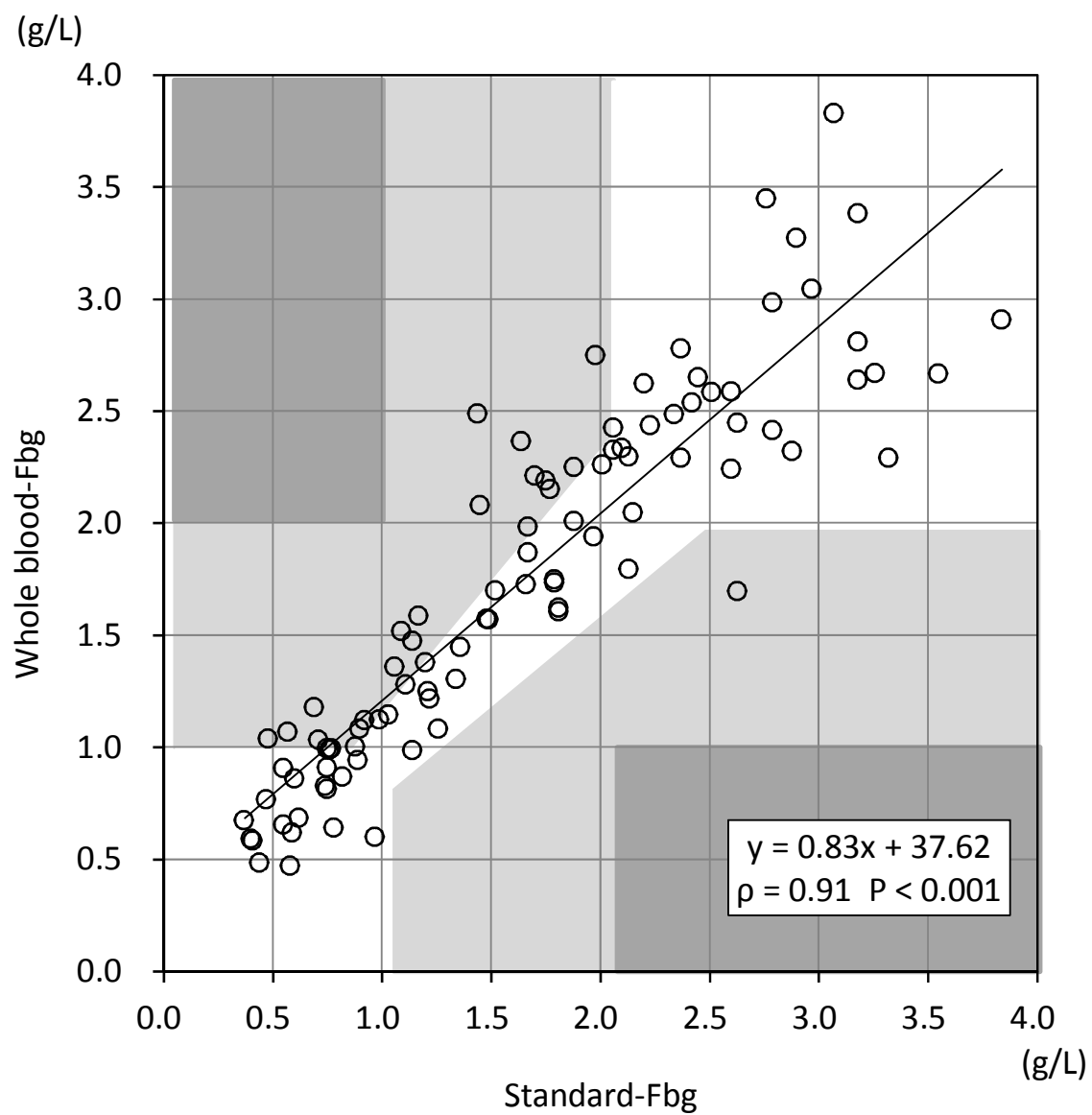


Figure 3

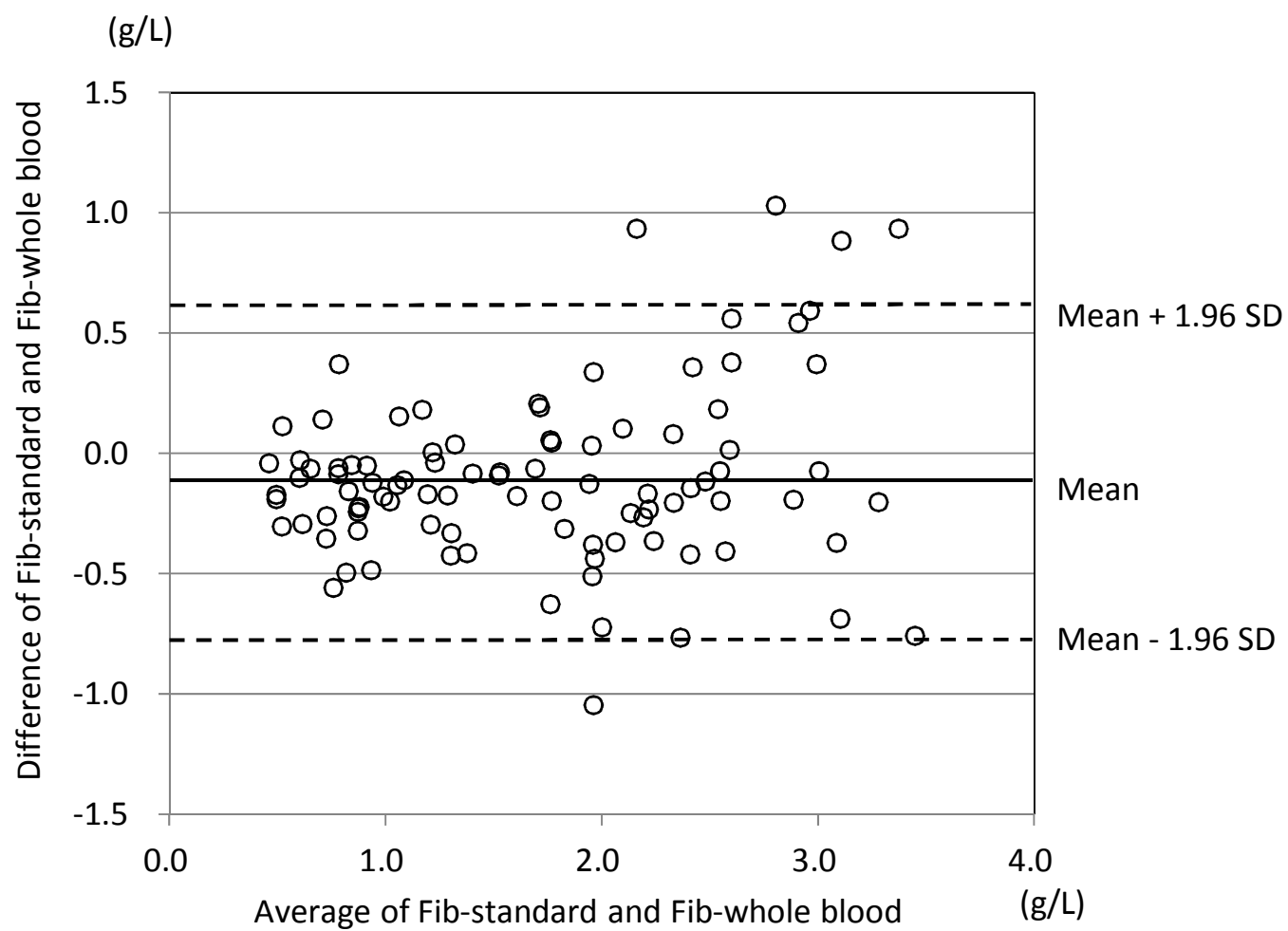


Figure 4

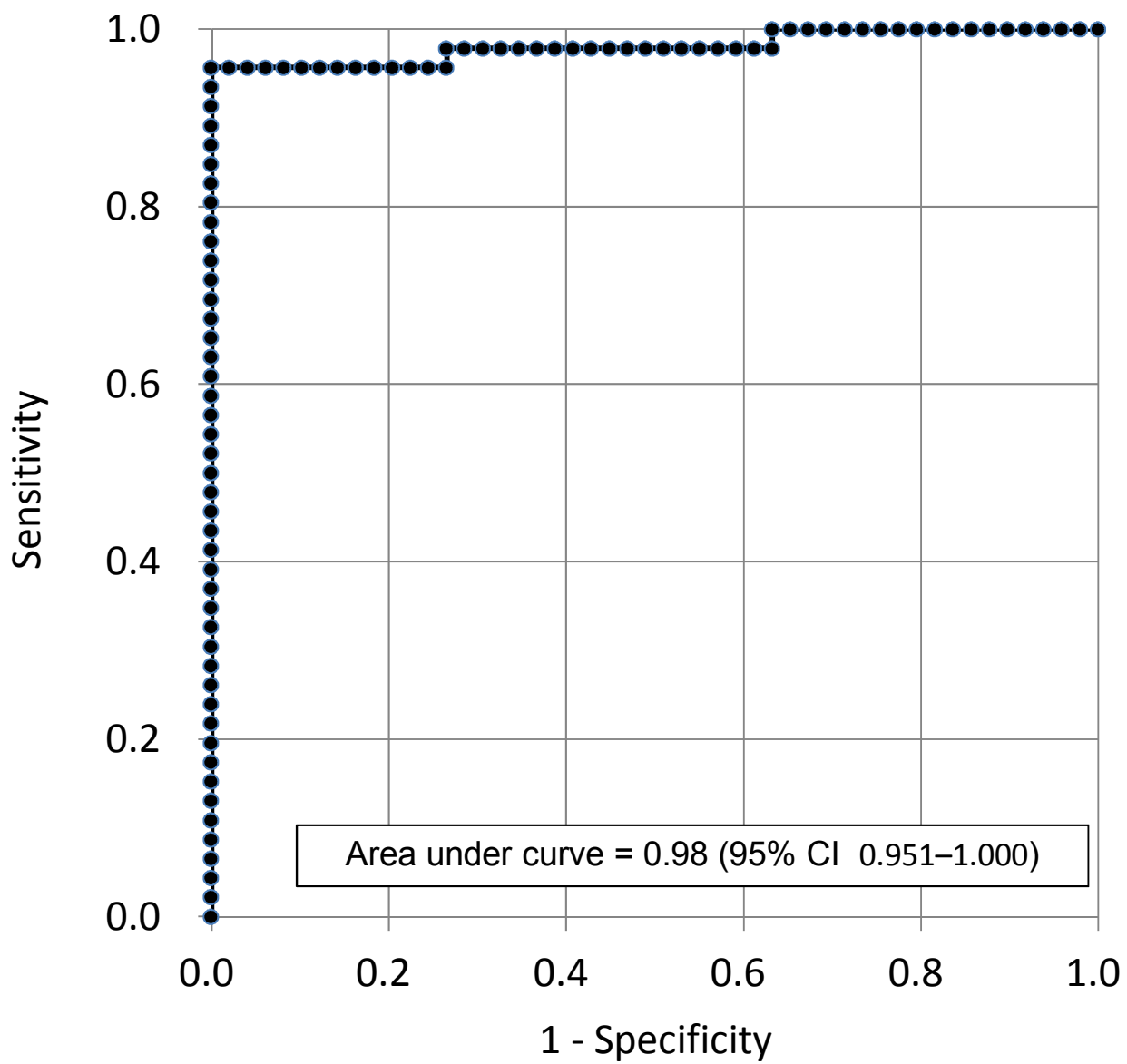


Figure 5