Performance of the Fully Automated Blood Coagulation Analyzer CS-5100

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We evaluated the basic performance of the fully automated blood coagulation analyzer CS-5100 (CS-5100; Sysmex Corporation, Kobe, Japan) for blood coagulation and fibrinolysis testing and compared its performance with that of another fully automated blood coagulation analyzer CA-7000 (CA-7000; Sysmex Corporation). CS-5100 showed good basic performance. ATIII especially has superior onboard reagent stability up to eight days, because of the use of a reagent cap which helps prevent evaporation of the reagent. Moreover, Fibrinogen and D-dimer have enhanced linearity.

Apart from routine testing, CS-5100 is also fully able to meet the demands of a 24-hour emergency testing setup. This study confirms the usefulness of CS-5100 to large and busy hemostasis laboratories.

Key Words Reagent Cap, Onboard Reagent Stability, Enhanced Linearity

INTRODUCTION

Very rapid and highly accurate blood coagulation and fibrinolysis testing has now become possible with the widespread use of fully automated analyzers that can simultaneously analyze several parameters using the principles of coagulation time method, synthetic substrate method, and immunoturbidimetry.

At our hospital, we had been using a fully automated CA-7000 blood coagulation analyzer (CA-7000; Sysmex Corporation, Kobe, Japan) [1] for blood coagulation and fibrinolysis testing. But this analyzer was becoming old. Besides that, a new analyzer that enabled 24 hour testing service became necessary as the hospital was designated as a Regional Disaster Medical Center in 2011. The fully automated CS-5100 blood coagulation analyzer (CS-5100; Sysmex Corporation) developed by Sysmex uses a multi-wavelength detection system that enables more parameters to be analyzed, functions like pre-analysis sample quality checking, and the high throughput of maximum 400 tests per hour. Furthermore, with its cap-piercing function and small volume sampling capability, it has improved ability to process multiple samples and handle multiple parameters. It also has improved cooling and operation of the reagent table, and all these features are expected to facilitate rapid testing [2]. We therefore analyzed the basic performance of CS-5100 and examined the correlation of its measured values with CA-7000 measurements.

MATERIALS AND METHODS

1. Specimens

Citrated plasmas (3.2% sodium citrate) of patients submitted to the clinical laboratory of our hospital for testing and of normal persons, and commercially obtained standard substances were used as test specimens.

2. Analyzers and reagents

The analyzer evaluated, control analyzer, and reagents used are listed in ***Table 1***. The analysis parameters were prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (Fbg), hepaplastin test (HpT), antithrombin III (ATIII), fibrin/fibrinogen degradation products (FDP) and D-dimer (DD).

Note: This article is translated and republished from the Sysmex Journal Web Vol.15 No.1, 2014. (Japanese)

3. Methods

1) Within-run reproducibility
Ten replicate measurements were made with Coagutrol IX and IIX (Coagutrol IX and IIX; Sysmex Corporation), FDP neo (FDP neo; Sysmex Corporation) reference standard, and D-dimer neo (D-dimer neo; Sysmex Corporation) reference standard.

2) Onboard reagent stability
Keeping the cooling function on, the reagent bottles were set on the CS-5100 reagent table with the seal open and after directly fitting the special anti-evaporation reagent, measurements were made daily for 5 days (8 days for ATIII, FDP and DD). For Coagutrol IX and IIX, FDP neo, and D-dimer neo, a new vial was prepared every day as specified in the package inserts.

3) Correlations
Correlations with the results obtained by CA-7000, the earlier analyzer model, were examined using citrated patient's plasma (3.2% sodium citrate) specimens.

4) Linearity of Fbg and DD data
High Fbg plasma was diluted with Owren Veronal buffer. For DD, the sample was diluted with D-dimer diluents neo. The dilutions used in both cases were 10/10, 8/10, 6/10, 4/10, 2/10 and 1/10, and 1/20 and 0/10 were also used for DD.

5) Calculation of normal reference ranges
The normal reference ranges of PT, APTT, Fbg, FDP and DD were calculated by the parametric method using measured data of 95 specimens of 3.2% citrate-added plasma of healthy individuals.

Table 1 *Analyzers and reagents used*

Analyzer / Parameter	Evaluated analyzer: CS-5100	Control analyzer: CA-7000
PT	Thromborel S	Thromborel S
APTT	Dade Actin	Dade Actin
Fbg	Thrombocheck Fib (L)	Thrombocheck Fib (L)
HpT	Compound factor H Kokusai	Compound factor H Kokusai
ATⅢ	Berichrom Antithrombin III	-
P-FDP	Latex Test BL-2 P-FDP	Nanopia® P-FDP
DD	LIAS AUTO D-dimer NEO	Nanopia® D-dimer

Table 2 *Within-run reproducibility (n = 10)*

Parameter	PT						APTT		Fbg		HpT	
Unit	sec	%	INR	sec	%	INR	sec	sec	mg/dL	mg/dL	%	%
Standard	Ⅸ			Ⅱ			Ⅸ	Ⅱ	Ⅸ	Ⅱ	Ⅸ	Ⅱ
Mean	12.1	97.0	1.0	19.0	42.1	1.6	29.1	77.7	290.0	109.9	108.6	31.0
SD	0.05	0.83	0.01	0.11	0.33	0.01	0.07	0.42	3.81	3.00	0.78	0.16
CV (%)	0.43	0.85	0.50	0.58	0.78	0.42	0.24	0.54	1.31	2.73	0.72	0.53

Parameter	ATⅢ	
Unit	%	%
Standard	Ⅸ	Ⅱ
Mean	104.2	34.0
SD	0.67	0.41
CV (%)	0.65	1.20

Parameter	FDP		DD	
Unit	μg/mL		μg/mL	
Standard	L	H	L	H
Mean	7.0	25.8	1.8	11.0
SD	0.11	0.23	0.04	0.10
CV (%)	1.55	0.88	2.37	0.90

*** Standards used**
Coagutrol IX and IIX
FDP Neo standard
D-dimer Neo standard

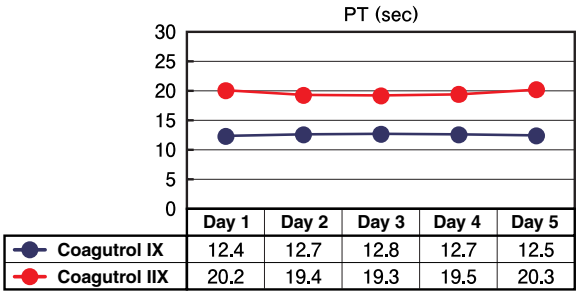
RESULTS

1) Within-run reproducibility

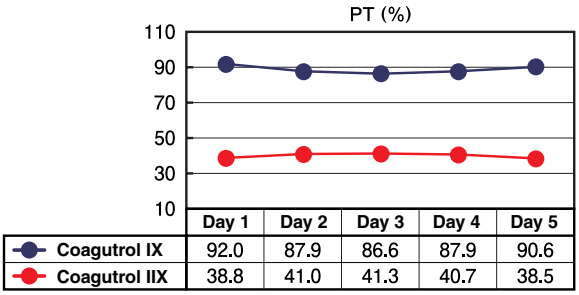
The coefficient of variation (CV%) of all parameters was in the range 0.24-2.73% (***Table 2***).

2) Onboard reagent stability

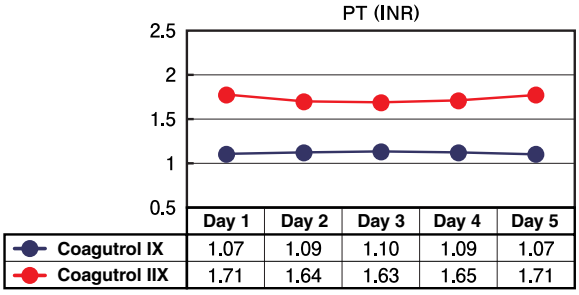
The variation in the measured values was within ±10% of the first day's results up to the 5th day for PT, APTT and



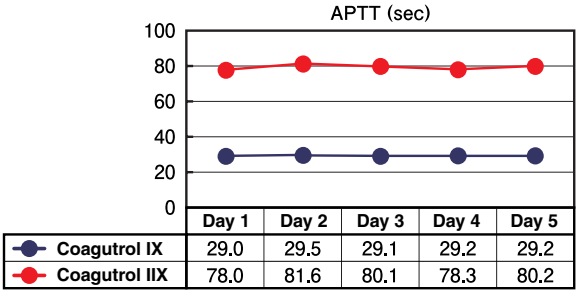
	Day 1	Day 2	Day 3	Day 4	Day 5
Coagutrol IX	12.4	12.7	12.8	12.7	12.5
Coagutrol IIX	20.2	19.4	19.3	19.5	20.3



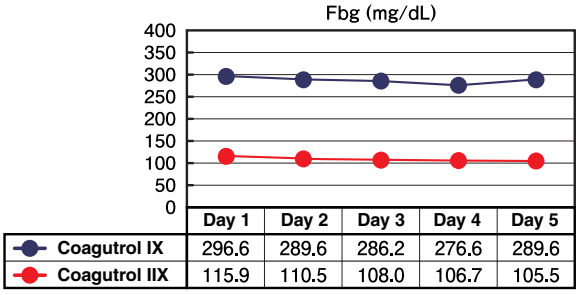
	Day 1	Day 2	Day 3	Day 4	Day 5
Coagutrol IX	92.0	87.9	86.6	87.9	90.6
Coagutrol IIX	38.8	41.0	41.3	40.7	38.5



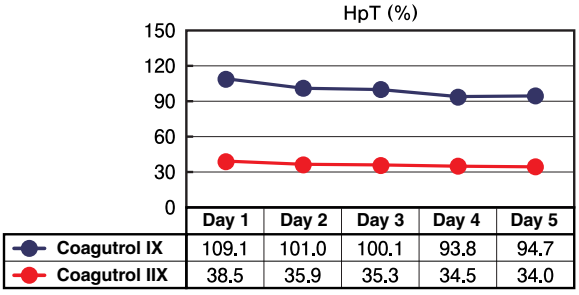
	Day 1	Day 2	Day 3	Day 4	Day 5
Coagutrol IX	1.07	1.09	1.10	1.09	1.07
Coagutrol IIX	1.71	1.64	1.63	1.65	1.71



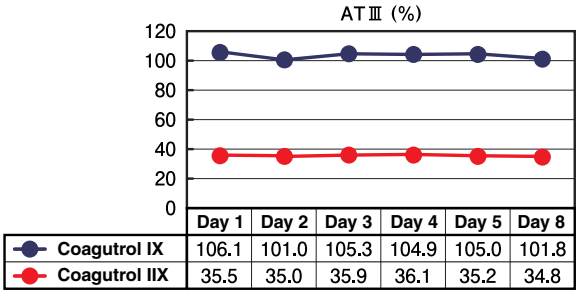
	Day 1	Day 2	Day 3	Day 4	Day 5
Coagutrol IX	29.0	29.5	29.1	29.2	29.2
Coagutrol IIX	78.0	81.6	80.1	78.3	80.2



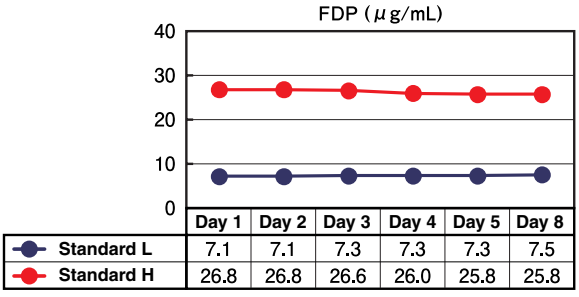
	Day 1	Day 2	Day 3	Day 4	Day 5
Coagutrol IX	296.6	289.6	286.2	276.6	289.6
Coagutrol IIX	115.9	110.5	108.0	106.7	105.5



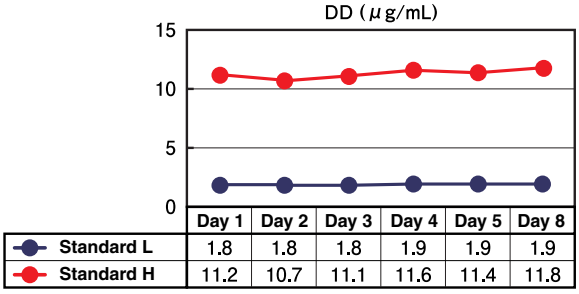
	Day 1	Day 2	Day 3	Day 4	Day 5
Coagutrol IX	109.1	101.0	100.1	93.8	94.7
Coagutrol IIX	38.5	35.9	35.3	34.5	34.0



	Day 1	Day 2	Day 3	Day 4	Day 5	Day 8
Coagutrol IX	106.1	101.0	105.3	104.9	105.0	101.8
Coagutrol IIX	35.5	35.0	35.9	36.1	35.2	34.8



	Day 1	Day 2	Day 3	Day 4	Day 5	Day 8
Standard L	7.1	7.1	7.3	7.3	7.3	7.5
Standard H	26.8	26.8	26.6	26.0	25.8	25.8



	Day 1	Day 2	Day 3	Day 4	Day 5	Day 8
Standard L	1.8	1.8	1.8	1.9	1.9	1.9
Standard H	11.2	10.7	11.1	11.6	11.4	11.8

Fig. 1 *Onboard reagent stability*

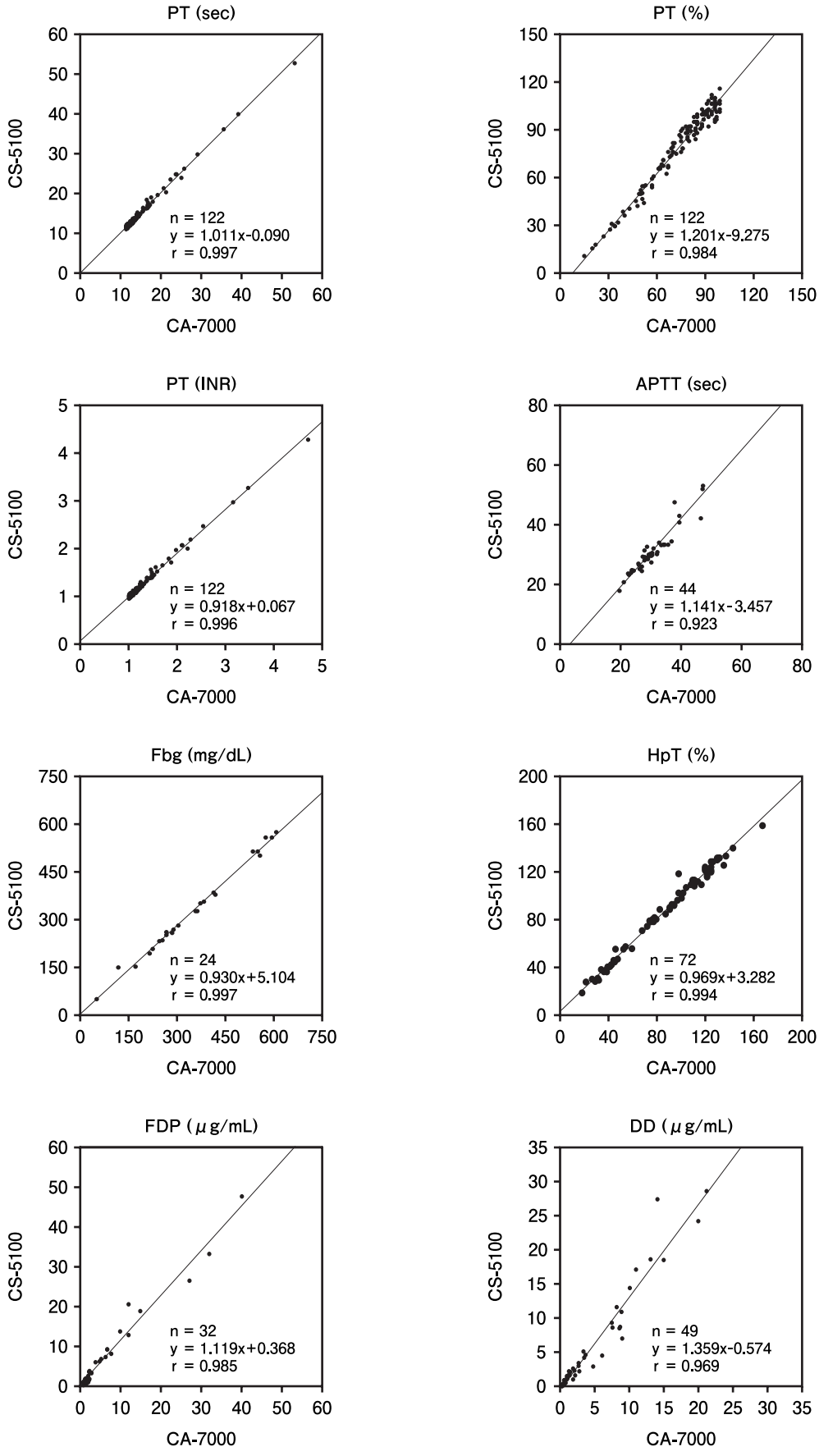


Fig. 2 *Correlation diagrams*

Fbg, up to the 3rd day for HpT, and up to the 8th day for ATIII, FDP and DD (***Fig. 1***).

3) Correlations
Correlations between measurements by CS-5100 and CA-7000 are shown in ***Fig 2***. The coefficients of correlation r were in the range 0.923-0.997 (***Table 3***).

4) Linearity of Fbg and DD data
Linearity was seen up to 750 mg/dL for Fbg, and up to 98 µg/mL for DD (***Fig. 3***).

5) Calculation of normal reference ranges
The normal reference ranges were 10.1-12.4 for PT (sec), 84.4-137.4 for PT (% activity), and 0.88-1.09 for PT (INR). The ranges were 24.3-39.3 sec for APTT, 163-356 mg/dL for Fbg, 2.98 µg/mL or less for FDP, and 1.074 µg/mL or less for DD (***Fig. 4***).

Table 3 *Table of correlations between results obtained with CA-7000 and CS-5100*

X : CA-7000 Y : CS-5100

Parameter	n	r	Regression equation
PT (sec)	122	0.997	y = 1.011x - 0.090
PT (%)	122	0.984	y = 1.201x - 9.275
PT (INR)	122	0.996	y = 0.918x+0.067
APTT (sec)	44	0.923	y = 1.141x - 3.457
Fbg (mg/dL)	24	0.997	y = 0.930x+5.104
HpT (%)	72	0.994	y = 0.969x+3.282
FDP (µg/mL)	32	0.985	y = 1.119x+0.368
DD (µg/mL)	49	0.969	y = 1.359x - 0.574

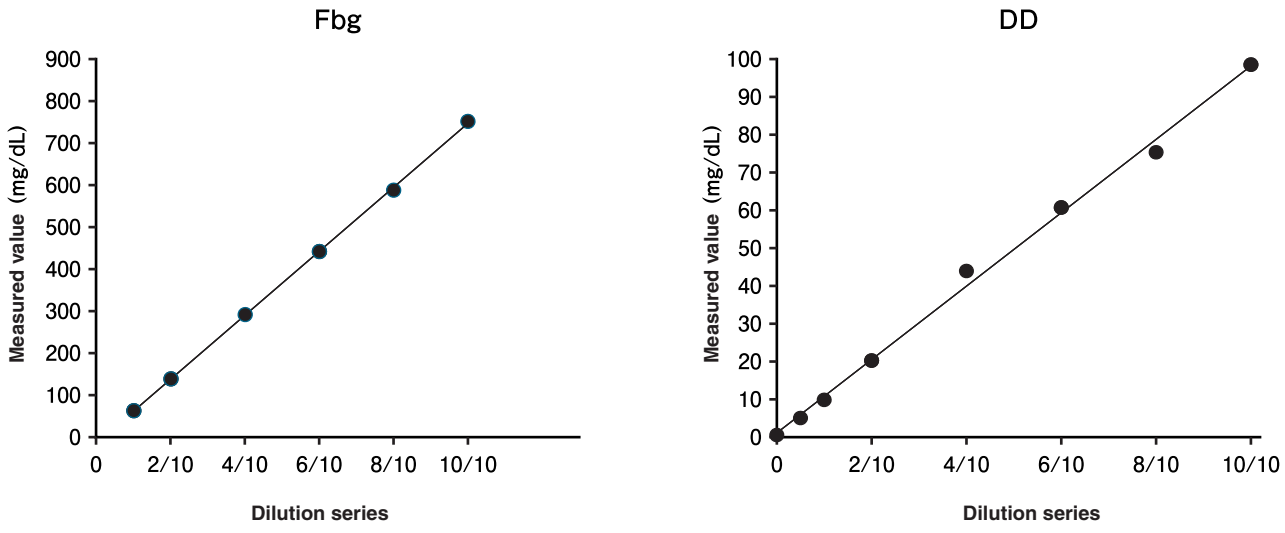


Fig. 3 *Linearity of Fbg and DD data*

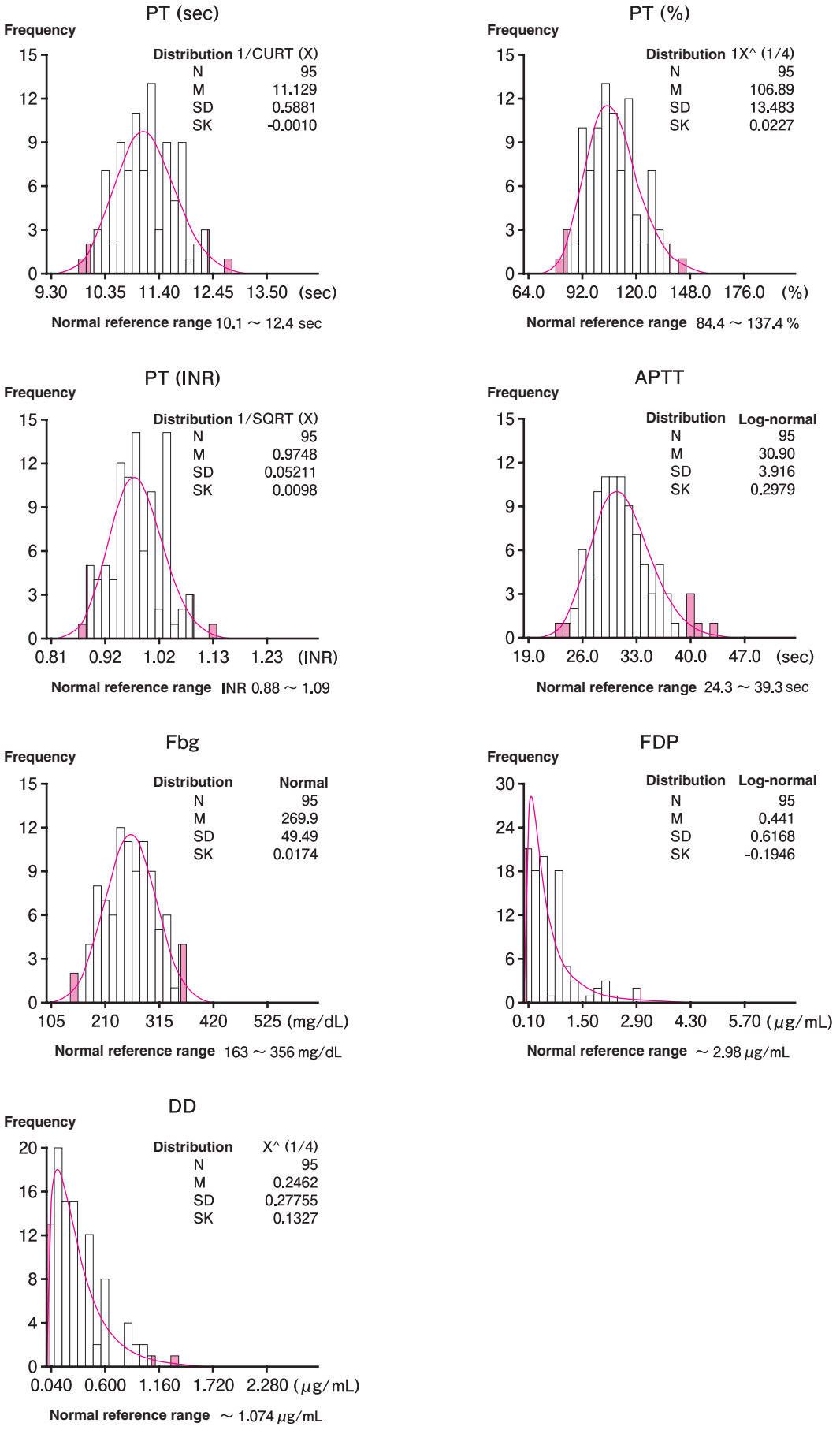


Fig. 4 *Normal reference ranges*

DISCUSSION

Blood coagulation and fibrinolysis testing is essential for diagnosis, understanding the pathophysiology, and monitoring of treatment, of hemorrhagic and thrombotic diseases [3], and for diagnosis and understanding the pathophysiology of liver diseases. As a regional disaster medical center, our hospital is now required to have a 24 hour testing setup.

Our present study found that the within-run reproducibility of measured values was good for all the parameters, the CV being ≤ 3%. This was similar to results of investigations reported so far [4,5] for CS-5100, and better than those reported for the earlier model CA-7000 [1].

Our examination of onboard reagent stability with seal opened and capped reagent bottles kept in the analyzer for 24 hours a day showed that the results of measurement of PT, APTT and Fbg were stable for 5 days, and those ATIII, FDP and DD for 8 days. With HpT, the measured value started to decrease from the 4th day. This seems to be the appropriate result, as the package insert itself mentions that the stability of the reagent is 4 days at 2-8°C. Our study confirmed that onboard reagent stability was better in CS-5100 than in CA-7000. This is because of the structure of the reagent table of the new analyzer. The interior of the reagent table of CS-5100 is maintained at the low temperature of 10°C, and it has a built-in fan which makes the temperature distribution within the table uniform, and thus contributes to better reagent stability. Especially with the ATIII reagents, which are particularly prone to drying, the fitting of reagent caps reduced evaporation which kept the reagents stable for 8 days.

Correlation of the measured values with those of CA-7000 was good, the correlation coefficients r being 0.923-0.997. The measured values of DD were higher with CS-5100, which increased the slope of the line slightly. This was because of the difference in the reagents used, LIAS AUTO D-dimer NEO with CS-5100 and Nanopia® D-dimer (Nanopia® D-dimer; SEKISUI MEDICAL Co., Ltd., Tokyo, Japan) with CA-7000.

Linearity could be confirmed up to the higher concentrations of 750 mg/dL for Fbg and 98 μg/mL for DD, which was significantly better than CA-7000. Therefore, we can confidently expect that the number of retests after dilution would be reduced because of this expanded measurement range.

The normal reference ranges were confirmed to show no major difference from those used with CA-7000. Therefore, smooth switchover to CS-5100 could be achieved without causing any confusion at the point of care.

CONCLUSION

Our investigation showed that compared to the earlier model, CS-5100 had better within-run reproducibility, onboard reagent stability and linearity of Fbg and DD measured values. Examination of correlations and normal reference ranges showed that it was at par with CA-7000, and that data continuity could be maintained. The above results suggest that with CS-5100, apart from routine testing, we can satisfactorily handle 24-hour emergency testing, as required for a regional disaster medical center. Thus the usefulness of CS-5100 has been confirmed.

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