Evaluation of the Fully Automated Blood Coagulation Analyzer CA-650

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We evaluated the Fully Automated Blood Coagulation Analyzer CA-650 (CA-650; Sysmex Corporation, Kobe, Japan) for performance of coagulation and fibrinolysis assays. Results of within-run reproducibility and on-board stability of the reagents were good. There was also a good correlation of results from CA-650 with the Fully Automated Blood Coagulation Analyzer CA-500 Series (CA-500 Series; Sysmex Corporation, Kobe, Japan). The analytical performance of CA-650 supports its use in a routine coagulation testing laboratory.

Key Words CA-650, Compact, Usability

INTRODUCTION

The importance of blood coagulation testing has increased in recent years due to the increased incidence of thrombosis in the aged population and other diseases arising mainly from thrombus formation. Against this background, various types of blood coagulation analyzers have been developed. The Sysmex CA-600 series of analysers (CA-600 series; Sysmex Corporation, Kobe, Japan) are compact, fully automated coagulation analyzers suitable for low volume haemostasis laboratories which handle only small numbers of samples daily, for stat laboratories or as a powerful backup instrument in larger laboratories. The CA-600 series of analysers consist of the CA-620 and CA-650 and have now replaced the previous CA-500 series of analysers (CA-500 series; Sysmex Corporation, Kobe, Japan), CA-510, CA-530 and the CA-550.

The Yonaha General Hospital, to which the first author is affiliated, has recently replaced their Sysmex CA-510 fully automated coagulation analyzer, with a Sysmex CA-650 analyser.

We evaluated the basic performance of CA-650 using clinical samples and commercial controls and compared the performance with that of CA-500 series analyzers including CA-510 and CA-550.

MATERIALS AND METHODS

1. Analysis samples

One hundred and twenty patients plasma samples were collected in sodium citrate (3.2%) tubes and submitted for analysis to our clinical laboratory. Sysmex and SIEMENS Commercial Controls were also used in the study and are listed in ***Table 1***.

2. Analyzers

Analyzer evaluated: Sysmex CA-650

The analyzer performance of the CA-650 was compared with the existing CA-510 of the hospital laboratory for parameters measured by the clotting time method (PT, APTT, Fbg, TTO and HpT), and with a CA-550 for specialized chromogenic and immunoassays such as AT, FDP, and D-dimer.

3. Analysis reagents

The parameters analyzed and the reagents used in the study are listed in ***Table 2***. PT (prothrombin time), APTT (activated partial thromboplastin time), Fbg (fibrinogen), TTO (thrombotest value) and HpT (hepaplastin test value) were determined by the clotting time method. The

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Table 1 *Controls used*

Parameter	Control
PT	Coagtrol IX/IIX
APTT	Coagtrol IX/IIX
Fbg	Coagtrol IX/IIX
TTO	Coagtrol IX/IIX
HpT	Coagtrol IX/IIX
AT	Control Plasma N
	Control Plasma P
FDP	FDP CONTROL NEO
D-dimer	D-Dimer CONTROL NEO

Table 2 *Analysis reagents*

Parameter	Reagent name
PT	Thromborel® S
APTT	Thrombocheck APTT-SLA
Fbg	Dade Thrombin Reagent
TTO	Compound Factor T Kokusai
HpT	Compound Factor H Kokusai
AT	Berichrom® Antithrombin III Auto B
FDP	Latex Test BL-2 P-FDP
D-dimer	LIAS AUTO D-Dimer NEO

chromogenic substrate method was used for AT (anti-thrombin) and immunoturbidimetry was used for FDP (fibrinogen/fibrin degradation products) and D-dimer (cross-linked fibrin degradation products) assays.

4. Methods

1) Within-run reproducibility
Each of the controls were analyzed 20 times consecutively and the coefficient of variation (CV%) was calculated to examine the within-run reproducibility.

2) On-board reagent stability
Each of the reagents was set, with evaporation cap opened 24 hours, in the reagent holder cooled to 15°C and the controls for the coagulation time method parameters and AT were analyzed over 6 days (120 hours from setting of the reagent). FDP and D-dimer controls were analyzed over 7 days (144 hours).

3) Correlations
Linear regression equations and coefficients of correlation were calculated by comparing measured values of patients' plasma obtained using CA-650 , CA-510 and CA-550 analysers.

RESULTS

1) Within-run reproducibility
CV was 0.39-2.30% for the clotting time method parameters, 1.22-3.95% for AT, and 1.66-5.52% for FDP and D-dimer (***Table 3-A*** and ***Table 3-B***).

2) On-board reagent stability
The results of onboard stability of the reagents are shown in ***Fig. 1***. Measured values of PT, APTT, TTO, HpT and AT were stable for 6 days, Fbg for 4 days, and FDP and D-dimer for 7 days.

3) Correlations
The slopes of linear regression equations and correlation coefficients between the results from the CA-650 and CA-500 series analyzers for the 120 samples showed that the slope and correlation coefficient were respectively 0.88-1.20 and 0.977-0.994 for the clotting time method parameters, 0.92 and 0.986 for AT, 0.99 and 0.984 for FDP, and 0.99 and 0.998 for D-dimer (***Fig. 2***).

DISCUSSION

With the increasing number and diversity of requests for blood coagulation tests, there is high demand from large-scale clinical laboratories for multi-parameter high throughput coagulation analyzers. On the other hand, there is also a strong demand for compact, low-cost and fully automated analyzers for small laboratories and for emergency testing. These compact analyzers are also often used in large laboratories as backup for the main analyzers. CA-650 provides strong performance and high quality results for routine tests, but also provides added value through a wide range of speciality testing to further investigate haemostatis disease status. We have verified the basic performance of CA-650 after the induction of this analyzer in our laboratory.
Our evaluation of the basic performance of CA-650 in the analysis of PT, APTT, Fbg, TTO, HpT, AT, FDP and D-dimer showed good performance for all parameters, as per the within-run reproducibility stated in the analyzer specifications (CV ≤ 2% for PT and APTT, ≤ 4% for Fbg, TTO and HpT, ≤ 5% for AT, and ≤ 10% for FDP and D-dimer). The within-run reproducibility (CV%) for clotting time method parameters and chromogenic substrate method parameters measured by CA-650 was comparable to the within-run reproducibility of the same parameters CA-500 series (CV 0.34-2.08% for coagulation time method parameters and 1.271-2.536% for chromogenic substrate method parameters) [1)]. As for the onboard stability of reagents, measured values of PT,

Table 3-A *Within-run reproducibility*

Parameter	PT					
Reagent	Thromborel® S					
Sample	Normal control			Pathological control		
Unit	sec	%	INR	sec	%	INR
1	10.8	88.3	1.08	18.3	39.3	1.76
2	10.8	88.3	1.08	18.2	39.6	1.76
3	10.7	89.7	1.07	18.2	39.6	1.76
4	10.8	88.3	1.08	18.1	39.8	1.75
5	10.7	89.7	1.07	18.1	39.8	1.75
6	10.6	91.0	1.06	18.1	39.8	1.75
7	10.7	89.7	1.07	18.2	39.6	1.76
8	10.8	88.3	1.08	18.0	40.1	1.74
9	10.7	89.7	1.07	18.2	39.6	1.76
10	10.6	91.0	1.06	18.2	39.6	1.76
11	10.7	89.7	1.07	18.1	39.8	1.75
12	10.7	89.7	1.07	18.2	39.6	1.76
13	10.8	88.3	1.08	18.2	39.6	1.76
14	10.8	88.3	1.08	18.3	39.3	1.76
15	10.8	88.3	1.08	18.2	39.6	1.76
16	10.7	89.7	1.07	18.2	39.6	1.76
17	10.8	88.3	1.08	18.2	39.6	1.76
18	10.8	88.3	1.08	18.3	39.3	1.76
19	10.8	88.3	1.08	18.2	39.6	1.76
20	10.8	88.3	1.08	18.0	40.1	1.74
Mean	10.75	89.06	1.075	18.18	39.65	1.756
SD	0.07	0.94	0.01	0.09	0.22	0.01
CV (%)	0.64	1.05	0.64	0.47	0.55	0.39
MAX	10.8	91.0	1.08	18.3	40.1	1.76
MIN	10.6	88.3	1.06	18.0	39.3	1.74

Parameter	APTT	
Reagent	Thrombocheck APTT-SLA	
Sample	Normal control	Pathological control
Unit	sec	
1	27.3	61.7
2	27.4	61.8
3	27.2	61.5
4	27.4	61.6
5	27.3	61.5
6	27.3	61.5
7	27.3	61.5
8	27.3	61.4
9	27.2	61.4
10	27.3	61.0
11	27.4	61.5
12	27.6	62.5
13	27.5	62.1
14	27.5	61.7
15	27.5	61.2
16	27.4	62.1
17	27.3	61.6
18	27.3	61.2
19	27.2	61.4
20	27.5	61.9
Mean	27.36	61.61
SD	0.11	0.35
CV (%)	0.42	0.57
MAX	27.6	62.5
MIN	27.2	61.0

Parameter	Fbg	
Reagent	Dade Thrombin Reagent	
Sample	Normal control	Pathological control
Unit	mg/dL	
1	249.9	108.5
2	246.1	109.8
3	242.5	107.9
4	238.9	107.9
5	246.1	101.9
6	242.5	107.2
7	246.1	107.9
8	246.1	109.1
9	246.1	106.6
10	249.9	104.2
11	238.9	110.5
12	249.9	106.0
13	246.1	106.6
14	242.5	106.6
15	238.9	104.8
16	249.9	109.1
17	238.9	101.9
18	238.9	106.6
19	238.9	103.0
20	242.5	106.0
Mean	243.98	106.61
SD	4.17	2.45
CV (%)	1.71	2.30
MAX	249.9	110.5
MIN	238.9	101.9

Parameter	TTO	
Reagent	Compound Factor T Kokusai	
Sample	Normal control	Pathological control
Unit	%	
1	125.6	50.3
2	127.9	51.2
3	126.7	50.1
4	129.0	50.8
5	132.6	49.7
6	129.0	50.5
7	129.0	50.3
8	130.2	50.3
9	137.6	49.3
10	127.9	51.2
11	129.0	49.9
12	130.2	49.7
13	131.4	51.2
14	132.6	49.9
15	129.0	48.9
16	130.2	50.1
17	133.8	49.9
18	132.6	50.1
19	133.8	50.1
20	133.8	49.3
Mean	130.595	50.14
SD	2.91	0.63
CV (%)	2.23	1.26
MAX	137.6	51.2
MIN	125.6	48.9

Parameter	HpT	
Reagent	Compound Factor H Kokusai	
Sample	Normal control	Pathological control
Unit	%	
1	101.7	41.7
2	103.5	41.1
3	100.0	42.7
4	104.4	42.7
5	100.9	41.9
6	104.4	42.7
7	103.5	42.0
8	102.6	41.8
9	102.6	42.3
10	105.4	42.0
11	102.6	42.4
12	106.3	42.8
13	106.3	41.4
14	108.2	42.6
15	106.3	43.1
16	105.4	41.5
17	107.2	41.7
18	108.2	41.7
19	106.3	41.8
20	107.2	41.4
Mean	104.65	42.065
SD	2.41	0.56
CV (%)	2.30	1.33
MAX	108.2	43.1
MIN	100	41.1

Table 3-B *Within-run reproducibility*

Parameter	AT	
Reagent	Berichrom® Antithrombin III Auto B	
Sample	Normal control	Pathological control
Unit	%	
1	98.7	33.0
2	97.2	31.8
3	98.6	31.9
4	100.5	32.8
5	99.8	32.1
6	100.8	32.1
7	100.0	32.1
8	99.6	31.8
9	100.7	30.8
10	100.0	32.9
11	99.8	32.3
12	99.2	32.1
13	100.8	32.5
14	99.6	32.3
15	100.3	28.6
16	101.1	33.7
17	96.6	34.1
18	100.8	34.1
19	99.6	32.8
20	101.1	34.5
Mean	99.74	32.42
SD	1.22	1.28
CV (%)	1.22	3.95
MAX	101.1	34.5
MIN	96.6	28.6

Parameter	FDP	
Reagent	Latex Test BL-2 P-FDP	
Sample	Low concentration control	High concentration control
Unit	μg/mL	
1	10.0	25.9
2	9.6	26.1
3	9.3	26.1
4	10.0	27.2
5	10.0	26.3
6	9.6	25.7
7	9.3	26.3
8	8.9	26.1
9	10.3	26.1
10	9.6	26.1
11	10.0	27.0
12	8.9	27.0
13	10.6	26.3
14	9.6	26.6
15	10.6	27.2
16	10.9	27.0
17	9.6	26.4
18	10.0	26.4
19	9.6	26.6
20	9.3	26.6
Mean	9.79	26.45
SD	0.54	0.44
CV (%)	5.52	1.66
MAX	10.9	27.2
MIN	8.9	25.7

Parameter	D-dimer	
Reagent	LIAS AUTO D-Dimer NEO	
Sample	Low concentration control	High concentration control
Unit	μg/mL	
1	1.9	11.7
2	2.1	11.5
3	2.1	11.3
4	2.1	11.5
5	2.1	11.5
6	1.9	11.5
7	1.8	11.6
8	2.1	11.5
9	2.2	11.6
10	1.9	11.2
11	2.0	11.7
12	2.1	11.9
13	2.0	11.6
14	2.0	11.6
15	2.1	11.7
16	2.0	11.9
17	2.0	11.8
18	2.1	11.9
19	2.1	12.1
20	2.0	11.9
Mean	2.03	11.65
SD	0.1	0.22
CV (%)	4.82	1.90
MAX	2.2	12.1
MIN	1.8	11.2

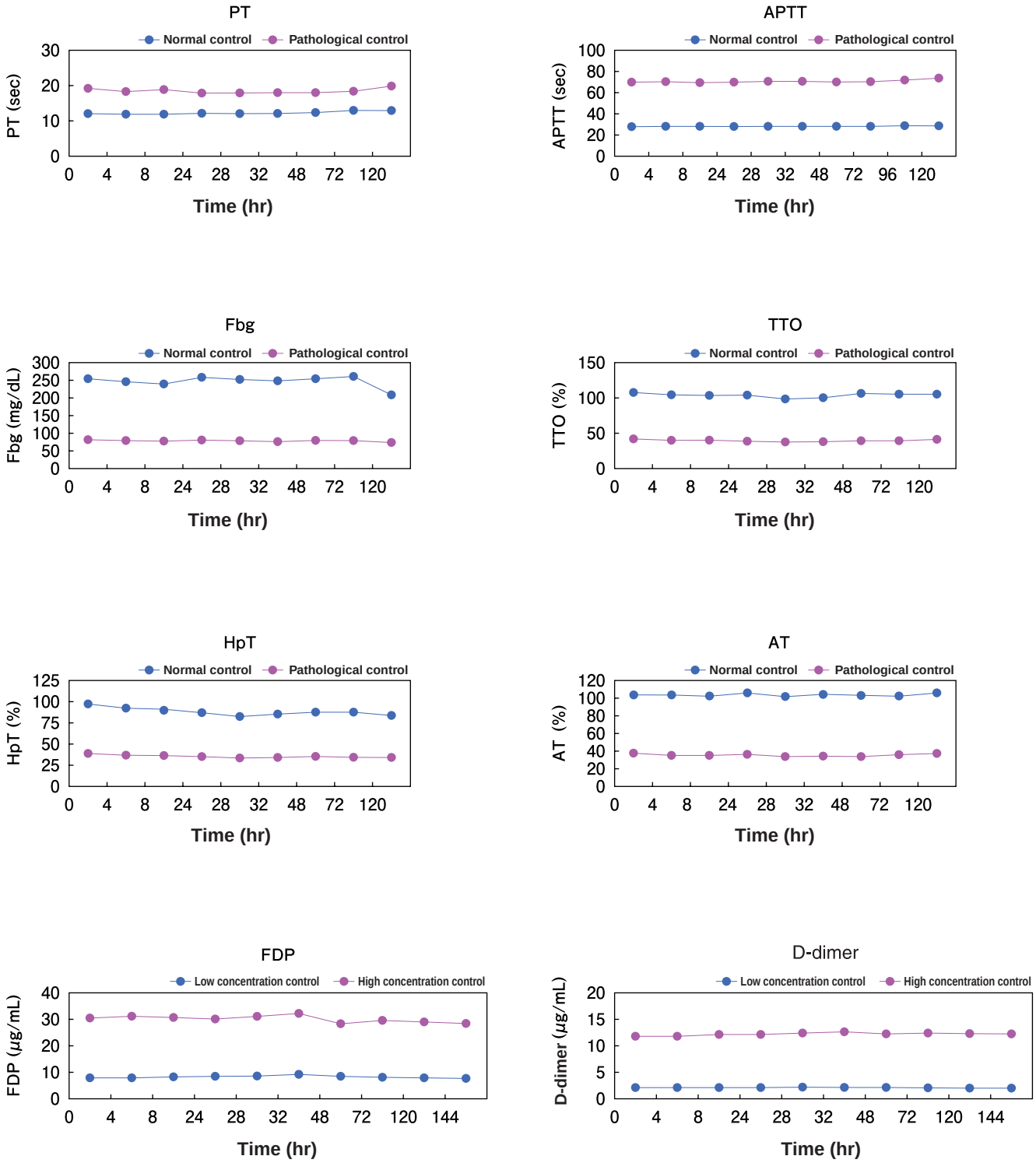

Fig. 1 *Onboard reagent stability*

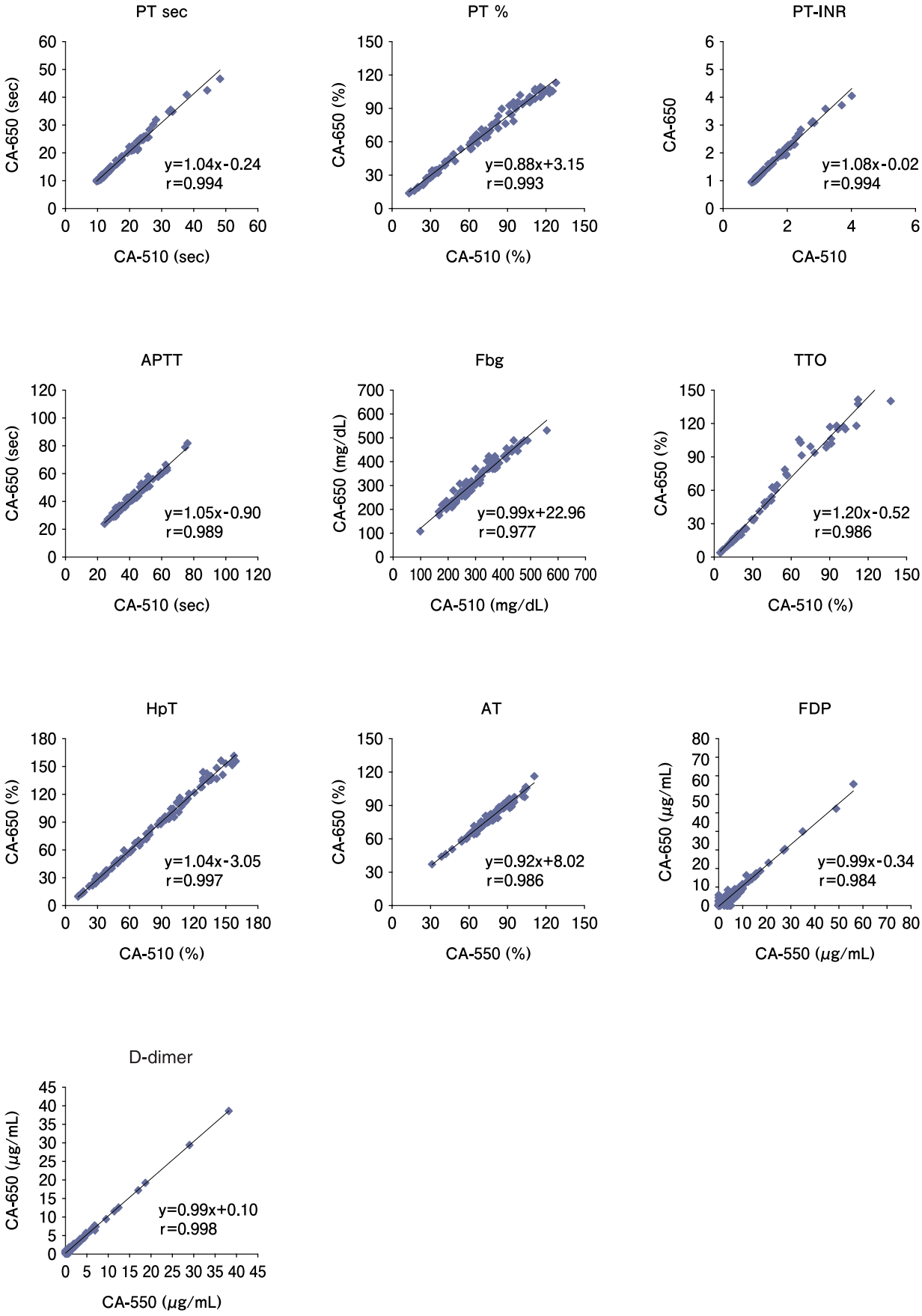

Fig. 2 *Correlations*

APTT, TTO, HpT and AT were stable for 6 days, Fbg for 4 days, and FDP and D-dimer for 7 days. The results obtained by the CA-650 and CA-500 series of analysers showed good correlation in all parameters, with the data points scattered closely around the regression lines (***Fig. 2***). Low concentration samples gave variable results for FDP. This is believed to be due to the reduced analysis accuracy as the value of this parameter fell below the measurement range.

CA-650 has the basic platform [2] of the CA-500 series, but it has a new exterior design and improved features to promote ease of use. CA-650 is capable of three measurement principles, namely, clotting time method, chromogenic substrate method and immunoturbidimetry. The data memory has been doubled to 600 samples (3000 tests) from the 300 samples (1500 tests) from the CA-500 series [3]. When a new calibration line is prepared, the previous curve is automatically saved as a backup. It is also possible to retain three calibration curves by manual operation (with software Ver. 00-04 and later).

CA-650 is operated in almost the same way as the CA-500 series analyzers, and this facilitated smooth transition from CA-510 to the new CA-650 analyzer at our hospital. The CA-510 was capable of analyzing only parameters measured by the clotting time method. Now, the introduction of the CA-650 has enabled the analysis of additional parameters measured by the chromogenic substrate method and immunoturbidimetry .

In recent years, there has been an increase in the number of FDP and AT tests performed at our hospital. The number of tests performed in our clinical laboratory is small, however AT tests account for a large proportion of the coagulation tests due to the obstetrics department. Therefore the FDP and AT testing capability of this compact analyzer is a major advantage. Additionally, the touch panel is now in color unlike in CA-510, which makes it easy to read and operate. The capacities of the rinse fluid bottle and waste fluid bottle have been increased to 5 L (standard) and 2 L (optional), which would reduce the time spent in changing the washing fluid, and waste fluid disposal.

Based on the above results, we can say that the CA-650 is excellent for day-to-day routine and specialized haemostasis testing.

CONCLUSION

CA-650 showed good basic performance in the present study. CA-650 was developed as a redesigned model of the CA-500 series analyzers. It is operated almost the same as the CA-500 series of analysers and has improved user functionality. Thus, the CA-650 is considered beneficial for day-to-day routine testing.

References

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