Introduction of Products

Overview and Features of the Automated Hematology Analyzer

XN-L Series

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INTRODUCTION

In recent years, healthcare infrastructures have been steadily constructed in emerging markets. In addition, rapid rates of economic growth have made healthcare information more accessible worldwide.

Thus, people have become more aware of health and healthcare, with dramatically increasing demands for medical care and clinical testing. In developed countries, regional needs have diversified, such as medical cost suppression due to the aging society and widely-spreading personalized healthcare.

To address the dynamic healthcare terrain, we launched the XN-Series in 2011, which improved the efficiency and clinical values of blood cell count testing. Now we introduce the XN-L series; compact automated hematology analyzers that are based on XN series functionality, operability, and clinical parameters [1-3] (***Fig. 1***). These analyzers are among the world's smallest and are equipped with advanced testing modalities including reticulocyte (RET) measurement functions, a low WBC mode, and body fluid mode. The XN-L also has the features of conventional products including: 8 CBC parameters, 6 WBC classifications, and trace analyte measurement. This series includes superior service and support systems that correspond to the Sysmex Network Communication Systems (SNCS®) [4], contributing to safe and efficient laboratory test environments. One analyzer in this line, the XN-550, features automated Rerun/Repeat/Reflex functions as an added capability. Furthermore, this product line is already equipped to provide future enhancements, including an optional application to detect the infected erythrocytes in malarial infection, which is one of the three most prevalent infections worldwide. Sysmex is committed to advancing hematology technologies in order to further develop the clinical use of the automated blood cell analyzer. In this report, XN-L series will be introduced.

Fig. 1 *XN-L series Automated Hematology Analyzers*

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MAIN SPECIFICATIONS

1. Name

1) Name: Automated Hematology Analyzer XN-L series
2) Model: XN-550 (Sampler type)
XN-450 (Cap-piercing type)
XN-350 (Open type)

2. Applications

These devices are hematology analyzers for blood testing using human blood. Blood should be anticoagulated with EDTA-2K, EDTA-3K, and EDTA-2Na for use on the analyzers. Body fluids, such as cerebrospinal, pleural, peritoneal, and synovial fluids, can also be measured.

3. Reportable parameters

There are 35 reportable whole blood parameters and 7 reportable body fluid parameters. For details, see ***Table 1***.

4. Main research parameters

Fragmented red blood cell count (FRC#), fragmented red blood cell ratio (FRC%), high fluorescent lymphocyte count (HFLC#), and high fluorescent lymphocyte ratio (HFLC%).

5. Sample volume

Sample volumes to be aspirated are 25μL and 70μL for whole blood and diluted blood/body fluid, respectively. For details, see ***Table 2***.

6. Throughput

Throughput is up to approx. 70 samples per hour. For details, see ***Table 3***.

7. Dimensions and weight

Dimensions (width × depth × height) and weights are shown in ***Table 4***.

8. Reagents

Reagents and their measurement channels are shown in ***Table 5***.

Table 1 *Reportable parameters*

Analysis Mode	Discrete	Detector/Channel	Parameter
Whole Blood mode	CBC	RBC/PLT, HGB, WDF	WBC, RBC, HGB, HCT, MCV, MCH, MCHC, PLT RDW-SD, RDW-CV, PDW, MPV, P-LCR, PCT
	DIFF	WDF	NEUT#, LYMPH#, MONO#, EO#, BASO#, NEUT%, LYMPH%, MONO%, EO%, BASO%, IG#, IG%
	RET	RET*	RET#, RET%, IRF, LFR, MFR, HFR, RET-He, IPF#, IPF
Body Fluid mode*	—	RBC, WDF	RBC-BF, WBC-BF, MN#, PMN#, MN%, PMN%, TC-BF

* The availability of functions depends on the system configuration.

Table 2 *Sample volume*

XN-550/XN-450

Analysis method	Specimen	Test tube	Cap	Aspirated sample volume	Required sample volume
Sampler analysis (XN-550)	Whole blood	Regular sample tube	Close	25μL	1mL
		RBT micro collection tube	Close		250μL
Manual analysis	Whole blood	Regular sample tube	Close	25μL	1mL
			Open		300μL
		RBT micro collection tube	Close		250μL
		Micro collection tube	Open		100μL
	Diluted blood	Regular sample tube	Open	70μL*1	300μL
		Micro collection tube	Open		140μL
	Body fluid*2	Regular sample tube	Close	70μL	1mL
			Open		300μL
		Micro collection tube	Open		140μL

*1: Use diluted blood prepared by diluting 20μL of whole blood1:7.
*2: The availability of body fluid analysis function depends on the system configuration.

XN-350

Analysis method	Specimen	Test tube	Cap	Aspirated sample volume
Manual analysis	Whole blood	Regular sample tube	Open	25μL
	Diluted blood			70μL
	Body fluid*			

* The availability of body fluid analysis function depends on the system configurations.

Table 3 *Throughput*

Analysis mode	Discrete	Throughput
Whole blood	CBC	Approx. 60 samples/hour (approx. 70 samples/hour*1)
	CBC+DIFF	
	CBC+RET*2	Approx. 35 samples/hour
	CBC+DIFF+RET*2	
Low WBC*2	CBC+DIFF	Approx. 55 samples/hour
	CBC+DIFF+RET*2	Approx. 30 samples/hour
Pre-Dilution	CBC	Approx. 60 samples/hour
	CBC+DIFF	
	CBC+DIFF+RET*2	Approx. 30 samples/hour
Body fluid*2	—	Approx. 30 samples/hour

*1: The throughput depends on the system configuration.
*2: The availability of functions depends on the system configurations.

Table 4 *Dimensions and weight*

		Dimensions (width × depth × height)	Weight
XN-550	Analyzer Monitor	Approx. 450 × 660 × 450 mm Approx. 267 × 205 × 240 mm	Approx. 53 kg Approx. 3 kg
XN-450	Analyzer	Approx. 450 × 460 × 440 mm	Approx. 35 kg
XN-350	Analyzer	Approx. 450 × 460 × 510 mm	Approx. 35 kg

Table 5 *Reagents*

Channel	Reagent type	Product name
Each channel	Diluent (concentrated reagent)	CELLPACK DST*1
	Diluent	CELLPACK DCL
HGB channel	Hemolytic agent	SULFOLYSER
WDF channel	Hemolytic agent	Lysercell WDF
	Stain solution	Fluorocell WDF
RET channel*2	Diluent	CELLPACK DFL
	Stain solution	Fluorocell RET

*1: Use of CELLPACK DST depends on the system configuration.
*2: The availability of functions depends on the system configurations.

TECHNOLOGY

1. Measurement principles

1) Flow cytometry

The XN-L uses reliable flow cytometry technology using a semiconductor laser which inherits the technology of XN-Series [4] to provide high-performance measurements in a compact design. Blood cells are treated with specific reagents, and are expanded on multi-dimensional scattergrams through the conversion of forward scattered -, side scattered-, and side fluorescent light into electrical impulses. Each scattergram is analyzed using original technologies to calculate measurements (***Table 6***). The low WBC and body fluid modes improve accuracy by increasing the amount of blood cells counted. Also, reticulocyte hemoglobin equivalents (RET-He) and immature platelet fraction (IPF) are determined.

2) Hydro dynamic focusing method (direct current: DC detection method) [5]

Red blood cell and platelet counts are determined using Hydro dynamic focusing method. In principle, the coincidence and recount of blood cells are minimized, facilitating accurate measurements of blood counts and volumes.

3) SLS hemoglobin method [6]

Hemoglobin concentrations are determined by the SLS hemoglobin method without using toxin or special oxidizing agents. In principle, blood cells are lysed with sodium lauryl sulfate (SLS), followed by colorimetric measurements. This method is suitable for automation.

2. Body fluid mode [1]

The devices are equipped with a body fluid mode. Without sample pretreatment, white blood cell (WBC-BF) and red blood cell (RBC-BF) counts as well as mononuclear (MN#, MN%) and polymorphonuclear (PMN#, PMN%) leukocyte ratios can be determined and reported. The measurement accuracy is improved by increasing the particle counts approximately tenfold in white blood cells and threefold in red blood cells, when compared to the whole blood mode.

3. Low WBC mode [2,3]

The devices are equipped with a low WBC mode, facilitating the accurate determination of low WBC counts. In principle, sample volume to be measured is doubled, as compared with the whole blood mode, thereby improving the measurement accuracy.

4. Automated dispensing function of diluent

The devices dispense 120µL of CELLPACK DCL into an empty micro collection tube. Subsequently, diluted blood prepared with 20µL of sample can be measured. This facilitates the measurement of small blood volumes which is especially useful for patient populations including geriatric and infant.

Table 6 *Measurement channels and detection parameters*

Channel	Detection parameters	Detection parameters
WDF	White blood cell count	Forward scattered light - side scattered light (CBC)
	WBC 6 differentiation for white blood cell	Side scattered light - side fluorescence light (CBC + DIFF)
RET*	Reticulocyte	Side fluorescence light - forward scattered light

* The availability of functions depends on your system configurations.

BASIC PERFORMANCE

1. Within-run reproducibility

1) Whole blood mode

Within-run reproducibility was demonstrated using three blood samples from healthy volunteers each with 10-consecutive measurements in whole blood mode. Results are shown in ***Table 7***. The CV values of main parameters were WBC : 1.3 - 2.0%, RBC : 0.3 - 0.7%, HGB : 0.3 - 0.5%, HCT : 0.2 - 0.8%, PLT-I : 2.0 - 2.2%, and PLT-O : 0.8 - 2.1%.

2) Body fluid mode

Within-run reproducibility in body fluid mode was demonstrated by preparing samples in three different concentrations using quality control material (XN CHECK BF) and measuring each in 10-consecutive runs. This data is shown in ***Table 8***. The CV values of main parameters were WBC-BF : 5.6 - 9.3%, RBC-BF : 2.4 - 10.6% , and TC-BF# : 5.6 - 9.3%.

2. Correlation

1) Whole blood mode

A correlation between XN-550 (XN-L series) and XN-1000 (XN-Series) in the whole blood mode using patient blood samples (EDTA-2K added, N = 106, provided by the Improvement for Measurement and Diagnostic Technique Project at Department of Laboratory Tests, University of Tsukuba Hospital, Japan) is shown in ***Fig. 2***. The correlation coefficients (r) of main parameters were WBC : 0.9974, RBC : 0.9984, HGB : 0.9987, HCT : 0.9976, and PLT : 0.9982.

2) Body fluid mode

A correlation between XN-550 (XN-L series) and XN-1000 (XN-Series) using 20 celomic fluid, 12 cerebrospinal fluid, and 23 peritoneal dialysate in the body fluid mode is shown in ***Fig. 3***. The correlation coefficients (r) of each parameter was WBC-BF : 0.9994, RBC-BF : 0.9995, and TC-BF# : 0.9993.

3. Minimum detection sensitivity

1) Whole blood mode

Minimum sensitivities (limit of blank : LoB, limit of detection : LoD, and limit of quantitation : LoQ) in measuring a quality control material (e-CHECK) for which the concentration has been adjusted and CELLPACK DCL in the whole blood mode are shown in ***Table 9***. The minimum detection sensitivities of main parameters were WBC (CBC + DIFF mode) : 0.01 × 10^9/L, RBC : 0.00 × 10^{12}/L, and PLT : 1 × 10^9/L.

2) Low WBC mode

Minimum sensitivities (LoB, LoD, and LoQ) in measuring a quality control material (e-CHECK) for which the concentration has been adjusted and CELLPACK DCL in the low WBC mode are shown in ***Table 10***. The minimum detection sensitivities of main parameters were WBC : 0.01 × 10^9/L, RBC : 0.00 × 10^{12}/L, and PLT : 1 × 10^9/L.

3) Body fluid mode

Minimum sensitivities (LoB, LoD, and LoQ) in measuring a quality control material (e-CHECK) for which the concentration has been adjusted and CELLPACK DCL in the body fluid mode are shown in ***Table 11***. The minimum detection sensitivities of main parameters were WBC-BF : 0.001 × 10^9/L, RBC-BF : 0.000 × 10^{12}/L, and TC-BF# : 0.001 × 10^9/L.

Table 7 *Within-run reproducibility of the whole blood mode*

		WBC-C*1 (10^9/L)	WBC-D*2 (10^9/L)	RBC (10^{12}/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	PLT-I (10^9/L)	PLT-O (10^9/L)
1	AVE.	6.948	6.915	5.206	162.7	0.5020	96.43	31.25	324.1	312.1	298.2
	SD	0.140	0.138	0.014	0.7	0.0012	0.07	0.16	1.9	6.2	2.3
	CV	2.0%	2.0%	0.3%	0.4%	0.2%	0.1%	0.5%	0.6%	2.0%	0.8%
2	AVE.	9.091	9.012	5.014	148.0	0.4682	93.38	29.52	316.0	259.6	250.6
	SD	0.117	0.114	0.035	0.7	0.0035	0.15	0.23	2.6	5.6	4.1
	CV	1.3%	1.3%	0.7%	0.5%	0.8%	0.2%	0.8%	0.8%	2.2%	1.6%
3	AVE.	3.661	3.638	4.783	154.2	0.4672	97.68	32.25	330.1	174.5	170.6
	SD	0.046	0.048	0.030	0.4	0.0030	0.11	0.22	2.1	3.8	3.7
	CV	1.3%	1.3%	0.6%	0.3%	0.7%	0.1%	0.7%	0.6%	2.2%	2.1%

		NEUT% (%)	LYMPH% (%)	MONO% (%)	EO% (%)	BASO% (%)	RET% (%)	RET# (10^9/L)	RET-He (pg)
1	AVE.	56.59	34.51	5.48	2.89	0.53	2.437	126.87	33.11
	SD	0.82	0.91	0.22	0.22	0.14	0.055	2.74	0.06
	CV	1.5%	2.6%	4.0%	7.6%	26.8%	2.3%	2.2%	0.2%
2	AVE.	74.78	14.19	8.56	2.07	0.40	1.966	98.57	32.60
	SD	0.51	0.52	0.45	0.17	0.09	0.053	2.67	0.09
	CV	0.7%	3.6%	5.2%	8.2%	23.6%	2.7%	2.7%	0.3%
3	AVE.	44.86	46.58	6.49	1.50	0.57	1.086	51.94	33.96
	SD	0.69	0.78	0.40	0.29	0.15	0.061	2.79	0.19
	CV	1.5%	1.7%	6.1%	19.4%	26.2%	5.6%	5.4%	0.6%

*1 WBC-C: The total white blood cell count measured from the forward scattered light and side scattered light of WDF channel (CBC mode).
*2 WBC-D: The white blood cell count measured from the WDF channel (CBC + DIFF mode).

Table 8 *Within-run reproducibility of the body fluid mode*

		WBC-BF (10^9/L)	RBC-BF (10^{12}/L)	TC-BF (10^9/L)
1	AVE.	0.0104	0.0066	0.0104
	SD	0.0008	0.0007	0.0008
	CV	8.1%	10.6%	8.1%
	MAX	0.012	0.008	0.012
	MIN	0.009	0.006	0.009
2	AVE.	0.0211	0.0118	0.0211
	SD	0.0020	0.0006	0.0020
	CV	9.3%	5.4%	9.3%
	MAX	0.025	0.013	0.025
	MIN	0.018	0.011	0.018
3	AVE.	0.0464	0.0268	0.0464
	SD	0.0026	0.0006	0.0026
	CV	5.6%	2.4%	5.6%
	MAX	0.050	0.028	0.050
	MIN	0.043	0.026	0.043

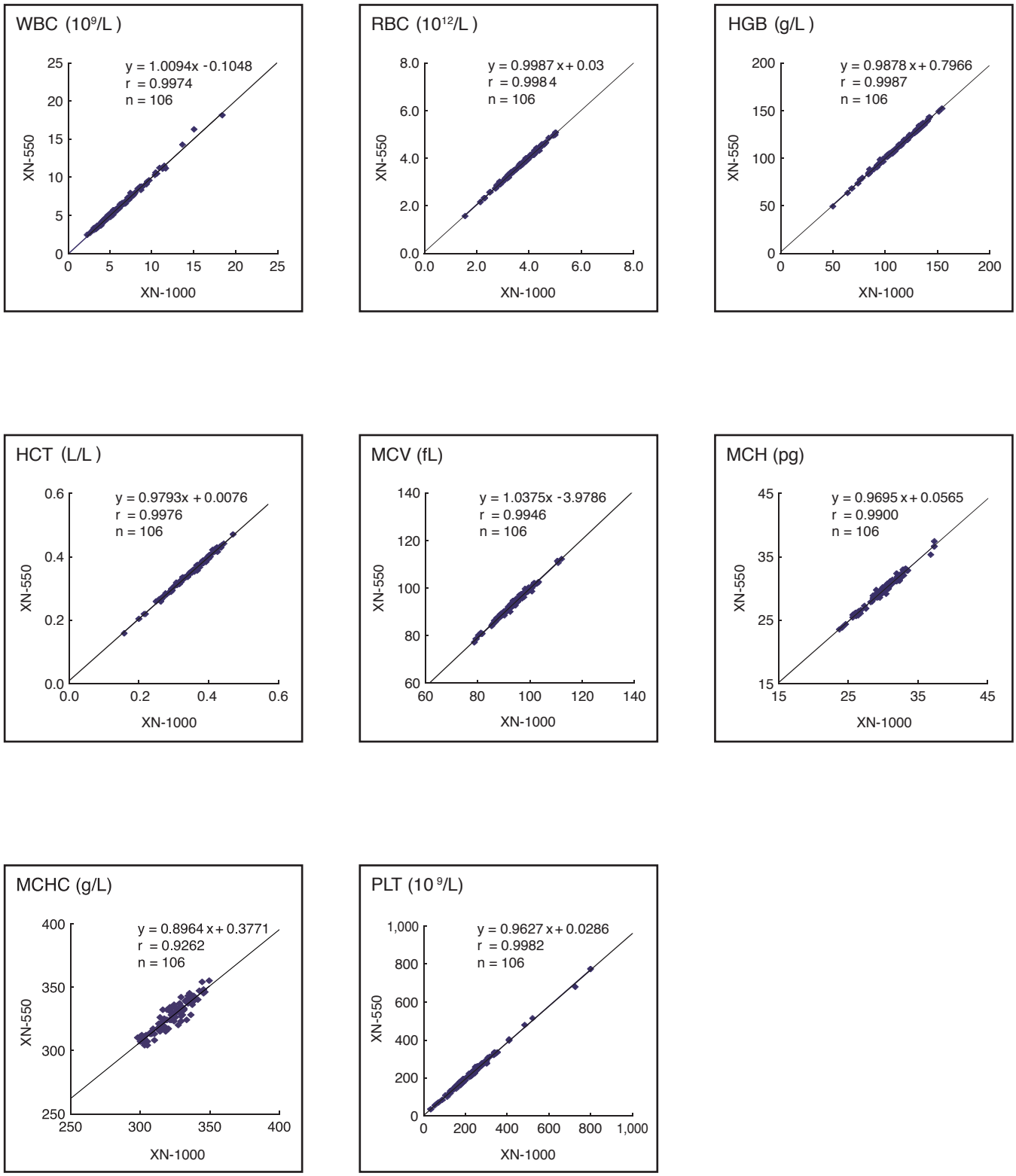


Fig. 2-1 *Correlations among CBC 8 parameters*

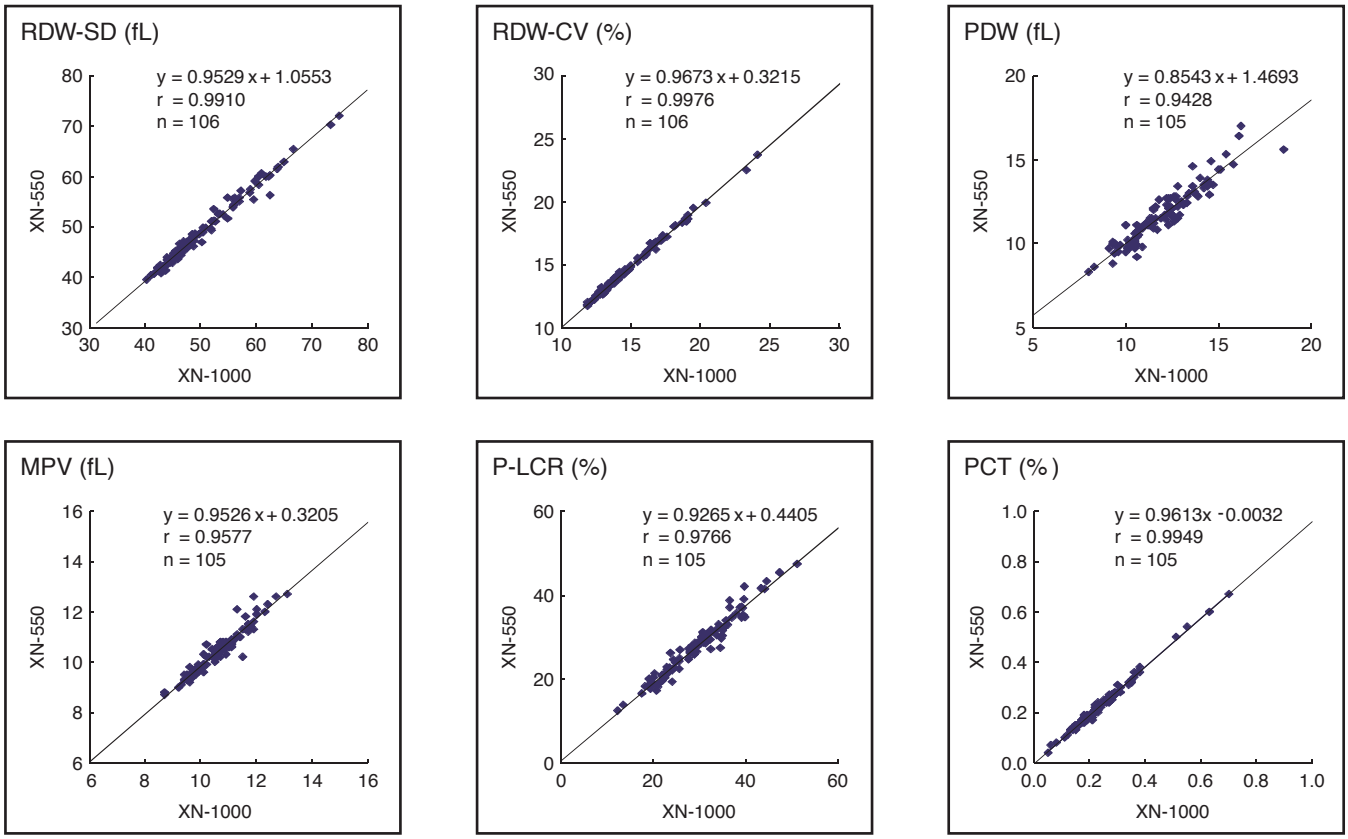


Fig. 2-2 *Correlations among analytical parameters*

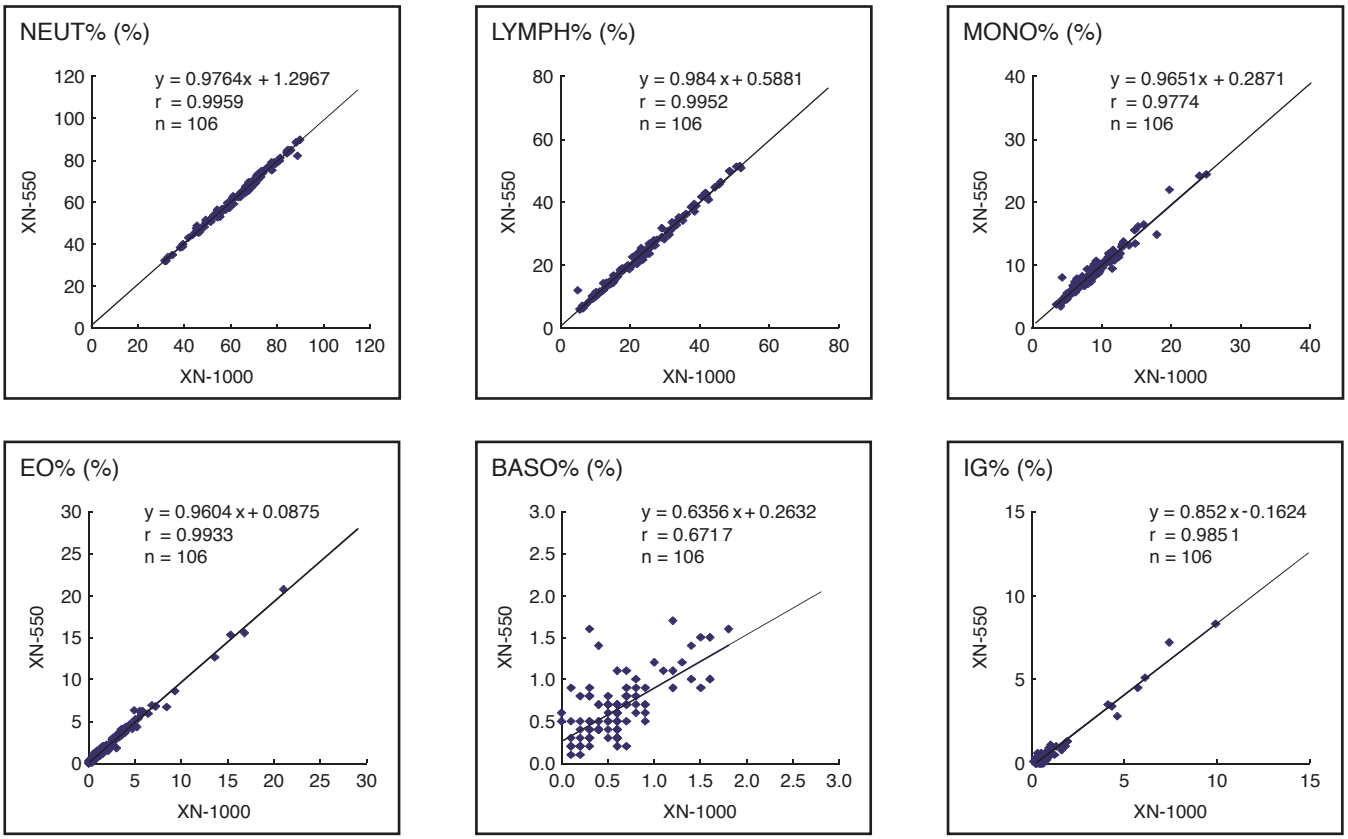


Fig. 2-3 *Correlations among WDF channel parameters*

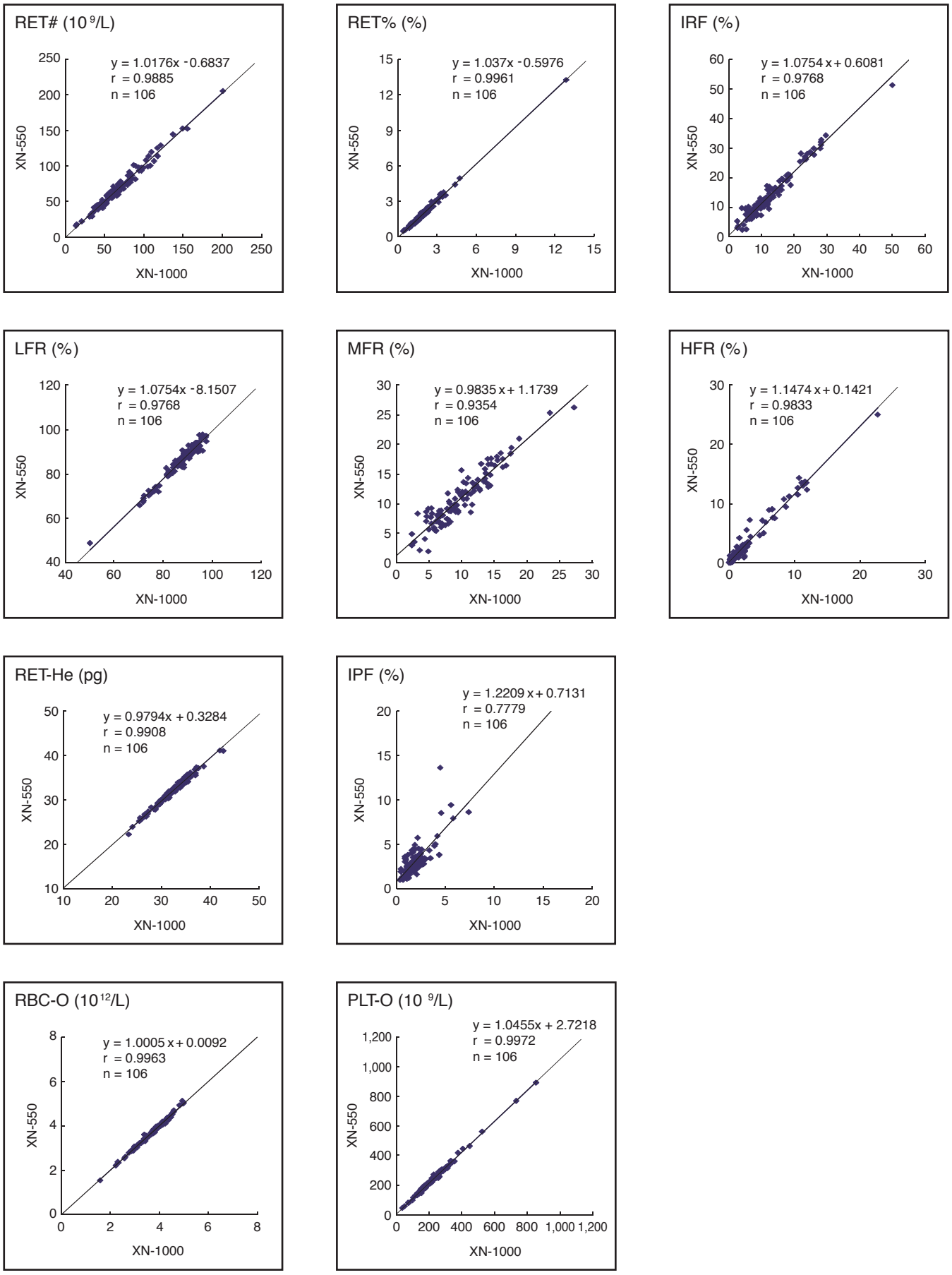
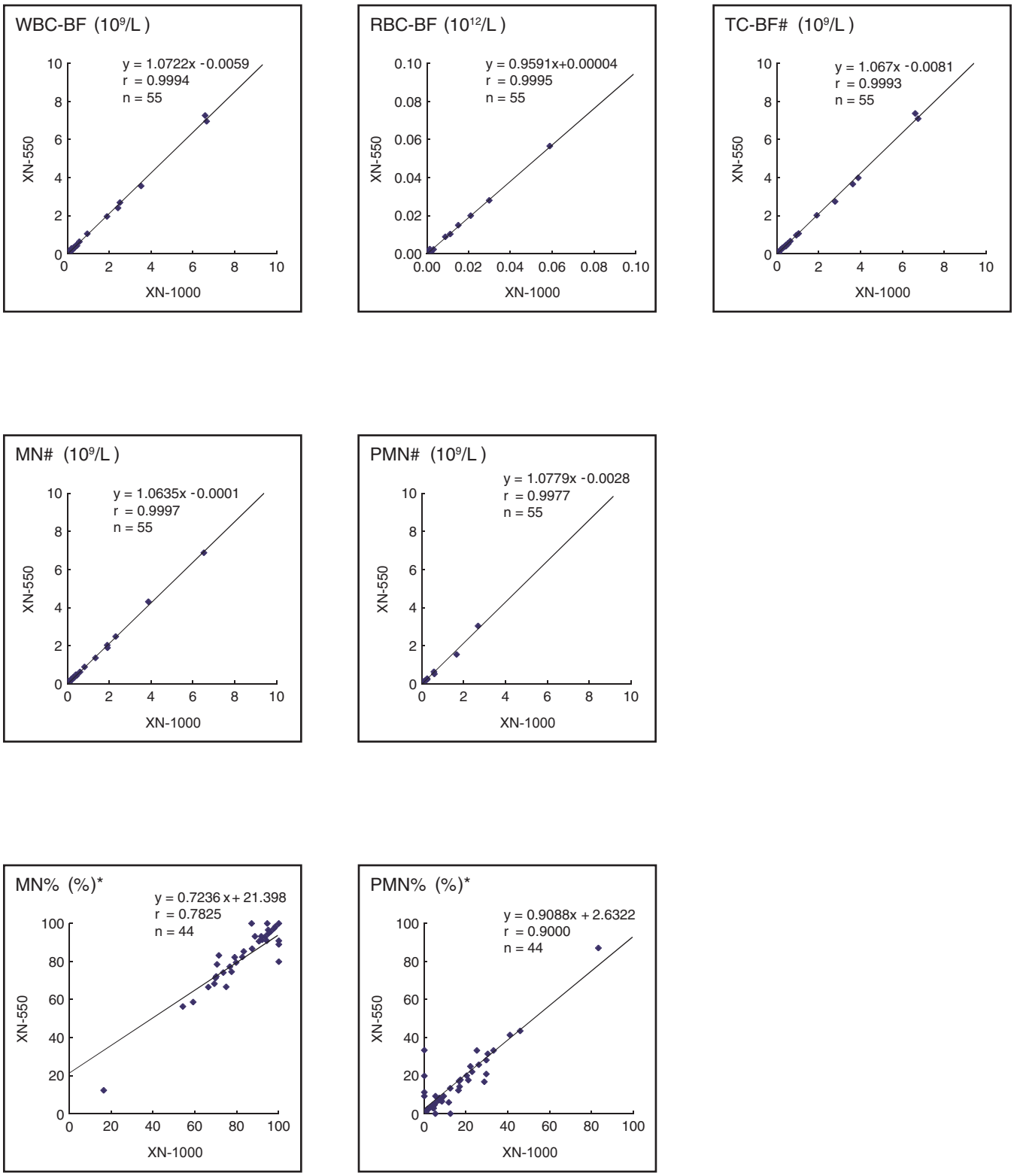


Fig. 2-4 *Correlations among RET channel parameters*



* MN% and PMN% parameters: N= 44, as samples not satisfying the LoQ (WBC-BF < 0.003×10^9/L) were excluded.

Fig. 3 *Correlations among body fluid parameters*

Table 9 *Minimum detection sensitivity of the whole blood mode*

	WBC-C (10^9/L)	WBC-D (10^9/L)	RBC (10^{12}/L)	HGB (g/L)	HCT (L/L)	PLT-I (10^9/L)	PLT-O (10^9/L)
LoB	0.01	0.00	0.00	0	0.000	0	0
LoD	0.02	0.01	0.00	0	0.000	1	1
LoQ	0.03	0.02	0.00	0	0.000	2	2

Table 10 *Minimum detection sensitivity of the low WBC mode*

	WBC-C (10^9/L)	RBC (10^{12}/L)	HGB (g/L)	HCT (L/L)	PLT-I (10^9/L)	PLT-O (10^9/L)
LoB	0.00	0.00	0	0.000	0	0
LoD	0.01	0.00	0	0.000	1	1
LoQ	0.01	0.00	0	0.000	2	2

Table 11 *Minimum detection sensitivity of the body fluid mode*

	WBC-BF (10^9/L)	RBC-BF (10^{12}/L)	TC-BF# (10^9/L)
LoB	0.000	0.000	0.000
LoD	0.001	0.000	0.001
LoQ	0.002	0.001	0.002

FEATURES

In spite of its small size, XN-L series can provide various healthcare information (RET, RET-He, and body fluid parameters) which may assist clinicians in diagnostic decisions.

RET-He reflects the hemoglobin levels in reticulocytes and is a sensitive indicator of iron utilization in erythropoiesis. Thus, it should facilitate the treatment and management of anemia in patients with chronic kidney disease [7] and improve the safety of autologous blood donation [8].

The XN-L series allows the measurements of white blood cells, red blood cells, mononuclear cells, and polymorphonuclear leukocytes in the body fluid mode. Thus, it allows users to make rapid and objective reports of measurements from emergency tests at non-business hours, as well as from daily practices. This feature should be particularly useful in the diagnosis of central nervous system infection. In addition, it may be utilized as screening information for cytology to detect tumor cells[9].

The XN-L series is also equipped with a PLT-I/PLT-O switching function. The impedance platelet count (PLT-I) comes from the hydro dynamic focusing method, while the optical platelet count (PLT-O) is measured in the RET channel using flow cytometry. Usually, the PLT-I is employed as platelet count, while the PLT-O is automatically reported as platelet count for samples with abnormal platelet particle size distributions, such as those with fragmented red blood cells [10].

This function facilitates reporting of more reliable platelet counts.

In addition, with customers' analytical devices and our customer support centers connected on-line, the XN-L series provides real-time quality control and fault monitoring/repair support on the outsourcing basis, and SNCS® service function providing information on the web [4, 11]. More than 24,000 devices are connected on the web around the world, facilitating reporting of accurate measurements and maintenance of devices.

ADDITIONAL VALUES

Like XN-Series, the XN-L series also provides parameters such as immature granulocyte (IG) count and IPF.
Studies have shown that IG may facilitate the detection of inflammatory reaction easier and quicker when combined with existing parameters, such as C-reactive protein and erythrocyte sedimentation rate [12].
Reticulated platelet counts reflect the platelet production ability of the bone marrow. The XN-L series allows automatic measurement of its related parameter IPF. IPF has been reported useful in predicting platelet recovery time after chemotherapy or hematopoietic stem cell transplantation [13] and may aid clinicians in the differential diagnosis of thrombocytopenic disorders, such as immunological thrombocytopenia (e.g., idiopathic thrombocytopenic purpura) [14].

CONCLUSIONS

This report introduced the newly released Automated Hematology Analyzer XN-L series. Using many of the same technologies as the higher throughput XN-series, these compact analyzers contribute to accurate measurement techniques and testing efficiency and can be customized to fit the unique needs of each customer. In addition, it employs systems developable onward so that the wide spread usage of hematology analyzers in clinical practice can be expected in future.

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