Evaluation of the Sysmex XT-2000*i*, a New Automated Haematology Analyser

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The XT 2000i is a recently released automated haematology analyser that was evaluated during a three-month-period. For measurement of the haemoglobin (HGB) concentration the sodium lauryl sulphate (SLS) method is used, while red blood cells (RBC, RBC-I) and platelets (PLT, PLT-I) are counted by impedance technology. White blood cells (WBC), reticulocytes (RET), platelets (PLT, optical measurement; PLT-O) and red blood cells (RBC, optical measurement; RBC-O) are counted by flow cytometry using a polymethine fluorescence dye.

Reproducibility, carryover and linearity were analysed. The correlation study was performed with the Sysmex XE-2100 and included a comparison of sample flagging. Instrument flagging data were also checked against microscopy differentials according to the recommendations of the National Committee for Clinical Laboratory Standards (NCCLS).

The correlation coefficients for complete blood cell count (CBC) and automated differentials obtained by comparison with the XE-2100 were good, except for the reticulocyte fractions. Sensitivity, specificity and efficiency of the various flags were adequate compared to microscopy differentials.

(Sysmex J Int 12 : 71-75, 2002)

Key Words Automated Hematology Analyzer, XT-2000*i*, Complete Blood Count, Platelets

Received 6 December, 2002; Accepted 13 December, 2002

INTRODUCTION

Automated haematology analysers are increasingly able to process the great majority of blood cell counts including the automated white blood cell (WBC) differential. Instrument manufacturers generally invest in development of new technologies or improvements of existing approaches.

The Sysmex XT-2000*i* is a newly developed haematology analyser based on the same technologies as the Sysmex XE-2100, but without the counting of nucleated red blood cells (NRBC) and without the IMI-channel[1]. The haemoglobin (HGB) is measured with the colorimetric sodium lauryl sulphate (SLS) method. Leukocytes are counted using multi-angle scatter separation; a WBC differential can be performed by a combination of the scatter signals and the polymethine fluorescence dye signal. Platelets (PLT) and red blood cells (RBC) are normally counted by impedance technology (PLT-I, RBC-I) but can also be counted in the reticulocyte mode using optical methods (scatter signals and fluorescence signal; PLT-O, RBC-O). Reticulocytes (RET) are counted by side fluorescence signals from the DNA/RNA content, which are stained by the fluorescent polymethine dye.

The analyser has a maximum throughput of 80 samples per hour, and uses 150 µL of blood in the closed sample mode, 85 µL in the open sample mode and 40 µL in the capillary mode. The analyser can be run in the following parameter selections: complete blood cell count (CBC), CBC + differential, CBC + RET and CBC + differential + RET.

The correlation of the CBC, automated WBC differential and RET data were performed against the Sysmex XE-2100. The instrument flagging of the WBC differential was checked microscopically.

MATERIALS AND METHODS

The XT-2000*i* tested was a production model and initially checked and adjusted by the manufacturer. During the evaluation period daily quality control samples were run on the XT-2000*i* as well as the XE-2100. All samples used for the evaluation study were anticoagulated with K_3EDTA and processed in parallel on both analysers.

For reproducibility 10 consecutive analyses from a single specimen were analysed in the manual mode. The following specimens were analysed: (a) low WBC, RBC, PLT, RET, (b) normal WBC, RBC, PLT, RET, and (c) high WBC, RBC, PLT, RET.

For linearity a specimen with high blood cell counts was diluted (100%, 80%, 60%, 40 %, 20%, 10%, 5%) in autologous plasma yielding the following concentrations:

RBC $0.38 – 8.27 \times 10^{12}$/L
WBC $9.2 – 21.2 \times 10^{9}$/L, and $0.75 – 8.72 \times 10^{9}$/L
PLT $62 – 1287 \times 10^{9}$/L, and $19 – 102 \times 10^{9}$/L
RET $16 – 200 \times 10^{9}$/L

The carryover study was performed according to the International Council for Standardization in Haematology (ICSH) protocol by using 3 specimens of low and high WBC, RBC, and PLT concentrations[2]. For each sample the carryover can be calculated by the formulae:

$$Carryover\ (\%) = \frac{l3\text{-}l3}{h3\text{-}l3} \times 100$$

where l1, l2 and l3 are the first, second and third analysis of the sample with the low cell counts, and h1, h2 and h3 are the first, second and third analysis of the sample with the high cell counts.
To compare the analyser, 100 normal and 100 abnormal samples with a mixture of abnormal cell types such as immature white cells and blasts and where the analyser reports a complete 5-part WBC differential were analysed. Data were analysed using paired t-test, regression analysis by Passing-Bablok[3] and Bland-Altman analysis[4].
Comparison of flags produced by the XT-2000*i* and manual methods (400-cell differential by two technologists each performing a 200-cell count) was made by analysing 100 normal and 100 abnormal samples.
All specimens were processed within 6 hours including the preparation of a blood smear. The smears were stained using the May-Grünwald Giemsa staining method. A microscopic 400-cell differential count was performed according to the NCCLS H20-A protocol[5]. Flag sensitivity, specificity and efficiency were calculated using the following formulae:

$$\text{Sensitivity:} \frac{\text{true positive}}{\text{true positive} + \text{false negative}} \times 100$$

$$\text{Specificity:} \frac{\text{true negative}}{\text{false positive} + \text{true negative}} \times 100$$

Efficiency:

$$\frac{\text{true positive} + \text{true negative}}{\text{true positive} + \text{true negative} + \text{false positive} + \text{false negative}} \times 100$$

For band cells we used the criteria of the Dutch Society for Laboratory Haematology in this study, as described earlier by Lee, et al.[6]: constrictions of one half to one third of the nuclear width are considered to represent the lobulation of a segmented neutrophil. The reference value for band cells in human blood is less than 7%. More than 6% band cells or more than 1% metamyelocytes or other immature granulocytes (IG) are considered positive for left shift.

RESULTS

Reproducibility

Coefficients of variation (CV) for all parameters demonstrated good results and are listed in ***Table 1*** for the WBC, RBC, PLT-I, PLT-O and RET.

Carryover

For the WBC the carryover was 0.12%, for the RBC 0%, and for the PLT-I and PLT-O 0% and 0.75%, respectively.

Comparison of the XE-2100 and XT-2000*i*

The comparability was tested by measuring 100 normal and 100 abnormal samples with a mixture of flagging. The results are listed in ***Table 2***. Furthermore Bland-Altman plots were made for the comparison of both analysers (***Fig. 1***).

Table 1 *Reproducibility of the XT-2000i analyser*

Parameter	Unit	Mean	SD	CV%
WBC	$\times 10^9$/L	1.78	0.03	1.90
WBC	$\times 10^9$/L	6.29	0.09	1.44
WBC	$\times 10^9$/L	17.14	0.36	2.10
RBC	$\times 10^{12}$/L	2.44	0.01	0.29
RBC	$\times 10^{12}$/L	3.78	0.03	0.75
RBC	$\times 10^{12}$/L	5.84	0.03	0.57
PLT-I	$\times 10^9$/L	19.4	0.70	3.64
PLT-I	$\times 10^9$/L	164.6	5.66	3.44
PLT-I	$\times 10^9$/L	1109.7	14.83	1.34
PLT-O	$\times 10^9$/L	21.2	0.83	3.90
PLT-O	$\times 10^9$/L	189.2	5.66	2.99
PLT-O	$\times 10^9$/L	1247.9	20.51	1.64
RET	%	0.16	0.08	53.03
RET	%	1.01	0.01	0.30
RET	%	3.97	0.16	3.92

Table 2 *Comparison of the XE-2100 and the XT-2000i analysers for the CBC, RET, and WBC differentiation*

Parameter	Unit	Intercept	Slope	Correlation coefficient
WBC	$\times 10^9$/L	– 0.0216	0.983	0.998
PLT-r*	$\times 10^9$/L	– 4.38	1.020	0.992
PLT-I	$\times 10^9$/L	– 1.79	1.013	0.992
PLT-O	$\times 10^9$/L	1.36	0.888	0.996
RBC	$\times 10^{12}$/L	– 0.1515	1.035	0.998
HGB	mmol/L	– 0.100	1.000	0.998
HCT	L/L	– 0.0022	0.979	0.995
MCV	fL	– 2.400	1.000	0.991
MCH	fmol/L	0.0102	1.015	0.987
MCHC	mmol/L	0.0400	1.000	0.914
RET	$\times 10^9$/L	– 0.0014	1.315	0.976
RET-LFR	%	– 17.047	1.176	0.899
RET-MFR	%	– 0.859	1.206	0.846
RET-HFR	%	0.00	1.016	0.829
NEUT	$\times 10^9$/L	5.19	0.994	0.998
LYMPH	$\times 10^9$/L	0.62	0.962	0.995
MONO	$\times 10^9$/L	– 0.99	0.776	0.957
EO	$\times 10^9$/L	0.000	1.000	0.855
BASO	$\times 10^9$/L	0.000	1.000	0.855

*PLT-r is the reported count value.
PLT-r means the PLT count value reported for each sample by each analyser; This may be either the PLT-I or PLT-O value, depending on which value was considered most reliable in each case by the "switching algorithm" in the XE-2100 and the XT-2000*i*.

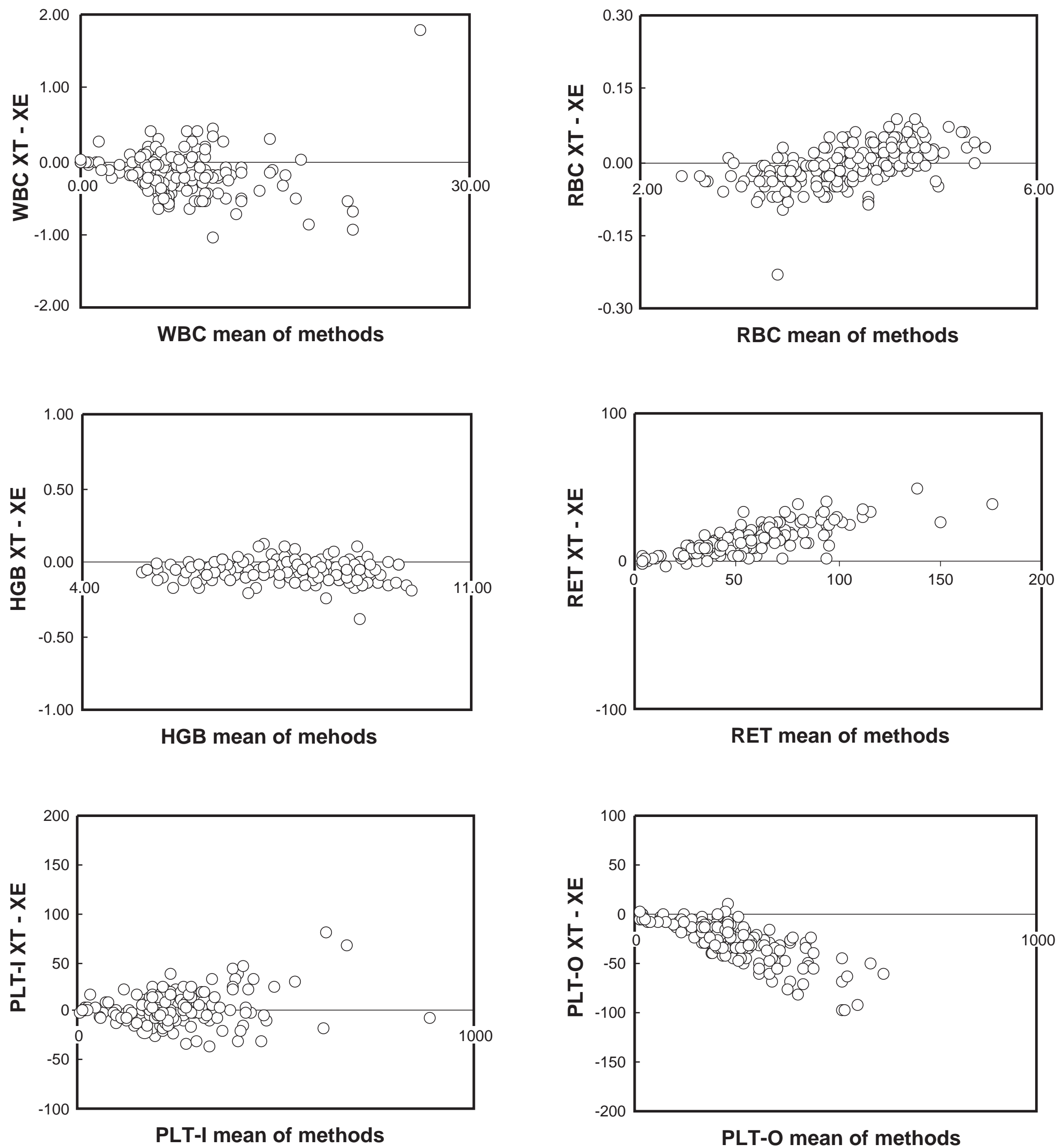

Fig. 1 Bland-Altman plots of various parameters for the comparison of the XE-2100 and XT-2000i

Linearity

Linearity data for the samples measured on the XT-2000*i* showed good correlation for all cells and are presented in ***Table 3***.

Comparison of XE-2100 and XT-2000*i* abnormal flagging capabilities

The comparison of the flagging messages of both analysers is summarized in ***Table 4***. The settings of the Q-flags for the XT-2000*i* were performed by the manufacturer, whereas the settings for the XE-2100 were performed by the evaluating laboratory.

Specificity and sensitivity of XT flagging data

The comparison of the analyser flagging with the microscopic 400-cell differential is summarized in ***Table 5***.

Table 3 *Linearity of the XT-2000i analyser*

Parameter	unit	range	r^2
Open mode			
RBC-I	× 10^{12}/L	8.27 – 0.38	0.9987
RBC-O	× 10^{12}/L	8.12 – 0.37	0.9995
HGB	mmol/L	15.0 – 0.7	0.9995
PLT-I	× 10^9/L	1,287 – 62	0.9954
PLT-I	× 10^9/L	102 – 19	0.9929
PLT-O	× 10^9/L	1,669 – 82	0.9954
PLT-O	× 10^9/L	101 – 13	0.9822
WBC	× 10^9/L	219.2 – 9.2	0.9993
WBC	× 10^9/L	8.72 – 0.75	0.9986
RET	× 10^9/L	200.0 – 15.8	0.9552
Capillary mode			
RBC-I	× 10^{12}/L	6.94 – 0.36	0.9937
RBC-O	× 10^{12}/L	6.86 – 0.35	0.9931
HGB	mmol/L	12.8 – 0.7	0.9939
PLT-I	× 10^9/L	1,287 – 62	0.9946
PLT-I	× 10^9/L	101 – 13	0.9822
PLT-O	× 10^9/L	1,870 – 89	0.9975
PLT-O	× 10^9/L	87 – 13	0.9591
WBC	× 10^9/L	244.1 – 12.1	0.9948
WBC	× 10^9/L	7.76 – 0.82	0.9960
RET	× 10^9/L	170.7 – 20.4	0.9485

Table 4 *Comparison of flagging of the XE-2100 and the XT-2000i analysers*

AL/ALB*1	XE —	XE +
XT —	207	4
XT +	9	1

Blasts	XE —	XE +
XT —	208	6
XT +	8	8

IG*2	XE —	XE +
XT —	151	3
XT +	3	43

LS*3	XE —	XE +
XT —	205	1
XT +	5	11

NRBC*4	XE —	XE +
XT —	195	5
XT +	17	13

PC*5	XE —	XE +
XT —	196	9
XT +	7	18

*1 AL/ALB = Atypical lymphocytes? or Abnormal lymphocytes?/Blasts?
Q-flags for XE-2100 and XT-2000*i* = 160
*2 IG = Immature Granulocytes? Q-flags for XE-2100 and XT-2000*i* = 160
*3 LS = Left Shift? Q-flags for XE-2100 and XT-2000*i* = 160
*4 NRBC = Nucleated red blood cells. A positive result for the XT-2000*i* is a flagging message; for the XE-2100 an NRBC count of more than 0.5% is considered as positive.
*5 PC = Platelet Clumps?

Table 5 *Specificity and sensitivity of the XT-2000i analyser flagging*

Flag	Specificity (%)	Sensitivity (%)	Efficiency (%)
Abnormal lymphocytes/ blasts? Atypical lymphocytes?	71.0	92.0	89.9
Blasts?	96.6	100.0	96.0
Immature Granulocytes?	79.7	100.0	81.3
Left Shift?	95.6	70.4	92.6
NRBC?	92.5	81.3	91.7
Red Cell suspect flags *	98.1	53.3*	95.2
Platelet Clumps?	90.3	66.7	95.2

*Microscopic red cell criteria not recognised by the instrument included: spherocytes, elliptocytes, schistocytes, target cells, basophilic stippling.

DISCUSSION

In this study we evaluated the Sysmex XT-2000*i*. With almost 500 measured samples representative for a routine haematology laboratory, linearity, reproducibility, and carryover were evaluated (in both open and capillary modes). All features can be described as satisfactory to excellent.

Furthermore various parameters measured by the XT-2000*i* were compared with the measurements performed with the Sysmex XE-2100. Statistical analysis revealed that the correlation was very good, but that for the RET count and the optical platelet (PLT-O) count differences were observed. Both parameters are obtained from the same instrument channel and it is interesting to note that the differences increase in a linear manner with increasing concentration. This suggests that these differences may be due to a calibration anomaly. With regard to the flagging performance it was found in general that both analysers performed identically.

Flagging capabilities of the XT-2000*i* are similar to those of the XE-2100.

The Sysmex XT-2000*i* would be a very useful analyser in variously sized laboratories.

ACKNOWLEDGEMENTS

We would like to thank Sysmex Europe and Goffin Meyvis for the opportunity to evaluate the Sysmex XT-2000*i*.

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