Clinical performance of Medonic™ M51 5-part hematology analyzer

A complete blood count (CBC) is frequently requested by physicians to obtain information about a patient's blood status, and tests are routinely performed in clinical laboratories. Medonic M51 hematology analyzer provides information on 29 parameters (20 for use in IVD, 9 for RUO) for the CBC, including red blood cells (RBC) and platelets (PLT), hemoglobin (HGB), as well as a 5-part differential of white blood cells (WBC). This work evaluates the performance of Medonic M51 compared with a reference system for the 20 IVD parameters. The results show good agreement between the systems, indicating reliable use of Medonic M51 in routine hematology analyses.

Introduction

Hematological tests can be used to help diagnose and monitor numerous blood-related conditions, including anemia, infections, and certain forms of cancer. Although manual microscopy is often considered the ultimate method for cellular and morphological analyses, automated hematology analyzers are routinely used for CBC and WBC differentials in clinical laboratories. In addition, automated analyzers can provide much more information than a manual count.

Medonic M51 is a 5-part hematology analyzer from Boule Diagnostics (Figure 1). As most hematology analyzers, Medonic M51 uses electrical impedance for CBC and spectrophotometry for determination of HGB. For the WBC differential, however, measurement methods differ between analyzers. Medonic M51 uses a tri-angle laser-scatter method for the 5-part differential of WBC (Figure 2).

This study validates the performance of Medonic M51 against a reference system, using normal and abnormal fresh whole blood samples collected from patients for routine analysis.

Figure 1. Medonic M51 is an entry-level 5-part hematology analyzer intended for the cost-minded clinical laboratory. The user-friendly design makes system operations easy. Robust software and hardware components ensure a reliable system performance. With its small footprint, Medonic M51 is well suited for the typical physician office laboratory.

Materials and methods

Instruments and reagents

Medonic M51 5-part hematology analyzer and its associated reagents, calibrator, and control material were used as test system. As reference system, the Sysmex™ XN-1000 hematology analyzer and its associated reagents, calibrator, and control material (Sysmex Corp.) were used.

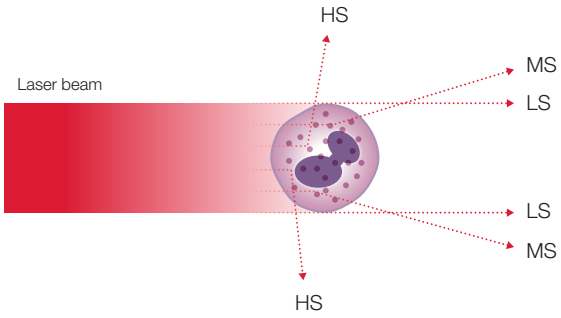


Figure 2. Medonic M51 uses laser-based flow cytometry for WBC, with separate channels for 4-part and BASO differential. Low angle signal (about 1° to 5°) represents the cell volume information, middle angle signal (about 7° to 20°) represents the cell nucleus information, high angle signal (about 90°) represents the cell nucleus and cytoplasm information.

Abbreviations and acronyms: Basophiles, BASO; complete blood count, CBC; eosinophils, EOS; hematocrit, HCT; hemoglobin, HGB; *in vitro* diagnostics, IVD; lymphocytes, LYM; mean cell volume, MCV; mean corpuscular hemoglobin, MCH; mean corpuscular hemoglobin concentration, MCHC; mean platelet volume, MPV; monocytes, MONO; neutrophils, NEU; platelets, PLT; platelet distribution width, PDW; red blood cells, RBC; red cell distribution width, RDW; research use only, RUO; white blood cells, WBC.

Quality control

Controls were analyzed daily, before and after sample analysis according to manufactures' advice. Background values were determined prior to control analysis.

Analysis of clinical samples

Fresh normal and abnormal human whole blood samples, collected for routine analyses, were analyzed in singlicate on both test and reference systems (n = 184) as well as by manual microscopy (n = 150). Normal ranges established by the Mayo Clinic were used for selecting samples for co-calibration of the analyzers. Selected values were combined for both male and female adults. As the difference in values for the main parameters between the test and the reference systems was small, the analyzers were not co-calibrated prior to the statistical analyses, except for RBC (and thereby HCT), for which the difference between the means of RBC between the analyzers was about 5.5%.

The specification limits for the correlation coefficient (r) and bias between test and reference systems are given in Table 1.

Table 1. Specification limits for performance evaluation of a new method or analyzer

Parameter	Unit	Specification limits	
		r	Bias
WBC	10^9/L	≥ 0.99	≤ ± 5%
NEU	%	≥ 0.90	≤ ± 5
LYM	%	≥ 0.90	≤ ± 5
MONO	%	≥ 0.75	≤ ± 5
EOS	%	≥ 0.80	≤ ± 5
BASO	%	≥ 0.56	≤ ± 5
NEU	10^9/L	≥ 0.90	NA
LYM	10^9/L	≥ 0.90	NA
MONO	10^9/L	≥ 0.75	NA
EOS	10^9/L	≥ 0.80	NA
BASO	10^9/L	≥ 0.56	NA
RBC	10^{12}/L	≥ 0.99	≤ ± 3%
HGB	g/dL	≥ 0.98	≤ ± 2.5%
MCV	fL	≥ 0.95	≤ ± 3%
HCT	%	≥ 0.98	≤ ± 1
RDW	%	≥ 0.90	≤ ± 2
MCH	pg	NA	NA
MCHC	g/dL	NA	NA
PLT	10^9/L	≥ 0.95	≤ ± 7%
MPV	fL	≥ 0.80	≤ ± 10%

NA = not applicable

Statistical analyses

Using Analyse-it statistics add-in for Microsoft Excel®, the strength of the relationship between the cell count in the test and the reference systems was measured using Pearson correlation coefficient (r). The correlations were ranked as "excellent" for r = 0.93–1.00, "good" for r = 0.80–0.92, "fair" for r = 0.59–0.79, and "poor" for r < 0.59. Passing-Bablok regression analysis and Bland Altman difference plots for estimation of agreement and possible systematic bias between the test and the reference systems were performed on matched samples.

Study design

The following standards were used as guidance for study design:

- Validation, Verification, and Quality Assurance of Automated Hematology Analyzers; Approved Standard – Second Edition. CLSI H26-A2
- Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition. CLSI EP09-A3
- Performance evaluation of in vitro diagnostic medical devices. EN 13612

Results

Comparison of test and reference systems

Descriptive statistics of parameter measured with the test and reference systems are presented in Table 2. For CBC only, all samples were included (n = 184). For WBC differential, samples flagged as suspicious with the reference system (n = 55) were removed.

At a 5% significance level, no statistically significant differences were observed between means of the parameters obtained with the test and the reference systems. Correlation between the test and reference systems, as evaluated by Passing-Bablok regression analysis, was shown to be "excellent" for most parameters; "good" for MCHC, MONO, RDW, and MPV; and "fair" for BASO. The correlation coefficients were all above specification limits (Table 3). The slopes were close to 1 except for MCHC, RDW, and MPV. The intercepts were close to 0, except for some of the parameters, as presented in Table 3 and Figure 3.

Bias estimates, obtained from Bland-Altman difference plots for method comparison, between the test and the reference systems were relatively low and within the specification limits for most parameters (Table 3, Figure 3).

Table 2. Descriptive statistics of parameter values obtained with the test and reference systems

Analyte	Unit	N	Sysmex XN-1000							Medonic M51						
			Mean	SD	Min	Max	Median	1st Q	3rd Q	Mean	SD	Min	Max	Median	1st Q	3rd Q
WBC*	10^9/L	184	21.1	37.8	0.56	225	8.70	5.82	14.58	20.7	38.3	0.67	233	8.13	5.57	13.4
NEU*	%	129	65.3	13.1	30.1	91.9	65.4	55.7	74.7	66.7	13.7	30.9	93.4	67.0	57.0	75.9
LYM*	%	129	22.5	12.2	3.40	59.1	20.6	13.5	31.5	23.1	12.4	3.60	58.1	21.1	13.8	31.8
MONO*	%	129	8.71	2.90	2.30	19.7	8.40	6.50	10.3	7.26	2.75	1.90	16.0	7.20	5.27	8.70
EOS*	%	129	2.21	2.31	0.00	12.5	1.50	0.57	3.20	2.19	2.18	0.00	13.0	1.60	0.70	3.03
BASO*	%	129	0.54	0.35	0.00	1.70	0.50	0.30	0.70	0.81	0.40	0.30	2.90	0.80	0.50	1.00
NEU*	10^9/L	129	6.75	4.57	0.69	22.3	5.38	3.50	8.40	6.56	4.51	0.72	24.2	5.16	3.47	8.17
LYM*	10^9/L	129	1.77	0.76	0.49	3.72	1.63	1.23	2.17	1.73	0.73	0.46	3.82	1.61	1.21	2.08
MONO*	10^9/L	129	0.79	0.42	0.19	2.73	0.71	0.50	0.98	0.63	0.36	0.14	2.31	0.57	0.37	0.77
EOS*	10^9/L	129	0.19	0.25	0.00	2.05	0.13	0.04	0.27	0.18	0.19	0.00	1.14	0.11	0.05	0.24
BASO*	10^9/L	129	0.05	0.03	0.00	0.21	0.04	0.03	0.06	0.07	0.03	0.01	0.21	0.06	0.04	0.09
RBC†	10^{12}/L	184	4.45	1.30	1.10	7.80	4.46	3.47	5.49	4.54	1.26	1.20	7.66	4.57	3.57	5.54
HGB	g/L	184	127	33.1	45.0	209	124	102	149	127	32.9	45.0	206	124	104	147
MCV	fL	184	89.1	8.05	65.8	123	89.0	84.0	93.1	87.0	7.55	65.7	123	87.0	83.0	90.9
HCT†	%	184	39.1	10.4	9.70	62.4	38.8	31.7	46.4	39.3	10.6	10.4	64.2	39.4	31.7	46.2
MCH	g/dL	184	29.2	3.29	19.9	45.0	29.2	27.6	30.7	30.0	3.17	21.8	44.6	30.0	28.1	31.6
MCHC	pg	184	327	21.2	290	464	324	314	334	344	16.1	319	458	341	334	350
RDW	%	184	15.0	2.97	11.4	28.9	14.2	13.1	16.2	14.3	2.09	12.1	25.5	13.7	13.0	15.0
PLT	10^9/L	184	380	502	2.00	2677	245	156	427	405	617	6.00	3521	233	153	409
MPV	10^9/L	175	10.7	1.06	8.50	13.7	10.6	9.90	11.48	9.98	1.18	7.30	12.8	9.90	9.20	10.8

* Non-flagged WBC and WBC differential count

† The test and the reference analyzers were co-calibrated.

Table 3. Comparison of test and reference systems

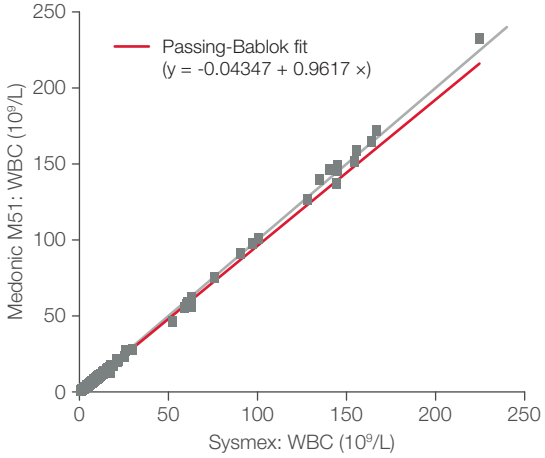
Analyte	Unit	N	Sysmex XN-1000 vs Medonic M51									
			r	I	95% CI		S	95% CI		Bias	95% CI	
WBC*	10^9/L	184	1.00	- 0.04	- 0.19	0.04	0.96	0.95	0.98	- 4.11%	- 4.90%	- 3.32%
NEU*	%	129	0.99	- 1.51	- 3.33	0.34	1.04	1.01	1.06	1.33	0.94	1.72
LYM*	%	129	0.99	0.20	- 0.09	0.45	1.01	1.00	1.03	0.61	0.38	0.84
MONO*	%	129	0.87	- 0.91	- 1.79	- 0.20	0.98	0.90	1.07	- 1.45	- 1.70	- 1.19
EOS*	%	129	0.96	0.05	0.00	0.13	0.98	0.92	1.00	- 0.02	- 0.13	0.10
BASO*	%	129	0.66	0.30	0.13	0.30	1.00	1.00	1.30	0.27	0.21	0.32
NEU*	10^9/L	129	1.00	- 0.05	- 0.11	0.02	0.97	0.96	0.99	- 3.25%	- 4.10%	- 2.40%
LYM*	10^9/L	129	0.99	0.03	- 0.03	0.08	0.95	0.92	0.99	- 2.34%	- 3.61%	- 1.07%
MONO*	10^9/L	129	0.93	- 0.03	- 0.05	0.00	0.86	0.81	0.91	- 25.0%	- 28.9%	- 21.0%
EOS*	10^9/L	129	0.95	0.01	0.00	0.01	0.92	0.87	0.96	16.5%	4.9%	28.1%
BASO*	10^9/L	129	0.69	0.01	0.00	0.02	1.20	1.00	1.50	41.6%	32.5%	50.8%
RBC†	10^{12}/L	184	1.00	0.20	0.16	0.25	0.98	0.97	0.99	2.63%	2.24%	3.03%
HGB	g/L	184	1.00	0.00	- 1.00	2.59	1.00	0.98	1.00	0.07%	- 0.34%	0.48%
MCV	fL	184	0.96	4.19	- 0.64	8.66	0.93	0.88	0.98	- 2.33%	- 2.71%	- 1.95%
HCT†	%	184	0.99	- 0.77	- 1.60	0.01	1.02	1.00	1.04	0.14	- 0.03	0.31
MCH	g/dL	184	0.97	2.13	0.93	2.93	0.95	0.92	0.99	2.81%	2.44%	3.19%
MCHC	pg	184	0.86	116	94.9	138	0.69	0.63	0.76	5.16%	4.67%	5.64%
RDW	%	184	0.92	4.30	3.73	4.93	0.67	0.62	0.71	- 0.67	- 0.87	- 0.48
PLT	10^9/L	184	0.99	2.45	- 4.81	7.73	0.99	0.96	1.04	2.62%	0.24%	5.00%
MPV	10^9/L	175	0.85	- 2.35	- 3.05	- 1.41	1.17	1.08	1.23	- 6.46%	- 7.36%	- 5.56%

r = Pearson correlation coefficient, I = intercept, CI = confidence interval, S = slope

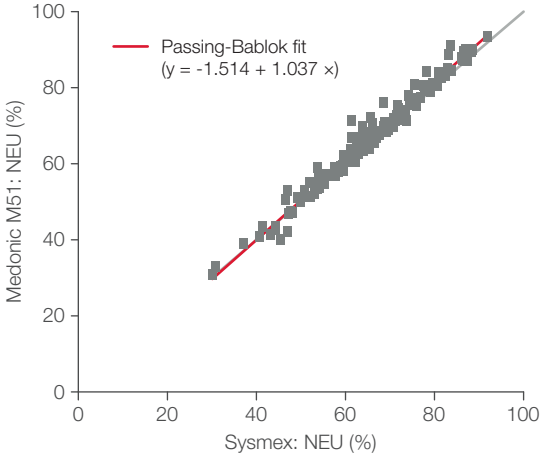
* Non-flagged WBC and WBC differential count

† The test and the reference analyzers were co-calibrated.

(A)


Passing-Bablok fit
(y = -0.04347 + 0.9617 ×)
Medonic M51: WBC (10⁹/L)
Sysmex: WBC (10⁹/L)
0
50
100
150
200
250

(B)


Passing-Bablok fit
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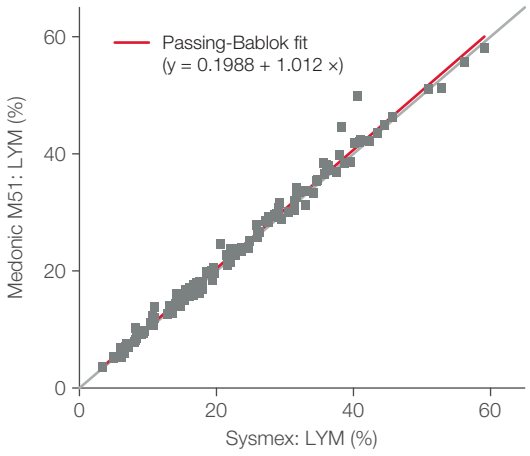
Medonic M51: NEU (%)
Sysmex: NEU (%)
0
20
40
60
80
100

(C)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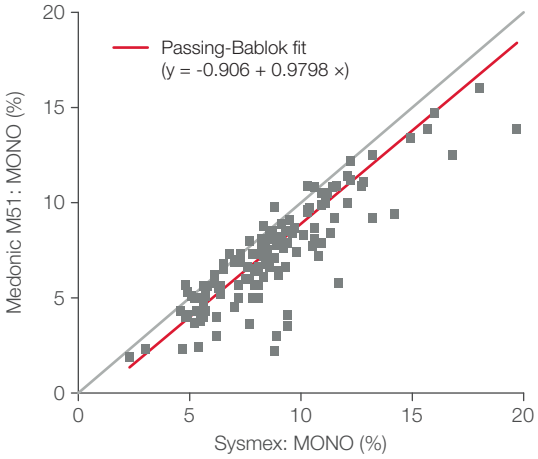
Medonic M51: LYM (%)
Sysmex: LYM (%)
0
20
40
60

(D)


Passing-Bablok fit
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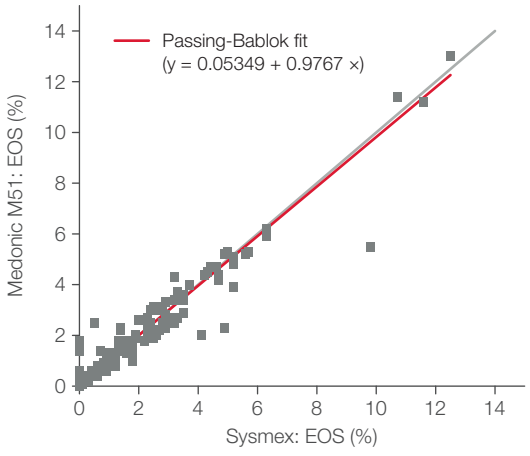
Medonic M51: MONO (%)
Sysmex: MONO (%)
0
5
10
15
20

(E)


Passing-Bablok fit
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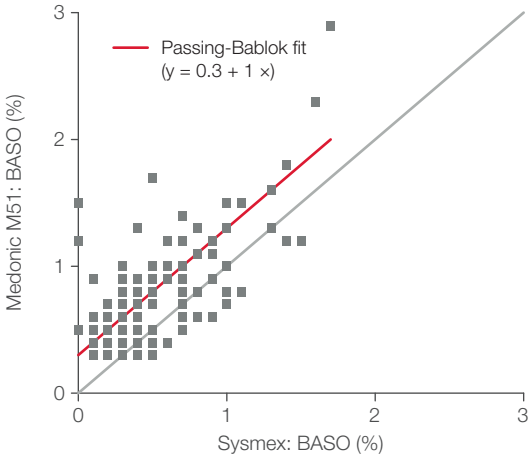
Medonic M51: EOS (%)
Sysmex: EOS (%)
0
2
4
6
8
10
12
14

(F)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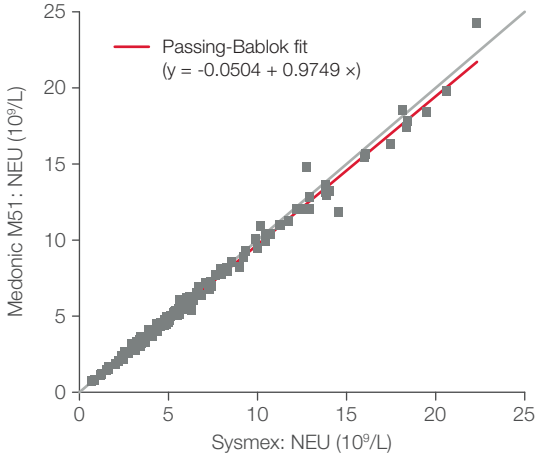
Medonic M51: BASO (%)
Sysmex: BASO (%)
0
1
2
3

(G)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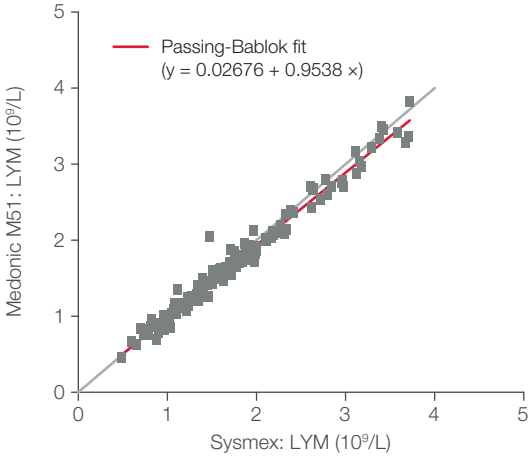
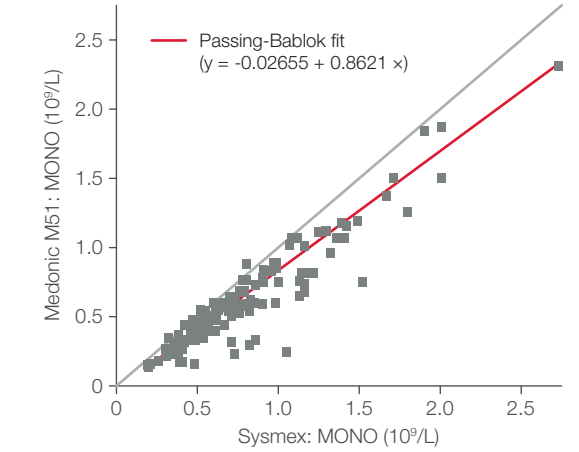
(y = -0.0504 + 0.9749 ×)
Medonic M51: NEU (10⁹/L)
Sysmex: NEU (10⁹/L)
0
5
10
15
20
25

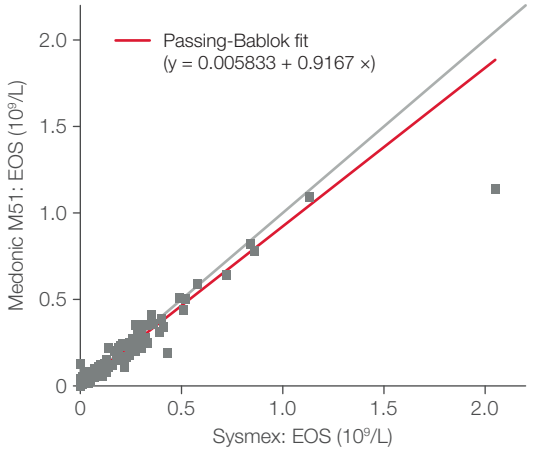
(H)


Passing-Bablok fit
(y = 0.02676 + 0.9538 ×)
Medonic M51: LYM (10⁹/L)
Sysmex: LYM (10⁹/L)
0
1
2
3
4
5

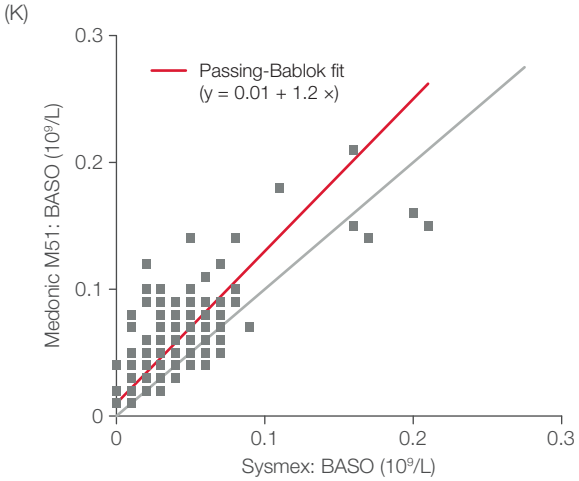
(I)


Passing-Bablok fit
(y = -0.02655 + 0.8621 ×)
Medonic M51: MONO (10⁹/L)
Sysmex: MONO (10⁹/L)
0
0.5
1.0
1.5
2.0
2.5

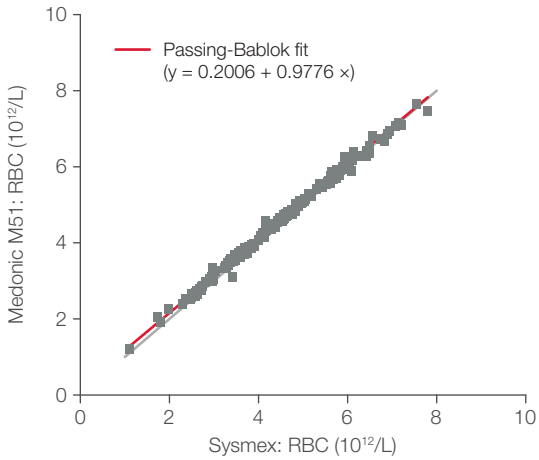
(J)


Passing-Bablok fit
(y = 0.005833 + 0.9167 ×)
Medonic M51: EOS (10⁹/L)
Sysmex: EOS (10⁹/L)
0
0.5
1.0
1.5
2.0

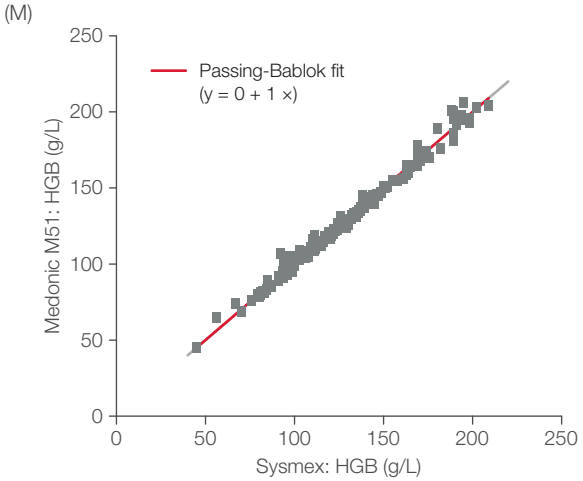
(K)


Passing-Bablok fit
(y = 0.01 + 1.2 ×)
Medonic M51: BASO (10⁹/L)
Sysmex: BASO (10⁹/L)
0
0.1
0.2
0.3

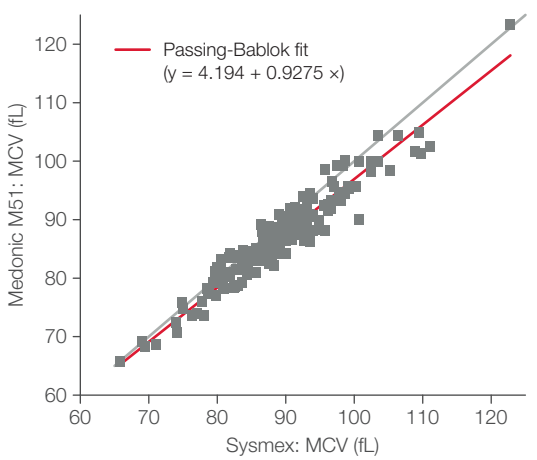
(L)


Passing-Bablok fit
(y = 0.2006 + 0.9776 ×)
Medonic M51: RBC (10¹²/L)
Sysmex: RBC (10¹²/L)
0
2
4
6
8
10

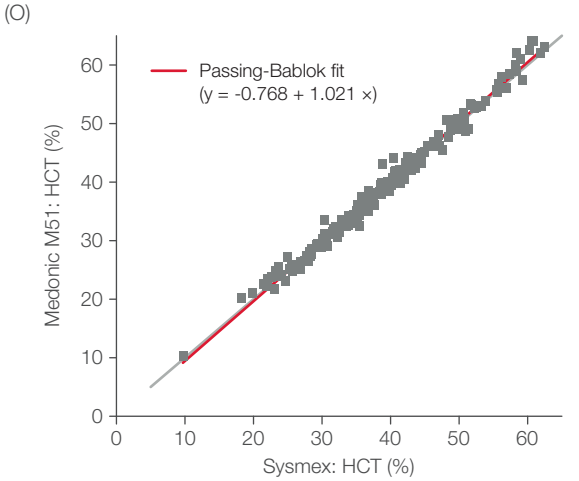
(M)


Passing-Bablok fit
(y = 0 + 1 ×)
Medonic M51: HGB (g/L)
Sysmex: HGB (g/L)
0
50
100
150
200
250

(N)


Passing-Bablok fit
(y = 4.194 + 0.9275 ×)
Medonic M51: MCV (fL)
Sysmex: MCV (fL)
60
70
80
90
100
110
120

(O)


Passing-Bablok fit
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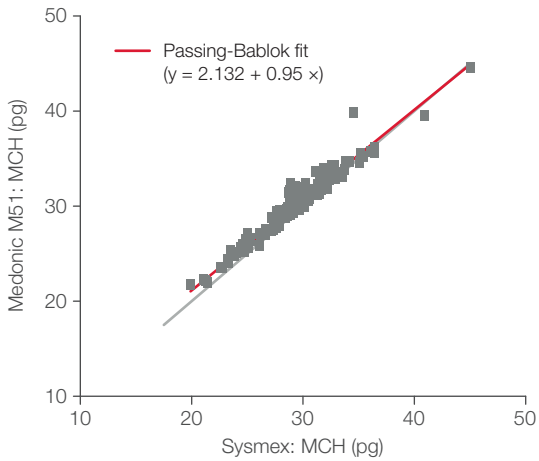
Medonic M51: HCT (%)
Sysmex: HCT (%)
0
10
20
30
40
50
60

(P)


Passing-Bablok fit
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Medonic M51: MCH (pg)
Sysmex: MCH (pg)
10
20
30
40
50

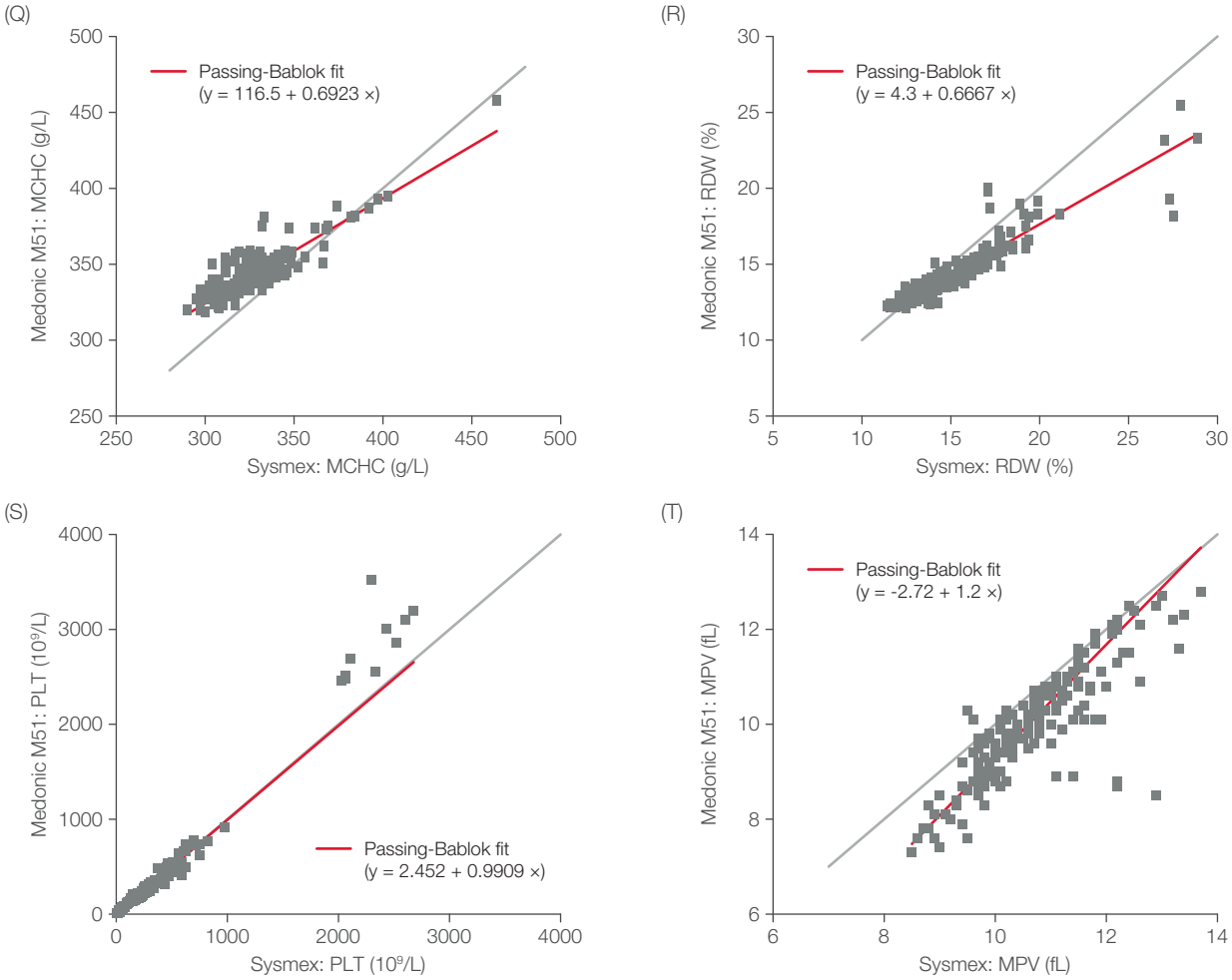


Figure 3. Agreement between the test and the reference systems. Passing-Bablok regression graphs for WBC (A), NEU% (B), LYM% (C), MONO% (D), EOS% (E), BASO% (F), NEU (G), LYM (H), MONO (I), EOS (J), BASO (K), RBC (L), HGB (M), MCV (N), HCT (O), MCH (P), MCHC (Q), RDW% (R), PLT (S), and MPV (T). In regression plots, the gray line corresponds to identity (x = y) and the red line corresponds to best fit.

Comparison of test and reference system with manual microscopy

The correlation between the WBC differential count using the test system versus manual microscopy, evaluated by Passing-Bablok regression analysis, was “excellent” for NEU (%), “good” for EOS and NEU (absolute count), “fair” for LYM, but “poor” for MONO and BASO (Table 4, Figure 4). The correlation between the WBC differential count using the reference system versus manual microscopy was comparable to what was obtained with the test system, except for LYM where the correlation was “good” (Table 4).

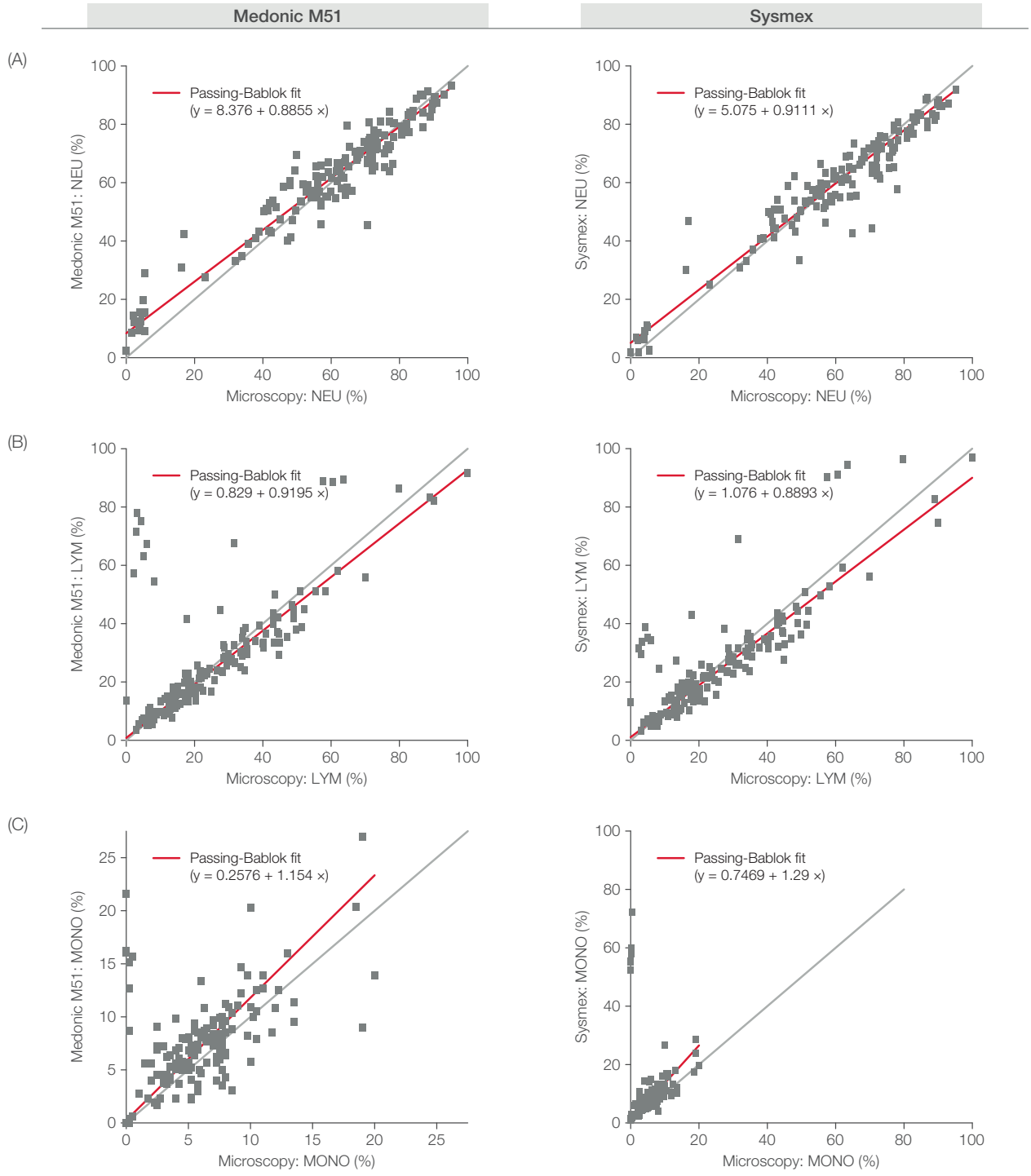
The bias estimates, obtained from the Bland-Altman difference plots for method comparison, between the test system versus manual microscopy were relatively low for the percent count and high for the absolute count of the WBC differential (Table 4). Poor agreement was observed for BASO and MONO. The results were comparable to what was obtained with the reference system versus manual microscopy (Table 4) with both systems showing a positive bias and the reference system deviating more than the test system.

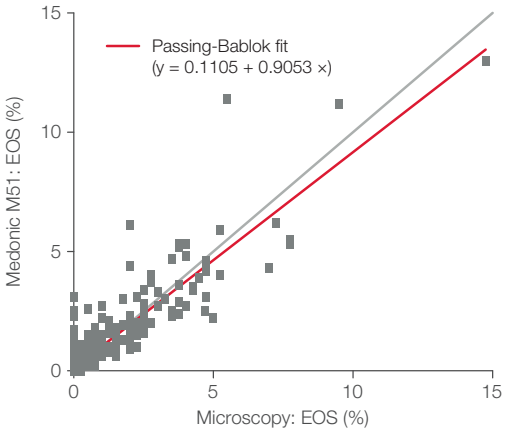
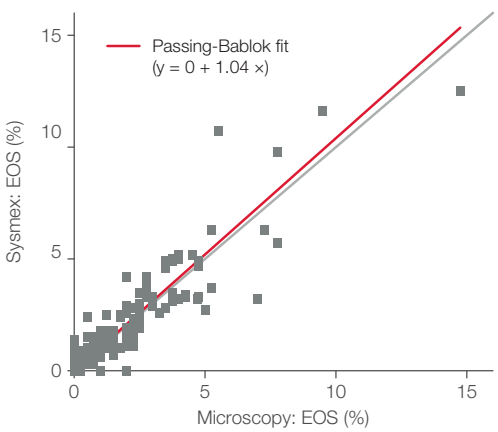
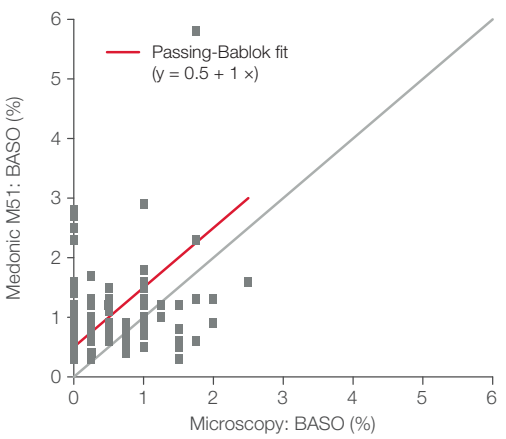
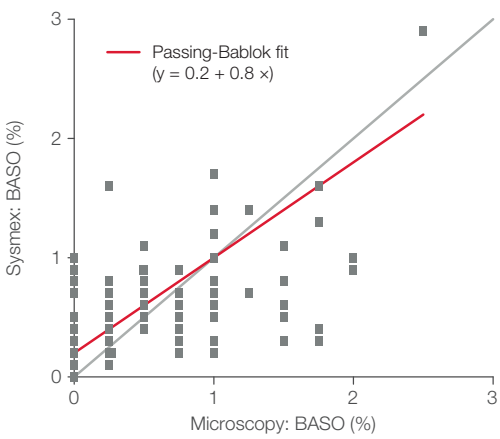
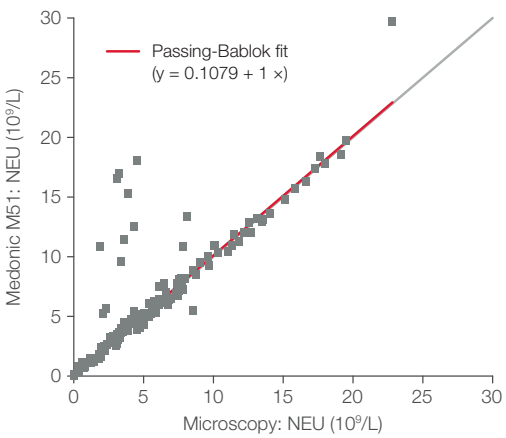
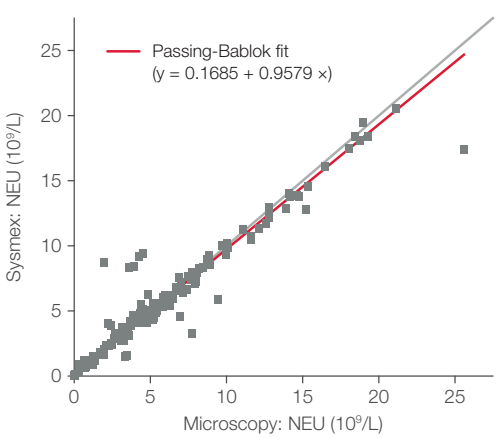
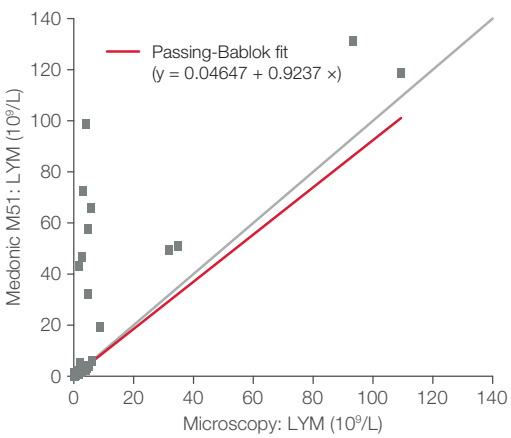
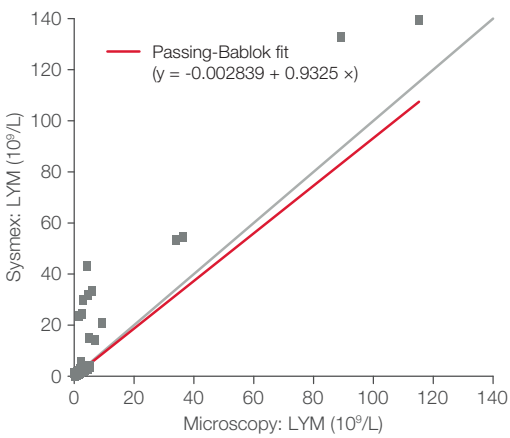
With high WCB counts, it can be difficult for the analyzer to differentiate the subpopulations. As shown for MONO in Figure 5, for example, when removing samples with WBC counts above 50 × 10^9/L, the correlation between systems improves. Although a bias between the systems, Medonic M51 was closer to manual microscopy than the reference system. As laboratories are obliged to establish and maintain reference intervals for measurands, this will mitigate the observed bias.

Table 4. Comparison of WBC differential count (n = 150) for the test and reference systems with the manual microscopy

Analyte	Unit	Medonic M51				Sysmex XN-1000			
		r	I	S	Bias	r	I	S	Bias
NEU%	%	0.96	8.38	0.89	1.78	0.96	5.08	0.91	- 0.70
LYM%	%	0.70	0.83	0.92	2.27	0.86	1.08	0.89	0.30
MONO%	%	0.49	0.26	1.15	1.52	NA	0.75	1.29	5.10
EOS%	%	0.87	0.11	0.91	0.13	0.91	0	1.04	0.06
BASO%	%	0.27	0.50	1.00	0.49	0.58	0.20	0.80	0.09
NEU	10^9/L	0.85	0.11	1.00	13.2%	0.96	0.17	0.96	3.94%
LYM	10^9/L	0.77	0.05	0.92	6.73%	0.94	0	0.93	3.19%
MONO	10^9/L	0.15	0	1.20	20.4%	NA	0.02	1.36	46.3%
EOS	10^9/L	0.91	0.01	0.90	35.2%	0.93	0	1.04	17.2%
BASO	10^9/L	NP	NP	NP	107%	0.42	0.02	0.89	77.5%

r = Pearson correlation coefficient, I = intercept, S = slope



	Medonic M51	Sysmex
(D)		
(E)		
(F)		
(G)		

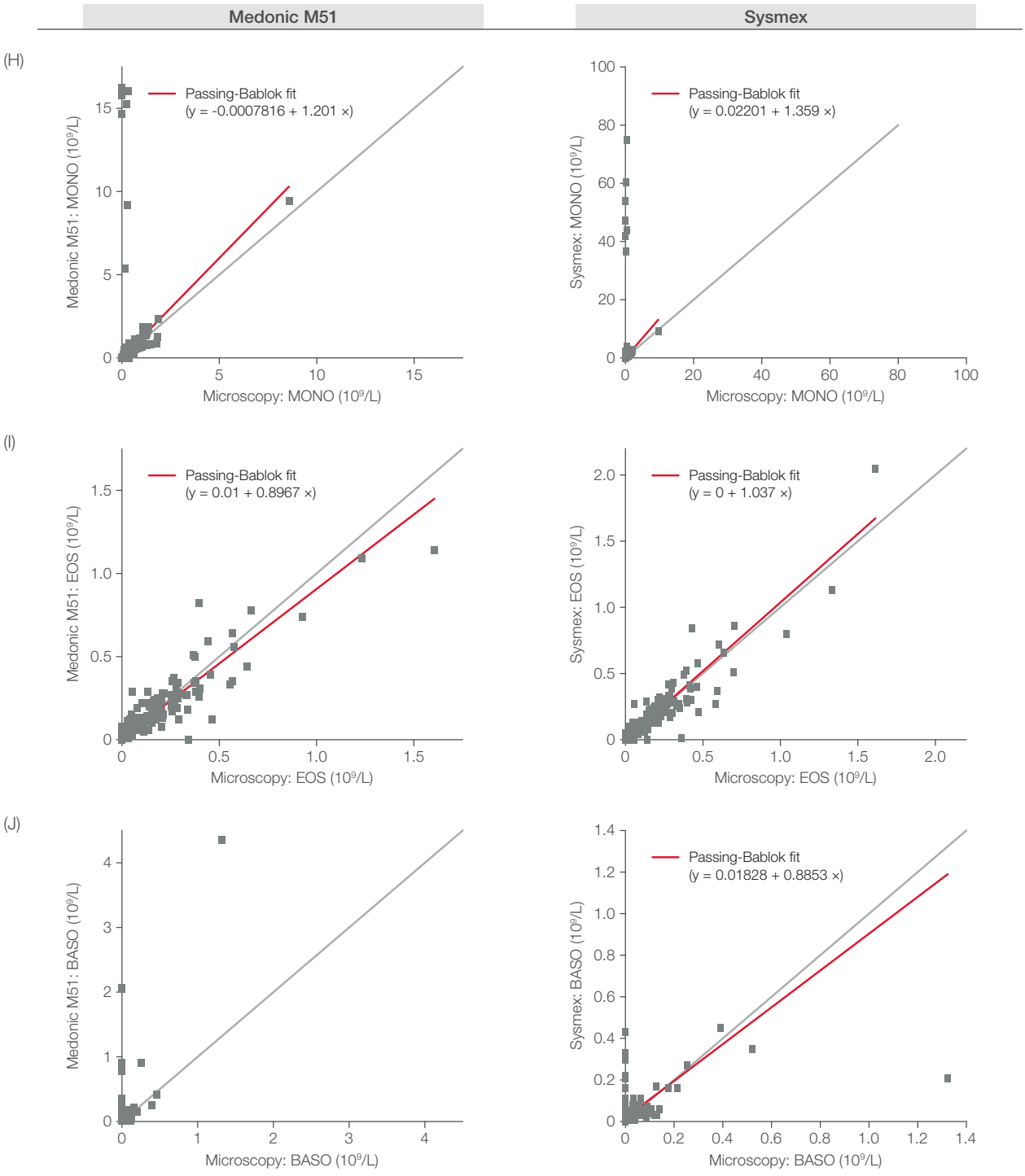


Figure 4. Agreement between WBC differential count using the test and reference systems versus he manual microscopy for NEU% (A), LYM% (B), MONO% (C), EOS% (D), BASO% (E), NEU (F), LYM (G), MONO (H), EOS (I), and BASO (J). In Passing-Bablok regression plots, the gray line corresponds to identity (x = y) and the red line corresponds to best fit.

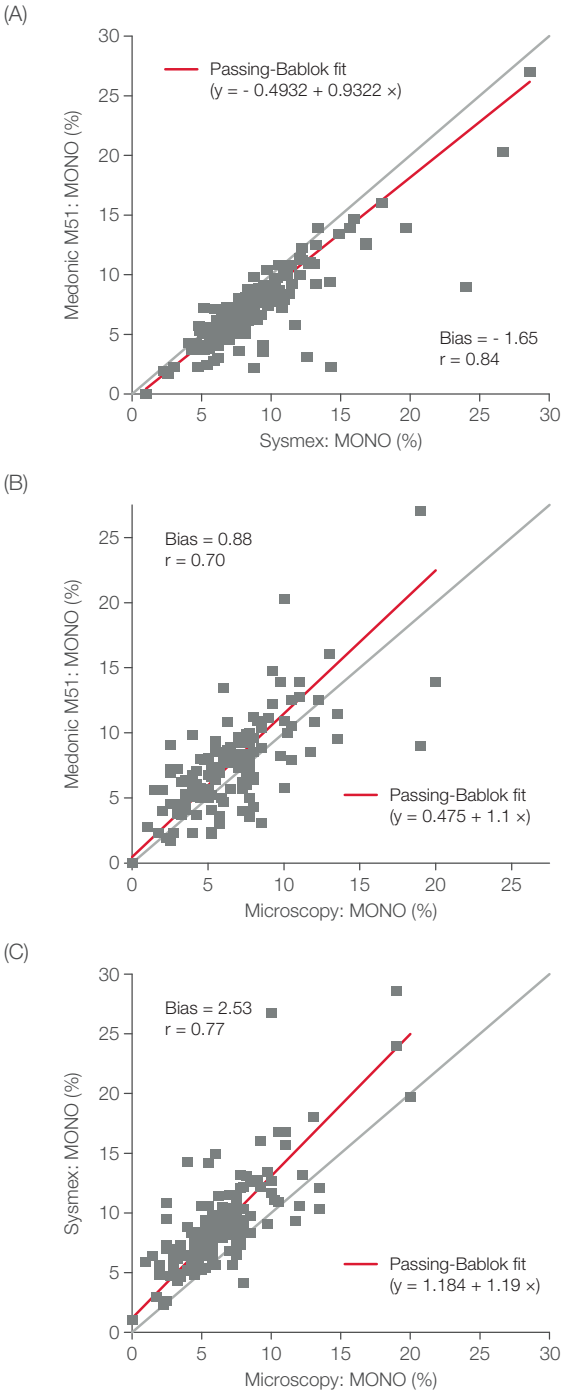


Figure 5. Agreement of the MONO count between (A) the test and the reference system, (B) the test system and manual microscopy, and (C) the reference system and manual microscopy using samples with WBC < 50 × 10^9/L (n = 138). In the regression plots, the gray line corresponds to identity (x = y) and the red line corresponds to best fit.

Discussion

The performance of the Medonic M51 5-part hematology analyzer was compared to that of the Sysmex XN-1000 5-part hematology analyzer. Medonic M51 operates with the same technology as Sysmex XN-1000, except for the WBC differential count, where Sysmex XN-1000 uses fluorescence flow cytometry whereas Medonic M51 uses laser-based flow cytometry. Any significant difference in the observed means can most likely be attributed to the different detection and calculation methods between the two systems.

In general, the results show excellent to good correlations and relatively low bias estimates between the test and reference systems, indicating that the systems are in good agreement.

The WBC differential using Medonic M51 agreed well with manual microscopy, except for BASO and MONO. In the comparison between the analyzers, MONO showed a proportional negative bias, which became constant when expressed in relative terms. In the comparison between the analyzers and manual microscopy, both analyzers showed a positive bias, with Sysmex XN-1000 deviating more than Medonic M51.

Conclusion

Overall, the performance of the Medonic M51 test system was approved for all parameters according to the specification limits when compared to the Sysmex XN-1000 reference system. As the analyzers provided similar correlation and bias estimates compared with manual microscopy, the performance of Medonic M51 is considered acceptable. These results indicate that the performance of Medonic M51 5-part hematology analyzer is acceptable for routine hematology analysis.

Disclaimer

The results and conclusions presented in this study are valid for this specific study only. Other study conditions and assumptions could have significant impact on the outcome.

Acknowledgement

We thank Dr. Anders Kallner, Karolinska Institute, Solna, SE for valuable discussions.

Ordering information

Product	Description	Product code
Medonic M51	5-part hematology analyzer	1620020
Medonic M51-D Diluent	Diluent, 20 L	1504510
Medonic M51-L1 Lyse	Lyse 1, 200 mL	1504511
Medonic M51-L2 Lyse	Lyse 2, 500 mL	1504512
Boule EasyCleaner	Cleaner, 50 mL	1504513
Boule Cal-5Diff A1	Calibrator, 1 × 3 mL	1504517
Boule Con-5Diff A1 Tri	Control low, normal, and high, 3 × 2 × 3 mL	1504518

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