Empowering WBC Differential with Digital Morphology

HemaBook Chapter 23

Throughout human history, the number 3 has always had a unique significance. In Ancient Greek philosophy, the number 3 was considered as the perfect number, the number of harmony, wisdom and understanding.

Time is divided into three stages	There are three physical states	Space consists of three dimensions
present, past, future		SF Cube length, width and height

Recently, the MC-80 Digital Morphology Analyzer underwent rigorous evaluation by 3 top university hospitals worldwide, quickly earning global recognition. The International Journal of Laboratory Hematology recently published three professional evaluation reports on the WBC differential performance of MC-80, providing insights from different perspectives.

MC-80 in Onco-hematology

Rome, Italy

Stain: May-Grünwald-Giemsa (Carlo Erba Reagenti/ Merck KGaA)

"Advances in technology mean that moving from microscopes to digital alternatives can now be achieved without sacrificing image quality." Professor Gina Zini shares her views on the main benefits of digital development, including better quality screening, time savings for busy morphologists, better clinical collaboration, and improved training in the interview.1 Prof. Zini is very concerned about the application of this technology in the most challenging hematology departments. After conducting a systematic and rigorous evaluation of the MC-80, she called this work "artificial intelligence and blood film"! 2

Artificial intelligence and the blood film: Performance of the MC-80 digital morphology analyzer in samples with neoplastic and reactive cell types

Gina Zini[1,2] | Francesca Mancini[3] | Elena Rossi[1,2] | Stefania Landucci[3] | Giuseppe d'Onofrio[1]

It's a two-university study. A vast proportion of samples from hematology patients with blood disorders and a few with viral infections (591 patients in total) were selected to include most types of cells that do not normally circulate in the peripheral blood.

Sample selection & collection & anonymization

"La Sapienza" University – Hematology laboratory, Rome

Smearing, fixing and staining of four peripheral blood smears

Slide A. Manually prepared	Slide B. Manually prepared	Slide C. by SC-120	Slide C. by SC-120

"La Sapienza" University - Hematology laboratory, Rome

Morphology Examination

Slide A. Manual differetiation I	Slide B. Manual differentiation II	Slide C. MC-80 pre-classification	Slide D. MC-80 pre-classification
"La Sapienza" University - Hematology laboratory, Rome	Fondazione Policlinico Universitario A. Gemelli IRCSS – Università Cattolica del S. Cuore, Rome		

Validation

Manual differetiation	MC-80 Post-classification
Supervised differential from a thirdmorphologist, in case of discrepancies between the two manual differentials	Slide C. validation at screen of MC-80 sample differential

Fondazione Policlinico Universitario A. Gemelli IRCSS – Università Cattolica del S. Cuore, Rome

Data analysis & statistics

Fondazione Policlinico Universitario A. Gemelli IRCSS – Università Cattolica del S. Cuore, Rome

Duplicate analysis (two runs of each of 413 films)

The results confirm the excellent internal consistency of the MC-80 differential count, even in the presence of abnormal cells.

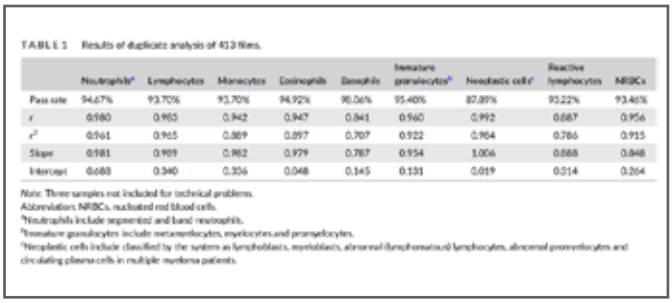


TABLE 1 Results of duplicate analysis of 413 films.

	Neutrophils[a]	Lymphocytes	Monocytes	Eosinophils	Basophils	Immature granulocytes[b]	Neoplastic cells[c]	Reactive lymphocytes	NRBCs
Pass rate	94.67%	93.70%	93.70%	94.92%	98.06%	95.40%	87.89%	93.22%	93.46%
r	0.980	0.963	0.942	0.947	0.841	0.960	0.992	0.887	0.956
r^2	0.961	0.965	0.889	0.897	0.707	0.922	0.984	0.786	0.915
Slope	0.981	0.989	0.982	0.979	0.787	0.954	1.006	0.888	0.848
Intercept	0.680	0.340	0.336	0.048	0.145	0.131	0.019	0.014	0.264

Note: Three samples not included for technical problems.
Abbreviation: NRBCs, nucleated red blood cells.
[a]Neutrophils include segmented and band neutrophils.
[b]Immature granulocytes include metamyelocytes, myelocytes and promyelocytes.
[c]Neoplastic cells include classified by the system as lymphoblasts, myeloblasts, abnormal (lymphomatous) lymphocytes, abnormal promyelocytes and circulating plasma cells in multiple myeloma patients.

Distributional inaccuracy

The correlation coefficients (r) between MC-80 post-classification results and manual differential (reference) for the five types of normal leukocytes and the four primary populations of abnormal cells are high for all types of cells except for reactive lymphocytes.

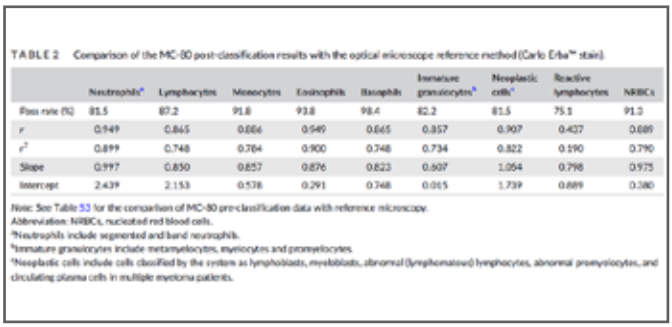


TABLE 2 Comparison of the MC-80 post-classification results with the optical microscope reference method (Carlo Erba™ stain).

	Neutrophils[a]	Lymphocytes	Monocytes	Eosinophils	Basophils	Immature granulocytes[b]	Neoplastic cells[c]	Reactive lymphocytes	NRBCs
Pass rate (%)	81.5	87.2	91.8	93.8	98.4	82.2	81.5	75.1	91.3
r	0.949	0.845	0.884	0.949	0.845	0.857	0.907	0.427	0.689
r^2	0.899	0.748	0.784	0.900	0.748	0.734	0.822	0.190	0.790
Slope	0.997	0.850	0.857	0.876	0.823	0.607	1.054	0.798	0.975
Intercept	2.439	2.153	0.578	0.291	0.348	0.015	1.739	0.889	0.380

Note: See Table S3 for the comparison of MC-80 pre-classification data with reference microscope.
Abbreviation: NRBCs, nucleated red blood cells.
[a]Neutrophils include segmented and band neutrophils.
[b]Immature granulocytes include metamyelocytes, myelocytes and promyelocytes.
[c]Neoplastic cells include cells classified by the system as lymphoblasts, myeloblasts, abnormal (lymphomatous) lymphocytes, abnormal promyelocytes, and circulating plasma cells in multiple myeloma patients.

The results between pre-classification and the post-classification MC-80 results are compared too. It's reported, differences between the major normal leukocyte classes were minimal, while the most relevant adjustments due to the operators' revision (post-classification) were observed for basophils and reactive lymphocytes.

Explanation of outliers (distributional disagreements)

Dysplastic neutrophils
- abnormal chromatin condensation
- cytoplasmic granulation

Lymphoma cells
- Mind multiple flags from the blood cell counter and the digital analyzer
- Validation by the side review by an expert morphologist (pathologist or hematologist)

Clinical sensitivity: Identification of films with pathological cells

- The MC-80 displays extremely good sensitivity in identifying immature granulocytes.

Immature granulocytes

- The MC-80 displays good efficiency and sensitivity in identifying reactive lymphocytes.

Reactive lymphocytes

- It has a sensitivity of 97.5% and a predictive value of a negative result equal to 96.9% for NRBC.

NRBC

- All samples were flagged by the digital morphology analyzer. Expert morphological review under the microscope is recommended.

Neoplastic cells

TABLE 3 Specific performance of the MC-80 in identifying films with specific types of cells that do not normally circulate in the blood of healthy subjects.

	Granulocyte precursors (>1%)	Neoplastic cells[a] (>0%)	Reactive lymphocytes (>3%)	NRBCs (>1/100 WBC)
Sensitivity	98.8%	83.8%	93.6%	97.5%
Specificity	87.7%	86.1%	92.9%	89.9%
PV of positives	83.5%	80.6%	81.1%	81.4%
PV of negatives	99.2%	88.4%	97.8%	96.9%
Total efficiency	92.0%	85.2%	95.2%	92.0%

[a]Neoplastic cells include cells classified by the system as lymphoblasts, myeloblasts, abnormal (lymphomatous) lymphocytes, abnormal promyelocytes, and circulating plasma cells in multiple myeloma patients.
Abbreviations: NRBCs, nucleated red blood cells; PV, predictive value.

Conclusion (excerpted from "Abstract - Conclusion")

"Our study highlights the outstanding diagnostic performance of this artificial intelligence–based blood film analyzer for hematology patients with circulating abnormal cells. We appreciated the morphological harmonization of cells observed on the screen and those seen in the microscope."

MC-80 in a State-of-the-art Fully Automated Core Laboratory

Barcelona, Spain

Stain: May-Grünwald-Giemsa (RAL)

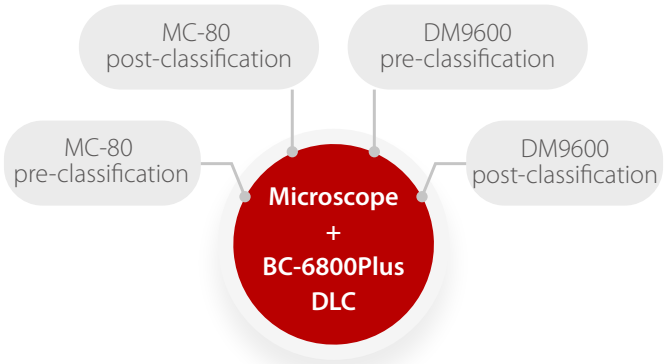
Performance of the new MC-80 automated digital cell morphology analyser in detection of normal and abnormal blood cells: Comparison with the CellaVision DM9600

Anna Merino | Javier Laguna | María Rodríguez-García | Judit Julian | Alexandra Casanova | Angel Molina

A total of 445 samples were used, and WBC pre-classification values with the MC-80 and DM9600 were compared with the manual reference (microscope), Mindray BC-6800Plus differentials (only normal samples), and confirmed or reclassified images (post-classification). [3]

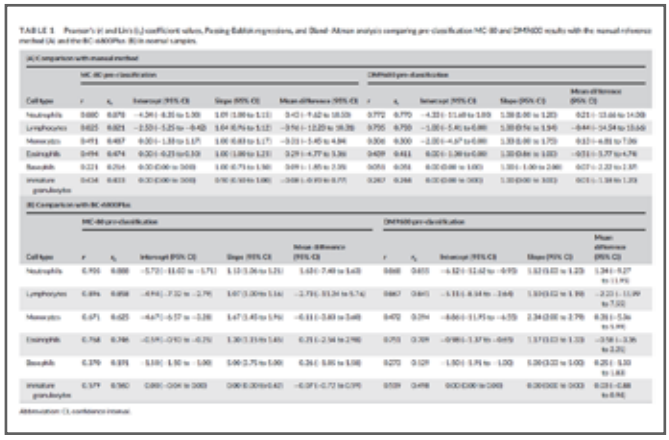
Comparative study and statistical analysis

The pre-classification and post-classification of WBC using the MC-80 and DM9600 in normal samples were compared with the manual reference method using the microscope and with the differential leukocyte count (DLC) obtained on the BC-6800Plus.



Comparison with DM9600 - routine cell types

Table 1 shows the pre- and post-classification percentages of WBC obtained using the MC-80, which exhibited a strong correlation and concordance for all types of leucocytes, including immature granulocytes (IG) (values between 0.91 and 1).



Comparison with DM9600 – blast cells and immature granulocytes

As observed in samples from acute leukemia patients, when comparing pre- and post-classification percentages of blast cells in this group of patients, the MC-80 exhibited the highest correlation and concordance values.

In samples from patients with myelodysplastic syndromes (MDS) /myeloproliferative neoplasm (MPN), percentages of blast cells using the microscope were similar to pre- and post-classification values provided by the MC-80 and the DM9600.

The pre- and post-classification percentages of immature granulocytes (IG) provided by MC-80 showed much higher correlation and concordance values in patients with infections, especially in the pre-classification.

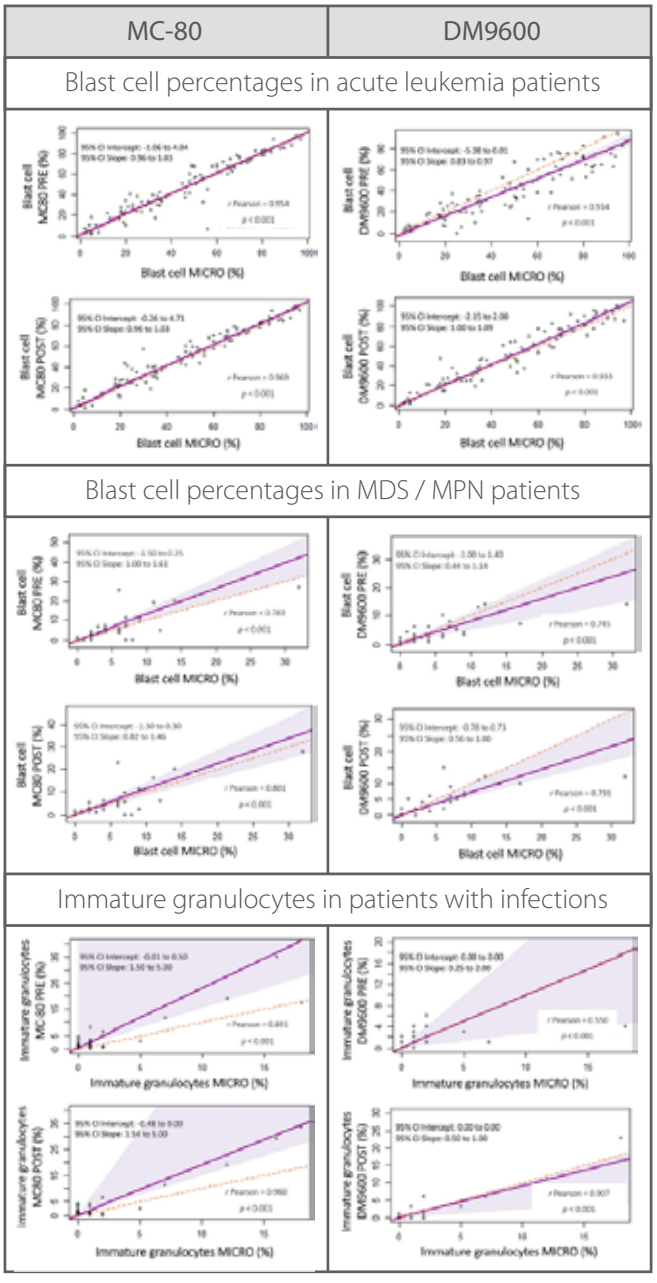
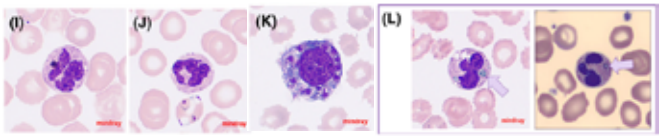


FIGURE 2 Passing-Bablok regressions and correlation coefficient values of reference manual method and pre- and post-classification results provided by Mindray MC-80 and CellaVision® DM9600. (A) Blast cell percentages in acute leukemia patients; (B) Blast cell percentages in myelodysplastic syndromes/myeloproliferative neoplasm patients; and (C) Immature granulocytes in patients with infections. POST, post-classification percentages; PRE, pre-classification percentages.

"Discussion" Highlights

- Correlation and concordance between pre- and post-classification using the MC-80 were higher than with DM9600, suggesting that reviewing samples in the MC-80 may be faster.

- The images provided by the MC-80 showed good quality for the specialists to recognize malignant cells, dysplastic cells, malaria, Leishmania and inclusions such as green crystals in neutrophils.



Conclusion (excerpted from "Abstract - Conclusion")

"We found that the MC-80 shows high performance for WBC differentials for both normal samples and patients with hematological diseases."

MC-80 in a Large Multi-microscope Laboratory

Bangkok, Thailand

Stain: Wright-Giemsa (Baso Diagnostics)

Nine hundred and thirty-four samples (100 normal and 834 blood samples triggered a flag on the hematology analyzers) were randomly collected.[4]

Precision

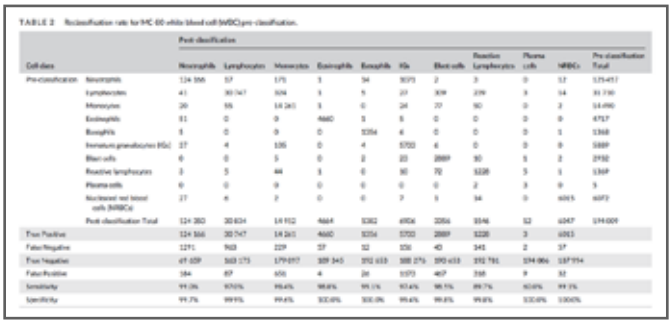
The WBC counts of 24 selected samples ranged from 2.74 x 109/L to 62.33 x 109/L. All cell types showed acceptable precision.

TABLE 1 Precision of MC-80

Cell class	n (cases)	Median percentage (range)	Median SD (range)	Median CV (range)
Segmented neutrophils	50	43.4 (0.5-92.1)	1.0 (0.2-3.4)	2.5 (0.4-42.2)
Band forms	50	5.7 (0-22.0)	0.7 (0-3.4)	10.4 (0-51.6)
Lymphocytes	50	33.1 (1.1-65.7)	0.6 (0.2-2.4)	5.6 (0.7-53.7)
Monocytes	50	9.2 (0.9-28.2)	0.6 (0-2.2)	6.2 (0-41.2)
Eosinophils	40	2 (0.5-13.2)	0.2 (0-2.6)	12.2 (0-73.6)
Basophils	34	0.7 (0.5-10)	0.2 (0-1)	34.6 (0-57.9)
Metamyelocytes	30	1.9 (0.5-24.4)	0.2 (0-1.4)	14.6 (0-60.4)
Myelocytes	35	1.3 (0.5-15)	0.2 (0-1.8)	20.1 (0-57.9)
Promyelocytes	22	0.8 (0.5-4.6)	0 (0-0.7)	29.8 (0-51.6)
Blasts	23	1.0 (1.5-9.0)	0 (0-1.6)	9.6 (0.9-51.6)
Reactive lymphocytes	33	0.6 (0.5-4.2)	0.2 (0-1.4)	46.4 (0-59.2)
Plasma cells	6	4.0 (1.0-7.9)	1.1 (0.5-2.8)	42.1 (11.8-50.5)
Nucleated red blood cells	28	0.9 (0.5-55.4)	0.1 (0-1.5)	5.8 (0-67.1)

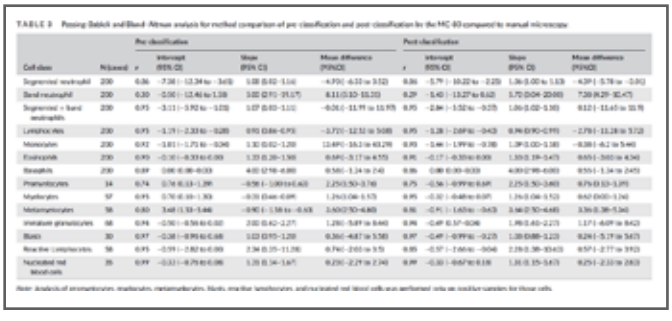
Cell identification performance

The cell identification performance was analyzed on 194,009 cells from 934 blood smears. Overall, the specificity of cell identification was higher than 95% for all cell classes, and sensitivity greater than 95% for most cell classes. The lowest sensitivity was found in plasma cells. It should be noted that the total number of analyzed plasma cells was considerably low (n = 5).



Method comparison study

Compared to manual counting, MC-80 yields a good correlation (r > 0.90) and minimal differences for most cell classes. The highest correlation was found in nucleated red blood cells (NRBC) (r = 0.99).



Conclusion

In conclusion, the performance of the WBC differential of the newly released Mindray MC-80 automated digital cell morphology analyzer is acceptable compared to the manual differential.

The number 3 holds great inspiration.
3 esteemed morphologists, through their remarkable work on MC-80's 3-year evaluation, have instilled incredible confidence in the analyzer. This has established MC-80 as a trusted tool for serving laboratories worldwide.

References

[1]https://www.htworld.co.uk/insight/opinion/digital-morphology-what-advances-mean-for-modern-laboratories-and-why-continued-innovation-is-imperative-hm23/

[2]Zini G, Mancini F, Rossi E, Landucci S, d'Onofrio G. Artificial intelligence and the blood film: Performance of the MC-80 digital morphology analyzer in samples with neoplastic and reactive cell types. Int J Lab Hematol. 2023 Dec;45(6):881-889. doi: 10.1111/ijlh.14160. Epub 2023 Aug 28. PMID: 37641457.

[3]Merino A, Laguna J, Rodríguez-García M, Julian J, Casanova A, Molina A. Performance of the new MC-80 automated digital cell morphology analyser in detection of normal and abnormal blood cells: Comparison with the CellaVision DM9600. Int J Lab Hematol. 2023 Sep 25. doi: 10.1111/ijlh.14178. Epub ahead of print. PMID: 37746889.

[4]Khongjaroensakun N, Chaothai N, Chamchomdao L, Suriyachand K, Paisooksantivatana K. White blood cell differentials performance of a new automated digital cell morphology analyzer: Mindray MC-80. Int J Lab Hematol. 2023 Oct;45(5):691-699. doi: 10.1111/ijlh.14119. Epub 2023 Jun 20. PMID: 37338111.

mindray

healthcare within reach

Follow Mindray on Social Media

Linked in @Mindray

@Mindray Global

Wechat

www.mindray.com

P/N: ENG-Quick Facts About Erythrocyte Sedimentation Rate (ESR) Part A-210X4P-20231010

©2023 Shenzhen Mindray Bio-Medical Electronics Co.,Ltd. All rights reserved.