Digital Image Analysis of Blood Cells

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KEYWORDS

• ANC • Automated blood cells analyzers • Differentials • Digital image • CellaVision

KEY POINTS

- The performance of modern hematology analyzers is suboptimal in identifying specific blast cells, whereas manual review is still required in the presence of immature granulocyte flags or abnormal white blood cell distribution.
- The Beckman Coulter HematoFlow analyzer is a promising new technique but cytology remains the gold standard because to date it is the only modality to reach a definitive diagnosis in many cases.
- Automated microscopy count shows good correlation with the reference manual microscopy count and may replace the regular microscope in high-volume hematology laboratories and in adult samples.

INTRODUCTION

The complete blood cell (CBC) count is one of the most commonly ordered laboratory tests. Blood cell differential counts, and morphologic analysis of white blood cells (WBC), red blood cells (RBCs), and platelets, are an important diagnostic value in malignant and benign hemopathies. The acute myeloid leukemia (AML) classification is still based on cytology and cytology is an important diagnostic criterion in the myelodysplastic syndromes and classification of their different subtypes. Most of the RBC and platelet disorders have unique features for either red cell or platelet morphology, which can then guide the selection of additional tests. Thus, it is imperative to guarantee high levels of consistency and quality and maintenance of expertise in hematology laboratories. The interpretation of manual blood cell differential count, WBC, RBC, and platelet cytology is one of the most important and difficult tasks in a hematology laboratory; unfortunately, it is also less recognized and valued than flow cytometry or molecular biology.

Conflicts of interest: The author has nothing to disclose.

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Clin Lab Med 35 (2015) 105–122
http://dx.doi.org/10.1016/j.cll.2014.10.005 **labmed.theclinics.com**
0272-2712/15/$ – see front matter

Abbreviations

ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
ANC	Absolute neutrophil count
CBC	Complete blood cell
FCM	Flow cytometric
MDS	Myelodysplastic syndromes
r^2	Correlation coefficient
RBC	Red blood cell
WBC	White blood cell

In performing automated blood cell differential counting, hematology analyzers can flag abnormalities in RBCs and reticulocytes, WBCs, and platelets, which trigger examination of a peripheral blood smear. Until the last century, all the blood smears that required an examination were analyzed manually by light microscopy. Manual light microscopic examination is still the gold standard and, according to the Clinical and Laboratory Standards Institute guidelines in the United States, requires the manual differential count of 200 cells performed by 2 experienced laboratory staff members (technologists, scientists, biologists). However, manual blood smear examination is time consuming, labor intensive, and as stated requires highly experienced, well-trained laboratory staff. Furthermore, it remains subjective and it is difficult to apply proper quality control. There is substantial variability between staff members and even in the microscopic examination of the same smear by the same person at different times; manual cell counting remains subject to significant statistical variance because of the low number of cells counted.[1–4] In addition, constant budget pressures have resulted in staff reductions for many hematology laboratories, with more work being done by fewer laboratory staff members. The development of analytical platforms capable of analyzing thousands of samples per day has prompted research and development for the automation of the manual morphologic analysis of blood cells.

HISTORY OF DIGITAL IMAGING INSTRUMENTS FOR PERIPHERAL BLOOD

The first automated morphologic analysis system was the Cydac Scanning Microscope System (Cydac, Uppsala, Sweden) in 1966.[5] Further developments lead to the LARC (leukocyte automatic recognition computer) (Corning Medical, Raleigh, NC), the Hematrak (Geometric Data, Wayne, PA), the Coulter Diff3 and Diff4 (Coulter S-Plus WBC histogram, Coulter Electronics, Hialeah, FL), and the ADC 500 (Abbott Laboratories, Abbott Park, IL).[6] However, these systems were too slow; with limited automation and, most importantly, did not prove their superiority, or at least their equivalence, compared with the reference method, the manual microscopy examination. In the early 2000s, CellaVision (CellaVision AB, Lund, Sweden) produced a new generation of automated morphologic analysis system for peripheral blood smears and fluids, initially called Diffmaster Octavia (2001), DM8, DM96 (2004) (**Fig. 1**), and recently the CellaVision DM1200.

DIGITAL IMAGE MICROSCOPY WITH THE CELLAVISION INSTRUMENT

Barcode-labeled, May Grünwald Giemsa (MGG)/Wright Giemsa/Wright stained glass slides are placed into a magazine. The DM96 instrument can be loaded with up to 8 magazines, each containing up to 12 slides, and operates with a