Next-Generation Morphology (NGM) Enables Advanced Digital Analysis of Myelodysplastic Syndromes in Peripheral Blood Smears

A multilayer morphometric approach delivers high-resolution Full-Field imaging and quantitative insights into myelodysplasia using the Scopio Labs X100 digital system. [1 a p1, a-c p3 Katz]

Background

Morphological analysis has not kept pace with molecular and flow cytometry advancements using AI tools, remaining largely manual, low in sensitivity, and constrained by technological and theoretical limitations. [1 b p1 Katz]

A fundamental trade-off between field of view and resolution restricts high-magnification imaging (×100) to only 100—200 leukocytes, limiting analytical sensitivity to around 10^{-2}. [1 c p1, d p3 Katz]

Achieving high-resolution, large-scale ("big data") imaging within practical timeframes remains challenging. [1 d p1 Katz]

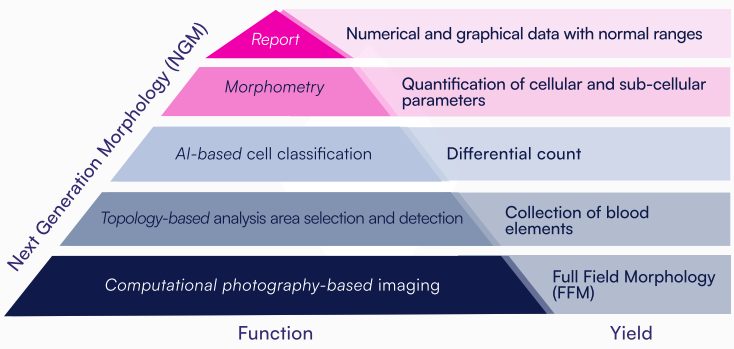
~80% of practitioners continue to rely on manual microscopy for peripheral blood smear(PBS) analysis. [1 e p3 Katz]

A prospective study evaluated next-generation morphology (NGM) The Scopio Labs X100 platform was used to test NGM performance by analyzing peripheral blood smears (PBS) from myelodysplastic syndrome (MDS) patients and age-matched controls. [1 e p1, c p3 Katz]

" NGM directly addresses the gaps in high-resolution digitization detailed previously, and unlock the diagnostic and research potentials of morphology in hematology." [1 f p3 Katz]

Methodology

- Stained PBS utilizing a May—Grunwald—Giemsa protocol were analyzed from 37 myelodysplastic syndrome (MDS) patients and 30 age-matched controls. [1 e p1, a p11 Katz]
- A low-magnification objective coupled with an illumination array captured multiple large field-of-view (FOV) low-resolution images. Each image was taken under different wavelengths and illumination angles, capturing unique data patterns from the sample. [1 g p3 Katz] A high-resolution image was computationally reconstructed from these multiple low-resolution inputs using physical imaging models. [1 h p3 Katz]
- AI and machine learning (ML) algorithms were integrated with traditional computer vision for cell detection and classification: [1 i p3 Katz]



Neutrophils granulation index:

Using a simple dimensionality reduction-based algorithm, a single grading scale without units (granulation index [GI]) was created from the parameters. A dataset of representative samples for each neutrophil population (hypogranulation, normal, toxic granulation, five of each) was used to cover the entire granulation spectrum in the scale creation. [1 a p4 Katz]

RBC morphometry:

Once RBCs are properly segmented, geometric-based features can be extracted with image processing algorithms. The cell size is derived from the segment size and is quantified in area units (µm2). The deformation of the cell contour is derived from the normalized distribution of the contour distances from the cell center point and is quantified in length units (µm). [1 b p4 Katz]

IPSS-R MDS patient's stratification and statistics:

The Revised International Prognostic Scoring System (IPSS-R) assessed MDS risk using CBC parameters (hemoglobin, ANC, platelets), cytogenetics, and blast percentage, with scores >2.5 classified as high-risk. Demographic and laboratory data were analyzed using univariate and multivariate Cox regression, adjusted for age, gender, and morphometric variables, to identify independent predictors of MDS risk ($p < 0.05$ considered significant). [1 a p5 Katz]

1 Clinical Site [1 a p11 Katz]

Tel Aviv Sourasky Medical Center [1 j p3 Katz]

What Did They Evaluate?

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- Utilization of next-generation morphology (NGM) for precise quantitative analysis of myelodysplasia in PBS [1 k p3 Katz]

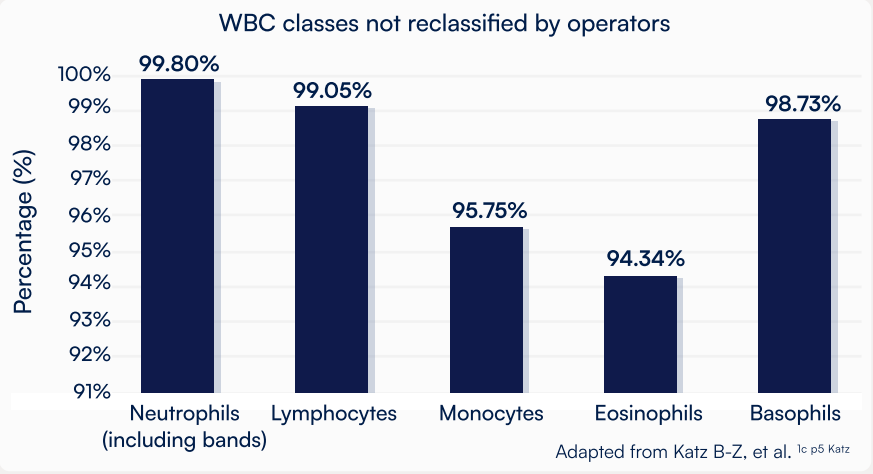
Results

>94% of the WBCs belonging to the five major WBC classes were correctly classified by the system [1 b p5 Katz]

274,856 cells analyzed [1 c p5 Katz]
Representing 1374 PBS

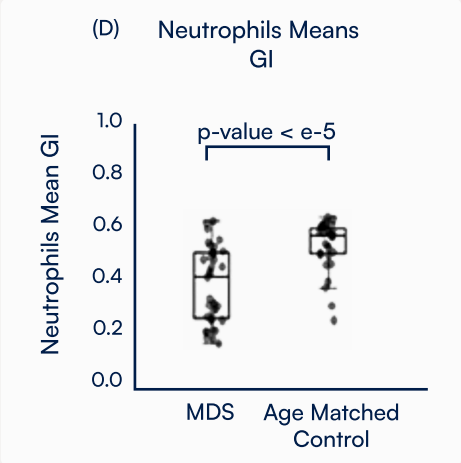
These cells were rarely reclassified by human operators—accuracy was highest for neutrophils (99.8%) and basophils (98.73%). [1 c p5 Katz]

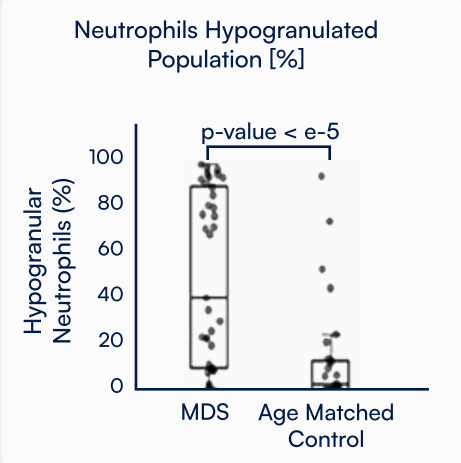
- **Only 0.41% of cells were initially unclassified;** operators most often reassigned these as neutrophils (26.68%) or blasts (12.85%), while 39.89% remained unclassified. [1 e p5 Katz]
- **Blasts were correctly identified 79.91% of the time,** with misclassifications mainly as lymphocytes or monocytes. [1 f p5 Katz]



Significant reduction in mean GI in MDS

- Due to the high accuracy of AI-based neutrophil classification, neutrophils were evaluated automatically - without human review - in 37 MDS samples and 30 age-matched control samples. [1 g p5, a p6 Katz]



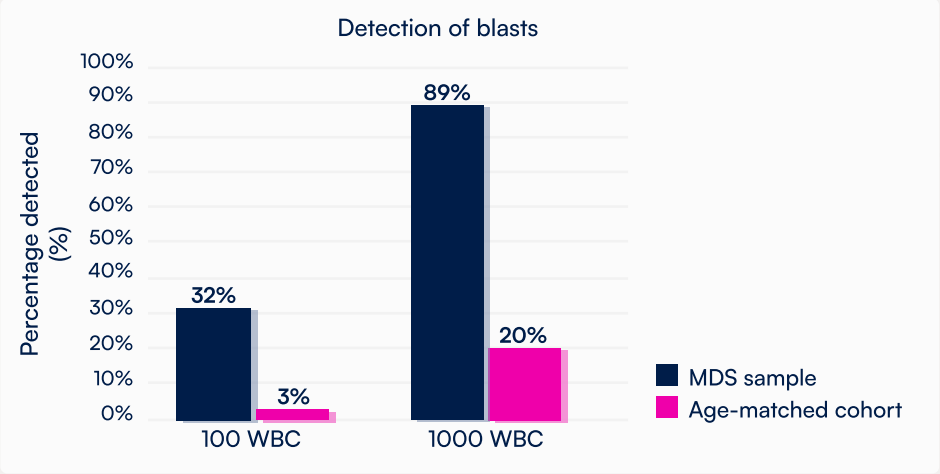


Adapted from Katz B-Z, et al. [1 a p8 Katz]

- Mean GI significantly reduced in MDS vs controls (0.38 ± 0.14 vs 0.53 ± 0.10, $p < 10^{-5}$). [1 a p7 Katz]
- Hypogranulated neutrophils increased (49.6% vs 13.2%, $p < 10^{-5}$). [1 b p7 Katz]

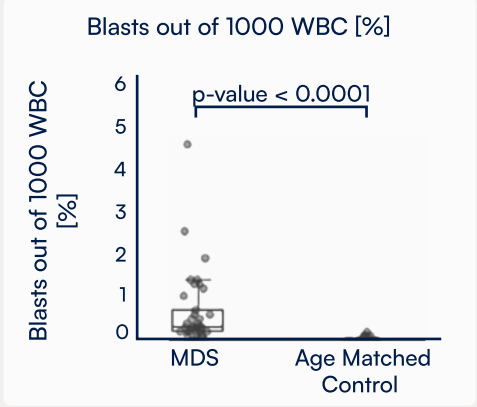
Enhanced detection sensitivity for blast enumeration

- Blasts percentage per 100 (according to the current practice) or 1000 (now provided by the FFM) WBC counts/sample in 37 MDS and 30 age-matched control samples. [1 b p8 Katz]
- A highly significant difference ($p < 10^{-9}$) in the detection of blasts was noted in 1000 WBC counts per sample. [1 c p8 Katz]



Adapted from Katz B-Z, et al. [1 c,d p8 Katz]

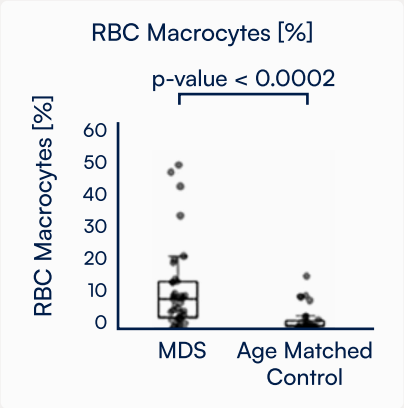
- The percentage of blasts per 1,000 WBCs in MDS samples was 0.65 ± 0.87% (range: 0—4.50%), which was significantly higher ($p < 0.0001$) than in age-matched controls, who showed 0.02 ± 0.05% blasts (range: 0—0.20%). [1 e p8 Katz]

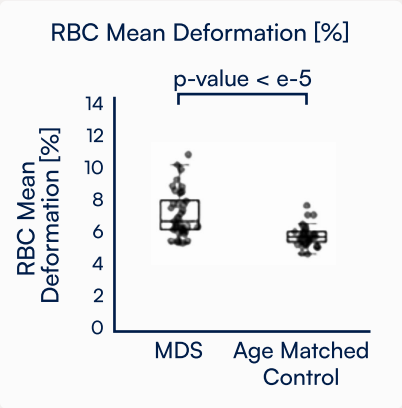


Adapted from Katz B-Z, et al. [1 a p9 Katz]

Detection of RBC morphometry

- **At least 152,310 red blood cells (RBCs) were analyzed** per peripheral blood smear (PBS) to ensure a 95% confidence interval for detecting RBC abnormalities occurring at a 1% frequency. [1 f p8 Katz]





Adapted from Katz B-Z, et al. [1 a p10 Katz]

- **Macrocytosis was significantly higher in MDS samples** (11.44 ± 11.89%, range 0.64—46.83%) compared with age-matched controls (2.85 ± 3.72%, range 0.34—15.30%; $p < 0.0002$). [1 g p8 Katz]
- **MDS samples also had a significantly higher proportion of deformed RBCs** (7.24 ± 1.42%, range 5.4—10.82%) than controls (5.86 ± 0.67%, range 4.75—7.74%; $p < 10^{-5}$). [1 h p8 Katz]

Conclusions

The Next-Generation Morphology (NGM) platform using Scopio Labs' X100 scanner and application enables:

- High-resolution, large-field imaging digital PBS analysis. [1 a p1 Katz]
- Sensitive detection of morphologic abnormalities in MDS. [1 g p1 Katz]
- Objective, quantitative morphometry supporting risk stratification. [1 a p1 Katz]
- Opportunities for remote diagnostics and research into hematologic dysplasia. [1 b p9 Katz]

Read the full publication

1. Katz B-Z, Moshe Y, Bensity D, Luttwak E, Brazilai M, Oster HS, et al. Next-generation morphology, a novel multilayer morphometric digital analysis, reveals both the basic topology and new trends of myelodysplasia of peripheral blood specimens. Br J Haematol. 2025;00:1—12. doi:10.1111/bjh.70110