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Automated digital morphometry of peripheral blood smears detects both infrequent events and cellular population patterns in myelodysplastic syndrome

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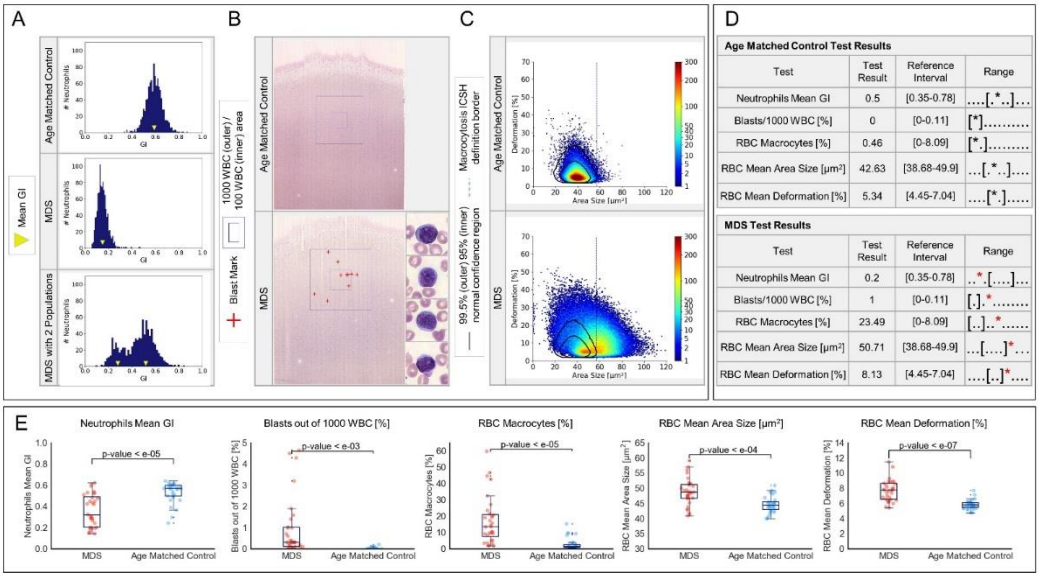
Introduction: Current diagnosis of myelodysplastic syndrome (MDS) is based on invasive bone marrow aspirate, followed by subjective morphological analysis. The novel Full-Field Morphology (FFM) technology developed by Scopio Labs performs peripheral blood smear (PBS) analysis on a large scale of 1000 fields of 100X view in a routine manner, allowing a precise and highly sensitive automated quantification of cellular and sub-cellular morphological parameters. In this study, we applied this digital morphometric approach to compare PBS morphology of MDS patients with age-matched controls. **Methods:** 32 MDS and 30 age-matched control PBS were scanned by the Scopio Labs system, and evaluated according to three distinct morphological features with known significance in MDS: blast percentage per 100 or 1000 WBC; neutrophil cytoplasmic granulation per 1000 neutrophils; RBC morphology of at least 150,000 RBC. Quantitative determination of neutrophils granulation, was measured by Granulation Index (GI, between 0-1) and GI Distribution Width (GIDW, between 0-1). RBC measurements included the quantitative measurements of RBC size, namely macro- and microcytosis, and RBC contour changes (deformation), i.e. the percent of RBC that deviate from normal RBC shape. **Results:** The mean GI of MDS samples was 0.36±0.15 (A,E), significantly ($p<10^{-4}$) lower compared with the mean GI of age-matched control samples 0.53±0.10 (A,E). Mean GI were highly diverse among MDS samples compared with age-matched controls (E). Interestingly, two sub-populations of neutrophils were detected in some of the MDS samples, differ in their mean GI (A). Such fingerprint, suggesting the presence of an abnormal and normal clones, was not detected in the control samples (A). Blasts were detected in 13/32 (41%) of MDS samples compared with 1/30 (3%) of age-matched controls, when counts were performed per 100 WBC. However, when 1000 WBC were analysed, blasts were detected in 27/32 (84%) of MDS samples compared with 6/30 (20%) of age matched controls, a highly significant difference ($p<10^{-6}$) (B). The percentage of blasts per 1000 WBC counts/sample of MDS samples was 0.92±1.35%, significantly (P<0.0008) higher compared with the percentage of blasts per 1000 WBC counts/sample of age-matched control samples 0.02±0.05% (E). RBC analysis revealed significant differences between MDS and age-matched samples (C). As expected, mean RBC size and % of were significantly ($p<10^{-5}$) higher in the MDS samples compared with the age matched controls (E). We found that MDS PBS contained significantly ($p<10^{-6}$) higher number of abnormally-shaped RBC (E). Representative summaries of morphometric analyses of MDS and age-matched control are shown in (D).



Age Matched Control Test Results

Test	Test Result	Reference Interval	Range
Neutrophils Mean GI	0.5	[0.35-0.78]	....[.*..]...
Blasts/1000 WBC [%]	0	[0-0.11]	[*].....
RBC Macrocytes [%]	0.46	[0-8.09]	[*.].....
RBC Mean Area Size [µm²]	42.63	[38.68-49.9]	...[.*..]....
RBC Mean Deformation [%]	5.34	[4.45-7.04]	....[*.].....

MDS Test Results

Test	Test Result	Reference Interval	Range
Neutrophils Mean GI	0.2	[0.35-0.78]	..*.[....]...
Blasts/1000 WBC [%]	1	[0-0.11]	[.].*.....
RBC Macrocytes [%]	23.49	[0-8.09]	[..]..*.....
RBC Mean Area Size [µm²]	50.71	[38.68-49.9]	...[....]*...
RBC Mean Deformation [%]	8.13	[4.45-7.04]	....[..]*....

Conclusion: Our study demonstrates that FFM-based digital PBS analysis enables the detection and quantification of unique WBC and RBC morphologic alterations associated with MDS.