L'impiego dell'intelligenza artificiale

artificial intelligence applied to the identification and classification of blood cells

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Disclosures of Gina Zini

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Mindray					x		

The 5th IASTED International Multi-Conference Computers and Advanced Technology in Education (CATE 2002)

Topic: Decision Support System in Medicine
Contribution: Oral Presentation
Title: Neural Network Project applied to a routine hematological analyser

Authors: G.Zini, G. Mistretta, G. Giordano, G. d'Onofrio

Research Center for Clinical evaluation of Hematological Analyser Systems
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ELSEVIER

Clinica Chimica Acta 333 (2003) 195–201

www.elsevier.com/locate/clinchim

Neural network in hematopoietic malignancies

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Hematology, October 2005; 10(5): 393–400

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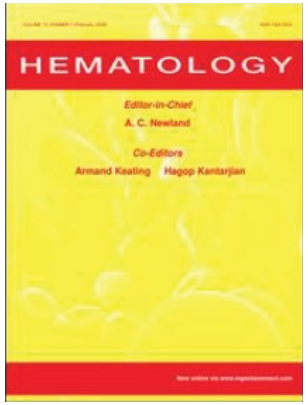

ARTIFICIAL INTELLIGENCE

Artificial intelligence in Hematology

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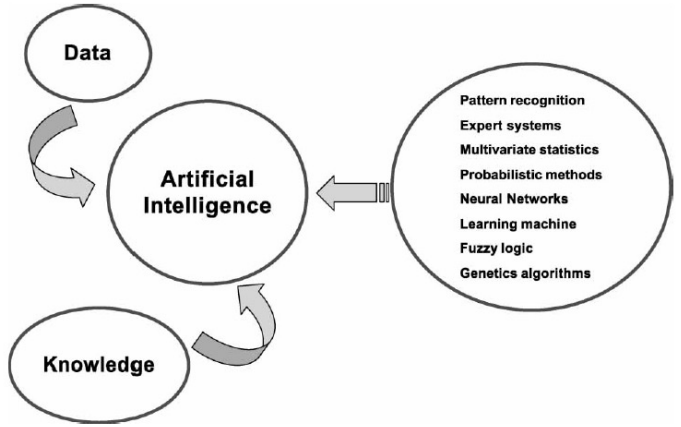
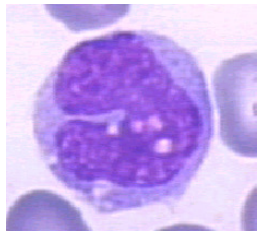
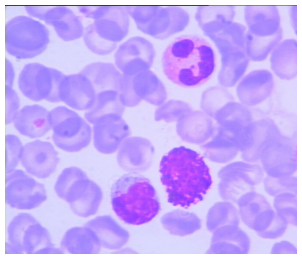
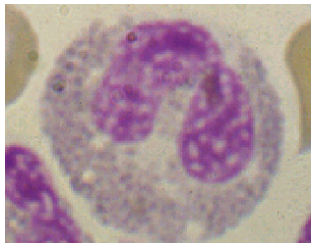


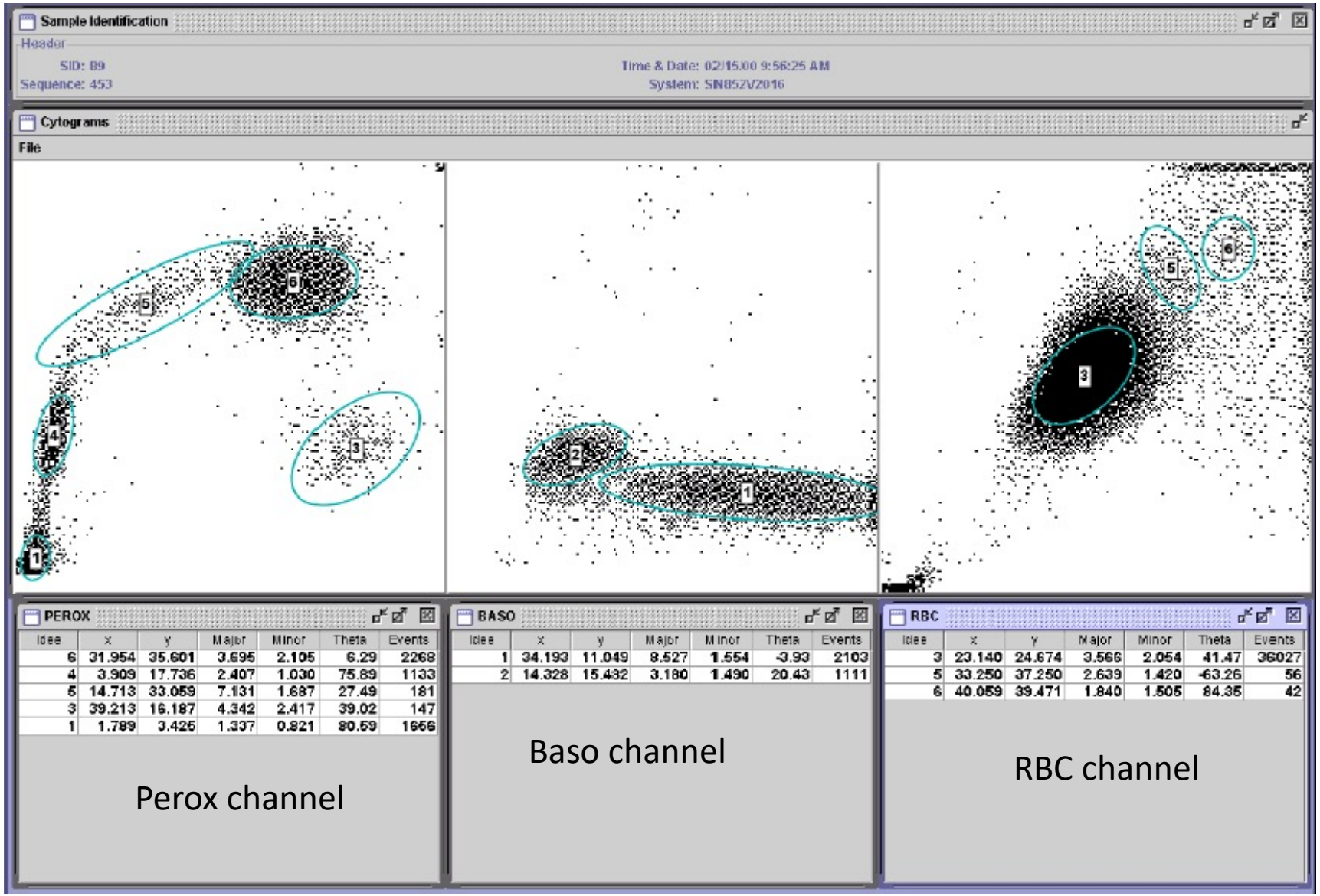
Figure 5. Computational artificial intelligence: relationships among different related tools.

Normal





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4 3.909 17.736 2.407 1.030 75.89 1133
5 14.713 33.059 7.131 1.687 27.49 181
3 39.213 16.187 4.342 2.417 39.02 147
1 1.789 3.425 1.337 0.821 80.59 1656
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BASO
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1 34.193 11.049 8.527 1.554 -3.93 2103
2 14.328 15.432 3.180 1.490 20.43 1111
Baso channel
RBC
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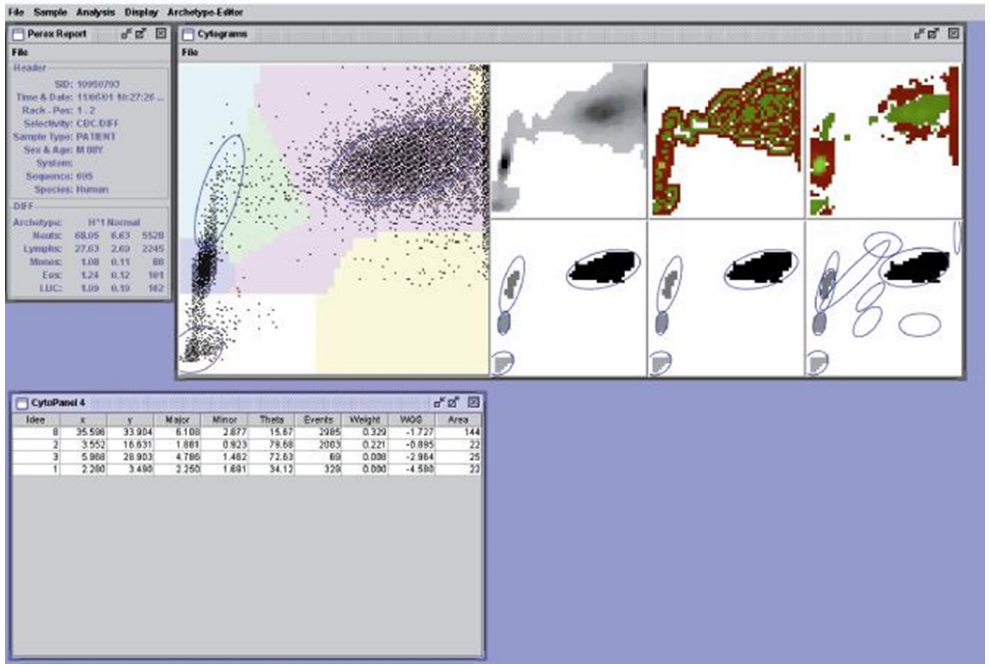
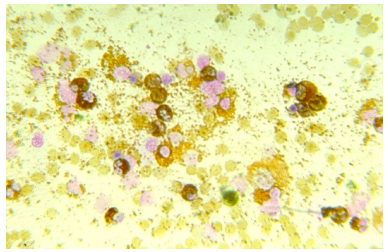
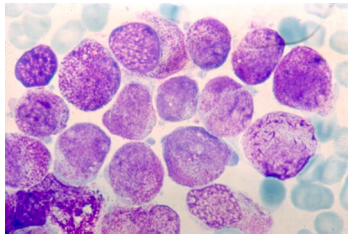
6 40.059 39.471 1.840 1.505 84.35 42
RBC channel

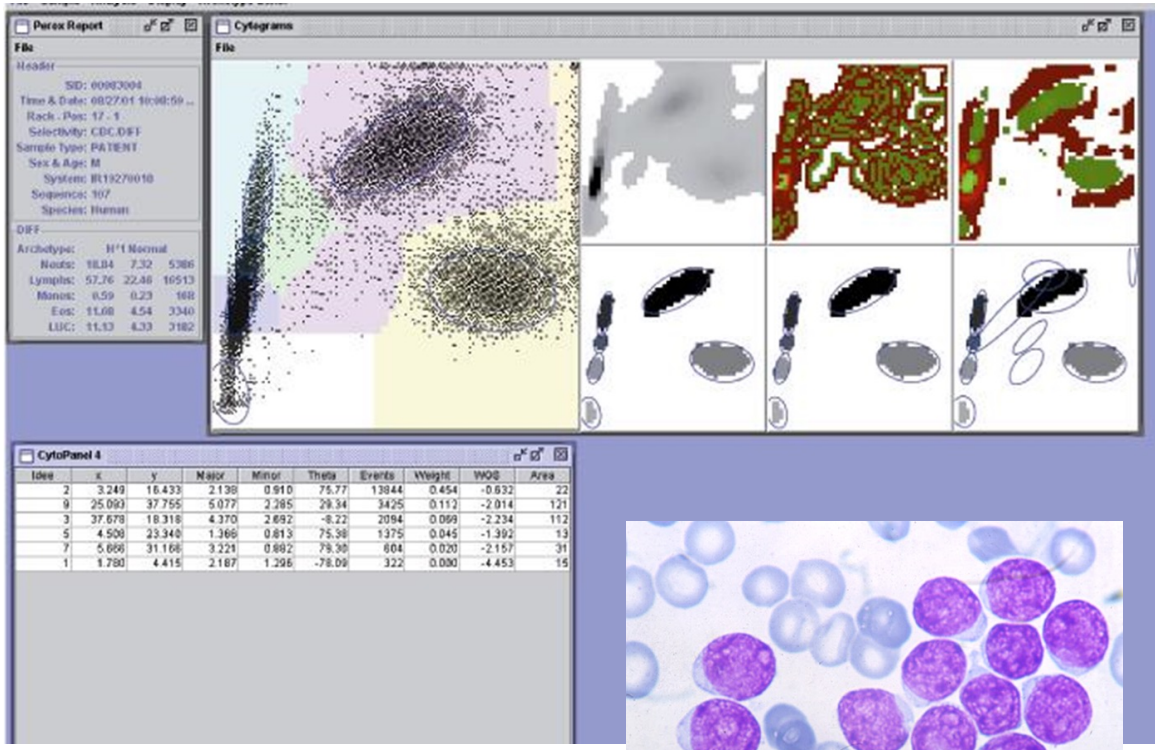
Acute Promyelocytic Leukemia







Acute Lymphoblastic Leukemia

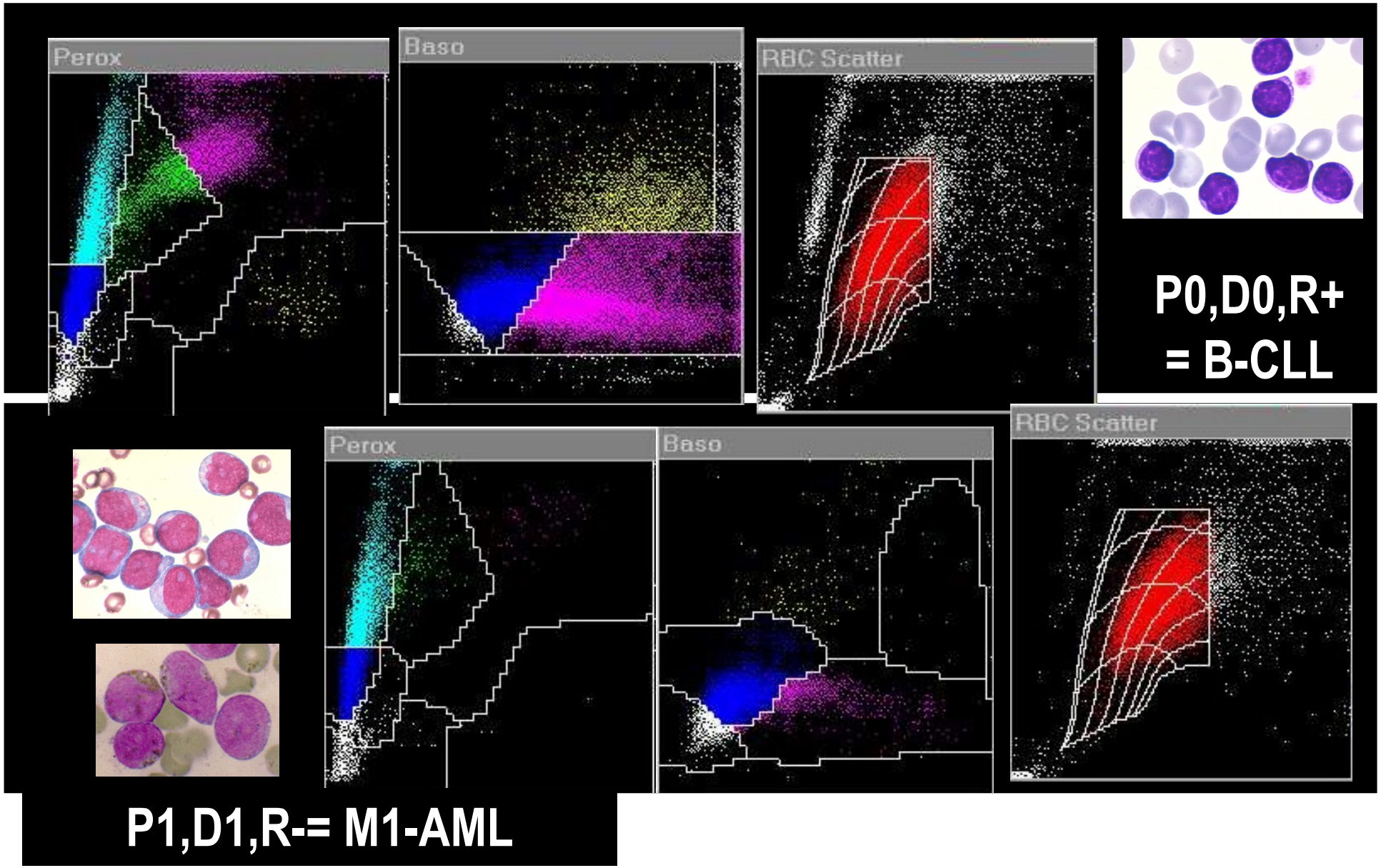


PANDA method

P eroxidase
A ctivity
N uclear
D ensity
A nalysis

PANDA Classification Score

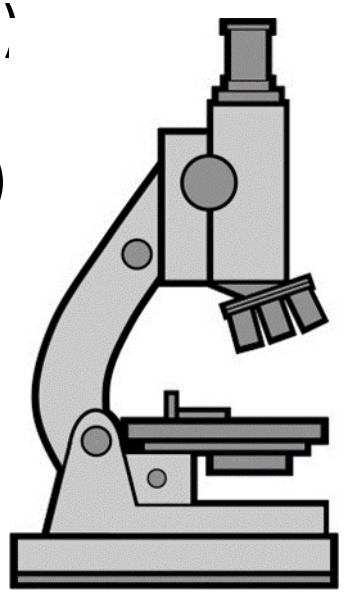
D (0 to 2): Nuclear Density
P (0 to 6): Peroxidase Activity
(R) Cell Size/Density



Cell identification at the microscope: a decision making process

Factors influencing decision making:

- Past experience (Juliusson, Karlsson, & Gärling, 2005)
- Cognitive biases, i.e. analog vs digital (Stanovich & West, 2008)
- Age and Individual differences (Bruin, Parker, & Fischoff, 2007)
- Belief in personal relevance (Acevedo, & Krueger, 2004)
- Escalation of committment



Heuristics

- are general decision-making strategies people use that are based on little information, very often derived from previous experiences with similar problems
- are mental shortcuts that reduce the cognitive burden associated with decision making
- reduce work in decision making in several ways:
  - offer the user the ability to scrutinize few signals
  - diminish the work of retrieving and storing information in memory

Representative heuristic (RH), is an extremely economical heuristics in the event that one of two things is recognizable, people will tend to choose the recognized thing (Pachur, & Hertwig, 2006).

In the field of medicine missed medical diagnoses are mainly attributable to representative heuristics (Redelmeier, 2005)

Heuristics primarily serves the purpose of reducing the effort associated with a task (Shah & Oppenheimer, 2008)

Cell identification at the microscope: a decision-making process based on negotiation avoids bias

- Recognition skills depend on two related processes: the perception of familiarity or unfamiliarity (a rapid intuitive process based on previous experience), and recollection (a slower conscious recall of knowledge) (Henson et al., 1999; Wagner et al., 1998)
- Anchoring and adjustment heuristic is the foundational decision making heuristic in situations where some estimate of value is needed (Epley, & Gilovich, 2006)
- The practical application of the anchoring and adjustment heuristic is in negotiation
- People tend to make a decision which tends to gravitate towards the anchor side
- Negotiation requires effort where actual values tend to be farther away from the anchor initially planted.
- Such work is important in avoiding anchor bias
  (Epley and Gilovich, 2006)

Virtual microscopy & virtual smear

- The computer and the digital camera offer unprecedented possibilities for improving hematology education, research and patient service.

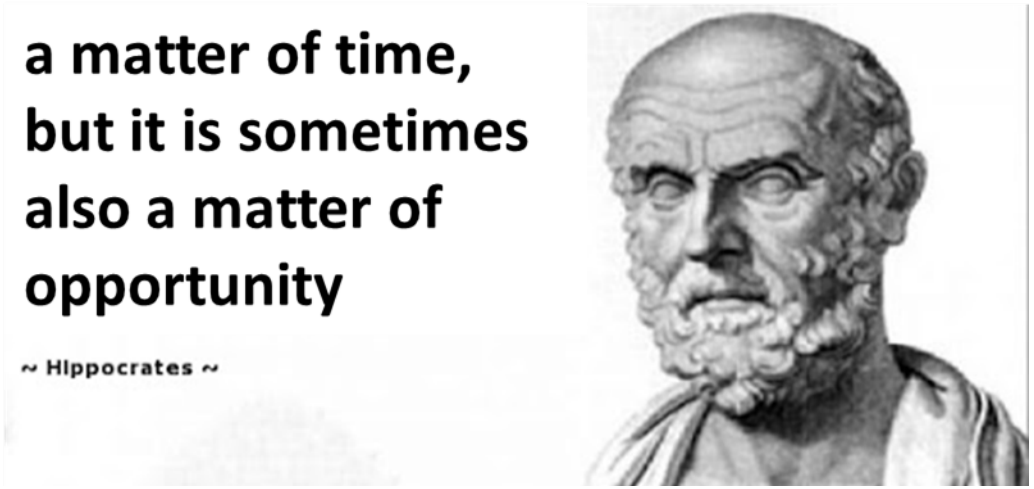
- Peripheral blood smear images of exceptional quality can be acquired rapidly and conveniently.

- Images are immediately available for incorporation into websites or digital publications, printing, transfer to other individuals by e-mail or other applications.

- These images are essentially indistinguishable from conventional film images.

Valuable reasons why virtual microscopy is destined to irreversibly replace the OM

We can borrow this phrase from Hippocrates about healing



Virtual microscopy & virtual smear

- With further advances in computer speed and internet streaming technology, virtual microscopy could easily replace the real microscope in pathology education.
- Hematology education may be completely revolutionized and make the conventional lecture and laboratory format obsolete very soon.
- Patient care may be enhanced by the transmission of digital images to separate locations and individuals for consultation, education and research.
- Diagnostic accuracy and reproducibility, standardization and harmonization do represent the main aspects of this technology applied to hematology.
- Technology implementation does allow to apply to the digital images those typical functions of the optical microscope, such as focusing, enlargement and zooming.

Main causes of Cell ID error

Main causes	Human	Solution: individual	Tools	Solution: worldwide
Competence/software	Yes	Time (individual output)	Yes	Time
Optical microscope fatigue	Yes	None	No	n/a
Workload	Yes	None	No	n/a
Uncertainty	Yes	Time to minimize	No	Software improvement (minimize unclassified cells)
Impact on TAT	Often	None	No	n/a
Representative heuristic (no negotiation errors)	Yes	None	No	n/a

Improving outcome requires a fruitful reciprocal approach

- Humans can be more easily trained by using media: i) quantitative and qualitative access to all cell types, ii) optimization and personalizayion of training time, iii) reduced physical fatigue reduction, iv) harmonization of cells ID and their nomenclature. Routine optical microscopy activity will be limited to those difficult cells requiring human decision-making complexity.
- Tools can carry out the most of pre-classification activity with appropriateness reserving the microscopic activity for cases that require human decision-making complexity to pre-classify.

Whole slide imaging (WSI) today

Several applications in **Pathology**

- Education, Training and Competency Testing
- Telepathology has been validated for second opinion in challenging cases of surgical pathology, cytopathology, and immunohistochemistry
- Experts can seek experts' opinion on cases (no expense/delay in international shipping) as well as intra-operative section diagnosis through remote
- 2017 approval of US FDA for primary diagnosis in surgical pathology "on the basis of non-inferiority of WSI vis-à-vis glass slide with respect to diagnostic concordance and the reproducibility of repeated scanning"
- Main limitations: limited diffusion, scanning time and massive data storage capacity

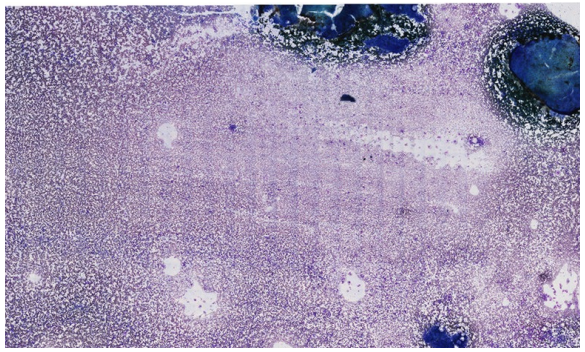
Validating Whole Slide Imaging
for Diagnostic Purposes in Pathology

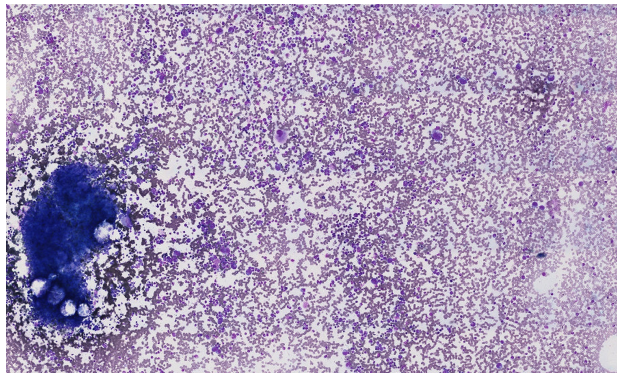
Guideline from the College of American Pathologists Pathology and Laboratory Quality Center

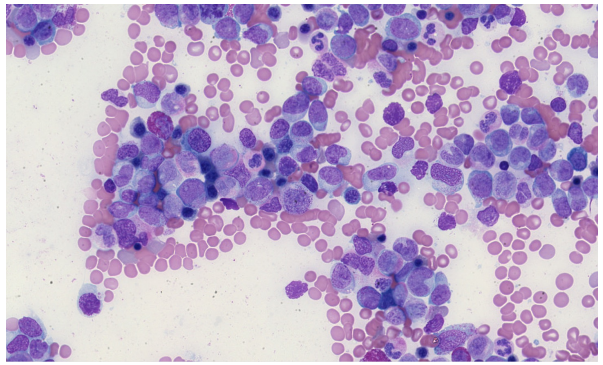
Liron Pantanowitz, MD; John H. Sinard, MD, PhD; Walter H. Henricks, MD; Lisa A. Fatheree, BS, SCT(ASCP); Alexis B. Carter, MD;

Few applications in **Hematology**

- Education, Training, and Competency Testing
- Telehemathology for second opinion in challenging cases (very rare reports)
- Main limitations: very limited diffusion, scanning time and massive data storage capacity





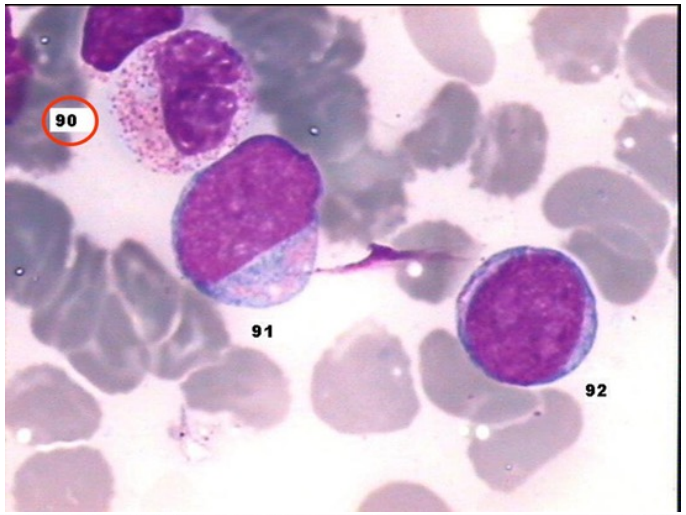


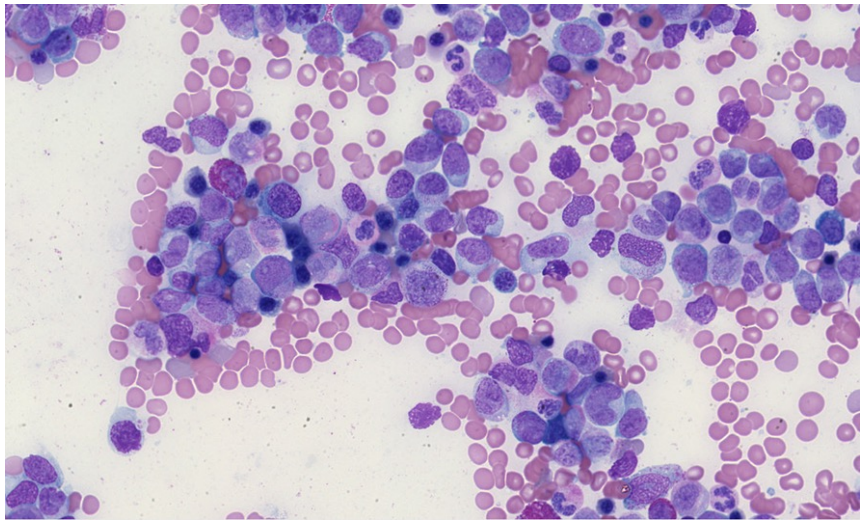
ELN WP10 Diagnostics Morphology

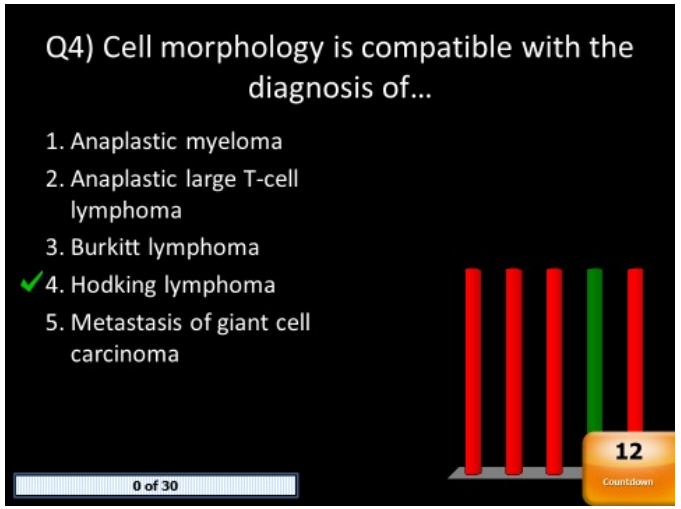
ELN Foundation
European LeukemiaNet

12-year activities 2007-2019:16 morphological exercises

4 ELNWP10 workups available on the net.jpg/.tiff based
8 ELNWP10 workups available via net WSI based
4 SWG EHA-ELN workups in presence .jpg/.tiff based







ELN Foundation
European LeukemiaNet

ELN WP10 Diagnostics Morphology

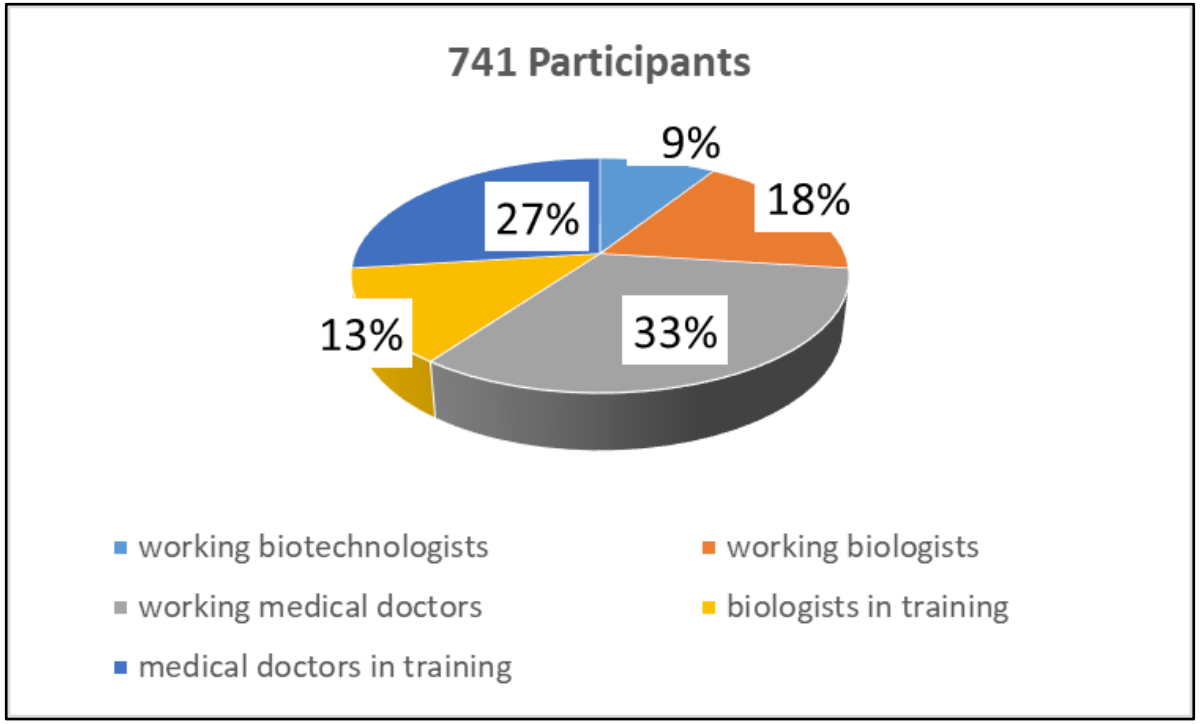
- 12-year activities 2007-2019: 16 morphological exercises

- 741 participants:

69 (9%) biotechnologists

437 (51%) graduates working in the laboratory or clinic [136 (18%) biologists and 241 (33%) medical doctors]

295 (40%) graduate on training [97(13 %) biologists and 198 (27%) medical doctors)



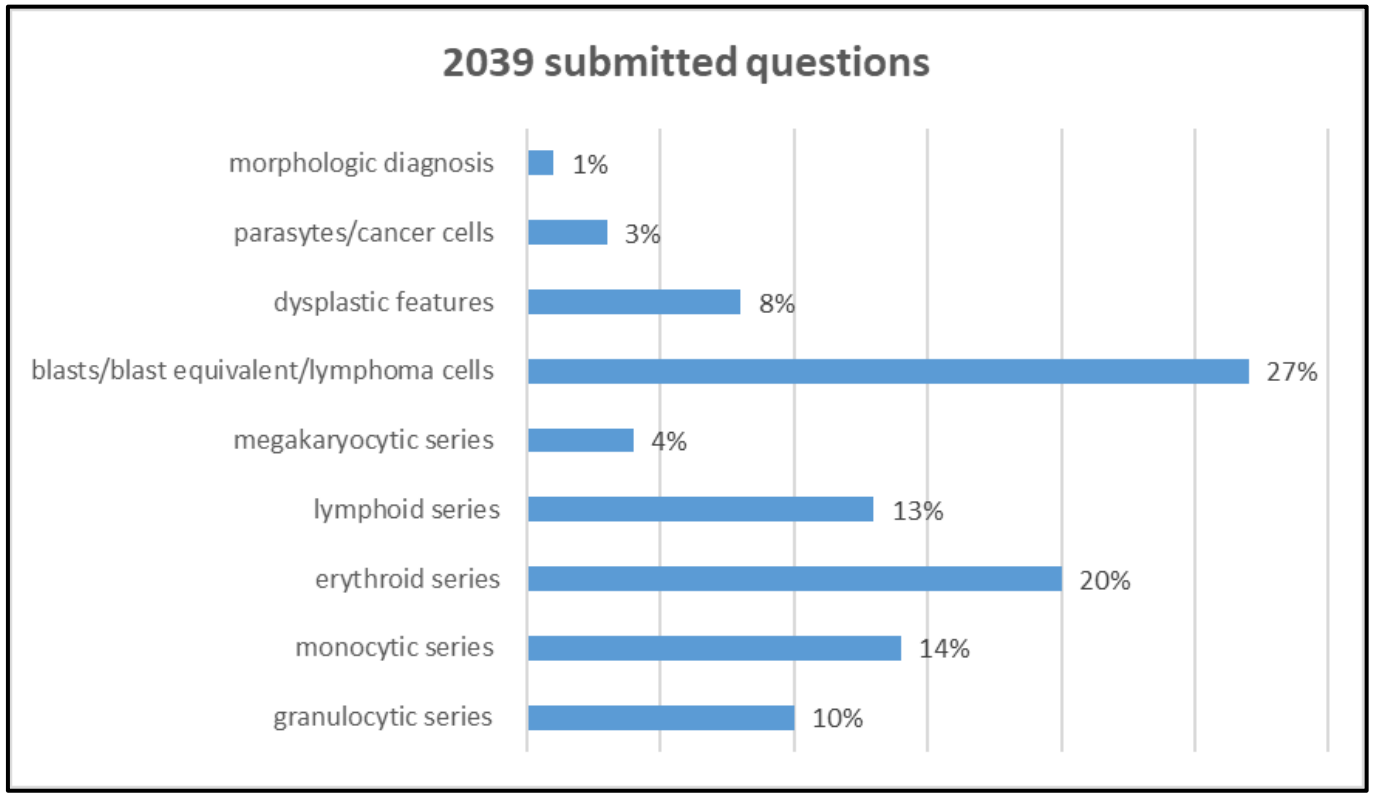
ELN WP10 Diagnostics Morphology

- 12-year activities 2007-2019: 16 morphological exercises

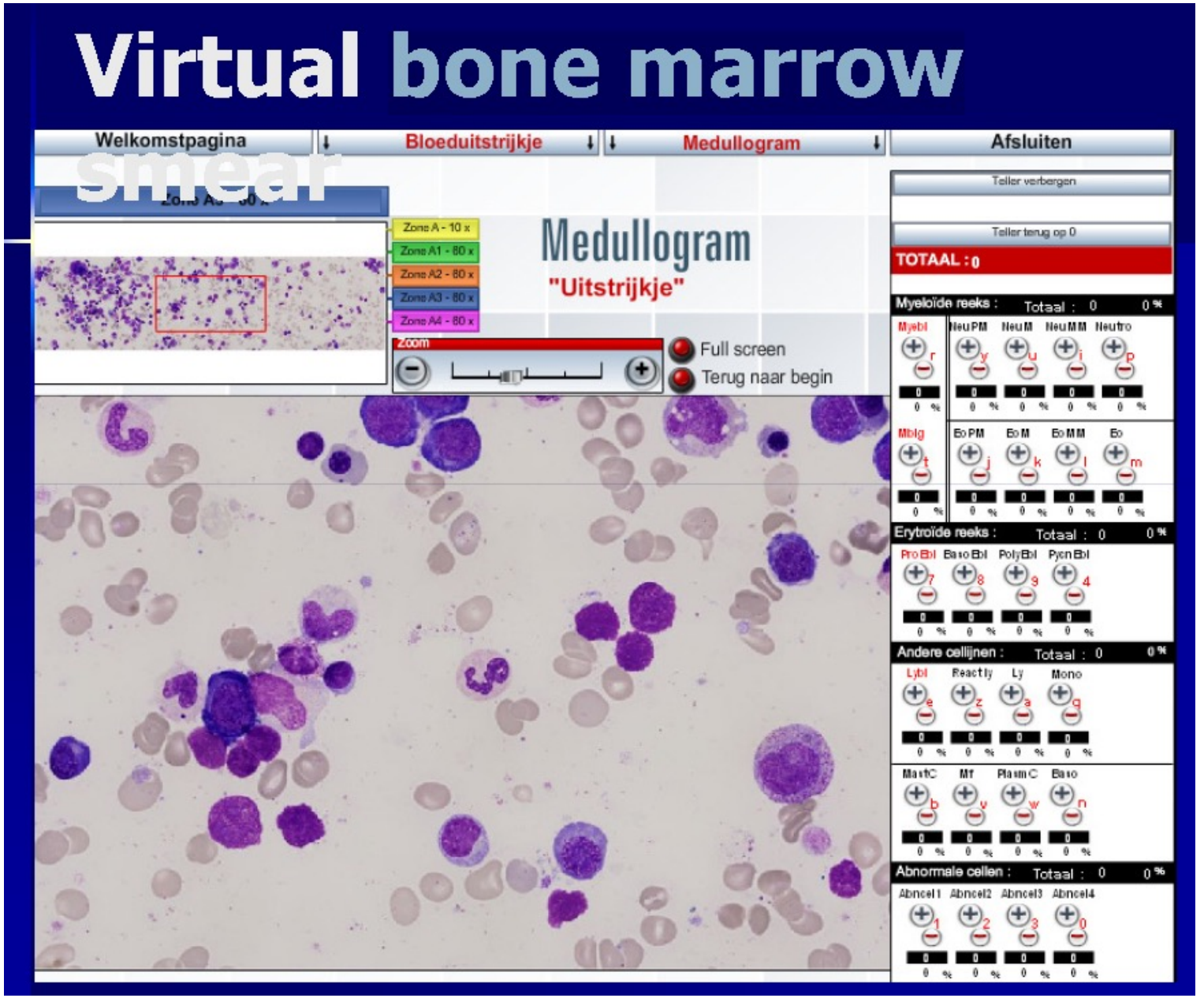
- 2.039 submitted questions

- Cell lineage and subgroups distribution:

granulocytic series 204 (10%),
monocytic series 281 (13,78%),
erythroid series 410 (20,1%)
lymphoid series 273 (13,3%)
megakaryocytic series 80 (3,92%)
blasts/blast equivalent/lymphoma cells 554 (27,1%)
dysplastic features 163 (7,99 %)
parasytes/cancer cells 58 (2,84%)
morphologic diagnosis 16 (0,8%).



Dutch site


Virtual bone marrow
Welkomstpagina
Bloeduitstrijkje
Medullogram
Afsluiten
smear
Zone A - 10 x
Zone A1 - 80 x
Zone A2 - 80 x
Zone A3 - 80 x
Zone A4 - 80 x
Medullogram
"Uitstrijkje"
Zoom
Full screen
Terug naar begin
Teller verbergen
Teller terug op 0
TOTAAL : 0
Myeloïde reeks : Totaal : 0 0 %
Myebl
NeuPM
NeuM
NeuMM
Neutro
Mbig
EoPM
EoM
EoMM
Eo
Erytroïde reeks : Totaal : 0 0 %
ProEbl
BasoEbl
PolyEbl
PycnEbl
Andere cellijnen : Totaal : 0 0 %
Lybl
Reactly
Ly
Mono
MastC
Mf
PlasmC
Baso
Abnormale cellen : Totaal : 0 0 %
Abncel1
Abncel2
Abncel3
Abncel4

Review of the UK NEQAS (H) digital morphology pilot scheme for continuing professional development accessed via the internet

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doi:10.1111/j.1751-553X.2008.01086.x

Received 21 April 2008; accepted for publication 13 June 2008

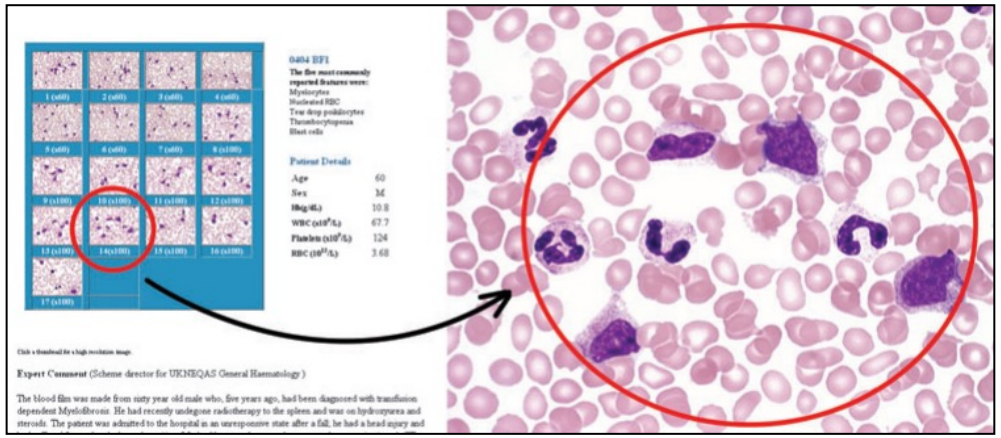
Keywords
Quality control, laboratory practice, morphology, blood, bone marrow

SUMMARY

UK NEQAS (H) developed and instigated a pilot scheme for digital morphology, which was accessed by participants over the internet in order to assess the viability of using high quality images as an educational tool for continuing professional development. The pilot scheme was trialled over a 2-year period with eight releases totalling 16 morphology cases. Digital images allowed participating individuals to examine and comment on exactly the same cells and compare their findings with those of other participants, consensus data from traditional glass slide surveys and expert opinion. Feedback from participants on their experience was then relayed back to the development team by UK NEQAS (H) in order to drive the educational format and to ensure that any new scheme would meet the requirements of the users.

INTRODUCTION

The United Kingdom National External Quality Assurance Scheme for General Haematology [UK NEQAS (H)] collaborated with a team of medical, scientific and academic staff from the Manchester Royal Infirmary (MRI) and Manchester Universities to develop an internet-based pilot scheme for digital morphology. The aim of the collaboration was to explore the use of digital images for the morphological examination of peripheral blood cells in an external quality assessment (EQA) setting. This pilot scheme was credited by



Clin. Lab. Haem.
2005, **27**, 357–362

REVIEW

Digital imaging of haematological morphology

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Department of Clinical Haematology, Central Manchester and Manchester Children's University Hospitals, Manchester, UK

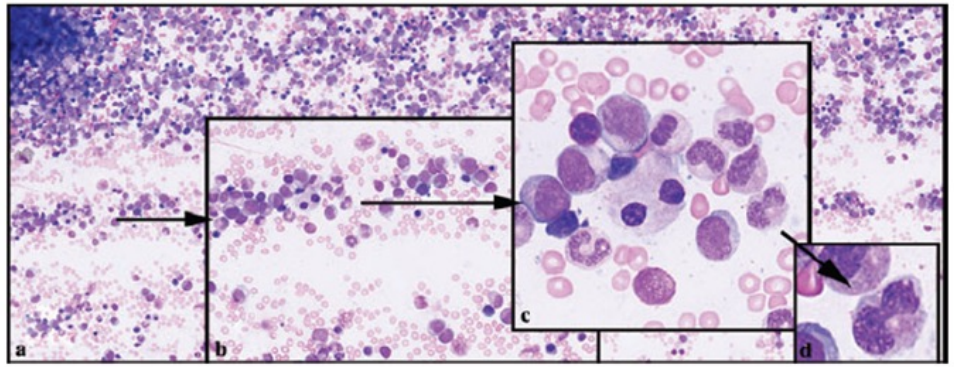


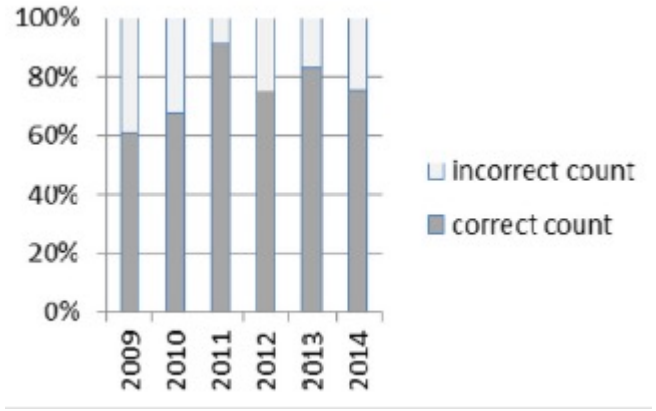
Figure 2. The background panel shows a digital slide prepared from 60 separate ×60 oil-immersion microscopic fields. Panels (b and c) show magnified images of details from the main slide, illustrating the cytological detail of a micromegakaryocyte, several blast cells and dysplastic maturing myeloid cells. Panel (d) shows a dysplastic neutrophil at high magnification. Please note this image is a printed reproduction and does not therefore precisely reproduce the quality of the original image.

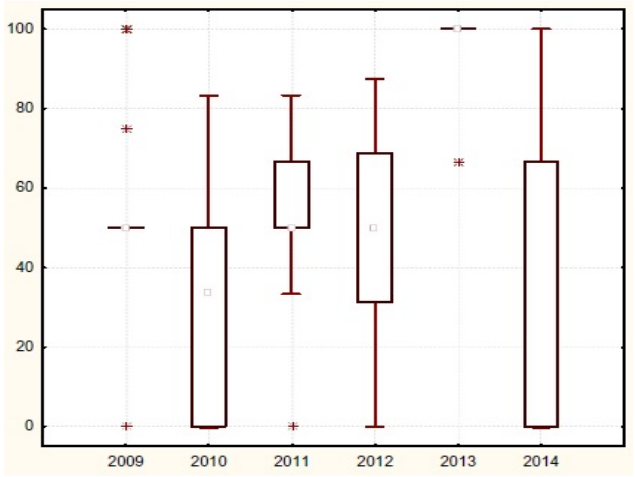
External bone marrow cytological examination quality assurance (EQAhem) — summary after 6 years in Poland (Lewandowsky et al, Ann Hematol online, July 2015)

assessment of the whole process of bone marrow examination

- ✓ participants assess blood and bone marrow smears
- ✓ identify selected cells from photographs
- ✓ and interpret laboratory data together with microscopic results

blast count





dysplastic cells

Digital morphology applied to PB virtual slide reviewing and validation in hematology

- DM96, DM1200 and DM9600 CellaVision AB, (Lund, Sweden)
- The DI-60 Integrated Slide Processing System (Sysmex, Kobe, Japan)
- Vision Hema (West Medica, Perchtoldsdorf, Austria)
- EasyCell Assistant (Medica Corporation; Bedford, MA, USA
- Nextslide (Nextslide Imaging, LLC, Cleveland, OH, USA)
- COBAS 511 (Roche Diagnostics, Indianapolis, IN, USA)
- HemaCAM (Fraunhofer Institute for Integrated Circuits IIS)
- Minday MC-80

Literature overview summary

- Important advantages of digital morphology include the ability to easily consult colleagues, reference abnormal cells, utilize archived images for education, quality assurance and competency assessment, archival, retrieval and expert consultation from remote sites.
- Most studies are based on local validation protocols applied to the routine workload.

Received: 8 January 2019 | Revised: 25 March 2019 | Accepted: 4 April 2019
DOI: 10.1111/ijlh.13042

REVIEW

ISLH International Journal of Laboratory Hematology WILEY

Digital morphology analyzers in hematology: ICSH review and recommendations

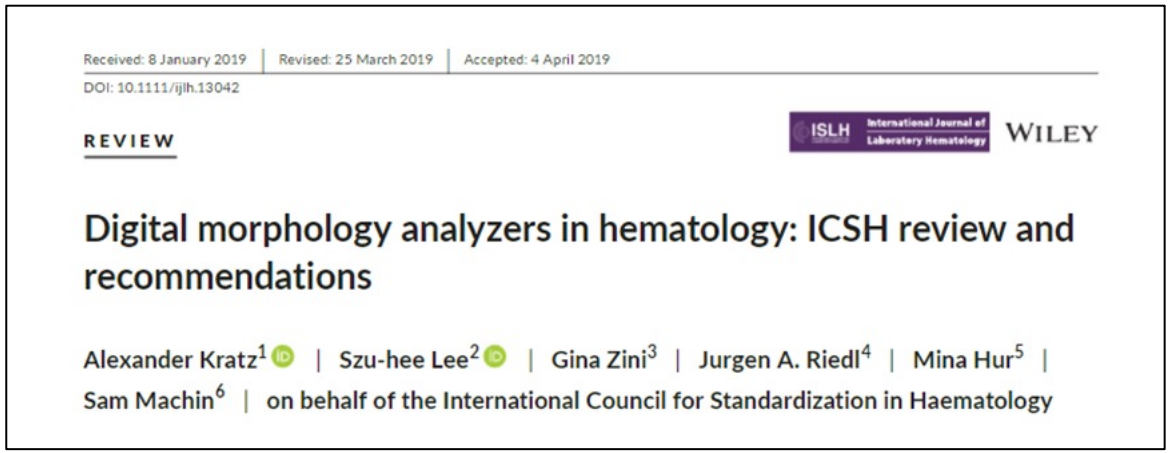
Alexander Kratz[1] | Szu-hee Lee[2] | Gina Zini[3] | Jurgen A. Riedl[4] | Mina Hur[5] | Sam Machin[6] | on behalf of the International Council for Standardization in Haematology

A morphological review step can then often be performed quickly with digital morphology. The operator can validate the differential on digital images, and, if needed, also perform a manual microscopic review as a final check.

Recommendations (I)

- Appropriate use of digital imaging in conjunction with automated cell counters: selection of samples to be digitized should be based on rules that use the flagging systems of the institution's automated analyzer as well as automated rules based on the specific needs of the laboratory.
- Always reconcile the flags of the automated analyzer with the report of the digital imaging. In the presence of any discrepancy, a manual differential with the microscope should be performed.

Recommendations (II)



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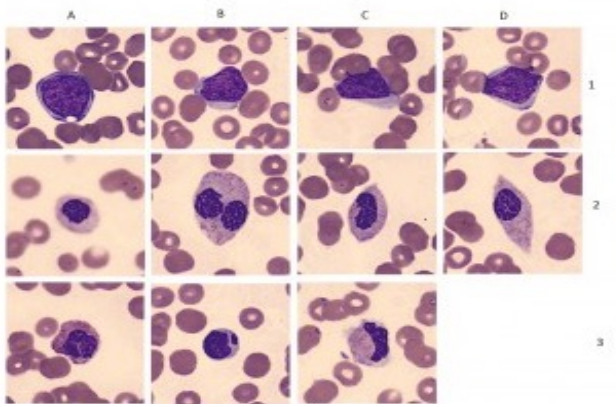
Digital morphology analyzers in hematology: ICSH review and recommendations

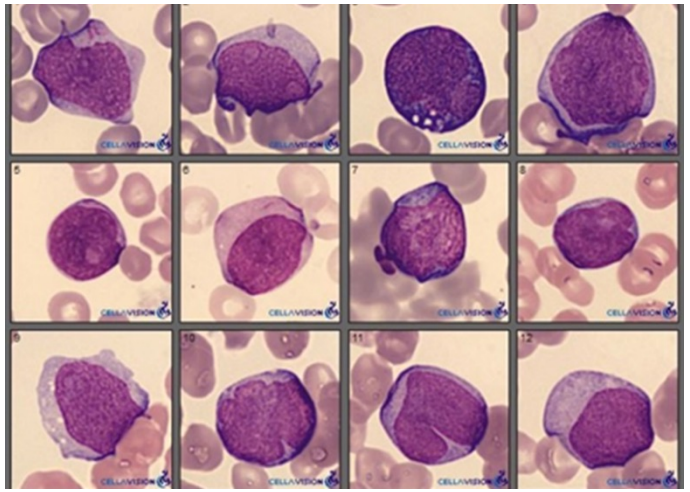
Alexander Kratz[1] | Szu-hee Lee[2] | Gina Zini[3] | Jurgen A. Riedl[4] | Mina Hur[5] | Sam Machin[6] | on behalf of the International Council for Standardization in Haematology

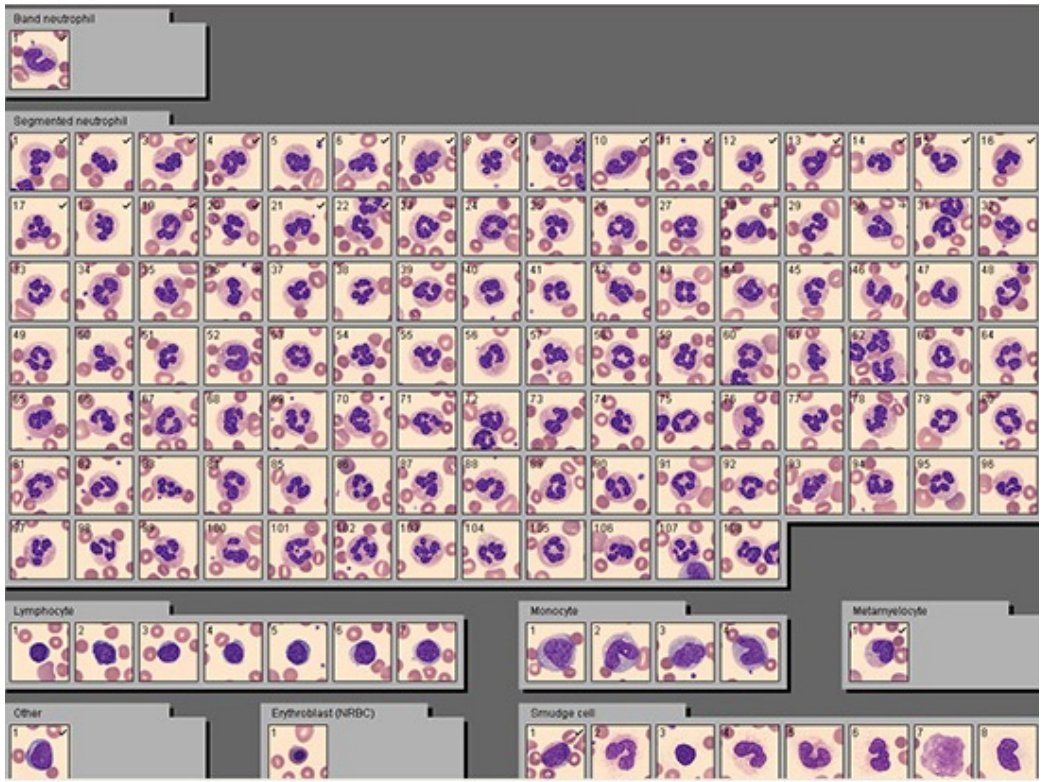
- There may be substantial differences between digital systems that use slides that were prepared and stained manually versus systems that use automated slidemakers and stainers: robust correlation studies on differences in morphological details and color matching between the two methods are lacking.

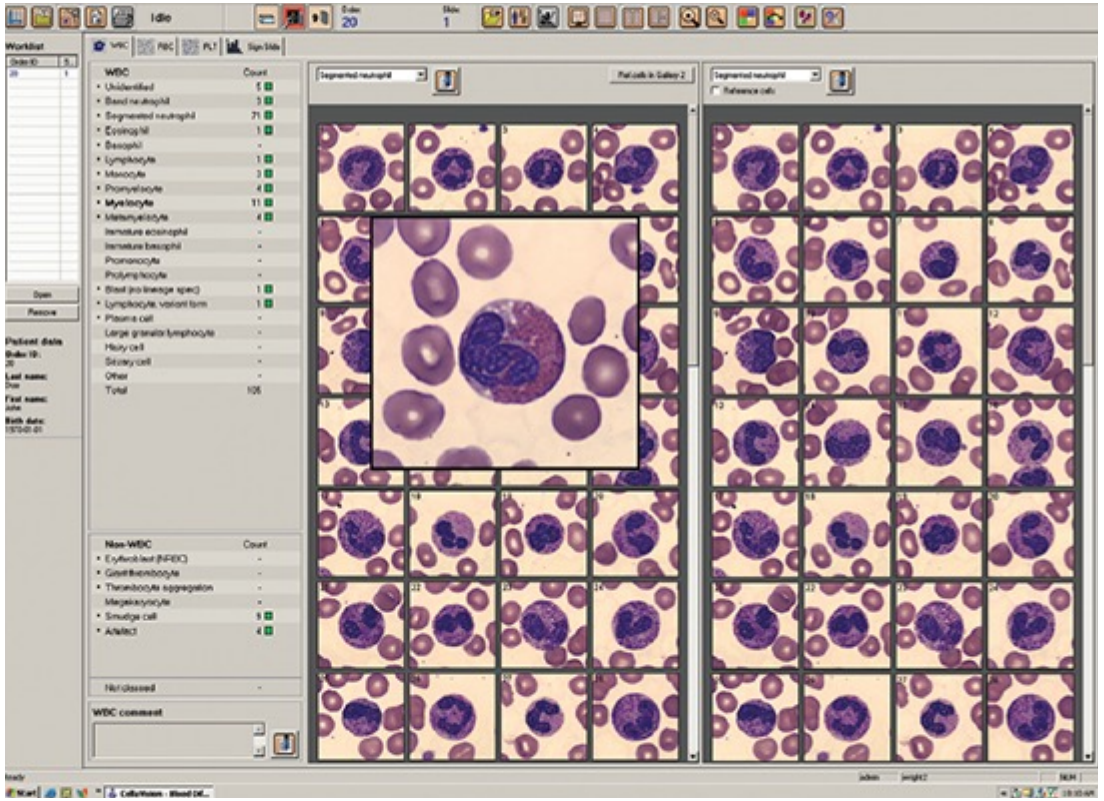
- In automatically prepared films, cells may appear larger and thinner, and there may be chromatic differences compared to cells stained with panoptical stains. In the presence of abnormal cells or in pediatric samples of lymphocytes, the size, thickness, and color differences can lead to incorrect cell identification, often resulting in an overestimation of blast cells. We strongly recommend that operators should be trained on this “new morphology” just as they are trained in the interpretation of cytograms from automated cell counters.



Automated DM Applied to PB







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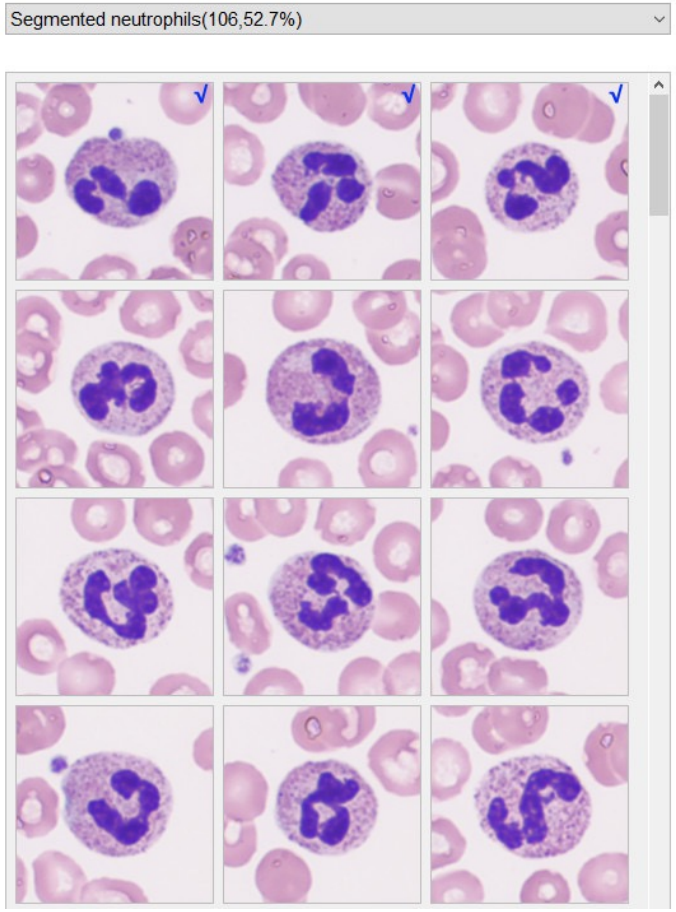
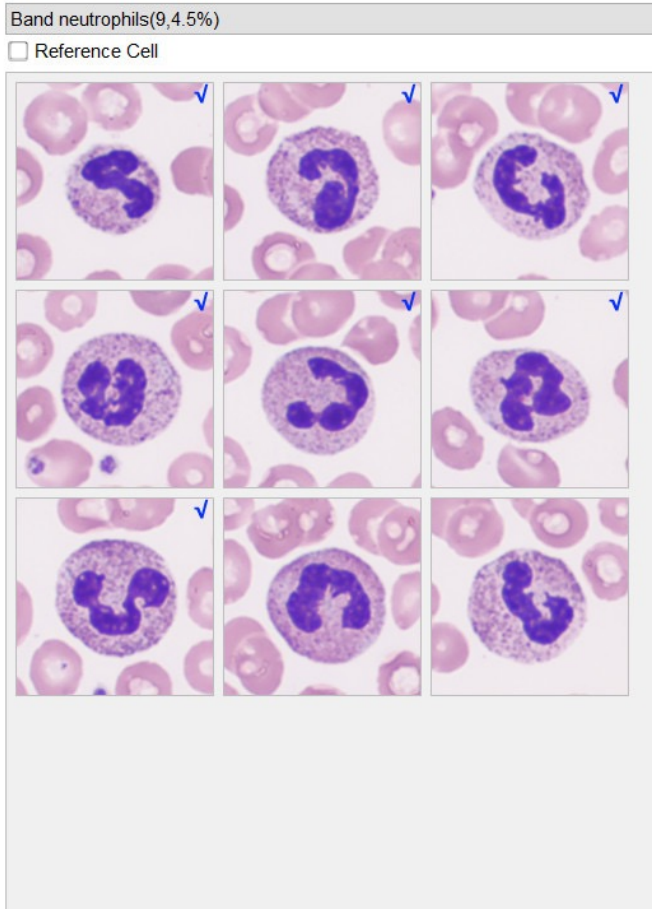
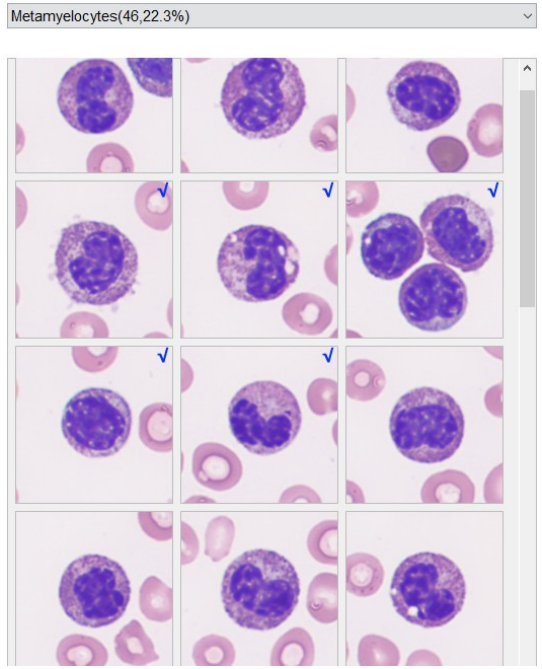
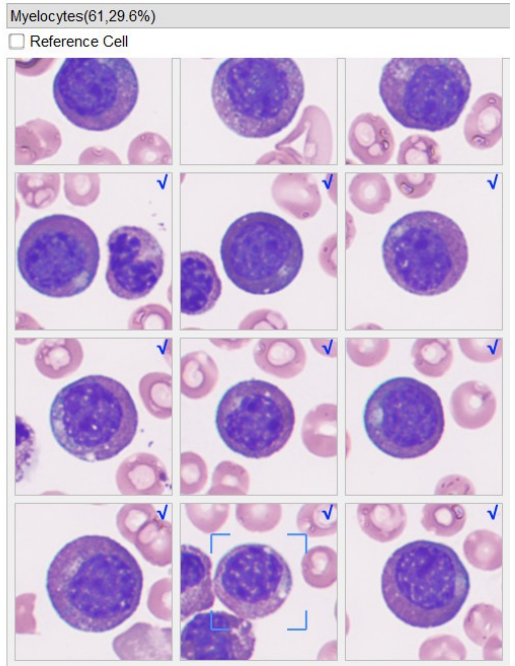








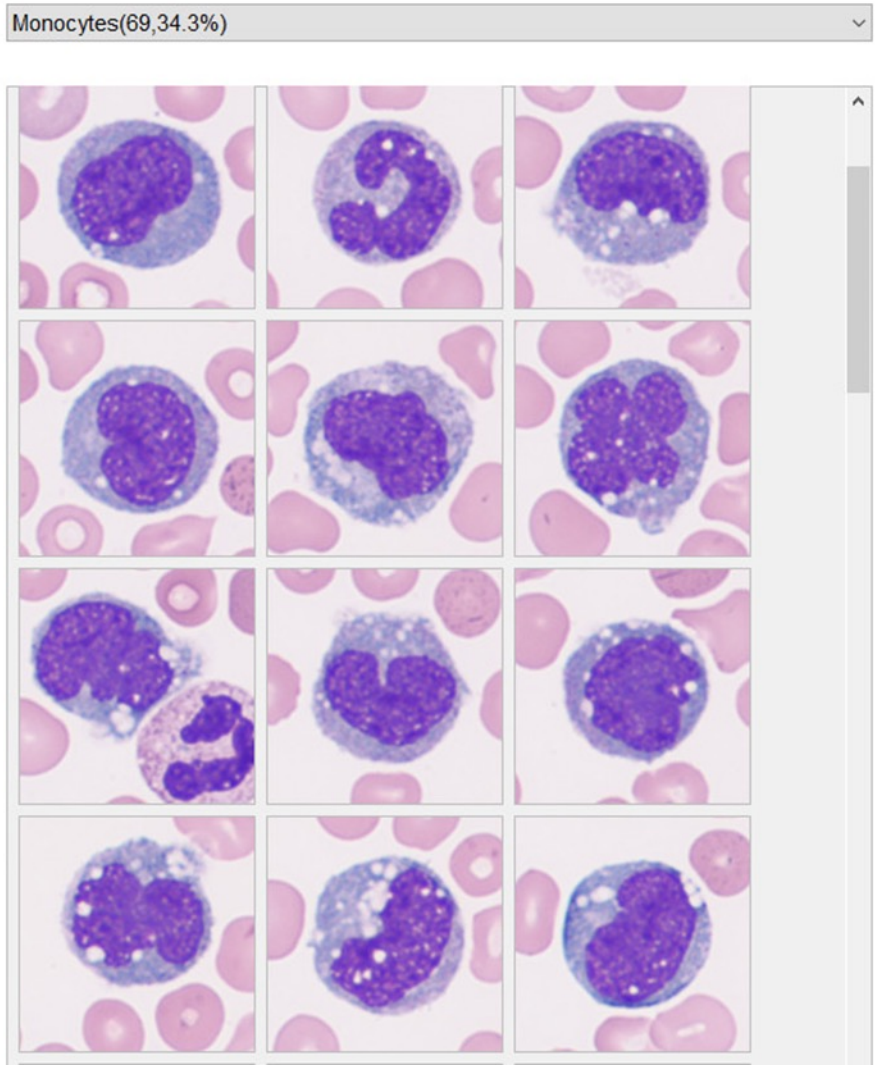
Granulocytic series

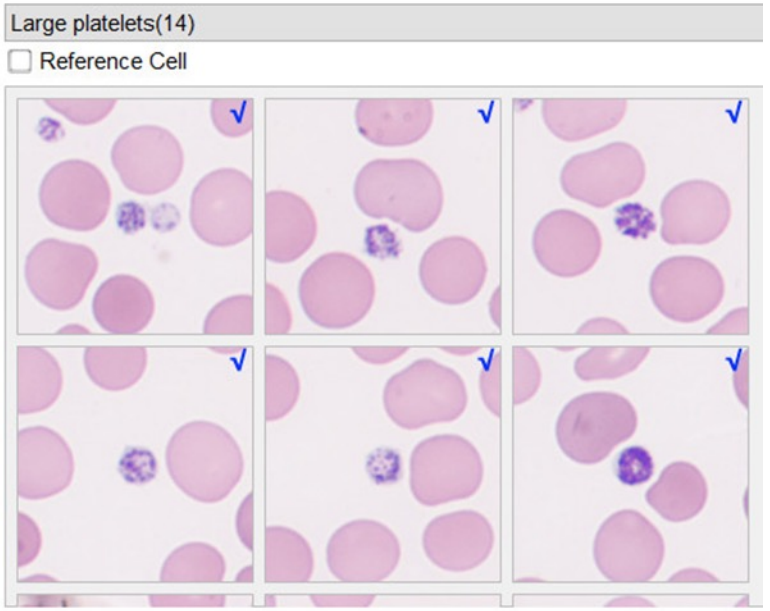
Band cell definition: any cell of the granulocytic (leukocytic) series that has a nucleus that could be described as a curved or coiled band, no matter how marked the indentation, if it does not completely segment the nucleus into lobes connected by a filament.

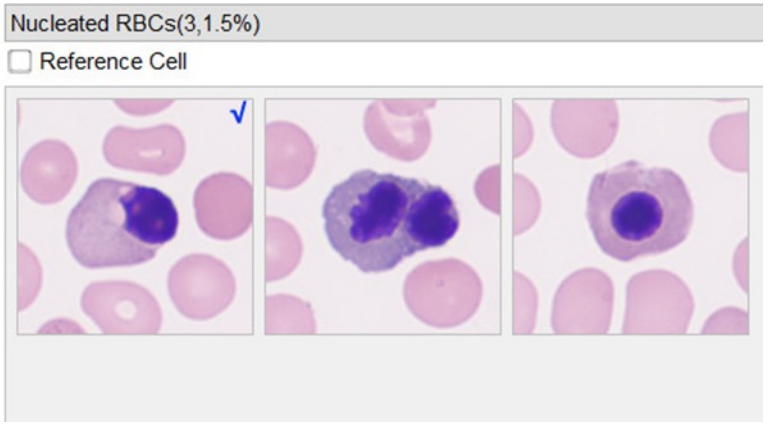
Automated DM applied to PB

Nucleated cells&others

	WBC (Total 201,100.0%)	Count	%	
	Unidentified			
L	Segmented neutrophils	43	21.4	E
!	Band neutrophils	38	18.9	E
L	Lymphocytes	8	4.0	E
H	Monocytes	69	34.3	E
	Eosinophils			
	Basophils			
!	Metamyelocytes	10	5.0	•
!	Myelocytes	30	14.9	E
	Promyelocytes			Ⓔ
!	Blast cells	3	1.5	E
	Reactive lymphocytes			
	Plasma			
	Abnormal lymphocytes			
	Abnormal promyelocytes			
	Non-WBC (Total 40)	Count	%	
!	Nucleated RBCs	3	1.5	E
	Giant platelets	2		E

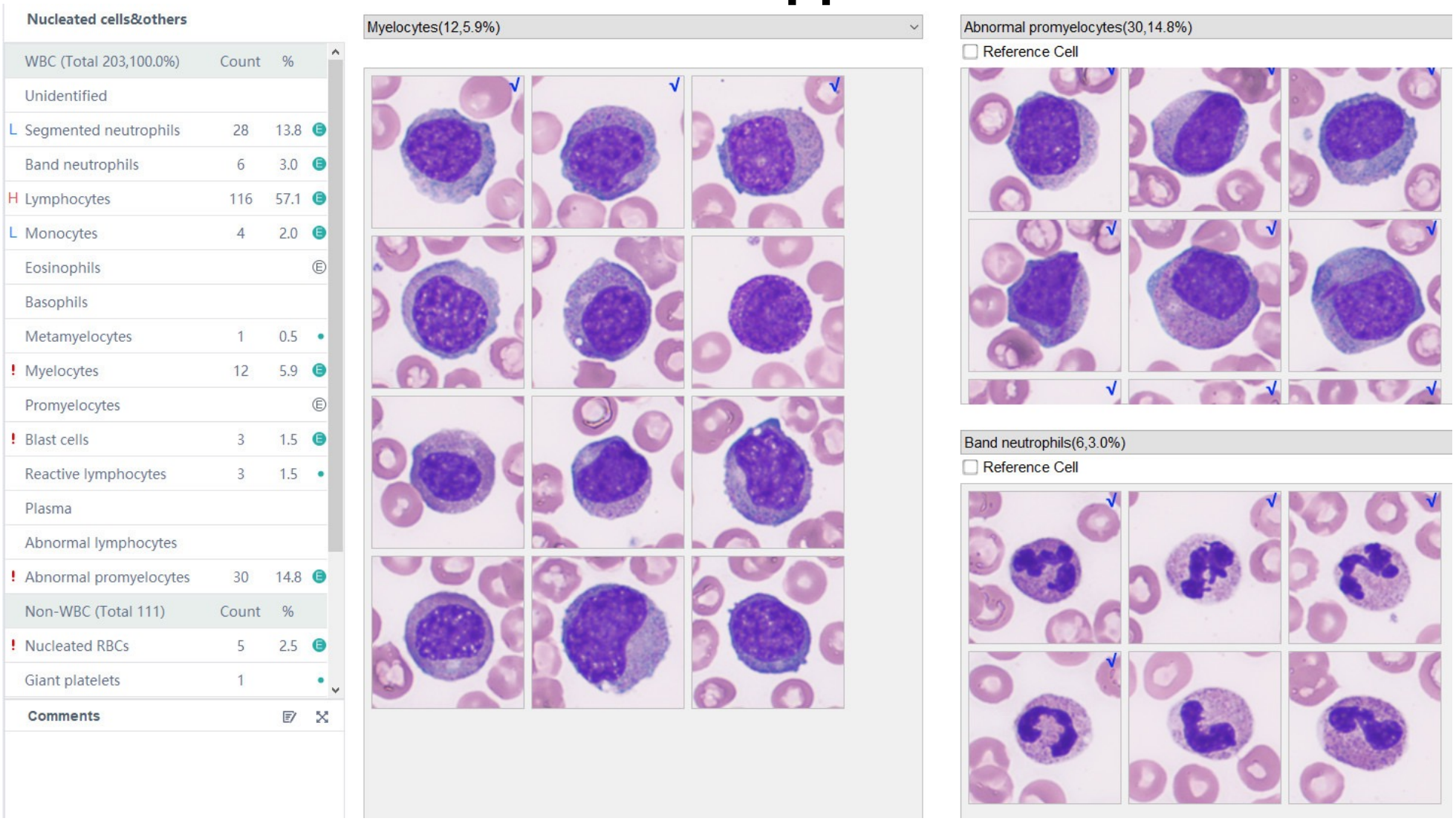






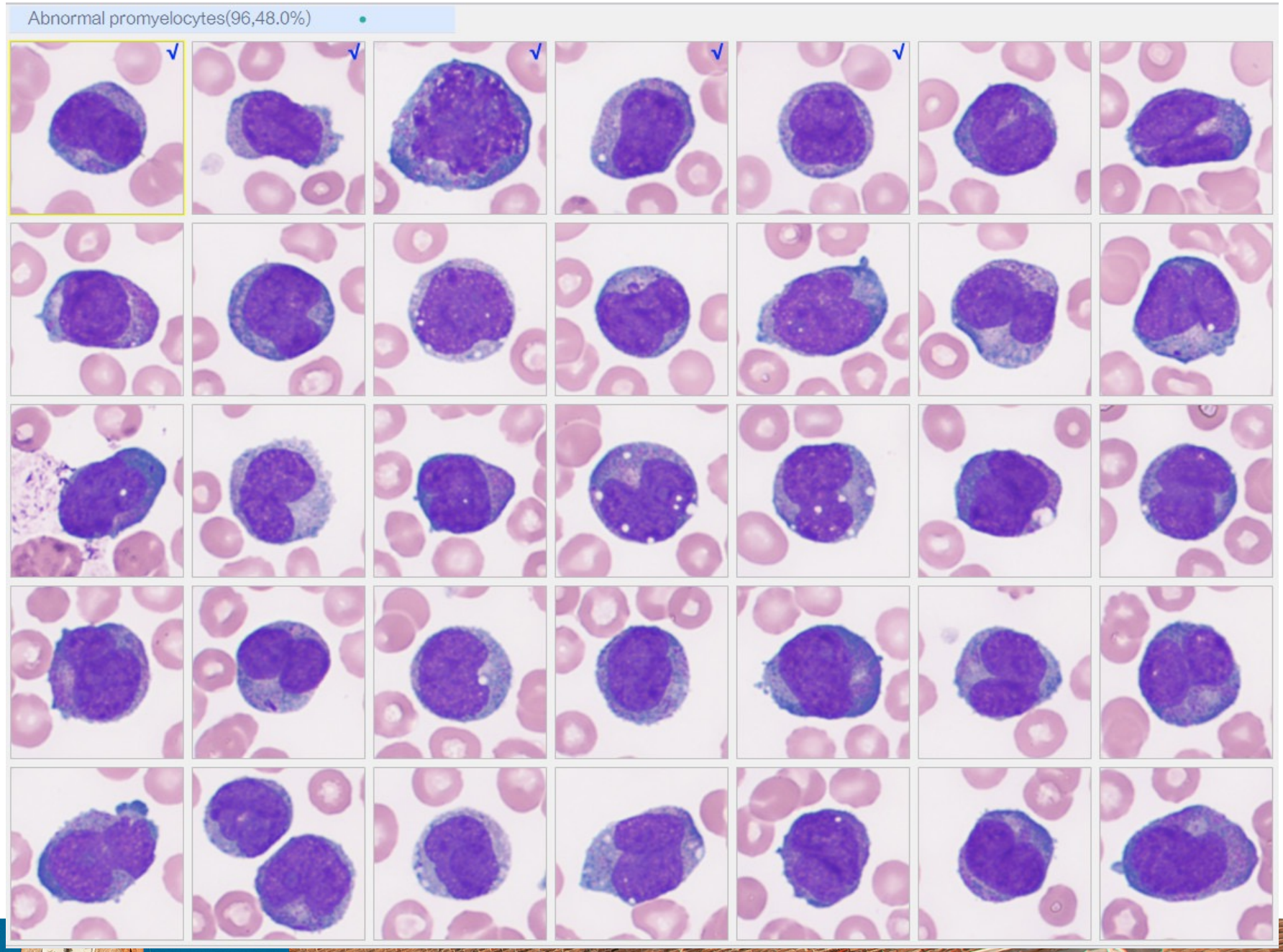
Monocytes, large Plts, NRBC

Automated DM applied to PB



Acute promyelocytic leukemia, hypergranular (treated)

Acute promyelocytic leukemia microgranular DGN



Thank you for listening

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