Artificial Intelligence – Hematology Laboratory

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Shortages in pathologists and lab staff are impacting support for intraoperative frozen section (IFS) consultation and rapid on-site evaluation (ROSE). Historically IFS and ROSE have required a pathologist's physical presence in the location where samples are being prepared. This webinar will examine how telepathology and whole slide imaging have advanced to a point where they can be used to convert support of IFS and ROSE from on-site to remote

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Presentation outline

- Automated digital cell morphology
  - Brief history / timeline
  - Systems on the market
    - CellaVision focus
  - Benefits
- Immunofluorescence patterns - AIM

ADCM

automated digital cell morphology

WBC, RBC and platelet pre-classifications operate as a decision support system (DSS), requiring the operator to review the pre-classified data generated by the system, approve, or correct it.

So far, DSS is the only mode cleared by the FDA for such analyzers.

- Adaptive Monolayer Detection algorithm, designed to identify the clinically relevant area and adapt for optimal review
- No instrument learning

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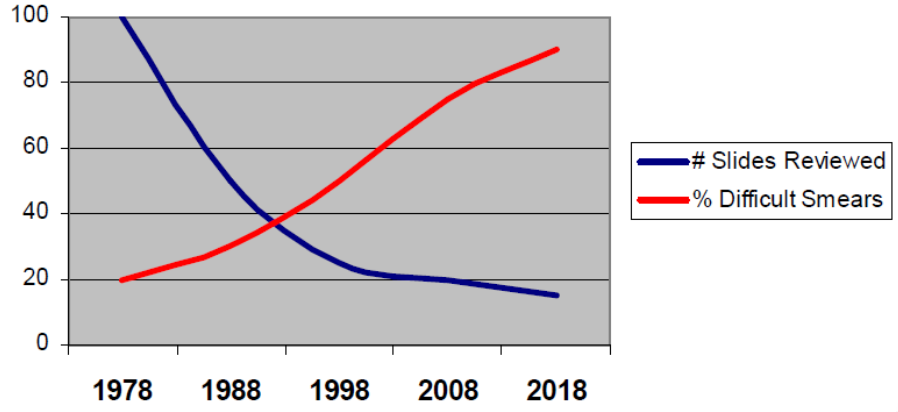
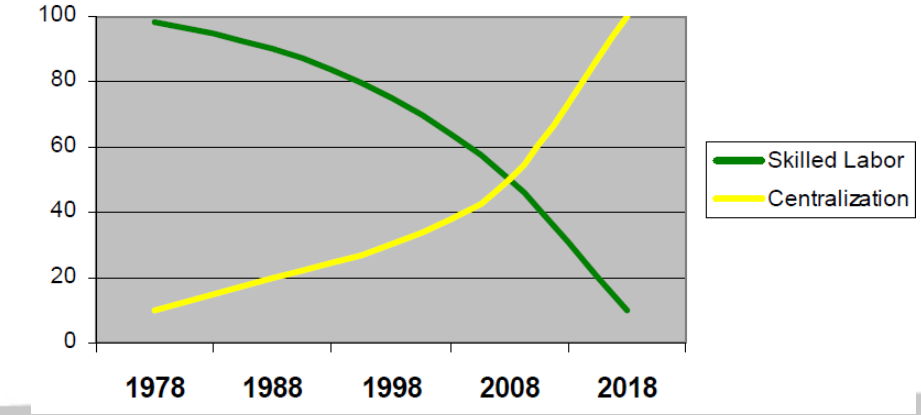
Goals for successful product and reasons driving implementation

- Improve efficiency in training MLT
  - Efficiency, proficiency, connectivity, ergonomics
- Real-time collaboration with Pathologist especially from remote facilities
  - Remove geographical constraints from smear review
- Declining availability of medical technologists
- Need for greater level of standardization and quality assurance
- Impact on Pathologist
  - Convenient access to pending slides for review
  - Easy image capture for use in applications
  - Remote access from home





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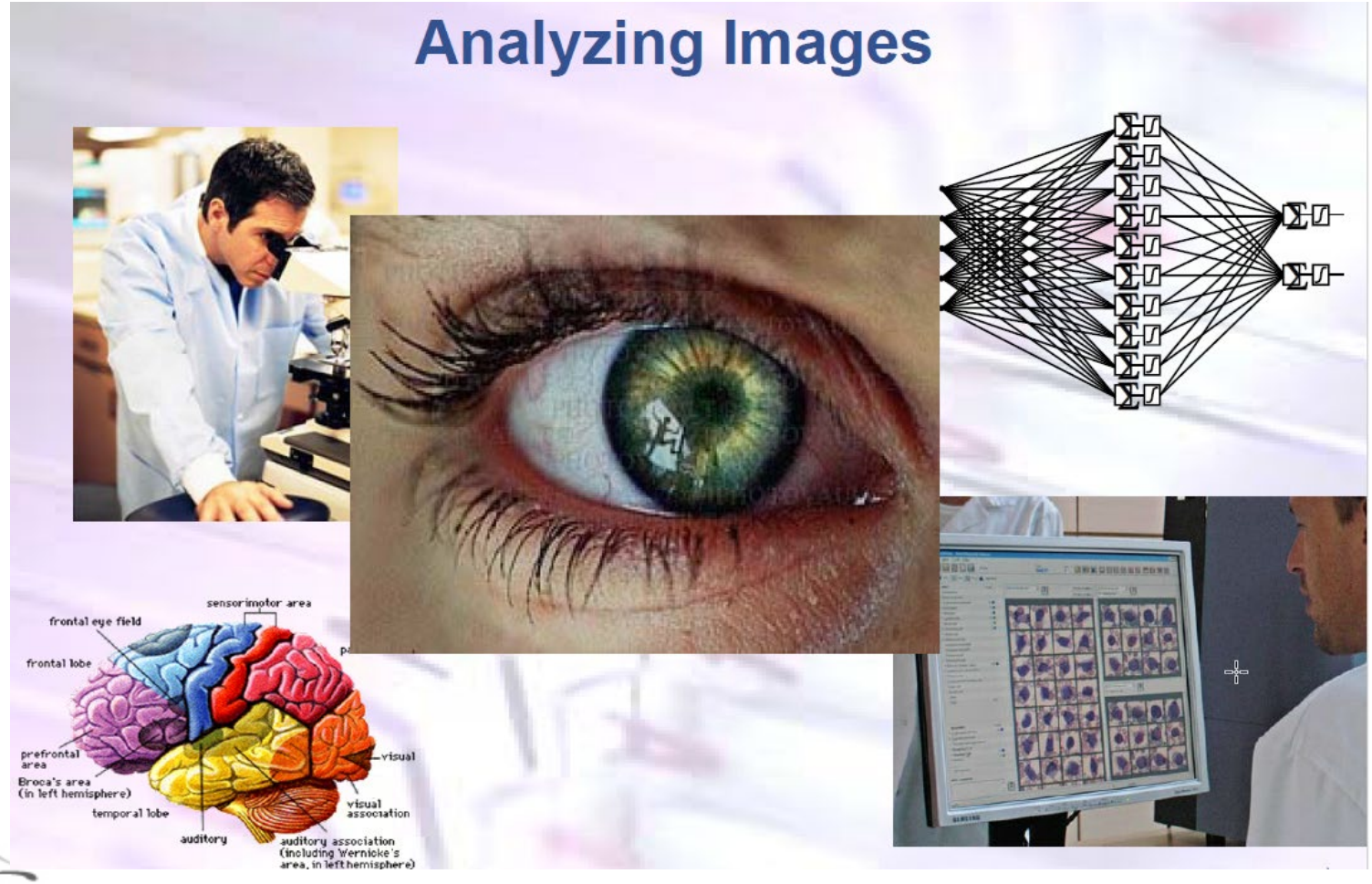
Pattern recognition



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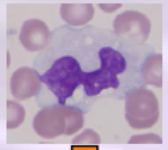
Input

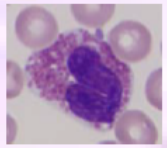


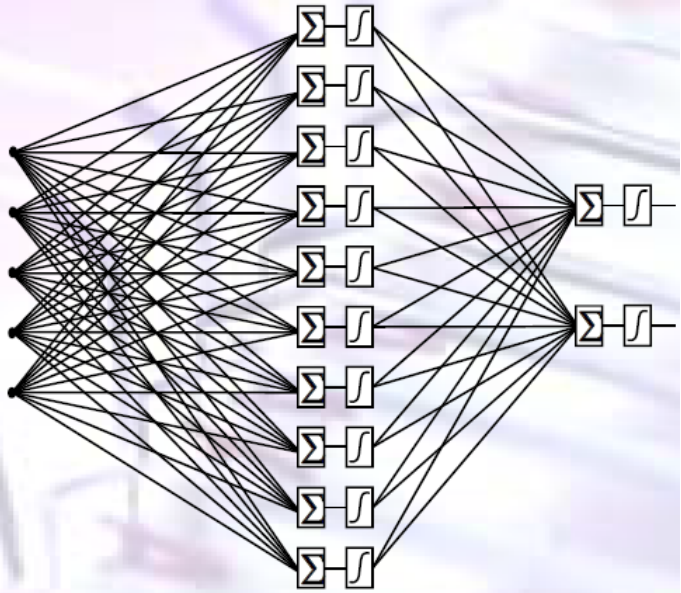
360 features based on 6 main groups:

- Form
- Colour
- Texture
- Detection
- Markov
- Wavelets

FEATURES

Feature extraction





ANN

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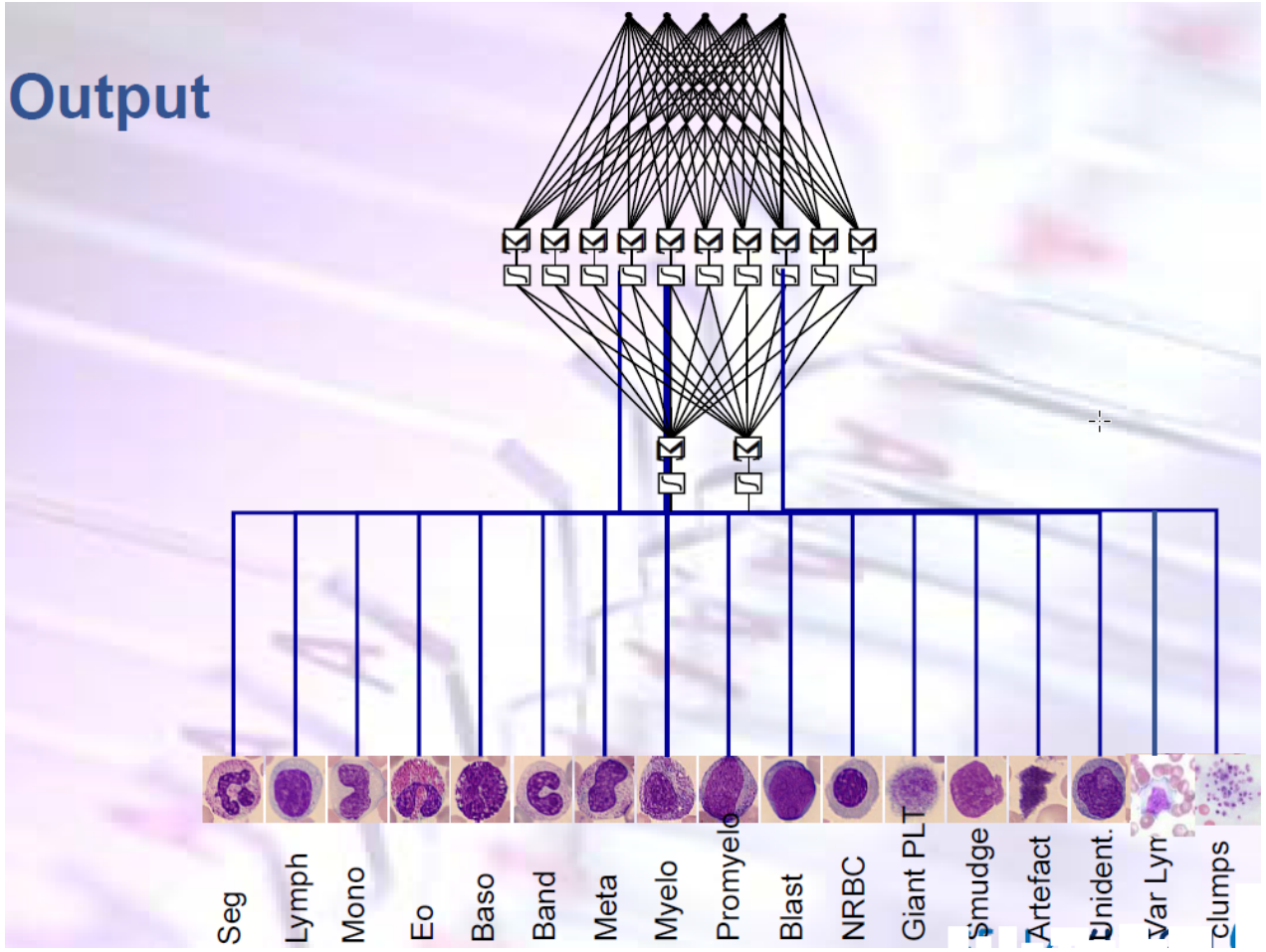
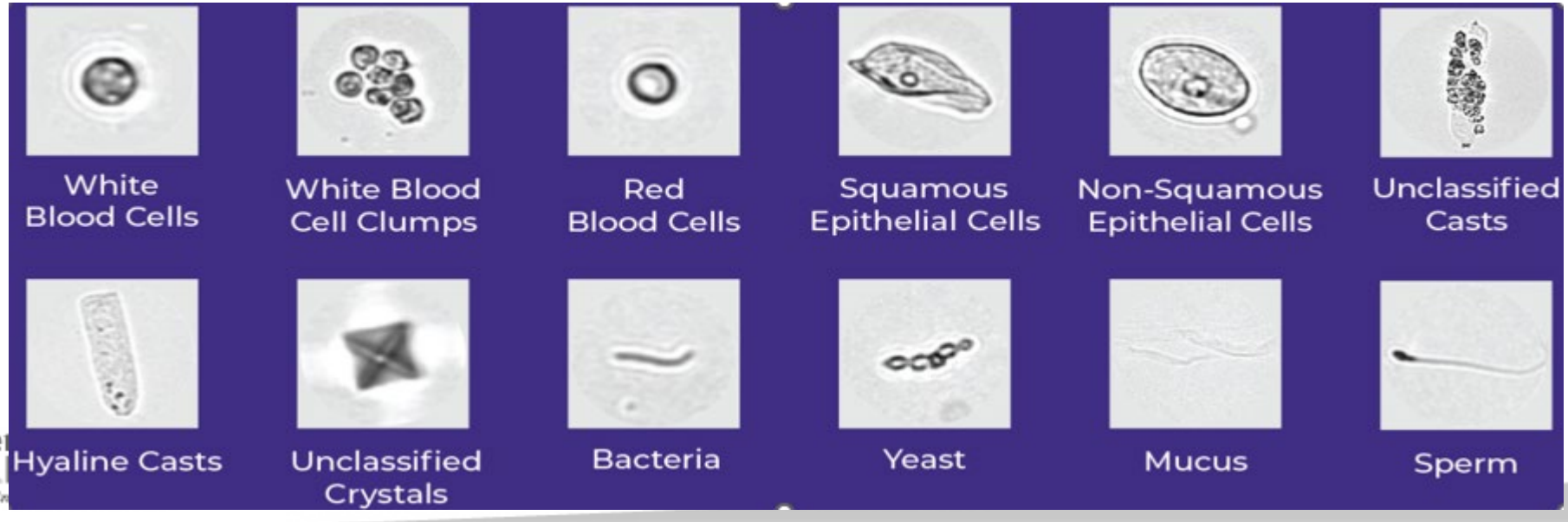
Output


Seg
Lymph
Mono
Eo
Baso
Band
Meta
Myelo
Promyelo
Blast
NRBC
Giant PLT
Smudge
Artefact
Unident.
Var Lym
Clumps

Urinalysis

DxU Microscopy Series Urine Microscopy Analyzer

- reducing manual microscopic review rates to less than 3%.
- achieved using Digital Flow Morphology technology + APR Software to capture digital images.
- APR Software evaluates the size, shape, contrast and texture of the urine particles and evaluates each digital image to identify and classify the urine particles into one of 12 primary categories. The operator has the option to further subclassify particles into 27 additional categories.



Pre-requisite for successful ADCM

- Ease of use
- Interface ease
- Throughput
- Good pre-classification rates
- Slide stain quality

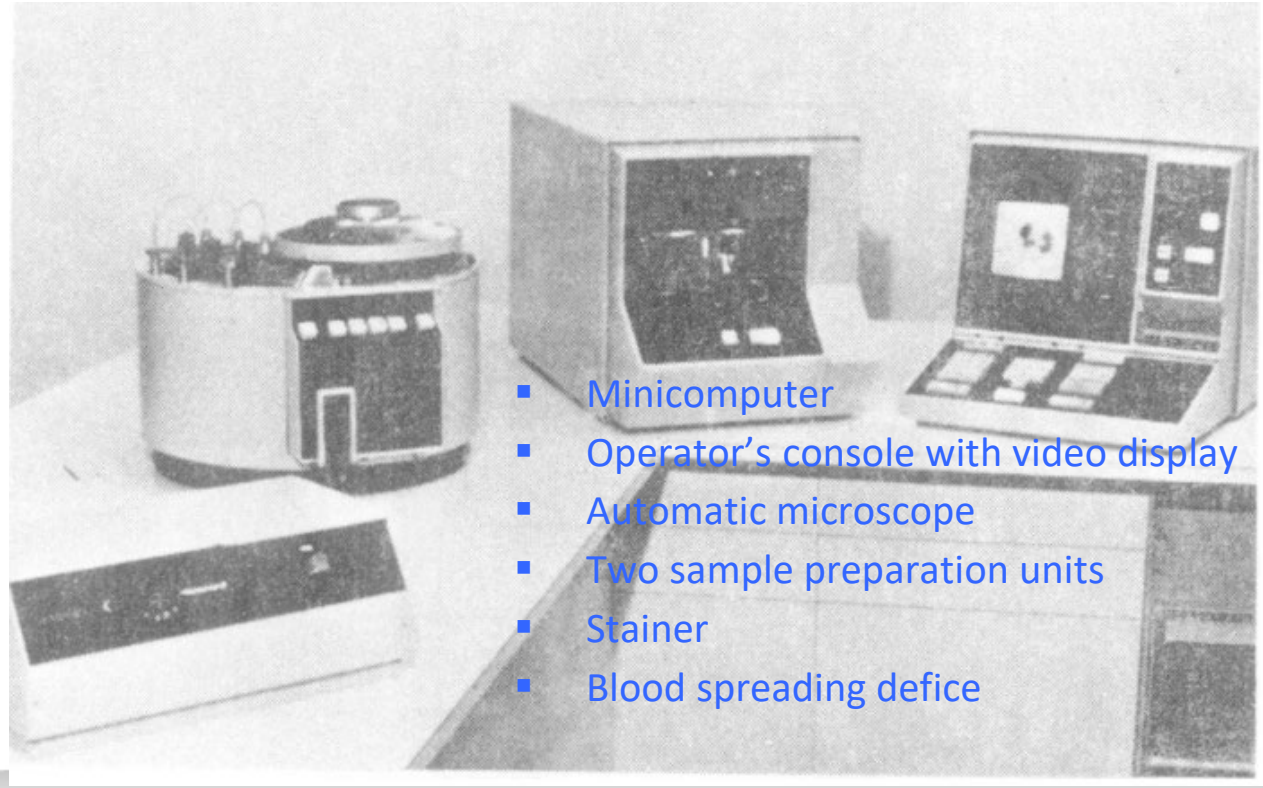
DIFF-Line (CellaVision):

a complete workflow for smearing, staining, and analyzing peripheral blood smears in hematology labs that handle a smaller amount of daily blood samples.

Brief history of digital morphology in Hematology

- Several attempts have been made to automate the identification of WBCs on a peripheral blood smear, dating back to the **1970s**. One of the first commercial image analyzers was the **LARC**® (Leukocyte Automatic Recognition Computer), manufactured by Corning Glass.
- The system required spun slides and could classify the five normal cell types. Abnormal cell types were placed in a separate category for manual review through the microscope oculars. The system used nine cell features and a decision tree for the cell classification.

- Tedious
- Time consuming
- Sensitive to subjective error
- Aim to improve quality of results



- Minicomputer
- Operator's console with video display
- Automatic microscope
- Two sample preparation units
- Stainer
- Blood spreading defice

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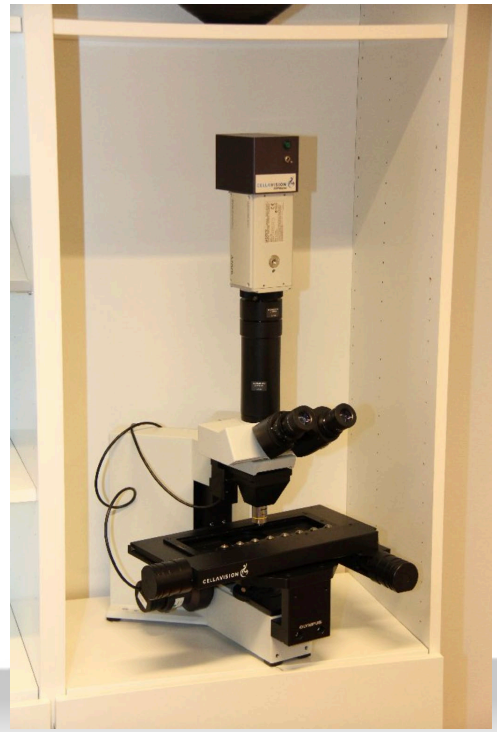
Brief history of digital morphology in Hematology

- Another analyzer, the **diff3**®, was developed by Perkin Elmer. It required spun slides and could classify 10 cell classes and could be loaded with a 14-slide magazine.
- **1980s**: Geometric Data Corp. Developed analyzer **Hematrak**®;
  used by more than 1000 laboratories at its height of popularity.
  Classification of the cells based on 100 extracted cell features

- In **1994**, CellaVision was founded in Sweden.



- In **2001**, CellaVision AB launched the **DiffMaster™ Octavia**.
  - modified standard microscope for high-speed movements
  - an automated 8-slide stage
  - a control box for illumination and stage movements
  - a high-speed CCD camera
  - software for pre-classifying white and red blood cells

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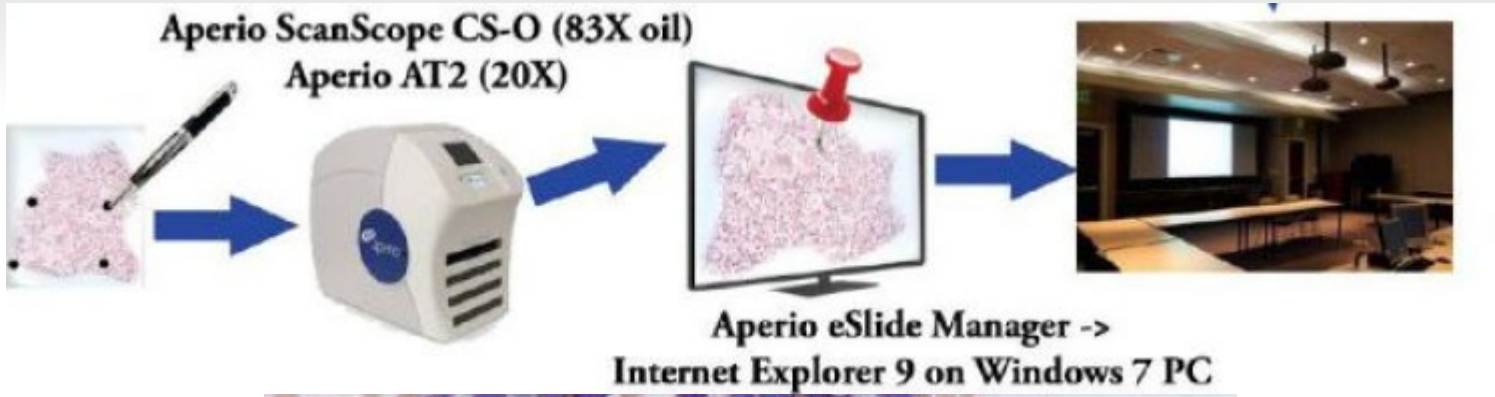
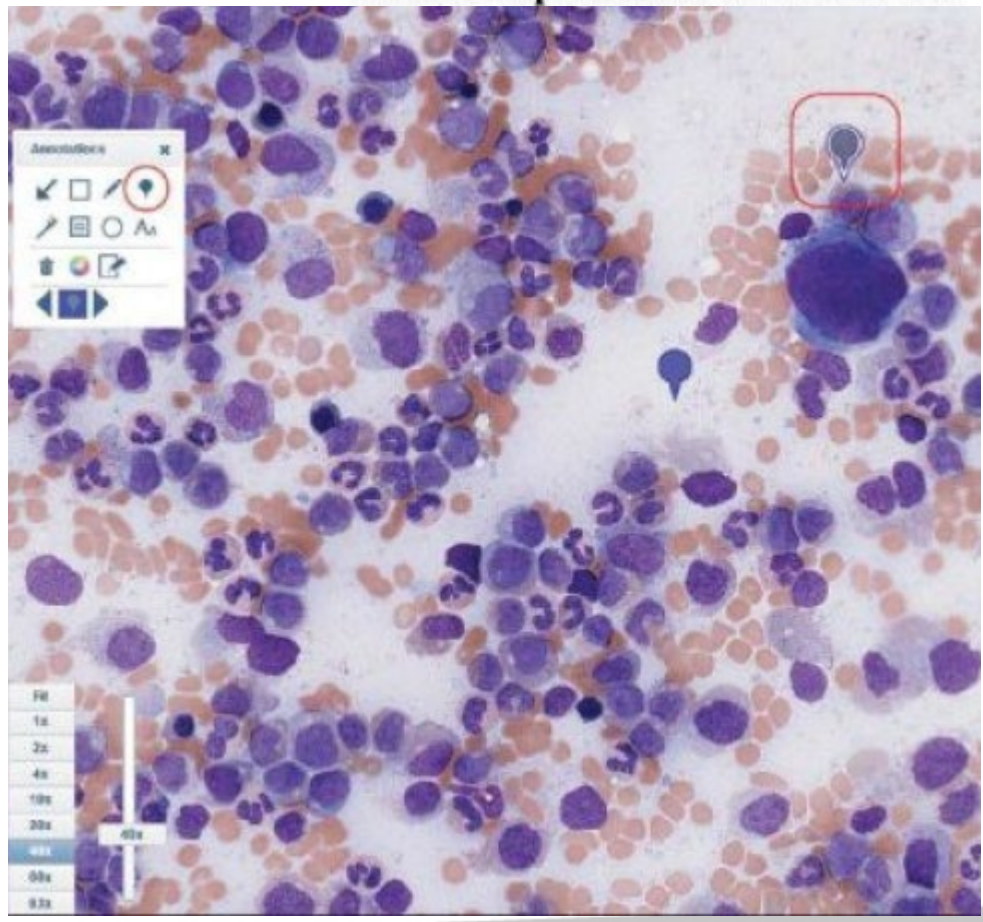
Aperio

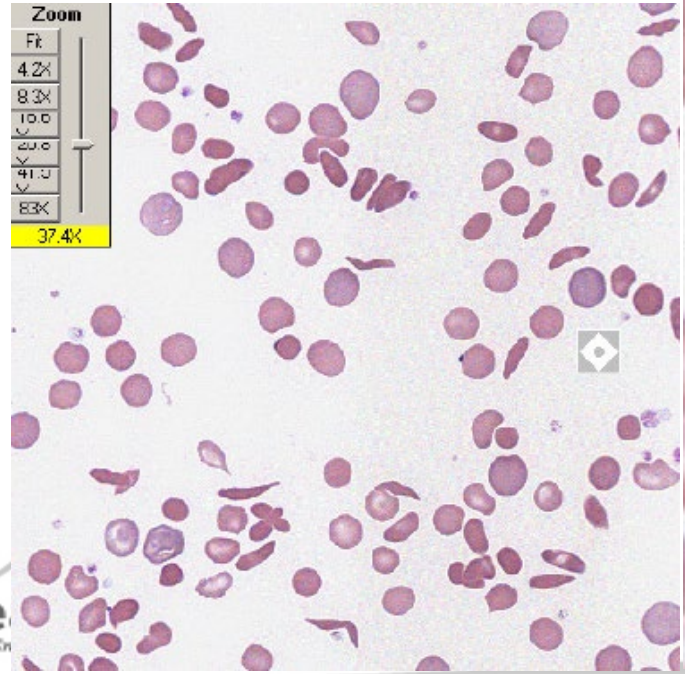


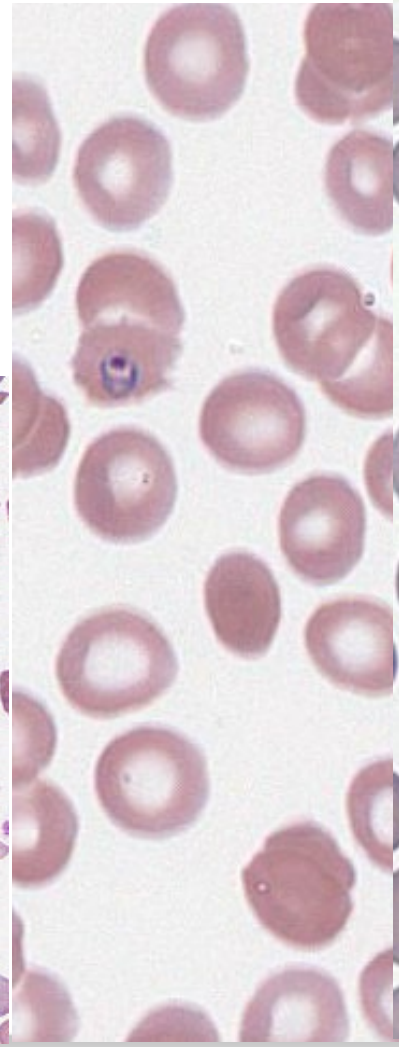
- Hi / lo power whole slide scanning
- High quality images
- No AI / pre-classification
- Does not meet large lab throughput needs

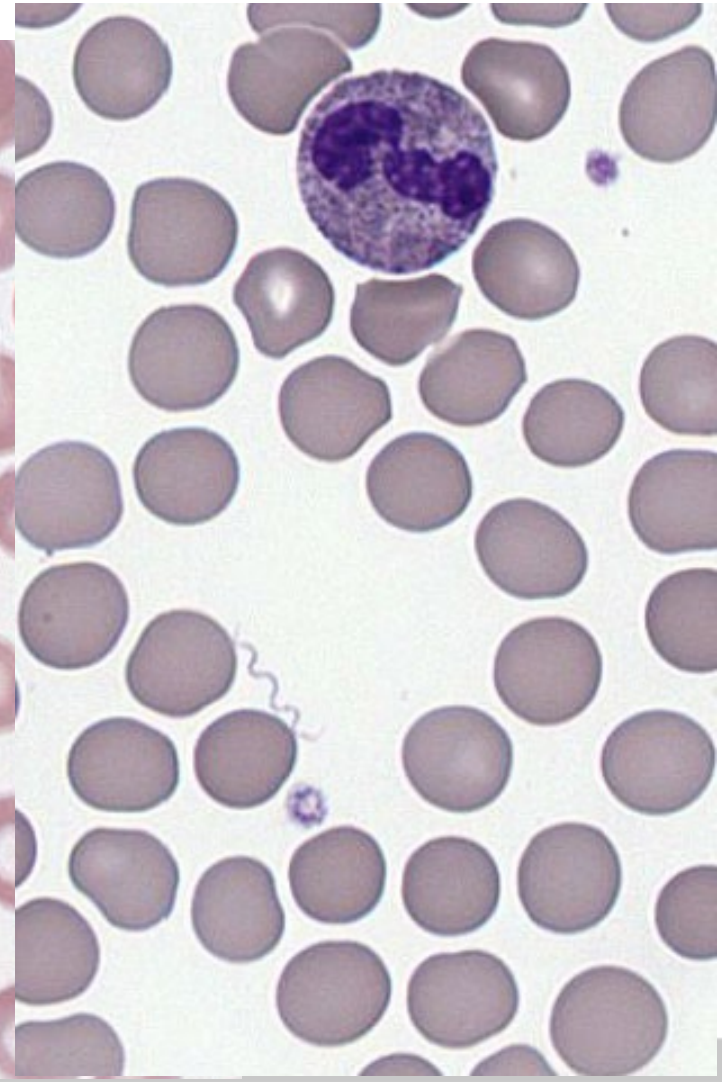


Panoptiq ViewsIQ

- Software
- PC
- Monitor
- Digital camera







Panoramic digital slide scanners

	Pannoramic DESK	Pannoramic MIDI	Pannoramic SCAN	Pannoramic 250 Flash II
Slide capacity	1	12	150	250

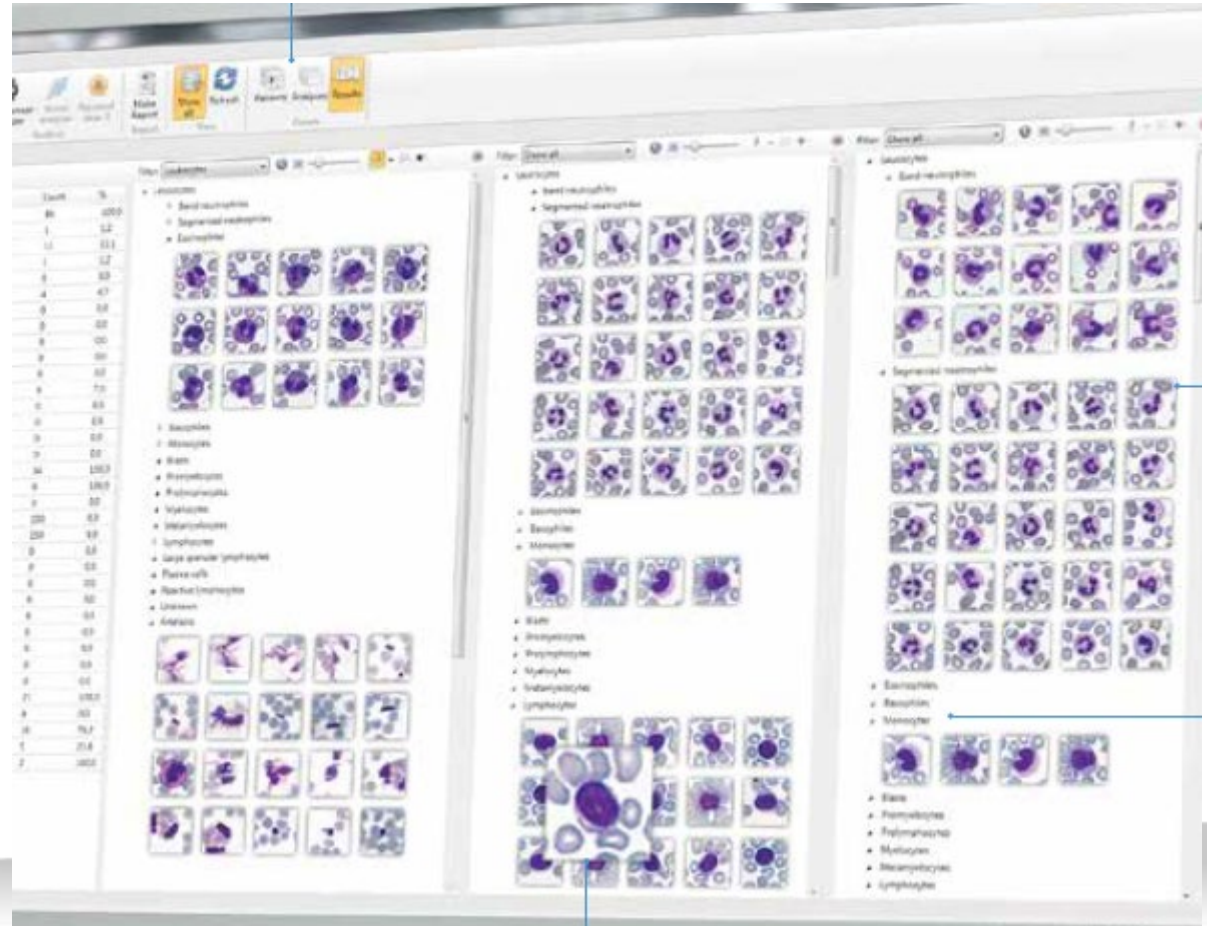
- High volume / auto loading
- No AI (pre-classification), LIS interface

Vision Hema Pro

Slide tray loading

Vision Hema Pro

- Autmoatic scanning
- ID and pre-classification of blood cells.
- Quick validation of results



Scopio Labs X100 Full Field PBS

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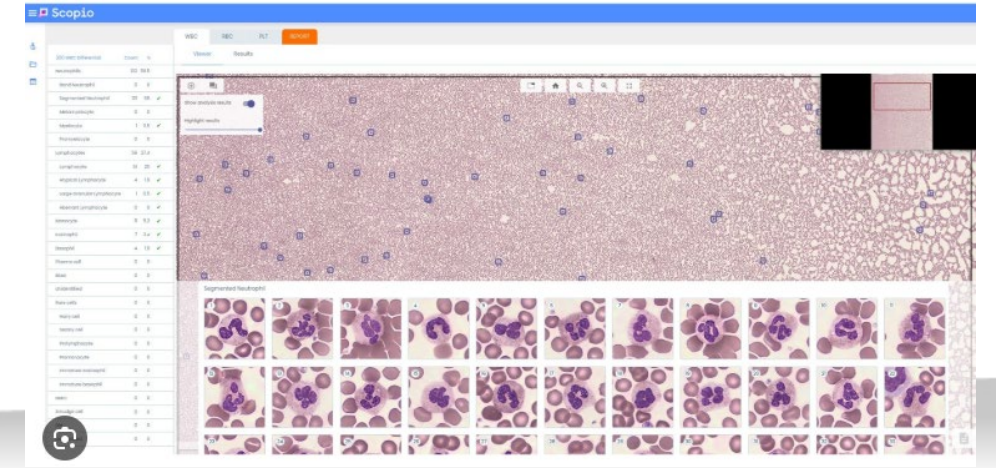
Scopio Labs X100 Full Field PBS

- High resolution full field viewing of peripheral blood specimens combined with AI-based morphological analysis
- Current digital cell imaging systems perform peripheral blood smear (PBS) analysis in limited regions of the PBS and require the support of manual microscopy without achieving full digital microscopy.
- WBC pre-classification via AI to neutrophils, lymphs, mono, eos, baso, pro, meta, meylo, blast, variant lymph, plasma cells, NRBC, smudge (same as cellavision)
- On average, scan and pre-classification times were 4 minutes per slide, but were up to 7 minutes for long smears. Slower than cellavision



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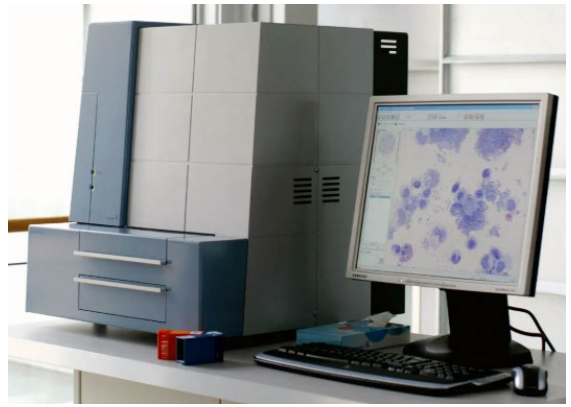
Brief history of digital morphology in VCH Hematology

- 2003: **CellaVision** DM96 VGH Oct 2007
  - 96 slide capacity, 8 magazines



- 2010: DM1200
  LGH 2010, RHS 2015

- 2014 DI-60

Integrated onto Sysmex cell counter line

CellaVision

360 features are calculated.

- Form
- Colour
- Texture (granules..)
- Detection (vacuoles..)
- Markov (probability functions)
- Wavelets
- Size
- Nuclear: cytoplasmic ratio…

Artificial Neural Networks

- Not about pre-classification accuracy but about providing tools to improve the speed and accuracy of the MLT

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WBC pre-classification accuracy

Pre-classification data absolute			
Cell-class	n1	n2	n3
Segmented neutrophil	3437	3436	3623
Eosinophil	182	182	186
Basophil	57	55	56
Lymphocyte	1306	1277	1414
Monocyte	452	423	429
Band neutrophil	185	0	0
Var Ly	62	3	3
Plasma	0	0	0
Promyelocyte	7	5	5
Myelocyte	45	42	43
Metamyelocyte	50	48	49
Blast cell	390	342	424
Smudge cell	77	77	77
Erythroblast (NRBC)	79.8	79.8	93.8
Artefact	14	0	4
Giant thrombocyte	0	0	0

Pre-classification data relative		
Cell-class	Pre-classifying agreement	In agreement with final result
Segmented neutrophil	100.0%	94.8%
Eosinophil	100.0%	97.8%
Basophil	96.5%	98.2%
Lymphocyte	97.8%	90.3%
Monocyte	93.6%	98.6%
Var Ly	4.8%	100.0%
Promyelocyte	71.4%	100.0%
Myelocyte	93.3%	97.7%
Metamyelocyte	96.0%	98.0%
Blast cell	87.7%	80.7%
Smudge cell	100.0%	100.0%
Erythroblast (NRBC)	100.0%	85.1%
Artefact	0.0%	0.0%
	Pre-classifying agreement	In agreement with final result
SN, Ly, Mo	98.9%	94.0%
SN, Ly, Mo, Bas, Band, Eos	95.6%	94.1%

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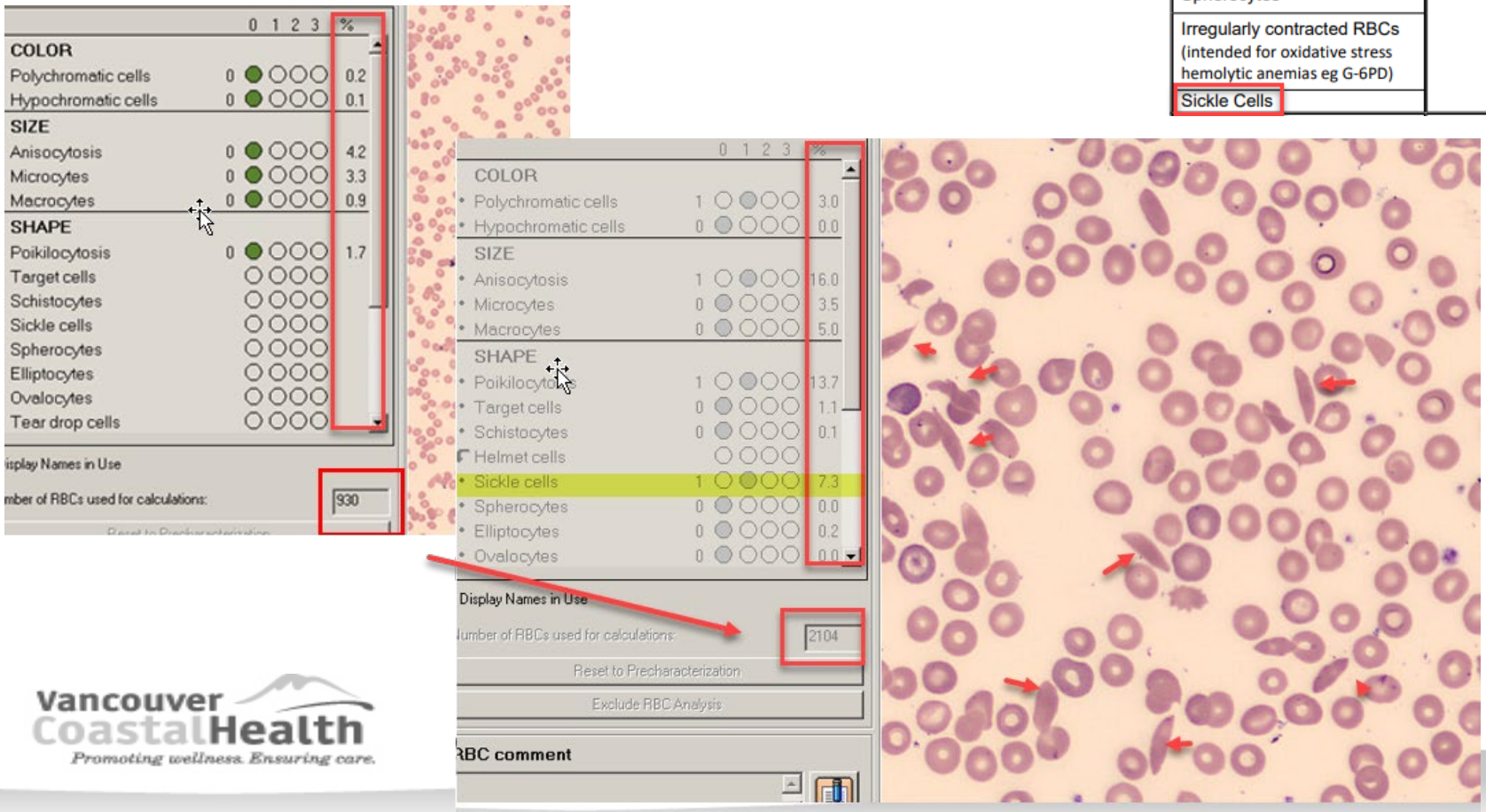
Advanced RBC Software - CellaVision

- ~ 2500 RBC vs ~ 900
- ‘persistent’ zooming
- Improved scan area

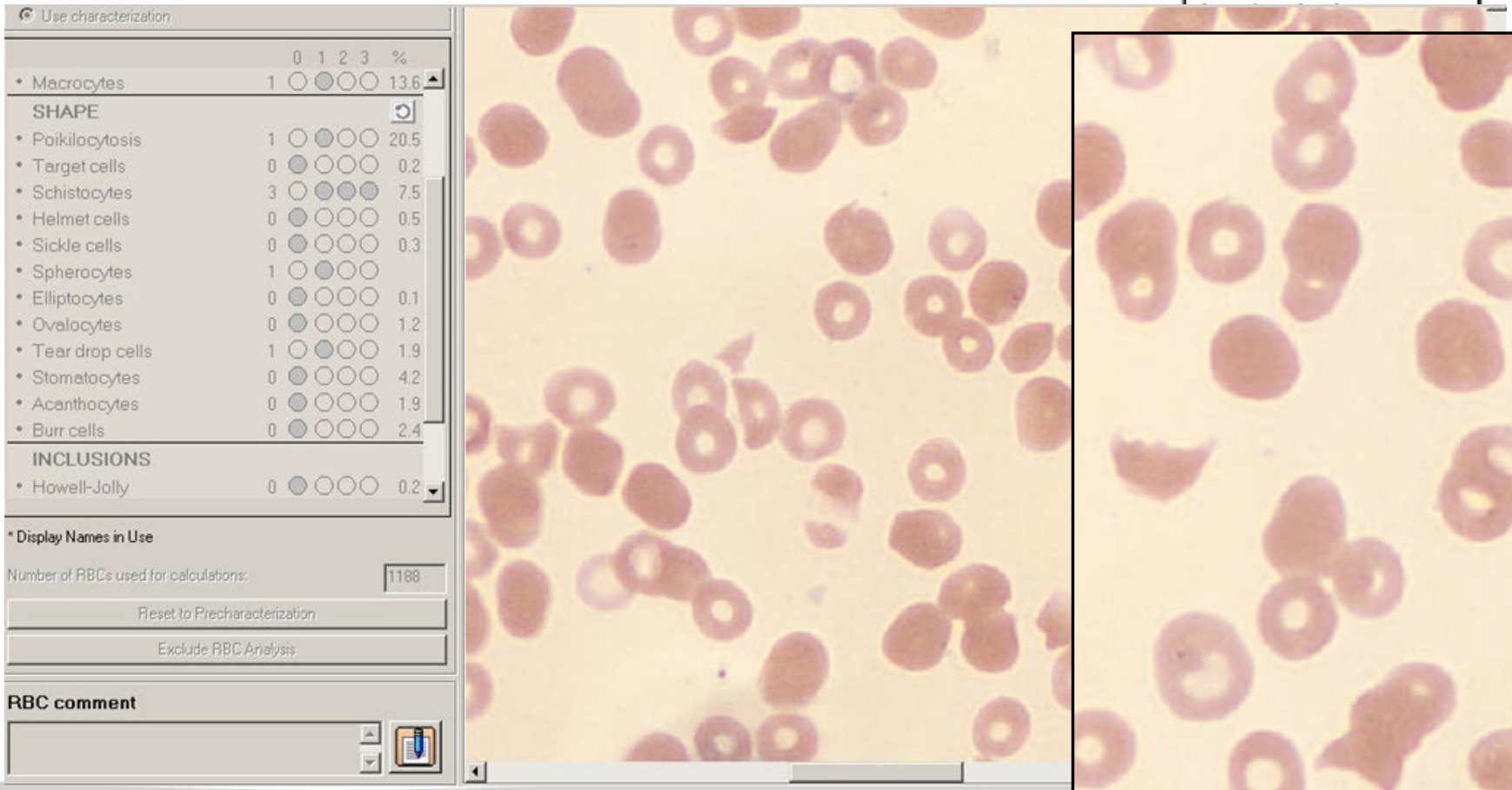
Parameter	Report as		Pathologist referral Criteria (First Time Only)	Critical Value Requires immediate pathologist consultation & phoning to the ordering physician or ward
Bite Cells Blister Cells Schistocytes **(includes Helmet cells) do NOT report in absence of thrombocytopenia / dropping platelets** Spherocytes Irregularly contracted RBCs (intended for oxidative stress hemolytic anemias eg G-6PD)	**2% - 20%** of RBC's affected: **Present**	**> 20%** of RBC's affected: **Many**	Refer **> 2%** fragmentation with thrombocytopenia and anemia	Severe anemia (HB <75 g/L) with spherocytes, polychromasia. Schistocytes and ↓ PLT (<100) or falling platelet count **+ / -** polychromasia
Sickle Cells			Refer any Sickle Cells not previously referred (confirmed)	Sickle cells – 1st time

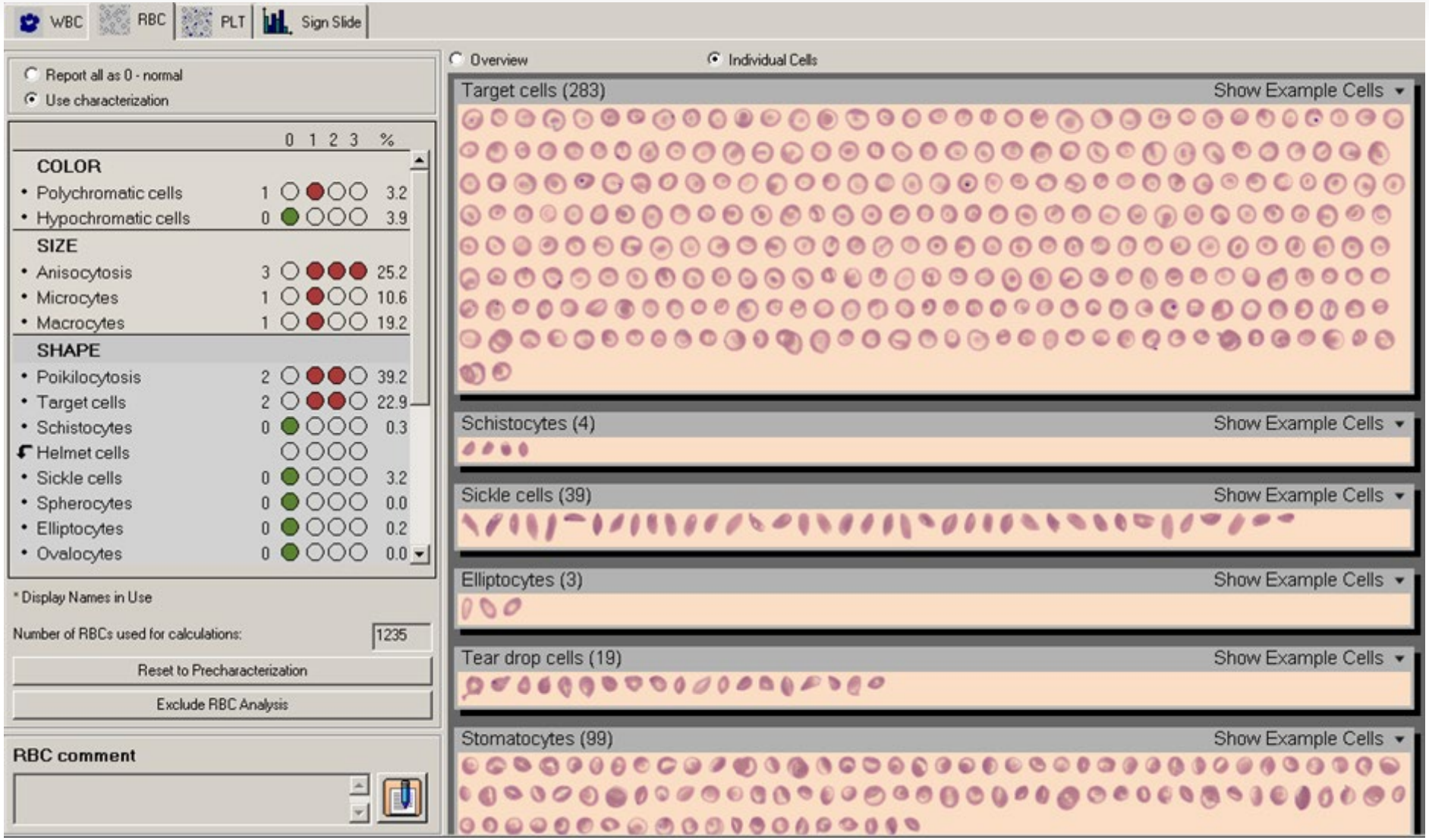


MAHA (micro angiopathic hemolytic anemia)

3050 Peripheral Blood Film Handling and Reporting

Parameter	Report as		Pathologist referral Criteria (First Time Only)	Critical Value Requires immediate pathologist consultation & phoning to the ordering physician or ward
Bite Cells Blister Cells Schistocytes **(includes Helmet cells)** **do NOT report in absence of thrombocytopenia /**	**2% - 20%** of RBC's affected: **Present**	**> 20%** of RBC's affected: **Many**	Refer **> 2%** fragmentation with thrombocytopenia and anemia …er any Sickle Cells …previously referred …nfirmed)	Severe anemia (HB <75 g/L) with spherocytes, polychromasia. Schistocytes and ↓ PLT (<100) or falling platelet count **+ / -** polychromasia Sickle cells – 1st time




WBC
RBC
PLT
Sign Slide
Report all as 0 - normal
Use characterization
0 1 2 3 %
COLOR
• Polychromatic cells 1 3.2
• Hypochromatic cells 0 3.9
SIZE
• Anisocytosis 3 25.2
• Microcytes 1 10.6
• Macrocytes 1 19.2
SHAPE
• Poikilocytosis 2 39.2
• Target cells 2 22.9
• Schistocytes 0 0.3
Helmet cells
• Sickle cells 0 3.2
• Spherocytes 0 0.0
• Elliptocytes 0 0.2
• Ovalocytes 0 0.0
* Display Names in Use
Number of RBCs used for calculations: 1235
Reset to Precharacterization
Exclude RBC Analysis
RBC comment
Overview
Individual Cells
Target cells (283) Show Example Cells
Schistocytes (4) Show Example Cells
Sickle cells (39) Show Example Cells
Elliptocytes (3) Show Example Cells
Tear drop cells (19) Show Example Cells
Stomatocytes (99) Show Example Cells

Brief history of digital morphology in VCH Hematology

- 2019: CellaVision DC-1

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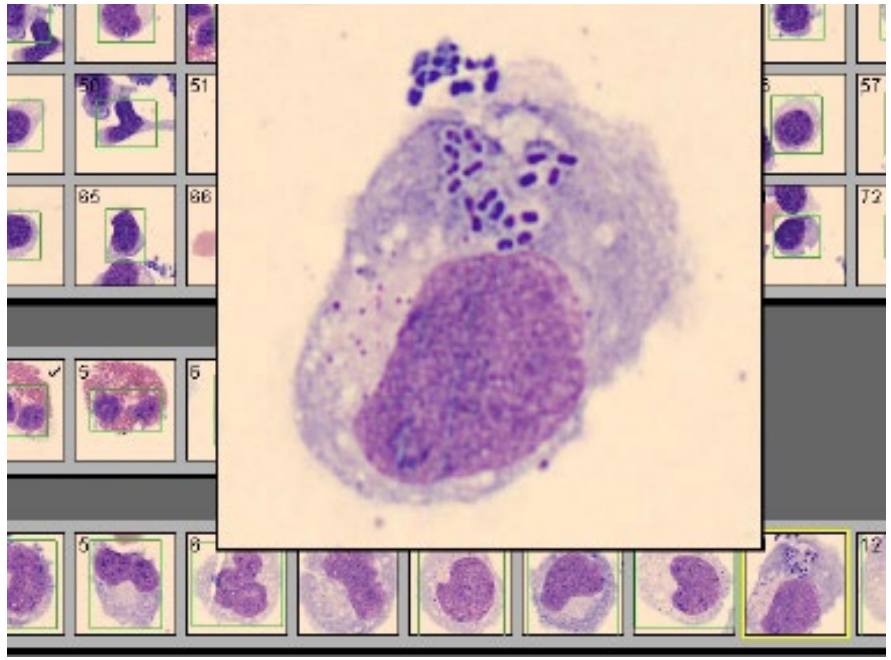
Body Fluid software

- 10 User-defined body fluid WBC classes
- 5 User-defined body fluid non-WBC classes
- CellaVision pre-classifies:
  - Neutrophils
  - Lymphocytes
  - Eosinophils
  - Macrophage
  - Other
  - Smudge cells
  - Artefact
  - Unidentified



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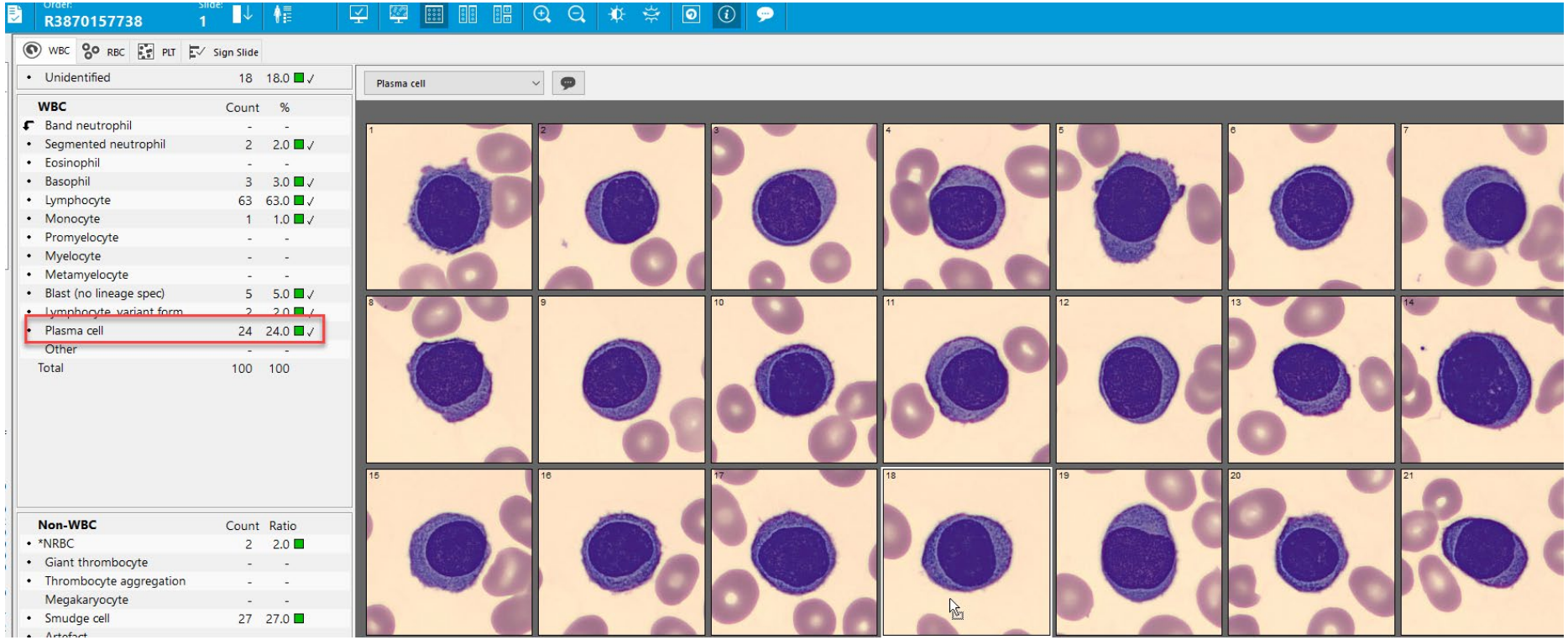
Cellavision

Future applications – no momentum

- Malaria
  - Less compelling in age of NAT / PCR
- Bone marrow neural network
  - Inconsistent thickness of films
  - dysplasia

Inherent bias in people, no inherent bias in ANN



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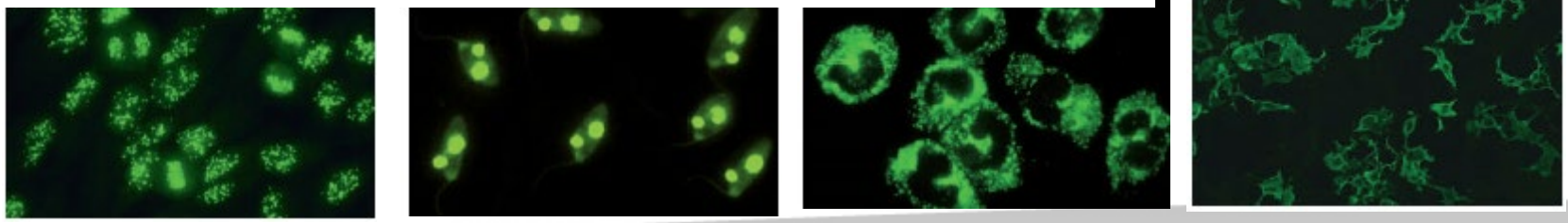
Immunofluorescence Patterns – AIF

- Automated IIFT pattern recognition and calculation of the antibody titer based on deep learning/deep convolutional neural networks
- Security and traceability thanks to automated identification of slides by means of matrix codes

Performance analysis of automated evaluation of antinuclear antibody indirect immunofluorescent tests in a routine setting

concordance of 99.3% was observed within the range of 1 titer step difference between EPa and observer.

Conclusions The ANA IIF results reported by the EPa software are in very good agreement with the results reported by the observer with respect to being negative/positive, pattern recognition and titer, making automated ANA IIF evaluation an objective and time-efficient tool for routine testing.



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