cancilico
AI DIAGNOSTICS

Instructions for use

MyeloAID-RUO

Version 1.0

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For Research Use Only

Preface

We would like to thank you for the purchase of our product. MyeloAID-RUO is an AI-based software to digitize morphological differentiation of bone marrow for research use only.

If you have any questions about the content of these instructions for use or the use of the product, please contact us support@cancilico.com. Your opinion is important to us. Please feel free to let us know your wishes and criticism regarding the product. We will analyse your feedback and take it into account for the next version.

Your Cancilico Team

Table of contents

1 General Information

1.1 License Terms, Citation

If you use the Cancilico Research Suite for research and studies, please mention our software in your publication:

- Reference List Entry: Cancilico GmbH. (2025). MyeloaAID RUO (Version 1.0) in PathoZoom Scan & LiveView.
- In-Text: “The analysis was conducted using the Cancilico MyeloAID-RUO (Version 1.0).”
- Your right to use the Software is contingent upon a valid license obtained through Cancilico or one of our valid partners.
    - Subscriptions for use of MyeloAID-RUO are currently available at: Smart in Media AG.
    - Purchasing Smart in Media's “Pathozoom Scan & Live View” product, includes up to 20 free analyses with MyeloAID-RUO. For usage exceeding this limit, a separate subscription based on usage volume must be acquired through Smart in Media. Your right to use the Software beyond the free tier is contingent upon maintaining a valid and active subscription with Smart in Media.

The license terms of the currently valid end-user license agreement (EULA) apply. These can be viewed at https://cancilico.com/eula-sim-ruo/

2 Intended Purpose

2.1 Research Use Only

MyeloAID-RUO is a stand-alone software used for the morphological differentiation of digital bone marrow aspirates for research use only (RUO).

Unlike in vitro diagnostic medical devices (IVDs), RUOs are dedicated to facilitating research initiatives and are not intended for direct medical procedures with human patients. RUO products can be used for Fundamental Research or Pharmaceutical Research, for example. In essence, RUO products provide researchers and physicians with the necessary tools to conduct experiments and studies, contributing to the overall progress in medical research. Their intended use in laboratory settings supports the development of new technologies and innovative solutions for various research applications.

2.2 Functions

MyeloAID-RUO detects, counts, and classifies nucleated cells into cell classes by quantitative and qualitative measures based on AI models (see chapter 4 for more details on cell classes).

The area to be analyzed runs through a quality check and the detection model to detect the nucleated cells. Each detected cell is assigned an ID, coordinates and a bounding box. The classification model then assigns each cell to one cell class on the basis of training data. Optionally, user corrections in the form of changes in the assigned cell classes can be fed back as input to the software module. The results of the analysis are shown as a frequency distribution of the cell classes.

2.3 Supported samples

2.3.1 Sample preparation

Bone marrow samples are collected by a medical technical assistant, nurse, or physician from aspirates or trephine biopsy of iliac crest, tibia or sternum.

Bone marrow smears are prepared without delay after aspiration. Bone marrow smears should be dried for at least 30 minutes before staining.

2.3.2 Properties

The Cancilico Research Suite supports samples with the following properties.

Table 1: Properties of digitized microscope images

	Digitized Microscope Images
Samples	bone marrow aspirate smear
Stains	May-Grunwald-Giemsa
Formats	• .png (Portable Network Graphics) specification: https://www.w3.org/TR/2003/REC-PNG-20031110/ • .jpg/.jpeg (JPEG File Interchange Format) specification: https://www.w3.org/Graphics/JPEG/jfif3.pdf
Recommended Image Resolution	0.12 mpp (microns per pixel) to 0.02 mpp
Recommended Image Size	30x30 to 400x400 microns

3 Important notes

Please note that:

- The analysis tools are AI-based and have been trained using selected data. Our data corpus does not cover 100% of possible diseases, age ranges and scanner/microscope hardware which is why there may be uncertainties in the analysis of the AI. Please check the results conscientiously.
- MyeloAID has been trained on images taken with the following microscopes and scanners, results on other imaging hardware may vary:
    - Pannoramic SCAN 150
    - Pannoramic SCAN 1000
    - Glissando 20SL
    - Nikon Eclipse Ni-L
    - Axio Imager Z2
    - Nikon Eclipse E600
    - Bioview Duet 3
- MyeloAID does not filter input images, it will still execute and try to find and classify cells on samples with different stainings, different tissues and even on nonsensical input images.
- Please calibrate your microscope/scanner according to the manufacturer's instructions before using the AI analysis. Wrong magnification calibration will lead to dramatic degradation of prediction accuracy
- Your changes to the analysis results of the AI will be analyzed and potentially incorporated as feedback into the training of the AI in order to improve it. We store the correction data for this purpose.
- Please review table 2 to see exactly how cell classes that MyeloAID outputs are defined. Especially review which cells are and are not classified as blasts

4 Cell Types

Table 2: List of cell types distinguished by the AI. Classes marked with an asterisk do not count to nucleated differential count (only total number of objects). Definitions of cell types were created with our experts and derived from "Atlas der klinischen Hämatologie" (Löffler, H., Rastetter, J., & Haferlach, T., 2004) and ICSH guidelines.

Cell Types	Key Features
Blast	• Large cell with round/oval nucleus (12-20 µm in diameter) • high nuclear-cytoplasmatic ratio • Fine, dense chromatin pattern • 2-6 well-defined, light blue nucleoli • Minimal or no granulation • Scant basophilic (light blue) cytoplasm **ATTENTION:** • Megakaryoblasts are classified as **Megakaryocytes**, not as **Blasts** • Monoblasts (blasts with discrete monocytic features) are classified as **Blasts**
Myeloid Lineage - Neutrophil	
Promyelocyte	• Larger than blast (20-25 µm in diameter) • Round nucleus with up to 6 nucleoli • Abundant and coarse primary/non-specific azurophilic granules • Visible Golgi zone (lighter area near nucleus) • bluish to lighter blue cytoplasm **ATTENTION:** • Atypical Promyelocytes are classified as **Promyelocytes,** not as **Blasts**!

Myelocyte	• smaller than promyelocyte (14-20 µm in diameter) • Oval/eccentric nucleus, rarely nucleoli • Nucleus-to-cytoplasm ratio approximately 1:1 • Specific granules appear (neutrophilic, eosinophilic, or basophilic) • cytoplasm is lighter with a faint blue hue
Metamyelocyte	• Kidney-shaped/indented nucleus • Indentation less than halfway across nucleus • No nucleoli • Abundant specific granulation
Band Granulocyte	• Nucleus shaped like a curved band/horseshoe • No segmentation or early segmentation • Condensed chromatin • Abundant specific granulation • Nuclear ends may nearly touch but remain separate
Segmented Granulocyte	• 3-5 (rarely more) nuclear segments connected by thin filaments • Condensed chromatin • Cytoplasm filled with specific granules • Most mature form with maximum granulation • size 10-15 µm in diameter
Eosinophil	• Abundant large bright orange-red granules • immature eosinophilic cells may appear “dirty” due to basophilic cytoplasm, those immature eosinophils may have azurophilic granules in addition to the orange-red granules
Basophil	• Coarse dark purple-blue granules • granules often obscure nucleus
Monocyte	• Large cell with abundant cytoplasm • Kidney-shaped/lobulated/folded nucleus, comprises 50% or less of cell volume

	• Fine, lacy chromatin • Gray-blue cytoplasm with occasional fine azurophilic granulation, characteristic "ground glass" appearance • May have vacuoles in cytoplasm • May show pseudopods during motility • No visible nucleoli • 12-20 µm in diameter **Distinctive features:** • Characteristic horseshoe/kidney-shaped nucleus • Highest cytoplasm-to-nucleus ratio of the three stages (Promonocyte, Immature Monocyte, Monocyte) • Mature "ground glass" cytoplasmic appearance • Most prominent vacuolization • May show cytoplasmic projections
Lymphoid Lineage	
Lymphocyte	• Small to medium size (6-9 µm, smaller than neutrophils) • Dense, round, eccentric nucleus that nearly fills the cell • the nucleus has typically the size of an erythrocyte (~7 µm) • Condensed chromatin • Thin rim of clear blue cytoplasm • No granulation or occasional azurophilic granules
Plasma Cell	• Medium to large cell 14-20 µm in diameter • intense basophilic cytoplasm • prominent golgi zone attached to the eccentric nucleus in a “half-moon” shape (shape is often referred to as a “fried egg”) • If plasma cells group in 2 to 3 cells it is often an indicator for malignant plasma cells • infrequently they may appear with an azurophilic rim (so called “burning plasma cell”)

Erythroid Lineage	
Proerythroblast	• a large cell with a high nuclear-to-cytoplasmic ratio • fine chromatin • visible nucleoli • deeply basophilic cytoplasm • 15-22 µm in diameter • occasionally white spots/margins in the cytoplasm close to the nucleus
Erythroblast	Supercategory for **Basophile Erythroblast, Polychromatic Erythroblast, Orthochromatic Erythroblast** **Basophile Erythroblast:** • Smaller than a proerythroblast (8-15 µm in diameter) • nuclear-to-cytoplasmic ratio shifts towards cytoplasm • more condensed chromatin • usually no visible nucleoli • intensely basophilic cytoplasm **Polychromatic Erythroblast** • Characterized by a smaller, more condensed nucleus • greyish or lilac appearance, color may appear fainter than in basophil erythroblasts but not as faint as in orthochromatic erythroblasts **Orthochromatic Erythroblast** • smaller than predecessors (7-10 µm in diameter) • small, dense, pyknotic nucleus (often eccentric) • faint gray-bluish cytoplasm
Erythrocyte*	• Standard size 7-8 µm in diameter • No nucleus • Consistent pink/salmon color on Wright-Giemsa stain • No basophilic staining (no RNA)
Megakaryocyte Lineage	

Megakaryocyte*	• Very large cell (40-100 µm) • Multilobed nucleus • Abundant granular cytoplasm • Platelets form at the periphery (can be seen as protrusions on the outer margins of the cell) • Young megakaryocytes have dark blue cytoplasm, 1-2 nuclei and only scarce reddish granules, they may be slightly larger than promyelocytes **ATTENTION** • All stages of megakaryopoiesis are listed under 'Megakaryocyte' including Megakaryoblasts.
Thrombocyte*	• platelets (thrombocytes) are anucleated cytoplasmic fragments • typically 2-4 µm in diameter
Stromal Cells	
Mast Cell	• Normally within a spongiosa particle, can be outside a particle, • Filled with abundant deep purple, fine granular granules • Due to smear technique, mast cells outside a particle often appear with a "tail" and are typically "bursted" • Mastoblasts or promastocytes have a relatively large nucleus with a blurred structure and sparse granulation • Mastocytes are large cells (15 - 30 µm in diameter) and have a round, compact nucleus that is similar in structure to that of lymphocytes or plasma cells
Macrophage*	• Typically a large cell (often 15-80 µm in diameter) • abundant, often irregularly shaped (ameboid) cytoplasm that can appear pale blue-gray and may contain vacuoles or visible ingested material (e.g., cellular debris, old red blood cells, pigment like hemosiderin)

	• nucleus is usually eccentric (off-center), and can be round, oval, kidney-shaped (reniform), or indented, with chromatin that is often finer or more dispersed than that of a monocyte, though it can also be more condensed • Nucleoli may or may not be prominent
Other	
Smudge Cell*	• Any object clearly identifiable as a destroyed cell **ATTENTION:** • Smudge Cell definition is different from Smudge Cell definition in peripheral blood
Mitotic Cell*	• Any cell that is currently undergoing mitosis • Absence of distinct nuclear membrane
Apoptotic Cell*	• Any cell that is clearly undergoing programmed cell death • most cells are shrinking • nucleus is pyknotic • cell rim is typically intact • sometimes, original cell is no longer identifiable
Fat Vacuole*	• round/oval, colorless • usually larger than most nucleated cells
Not Recognizable (NR) Cell medical*	• Any object, that is clearly identifiable as a nucleated cell, but difficult to classify into the given categories due to morphological/pathological reasons
Not Recognizable (NR) Cell technical*	• Not identifiable non-nucleated cells or nucleated cell, that is not identifiable due to **technical reasons**, e.g.: pixel resolution, staining errors, damaged or corrupted sample, out of focus or blurry, corrupted image data

Artifact*	• Any object, that is not a cell (and not a Fat Vacuole) • e.g. staining residual, cytoplasmic remnants, remnants of completely destroyed cells
Other cell*	• Any cell, that does not fit into the other cell types • eg.: skin cell

5 Use of the product

Please refer to Smart in Media's PathoZoom® Scan & LiveView user manual for instructions on how to use the product.

6 Maintenance

6.1 Troubleshooting

6.1.1 Image Quality Guidelines

Many analysis issues stem from image quality problems. Before contacting support, ensure your images meet these requirements:

- **Magnification**: images are recommended to have **0.12 mpp or less**. This can be achieved with microscopes/scanners with 40x or higher magnification, depending on adapter magnification, camera sensor size and other hardware factors. Please check your imaging hardware specifications for the exact values
- **Proper focus** - cells should have sharp, clearly defined borders and visible granules.
- **Appropriate brightness and contrast** - avoid over- or under-exposed images
- **Clear cell morphology** - nuclei and cytoplasm should be distinguishable
- **Correct microns-per-pixel (mpp) calibration** - do not rescale images after capture
- **May-Grunwald-Giemsa staining** - other stains are not supported

6.1.2 Common Issues and Solutions

Issue	Possible Cause	Solution
Performance Issues		
Image analysis is very slow	The AI model requires a warmup period of up to 30s. Regular warmup occurs in the background.	Wait 30s before continuing. If analysis still takes more than 5s per image, contact support.

Software unresponsive or crashes	This is most likely caused by the product integrating MyeloAID. Common issues are related to browser cache issues, memory overload, or system resources exceeded	Refer to the vendor's FAQ. Common solutions: - In a web application, refresh browser (F5), clear cache or try a different browser. - In a desktop application, restart the software and close other applications to reduce system load.
Analysis Quality Issues		
Analysis failing with "bad request" error	Image contains no nucleated cells or severe quality issues	Refer to Section 6.1.1 Image Quality Guidelines. Move to an area with clear, recognizable cells.
Image resolution error: "mpp below 0.4 mpp"	Resolution below 0.4 mpp threshold	Refer to Section 6.1.1 Image Quality Guidelines. Use minimum 40x magnification. Verify correct magnification setting in microscope software (e.g., 50x in Scan & LiveView).
High number of "Not Recognizable" cells	a) Cells smaller than 30x30 pixels b) Over-stained, blurry, or poor-quality samples	Refer to Section 6.1.1 Image Quality Guidelines. If the issue persists, try a different sample area or re-prepare the slide.
Classification results seem inaccurate	Poor image quality, incorrect staining, wrong	Refer to Section 6.1.1 Image Quality Guidelines. Verify: - May-Grunwald-Giemsa

	sample type, or calibration issues	staining used - Bone marrow sample - Proper calibration
Results/Export Issues		
Results not saving or exporting	Most likely related to storage space. In a web application causes might also be browser permissions or active popup blockers	Ensure sufficient disk space, In a web application, check browser storage permissions and disable popup blocker temporarily

6.1.3 When to Contact Support

If the above solutions do not resolve your issue, please contact support@cancilico.com with:

- Detailed description of the problem
- Steps you've already tried
- Screenshot of any error messages
- Information about your browser and operating system
- Sample images (if applicable and permissible)

6.2 Updates

Model updates by Cancilico are automatically made available in Smart in Media's PathoZoom® Scan & LiveView. At present, it is not possible to select different versions. This means that only the currently published model is available.

7 Change History

Date	Version	Alteration
19.09.2025	1.0	Initial Creation