MetaSystems White Paper

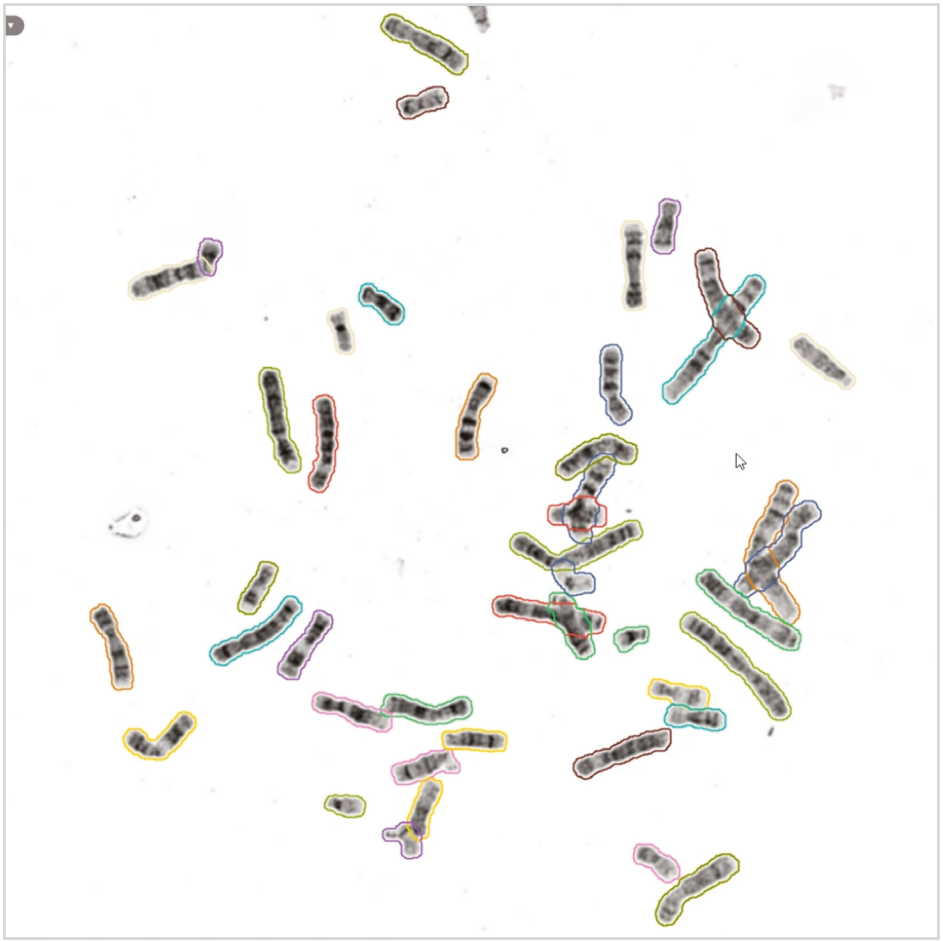
How Our Users Take Advantage of Deep Learning in Ikaros

Deep Neural Networks (DNNs) are transforming digital chromosome processing by supporting key steps in karyogram preparation. Integrated into Ikaros, these networks support chromosome separation and classification. This white paper examines the available publications, highlights practical experience, and discusses the role of AI as a tool that supports cytogenetics professionals while preserving human expertise and control.

WHITE PAPER

At a Glance

- Customized Deep Neural Networks (DNNs) in Ikaros can be implemented to separate and classify banded chromosomes for generating karyogram proposals.
- Ikaros supports the most common chromosome banding methods and enables the processing of metaphase cells from different tissue types, including lymphocytes, bone marrow, amniotic fluid, and chorionic villi.
- Cytogenetics professionals retain control over review and full interpretation.



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Modern Cytogenetics and the Need for Efficient Digital Workflows

Karyotyping remains an integral component of routine operations in many cytogenetics laboratories worldwide. The interpretation of banded metaphase chromosomes, however, is a complex and highly specialized task. After suitable metaphase cells have been identified and captured, individual chromosomes must be accurately segmented, classified according to their characteristic banding patterns, and arranged into a standardized karyogram. This process requires extensive expertise, careful visual assessment, and considerable hands-on time.

At the same time, cytogenetics laboratories are facing growing operational challenges. Increasing sample volumes, continued pressure to reduce turnaround times, and a global shortage of experienced cytogeneticists place significant demands on laboratory workflows. In addition, laboratories strive for greater standardization and reproducibility to minimize inter-operator variability while maintaining high quality.

Digital imaging systems have substantially improved chromosome analysis by replacing conventional microscopy with automated image acquisition and on-screen evaluation. Building on these advances, artificial intelligence (AI) has emerged as the next step. By applying deep learning algorithms to chromosome segmentation and classification, AI can accelerate time-consuming workflow steps.

Ikaros, MetaSystems' software solution for chromosome processing, integrates the possibility to leverage AI-assisted chromosome segmentation and classification in a comprehensive digital workflow. Combining metaphase image processing, customized and user-validated Deep Neural Network-based chromosome segmentation and classification, and expert-guided review, the software is designed to support cytogeneticists in routine operations while preserving full user control over the final interpretation. Rather than replacing the expertise of the cytogeneticist, AI can serve as a support tool that can increase efficiency and allows laboratory professionals to focus on assessment instead of repetitive manual tasks.

Deep Learning in Chromosome Processing

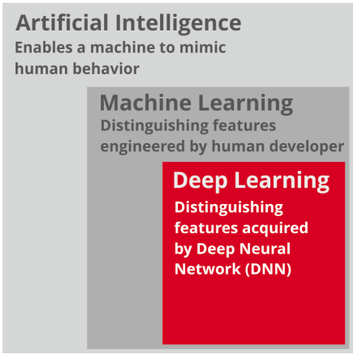
For many years, automated chromosome processing in Ikaros relied primarily on rule-based image processing algorithms (machine learning). These methods used predefined mathematical features such as chromosome length, centromere position, arm ratio, and banding intensity to identify and classify chromosomes. While effective under ideal imaging conditions, their performance was often limited when chromosome morphology varied, banding patterns were less distinct, or chromosomes overlapped.

Recent advances in artificial intelligence, particularly in Deep Learning, have fundamentally changed automated image analysis. Unlike conventional algorithms that depend on manually defined classification rules, Deep Neural Networks (DNNs) learn relevant image features directly from large datasets during the training process. By analyzing thousands of annotated chromosome images, the network progressively learns to recognize complex banding patterns, chromosome morphology, and subtle visual characteristics that distinguish individual chromosome pairs.

The latest generations of Ikaros incorporate the possibility to train user-specific Deep Neural Networks for chromosome segmentation and classification. Following metaphase acquisition, these networks can be configured to segment and assign each chromosome to its corresponding class based on the features obtained from the user-classified training images. The classified chromosomes are then automatically arranged into a preliminary karyogram for expert review.

Rather than replacing the expertise of the cytogeneticist, the AI-assisted workflow is designed to accelerate routine processing while maintaining full user control. Users can review the automatically generated karyogram, verify chromosome assignments, perform corrections where necessary, and finalize the interpretation. Only after the operator has finalized the karyogram will it be marked as complete and saved as a result. This collaborative approach combines the speed of artificial intelligence with the experience and judgment of trained laboratory professionals.

▼ *Deep learning is a subfield of artificial intelligence. The Deep Neural Network (DNN) acquires features without human interaction to distinguish images.*



User Experience in Routine Cytogenetics

How does Deep Learning perform in everyday cytogenetics? And what difference can AI-assisted chromosome processing make in a laboratory setting? The following publications and laboratory reports explore these questions from different perspectives. They describe the experience of cytogenetics laboratories using Deep Neural Networks (DNNs) in Ikaros to support chromosome segmentation and classification. These experiences represent different studies, specimen types, and evaluation methods; they should therefore be interpreted within their respective contexts. The following sections examine the individual publications and user experiences in detail, outlining their study designs, key results, and practical relevance for laboratories using Deep Neural Networks (DNNs) Ikaros.

References

Research Paper

(1). Vajen B, Hänselmann S, Lutterloh F, *et al.* Classification of fluorescent R-band metaphase chromosomes using a convolutional neural network is precise and fast in generating karyograms of hematologic neoplastic cells. *Cancer Genetics* **2022**;260–261:23–29. https://doi.org/10.1016/j.cancergen.2021.11.005

Conference Abstracts

(2). Xu X, Slagter D, VanDeWalker T, *et al.* P589: Improved efficiency of G-band chromosome analysis via deep neural network workflow. *Genetics in Medicine Open* **2023**;1:100636. https://doi.org/10.1016/j.gimo.2023.100636

(3). Fedderson RB, Tambunga B, Vitier G, *et al.* P421: AI-assisted karyotyping improves efficiencies at scale in the cytogenetics laboratory. *Genetics in Medicine Open* **2023**;1(1 Suppl.):100468. https://doi.org/10.1016/j.gimo.2023.100468

(4). Borri D, Kishimoto RK, Santos MFMD, *et al.* Implementation of a commercial model of artificial intelligence for karyotyping. *Hematology, Transfusion and Cell Therapy* **2023**;45(Suppl. 4):S837–S838. https://doi.org/10.1016/j.htct.2023.09.1510

(5). Avenarius M, Teierle S, Culley L, *et al.* 2: Artificial intelligence-assisted conventional chromosome analysis to explore clonal dynamics in chronic lymphocytic leukemia. *Genetics in Medicine Open* **2025**;3(Suppl. 1):101919. https://doi.org/10.1016/j.gimo.2024.101919

Blog Article

(6). MLL Münchner Leukämielabor GmbH. Chromosome Analysis 5.0 – Automation, Digitization and Artificial Intelligence. October 6, **2022**. https://www.mll.com/en/chromosome-analysis-5-0-automation-digitization-and-artificial-intelligence

(1). Improved Chromosome Classification and Workflow Efficiency Through Deep Learning

Vajen *et al.* investigated whether a Deep Neural Network (also called convolutional neural network)-based approach could improve chromosome classification of fluorescent R-banding and support routine karyotyping workflows in hematologic neoplasms. The study was conducted at the Department of Human Genetics at Hannover Medical School, Germany, and evaluated the ability of deep learning to identify individual chromosomes, predict their correct orientation, and accelerate the generation of karyograms.

For the development of the DNN, the authors used a large dataset of routine diagnostic karyograms collected between 2012 and 2019. The dataset comprised 330,131 normal karyograms generated from fluorescence R-banded metaphases. Approximately 78% of the cases originated from bone marrow samples and 22% from peripheral blood samples. The dataset was divided into independent training, validation, and test sets, with 297,119 karyograms used for training and 16,506 karyograms reserved for final evaluation.

The Deep Neural Network was trained to classify individual chromosomes into the 24 human chromosome classes (chromosomes 1–22, X, and Y) and to predict the correct chromosome orientation for automated karyogram arrangement. Training of the neural network took place at our MetaSystems headquarters in Germany. After development, the DNN was integrated into the Ikaros karyotyping software workflow.

The evaluation demonstrated a high level of classification performance. The DNN correctly identified 98.8% of individual chromosomes in the independent test dataset. In addition, the network predicted chromosome orientation with high precision, achieving a median absolute rotation error of only 2°.

Beyond technical performance, the study evaluated the impact of DNN support on routine laboratory workflow. Two observers analyzed 200 metaphases from 20 individuals diagnosed with hematologic neoplasms, including acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), and chronic myeloproliferative disorders. Each metaphase was analyzed both with the conventional automated classification approach and with DNN-assisted classification.

The authors report that the integration of the DNN substantially reduced the number of manual correction steps required to generate a final karyogram. While the conventional workflow required an average of 19.1 correction steps per karyogram, only 0.15 correction steps were required when DNN support was applied. As a result, the average hands-on time required for karyogram generation was reduced from 102.3 seconds to 58.6 seconds, representing a time saving of approximately 43%.

Importantly, the study demonstrated that AI assistance can support cytogeneticists without replacing expert review. The DNN generated a preliminary chromosome classification and arrangement that could be verified and adjusted by trained professionals. This approach combines the consistency and speed of artificial intelligence with the diagnostic expertise required for the interpretation of complex cytogenetic findings.

The results provide strong evidence that deep learning-based chromosome classification can improve the initial automated classification performance in the evaluated study setting. By integrating DNN-based classification into Ikaros, artificial intelligence becomes a practical tool to reduce repetitive manual tasks and support standardized digital karyotyping.

> "My former laboratory at Hannover Medical School supported MetaSystems in adapting the AI functionality to the segmentation and classification of fluorescent R-banding (Vajen *et al.*, PMID 34839233).
>
> With the help of the adapted AI, we were able to save more than 40% processing time with the karyotyping software Ikaros.
>
> As the new head of amedes genetics, I am pleased to see that the cytogenetic laboratory is equipped with solutions by MetaSystems for metaphase finding, karyotyping and FISH as well."
>
> *Prof. Dr. Gudrun Göhring*
> *Medical Director of Genetics*
> *MVZ amedes genetics for interdisciplinary laboratory diagnostics*
> *Hannover, Germany*

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(2). Impact of DNN-Assisted Chromosome Classification on Case Processing Time

Xu *et al.* evaluated whether integrating a Deep Neural Network for chromosome classification into an established digital chromosome analysis workflow could reduce the time required to complete routine karyotyping. The study was conducted at Mayo Clinic in collaboration with our U.S. colleagues from MetaSystems Group Inc. and addressed the persistent challenge of labor-intensive chromosome analysis in clinical cytogenetics laboratories.

The evaluation included 90 prospectively collected clinical cases: 45 normal congenital peripheral blood cases and 45 normal neoplastic bone marrow cases. Six cytogenetic technologists with varying levels of experience participated. Each case was first processed using the routine clinical workflow incorporating the DNN, with a complete 20-cell study performed. The same case images were subsequently analyzed without DNN support in a separate, blinded environment. A washout period of at least one month was used between the two assessments. The authors then compared the average time required to complete each case under the two workflows.

The results demonstrated substantial reductions in case-processing time when the DNN was incorporated. For normal peripheral blood cases, the average time decreased from 119.6 minutes without DNN support to 55.1 minutes with DNN support, corresponding to a reduction of 53.9%. For normal bone marrow cases, the average time decreased from 104.9 minutes to 60.6 minutes, representing a reduction of 42.2%. These findings indicate that DNN-assisted chromosome classification can reduce the time technologists spend preparing and reviewing karyograms within a complete workflow.

The study supports the practical value of integrating AI into digital chromosome analysis, particularly in laboratories managing substantial case volumes or facing shortages of experienced cytogenetics personnel. By reducing hands-on processing time, DNN-assisted workflows may help laboratories allocate their expertise more efficiently while retaining professional oversight of chromosome evaluation and final interpretation.

Overall, Xu *et al.* provide workflow-level evidence that integrating a DNN for chromosome classification into digital karyotyping can substantially reduce case-processing time in a clinical cytogenetics laboratory.

(3). AI-Assisted Karyotyping Improves Efficiencies at Scale in the Cytogenetics Laboratory

Fedderson *et al.* evaluated the implementation of Deep Neural Network based algorithms for chromosome segmentation and classification in a digital chromosome analysis workflow at an academic reference laboratory. The study addressed the need to improve laboratory efficiency amid staffing shortages and increasing demands for flexible working arrangements, while maintaining the quality of cytogenetic services.

The study included G-banded metaphase images from bone marrow, peripheral blood, and prenatal specimens. A total of 51 images representing 40 cases were used to evaluate chromosome segmentation, while 65 images representing 28 cases were used to evaluate chromosome classification. Both normal and abnormal cases were included. Multiple independent analyzers participated in the evaluation, and the DNN-assisted workflow was compared with previously validated workflows using earlier versions of the Ikaros software.

The results demonstrated a substantial improvement in chromosome classification. Average classification accuracy increased from 65% with the previous software-assisted classification approach to 97% with DNN support. The greatest improvement was observed in peripheral blood specimens, where classification accuracy increased from 49% to 95%. Accuracy was defined as the proportion of chromosomes correctly assigned to their respective classes in the karyogram; chromosome orientation was not included in this assessment.

The DNN-assisted workflow also reduced the number of processing steps by an average of 15. In terms of processing time, the authors reported savings of 20 seconds per image for chromosome segmentation and 33.5 seconds per image for chromosome classification. The segmentation function showed particular utility for bone marrow preparations, which generally contain shorter chromosomes with less overlap.

These findings demonstrate the potential of DNN-based support to improve both the efficiency and consistency of digital karyotyping workflows. By reducing repetitive manual operations and improving initial chromosome classification, AI-assisted processing allows cytogeneticists to devote more attention to reviewing chromosome morphology, evaluating banding patterns, and identifying abnormalities.

Overall, Fedderson *et al.* demonstrate how integrating DNN-based segmentation and classification into an established digital workflow can support more efficient karyogram preparation while retaining the expert review required for cytogenetic interpretation.

(4). Implementation of a Commercial AI Model for Routine Karyotyping

Borri *et al.* evaluated the implementation of the Deep Neural Network based algorithms for chromosome segmentation and classification integrated into the Ikaros software. The objective was to validate the performance of the commercial AI model under routine laboratory conditions and to quantify its impact on chromosome analysis workflows.

The evaluation included 120 routine metaphases, comprising 55 bone marrow metaphases (300–400 band resolution) from patients with hematological malignancies and 65 peripheral blood metaphases (approximately 550 band resolution) from constitutional cytogenetic analyses. The dataset also included metaphases with numerical and structural chromosomal abnormalities as well as challenging cases containing multiple overlapping chromosomes.

The authors compared conventional manual analysis with the AI-assisted workflow, measuring the total hands-on time required for chromosome segmentation, chromosome classification, and expert review.

For bone marrow samples, the average analysis time decreased from 74 ± 30 seconds per metaphase to 23 ± 19 seconds when the DNN-assisted workflow was used. This corresponds to an average productivity gain of 68.6%, while requiring correction of only approximately one incorrectly paired chromosome per metaphase.

Even greater improvements were observed for peripheral blood samples. The average analysis time was reduced from 138 ± 56 seconds to 29 ± 16 seconds per metaphase, representing a productivity gain of 78.7%. Despite the considerable reduction in hands-on time, the average chromosome pairing error remained low at 2.6 chromosomes per metaphase and could be readily corrected during expert review.

In the cited publication, the authors reported shorter turnaround times following implementation of a DNN-assisted workflow. Multiple workflow-related factors may have contributed to these observations. According to the authors, the turnaround time for constitutional karyotyping was reduced from 21 days to 15 days, while the turnaround time for oncohematological karyotyping decreased from 14 days to 7 days.

The study demonstrates that AI-assisted chromosome analysis can be integrated successfully into routine clinical diagnostics using commercially available Ikaros software. Importantly, the authors emphasize that artificial intelligence functions as a support technology rather than an autonomous system. Automated chromosome segmentation and classification substantially reduce repetitive manual work, while experienced cytogeneticists remain responsible for reviewing the generated karyograms and establishing the final interpretation.

(5). AI-Assisted Karyotyping to Explore Clonal Dynamics in Chronic Lymphocytic Leukemia

Avenarius *et al.* investigated whether AI-assisted karyogram preparation could support more extensive conventional chromosome analysis in patients with chronic lymphocytic leukemia (CLL). At the Ohio State University, the laboratory validated and implemented Ikaros software incorporating AI-assisted karyogram preparation to address the time-consuming nature of conventional chromosome analysis, particularly in cases with complex karyotypes.

The DNN-assisted workflow uses artificial intelligence to separate individual chromosomes from metaphase images, assign chromosome classifications, and generate preliminary karyograms with confidence indicators for chromosome placement. According to the authors, implementation substantially reduced the time required to prepare karyograms across analyzed cells. During the first seven months of use, the laboratory's monthly average case turnaround time improved by 1.5 days.

Building on these workflow improvements, the investigators explored whether analyzing more than the conventional 20 metaphases could provide additional information about clonal evolution and prognostically relevant chromosomal abnormalities in newly diagnosed CLL, which were subsequently interpreted by the clinical laboratory team. In a preliminary evaluation, they analyzed 40–50 metaphases in each of eight cases.

Four of the eight cases provided a more complete understanding of clonal evolution and/or additional cytogenetic findings that the authors considered clinically relevant. The expanded analysis performed by the investigators resulted in different prognostic classifications in two cases: one case was reclassified from non-complex to complex, while another was reclassified from complex to highly complex.

These preliminary findings suggest that reducing the time required for karyogram preparation may create opportunities to examine more metaphases in selected cases. In CLL, where chromosomal abnormalities and clonal evolution can contribute to prognostic assessment, expanded analysis may reveal findings that are not captured by a more limited examination.

However, the study does not establish that AI itself improves the detection of chromosomal abnormalities or changes clinical outcomes. The additional findings resulted from analyzing more metaphases, enabled in part by a more efficient workflow. The expanded analysis involved only eight cases, and the authors emphasized that further studies are needed to determine whether routinely examining additional cells has a clinical rationale in CLL or other neoplastic diseases.

Overall, this report illustrates a potential downstream benefit of AI-assisted karyotyping: by reducing the time required for routine chromosome processing, it may make more extensive metaphase evaluation feasible in selected clinical cases.

(6). AI in Routine Chromosome Analysis: Experience from MLL

In a website article published in October 2022, MLL Münchner Leukämielabor described how artificial intelligence had been integrated into their routine chromosome analysis. The laboratory had progressively automated several stages of its laboratory processes and collaborated with MetaSystems to develop Deep Neural Networks (DNNs) for chromosome object recognition, quality assessment, and classification.

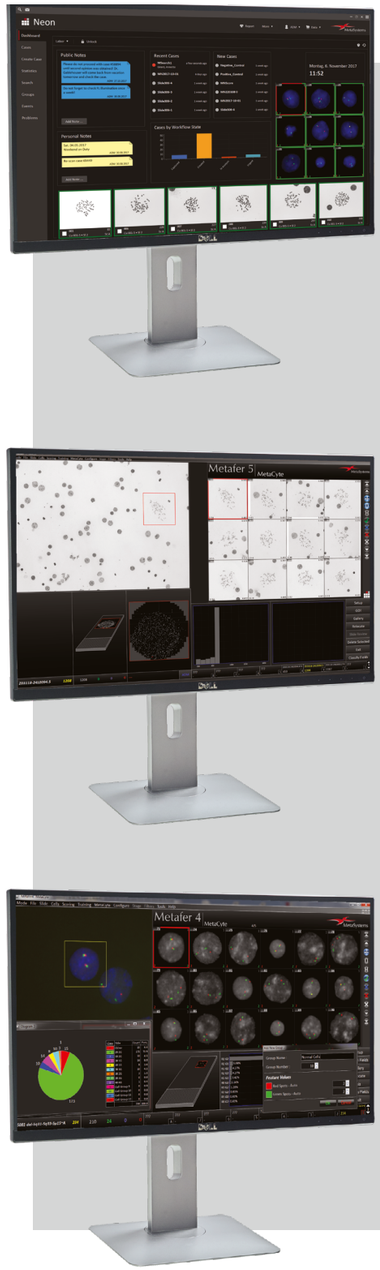
According to MLL, AI-based algorithms had been used routinely since the end of 2019 and were continuously developed. The integrated workflow enabled automated generation of karyograms, eliminating manual image-processing steps that had previously required substantial technologist input. MLL reported that manually creating a karyogram typically took approximately two to three minutes, whereas the AI-assisted workflow required approximately 25 seconds, including subsequent verification by a cytogeneticist.

The laboratory also reported improvements in overall turnaround time following the introduction of AI. The proportion of cases reported within five days or less increased from approximately 30% before implementation to almost 50% afterward. At the same time, the proportion of cases with a turnaround time exceeding seven days decreased from 28% to 15%.

This report illustrates how AI-assisted chromosome analysis can contribute to efficiency improvements beyond individual image-processing steps. By reducing the time required to prepare karyograms and supporting the systematic assessment of metaphases, AI can help laboratories optimize routine workflows while retaining expert review and interpretation. The findings should nevertheless be interpreted in the context of the report's design. The article describes MLL's implementation experience but does not provide peer review.

Overall, MLL's experience provides practical evidence that integrating AI into an established, highly automated cytogenetics laboratory can reduce hands-on processing time and contribute to shorter reporting times in routine operations.

> "Our lab had the opportunity to be the first user to test the betaversion of MetaSystems' new AI-based karyotyping software Ikaros.
>
> We experienced a time gain of up to 50% in the karyotype analysis of bone marrow metaphases. This enormous gain in efficiency allows us to keep pace with the ever-increasing workload in times of shortage of personnel resources."
>
> *Prof. Dr. Claudia Haferlach*
> *MD from MLL (Münchner Leukämielabor GmbH, Germany)*



MORE SOFTWARE & SERVICES

Neon 2.0

Neon 2.0 serves as the central platform for managing case and image data generated with Ikaros 7.0 and Metafer 4.4. Neon 2.0 organizes all relevant images, results, and metadata in a structured, case-based format. Its powerful search functions, multi-user capability, and compatibility with Laboratory Information Systems (LIS) support efficient collaboration across workstations. By ensuring secure data handling, full traceability, and seamless workflow integration, Neon 2.0 enables laboratories to manage complex imaging and analysis processes with clarity and efficiency.

Metafer 4.4

Metafer 4.4 is the latest version of MetaSystems' versatile platform software Metafer, designed to automate slide scanning and image processing. Metafer enables automated imaging of up to 800 slides per session while supporting a wide range of contrasting methods, including brightfield, fluorescence, phase contrast, and darkfield. Its modular design and scanning parameters provide precise measurements, customizable workflows, and well-structured access to image data. User-trainable classifiers allow flexible adaptation to specimen-specific requirements.

Customization Packages

Customization packages are a service offered to tailor workflows to the specific needs of individual labs. The Customization Package Metaphase DNN enhances the workflow to find metaphases on a slide by using Deep Neural Networks (DNN) to automatically detect suitable metaphases from low-magnification scans. Complementing workflows in cytogenetics, the Customization Package Spot Counting streamlines FISH analysis by automatically locating suitable nuclei, detecting and enumerating fluorescent signals, and allowing parameter adjustments tailored to specific probe layouts and fluorochromes. These packages are intended to support workflow automation and may help reduce manual workload depending on specimen quality, laboratory procedures, and user expertise.

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About MetaSystems

For 40 years, MetaSystems has been developing innovative solutions for automated microscopy-based imaging for the healthcare and biotechnology sectors. Our headquarters are located in the southwest of Germany near Heidelberg.

We are a global company with an international team working in Germany and in our subsidiaries in North and South America, Europe, India, China and Japan. Our customers can be found in institutes, hospitals, and universities in over 100 countries around the world.

We continuously develop our products in close connection with our users, thus combining innovation with tradition. Our modern approaches include an advanced workflow management and the use of artificial intelligence. In many segments, this has enabled us to achieve an international top position.



CE IVD Ikaros 7.0 and Metafer 4.4 are classified as in vitro diagnostic Software as Medical Device (SaMD) Class A in the European Union in accordance with the In Vitro Diagnostics Regulation (EU) 2017/746 (IVDR) and carries the CE label unless otherwise indicated.

Neon 2.0 is classified as an accessory for in vitro diagnostic medical devices (IVD) in the European Union in accordance with the In Vitro Diagnostics Regulation (EU) 2017/746.

MetaSystems products are used in many countries worldwide. Use all MetaSystems IVD products only within the scope of their intended purpose and the regulations of the respective country or region.

Hardware components supplied by third-party manufacturers are not included in MetaSystems IVD products.

MetaSystems software provides, among other functions, features to assist users with image processing. These include, but are not limited to, the use of machine and deep learning algorithms for pattern recognition. The output generated in this process should be regarded as preliminary suggestions and, in any case, mandatorily requires review and assessment by trained experts.

MetaSystems offers **Customization Packages** for application workflows that have been successfully implemented for customer labs using standard Metafer platform functionality. It is expected that they can be implemented for other customer labs using similar workflows and slide preparation procedures. If a Customization Package is purchased, MetaSystems product specialists will - based on their experience from other similar application cases - support the customer lab in adapting the Metafer software configuration to their needs. The performance of the solution will depend on the quality of the customer slides and the expertise of the users, MetaSystems cannot specify or guarantee any performance parameters. The validation of the solution for clinical use is the sole responsibility of the customer lab.

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