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Review Article

From Microscopy to Precision Hematology: The Evolution of Artificial Intelligence in Hematologic Diagnostics

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ABSTRACT

Hematologic diagnostics has evolved considerably over the past decades, progressing from reliance on manual microscopic examination to increasingly sophisticated digital and artificial intelligence (AI)-enabled diagnostic systems. This transformation has been driven by the growing complexity of hematologic diseases, advances in molecular medicine, and the need for faster, more standardized, and more reproducible diagnostic approaches. AI has emerged as a transformative technology capable of enhancing image interpretation, automating routine laboratory processes, and integrating diverse sources of diagnostic information to support precision medicine. This narrative review critically examines the evolution of hematologic diagnostics from conventional microscopy to AI-assisted practice and explores how AI is reshaping diagnostic workflows across the hematologic diagnostic pathway. Current evidence indicates that AI has substantially improved blood smear analysis, bone marrow evaluation, disease detection and classification, and clinical decision support while reducing observer variability and improving laboratory efficiency. Moreover, the integration of morphology with flow cytometry, cytogenetics, genomics, laboratory findings, and clinical metadata is redefining hematologic diagnosis as a multidimensional, patient-centered process. Despite these advances, important challenges remain, including limited external validation, dataset heterogeneity, algorithm transparency, interoperability, regulatory oversight, and equitable implementation across diverse healthcare settings. The review further identifies key evidence gaps and proposes the Precision Hematology Evolution Framework (PHEF) as a conceptual model illustrating the transition from morphology-based diagnosis to AI-enabled precision hematology. Collectively, the evidence suggests that AI is best viewed as an enabling technology that augments expert clinical interpretation rather than replacing it. Continued multidisciplinary collaboration, rigorous validation, and responsible governance will be essential to fully realize the promise of AI in delivering more accurate, personalized, and equitable hematologic care.

Keywords: Artificial Intelligence; Hematologic Diagnostics; Digital Pathology; Precision Hematology; Machine Learning

Introduction

Hematologic disorders, including anemia, leukemia, lymphoma, myeloma, and inherited blood diseases, remain a major cause of morbidity and mortality worldwide. Accurate and timely diagnosis is fundamental to effective disease management, influencing treatment selection, prognostic assessment, and long-term patient outcomes. For decades, hematologic diagnosis has relied heavily on microscopic examination of peripheral blood smears and bone marrow specimens, where experienced hematologists and hematopathologists identify subtle morphological features that distinguish normal from abnormal cells. Bone marrow cytomorphology in particular remains an important cornerstone of hematological diagnosis and is still performed manually many times each day [2]. Despite remarkable advances in laboratory medicine, microscopic morphology continues to serve as the diagnostic cornerstone for many hematologic conditions [3].

However, the diagnostic landscape of hematology has become increasingly complex. The growing recognition of molecular heterogeneity within hematologic diseases, coupled with advances in genomics, flow cytometry, cytogenetics, and next-generation sequencing, has transformed disease classification and clinical decision-making; the current World Health Organization classification of hematolymphoid tumours is now explicitly rooted in molecular biology [9]. Modern hematologic diagnosis now requires the integration of diverse and often high-dimensional datasets that extend well beyond conventional morphology, drawing together imaging, pathology, omics, and laboratory parameters [17]. At the same time, rising laboratory workloads, shortages of specialized hematopathologists, and the inherent subjectivity of manual slide interpretation have exposed important limitations of traditional diagnostic approaches, highlighting the need for more efficient, standardized, and reproducible methods. Manual analysis of blood cells is typically slow, laborious, and error prone, and automated analysis can substantially reduce the workload of hematologists while providing fast, accurate results to support the diagnostic process [1].

Artificial intelligence (AI) has emerged as one of the most promising innovations addressing these challenges. Through machine learning and deep learning algorithms, AI has demonstrated considerable potential in automating blood cell recognition, detecting hematologic malignancies, interpreting bone marrow morphology, integrating multimodal diagnostic data, and supporting clinical decision-making; across the field it has been applied to hematopathological, laboratory, genomic, and clinical data to inform diagnosis, prognosis, and treatment planning [16]. AI-based decision-support systems in particular hold substantial promise as part of clinical practice in detecting hematological malignancy [6]. Rather than functioning solely as a tool for automation, AI is increasingly reshaping how hematologic information is analyzed, interpreted, and translated into patient care, with an impact that extends across clinicians, health systems, and patients [18], paving the way toward precision hematology, and its integration into routine practice to support hematologists' decision-making is widely regarded as inevitable [7].

Although numerous narrative and systematic reviews have described specific AI applications in hematology, most concentrate on individual technologies or disease-specific use cases. Comparatively little attention has been given to examining how AI has fundamentally transformed diagnostic paradigms, assessing the maturity and limitations of current evidence, or outlining the critical steps required for widespread clinical implementation. This review addresses these gaps by tracing the evolution of hematologic diagnostics from conventional microscopy to AI-assisted practice, synthesizing evidence across major diagnostic domains, critically evaluating current achievements and persistent challenges, identifying key knowledge gaps, and proposing a conceptual framework to guide the continued advancement of precision hematology.

Narrative Review Methodology

This narrative review was conducted to synthesize current evidence on the evolution of artificial intelligence (AI) in hematologic diagnostics and its implications for precision hematology. A structured literature search was performed using PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar to identify relevant peer-reviewed publications published between January 2015 and May 2026, while seminal studies published before this period were included when considered foundational to the development of AI in medical imaging and hematology. Search terms included combinations of *artificial intelligence, machine learning, deep learning, hematology, hematologic diagnostics, digital pathology, bone marrow, peripheral blood smear, precision hematology, computer vision, clinical decision support, and digital health.* Additional articles were identified through manual

screening of reference lists from relevant reviews and key publications.

Studies were selected based on their relevance to AI applications in hematologic diagnostics, including image interpretation, disease detection and classification, workflow optimization, multimodal data integration, and precision medicine. Priority was given to recent systematic reviews, high-quality original research, multicenter studies, consensus statements, and landmark publications that significantly advanced the field. Articles not directly related to hematologic diagnostics or lacking sufficient methodological detail were excluded. As a narrative review, this study did not follow a formal systematic review protocol or PRISMA methodology; instead, the objective was to provide a critical synthesis of the current evidence, identify persistent knowledge gaps, and propose a conceptual framework to guide future research and clinical implementation.

The Evolution of Hematologic Diagnostics: Why Change Was Necessary

The history of hematologic diagnostics is often portrayed as a sequence of technological innovations. However, the transition from manual microscopy to digital and AI-assisted diagnostics was driven less by technological progress itself than by the growing complexity of hematologic diseases and the changing demands of clinical practice. Each stage of this evolution emerged in response to limitations that increasingly challenged the ability of existing diagnostic methods to deliver timely, accurate, and comprehensive patient care.

For much of the twentieth century, microscopic examination of peripheral blood smears and bone marrow aspirates formed the cornerstone of hematologic diagnosis. Morphological assessment enabled clinicians to identify abnormalities in blood cell size, shape, maturation, and distribution, providing essential information for diagnosing anemias, leukemias, lymphomas, and other hematologic disorders. The expertise of hematologists and hematopathologists in recognizing subtle cellular features made microscopy an indispensable diagnostic tool, particularly in settings where advanced laboratory technologies were unavailable.

Despite its enduring value, morphology-based diagnosis has important limitations. Interpretation is inherently subjective and depends heavily on individual expertise, and manual bone marrow evaluation has been shown to be subject to substantial inter- and intra-observer variability that can affect diagnostic consistency, particularly in borderline or rare cases [2]. This variability among and within hematologists reflects differences in expertise, experience, and the subjective nature of manual review, and is compounded by the time-consuming and poorly reproducible character of manual assessment [3]. Simultaneously, increasing laboratory workloads and a global shortage of experienced hematopathologists have placed considerable pressure on healthcare systems, making manual slide review both time-consuming and difficult to sustain. More importantly, advances in molecular genetics, cytogenetics, flow cytometry, and next-generation sequencing have fundamentally reshaped disease classification [9]. Modern hematologic disorders are now understood as biologically heterogeneous entities whose diagnosis and prognosis often depend on integrating morphological, immunophenotypic, cytogenetic, and genomic information, an integration that conventional microscopy alone cannot provide. Indeed, because manual morphology is inherently qualitative, it is difficult to combine with other diagnostic methods that offer more quantitative data [2].

These challenges accelerated the adoption of automated hematology analyzers, digital imaging systems, and whole-slide pathology, which improved standardization, workflow efficiency, and remote accessibility while generating large volumes of high-quality digital data. Digital morphology analyzers, for example, use artificial neural networks to preclassify cells from digital blood-smear images, although a skilled morphologist is still required to review and reclassify cells before results can be released [21]. Although these technologies enhanced laboratory performance, they primarily digitized existing processes rather than transforming diagnostic reasoning. Nevertheless, they established the digital infrastructure necessary for artificial intelligence to emerge as the next stage in hematologic diagnostics.

Viewed collectively, the evolution of hematologic diagnostics reflects a response to increasingly complex clinical needs rather than a simple progression of laboratory technologies. Artificial intelligence represents the logical continuation of this trajectory, offering the capability to integrate multidimensional diagnostic data, reduce variability, and support more precise, individualized clinical decision-making.

The progressive transformation from morphology-based diagnosis to artificial intelligence reflects the historical evolution of hematologic diagnostics in response to increasing diagnostic complexity rather than technological advancement alone. Figure 1 provides a chronological overview of

the major developmental stages that have shaped modern hematologic practice, illustrating how successive technological innovations progressively expanded diagnostic capability and prepared the foundation for precision hematology.

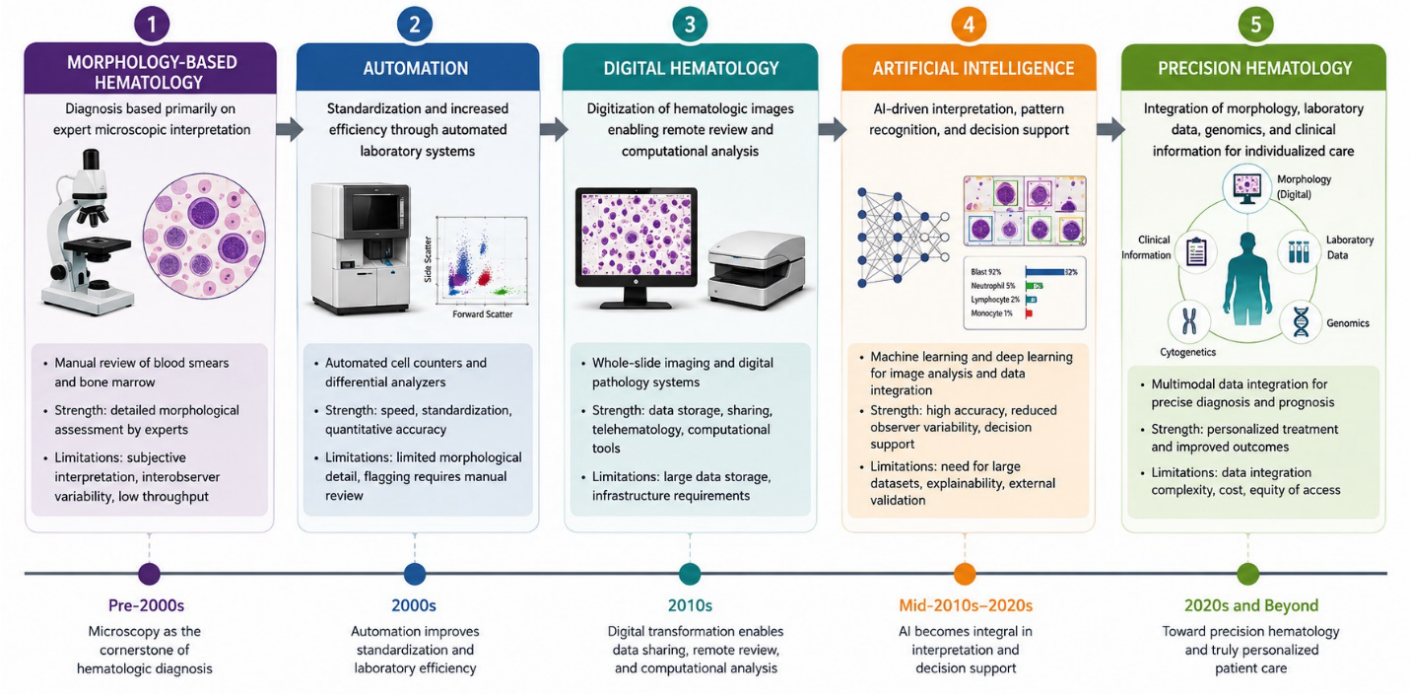

Figure 1. Evolution of Hematologic Diagnostics.

The evolution of hematologic diagnostics from morphology-based hematology to precision hematology. The framework illustrates five successive stages: (1) Morphology-Based Hematology, where diagnosis relied primarily on expert microscopic interpretation; (2) Automation, characterized by automated hematology analyzers that improved standardization and laboratory efficiency; (3) Digital Hematology, marked by whole-slide imaging and digital pathology that enabled computational analysis and remote consultation; (4) Artificial Intelligence, where machine learning and deep learning enhanced image interpretation, pattern recognition, and clinical decision support; and (5) Precision Hematology, which integrates morphology, laboratory findings, genomics, cytogenetics, and clinical information to support individualized diagnosis and management. Rather than depicting isolated technological advances, the figure illustrates the progressive shift from subjective morphology-centered diagnosis toward integrated, data-driven precision care. The major transitions in hematologic diagnostics and their distinguishing characteristics are summarized in Table 1, illustrating the progression from morphology-based practice to precision hematology.

Table 1. Evolution of Diagnostic Paradigms in Hematology

Diagnostic Paradigm	Primary Diagnostic Approach	Reproducibility	Data Integration	Scalability	Clinical Utility
Morphology-Based Hematology	Manual microscopic examination of peripheral blood smears and bone marrow by expert hematologists	Moderate; dependent on operator expertise and susceptible to interobserver variability	Low; morphology assessed largely in isolation	Limited by specialist availability and manual workload	Foundation for hematologic diagnosis; effective for morphological assessment but limited for complex disease characterization
Automation	Automated hematology analyzers for cell counting, differential analysis,	High for standardized quantitative measurements	Low to moderate; primarily laboratory parameters	High; capable of processing large sample volumes efficiently	Improved laboratory efficiency, standardization, and turnaround time while

Diagnostic Paradigm	Primary Diagnostic Approach	Reproducibility	Data Integration	Scalability	Clinical Utility
	and laboratory flagging				reducing manual workload
Digital Hematology	Whole-slide imaging, digital pathology, and computerized image management	High; standardized digital image acquisition and review	Moderate; integrates digital morphology with laboratory information systems	High; supports remote consultation, telehematology, and digital archiving	Facilitates collaborative diagnosis, education, computational analysis, and data sharing
AI-Assisted Diagnostics	Machine learning and deep learning for image interpretation, abnormal cell detection, disease classification, and decision support	High under validated conditions; performance depends on dataset quality and external validation	High; integrates imaging, laboratory parameters, and selected molecular data	High; enables automated screening and prioritization of abnormal cases	Enhances diagnostic accuracy, reproducibility, workflow efficiency, and clinical decision support while augmenting expert interpretation
Precision Hematology	Multimodal integration of morphology, laboratory findings, genomics, cytogenetics, flow cytometry, and clinical information	Potentially very high through comprehensive evidence integration	Very high; combines multidimensional patient data for individualized assessment	Emerging; dependent on digital infrastructure, interoperability, and validated AI ecosystems	Supports personalized diagnosis, prognostic stratification, treatment selection, disease monitoring, and precision patient management

Artificial Intelligence as a Paradigm Shift in Hematology

Artificial intelligence (AI) represents a fundamental shift in hematologic diagnostics, moving beyond the automation of routine laboratory tasks to augmenting clinical interpretation and decision-making. Unlike conventional automated systems, which primarily perform predefined functions such as cell counting and flagging abnormal results, AI is capable of learning complex patterns from large datasets, recognizing subtle morphological features, and integrating diverse sources of clinical information. Deep learning, in particular, allows computational models composed of multiple processing layers to learn representations of data at successive levels of abstraction, discovering intricate structure without hand-engineered features [29]. This transition reflects a change in the role of computational tools, moving from executing repetitive processes to supporting diagnostic reasoning in increasingly complex clinical environments.

A defining strength of AI lies in its ability to recognize intricate patterns that may not be readily apparent through manual examination alone. Building on landmark demonstrations that deep neural networks can match specialist performance in medical image classification, such as dermatologist-level classification of skin cancer from clinical images [22], deep learning models trained on large annotated collections of peripheral blood and bone marrow images have demonstrated remarkable capability in identifying abnormal cell populations and classifying hematologic disorders with a high degree of accuracy; in one landmark study, convolutional neural networks trained on more than 170,000 expert-annotated bone marrow images from 945 patients outperformed prior feature-based approaches for single-cell classification [2]. More importantly, AI extends beyond image analysis by integrating laboratory parameters, flow cytometry findings, cytogenetic abnormalities, genomic profiles, and relevant clinical information; AI-based models have already been shown to differentiate cells, detect malignant cell populations, support chromosome banding analysis, and interpret clinical variants, contributing to early detection and prognosis [7]. Such multimodal analysis supports a more comprehensive understanding of disease biology and aligns closely with the principles of precision medicine, where diagnosis is informed by multiple complementary sources of evidence rather than morphology in isolation.

The integration of AI into diagnostic workflows also has important implications for clinical decision-making. By providing standardized image interpretation and quantitative assessments, AI can reduce the interobserver variability that has long challenged morphology-based diagnosis [2]. Consistent evaluation of blood films and bone marrow specimens

may improve diagnostic reproducibility across institutions while supporting less experienced clinicians in complex cases. Rather than replacing hematologists, AI functions as a decision-support system that prioritizes abnormal findings, assists in differential diagnosis, and enables experts to focus on cases requiring higher levels of clinical judgment.

Current evidence increasingly supports the diagnostic potential of AI in hematology. Across numerous studies, deep learning approaches consistently outperform traditional machine learning methods and conventional image-processing techniques in blood cell classification and morphology recognition, and the field has shifted markedly toward convolutional neural networks as datasets have grown larger [1]. In bone marrow cytomorphology, deep learning has produced accuracy improvements that surpass traditional manual methods [3]. Reported diagnostic accuracies are frequently comparable to those achieved by experienced hematopathologists under controlled research settings. However, these promising findings should be interpreted with caution. Many AI models have been developed using retrospective, single-center datasets that may not adequately represent the diversity of real-world clinical practice [4]. Limited external validation, concerns regarding algorithm transparency, and uncertainty surrounding integration into routine workflows continue to restrict widespread clinical adoption. Consequently, the future success of AI in hematology will depend not only on improving algorithmic performance but also on demonstrating robustness, explainability, and clinical utility across diverse healthcare settings.

AI Across the Hematologic Diagnostic Pathway: What Has Changed?

The impact of artificial intelligence (AI) in hematology extends beyond improving individual diagnostic tests; it is reshaping the entire diagnostic pathway. Rather than functioning as isolated tools, AI applications increasingly support interconnected stages of laboratory practice, from image interpretation and disease classification to the integration of multimodal data for personalized clinical decision-making. This evolution reflects a shift from interpreting single laboratory findings to generating comprehensive diagnostic insights that combine morphology with molecular and clinical information.

Image Interpretation

The earliest and most mature application of AI in hematology is image interpretation. Traditionally, peripheral blood smear examination and bone marrow morphology relied on the expertise of hematologists to identify subtle differences in cell size, shape, staining characteristics, and maturation patterns. While highly informative, manual interpretation is time-intensive and subject to considerable interobserver variability, particularly in diagnostically challenging cases [3].

Recent advances in deep learning have substantially improved the automated analysis of hematologic images. AI models can accurately classify red blood cells, white blood cells, and platelets, perform automated differential counts, quantify blast cells, and detect morphologic abnormalities associated with both benign and malignant hematologic conditions. For example, convolutional neural network–based systems have reported classification accuracies exceeding 95% under controlled validation conditions for peripheral blood smear analysis, while deep-learning approaches applied to bone marrow morphology have demonstrated diagnostic performance comparable to experienced hematopathologists in expert-annotated datasets. These improvements have translated into greater diagnostic consistency, reduced observer variability, and shorter laboratory turnaround times. However, reported performance varies considerably across studies because of differences in staining protocols, scanner platforms, image quality, and dataset composition, highlighting the need for standardized multicenter validation before widespread clinical implementation [1,2,12].

Across published studies, AI-assisted image analysis has consistently demonstrated improvements in diagnostic efficiency, reproducibility, and turnaround time. However, performance remains influenced by factors such as staining protocols, image acquisition systems, scanner resolution, and the diversity of training datasets. Consequently, algorithms developed within a single institution often experience reduced performance when applied to external populations, emphasizing the importance of multicenter validation and standardized imaging protocols [4]. Machine-learning models are demonstrably sensitive to how slides are pre-processed and require appropriate training if they are to serve as universal diagnostic aids [28].

Disease Detection and Classification

Beyond image interpretation, AI increasingly contributes to disease detection and diagnostic classification. Rather than relying solely on predefined morphological criteria, AI models identify complex relationships among cellular characteristics that may facilitate earlier and more accurate recognition of hematologic disorders. Applications have been reported across a broad spectrum of conditions,

including acute and chronic leukemias, lymphomas, anemias, and inherited hemoglobinopathies.

In leukemia diagnostics, AI has demonstrated considerable promise in detecting blast cells, distinguishing leukemia lineages, and supporting disease classification using integrated morphologic and laboratory features. Deep-learning algorithms have consistently achieved excellent diagnostic discrimination in experimental settings, with several studies reporting areas under the receiver operating characteristic curve exceeding 0.95 and diagnostic accuracies comparable to expert hematopathologists for selected leukemia subtypes [6,11,30]. Despite these encouraging findings, most studies remain retrospective and rely on carefully curated datasets, emphasizing the need for prospective external validation across heterogeneous clinical environments. Similar approaches have been explored for characterizing anemia subtypes and screening for inherited disorders such as sickle cell disease using automated blood smear analysis. A deep-learning framework applied to smartphone-based microscopy images achieved approximately 98% screening accuracy among 96 patients, demonstrating the potential of low-cost AI-assisted diagnostics in resource-constrained settings [5]. Nevertheless, this result should be interpreted cautiously because it was derived from a relatively small cohort, and larger multicenter studies involving more diverse patient populations are required before such systems can be considered broadly generalizable for routine clinical practice [5]. Deep learning has also been used to differentiate myelodysplastic syndromes from aplastic anemia on peripheral blood smears with high reported sensitivity and specificity [13], to identify acute promyelocytic leukemia, a hematologic emergency, from bone marrow smears [15], and to classify non-Hodgkin lymphoma subtypes on whole-slide histopathology images [14]. Beyond malignant and inherited disorders, image-analysis and machine-learning methods have been widely applied to detect blood-borne parasites such as malaria on microscopic blood films [27].

Despite these encouraging findings, current evidence indicates that AI performs most effectively as a clinical decision-support system rather than an autonomous diagnostic platform. Human expertise remains essential for interpreting atypical findings, resolving conflicting results, and incorporating clinical context into final diagnostic decisions. Accordingly, the greatest benefit of AI lies in augmenting specialist expertise, improving diagnostic confidence, and reducing oversight of subtle abnormalities rather than replacing clinician judgment [3].

Precision Diagnostics

Perhaps the most transformative contribution of AI is its ability to integrate multiple diagnostic modalities into a unified clinical assessment. Contemporary hematologic diagnosis increasingly depends on information derived from flow cytometry, cytogenetic analysis, genomic sequencing, laboratory biomarkers, and patient-specific clinical characteristics. Individually, each modality provides valuable but incomplete information; collectively, they offer a far more comprehensive understanding of disease biology.

AI provides a powerful framework for integrating these heterogeneous datasets, enabling recognition of complex relationships that may be difficult to identify through conventional analysis [23]. Notably, incorporating complementary data such as flow cytometry or molecular genetics has been anticipated to further improve the quality of predictions obtainable from neural networks [2]. In cytogenetics specifically, deep neural network classifiers have been developed to automate chromosome banding analysis and karyotyping, tasks that remain labor-intensive and dependent on highly experienced specialists [26]. By combining morphologic findings with immunophenotypic profiles, genomic alterations, cytogenetic abnormalities, and relevant clinical metadata, AI supports more accurate disease classification, refined prognostic stratification, prediction of treatment response, and individualized therapeutic planning. This multidimensional approach is particularly valuable in hematologic malignancies, where molecular heterogeneity increasingly guides diagnosis and targeted treatment selection.

Collectively, the literature demonstrates that the greatest value of AI in hematologic diagnostics lies not in replacing microscopic examination but in expanding its interpretive capacity through the integration of complementary diagnostic information. Rather than serving as a substitute for expert clinical judgment, AI functions as an enabling technology that connects imaging, laboratory, molecular, and clinical data into a coherent diagnostic framework. This progression marks the transition from isolated test interpretation toward precision hematology, where diagnostic decisions are increasingly informed by multidimensional evidence tailored to the individual patient.

Current Evidence: Consensus, Controversies, and Knowledge Gaps

The expanding body of literature on artificial intelligence (AI) in hematologic diagnostics demonstrates substantial progress, yet it also reveals important inconsistencies that warrant careful interpretation. While many studies report impressive diagnostic performance, differences in study design, datasets, validation strategies, and clinical settings make it difficult to determine the true readiness of AI for routine clinical practice. A critical synthesis of the evidence shows that the field has reached consensus in several areas, while significant controversies and knowledge gaps remain.

Quantitative evidence across the literature consistently demonstrates the high diagnostic potential of AI systems in hematology. Reported accuracies for blood-cell classification and leukemia detection frequently exceed 90%, with several deep-learning models achieving sensitivities and specificities comparable to experienced hematopathologists under controlled research conditions [2,6,11]. Nevertheless, these impressive performance metrics should be interpreted within the context of study design. Many investigations rely on retrospective analyses, relatively small patient cohorts, or single-center datasets, all of which may overestimate real-world performance. Consequently, diagnostic accuracy alone should not be considered sufficient evidence for clinical implementation without robust external validation and prospective multicenter evaluation.

Despite these encouraging findings, several important controversies continue to shape discussions regarding AI implementation in hematology. Although many algorithms achieve expert-level performance in research settings, their readiness for routine clinical use remains uncertain. Questions persist regarding the explainability of complex deep learning models, whose classification decisions do not lend themselves to direct human interpretation and which are often the least explainable among high-performing models [2,4]. Explainability is not a purely technical matter but raises intertwined medical, legal, ethical, and societal questions that bear directly on clinical adoption [20]. This lack of transparency may reduce clinician trust, particularly when AI recommendations conflict with expert opinion. Regulatory approval also remains an evolving challenge, as regulation must balance the pace of innovation with the potential for harm and be supported by thoughtful post-market surveillance [4]. Although the number of approved AI- and machine-learning-based medical devices has increased substantially since 2015, no dedicated regulatory pathway for such devices yet exists in the USA or Europe [8]. Even the most capable tool can prove ineffective if it is misapplied or its results are misinterpreted, underscoring the need for hematologists to understand the fundamentals of the systems they use [7]. Furthermore, relatively few studies have evaluated the cost-effectiveness of AI implementation, leaving uncertainty about whether improvements in diagnostic performance justify the financial investment required for digital infrastructure, software maintenance, and workforce training. The question of clinical responsibility also remains unresolved, particularly when diagnostic errors involve both human experts and AI-assisted systems. Current regulatory frameworks generally regard AI as a clinical decision-support tool rather than an autonomous decision-maker, meaning that ultimate responsibility for diagnosis continues to rest with the supervising clinician. However, as AI systems become increasingly sophisticated and influential in clinical workflows, determining liability when human judgment and algorithmic recommendations diverge remains an important unresolved legal and ethical challenge. Future regulatory frameworks will need to establish clear standards for accountability, documentation, human oversight, and post-deployment monitoring to ensure patient safety while fostering clinician confidence in AI-assisted diagnostics.

The variability observed across published studies is largely attributable to methodological differences rather than contradictory evidence. Many AI models are trained using datasets collected from single institutions, limiting their ability to generalize across diverse patient populations and laboratory environments; indeed, most AI systems remain far from achieving reliable generalizability for medical data [4]. Differences in staining techniques, slide preparation, scanner resolution, and image acquisition protocols can substantially influence algorithm performance. In addition, models may inadvertently exploit unreliable confounders, further impairing their ability to generalize to new datasets [4]. The limited use of external validation further restricts confidence in reported performance; a systematic review found that only 6% of 516 eligible medical-imaging AI studies performed external validation [4].

Several important knowledge gaps must also be addressed before AI can become an integral component of routine hematologic diagnostics. Current evidence remains limited for rare hematologic disorders, where insufficient training data hinder robust algorithm development. Pediatric hematology is similarly underrepresented despite important biological differences from adult disease. Most AI research has been conducted in well-resourced

academic centers, with comparatively little evidence from low- and middle-income countries where digital infrastructure and laboratory resources differ substantially. Finally, there is a shortage of prospective clinical trials evaluating the long-term impact of AI on diagnostic accuracy, patient outcomes, workflow efficiency, and healthcare costs, and large-scale multicenter validation studies are needed to confirm clinical utility [3]. Reflecting this need, dedicated reporting standards now emphasize that interventions involving AI should undergo rigorous, prospective evaluation to demonstrate impact on health outcomes [25]. Addressing these gaps will be essential for translating promising research findings into safe, equitable, and sustainable clinical practice. To provide an integrated overview of the current state of the field, Table 2 synthesizes the evidence across major diagnostic domains, identifying areas of agreement, persistent controversies, knowledge gaps, and future research priorities.

Table 2. Thematic Synthesis of Current Evidence on Artificial Intelligence in Hematologic Diagnostics

Diagnostic Domain	Current Evidence	Areas of Consensus	Major Controversies	Knowledge Gaps	Future Research Priorities
Image Interpretation	AI demonstrates high accuracy in peripheral blood smear analysis, bone marrow morphology, automated differential counts, and abnormal cell detection	Deep learning consistently improves image classification accuracy and reduces observer variability	Generalizability across institutions, image standardization, and algorithm explainability remain uncertain	Limited multicenter validation and insufficient evaluation under routine clinical conditions	Development of robust multicenter datasets, standardized imaging protocols, and explainable AI models
Disease Detection and Classification	AI supports detection and classification of leukemias, lymphomas, anemias, and hemoglobinopathies using morphologic and laboratory features	AI performs best as a clinical decision-support tool rather than an autonomous diagnostic system	Clinical readiness, regulatory approval, and responsibility for AI-assisted decisions remain unresolved	Limited evidence for rare hematologic disorders, pediatric populations, and prospective clinical implementation	Large prospective clinical trials, external validation, and evaluation across diverse patient populations
Workflow Optimization	AI improves laboratory efficiency by prioritizing abnormal specimens, reducing manual review, and shortening turnaround time	AI enhances productivity while allowing specialists to focus on diagnostically complex cases	Cost-effectiveness, workforce adaptation, and long-term operational sustainability require further study	Limited evidence regarding implementation in resource-constrained laboratories and routine healthcare systems	Health economic analyses, implementation science research, and integration with laboratory information systems
Precision Diagnostics	AI integrates morphology with flow cytometry, cytogenetics, genomics, laboratory findings, and clinical metadata to support individualized diagnosis	Multimodal data integration represents the future direction of hematologic diagnostics	Interoperability, data governance, privacy, and clinician trust remain significant challenges	Few studies evaluate comprehensive multimodal AI platforms or long-term patient outcomes	Development of multimodal AI, federated learning, real-time clinical decision support, and integration with electronic health records

Challenges and Future Directions: Building the Path to Precision Hematology

Despite remarkable advances in artificial intelligence (AI), its successful integration into hematologic diagnostics depends on addressing a series of interconnected technical, clinical, ethical, and regulatory challenges. These challenges should not be viewed as isolated obstacles but as components of a broader implementation ecosystem in which progress in one domain often influences outcomes in another. Overcoming these barriers will be essential to realizing the full potential of AI-driven precision hematology.

From a technical perspective, the reliability of AI systems is fundamentally dependent on the quality and diversity of the data used for their development [1]. Variations in staining protocols, slide preparation,

image resolution, and laboratory workflows can significantly affect algorithm performance, limiting reproducibility across institutions. Consequently, models trained on homogeneous datasets may perform well in controlled environments but fail to generalize to broader clinical populations [4]. Equally important is algorithm robustness, the ability to maintain consistent performance despite differences in patient characteristics, imaging platforms, or laboratory practices. Another major challenge is interoperability, as healthcare data are often siloed across imaging archives, pathology systems, and electronic health records that are difficult to integrate [4]; because much medical data sits in these silos and privacy concerns restrict access, machine learning is often prevented from reaching its full potential [10]. AI systems must therefore connect seamlessly with laboratory information systems, digital pathology platforms, and hospital electronic health records to support routine clinical workflows. Furthermore, improving explainability remains a priority, as clinicians are more likely to trust AI recommendations when the reasoning behind predictions is transparent and clinically interpretable [4].

Clinical implementation presents an equally important set of challenges. Introducing AI into established diagnostic workflows requires careful consideration of how clinicians interact with decision-support systems without disrupting existing practices. Trust remains central to adoption. Hematologists are unlikely to rely on AI-generated recommendations unless these systems demonstrate consistent accuracy, transparency, and added clinical value across diverse patient populations. Robust external validation through multicenter prospective studies is therefore essential to establish clinical reliability and ensure that algorithms perform equitably across different healthcare settings [3,4].

Ethical and regulatory considerations further shape the pathway toward implementation. AI systems require access to large volumes of patient data, raising legitimate concerns regarding privacy, informed consent, data governance, cybersecurity, and compliance with evolving regulatory requirements. Algorithmic bias remains another major concern because models trained on datasets that inadequately represent demographic, geographic, or socioeconomic diversity may produce systematically unequal diagnostic performance across patient populations. A widely cited example is the health-management algorithm described by Obermeyer and colleagues, which underestimated the healthcare needs of Black patients because healthcare expenditure was used as a proxy for disease burden [19]. Similar biases could emerge in hematologic diagnostics if training datasets fail to capture the diversity of disease presentation across different populations. Consequently, fairness assessment, external validation across diverse patient cohorts, and continuous post-deployment performance monitoring should become integral components of AI governance.

These challenges may be particularly pronounced in low- and middle-income countries, where implementation is frequently constrained by limited digital infrastructure, shortages of specialized personnel, fragmented health-information systems, and restricted financial resources. AI has the potential to improve access to expert diagnostic support in underserved regions through digital pathology and telehematology; however, algorithms developed using data from high-income countries may not perform optimally in settings with different disease epidemiology, laboratory practices, or imaging technologies. Future research should therefore prioritize geographically diverse datasets, equitable international collaborations, and context-specific validation studies to ensure that advances in AI contribute to reducing, rather than widening, global disparities in hematologic care.

Looking ahead, future research should move beyond developing increasingly accurate image-classification algorithms toward creating trustworthy, interoperable, and clinically integrated diagnostic ecosystems. Advances in multimodal AI, foundation models, federated learning, explainable AI, and generative AI offer important opportunities to combine imaging, laboratory testing, genomics, cytogenetics, and clinical information within unified decision-support systems. Nevertheless, technological innovation alone will not be sufficient. Sustainable implementation will require prospective multicenter validation, internationally harmonized regulatory standards, robust governance frameworks, transparent reporting, continuous monitoring of algorithm performance, and comprehensive clinician education to ensure that AI is deployed safely, equitably, and responsibly across diverse healthcare settings[10,24].

While Figure 1 summarizes the historical evolution of hematologic diagnostics, it does not explain how these technological advances interact to enable precision hematology in contemporary clinical practice. To address this conceptual gap, we propose the Precision Hematology Evolution Framework (PHEF) (Figure 2). Unlike the historical timeline presented in Figure 1, the PHEF is an implementation-oriented conceptual framework that illustrates how successive technological developments converge to support intelligent, multimodal, patient-centered

diagnosis. Beyond depicting the five developmental stages, the framework integrates the principal diagnostic data sources, AI-enabled analytical capabilities, clinical decision-support functions, and anticipated patient-centered outcomes. In doing so, the PHEF provides a conceptual roadmap for translating technological innovation into clinically actionable precision hematology and highlights the key enablers required for future implementation.

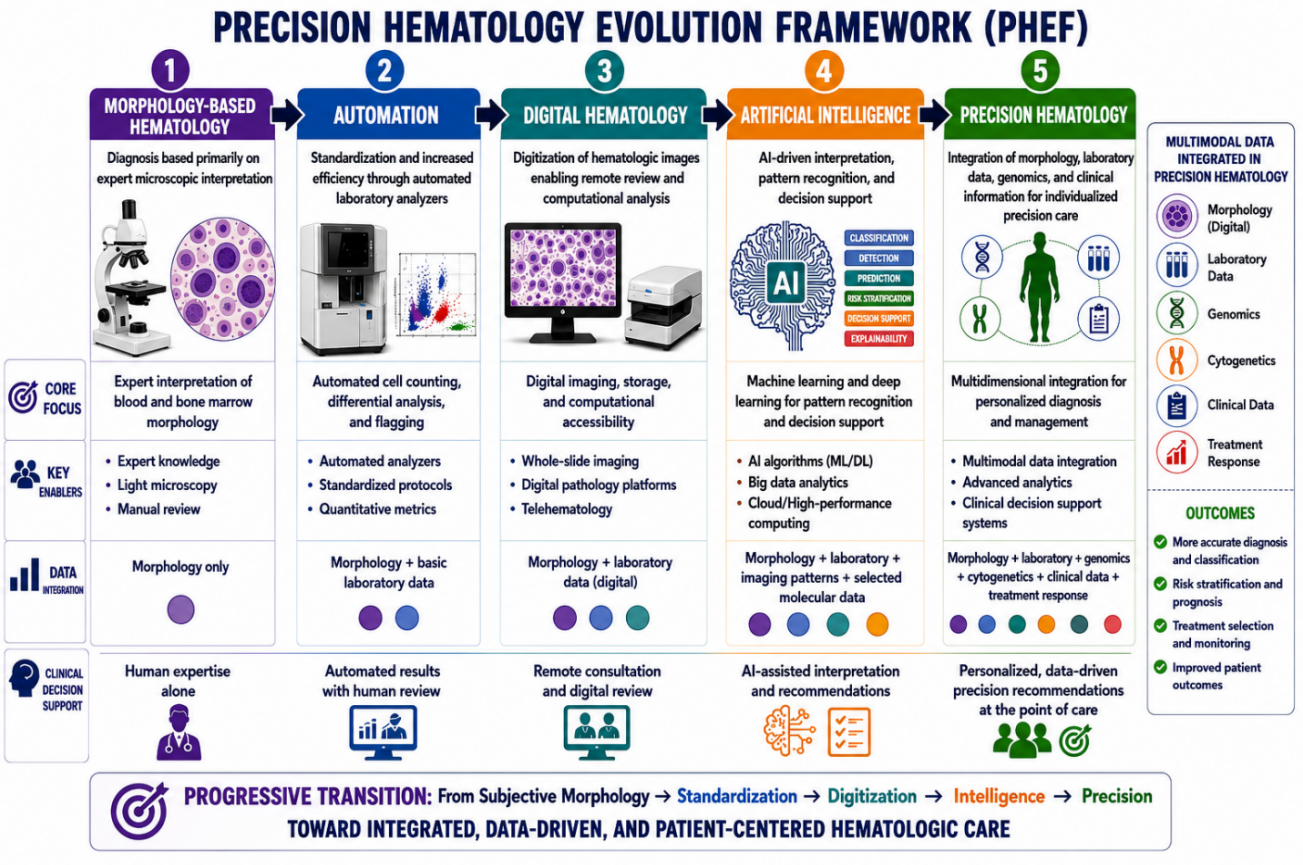

Figure 2. Precision Hematology Evolution Framework (PHEF).

Conceptual implementation framework illustrating how successive advances in hematologic diagnostics converge through multimodal data integration, AI-assisted analysis, and clinical decision support to enable precision hematology.

The principal contribution of the PHEF is that it extends beyond a descriptive account of technological evolution by providing an implementation-oriented framework that links diagnostic technologies, multimodal data integration, AI-assisted decision support, and clinical outcomes within a unified model for precision hematology.

Emerging Role of Generative AI and Large Language Models in Hematology

Recent advances in generative artificial intelligence (GenAI) and large language models (LLMs) represent a new frontier in hematologic diagnostics and clinical decision support. Unlike conventional machine-learning models that are typically designed for narrowly defined classification tasks, LLMs are capable of processing and synthesizing large volumes of unstructured clinical information, including pathology reports, laboratory results, clinical notes, and scientific literature. These capabilities may improve diagnostic documentation, facilitate evidence retrieval, assist multidisciplinary case discussions, and support educational activities for clinicians and trainees.

In hematology, emerging applications include automated summarization of complex diagnostic reports, integration of molecular and clinical findings into structured interpretations, clinical decision-support during multidisciplinary meetings, and assistance with guideline interpretation. When combined with image-analysis algorithms and multimodal AI systems, generative AI may contribute to more comprehensive diagnostic workflows by linking morphologic findings with genomic, cytogenetic, laboratory, and clinical information. Such developments align closely with the broader vision of precision hematology, where multiple data sources are synthesized to support individualized patient management.

Despite this promise, important limitations currently restrict routine clinical implementation. Large

language models may generate inaccurate or fabricated information, propagate biases present in their training data, or provide recommendations that lack transparency and verifiability. Their performance also depends on the quality, completeness, and representativeness of the clinical information provided. Consequently, outputs generated by LLMs should be regarded as decision-support rather than autonomous clinical recommendations and must always be interpreted within the context of expert clinical judgment. Future research should evaluate how generative AI can be safely integrated with validated diagnostic algorithms, robust governance frameworks, and prospective clinical evaluation to ensure accuracy, accountability, and patient safety.

Practical Implications

The integration of artificial intelligence into hematologic diagnostics has implications that extend well beyond laboratory innovation, influencing clinical practice, workforce development, healthcare delivery, and patient outcomes. For clinical hematologists and hematopathologists, AI functions as a decision-support tool that enhances diagnostic confidence by improving the consistency of image interpretation, prioritizing high-risk cases, and facilitating the integration of morphological, laboratory, and molecular findings. Rather than replacing specialist expertise, AI has the potential to reduce routine workload, allowing clinicians to focus on complex cases that require nuanced clinical judgment. In practice, a hybrid model that combines automated analysis with expert manual review is likely to be essential for maximizing accuracy and fostering trust in results [3].

For laboratory scientists, AI-assisted workflows can improve efficiency by automating repetitive analytical tasks, reducing turnaround times, and strengthening quality assurance through standardized image analysis [1]. At the institutional level, hospital administrators may benefit from improved laboratory productivity, more efficient resource utilization, and enhanced diagnostic capacity, although these advantages must be balanced against the costs of digital infrastructure, software implementation, staff training, and ongoing system maintenance.

The growing role of AI also has important implications for medical education. Future hematologists, hematopathologists, and laboratory professionals will require training not only in conventional morphology but also in AI literacy, digital pathology, data interpretation, and the ethical use of intelligent diagnostic systems. Preparing the workforce to collaborate effectively with AI will be essential for its responsible adoption.

At the healthcare system level, AI offers opportunities to improve diagnostic equity by expanding access to expert-level decision support, particularly in underserved and resource-constrained settings. For many low- and middle-income countries, where shortages of specialist personnel remain a significant challenge, validated AI systems could strengthen diagnostic services through telehematology and digital consultation networks. Low-cost, automated approaches have already been shown to screen for conditions such as sickle cell disease in resource-limited settings, where trained personnel for microscopic inspection are scarce [5]. Ultimately, the greatest beneficiaries are patients. Earlier detection, greater diagnostic precision, more consistent interpretation, and increasingly personalized treatment decisions have the potential to improve clinical outcomes while making high-quality hematologic care more accessible across diverse healthcare settings.

Successful implementation will also depend on establishing institutional governance structures that define responsibility for AI-assisted decisions, monitor algorithm performance after deployment, and ensure that clinicians remain actively engaged in all final diagnostic decisions. Maintaining meaningful human oversight will be essential for preserving patient safety, professional accountability, and public trust as AI becomes increasingly integrated into hematologic practice [31].

Conclusion

The evolution of hematologic diagnostics reflects a series of paradigm shifts driven by the growing complexity of disease biology and the increasing demand for more accurate, efficient, and individualized patient care. What began as a discipline centered on microscopic morphology has progressed through automation and digital pathology to the emergence of artificial intelligence as a transformative component of modern diagnostic practice. This transition is not simply a technological advancement but a fundamental redefinition of how hematologic diseases are identified, interpreted, and managed.

Current evidence demonstrates that AI has considerable potential to improve diagnostic efficiency, enhance consistency, and integrate diverse sources of clinical information. However, its greatest contribution

lies in augmenting, not replacing, the expertise of hematologists, hematopathologists, and laboratory scientists. Human judgment remains indispensable for contextualizing complex findings, addressing diagnostic uncertainty, and making patient-centered clinical decisions.

Emerging generative AI and large language models may further extend these capabilities by facilitating knowledge synthesis, clinical documentation, and multidisciplinary decision support, although their safe integration into hematologic practice will require rigorous validation, transparent governance, and continued human oversight.

Looking forward, the future of hematology will depend on the successful integration of morphology, laboratory testing, molecular profiling, cytogenetics, and clinical information within intelligent diagnostic ecosystems. Realizing this vision requires more than technological innovation; it demands rigorous clinical validation, transparent and explainable AI systems, representative and equitable datasets, multidisciplinary collaboration, and robust ethical and regulatory frameworks that ensure patient safety and public trust.

Ultimately, the future of hematologic diagnostics lies not in choosing between human expertise and artificial intelligence, but in creating an intelligent partnership where AI enhances clinical judgment, integrates multidimensional evidence, and enables truly personalized, precision-based hematologic care.

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References

1. Asghar R, Kumar S, Shaukat A, Hynds P. Classification of white blood cells (leucocytes) from blood smear imagery using machine and deep learning models: A global scoping review. PLoS One. 2024;19(6):e0292026. https://doi.org/10.1371/journal.pone.0292026
2. Matek C, Krappe S, Münzenmayer C, Haferlach T, Marr C. Highly accurate differentiation of bone marrow cell morphologies using deep neural networks on a large image data set. Blood. 2021;138(20):1917–27. https://doi.org/10.1182/blood.2020010568
3. Lin Y, Chen Q, Chen T. Recent advancements in machine learning for bone marrow cell morphology analysis. Front Med. 2024;11:1402768. https://doi.org/10.3389/fmed.2024.1402768
4. Kelly CJ, Karthikesalingam A, Suleyman M, Corrado G, King D. Key challenges for delivering clinical impact with artificial intelligence. BMC Med. 2019;17(1):195. https://doi.org/10.1186/s12916-019-1426-2
5. de Haan K, Ceylan Koydemir H, Rivenson Y, Tseng D, Van Dyne E, Bakic L, et al. Automated screening of sickle cells using a smartphone-based microscope and deep learning. npj Digit Med. 2020;3:76. https://doi.org/10.1038/s41746-020-0282-y
6. Boldú L, Merino A, Acevedo A, Molina A, Rodellar J. A deep learning model (ALNet) for the diagnosis of acute leukaemia lineage using peripheral blood cell images. Comput Methods Programs Biomed.

2021;202:105999. https://doi.org/10.1016/j.cmpb.2021.105999

7. Walter W, Pohlkamp C, Meggendorfer M, Nadarajah N, Kern W, Haferlach C, et al. Artificial intelligence in hematological diagnostics: Game changer or gadget? Blood Rev. 2023;58:101019. https://doi.org/10.1016/j.blre.2022.101019
8. Muehlematter UJ, Daniore P, Vokinger KN. Approval of artificial intelligence and machine learning-based medical devices in the USA and Europe (2015–20): a comparative analysis. Lancet Digit Health. 2021;3(3):e195–203. https://doi.org/10.1016/S2589-7500(20)30292-2
9. Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Leukemia. 2022;36(7):1703–19. https://doi.org/10.1038/s41375-022-01613-1
10. Rieke N, Hancox J, Li W, Milletarì F, Roth HR, Albarqouni S, et al. The future of digital health with federated learning. npj Digit Med. 2020;3:119. https://doi.org/10.1038/s41746-020-00323-1
11. Matek C, Schwarz S, Spiekermann K, Marr C. Human-level recognition of blast cells in acute myeloid leukaemia with convolutional neural networks. Nat Mach Intell. 2019;1(11):538–44. https://doi.org/10.1038/s42256-019-0101-9
12. Acevedo A, Alférez S, Merino A, Puigví L, Rodellar J. Recognition of peripheral blood cell images using convolutional neural networks. Comput Methods Programs Biomed. 2019;180:105020. https://doi.org/10.1016/j.cmpb.2019.105020
13. Kimura K, Tabe Y, Ai T, Takehara I, Fukuda H, Takahashi H, et al. A novel automated image analysis system using deep convolutional neural networks can assist to differentiate MDS and AA. Sci Rep. 2019;9:13385. https://doi.org/10.1038/s41598-019-49942-z
14. Steinbuss G, Kriegsmann M, Zgorzelski C, Brobeil A, Goeppert B, Dietrich S, et al. Deep learning for the classification of non-Hodgkin lymphoma on histopathological images. Cancers (Basel). 2021;13(10):2419. https://doi.org/10.3390/cancers13102419
15. Eckardt JN, Schmittmann T, Riechert S, Kramer M, Sulaiman AS, Sockel K, et al. Deep learning identifies acute promyelocytic leukemia in bone marrow smears. BMC Cancer. 2022;22(1):201. https://doi.org/10.1186/s12885-022-09307-8
16. Radakovich N, Nagy M, Nazha A. Artificial intelligence in hematology: current challenges and opportunities. Curr Hematol Malig Rep. 2020;15(3):203–10. https://doi.org/10.1007/s11899-020-00575-4
17. Nazha A, Elemento O, Ahuja S, Lam B, Miles M, Shouval R, McWeeney S, Sirhan S, Srisuwananukorn A, Haferlach T. Artificial intelligence in hematology. Blood. 2025;146(19):2283–92. https://doi.org/10.1182/blood.2025029876
18. Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. Nat Med. 2019;25(1):44–56. https://doi.org/10.1038/s41591-018-0300-7
19. Obermeyer Z, Powers B, Vogeli C, Mullainathan S. Dissecting racial bias in an algorithm used to manage the health of populations. Science. 2019;366(6464):447–53. https://doi.org/10.1126/science.aax2342
20. Amann J, Blasimme A, Vayena E, Frey D, Madai VI. Explainability for artificial intelligence in healthcare: a multidisciplinary perspective. BMC Med Inform Decis Mak. 2020;20(1):310. https://doi.org/10.1186/s12911-020-01332-6
21. Kratz A, Lee SH, Zini G, Riedl JA, Hur M, Machin S. Digital morphology analyzers in hematology: ICSH review and recommendations. Int J Lab Hematol. 2019;41(4):437–47. https://doi.org/10.1111/ijlh.13042
22. Esteva A, Kuprel B, Novoa RA, Ko J, Swetter SM, Blau HM, et al. Dermatologist-level

classification of skin cancer with deep neural networks. Nature. 2017;542(7639):115–8. https://doi.org/10.1038/nature21056

23. Acosta JN, Falcone GJ, Rajpurkar P, Topol EJ. Multimodal biomedical AI. Nat Med. 2022;28(9):1773–84. https://doi.org/10.1038/s41591-022-01981-2
24. Moor M, Banerjee O, Abad ZSH, Krumholz HM, Leskovec J, Topol EJ, et al. Foundation models for generalist medical artificial intelligence. Nature. 2023;616(7956):259–65. https://doi.org/10.1038/s41586-023-05881-4
25. Liu X, Cruz Rivera S, Moher D, Calvert MJ, Denniston AK; SPIRIT-AI and CONSORT-AI Working Group. Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the CONSORT-AI extension. Nat Med. 2020;26(9):1364–74. https://doi.org/10.1038/s41591-020-1034-x
26. Haferlach C, Hänselmann S, Walter W, Volkert S, Zenger M, Kern W, et al. Artificial intelligence substantially supports chromosome banding analysis maintaining its strengths in hematologic diagnostics even in the era of newer technologies. Blood. 2020;136(Suppl 1):47–8. https://doi.org/10.1182/blood-2020-137463
27. Poostchi M, Silamut K, Maude RJ, Jaeger S, Thoma G. Image analysis and machine learning for detecting malaria. Transl Res. 2018;194:36–55. https://doi.org/10.1016/j.trsl.2017.12.004
28. Syrykh C, Abreu A, Amara N, Siegfried A, Maisongrosse V, Frenois FX, et al. Accurate diagnosis of lymphoma on whole-slide histopathology images using deep learning. npj Digit Med. 2020;3:63. https://doi.org/10.1038/s41746-020-0272-0
29. LeCun Y, Bengio Y, Hinton G. Deep learning. Nature. 2015;521(7553):436–44. https://doi.org/10.1038/nature14539
30. Alcazer V, Le Meur G, Roccon M, Barrière S, Le Calvez B, Badaoui B, et al. Evaluation of a machine-learning model based on laboratory parameters for the prediction of acute leukaemia subtypes: a multicentre model development and validation study in France. Lancet Digit Health. 2024;6(5):e323–33. https://doi.org/10.1016/S2589-7500(24)00044-X