



Editorial

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Artificial Intelligence and Hematologic Malignancies



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Abstract

Artificial Intelligence holds immense potential to reshape hematology by automating complex tasks, enhancing diagnostic precision, prognostic accuracy, and therapeutic decision-making. Application of AI-based image analysis in assessing PD-L1 expression in diffuse large B-cell lymphoma (DLBCL) exemplifies how AI can enhance biomarker quantification and guide immunotherapy decisions. By leveraging deep learning algorithms, researchers have achieved high concordance with pathologist assessments, especially in fine needle biopsy samples, improving objectivity and reproducibility. The integration of AI into hematology demands robust validation, standardized protocols, and transparent models to ensure reliability and clinical trust.

Keywords: Artificial Intelligence; PD-L1; Hematologic Malignancies; Molecular Genetic

Abbreviations: AI: artificial intelligence; CBC: Complete blood count; ML: machine learning; DL: deep learning; MDS: myelodysplastic syndrome; MPN: Myeloproliferative neoplasms.

Introduction

Delays in diagnosing hematological diseases are primarily attributed to the complexity of symptoms and challenges in accurate disease diagnosis. Complete blood count (CBC) is typically the initial diagnostic tool to detect hematologic malignancies. It reveals abnormal blood cell count and morphological distortion in cells. Another challenging aspect is the detection of abnormal blood cell components. The current manual method for counting and recognition of abnormal cells is prone to inaccurate results making them dependent on the availability of highly skilled medical professionals [1].

Current Applications and Advances of AI in Hematological Malignancies

AI-based methods have been applied in hematology, it can be effectively utilized for the automated quantification of white and red blood cells, as well as for the rapid and accurate assessment of their morphology from digital microscopy, support the evaluation of flow cytometric data, aid in karyotyping, develop personalized models integrating multiple data sources, estimate the response to certain therapies and accurately predict the prognosis of various leukemias [2].

Morphology of Blood Cells

AI can be applied in the automated counting of white and red blood cells [3] and in the verification of cells morphology quickly and correctly. Its integration into diagnostic workflows can significantly reduce missed diagnoses. The most notable improvement has been observed in the identification of immature granulocytes—such as promyelocytes, myelocytes, and metamyelocytes—followed by abnormal lymphocytes, reactive lymphocytes, and blast cells.

In contrast, enhancement in detecting nucleated red blood cells and plasma cells have been the least significant [4]. AI has shown considerable promise in the classification of different lymphoid cell types, as well as in distinguishing between 17 and 21 cell types of different lineages and maturation stages. This includes the accurate identification of rare cell subsets and leukemic cells [3]. Blast cells may be ignored in manual differentiation when their proportion is low [4]. AI can differentiate between myeloblasts and lymphoblasts [3]. The interpretation of bone marrow smears is much more difficult and complex task [3].

Limitation: AI had insufficient ability to identify abnormal lymphocytes, as it is easily confused with small blast cells or other

cells [4]. Deep learning (DL) models for assisted interpretation of bone marrow smears could only yield moderate results [3].

Cytogenetics

Recent advancements in artificial intelligence (AI) have demonstrated considerable potential in the detection of numerical chromosomal abnormalities in tumor cytogenetics. Emerging evidence suggests that, beyond numerical anomalies, AI may also be capable of identifying structural aberrations in karyograms through automated analysis, paving the way for more comprehensive diagnostic capabilities [5].

Limitation: Misclassification errors frequently arise among chromosomes that exhibit high similarity in size, shape, and appearance [5].

Immunophenotyping

Flow cytometry generates large amounts of data. On average, each sample yields measurements from more than 50,000 individual cells. These data are typically analyzed by plotting the expression of the selected markers against one other [5]. Few attempts have been made for disease classification using flow cytometry data without preceding image transformation. Different machine learning (ML) techniques have been applied for identification of various hematologic malignancies including AML, CLL and lymphomas. Furthermore, AI-driven approaches have been employed to standardize the interpretation of minimal residual disease (MRD) measurements obtained via flow cytometry. AI demonstrates high predictive accuracy in predicting the clinical outcome of AML and myelodysplastic syndrome (MDS) patients with high accuracy [3].

Molecular genetics

The integration of ML and DL techniques into clinical genomic analysis holds significant promise. These advanced methods can rapidly recognize DNA sequence patterns, mutations, and disease markers faster than traditional methods. It forms the basis for automated disease classification and is required for clinical decision-making [3].

Clinical application of AI in diagnosis of hematological malignancies

Myelodysplastic Syndrome (MDS)

- Differentiate between MDS and aplastic anemia.
- Identify the diagnostic and prognostic associations between genetic variants and morphological changes.
- Identify molecular signatures strongly associated with response to hypomethylating agents [3].

Acute Myeloid Leukemia (AML)

- Automated identification and annotation of individual cells for the classification of different types of AML [3].

- Correlation of distinct morphological features to certain genetic aberrations, for simple and fast prescreening [2].

- Identify a prognostic 3-gene signature that separated AML patients of European LeukemiaNet (ELN) into subgroups with different survival probabilities.

- Pinpoint patients with NPM1mut AML cohort who are at high risk of relapses according to a genetic score.

- Assign AML patients with RUNX1-RUNX1T1 to favorable and poor risk classes [3].

- Differentiation of malignant and healthy cells for ALL diagnosis and ALL subtype classification [3].

Myeloproliferative Neoplasms (MPN)

- Discrimination of reactive and myeloproliferative neoplasms (MPN) samples [3].

- Distinction of Philadelphia chromosome-negative MPN (Ph-negative MPNs) by combining the readout of a hematology analyzer with morphological parameters automatically extracted from PB smears. The system had more than 90% sensitivity and more than 90% specificity compared to human experts.

Lymphomas

- DL algorithm can detect MYC+ DLBCL areas on standard hematoxylin and eosin (H&E)-stained slides of tissue biopsies and resections. It has a sensitivity of 0.93, which could save up to 34% of genetic tests [2].

- Accurate quantification of PD-L1 expressions on immunohistochemistry (IHC) whole slide images to improve the targeted immunotherapy development in DLBCL patients [6].

Other indications

- Differentiate various bone marrow disorders by integration of clinical data, peripheral blood values, and mutational data, into a genoclinical model.

- Molecular genetic data can help in clinical diagnosis and for prognostication and the prediction of drug-responses [3].

- Larger gene panels and DL-based approaches can be applied in patient classification, biomarker detection, and predicting clinical response to anticancer drugs [3].

Current Challenges for Clinical Implementation Of AI-Based Methods in Hematology

These models can often fall into several key pitfalls

Generalizability

The difference in various parameters, such as the selected genes, the selected staining technique, or the used antibodies and hotspots of a testing panel between different laboratories, institutions, and hospitals, impedes the generalization of the

developed methods [3].

Overfitting

The capability of the algorithm to extract meaningful features and to reliably identify the phenotype is restricted by its inability to obtain sufficient training material of rare cells in morphology, immunophenotyping and rare chromosomal abnormalities in tumor cytogenetics. For some instances, the available training data is also limited in its complexity, capturing only part of the biological variability. In ML, the danger of the inability to learn the training data too well is that a model can make excellent, precise predictions about those data but make very poor predictions on external data due to the sometimes-limited training material. There is a high risk of significantly worse performances for unseen data resulting in overfitting [3]. There is a potential of improving the performance of AI technologies by constant learning [3].

Lack of interpretability

Many AI models, especially DL ones, function as “black boxes,” making it difficult to understand how they arrive at decisions. Interpretability refers to the ability of AI to explain or present to humans why ML models make their model’s decisions and which variables in the model weigh most heavily in its prediction not just what decisions they make.

Data Quality

Training AI algorithms relies heavily on high-quality, representative data. Biases in patient selection or data quality can lead to inaccurate models [3].

Data Quantity

The performance of the algorithms largely depends on the availability of extensive standardized digital data to train the algorithms [3]. ML algorithms are notoriously data-hungry. Increasing numbers of cases reduces the likelihood of overfitting and increases model accuracy. There is no “golden number” at which every model saturates with enough patients or cases to generate stable, useful predictions; however, simulations suggest that the optimal number can be in the several thousands, with DL often requiring orders of magnitude more [3].

Class Imbalance

Class imbalance is a common challenge in AI, especially in ML classification tasks. It occurs when one class in the dataset significantly outnumbers the others—in an image classification problem. This imbalance can lead to biased models that perform well on the majority class but poorly in the minority class [3].

Uncertainty and Confidence

Clinical ML articles often propose models that do not provide indication of the degree of uncertainty associated with a particular result. Confidence and uncertainty in AI shape how machines make decisions and how humans interpret those decisions.

Confidence

A model’s belief in the correctness of its prediction, often expressed as a probability (e.g., 90% sure this image is a cat). Uncertainty: The degree to which a model is unsure about its prediction. It helps to identify when a model might be wrong or when more data is needed. Chronic Lymphocytic Leukemia Treatment-Infection Model (CLL-TIM) is an excellent example of this approach [3]. CLL-TIM-a ML-based tool designed to predict whether a newly diagnosed CLL patient is at high risk of infection or needs treatment within the next two years [3].

Conclusion

The road to widespread clinical adoption of AI in hematology is paved with challenges-such as overfitting, lack of generalizability, interpretability concerns and data limitations. Addressing these issues requires continuous model refinement. As AI continues to evolve, its thoughtful integration into hematologic practice could lead to more accurate diagnoses, better patient outcomes, and a new era of data-driven hematology.

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