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POSTER ABSTRACTS

803.EMERGING TOOLS, TECHNIQUES, AND ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

Leveraging AI for Predicting Genetic Alterations in Multiple Myeloma through Morphological Analysis of Bone Marrow Aspirates

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The diagnosis of multiple myeloma (MM) heavily relies on the cytomorphological analysis of bone marrow aspirate (BMA), supplemented by cytometry and genetic analysis of cytogenetic alterations, which hold critical prognostic and therapeutic implications. Key genetic alterations such as translocation t(11;14), ,gain 1q (+1q), deletion (del) 17p, and del1p are critical for determining disease prognosis and/or treatment strategies. However, the current diagnostic processes are time-consuming and resource-intensive, necessitating the need for more efficient methods. The primary aim of this study is to develop an AI system capable of screening and identifying patients with these genetic alterations based solely on the morphological features of BMA samples analyzed through automated optical microscopy. This approach seeks to enhance diagnostic accuracy, streamline the detection of genetic abnormalities, and facilitate early screening, thereby informing more effective and personalized treatment plans for MM patients.
BMA samples from non MM patients, MM patients without the targeted genetic alterations, and MM patients with confirmed alterations (t(11;14), +1q, del17p, del1p) were analyzed by digitizing 40 fields (100x) per patient using a 3D-printed device that attaches a mobile application to an optical microscope. Firstly, an AI algorithm was developed using a database of over 400,000 manually labeled cells, enabling automatic identification of nucleated cells and classification into plasma cells and non-plasma cells. Subsequently, another AI algorithm was designed to recognize morphological patterns of PC indicative of the genetic alterations. This algorithm is based on a Multiple Instance Learning (MIL) architecture, utilizing features extracted

from each cell by a foundational model trained through self-supervised learning on a database of over 1.4 million BMA cells. The dataset was divided into 66% for training and 33% for testing, ensuring patient-level independence between the sets.
A total of 946 digitized cases were analyzed, comprising 250 MM patients and 696 non-MM patients. Among the MM patients, 109 did not have the targeted genetic alterations, while 141 MM had specific genetic alterations. Of these, 80 had t(11;14), 64 had +1q, 24 had del17p, and 28 had del1p, with some patients presenting multiple alterations. The AI algorithm for detecting plasma cells achieved a ROC-AUC of 98%. On average, 174 plasma cells were detected and analyzed per BMA sample. The AI algorithm designed to identify patients with these genetic alterations based on morphological analysis of plasma cells demonstrated high efficacy. For t(11;14), the algorithm achieved an AUC of 92.50%, with a sensitivity of 91.67% and a specificity of 92,20%. For +1q, the AUC was 96.00%, with a sensitivity of 89.47% and a specificity of 93.94%. For del1p, the AUC was 96.80%, with a sensitivity of 100.00% and a specificity of 96.17%. For del17p, the AUC was 86.00%, with a sensitivity of 100.00% and a specificity of 80.39%.
Our results underscore the potential of applying AI models to the morphological analysis of plasma cells in BMA samples for the detection of multiple genetic alterations, confirming a significant correlation between cell morphology and genetics in MM cases. The developed AI algorithm accurately identifies the presence of morphological features suggestive of t(11;14), +1q, del17p, and del1p with high sensitivity and varying specificity. Clinically, this AI-driven approach could simplify the diagnosis and prognosis of MM patients, enabling more targeted therapeutic interventions. Overall, the algorithm demonstrated high sensitivity across all alterations, with specificity varying by alteration. The exceptionally high sensitivity and specificity for del1p, and the high sensitivity for del17p, in particular, highlight the potential of AI in accurately identifying these clinically significant genetic alterations based on morphology. Improved performance for other alterations may be achieved through increasing sample sizes, refining model architectures, or incorporating additional predictive variables. This advancement holds promise for integrating AI tools into routine clinical practice, potentially reducing the need for extensive genetic testing and accelerating the decision-making process for personalized MM treatment strategies.

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