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803.EMERGING TOOLS, TECHNIQUES AND ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

Machine Learning Models Predict Molecular Genetic Subtypes of Multiple Myeloma from Whole-Slide Bone Marrow Aspirate Smears

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Multiple myeloma (MM) is a plasma cell neoplasm and the second most common hematologic malignancy. Current guidelines recommend multiple myeloma cases undergo karyotyping and fluorescence in situ hybridization (FISH) analysis on bone marrow biopsy samples to assess for specific recurrent genetic abnormalities. Results of this testing help to predict differences in patient prognosis over time and to guide appropriate selection of therapy. Refinements in risk stratification incorporated additional complex molecular testing which, along with karyotyping and FISH, are costly and not available to all patients. Myeloma cell cytomorphologies have been associated in a subset of cases with more aggressive disease, when plasmablastic, and with a subset of t(11;14) cases, when lymphoplasmacytoid. Nonetheless, cellular features as assessed by manual microscopy have not been shown to identify biologic subtypes of disease reproducibly and broadly, such that these features are not a component of current prognostic systems. Whether accurate risk-stratification information can be extracted from microscopic images of myeloma cells through machine-based approaches is uncertain. Thus, in this study, we tested the feasibility of using machine learning models to predict multiple myeloma molecular genetic subtypes from analysis of neoplastic plasma cell morphology on Wright-stained aspirate smears. We first improved upon a previously developed computational pipeline that identifies and classifies hematopoietic cells from scanned whole-slide images (400x) of bone marrow aspirate smears, including classification of plasma cells with 94% accuracy. Using this pipeline, we obtained images from all plasma cells (up to 68,569 plasma cells per slide) from aspirate smears of 18 patients without plasma cell neoplasms and 96 patients with plasma cell neoplasms (including 20 with t(11;14) and 23 with gain(1q); 44 with standard risk FISH and 22 with high risk FISH (t(4;14), t(14;16), del(17p), or >4 copies 1q+)). We then developed convolutional neural network (CNN)-based multi-instance machine learning models to perform patient-level classifications of disease status and molecular genetic classification from image-level analysis of plasma cell cytomorphology. These models demonstrated strong performance for classifying patients without versus with plasma cell neoplasms (AUROC 0.80), and are capable of making patient-level predictions of multiple myeloma molecular genetic subtypes (t(11;14), AUROC 0.73; gain(1q), AUROC 0.71) as well as prediction of FISH risk level (AUROC 0.68). Finally, by assessing cell attention scores and CNN model weights, this machine learning pipeline can assess which individual plasma cells and which specific morphologic features provided the most utility in the prediction of molecular genetic subtypes for individual patients, hence providing explainability for model output. Importantly, our findings suggest that cytomorphologic features of plasma cells on routine aspirate smear slides contain information, extractable through machine-based approaches, that correlates with molecular genetic subtypes employed for risk stratification. With further refinement these promising computational digital pathology models can potentially yield tools not only for use in low resource settings, but also provide a potential basis for development of multimodal models that incorporate and improve upon results of currently used risk stratification tools.

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