An Online Decision Support System for Diagnosing Hematopoietic Malignancies By Flow Cytometry Immunophenotyping

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Abstract
An online decision support system for hematopoietic neoplasm based on virtual flow has been developed. Rules were implemented via eXtensible Markup Language (XML). 153 cases representing 28 different hematopoietic neoplasms were correctly classified. Further testing for unknown cases is undergoing.

Introduction
Flow cytometry is an essential tool to characterize hematologic malignances. Almost all laboratories use stand-along software to analyze flow cytometry data, coupled with manual interpretation which is time-consuming since multi-steps need to be taken. The process is error-prone due to manual data input. For pathologists who are not subspecialized in hematopathology, an online automated interpretation system will be useful in making diagnosis. For expert Hematopathologist, such system can be used for screening assessment. It can also sever as teaching tool for pathology residents.

Methods and Results
Several stand-alone systems have been built for automated analysis of flow cytometry immunophenotyping results for malignant lymphoma and leukemia\textsuperscript{1,2}. In this study, a knowledge-based decision support system to interpret online flow cytometry results for hematopoietic neoplasms have been developed as a complete Client-Server application by using Java programming and XML technology. The listmode flow cytometry data files are imported to the online decision support system where gating, dotplot, histogram and contour plot can be performed. Upon gating, the cell clusters of designation (CD markers) results are generated in percentage of cell population, based on which the positive or negative designation for CD markers is automatically assigned. By analyzing 273 of flow cytometry data profiles including both normal condition and hematopoietic neoplasms, we have set the threshold for CD markers’ positivity and B cell clonality (kappa and lambda ratio less than 0.5 or more than 4). Our expertise on diagnosing hematologic disorder is utilized in developing a semantic network of knowledge base. Confidence level of final differential diagnosis is calculated through a formula from the confidence factor of CD markers in making a particular diagnosis. Inference engine was implemented by JAVA programming (version 1.5.0) and XML (version 1.0) where tree structure and search algorithm are employed. The decision support system is hosted in an Apache-Jakarta Tomcat server container (version 5.5.20). A set of 153 flow cytometry listmode data files following flow cytometry data standard 2.0 with distinctive immunphenotyping profile covering both normal and 28 different hematopoietic neoplasms using World Health Organiztition (WHO) criteria are fed into the system and correct diagnosis was made. To further validate this online decision support system, a large case volume with unknown diagnosis will be tested. This is the first reported online decision support system implemented with XML and JAVA programming to interpret flow cytometry immunophenotyping results for hematopoietic neoplasms.

Conclusion
The website (http://www.flowcytometryonline.com) has been setup for online decision support where listmode data files located either in Sever side or Client side can be accessed and analyzed. Stand-alone application is also provided when internet access is limited. The system is expected to facilitate clinical diagnosis of hematologic neoplasms.

References