Image-Based Detection of High-Grade B-Cell Lymphomas (DH-L)

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INTRODUCTION

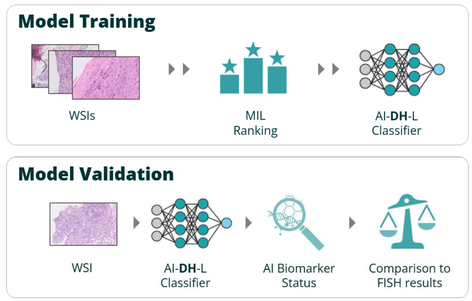
- Aggressive B-cell Non-Hodgkin Lymphomas (B-NHL) are divided into two main categories:
  - Diffuse large B-cell lymphoma (DLBCL) accounting for 90% of cases
  - High-grade B-cell lymphoma (HGBL)
- Diagnosis of HGBL with *MYC* and *BCL2* and/or *BCL6* rearrangements (double-hit lymphoma; DH-L) is confirmed by fluorescence in situ hybridization (FISH) analysis[1].
- Accurate and rapid diagnosis of DH-L is obligatory, when considering more aggressive treatment regimens (other than R-CHOP), suggested in these patients[2].

OBJECTIVE

To establish a novel tool for diagnosing DH-L directly from scanned Hematoxylin and Eosin (H&E) biopsy slides, by applying digital imaging technologies supported by machine learning algorithms.

METHOD

- H&E whole slide images (WSIs), prepared from biopsies obtained from lymph nodes as well as extra-nodal organs of patients with aggressive B-cell lymphoma histology, were collected from the pathology department at Tel-Aviv Sourasky Medical center (TASMC).
- Advanced Convolutional Neural Network (CNN) analysis was used to generate the aggressive B-NHL classifier (powered by Imagene-AI).



MIL=multiple instance learning

STUDY COHORT

- Cases were randomly divided into a training and a validation set (no significant differences were found between the sets).

Patients characteristics

	Training set (n=33)	Validation set (n=26)
Male, n (%)	18 (54.5)	16 (61.5)
GCB, n (%)	13 (39.4)	14 (53.8)
Lymph node samples, n (%)	14 (42.4)	6 (23.1)
Extra nodal samples, n (%)	19 (57.6)	20 (76.9)

RESULTS

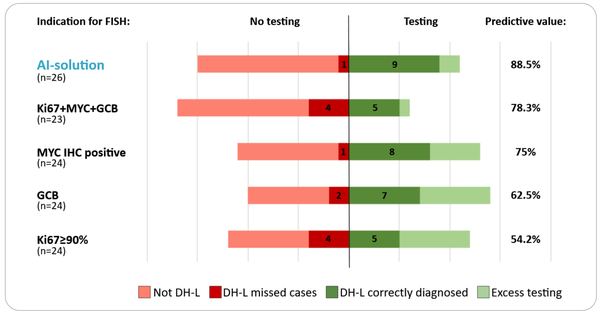
- H&E WSIs of the validation set samples were analysed using the AI-DH-L Classifier.
- The Classifier performance was evaluated compared to the official results obtained by FISH analysis.

AI-DH-L Classifier performance

	Official results		AI-Classifier results				AI-Classifier performance			
Total	**# P**	**# N**	**# TP**	**# TN**	**# FP**	**# FN**	**Sensitivity**	**Specificity**	**Accuracy**	**AUC**
26	10	16	9	14	2	1	90%	87.5%	88.46%	0.94

P=positive, N=negative, TN=true negative, TP=true positive, FP=false positive, FN=false negative

- Current criteria for employing FISH analysis to detect DH-L cases rely on **Ki67** expression, **MYC** expression, or diagnosis of **GCB**. However, all were found to be insufficiently specific[3].
- The AI-DH-L Classifier demonstrated high predictive values as a screening tool.



Predictive values of conventional features vs. the AI-DH-L -classifier *for correctly deciding whether to perform FISH testing.*
Presented are the number of samples in the relevant bars and predictive values for each screening method used (bright red and dark green bars).

CONCLUSIONS

- Here we present an AI-solution for the identification of DH-L patients.
- Current features used as criteria for FISH testing for the detection of DH-L cases display unacceptable rates of false negative cases demanding the development of new screening methods.
- The AI-DH-L Classifier demonstrated high performances and displayed superior predictive values compared to current conventional criteria used as a screening tool for guiding FISH testing.
- Interestingly, the AI-DH-L Classifier identified 2 cases with complex Burkitt manifestation and FISH results as DH-positive. While requiring further investigation, this suggests that the Classifier might identify cases that otherwise would have not been identified as DH with the conventional methods.

VISION

- Image-based prediction of biomarker status provides a fast, accessible and standardized method.
- The AI solution presented here uses routinely prepared pathological slides for the prediction of biomarker status without the requirement for additional material or substantial human labor.
- Implementation of such a system within the medical center can support real-time molecular profiling of B-NHL patients, defining a specific group of patients that would benefit from subsequent FISH testing, thereby, ultimately improving patient care.

REFERENCES

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