9° WORKSHOP
IN EMATOLOGIA TRASLAZIONALE
DELLA SOCIETÀ ITALIANA DI EMATOLOGIA SPERIMENTALE

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Digital Pathology in Ematologia: Utile o Ridondante?

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Disclosures di Gianluca Asti

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

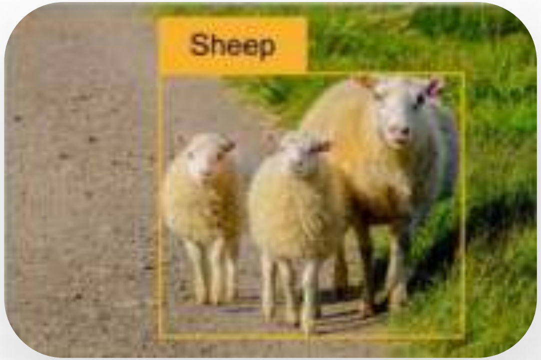
Bone marrow (BM) cytology and histopathology images are crucial for diagnosing and prognosticating myeloid neoplasms (MNs), but their high-dimensional data are underused.

Artificial Intelligence (AI) applied to tumor morphology (digital pathology, DP) has improved the use of tumor biopsies' data for various types of malignancies, accurately detecting patterns and converting complex image information into numerical features.

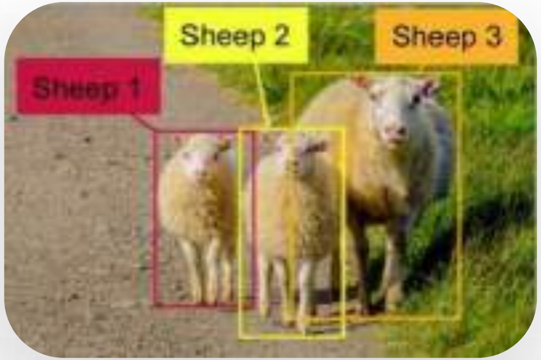
Here, we explored the potential of AI-based DP to improve personalized medicine in MNs which are characterized by high heterogeneity and a significant proportion of patients with unmet clinical needs.

What is Predictive AI

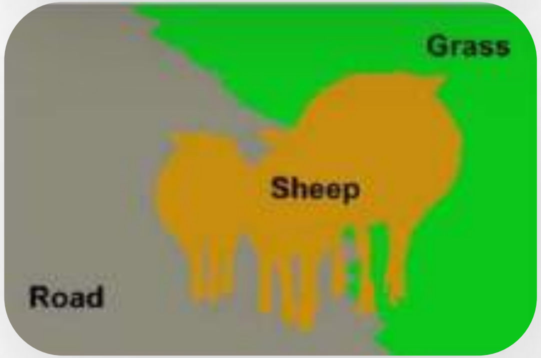
CLASSIFICATION AND LOCALIZATION



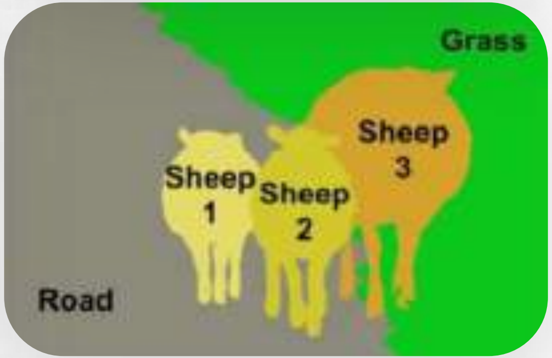
OBJECT DETECTION



SEMANTIC SEGMENTATION



INSTANCE SEGMENTATION



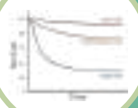
AIMS

This project was conducted by the GenoMed4All and Synthema consortia, to build AI-based features extraction tools from BM histopathological and cytological Whole Slide Images (WSI). High-dimensional data were used to

AIMS

1) assess diagnostic accuracy in MN patients

2) elucidate the association between morphologic features, clinical variables and molecular genetics

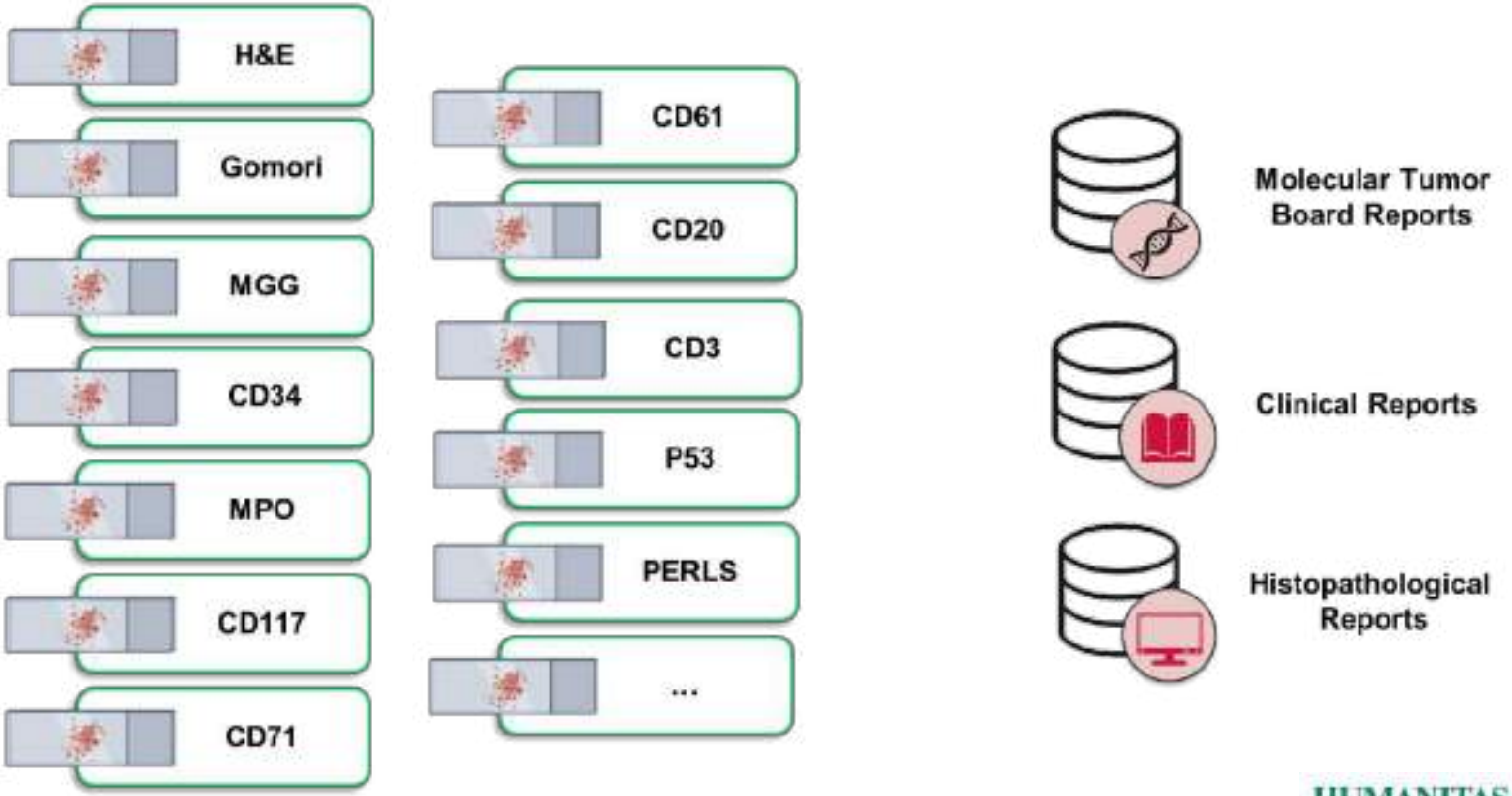


3) create an innovative tool for personalized risk assessments integrating morphological features with clinical and genomic information.

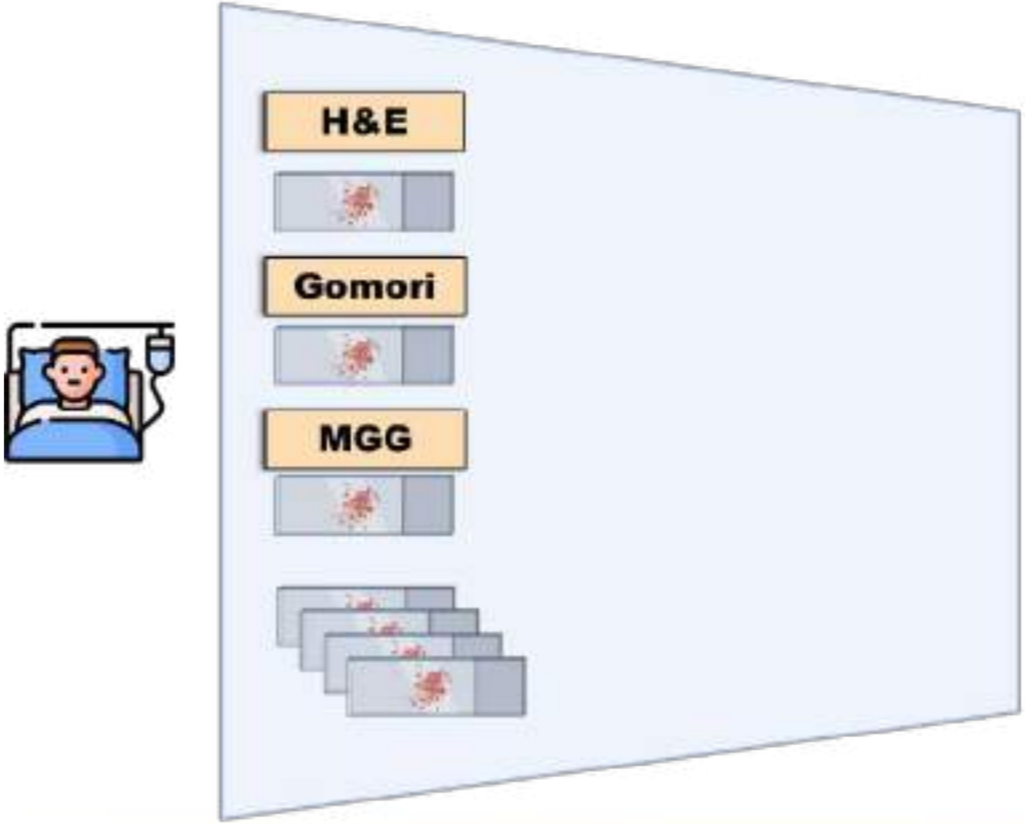
Myeloid Neoplasm Dataset

Patients Cohort Characteristics	All Patients (n = 1,167)
Age (y), median (range)	67 (20-96)
Gender (Male/Female), %	700/467, 60% ; 40%
Patient Diagnosis	
AML (%)	210 (18%)
MDS (%)	514 (44%)
MDS/MPN (%)	105 (9%)
MPN (%)	338 (29%)

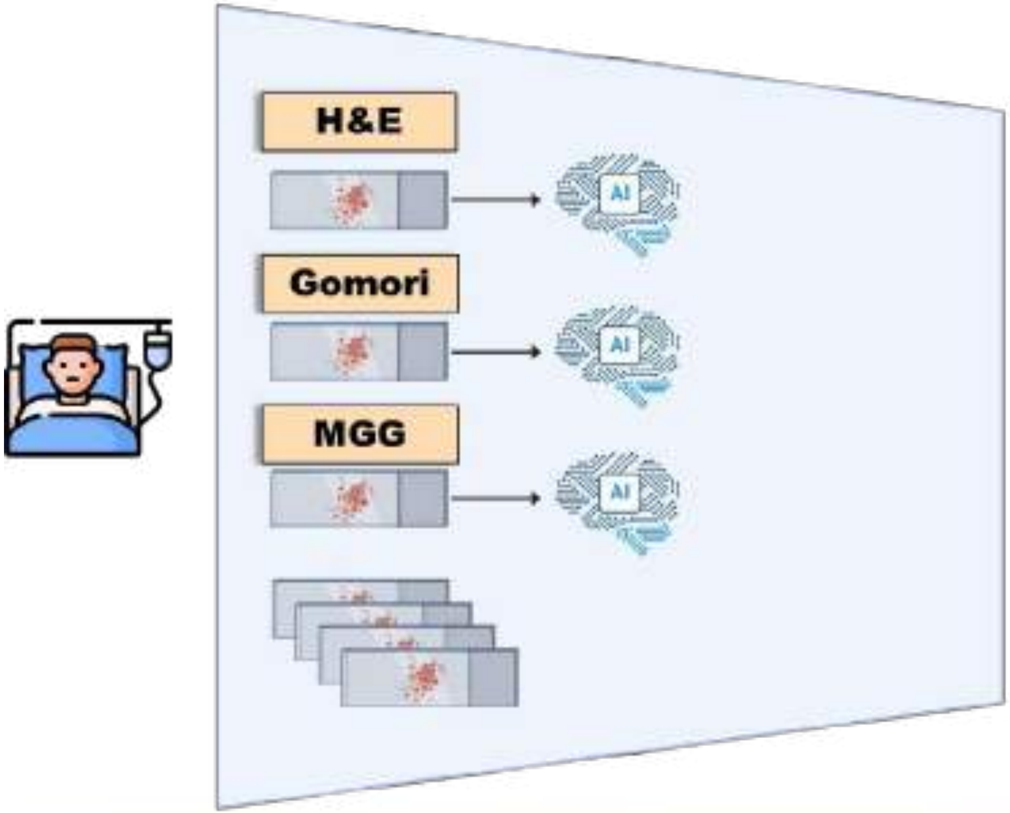
Myeloid Neoplasm Data Layer



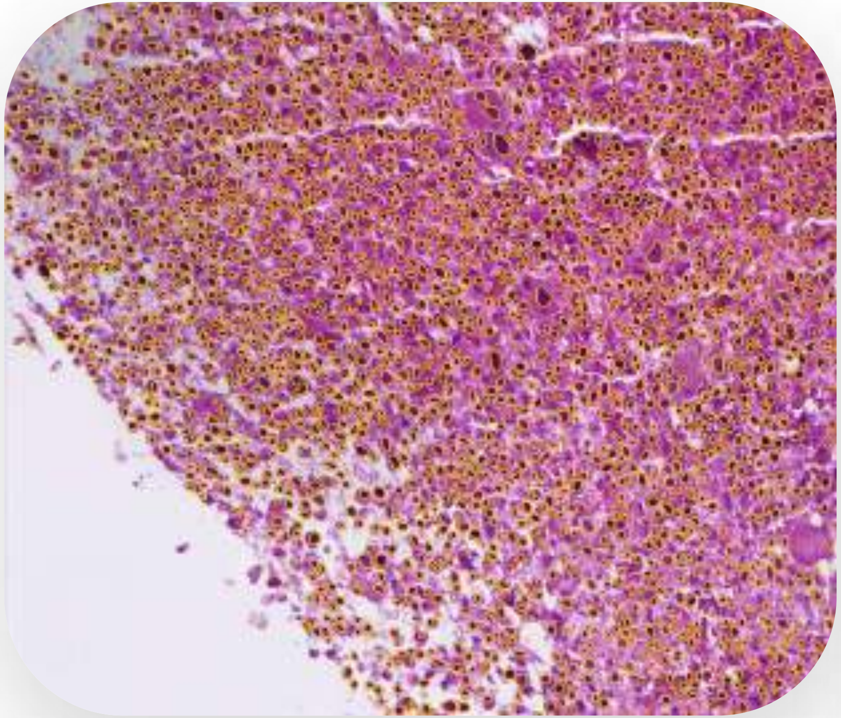
The Pipeline

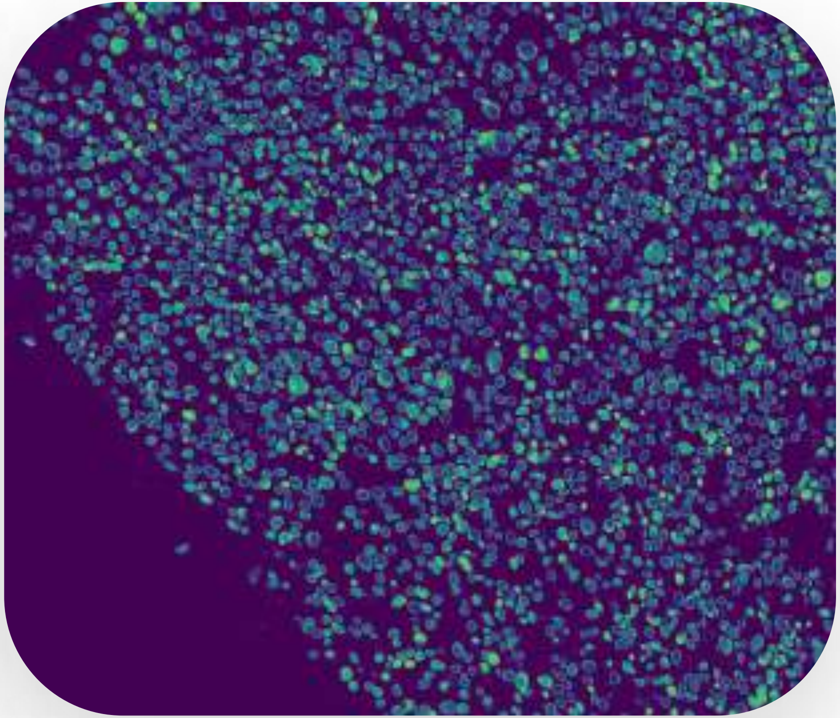


The Pipeline

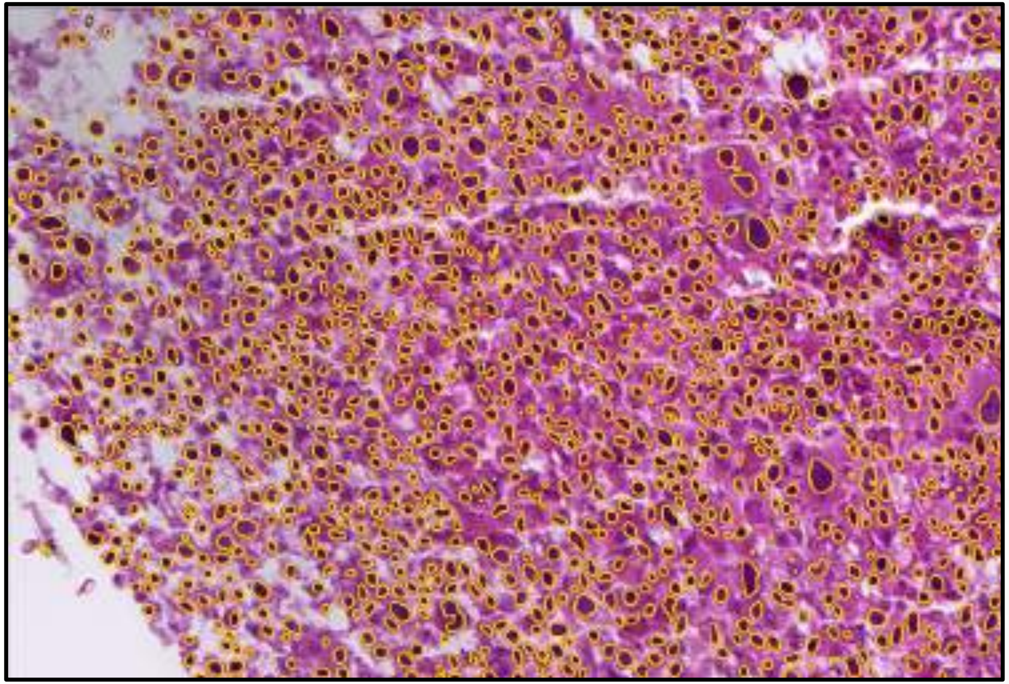


Features Extraction: Hematoxylin and Eosin





Features Extraction: Hematoxylin and Eosin

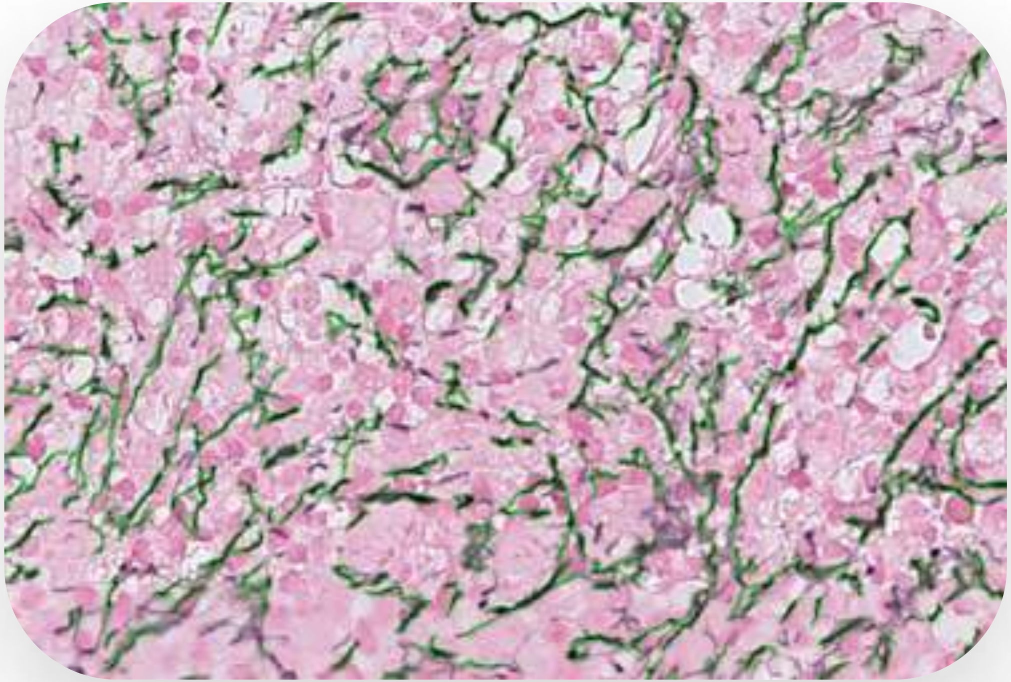


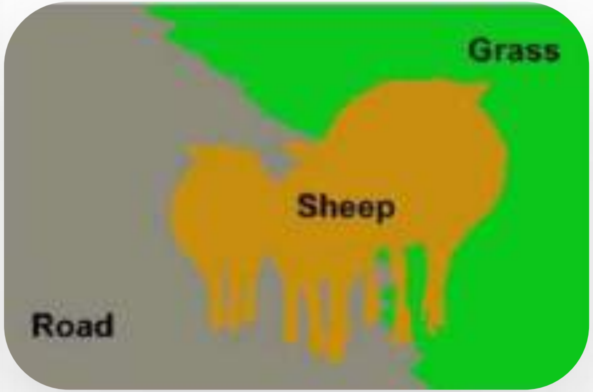
Morphological
Area
Perimeter
...

Color
Mean RGB
Mean HSV

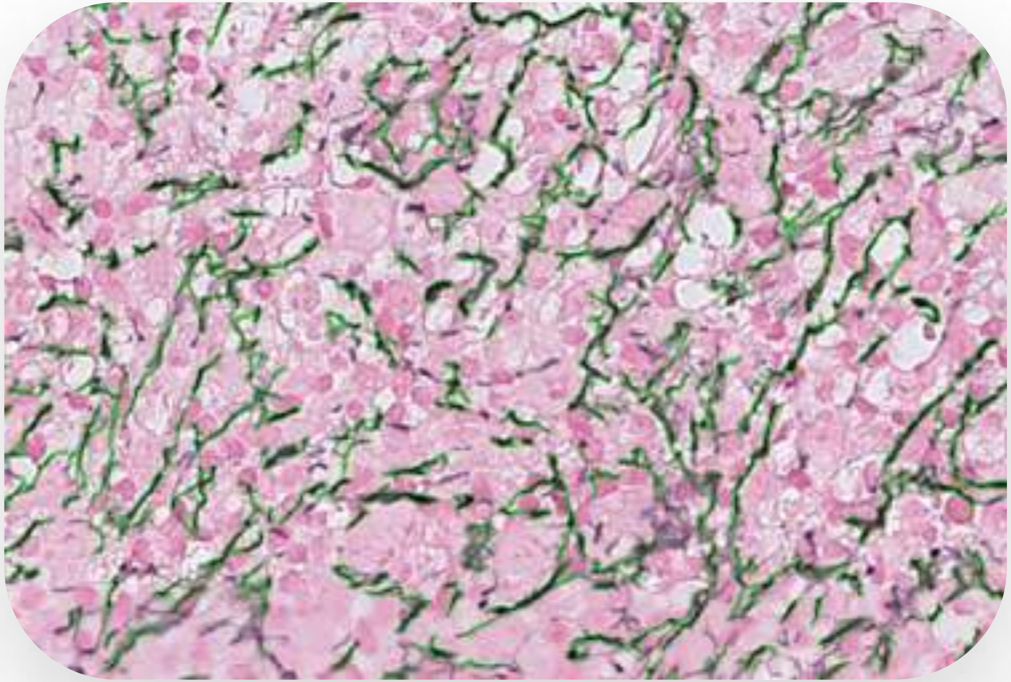
Haralick
Entropy
Contrast

Features Extraction: Gomori



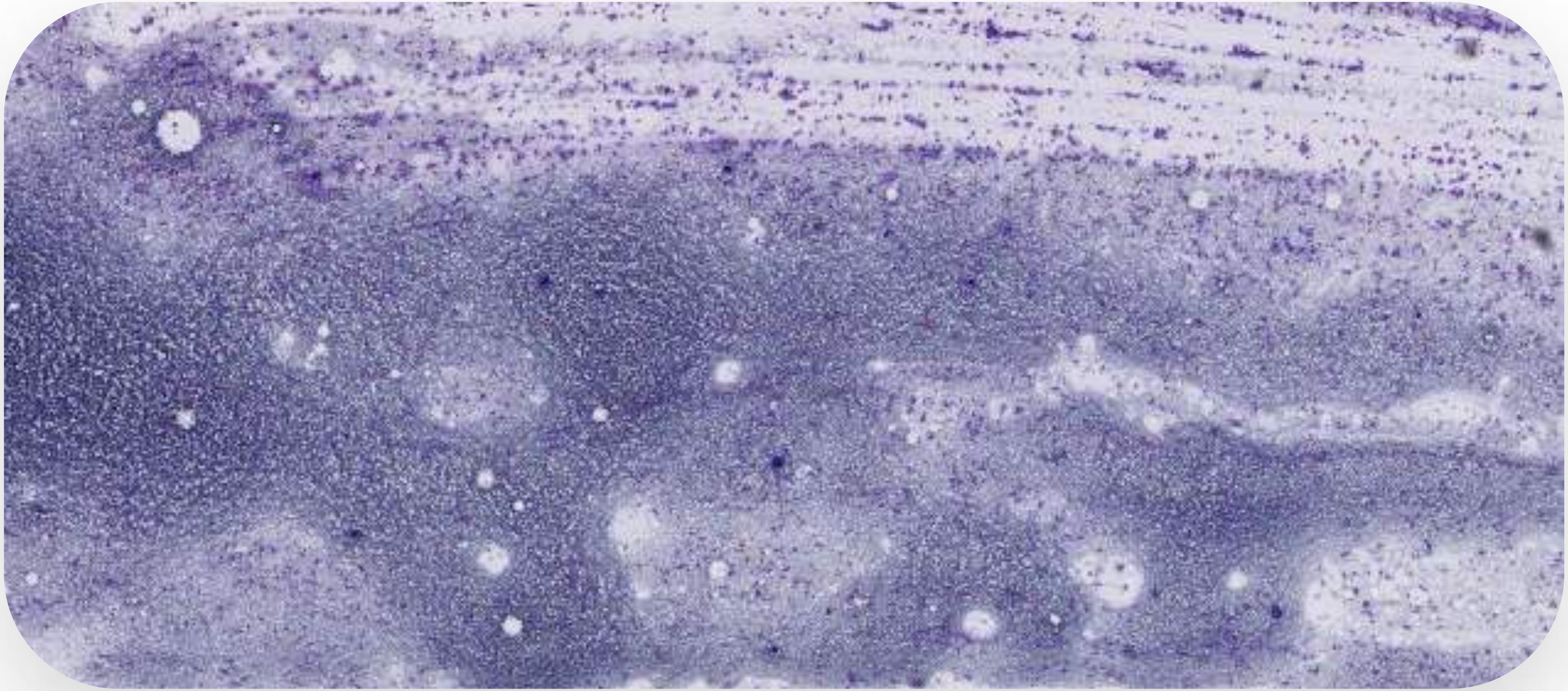


Features Extraction: Gomori

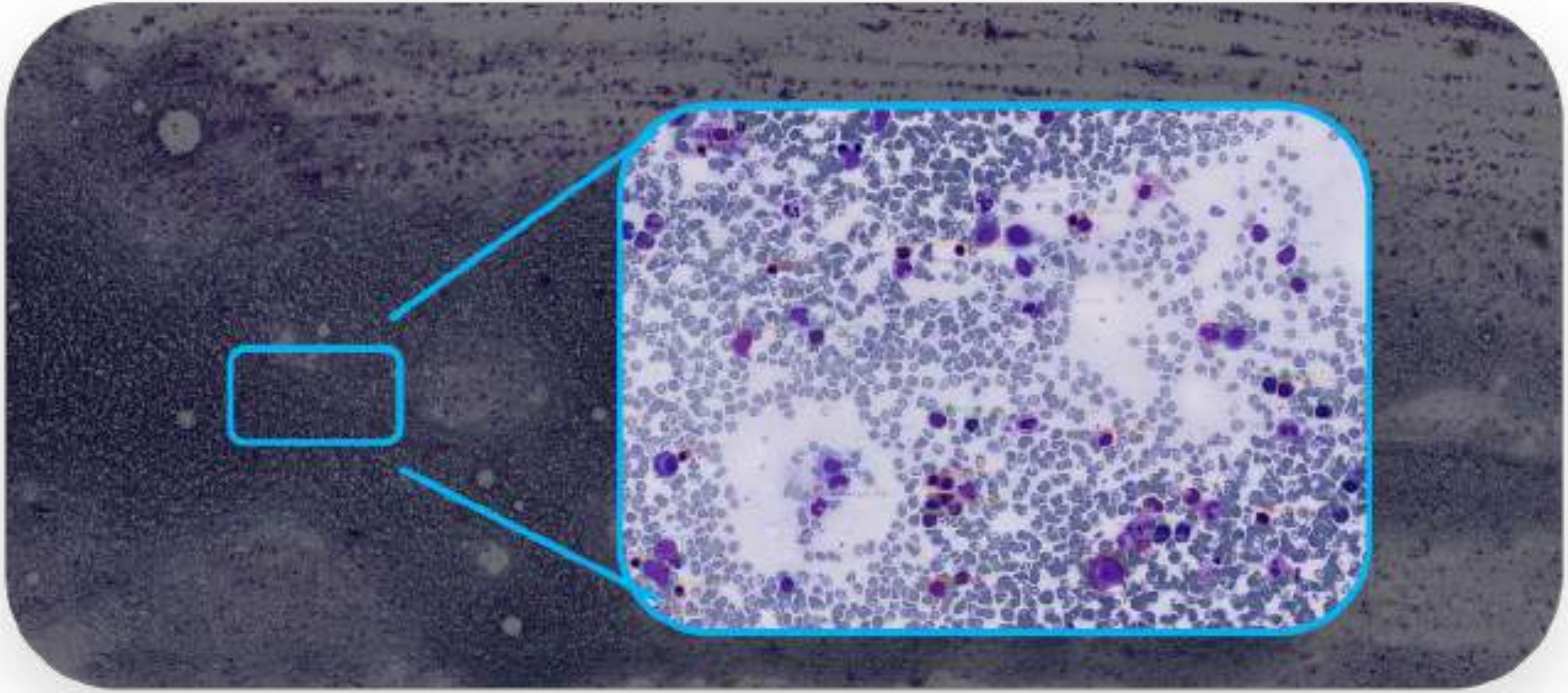


Fibrosis %

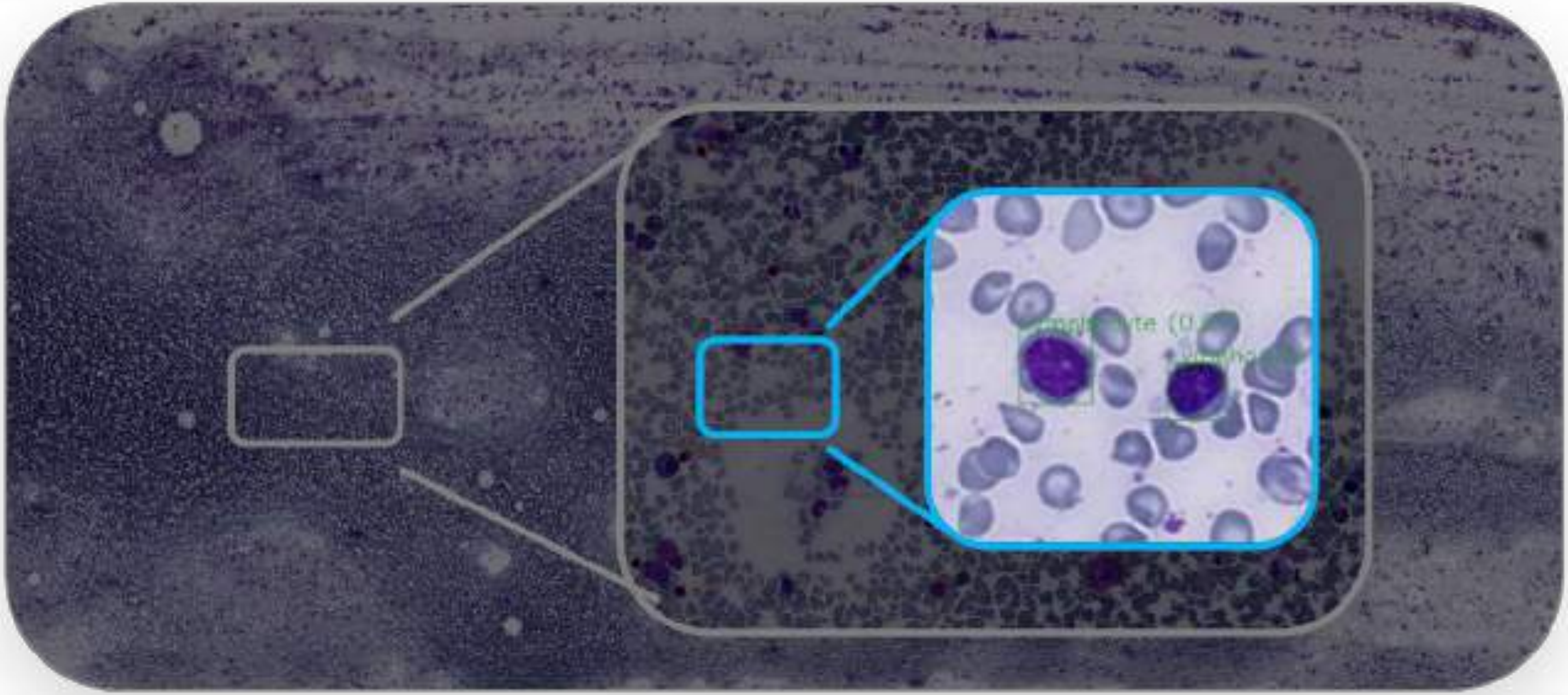
Features Extraction: May-Grunwald Giemsa



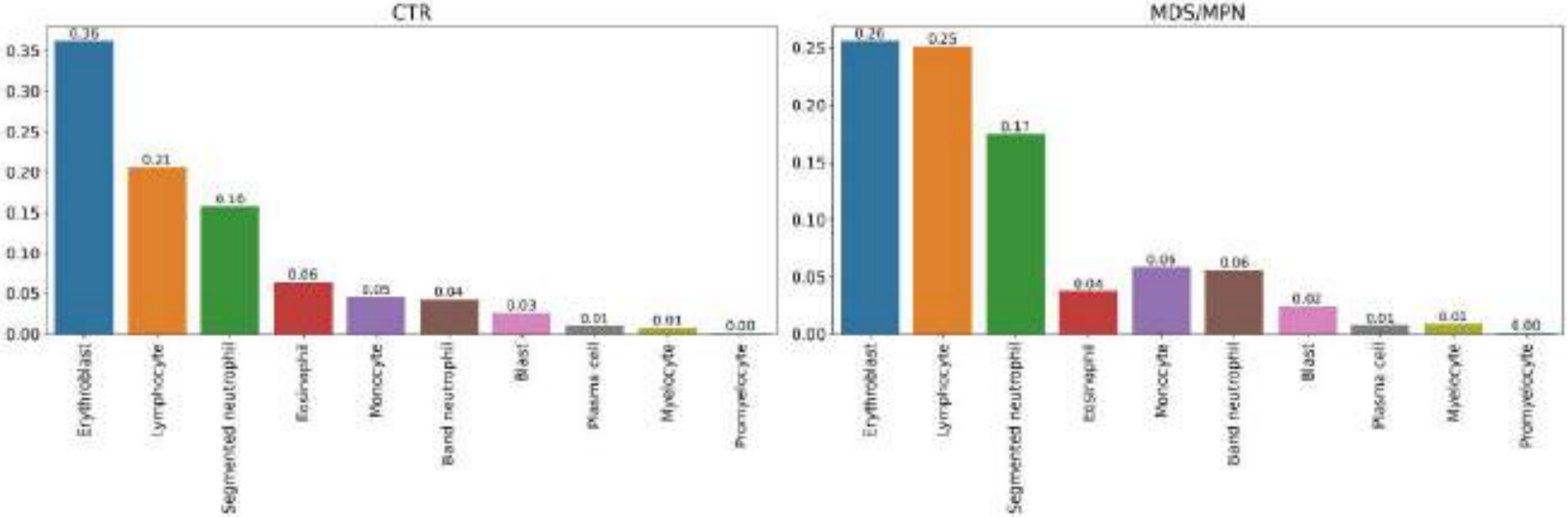
Features Extraction: *May-Grunwald Giemsa*



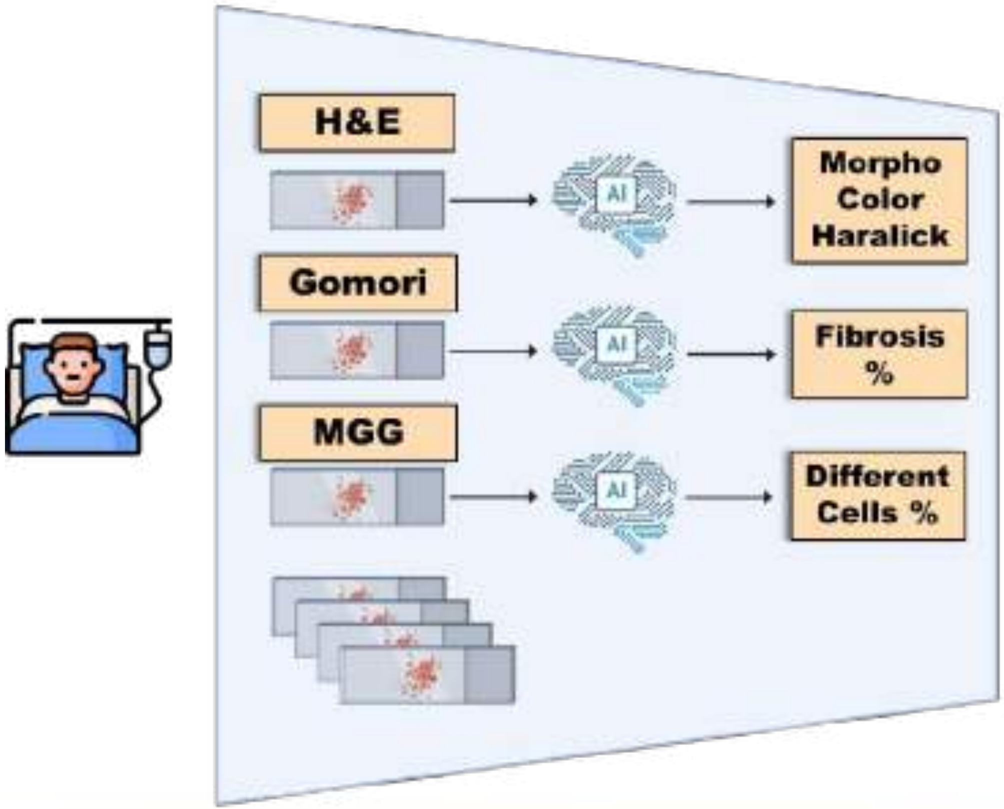
Features Extraction: May-Grunwald Giemsa



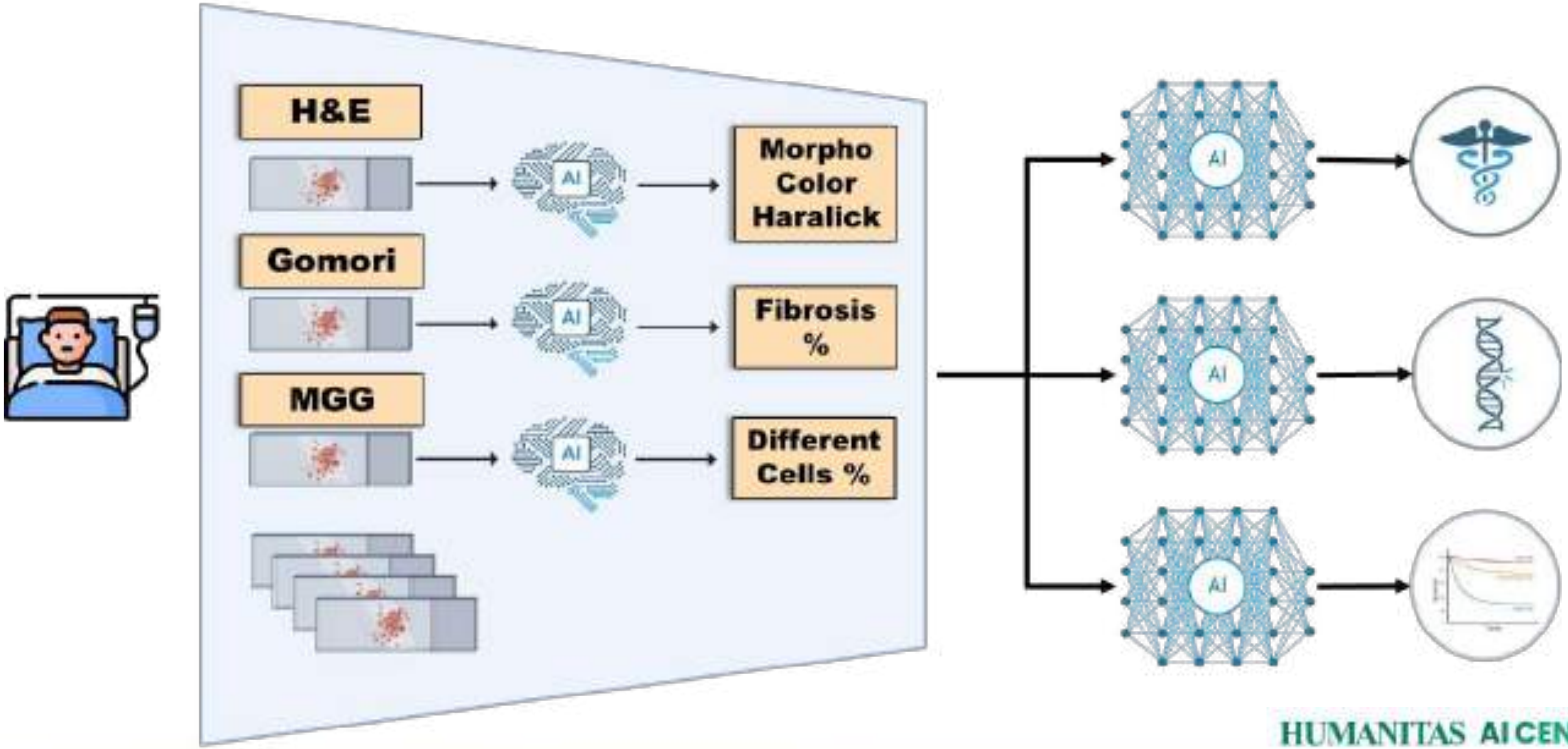
Features Extraction: May-Grunwald Giemsa



The Pipeline

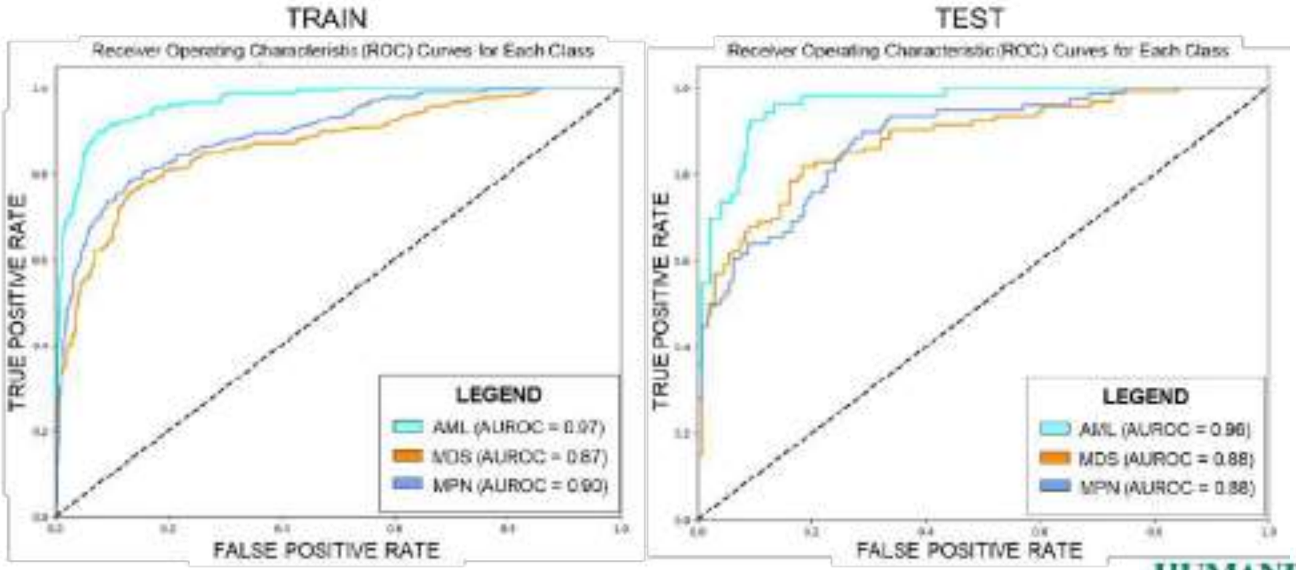


The Pipeline

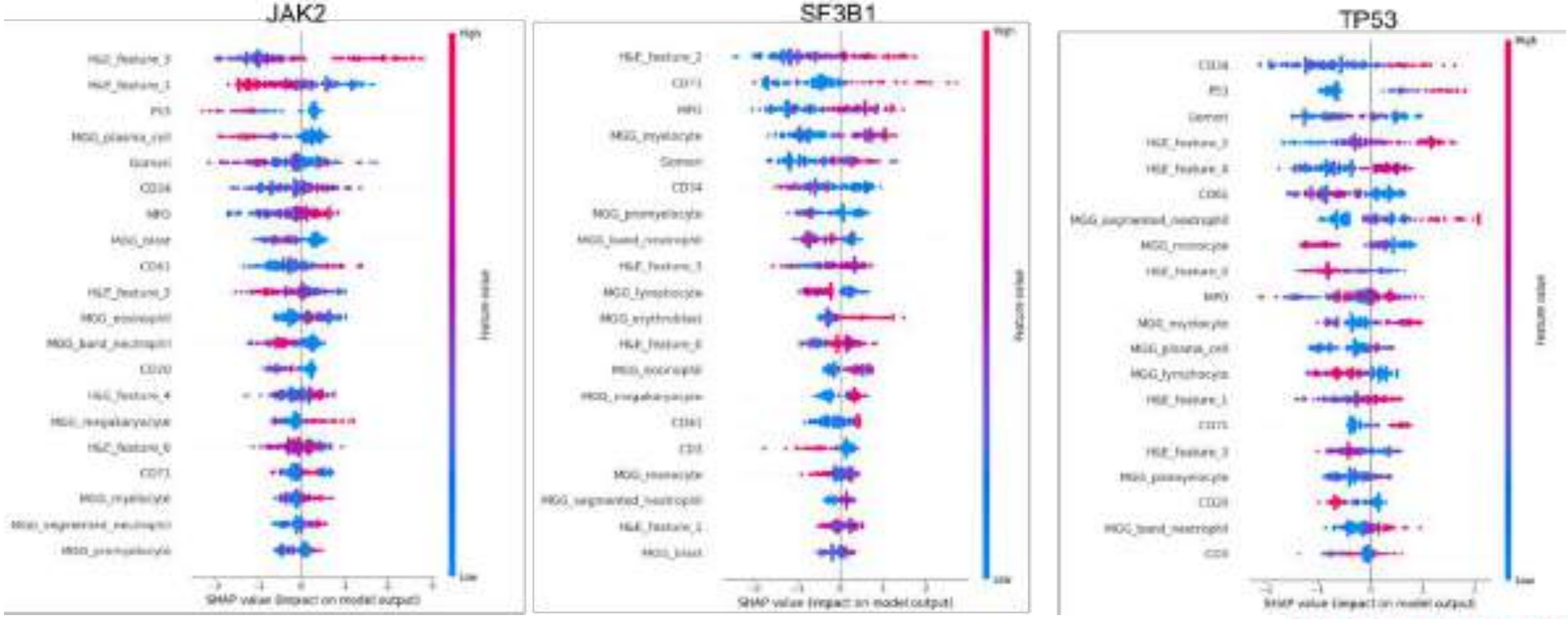


Results

A Deep Learning Model for multiclassification was trained using the WSI features to discriminate specific clinical entities among MN. The models predicted a correct diagnosis with an overall AUROC >0.91, suggesting that extracted features capture clinically relevant information.



Then we analysed the morphologic and molecular features association. Specific genomic profiles were predicted from WSI features with specialized XGBOOST models with high accuracy, in particular for SF3B1, JAK/STAT, TP53 and RUNX1 mutations (all with F1 Score > 90%). These findings underline the capability of the morphological features to capture the biological background of MN.



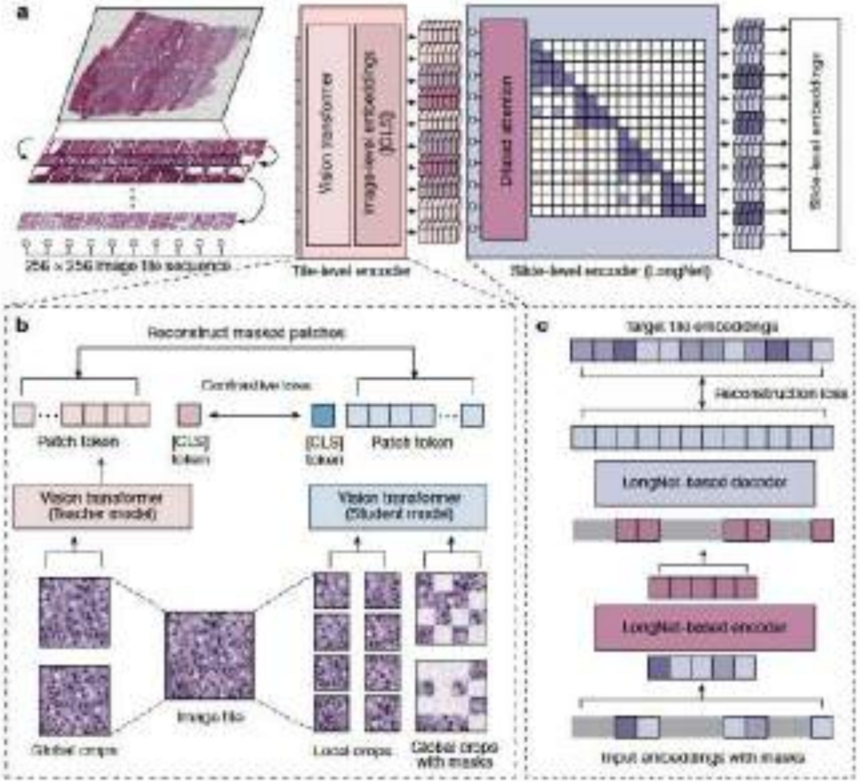
On these bases, we integrated morphological features into an innovative prognostic tool for personalized prediction of overall survival (OS) and leukemia-free survival (LFS) in MN. After the feature selection process (by using a L1-penalized Cox regression) morphological features were included in the model together with demographic, clinical and genomic information. Model discrimination was assessed using Harrell's concordance index (CI). Sequential integration of data layers into the model showed an increasing CI for OS and LFS, starting with 0.78 and 0.68, respectively with clinical and cytogenetic features alone; then raising CI up to 0.82 and 0.80 including somatic gene mutations; and finally reaching CI of 0.88 and 0.90 further integrating morphological features

Variables	Overall Survival C-Index	Leukemia Free Survival C-Index
Clinical	0.78	0.68
Clinical + Genomic + Karyotype	0.82	0.80
Clinical + Genomic + Karyotype + Imaging	0.88	0.90

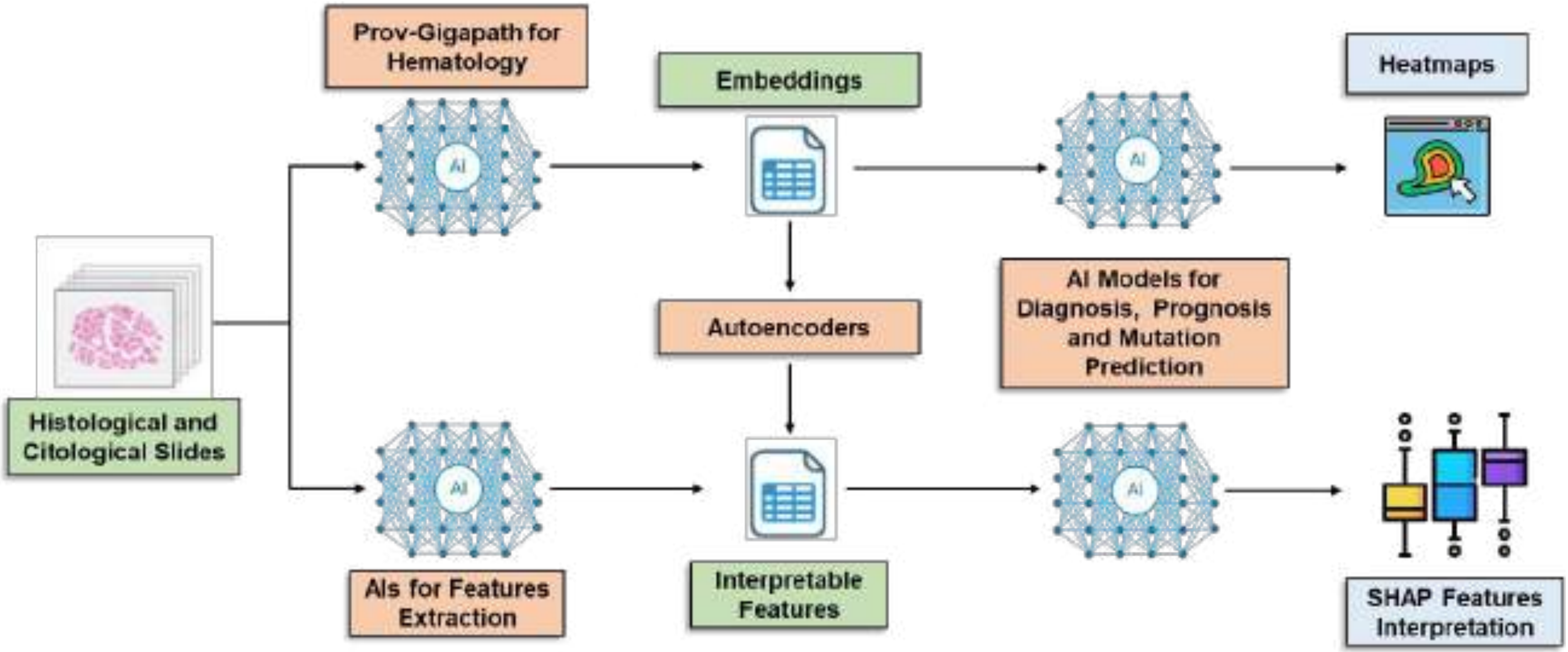
Next Steps

More Powerful than "Glass-Box" Models

- Low Explainability
- They focuses on only one staining at a time

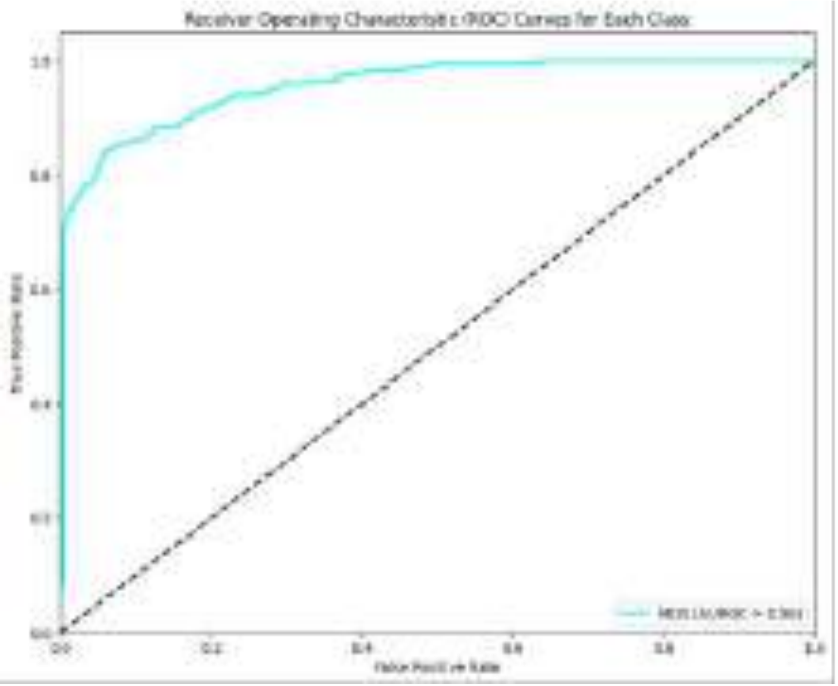


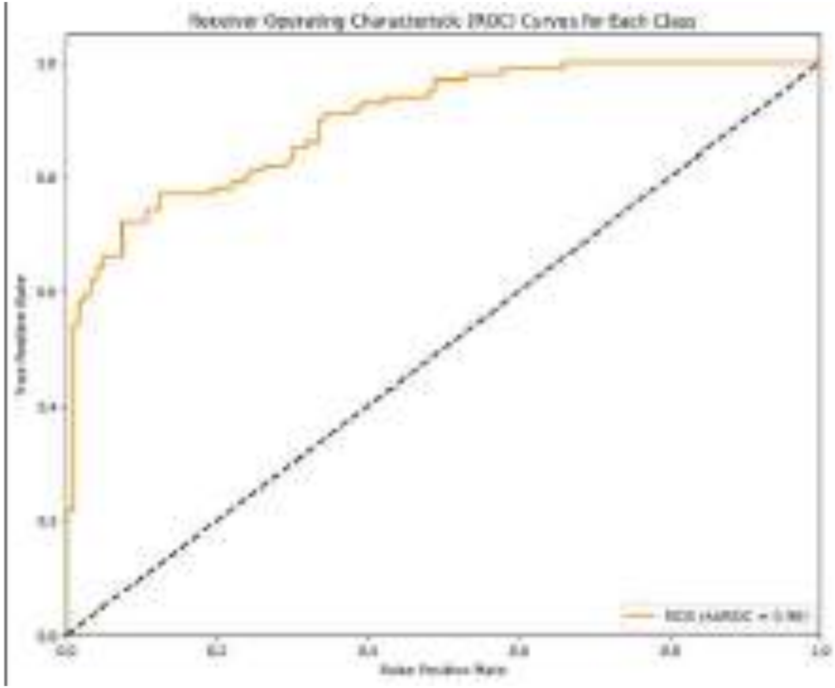
Next Steps



Prov-Gigapath for Hematology
AI
Embeddings
Heatmaps
AI
Histological and Citological Slides
Autoencoders
AI Models for Diagnosis, Prognosis and Mutation Prediction
AI
AI
Als for Features Extraction
Interpretable Features
SHAP Features Interpretation

Next Steps





Validation is currently ongoing on an independent MN population from MD Anderson Cancer Center, US.

Generative AI

PHASE 1
Analyzing data

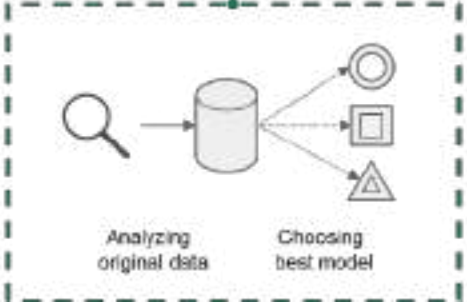
Analyzing the characteristic features in the original dataset to find their correlation and choose the right model and the effective configuration

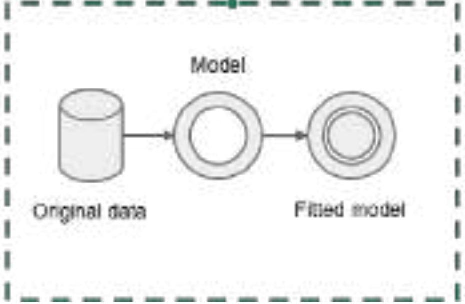
PHASE 2
Fitting model

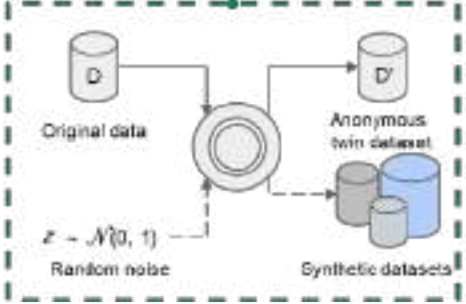
Fitting the model to learn an approximated distribution or process compatible with the original data

PHASE 3
Synthetizing data

Used the trained model to sample structurally and statistically comparable synthetic data







The importance of training

Prompt: Generate *cell images* of a patient of 80 years old with *acute leukemia*

The importance of training

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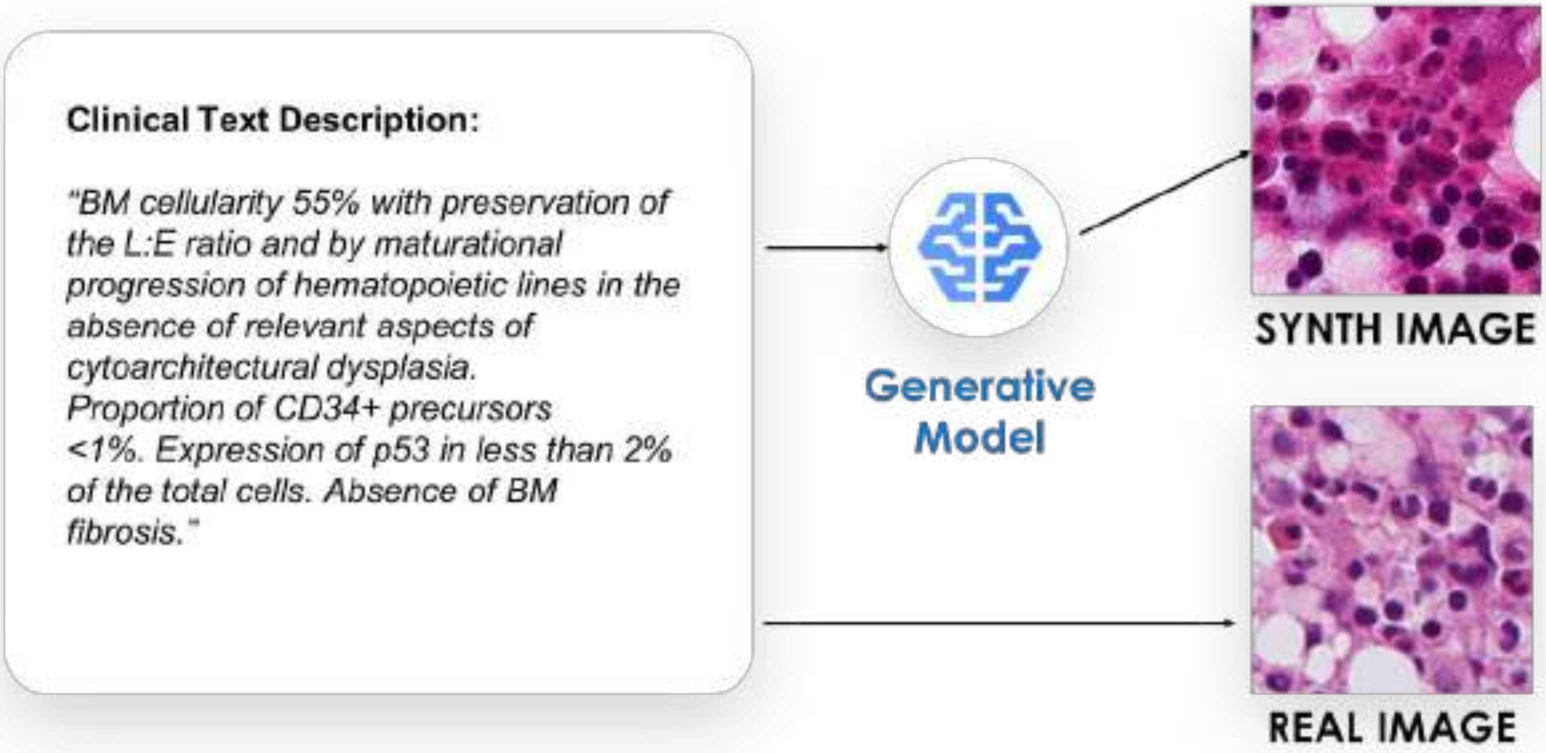
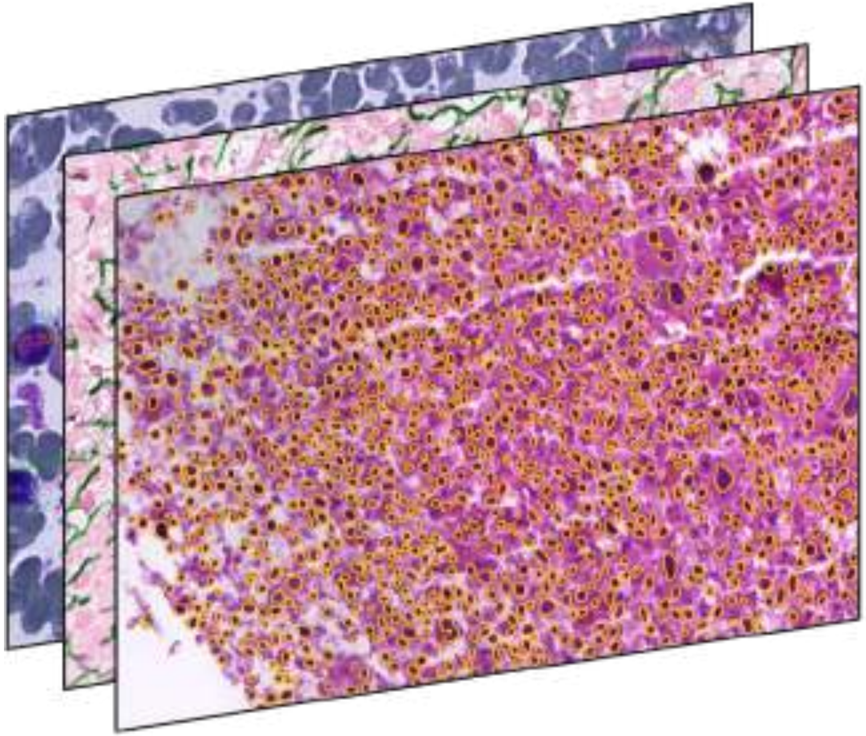
The importance of training

Prompt: Generate *cell images* of a patient of 80 years old with *acute leukemia*

Generation of synthetic images from textual information



Clinical validation on imaging data: features extraction



Morphological
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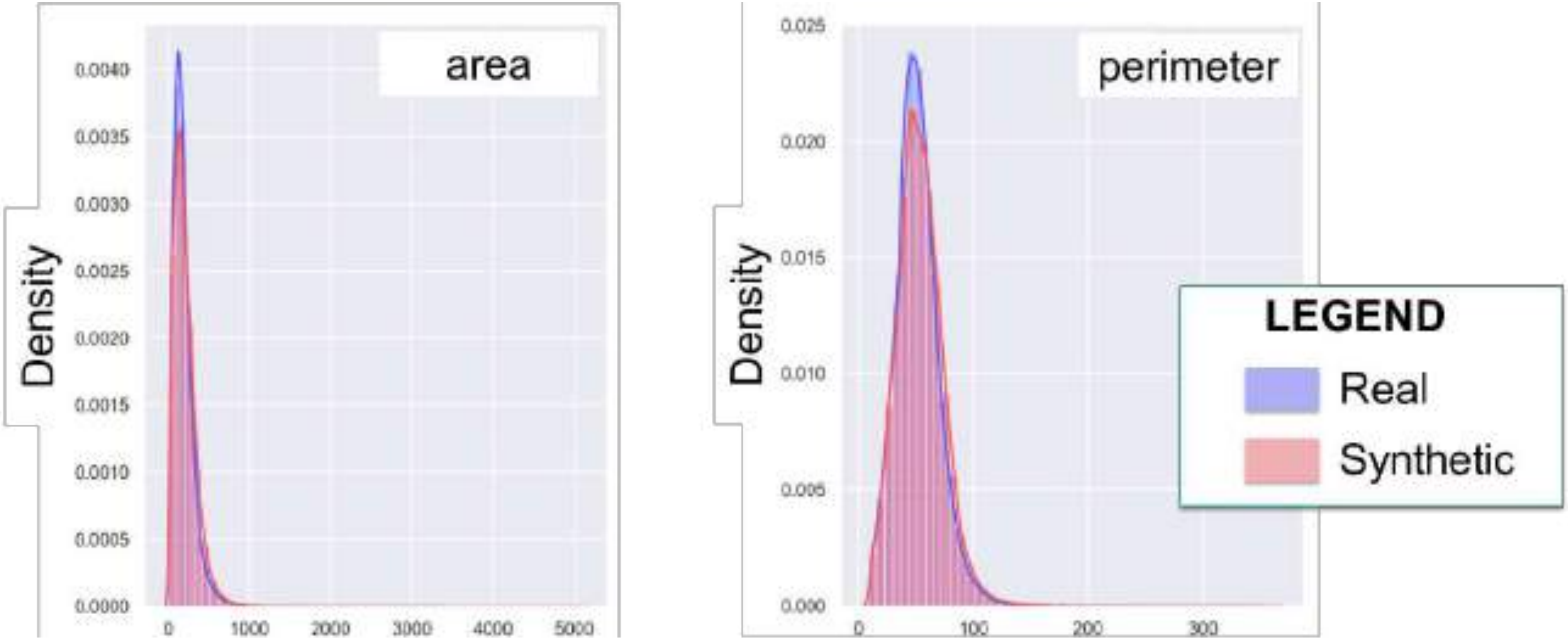
Synthetic Images Validation Framework

Distributions of Morphological Features extracted from Real and Synthetic H&E images



D'Amico S, et al. JCO Clin Cancer Inform. 2023 Jun;7:e2300021. doi:10.1200/CCI.23.00021.

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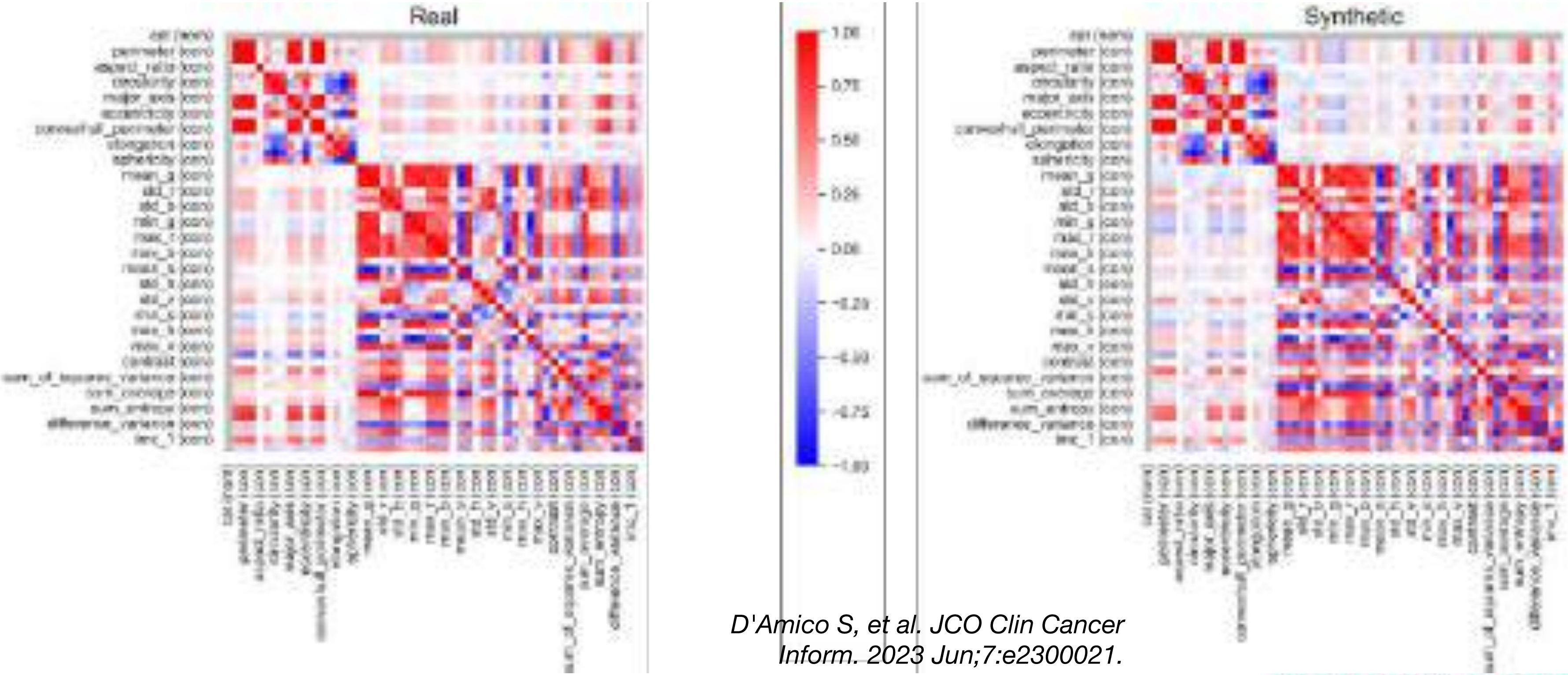
Synthetic Images Validation Framework

Correlation of Features extracted from Real and Synthetic H&E images



D'Amico S, et al. JCO Clin Cancer Inform. 2023 Jun;7:e2300021. doi:10.1200/CCI.23.00021.

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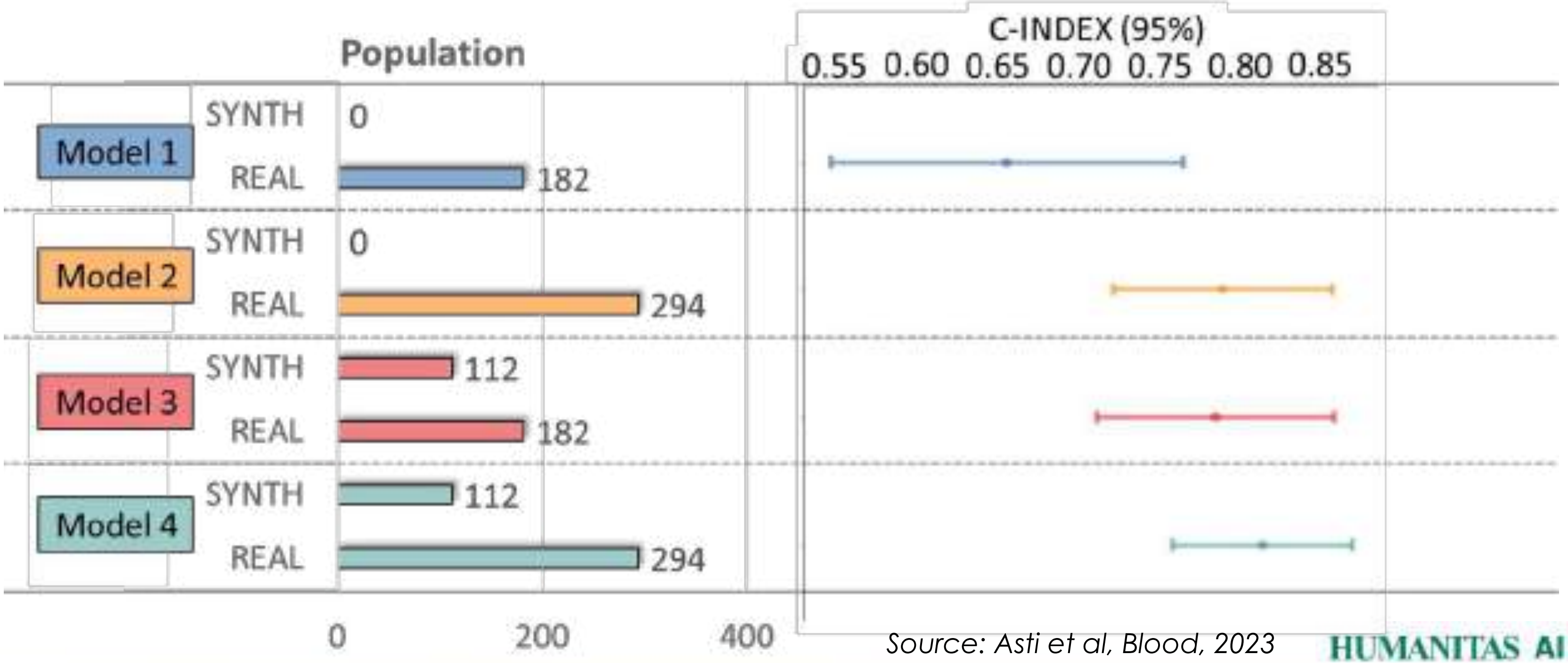
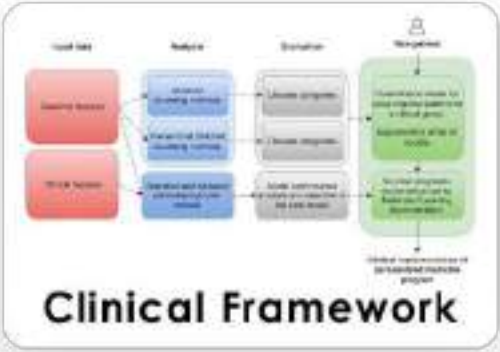
Clinical validation on imaging data: prognosis

Cox's proportional hazards model to predict individual probability of overall survival in patients affected with myeloid neoplasms.



Source: *Asti et al, Blood, 2023*

AI in healthcare



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train

AI POWER IS NOTHING WITHOUT TRAIN-ING

AIRC

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