FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE



CONVEGNO FISiM

Firenze, CSF Montedomini
"Il Fuligno"
23-24 ottobre 2026

Progetto *PATHroclus* per la digital pathology nelle neoplasie mieloidi

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Disclosures of Giulia Maggioni

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

Digital Pathology in Hematology: Challenges and Opportunities

Key Challenges

Data Fragmentation
Bone marrow images, annotations, and workflows are still poorly standardized across institutions.

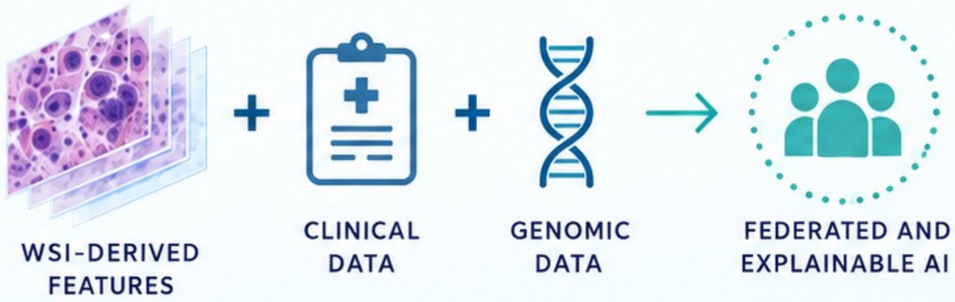
Privacy and Sharing Constraints
Large whole-slide images and data-protection rules make cross-institutional data sharing difficult.

Limited Standardization
Most current tools focus on a single stain, a single center, or a single task, with no shared standard for feature extraction.

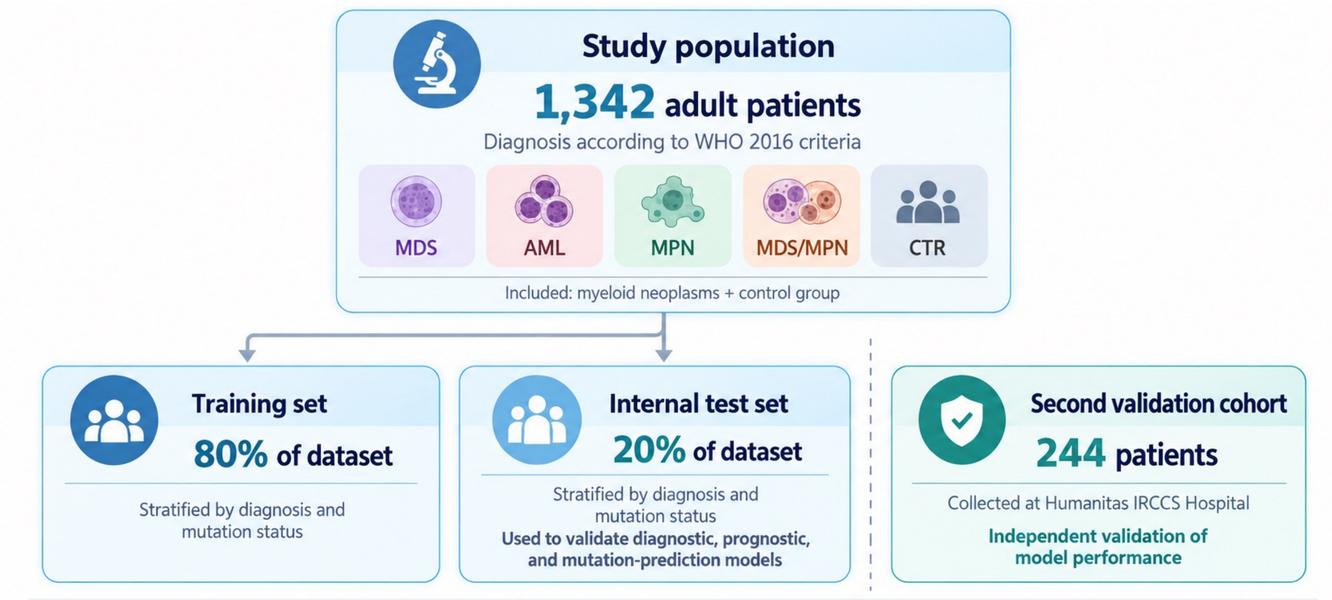
Limited Explainability
Many AI predictions remain difficult to interpret and therefore hard to translate into routine clinical practice.

Main Gap and Opportunity

No available platform currently combines **WSI-derived features** with **clinical** and **genomic data** in a **federated, explainable framework** for hematology.



Project cohort



Aims

1) Assess diagnostic accuracy in MN patients

2) Mutation prediction

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

PATHroclus platform

INPUT

- Digital pathology slides

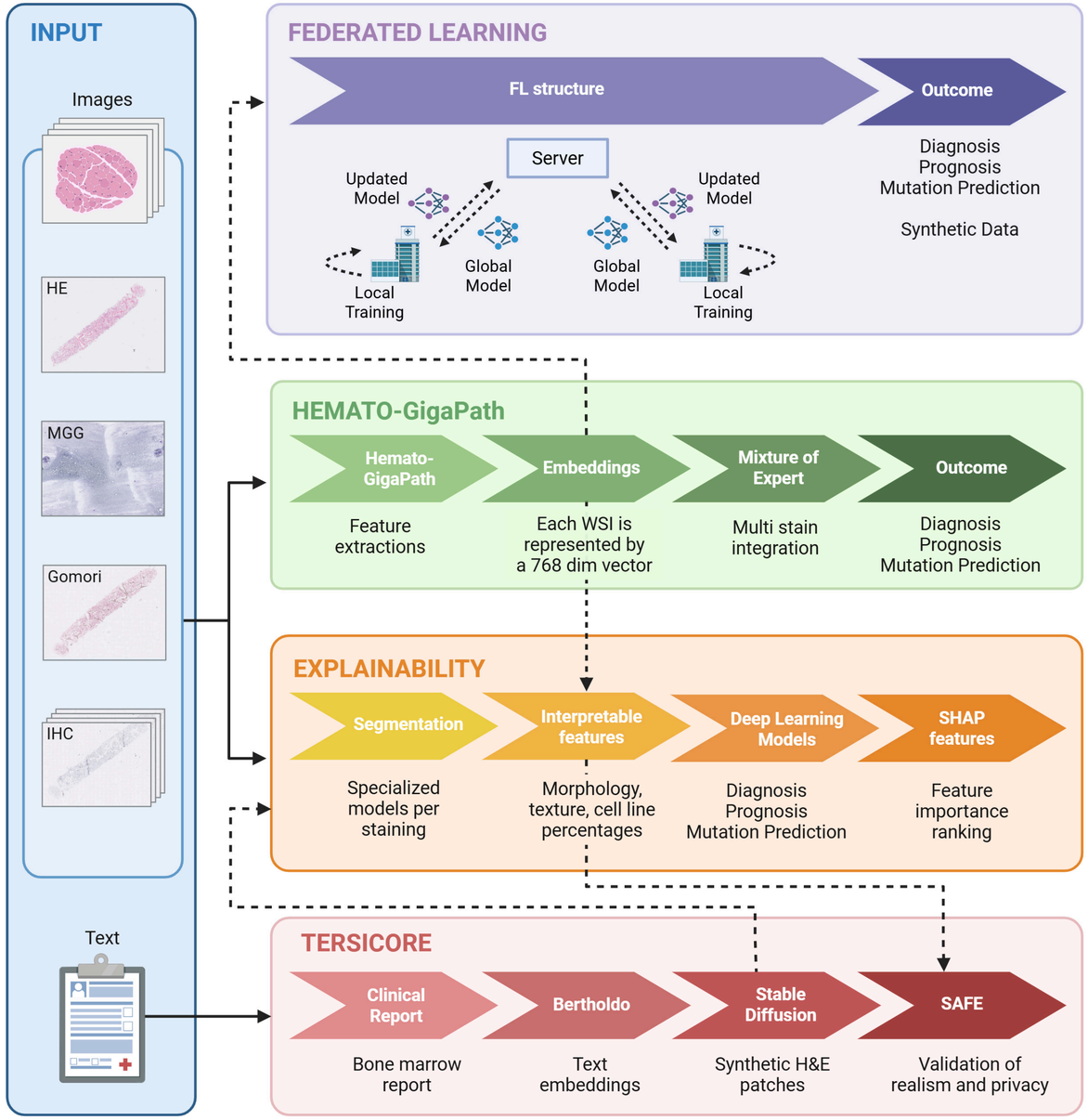
FOUR DIFFERENT MODULES

- **HEMATO - GigaPath**
  Foundation model for hematology

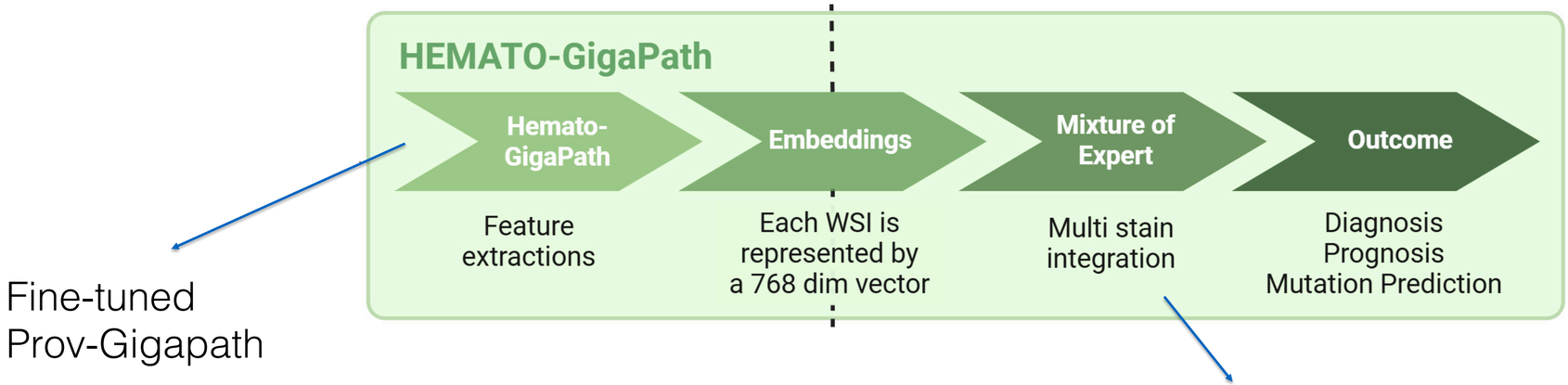
- **Explainability**
  SHAP-based interpretability for diagnosis and prognosis predictions

- **Tersicore**
  Synthetic H&E patch generation with privacy validation

- **Federated Learning - RAIL**
  Local training at each node; only model weights are shared



HEMATO-GigaPath Foundation Model

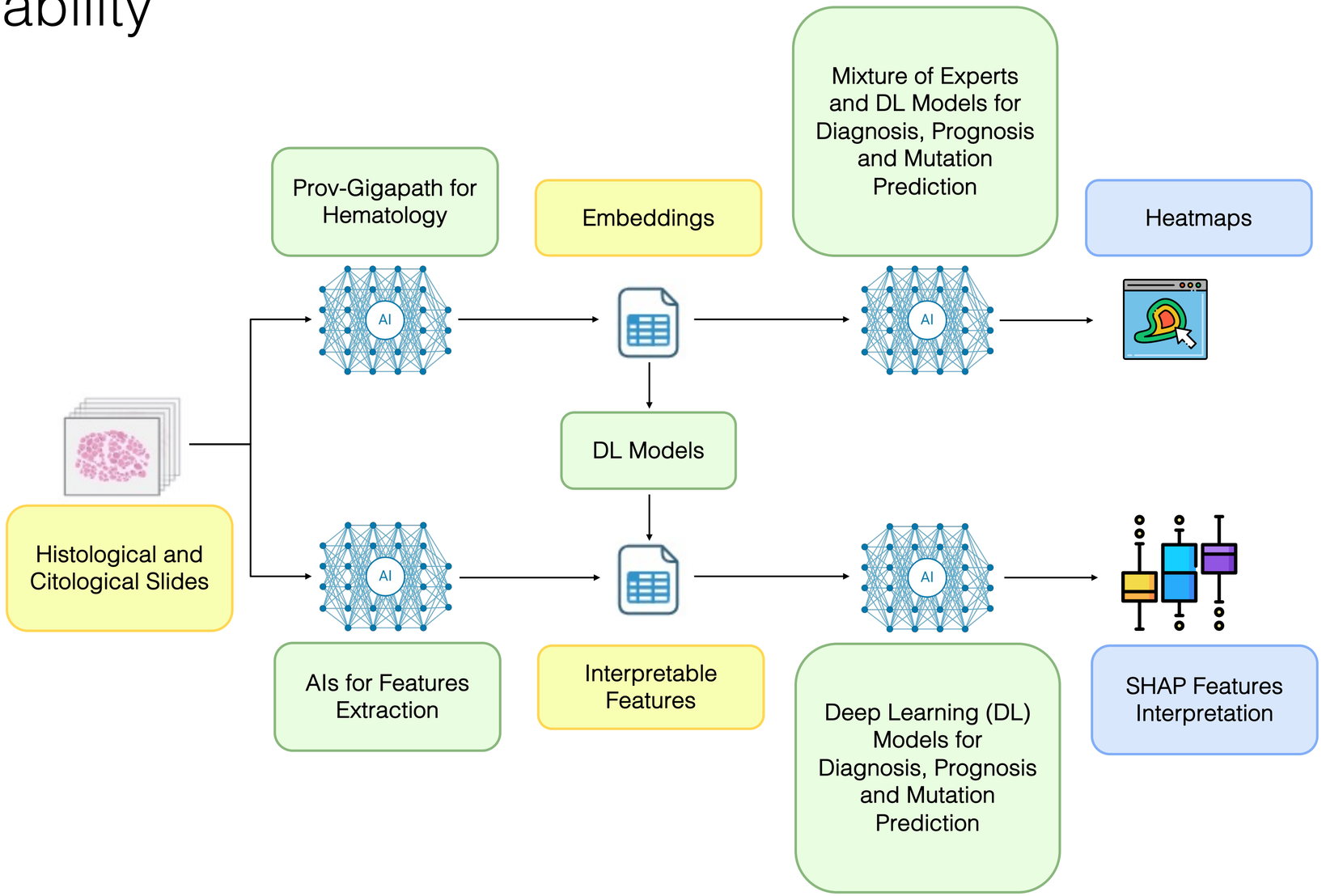


- ✓ Each staining is analyzed by a dedicated expert
- ✓ The model learns how much weight to assign to each expert for the final prediction

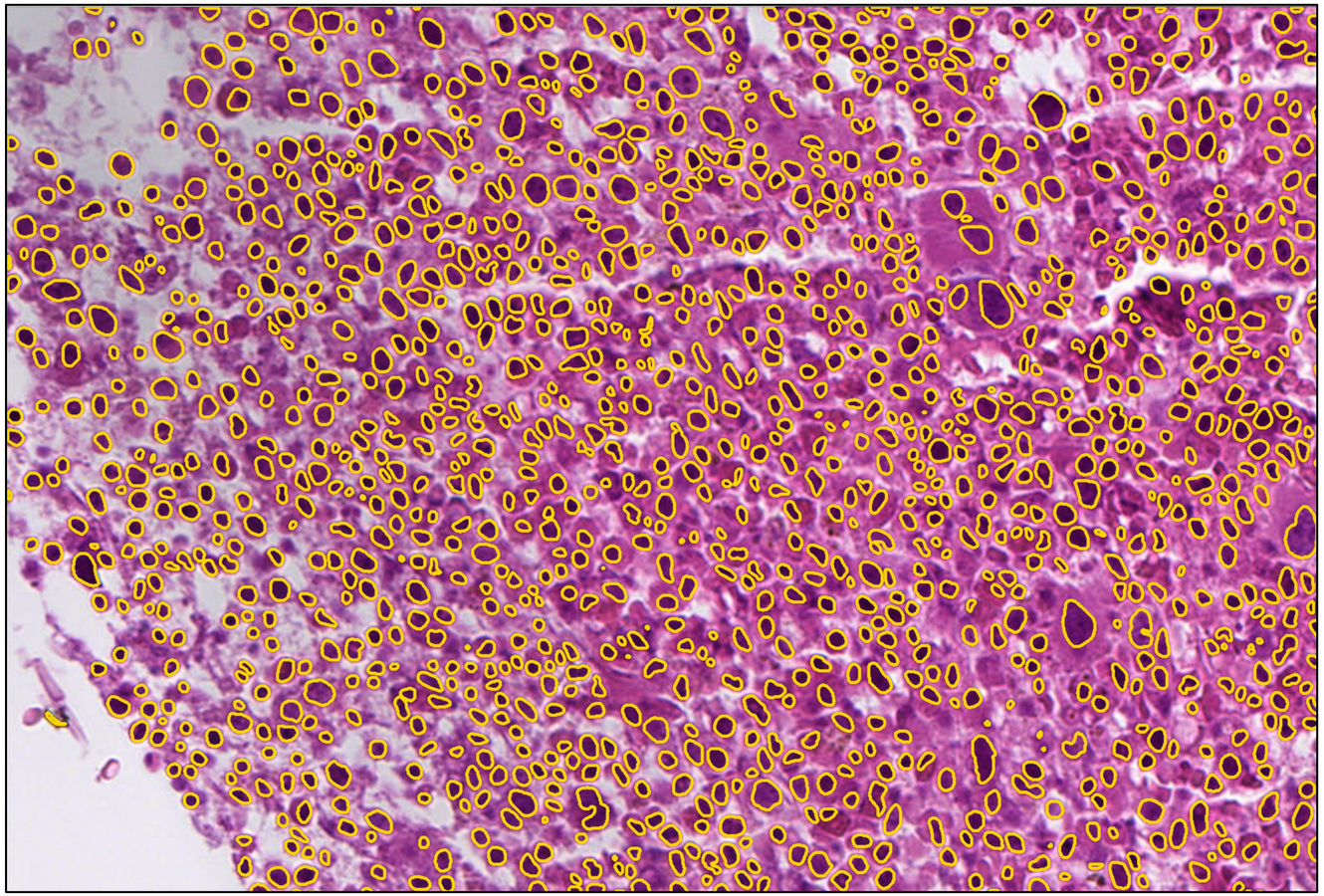
PRO — More Powerful than “Glass-Box” Models

CONS — Low Explainability

Explainability



HEMATOXYLIN & EOSIN STAINING:
NUCLEUS SEGMENTATION and FEATURES EXTRACTION

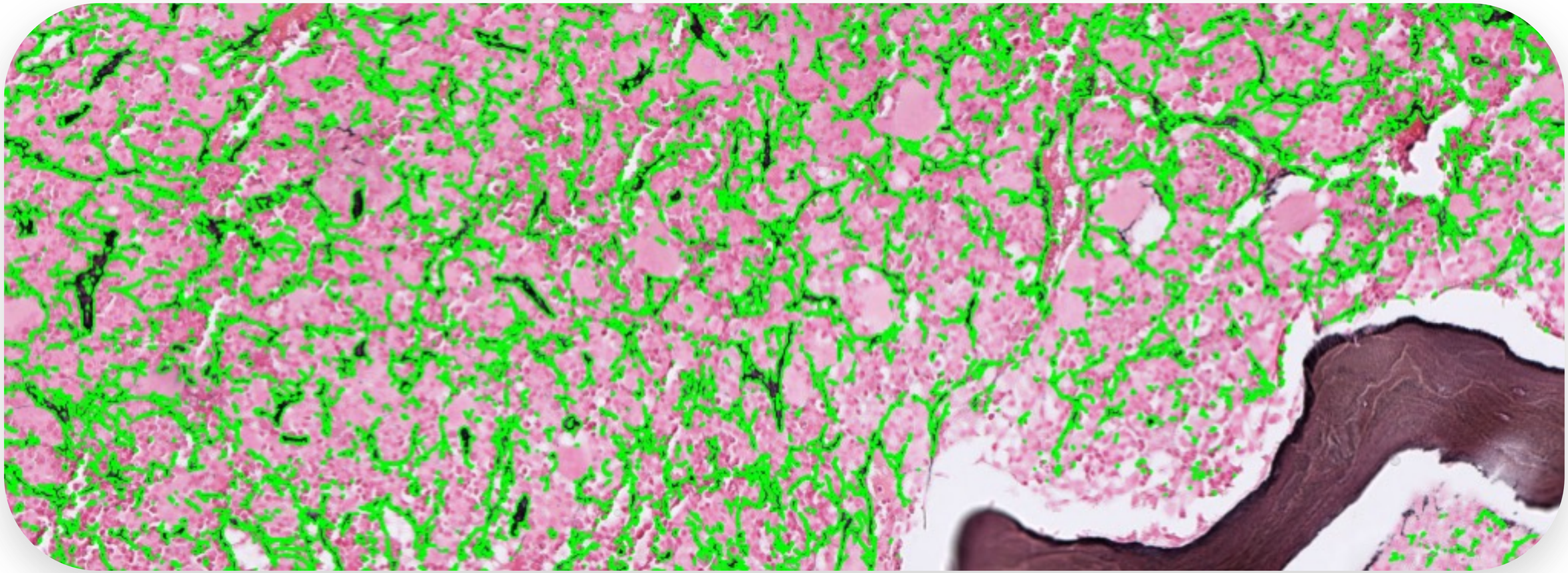


Morphological
Area
Perimeter
…

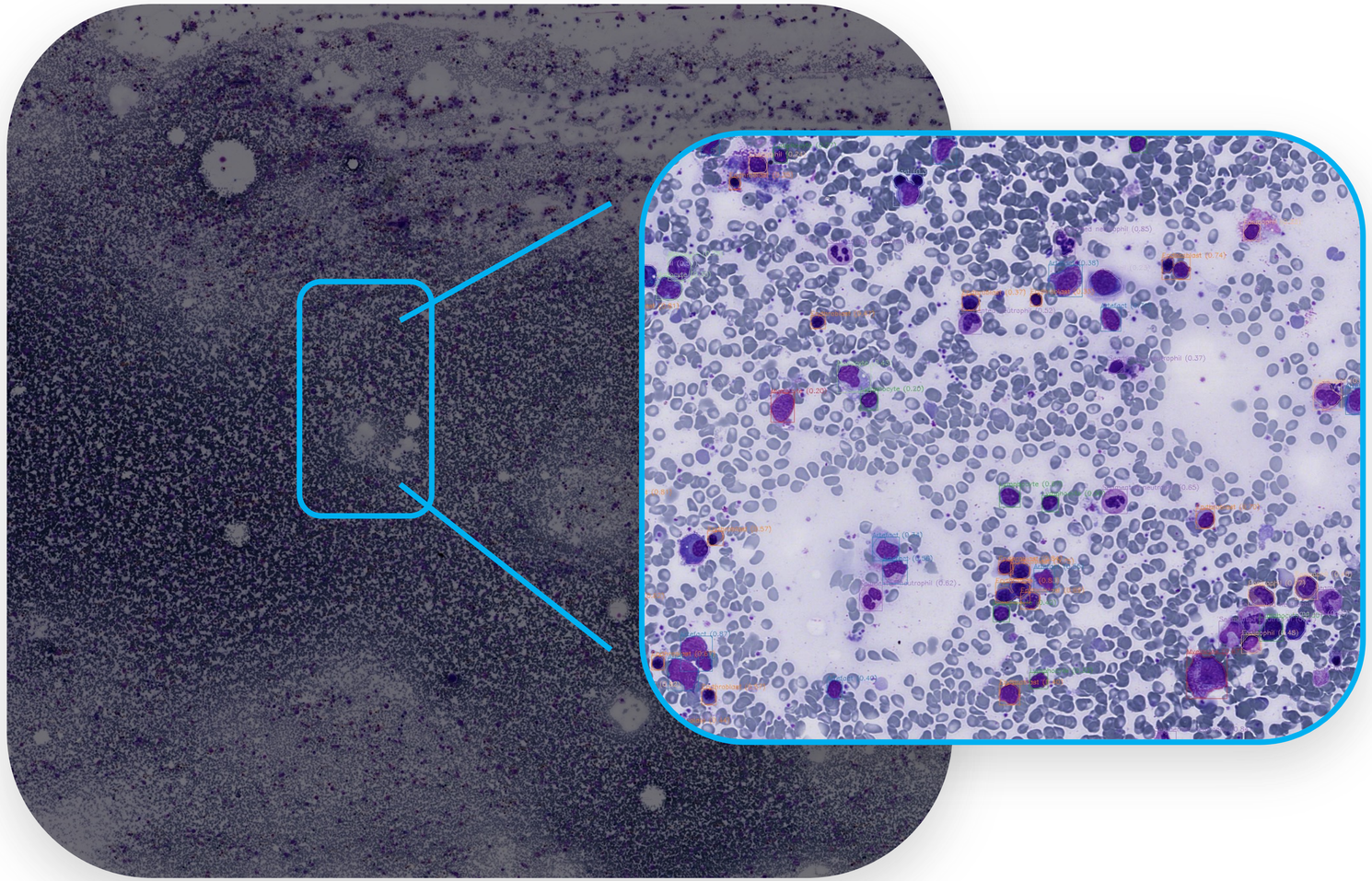
Color
Mean RGB
Mean HSV

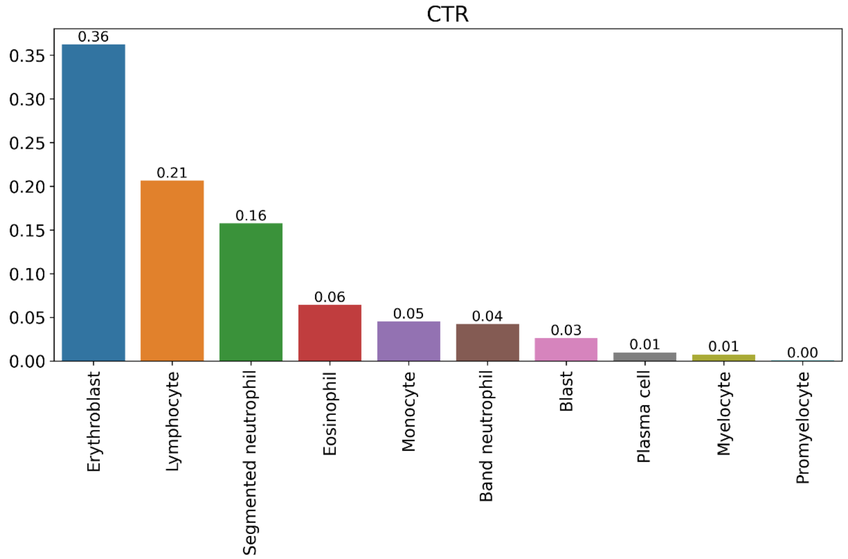
Haralick
Entropy
Contrast

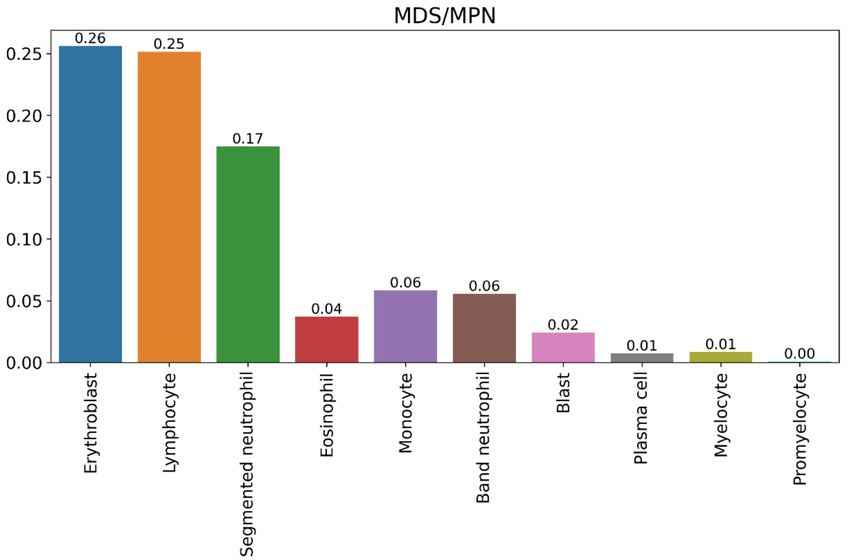
GOMORI STAINING – FIBROSIS SEGMENTATION



MAY-GRUNWALD GIEMSA – OBJECT DETECTION







Results from HEMATO-GigaPath

Result 1_Diagnostic Model

Internal Test Set

0.77	0.76	0.91
Accuracy	Balanced Accuracy	AUROC

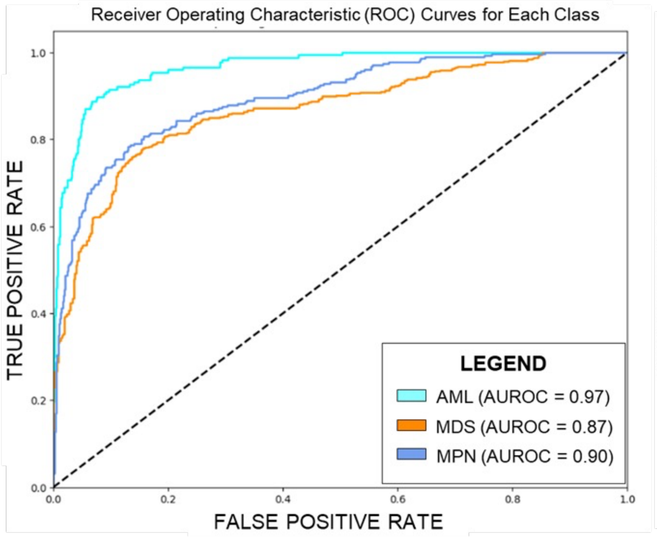
Independent Validation Cohort

0.71	0.89
Balanced Accuracy	Overall AUROC

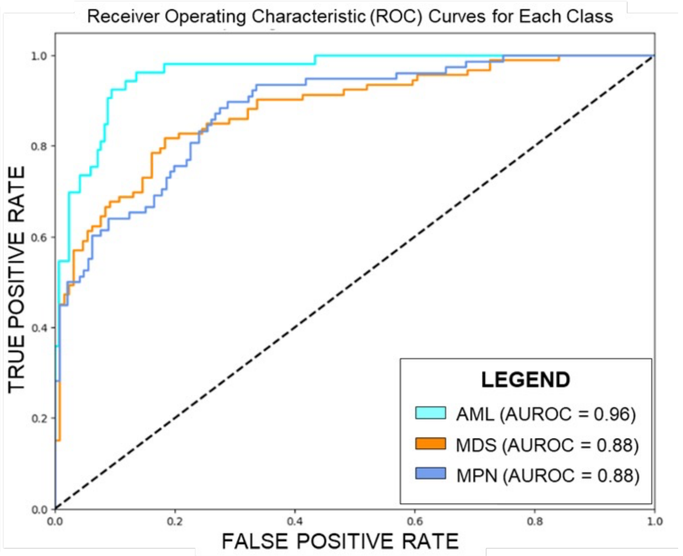
Class-specific AUROC in the Independent Cohort

AML	MPN	MDS
0.98	0.85	0.85

TRAIN



TEST

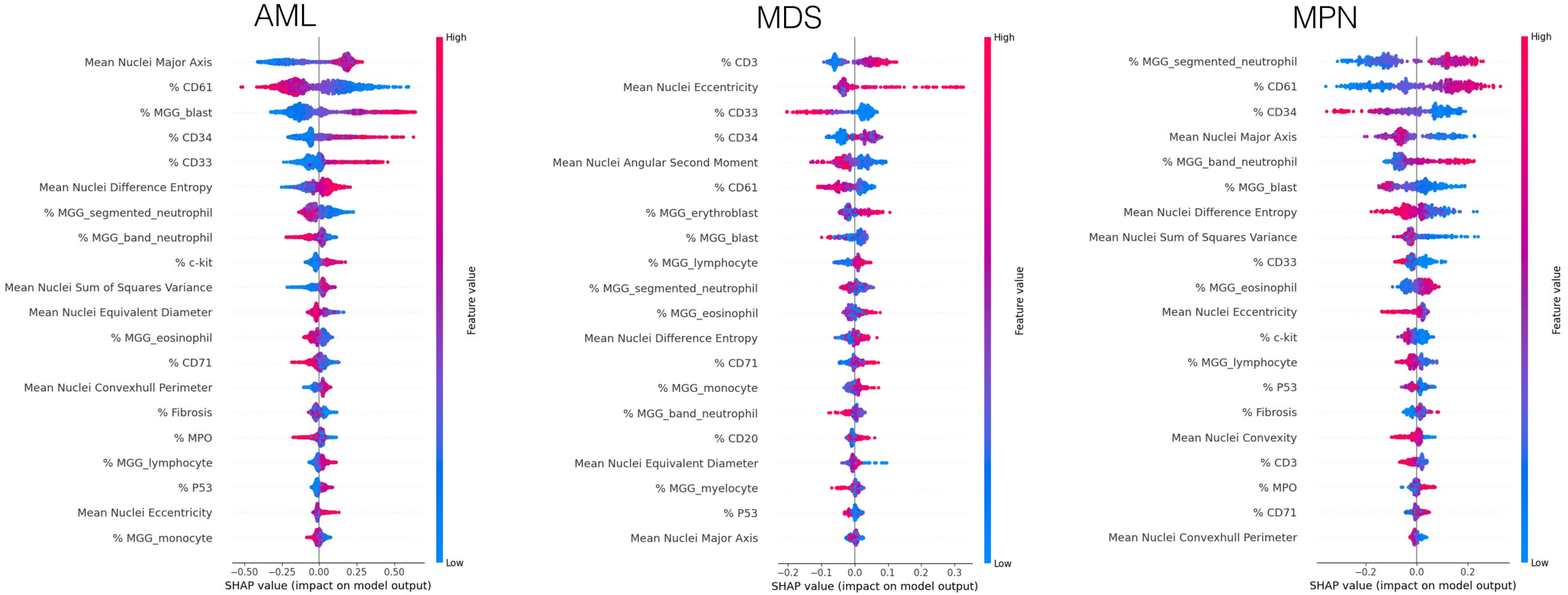


- ✓ Strong diagnostic performance was preserved in independent validation
- ✓ Multi-stain integration and fine-tuning are the key drivers

Explainability of the Diagnostic Model

The model is not a complete “black box”: SHAP analysis identified the morphological and immunophenotypic features driving each diagnostic prediction.

- **AML:** nuclear size/morphology, blast percentage, CD34 and CD33
- **MDS:** more distributed pattern, with multiple moderate morphological and immunophenotypic contributors
- **MPN:** segmented neutrophils and CD61



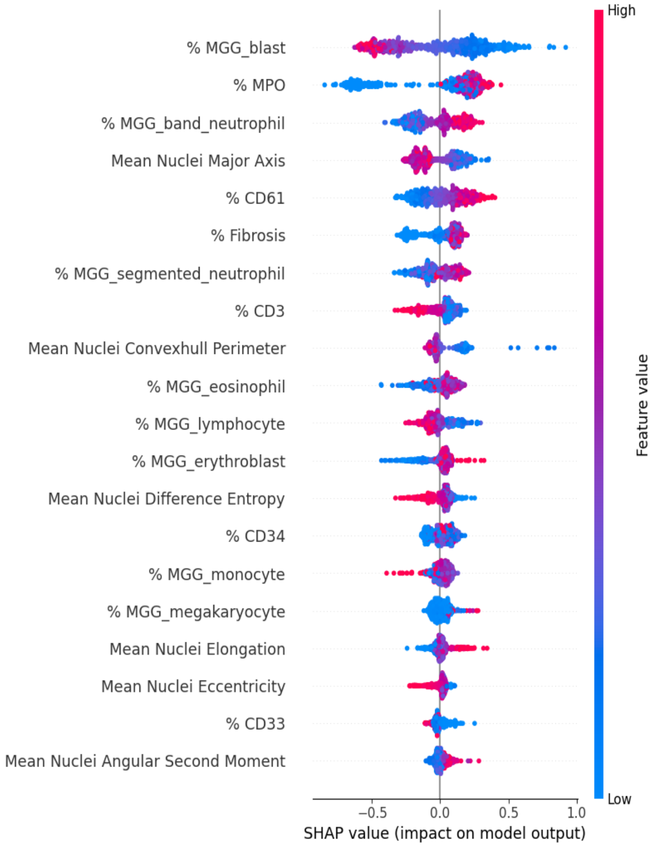
Result 2_Mutation prediction

Specific genomic profiles were predicted from WSI features with specialized XGBoost models with *heterogeneous performance across targets.*

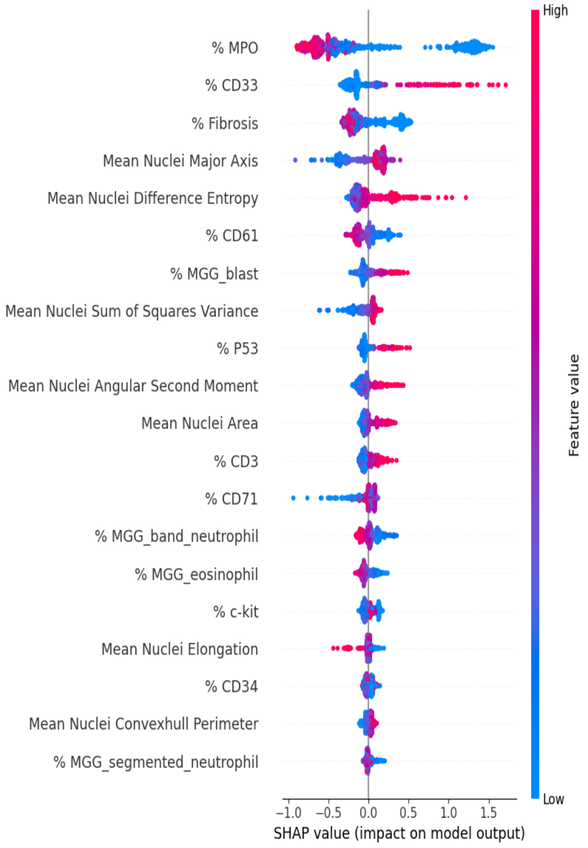
- **JAK2:** strongest performance, AUROC **0.93** internally and **0.92** in external validation
- **NPM1:** good external performance, AUROC **0.83**
- **FLT3, IDH1, SF3B1:** moderate performance

✓ SHAP analysis supports the presence of mutation-specific morphological patterns
✓ Foundation-model embeddings can capture clinically relevant genomic signals

JAK2



NPM1



Result 3_Prognostic Model

Novel prognostic tool for personalized prediction of OS and LFS in MN

Feature selection: L1-penalized Cox regression

Model includes:

- Clinical & cytogenetic data
- Somatic gene mutations
- Morphological features after PCA dimensionality reduction

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

Performance (Harrell's CI) improves with data integration

Federated Learning

Manager Node - Humanitas

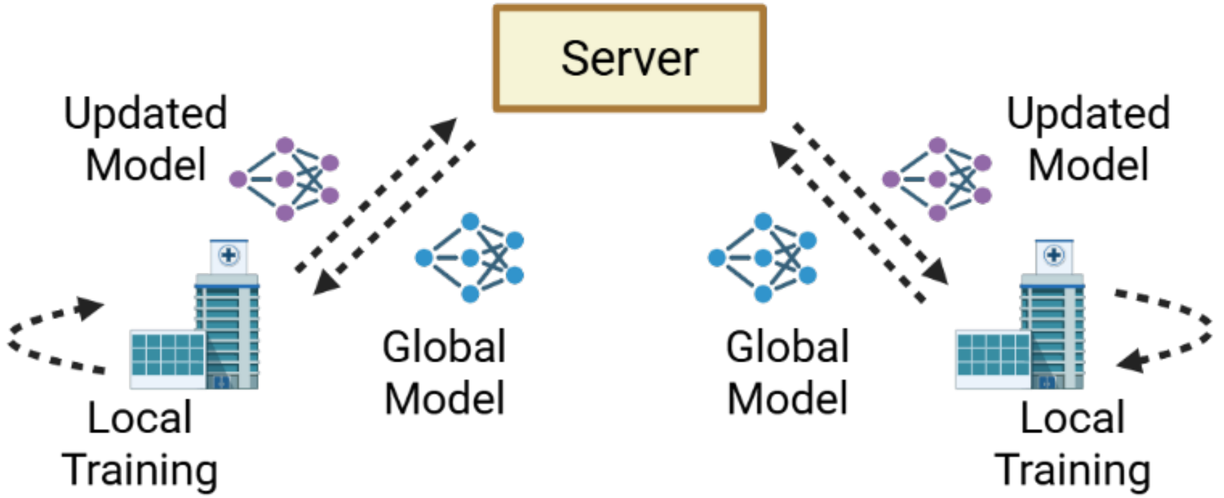
- Coordinate the training
- Aggregates the model weights

Worker Nodes - Each partner center

- Data stays local
- Only model updates travel to the server

Communication

- Based on Flower framework
- Docker containerized



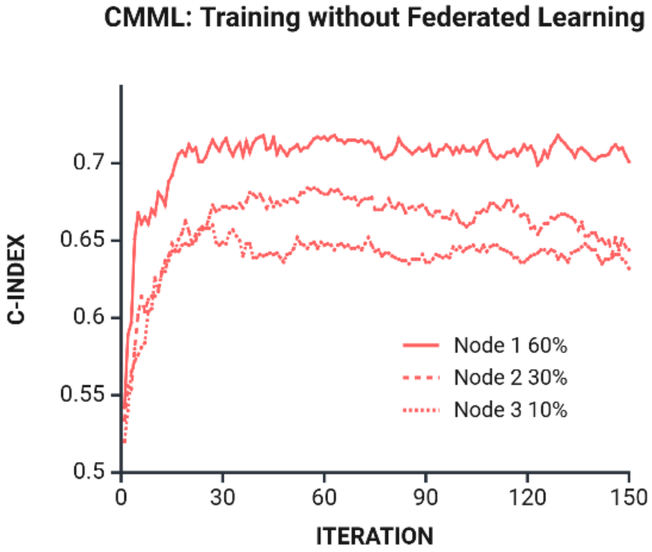
Federated Learning vs Isolated Training- CMML cohort

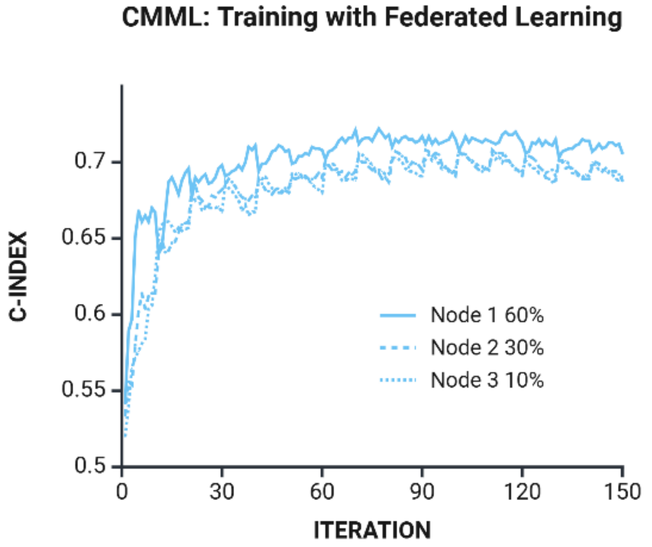
Setup

Model: UNIBO DeepSurv
Metric: C-Index
1337 patients (60/30/10%)
Variables: Clinical, Genomic, Karyotype
Task: Overall Survival

Key findings

- ✓ FL improved local performance compared to isolated training
- ✓ The largest benefit was observed in the smallest node





Federated Learning vs Isolated Training
MDS cohort imaging embeddings

Setup

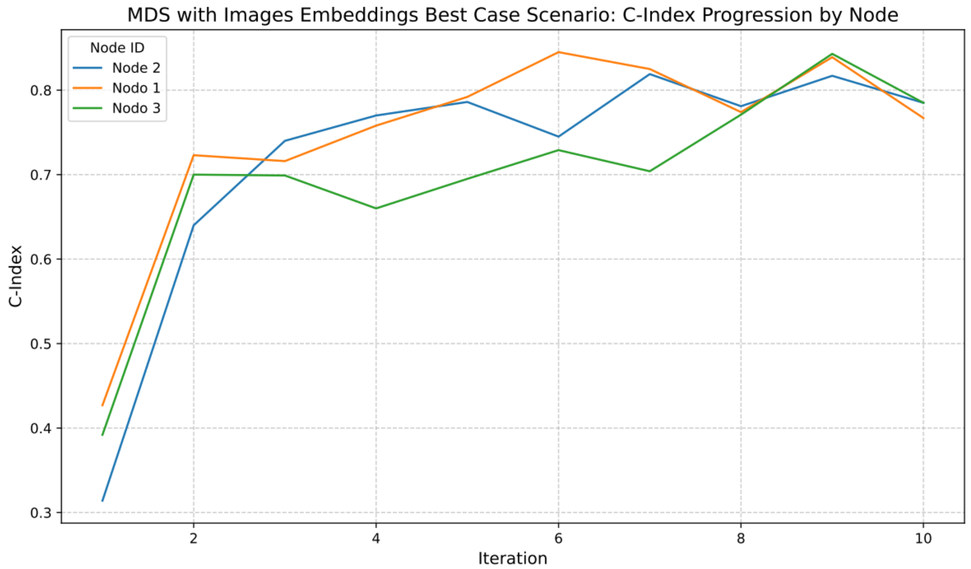
Model: UPM SAVAE
Metric: C-Index
860 patients (60/30/10%)
Variables: Clinical, Genomic, Karyotype, Embeddings
Task: Overall Survival

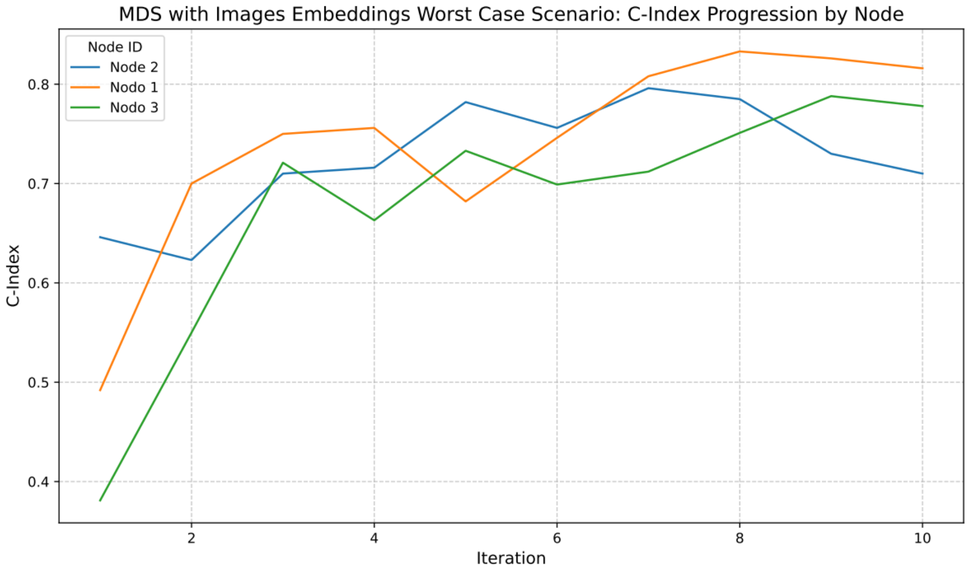
Scenarios

Best Case Scenario: all real-world data
Worst Case Scenario: missing some genomic and karyotype

Key findings

- ✓ Federated learning showed greater robustness to heterogeneous missing data
- ✓ Collaboration across centers can partially compensate for locally unavailable biomarkers

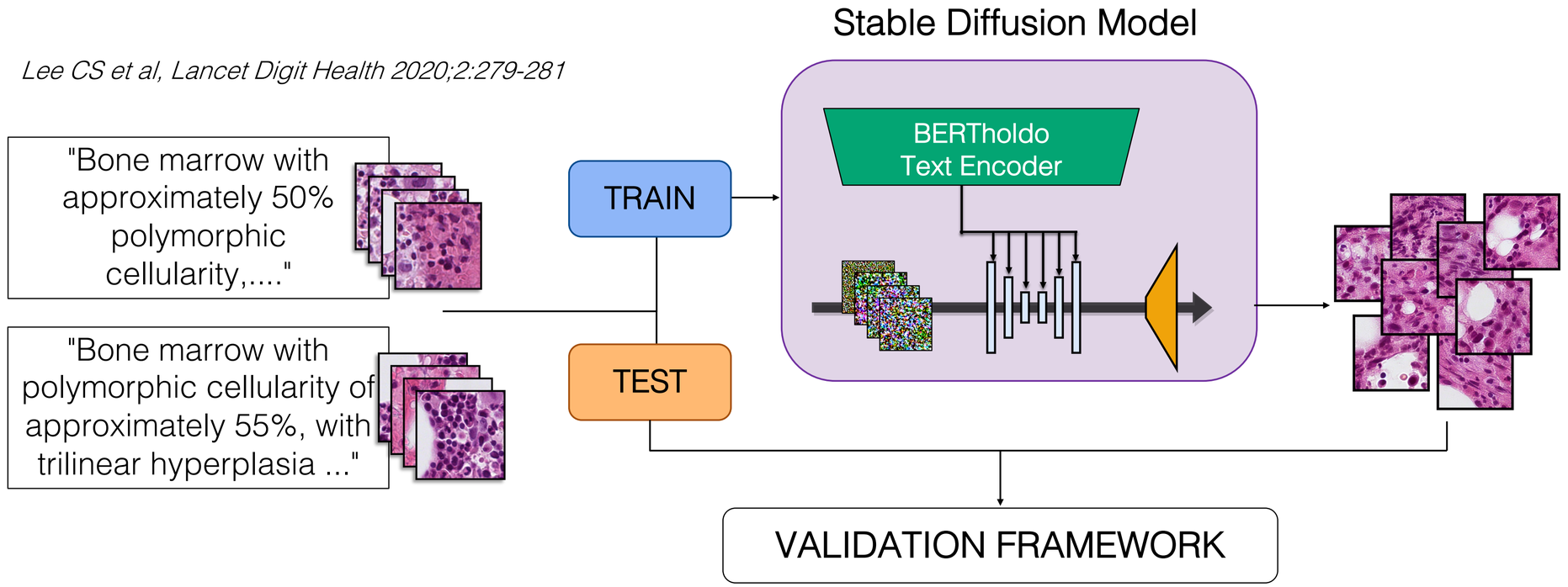


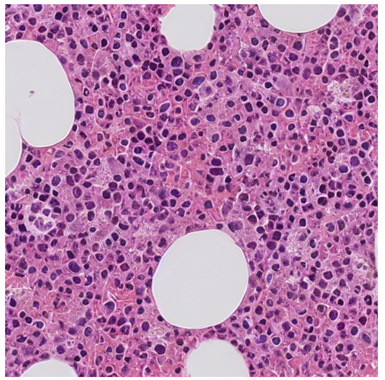


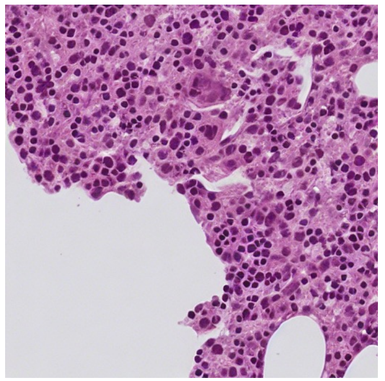
Tersicore

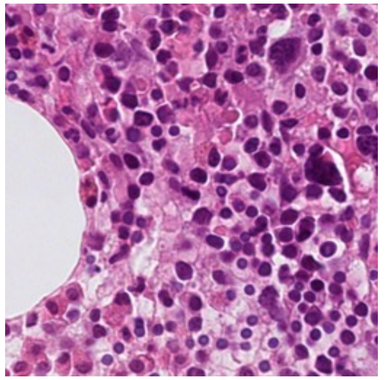
«**Clinical reports** are an **optimal** and **untapped source** of real-world **evidence**»

Lee CS et al, Lancet Digit Health 2020;2:279-281



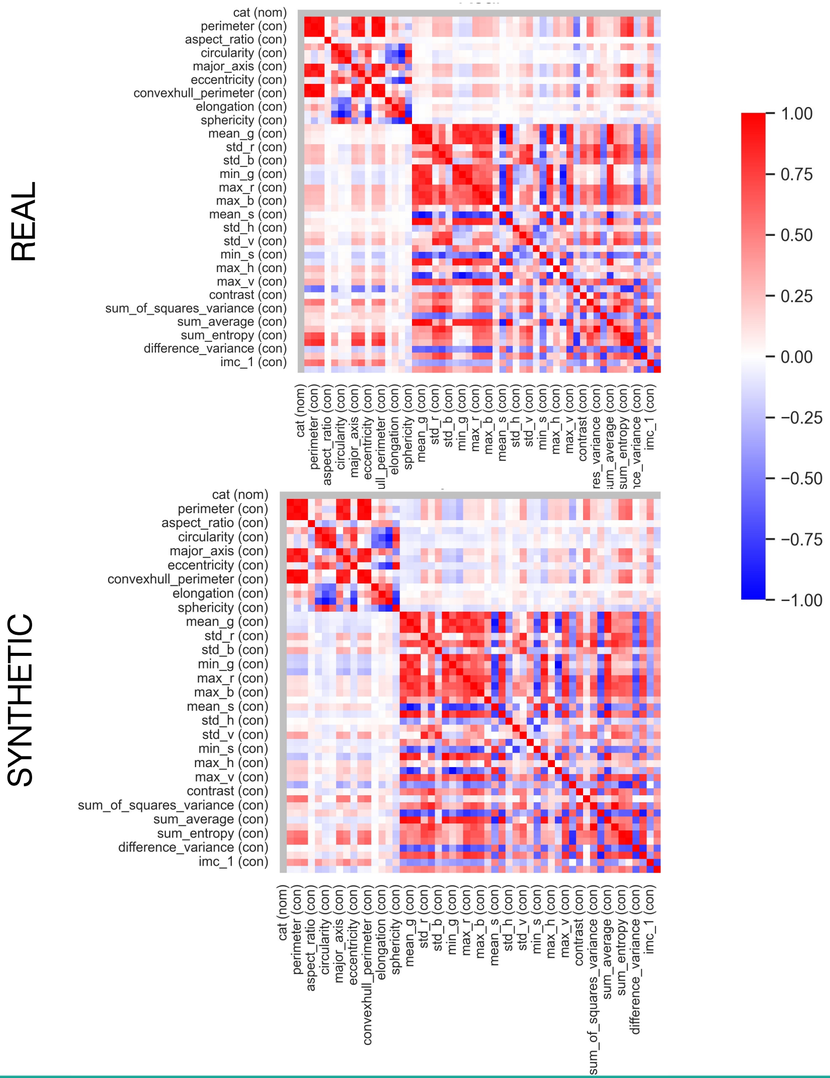




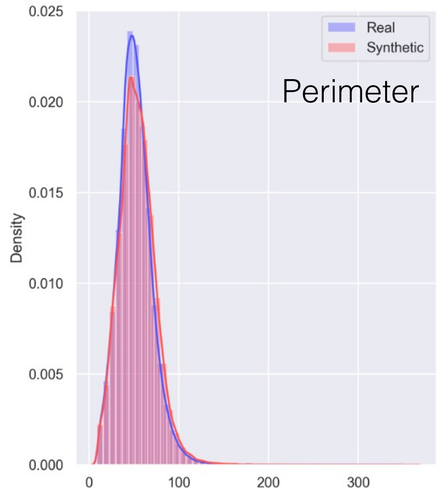


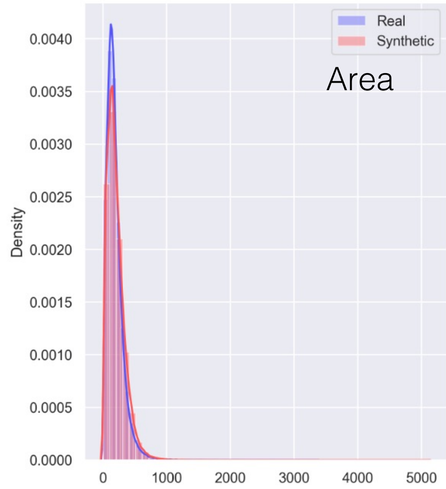
Synthetic images performance

Correlation of Features extracted from H&E images



Distributions of Morphological Features extracted from H&E images





- ✓ FID 8.3→ high similarity between the distributions of real and synthetic images
- ✓ MS-SSIM 0.028-0.216→ synthetic images were structurally diverse rather than repetitive

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

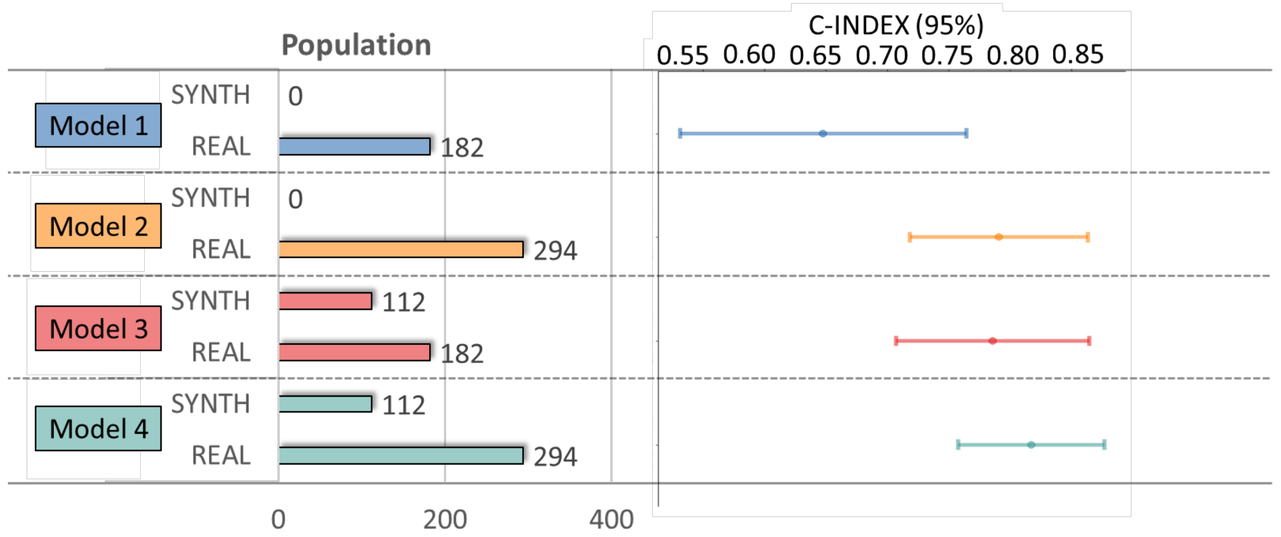
Synthetic images applications

1) <u>DIAGNOSTIC PERFORMANCE:</u>

Adding synthetic data **improves diagnostic performance**, increasing the F1-score from **54% to 64%** on the same real-world test set.

2) <u>PROGNOSIS:</u>

Synthetic patients preserved **prognostic performance comparable to additional real-world data**: **C-index 0.80 in both models**, with similar prognostic feature selection.



- ✓ Synthetic data are not simply realistic images, but appear to preserve clinically meaningful information.
- ✓ Potential tool to **overcome data scarcity**, particularly in rare hematologic diseases

Ongoing and future directions

1. **Predict treatment response**
   using integrated morphologic, clinical and genomic features
2. **Improve model explainability**
   by incorporating complementary interpretability frameworks
3. **Expand synthetic image generation**
   beyond H&E staining
4. **Deploy and validate the federated platform**
   across European partner centers through the EHA Innovation Grant
5. **Build a comprehensive multimodal database**
   integrating digital pathology, clinical and genomic data to support next-generation classification of myeloid and lymphoid malignancies

Consortium partners

- M. Della Porta — Humanitas
- P. Horrington — King's, UK
- A. Turki — Essen, DE
- J.M. Middeke — Dresden, DE
- A. Mosquera Orgeira — ES
- José Cardia — Lisbon, PT
- M. Ponzoni — OSR, IT

Take-home messages

- Digital pathology can extract clinically meaningful information from bone marrow images
- Explainability is achievable: SHAP-based analyses identify biologically plausible morphological and immunophenotypic drivers, reducing the «black box» nature of AI models
- Federated and synthetic-data approaches may overcome two major barriers in hematology AI: data sharing and data scarcity
- The ultimate goal is to transform digital morphology into an additional quantitative layer of clinically actionable information