



# Il progetto europeo GenoMed4All: sviluppi nella medicina personalizzata per la drepanocitosi

Mirco D'Agnolo

Dipartimento di Salute della Donna e del Bambino Università Degli Studi di Padova

Bologna, 2 Ottobre 2023

# XLVIII

CONGRESSO NAZIONALE

# AIEOP

**Bologna**

**2-4 Ottobre 2023**

***Il sottoscritto D'Agnolo Mirco***

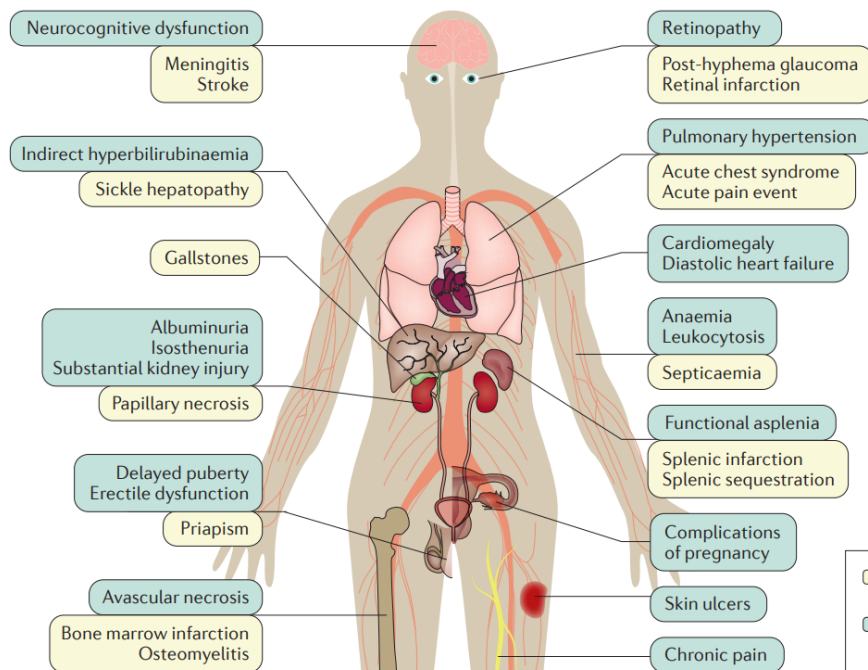
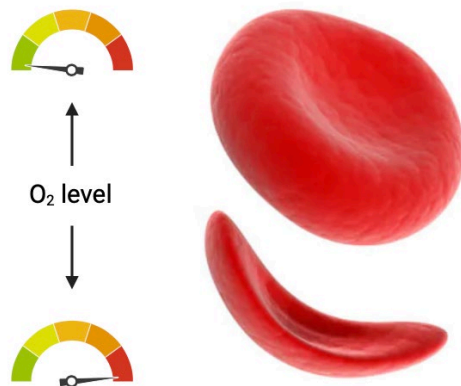
*ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-  
Regione del 5 novembre 2009,*

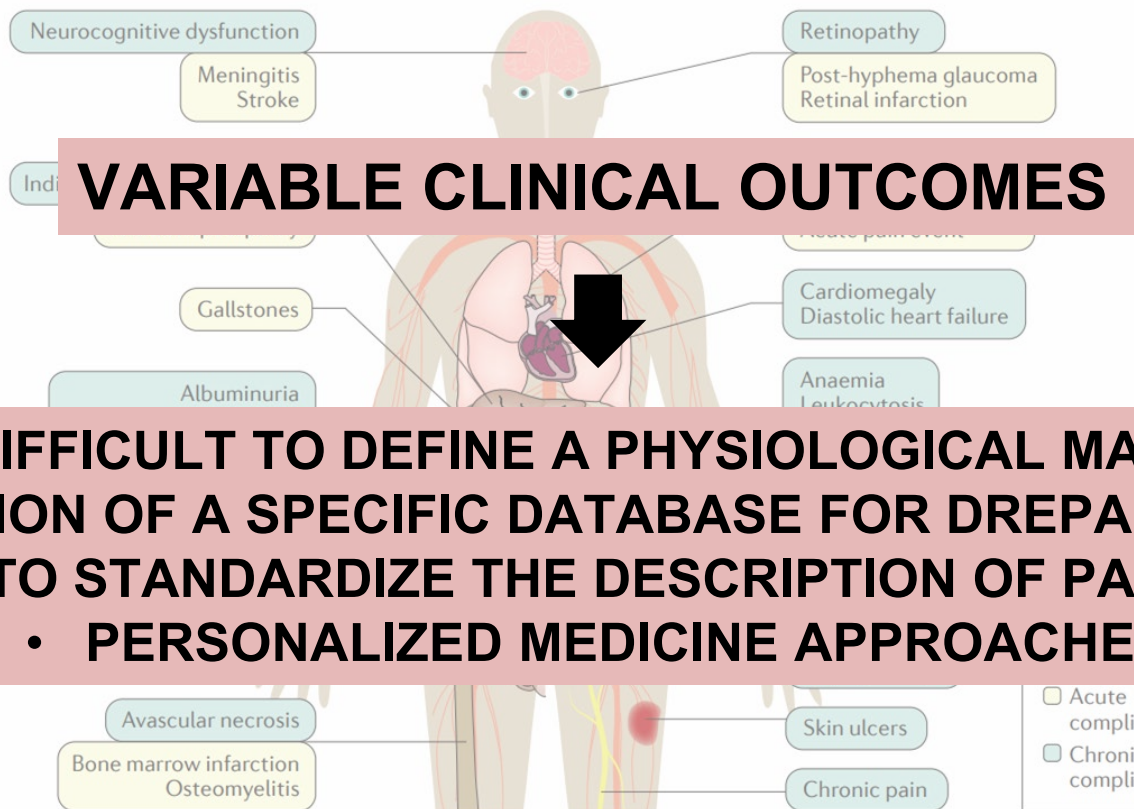
dichiara

☒ *che negli ultimi due anni NON ha avuto rapporti diretti di finanziamento con soggetti  
portatori di interessi commerciali in campo sanitario*

FROM A  
**SINGLE POINT MUTATION**

TO  
**VARIABLE CLINICAL OUTCOMES**





- **DIFFICULT TO DEFINE A PHYSIOLOGICAL MARKER**
- **CREATION OF A SPECIFIC DATABASE FOR DREPANOCYTOSIS**
- **NEED TO STANDARDIZE THE DESCRIPTION OF PARAMETERS**
  - **PERSONALIZED MEDICINE APPROACHES**

# GENOMED4ALL

*Genomics And Personalized Medicine For All Through  
Artificial Intelligence In Haematological Diseases*



## Diagnosis

AI algorithms for early  
identification of high-risk  
individuals



## Prognosis

Prediction algorithms for  
insights on disease  
development

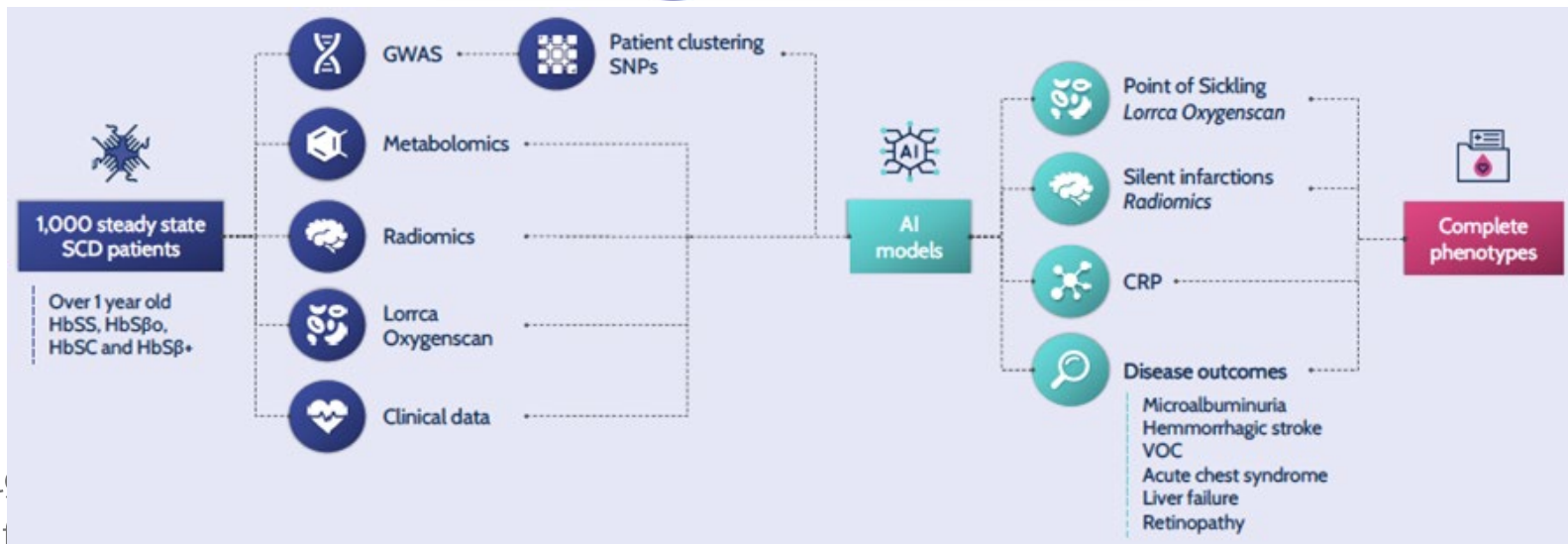


## Treatment

Clinical algorithms to aid  
decision-making in risk  
stratification



## GENOMED4ALL

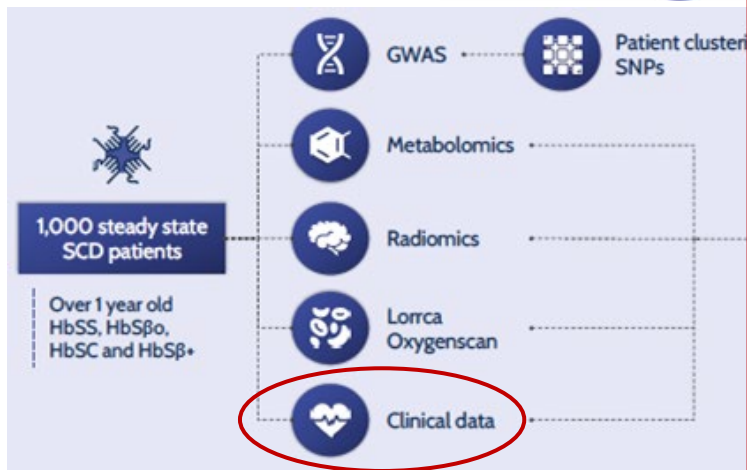


AI algorithms to aid  
identification of high-risk  
individuals

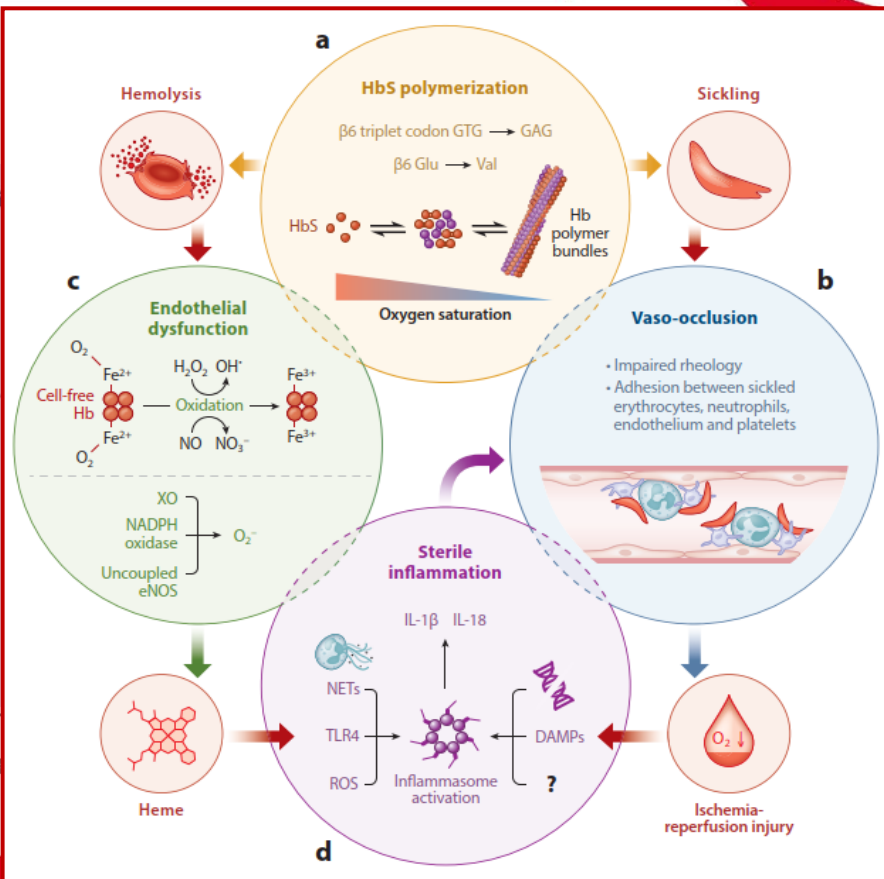
insights on disease  
development

decision making in risk  
stratification

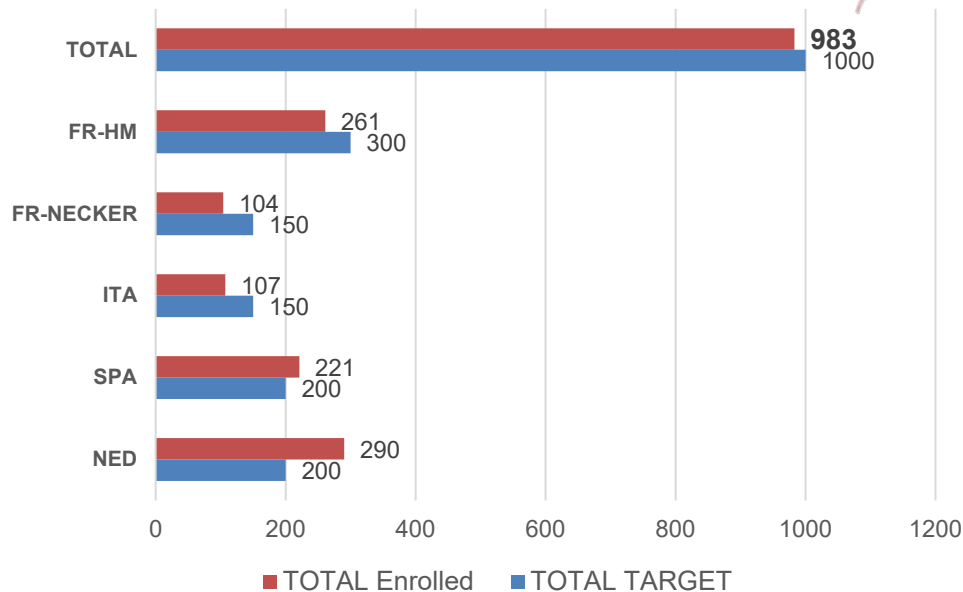
## GEN



AI algorithms for the identification of high-risk individuals



aid  
risk



Country	Clinical Data
NED	253
SPA	196
ITA	94
FR-NECKER	0
FR-HM	261
<b>TOTAL</b>	<b>804</b>



**Rare Anemia Disorders European Epidemiological Platform**

- Data dictionary and database in a GDPR compliant system
- Federated Learning

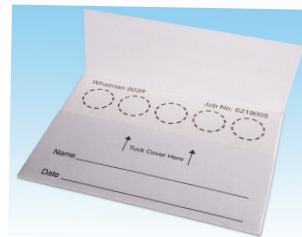


**METABOLOMICS**

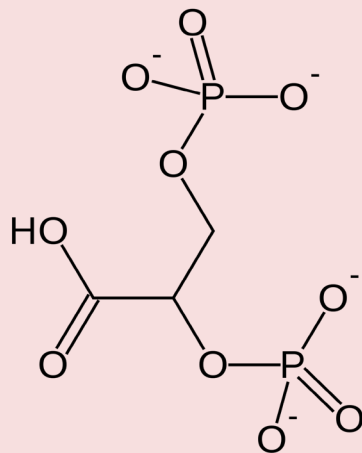
**Radiomics**

Genomics

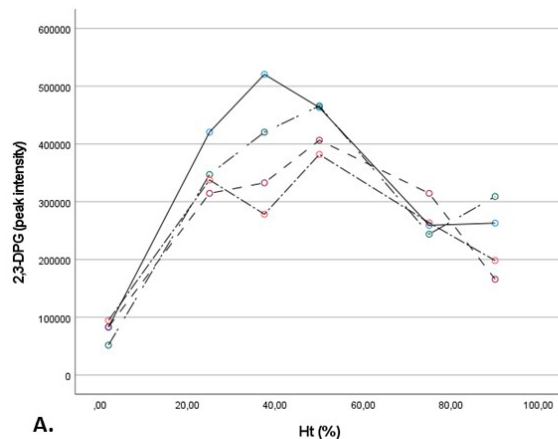
Point of Sickling



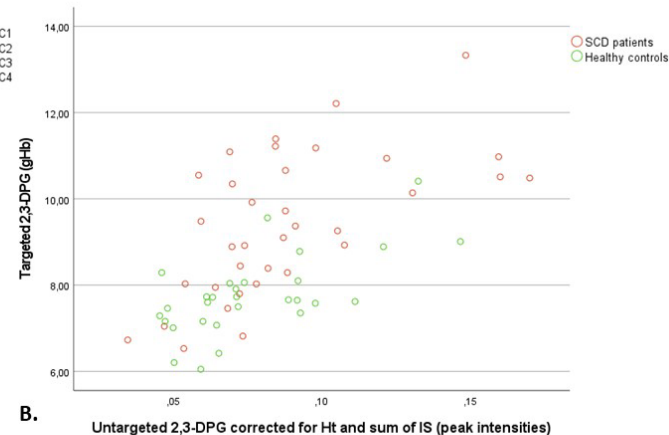
**1900+**  
**metabolites**



**2,3-diphosphoglycerate**



**A.**



**B.**

**Fig 1. 2,3-diphosphoglycerate (2,3-DPG) detection by untargeted- and targeted metabolomics**

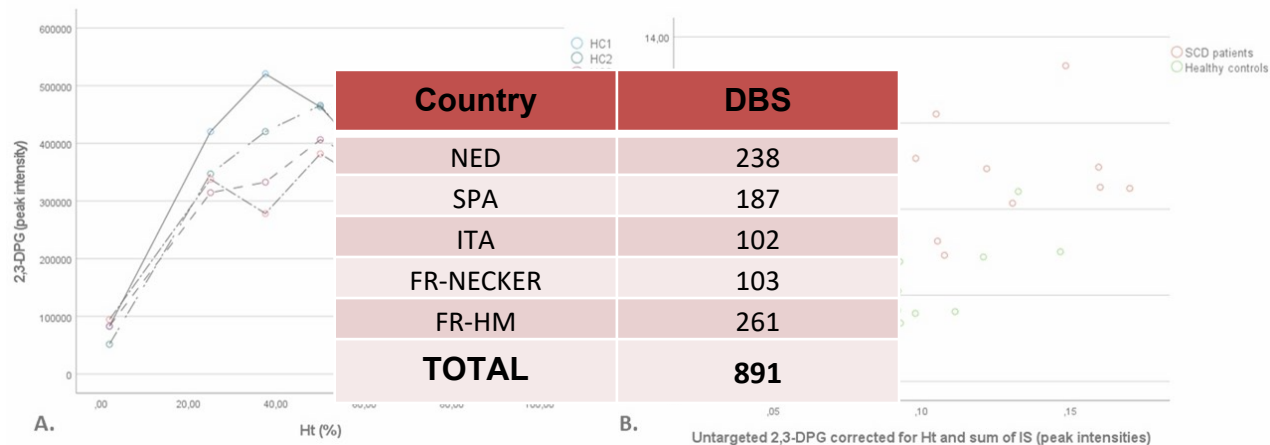
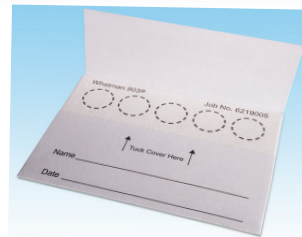
A) 2,3-DPG detected by untargeted metabolomics in dried blood spots with different Hematocrit (Ht) levels, 2,3-DPG is expressed by peak intensity. Spearman's correlation between Ht and 2,3-DPG is  $r = 0.060$  n.s. B) Correlation between untargeted and targeted detection of 2,3-DPG. 2,3-DPG detected via untargeted metabolomics corrected by  $(\frac{1-Ht}{Ht})$  and the sum of Internal Standard (IS) metabolites, expressed by peak intensities. Targeted 2,3-DPG expressed per gram Hemoglobin (gHb). Spearman's correlation between 2,3-DPG detected by both methods is  $r = 0.610$ ,  $p < 0.001$ .

**METABOLOMICS**

**Radiomics**

Genomics

Point of Sickling



**Fig 1. 2,3-diphosphoglycerate (2,3-DPG) detection by untargeted- and targeted metabolomics**  
A) 2,3-DPG detected by untargeted metabolomics in dried blood spots with different Hematocrit (Ht) levels, 2,3-DPG is expressed by peak intensity. Spearman's correlation between Ht and 2,3-DPG is  $r=0.060$  n.s. B) Correlation between untargeted and targeted detection of 2,3-DPG. 2,3-DPG detected via untargeted metabolomics corrected by  $(\frac{1-Ht}{Ht})$  and the sum of Internal Standard (IS) metabolites, expressed by peak intensities. Targeted 2,3-DPG expressed per gram Hemoglobin (gHb). Spearman's correlation between 2,3-DPG detected by both methods is  $r=0.610$ ,  $p<0.001$ .

Metabolomics

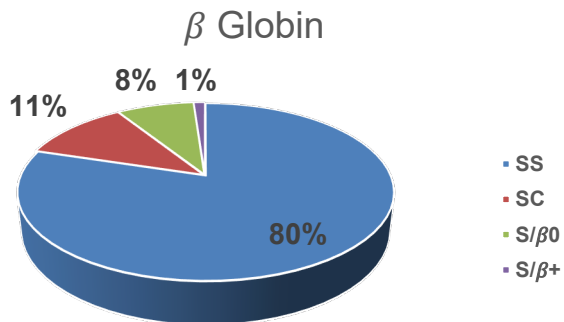
Radiomics

**GENOMICS**

Point of  
Sickling



Evaluation of  $\alpha$  and  $\beta$  globin gene mutation



Metabolomics

Radiomics

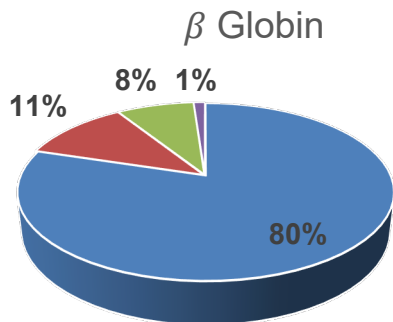
**GENOMICS**

Point of  
Sickling

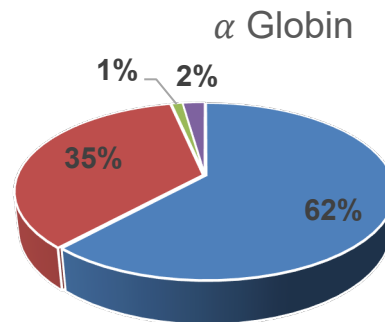


Evaluation of  $\alpha$  and  $\beta$  globin gene mutation

**Alpha Globin Strip Assay Kit**  
for the standardization of the  
measurements



- SS
- SC
- S/ $\beta^0$
- S/ $\beta^+$



- $\alpha\alpha/\alpha\alpha$
- -3,7/ $\alpha\alpha$
- -3,7/-3,7
- -3,7 $\alpha\alpha/\alpha\alpha$

Metabolomics

Radiomics

**GENOMICS**

Point of  
Sickling



Evaluation of  $\alpha$  and  $\beta$  globin gene mutation

Genome-wide Association Study  
(GWAS)

- 400 GM  $\rightarrow$  50 GM
- Sample collection:

Country	DNA
NED	216
SPA	161
ITA	100
FR-NECKER	103
FR-HM	261
<b>TOTAL</b>	<b>841</b>

Metabolomics

**RADIOMICS**

Genomics

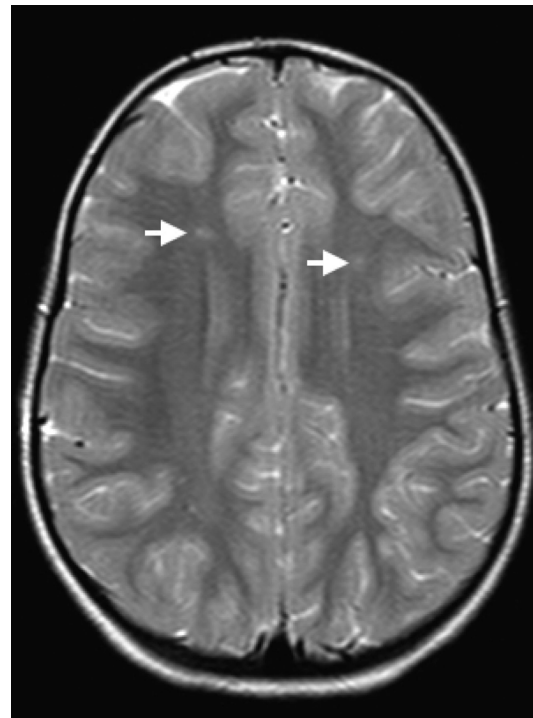
Point of  
Sickling

## CO04

### **OTTIMIZZAZIONE DIAGNOSTICA DEGLI INFARTI CEREBRALI SILENTI NELLA DREPANOCITOSI: USO DELLA RADIOMICA E DELL'INTELLIGENZA ARTIFICIALE NEL PROGETTO EUROPEO GENOMED4ALL.**

M.P. Boaro, R. Biondi, N. Biondini, G. Reggiani, M. D'Agnolo, M. Martella, A. Collado Gimbert, M.D.M. Manu Pereira, F. Alvarez, V. Pinto, V. Voi, G.B. Ferrero, M. Casale, G. Palazzi, G.L. Forni, S. Perrotta, G. Castellani, M. Minerva, R. Manara, J.M. Escudero Fernandez, N. Romano, M. Cirillo, F. Cavalleri, S. Zazo, M. de Montalembert, P. Bartolucci, E. van Beers, T. Sanavia, P. Fariselli, R. Colombatti (Padova, Bologna, Barcelona-ES, Madrid-ES, Genova, Orbassano, Napoli, Modena, Paris-FR, Creteil-FR, Utrecht-NL, Torino)

**Martedì 3 Ottobre 2023 – 10:50 am**



Manuscript in preparation  
*M.P. Boaro et. al.*

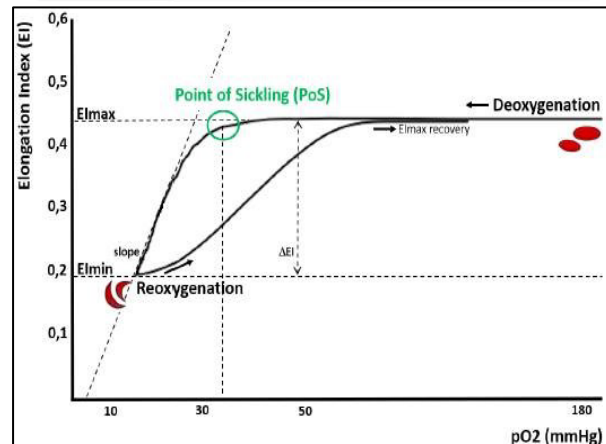
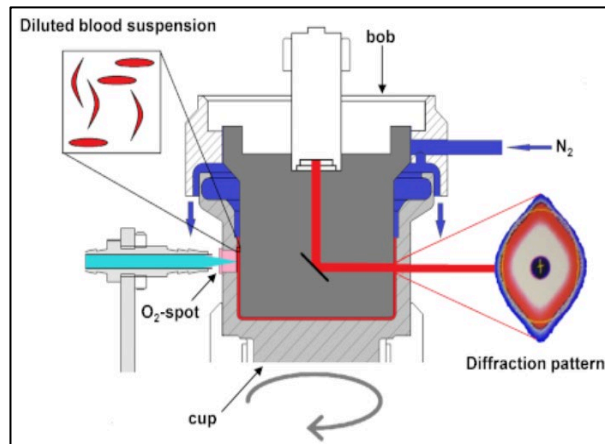
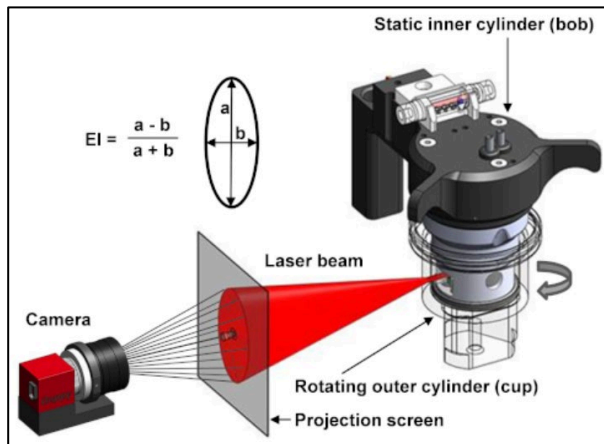
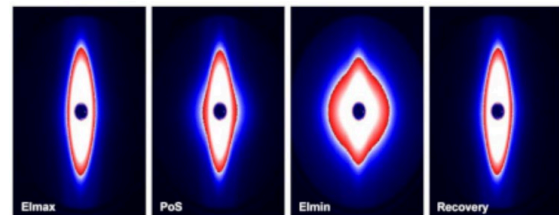


Metabolomics

Radiomics

Genomics

**POINT OF SICKLING**



Metabolomics

Radiomics

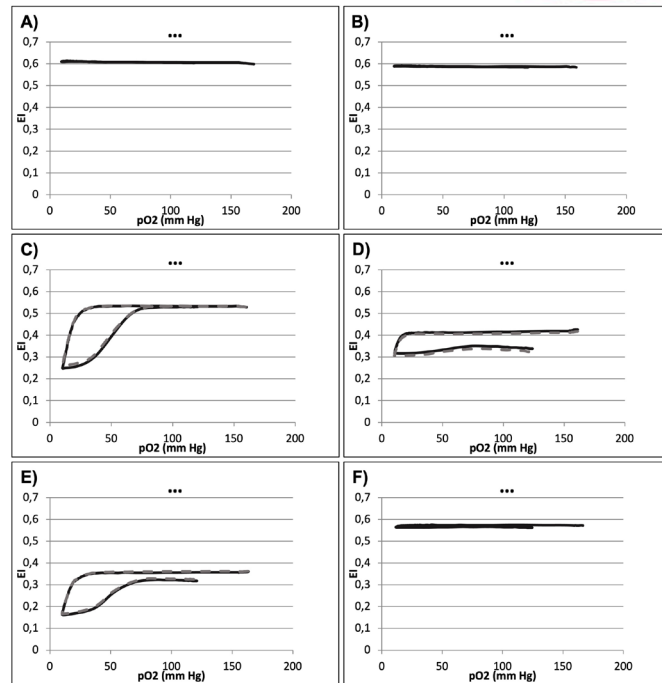
Genomics

**POINT OF SICKLING**



- Quality controls for measurements reproducibility (Cryo Straws)
- Sample collection:

Country	Oxygenscan
NED	149
SPA	128
ITA	102
FR-NECKER	67
FR-HM	209
<b>TOTAL</b>	<b>655</b>



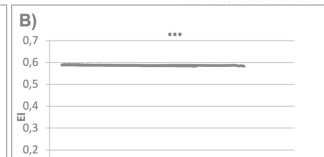
**Figure.** Oxygenscan curves for: A) healthy control; B) patient after HSCT; C) HbSS; D) HbSC; E) HbS/β<sup>0</sup>; F) HbS/β<sup>+</sup>

Metabolomics

Radiomics

Genomics

POINT OF  
SICKLING

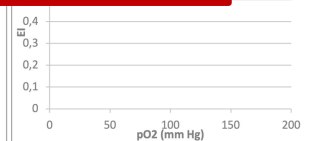
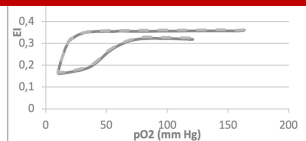


## P91

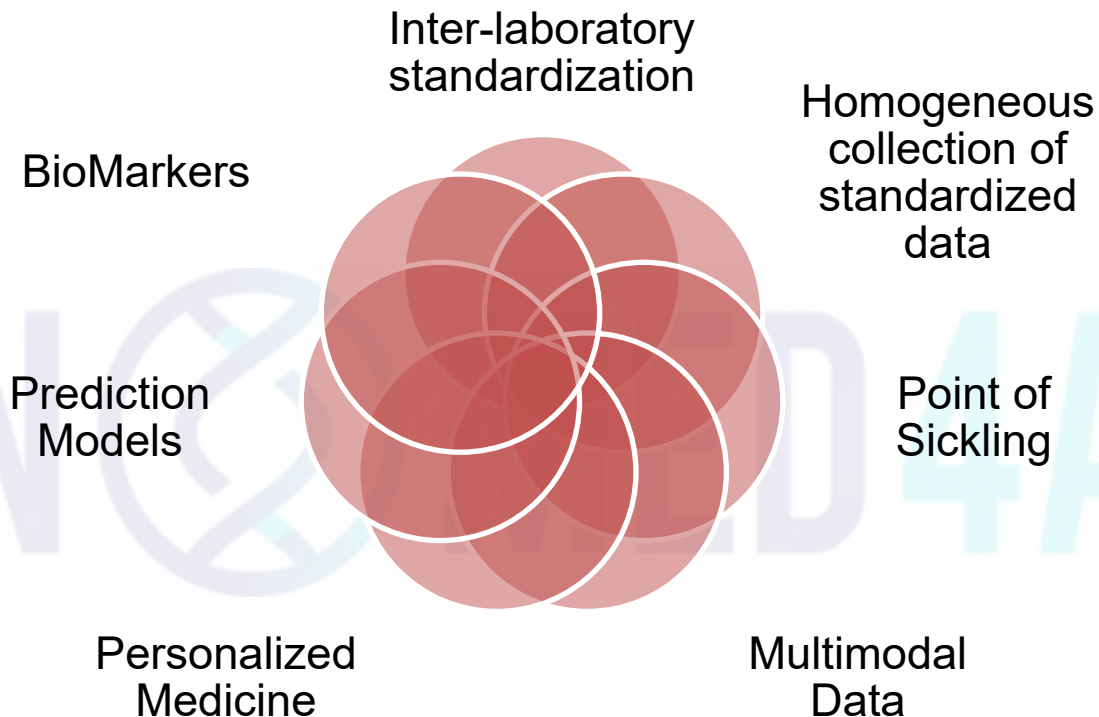
# STANDARDIZZAZIONE DEI PARAMETRI DI OXYGENSCAN PER L'OTTIMIZZAZIONE DELLA DIAGNOSTICA E DEL MONITORAGGIO TERAPEUTICO NELLA DREPANOCITOSI

M. D'agnolo, M. Martella, G. Reggiani, V. Munaretto, M.P. Boaro, R. Trapanese, M.D.M. Manu Pereira, A. Idrizovic, A. Collado Gimbert, M. Rab, G. Castellani, R. Colombatti (Padova, Barcelona-ES, Utrecht-NL, Bologna)

FR-NECKER	67
FR-HM	209
<b>TOTAL</b>	<b>655</b>



**Figure.** Oxygenscan curves for: A) healthy control; B) patient after HSCT; C) HbSS; D) HbSC; E) HbS/β<sup>0</sup>; F) HbS/β<sup>+</sup>

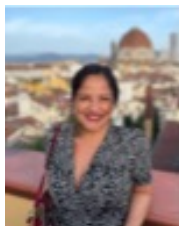


**STAY TUNED,  
WORK IN PROGRESS**



0%

100%



*Jackeline Elizabeth Maran*  
**Referente Sociale**



*Maria Paola Boaro*  
**Pediatra**



*Raffaella Colombatti*  
**Responsabile**



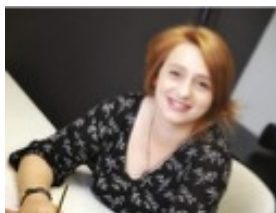
*Giulia Reggiani*  
**Pediatra**



*Maddalena Martella*  
**Biologa**



*Ilaria Baido*  
**Data Manager**



*Roberta Trapanese*  
**Data Manager**



*Martina Bonel*  
**Data Manager**



*Maria Elisa delle Fave*  
**Psicologa**



*Veronica Marchiori*  
**Psicologa**



*Alessandra Paratella*  
**Study Coordinator**



*Mirco D'Agnolo*  
**Biologo**

## **GRUPPO DREPANOCITOSI PADOVA**



**EuroBloodNet**

PROJECT PARTNERS  
**GENOMED4ALL**



**ThermoFisher**  
SCIENTIFIC



**Datawizard**



**HUMANITAS**  
RESEARCH HOSPITAL



ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS



**UMC Utrecht**



**ESIEE** **CINECA**  
PARIS



UNIVERSITÀ  
DEGLI STUDI  
DI PADOVA



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## **GRAZIE PER L'ATTENZIONE**

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### **CONTATTI:**

*Mirco D'Agnolo*

*Università degli Studi di Padova*

*Dipartimento di Salute della Donna e del Bambino*

*email: [mirco.dagnolo@unipd.it](mailto:mirco.dagnolo@unipd.it)*



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