



Ottimizzazione diagnostica degli infarti cerebrali silenti nella drepanocitosi : uso della radiomica e dell'intelligenza artificiale nel progetto Europeo GenoMed 4All.

Dr.ssa Maria Paola Boaro

Clinica di Oncoematologia Pediatria – Università di Padova

Bologna, 3 Ottobre 2023

**XLVIII**

CONGRESSO NAZIONALE

**AIEOP**

**Bologna**

**2-4 Ottobre 2023**

***La sottoscritta Maria Paola Boaro***

*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*

## **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, R. Colombatti, J. M. Escudero Fernandez, N. Romano, M. Cirillo, F. Cavalleri, S. Zazo, M. de Montalembert, P. Bartolucci, E. van Beers, T. Sanavia, P. Fariselli (Padova, Bologna, Barcelona-ES, Madrid-ES, Genova, Orbassano, Napoli, Modena, Paris – FR, Creteil – FR, Utrecht – NL, Torino)

## INTRODUZIONE

### SICKLE CELL DISEASE

Rare autosomal recessive disorder

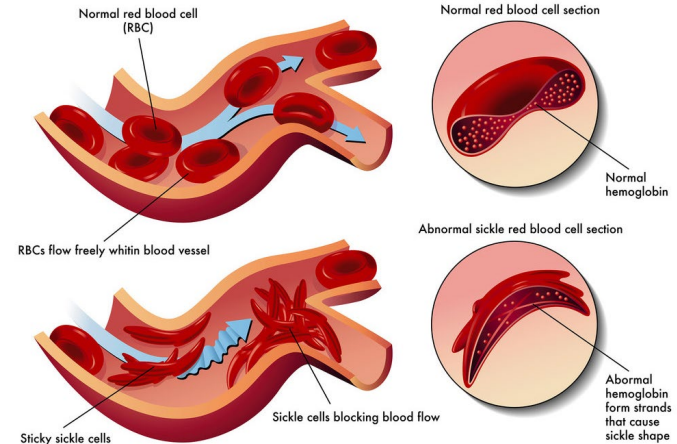
Point mutation *HBB* c.19 A>T → HbS

Selected by malaria in Africa and middle east regions

Sickle cells (rigid RBCs) → vaso-occlusive crisis and hemolysis

Acute and chronic complications

Decreased life expectancy and low Quality of Life



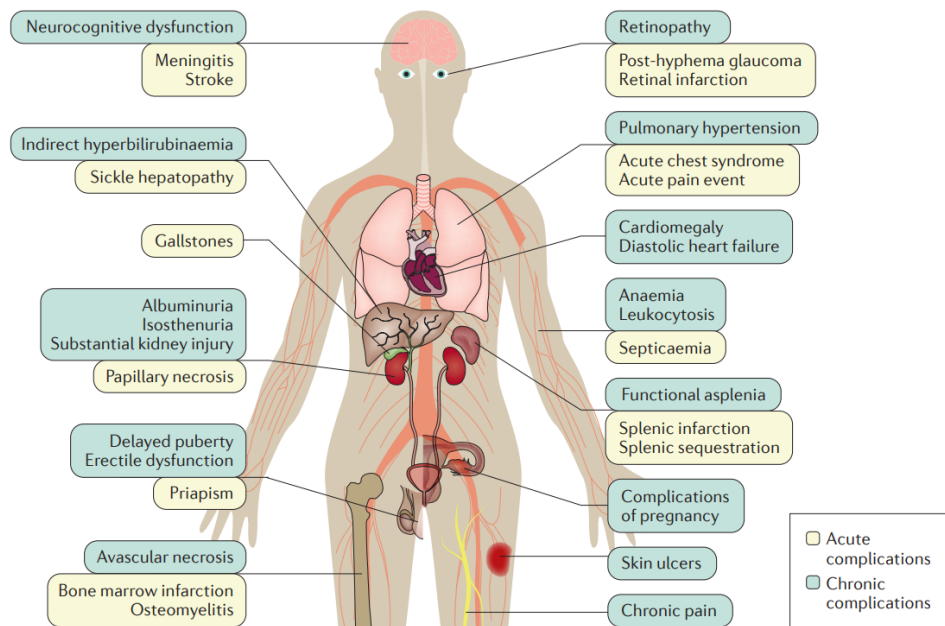


## INTRODUZIONE

## SICKLE CELL DISEASE

Chronic disease

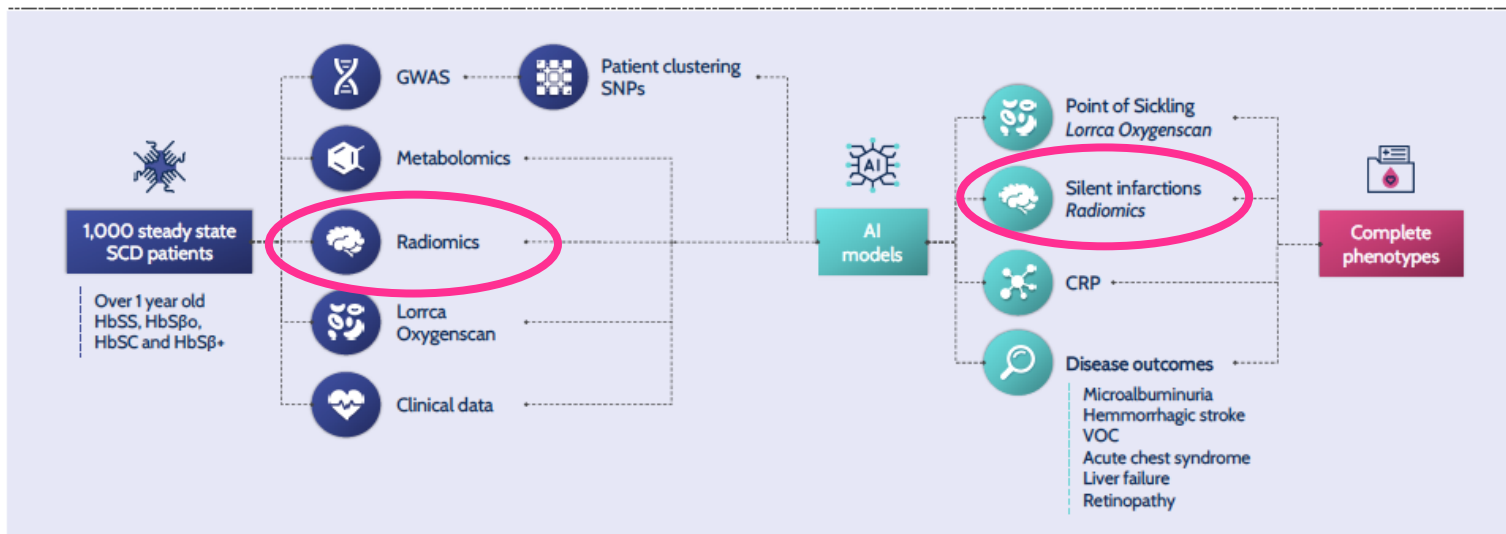
Multi systemic involvement



Kato G.J. et al. 2018 Nature reviews Disease Primers, 4 (18010); 1-22

## GENOMED4ALL

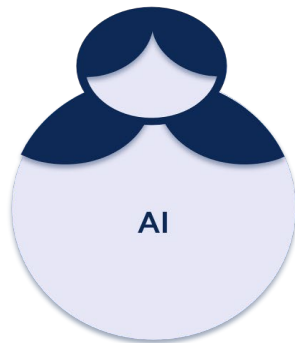
Genomics and Personalized Medicine for all through Artificial Intelligence in  
Haematological Diseases – Sickle Cell Disease use case



## INTRODUZIONE

### Artificial Intelligence

Any technique which enables computers to mimic human behaviour



### Machine Learning

A subset of AI techniques which use statistical methods to enable machines to improve with experience



### Neural Networks

A subset of ML algorithms inspired by the way neurons in the human brain operate



### Deep Learning

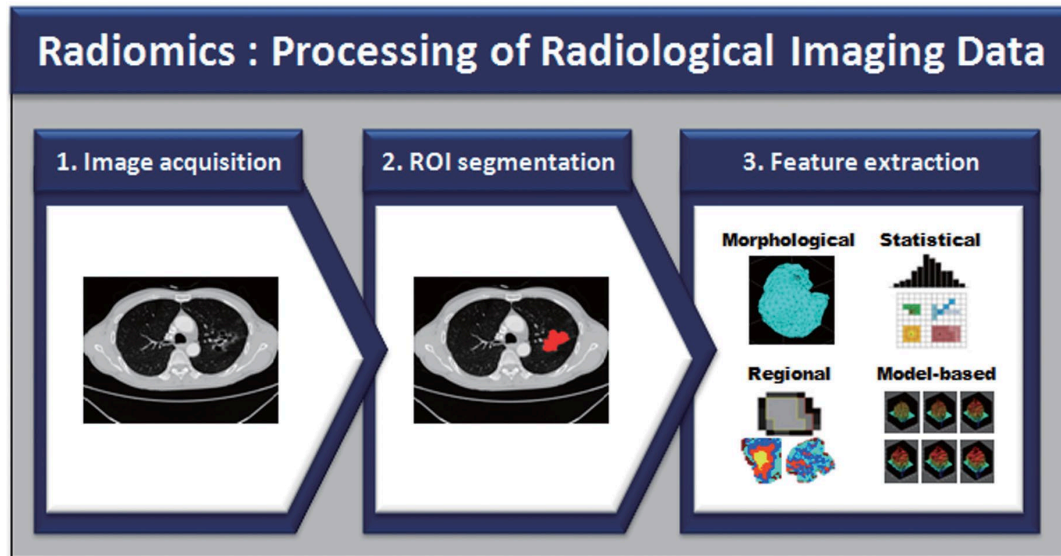
A subset of NN that makes computation of multi-layer neural networks feasible



## INTRODUZIONE

### RADIOMICS

Images are more  
than pictures,  
they are data



Lee G. et al. 2017 Precision and Future Medicine 1(1):10-31

Gilles R. et al. 2016, Radiology, 278 (2): 563-577



## **INTRODUZIONE**

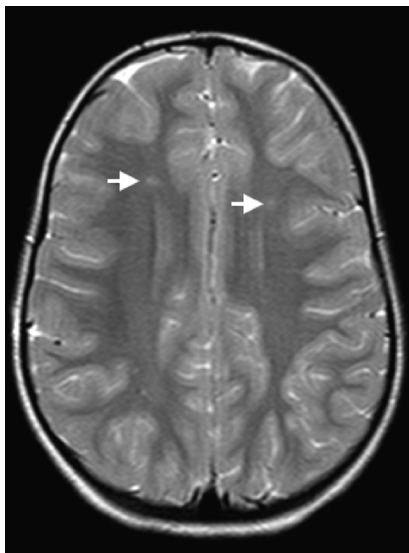
### **STANDARDIZED DEFINITION OF SILENT CEREBRAL INFARCT**

Presence of abnormalities on a magnetic resonance imaging (MRI) scan consistent with cerebral infarction (FLAIR T-2 weighted imaging) without a clinical history or abnormalities on physical examination that are consistent with a previous stroke. MRI lesions have to be at least 3 mm in diameter in children, whereas in adults a more restrictive definition is sometimes used which includes a lesion measuring at least 5 mm on MRI.

Estcourt LJ et al. Cochrane Database Syst Rev. 2020 Apr 6;4(4):CD012389.  
DeBaun MR et al. Blood 2012;119(16):3684-90.  
Casella JF et al. Pediatric Hematology & Oncology 2010;27(2):69-89

## INTRODUZIONE

### SILENT CEREBRAL INFARCT



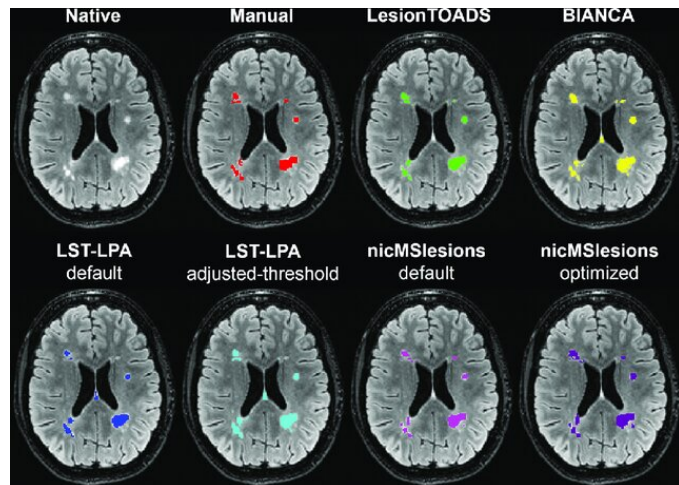
Significant MORBIDITY: affect 25% of children by the age of 6 and 40% by the age of 18 with consequences on cognition, schooling, working capacity and quality of life.

BARIERS TO SCREENING: Screening of neurological complications and chronic organ damage is suboptimal in Europe

Not all centers have expert neuroradiologists to identify SCI

PATHOPHYSIOLOGY AND RISK FACTORS incompletely understood

## OBIETTIVO DELLO STUDIO



To build new algorithms through Artificial Intelligence, for the segmentation of brain matter and automatic identification of SCI, distinguishing the pathological white matter hyperintensities (WMH) from the non-pathological ones

## MATERIALI E METODI

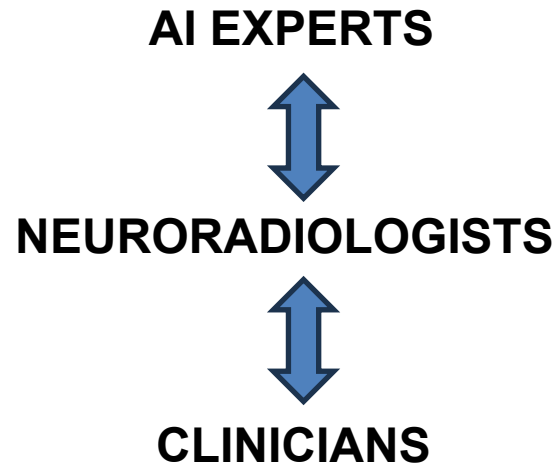
2D and 3D FLAIR sequences of anonymized brain MRI of SCD patients

445 MRI of 260 patients from 6 European EuroBlood Net Centers

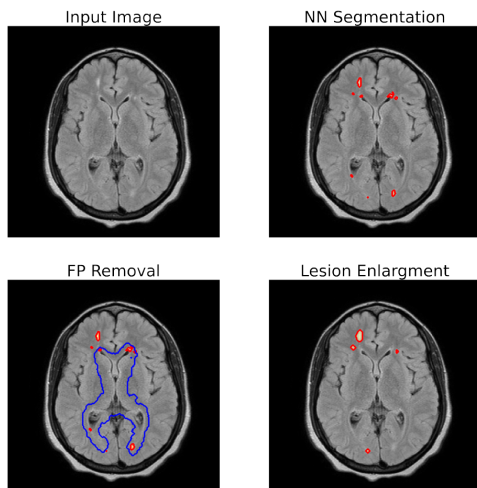
Different equipment: Siemens 1,5 and 3 T, Philips 1,5 T, GE 3 T

Open-source software:

Lesion Segmentation Tools and UNet for segmentation  
Freesurfer for brain extraction



## RISULTATI



**Figure:** Image Segmentation Pipeline. Clockwise: Input image, Neural Network results (thr=.45), Defined Area for FP removal, enlarged region by active contours

*wmh\_ibtTum*

- UNet Ensemble
- Open Source

### Pipeline

- Pre-trained UNet
- Find Ventricles  
Exclusion Regions
- Remove FP
- Active Contour:  
Enlarge Regions
- Remove FP by  
surrounding WM

### Brain extraction

MNI152 atlas on the T1 images



### Segmentation

#### Pre-Trained UNet Ensemble:

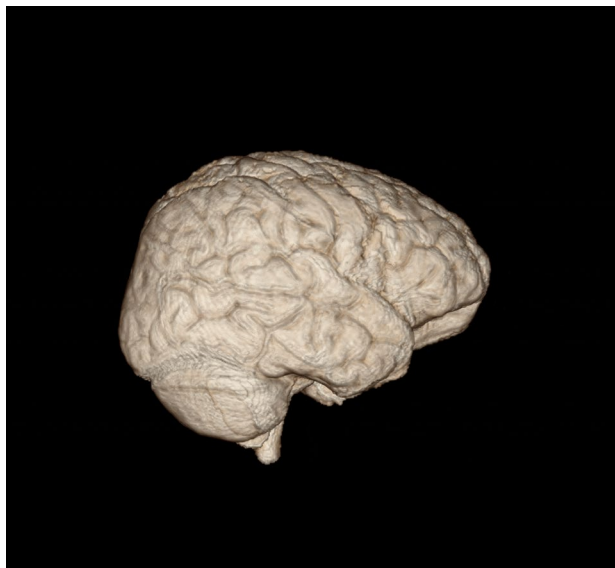
- *Winner of MICCAI WMH Segmentation Challenge*
- *Open Source*

#### Refinement:

- *Removal of False Positives*
- *Lesion Area Enlargement*



## RISULTATI



### Brain extraction

Registration of a brain atlas (in our project the ICBM MNI 152)

Masking and thresholding process.

Optimising Freesurfer from 20' to 2'

## RISULTATI

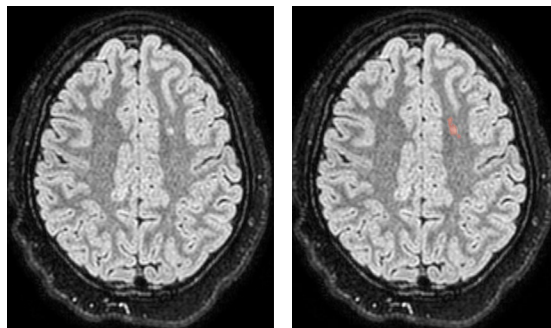
### FIRST PHASE

AI segmentation:  
First semi automatic  
SCI IDENTIFICATION  
(pre-processing – WMH  
segmentation – post  
processing)



### SECOND PHASE

Neuroradiologist manual  
labelization

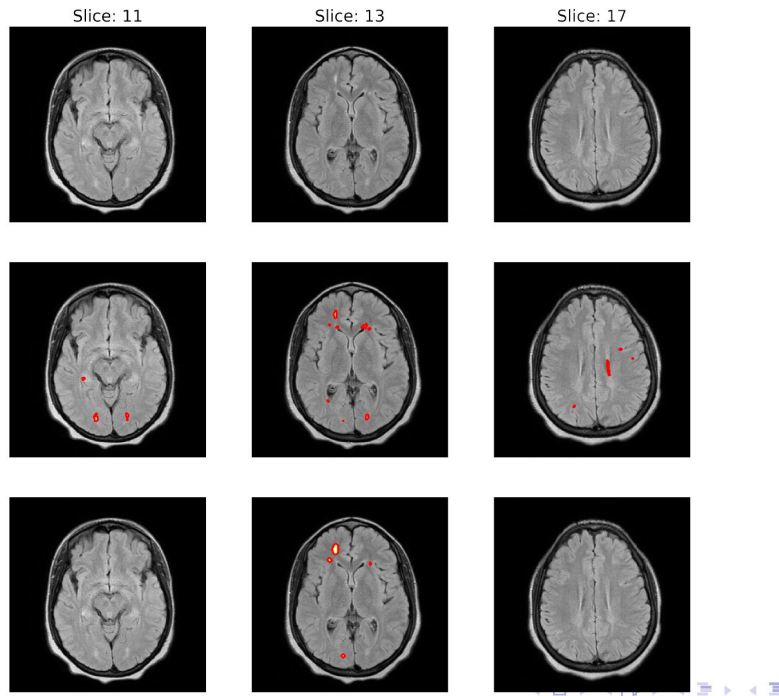


### THIRD PHASE

AI refinement:  
second training of  
NEURAL NETWORK  
with «correct labeling»

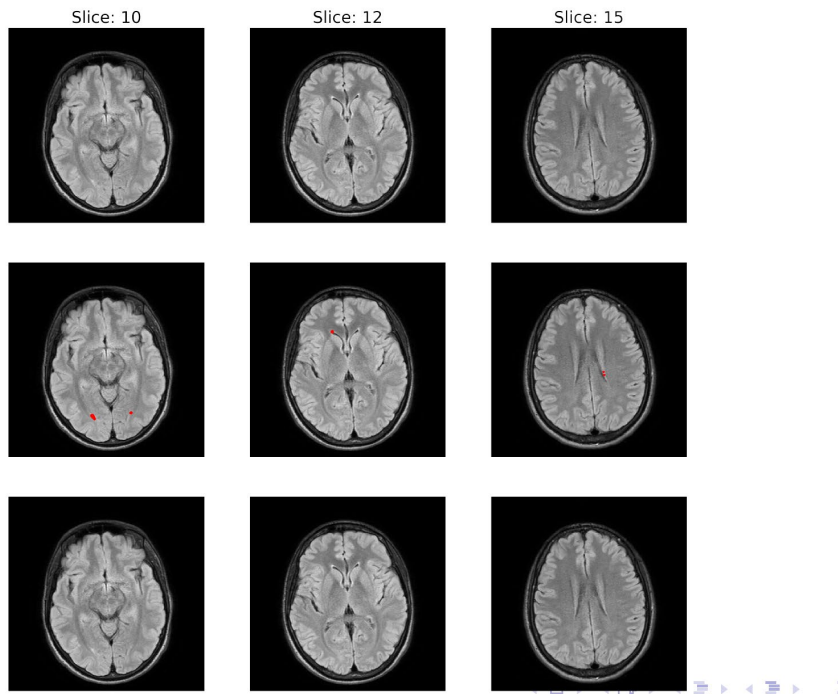
## Results

Patient: 1 Exam: 2020 Outcome: Altered



## Results

Patient:4 Exam:2016 Outcome: Not Altered



## **DISCUSSIONE E CONCLUSIONI**

### **AUTOMATIC DETECTION OF SCI THROUGH AI MODELS APPLIED TO**

- different datasets of anonymized images
- different equipment
- different phases of brain maturation (children, teenagers, adults)

**IS POSSIBLE**

FUTURE STEPS:

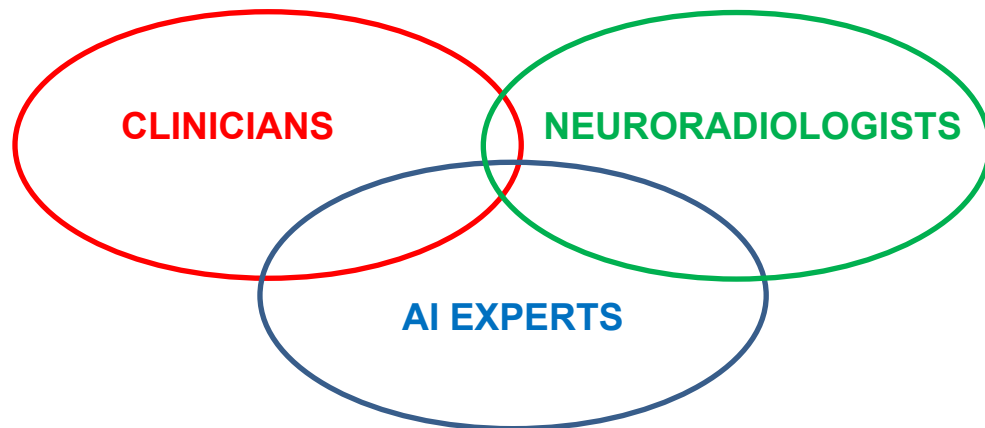
- features extraction and selection, to complete the whole radiomic process.
- correlation between SCI And clinical/hematological parameters
- prediction of risk of developing SCI In The Future

**REAL WORLD DATABASE**



## DISCUSSIONE E CONCLUSIONI

**THE CREATION OF A SPECIFIC ALGORITHM REQUIRES A CLOSE  
COLLABORATION IN THE MULTIDISCIPLINARY TEAM  
(CLINICIANS, NEURORADIOLOGISTS, AI EXPERTS)**



*Manuscript in preparation*

## THANKS TO RADIOMICS TEAM

«Core» SCD TEAM of  
GENOMED4ALL

**Raffaella Colombatti:**  
**coordinator of Radiomic Group**

Pablo Bartolucci  
Mariane de Montalembert  
Eduard Van Beers  
Maria Manu del Mar  
Anna Collado Gimbert  
Sigrid Van der Veen  
Anne Laure Phamhung-  
dalexandrydorengi

Neuroradiologists Team

Renzo Manara  
Matteo Minerva

ALL CENTERS  
CONTRIBUTING TO THE  
DATASET

For Italy: Padova, Genova  
Galliera, Napoli Vanvitelli,  
Torino Orbassano, Monza

Radiomics AI Team

Gastone Castellani  
Riccardo Biondi  
Nicholas Biondini  
Tiziana Sanavia  
Piero Fariselli  
Kostas Marias  
Nikolaos Papanikolaou  
Santiago Zazo  
Federico Alvarez

**EuroBloodNet**

## PROJECT PARTNERS

**GENMED4ALL**



**ThermoFisher**  
SCIENTIFIC



**Datawizard**



**HUMANITAS**  
UNIVERSITY HOSPITAL



ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS



**UMC Utrecht**



**ESIEE**  
PARIS

**CINECA**

**THANK YOU FOR YOUR  
ATTENTION**