Towards Multiple Sclerosis Assessment through Advanced MRI Biomarkers and Artificial Intelligence

Pedro M. Gordaliza[a,b,c], Joe Najm[b,d], Maxence Wynen[b,e,f], Nataliia Molchanova[b,c,g], Francesco La Rosa[d,h], Jean-Philippe Thiran[a,b,d], Pietro Maggi[f,i,j], Benoit Macq[e], Cristina Granziera[k,l], Martina Absinta[m,n], Meritxell Bach Cuadra[a,b,c]

[a] CIBM Center for Biomedical Imaging, Switzerland, [b] Radiology Department, Lausanne University and University Hospital, Switzerland [c] University of Lausanne, Switzerland, [d] Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland, [e] ICTeam, UCLouvain, Louvain-la-Neuve, Belgium, [f] Louvain Inflammation Imaging Lab (NIL), Institute of Neuroscience (IoNS), UCLouvain, Brussels, Belgium, [g] University of Applied Sciences of Western Switzerland, Switzerland, [h] Department of Neurology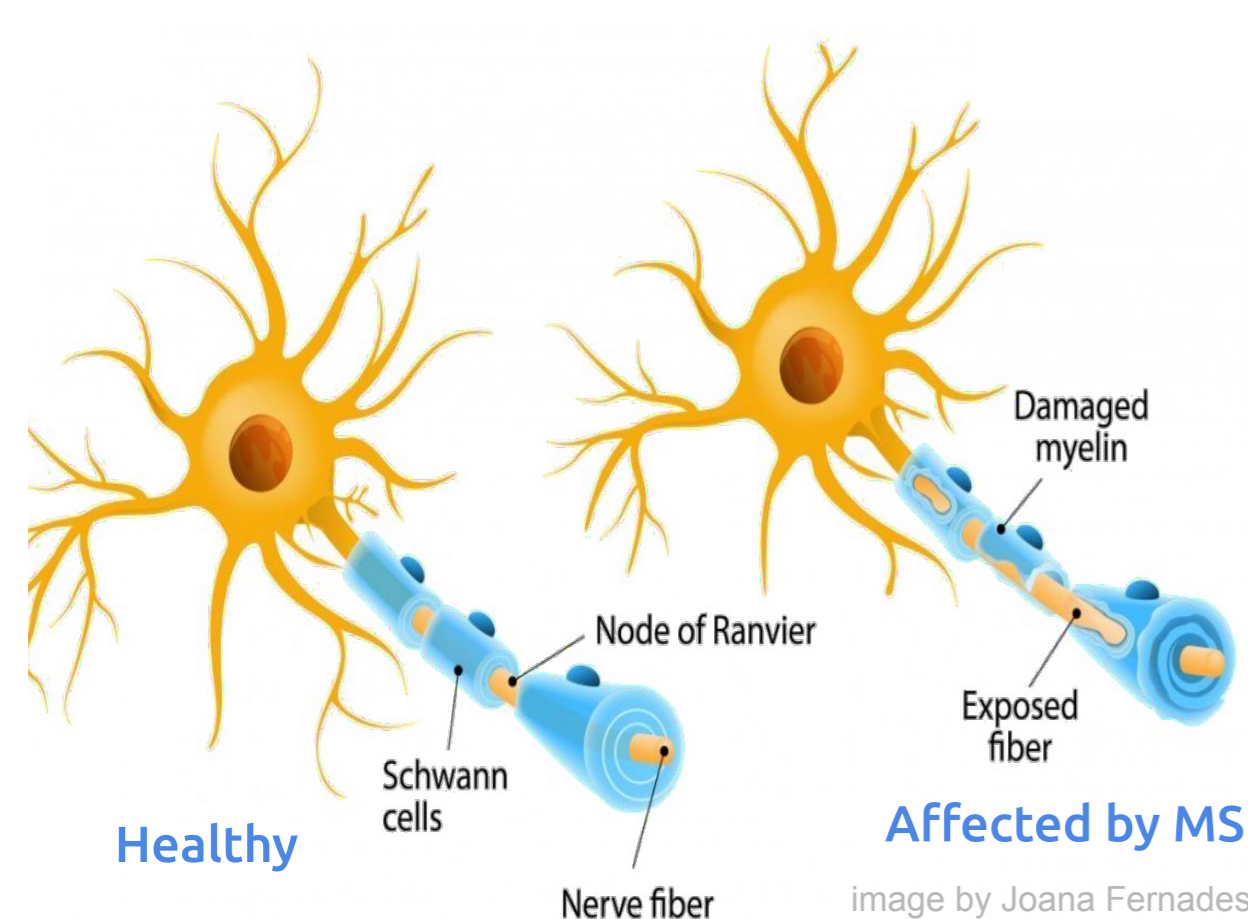, Icahn School of Medicine at Mount Sinai, New York, NY, USA, [i] Department of Neurology, Cliniques universitaires Saint-Luc, Université catholique de Louvain, Brussels, Belgium, [j] Department of Neurology, CHUV, Lausanne, [k] Translational Imaging in Neurology (ThINk) Basel, Department of Biomedical Engineering, University Hospital Basel and University of Basel, Switzerland, [l] Neurologic Clinic and Policlinic, MS Center and Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel, [m] IRCCS San Raffaele Hospital and San Raffaele University, Italy, [n] Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

BACKGROUND

Healthy — Affected by MS
Node of Ranvier, Damaged myelin, Schwann cells, Nerve fiber, Exposed fiber
image by Joana Fernades

- Approximately 2.3 million people worldwide live with Multiple Sclerosis (MS)[1].
- Autoimmune inflammatory disease of the central nervous system affecting myelin sheath damaging it and the nerves, degrading or interrupting the information flow.
- Degenerative disease, increased patient disability through time, without curation.

- MS lesion assessment in-vivo with MRI.
- During clinical practice, monitoring White Matter Lesions (WML).
- Advanced MRI sequences allow the discovery of more informative biomarkers for research: Cortical Lesions (CL), Parametric Rims (PRL) and Central Veins Sings (CVS)[2].

T1w, T2w, FLAIR Advanced Sequences: MP2RAGE, FLAWS, DIR, PSIR...

White matter lesions | Cortical lesions | Paramagnetic rims | Central vein sign (axial, sagittal, coronal)
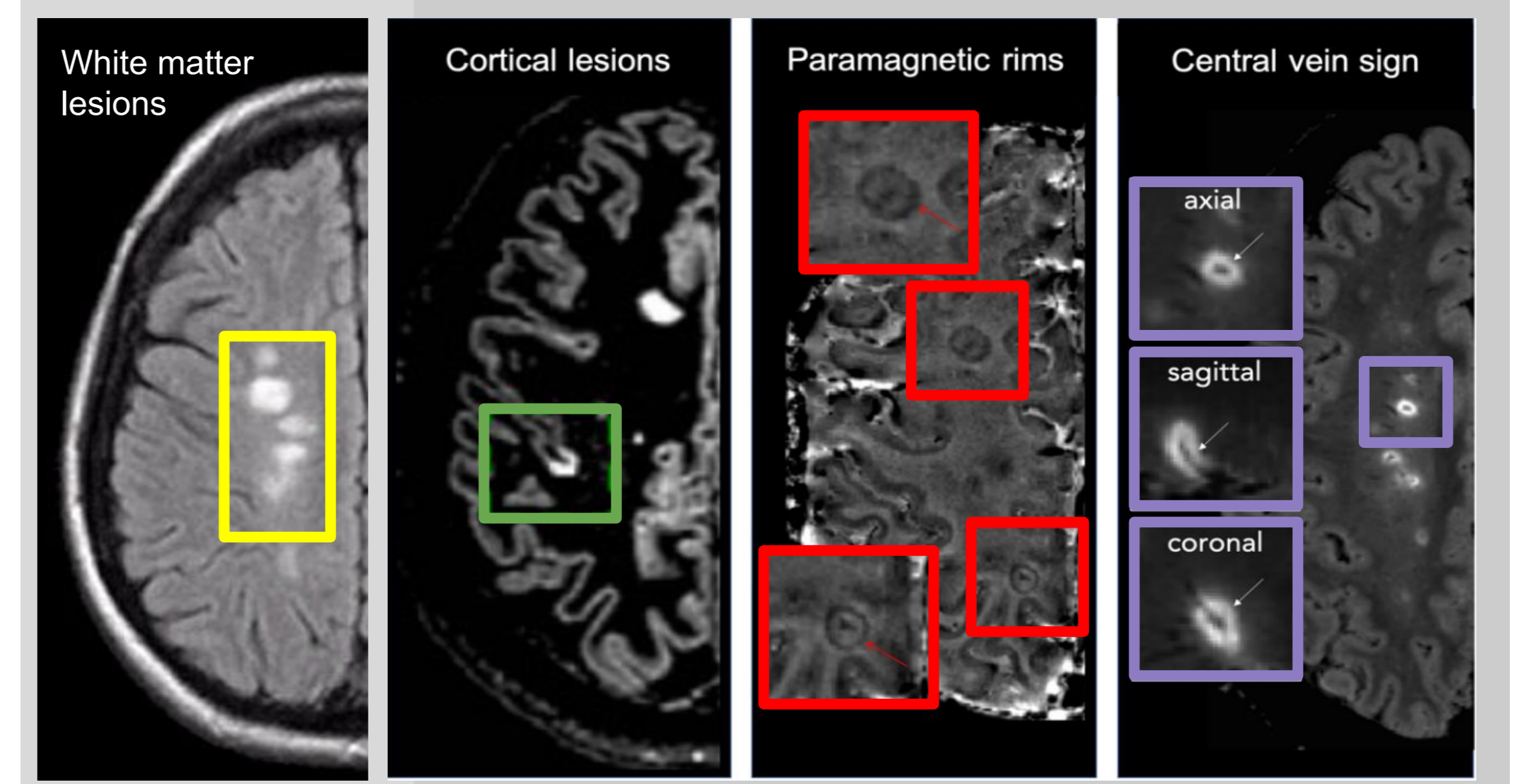
Differential diagnosis / Prognosis
Clinical assessment (McDonald Criteria)

[1] Filippi et al. *Nat. Rev. Dis. Primers*. 2018, [2] La Rosa et al. *NeuroImage Clin.* 2022

AIMS

MSxplain
Responsible AI in Multiple Sclerosis
Explainability, Interpretability, Uncertainty, Integration
HASLERSTIFTUNG

- Automated segmentation and/or detection of advanced biomarkers aligned with the **MSxplain** project goals:
  - Improve the automation model's generalization capabilities by identifying existence bias.
  - Increase confidence in the clinical decision-making process through new interpretability and explainability strategies.
  - Extract measures of MS progression modelling the possible cause and effects relations underlying the disease's biological mechanisms

[3] MSxplain project. https://wp.unil.ch/mial/research/projects/msxplain/

PROJECTS

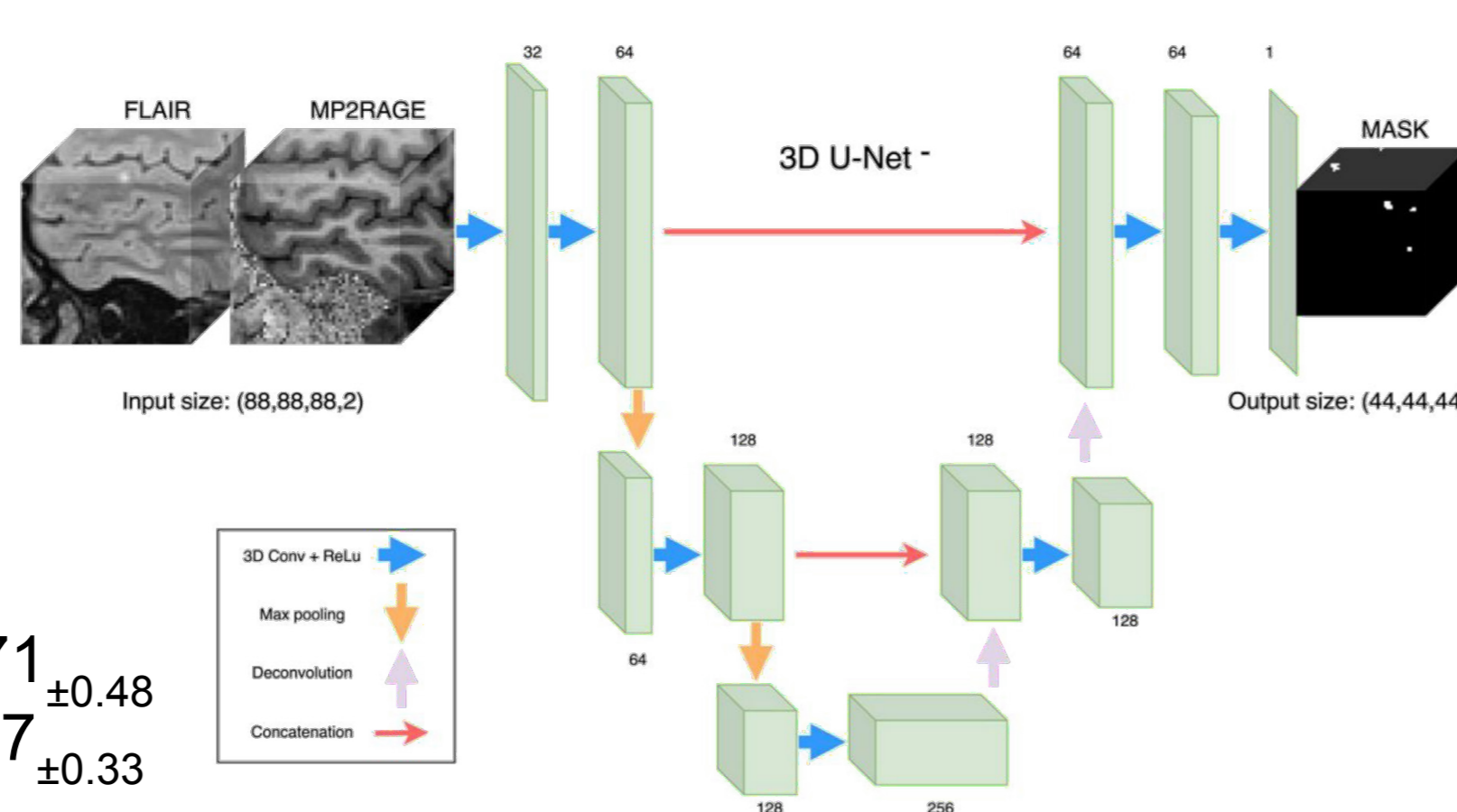| • CL Segmentation	• PRL Detection
• CL are present in all MS phenotypes and can be detected at early stages	• PRL biomarker for progression. PRL burden correlates with MS aggressiveness

Developed

○ **3D-UNET-[4]:**

- Experiment:
  Train = 54
  Test = 35

- Results:
  Dice = $0.60_{\pm 0.19}$
  True Positive Rate$_{CL}$ = $0.71_{\pm 0.48}$
  False Positive Rate = $0.27_{\pm 0.33}$

FLAIR MP2RAGE — 3D U-Net — MASK
Input size: (88,88,88,2) Output size: (44,44,44)

[4] La Rosa et al. *NeuroImage Clin.* 2020

○ **RIMnet[5]**
- Allows to differentiate selected patches

- Experiment:
  Rim+ = 462 patches
  Rim- = 4857 patches

- Results
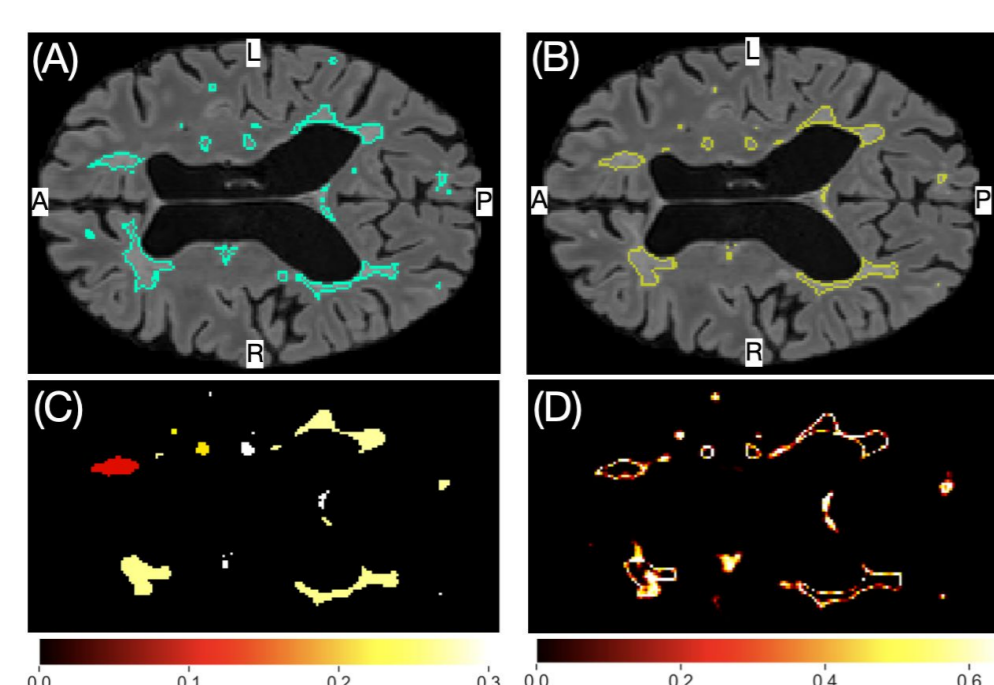 Phase input→AUC = 0.913
  Phase+Flair→AUC = 0.943

Phase, FLAIR → rim+ / rim-
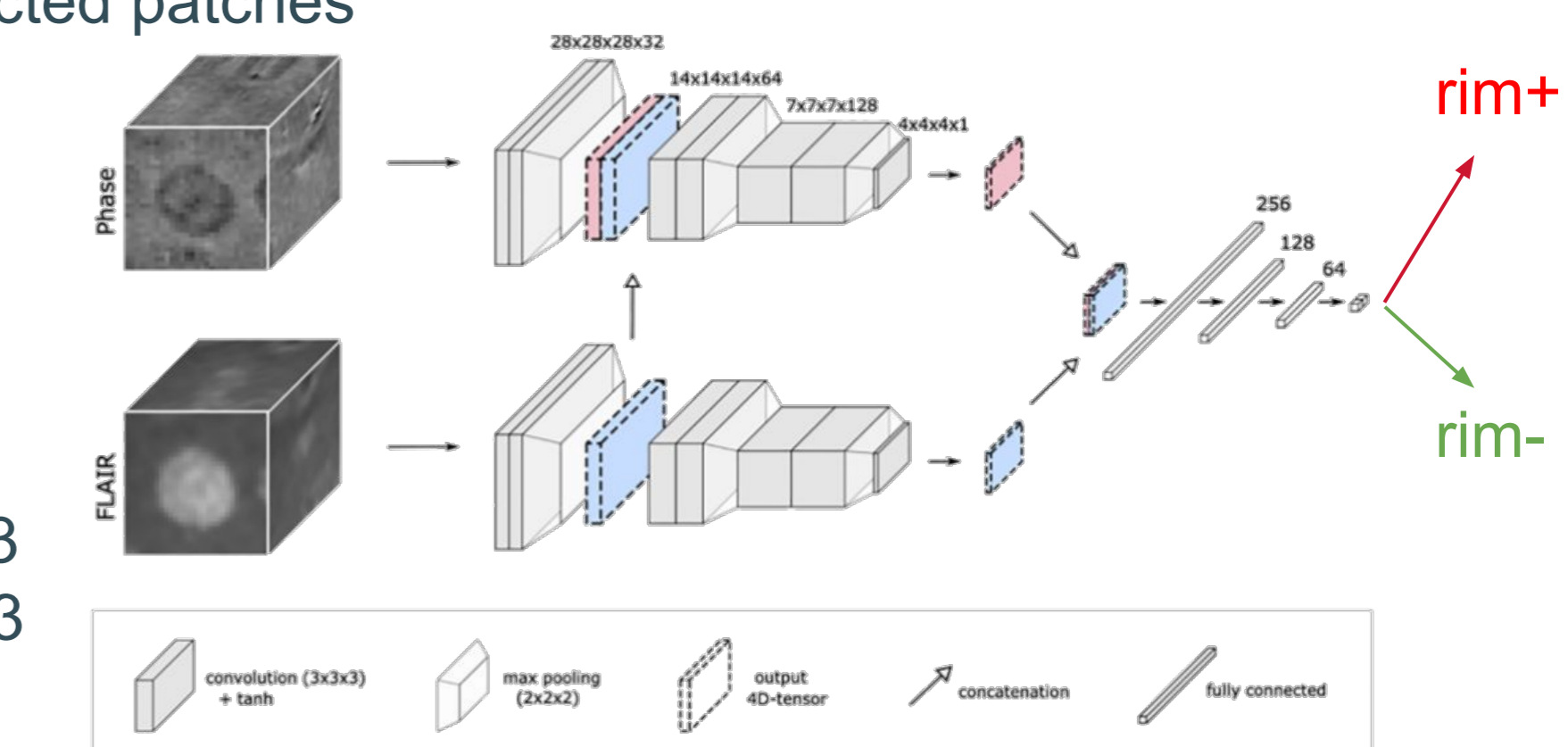
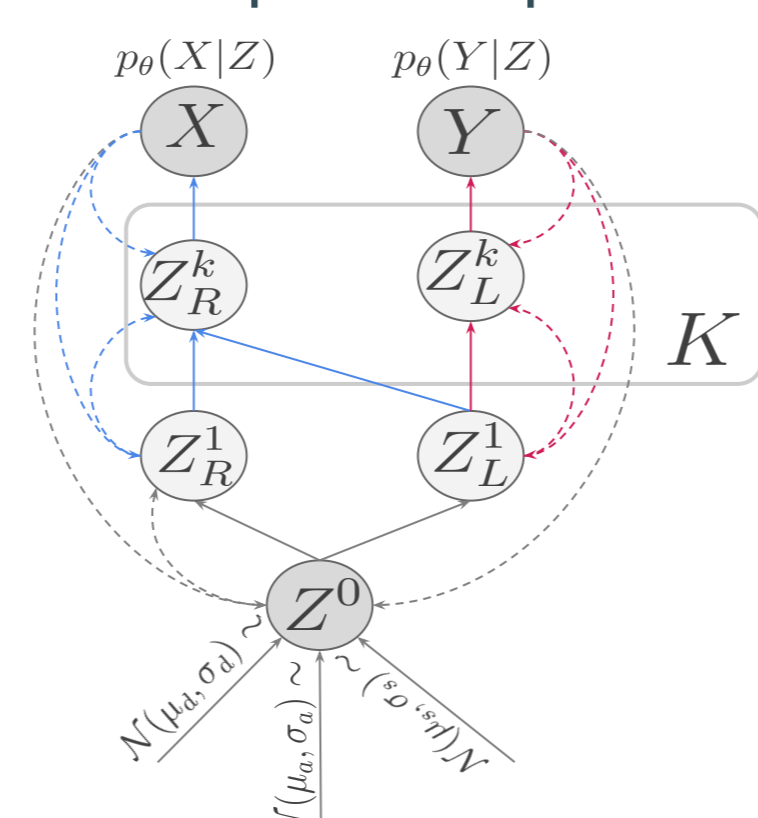[5] Barquero et al. *NeuroImage Clin.* 2020

Ongoing

○ **Uncertainty Estimation**
- Extended from our work in WML segmentation[6] (Check @NM poster!)
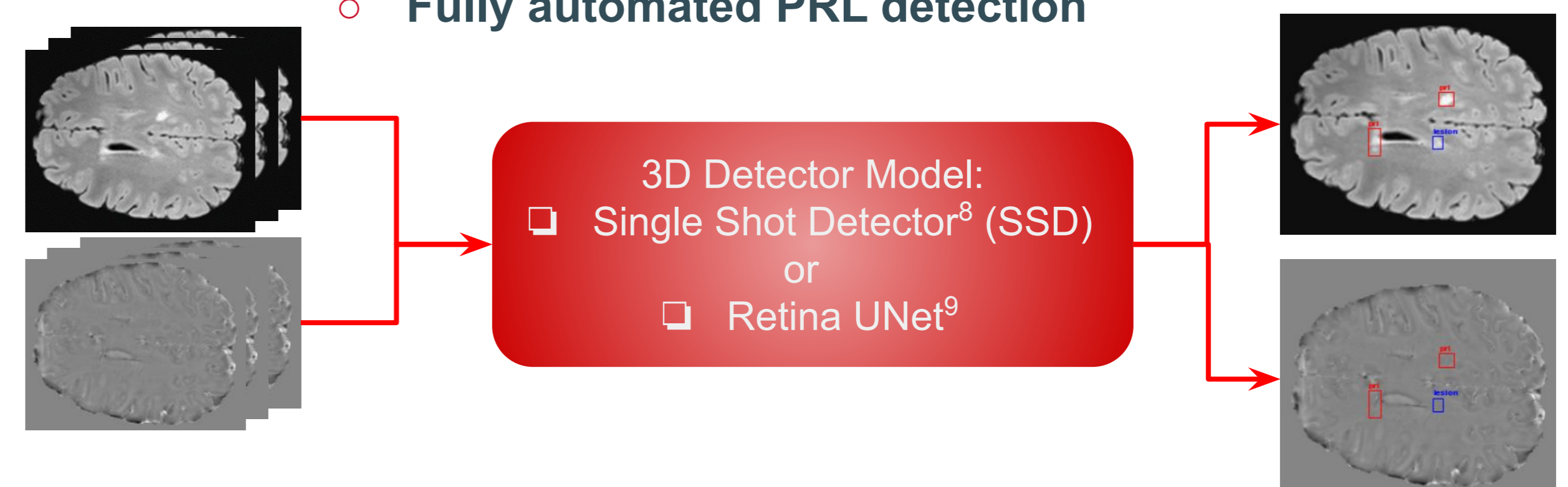

○ **Deep Causal Models**
- To deal with Domain Adaptation issues and improve explainability[7].

[6] Molchanova et al. *ISBI*. 2022

○ **Fully automated PRL detection**

3D Detector Model:
❑ Single Shot Detector[8] (SSD)
or
❑ Retina UNet[9]

- SSD model learning is based on cheaper annotations, lesions localization, than Retina UNet, instance lesion segmentation

[7] Gordaliza et al. *PhD Thes.* 2022 [8] Liu et al. *CVPR* 2015, [9] Baumgartner. *MICCAI* 2021