

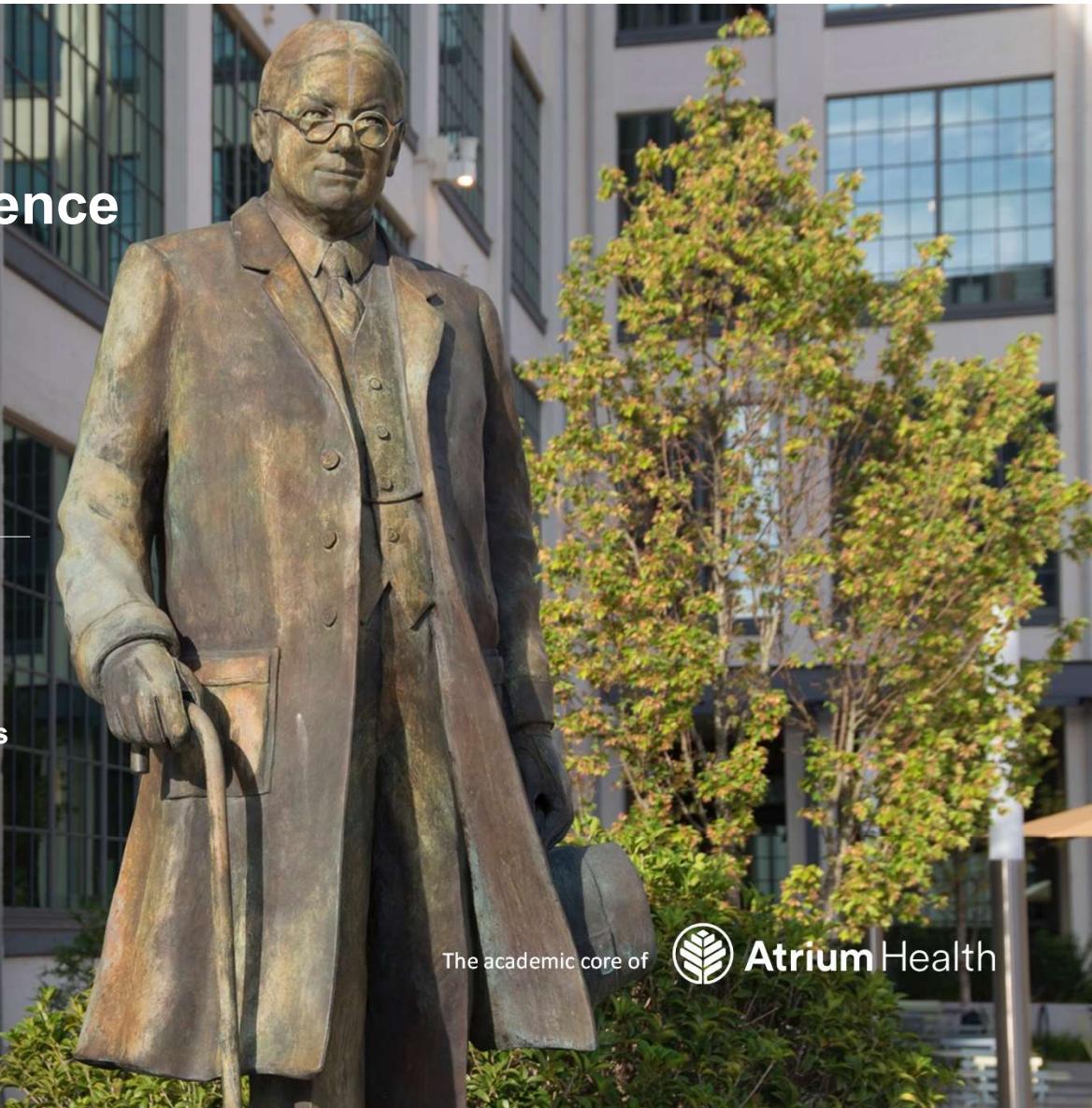
Application of Artificial Intelligence Research in Biomedical Informatics

- Informatics Bootcamp 2025

Da Ma
Assistant Professor
Center for Artificial Intelligence Research
Alzheimer's Disease Research Center
Biomedical Engineering | Internal Medicine | Geriatrics



**Wake Forest University
School of Medicine**



The academic core of

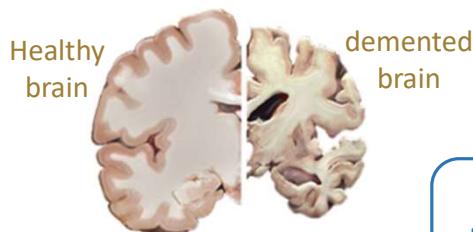


AI application in Biomedical/Health Informatics

- **Health / Biomedical Informatics:**
 - Interdisciplinary field that applies computing, data science, and information technology to improve health care, biomedical research, and public health outcomes.
 - AI-integrated health/biomedical informatics
 - enables the analysis capability for complex medical data (e.g. EHR, medical imaging, genomics/multiomics, sensoring data)
 - enhances disease prediction, personalized treatments, clinical decision-making, and biomedical research by.
- **Example Applications of**
 - **Topic 1:** Early Prediction, Disease Risk Stratification, Biomarker Identification
 - **Topic 2:** Disentangle Disease Heterogeneity
 - **Topic 3:** Biological Aging | Healthy Aging
 - **Topic 4:** Explainable AI for clinical translation
 - **Topic 5:** Bias control, domain adaptation, data harmonization

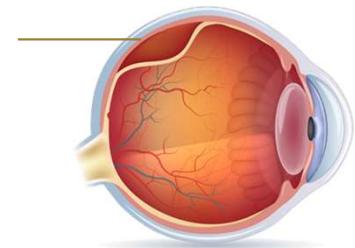


Example of Health/Biomedical Informatics



Neuroimaging informatics

Retinal detachment
fluid build up



AI-integrated
Biomedical Informatics

Precision
medicine

Brain-body Integrated
Health informatics

Genomics informatics

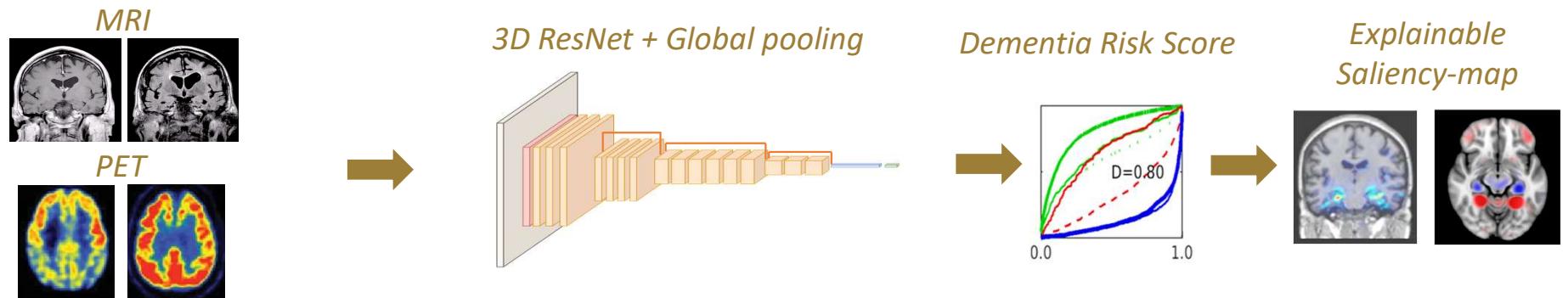


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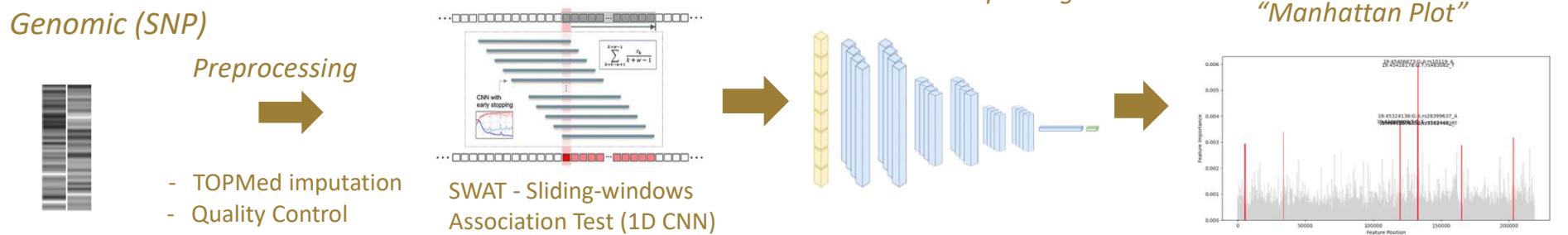
The academic core
of Atrium Health

Topic 1: Early prediction, disease risk stratification, biomarker identification

- “Multi-modal” neuroimaging dementia risk score

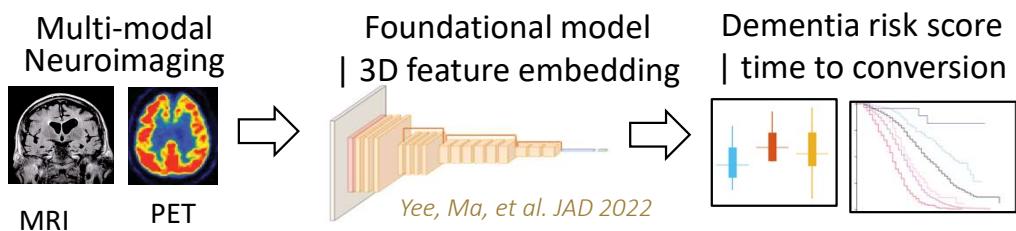


- Deep polygenic risk score

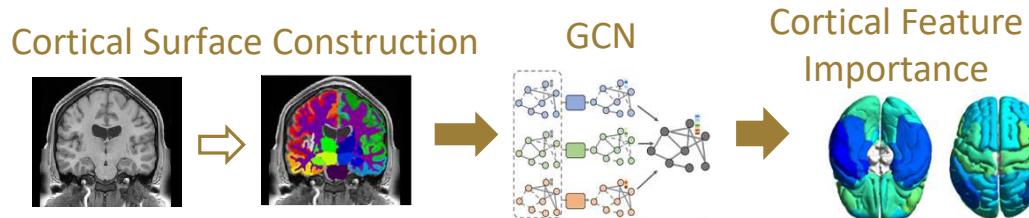


Topic 1: Early prediction, disease risk stratification, biomarker identification

- Multi-modal Neuroimaging dementia risk prediction



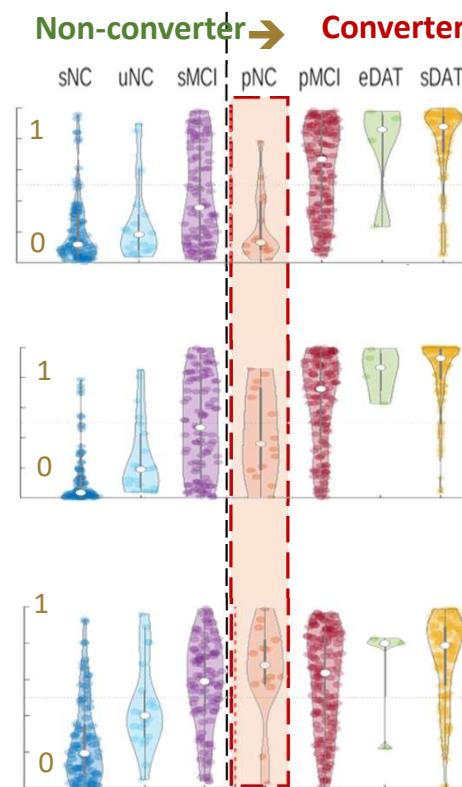
- Cortical-atrophy-based graph convolutional network (GCN)



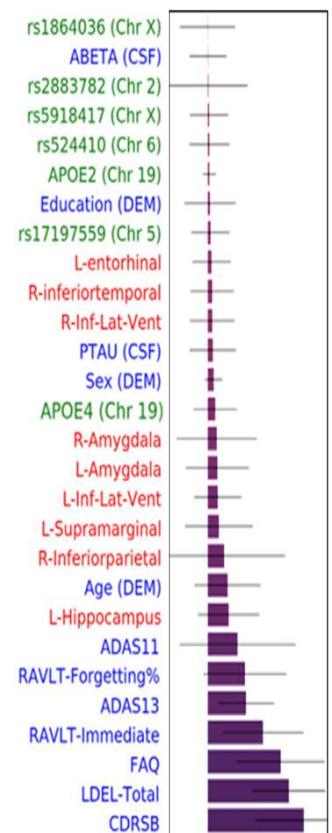
- Neuroimaging genomics dementia risk prediction



- Stratified dementia risk

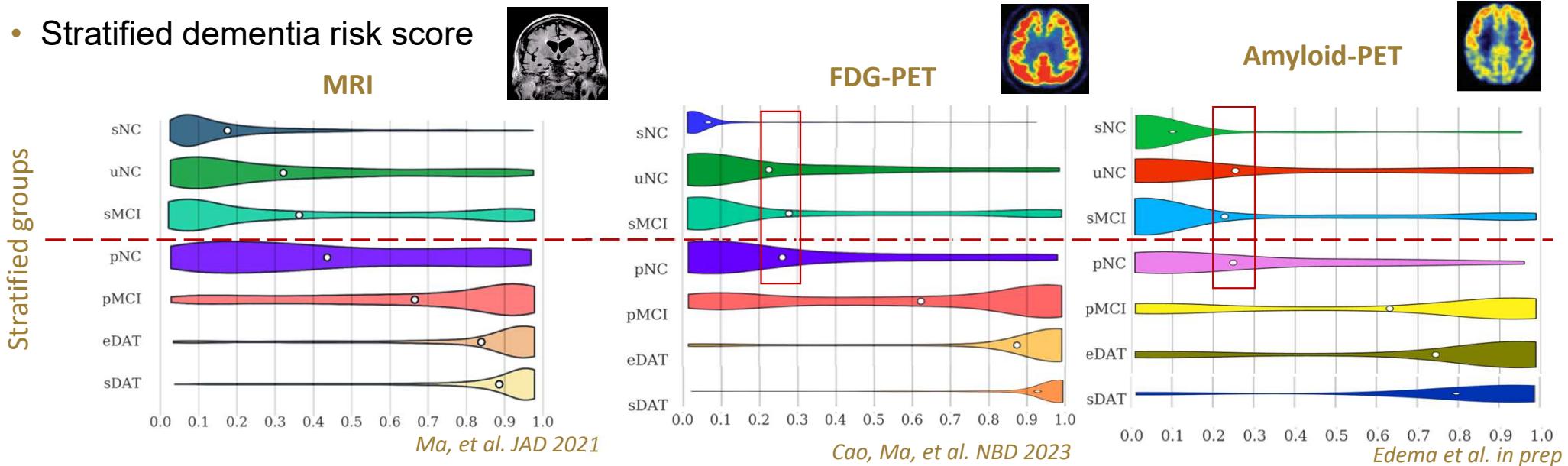


- Feature Importance

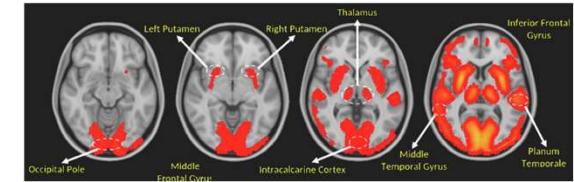
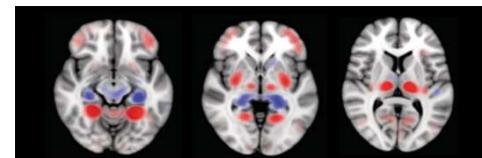
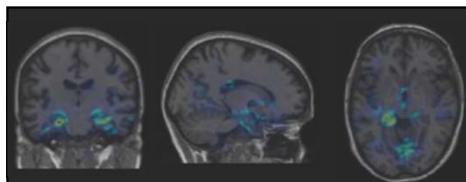


Case 2: Multi-modal Neuroimaging Dementia Risk Stratification

- Stratified dementia risk score

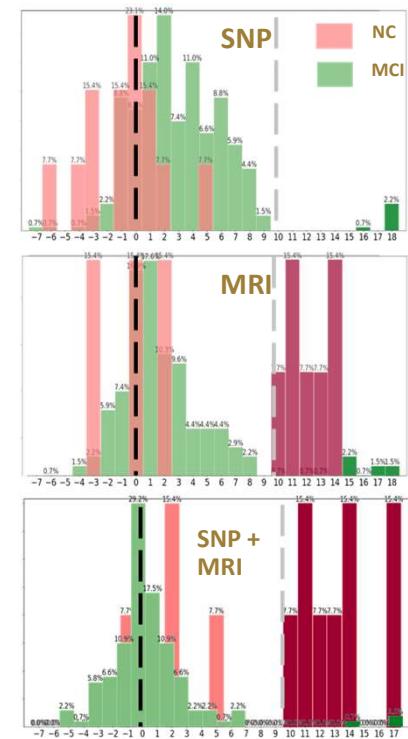
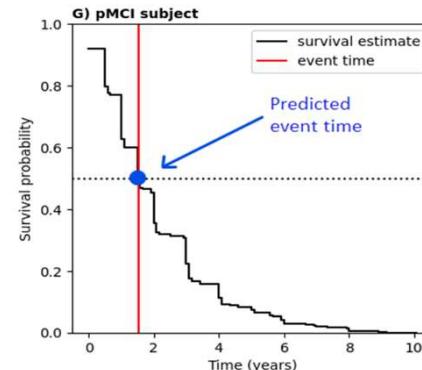
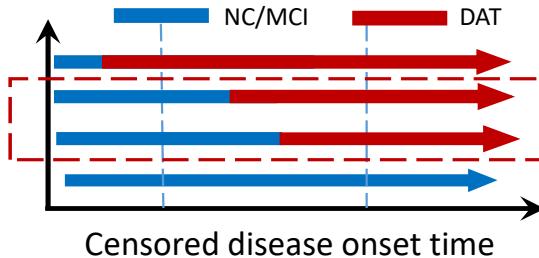
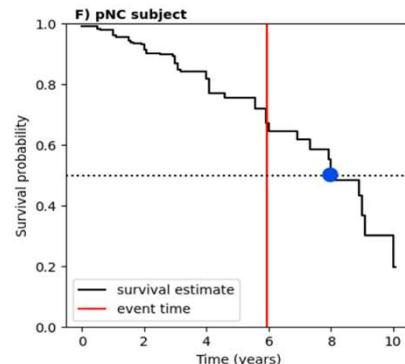
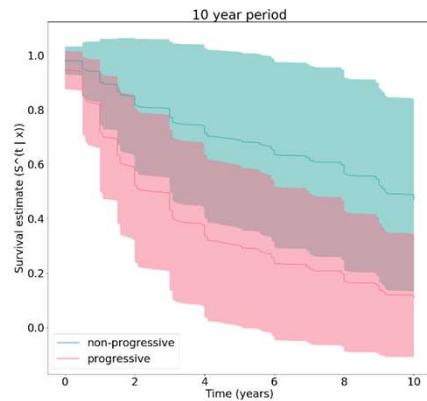


- Clinical explainability – guided-backpropagation



Case 3: Longitudinal disease onset and risk prediction

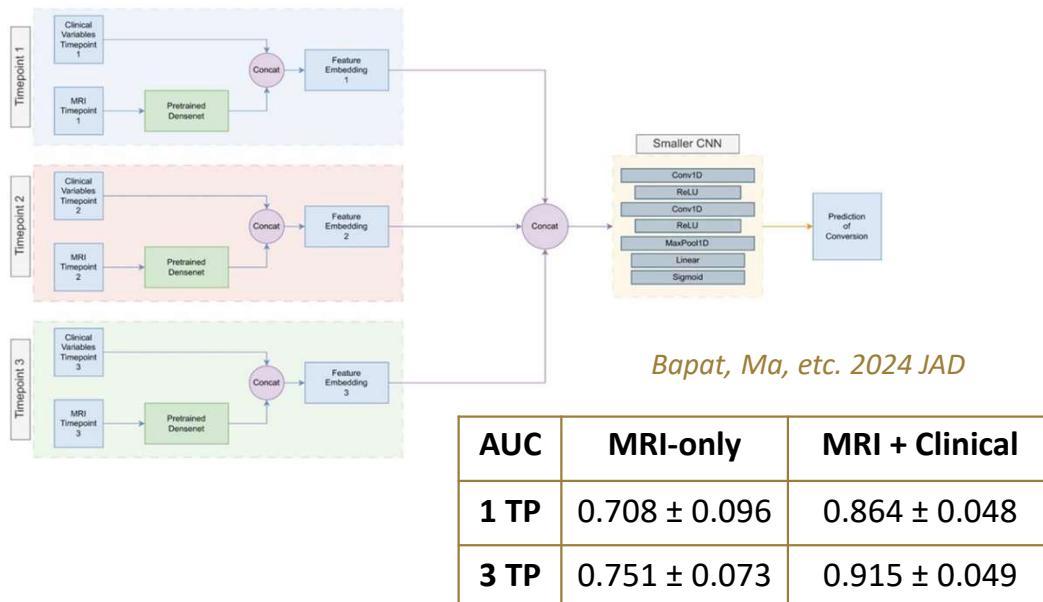
- Predict time-to-disease-onset
- Longitudinal stratification of at-risk population
 - Personalized management
 - Targeded clinical trial recruitment



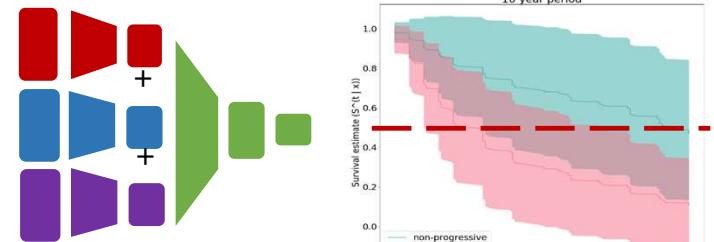
Mirabnahrazam et al.
JAD 2022 | NBA 2023

Case 4: Longitudinal Neuroimaging AD Risk Prediction

- Predict conversion to dementia in 4-years
- Fusion of 3 timepoints neuroimaging data
 - Cascade network
 - Combined with non-imaging feature



- Longitudinal survival analysis
- Fusion of 3-timepoints neuroimaging data

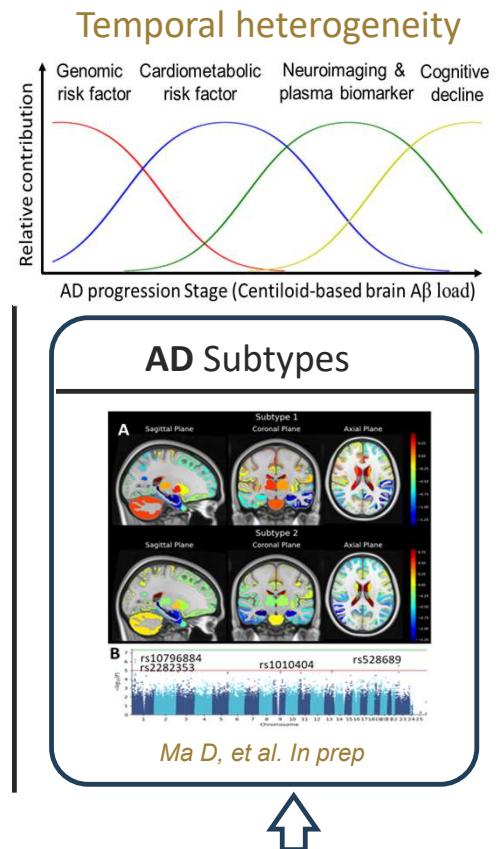
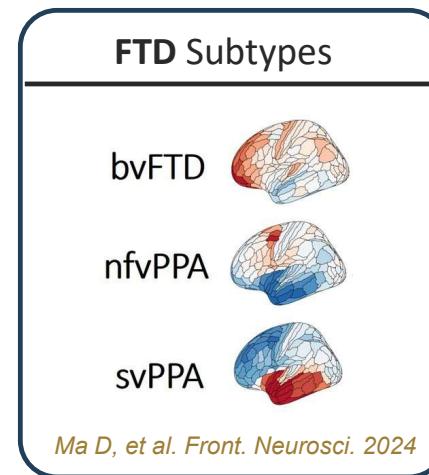
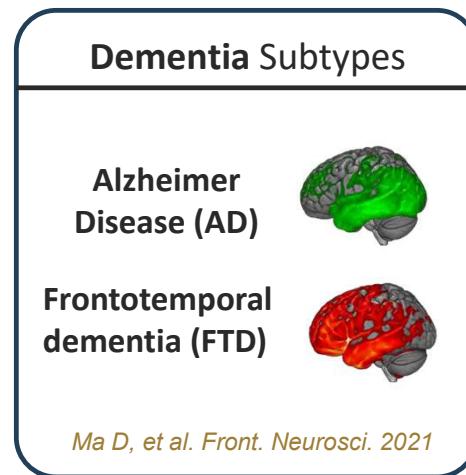
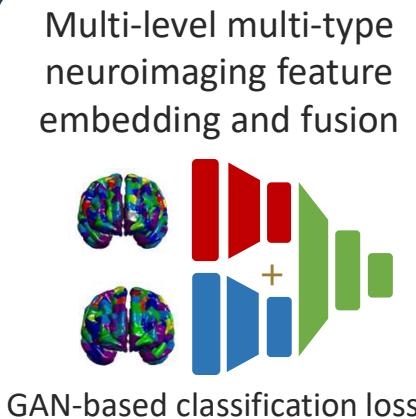


Kyriacou, etc. In prep

C_{idx}	MCI Conversion	AD Conversion
1 TP	0.603	0.756
3 TP	0.875	0.906

Area 2: Disentangle Disease Heterogeneity

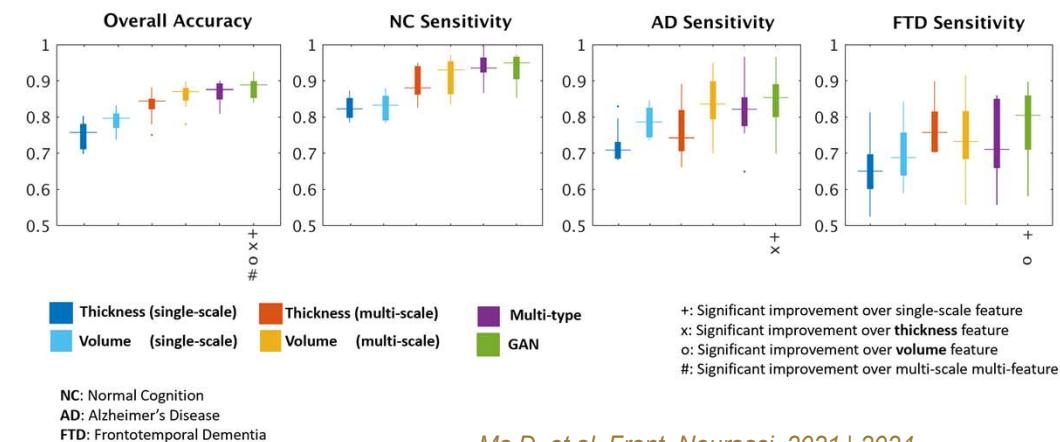
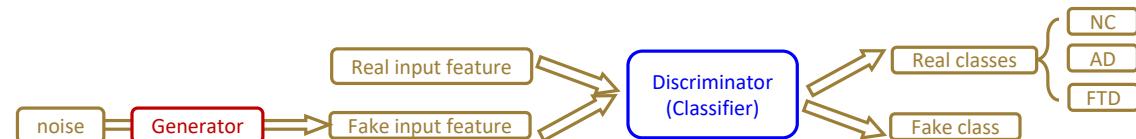
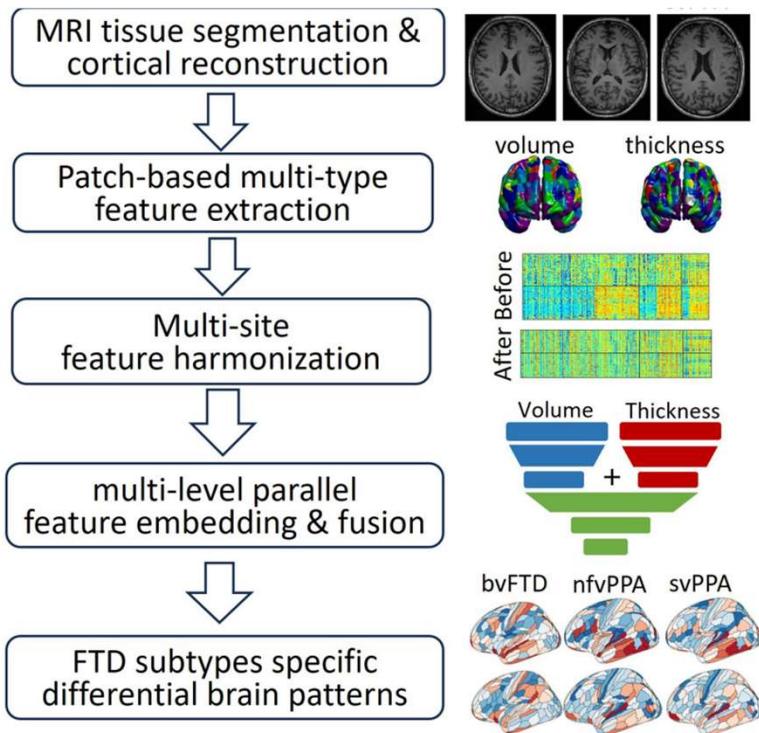
- Neuroimaging-based deep-learning classification for dementia subtyping
- Supervised classification | Unsupervised clustering
- Explainable AI dementia subtype neurodegenerative patterns



Unsupervised learning | Neuroimaging-plasma biomarker | genomics + cardiometabolic risk factor

Area 2: Disentangle Disease Heterogeneity

- Multi-modal Multi-type Generative Adversarial Network (GAN) based dementia subtyping

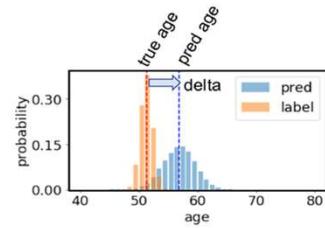
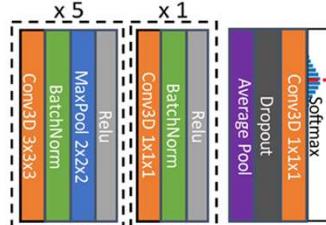


Ma D, et al. *Front. Neurosci.* 2021 | 2024

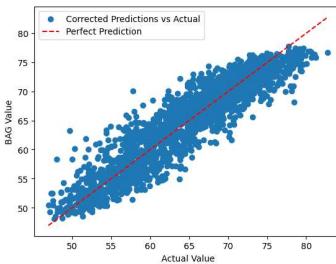
Area 3: Biological Aging | Healthy Aging

- Radiological Brain Aging

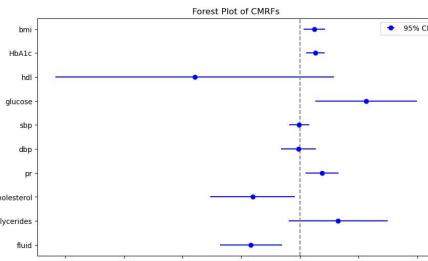
Soft-classification-base age prediction → Brain Age Gap (BAG)



Predicted brain age
v.s.
chronological age



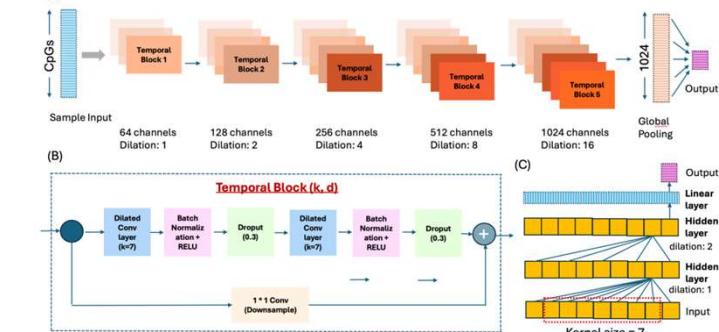
BAG v.s. CMRF
(Cardiometabolic
Risk Factors)



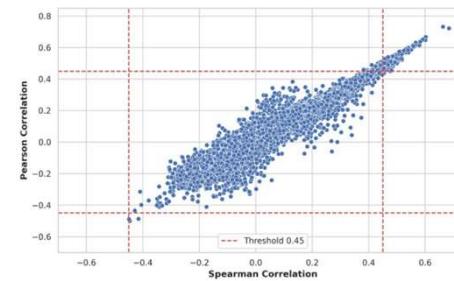
Tavakoli F, Ma D, et al. AAIC 2024

- Epigenomic Aging -- DNA Methylation Clock

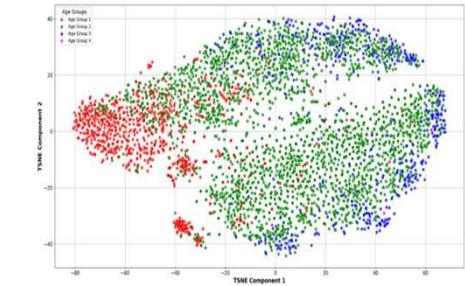
Temporal Convolutional Network (TCN): Temporal + dilation blocks



Biological v.s. chronological age



Age group clustering



Dip SA, Ma D, et al. 2024

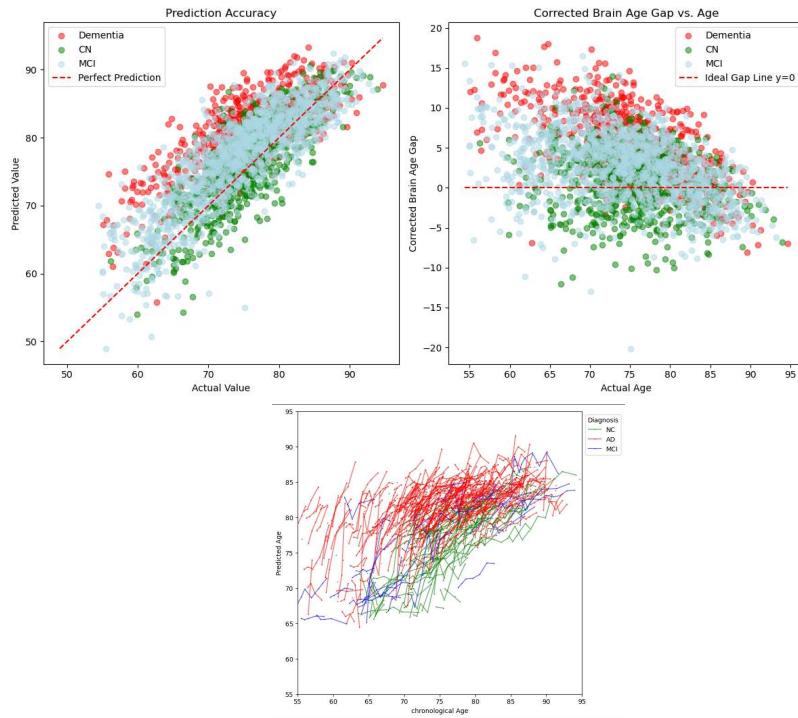


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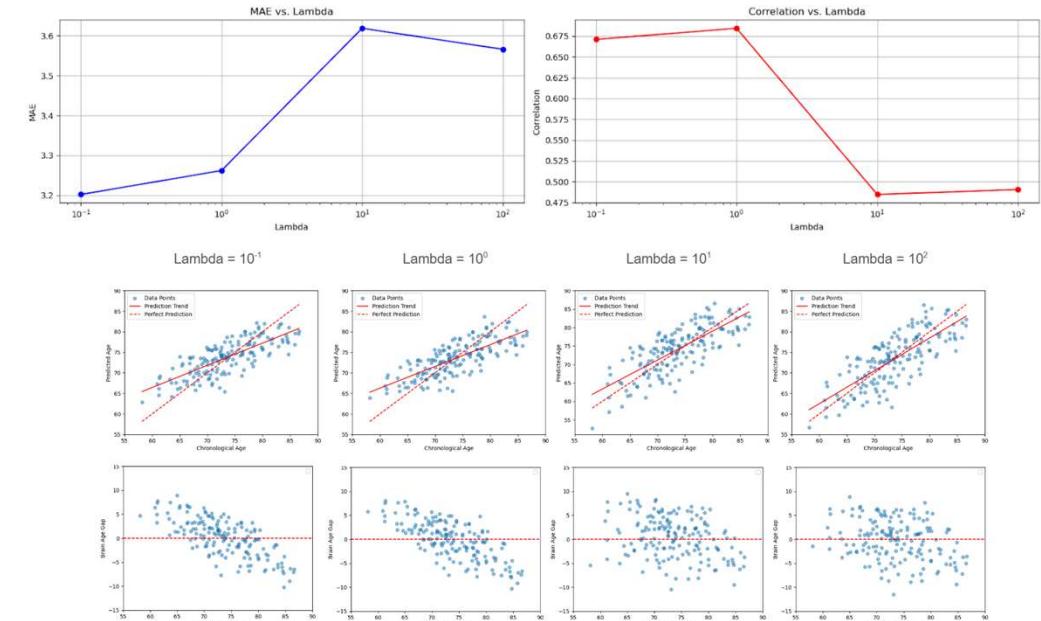
The academic core
of Atrium Health

Area 3: Biological Aging | Bias removal

- Age-dependent Bias in calculating brain aging

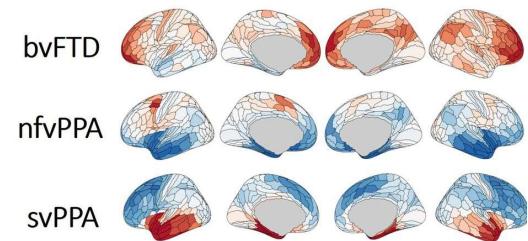
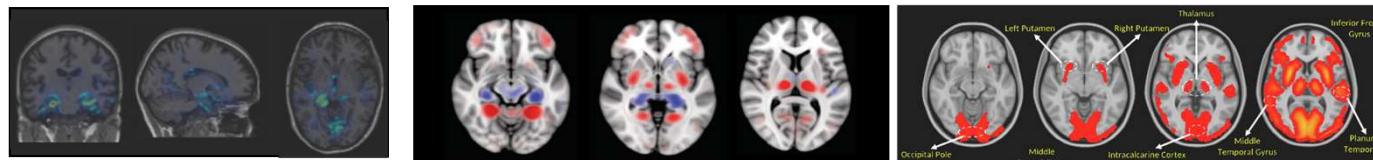


Negative correlation loss penaltitiation

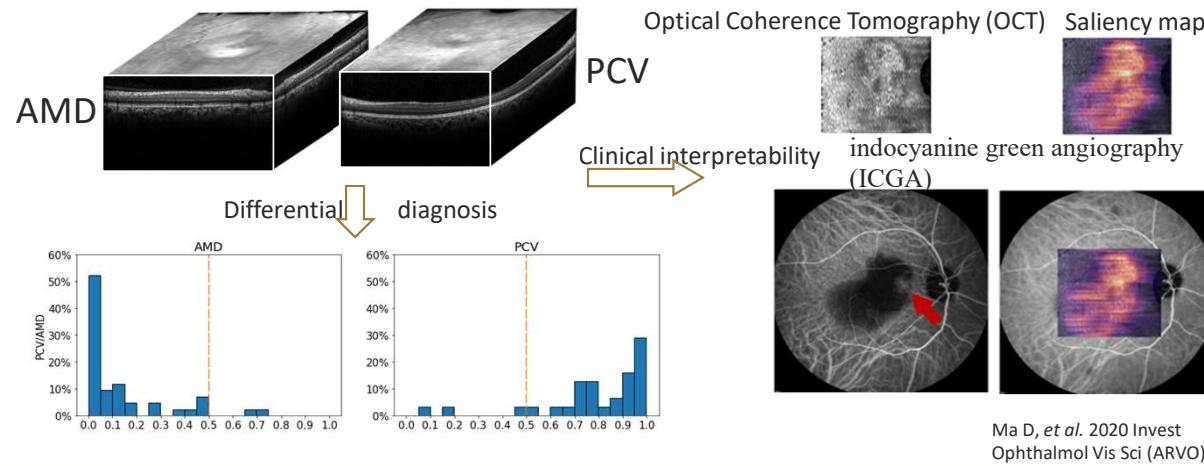


Topic 2: Explainable AI for biomedical informatics

- Explainability for Neuroimaging – guided-backpropagation | Integrated Gradient

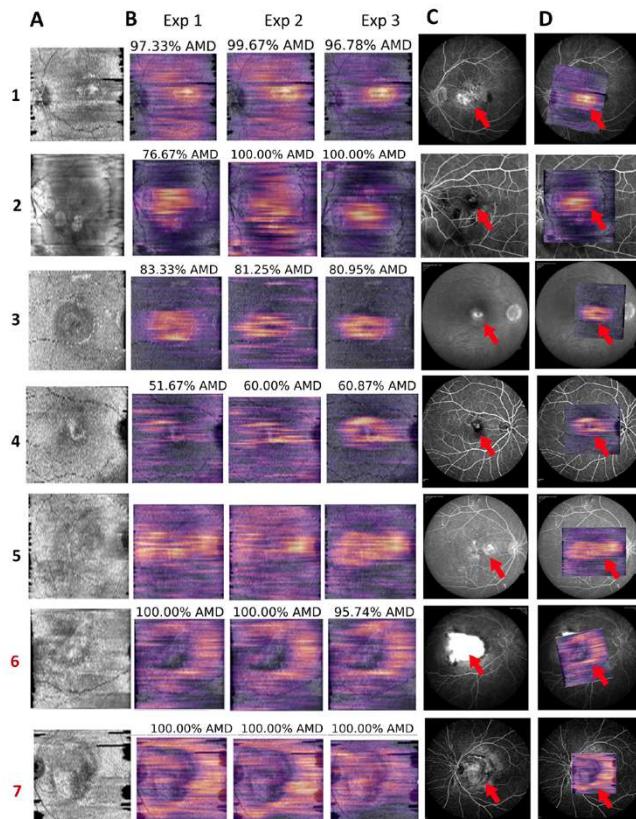


- Explainability for Retinal Imaging – 2.5D patch-wise Gradient-weighted Class Activation Mapping (Grad-CAM)

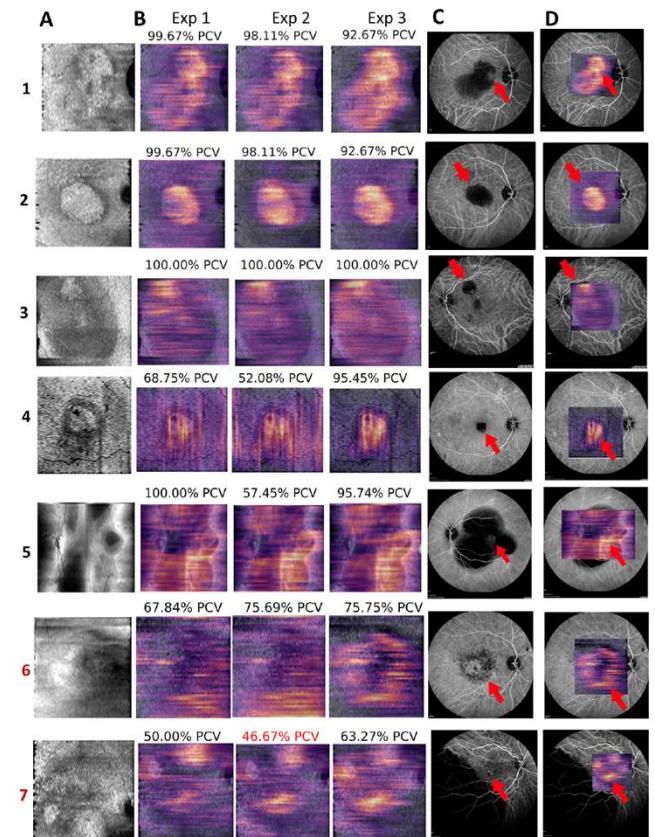


Topic 2 - Clinical Explainable Differential Diagnosis

AMD



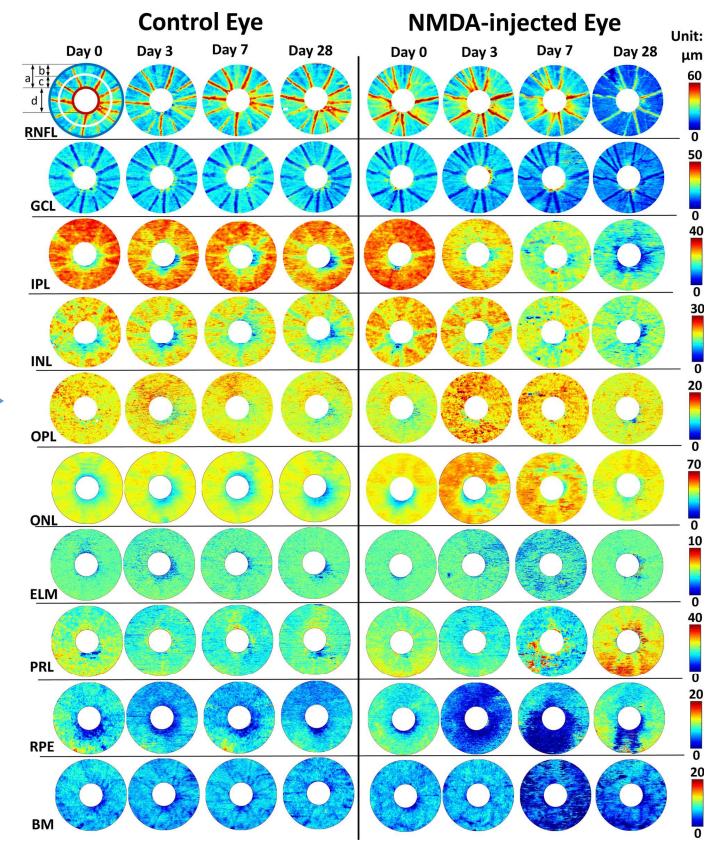
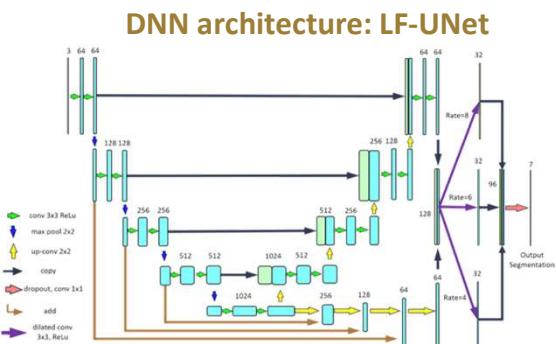
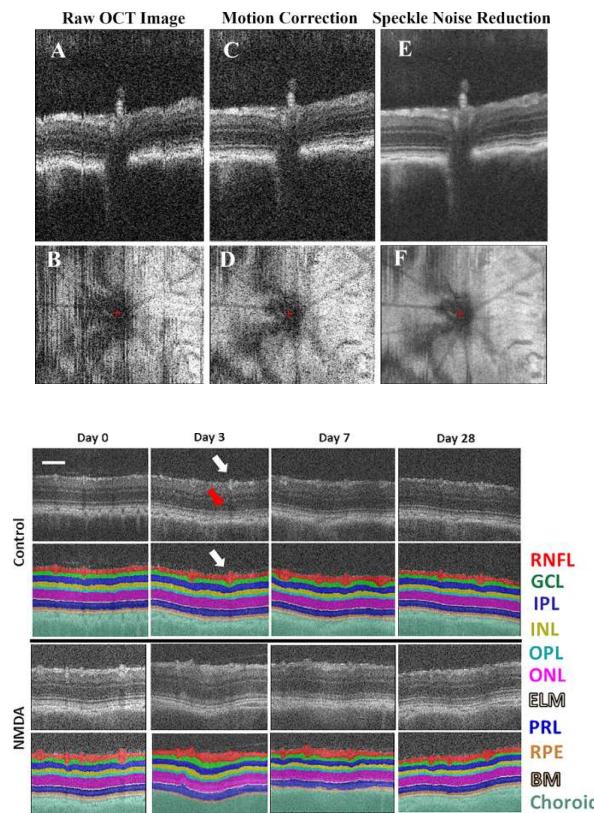
PCV



Ma D, et al. 2020 Invest Ophthalmol Vis Sci (ARVO)

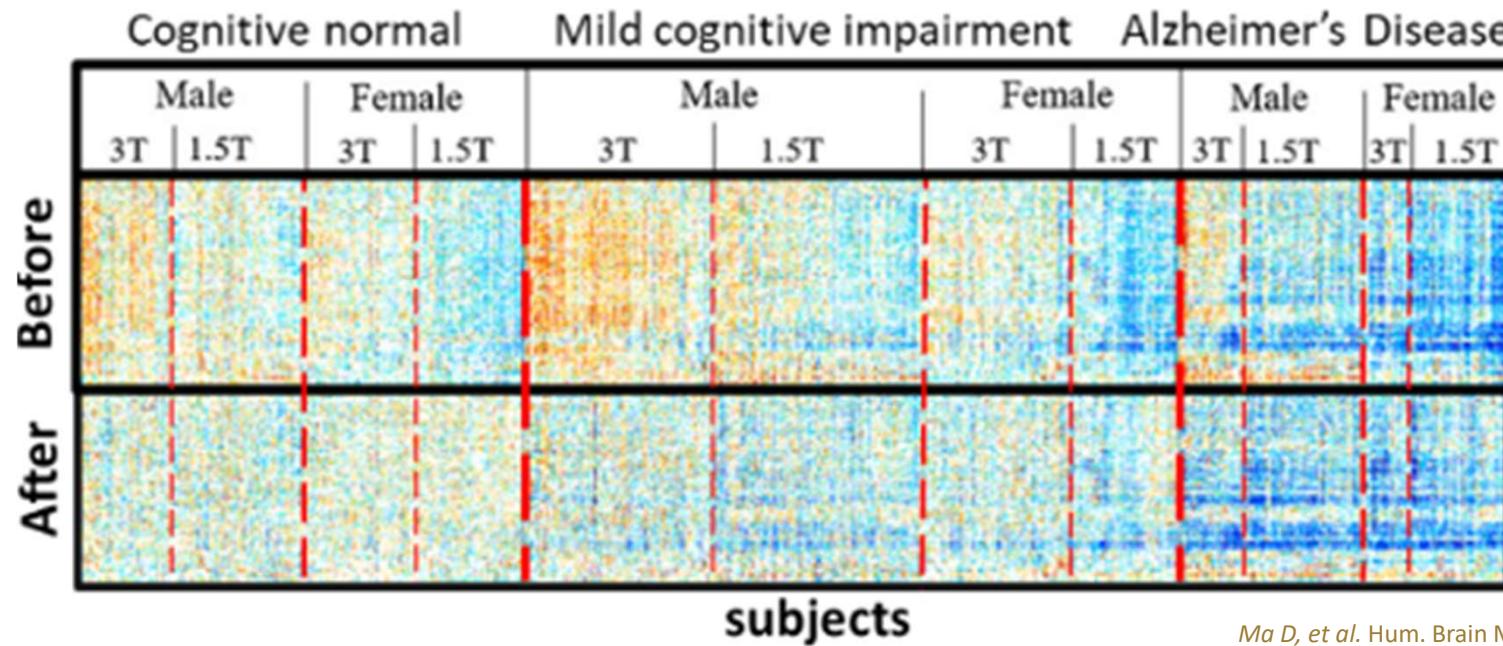


Topic 4: Explainable AI for biomedical informatics



Topic 5: Bias control, domain adaptation, data harmonization

- Effective feature harmonization is crucial for control population bias and ensure fairness AI

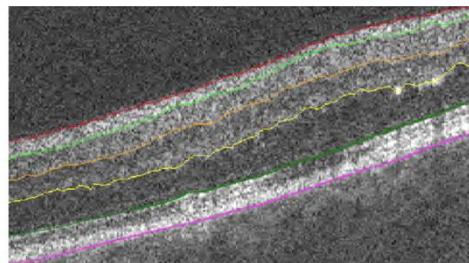


Ma D, et al. Hum. Brain Mapp. 2019

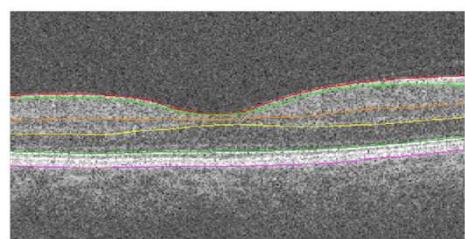


Topic 5: Bias control, domain adaptation, data harmonization

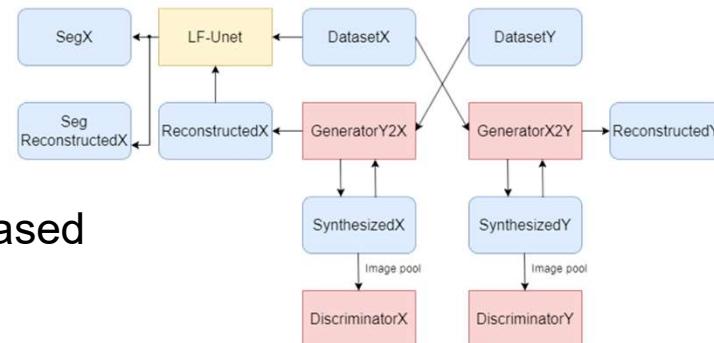
- Case 2: AI-based “Domain adaptation” to control out-of-distribution population bias



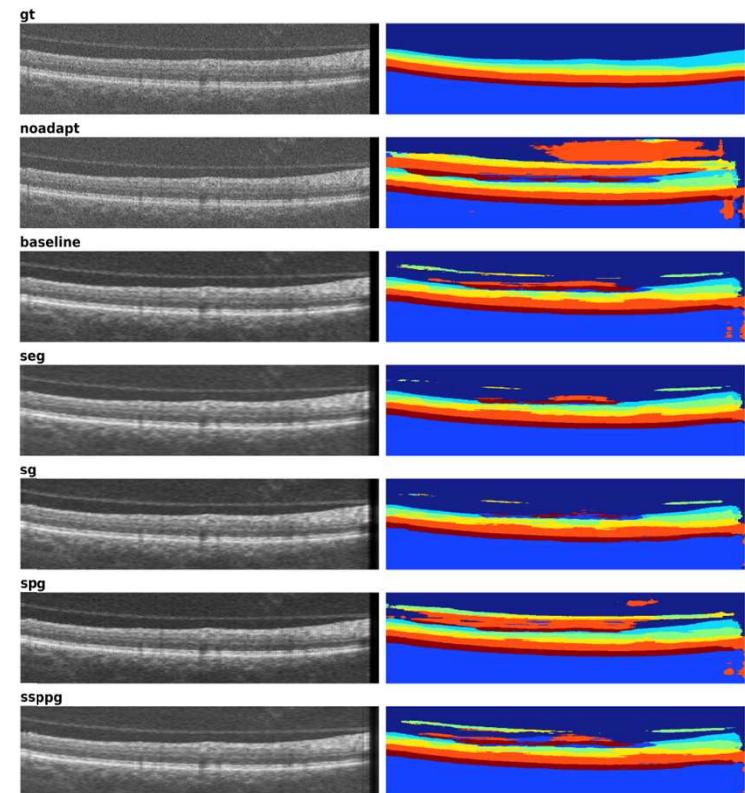
(a) Example of the segmentation of 5 inner retinal layers for Zeiss OCT Bscan



(b) Example of the segmentation of 5 inner retinal layers for Topcon OCT Bscan



- Generative-AI (GAN)-based “domain” adaptation



Chen S, Ma D, et al. Comput. Biol. Med. 2023

Move on to hands-on tutorial

