



**From CT to
CNNs:**

**Deep Learning for Neuroimaging-
Based Diagnosis of Alzheimer's and
Dementia**

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O Analytics for every brain scan

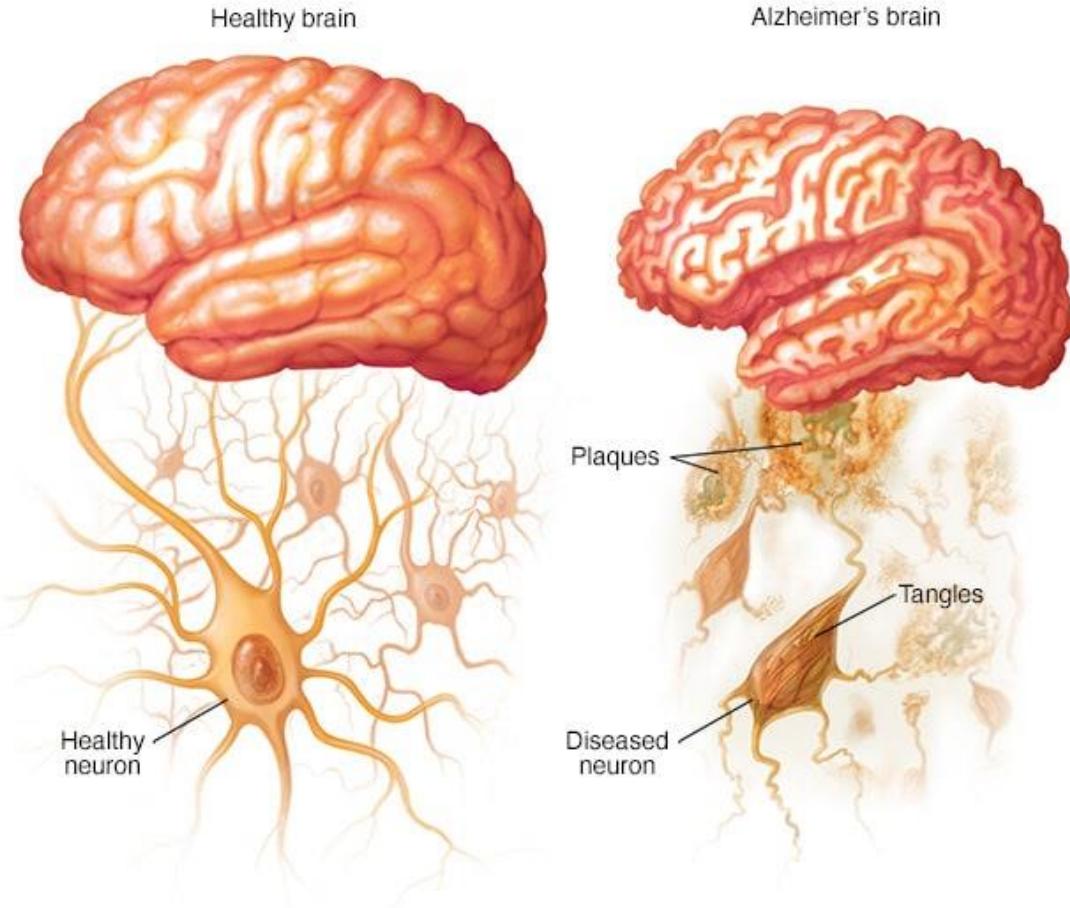
Precision Brain Health Solutions

Enabling data-driven diagnosis, patient insights & therapeutic development for brain diseases & disorders across the lifespan.

 GET STARTED



1. Alzheimer's disease
2. Diagnostic approaches for AD
3. Neuroimaging for AD diagnosis
4. Why use deep learning for neuroimaging?
5. Deep learning (nnUNET and MedNeXT)
6. Validation and inference on dementia dataset
7. RealAD study
8. Unified multimodal approach for early AD detection for therapy



What is AD?

A progressive neurological disorder and the leading cause of dementia ($\approx 2/3$ of cases)

Global Impact?

55+ million people live with dementia today.
Projected to reach **152 million by 2050**.
71% of future cases will be in **developing countries**.

Regional Stats

Europe (2019): **188 per 100,000** incidence rate.
Sweden: **160,000** with dementia; $\sim 2/3$ have AD

Economic Burden

\$818B in 2015 → Over **\$1 trillion in 2018**

Urgent Needs

Prevention

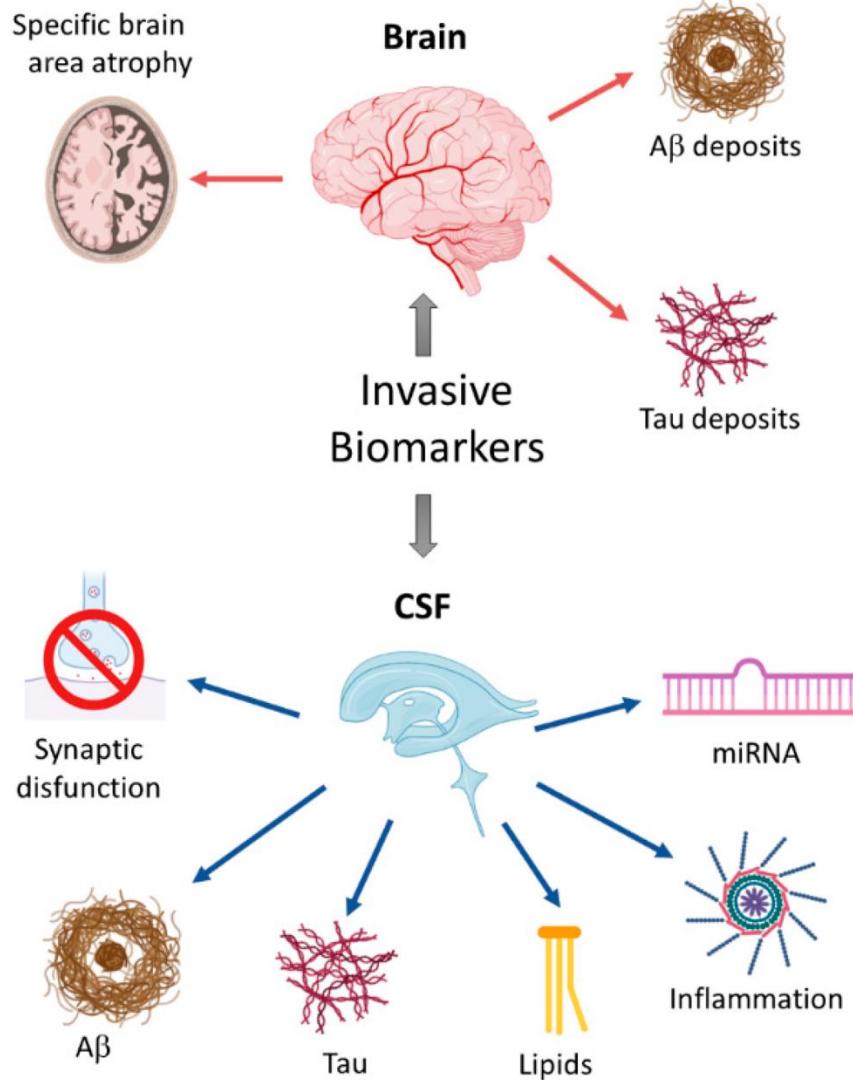
Faster diagnosis

Improved treatments

What unique test once used peanut butter to assess Alzheimer's disease?

- A) Taste test
- B) Smell test
- C) Texture test
- D) Vision test

Diagnostic Approaches for Alzheimer's Disease



1. Plasma and CSF Biomarkers

Plasma biomarkers: Blood-based tests detecting amyloid- β 42/40 ratio, phosphorylated tau (p-tau), and neurofilament light (NfL). Promising for non-invasive early detection.

CSF biomarkers: Lumbar puncture used to measure:

- ↓ Amyloid- β 42
- ↑ Total tau (t-tau)
- ↑ Phosphorylated tau (p-tau)

High sensitivity and specificity for Alzheimer's pathology

2. Cognitive Tests

Used to assess memory, attention, language, and executive function.

Common tools:

- **Mini-Mental State Examination (MMSE)**
- **Montreal Cognitive Assessment (MoCA)**
- **Clock Drawing Test**

Help monitor disease progression and support diagnosis.

Diagnostic Approaches for Alzheimer's Disease

3. Genetic Factors

Chromosome 21: Carries the APP gene (amyloid precursor protein); mutations or trisomy (as in Down syndrome) increase Alzheimer's risk.

APOE ε4 allele: The most significant genetic risk factor for late-onset Alzheimer's.

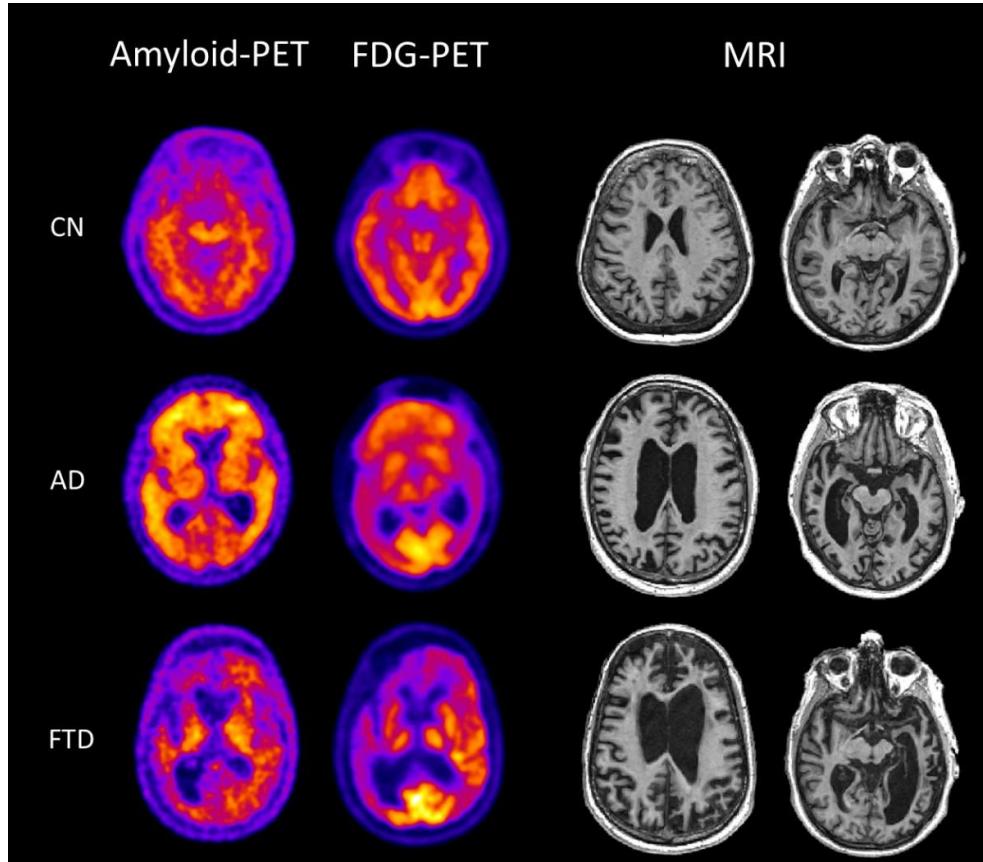
4. Neuroimaging

MRI: Detects brain atrophy, especially in the hippocampus and medial temporal lobe.

PET scans:

- **FDG-PET:** Shows reduced glucose metabolism in affected brain regions.
- **Amyloid PET:** Visualizes amyloid plaques.
- **Tau PET:** Tracks tau protein accumulation (neurofibrillary tangles).

Imaging is crucial for differential diagnosis and staging.



Which genetic mutation, discovered in Swedish families, is linked to early-onset Alzheimer's?

- A) APOE ε4
- B) Swedish mutation
- C) BRCA1
- D) Huntington's gene

BRAIN IMAGING



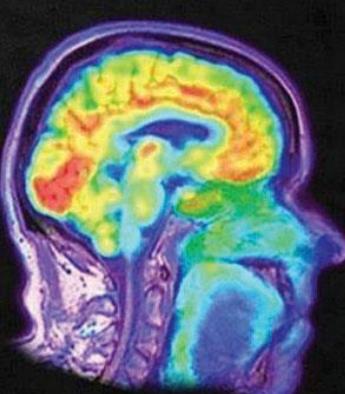
X-RAY



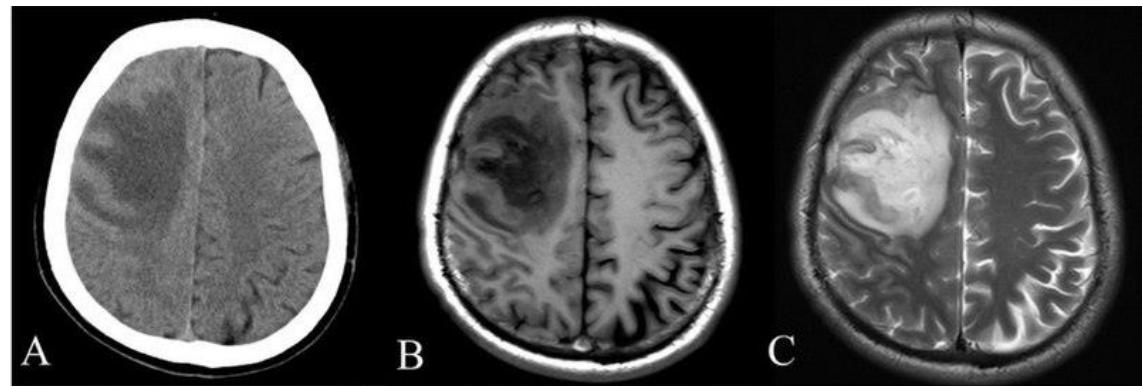
MRI



MRA



PET SCAN



To function correctly, MRI machines must be kept at what temperature?

- A) Room temperature
- B) 100°C
- C) 0 Kelvin
- D) 37°C

Why use Deep Learning for Neuroimaging?

1. Automated Feature Extraction

Learn complex patterns in brain scans (e.g., subtle atrophy, plaque distribution) without manual input

2. High Accuracy

Classify Alzheimer's stages (e.g., normal, MCI, AD) using CT, MRI or PET data

3. Early Detection

Identify disease-specific biomarkers and brain changes before clinical symptoms appear, improving early intervention

4. Scalability

Efficiently processes large volumes of imaging data, enabling population-scale screening and longitudinal analysis

5. Multimodal Integration

Combines multiple imaging types (MRI, PET) and even non-imaging data (e.g., genetics, CSF biomarkers) for improved diagnostic accuracy.

Datapool (relevant to segmentation tasks)

H70 Birth cohort

- 916 CT scans
- 744 paired MRI scans
- MRI Segmentations
 - SPM
 - Freesurfer
 - FSL
 - MAPER
 - Sythseg

Singapore Memory Clinic

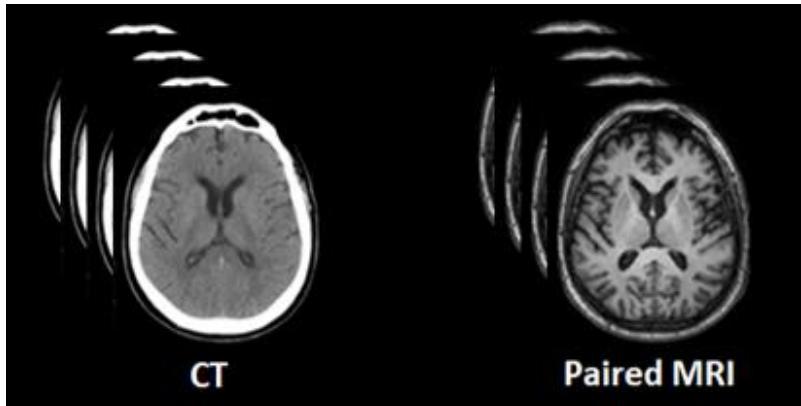
- 204 CT scans
- 244 MRI scans
- MRI Segmentations
 - SPM

Uppsala iNPH patients

- 62 CT scans
- 62 manual VCSF labels

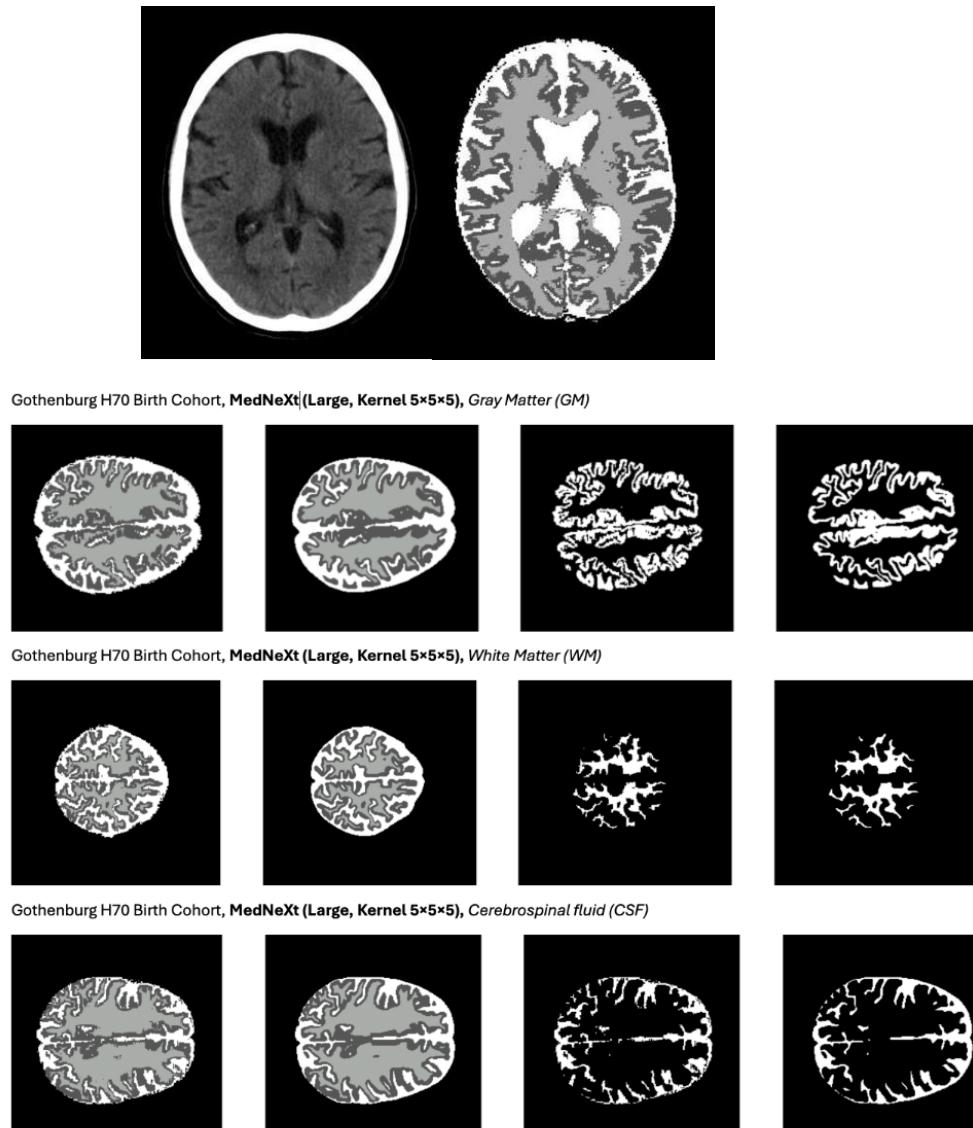
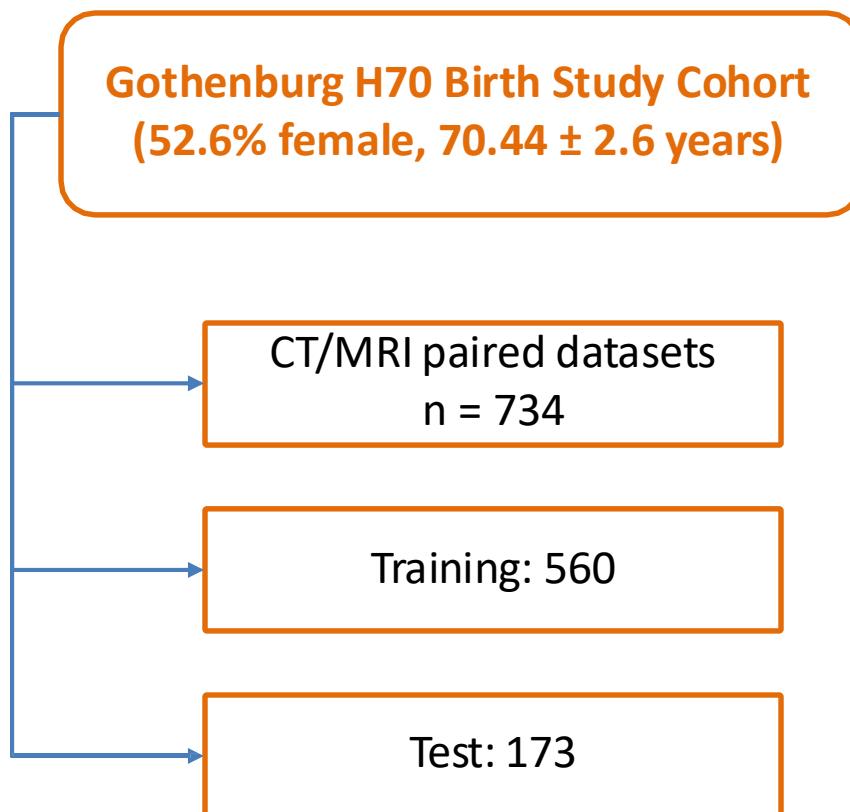
Constraints

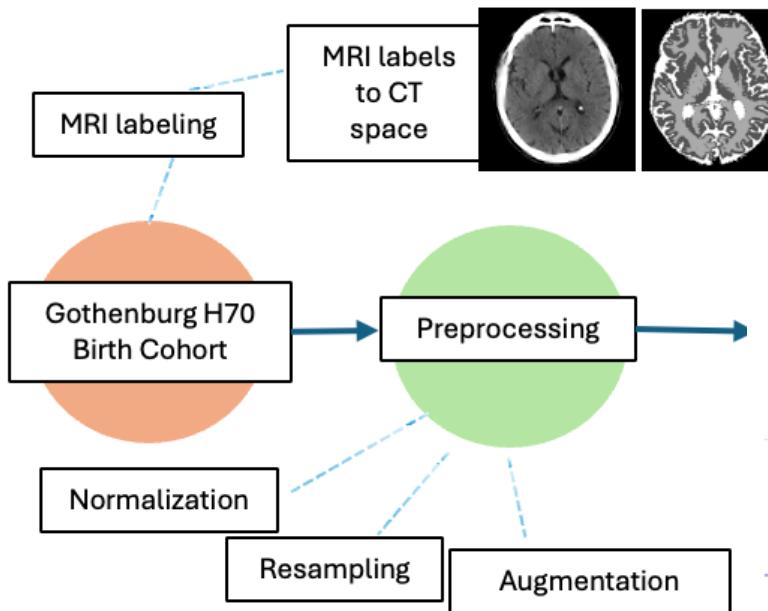
- Spatial resolution (Risk)
 - CT scans have a thickness of 5mm (512x512x30), and MRI scans have a thickness of 1mm (256x256x256)

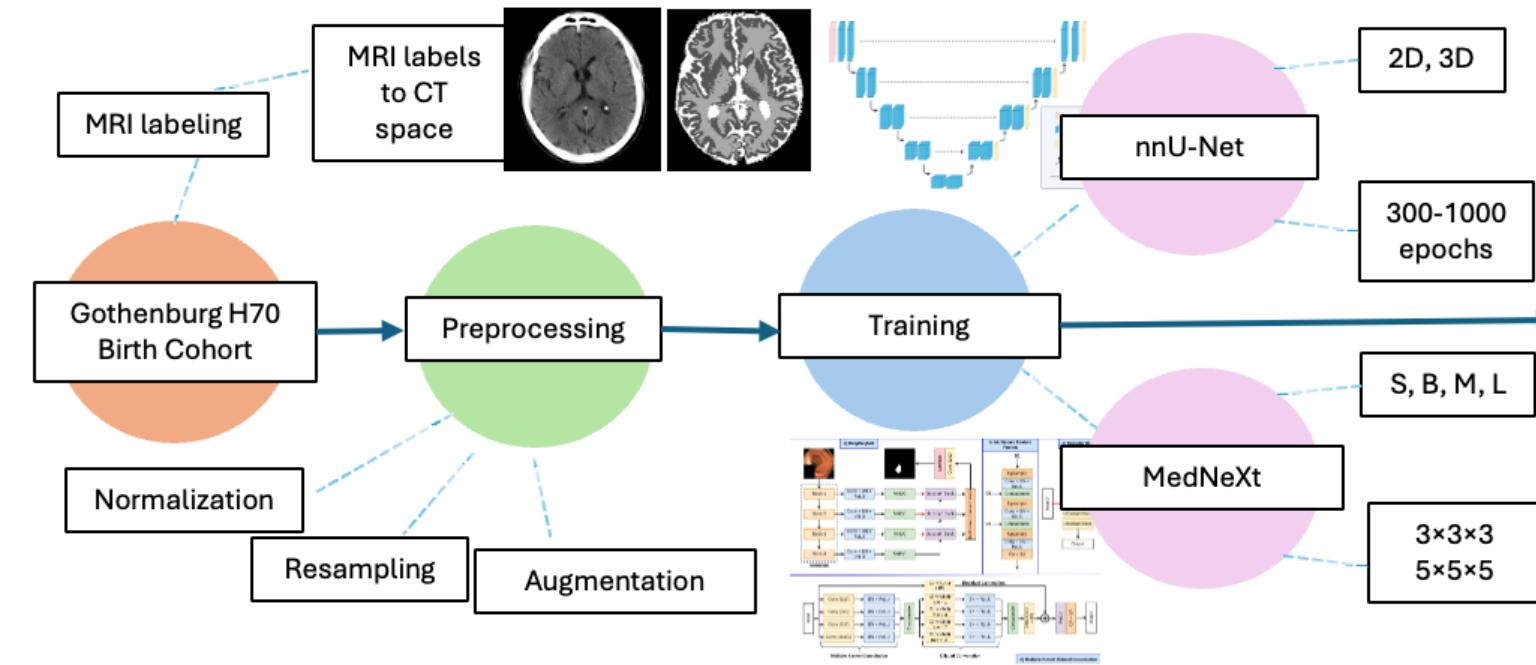


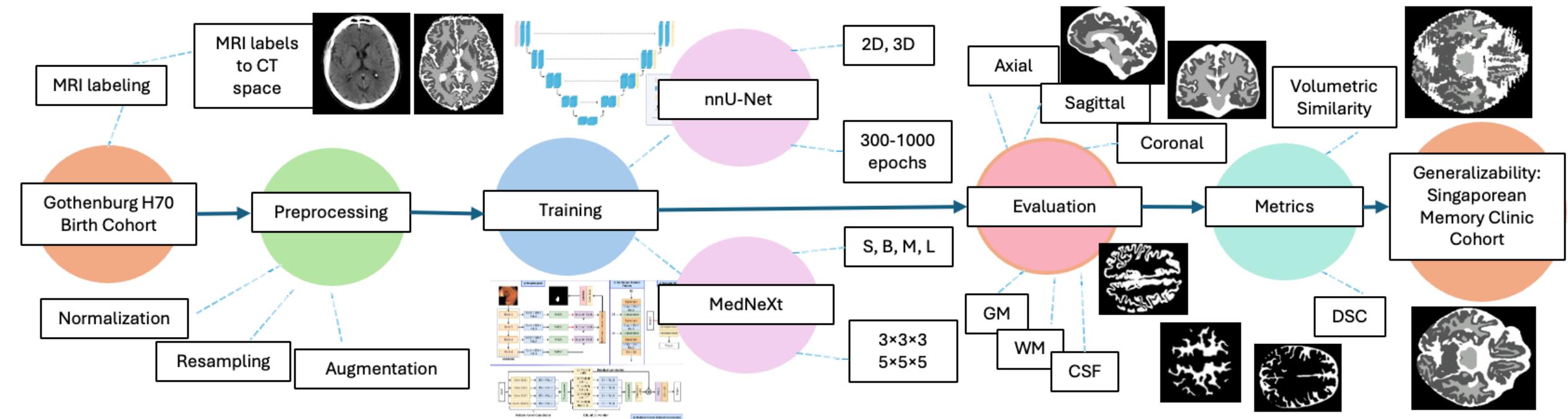
- Bone details and contrast resolution
- Generator functions used in MRI cannot be used in CT

Exploring nnU-Netv2 and MedNeXt in CT brain segmentation

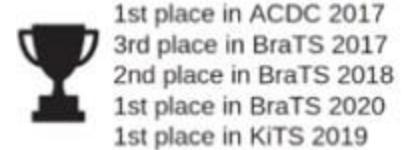








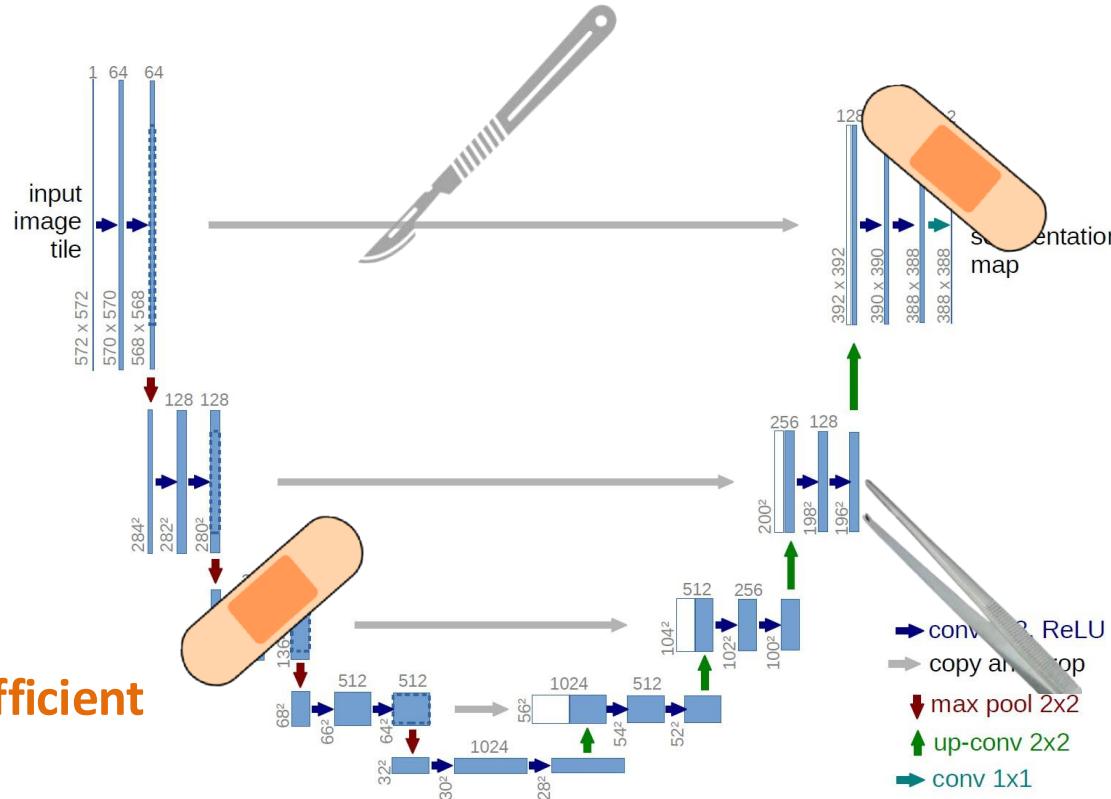
U-Net (Ronneberger et.al, 2015)



Encoder-Decoder
architecture

Skip connections

Versatile and efficient

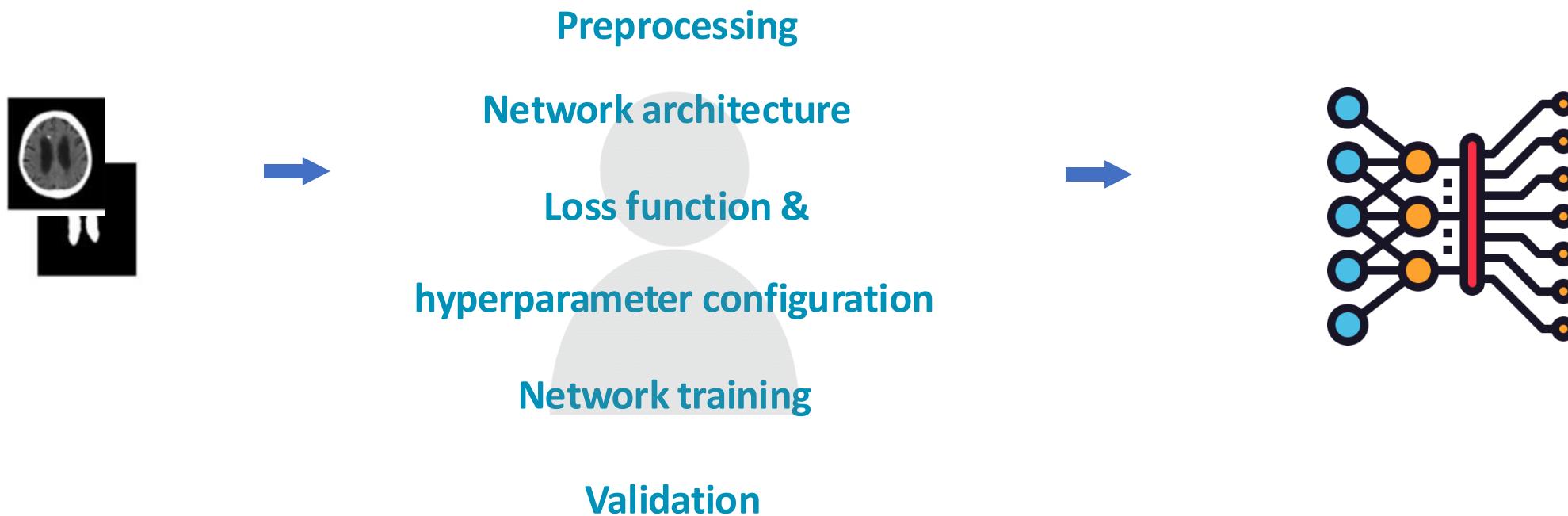


Standard specialised
layers

Fewer dependencies &
Compatibility

Modularity

Training a model from scratch



nnU-Net



nnU-Net: a self-configuring method for deep learning-based biomedical image segmentation

Fabian Isensee^{1,2,6}, Paul F. Jaeger^{1,6}, Simon A. A. Kohl^{1,3}, Jens Petersen^{1,4} and Klaus H. Maier-Hein^{1,5✉}

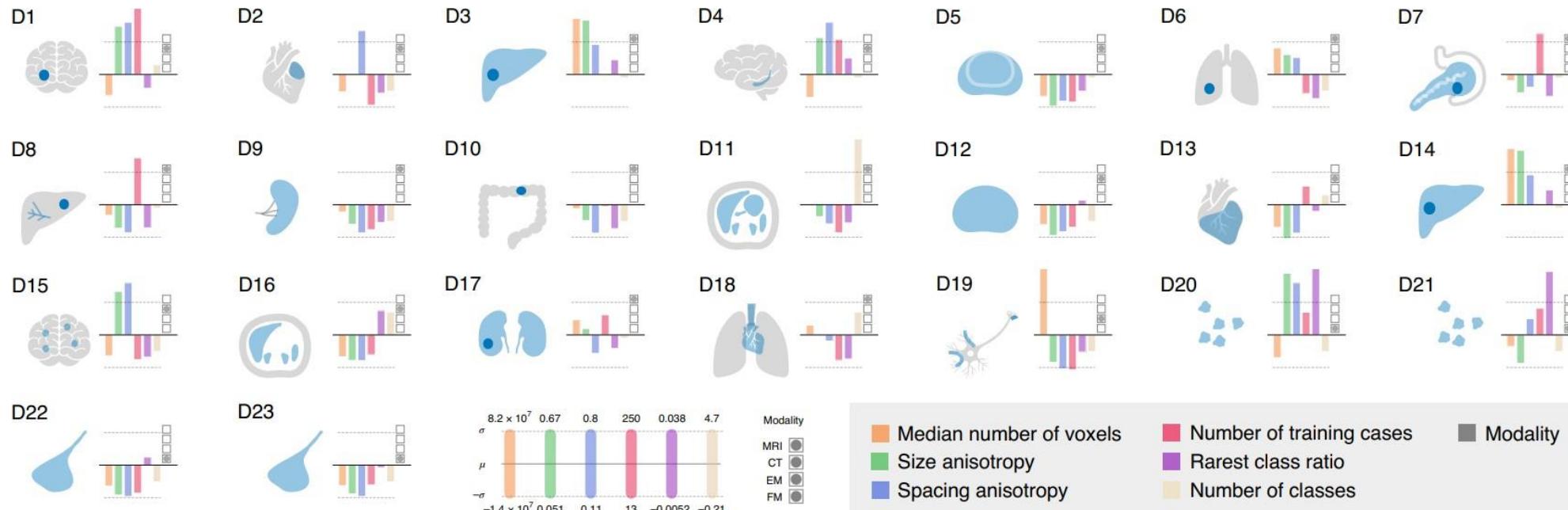
Biomedical imaging is a driver of scientific discovery and a core component of medical care and is being stimulated by the field of deep learning. While semantic segmentation algorithms enable image analysis and quantification in many applications, the design of respective specialized solutions is non-trivial and highly dependent on dataset properties and hardware conditions. We developed nnU-Net, a deep learning-based segmentation method that automatically configures itself, including preprocessing, network architecture, training and post-processing for any new task. The key design choices in this process are modeled as a set of fixed parameters, interdependent rules and empirical decisions. Without manual intervention, nnU-Net surpasses most existing approaches, including highly specialized solutions on 23 public datasets used in international biomedical segmentation competitions. We make nnU-Net publicly available as an out-of-the-box tool, rendering state-of-the-art segmentation accessible to a broad audience by requiring neither expert knowledge nor computing resources beyond standard network training.

- ✓ Holistic configuration of the entire pipeline
- ✓ Fast execution; standard deep learning hardware
- ✓ Designed for biomedical datasets

What does the 'nn' in nnU-Net stand for?

- A) Neural Network
- B) No New
- C) Nonlinear Node
- D) Next-Generation

nnU-Net: dataset fingerprint



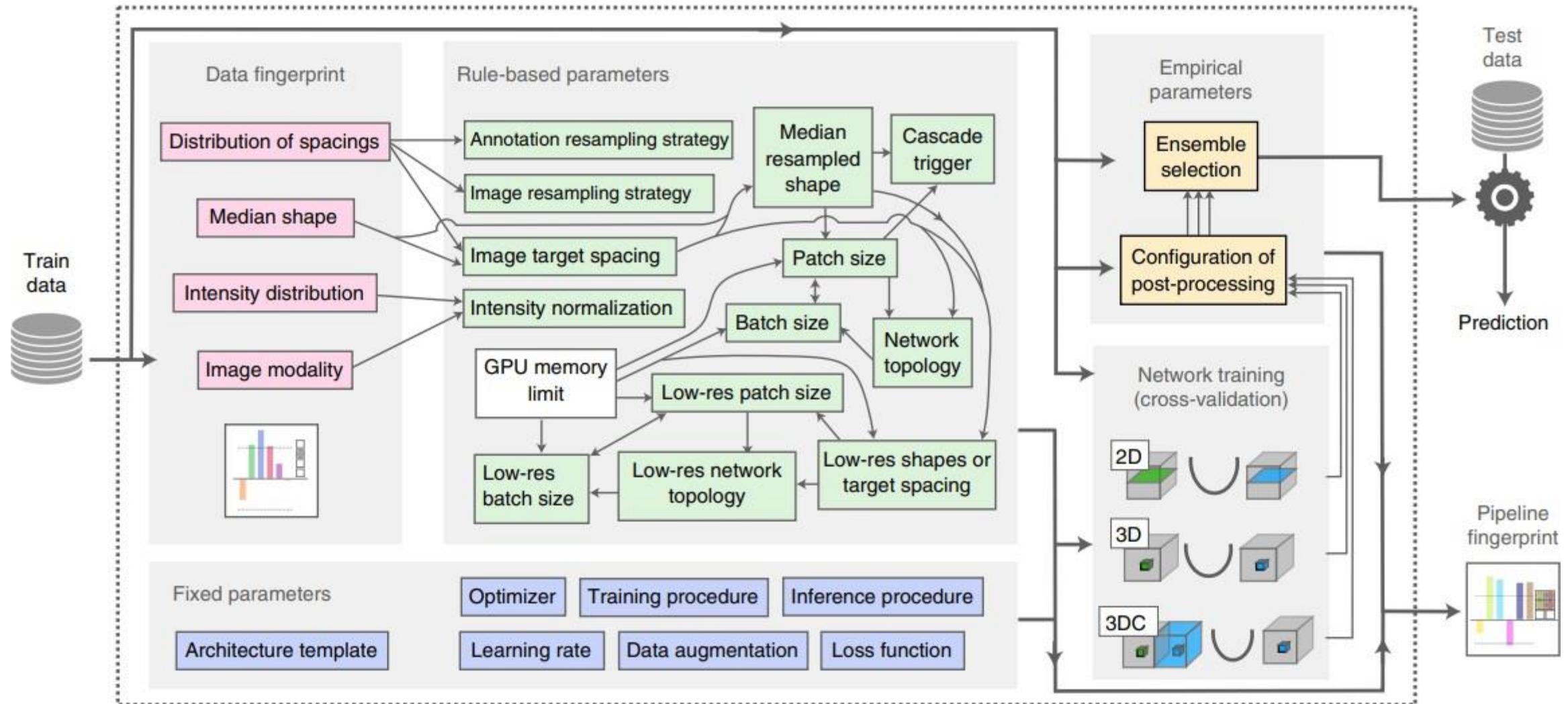
D1 MSD, brain tumor (edema, necrosis, enhancing tumor)
D2 MSD, heart (left atrium)
D3 MSD, liver (liver, liver tumor)
D4 MSD, hippocampus (anterior and posterior)
D5 MSD, prostate (peripheral zone, transition zone)
D6 MSD, lung (lung nodules)
D7 MSD, pancreas (pancreas, pancreatic tumor)
D8 MSD, hepatic vessel (hepatic vessels, liver tumors)

D9 MSD, spleen (spleen)
D10 MSD, colon (colon cancer)
D11 BCV-Abdomen (13 abdominal organs)
D12 PROMISE12 (prostate)
D13 ACDC (left and right ventricle, myocardium)
D14 LiTS (liver, liver tumor)
D15 MSLes (MS lesions)
D16 CHAOS (liver, spleen, left and right kidneys)

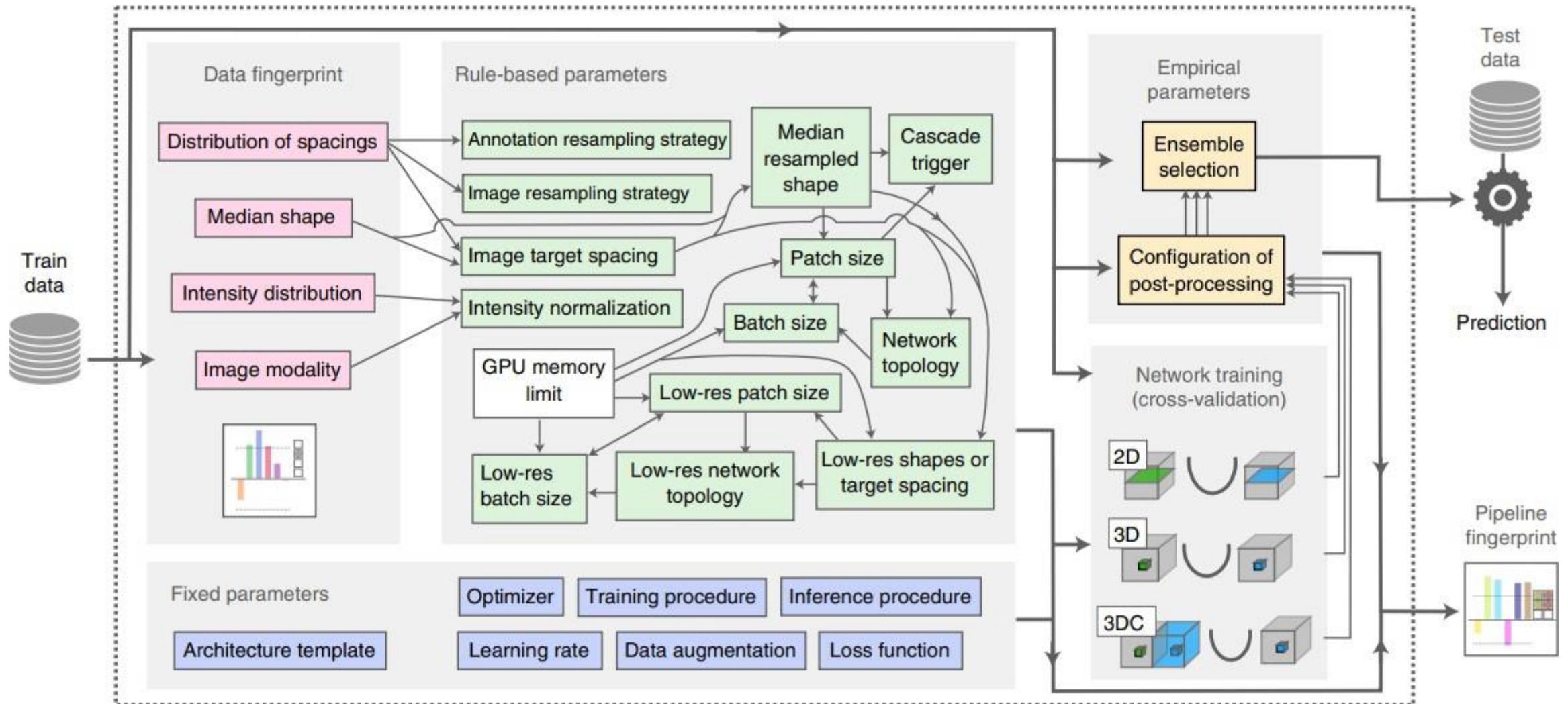
D17 KiTS (kidneys, kidney tumor)
D18 SegTHOR (heart, aorta, esophagus, trachea)
D19 CREMI (synaptic cleft)
D20 CTC - Fluo-N2DH-SIM+ (HL60 nuclei)
D21 CTC - Fluo-N3DH-SIM+ (HL60 nuclei)
D22 CTC - Fluo-C3DH-A549 (A549 cell)
D23 CTC - Fluo-C3DH-A549-SIM (A549 cell)

MSD, Medical Segmentation Decathlon; CTC, Cell Tracking Challenge

nnU-Net: Parameters



nnU-Net: Parameters



MedNeXt: Transformer-Driven Scaling of ConvNets for Medical Image Segmentation

Authors:  Saikat Roy,  Gregor Koehler,  Constantin Ulrich,  Michael Baumgartner,  Jens Petersen,  Fabian Isensee,  Paul F. Jäger,  Klaus H. Maier-Hein | [Authors Info & Claims](#)

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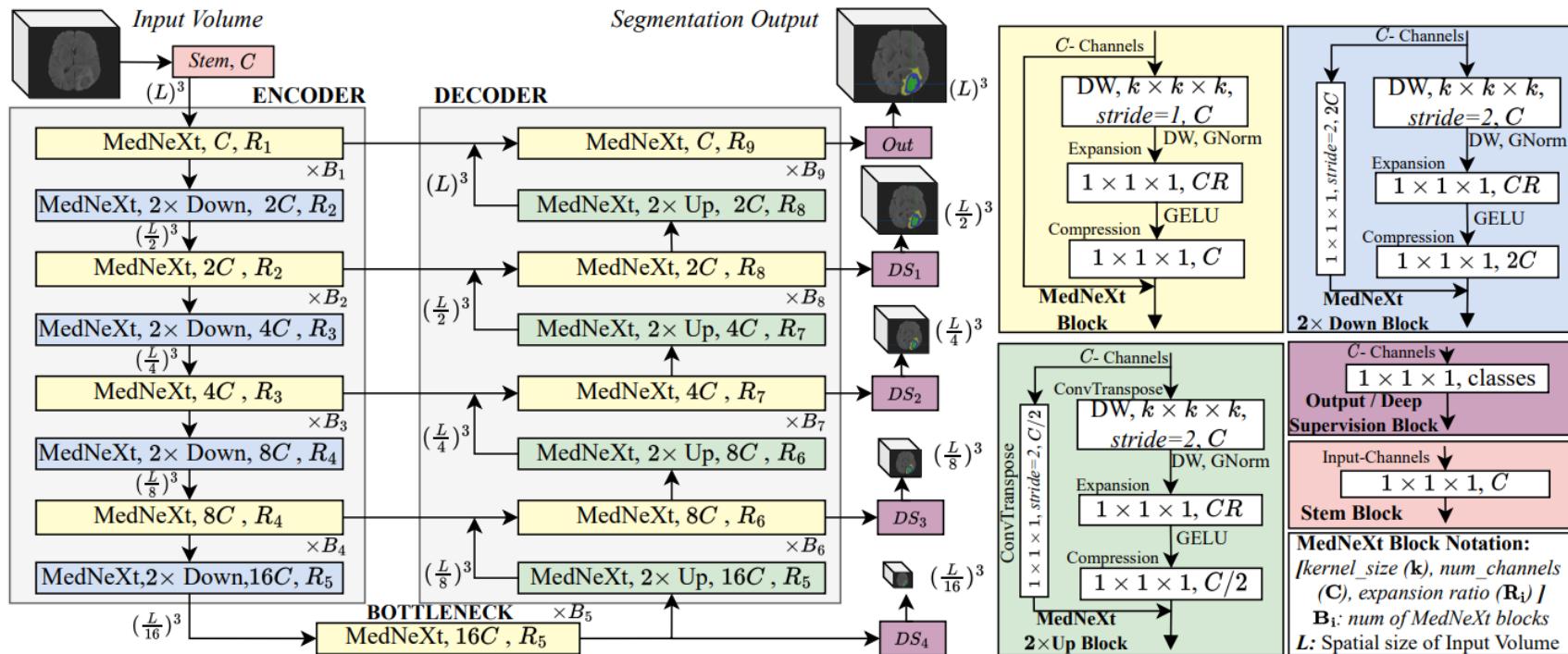
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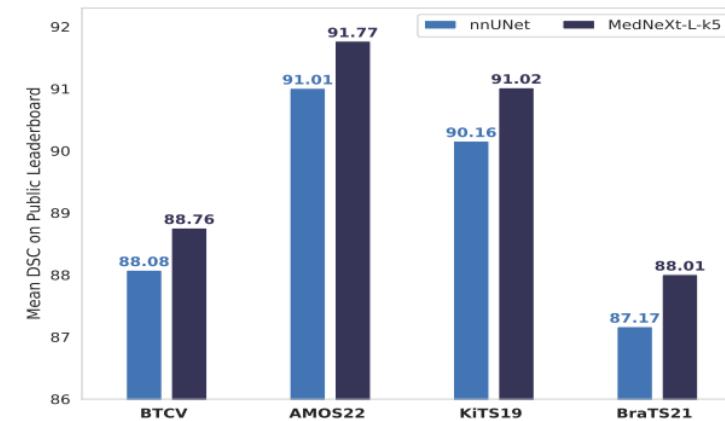
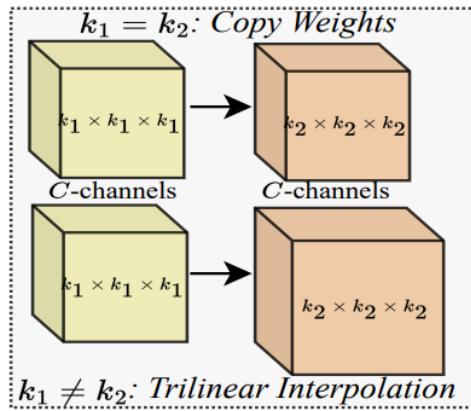
Abstract

There has been exploding interest in embracing Transformer-based architectures for medical image segmentation. However, the lack of large-scale annotated medical datasets make achieving performances equivalent to those in natural images challenging. Convolutional networks, in contrast, have higher inductive biases and consequently, are easily trainable to high performance. Recently, the ConvNeXt architecture attempted to modernize the standard ConvNet by mirroring Transformer blocks. In this work, we improve upon this to design a modernized and scalable convolutional architecture customized to challenges of data-scarce medical settings. We introduce MedNeXt, a *Transformer-inspired* large kernel segmentation network which introduces – 1) A *fully* ConvNeXt 3D Encoder-Decoder Network for medical image segmentation, 2) Residual ConvNeXt up and downsampling blocks to

- ✓ Composed purely of ConvNeXt blocks
- ✓ Preserve contextual richness
- ✓ Prevent performance saturation, UpKern



(a) MedNeXt macro and block architecture



(b) UpKern Initialization

(c) Leaderboard Scores

Features

Architecture

Configuration

Hardware Requirements

Key Strengths

nnU-Net

U-Net-based, self-configuring

Fully automated; adapts to dataset characteristics

Works on standard deep learning hardware

Out-of-the-box performance without manual tuning

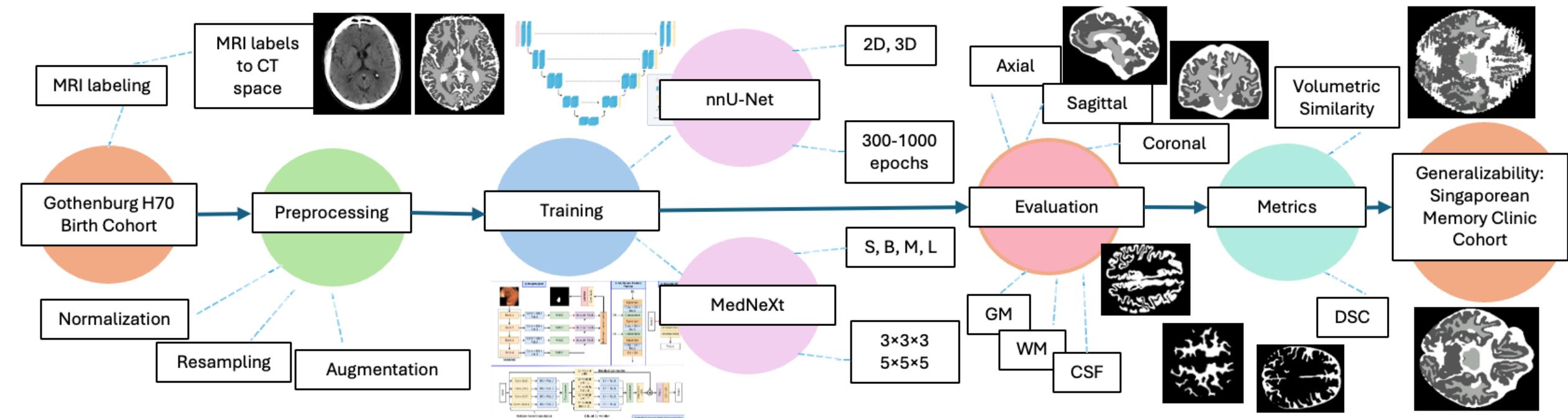
MedNeXt

ConvNeXt-inspired (modernized ConvNets)

Designed specifically for data-scarce medical settings

Focuses on scalability and efficiency

High performance in limited data scenarios; modular design



Model	Kernel size	Task	Parameters	Train(hrs)	Val(hrs)
Small (S)	$3 \times 3 \times 3$	H70_train	5.6M	48	2
Base (B)	$3 \times 3 \times 3$	H70_train	10.5M	48	2
Medium (M)	$3 \times 3 \times 3$	H70_train	17.6M	96	4
Large (L)	$3 \times 3 \times 3$	H70_train	61.8M	120	6
Large (L)	$5 \times 5 \times 5$	H70_train	63.0M	288	8

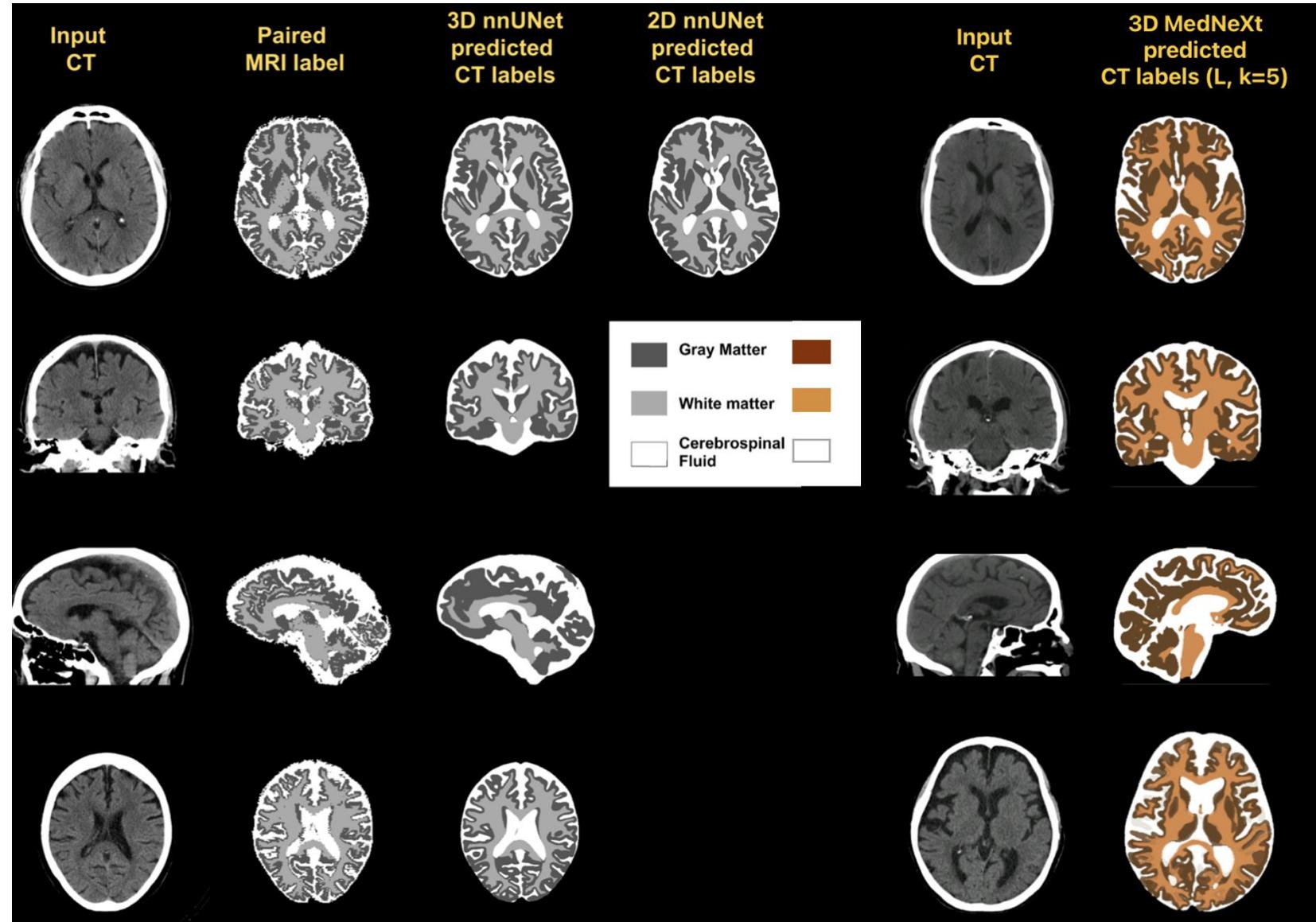
Performance of nnUNet Models Across Cohorts and Configurations

Dataset	Model	Epoch	Dice score coefficient (DSC)			Volumetric correlation(r)		
			GM	WM	CSF	GM	WM	CSF
H70 Axial	2D	300	0.79 ± 0.04	0.84 ± 0.03	0.76 ± 0.04	0.941	0.961	0.879
H70 Axial	2D	1000	0.80 ± 0.04	0.84 ± 0.03	0.77 ± 0.03	0.943	0.965	0.874
H70 Axial	3D	300	0.80 ± 0.04	0.84 ± 0.04	0.77 ± 0.03	0.892	0.870	0.860
H70 Axial	3D	1000	0.81 ± 0.04	0.86 ± 0.03	0.78 ± 0.04	0.952	0.970	0.875
H70 Coronal	3D	1000	0.70 ± 0.03	0.76 ± 0.02	0.69 ± 0.04	0.916	0.964	0.884
H70 Sagittal	3D	1000	0.74 ± 0.04	0.81 ± 0.03	0.73 ± 0.04	0.796	0.925	0.815
NUS Axial	3D	1000	0.66 ± 0.04	0.76 ± 0.03	0.68 ± 0.04	0.878	0.856	0.830

Performance of MedNeXt Models Across Cohorts and Configurations

Dataset	Model	Epoch	Dice score coefficient (DSC)			Volumetric correlation(r)		
			GM	WM	CSF	GM	WM	CSF
H70 Axial	S (3)	1000	0.81 ± 0.02	0.85 ± 0.03	0.78 ± 0.02	0.947	0.991	0.874
H70 Axial	B (3)	1000	0.81 ± 0.04	0.86 ± 0.04	0.78 ± 0.03	0.943	0.991	0.875
H70 Axial	M (3)	1000	0.82 ± 0.03	0.86 ± 0.02	0.78 ± 0.02	0.947	0.991	0.860
H70 Axial	L (3)	1000	0.82 ± 0.03	0.86 ± 0.03	0.79 ± 0.02	0.941	0.991	0.870
H70 Axial	L (5)	1000	0.82 ± 0.04	0.87 ± 0.02	0.79 ± 0.04	0.956	0.992	0.872
H70 Coronal	L (5)	1000	0.71 ± 0.03	0.78 ± 0.02	0.71 ± 0.04	0.928	0.971	0.894
H70 Sagittal	L (5)	1000	0.76 ± 0.03	0.83 ± 0.03	0.74 ± 0.02	0.852	0.955	0.842
NUS Axial	L (5)	1000	0.69 ± 0.04	0.78 ± 0.03	0.71 ± 0.02	0.888	0.991	0.865

nnUNet and MedNext
perform better in **3D**,
especially predicting the
GM, WM and CSF in coronal
and sagittal orientations



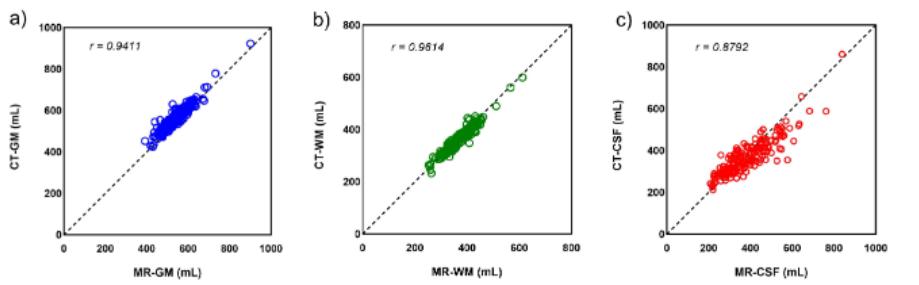
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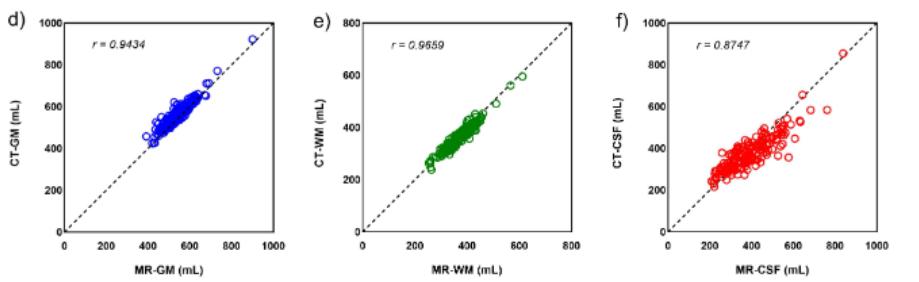
Performance of MedNeXt Models Across Cohorts and Configurations

Dataset	Model	Epoch	Dice score coefficient (DSC)			Volumetric correlation(r)		
			GM	WM	CSF	GM	WM	CSF
H70 Axial	S (3)	1000	0.81 ± 0.02	0.85 ± 0.03	0.78 ± 0.02	0.947	0.991	0.874
H70 Axial	B (3)	1000	0.81 ± 0.04	0.86 ± 0.04	0.78 ± 0.03	0.943	0.991	0.875
H70 Axial	M (3)	1000	0.82 ± 0.03	0.86 ± 0.02	0.78 ± 0.02	0.947	0.991	0.860
H70 Axial	L (3)	1000	0.82 ± 0.03	0.86 ± 0.03	0.79 ± 0.02	0.941	0.991	0.870
H70 Axial	L (5)	1000	0.82 ± 0.04	0.87 ± 0.02	0.79 ± 0.04	0.956	0.992	0.872
H70 Coronal	L (5)	1000	0.71 ± 0.03	0.78 ± 0.02	0.71 ± 0.04	0.928	0.971	0.894
H70 Sagittal	L (5)	1000	0.76 ± 0.03	0.83 ± 0.03	0.74 ± 0.02	0.852	0.955	0.842
NUS Axial	L (5)	1000	0.69 ± 0.04	0.78 ± 0.03	0.71 ± 0.02	0.888	0.991	0.865

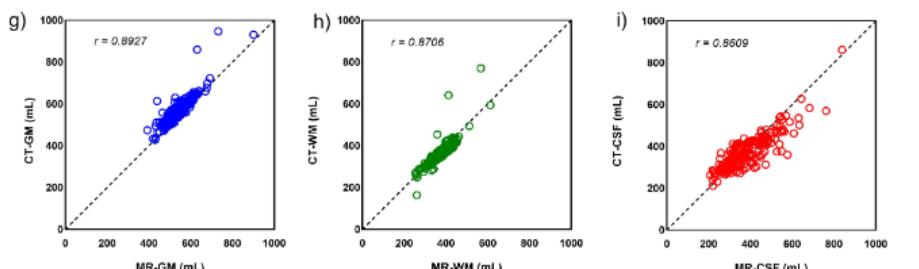
Predictions from 2D nnUNet trained with 300 epochs



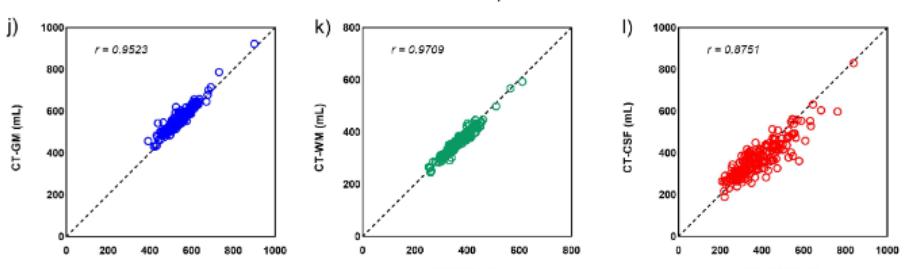
Predictions from 2D nnUNet trained with 1000 epochs



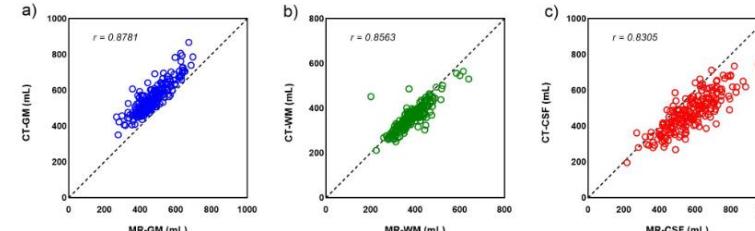
Predictions from 3D nnUNet trained with 300 epochs



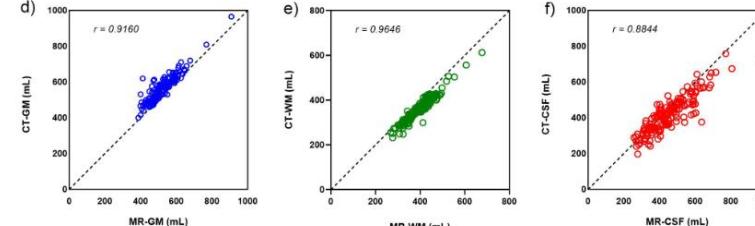
Predictions from 3D nnUNet trained with 1000 epochs



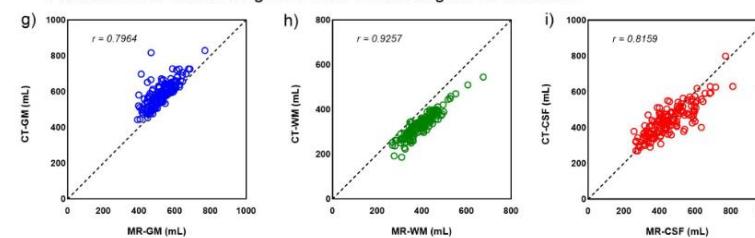
Predictions in Singaporean Memory Clinic axial CT datasets



Predictions in Gothenburg H70 Birth Cohort coronal CT datasets

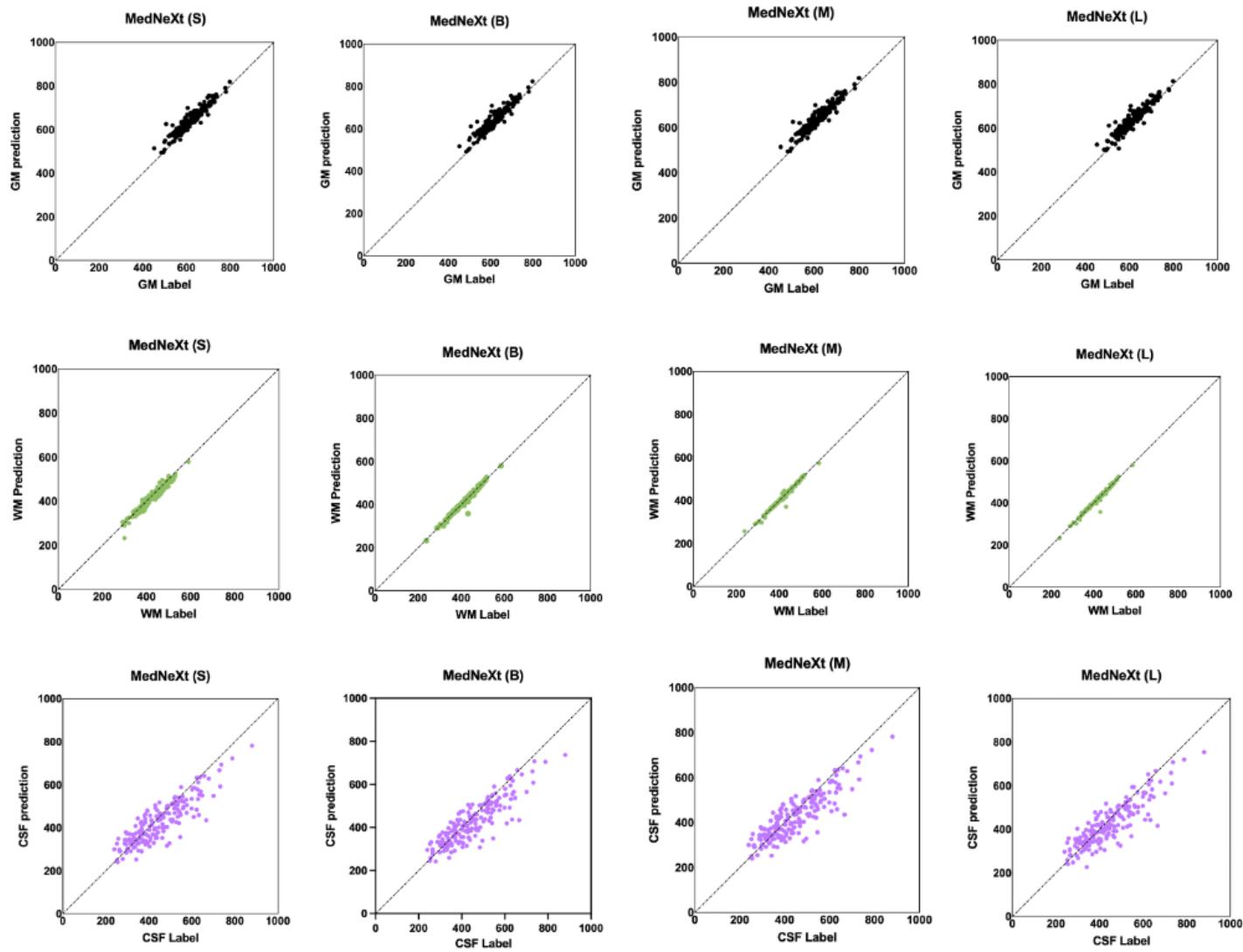


Predictions in Gothenburg H70 Birth Cohort sagittal CT datasets

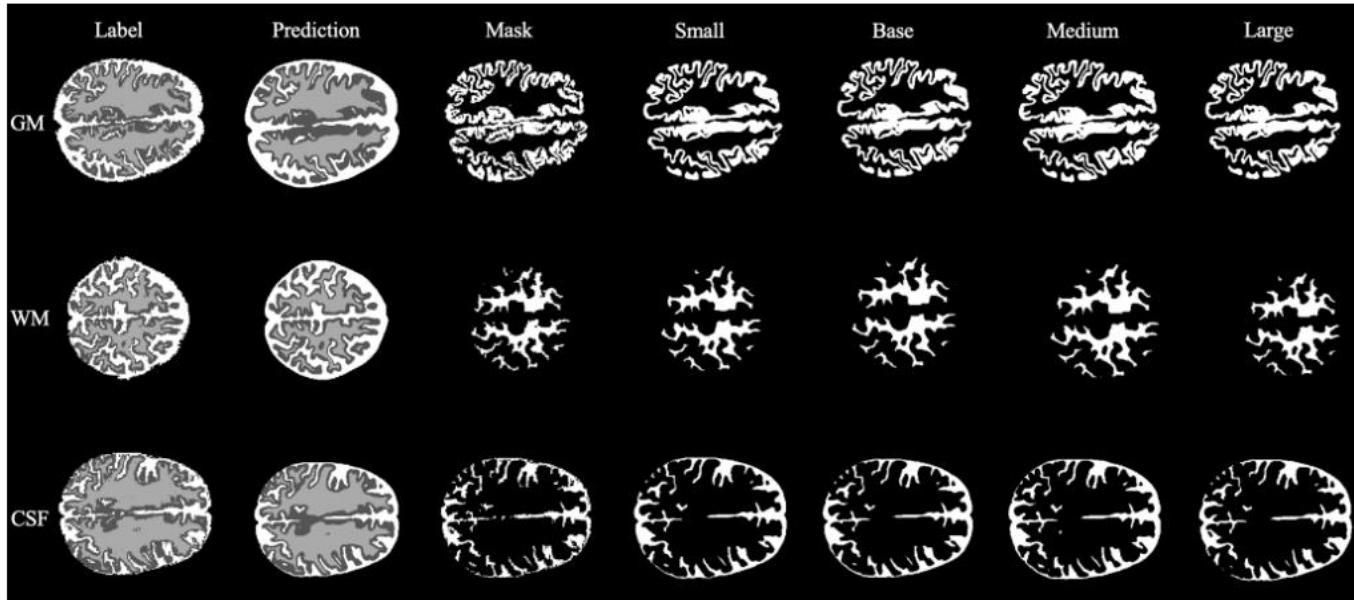


Correlation plots for 3D nnUNets (trained for 1000 epochs) CT predictions and paired ground truth MRI labels (GM, WM, and CSF) in NUS axial datasets ($n = 210$; a - c), H70 coronal ($n = 165$; d - f), and sagittal CT datasets ($n = 162$; g - i)

Correlation plots for 2D (trained for 300 epochs (a - c) and trained for 1000 epochs (d - f) and 3D nnUNets ((trained for 300 epochs (g - i) and trained for 1000 epochs (j- l) CT predictions and paired ground truth MRI labels (GM, WM, and CSF) in Gothenburg H70 Birth Cohort axial CT datasets ($n = 173$)

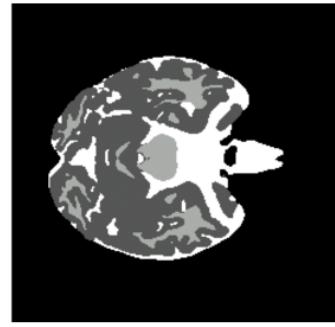
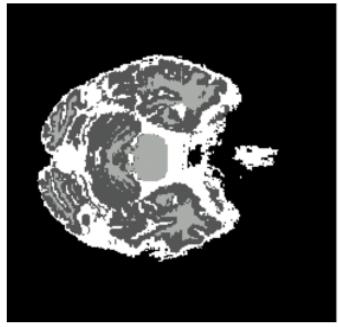


Correlation plots between 3D MedNeXt (Small, Base, Medium and Large, k=3) axial-CT predictions and paired ground truth MRI labels (GM: gray matter, WM: white matter, and CSF: cerebrospinal fluid) in Gothenburg H70 Birth Cohort (axial, n = 173)

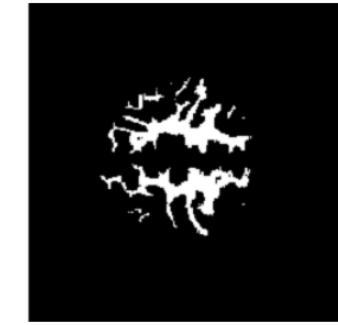


CT inputs and model outputs: The figure shows paired MRI ground truth labels for MedNeXt predictions (Small, Base, Medium and Large models) from H70 axial dataset of kernel size $3 \times 3 \times 3$ for GM: gray matter, WM: white matter, and CSF: cerebrospinal fluid

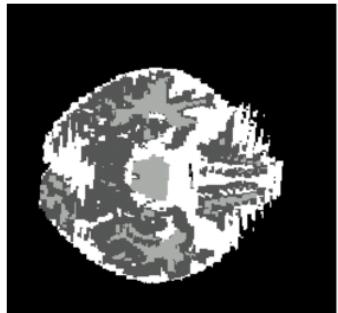
Singaporean Memory Clinic Cohort, **MedNeXt (Large, Kernel 5x5x5)**, Gray Matter (GM)



Singaporean Memory Clinic Cohort, **MedNeXt (Large, Kernel 5x5x5)**, White Matter (WM)



Singaporean Memory Clinic Cohort, **MedNeXt (Large, Kernel 5x5x5)**, Cerebrospinal fluid (CSF)



Predictions of the best performing model, MedNeXt-L on the Dementia cohort

3D nnUNet

Inference Time

Avg. 36s (2D) & 47s (3D) per image—efficient for real-time predictions and resource-constrained settings

Training Duration

Improved performance (e.g., DSC from 0.80 to 0.81 in GM) with 1000 epochs vs. 300 epochs

Cross-View Performance

DSC (Axial: 0.82, Coronal: 0.72, Sagittal: 0.76)

NUS Dementia Cohort

nnUNet (DSC: 0.70)

MedNeXt

Avg. 50s (small/base models) to 3 mins (large models)—longer inference time with improved performance

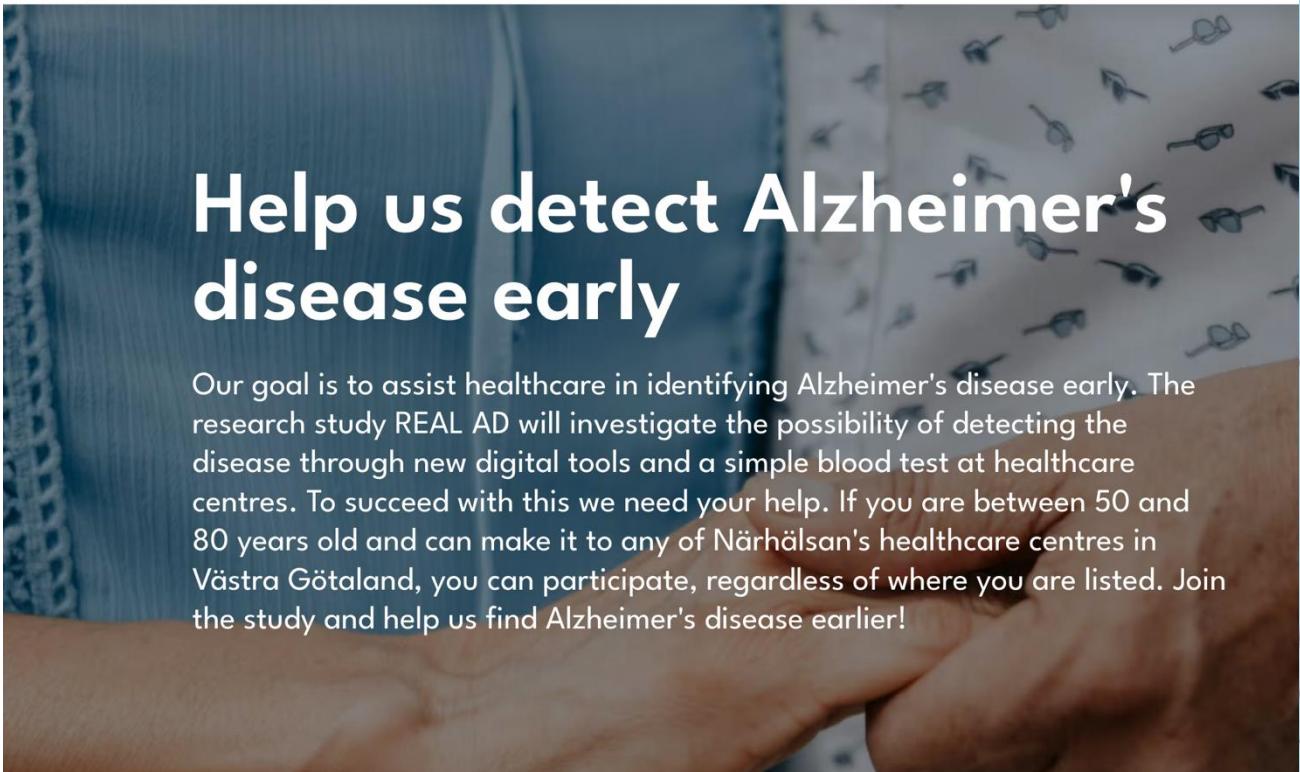
Longer training times (48h for small, 288h for large models), but higher accuracy (e.g., DSC from 0.81 to 0.82 in GM)

Better performance overall (Axial: 0.83, Coronal: 0.73, Sagittal: 0.78)

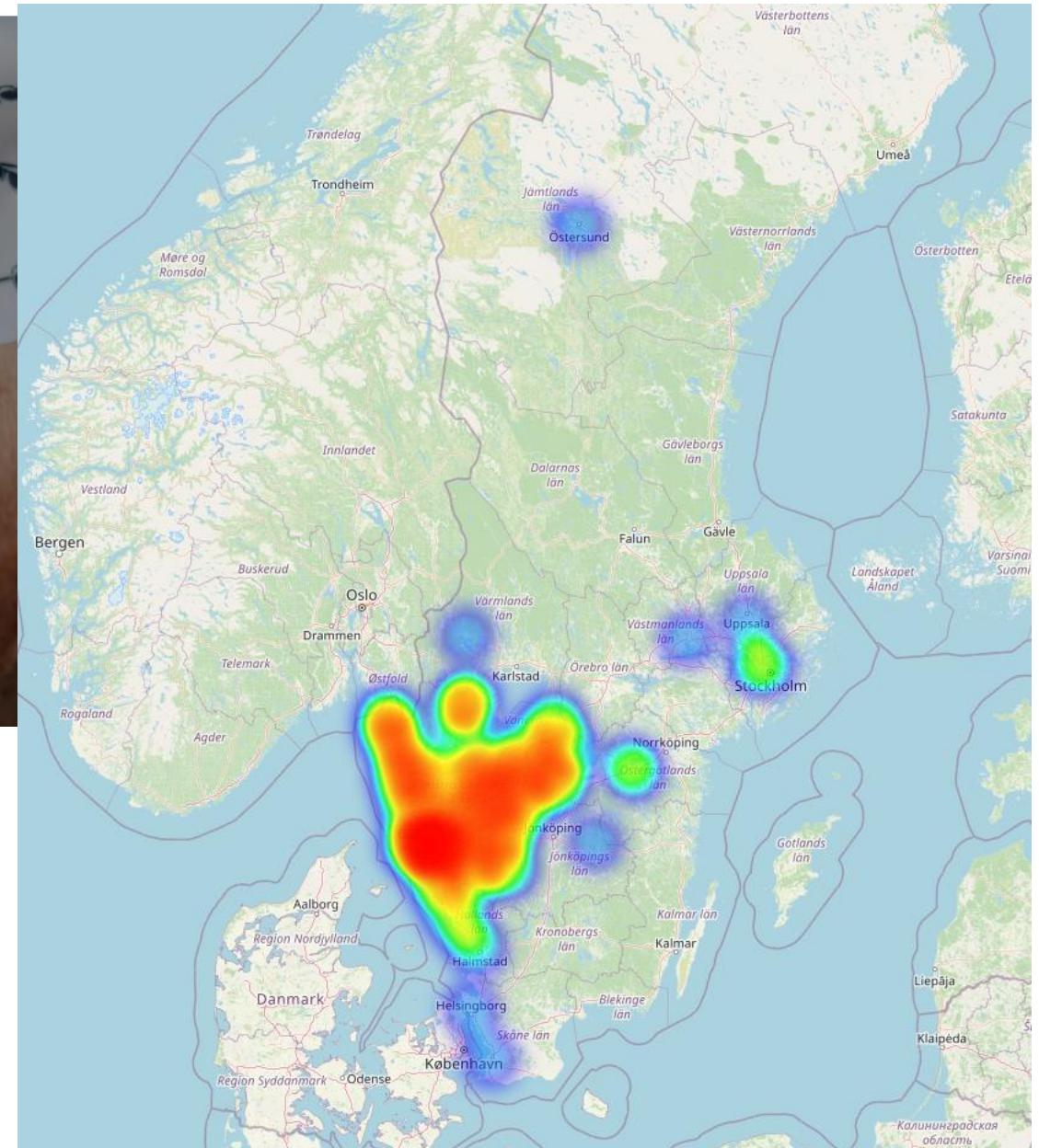
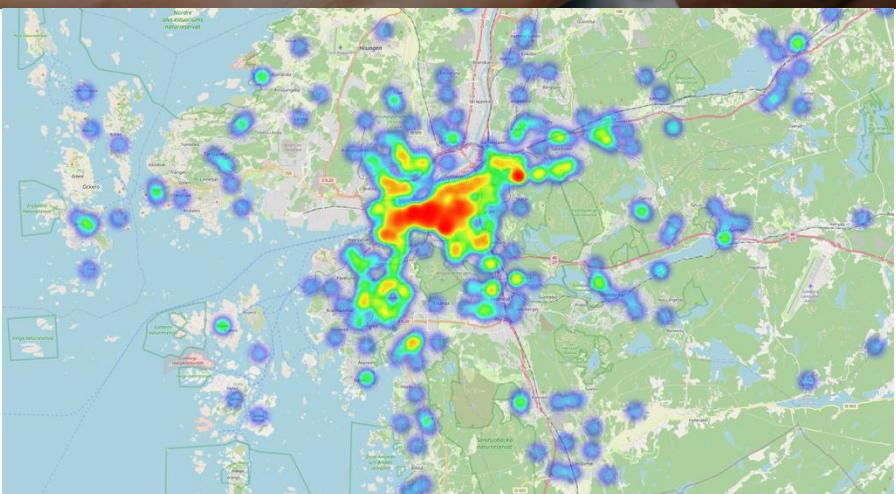
MedNeXt performed better (DSC: 0.73) vs. with clinically acceptable results.

Conclusions

1. MedNeXt requires more computational resources, limiting its use in resource-constrained environments
2. Orientation-aware considerations are crucial for clinical workflows, with axial yielding the best accuracy.



Our goal is to assist healthcare in identifying Alzheimer's disease early. The research study REAL AD will investigate the possibility of detecting the disease through new digital tools and a simple blood test at healthcare centres. To succeed with this we need your help. If you are between 50 and 80 years old and can make it to any of Närhälsan's healthcare centres in Västra Götaland, you can participate, regardless of where you are listed. Join the study and help us find Alzheimer's disease earlier!



1984

A β plaques
Neurofibrillary tangles
(NINCDS-ADRDA)

1992

CSF A β

CSF analysis based on immunoassay

1993

CSF t-tau

1995

CSF p-tau

2011

CSF A β CSF tau
(NIA-AA)

2012

DIAN results

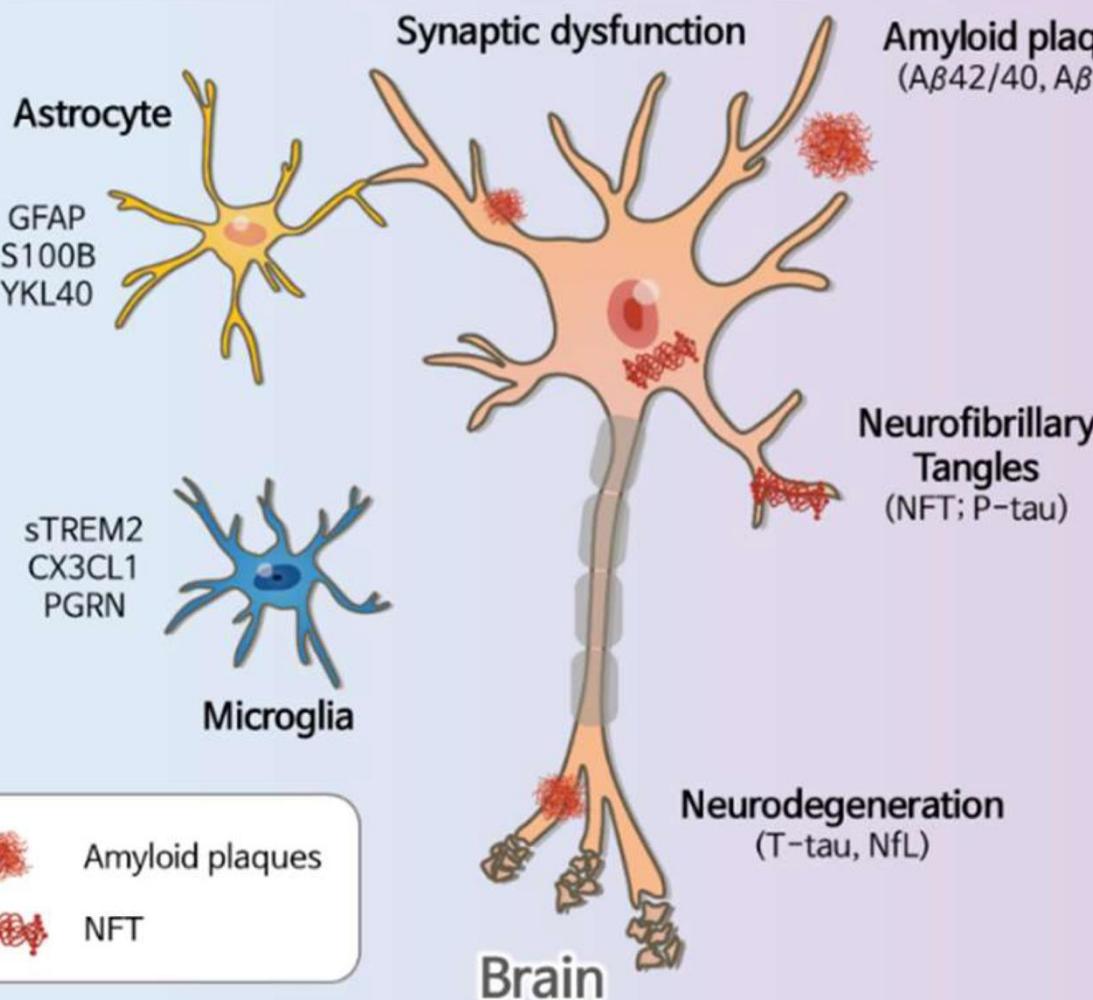
2018

ATN system
(NIA-AA)

Current - Future

Blood-based
biomarkers

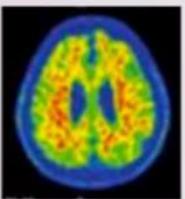
Alzheimer's disease biomarkers development timeline past-present-future



A

↓ A β 42/40
↓ A β 42

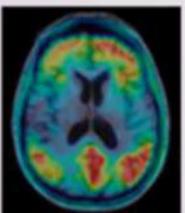
Amyloid PET



T

↑ P-tau181
↑ P-tau217

Tau PET

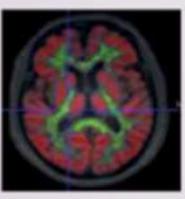


N

↑ T-tau
↑ NfL

FDG-PET

MRI



Primary AD biomarker
A β 42, T-tau, p-tau

Others
GFAP, NfL

Exosome

Lipids

miRNA

Blood

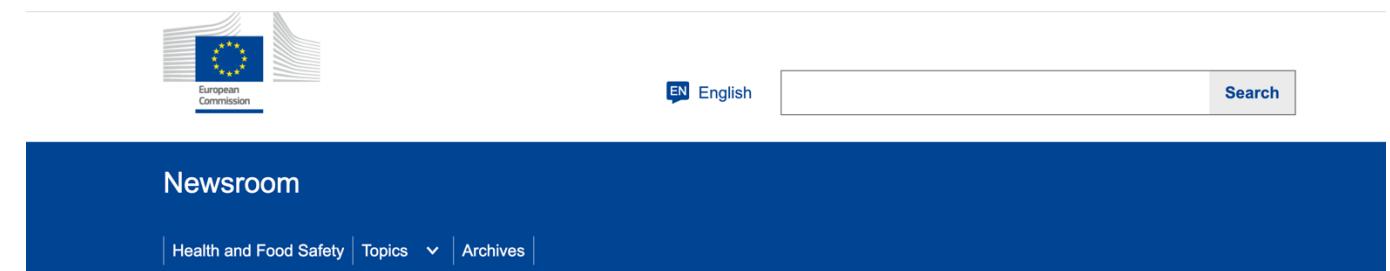
FDA Approves Eli Lilly's Donanemab for Early Symptomatic Alzheimer Disease

Author(s): [Isabella Ciccone, MPH](#)

The approval of donanemab marks the third antiamyloid therapy to gain the FDA's greenlight, following the conditional approval of aducanumab in 2021, and lecanemab in 2023—although aducanumab no longer remains on market after it was removed earlier this year.

The European Medicines Agency has recommended the refusal of the [marketing authorisation](#) for Kisunla, a medicine intended for the treatment of early Alzheimer's disease.

The Agency issued its opinion on 27 March 2025. The company that applied for authorisation, Eli Lilly Nederland B.V., may ask for a re-examination of the opinion within 15 days of receiving the opinion.



The screenshot shows the European Commission's website. At the top, there is the European Commission logo (a blue square with the EU flag) and a search bar. Below the header, a blue navigation bar contains the text "Newsroom" and links to "Health and Food Safety", "Topics", and "Archives". The main content area features a headline: "Commission authorises medicine for treatment of early Alzheimer's disease". Below the headline, there is a date: "date: 15/04/2025". Further down, there is a paragraph of text about the authorization and its conditions.

[OVERVIEW](#) > [PRESS RELEASE](#)

Commission authorises medicine for treatment of early Alzheimer's disease

date: 15/04/2025

The Commission has today granted EU authorisation for a medicine to treat mild cognitive impairment in the early stages of Alzheimer's disease, under strict conditions.

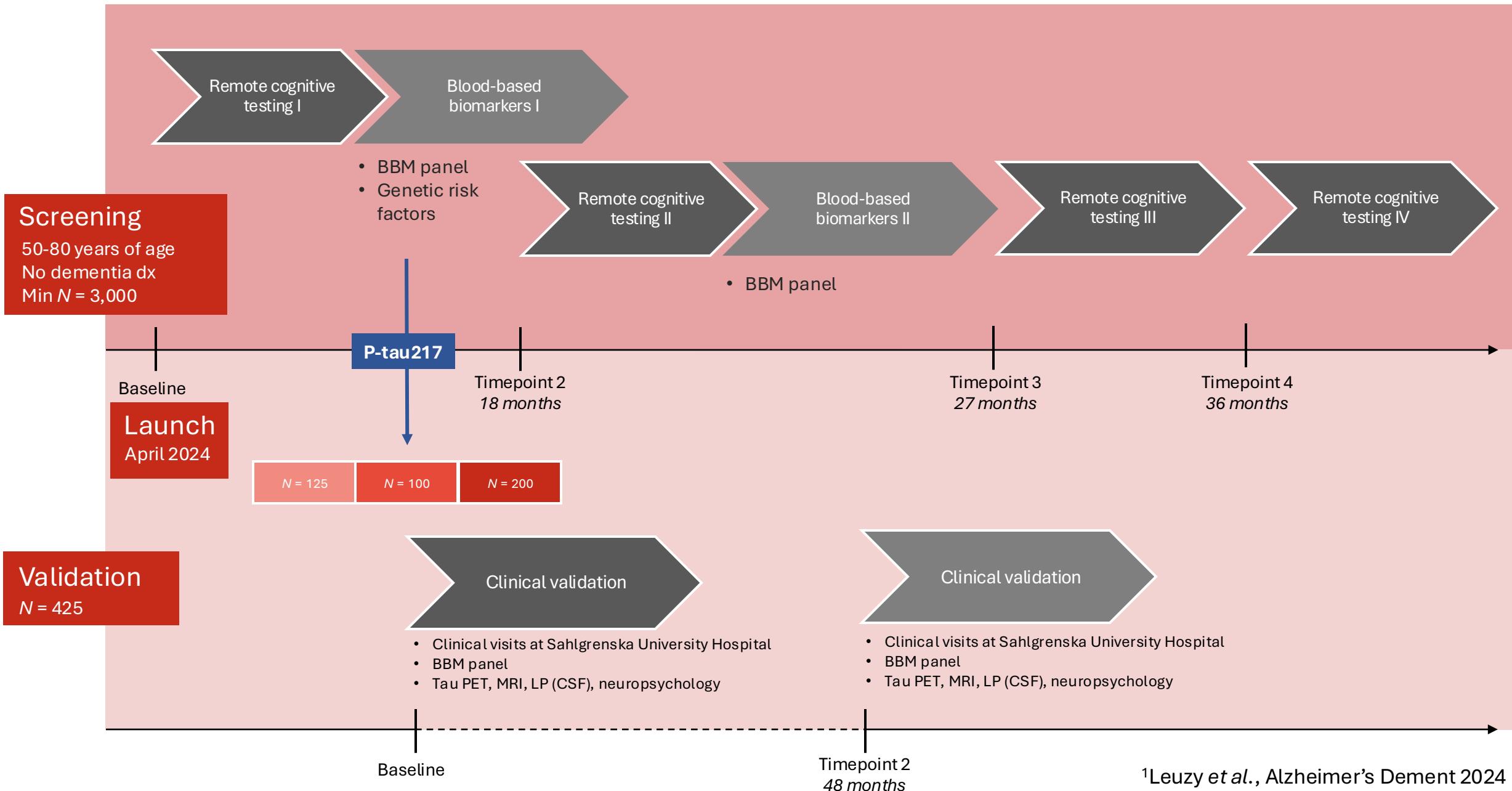
It is for use in people who have only 1 or no copy of the ApoE4 gene and who have amyloid beta plaques in the brain. It is the first such medicine to be authorised in the EU.

The authorisation is based on the positive scientific assessment of the European Medicines Agency, which concluded that the benefits of this medicine outweighed the risks in a particular population of patients with such disease and as long as risk minimisation measures are applied. Therefore, today's authorisation decision also sets strict conditions on the use of Leqembi, as well as clear risk mitigation requirements.

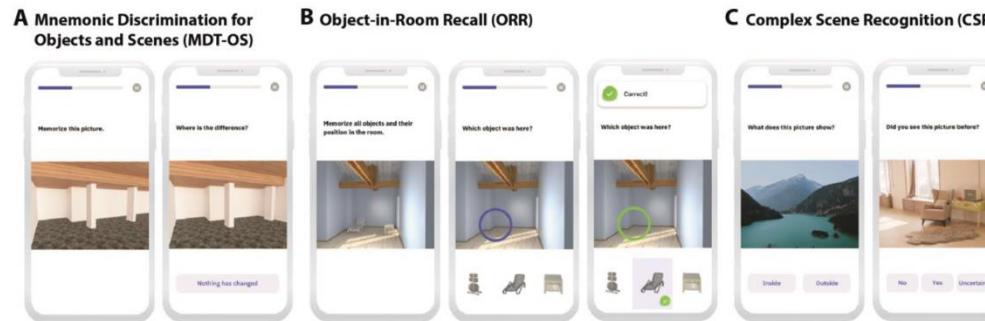


Validation of a realistic screening approach for

- 740,000 inhabitants between 50-80 y
- Highly digitalized society across all ages
- Diverse population
- Public primary care largest health care provider in Sweden
- Link with regional EMR



Step 2 | Cognitive testing

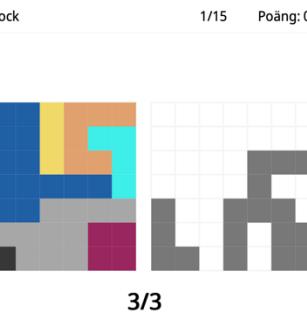


3 tests x 3 occasions (plus recall) over 3 months

¹Berron et al., npj Digital Medicine 2024
²Berron et al., Front Digit Health 2022



Hjälp (vanliga frågor) ⓘ (accounts+RealADexd14@h2cd.co.uk) ⓘ



6 test sessions over 3 months

¹Hampshire et al., NEJM 2024

Step 3 | Biomarker analyses

Roche Elecsys

- Ptau217
- Ptau181
- GFAP
- NFL
- ApoE (+/-)



Beckman-Coulter

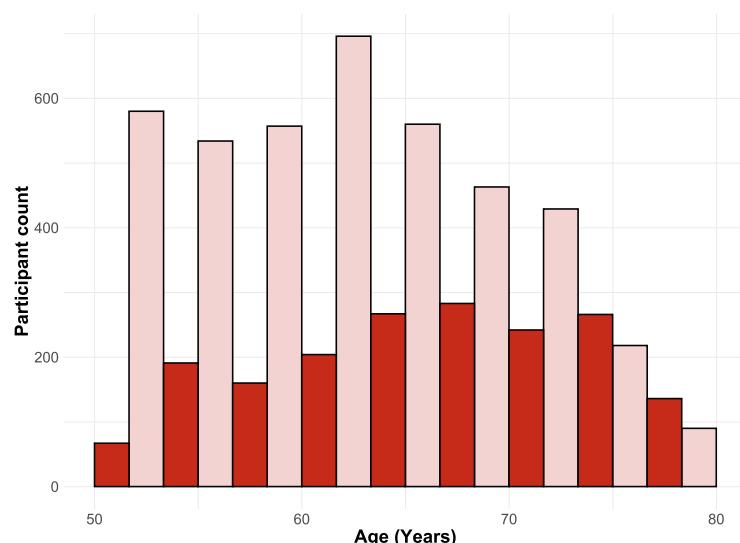
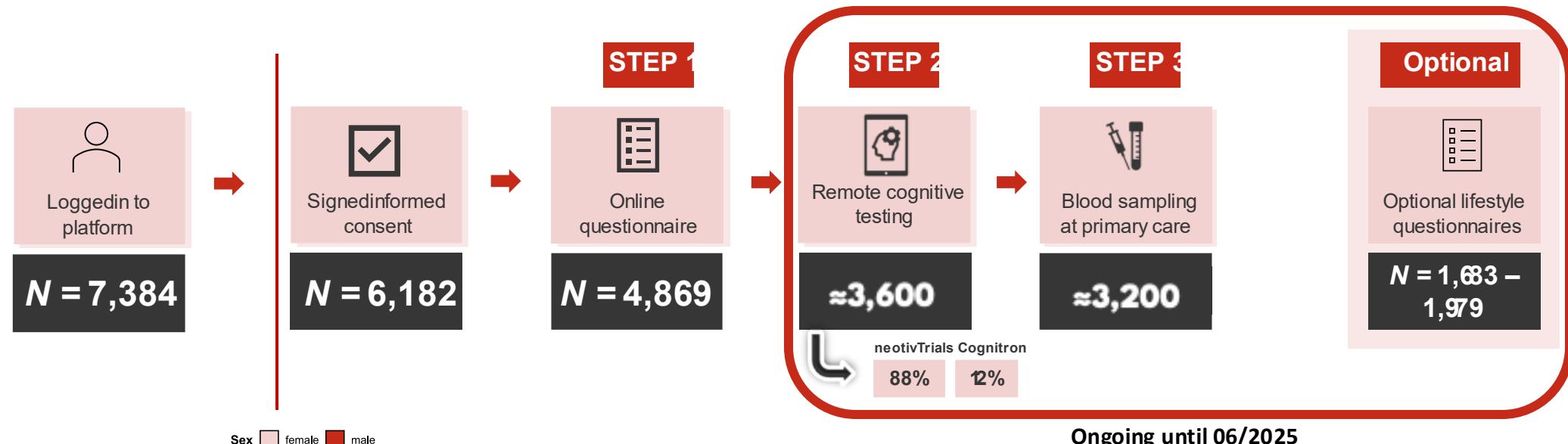
- A β 42
- Ptau217
- GFAP
- NFL
- ApoE



*Sub-cohorts to be analyzed with
C2N, Lumipulse*

To be continued...

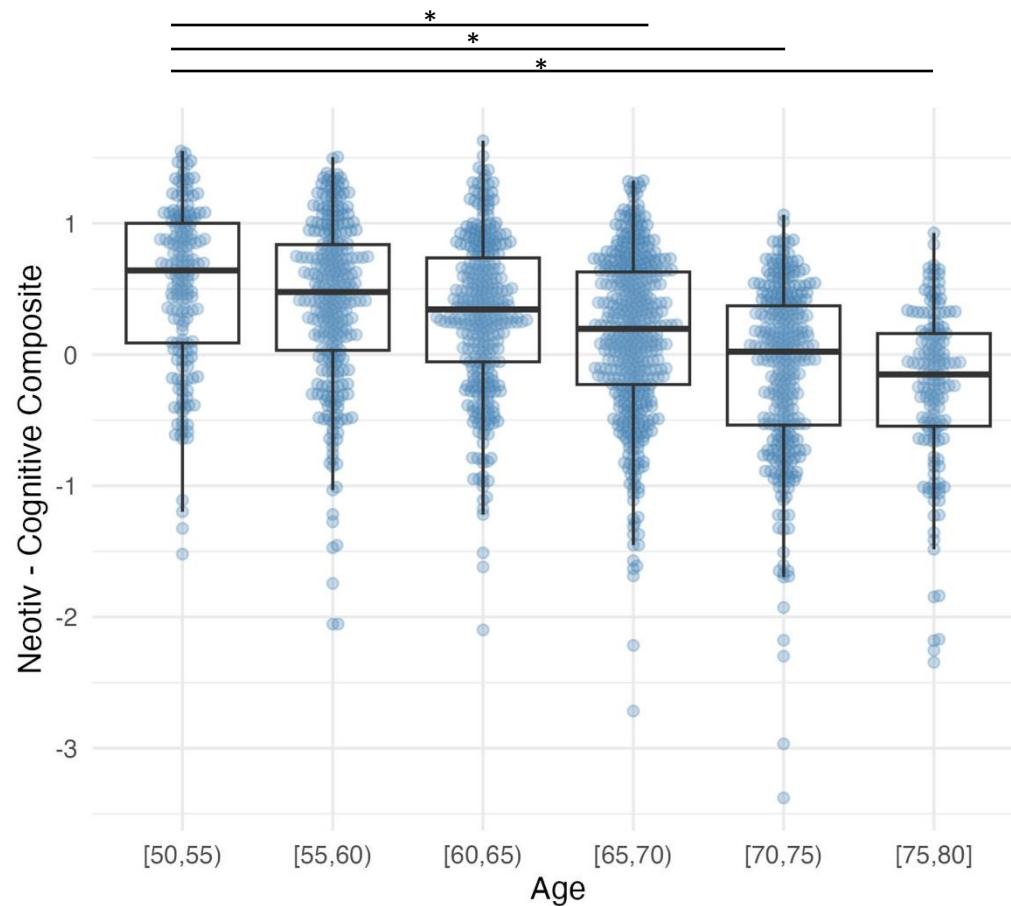
Participant numbers & demographics



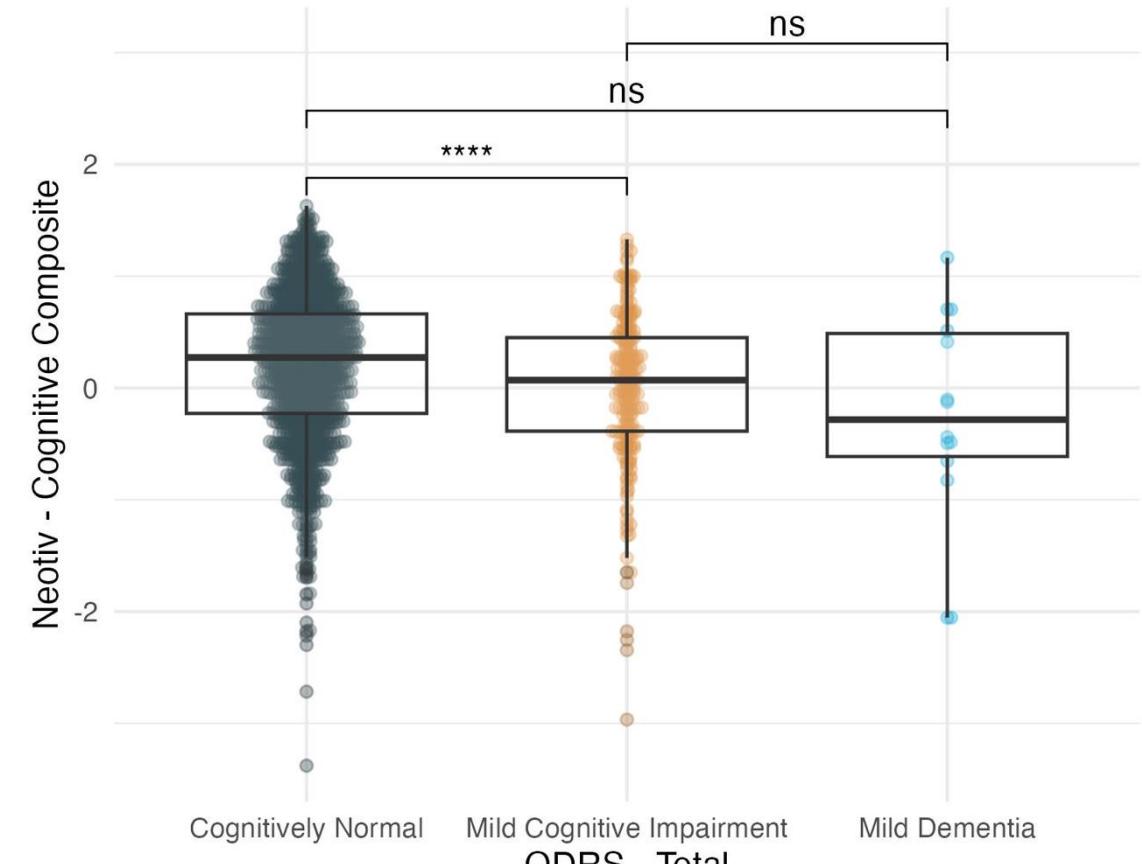
Age (y):	64.2 (7.7)	QDRS Category:	
Sex (female):	69%	Cognitively unimpaired	86%
ApoE E4+:	35%	Mild cognitive impairment	13%
Family history of dementia:	61%	Mild dementia	1%
Higher (tertiary) education:	64%		
Participants born in Sweden:	92%		
Parents born in Sweden:	82%		

Cognitive performance (neotiv)

vs age



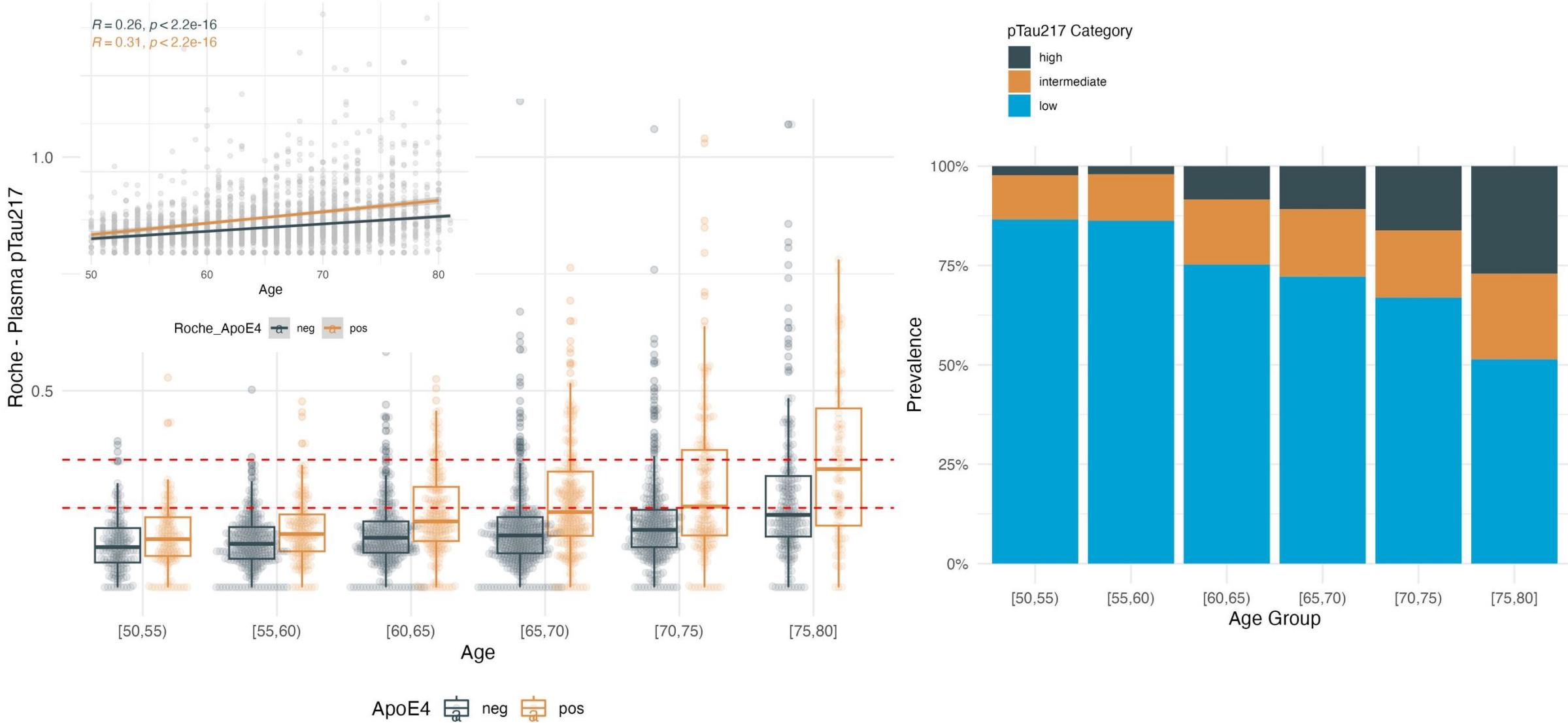
vs self-reported cognition



Preliminary dataset with neotivComposite (triple) and available ptau217 available: n = 1770

QDRS: Quick Dementia Rating System, Galvin A&D: DADM 2015; CU: QDRS normal; CI: QDRS MCI and mild dementia; * <0.05

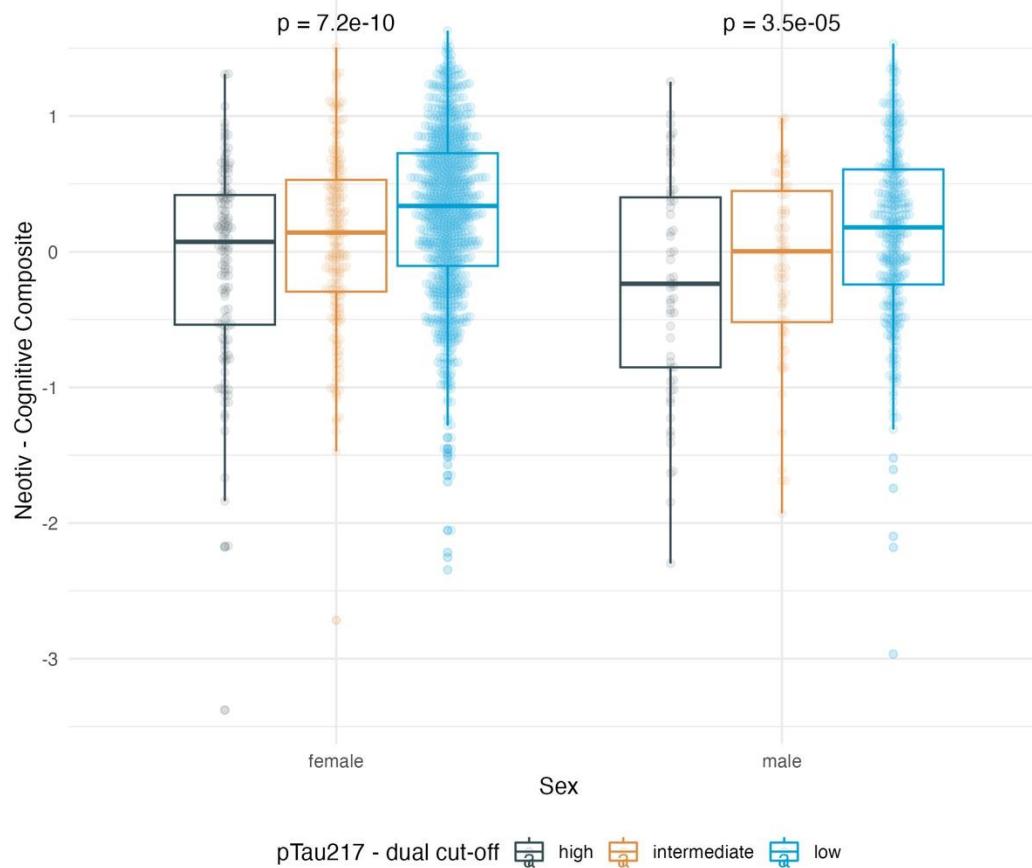
Plasma ptau217



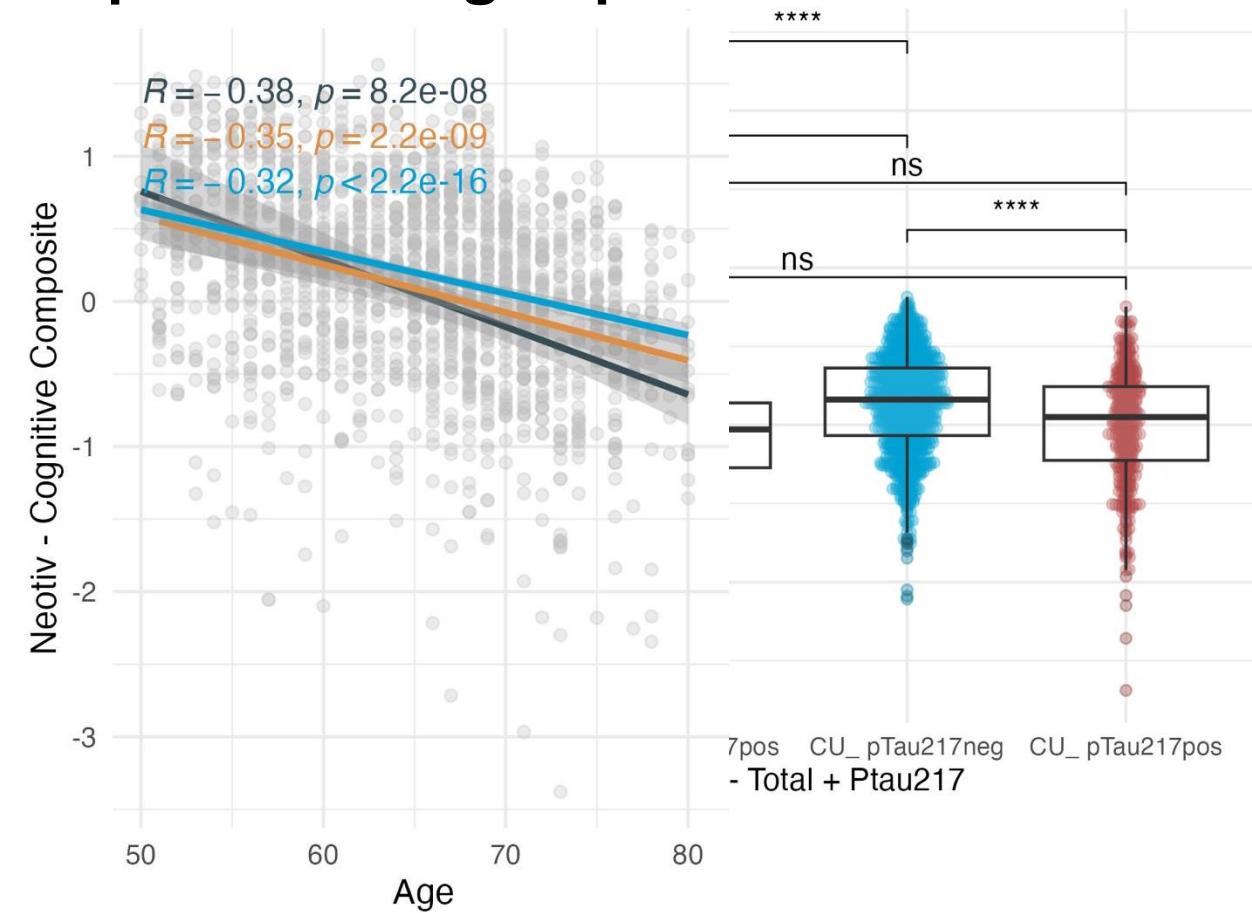
Preliminary dataset with neotivComposite and ptau217 available: $n = 1770$; Prototype Elecsys® pTau 217; Cut-Off from Internal Validation Study (90% sens/90%spec for Ab PET+)

Cognitive performance vs ptau217

Memory Composite vs ptau217



Subtle Impairment in self-reported CU ptau217 subgroups



Preliminary dataset with neotivComposite (triple) and available ptau217 available: $n = 1770$

QDRS: Quick Dementia Rating System, Galvin A&D: DADM 2015; CU: QDRS normal; CI: QDRS MCI and mild dementia; * <0.05

Future work....