

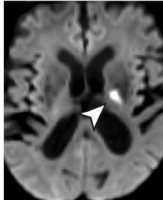
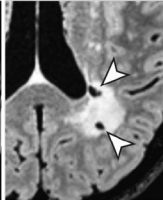
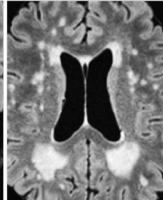
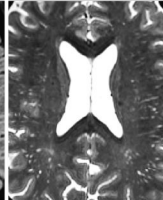
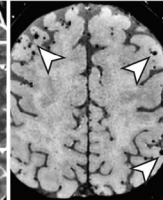
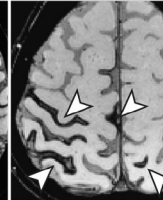
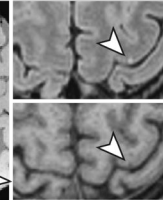
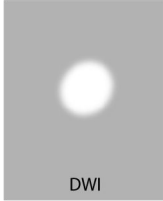


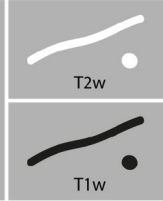
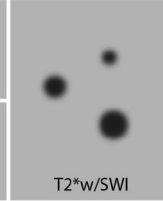


MIAAC
Medical Image Analysis Center

VCI Neuroimaging

Marco Duering

1

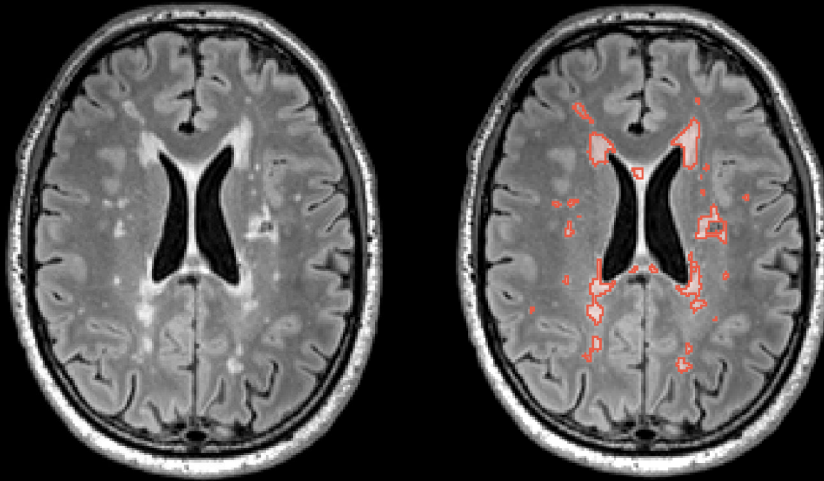
STRIVE-2

Recent small subcortical infarct	Lacune	White matter hyperintensity	Perivascular space	Cerebral microbleed	Cortical superficial siderosis	Cortical cerebral microinfarct
						
 DWI	 FLAIR	 FLAIR	 T2w T1w	 T2*w/SWI	 T2*w/SWI	 T2w T1w

STRIVE-2, Lancet Neurology 2023

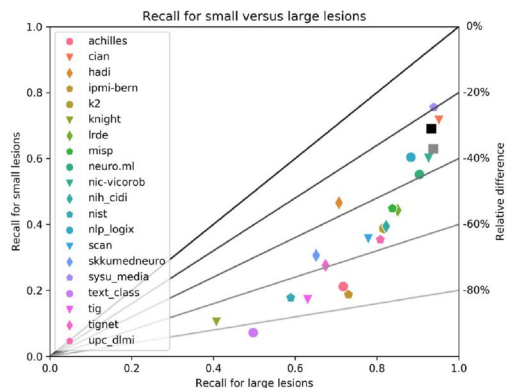
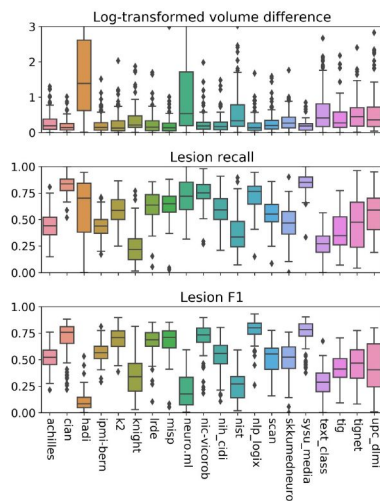
2

WMH segmentation



3

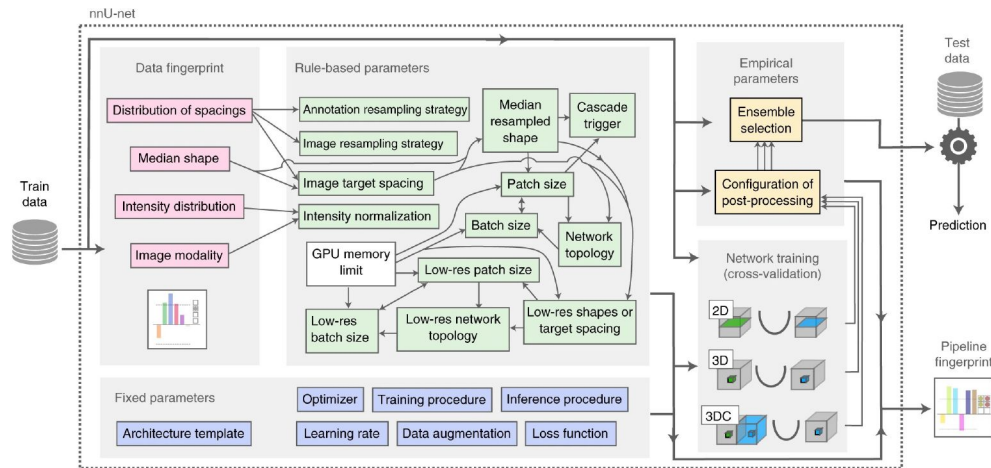
WMH segmentation – MICCAI Challenge 2017



Kuijf et al., IEEE Trans Med Imaging 2019

4

New method nnU-Net: Self-configuring U-Net

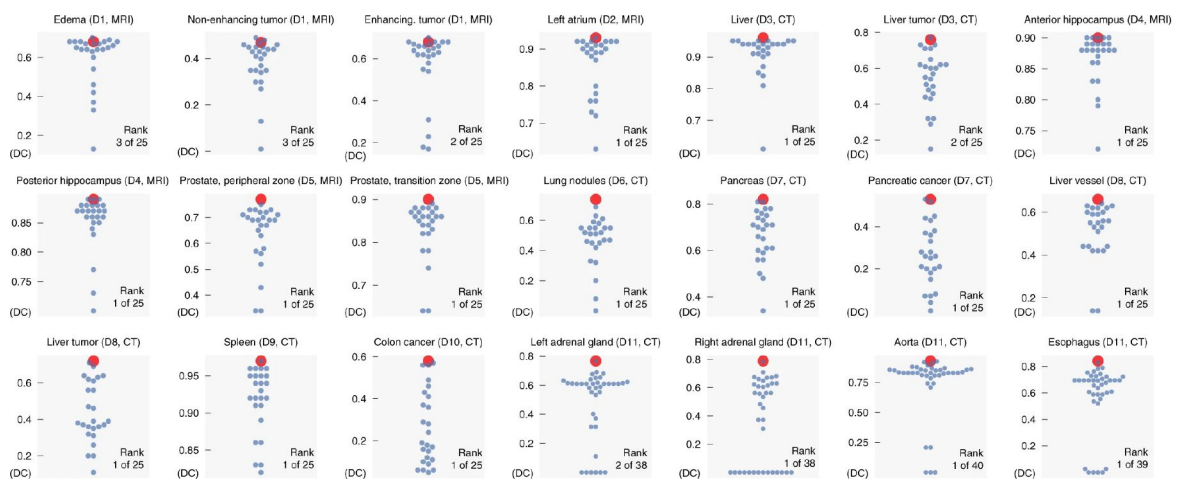


<https://github.com/MIC-DKFZ/nnUNet>

Isensee et al., Nature Methods 2021

5

nnU-Net: State-of-the-art performance

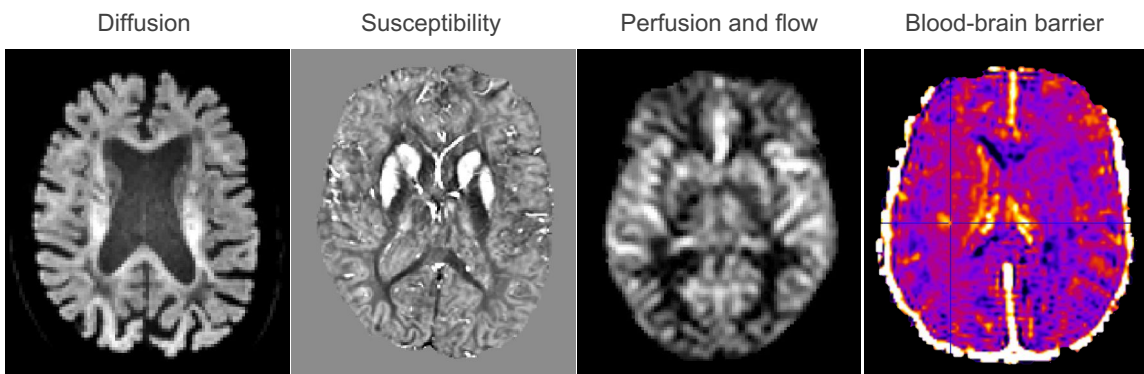


<https://github.com/MIC-DKFZ/nnUNet>

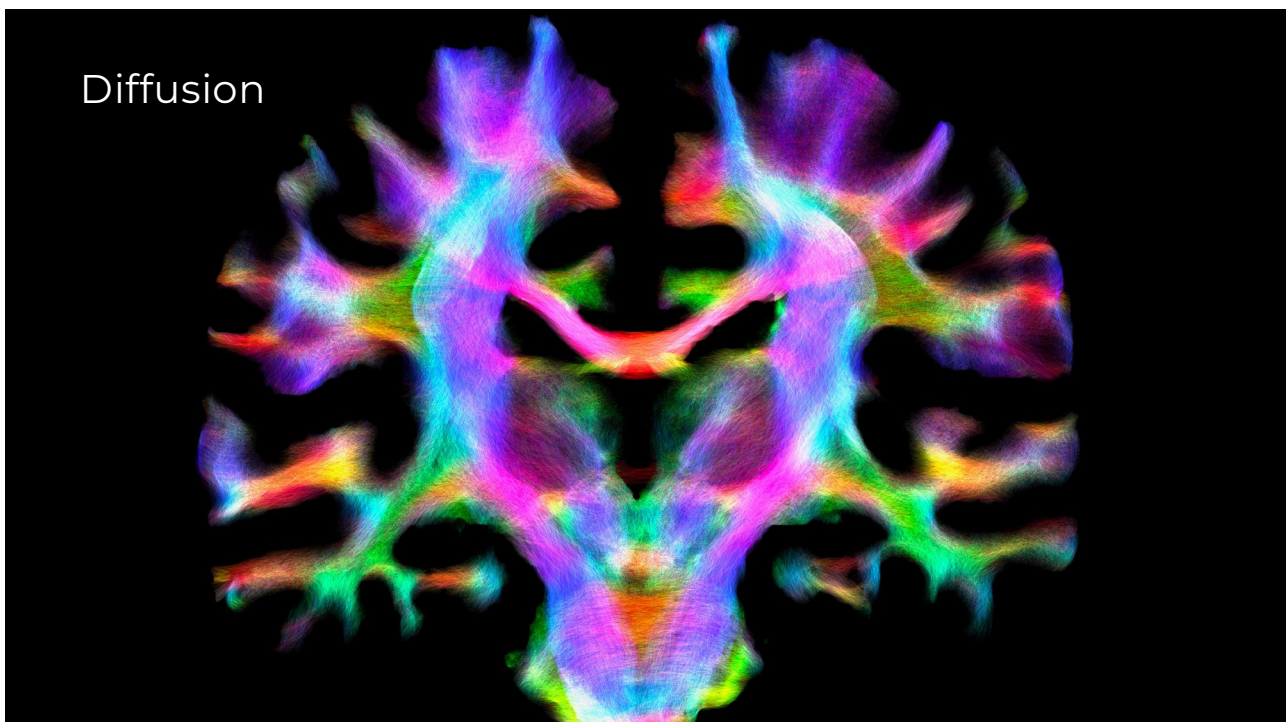
Isensee et al., Nature Methods 2021

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Quantitative Imaging Markers

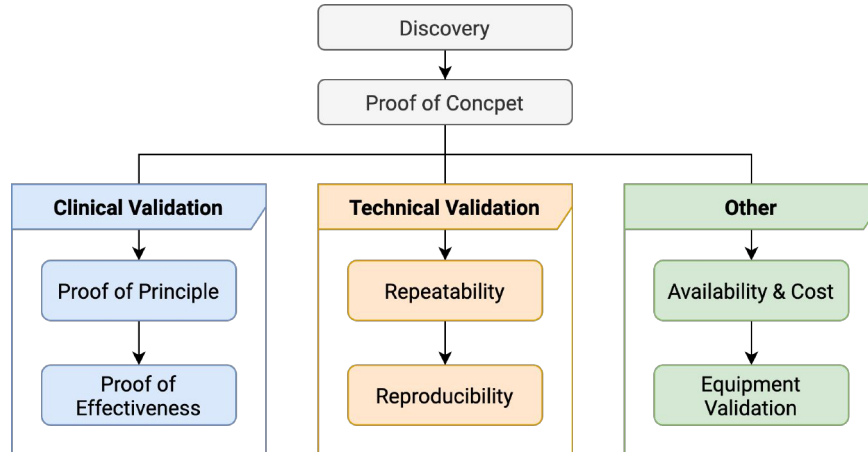


7



8

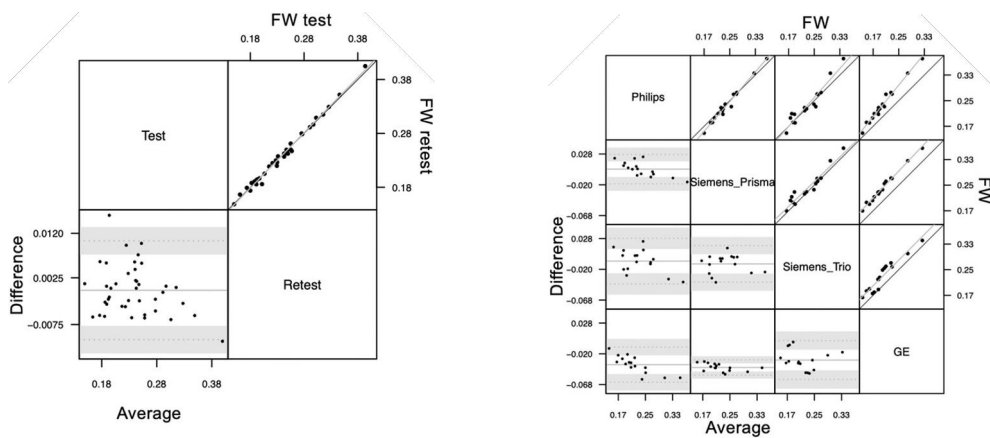
Biomarker Development



Adapted from: Smith et al., *HARNES Initiative, Alz Dement (Amst) 2019*

9

Technical Validation in the MarkVCID consortium



Maillard et al., *Alz Dement (Amst) 2022*

10

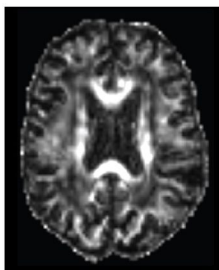
Clinical Validation of Imaging Markers

- **"Intended use"** clearly defined?
- Appropriate **datasets** and **statistics**? E.g.
 - Case/control and ROC analysis for diagnostic marker
 - Longitudinal data/analysis for monitoring marker
 - etc.
- **Added benefit** over existing/established markers?
- Validation against a **goldstandard**? Histopathology?

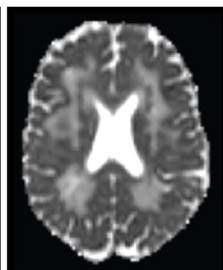


11

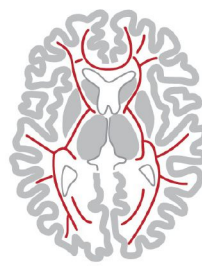
Added benefit of more complex methods?



Fractional anisotropy



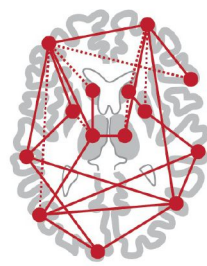
Mean diffusivity



Skeleton-based tract analysis



Identification of connected structures

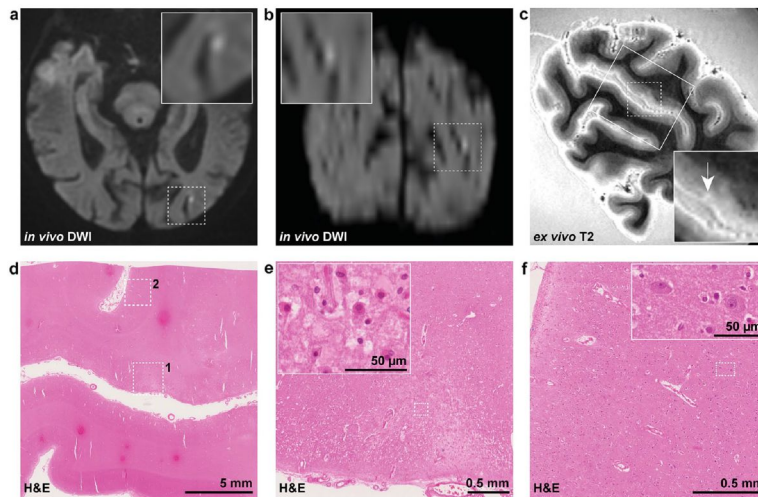


Altered whole brain network connectivity

Iadecola et al., JACC 2019
Konieczny et al., Neurology 2021
Dewenter et al., JCBFM 2022

12

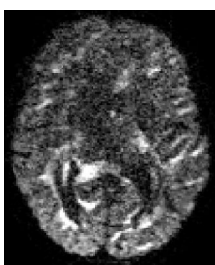
Histopathological correlation – DWI lesions



ter Telgte et al., *Acta Neuropathologica* 2020
Review; van Veluw, Arfanakis, Schneider, *Stroke* 2022

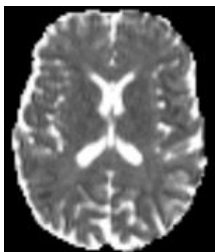
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Methodological Pitfalls – Diffusion MRI



Data requirements met?

- Tensor: ≥ 20 directions, b-value 700-1500 s/mm²
- Kurtosis: multi-shell (b=1000, b=2000)
- Tractography: > 30 or better > 60 directions
- Fixel-based analysis: $b \geq 2000$



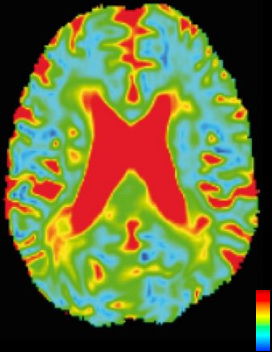
Known confounders addressed?

- CSF partial volume (atrophy!)
- Head motion
- Major artifacts

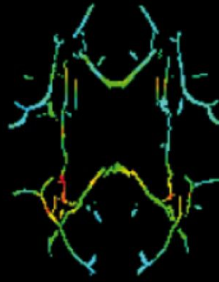
14

Peak width of skeletonized mean diffusivity (PSMD)

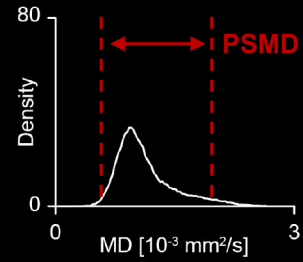
Diffusivity



Skeletonization



MD histograms



Baykara et al., *Annals of Neurology* 2016
 Review: Zanon Zotin et al., *Radiology* 2023

<https://github.com/miac-research/psmd>

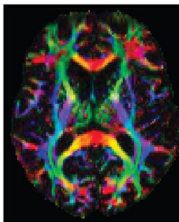


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From brain structure to vessel function

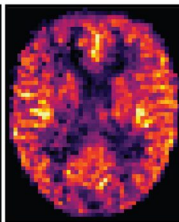
Quantitative imaging

Diffusion MRI
(tensor model)



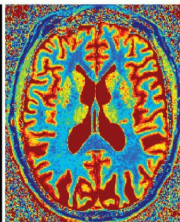
Fractional anisotropy
(color-coded)

Arterial spin labelling



Tissue perfusion
[ml/100mg/min]

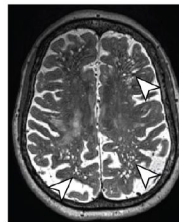
Quantitative relaxometry



Quantitative T1 map
[ms]

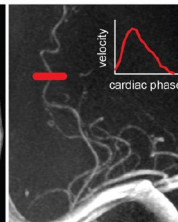
Vessel structure and function

High resolution imaging



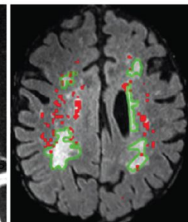
Enlarged perivascular spaces

Perforator imaging



7T angiography and single vessel blood flow metrics

Dynamic contrast enhanced MRI



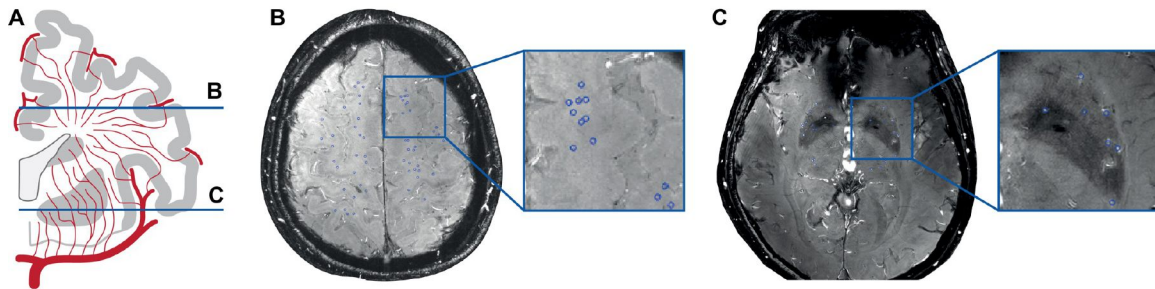
Blood-brain barrier permeability

Review: Vemuri, DeCarli, Duering, *Stroke* 2022



16

From brain structure to vessel function



Review: Van den Brink, Doubal, Duering, Int J Stroke 2023, MR images courtesy of Hilde van den Brink

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Take Home Messages

Lesion markers

- Segmentation **challenges**
- **nnU-Net** as benchmark method
- **Ground truth quality** equally important as algorithm performance!

Quantitative imaging markers

- Intended use → Targeted **validation** studies
- Requirements? Pitfalls? Added benefit?
- **Paradigm shift**: Lesions → Brain structure → Vessel function

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