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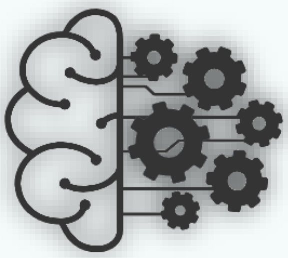
Towards application of AI to MS

State of the art



IX NapleSMeeting
1st Dec 2023, Napoli

Giuseppe Pontillo, MD, PhD

Amsterdam UMC
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Disclosures

Giuseppe Pontillo received research grants from MAGNIMS, ESNR, and ECTRIMS

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Outline

- Introduction
- AI for MRI acquisition and analysis
- AI for the diagnosis of MS
- AI for patient stratification
- Conclusions

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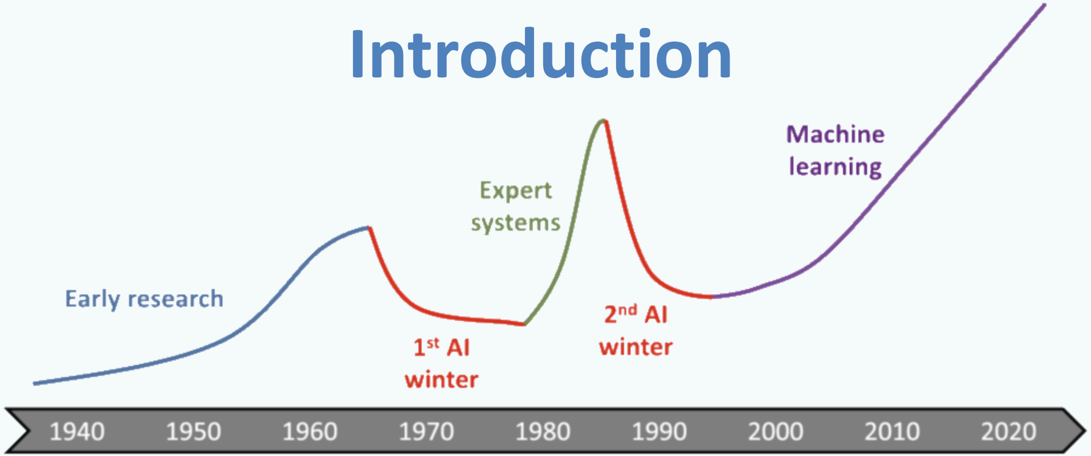
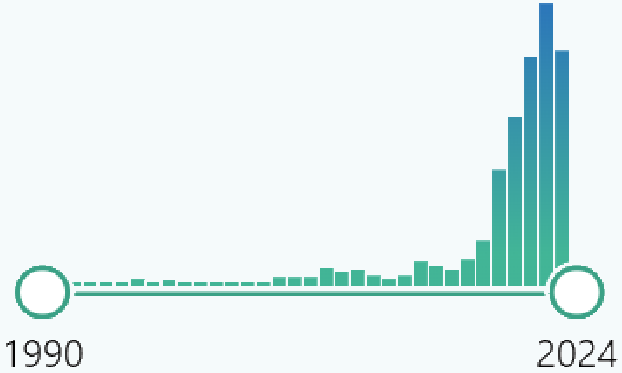
Introduction



Search query: "multiple sclerosis" AND ("artificial intelligence" OR "machine learning" OR "deep learning")



Colliot, et al. Machine Learning for Brain Disorders 2023

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Introduction

npj | Digital Medicine

www.nature.com/npjdigitalmed

REVIEW ARTICLE OPEN

Check for updates

Guidelines and quality criteria for artificial intelligence-based prediction models in healthcare: a scoping review

Anne A. H. de Hond[1,2,3,8] ✉, Artuur M. Leeuwenberg[4,8], Lotty Hooft[4,5], Ilse M. J. Kant[1,2,3], Steven W. J. Nijman[4], Hendrikus J. A. van Os[2,6], Jiska J. Aardoom[6,7], Thomas P. A. Debray[4], Ewoud Schuit[4], Maarten van Smeden[4], Johannes B. Reitsma[4], Ewout W. Steyerberg[2,3], Niels H. Chavannes[6,7] and Karel G. M. Moons[4]

Radiology: Artificial Intelligence — EDITORIAL

AI Reporting Guidelines: How to Select the Best One for Your Research

Michail E. Klontzas, MD, PhD • Anthony A. Gatti, PhD • Ali S. Tejani, MD • Charles E. Kahn, Jr, MD, MS

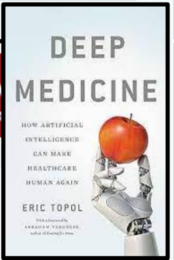
nature medicine

REVIEW A

https://doi.org/10.1038/s4

AI in health and medicine

Pranav Rajpurkar[1,4], Emma Chen[2,4], Oishi Banerjee[2,4] and Eric J. Topol[3] ✉



Radiology: Artificial Intelligence — SPECIAL REPORT

Artificial Intelligence and Radiology Education

Ali S. Tejani, MD • Hesham Elhalawani, MD • Linda Moy, MD • Marc Kohli, MD • Charles E. Kahn, Jr, MD, MS

Radiology: Artificial Intelligence — EDITORIAL

Will Artificial Intelligence Replace Radiologists?

Curtis P. Langlotz, MD, PhD

Radiology: Artificial Intelligence — EDITORIAL

Checklist for Artificial Intelligence in Medical Imaging (CLAIM): A Guide for Authors and Reviewers

John Mongan, MD, PhD • Linda Moy, MD • Charles E. Kahn, Jr, MD, MS

Lancet Digit Health. 2023 Jul;5(7):e400-e402. doi: 10.1016/S2589-7500(23)00090-0.

Position statement on clinical evaluation of imaging AI

Cathal McCague [1], Katherine MacKay [2], Ceilidh Welsh [3], Alex Constantinou [3], Rajesh Jena [4], Mireia Crispin-Ortuzar [5]; Imaging AI evaluation consensus group

IX NapleSMeeting
1 Dicembre 2023
Renaissance Naples Hotel Mediterraneo - Napoli

Amsterdam UMC
Universitair Medische Centra

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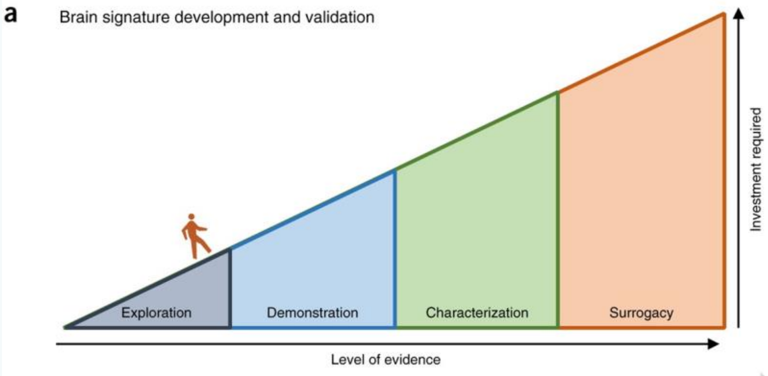
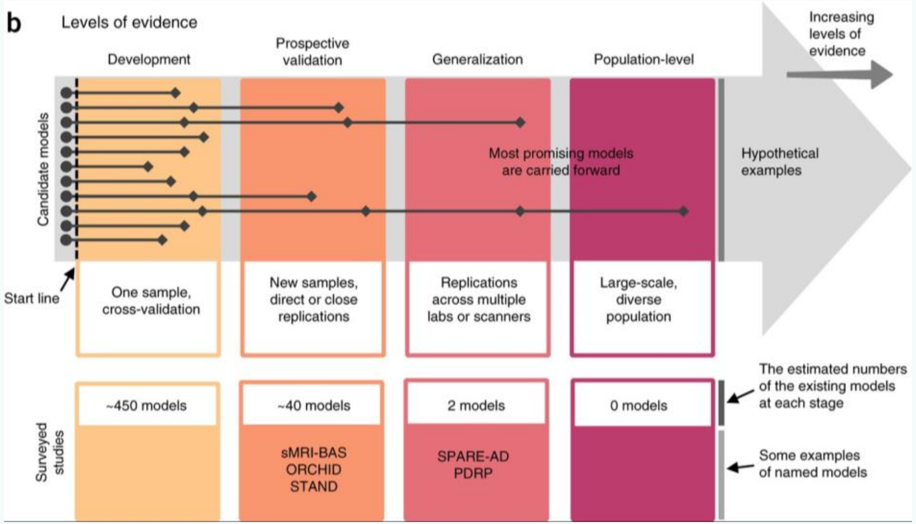
Introduction

Building better biomarkers: brain models in translational neuroimaging

Choong-Wan Woo, Luke J Chang, Martin A Lindquist & Tor D Wager

Nature Neuroscience **20**, 365–377 (2017) | Cite this article





Woo, et al. Nat Neurosci. 2017

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AI for MRI – *Protocol optimization/image synthesis*

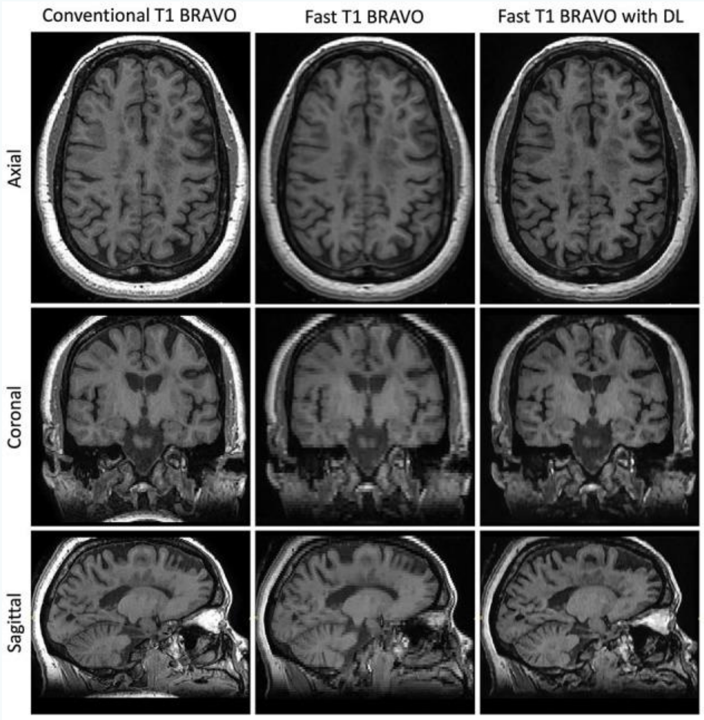
Accelerated Imaging

Applying Deep Learning to Accelerated Clinical Brain Magnetic Resonance Imaging for Multiple Sclerosis

Ashika Mani[1†], Tales Santini[2†], Radhika Puppala[3†], Megan Dahl[3], Shruthi Venkatesh[3], Elizabeth Walker[3], Megan DeHaven[3], Cigdem Isitan[3], Tamer S. Ibrahim[2], Long Wang[4], Tao Zhang[4], Enhao Gong[4], Jessica Barrios-Martinez[5], Fang-Cheng Yeh[5], Robert Krafty[6], Joseph M. Mettenburg[7] and Zongqi Xia[2,3]*

- Deep back-projection network to reconstruct higher-quality images from under-sampled k-space

- Comparable segmentation performance and association with clinical severity



2:57 min → 1:13 min

Mani, et al. Front Neurol 2021

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AI for MRI – *Protocol optimization/image synthesis*

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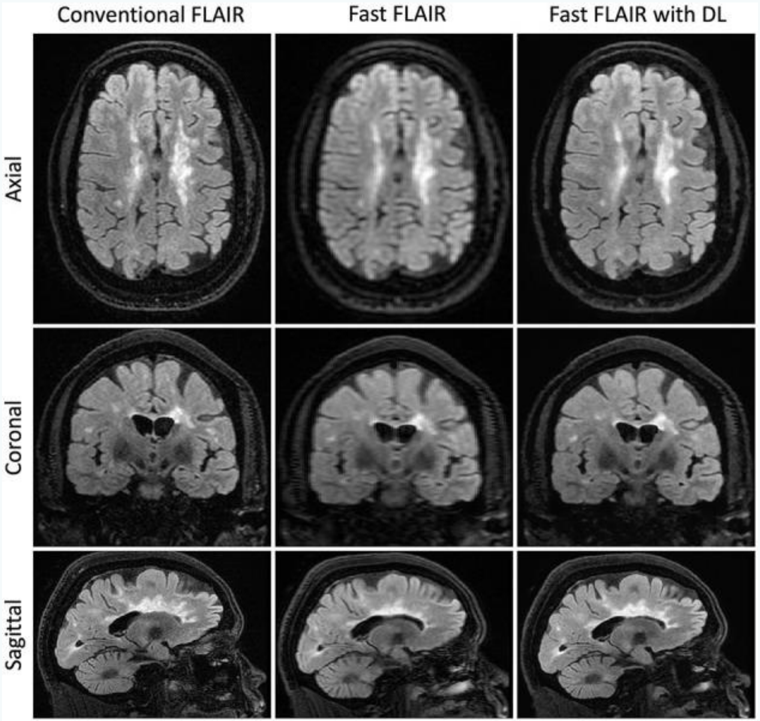


6:40 min → 1:13 min

Mani, et al. Front Neurol 2021

AI for MRI – *Protocol optimization/image synthesis*

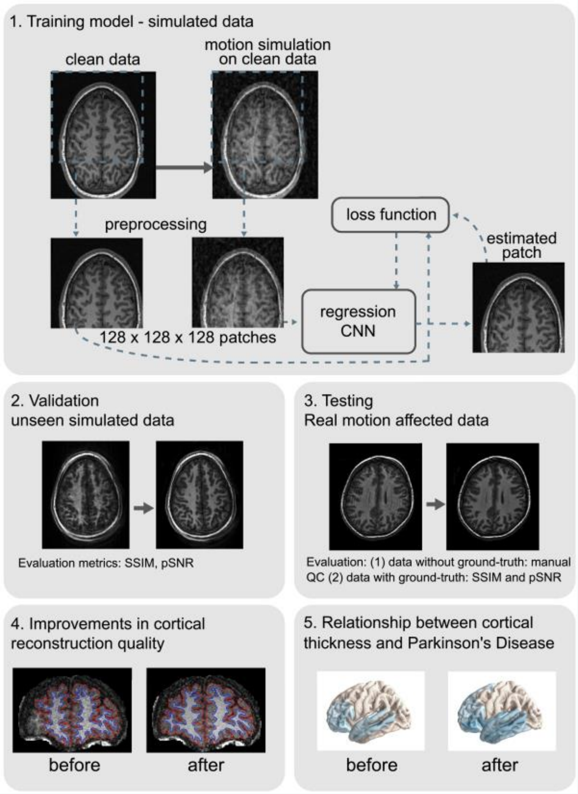
Image correction / Quality control

Retrospective motion artifact correction of structural MRI images using deep learning improves the quality of cortical surface reconstructions ☆

Ben A Duffy, Lu Zhao, Farshid Sepehrband, Joyce Min, Danny JJ Wang, Yonggang Shi, Arthur W Toga, Hosung Kim*, for the Alzheimer's Disease Neuroimaging Initiative

- Retrospective motion correction using a motion simulation model combined with a 3D convolutional neural network (CNN)

- Significant improvement in cortical surface reconstruction and association with clinical status



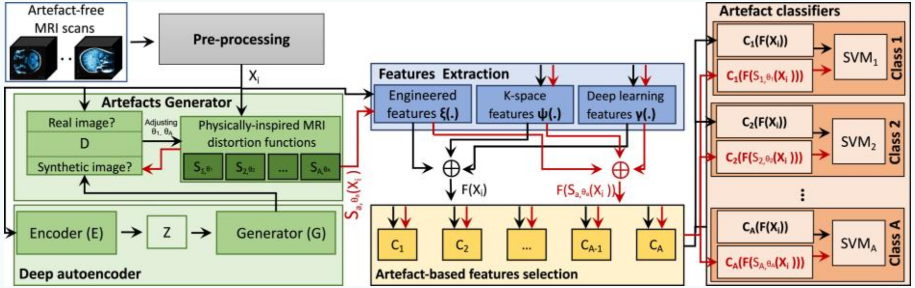
Duffy, et al. Neuroimage 2021

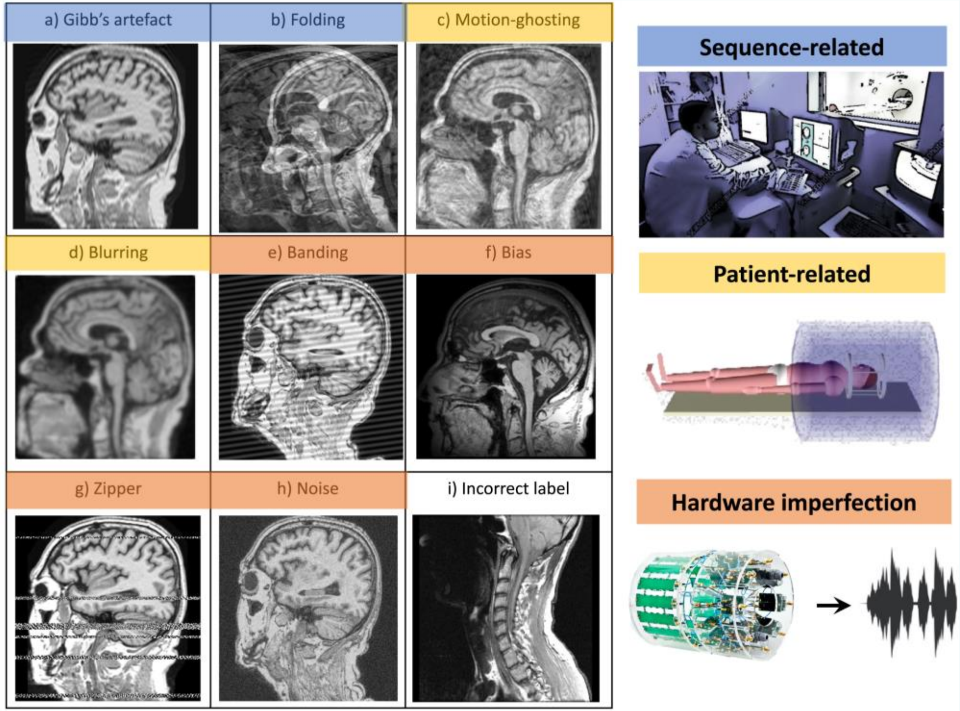
AI for MRI – *Protocol optimization/image synthesis*

Image correction / Quality control

An efficient semi-supervised quality control system trained using physics-based MRI-artefact generators and adversarial training

Daniele Ravi [a,d,e,*], for the Alzheimer's Disease Neuroimaging Initiative[1], Frederik Barkhof [c,b,d,f,g], Daniel C. Alexander [a,d], Lemuel Puglisi [d], Geoffrey J.M. Parker [b,d,f], Arman Eshaghi [a,d,f]





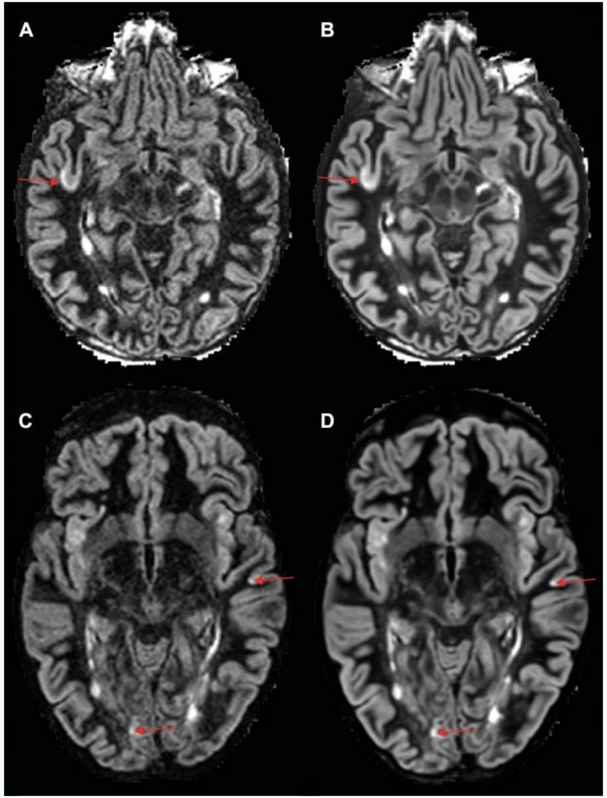
Ravi, et al. Med Image Anal 2023

AI for MRI – *Protocol optimization/image synthesis*

Contrast generation

Multicenter Evaluation of AI-generated DIR and PSIR for Cortical and Juxtacortical Multiple Sclerosis Lesion Detection

Piet M. Bouman, PhD • Samantha Noteboom, MSc • Fernando A. Nobrega Santos, PhD • Erin S. Beck, PhD • Gregory Bliault, MSc • Marco Castellaro, PhD • Massimiliano Calabrese, PhD • Declan T. Chard, PhD • Paul Eichinger, PhD • Massimo Filippi, PhD • Matilde Inglese, PhD • Caterina Lapucci, PhD • Andrzej Marciniak, PhD • Bastiaan Moraal, PhD • Alfredo Morales Pinzon, PhD • Mark Mühlau, PhD • Paolo Preziosa, PhD • Daniel S. Reich, PhD • Maria A. Rocca, PhD • Menno M. Schoonheim, PhD • Jos W. R. Twisk, PhD • Benedict Wiestler, PhD • Laura E. Jonkman, PhD • Charles R. G. Guttmann, PhD • Jeroen J. G. Geurts, PhD • Martijn D. Steenwijk, PhD



- Generative adversarial network (GAN) to generate DIR/PSIR from T1w and PD/T2w images

- High between-center (ICC= 0.81 for DIR, 0.75 for PSIR) and between-reader (ICC=0.76 for DIR, 0.85 for PSIR) reliability (N = 202)

Bouman, et al. Radiology 2023

AI for MRI – *Protocol optimization/image synthesis*

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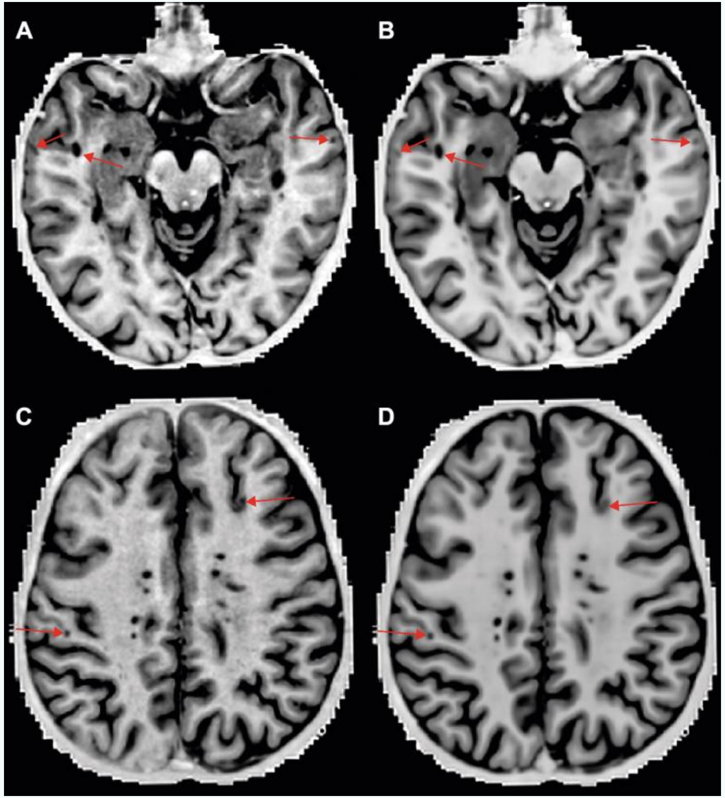

Bouman, et al. Radiology 2023

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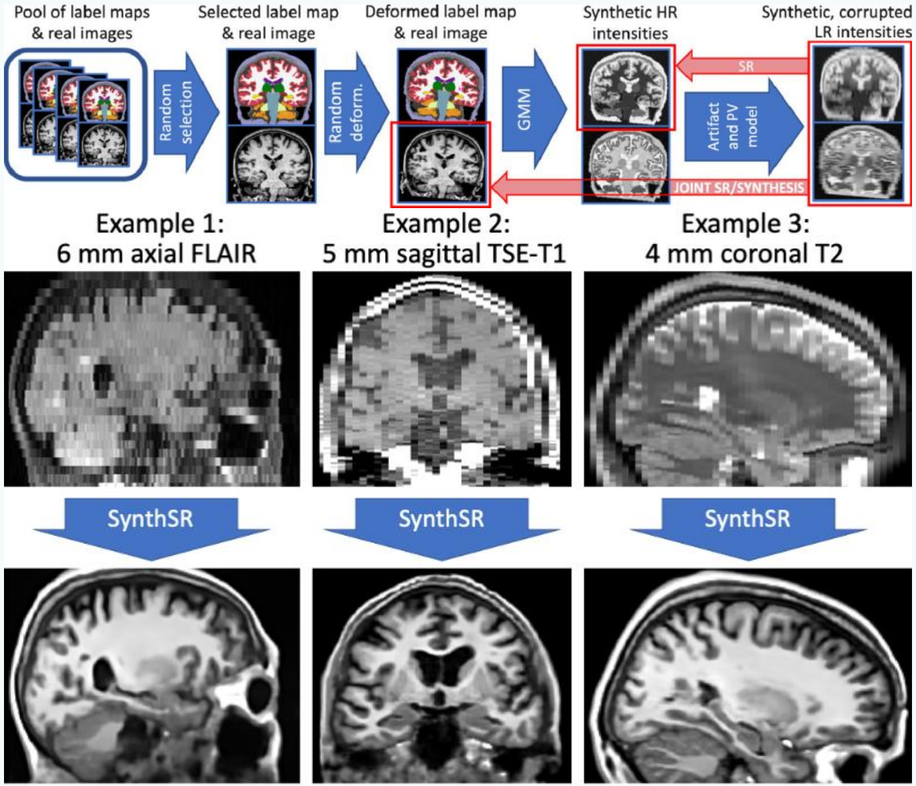
AI for MRI – *Protocol optimization/image synthesis*

Super-resolution

SynthSR: A public AI tool to turn heterogeneous clinical brain scans into high-resolution T1-weighted images for 3D morphometry

Juan E. Iglesias[1,2,3]*, Benjamin Billot[2], Yaël Balbastre[1], Colin Magdamo[4], Steven E. Arnold[4], Sudeshna Das[4], Brian L. Edlow[1,4,5], Daniel C. Alexander[2], Polina Golland[3], Bruce Fischl[1,3]

- Turns clinical brain MRI scans of any contrast, orientation, and resolution into high-resolution T1w scans suitable for 3D morphometry



Iglesias, et al. Science Advances 2023

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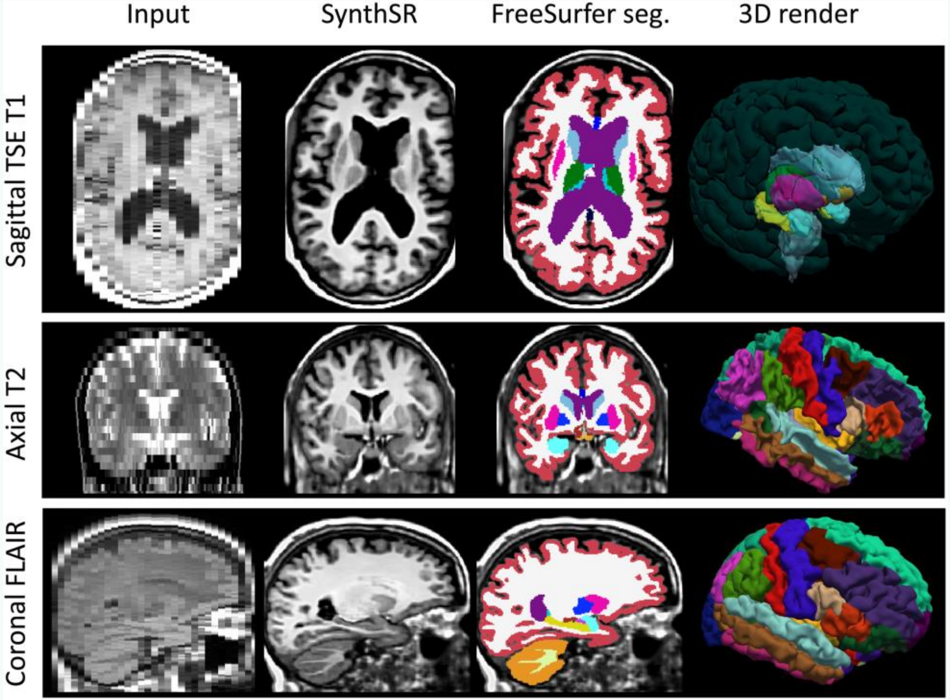

Iglesias, et al. Science Advances 2023

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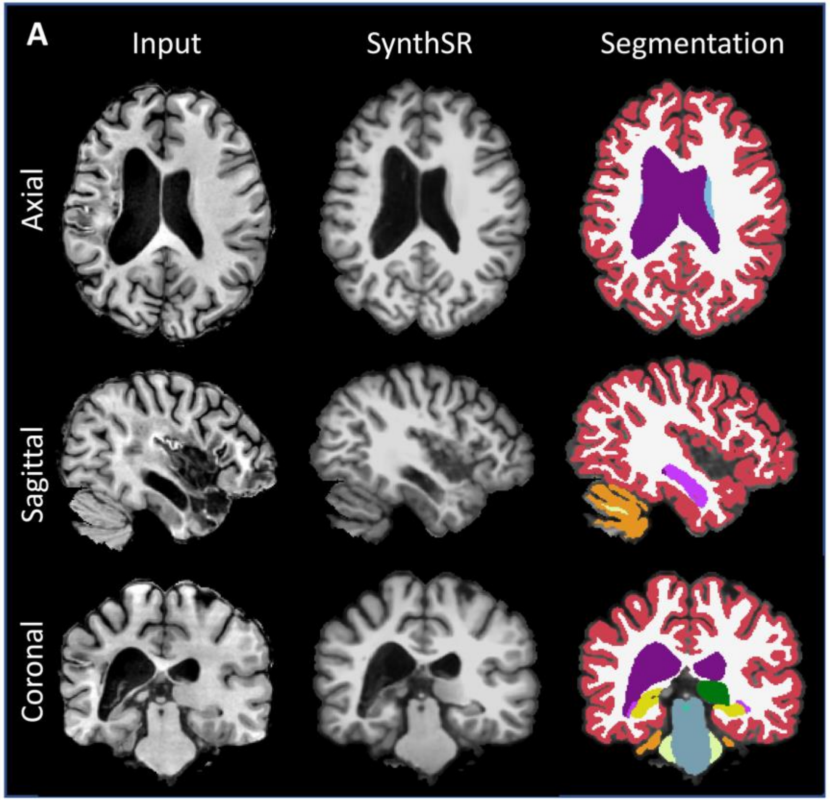
- Turns clinical brain MRI scans of any contrast, orientation, and resolution into high-resolution T1w scans suitable for 3D morphometry

- Performance on segmentation and registration tasks comparable to high-resolution T1w scans

- Robust to the presence of lesions



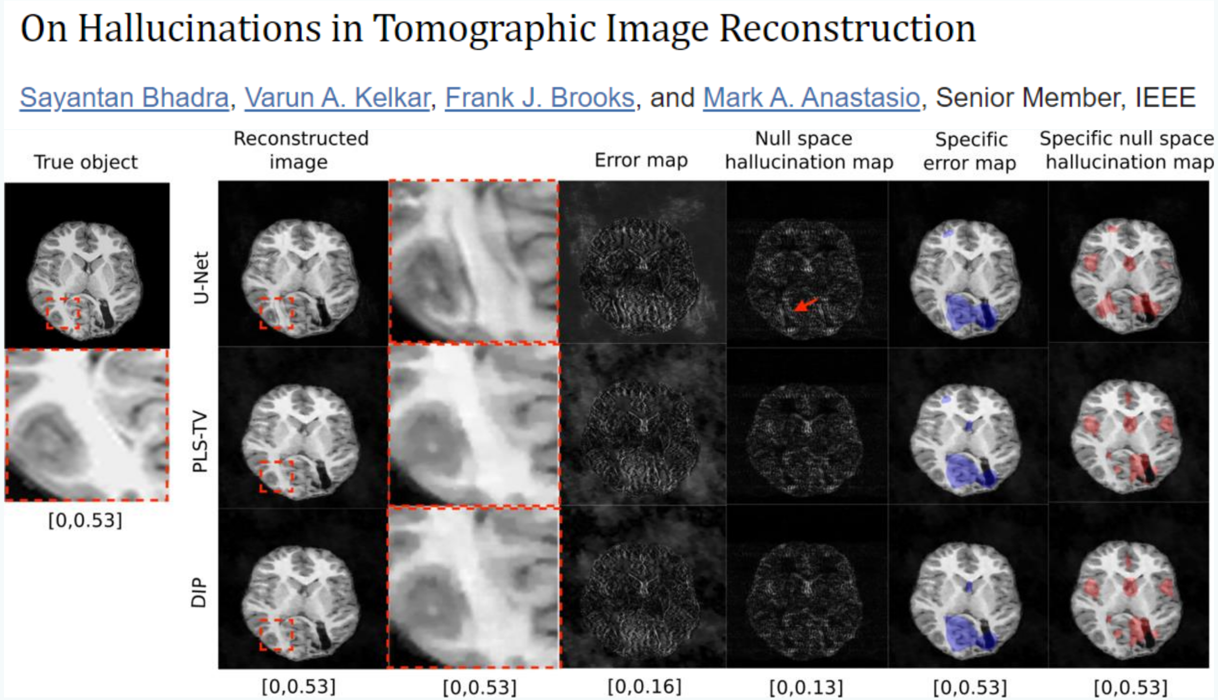
Iglesias, et al. Science Advances 2023

AI for MRI – *Protocol optimization/image synthesis*

Hallucinations

- DL-based image reconstructions are associated with the danger of creating false structures (hallucinations)!

- This risk can be quantified and analysed



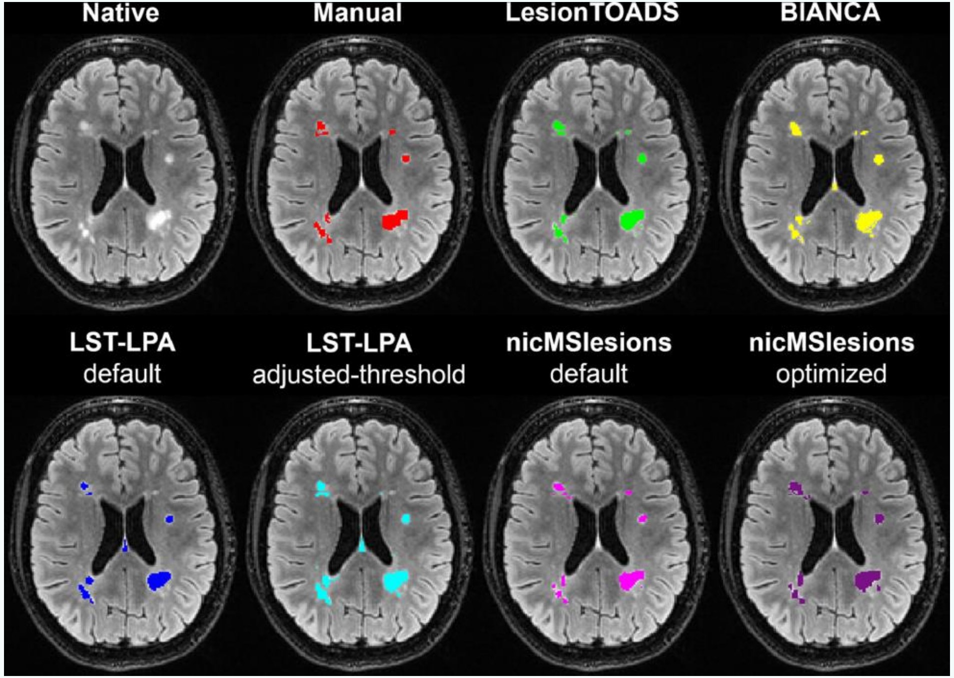
Bhadra, et al. IEEE Trans Med Imaging 2021

AI for MRI – *Lesion segmentation*

Comparing lesion segmentation methods in multiple sclerosis: Input from one manually delineated subject is sufficient for accurate lesion segmentation

M.M. Weeda[a,*], I. Brouwer[a], M.L. de Vos[a], M.S. de Vries[a], F. Barkhof[a,b], P.J.W. Pouwels[a], H. Vrenken[a]

- MICCAI and ISBI MS lesion segmentation challenges
- CNN-based strategies outperform alternative methods
- Best performance with supervised methods optimized to the local dataset (ICC > 0.97 and median Dice's SI > 0.64)



Weeda, et al. Neuroimage Clin 2019

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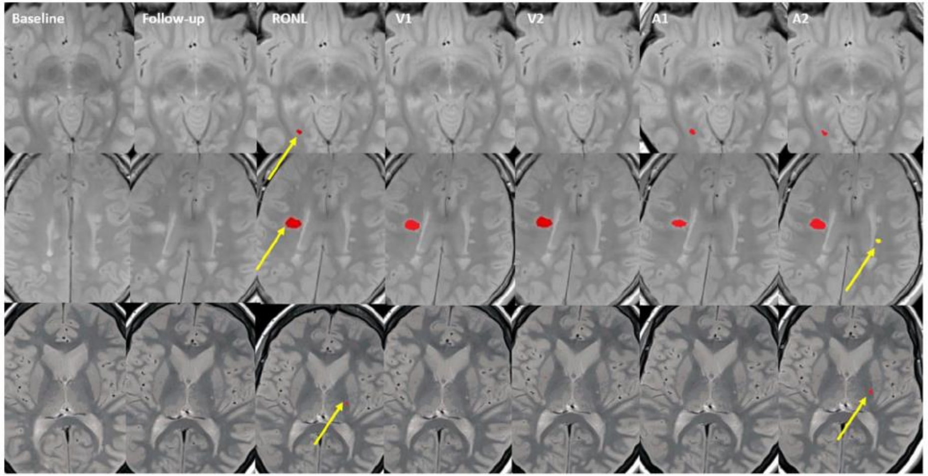
AI for MRI – *Lesion segmentation*

Assessment of automatic decision-support systems for detecting active T2 lesions in multiple sclerosis patients

Alex Rovira, Juan Francisco Corral, Cristina Auger, Sergi Valverde, Angela Vidal-Jordana, Arnau Oliver, Andrea de Barros, Yiken Karelys Ng Wong, Mar Tintoré, Deborah Pareto, Francesc Xavier Aymerich, Xavier Montalban, Xavier Lladó and Juli Alonso



- For new/enlarging T2 lesions, automated methods are more sensitive than visual assessment but many false positives

- Visually supervised automated methods could improve detection in clinical practice

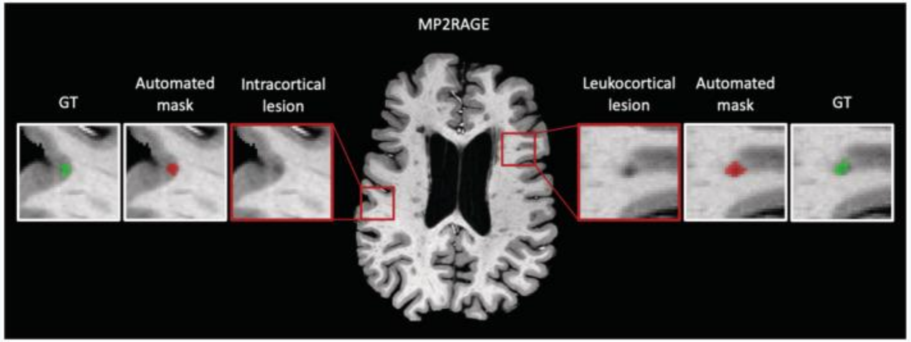
	V1	V2	A1	A2	V1A2
True negatives	62[a]	62[a]	52[a]	54[a]	62[a]
False negatives	9[a]	4[a]	3[a]	1[a]	2[a]
True positives	29[a]	34[a]	35[a]	37[a]	36[a]
False positives	0[a]	0[a]	10[a]	8[a]	0[a]
Sensitivity (CI)	76.32 (59.76–88.56)	89.47 (75.20–97.06)	92.11 (78.62–98.34)	97.37 (86.19–99.93)	94.74 (85.25–99.36)
Specificity (CI)	100.00 (CI: 94.22–100.00)	100.00 (94.22–100.00)	83.87 (72.33–91.98)	87.10 (76.15–94.26)	100.00 (94.22–100.00)
Accuracy (CI)	91.00 (83.60–95.80)	96.00 (90.07–98.90)	87.00 (78.80–92.89)	91.00 (83.60–95.80)	98.00 (92.96–99.76)

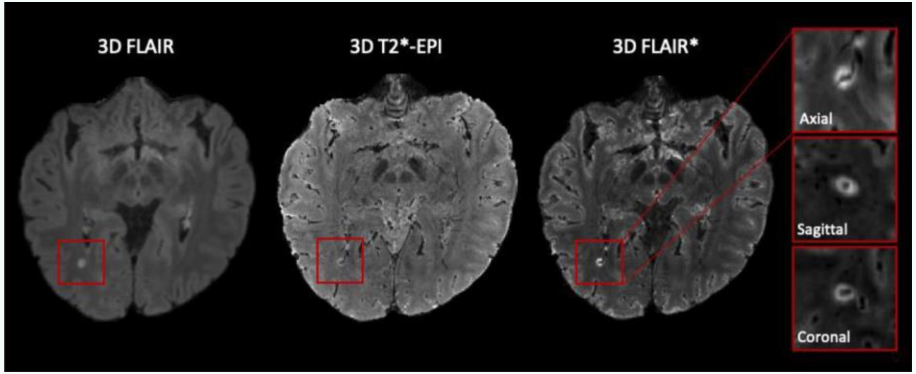
Rovira, et al. Mult Scler 2022

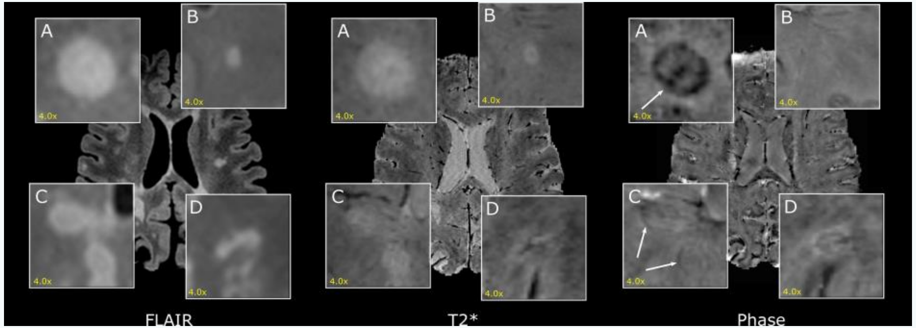
AI for MRI – *Lesion segmentation*

Cortical lesions, central vein sign, and paramagnetic rim lesions in multiple sclerosis: Emerging machine learning techniques and future avenues

Francesco La Rosa [a,b,c,*], Maxence Wynen [b,d,e,f], Omar Al-Louzi [g,h], Erin S Beck [c,g], Till Huelnhagen [a,f,i], Pietro Maggi [e,j,k], Jean-Philippe Thiran [a,b,f], Tobias Kober [a,f,i], Russell T Shinohara [l,m,n], Pascal Sati [g,h], Daniel S Reich [g], Cristina Granziera [o,p], Martina Absinta [q,r], Meritxell Bach Cuadra [b,f]







La Rosa, et al. Neuroimage Clin 2022

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AI for MRI – *Atrophy measurement*

A contrast-adaptive method
segmentation in multiple scl

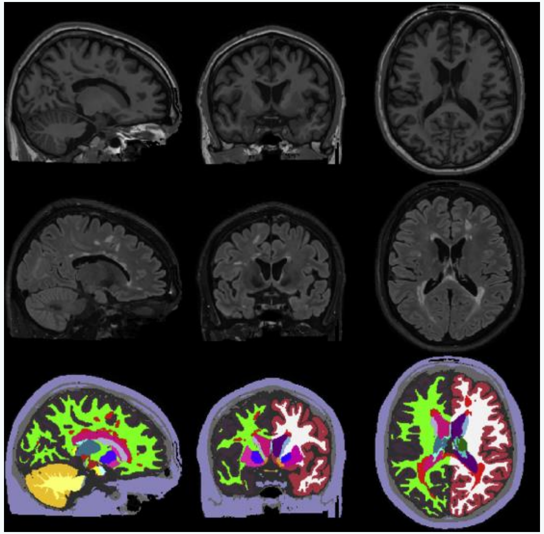
Stefano Cerri[a,b,*], Oula Puonti[b], Dom
Hartwig R. Siebner[b,e,f], Koen Van Le

SynthSeg: Segmentation of brain MRI sc
without retraining

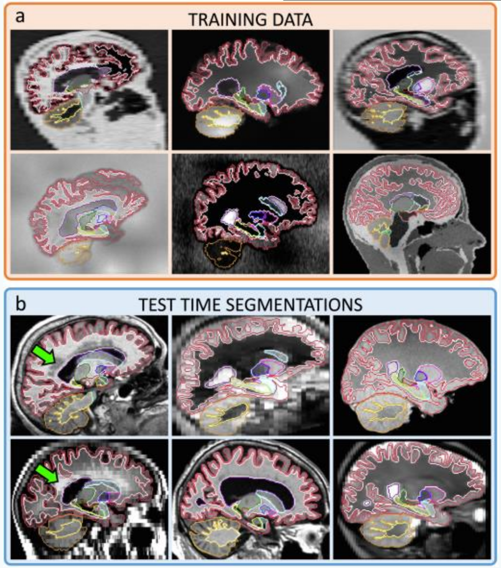
Benjamin Billot[a,*], Douglas N. Greve[b], Oula Puont
Bruce Fischl[b,e,f], Adrian V. Dalca[b,e], Juan Eugenio

Fully Automatic Method for Reliable Spinal Cord Compartment Segmentation in Multiple Sclerosis

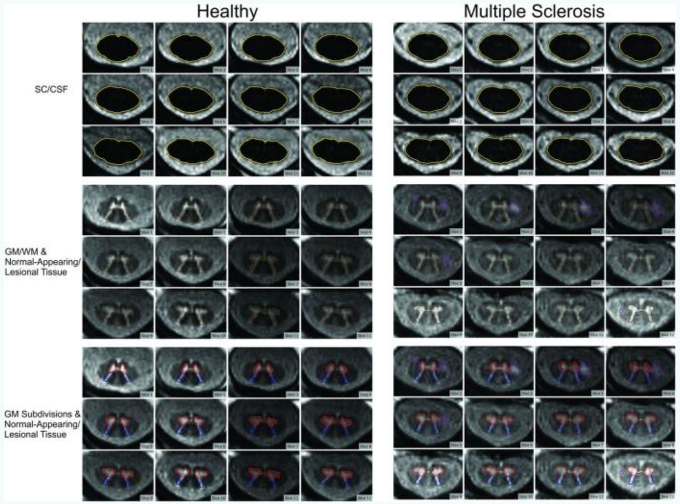
C. Tsagkas, A. Horvath-Huck, T. Haas, M. Amann, A. Todea, A. Altermatt, J. Müller, A. Cagol, M. Leimbacher, M. Barakovic, M. Weigel, S. Pezold, T. Sprenger, L. Kappos, O. Bieri, C. Granziera, P. Cattin, and K. Parmar



Cerri, et al. Neuroimage Clin 2022



Billot, et al. Med Image Anal 2023



Tsagkas, et al. AJNR 2023

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AI for MRI – *Quantitative reports*

Commercial volumetric MRI reporting tools in multiple sclerosis: a systematic review of the evidence

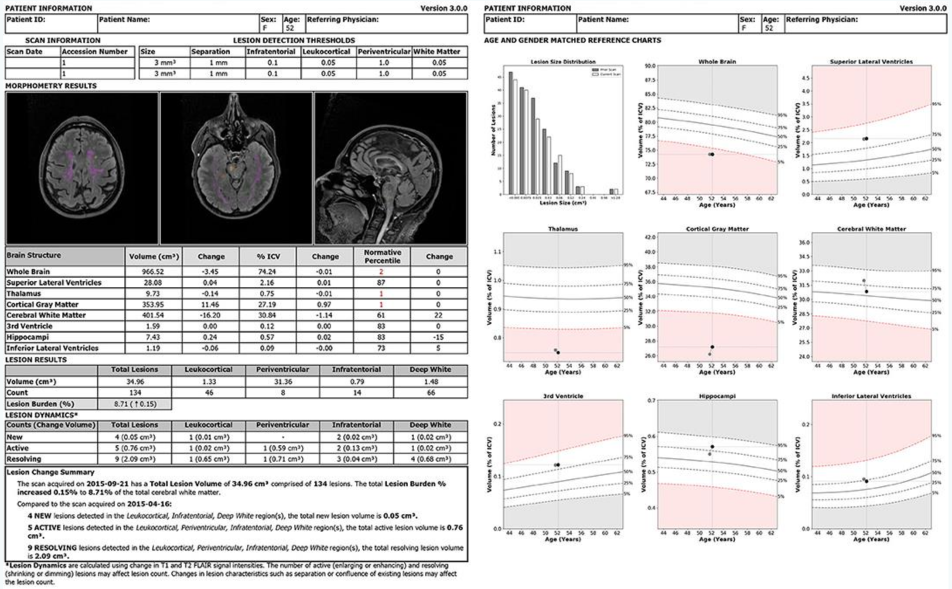
Zoe Mendelsohn[1,2,3,4,5] · Hugh G. Pemberton[1,2,6] · James Gray[7] · Olivia Goodkin[1,2,3] · Ferran Prados Carrasco[2,3,8] · Michael Scheel[4] · Jawed Nawabi[5,9] · Frederik Barkhof[1,2,3,10]

The utility of these tools should be critically evaluated:

- robustness of segmentation to inter-scanner variability and MR artifacts

- need for proven clinically-relevant cut-offs

- mandatory visual check



PATIENT INFORMATION Version 3.0.0

Patient ID:	Patient Name:	Sex: F	Age: 52	Referring Physician:

SCAN INFORMATION / LESION DETECTION THRESHOLDS

Scan Date	Accession Number	Size	Separation	Infratentorial	Leukocortical	Periventricular	White Matter
	1	3 mm³	1 mm	0.1	0.05	1.0	0.05
	1	3 mm³	1 mm	0.1	0.05	1.0	0.05

MORPHOMETRY RESULTS

Brain Structure	Volume (cm³)	Change	% ICV	Change	Normative Percentile	Change
Whole Brain	966.52	-3.45	74.24	-0.01	2	0
Superior Lateral Ventricles	28.08	0.04	2.16	0.01	87	0
Thalamus	9.73	-0.14	0.75	-0.01	1	0
Cortical Gray Matter	353.95	11.46	27.19	0.97	1	0
Cerebral White Matter	401.54	-16.20	30.84	-1.14	61	22
3rd Ventricle	1.59	0.00	0.12	0.00	83	0
Hippocampi	7.43	0.24	0.57	0.02	83	-15
Inferior Lateral Ventricles	1.19	-0.06	0.09	-0.00	73	5

LESION RESULTS

	Total Lesions	Leukocortical	Periventricular	Infratentorial	Deep White
Volume (cm³)	34.96	1.33	31.36	0.79	1.48
Count	134	46	8	14	66
Lesion Burden (%)	8.71 (↑0.15)				

LESION DYNAMICS*

Counts (Change Volume)	Total Lesions	Leukocortical	Periventricular	Infratentorial	Deep White
New	4 (0.05 cm³)	1 (0.01 cm³)	-	2 (0.02 cm³)	1 (0.02 cm³)
Active	5 (0.76 cm³)	1 (0.02 cm³)	1 (0.59 cm³)	2 (0.13 cm³)	1 (0.02 cm³)
Resolving	9 (2.09 cm³)	1 (0.65 cm³)	1 (0.71 cm³)	3 (0.04 cm³)	4 (0.68 cm³)

Lesion Change Summary

The scan acquired on **2015-09-21** has a **Total Lesion Volume** of **34.96 cm³** comprised of **134** lesions. The total **Lesion Burden %** **increased 0.15%** to **8.71%** of the total cerebral white matter.

Compared to the scan acquired on **2015-04-16:**

4 NEW lesions detected in the *Leukocortical, Infratentorial, Deep White* region(s), the total new lesion volume is **0.05 cm³.**

5 ACTIVE lesions detected in the *Leukocortical, Periventricular, Infratentorial, Deep White* region(s), the total active lesion volume is **0.76 cm³.**

9 RESOLVING lesions detected in the *Leukocortical, Periventricular, Infratentorial, Deep White* region(s), the total resolving lesion volume is **2.09 cm³.**

***Lesion Dynamics** are calculated using change in T1 and T2 FLAIR signal intensities. The number of active (enlarging or enhancing) and resolving (shrinking or dimming) lesions may affect lesion count. Changes in lesion characteristics such as separation or confluence of existing lesions may affect the lesion count.

PATIENT INFORMATION Version 3.0.0

Patient ID:	Patient Name:	Sex: F	Age: 52	Referring Physician:

AGE AND GENDER MATCHED REFERENCE CHARTS

Mendelsohn, et al. Neuroradiology 2022

Outline

- Introduction
- AI for MRI acquisition and analysis
- **AI for the diagnosis of MS**
- AI for patient stratification
- Conclusions

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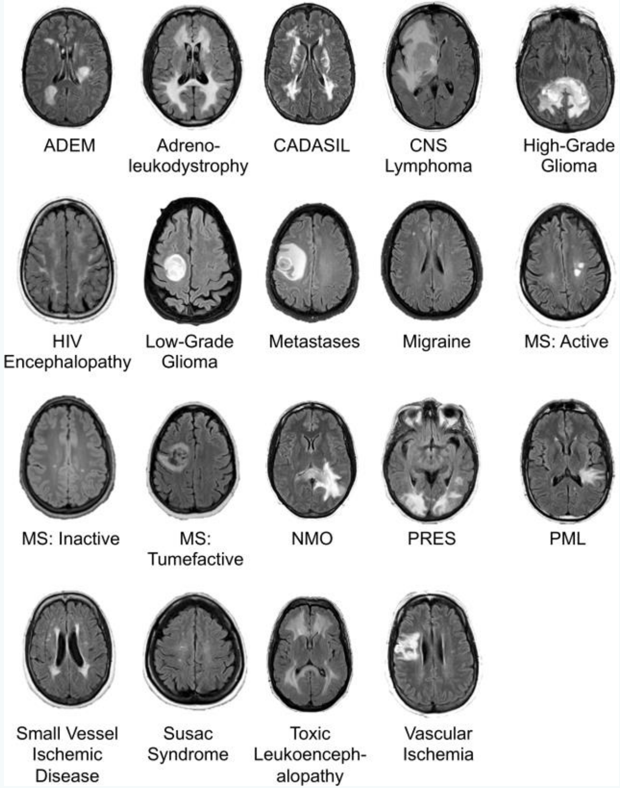
AI for the diagnosis of MS

Artificial Intelligence System Approaching Neuroradiologist-level Differential Diagnosis Accuracy at Brain MRI

Andreas M. Rauschecker, MD, PhD • Jeffrey D. Rudie, MD, PhD* • Long Xie, PhD • Jiancong Wang, BS • Michael Tran Duong, BA • Emmanuel J. Botzolakis, MD, PhD • Asha M. Kovalovich, MD • John Egan, MD • Tessa C. Cook, MD, PhD • R. Nick Bryan, MD, PhD • Ilya M. Nasrallah, MD, PhD • Suyash Mohan, MD • James C. Gee, PhD*

- AI system (DL+feature engineering+Bayesian classifier) for differential diagnosis across a range of brain diseases including MS (N~100)

- Performance similar to academic neuroradiologists (91% vs 86%, p=0.20), higher than neuroradiology fellows (77%, p=0.003), general radiologists (57%, p<0.001), and residents (56%, p<0.001)



Rauschecker, et al. Radiology 2020

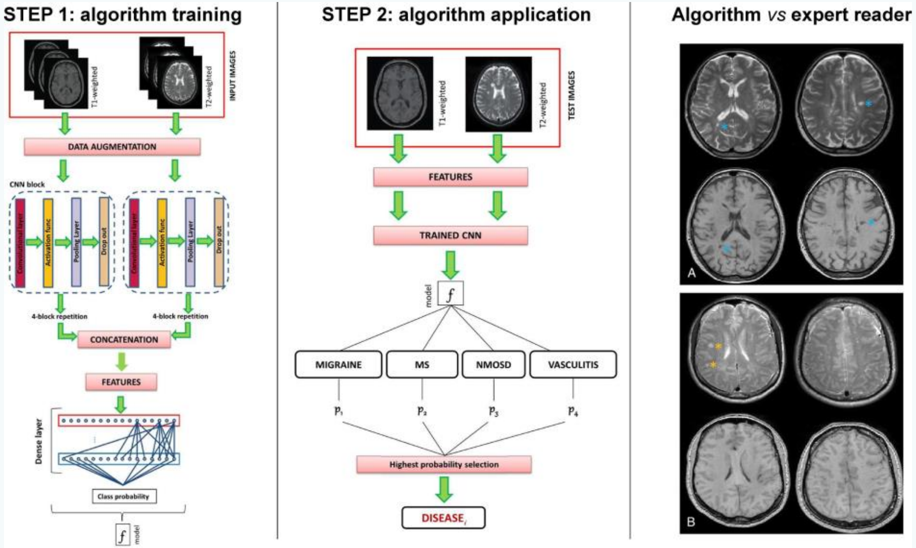
AI for the diagnosis of MS

Deep Learning on Conventional Magnetic Resonance Imaging Improves the Diagnosis of Multiple Sclerosis Mimics

Maria A. Rocca, MD,† Nicoletta Anzalone, MD,‡§ Loredana Storelli, PhD,* Anna Del Poggio, MD,‡ Laura Cacciaguerra, MD,*†§ Angelo A. Manfredi, MD,§|| Alessandro Meani, MSc,* and Massimo Filippi, MD*†§¶*

- CNN for differential diagnosis based on T1w and T2w across MS, NMOSD, migraine, and vasculitis (N=268)

- In the test set, deep learning was better than expert raters, highest diagnostic accuracy in MS (99% vs 73%% and 82%, p<0.001) and the lowest in NMOSD (88.6% vs 4.4%, p<0.001, for both raters)



Rocca, et al. Invest Radiol 2020

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Outline

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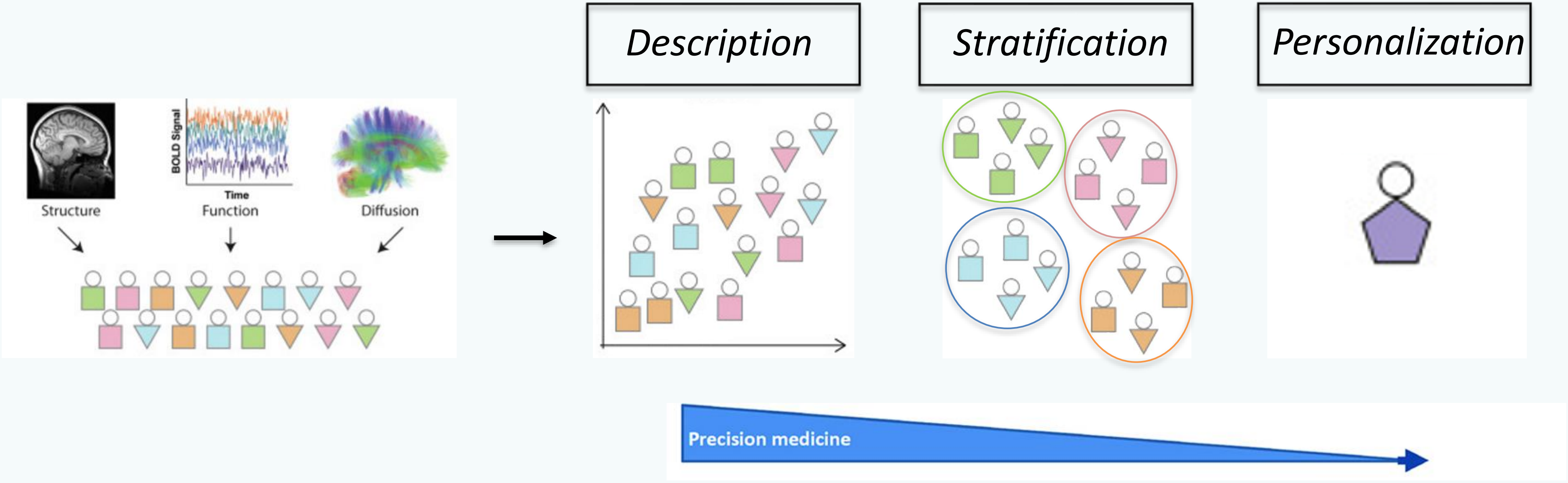
AI for patient stratification

MS is neurobiologically and phenotypically heterogeneous. MRI abnormalities are objective disease markers. Handling heterogeneity is crucial for personalized clinical management.



Colliot, et al. Machine Learning for Brain Disorders 2023

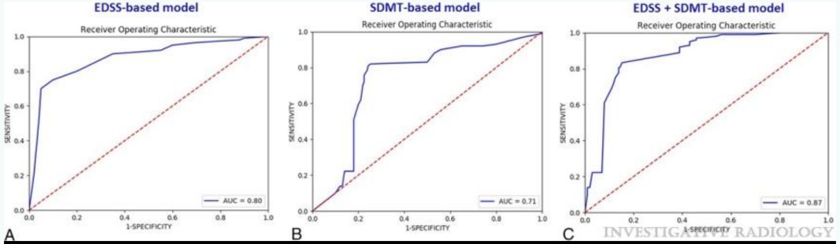
AI for patient stratification – *Predictive models*

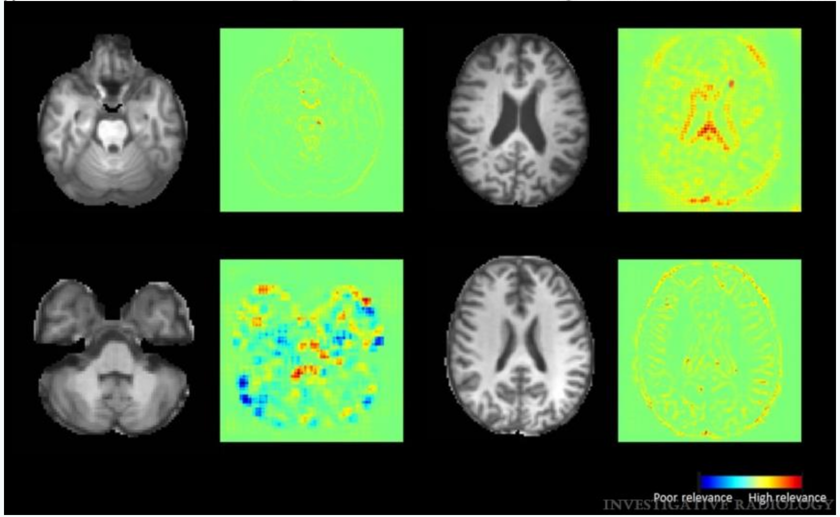
A Deep Learning Approach to Predicting Disease Progression in Multiple Sclerosis Using Magnetic Resonance Imaging

Loredana Storelli, PhD, Matteo Azzimonti, MD,*†‡ Mor Gueye, MD,*†‡ Carmen Vizzino, MSc,* Paolo Preziosa, MD, PhD,*† Gioachino Tedeschi, MD,§ Nicola De Stefano, MD, PhD,|| Patrizia Pantano, MD, PhD,¶# Massimo Filippi, MD,*†‡**†† and Maria A. Rocca, MD*†‡*

- CNN to predict 2-year EDSS, SDMT, and EDSS+SDMT worsening based on T1w and T2w scans (N=373)

- Out-of-sample accuracy was 83% (for EDSS), 68% (for SDMT), and 86% (for EDSS+SDMT, 70% for human raters)

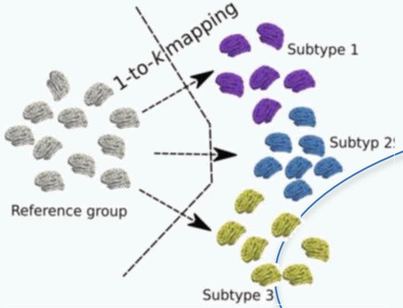




Storelli, et al. Invest Radiol 2020

AI for patient stratification – *Subtyping and DPM*

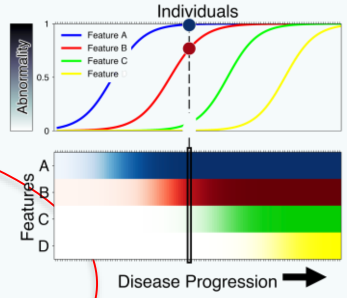
Family of (mostly unsupervised or semi-supervised) machine learning algorithms that estimate disease subgroups and/or the most probable order of events over the course of the disease



Subtyping

SuStaIn

Disease progression modelling



Phenotypic heterogeneity

Temporal heterogeneity

Colliot, et al. Machine Learning for Brain Disorders 2023

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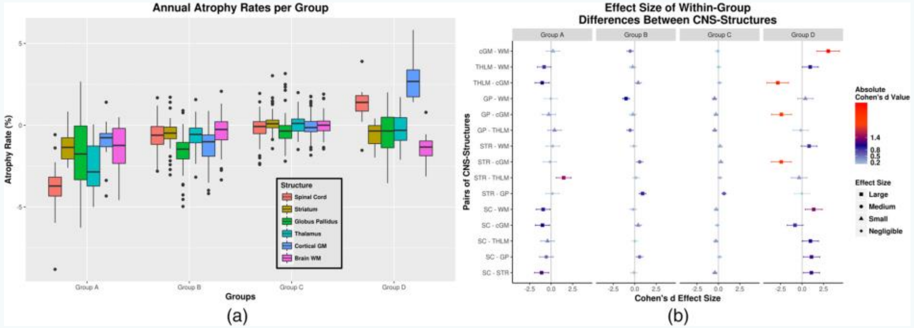
AI for patient stratification – *Subtyping*

Classification of multiple sclerosis based on patterns of CNS regional atrophy covariance

Charidimos Tsagkas[1,2,3] | Katrin Parmar[1,2] | Simon Pezold[4] | Christian Barro[1,5] | Mallar M. Chakravarty[6,7,8] | Laura Gaetano[9] | Yvonne Naegelin[1] | Michael Amann[1,3,4] | Athina Papadopoulou[1,2,10] | Jens Wuerfel[3,4,10] | Ludwig Kappos[1,2] | Jens Kuhle[1] | Till Sprenger[1,11] | Cristina Granziera[1,2] | Stefano Magon[1,12]



JAMA Neurology | Original Investigation

Identifying the Distinct Cognitive Phenotypes in Multiple Sclerosis

Ermelinda De Meo, MD; Emilio Portaccio, MD; Antonio Giorgio, MD; Luis Ruano, MD; Benedetta Goretti, MSc; Claudia Niccolai, MSc; Francesco Patti, MD; Clara Grazia Chisari, MSc; Paolo Gallo, MD; Paola Grossi, MSc; Angelo Ghezzi, MD; Marco Roscio, MSc; Flavia Mattioli, MD; Chiara Stampatori, MSc; Marta Simone, MD; Rosa Gemma Viterbo, MSc; Raffaello Bonacchi, MD; Maria A. Rocca, MD; Nicola De Stefano, MD; Massimo Filippi, MD; Maria Pia Amato, MD

Latent factor analysis on 1212 pwMS with BRB-N + Stroop

↓

5 cognitive phenotypes: Preserved, mild verbal memory/semantic fluency, mild multi-domain, severe attention/executive, severe multi-domain

Tsagkas, et al. Hum Brain Map 2021

De Meo, et al. JAMA Neurol 2021

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AI for patient stratification – *Disease progression modelling*

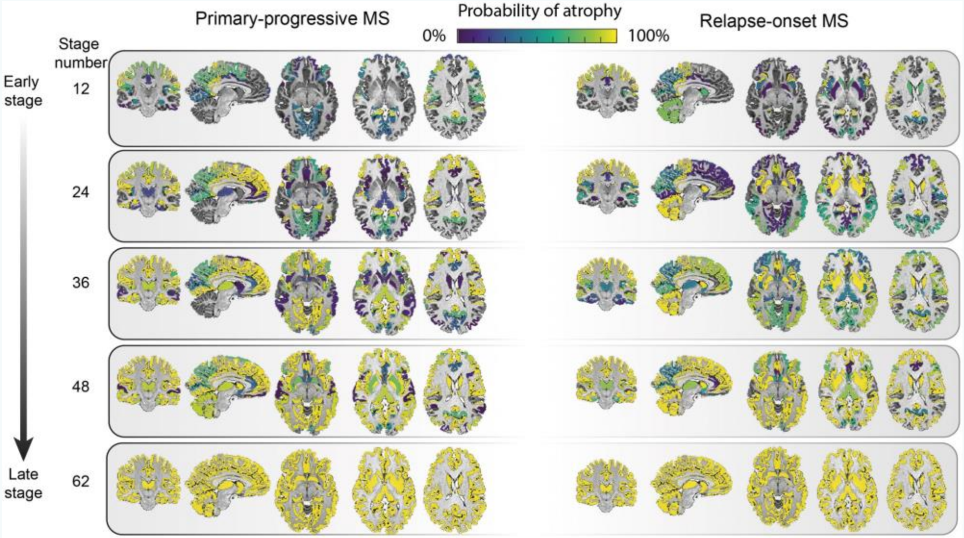
Progression of regional grey matter atrophy in multiple sclerosis

Arman Eshaghi,[1,2] Razvan V. Marinescu,[2] Alexandra L. Young,[2] Nicholas C. Firth,[2] Ferran Prados,[3] M. Jorge Cardoso,[3] Carmen Tur,[1] Floriana De Angelis,[1] Niamh Cawley,[1] Wallace J. Brownlee,[1] Nicola De Stefano,[5] M. Laura Stromillo,[5] Marco Battaglini,[5] Serena Ruggieri,[6,7] Claudio Gasperini,[6] Massimo Filippi,[8] Maria A. Rocca,[8] Alex Rovira,[9] Jaume Sastre-Garriga,[10] Jeroen J. G. Geurts,[11] Hugo Vrenken,[12] Viktor Wottschel,[12] Cyra E. Leurs,[13] Bernard Uitdehaag,[13] Lukas Pirpamer,[14] Christian Enzinger,[14,15] Sebastien Ourselin,[3,4] Claudia A. Gandini Wheeler-Kingshott,[1,16,17] Declan Chard,[1,4] Alan J. Thompson,[1] Frederik Barkhof,[1,3,4,12] Daniel C. Alexander[2] and Olga Ciccarelli[1,4] on behalf of the MAGNIMS study group*

- Event-based model on atlas-defined GM regional volumes (N=1417)

- Cingulate cortex, brainstem, thalamus are the first to become atrophic

- Stage change over time correlates with disability accumulation



Eshaghi, et al. Brain 2018

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AI for patient stratification – *Disease progression modelling*

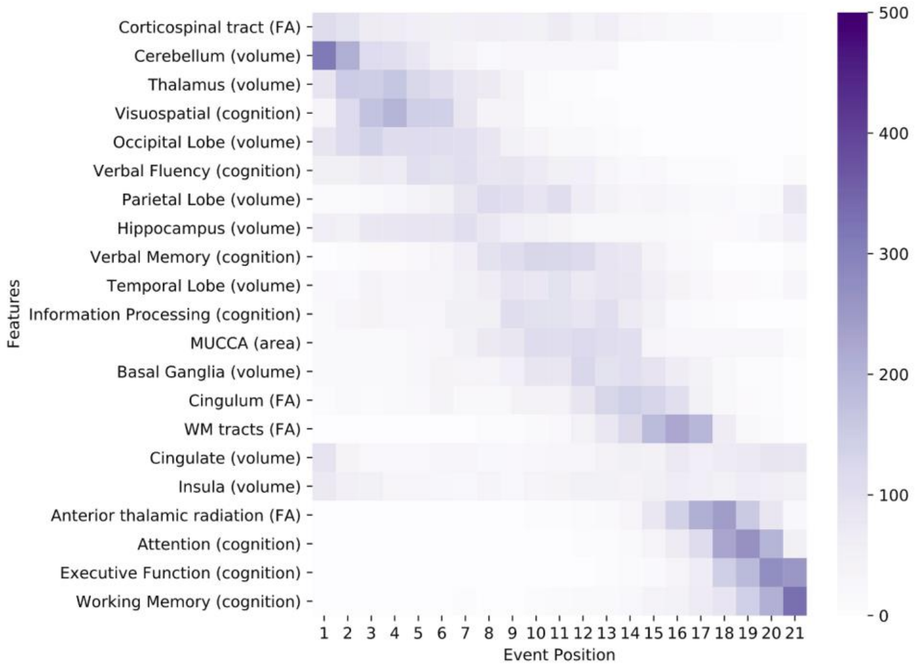
The sequence of structural, functional and cognitive changes in multiple sclerosis

Iris Dekker[a,b], Menno M. Schoonheim[c], Vikram Venkatraghavan[d], Anand J.C. Eijlers[c], Iman Brouwer[a], Esther E. Bron[d], Stefan Klein[d], Mike P. Wattjes[e], Alle Meije Wink[a], Jeroen J. G. Geurts[c], Bernard M.J. Uitdehaag[b], Neil P. Oxtoby[f], Daniel C. Alexander[f], Hugo Vrenken[a], Joep Killestein[b], Frederik Barkhof[a,f,g,1], Viktor Wottschel[a,1,*]

- EBM on T2-LL, brain and spinal cord volumes, rs-fMRI centrality, FA of major WM tracts, cognition (N=295)

- GM atrophy of the cerebellum, thalamus, and microstructural damage of the CST are early events

- Higher disability and impaired cognition are associated with earlier functional changes of the DMN and spinal cord atrophy



Dekker, et al. Neuroim Clin 2021

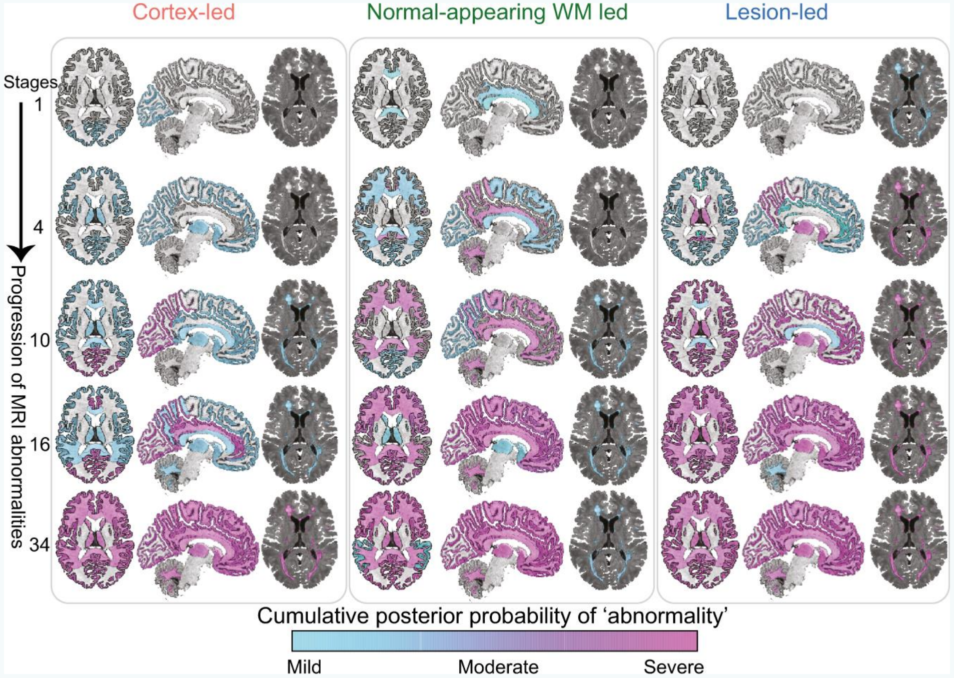
AI for patient stratification – *SuStaIn*

Identifying multiple sclerosis subtypes using unsupervised machine learning and MRI data

Arman Eshaghi[1,2], Alexandra L. Young[2,3], Peter A. Wijeratne[2], Ferran Prados[1,2,4], Douglas L. Arnold[5], Sridar Narayanan[5], Charles R. G. Guttmann[6], Frederik Barkhof[1,2,7,8], Daniel C. Alexander[2], Alan J. Thompson[1], Declan Chard[1,9,10] & Olga Ciccarelli[1,9,10]

- SuStaIn on T2-LL, GM (lobar) volumes, NAWM T1/T2 ratio (N=6322)

- Three MRI-driven phenotypes (Cortex, NAWM-, and Lesion-led)



Eshaghi, et al. Nat Comm 2021

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AI for patient stratification – *SuStaIn*

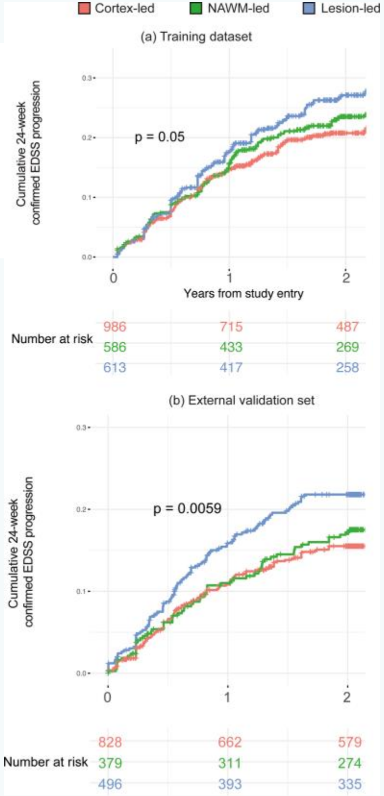
Identifying multiple sclerosis subtypes using unsupervised machine learning and MRI data

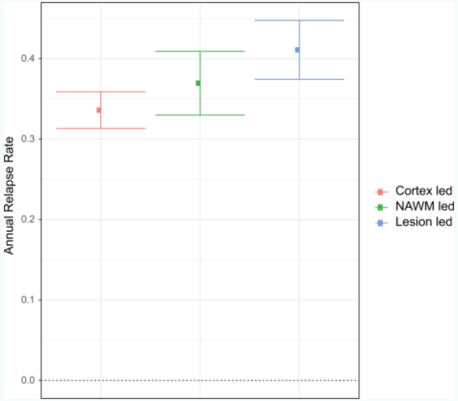
Arman Eshaghi[1,2], Alexandra L. Young[2,3], Peter A. Wijeratne[2], Ferran Prados[1,2,4], Douglas L. Arnold[5], Sridar Narayanan[5], Charles R. G. Guttmann[6], Frederik Barkhof[1,2,7,8], Daniel C. Alexander[2], Alan J. Thompson[1], Declan Chard[1,9,10] & Olga Ciccarelli[1,9,10]

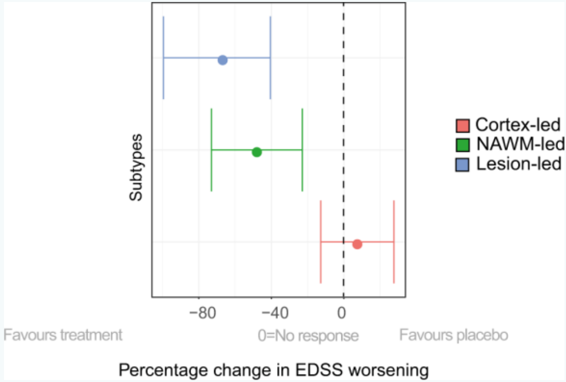
- SuStaIn on T2-LL, GM (lobar) volumes, NAWM T1/T2 ratio (N=6322)

- Three MRI-driven phenotypes (Cortex, NAWM-, and Lesion-led)

- Lesion-led subtype is associated with higher risk of CDP and relapse rate, and positive treatment response







Eshaghi, et al. Nat Comm 2021

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AI for patient stratification – *SuStaIn*

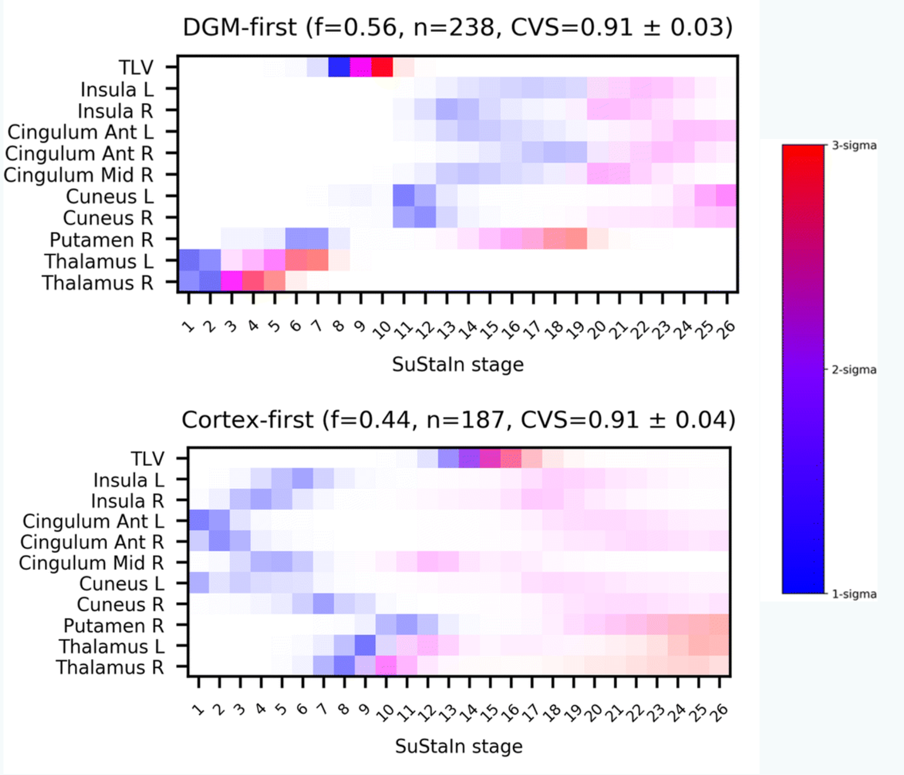
Stratification of multiple sclerosis patients using unsupervised machine learning: a single-visit MRI-driven approach

Giuseppe Pontillo[1,2] · Simone Penna[2] · Sirio Cocozza[1] · Mario Quarantelli[3] · Michela Gravina[2] · Roberta Lanzillo[4] · Stefano Marrone[2] · Teresa Costabile[5] · Matilde Inglese[6,7] · Vincenzo Brescia Morra[4] · Daniele Riccio[2] · Andrea Elefante[1] · Maria Petracca[4] · Carlo Sansone[2] · Arturo Brunetti[1]

- SuStaIn on T2-LL and GM volumes from AAL atlas (N=425)

- Two MRI-driven phenotypes (DGM-first, Cortex-first)

- Higher baseline stage and DGM-first subtype associated with long-term (10y) disability worsening, transition to SP course, and cognitive impairment



Pontillo, et al. Eur Radiol 2022

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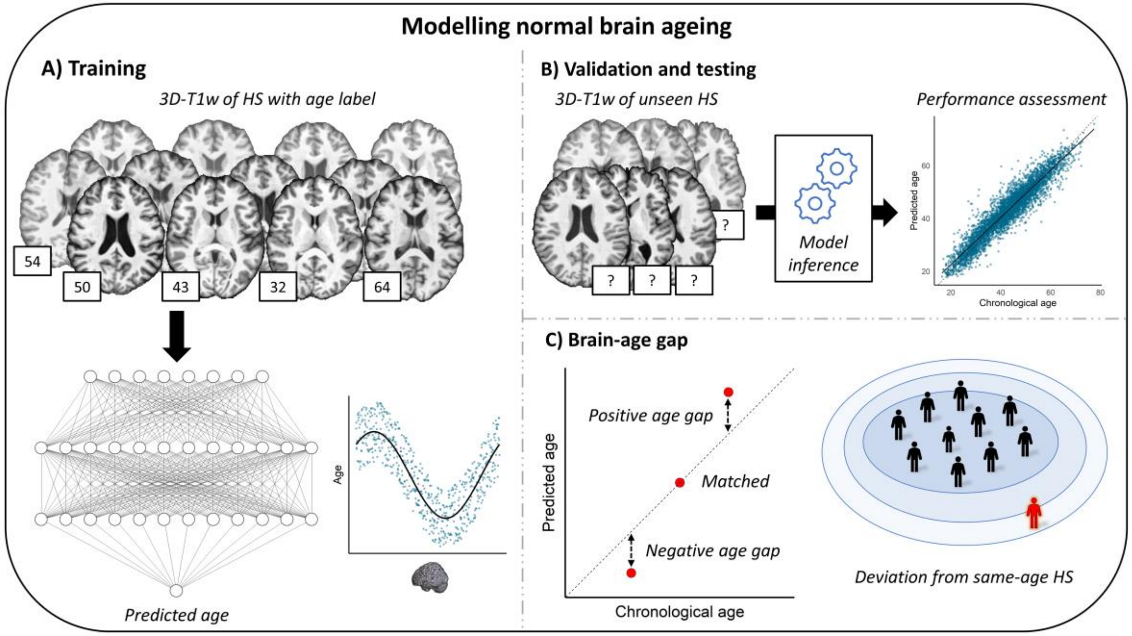
AI for patient stratification – *The brain-age paradigm*

- Using machine learning, chronological age is modeled as a function of (structural) brain MRI in healthy subjects

- The difference between predicted and chronological age (***brain-age gap***) as an <u>age-adjusted global metric of brain (structural) health</u>



Cole & Franke. Trends Neurosci 2017

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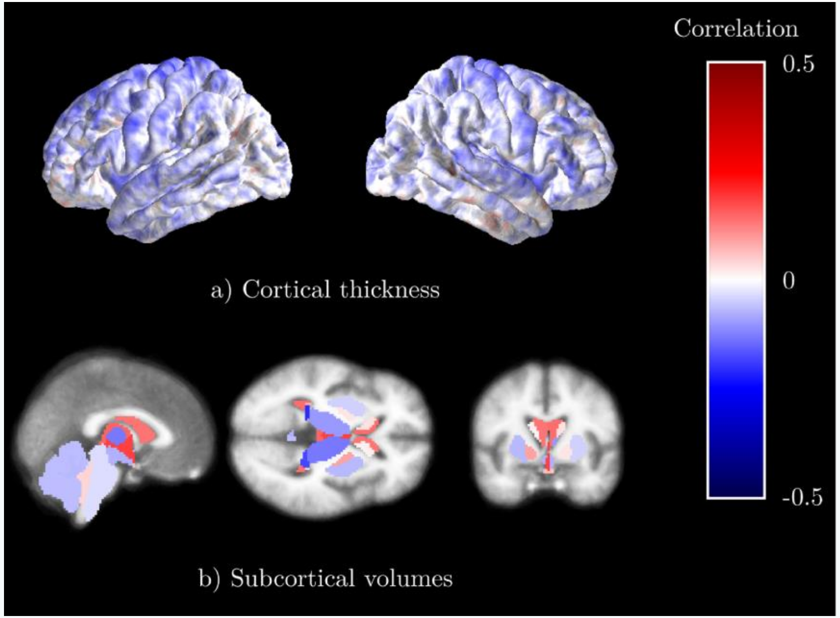
Brain aging in MS – *The brain-age paradigm*

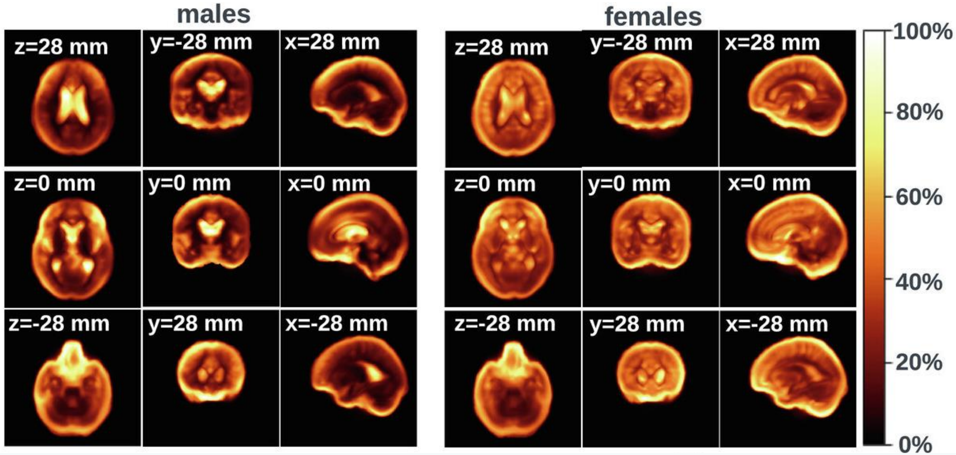
Deep neural networks learn general and clinically relevant representations of the ageing brain

Esten H. Leonardsen[a,b,*], Han Peng[c], Tobias Kaufmann[b,d], Ingrid Agartz[b,e,f], Ole A. Andreassen[b], Thomas Wolfers[a,b,1], Yunpeng Wang[a,1]



Anatomically interpretable deep learning of brain age captures domain-specific cognitive impairment

Chenzhong Yin[1], Phoebe Imms[2], Mingxi Cheng[1], Anar Amgalan[2], Nahian F Chowdhury[2], Roy J Massett[2], Nikhil N Chaudhari[2 3], Xinghe Chen[1], Paul M Thompson[3 4 5 6 7 8 9 10], Paul Bogdan[1], Andrei Irimia[2 3 5]; Alzheimer's Disease Neuroimaging Initiative

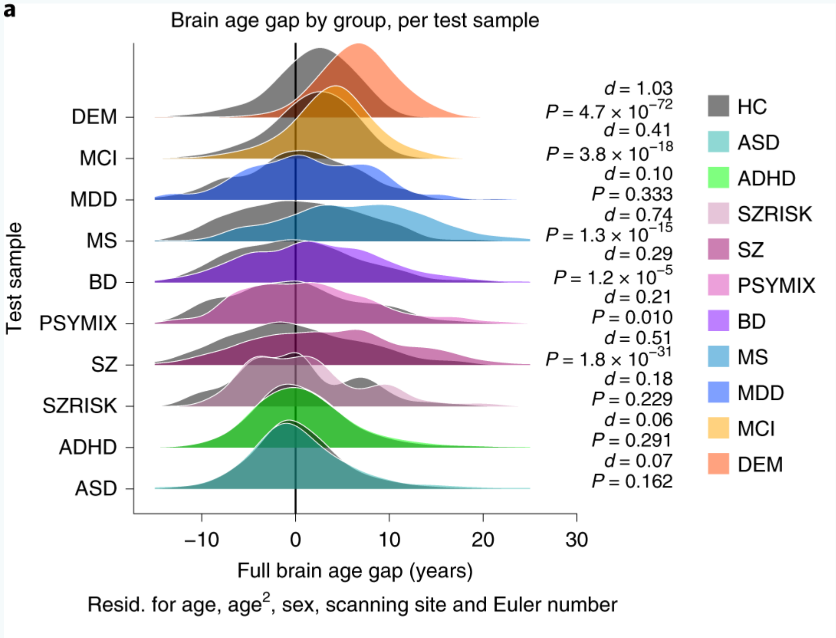


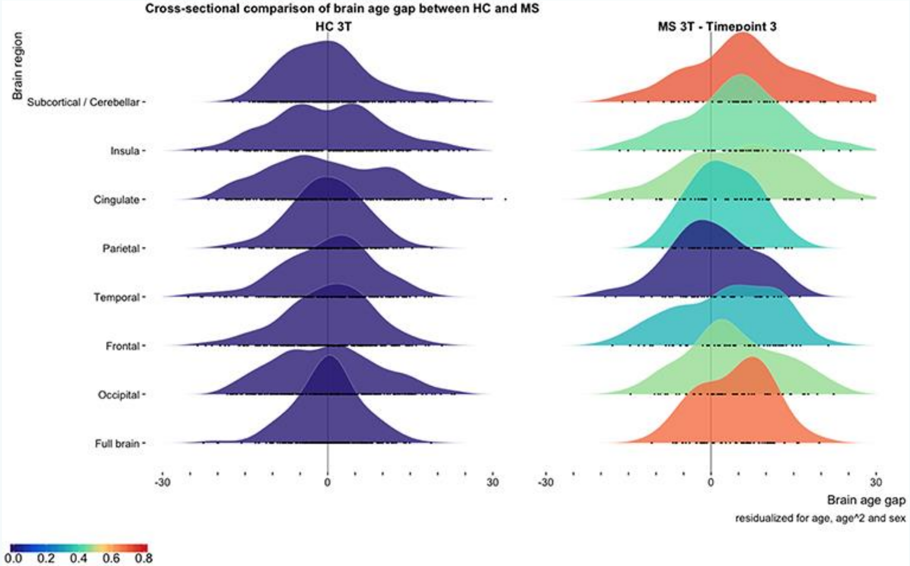
Leonardsen, et al. Neuroimage 2022

Yin, et al. PNAS 2023

Brain aging in MS – *The brain-age paradigm*

MS is associated with older appearing brains (i.e., positive brain-age gap)



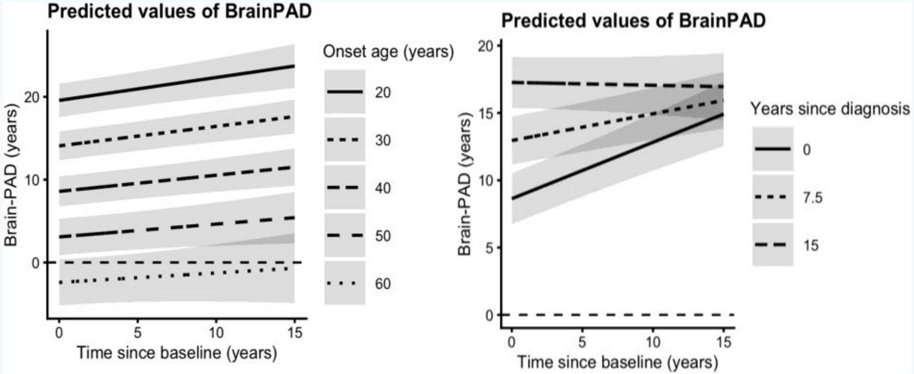


Kaufmann, et al. Nat Neurosci 2019

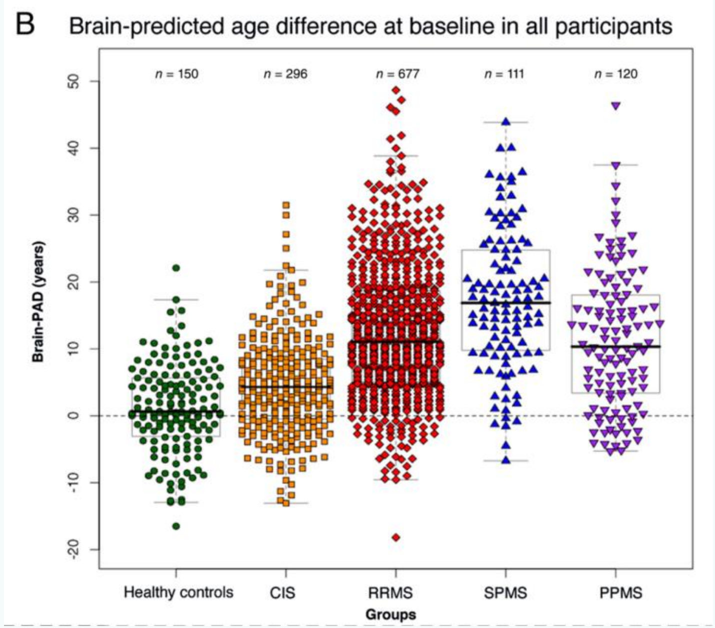
Hogestol, et al. Front Neurol 2019

Brain aging in MS – *The brain-age paradigm*

The brain-age gap increases over time…



and varies with clinical phenotype



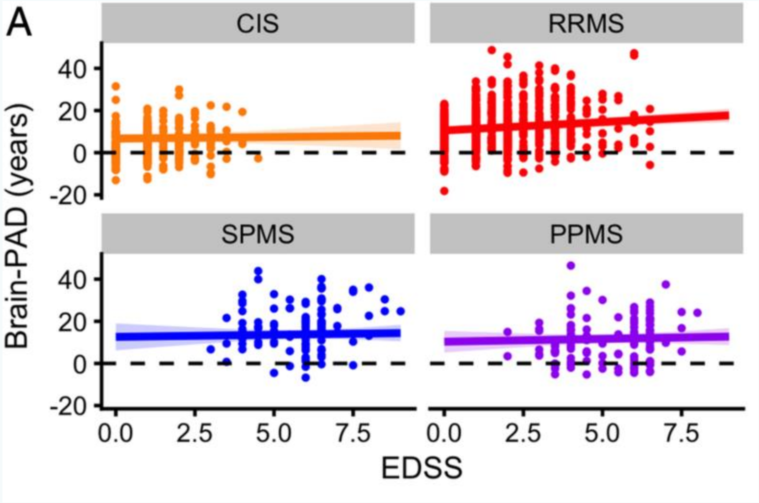
<u>EMM (years)</u>
CIS 6.7
RR 11.9
SP 13.3
PP 11.2

Cole, et al. Ann Neurol 2020

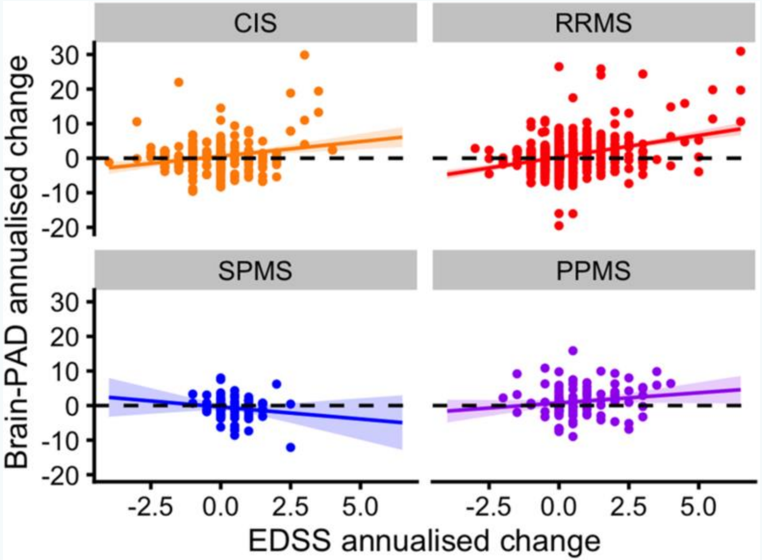
Brain aging in MS – *The brain-age paradigm*

The brain-age gap is associated with clinical disability

Cross-sectionally (b=0.64, p<0.001)



Longitudinally (r=0.26, p<0.001)



Cole, et al. Ann Neurol 2020

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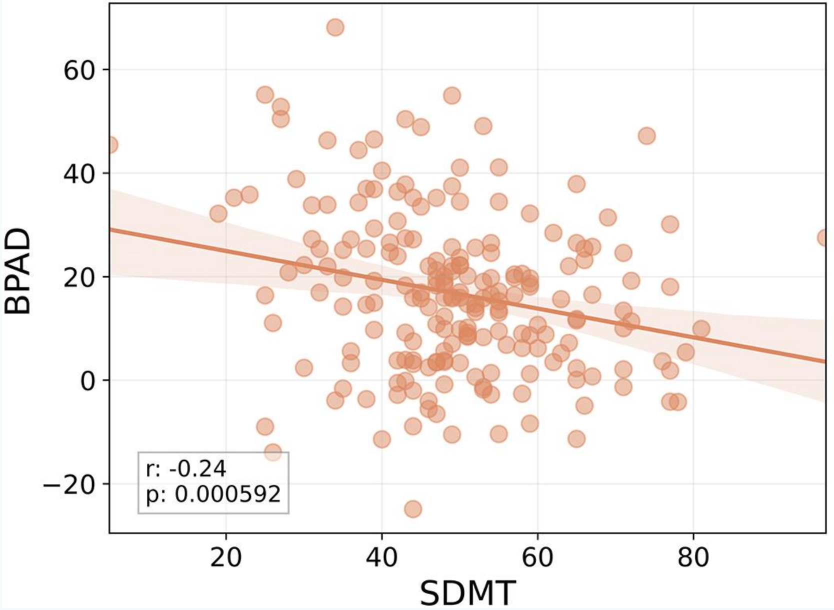
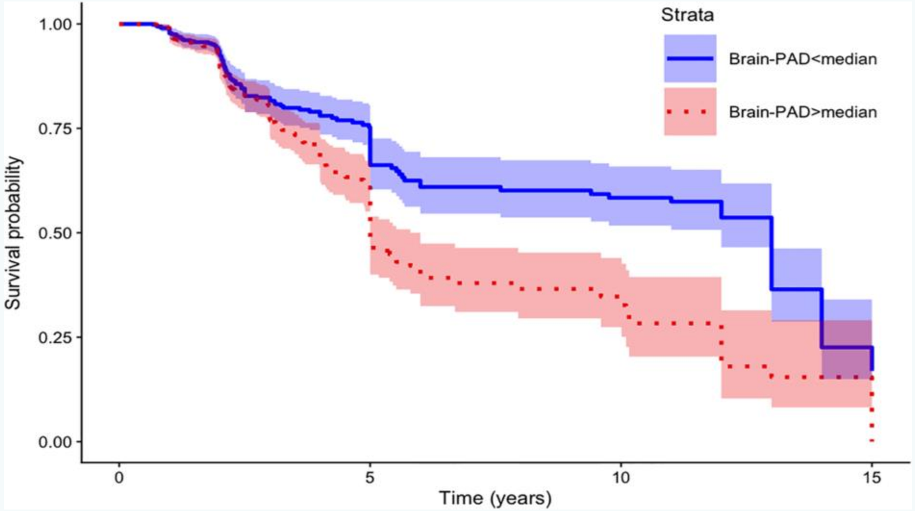
Brain aging in MS – *The brain-age paradigm*

The brain-age gap is associated with cognition…



and predicts disability worsening



Denissen, et al. Eur J Neurol 2022

Cole, et al. Ann Neurol 2020

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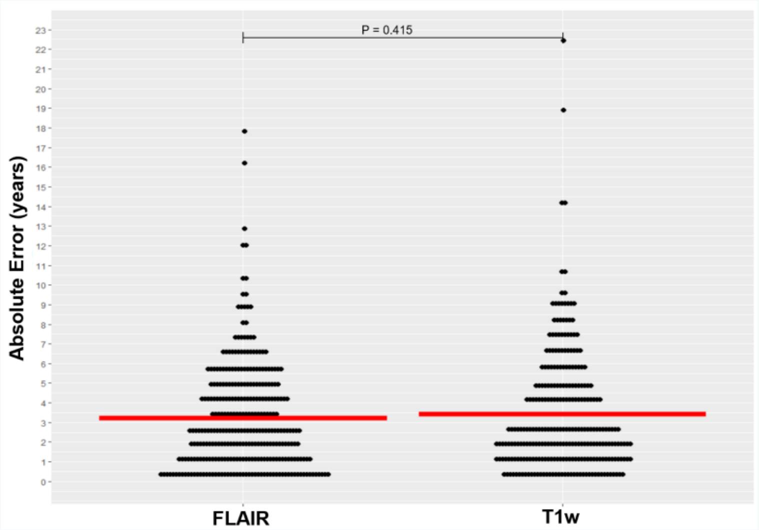
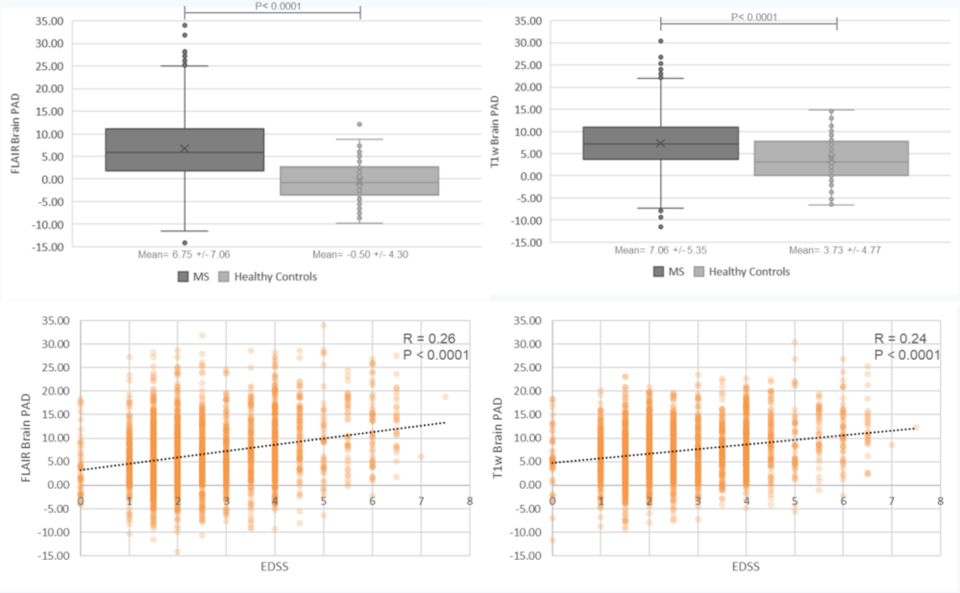
Brain aging in MS – *The brain-age paradigm*

Brain-age prediction is feasible on 3D-FLAIR scans (compared to T1w-based models)

Comparable predictive performance



Comparable sensitivity to MS and related disability



Colman, et al. ISMRM 2022

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Conclusions

- AI is all around us

Conclusions

- AI is all around us
- We are going towards generalist medical AI

Foundation models for generalist medical artificial intelligence

Michael Moor, Oishi Banerjee, Zahra Shakeri Hossein Abad, Harlan M. Krumholz, Jure Leskovec, Eric J. Topol & Pranav Rajpurkar

Nature **616**, 259–265 (2023) | Cite this article

Conclusions

- AI is all around us
- We are going towards generalist medical AI
- AI is transforming the (radiologist) profession

Foundation models for generalist medical artificial intelligence

Michael Moor, Oishi Banerjee, Zahra Shakeri Hossein Abad, Harlan M. Krumholz, Jure Leskovec, Eric J. Topol & Pranav Rajpurkar

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Will Artificial Intelligence Replace Radiologists?

Curtis P. Langlotz, MD, PhD

"Will AI replace radiologists?" is the wrong question. The right answer is:
Radiologists who use AI will replace radiologists who don't

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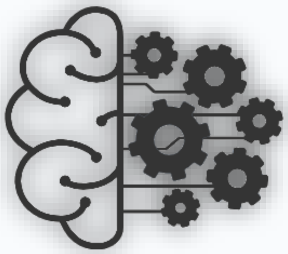

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