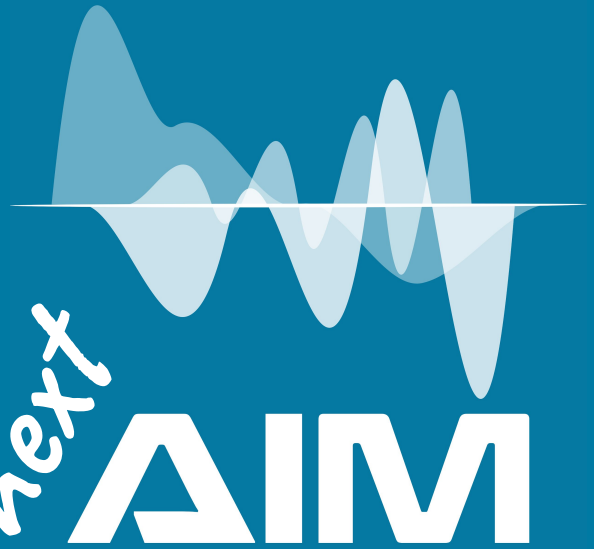
Artificial Intelligence in Medicine



Nuclear Medicine Neuroimaging Quantification

Enrico Peira
next_AIM general meeting
14.02.2023, Milano

DORIAN
evolving neuroimaging

INFN

Diagnosis ORiented ANalysis (DORIAN)

DORIAN delivers a fast and reliable tool for the **quantification** of medical imaging to support the early and differential diagnosis of neurodegenerative disorders. It provides clinicians and researchers with state-of-the-art robust, rater-independent and reproducible quantitative biomarkers to **better evaluate** dementias stage and progression, **complementing** their ability to write informed medical reports and improve on the early detection and diagnosis of neurodegenerative diseases.

Dorian recent activity

> Fondazione spin-off	[May 2020]
> Lab sessions @ Nucl. Med. school in Neurology	[Sep. 2021]
> EBAN finalist	[Mar.2022]
> Unicredit StartLab 3rd classified	[May 2022]
>> Amazon AWS academy invitation	[Sep. 2022]
> Lab sessions @ Nucl. Med. school in Neurology	[Oct. 2022]

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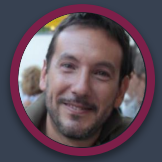
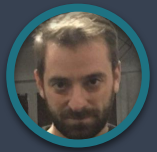


E. Peira
(INFN-GE)

R. Gianeri
(INFN-GE)



F. Sensi
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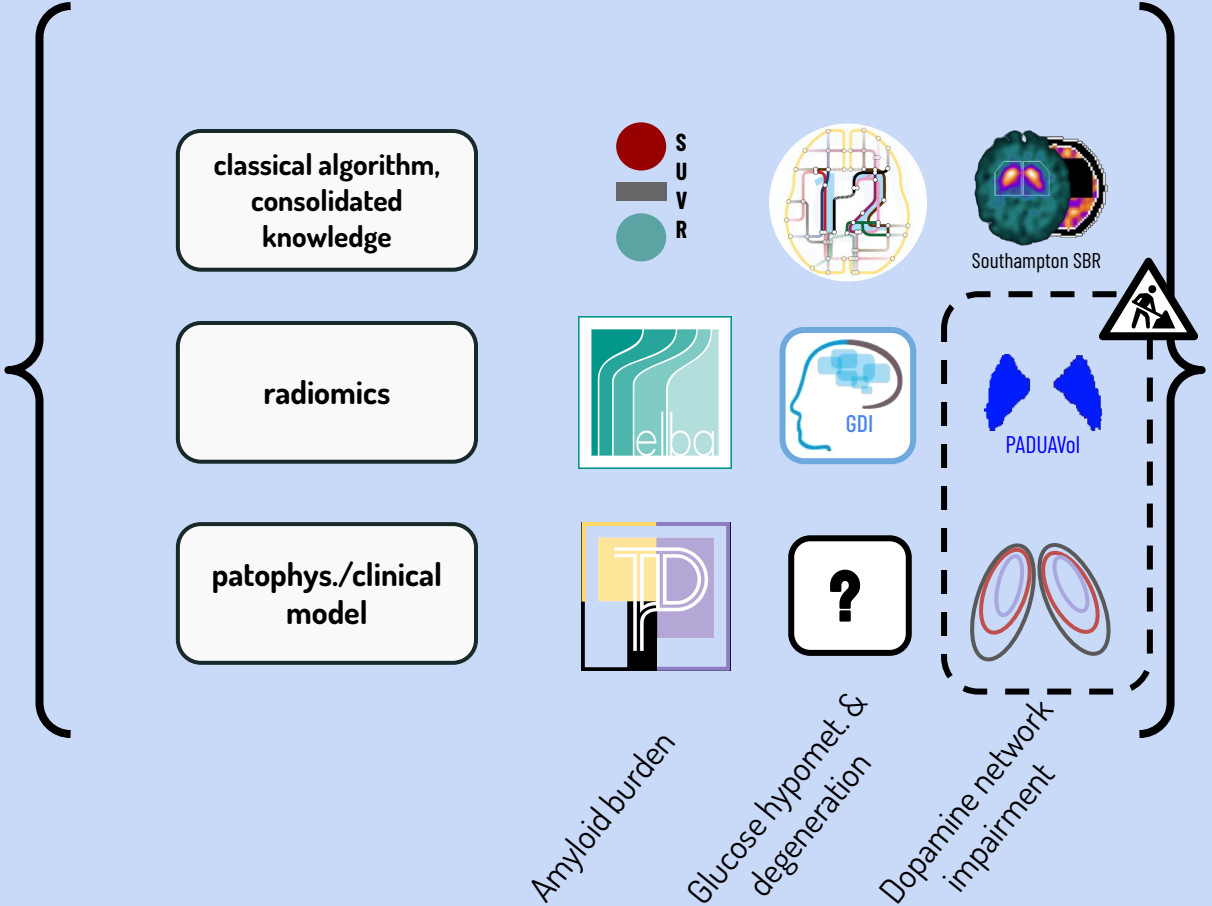
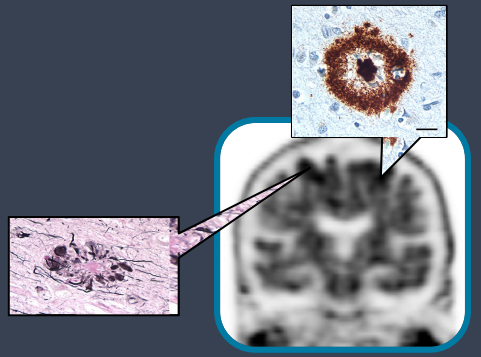
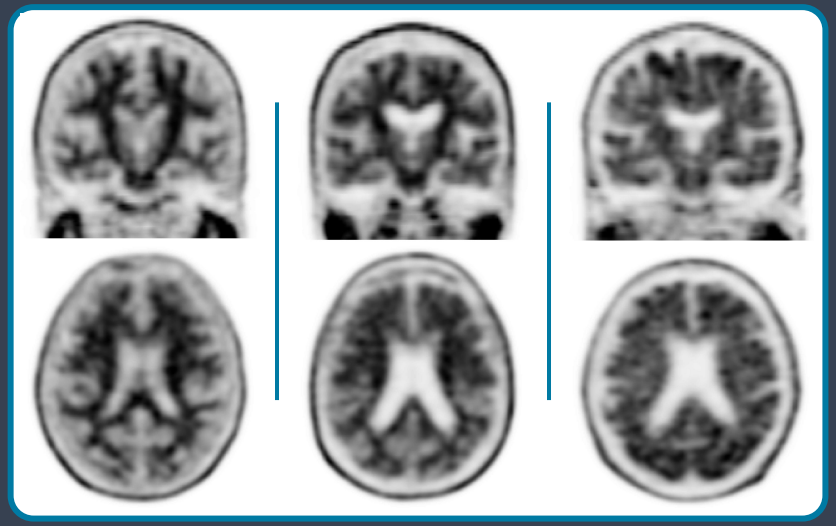

classical algorithm, consolidated knowledge
radiomics
patophys./clinical model
SUVR
elba
GDI
TD
?
Southampton SBR
PADUAVol
Amyloid burden
Glucose hypomet. & degeneration
Dopamine network impairment

AMYLOID BURDEN

What is amyloid PET?

- **In-vivo** assessment of **β-amyloid** in brain tissue
- **Aβ** plaques: pathological hallmark of Alzheimer's disease
- In clinical practice the amy-PET is visually inspected (**binary classification**)





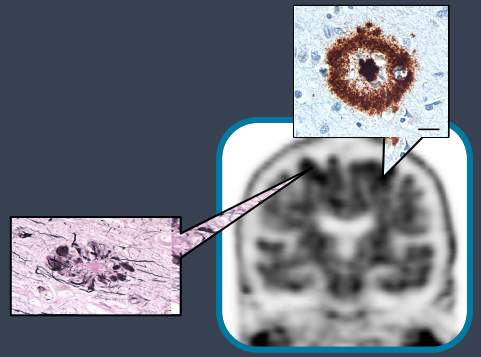
n ? p

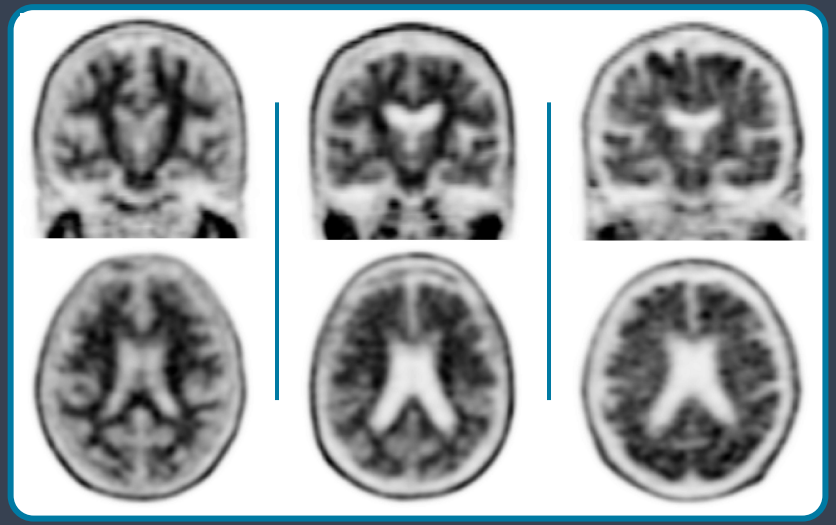
Why quantification ?

- **Spot borderline** (most clinically relevant cases)
- Provide a more detailed picture (**regionality**, **relationship** with other biomarkers)

What is amyloid PET?

- **In-vivo** assessment of **β-amyloid** in brain tissue
- **Aβ** plaques: pathological hallmark of Alzheimer's disease
- In clinical practice the amy-PET is visually inspected (**binary classification**)





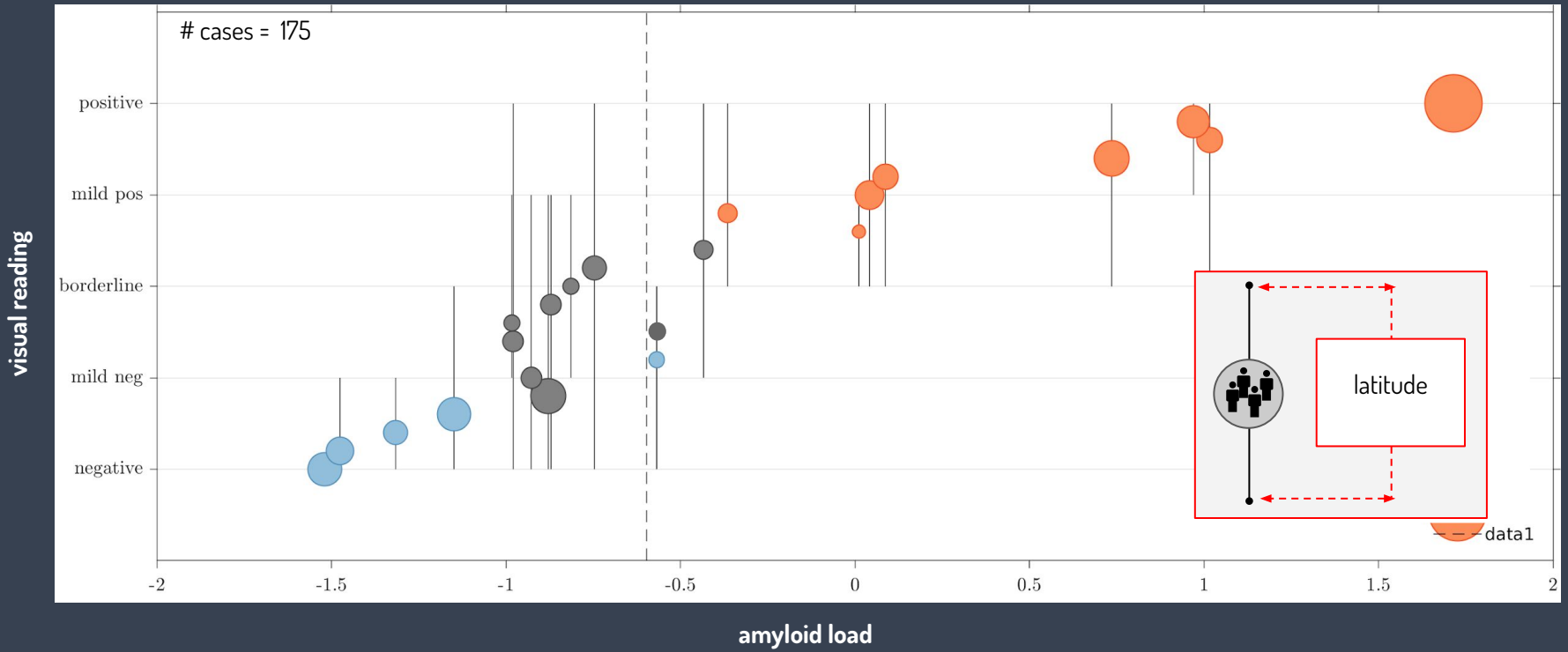
n ? p

Why quantification ?

- **Spot borderline**
- Provide a more de
with other biomar

Possibly even more critical with the approval of the first anti-amyloid treatment (June 2021)

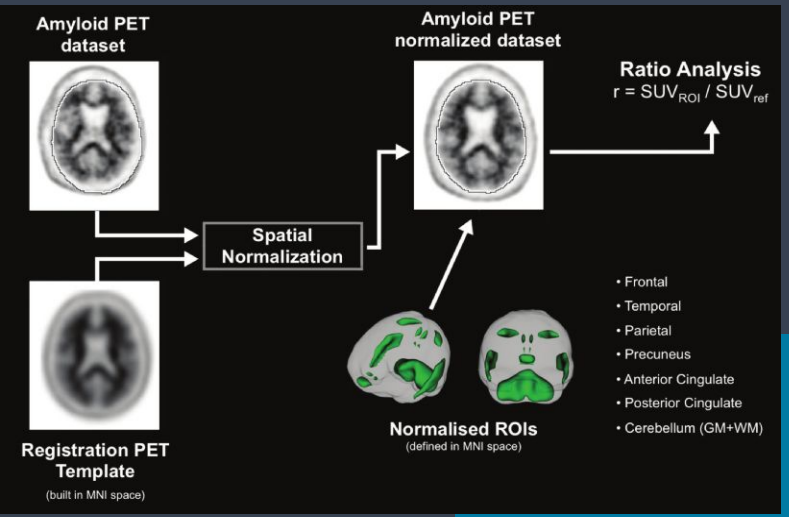
What happens in borderlines?



Chincarini et al.. "Semi-quantification and grading of amyloid PET: A project of the European Alzheimer's Disease Consortium (EADC)". Neuroimage: Clinical. 2019

Consolidated knowledge - SUVr

- register on a reference spatial frame (i.e. MNI)
- select reference (cerebellum, brain stem, ...) & target ROI (cortical)
- average counts (single/all ROI) and take the ratio



Positron emission tomography-computed tomography standardized uptake values in clinical practice and assessing response to therapy
Semin Ultrasound CT MR
Kinahan et al. (2010)

ratio of raw (mean) intensities
segmentation dependence
fixed target *ROI*
fixed ***reference*** *ROI*

very common quantification approach

automatic analysis software **available**

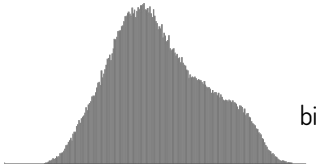
SUVr values/outcome critically depend on ROI **definitions** and **positioning**

Radiomic - ELBA

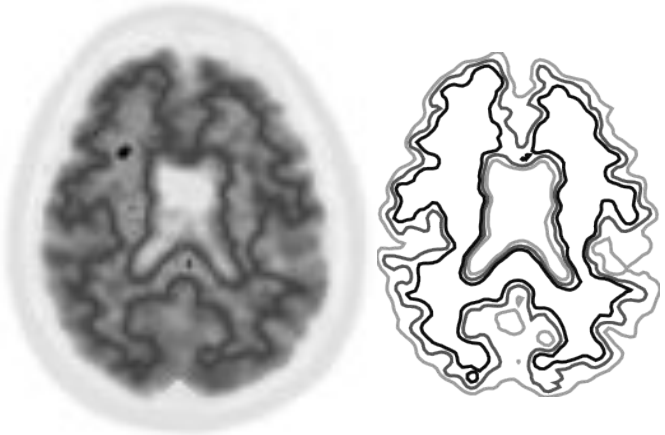
equal mix of geometric properties (sphericity) of iso-intensity surfaces & intensity statistics

no need for ROIs, no need for reference uptake!

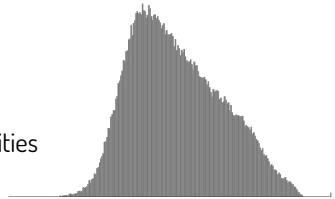
SUVr-independent evaluation of brain amyloidosis
Journal of Alzheimer's Disease,
Chincarini et al. (2016)

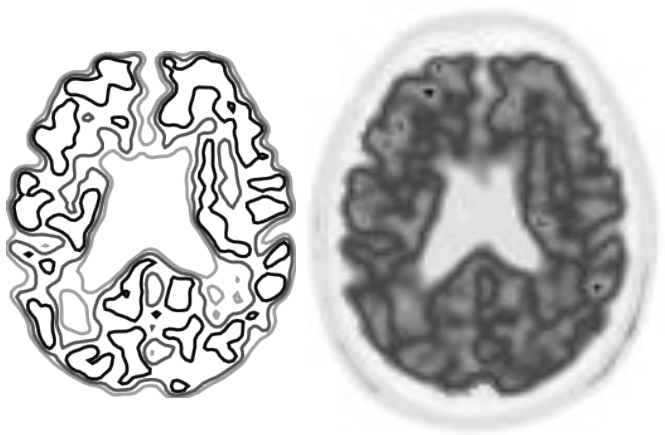


bias on lower intensities



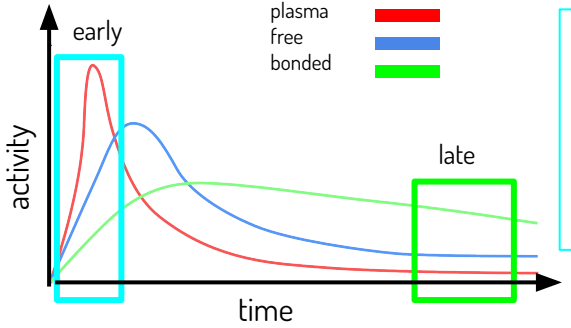
bias on higher intensities





Clinical model - TDr

REQUIREMENT: **early** acquisition, **proxy** of brain blood **perfusion** (Contractor 2012)

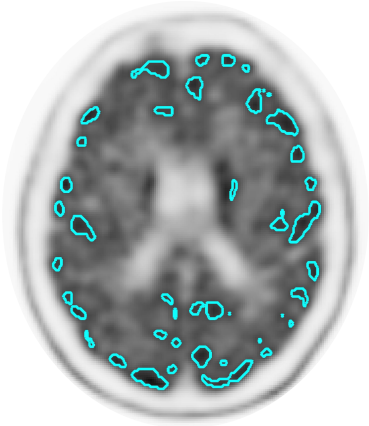


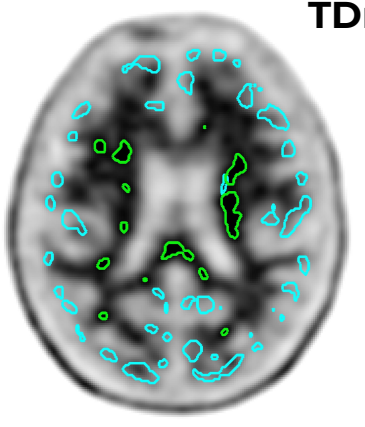
Target	**Reference**
highest uptake in the **early** scan (CBF) (Osch 2009)	highest uptake in the **late** scan (hot spot) (Fleisher 2017)

A kinetics-based approach to amyloid PET semi-quantification
EJNMMI,
Chincarini et al. (2020)

no segmentation
subject-dependent uptake *ROI*
subject-dependent ***reference*** *ROI*

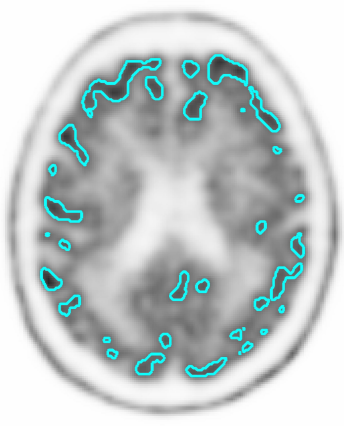
$$\textbf{TDr} = \frac{\langle I_{late} \rangle_{Target}}{\langle I_{late} \rangle_{Reference}} = \frac{\square}{\square}$$

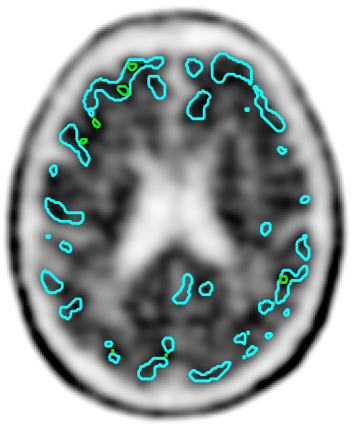




< **N**

> **P**

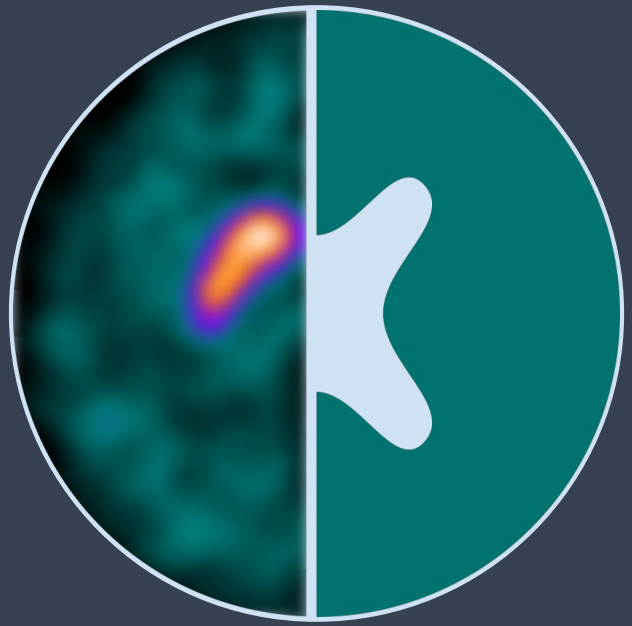




Validation

- 859 scan evaluated (615 clinical)
- Independent estimation of β-amyloid
- Tested on all commercially available tracer
- Excellent agreement with both visual and SUVr

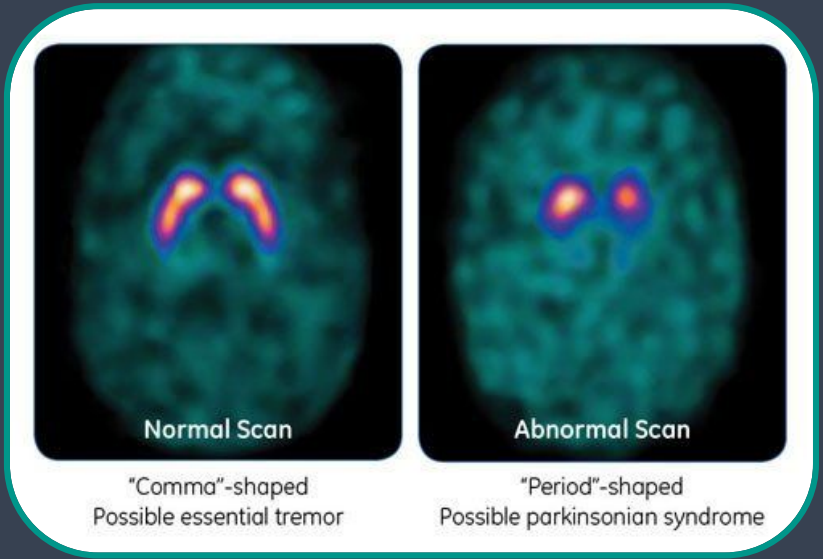
	Accuracy	Specificity	Sensitivity
		[95% CI]	
TDr	0.945 [0.937 0.951]	0.933 [0.931 0.934]	0.957 [0.928 0.970]
SUVr	0.862 [0.853 0.874]	0.836 [0.831 0.848]	0.893 [0.864 0.906]
ELBA	0.955 [0.944 0.958]	0.958 [0.958 0.959]	0.953 [0.930 0.957]

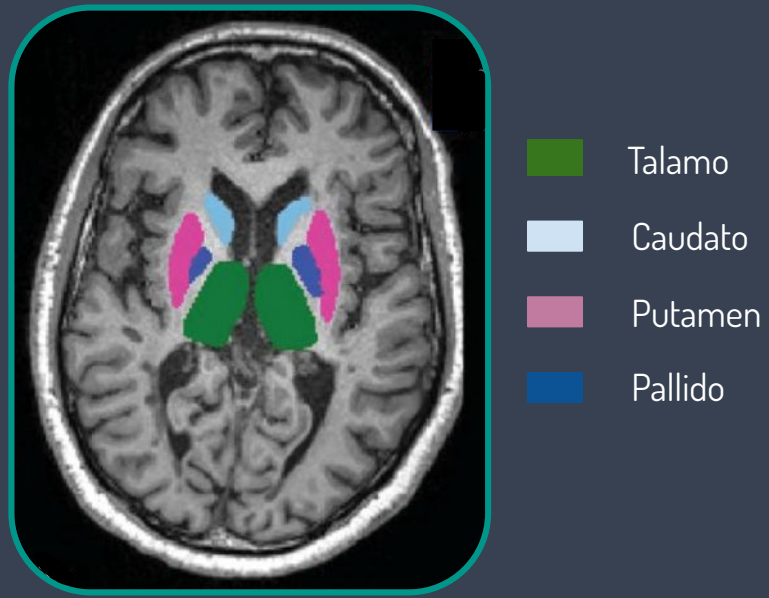


DOPAMINE TRANSPORTER

What is DaT-SPECT?

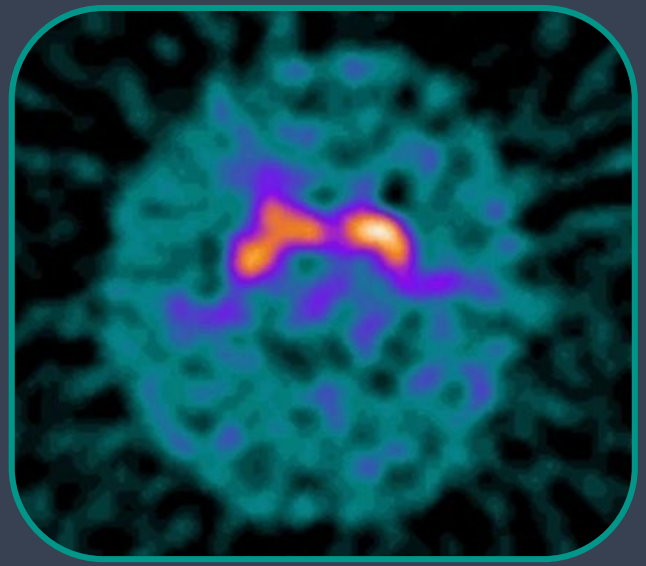
- 123-Ioflupane with SPECT: allow **in-vivo** assessment del **DaT** (dopamine transporter)
- **Marker** of nigrostriatal **dopaminergic** network **integrity** that is impaired in **Parkinson**
- **Visual assessment** in **clinical** practice (putamen uptake reduction, right-left imbalance)

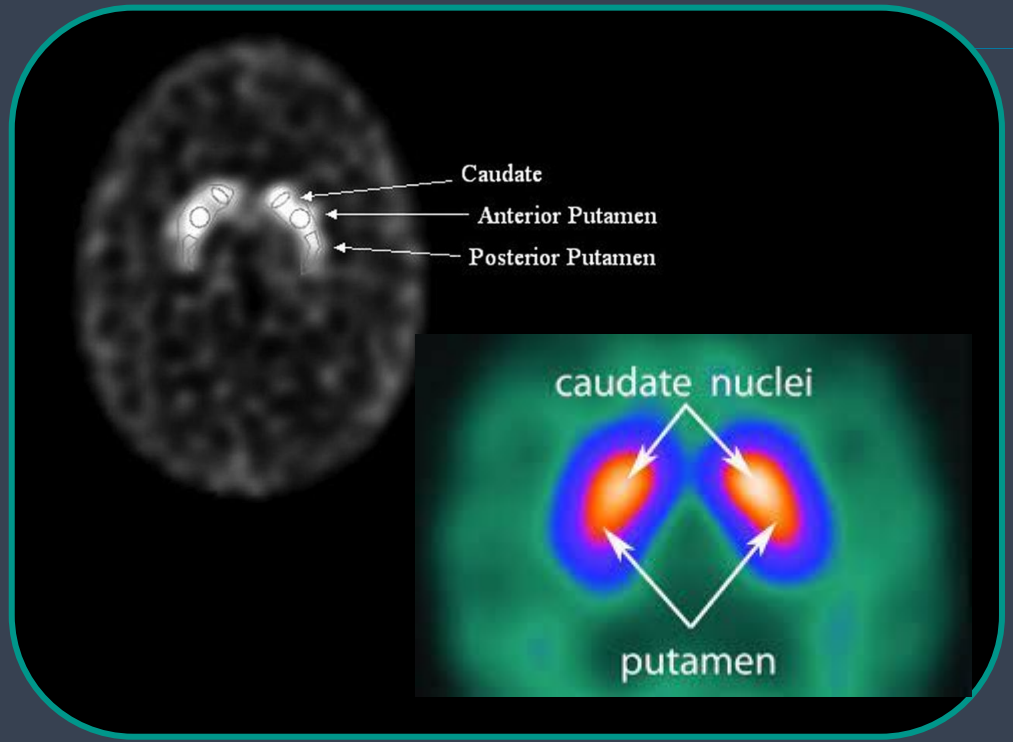




Main issues

- **PVE**: Low SPECT resolution and small target regions (6-12mm)
- Low **S/N ratio**

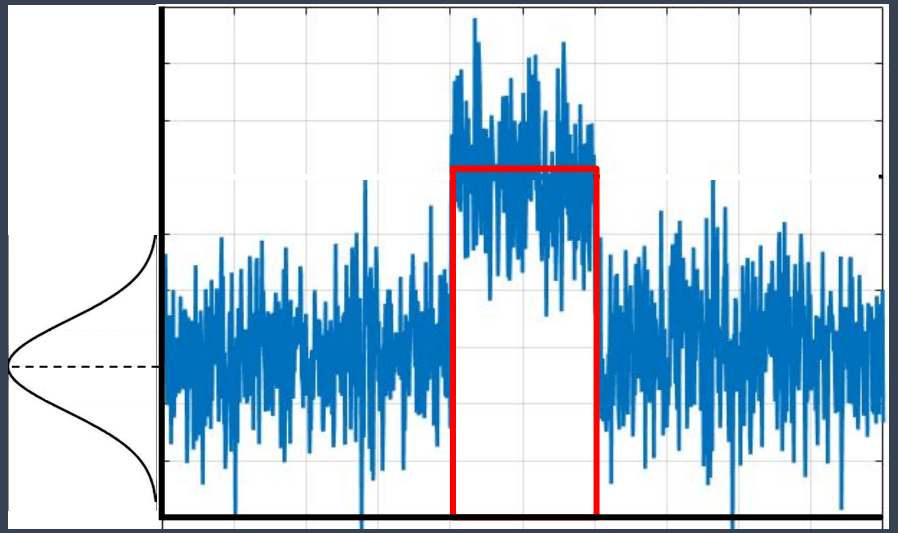


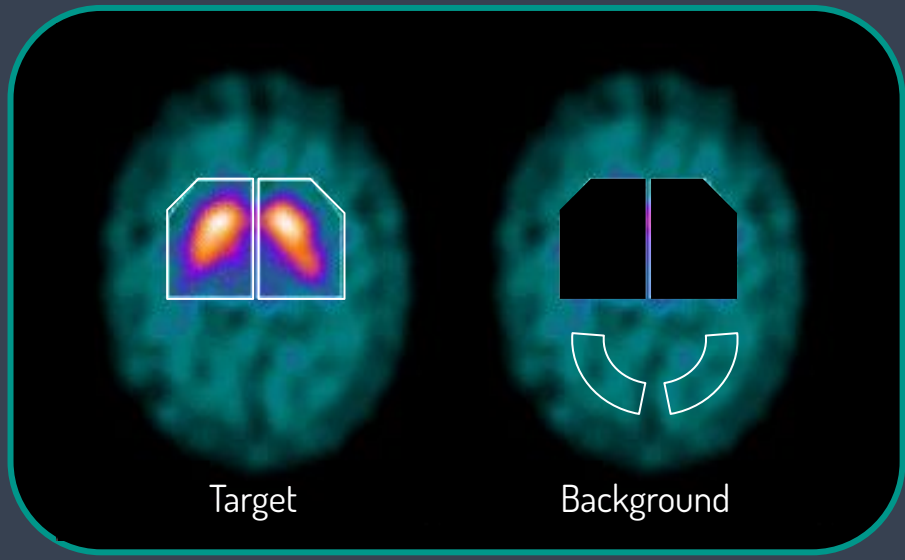


alignment and spatial **normalisation** are tricky!

Consolidated knowledge - Southampton SBR

- MNI normalization
- Assumption: no signal outside striatum
- Target voxels are distance weighted from the background distribution
- SBR (striatal vs occipital)

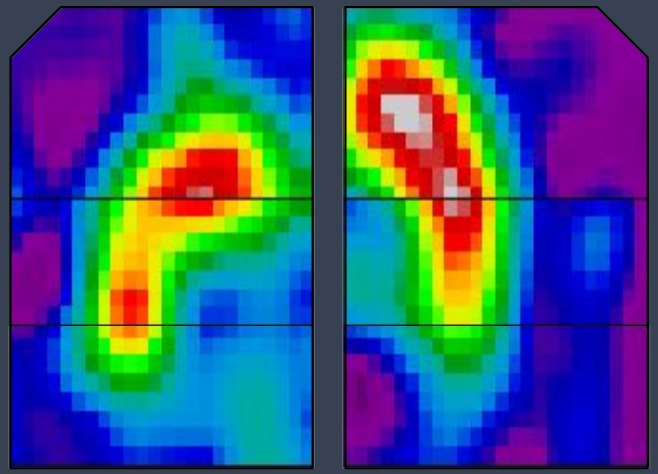


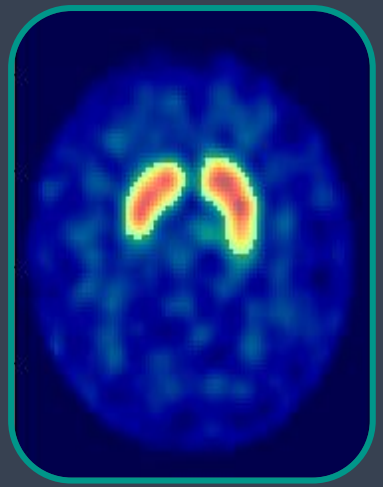


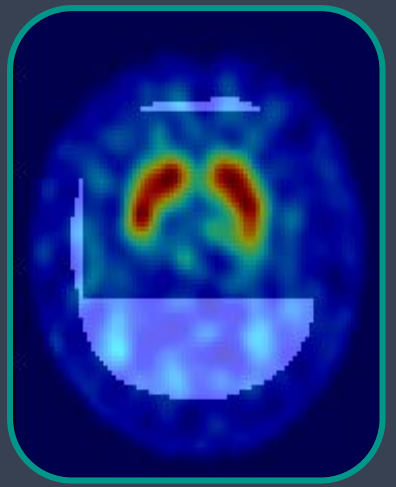
$$SBR = \frac{C_{Tgt} - C_{Bckg}}{C_{Bckg}}$$

Radiomic - PDIdx, PDVol

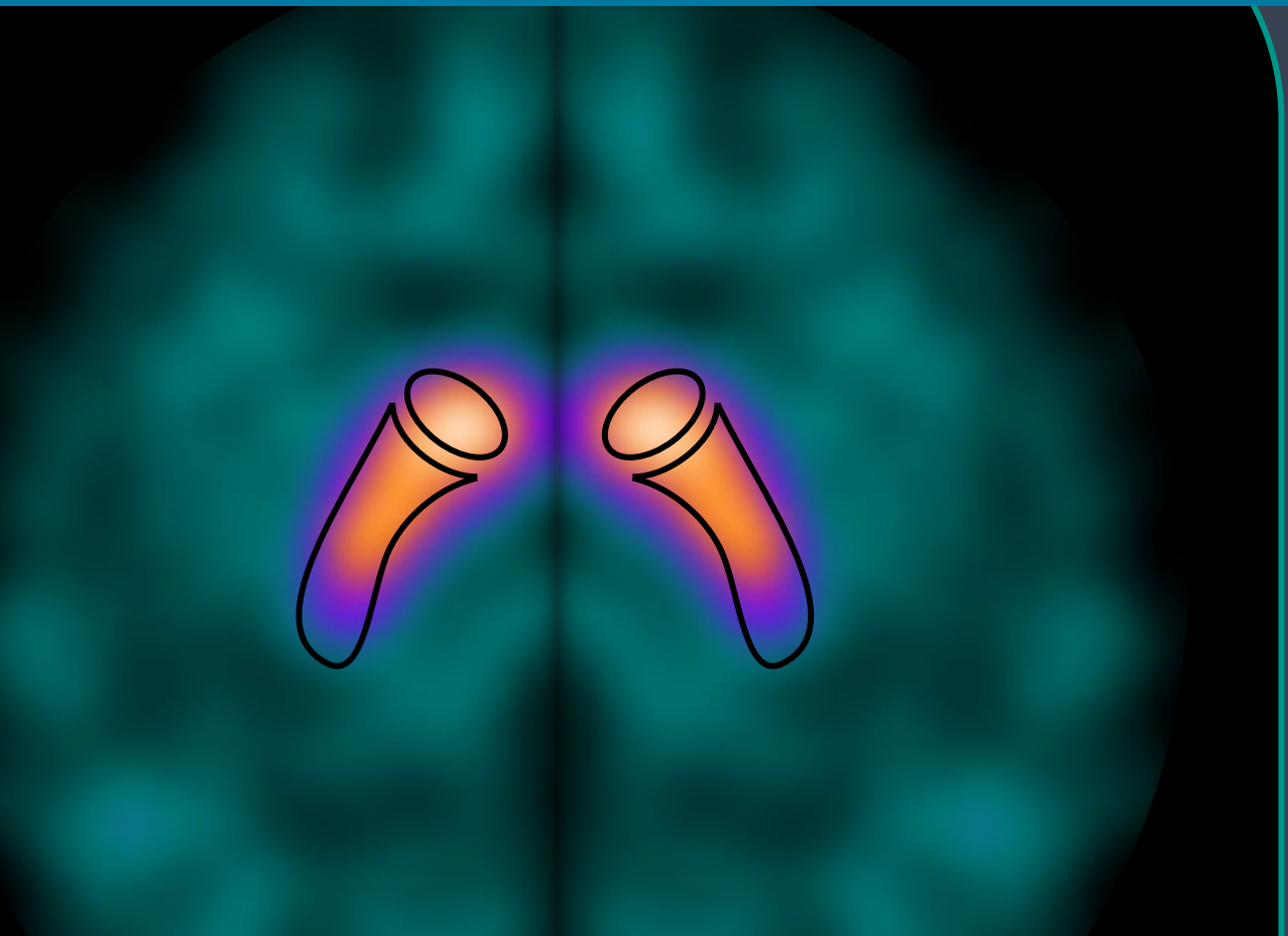
- MNI normalization
- Coarse segmentation based on the distance of striatal voxels from the background
- Left and right volume (PDVol)
- Average intensity / Background (PDIdx)





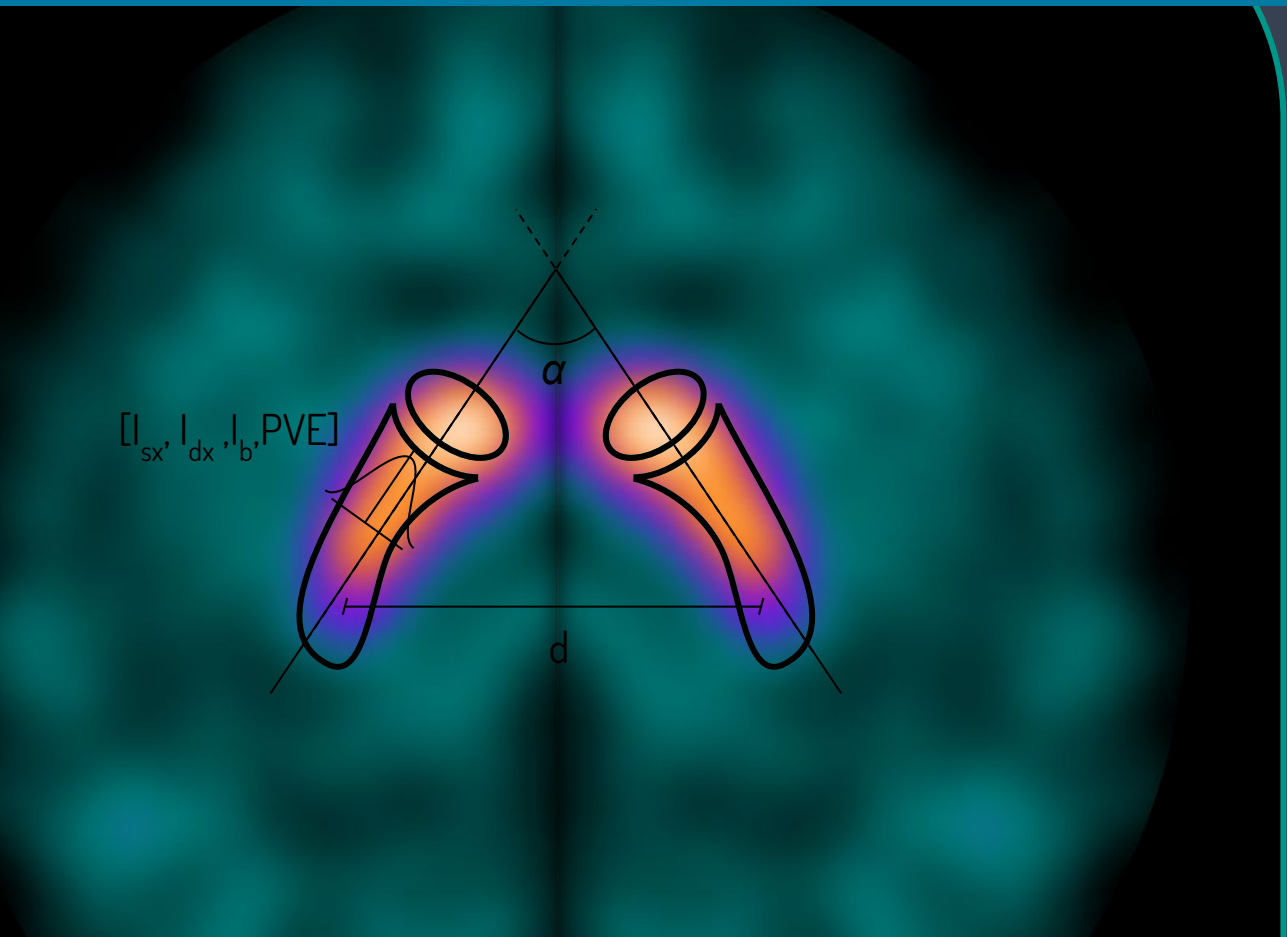


Clinical model - Striatal Matched SBR



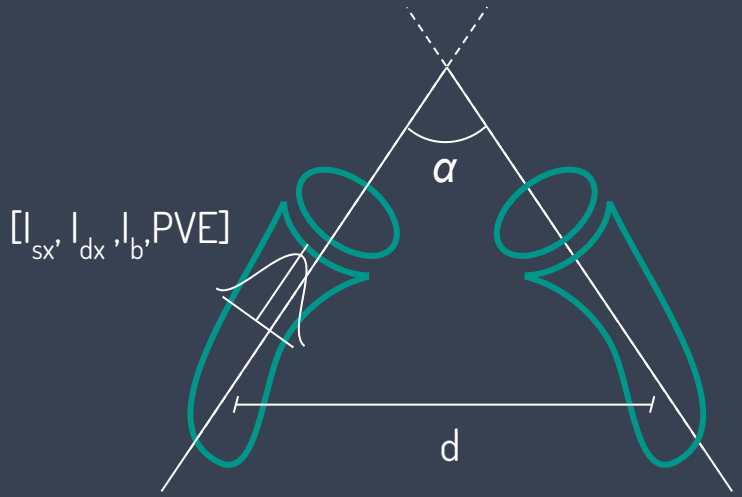
Dealing with data variability that affect processing

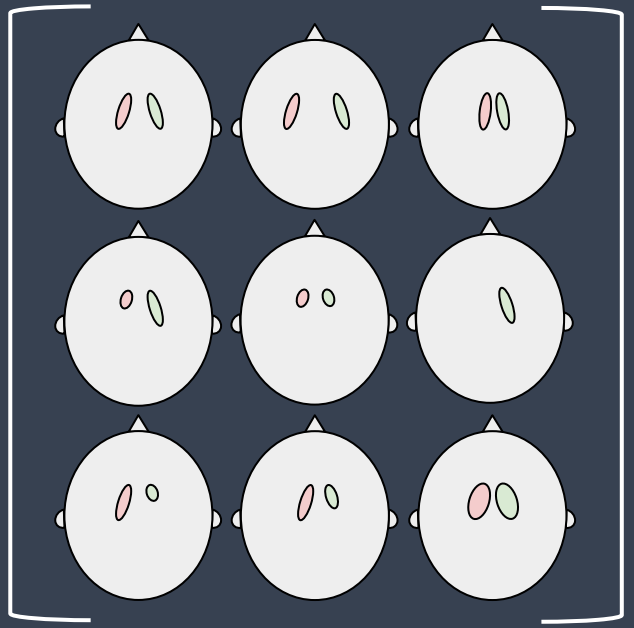
Clinical model - Striatal Matched SBR



Modelling pathophysiological characteristic (left/right/background intensity, tilting, distance, ...)

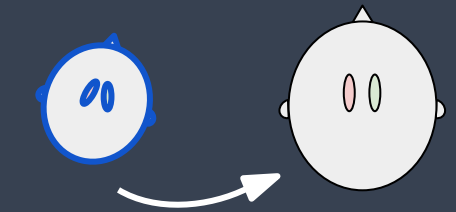
Clinical model - Striatal Matched SBR





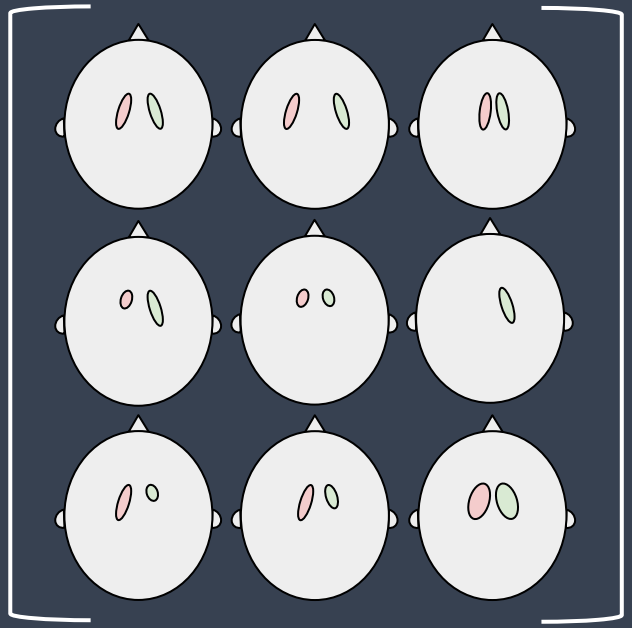
MNI template space

Clinical model - Striatal Matched SBR

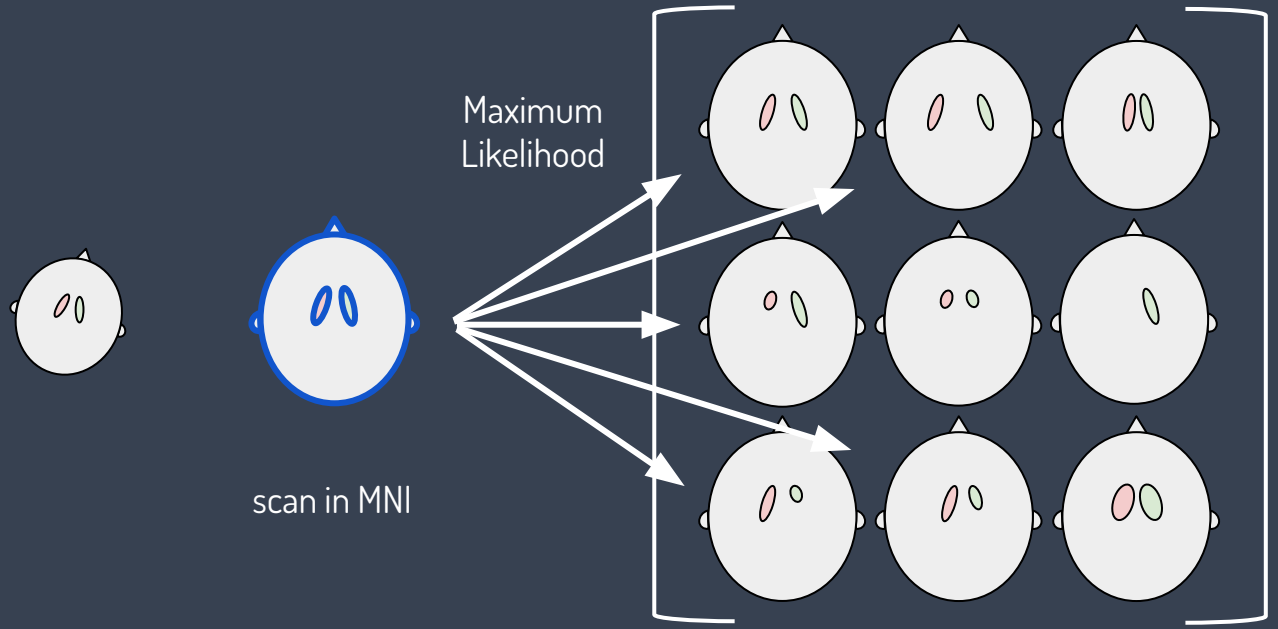


native scan

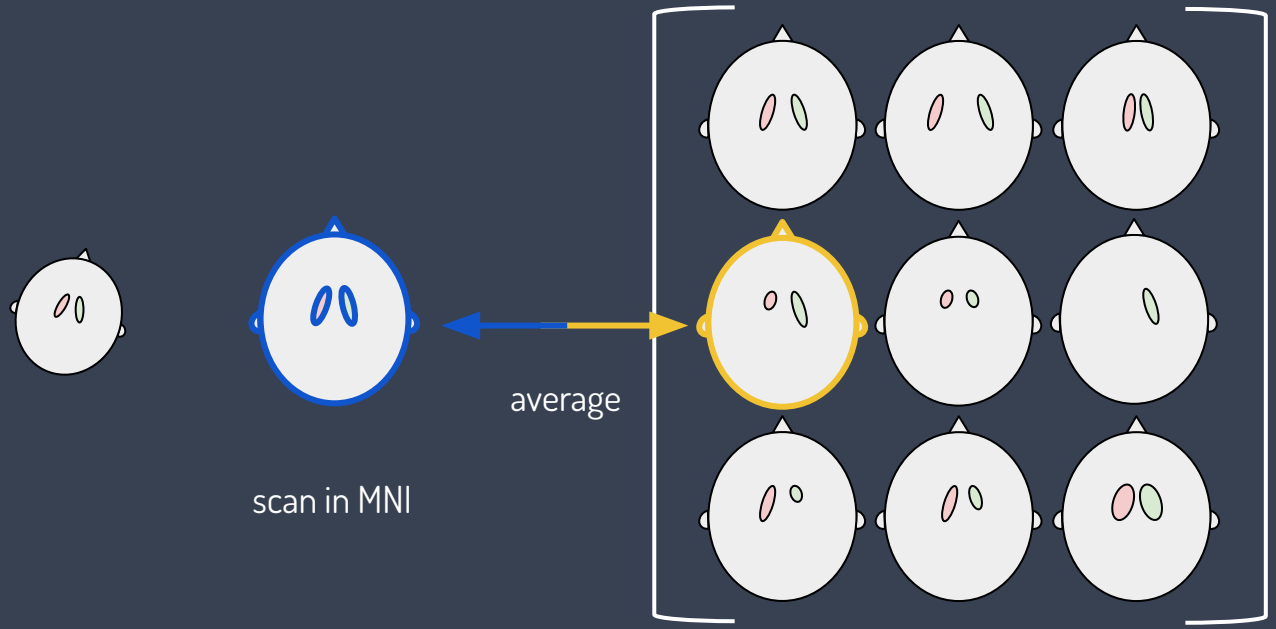
generic MNI
starting template



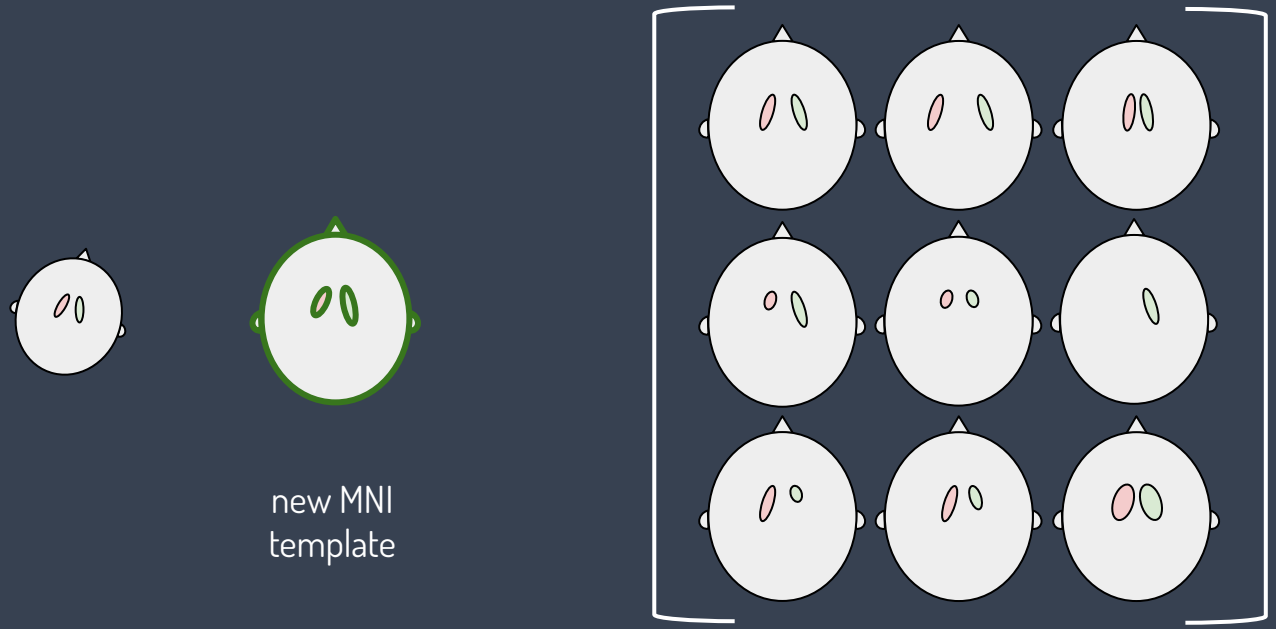
Clinical model - Striatal Matched SBR



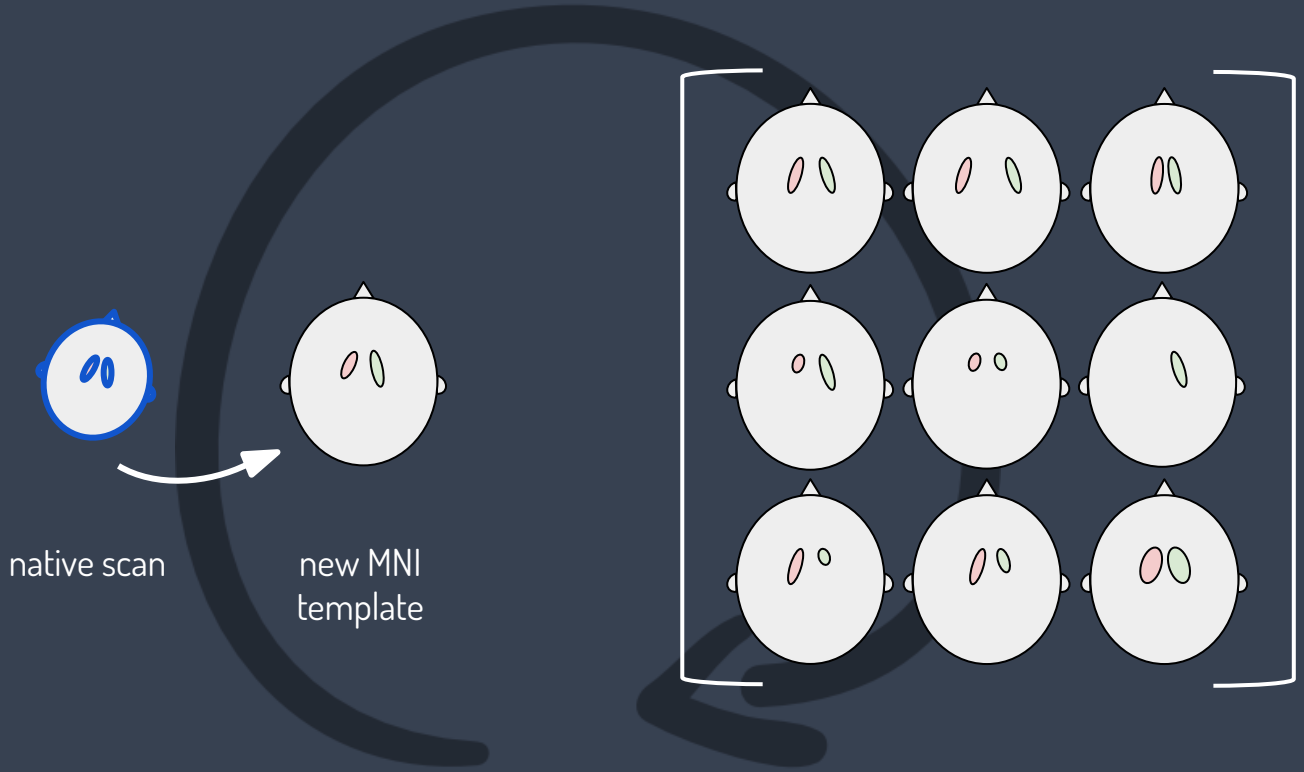
Clinical model - Striatal Matched SBR



Clinical model - Striatal Matched SBR



Clinical model - Striatal Matched SBR



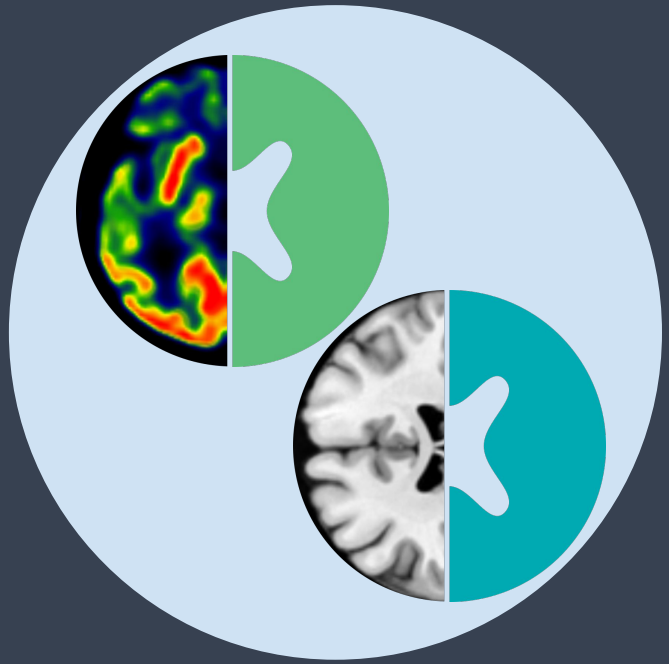
Iterative registration on a progressively averaging template

Clinical model - Striatal Matched SBR

- Multiple registration on a progressively averaged model allows the model (i.e. the estimated parameters) to converge to the mean parameters that best represent the input image, while at the same time overview the parameter precision
- By adding parameters I can update the method with the pathophysiological model
- You pay with computational cost (approx 1 min x registration on a "decent" hardware (multicore, min 32 GB memory) and possible convergence problems, but you can tune the iterations to achieve desired statistical error

$$SBR = \frac{C_{Tgt} - C_{Bckg}}{C_{Bckg}}$$

Iterative registration on a progressively averaging template



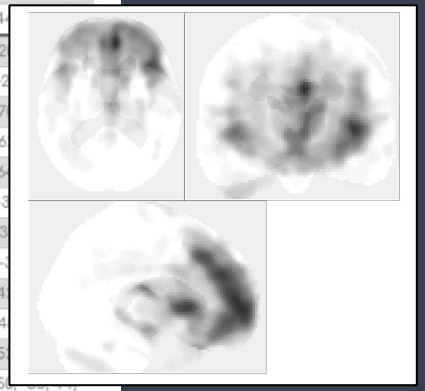
GLUCOSE HYPOMETABOLISM & NEURODEGENERATION

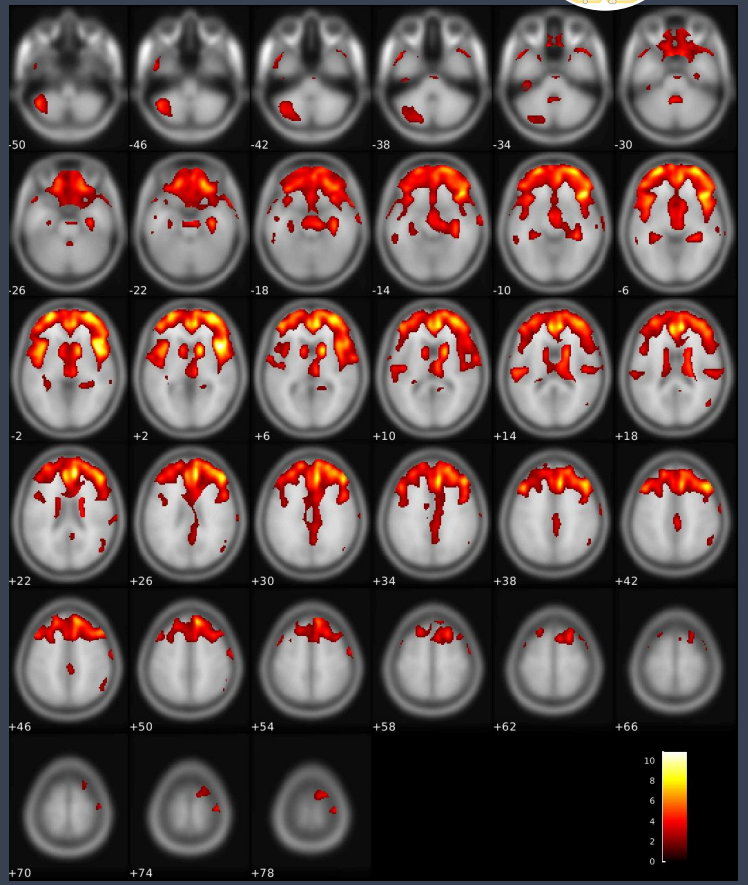
Consolidated knowledge - Voxel-wise (SPM)

- Voxel-wise analysis in SPM
- FDG hypometabolism T-maps

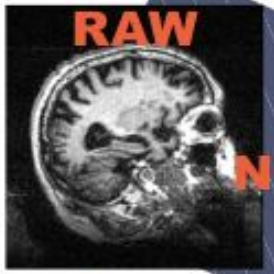
set-level		cluster-level				peak-level					coords
p	c	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	T	(Z_E)	p_{uncorr}	[mm]
1.000	9	0.000	0.000	53557	0.000	0.000	0.000	10.80	Inf	0.000	(44, 16, 0)
						0.000	0.000	10.18	Inf	0.000	(10, 44, 22)
						0.000	0.000	9.76	Inf	0.000	(46, 26, -10)
		0.962	0.863	1130	0.044	0.009	0.001	5.32	5.04	0.000	(-4
						1.000	0.236	3.17	3.10	0.001	(-2
		1.000	0.972	217	0.354	0.443	0.024	4.15	4.01	0.000	(-2
		1.000	0.972	218	0.353	0.751	0.048	3.87	3.75	0.000	(7
						1.000	0.886	2.14	2.12	0.017	(6
						1.000	0.954	1.97	1.96	0.025	(6
		1.000	0.972	548	0.146	0.927	0.084	3.65	3.54	0.000	(-3
						1.000	0.575	2.63	2.59	0.005	(-3
						1.000	0.969	1.91	1.90	0.029	(-
		1.000	0.972	108	0.521	0.998	0.173	3.32	3.24	0.001	(-4
		1.000	0.972	146	0.451	0.999	0.193	3.27	3.19	0.001	(4
						1.000	0.893	2.11	2.09	0.018	(5
		1.000	0.972	147	0.449	1.000	0.575	2.64	2.60	0.005	(5
						1.000	0.876	2.17	2.15	0.016	(54, -48, 46)
		1.000	0.972	161	0.427	1.000	0.703	2.48	2.45	0.007	(-56, -42, -12)
						1.000	0.987	1.83	1.82	0.035	(-56, -30, -22)

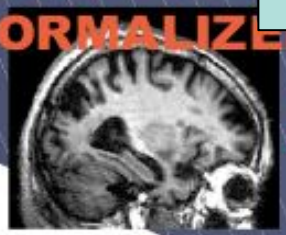
SPM report table.



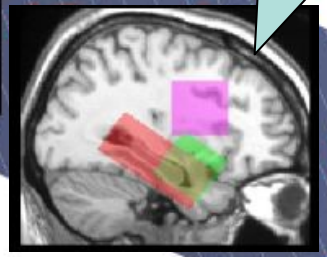


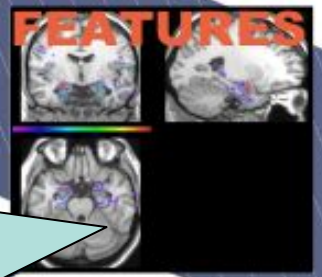
Radiomic - Global Disease Index





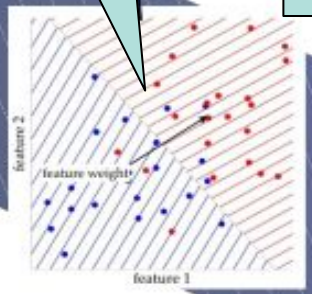
VOI placement
7 MTL volumes



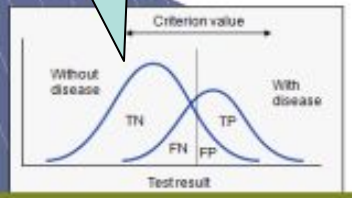


Relevant regions & features
A RF algorithm select those who discriminates CTRL / AD

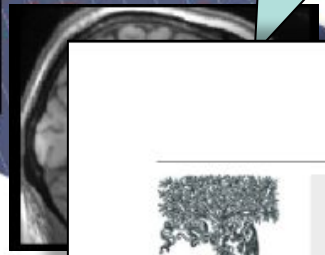
Classification
SVM classifier take feature subset from the RF and output the distance between the input set and the discriminating hyper surface.



Biomarker
A number is assigned to each input scan ranging from 1 (normalcy) to -1 (AD neurodegeneration)



Radiomic - Global Disease Index



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AD

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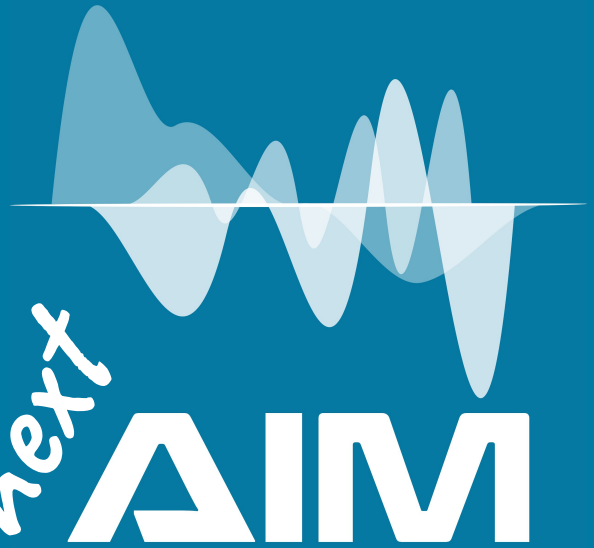
Local MRI analysis approach in the diagnosis of early and prodromal Alzheimer's disease☆

Andrea Chincarini [a,*], Paolo Bosco [a,b], Piero Calvini [a,b], Gianluca Gemme [a], Mario Esposito [a,b], Chiara Olivieri [c], Luca Rei [a,b], Sandro Squarcia [a,b], Guido Rodriguez [d], Roberto Bellotti [e,f], Piergiorgio Cerello [g], Ivan De Mitri [i,h], Alessandra Retico [j], Flavio Nobili [d]
and The Alzheimer's Disease Neuroimaging Initiative

Artificial Intelligence in Medicine



Thank you !

Enrico Peira
next_AIM annual meeting
14.02.2023, Milano

DORIAN
evolving neuroimaging

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