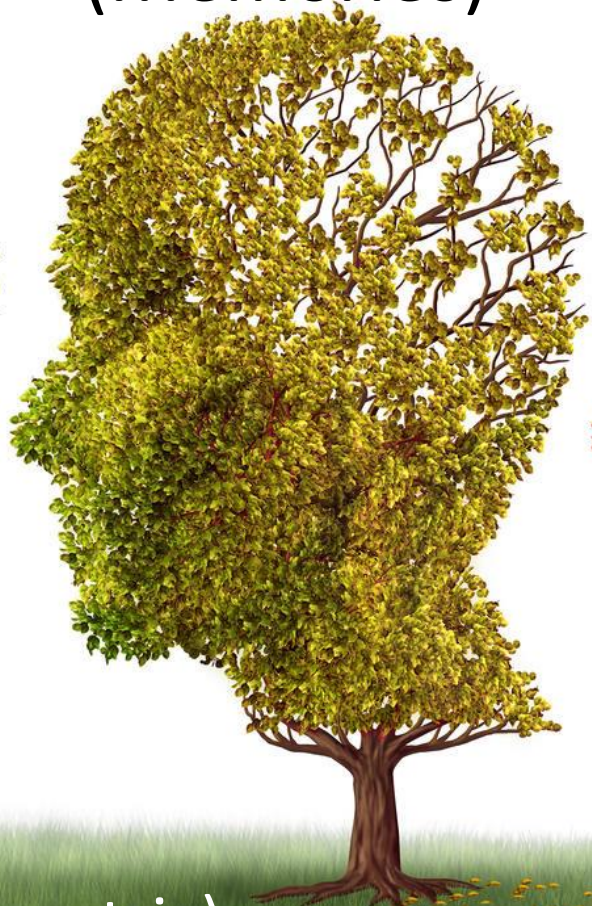


Herinneringen (Memories)



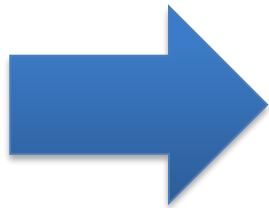
Annemie Ribbens (icometrix)
Sebastiaan Engelborghs (UAntwerpen)

23/11/2018

“Herinneringen” is gefinancierd binnen het Interreg V programma Vlaanderen-Nederland, het grensoverschrijdend samenwerkingsprogramma met financiële steun van het Europees Fonds voor Regionale Ontwikkeling. Meer info: www.grensregio.eu

icometrix - herinneringen

Retrospective and prospective evaluation of
selected biomarker profiles



Role of biomarkers

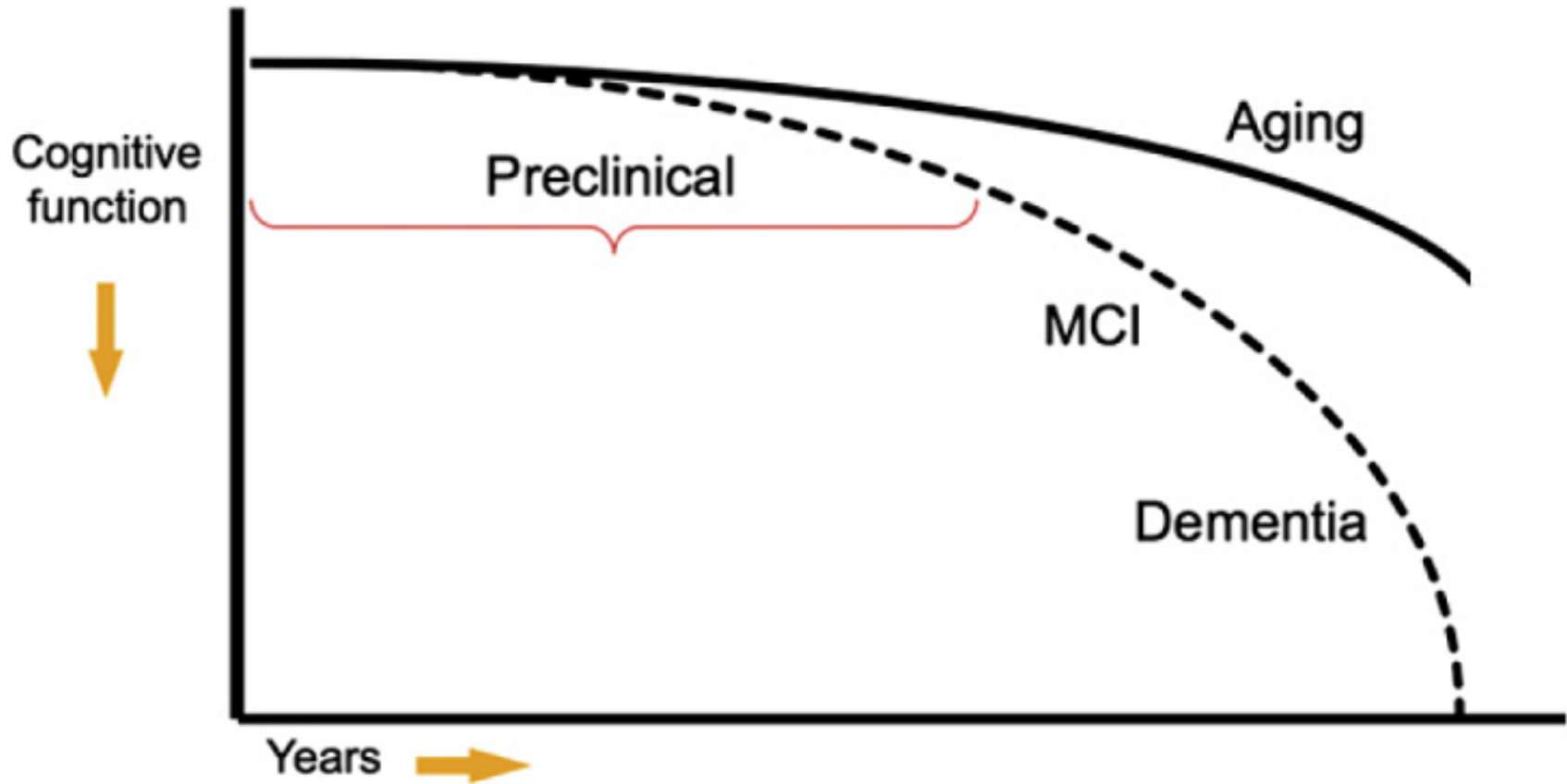


Biomarker validation in AD

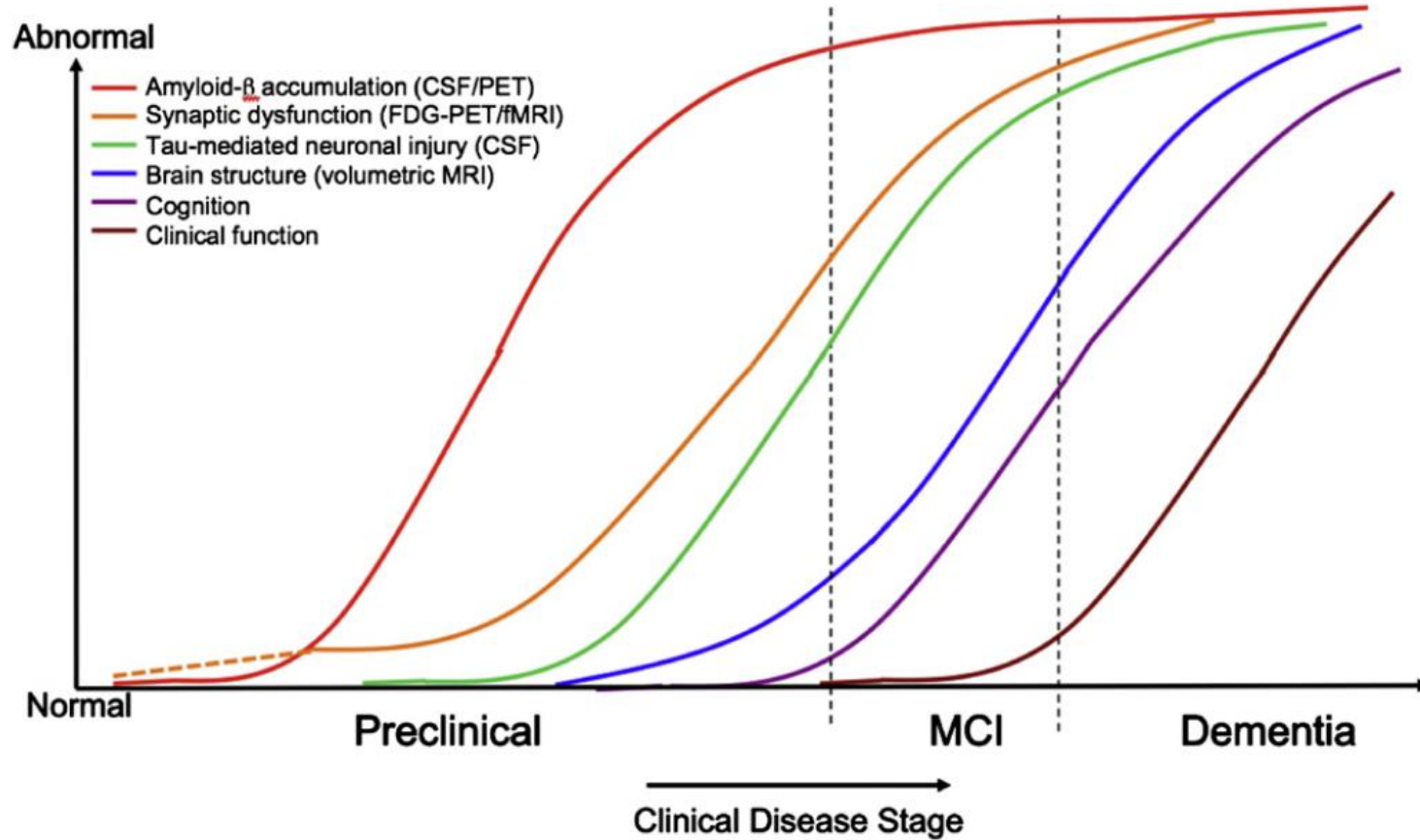
- Important to have an as homogeneous AD cohort as possible
- Important to apply biomarkers that reflect the neuropathology of AD



The continuum of AD



AD: biomarkers



Sperling et al. Alzheimer's & Dementia 2011, 7: 280-292



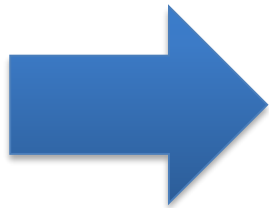
WP6 protocol

- Clinically diagnosed subjects:
 - Subjective cognitive decline: n=50
 - Mild cognitive impairment: n=50
 - AD dementia: n=50
- Neuropsychological exam, brain MRI scan, LP
- In case of normal AD CSF biomarkers: 'control' group



icometrix - herinneringen

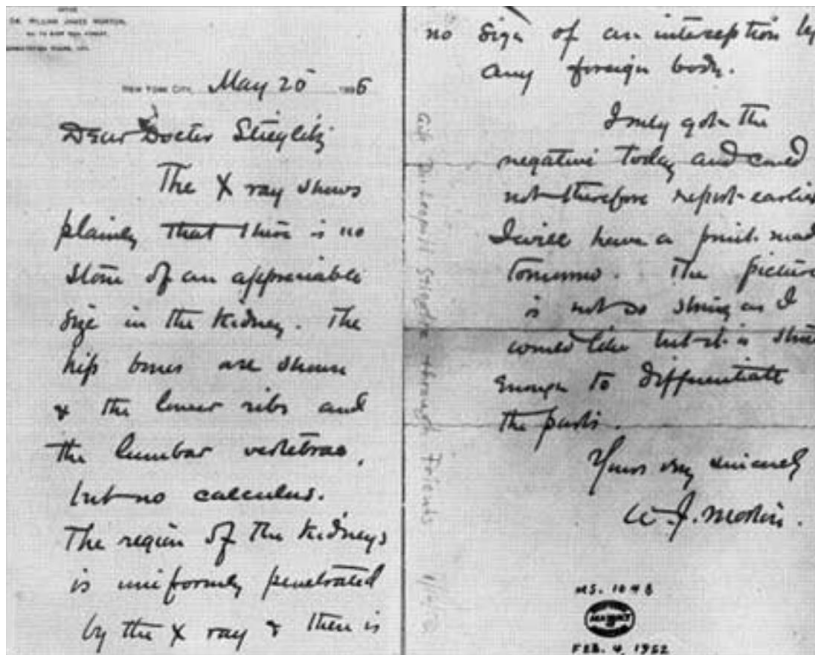
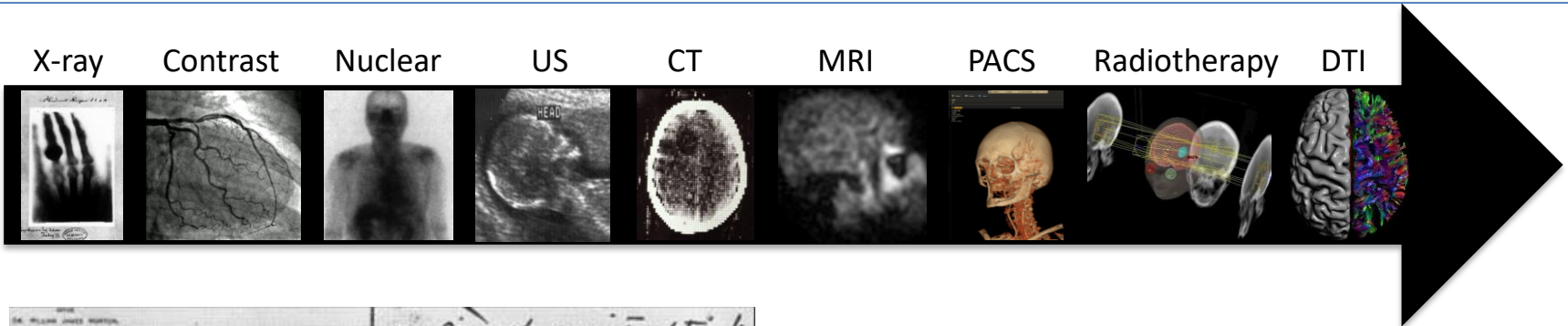
Retrospective and prospective evaluation of
selected biomarker profiles



imaging biomarkers



A brief history of radiology



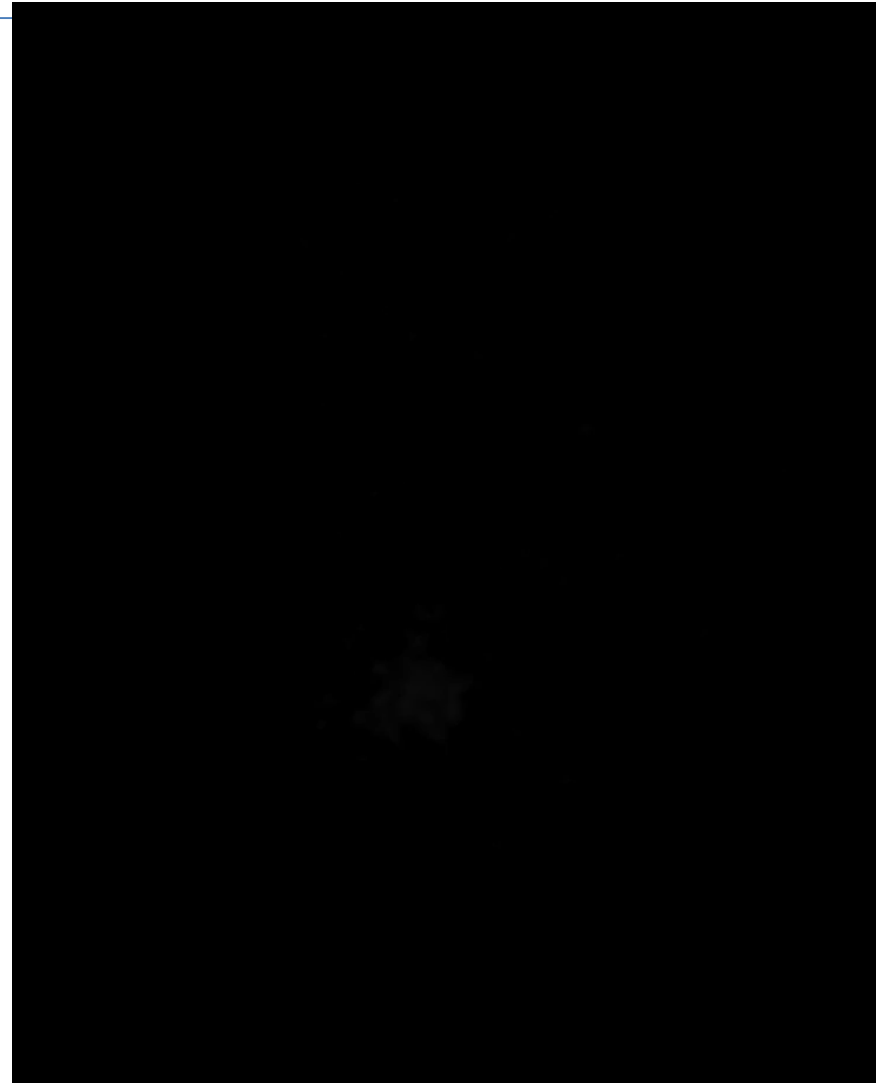
“Dear Dr Stieglitz: The X ray shows plainly that there is no stone of an appreciable size in the kidney. The **hip bones are shown** & the lower ribs and lumbar vertebrae, but no calculus. The region of the kidneys is **uniformly penetrated by the X ray** & there is no sign of an interception by any foreign body. I only got the negative today and **could not therefore report earlier**. I will have a print made tomorrow. The picture is not so strong as I would like, but **it is strong enough to differentiate the parts.**”

William James Morton, MD, May 1896



Radiological report today

Supratentorial, there are many T2-hyperintense lesions from the subcortical to the deep periventricular white matter in both hemispheres. Multiple lesions run perpendicular to the lateral ventricles. Moderate global cortical atrophy. No Gd enhancing lesions were seen.



Blood lab

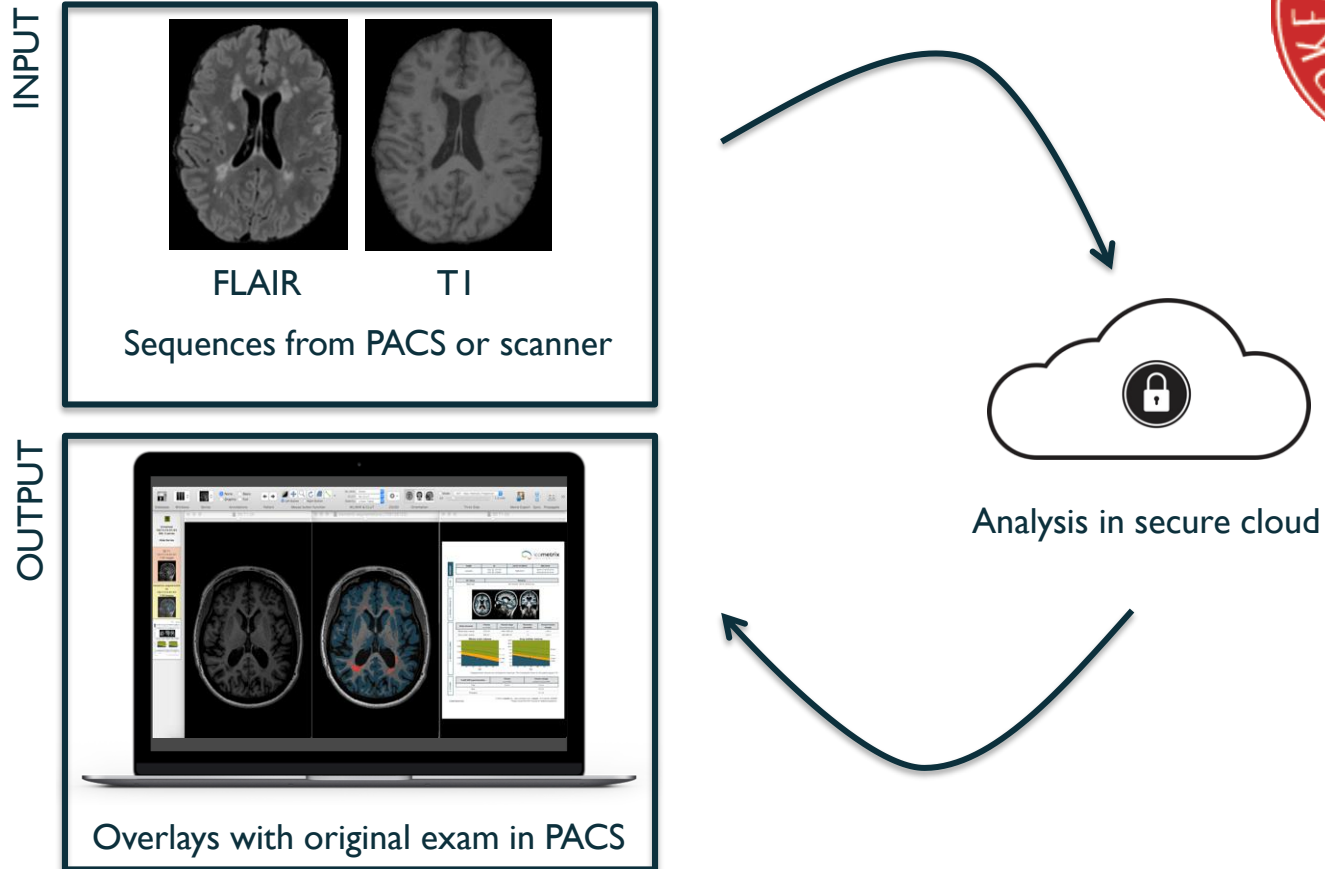


Patient Name		Date Drawn	Date Received	Date of Report
Doe, Jane		12/27/03	12/29/03	12/30/03
Sex	Age	Physician Name/Address		I.D. Number
F	37	CONCOURSE MEDICAL YOUR DOCTOR, M.D. ANYWHERE, USA 000000		654534565
Patient I.D./Soc. Sec. #		Time Drawn		Specimen Number
235463746		9:30AM		343477
TEST NAME	RESULT	ABNORMAL	NORMAL	UNITS
CHEM-SCREEN PANEL				
GLUCOSE			87.0	MG/DL
SODIUM			140.0	MMOL/L
POTASSIUM			4.6	MMOL/L
CHLORIDE			106.0	MMOL/L
CARBON DIOXIDE			28.0	MMOL/L
BUN			9.00	MG/DL
CREATININE			0.90	MG/DL
BUN CREATININE RATIO			10.0	
URIC ACID			6.00	MG/DL
CALCIUM			9.60	MG/DL
MAGNESIUM			2.09	G/DL
CHOLESTEROL			215.0	MG/DL
CHOL. PERCENTILE	H	75.0		PERCENTILE
TRIGLYCERIDES	H	230.0		MG/DL
PROTEIN, TOTAL			7.60	GM/DL
ALBUMIN			4.10	GM/DL
BILIRUBIN, TOTAL			0.41	MG/DL
BILIRUBIN, DIRECT			0.06	MG/DL
ALK PHOSPHATASE			69.0	UNITS/L
GGT			18.0	UNITS/L
AST (SGOT)	H	46.0		IU/L
ALT (SGPT)	H	65.0		IU/L
AMYLASE, SERUM			33.0	UNITS/L
COMPLETE BLOOD COUNT (CBC)				
WHITE BLOOD CELL (WBC) COUNT			5.10	THOUS./CU.MM
RED BLOOD CELL (RBC) COUNT	L	3.88		MIL./CU.MM
HEMOGLOBIN (HGB)			14.0	GM/DL
HEMATOCRIT (HCT)			42.3	PERCENT
MCV	H	109.0		FL
MCH	H	38.4		PG
MCHC			35.2	PERCENT
RDW			12.2	PERCENT
PLATELET COUNT, AUTO			243.0	THOUS./CU.MM
T-LYMPH SUBSETS				
CD4+ HELPER (36.0 PCT)			651	CU.MM
CD8+ SUPPRESS (44.0 PCT)			796	CU.MM
CD4/CD8 RATIO	L	0.81		RATIO
DIFFERENTIAL				
POLY (52.2 PCT)			2662	CU.MM
LYMPH (35.5 PCT)			1810	CU.MM
MONO (9.9 PCT)			504	CU.MM
EOS (1.9 PCT)			96	CU.MM
BAZO (0.5 PCT)			25	CU.MM

*These reference ranges are for females.

The ranges for men are: RBC=4.7-6.10,HGB=140-8.0,HCT=42.0-52.0

Imaging lab



Relevant imaging biomarkers

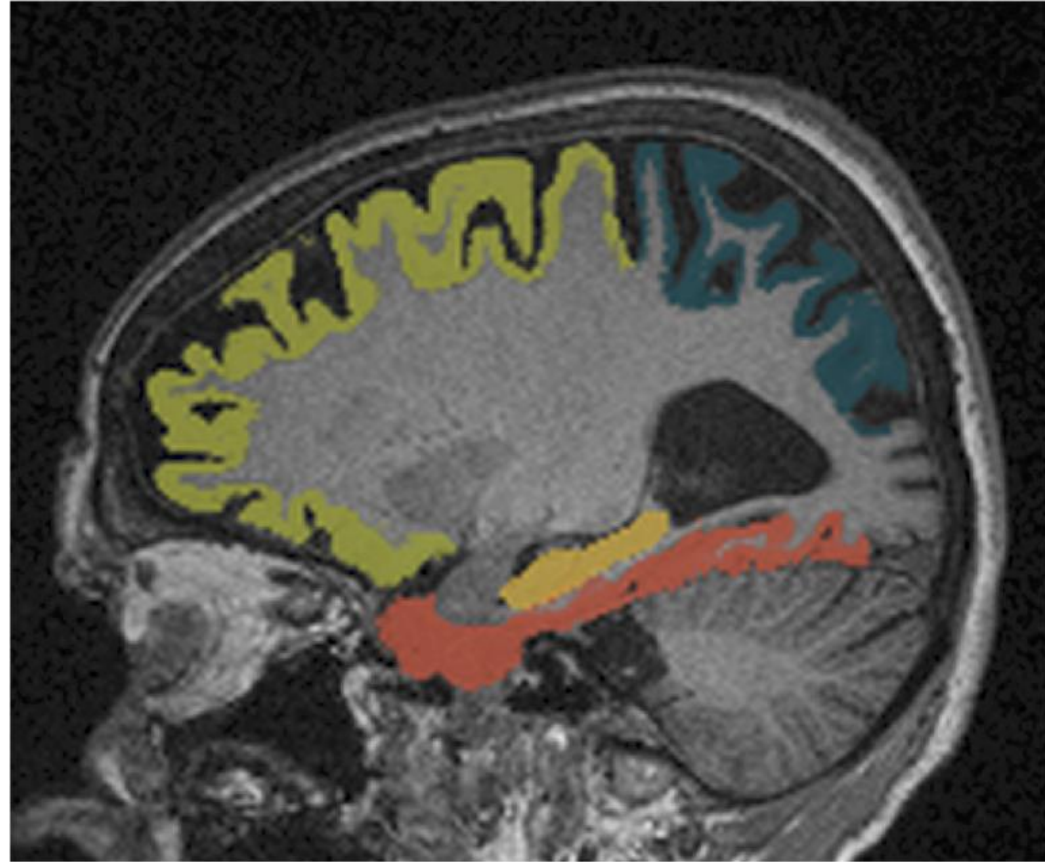
Global brain atrophy:

- Whole brain volume and atrophy
- Grey matter volume and atrophy
- White matter volume and atrophy

Local brain atrophy:

- Hippocampus
- Deep grey matter
- Cortical grey matter
- Frontal cortex
- Parietal cortex
- Temporal cortex

FLAIR white matter hyper-intensities
(*vascular*)



icobrain dm



icobrain dm

INFO	NAME	ID	YEAR OF BIRTH	MRI DATES
	icometrix dm	ICO-ID	1941	2015-09-29 2017-08-07
QC	STATUS		REMARKS	
	Approved		No remarks.	

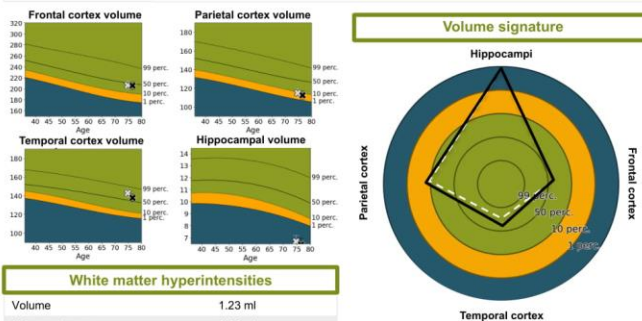
VISUAL RESULTS



BRAIN VOLUMES

	Frontal cortex	Parietal cortex	Temporal cortex	Hippocampi
Volume	206 ml*	112 ml*	138 ml*	6.4 ml*
Normal range	176 - 241 ml*	107 - 144 ml*	117 - 149 ml*	8.3 - 12.3 ml*
Normative percentile	38.6	6.3	71.0	< 1
Annualized volume change	-0.21 %	-1.19 %	-1.89 %	-2.09 %
Normal annualized volume change	-0.31 %	-0.36 %	-0.40 %	-0.95 %

FLAIR



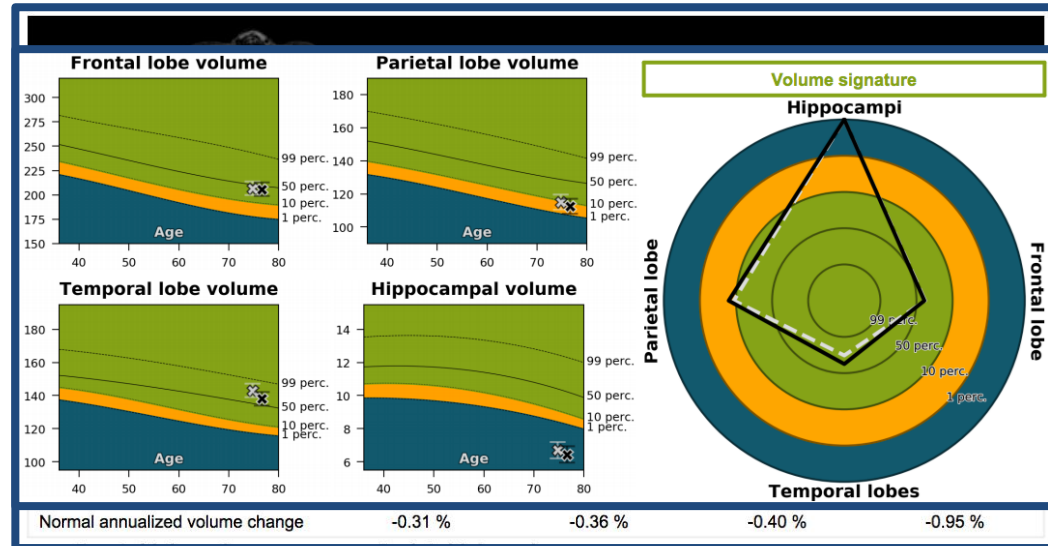
White matter hyperintensities
Volume
Volume change

* Displayed brain volumes are corrected for head size. The correction factor for this patient is 0.70.

SAMPLE

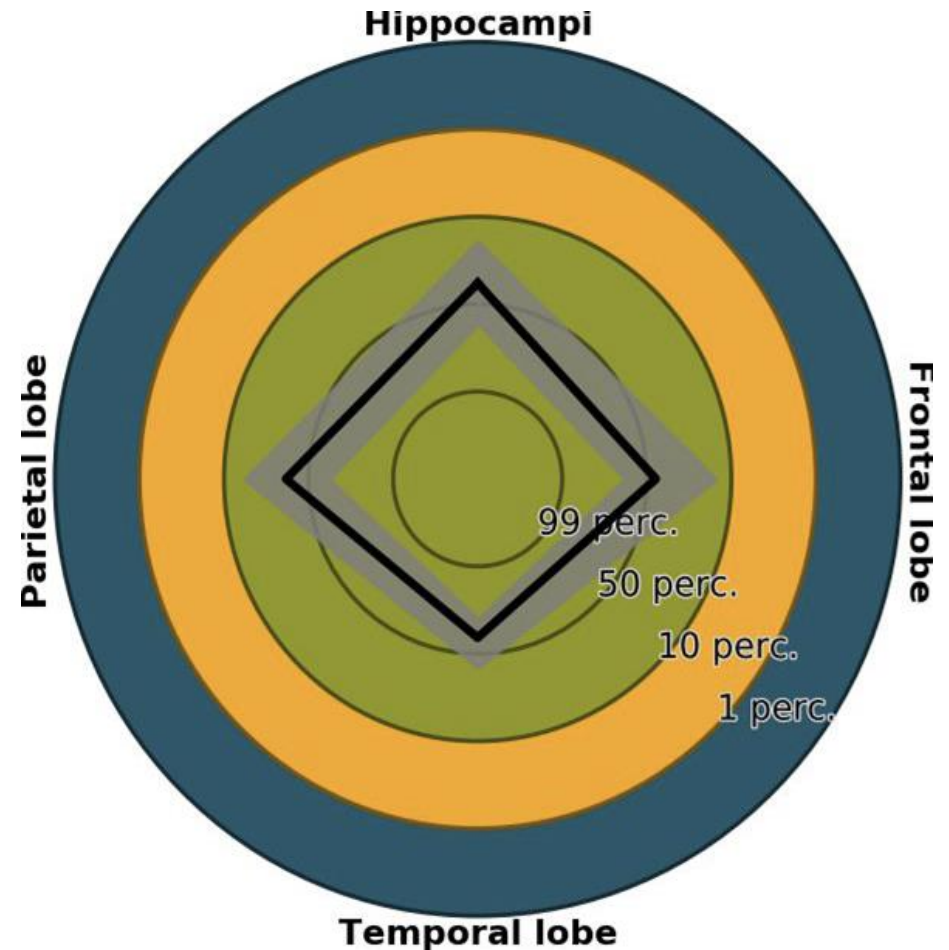
This report is approved for clinical use in the US, EU, AU, BR, CA and IN. Please visit www.icometrix.com or contact info@icometrix.com for more information.

icobrain 3.x.x Manufactured by icometrix NV, Kolonel Begaultlaan 1b/ 12, 3012 Leuven, Belgium.

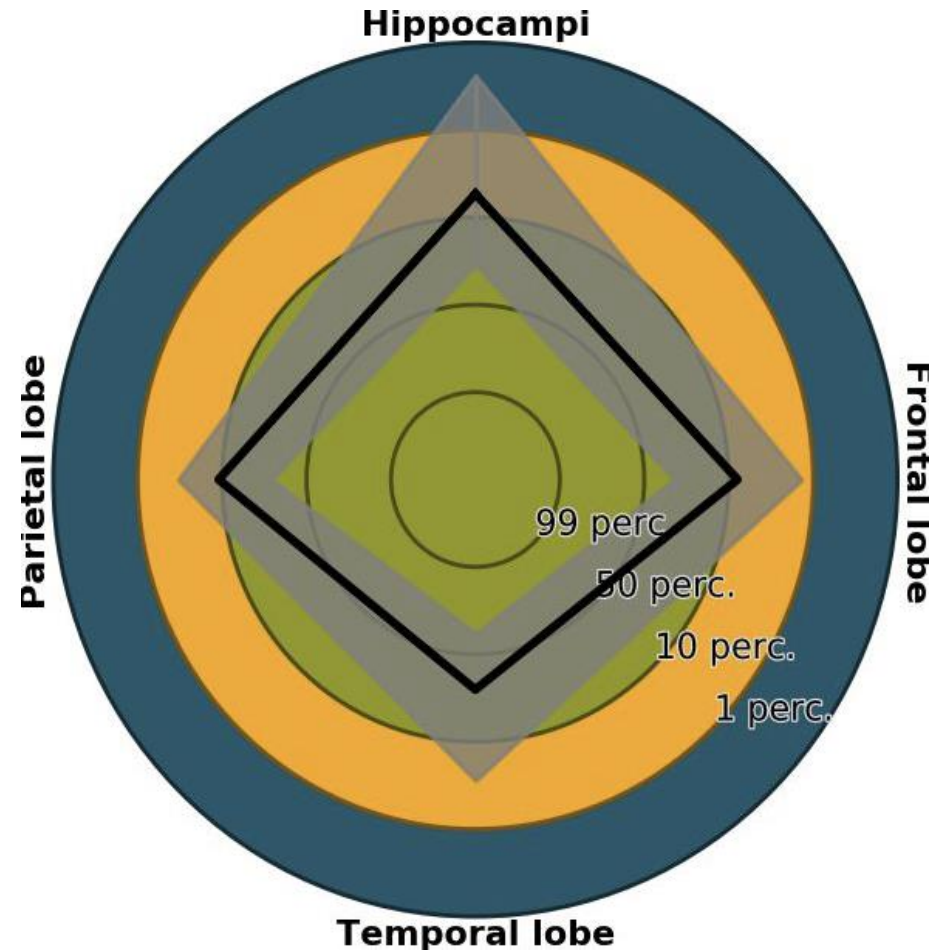


Dementia signatures

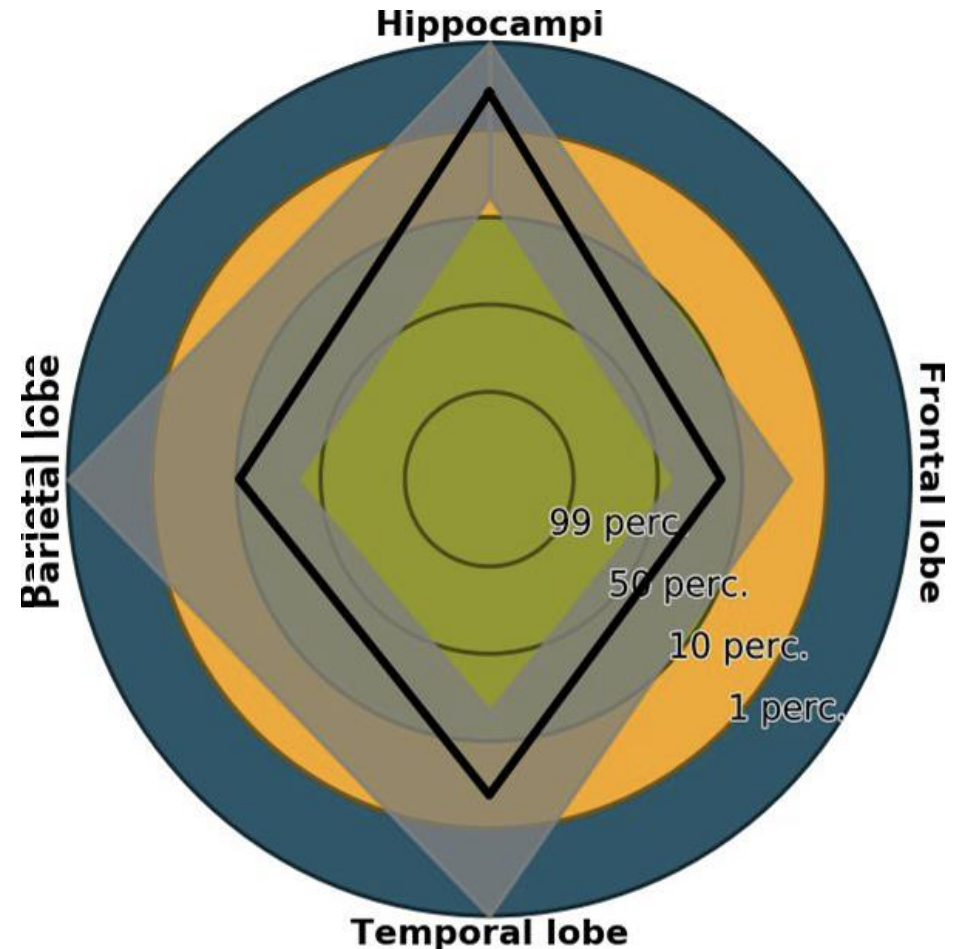
 HEALTHY SUBJECTS



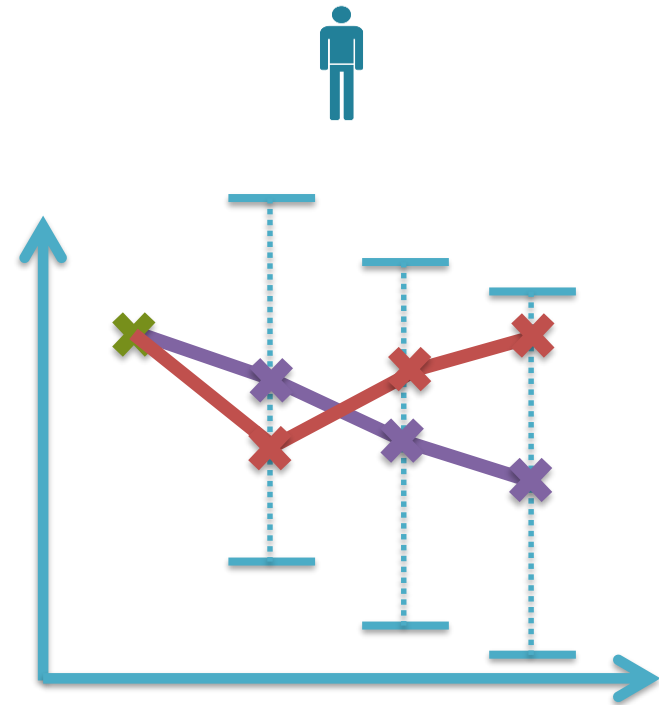
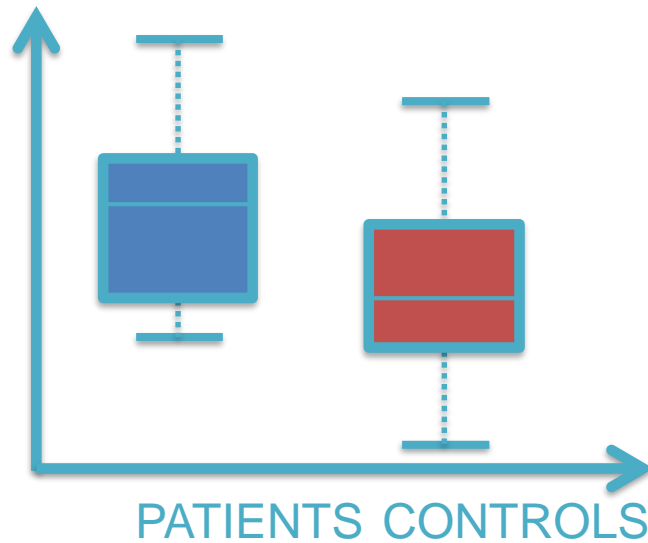
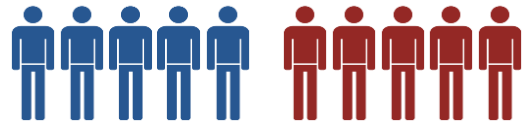
Dementia signatures



Dementia signatures



Assessment of individual patients

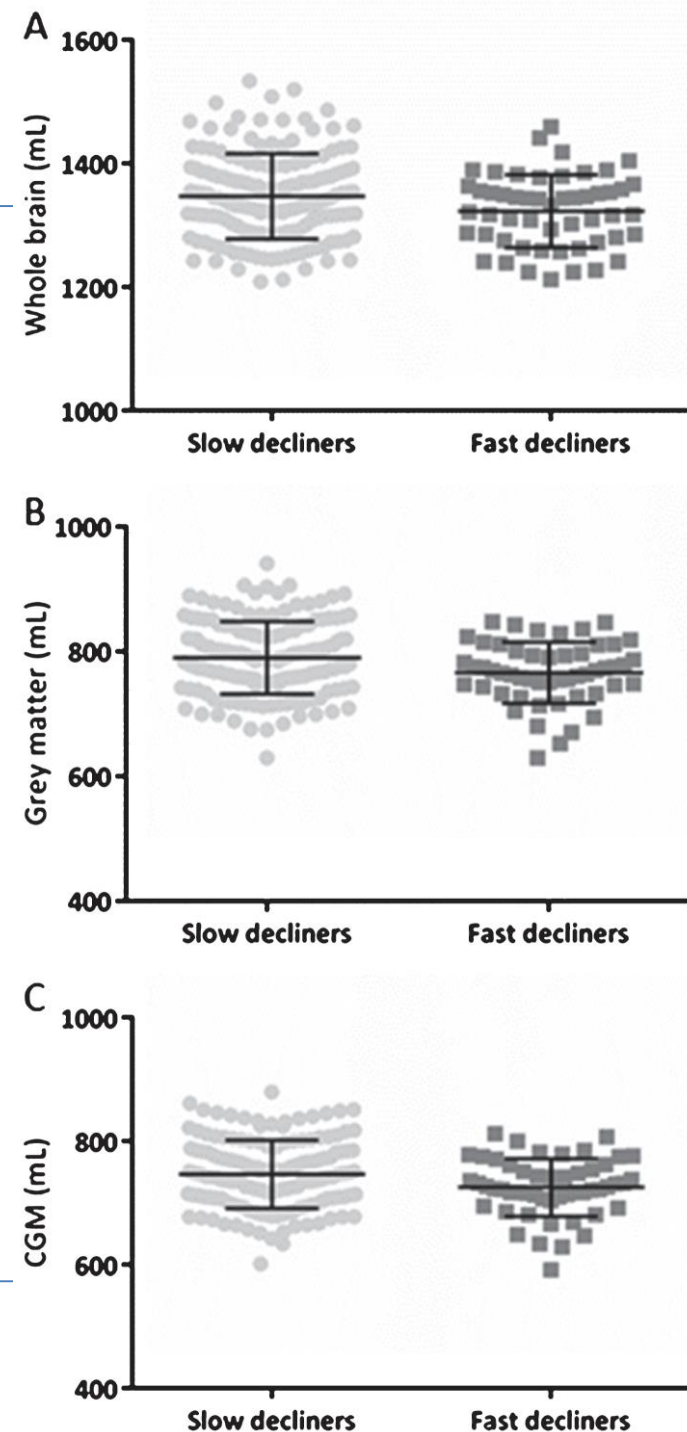


Disease assessment

REMEMBER – A Belgian multi-center MRI biomarker study

WB and GM volumes extracted by icometrix could be used to define the clinical spectrum of AD accurately and along with CGM, they are able to predict cognitive impairment based on (decline in) MMSE scores.[1]

- *Early diagnosis*
- *Clinical spectrum*
- *Disease prognosis*



[1] Niemantsverdriet et al. Journal of Alzheimer's disease, 2018



MRI vs. CSF markers

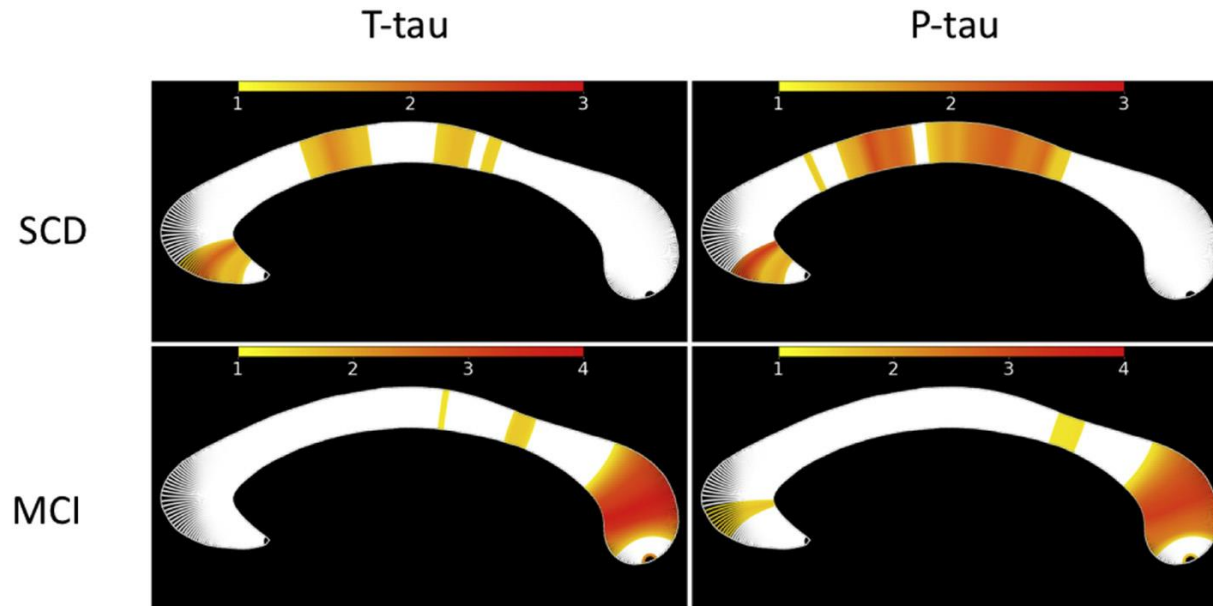


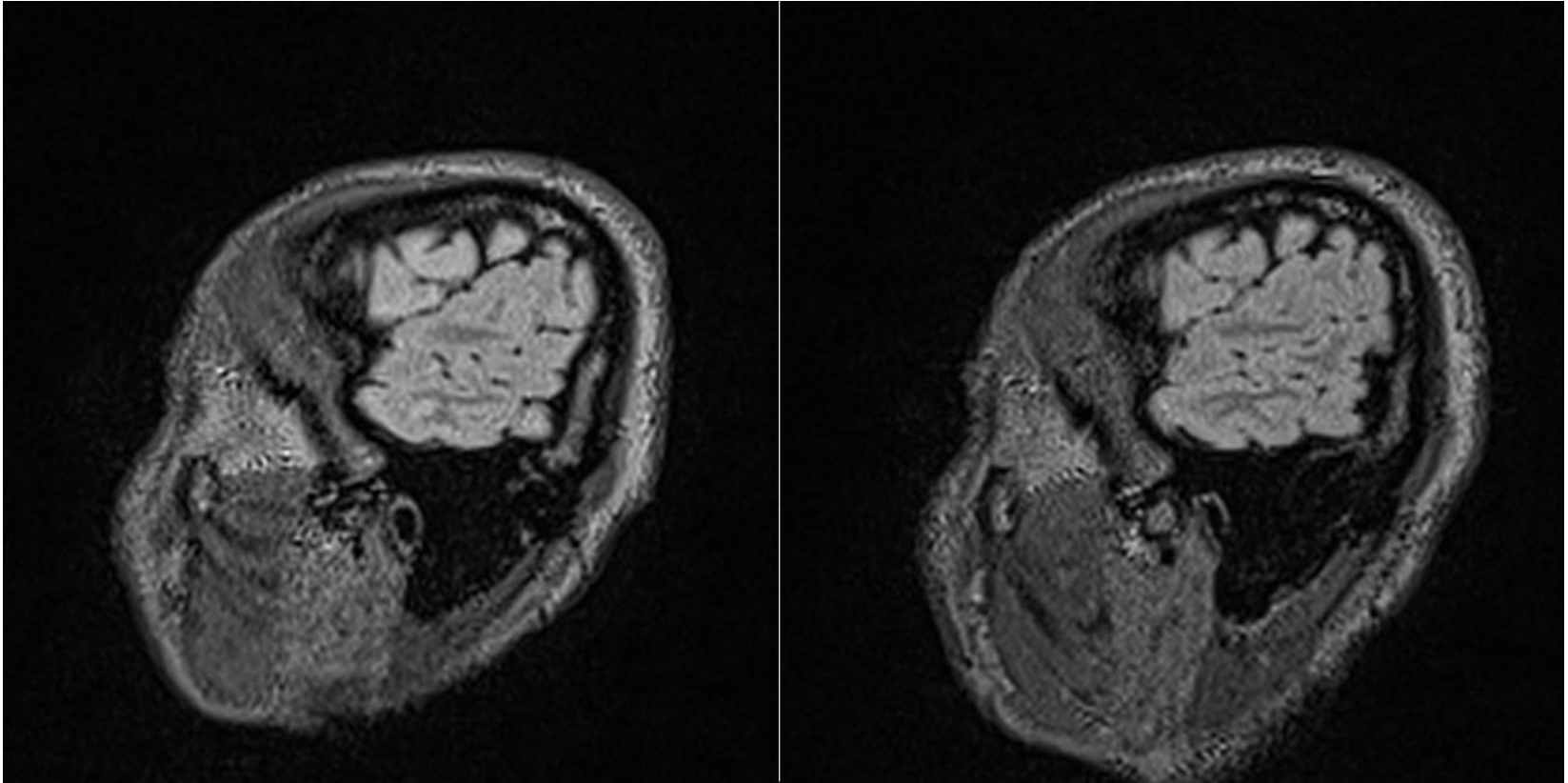
Fig: Correlation between CSF markers T-tau and P-tau and the callosal thickness profile. Significant streamlines are shown for $p < 0.05$. ^[1]

[1] Van Schependom et al., 2018



A clinical case

37-year-old with history of multiple sclerosis. Extremity weakness. Increasing loss of balance over 2 weeks.



A clinical case

Neuroradiologist 1 (EU)

Regression in size of several (about 10) lesions in both frontal lobes, of one occipital lesion and of all right cerebellar lesions and disappearance of one left frontolateral lesion.

Stability of the lesions in other locations.

Impression of progression of cortical atrophy.

CONCLUSION:

Favorable evolution with disappearance of one and regression of several other lesions.

Impression of slight cortical atrophy compared to the previous examination.

Neuroradiologist 2 (US)

1. New focus of punctate enhancement in the posterior right temporal lobe adjacent to the ventricular atrium. Diminished enhancement in previously seen right frontoparietal lesion.

2. New focus of T2 abnormality without enhancement right frontal lobe. Slight increase in size of left frontal T2 abnormality.

3. Multiple white matter lesions which are otherwise stable in the interval consistent with patient's clinical history of multiple sclerosis.



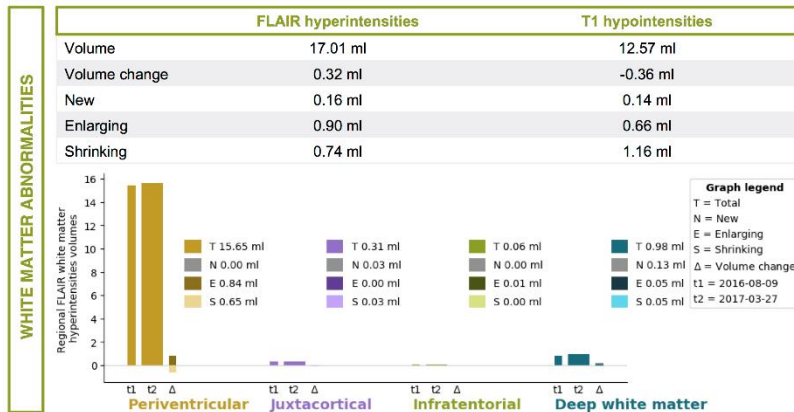
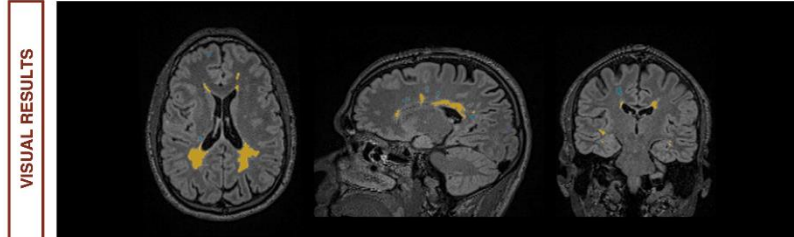
A clinical case

icobrain

icometrix
IMAGING BIOMARKER EXPERTS

INFO	NAME	ID	DATE OF BIRTH	MRI DATES
	icometrix	4147205	1979-03-29	2016-08-09 2017-03-27

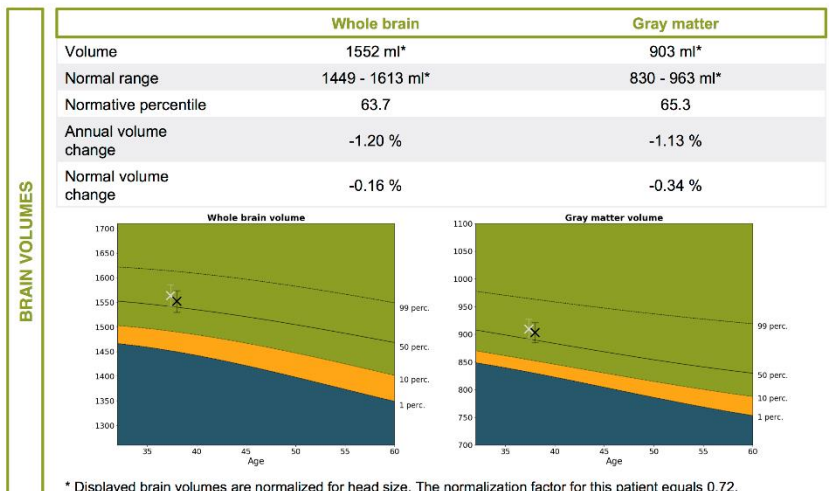
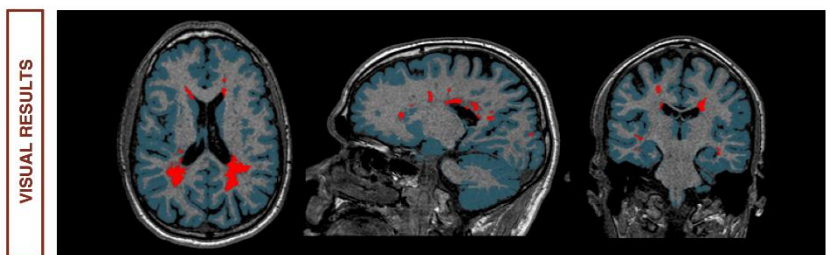
QC	STATUS	REMARKS
	Approved	No remarks. Not for clinical use.



icobrain

icometrix
IMAGING BIOMARKER EXPERTS

INFO	NAME	ID	DATE OF BIRTH	MRI DATES
	icometrix	4147205	1979-03-29	2016-08-09 2017-03-27



A clinical case

Neuroradiologist 1 (EU)

Regression in size of several lesions in both frontal lobes, of one occurring in the right cerebellar lesions, volume loss of 0.74ml.

Enlargement of several lesions (frontal and parietal) for a total volume of 0.90 ml. Two new lesions (frontal and parietal) for a total volume of 0.90 ml.

Progression of cortical atrophy with brain volume loss of 1.2% (gray matter volume loss of 1.2% both higher than the expected within that age category (0.34%).

CONCLUSION:

Progression of lesion load with two new lesions. Slight progression of global and cortical atrophy.

Neuroradiologist 2 (US)

1. New focus of punctate enhancement in the right frontal lobe adjacent to the previously described enhancement in the right parietal lesion.

2. R/T2 hyperintensity in the frontal, right parietal, and left frontal lobes, enlargement left frontal lobe abnormality.

3. FLAIR hyperintensity in the frontal lobe, 17.0 mL, increased by 1.1% interval.

4. Total brain volume decreased at 1522 mL, in the interval, with an interval decrease of 1.2%.

5. Please see included MSmetrix report for complete volumetric analysis.

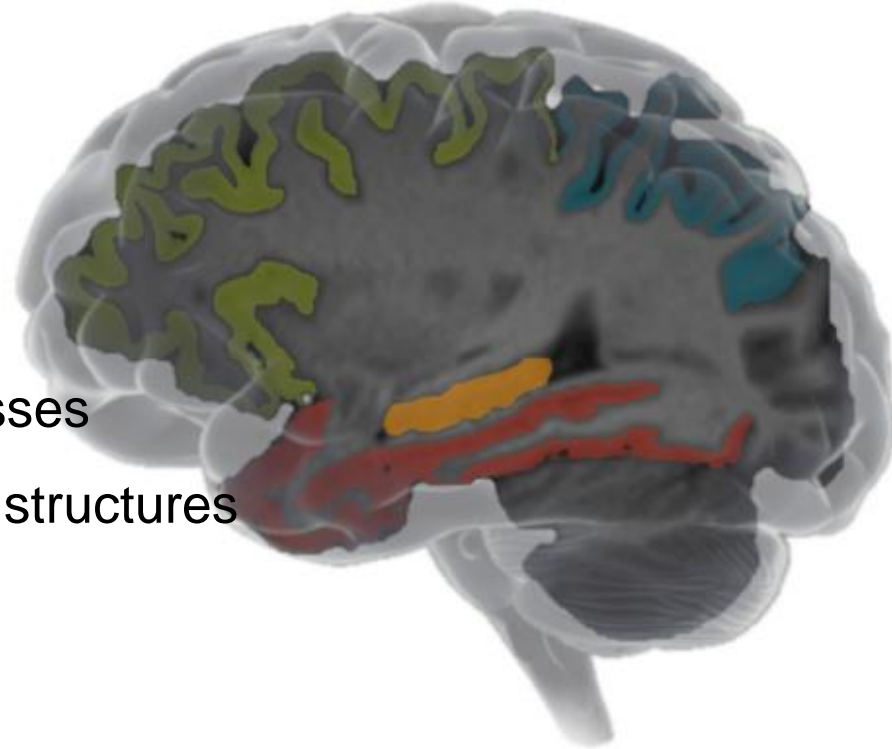
6. Please see included MSmetrix report for complete volumetric analysis.

1. Both radiologists changed their conclusion
2. Both radiologists felt more confident in their reading with the icobrain report
3. Numbers are added to the report
4. Reports were more accurate
5. Reports were more consistent
6. Reading time decreased from around 15 minutes to 5 minutes



Conclusion

- Objective information
- More information available
 - Global brain atrophy - tissue classes
 - Local brain atrophy - anatomical structures
 - Population graphs
- High accuracy, sensitivity and reproducibility



Early diagnosis & improved assessment and patient follow-up



Co-financiering

- Dit project is mede mogelijk gemaakt door co-financiering van:

