Molecular imaging in Nuclear Medicine

Applications in Artificial Intelligence
From Biomarkers to Theranostics

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The medical motives

- Need of **precise** and **early** characterization to:
  - diagnose and guide treatment of diseases otherwise incurable at later stages
  - evaluate efficiency of (expensive) therapeutics to not delay more effective treatment, and not cause unnecessary side effects

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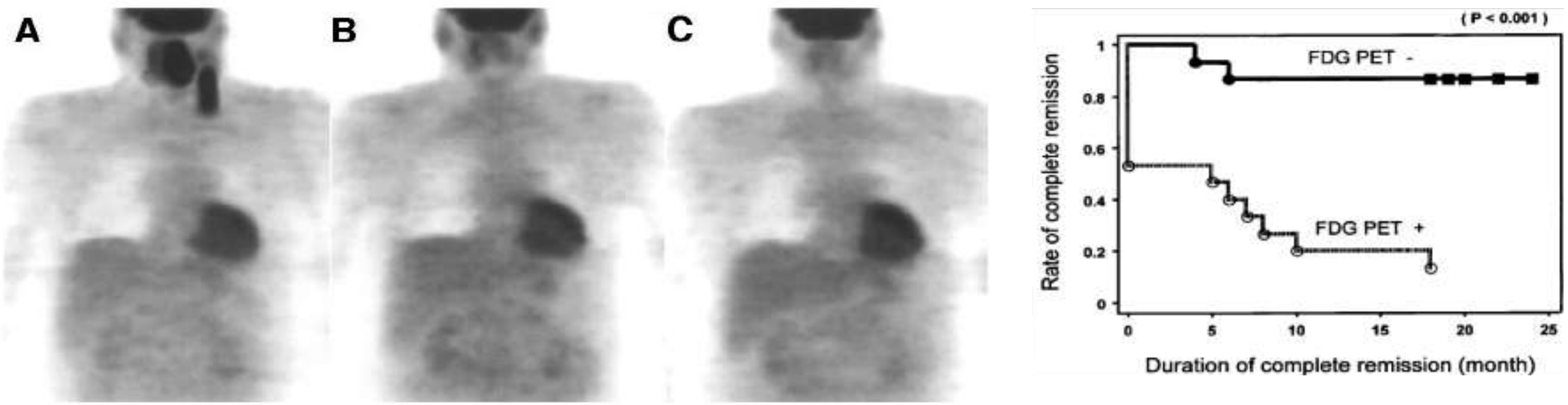
  - molecular changes precede morphological ones (***more sensitive for early diagnosis and evaluation***)

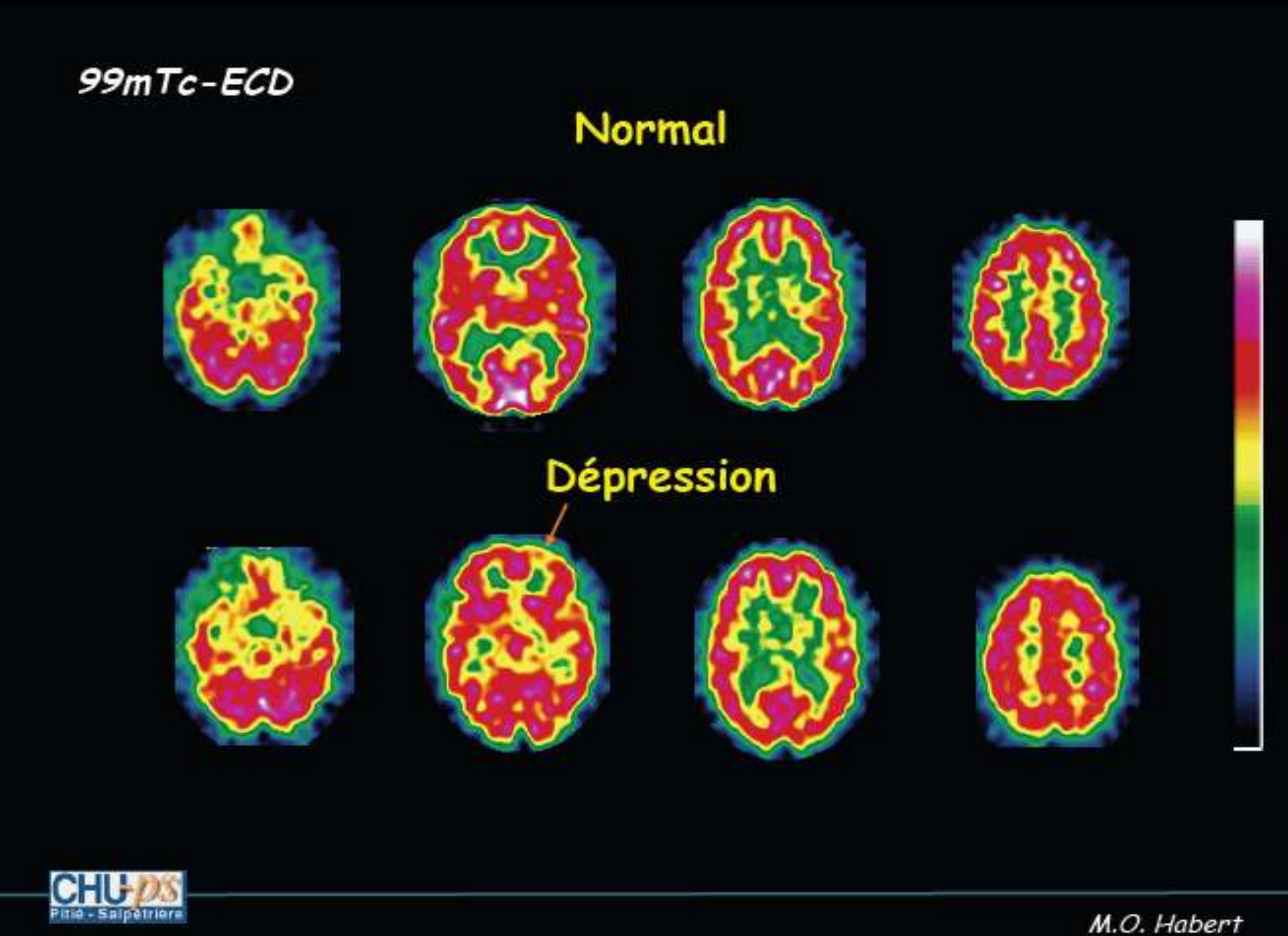
PET Predicts Prognosis After 1 Cycle of Chemotherapy in Aggressive Lymphoma and Hodgkin's Disease

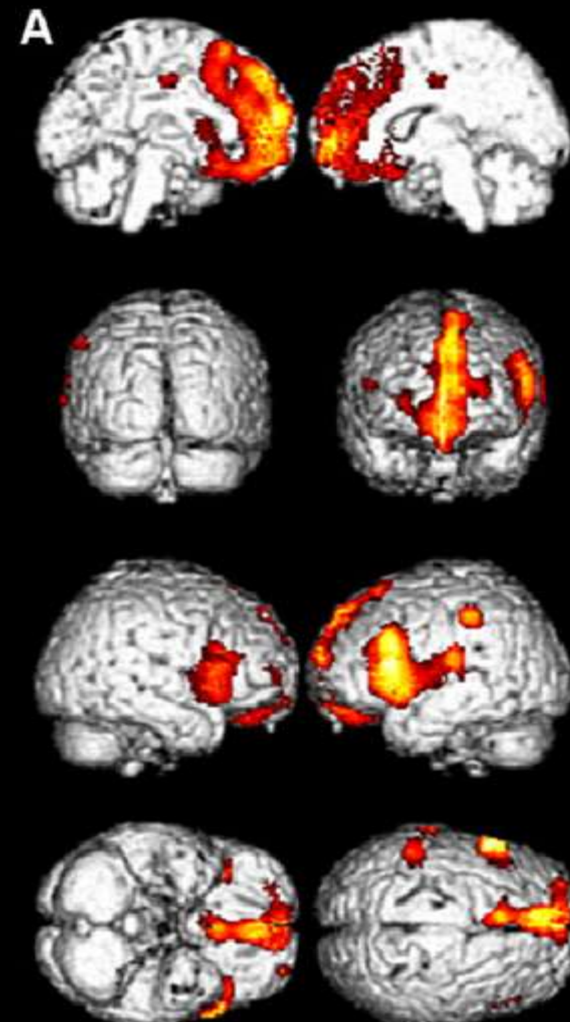
Lale Kostakoglu, MD[1]; Morton Coleman, MD[2]; John P. Leonard, MD[2]; Ichiei Kuji, MD[1]; Holly Zoe[1]; and Stanley J. Goldsmith, MD[1]



THE JOURNAL OF NUCLEAR MEDICINE • Vol. 43 • No. 8 • August 2002

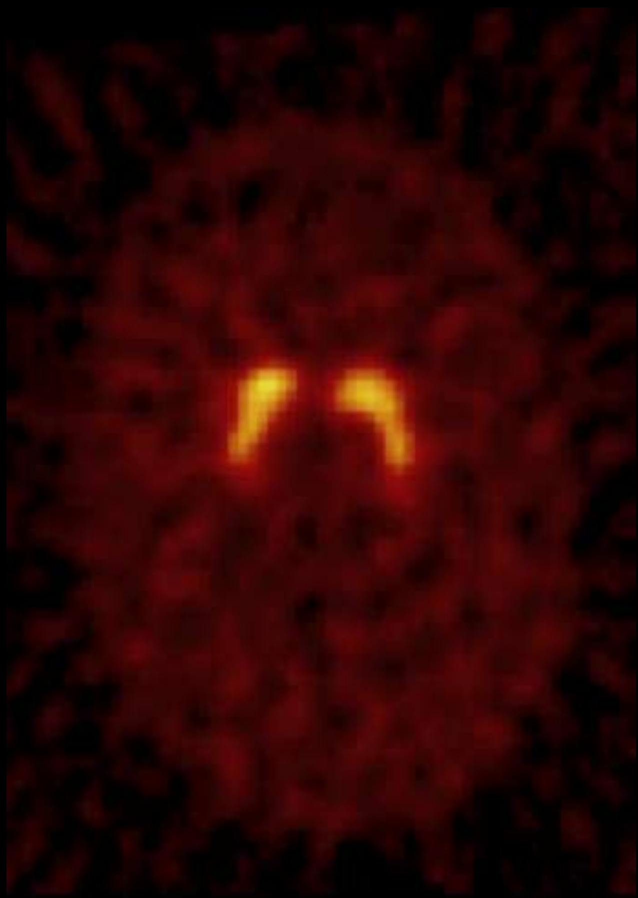
Brain hypoperfusion in patients with depression



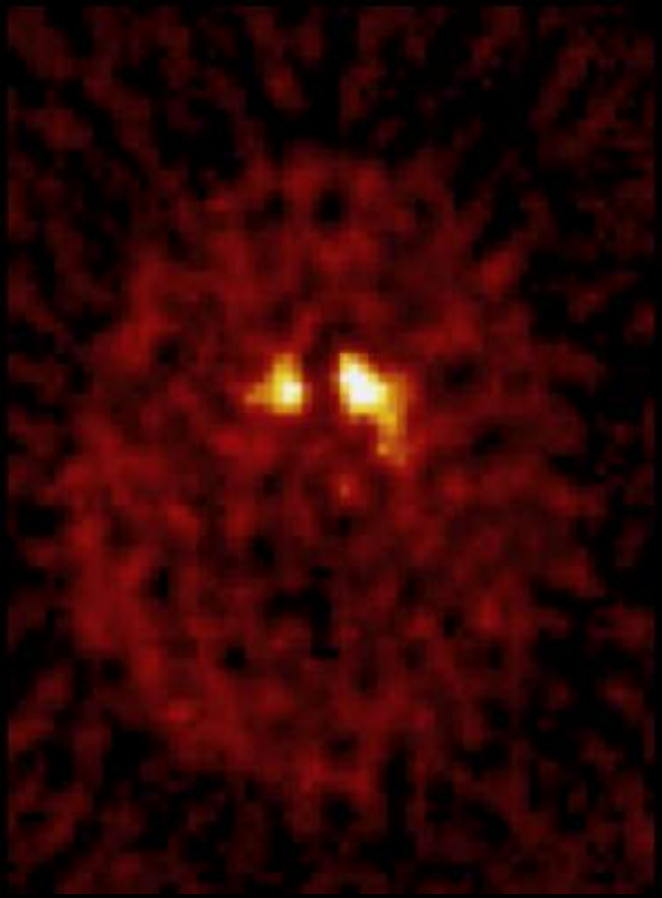


Richieri et al., EJNMMI 2011

50% of brain dopaminergic loss before first symptoms of Parkinson



Healthy subject

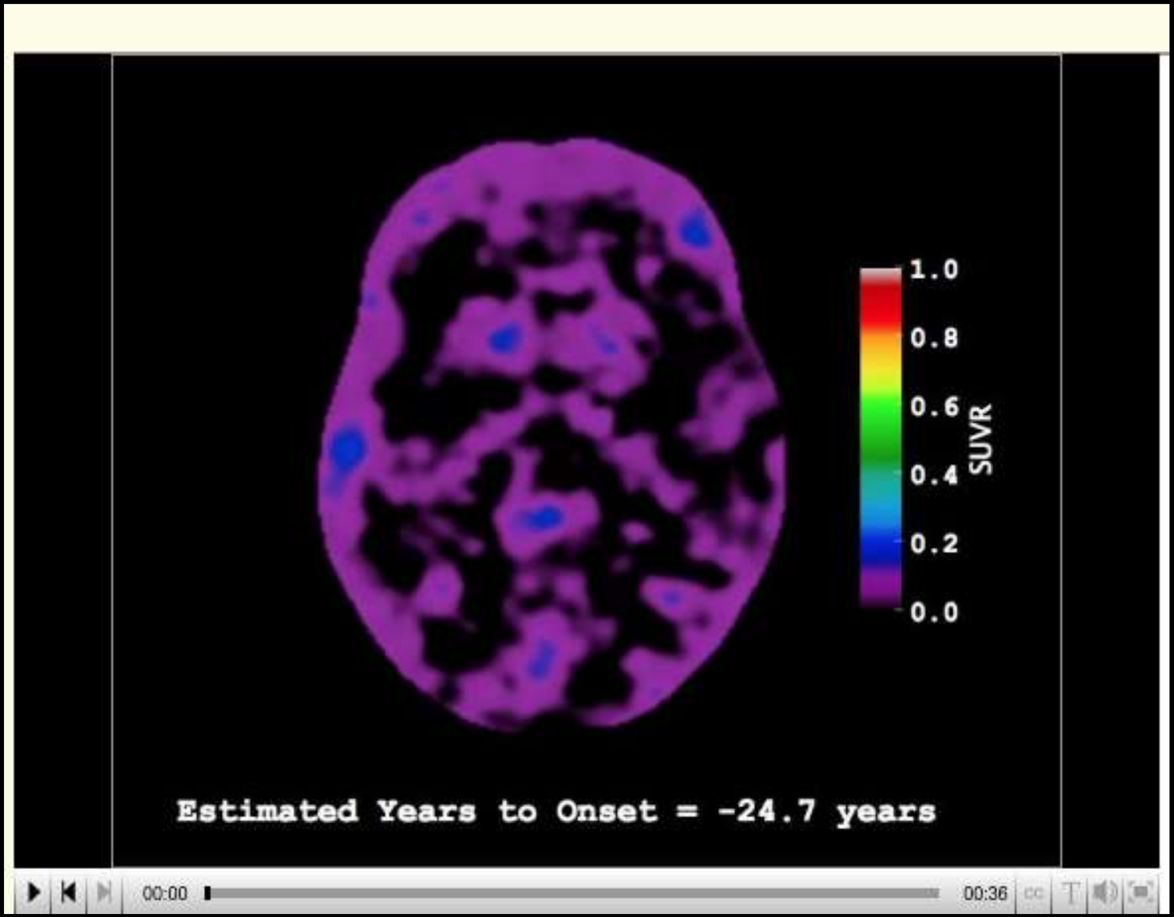


Patient with Parkinson's disease

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 AUGUST 30, 2012 VOL. 367 NO. 9

Clinical and Biomarker Changes in Dominantly Inherited Alzheimer's Disease

Randall J. Bateman, M.D., Chengjie Xiong, Ph.D., Tammie L.S. Benzinger, M.D., Ph.D., Anne M. Fagan, Ph.D., Alison Goate, Ph.D., Nick C. Fox, M.D., Daniel S. Marcus, Ph.D., Nigel J. Cairns, Ph.D., Xianyun Xie, M.S., Tyler M. Blazey, B.S., David M. Holtzman, M.D., Anna Santacruz, B.S., Virginia Buckles, Ph.D., Angela Oliver, R.N., Krista Moulder, Ph.D., Paul S. Aisen, M.D., Bernardino Ghetti, M.D., William E. Klunk, M.D., Eric McDade, M.D., Ralph N. Martins, Ph.D., Colin L. Masters, M.D., Richard Mayeux, M.D., John M. Ringman, M.D., Martin N. Rossor, M.D., Peter R. Schofield, Ph.D., D.Sc., Reisa A. Sperling, M.D., Stephen Salloway, M.D., and John C. Morris, M.D., for the Dominantly Inherited Alzheimer Network



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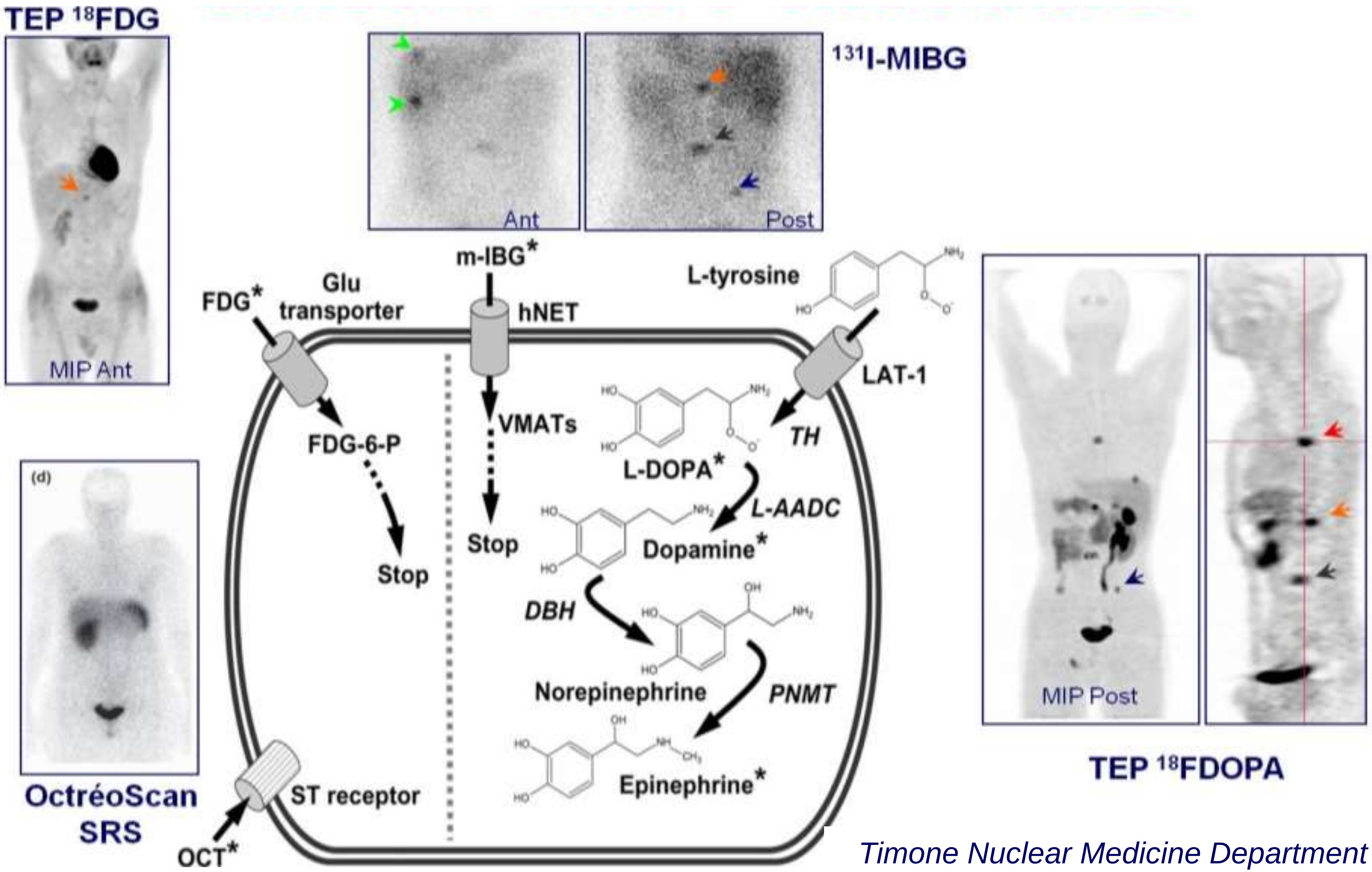
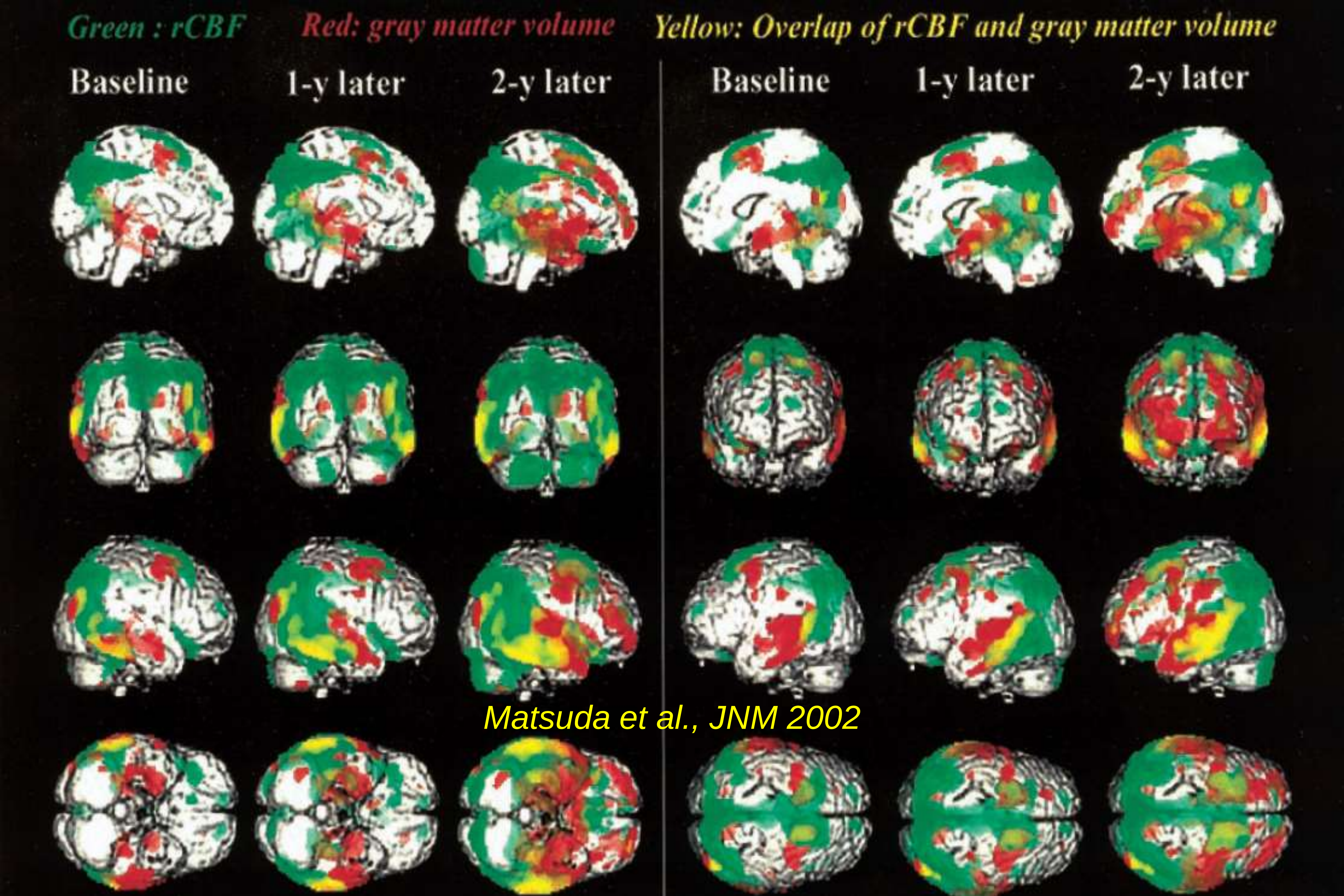
Molecular signature of neuro-endocrine tumors

Assistance Publique Hôpitaux de Marseille



Timone Nuclear Medicine Department


Green : rCBF
Red: gray matter volume
Yellow: Overlap of rCBF and gray matter volume
Baseline
1-y later
2-y later
Baseline
1-y later
2-y later
Matsuda et al., JNM 2002

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    - ✓ this molecular complexity is linked to prognosis, and therapy (***companion drugs***)

Lancet Neurol 2010; 9: 363–72

Published Online
March 1, 2010
DOI:10.1016/S1474-4422(10)70043-0

^{11}C-PiB PET assessment of change in fibrillar amyloid-β load in patients with Alzheimer's disease treated with bapineuzumab: a phase 2, double-blind, placebo-controlled, ascending-dose study

Juha O Rinne, David J Brooks, Martin N Rossor, Nick C Fox, Roger Bullock, William E Klunk, Chester A Mathis, Kaj Blennow, Jerome Barakos, Aren A Okello, Sofia Rodriguez Martinez de Liano, Enchi Liu, Martin Koller, Keith M Gregg, Dale Schenk, Ronald Black, Michael Grundman

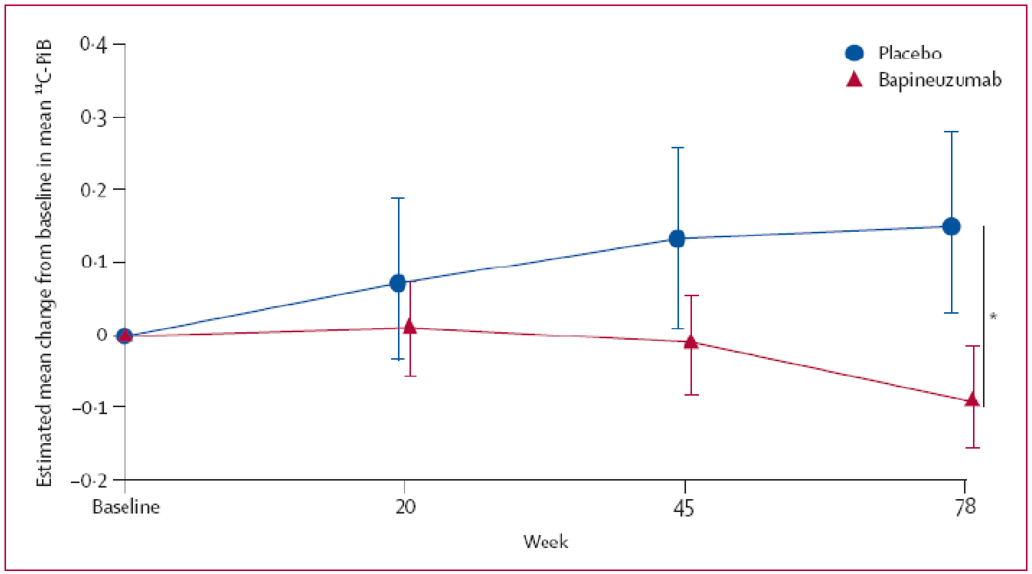
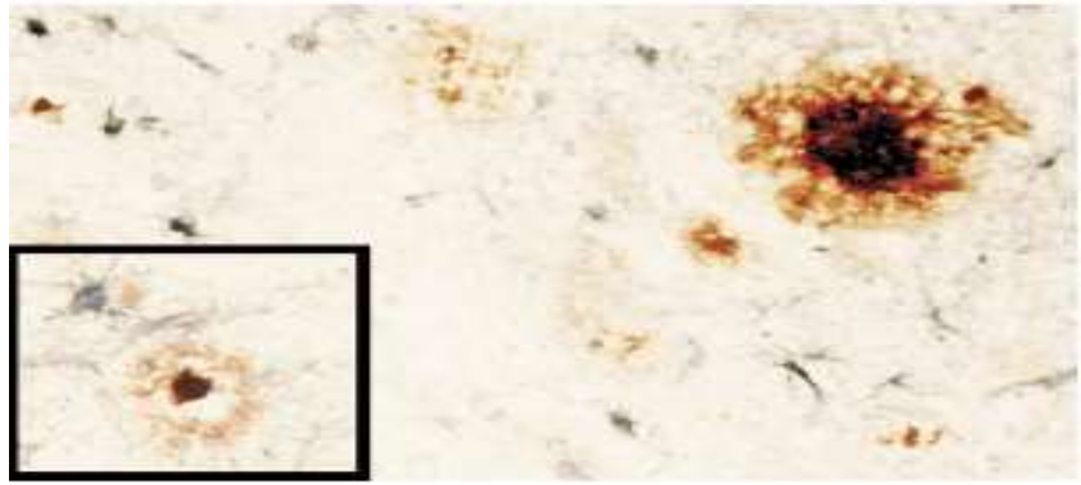
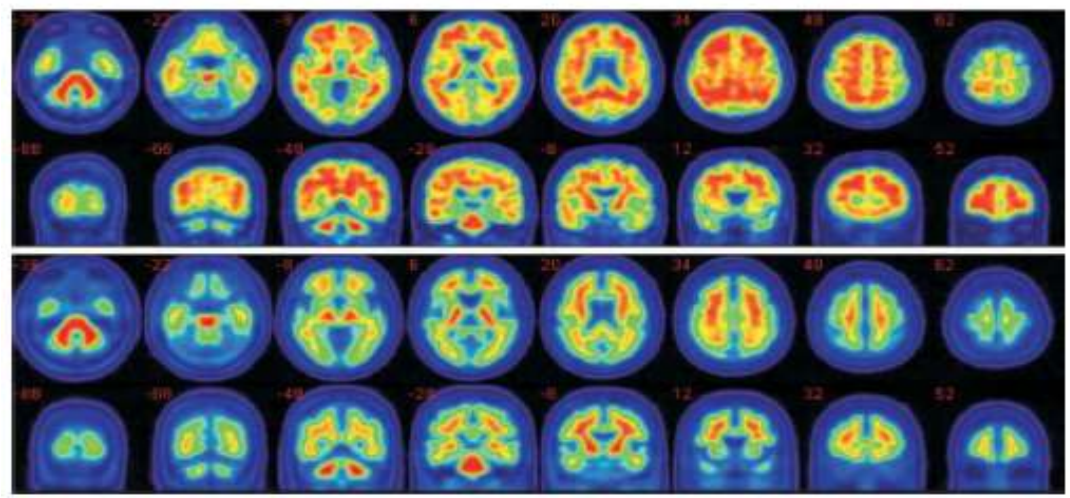


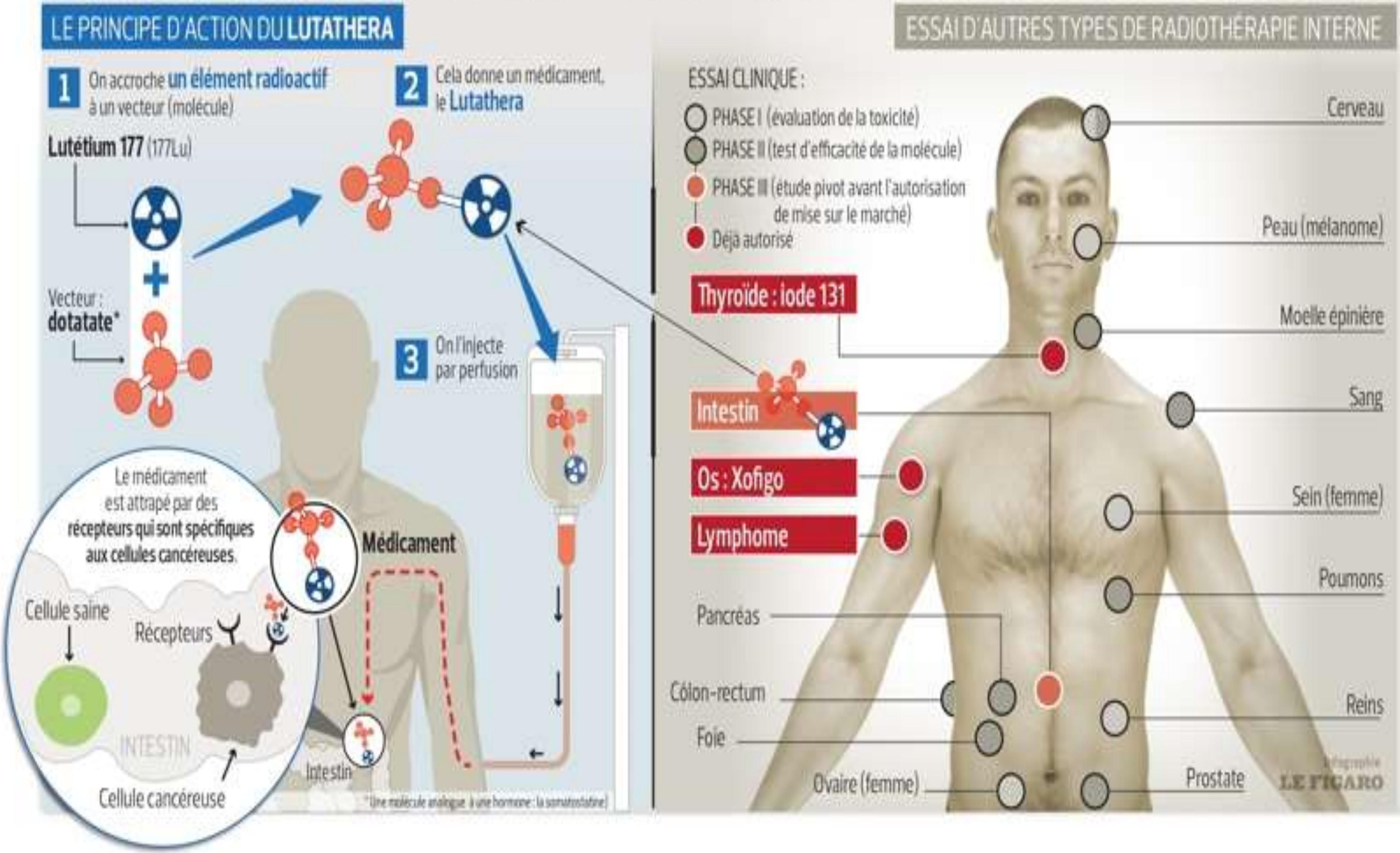
Figure 2: **Estimated change from baseline over time in mean ^{11}C-PiB PET**
Data are least squares means and 95% CIs. *Difference between patients in the placebo group and those in the bapineuzumab group at week 78=–0·24 (p=0·003). PiB=Pittsburgh compound B.



- ^{18}F-PIB Flutemetamol (GE Healthcare)



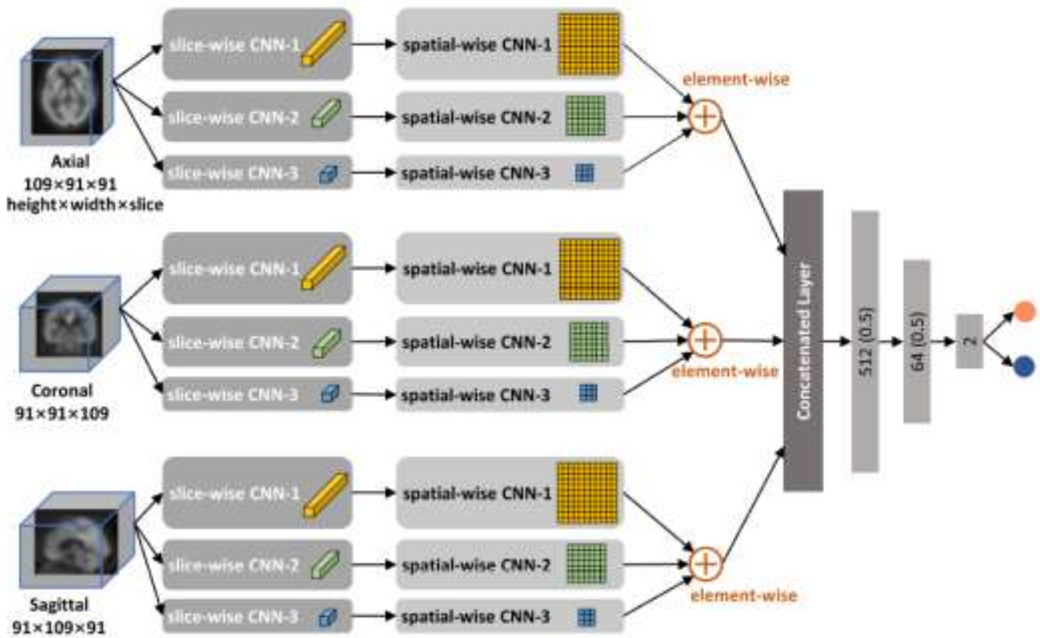
Attaquer les tumeurs de l'intérieur grâce à la radioactivité



Multi-view Separable Pyramid Network for AD Prediction at MCI Stage by ^{18}F-FDG Brain PET Imaging

Xiaoxi Pan, Trong-Le Phan, Mouloud Adel, Caroline Fossati, Thierry Gaidon, Julien Wojak, and Eric Guedj, for Alzheimer's Disease Neuroimaging Initiative

IEEE Transactions on Medical Imaging, vol. 40, no. 1, pp. 81-92, Jan. 2021



Category	Method	Data type	Subjects	ACC	SEN	SPE	AUC
Conventional methods	Hinrichs *et al.* [6]	MRI, ^{18}F-FDG PET	89AD + 94NC	84	84	82	87.16
	Padilla *et al.* [7]	^{18}F-FDG PET	53AD + 52NC	86.59	87.50	85.36	—
	Gray *et al.* [9]	^{18}F-FDG PET	50AD + 54NC	88.4	83.2	93.6	—
	Li *et al.* [10]	^{18}F-FDG PET	25AD + 30NC	89.1	92	86	97
	Zhu *et al.* 2014 [11]	MRI, ^{18}F-FDG PET, CSF*	51AD + 52NC	92.3	**92.3**	93.9	96.6
	Zhu *et al.* 2016 [12]	MRI, ^{18}F-FDG PET	51AD + 52NC	93.3	—	—	—
	Pan *et al.* 2019a [15]	^{18}F-FDG PET	237AD + 242NC	92.57	90.89	94.42	96.83
	Pan *et al.* 2019b [16]	^{18}F-FDG PET	237AD + 242NC	**94.20**	91.45	**96.76**	**97.42**
Emerging methods	Lu *et al.* [27]	^{18}F-FDG PET	226AD + 304NC	**93.58**	91.54	95.06	—
	Suk *et al.* [28]	MRI, ^{18}F-FDG PET	93AD + 101NC	92.20	88.04	**96.33**	**97.98**
	Liu *et al.* [30]	^{18}F-FDG PET	93AD + 100NC	91.2	91.4	91.0	95.3
	Yee *et al.* [33]	^{18}F-FDG PET	237AD + 359NC	93.5	**92.3**	94.2	97.6
	Huang *et al.* [34]	MRI, ^{18}F-FDG PET	465AD + 480NC	89.11	90.24	87.77	92.69
	MiSePyNet (Ours)	^{18}F-FDG PET	237AD + 242NC	93.13	90.32	95.49	97.11

*CSF = Cerebrospinal fluid

TABLE VIII
PERFORMANCE COMPARISON WITH STATE-OF-THE-ART METHODS FOR PMCI VS. SMCI(%)

Category	Method	Data type	Subjects	ACC	SEN	SPE	AUC
Conventional methods	Gray *et al.* [9]	^{18}F-FDG PET	53pMCI + 64sMCI	63.1	52.2	73.2	—
	Zhu *et al.* 2014 [11]	MRI, ^{18}F-FDG PET, CSF	43pMCI + 56sMCI	70.9	42.7	94.1	77.4
	Zhu *et al.* 2016 [12]	MRI, ^{18}F-FDG PET	43pMCI + 56sMCI	69.9	—	—	—
	Cheng *et al.* [14]	MRI, ^{18}F-FDG PET, CSF	43pMCI + 56sMCI	71.6	76.4	67.9	74.1
	Pan *et al.* 2019a [15]	^{18}F-FDG PET	166pMCI + 360sMCI	79.43	69.14	84.16	83.88
	Pan *et al.* 2019b [16]	^{18}F-FDG PET	166pMCI + 360sMCI	**80.48**	65.04	**87.95**	**85.67**
Emerging methods	Lu *et al.* [27]	^{18}F-FDG PET	112pMCI + 409sMCI	82.51	**81.36**	82.85	—
	Suk *et al.* [28]	MRI, ^{18}F-FDG PET	76pMCI + 128sMCI	70.75	25.45	**96.55**	72.15
	Yee *et al.* [33]	^{18}F-FDG PET	210pMCI + 427sMCI	74.7	74.0	75.0	81.1
	MiSePyNet (Ours)	^{18}F-FDG PET	166pMCI + 360sMCI	**83.05**	72.12	88.06	**86.80**

A multiparametric molecular imaging

A quantitative imaging to characterize molecular signatures

Understand, Diagnose, Select, Predict, Evaluate, Treat

Biomarker

Neuroscience

- ✓ *GLUT1*
- ✓ *Cerebral blood flow*
- ✓ *Dopamine transporter*
- ✓ *DOPA-decarboxylyase*
- ✓ *D2/3*
- ✓ *Noradrenergic reuptake*
- ✓ *5HT1-A*
- ✓ *Acetylcholinesterase*
- ✓ *NMDA receptor*
- ✓ *TSPO: microglia activation*
- ✓ *Amyloïd burden*
- ✓ *TAU phosphorylation*

Oncology

- ✓ *GLUT1*
- ✓ *LAT1*
- ✓ *Choline-kinase*
- ✓ *PSMA*
- ✓ *Tyrosine*
- ✓ *Somatostatin receptor*
- ✓ *Fluor*
- ✓ *VCAM-1*
- ✓ *Thymidine-kinase*
- ✓ *Hypoxia*

Gallium, for tailored peptide labeling

Companion Drug

Oncology/Neuroscience

- ✓ *Targeted therapy*
- ✓ *Anti-amyloïd*
- ✓ *Anti-TAU*
- ✓ *Anti-inflammatory*
- ✓ *DOPA*

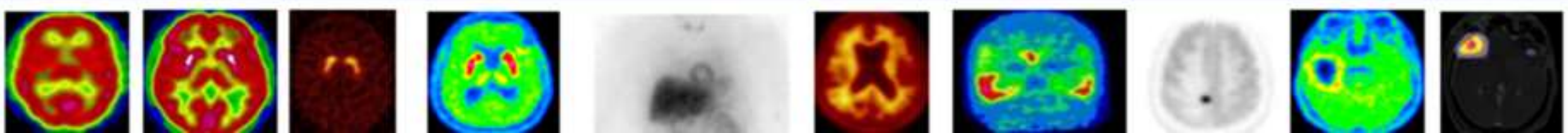
Theranostic

Oncology

- ✓ ^{131}Iodine
- ✓ *^{68}Ga/^{177}Lu-SSA*
- ✓ *^{90}Y/^{177}Lu-TheraSphere*

Extended to :

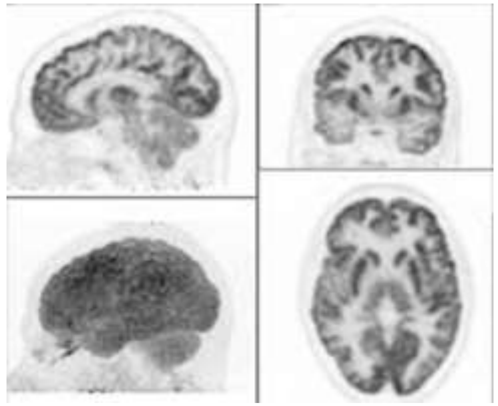
- ✓ *NOTES*
- ✓ *TMS/DBS*
- ✓ *Radiosurgery*
- ✓ *CBT*
- ✓ *Virtual Reality Exposure Therapy*



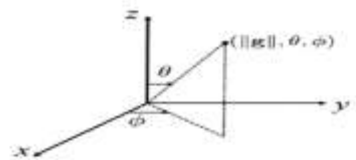
Spatial dimension

- Local approach: texture analysis

New digital PET detectors

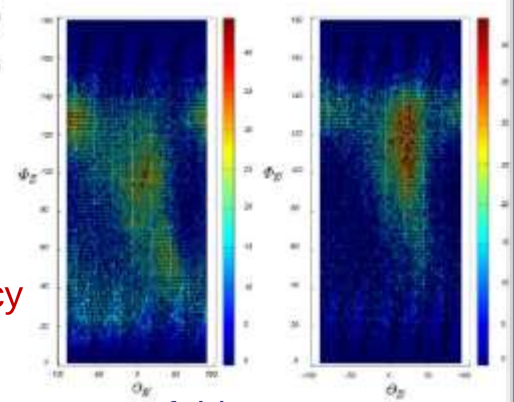


$$\begin{cases} G_x(m,n,k) = \rho(m,n,k).\sin\phi(m,n,k).\cos\theta(m,n,k) \\ G_y(m,n,k) = \rho(m,n,k).\sin\phi(m,n,k).\sin\theta(m,n,k) \\ G_z(m,n,k) = \rho(m,n,k).\cos\phi(m,n,k) \end{cases} \quad (2)$$



81 AD vs 61 HC: 92.96% of accuracy

Garali et al., EUVIP 2016
Nicesoft funding



Left hippocampus

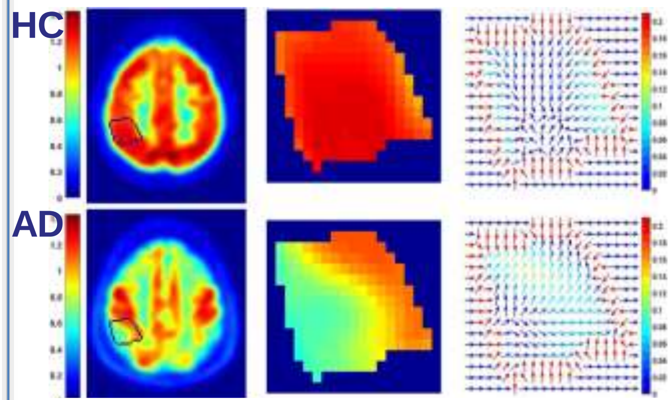


Table 8
Performance comparison for AD vs. pMCI vs. sMCI vs.NC(%).

Method	Subjects	ACC
Voxel	123AD + 123pMCI + 125sMCI + 123NC	60.57
ROI	123AD + 123pMCI + 125sMCI + 123NC	53.65
Our method	123AD + 123pMCI + 125sMCI + 123NC	**70.04**
Zhu et al. [30]	51AD + 43pMCI + 56sMCI + 52NC	56.29
Zhou et al. [33]	190AD + 157pMCI + 205sMCI+ 226NC	48

Pan et al., 2019
Computer Methods & Programs in Biomedicine

Spatial dimension

- Regional approach: metabolic connectivty on static images

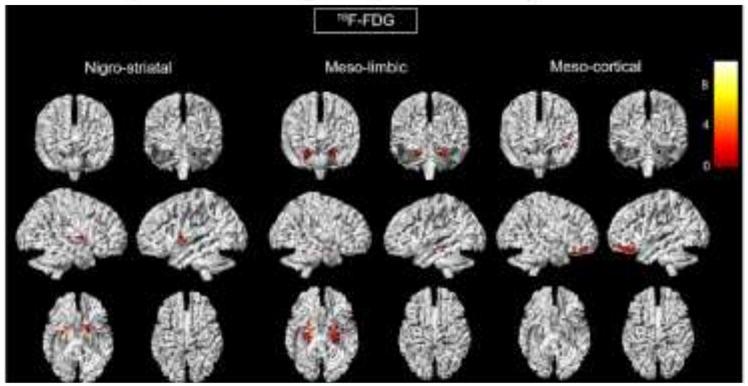
Pan et al., 2018
IEEE JBHI

Inter-regional correlation analyis, IRCA

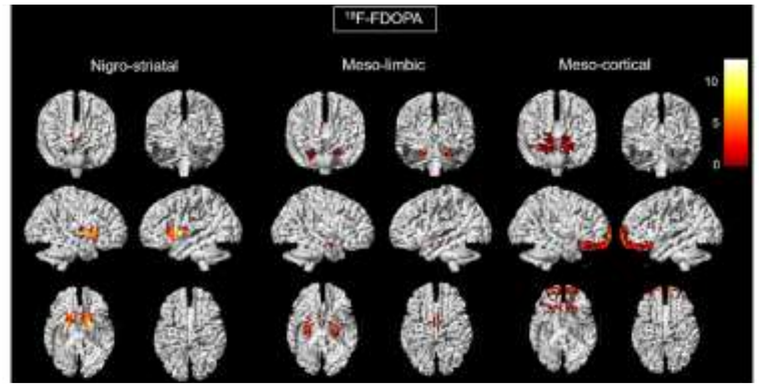
Verger et al., EJNMMI 2018

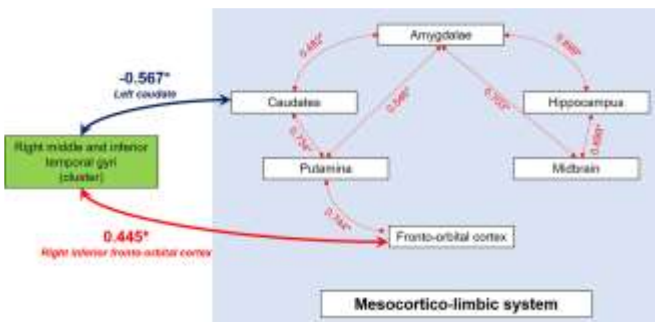
European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-019-04574-3
Published online: 18 November 2019

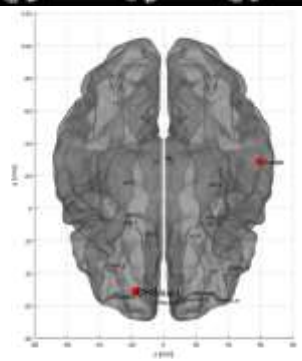
From metabolic connectivity to molecular connectivity: application to dopaminergic pathways



Midbrain connectivity

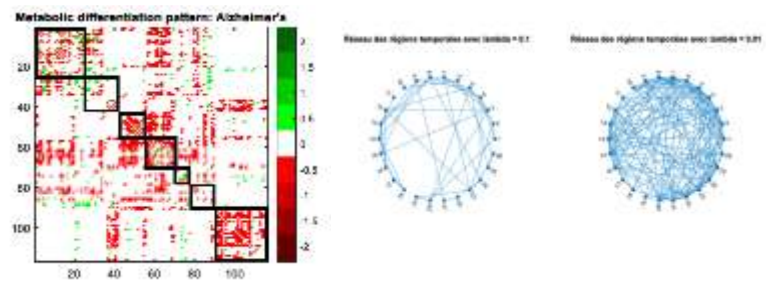






Graph theory

Verger et al, Human Brain Mapping 2018



Sparse precision matrix

Le et al, Computational Statistics & Data Analysis 2020

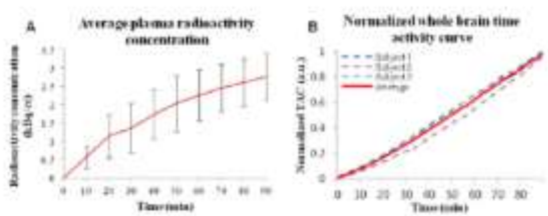
Temporal dimension

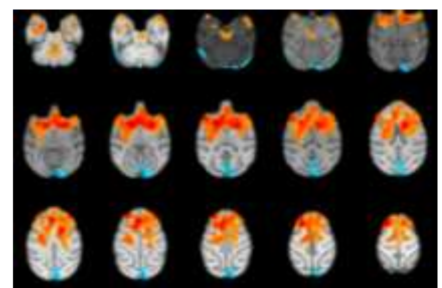
- Complex paradigms of activation, inside VR environment

Acrophobia, PTSD

Verger et al., EJNMMI Res 2018 & Eur. J. Psychotrauma 2020 ; Rousseau et al., EJNMMI 2019; <u>*collab. IRBA*</u>

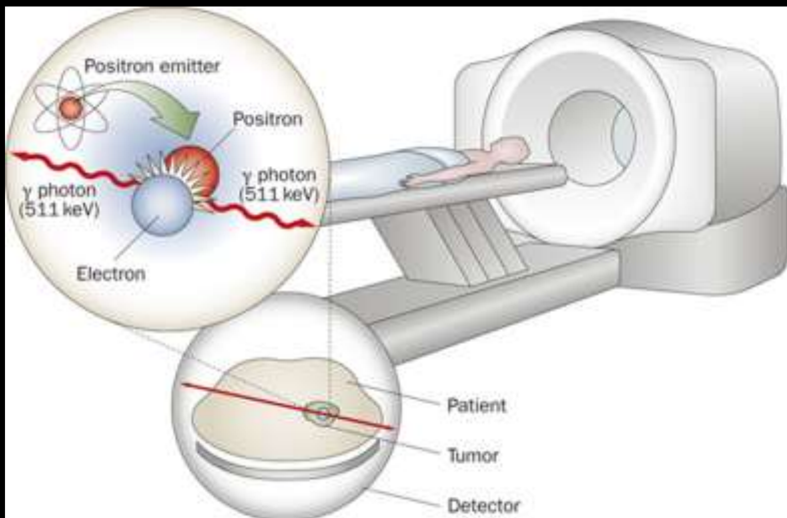
- Fonctional connectivity on dynamic images

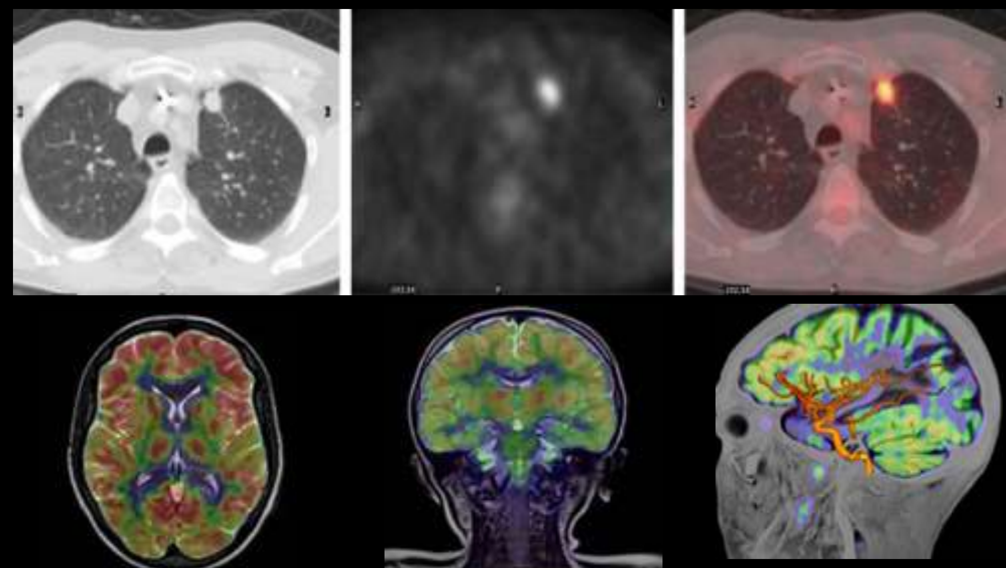




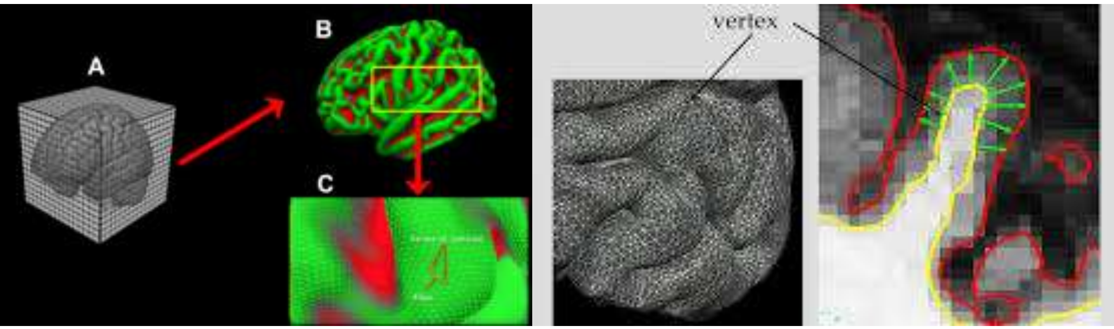
PNH project (@INT)

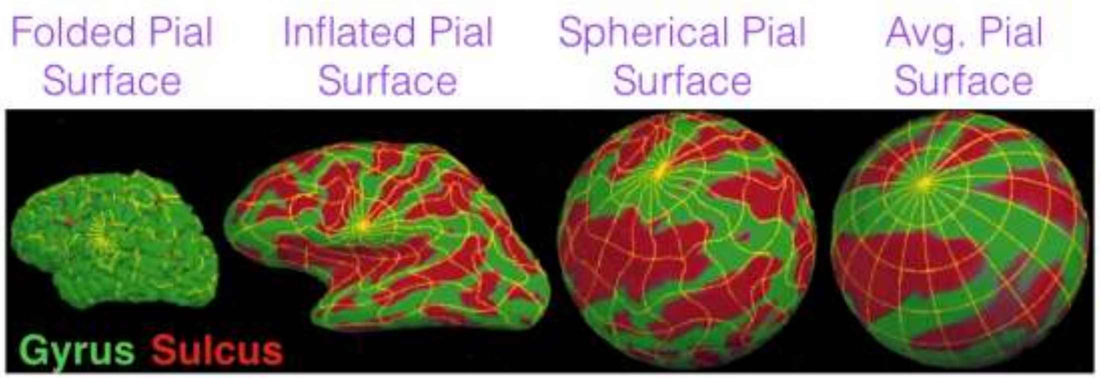
A multimodal imaging

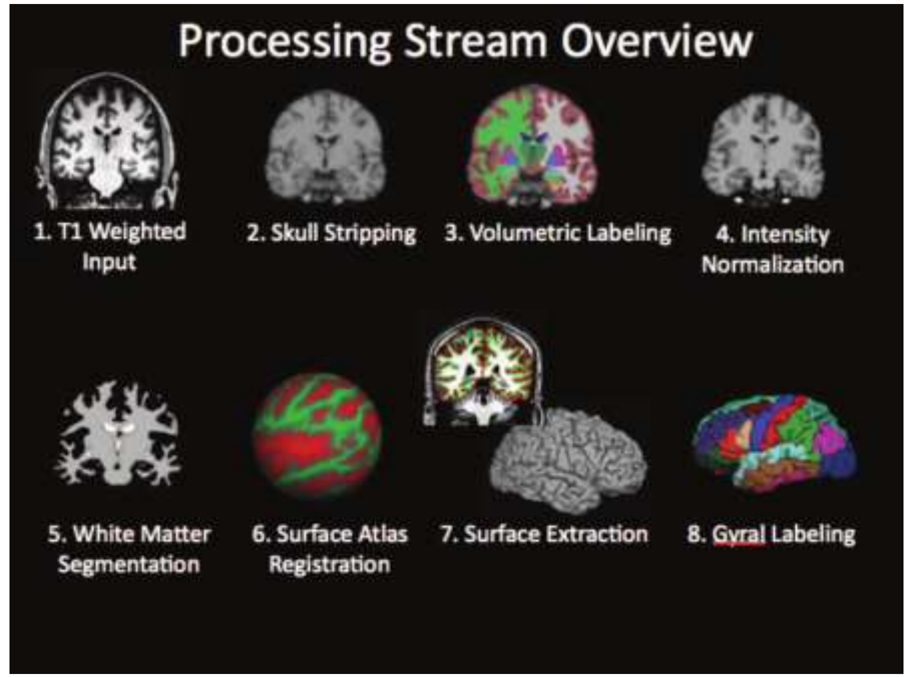




SURFACE - FREESURFER



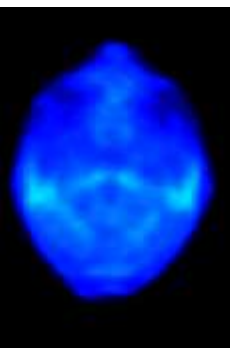


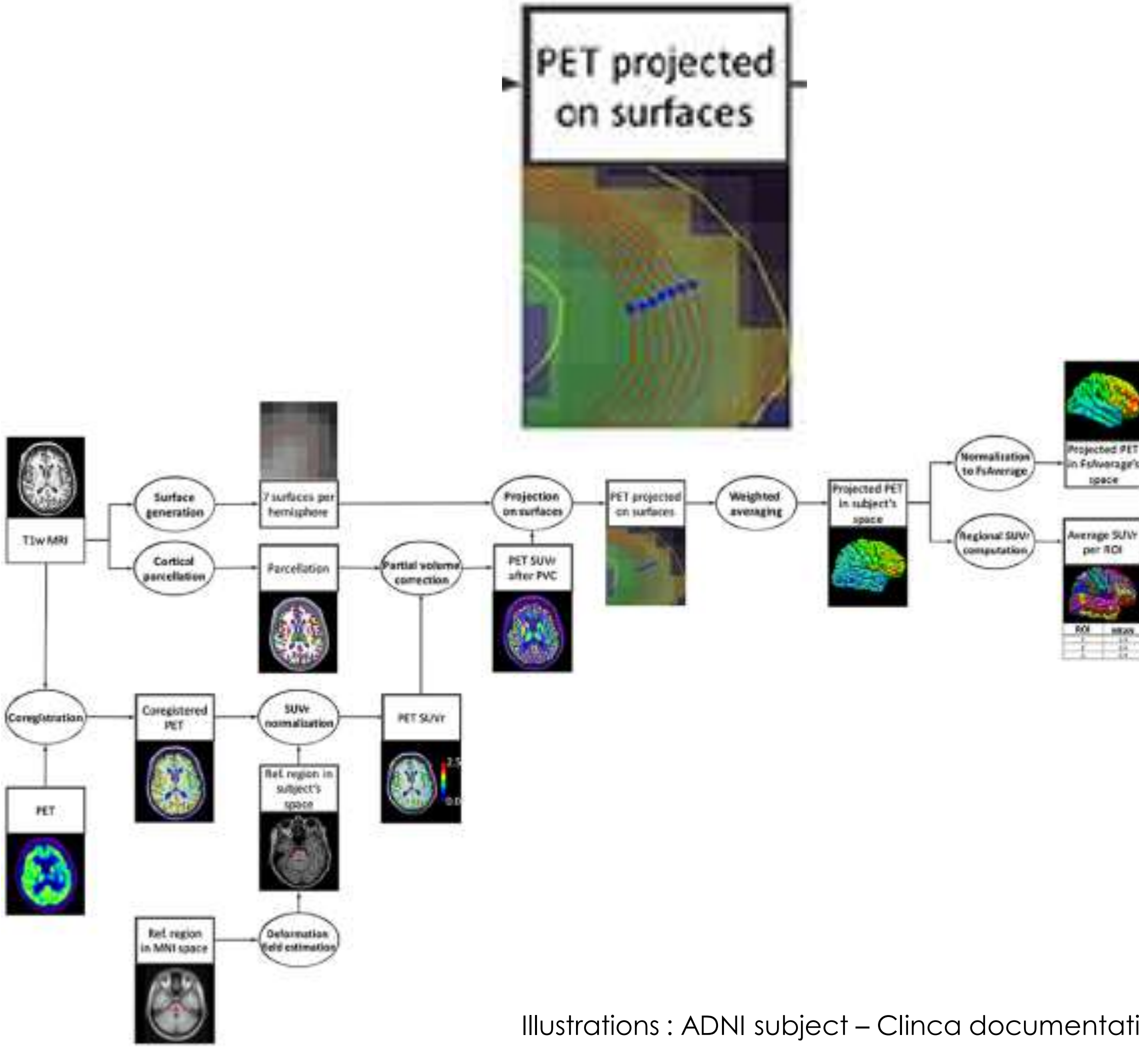


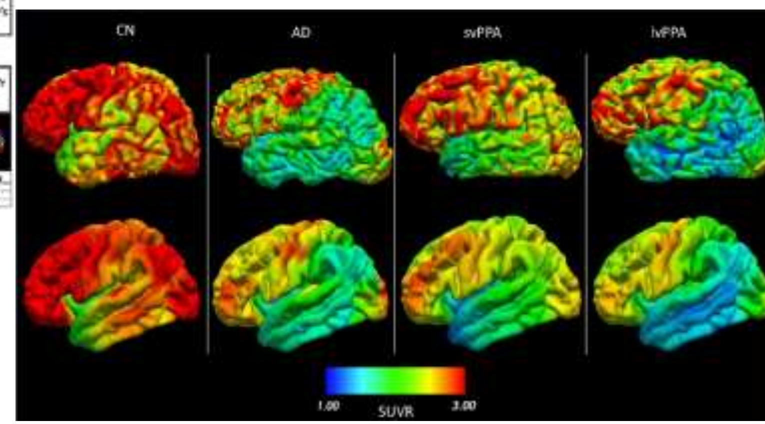
•Illustrations : DOI: 10.1037/neu0000446 - http://ielvis.pbworks.com/ - https://www.andysbrainblog.com/ - Anissa Rice

@Jacques-Yves Campion

SURFACE - CLINICA

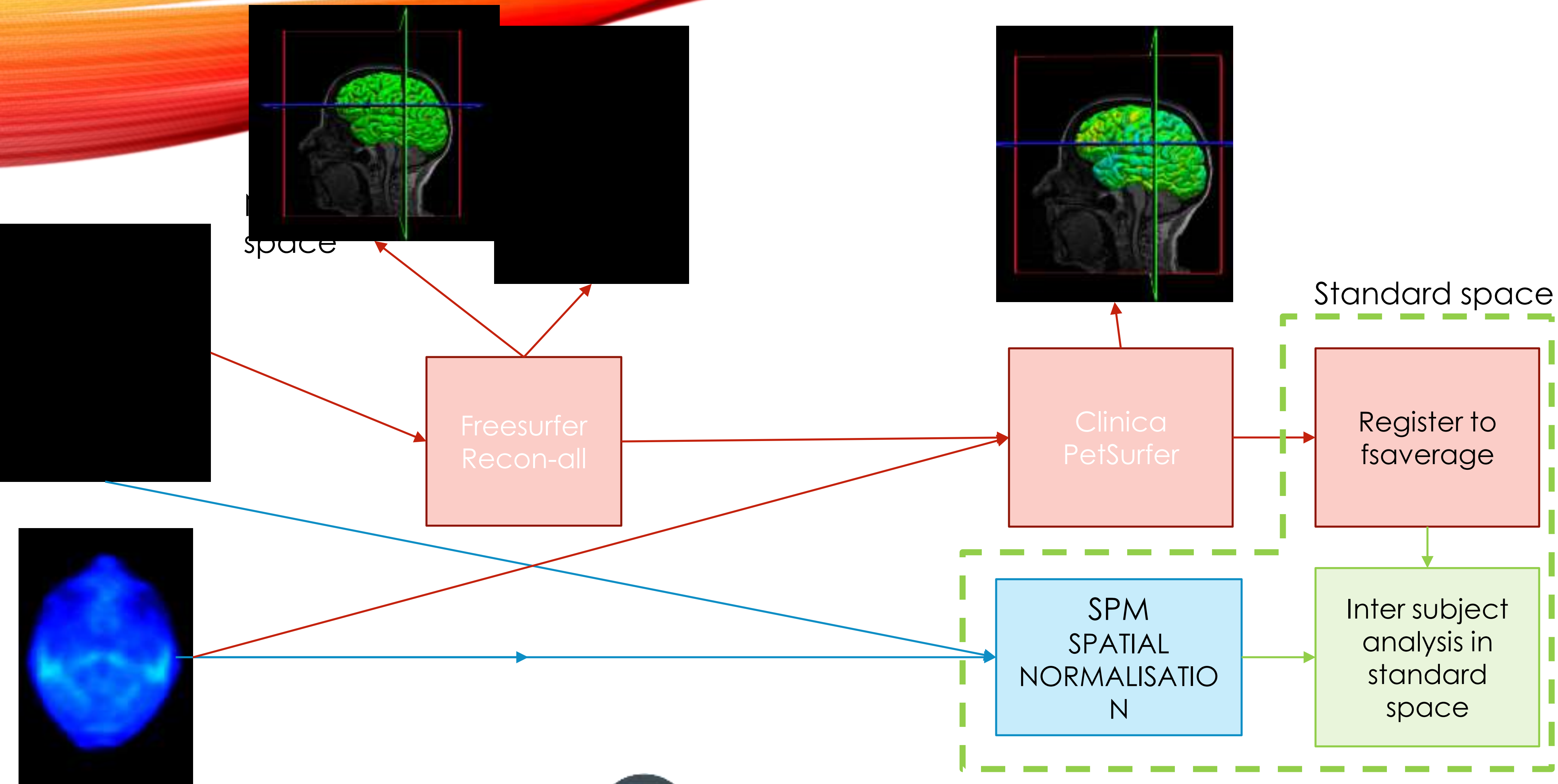






Illustrations : ADNI subject – Clinca documentation

@Jacques-Yves Campion



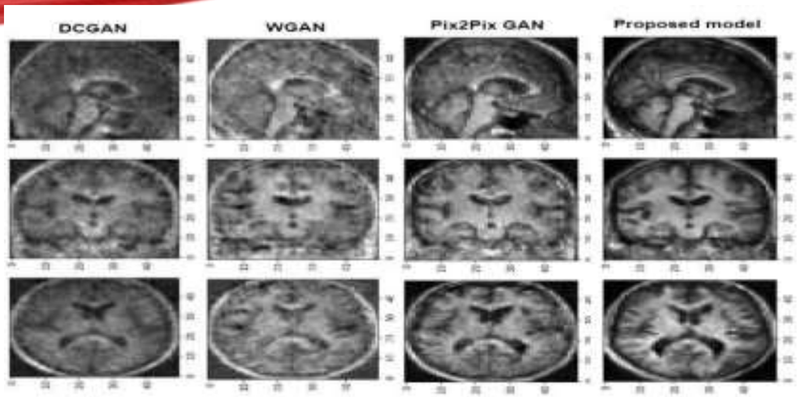
STATE OF THE ART AND IMPLEMENTATION

Illustrations : ADNI subject

@Jacques-Yves Campion

PET2MRI

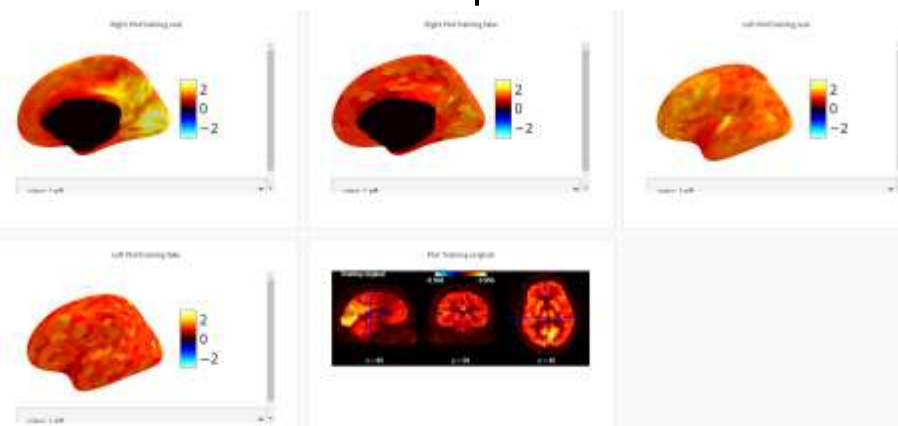
@FaridehBazangani



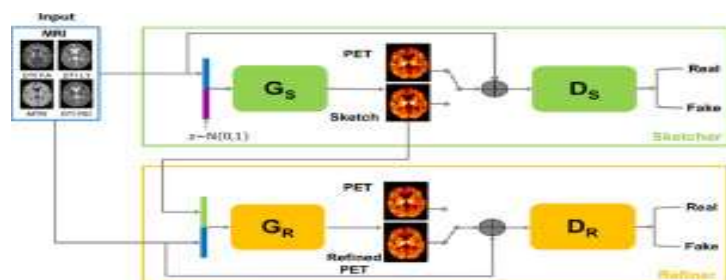
ARTIFICIAL INTELLIGENCE

PyTorch TorchIO Weights & Biases

« PETsurface » prediction



PETCritics



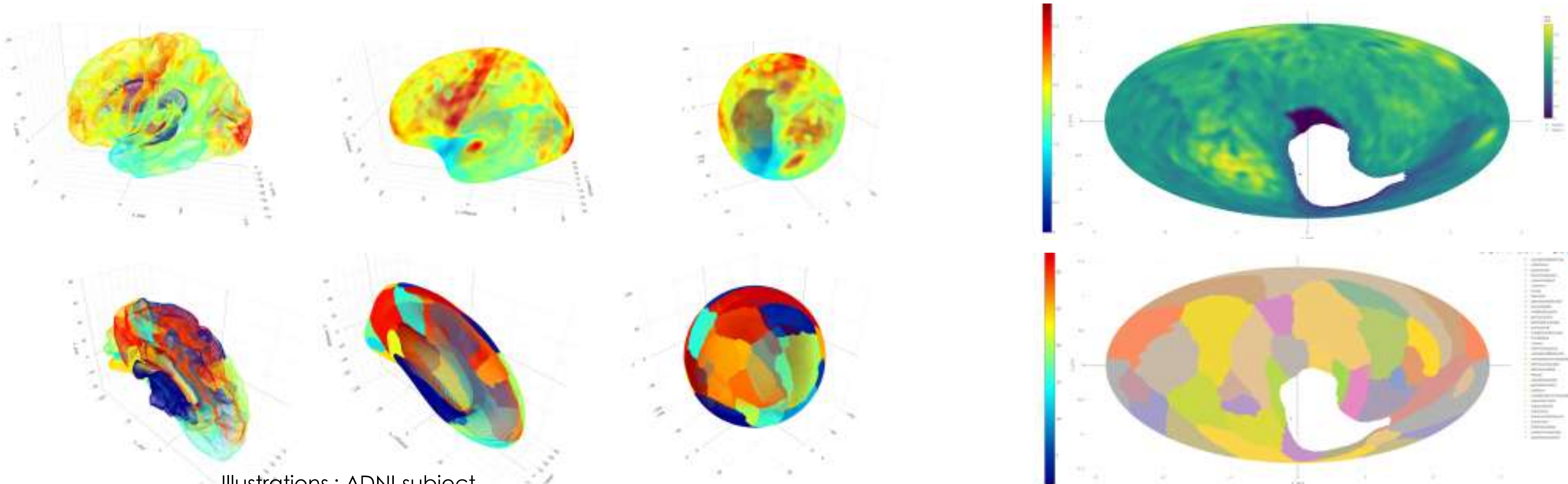
@Jacques-Yves Campion

2D PROJECTION VIEW

- Freesurfer tool to apply data to sphere
- 2D projection (mollweid)

➔New visualization for nuclear physician

➔Easier IA algorithms (2D vs 3D mesh)



Illustrations : ADNI subject

HOLOGRAPHIC VIEWS

- Convert Freesurfer data to 3D model
- Implement 3D model to Augmented Reality with web interface
- Create 3D interface in Mixed Reality with Hololens 2
- Statistics visualization
- Better patient ad interview
- Upgrade medical interaction and diagnosis

Illustrations : ADNI subject - https://www.philips.com/