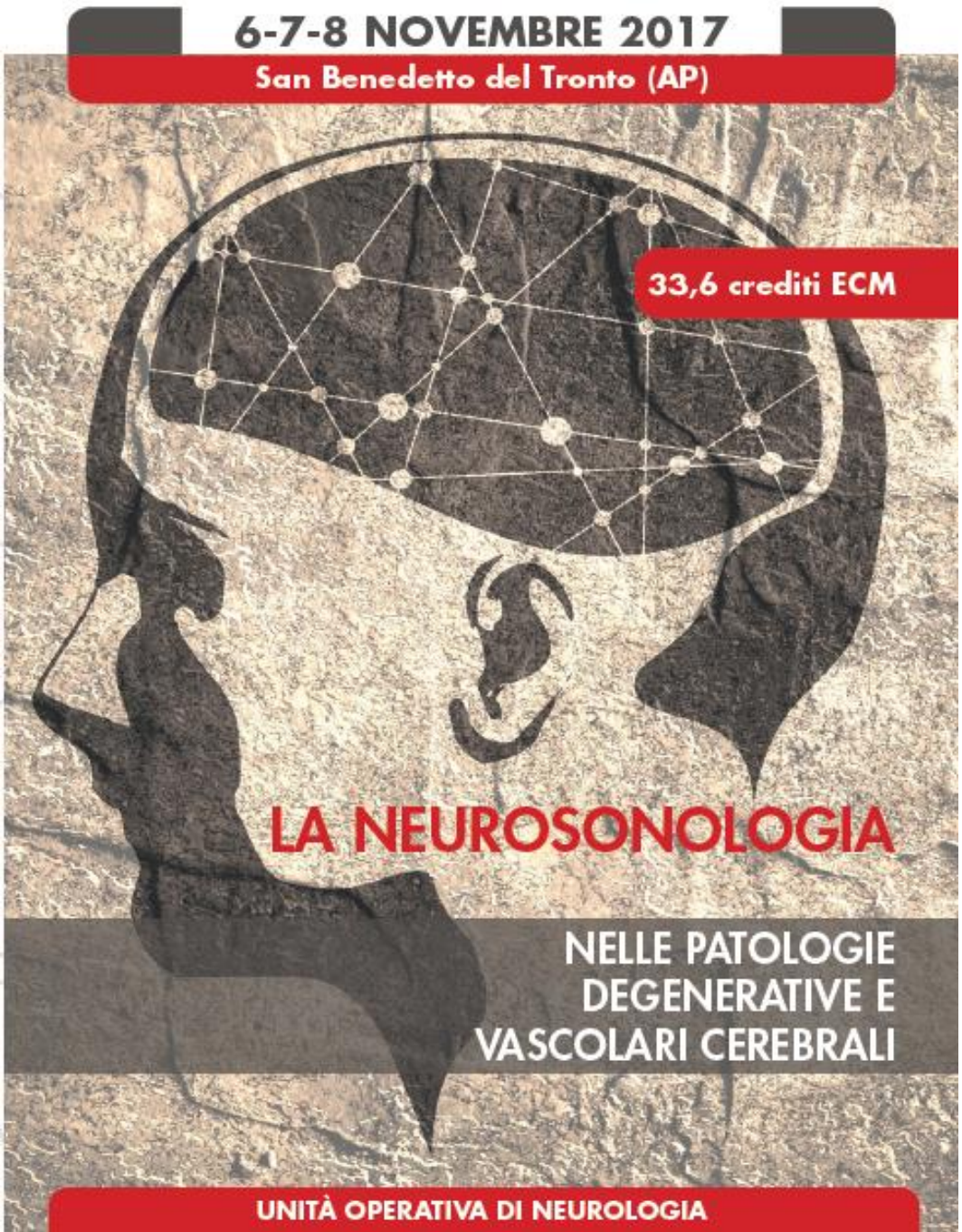

La "neurologia nucleare": nuova realtà diagnostica nelle patologie degenerative neurologiche

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SOD Medicina Nucleare
DIPARTIMENTO SCIENZE RADIOLOGICHE
OSPEDALI RIUNITI ANCONA

Le patologie degenerative cerebrali sono in continuo aumento a livello mondiale e rappresentano una sfida sia diagnostica sia terapeutica per il prossimo futuro.

La Medicina Nucleare, a differenza di altre metodiche, si avvale di radiofarmaci per valutare la funzione metabolica dei tessuti e/o dei sistemi in modo specifico, e quindi, fermo restando il rinnovo tecnologico delle apparecchiature, la “variabile evolutiva” è rappresentata prevalentemente dalla scoperta di nuovi radiofarmaci piuttosto che dall'hardware in uso.

In particolare in ambito neurologico, la Medicina Nucleare, ha fatto passi da gigante con “l'espansione“ di alcune metodiche (SPECT) e l'introduzione di nuove (PET/TC), come vedremo a breve.

Types and causes Of Dementia

TYPE	CAUSES
Parenchymatous Brain Disease	Alzheimers Disease, Parkinson's disease, Huntingtons's Chorea, Pick's Disease, Steel-Richardson syndrome (prog. Supranuclr palsy)
Vascular Dementia	Multiinfarct Dementia, Subcortical Vascular dementia (Binswanger's disease)
Toxic Dementia	Alcohol, Drugs, Heavy Metals, Bromide, CO, Benzodiazepines, Psychotropics
Metabolic Dementia	Chronic hepatic/uremic encephalopathy, dialysis dementia, Wilson's disease
Endocrinal	Pituitary, Parathyrois, Thyroid, Adrenal dysfunction
Deficiency Dementia	Pernicious anemia, Pellagra, Folic acid, Thiamine deficiency
Infections	AIDS, Neurosyphillis, Chronic Meningitis, Creutzfelft-Jacob disease
IOP ↑	Brain tumor, Head injury hematoma, hydrocephalus

Commonest: ALZHEIMERS DEMENTIA, MULTIINFARCT DEMENTIA, HYPOTHYROID DEMENTIA, AIDS DEMENTIA COMPLEX

.Gamma Camere (SPECT e SPECT/TC):

_ HMPAO-SPECT, ECD-SPECT (traccianti di perfusione).

_ ***123I-Ioflupane*** (tracciante che valuta l'integrità dei recettori

INCIDENZA DEL M. DI PARKINSON

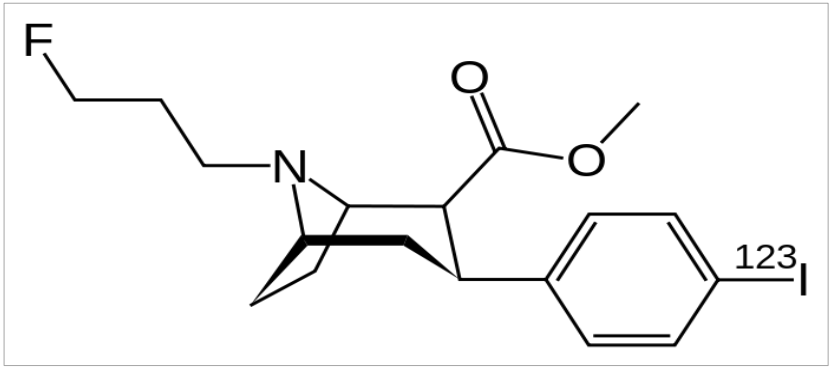
230.000 casi in Italia
1-2% della popolazione *over* 60 colpita
3-5% della popolazione *over* 85 colpita
L'età media di comparsa dei sintomi è intorno ai 60 anni, il **5%** dei pazienti può presentare una forma ad **esordio precoce**, con esordio prima dei 50 anni

INCIDENZA DELLA DEMENZA

Stima sulla base dei dati Europei:
prevalenza:
1.000.000 di persone
Incidenza *(annua)*
150.000-200.000 persone
La sua diffusione è in continua crescita: il World Alzheimer Report 2016 stima che dagli attuali 47 milioni di persone affetti da questa patologia, si giungerà a 131 milioni di malati entro il 2050.

123I-IOFLUPANE

integrità dei recettori presinaptici nei nuclei della base encefalica



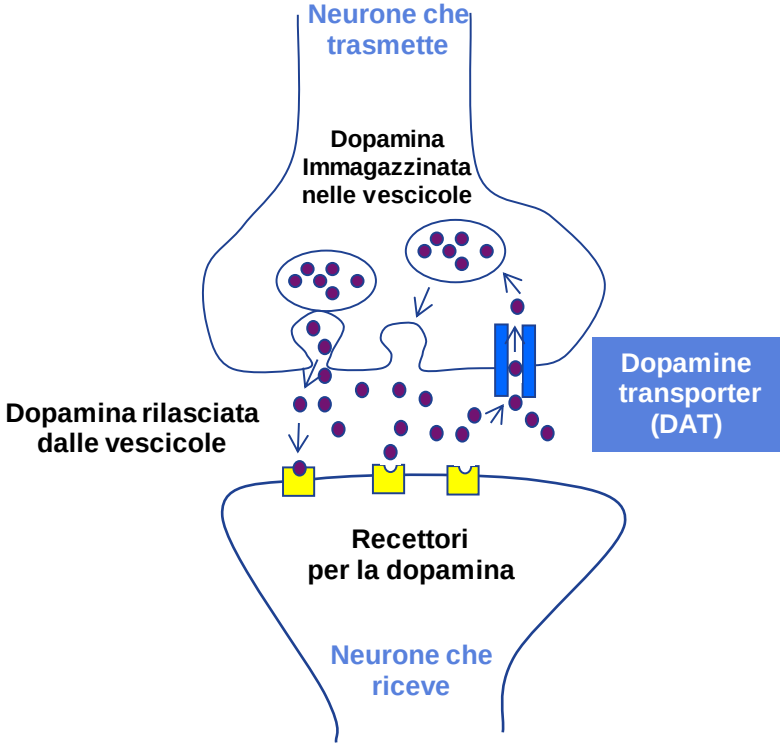
Radiofarmaco marcato con 123I pronto all'uso

Analogo della cocaina con

- Buona affinità per i DAT (0,6-30μM)
- Elevata selettività per i DAT
- Ottimali proprietà cinetiche (imaging in 3-6h)

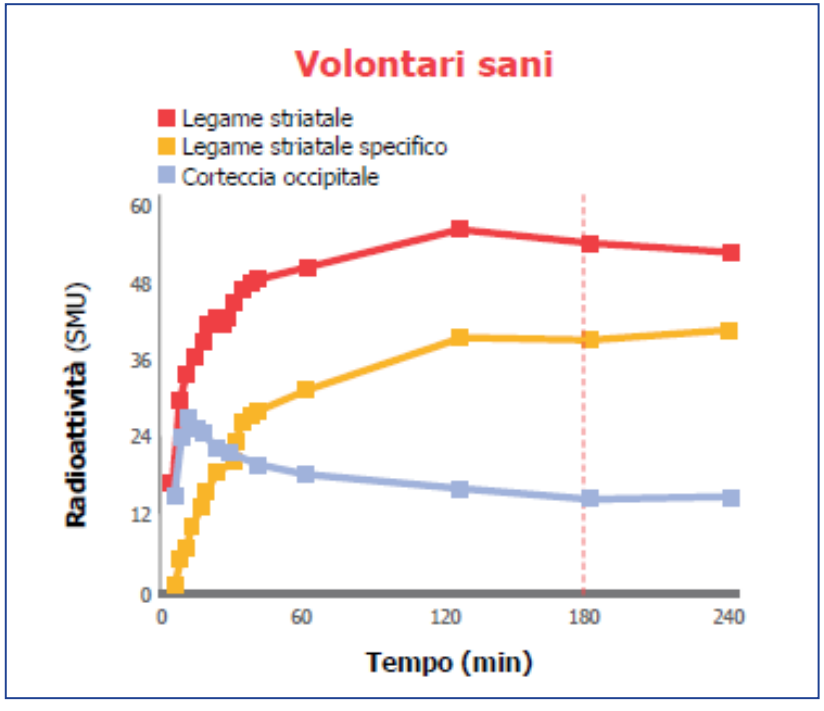
123I-IOFLUPANE

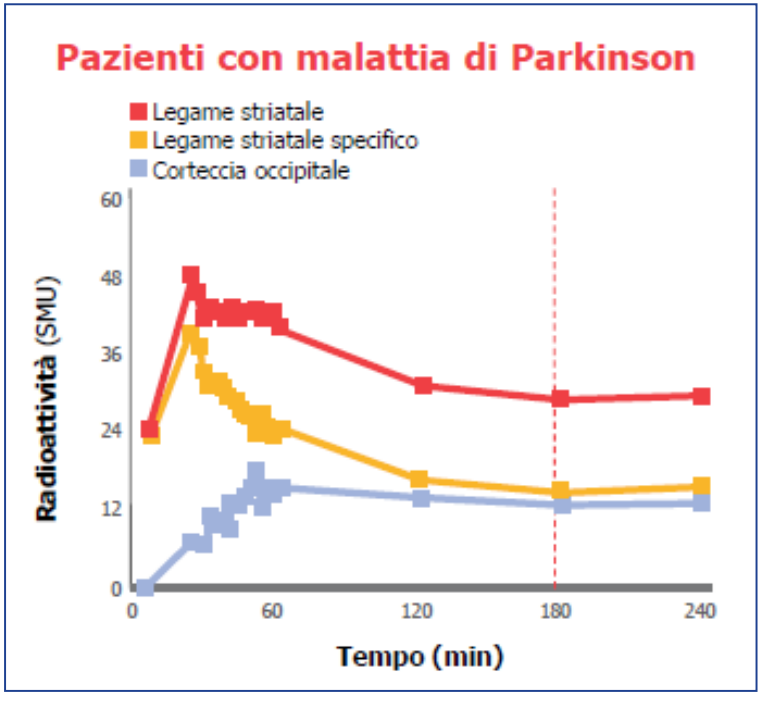
Fornisce una misura dell'integrità dei neuroni dopaminergici



- La Dopamine (DA) è sintetizzata nei neuroni presinaptici della **sostanza nera**
- Dopo essere stata immagazzinatia nelle vescicole presinaptiche , la DA è rilasciata nello spazio sinaptico
- La DA esercita la sua azione attivando i recettori dopaminergici localizzati sul neurone postsinaptico (striato)
- Un meccanismo di **reuptake** permette alla DA residua nello spazio intersinaptico di essere re-incorporata nel neurone presinaptico attraverso i **Trasportatori della Dopamina (DAT**)
- **Datscan** si lega selettivamente ai DAT

Attività specifica corticale





Booij et al. J Neurol Neurosurg Psychiatry 1997;62(2):133-40

	Region	FP-CIT			F-DOPA		
		Sensitivity (%)	Specificity (%)	AUC	Sensitivity (%)	Specificity (%)	AUC
Early-stage versus controls	Contralateral caudate	91	100	0.98	91	90	0.95
	Ipsilateral caudate	82	90	0.86	64	90	0.80
	Contralateral putamen	100	100	1.00	100	100	1.00
	Ipsilateral putamen	100	100	1.00	91	90	0.95
	Contralateral striatum	100	100	1.00	100	100	1.00
	Ipsilateral striatum	73	100	0.95	82	90	0.92
All patients versus controls	Contralateral caudate	100	91	0.98	90	96	0.98
	Ipsilateral caudate	100	82	0.94	90	86	0.91
	Contralateral putamen	100	100	1.00	100	100	1.00
	Ipsilateral putamen	100	96	0.99	100	89	0.98
	Contralateral striatum	100	100	1.00	100	100	1.00
	Ipsilateral striatum	100	86	0.98	90	93	0.97

Linee Guida & Imaging funzionale

LG ISS agg 2015

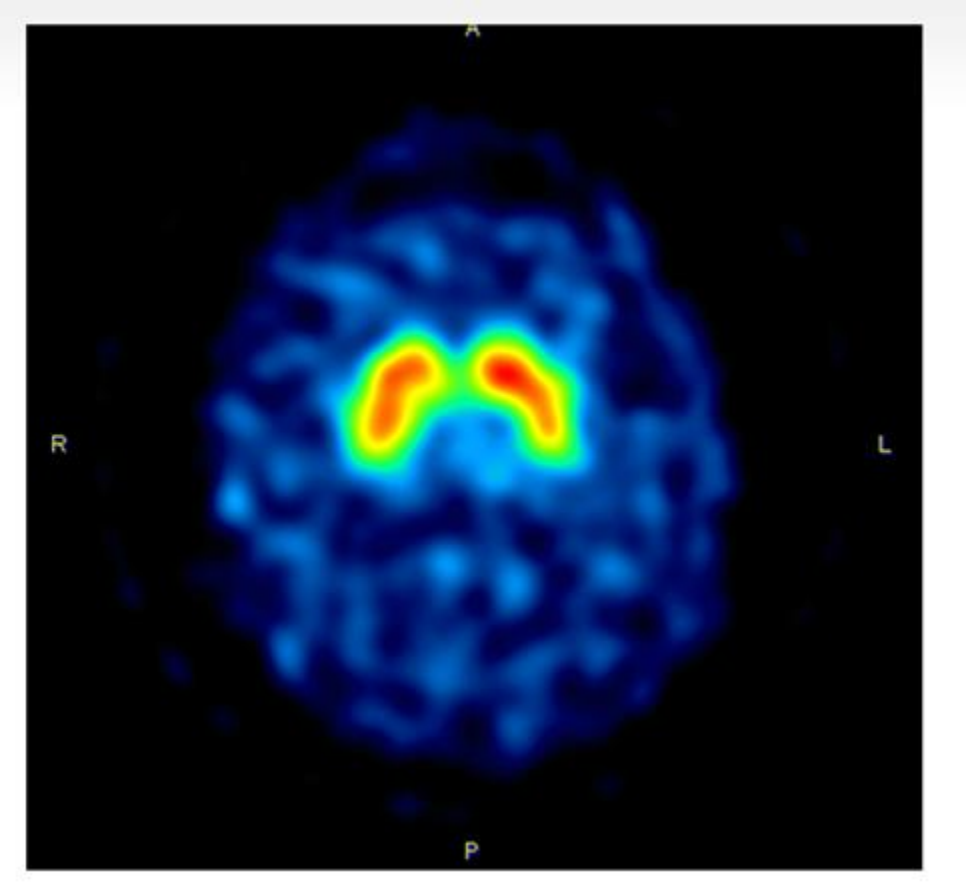
Raccomandazioni

«**La SPECT con** tracciante presinaptico **123I-Ioflupane (123I-FP-CIT, DaTScan**), **si conferma valida nel differenziare pazienti con malattia di Parkinson** in fase precoce e soggetti sani»

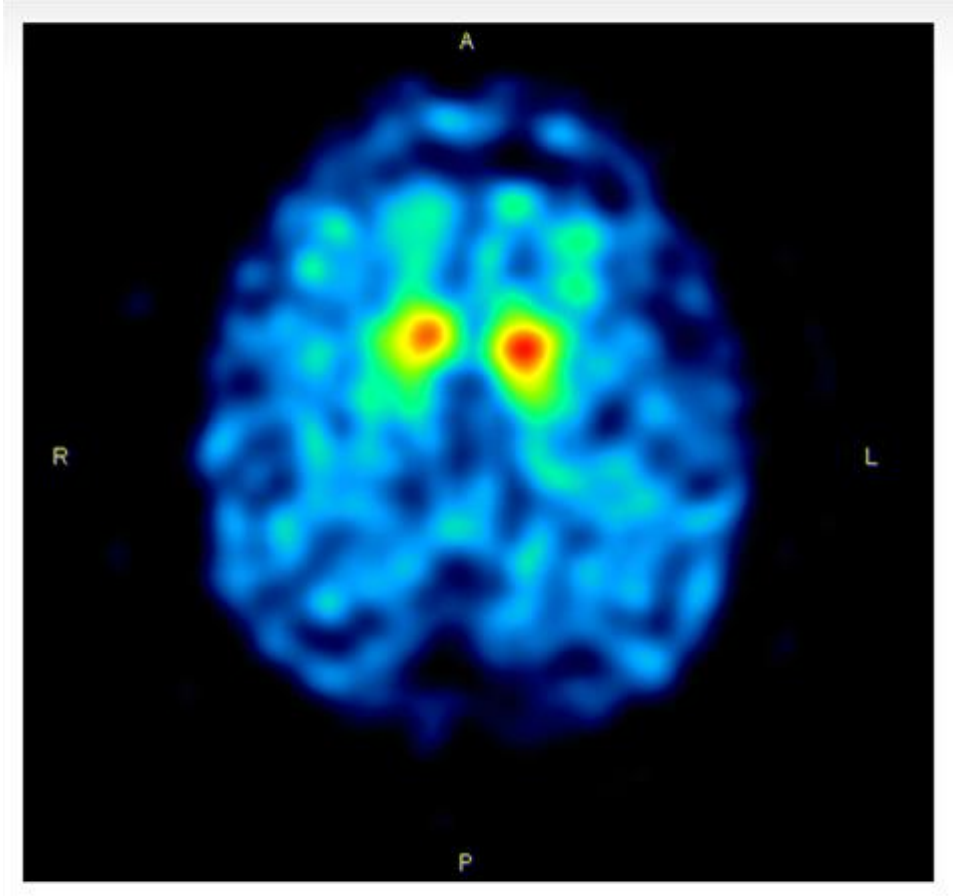
L'uso della 123I-FP-CIT SPECT può essere considerato come supporto, e non come sostituto, **alla diagnosi clinica** in pazienti in cui esiste un'incertezza diagnostica tra malattia di Parkinson e parkinsonismo non degenerativo/tremore.

L'uso della PET non è raccomandato come parte del percorso diagnostico per le sindromi parkinsoniane, se non in ambito di ricerca

Esame normale



Esame patologico

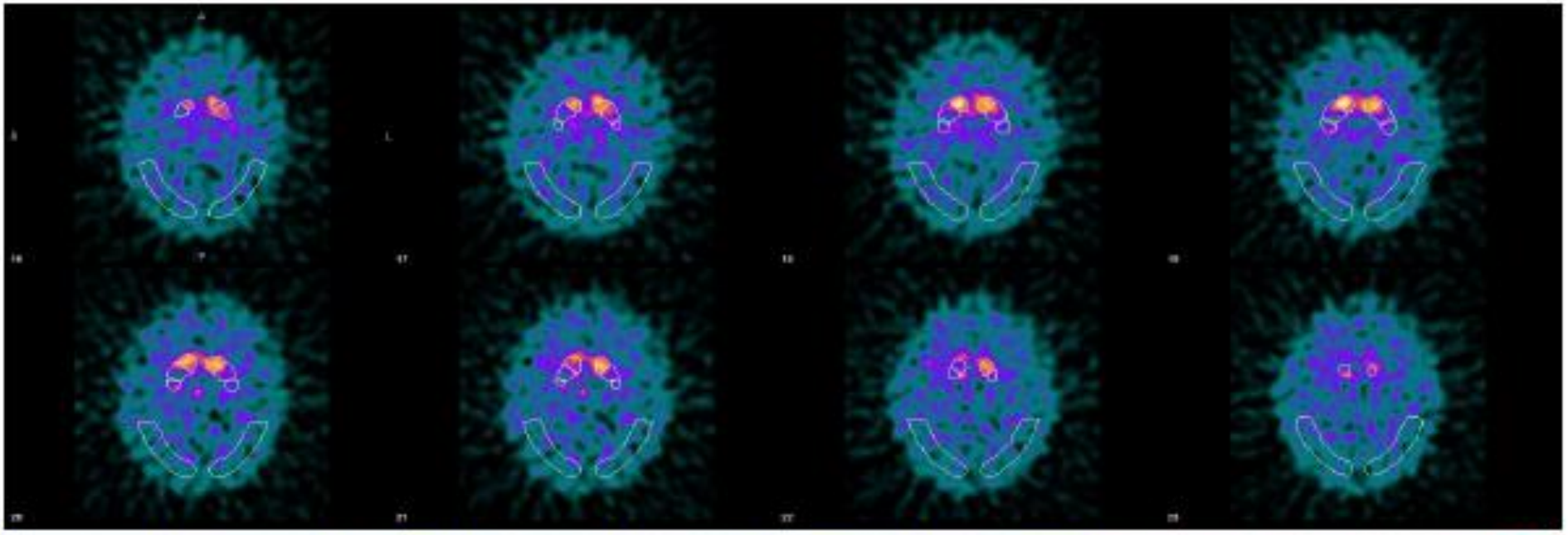


CASO CLINICO 1

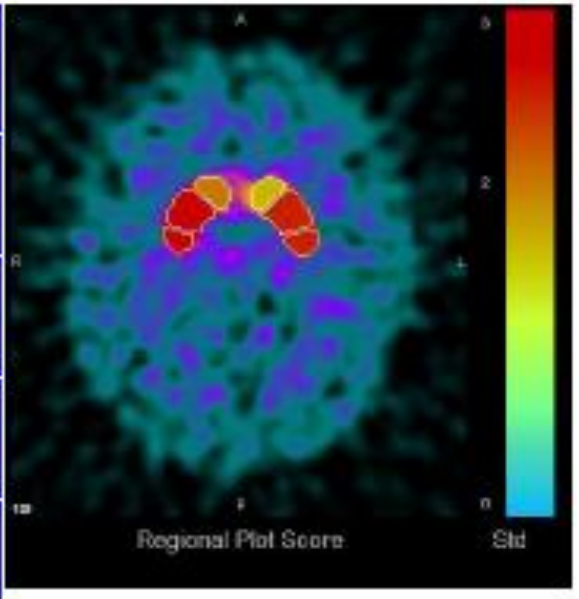
- Uomo, 57aa.
- Sindrome extrapiramidale acinetico-rigida.
- RM encefalo: ...non apprezzabili aree di focale alterazione del segnale del p
- EcoDoppler TSA: ...flusso carotideo normale, arterie vertebrali flusso preser
- Iperomocisteina modesta, THS nella norma.
- Terapia: Azilect 1 mg

  Normocis 400 mg

Gender: Male Recon Method: FBP w/Atten Correction NDB: GE - IRAC (SYS)



	Striatum Right	Striatum Left	Putamen Right	Putamen Left	Caudate Right	Caudate Left
Patient uptake	0.98	1.16	0.69	0.85	1.46	1.72
Normal (±1 SD)	2.54 (±0.63)	2.54 (±0.63)	2.39 (±0.61)	2.38 (±0.61)	2.78 (±0.66)	2.83 (±0.69)
Percent deviation	-61%	-54%	-71%	-64%	-48%	-39%
Num of SD from mean	-2.49	-2.20	-2.77	-2.50	-2.00	-1.61



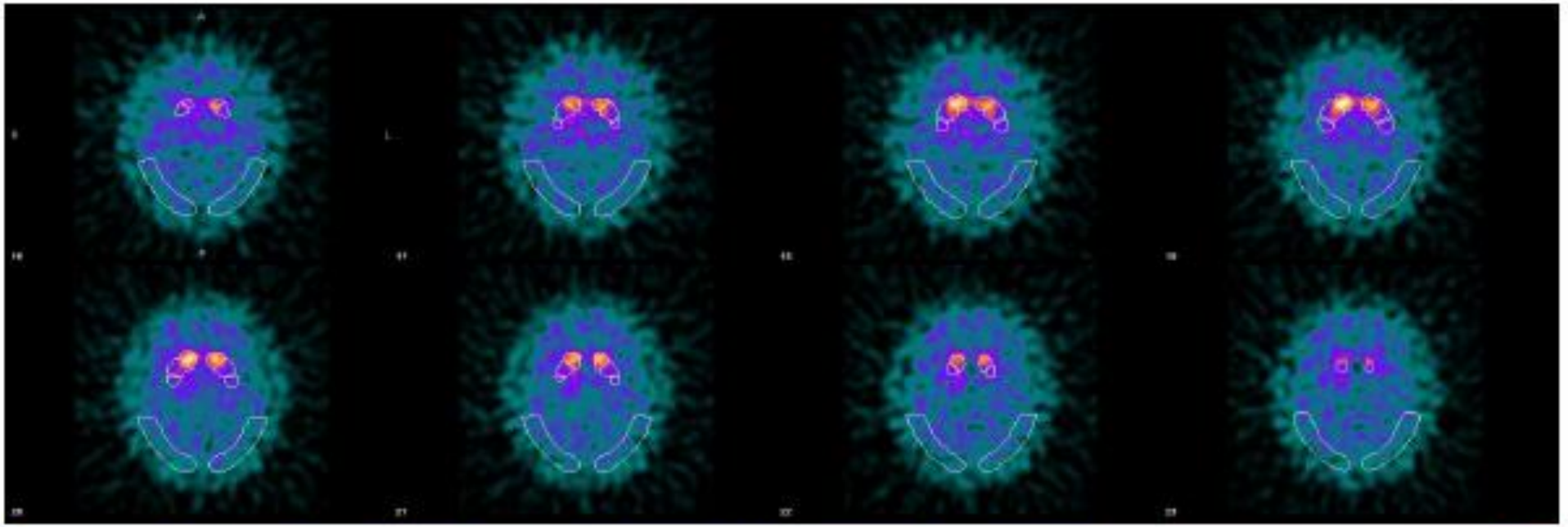
CASO CLINICO 2

- Uomo, 64aa.
- Tremore arto superiore destro prevalente a riposo insorto da circa un anno.
- RM encefalo: ...non alterazioni focali di segnale a carico del parenchima cer
- TC encefalo:...non evidenti alterazioni della densità diretta del parenchima e
- Terapia (da 4 mesi): Madopar 100 mg + 25 (2+1+1cps)

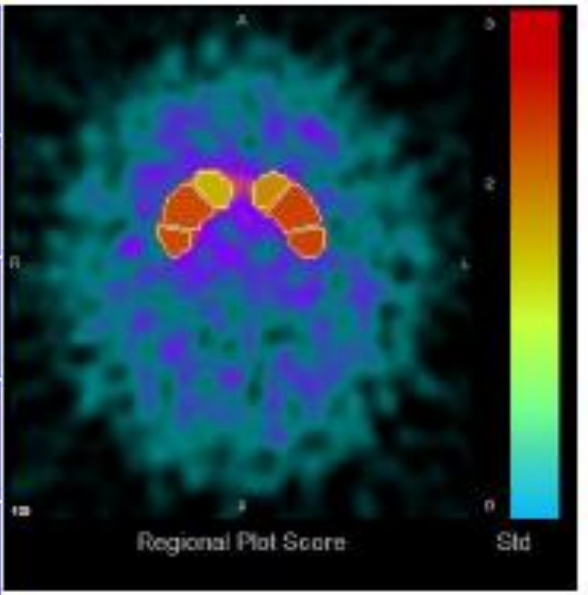
  Ropinorolo 4 mg RP

  Aidex 1 mg

Gender: Male Recon Method: FBP w/Atten Correction NDB: GE - IRAC (SYS)



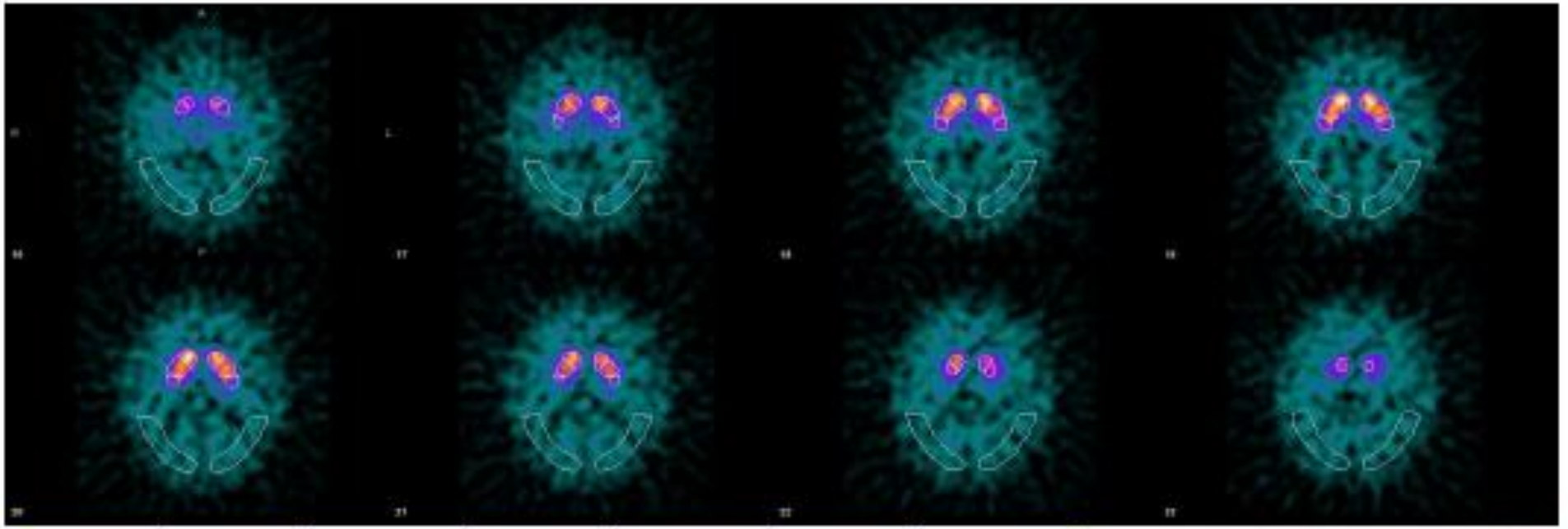
	Striatum Right	Striatum Left	Putamen Right	Putamen Left	Caudate Right	Caudate Left
Patient uptake	1.12	1.05	0.87	0.85	1.55	1.42
Normal (±1 SD)	2.39 (±0.63)	2.40 (±0.63)	2.24 (±0.61)	2.24 (±0.61)	2.64 (±0.66)	2.71 (±0.69)
Percent deviation	-53%	-56%	-61%	-62%	-41%	-48%
Num of SD from mean	-2.04	-2.17	-2.24	-2.28	-1.66	-1.88



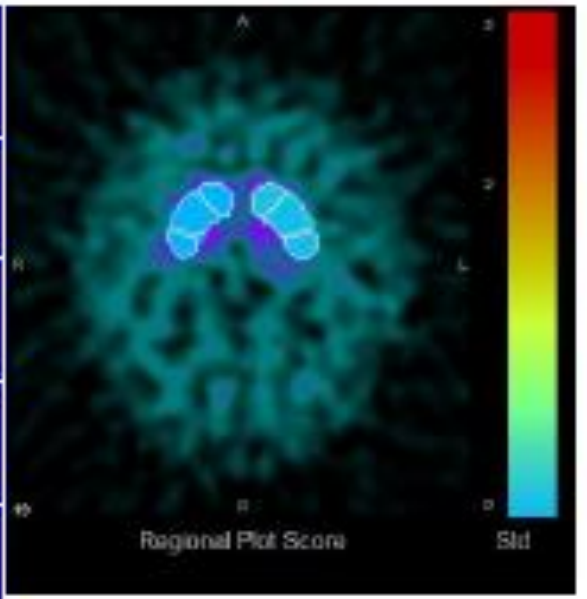
CASO CLINICO 3

- Uomo, 74aa.
- Riferito tremore al capo e della porzione distale arti superiori ad andamento
- Non deficit sensitivo-motori focali in atto. Lieve tremore posturale alla porzio
- TC encefalo:...non lesioni focali del parenchima cerebrale.
- Terapia: Rivotril 5 gtt/die.

Gender: Male Recon Method: FBP w/Atten Correction NDB: GE - IRAC (SYS)

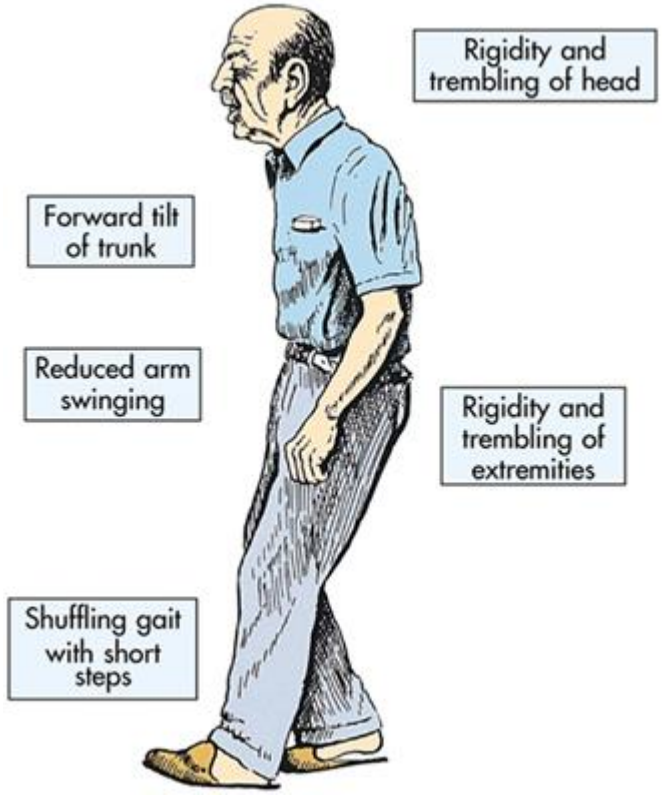


	Striatum Right	Striatum Left	Putamen Right	Putamen Left	Caudate Right	Caudate Left
Patient uptake	2.26	2.15	2.06	1.99	2.58	2.45
Normal (±1 SD)	2.22 (±0.63)	2.24 (±0.63)	2.06 (±0.61)	2.06 (±0.61)	2.48 (±0.66)	2.56 (±0.69)
Percent deviation	02%	-04%	00%	-04%	04%	-05%
Num of SD from mean	0.06	-0.14	0.00	-0.12	0.16	-0.17



123I-IOFLUPANE

- S. di Parkinson vs tremore essenziale.
- S. di Parkinson vs disturbi aspecifici dell'andatura e bradicinesia ne
- S. di Parkinson vs depressione/ansietà.
- Diagnosi differenziale nelle ***demenze***



Demenza con Corpi di Lewy (DLB)

Apetti chiave della patologia:

- Atrofia Cerebrale
- Corpi di Lewy*
- ***Perdita dei neuroni dopaminergici nigro-striatali***

***Corpi di Lewy**
Deposito anomalo di proteine nei neuroni, che ne alterano la normale funzione e causano morte neuronale.

Localizzati nella corteccia o nei gangli della base
La dislocazione correla con i sintomi

La diagnosi è difficile e spesso non viene correttamente identificata

- Se predomina il sintomo cognitivo -> può essere confusa con Alzheimer o Demenza Vascolare

- Se predomina il sintomo motorio -> può essere confusa con Parkinson Demenza

www.lbda.org/content/dlb-and-pdd-diagnostic-criteria

Mrak E et al, Dementia with Lewy bodies: Defi nition, diagnosis,and pathogenic relationship to Alzheimer's disease. Neuropsychiatric Disease and Treatment 2007:3(5) 619–625

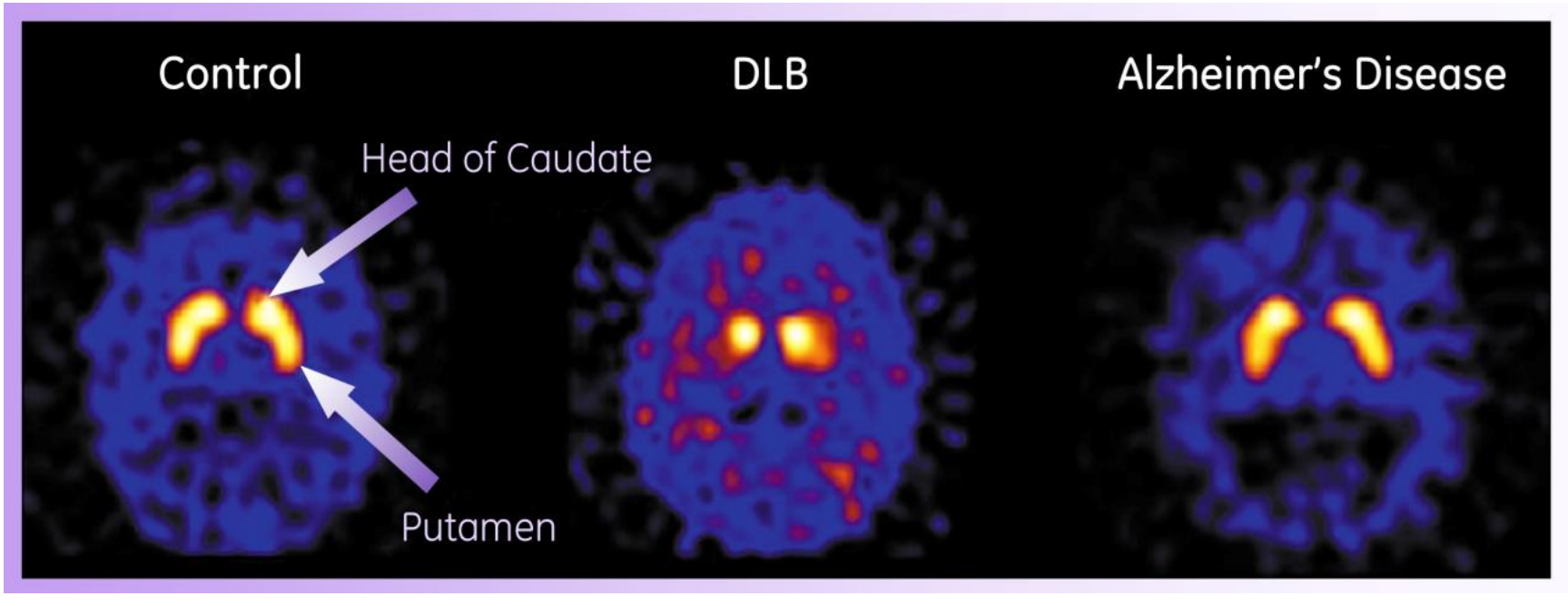
Malattia di Alzheimer

Progressivo deterioramento cognitivo (es. Perdita di memoria, deficit attentivo, disorientamento, caratteristiche neuropsichiatriche) che portano ad un declino sociale e funzionale

Aspetti chiave della patologia

- Atrofia Cerebrale
- Deficit Colinergico
- Deposito di amiloide
- Formazione di “grovigli” di proteina Tau

In che stato sono i neuroni dopaminegici nella sostanza nera?
Diagnosi differenziale tra AD e DLB



.PET/TC:

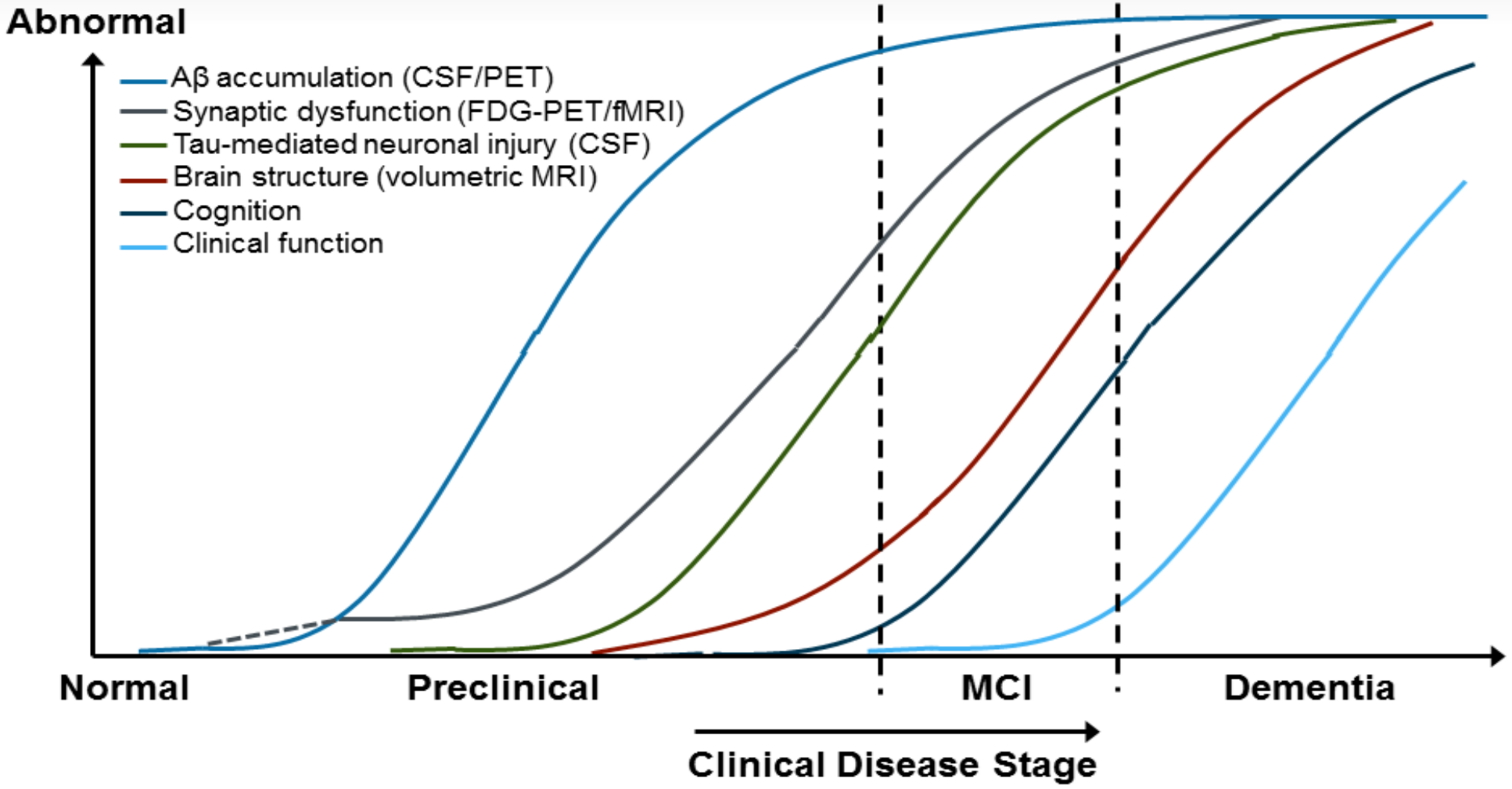
_ ***18F-FDG*** (metabolismo glucidico della corteccia cerebrale);

_ ***18F-florbetapir, 18F-florbetaben, 18F-flutemetamol***

_ 18F-DOPA (disfunzione dopaminergica presinaptica);

_ *(18F-...rilevazione proteina tau, in studio).*

Sequencing of Biomarkers



From Sperling RA, et al. *Alzheimers Dement.* 2011;7:280-292.

18F-FDG

metabolismo glucidico della corteccia cerebrale

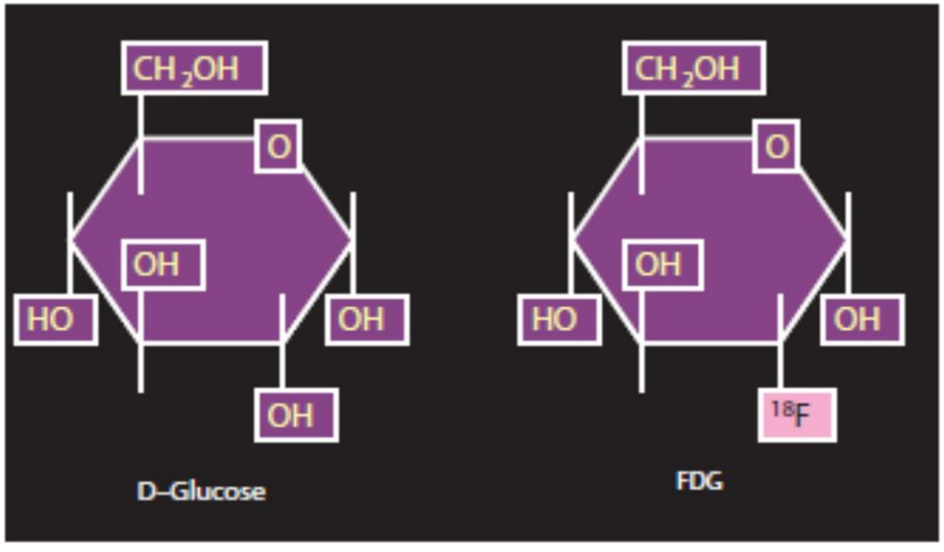


Fig. 3.3. [^{18}F]2-deoxy-2-fluoro-D-glucose (FDG). In FDG the hydroxyl group in the 2-position of D-glucose is replaced by ^{18}F

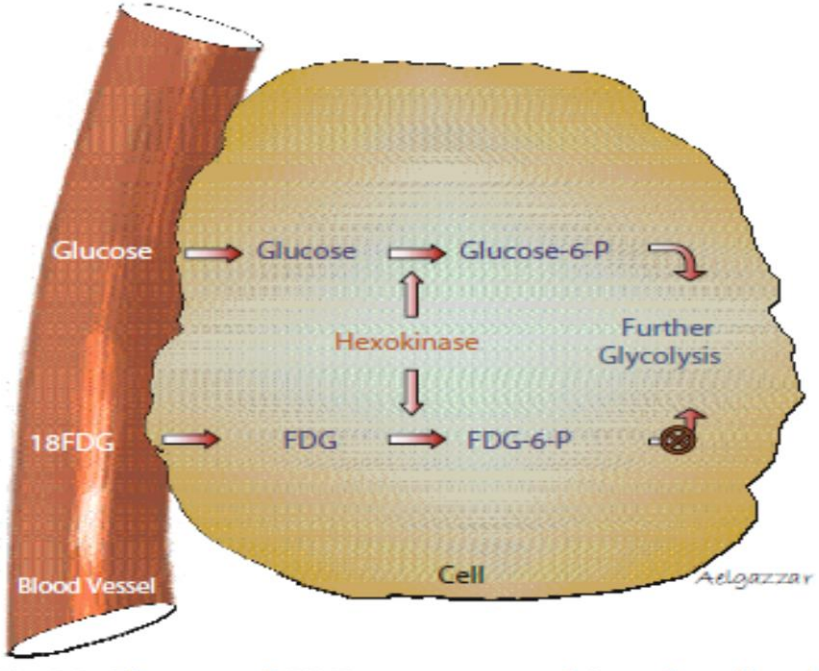


Fig. 3.2. Glucose and FDG are transported into the cell and phosphorylated, but FDG does not undergo further metabolism and accumulates in proportion to glucose utilization (increased in tumors, macrophages and ischemic myocytes)

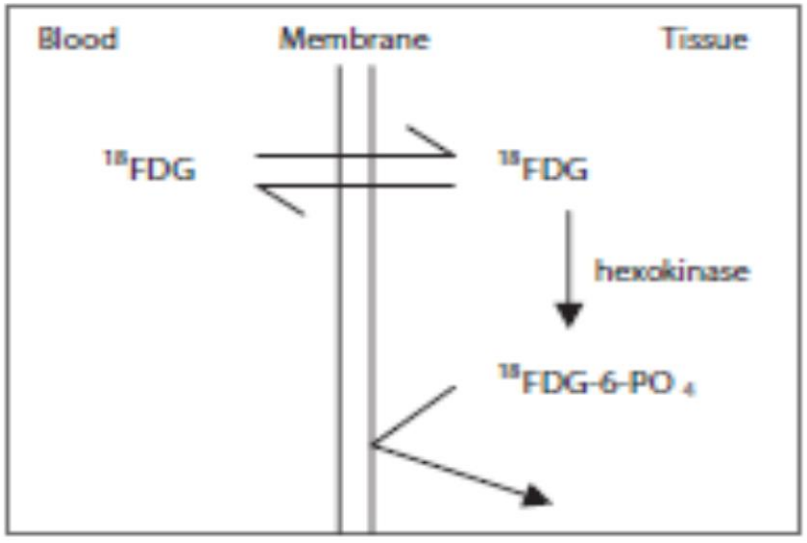


Fig. 2.3. Intracellular phosphorylation of ^{18}FDG to ^{18}FDG-6-PO_4 by hexokinase

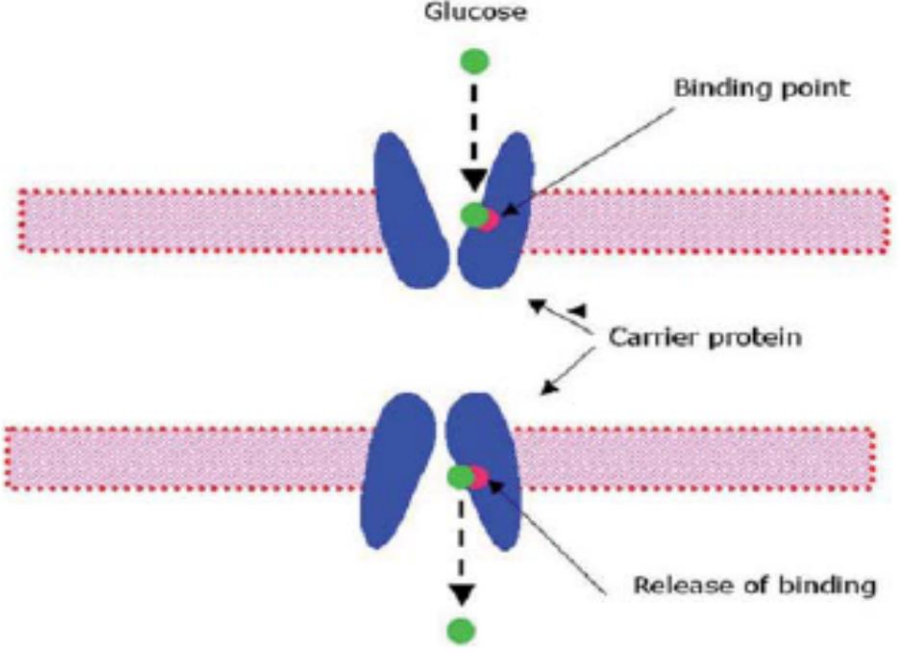
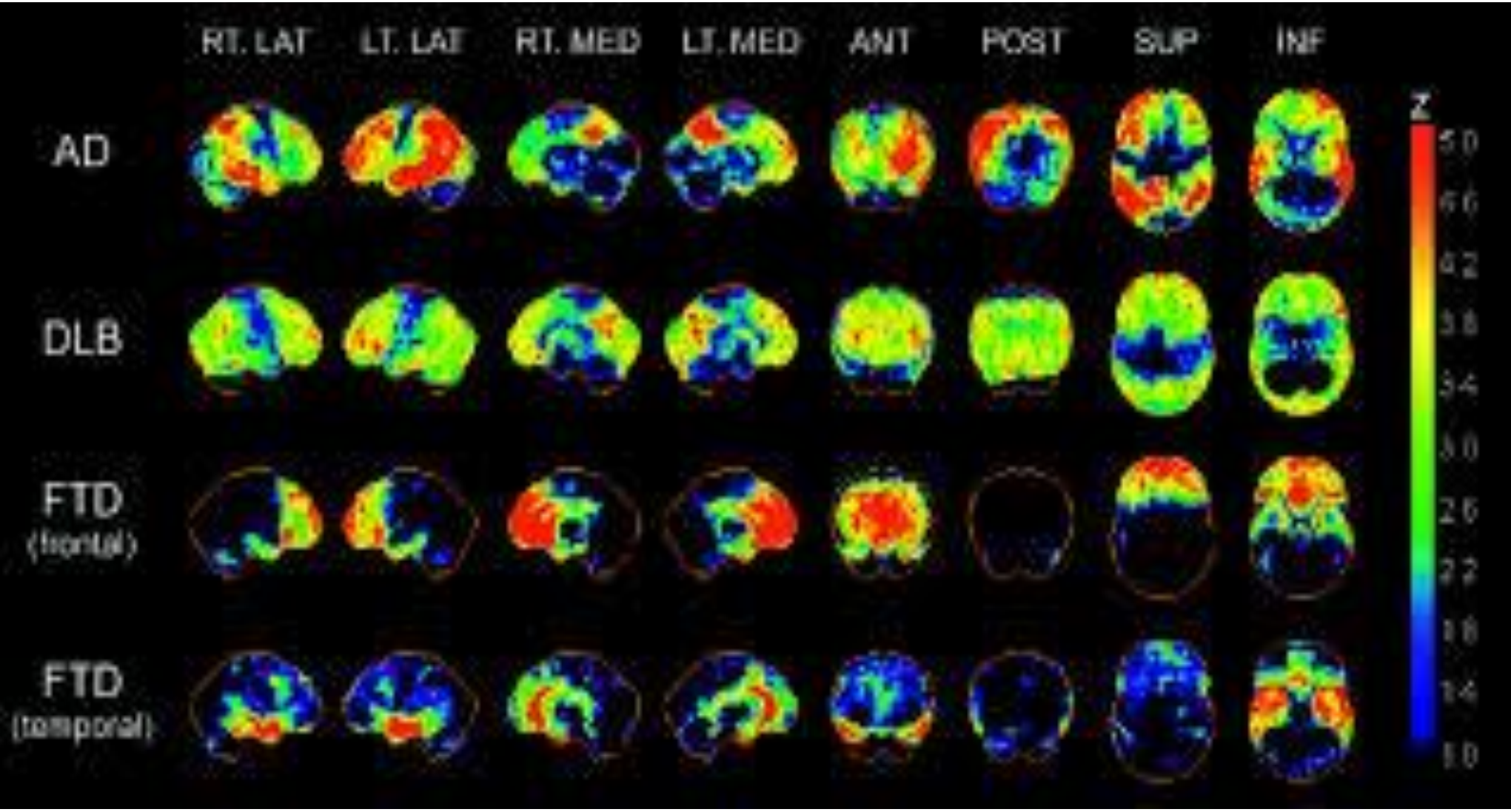


Table 3.1. Facilitative glucose transporters and their tissue locations

Trans-porter	Site of highest concentration
GLUT-1	Fetal tissue and placenta
GLUT-2	Intestine, kidney, liver and β cells of pancreas, brain
GLUT-3	Neurons in the brain
GLUT-4	Brown and yellow adipose tissue and skeletal muscle
GLUT-5	Small intestine
GLUT-7	Endoplasmic reticulum


RT. LAT
LT. LAT
RT. MED
LT. MED
ANT
POST
SUP
INF
AD
DLB
FTD
(frontal)
FTD
(temporal)
Z
50
46
42
38
34
30
26
22
18
14
10

CASO CLINICO 4

- Uomo, aa 55.
- Disturbi cognitivo-comportamentali esorditi un anno fa (memoria episodica, linguaggio, attenzione, sonno, alterazione sfera timica) progrediti nel tempo.
- RM : “...normali gli spazi liquorali...non evidenti alterazioni focali...”
- Esami ematochimici nella norma.
- APO E : non disponibile.
- ECG, EcoDoppler, EEG: non alterazioni di rilievo.
- MMSE: 20,2/30; ADL: 6/6; IADL: 5/5.

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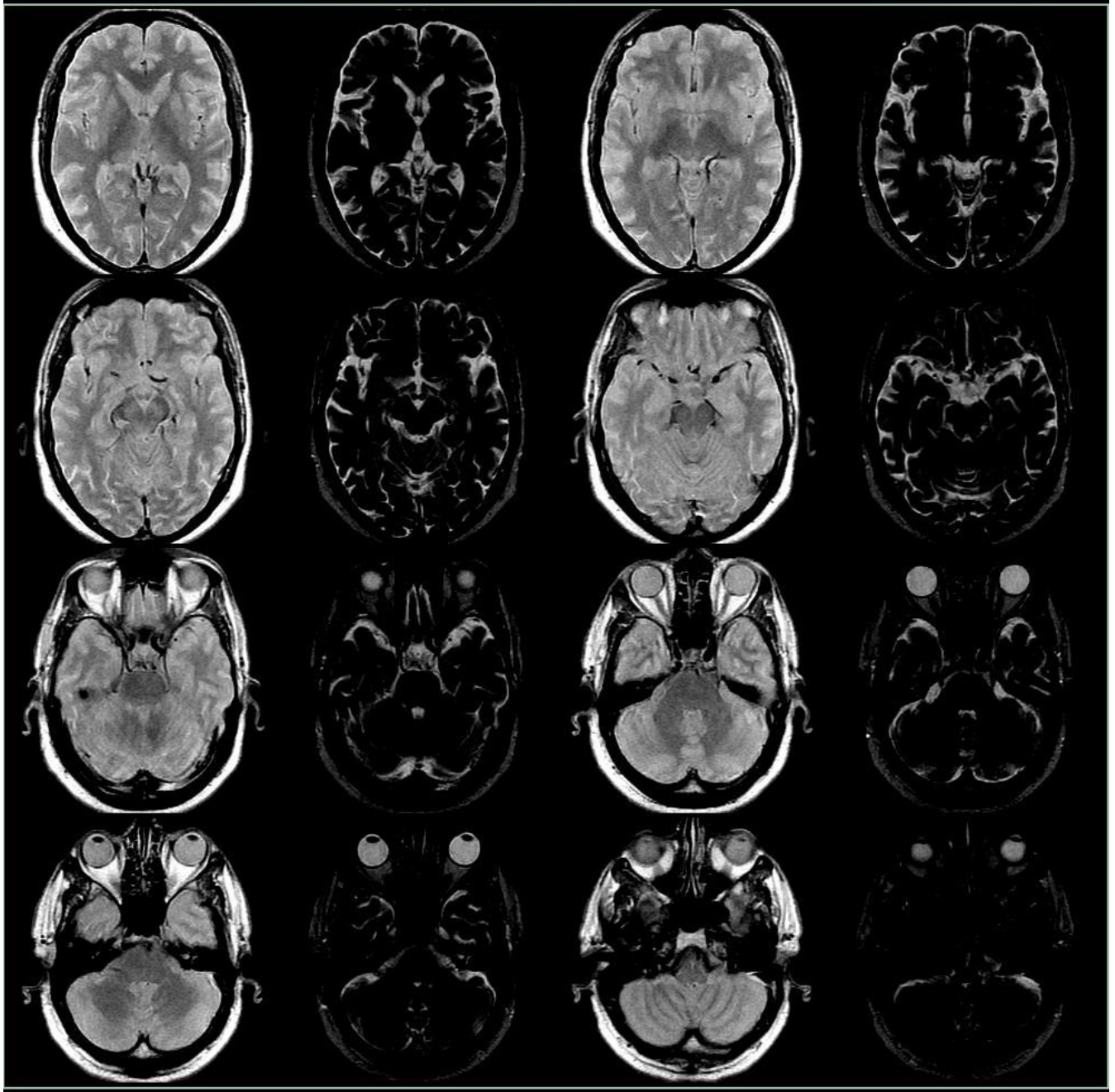

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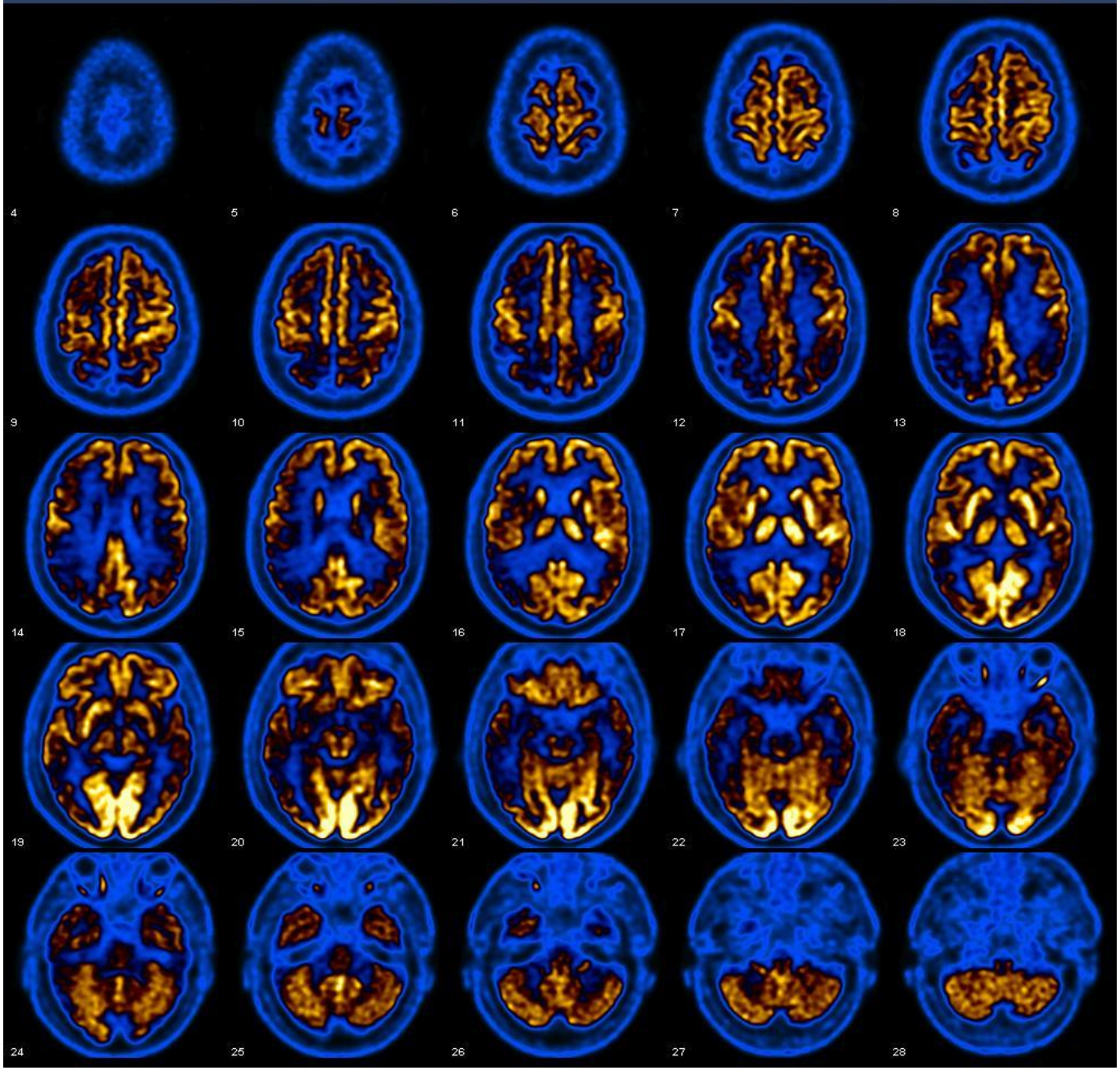
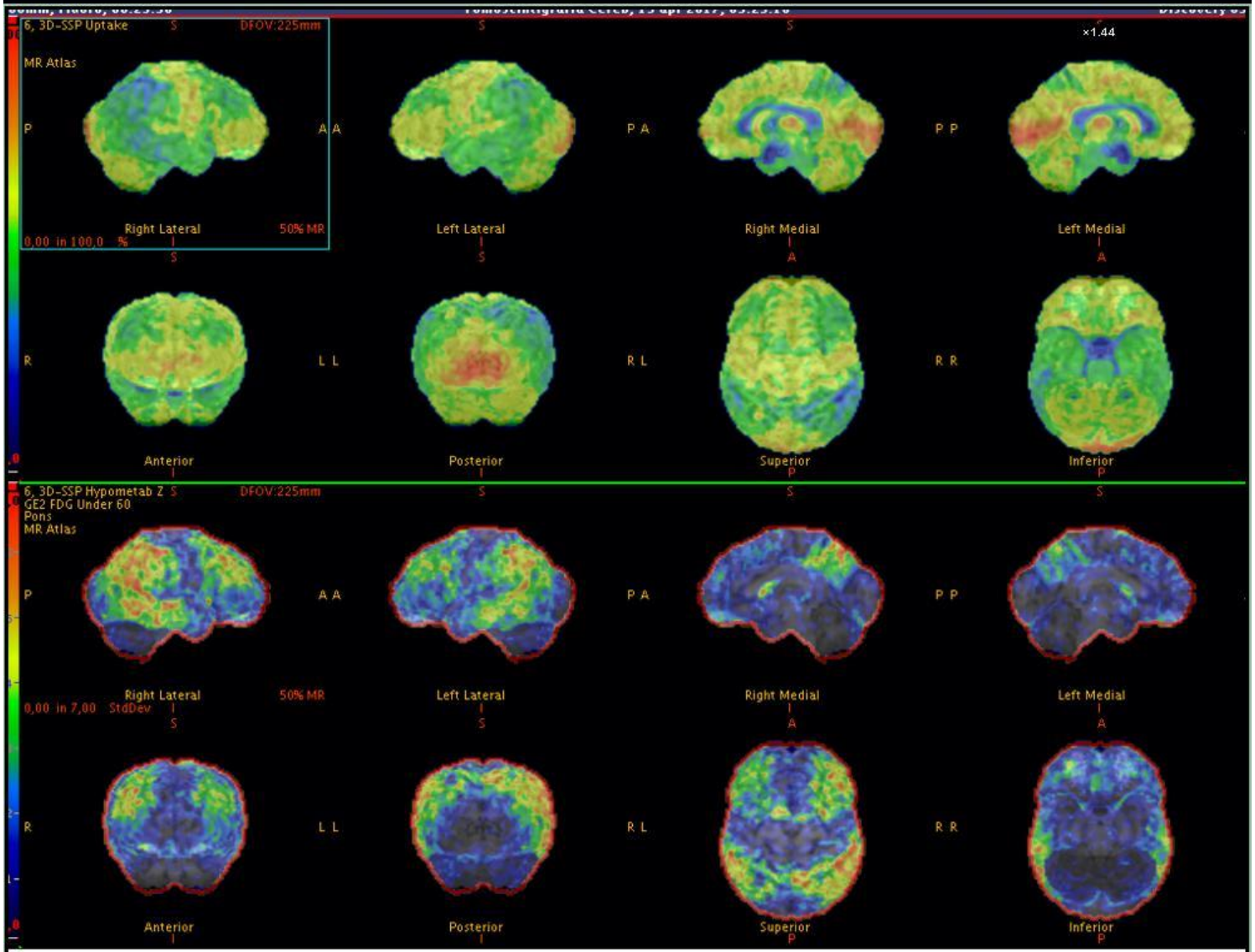
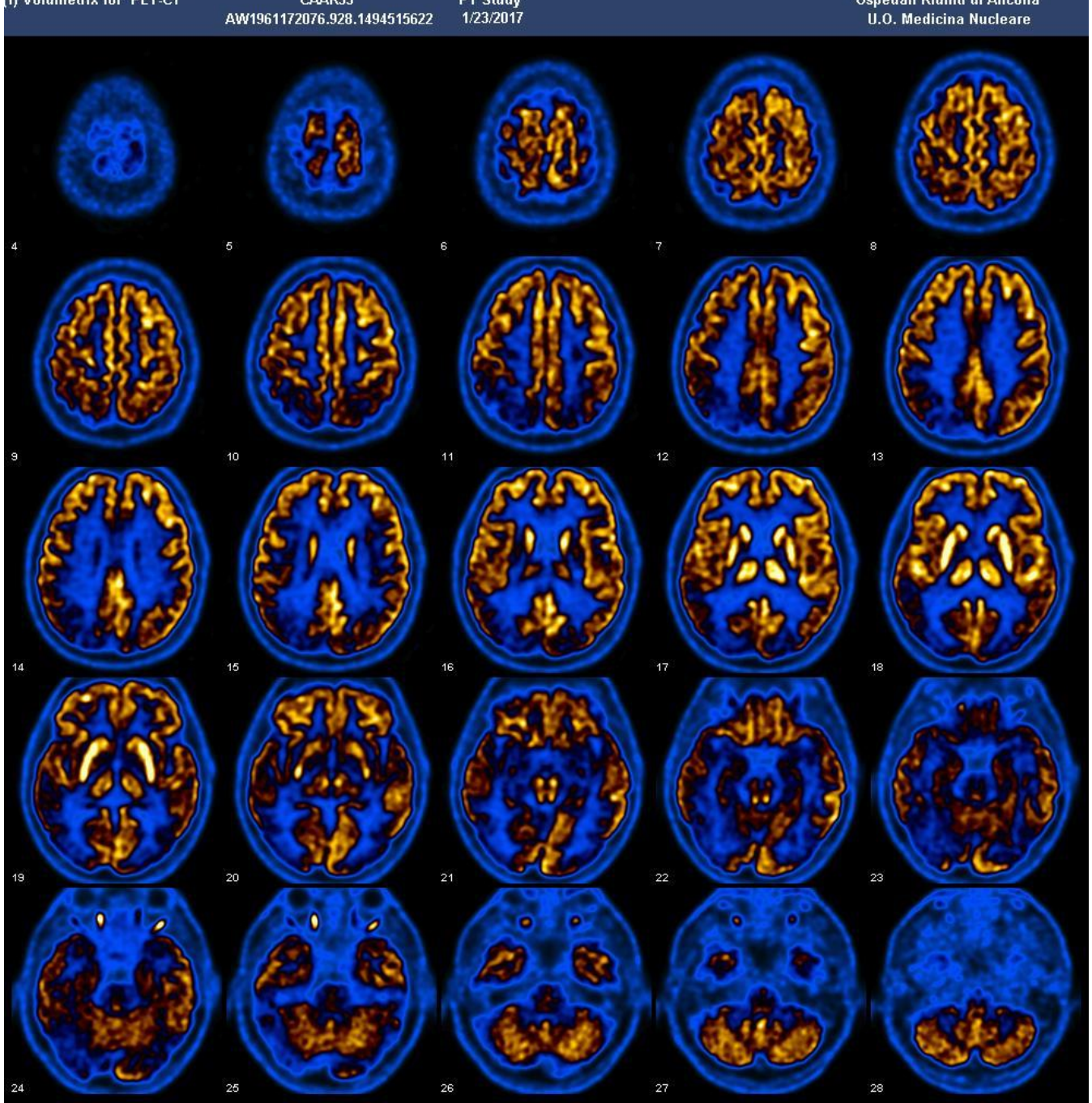



6, 3D-SSP Uptake
DFOV:225mm
MR Atlas
×1.44
Right Lateral
50% MR
0,00 in 100,0 %
Left Lateral
Right Medial
Left Medial
Anterior
Posterior
Superior
Inferior
6, 3D-SSP Hypometab Z
GE2 FDG Under 60
Pons
MR Atlas
DFOV:225mm
Right Lateral
50% MR
0,00 in 7,00 StdDev
Left Lateral
Right Medial
Left Medial
Anterior
Posterior
Superior
Inferior

CASO CLINICO 5

- Uomo, aa 61.
- RMN: “...piccola anomalia di sviluppo venoso in sede sottocorticale frontale anteriore sinistra... alcune piccole lacune di leucoencefalopatia di verosimile natura vascolare cronica prevalentemente in sede frontale...”
- Disturbo visuo-spaziale, episodi di disorientamento spaziale, diplopia.
- Esami ematochimici ed ECG nella norma.
- Atrofia corticale posteriore?


(1) Volumetrix for PET-CT
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PT Study
1/23/2017
Ospedali Riuniti di Ancona
U.O. Medicina Nucleare
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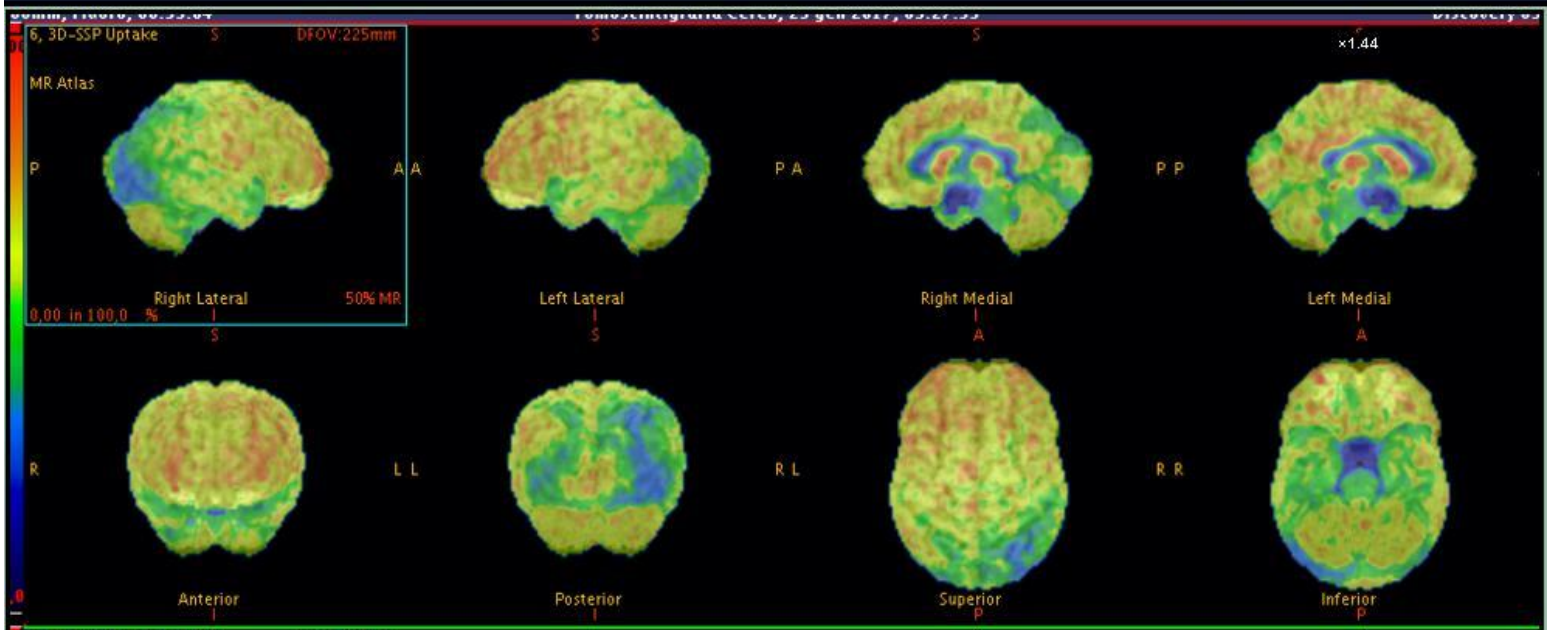
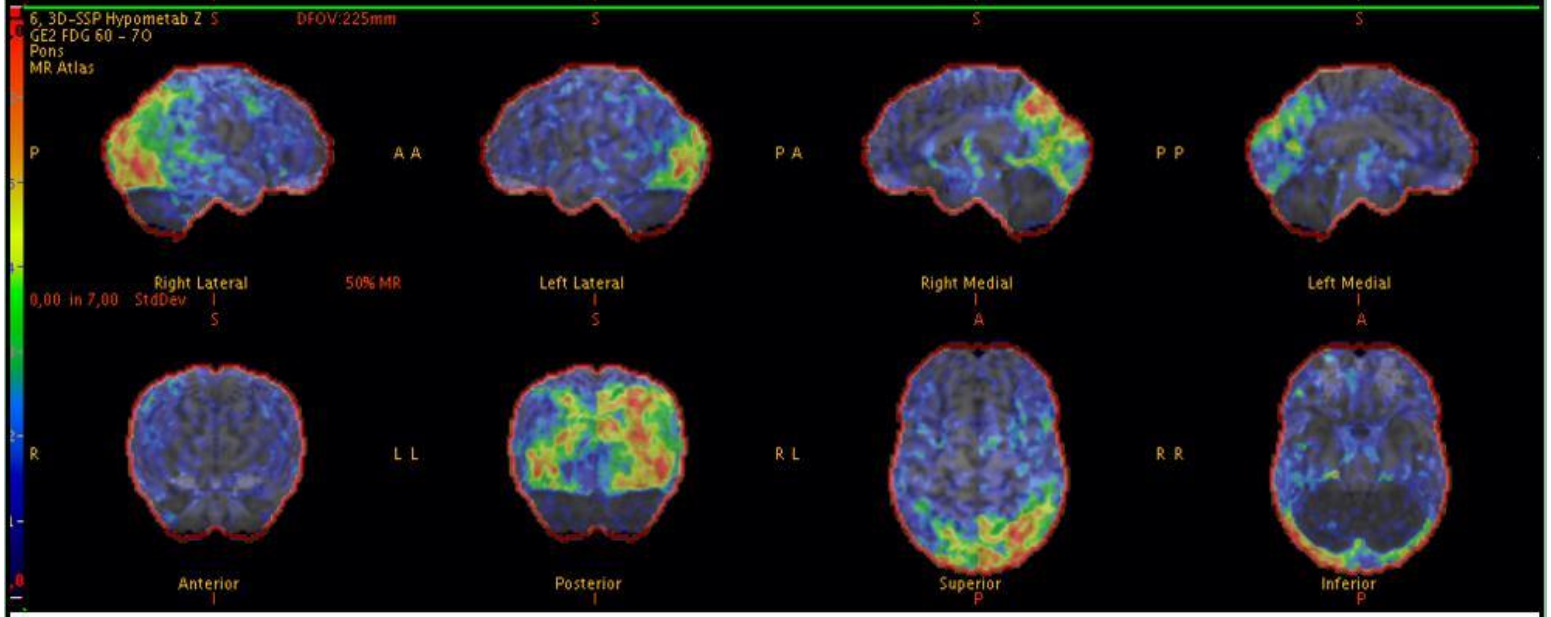




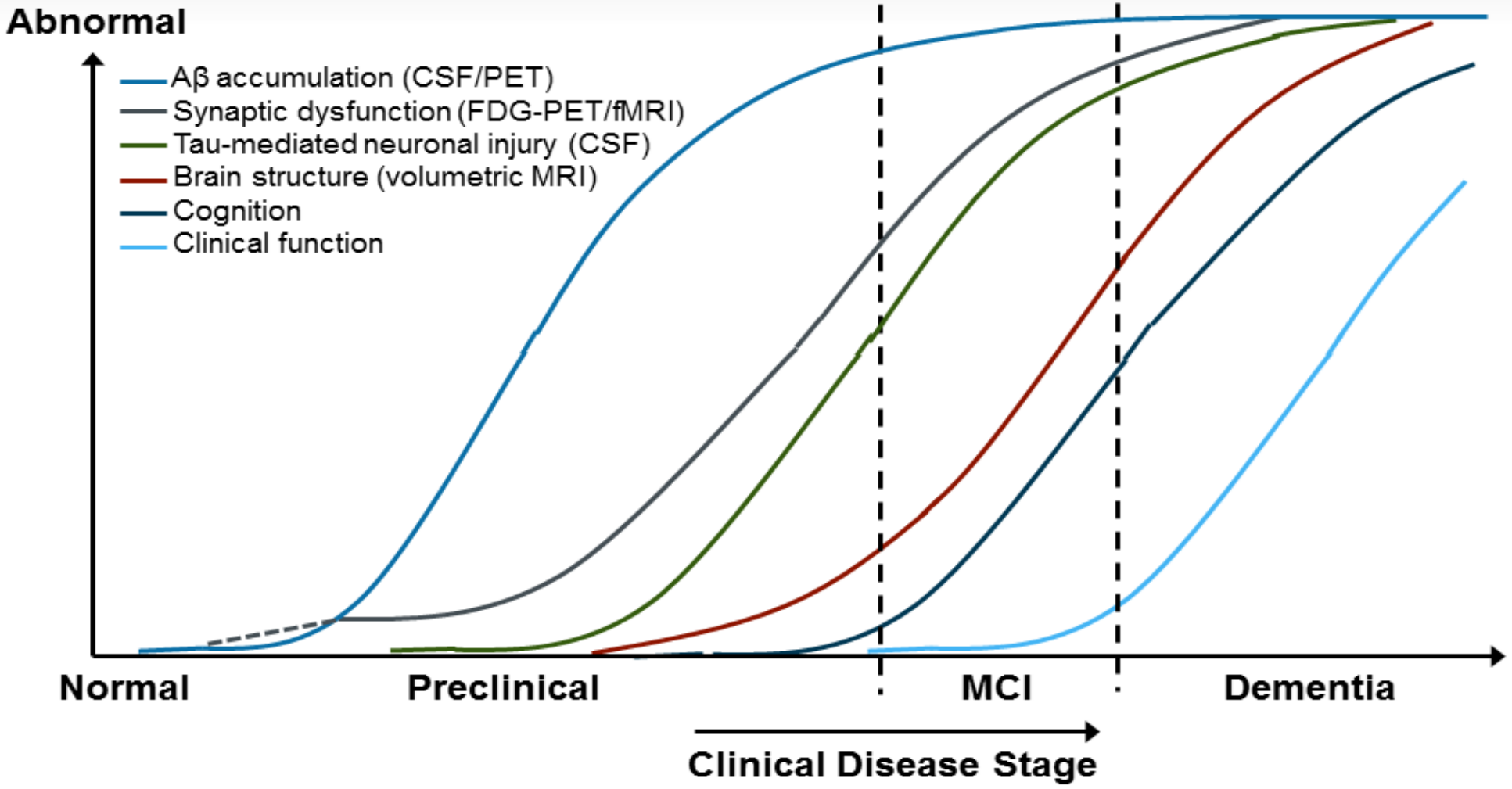
Clinical validity of brain fluorodeoxyglucose positron emission tomography as a biomarker for Alzheimer's disease in the context of a structured 5-phase development framework.

Garibotto V, Herholz K, Boccardi M, Picco A, Varrone A, Nordberg A, Nobili F, Ratib O; Geneva Task Force for the Roadmap of Alzheimer's Biomarkers.

Neurobiol Aging. 2017 Apr;52:183-195. doi: 10.1016/j.neurobiolaging.2016.03.033.

La tomografia cerebrale con fluorodesossiglucosio (FDG PET), misura il metabolismo del glucosio cerebrale, come biomarker per identificare l'AD clinico e prodromico.
Seguendo il quadro proposto per i biomarkers in oncologia ovvero utilizzando criteri omogenei con altri biomarcatori, si è verificato:
A - la FDG PET ha raggiunto pienamente la fase 1, ovvero *il razionale per l'uso*;
B - la fase 2, ovvero la *capacità di discriminare soggetti AD da controlli sani* o da altre forme di demenza, è quasi completa;
C - la fase 3, ovvero la *capacità di rilevazione precoce*, è in parte raggiunta.
D - la fase 4, ovvero l'uso routinario nei pazienti prodromici è in corso e solo i risultati preliminari possono essere estrapolati dalle osservazioni retrospettive.
E - la fase 5, ovvero quantificare l'impatto ed i costi, non è stata eseguita.
I risultati di questo studio dimostrano che sono necessari sforzi specifici per completare le prove della fase 3, in particolare è necessario confrontare e combinare FDG PET con altri biomarcatori e progettare studi prospettici di fase 4 come base per le valutazioni della fase 5.

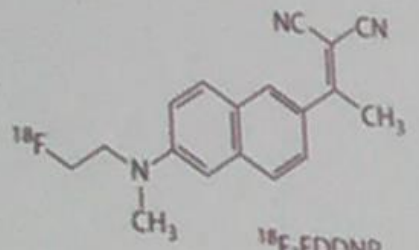
Sequencing of Biomarkers



From Sperling RA, et al. *Alzheimers Dement.* 2011;7:280-292.

PET/TC
RADIOFARMACI PER RILEVAZIONE BETA-AMILOIDE

Aβ Imaging in Humans



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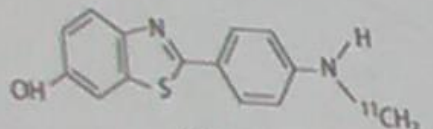

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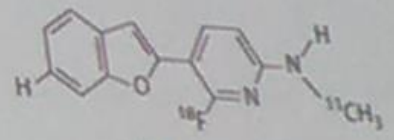

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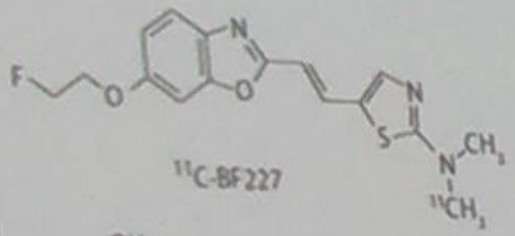

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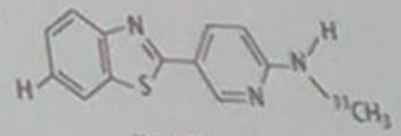

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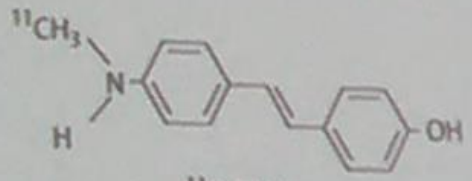
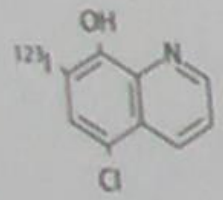
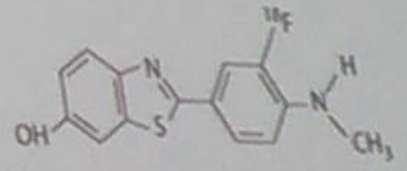


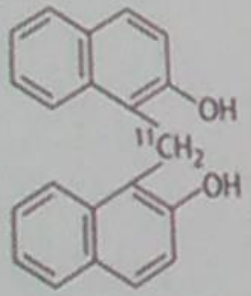
11C-SB13



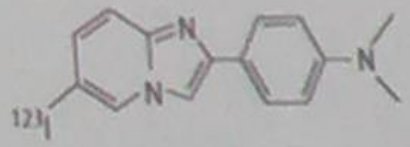
123I-CQ



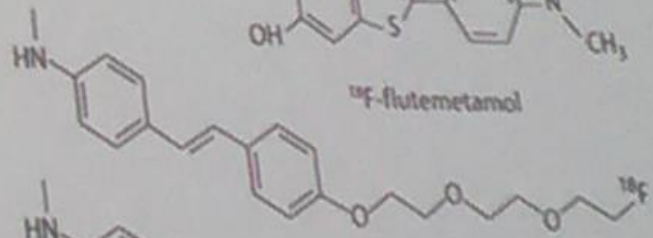
18F-flutemetamol



11C-ST1859



123I-IMPY



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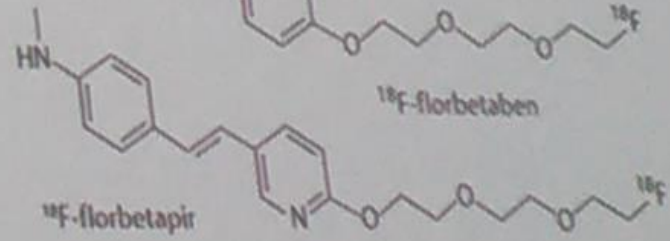


18F-florbetapir

Colorazione Silver staining con metodo di Bielschowsky per le placche neuritiche

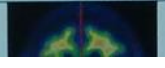
Nessuna

Rara

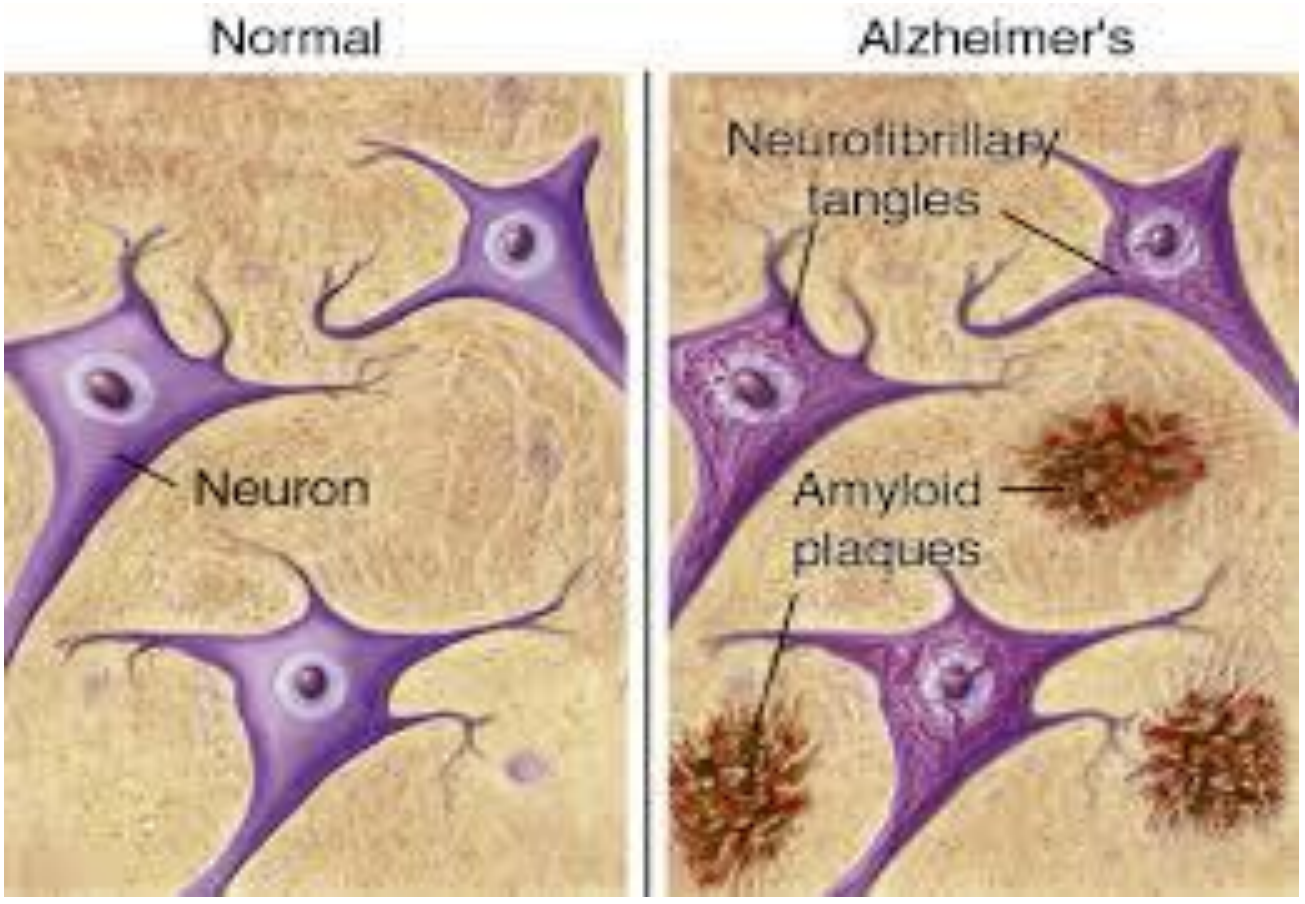
Moderata

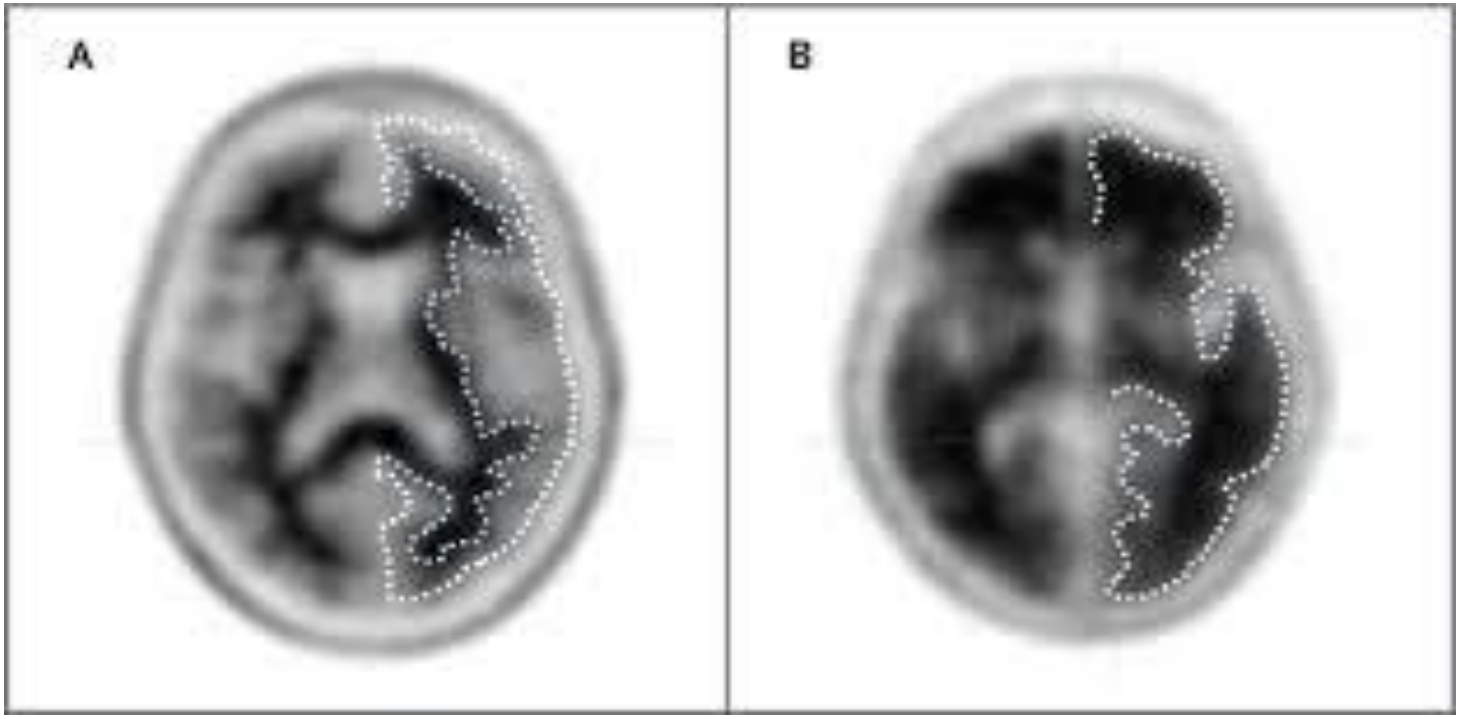
Frequente

Negativa



Positiva


Normal
Alzheimer's
Neuron
Neurofibrillary tangles
Amyloid plaques


A
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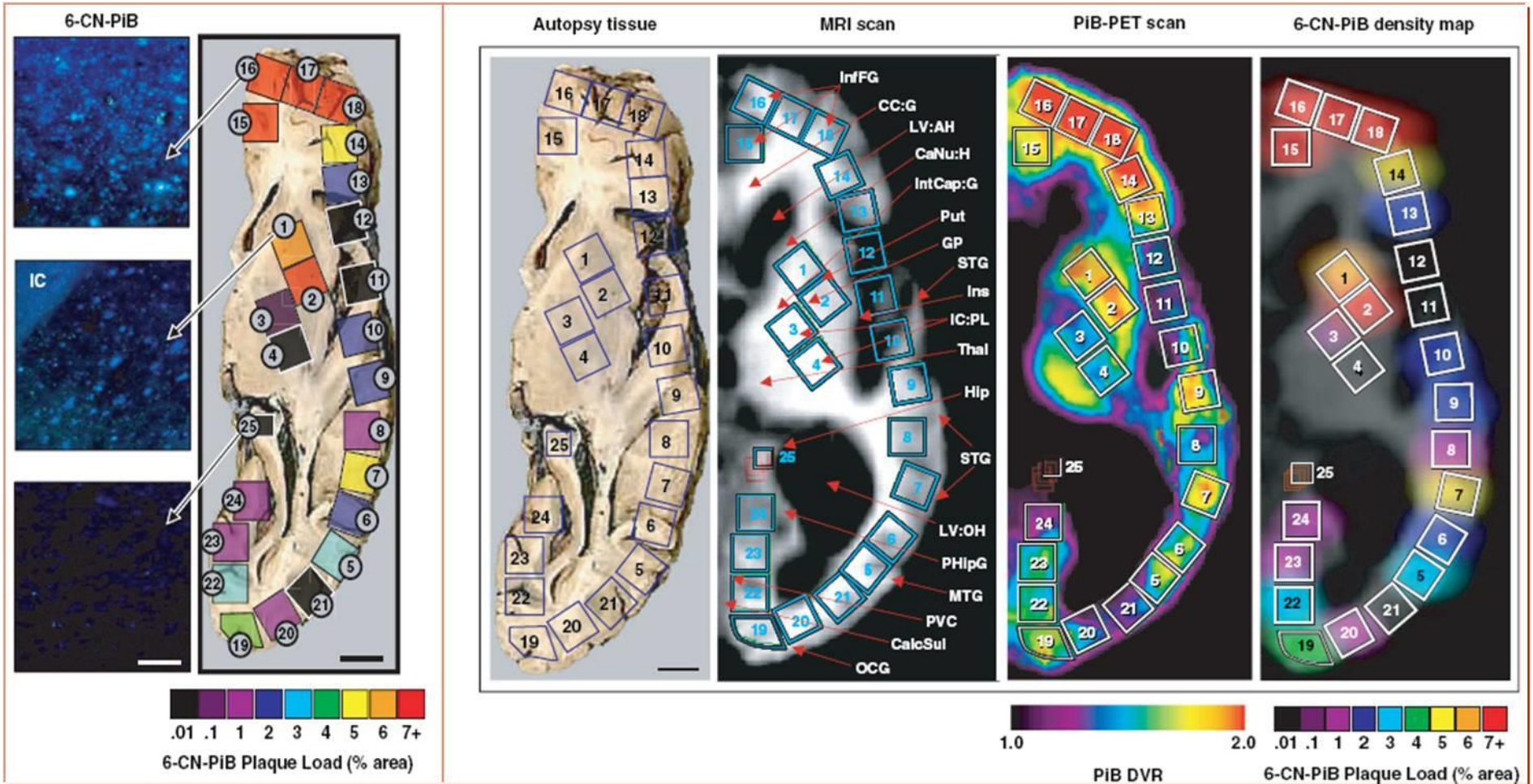
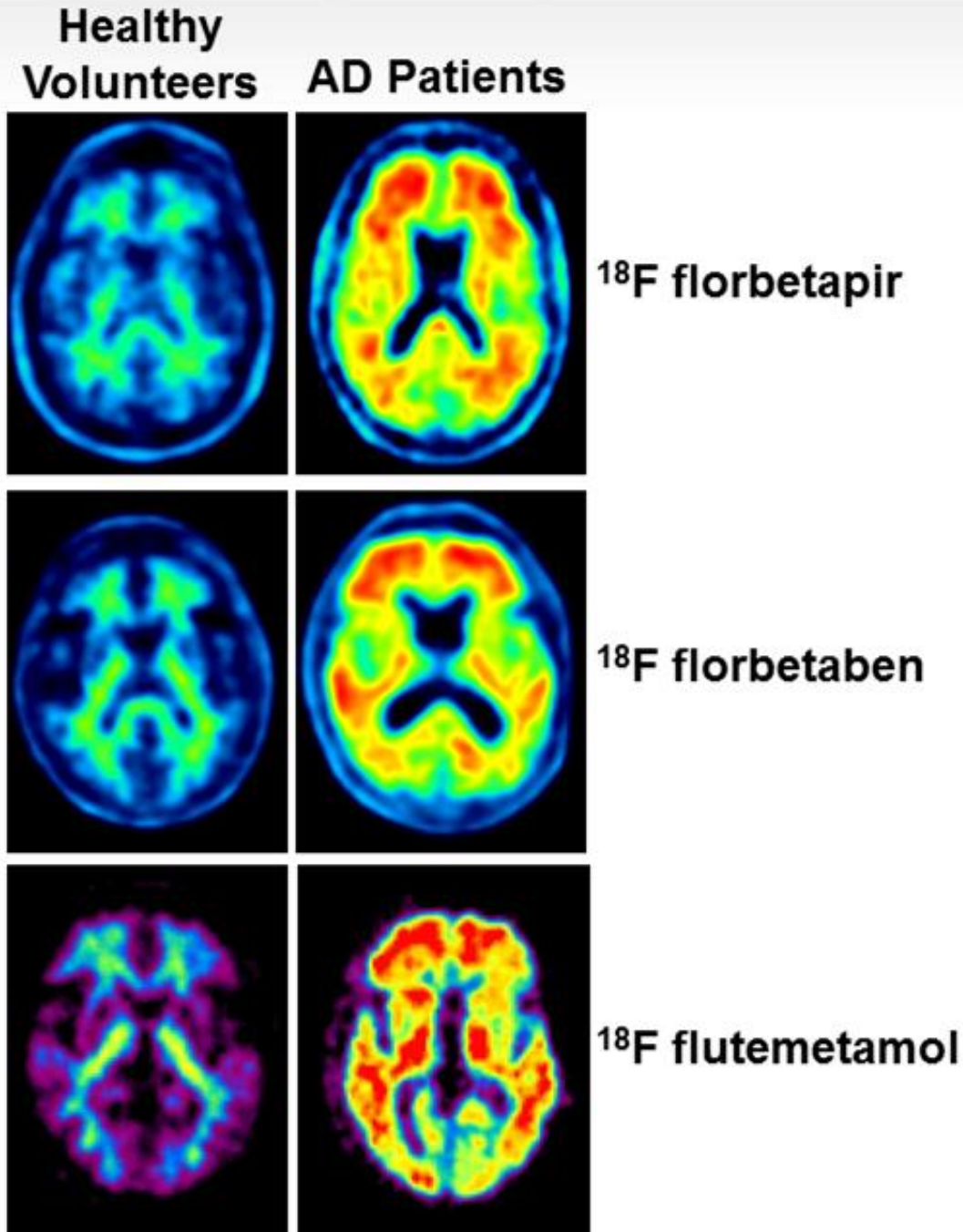
doi:10.1093/brain/awn016 *Brain* (2008), **131**, 1630–1645

Post-mortem correlates of *in vivo* PiB-PET amyloid imaging in a typical case of Alzheimer's disease

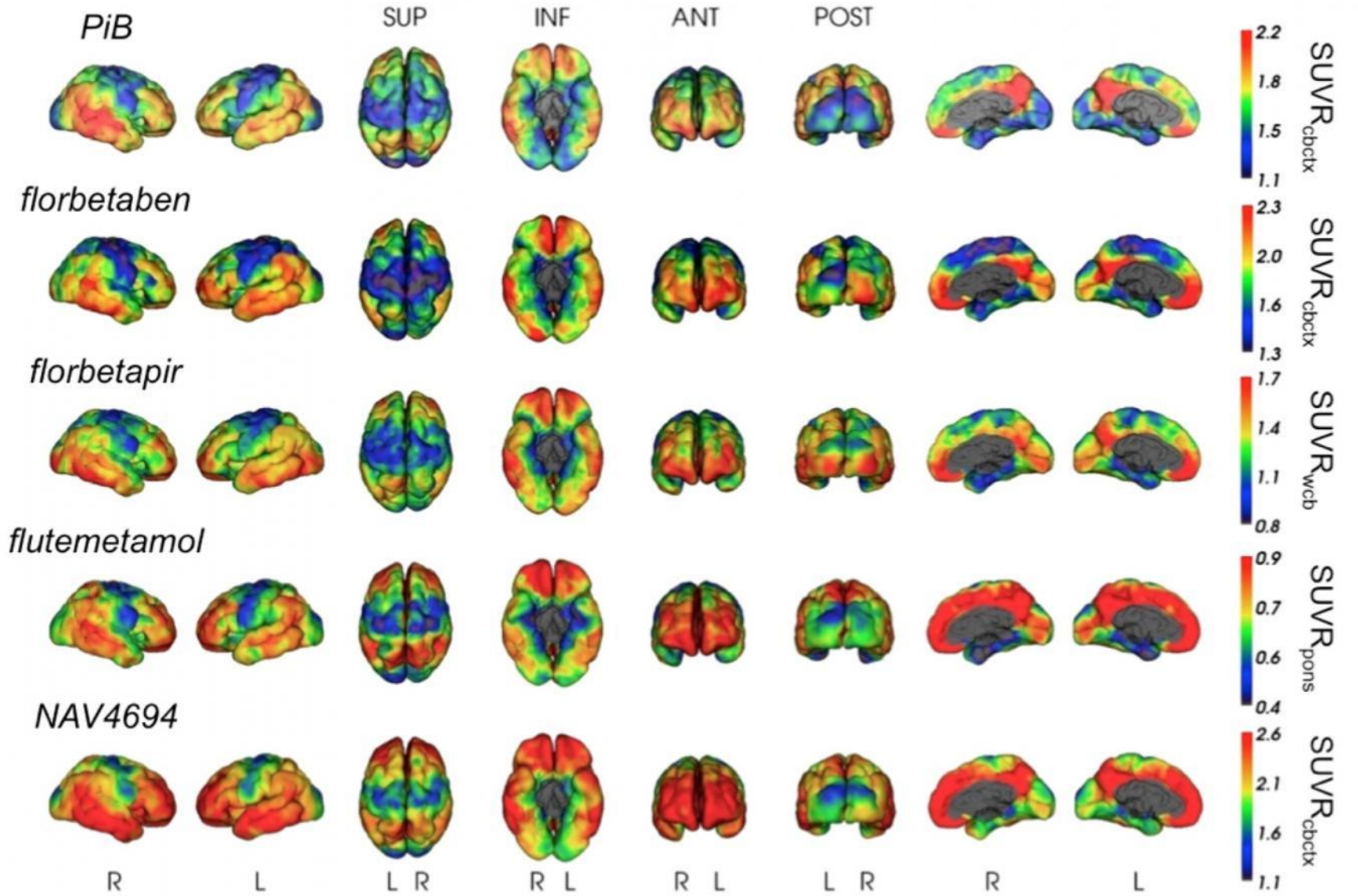
Milos D. Ikonomovic,[1,2] William E. Klunk,[2] Eric E. Abrahamson,[1] Chester A. Mathis,[3] Julie C. Price,[3]



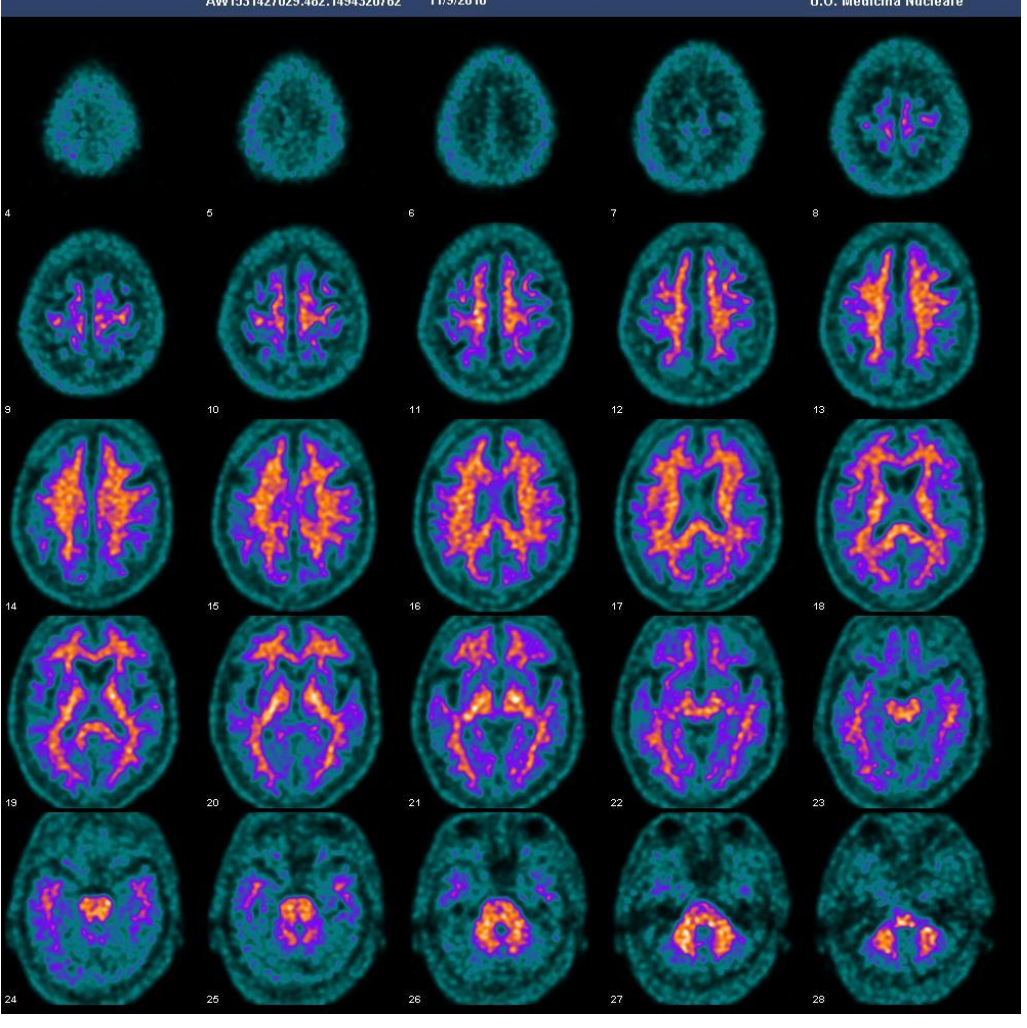


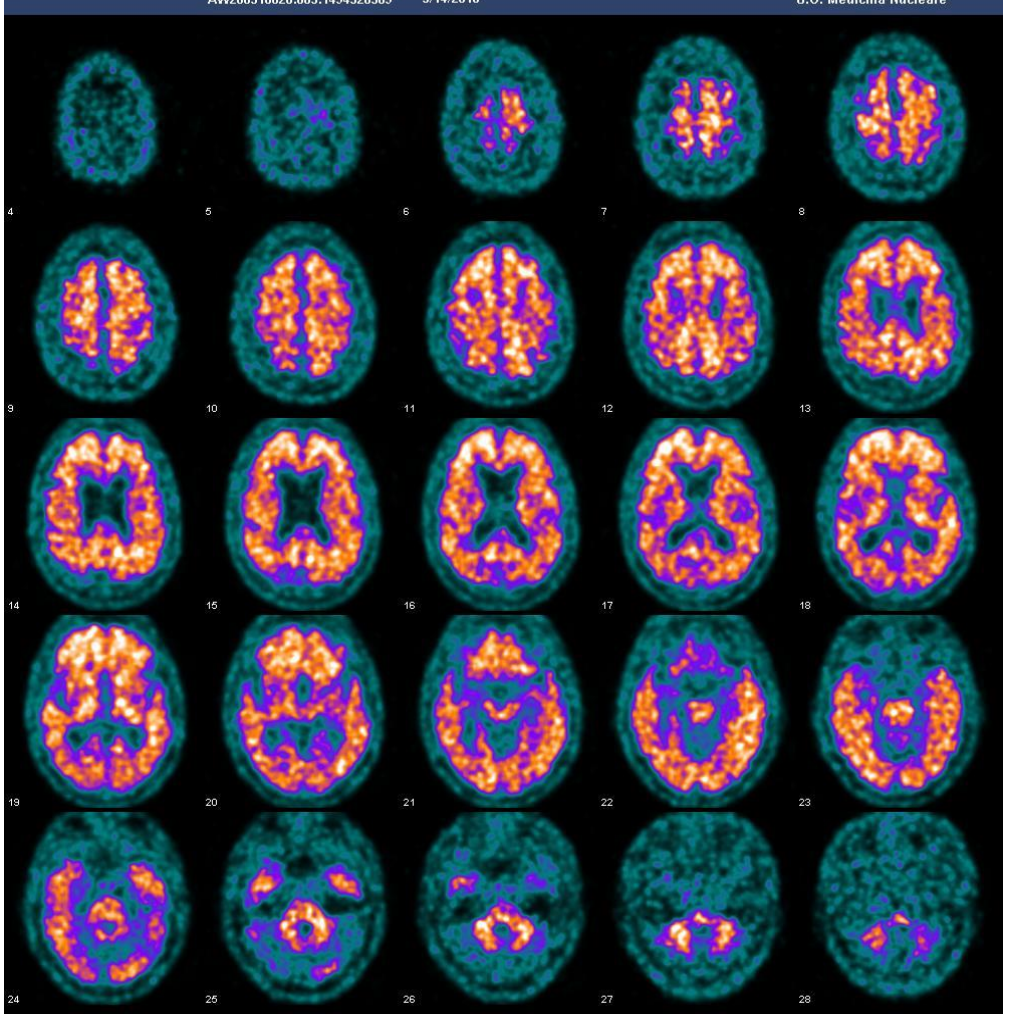
Images courtesy of John P. Seibyl, MD.

Aβ imaging in Alzheimer's disease



Images generated through CapAIBL® (*milxcloud.csiro.au*)
CSIRO Biomedical Imaging Group



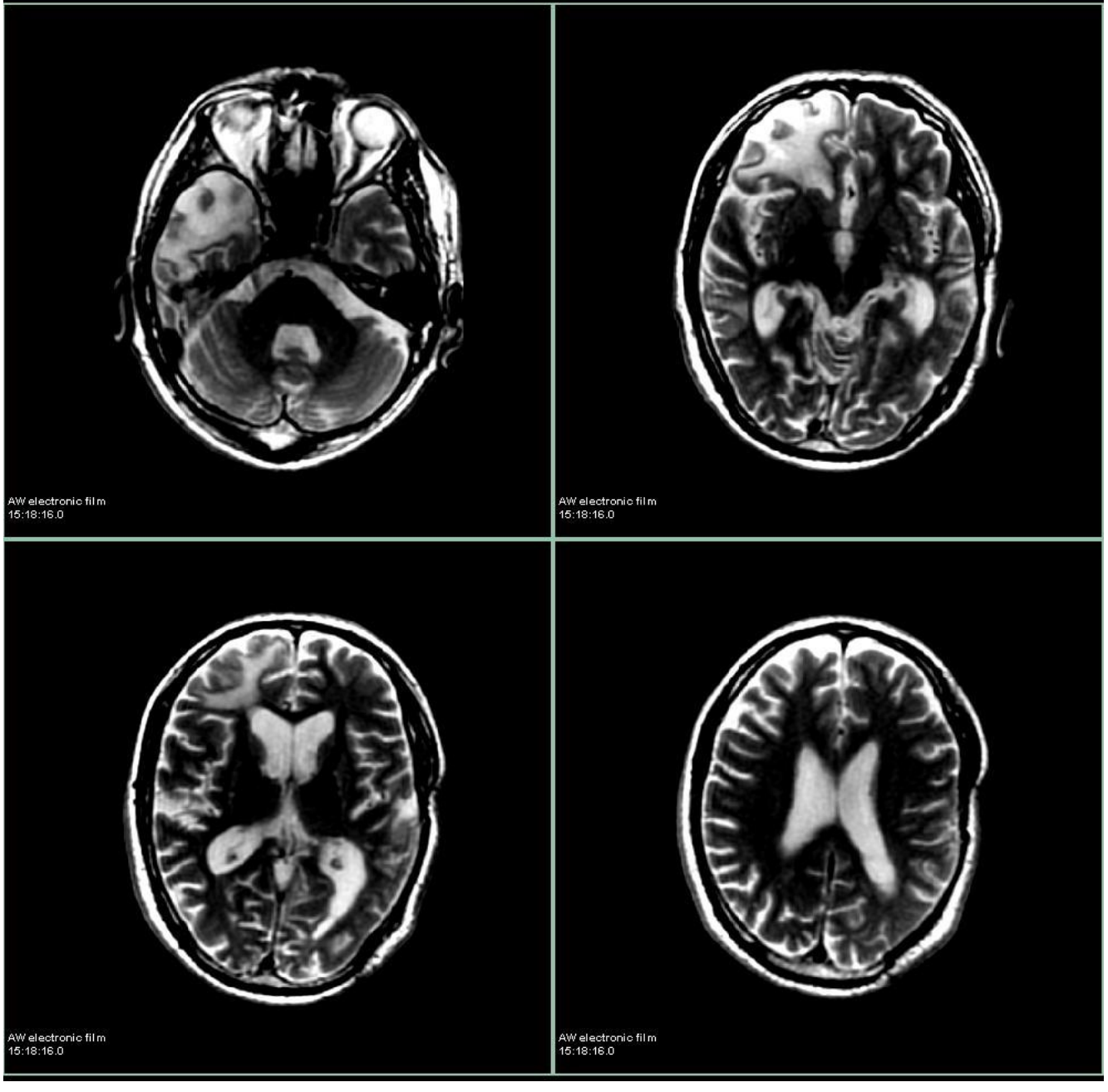


NORMALE

PATOLOGICO

CASO CLINICO 6

- Uomo, aa 65.
- 2007 trauma contusivo grave con ematoma sottotecale fronto-temporo-parietale sinistro (craniotomia te-pa sinistra).
- Comparsa di progressive alterazioni del comportamento e comparsa di disorientamento topografico.
- RM 11/2016: "..esiti gliotico-poroencefalici cortico-sottocorticali a sede fronto-temporale destra e temporale sinistra... gliosi post traumatica... accentuazione spazi liquorali periencefalici e ventricolari con assottigliamento del corpo calloso (a significato involutivo).
- Esami ematochimici nella norma (solo lieve incremento TSH).
- MMSE: 21/30, ALD: 6/6, IADL 5/5.


AW electronic film
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AW electronic film
15:18:16.0
AW electronic film
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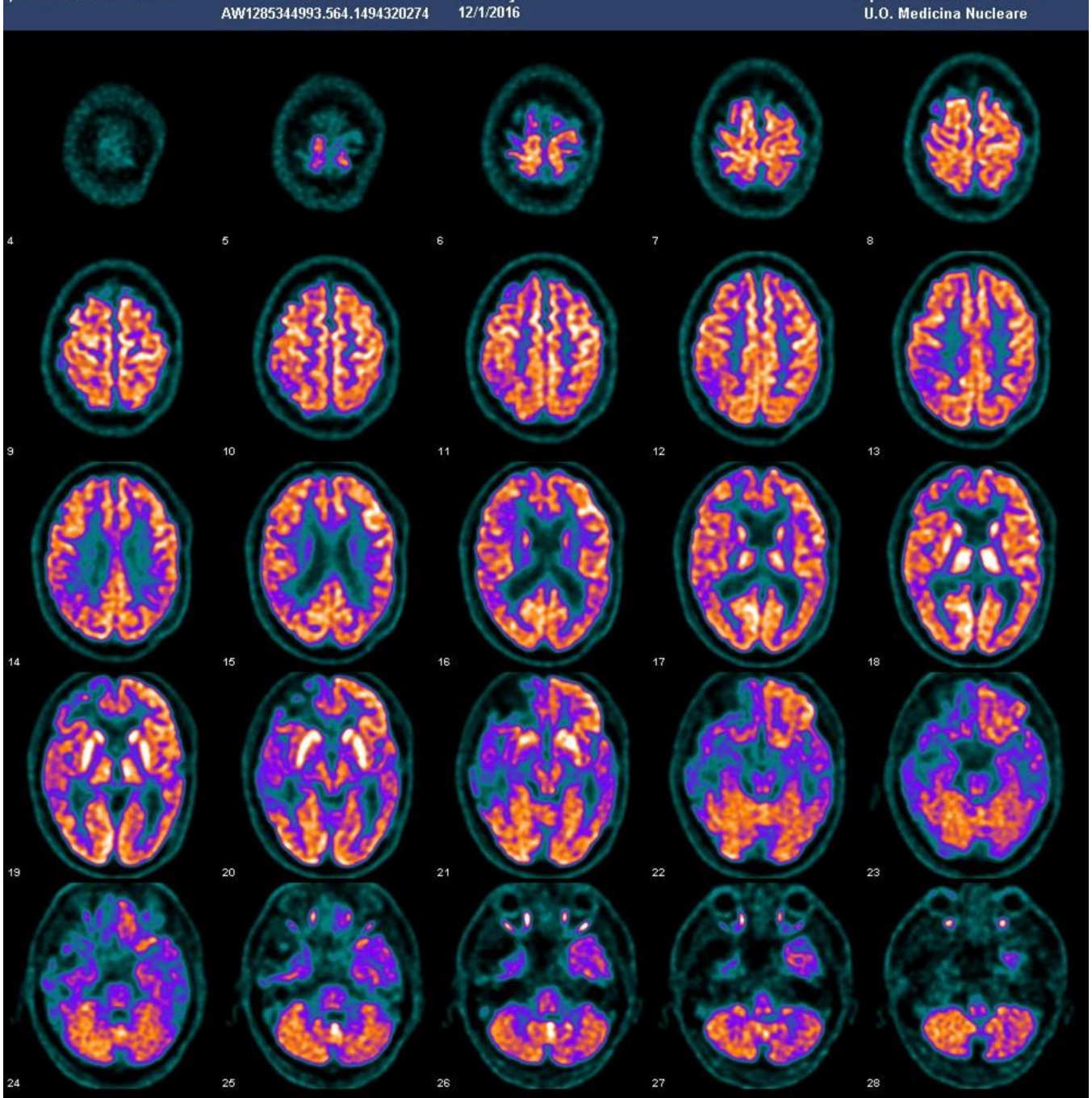
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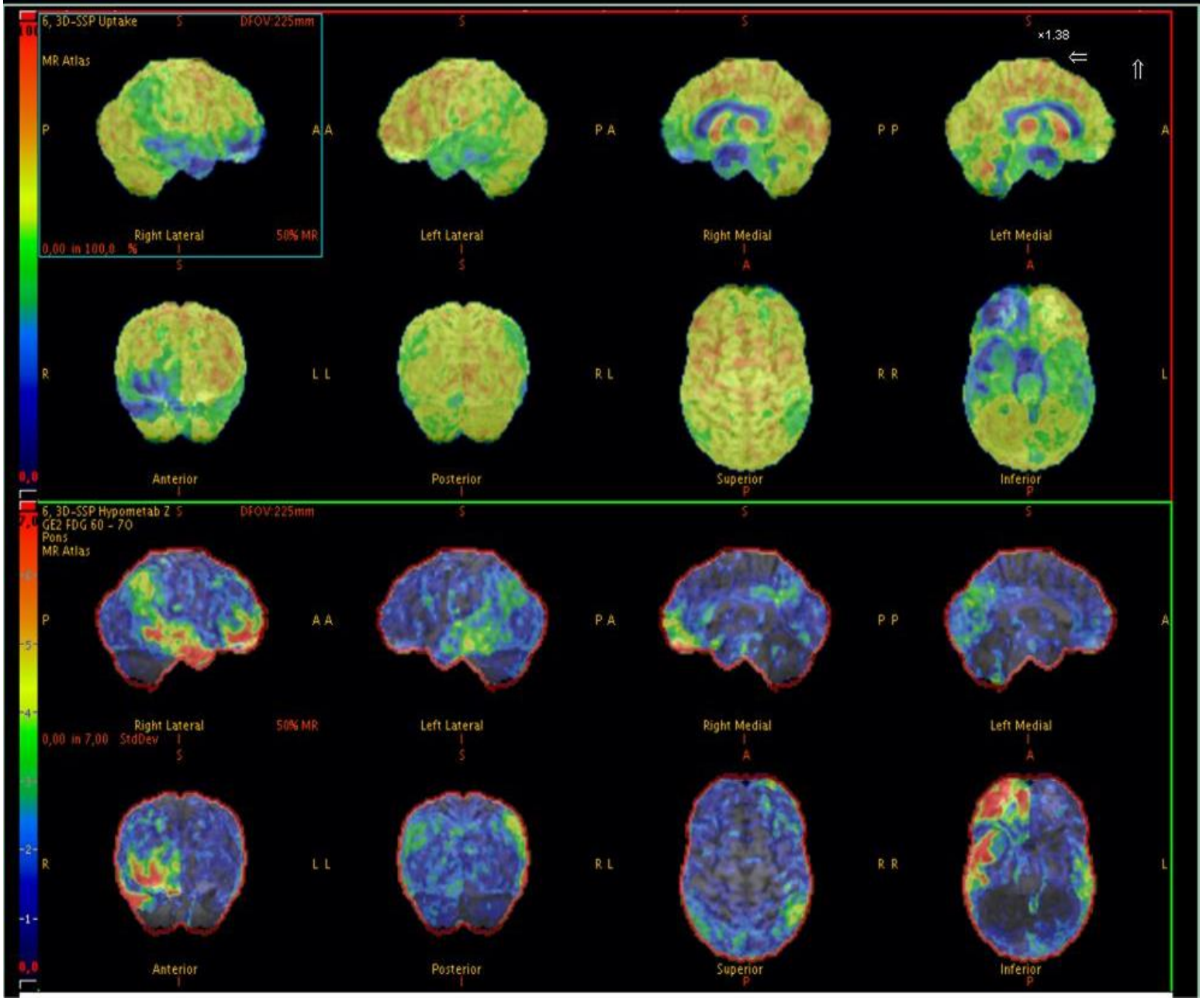
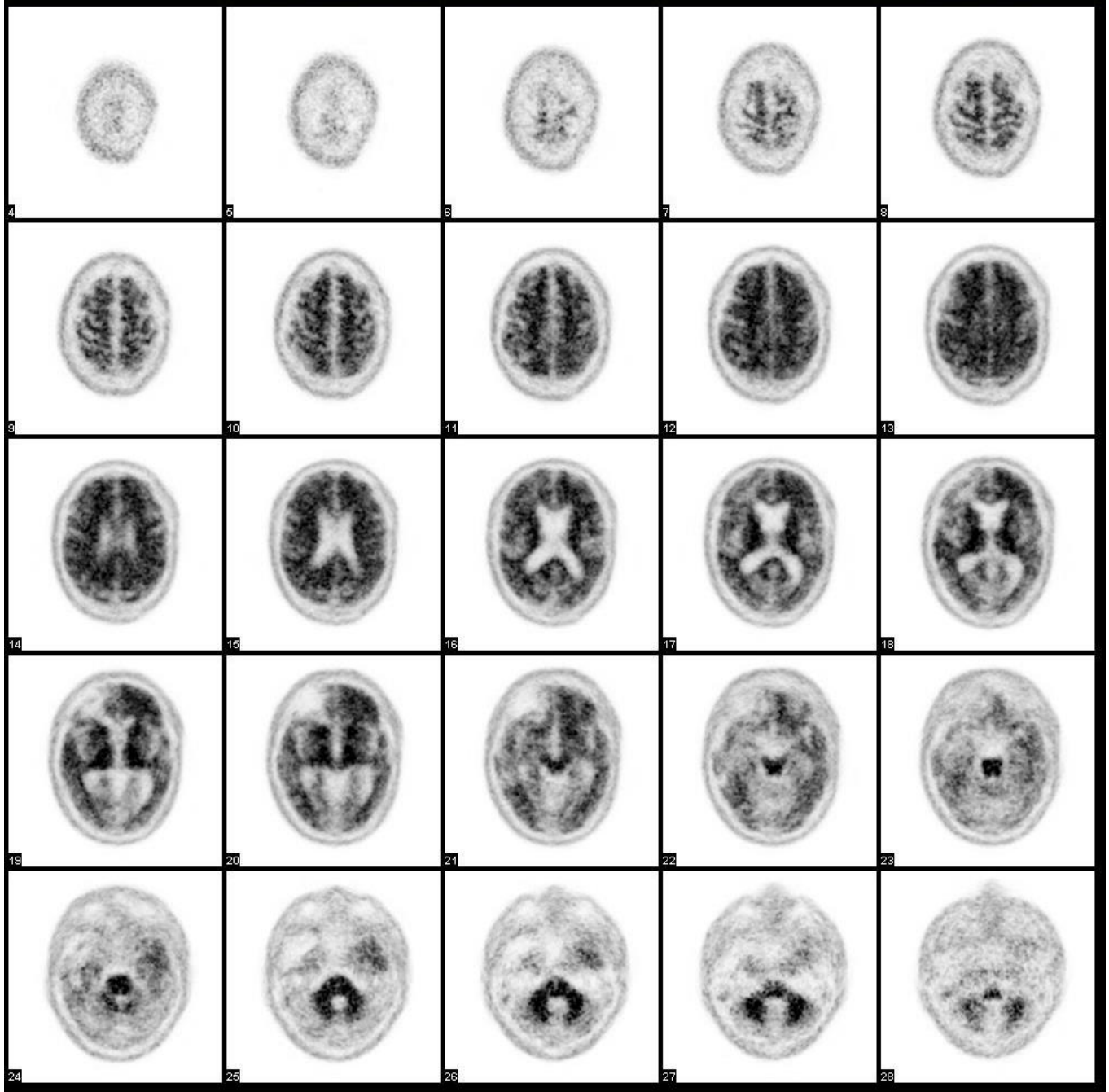

6, 3D-SSP Uptake
DFOV:225mm
MR Atlas
×1.38
Right Lateral
50% MR
0,00 in 100,0 %
Left Lateral
Right Medial
Left Medial
Anterior
Posterior
Superior
Inferior
6, 3D-SSP Hypometab Z
GE2 FDG 60 - 70
Pons
MR Atlas
DFOV:225mm
Right Lateral
50% MR
0,00 in 7,00 StdDev
Left Lateral
Right Medial
Left Medial
Anterior
Posterior
Superior
Inferior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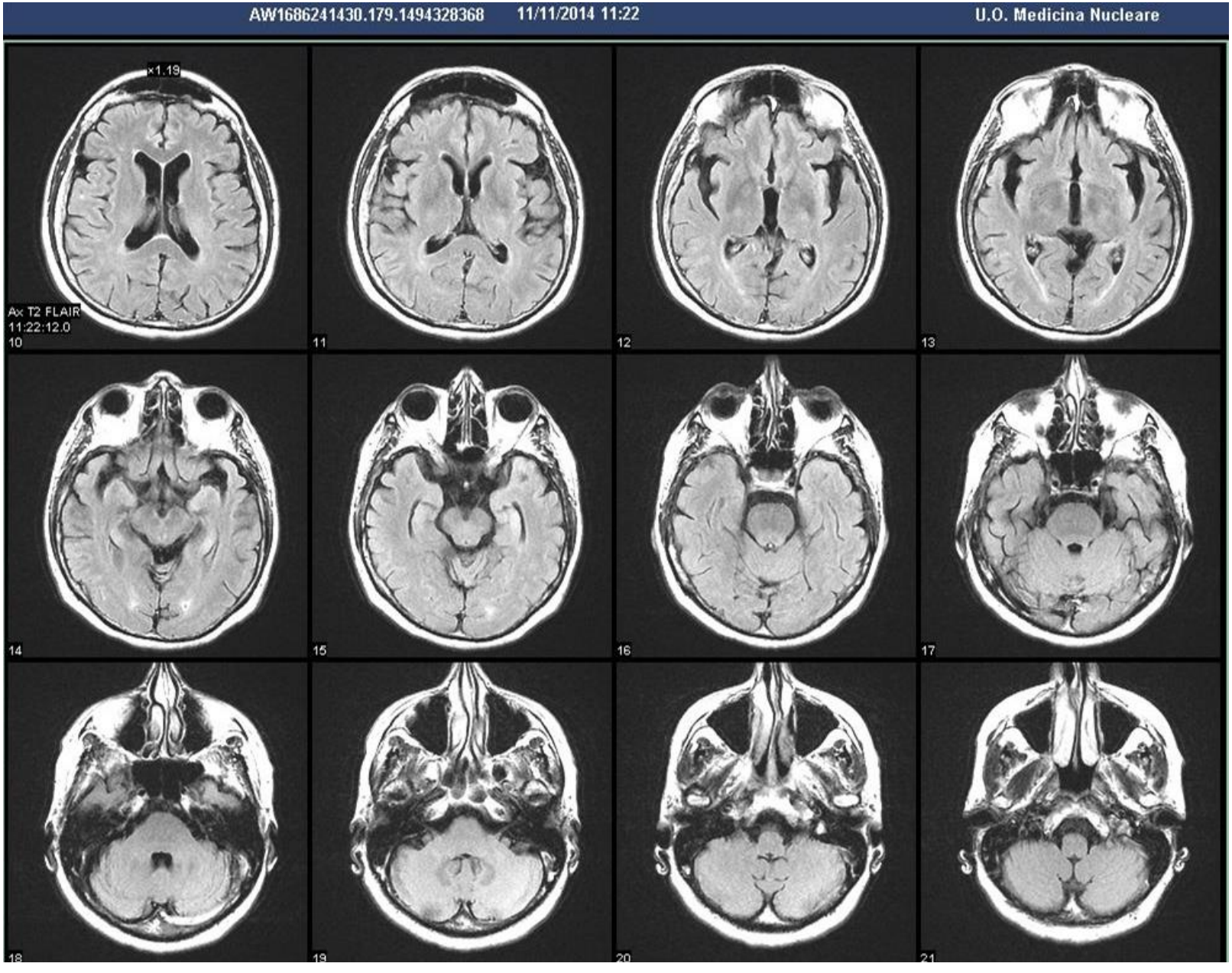
CASO CLINICO 7

- Donna, aa 65.
- Comparsa di disturbi della memoria negli ultimi tre anni. Familiarità positiva per AD (padre).
- 2014: MMSE: 27/30, ALD: 6/6, IADL 8/8.
- RM 11/2014: “..lieve dilatazione atrofica del sistema ventricolare edegli spazi subaracnoidei...iniziale minima condizione di sofferenza vascolare”.
- Esami ematochimici nella norma (solo lieve incremento TSH).
- Esegue nel 06/2015 PET 18-FDG.
- Esegue 02/2017 PET 18-Florbetapir.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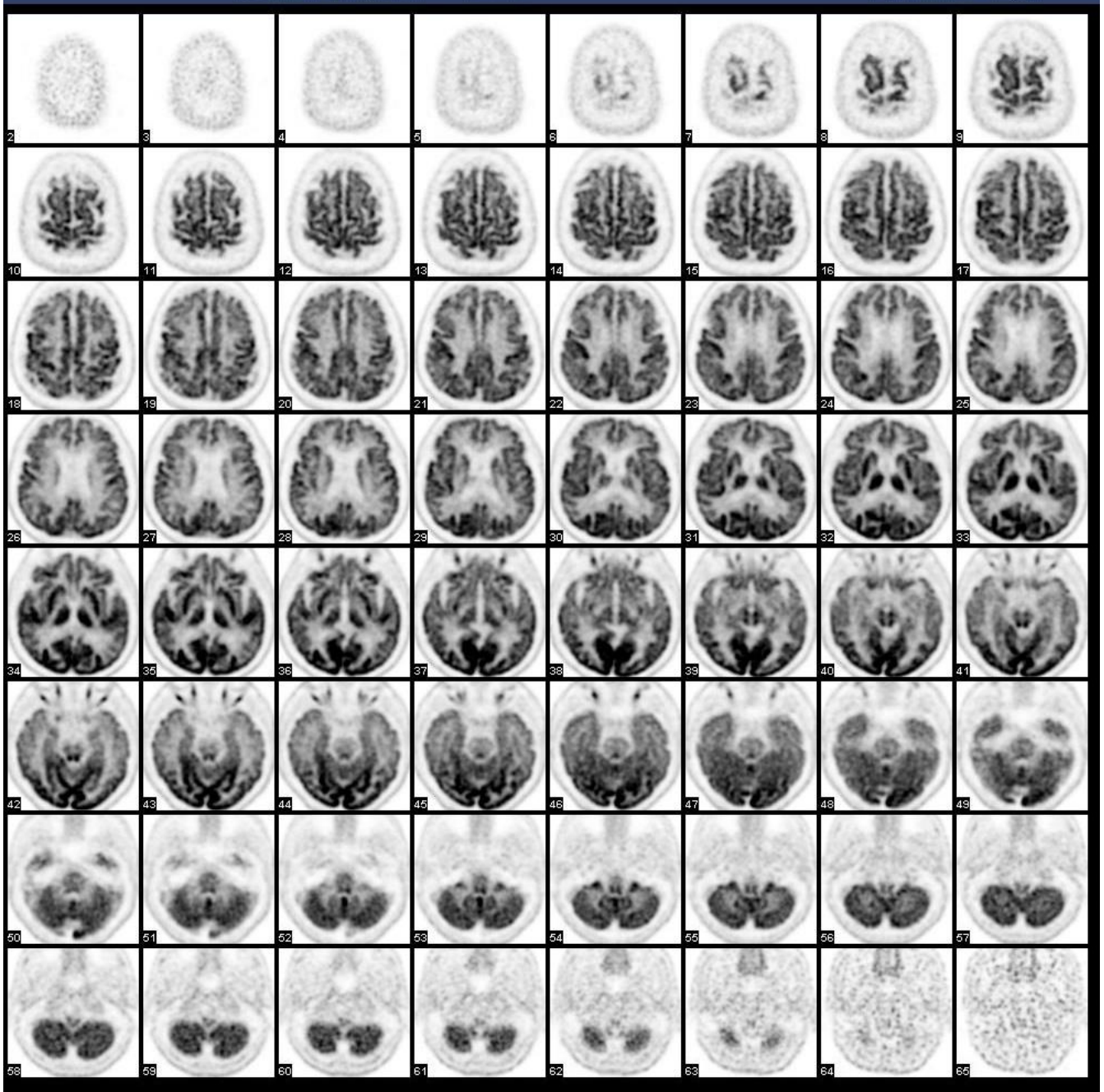
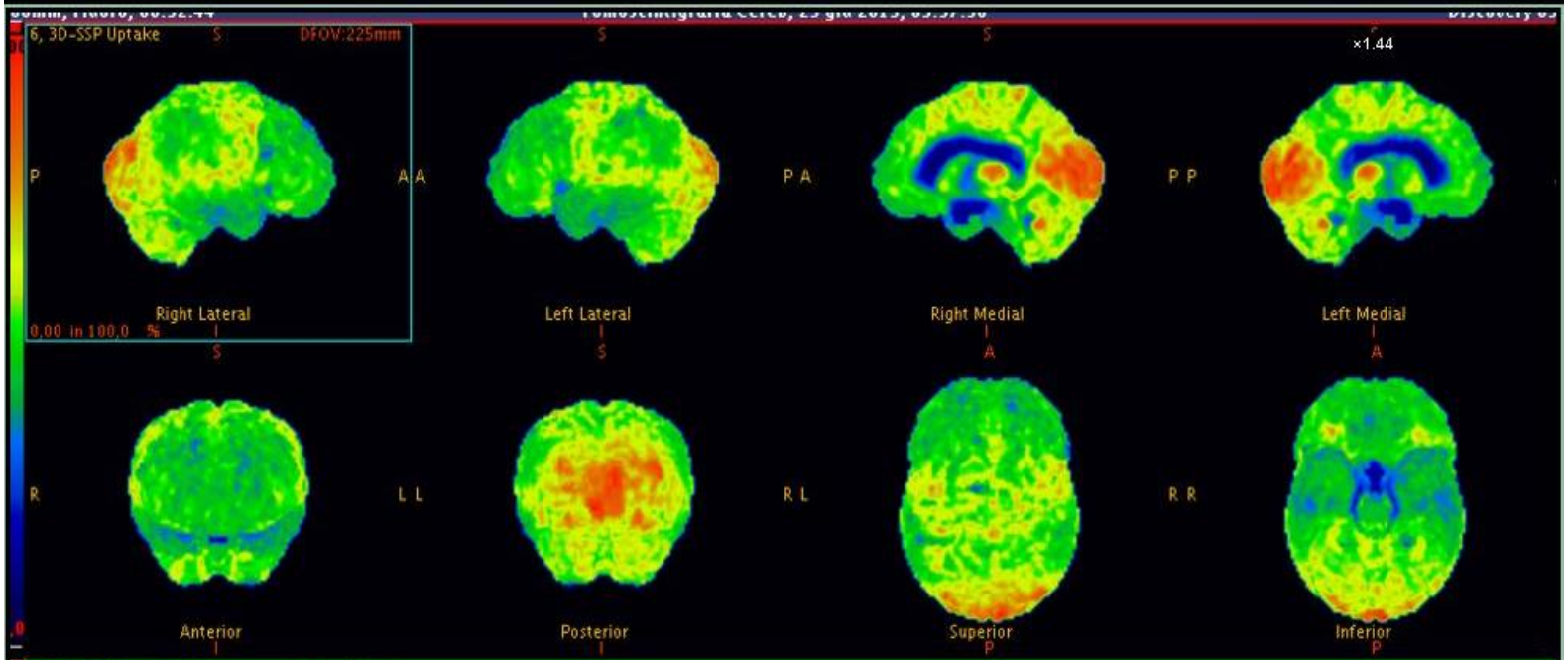
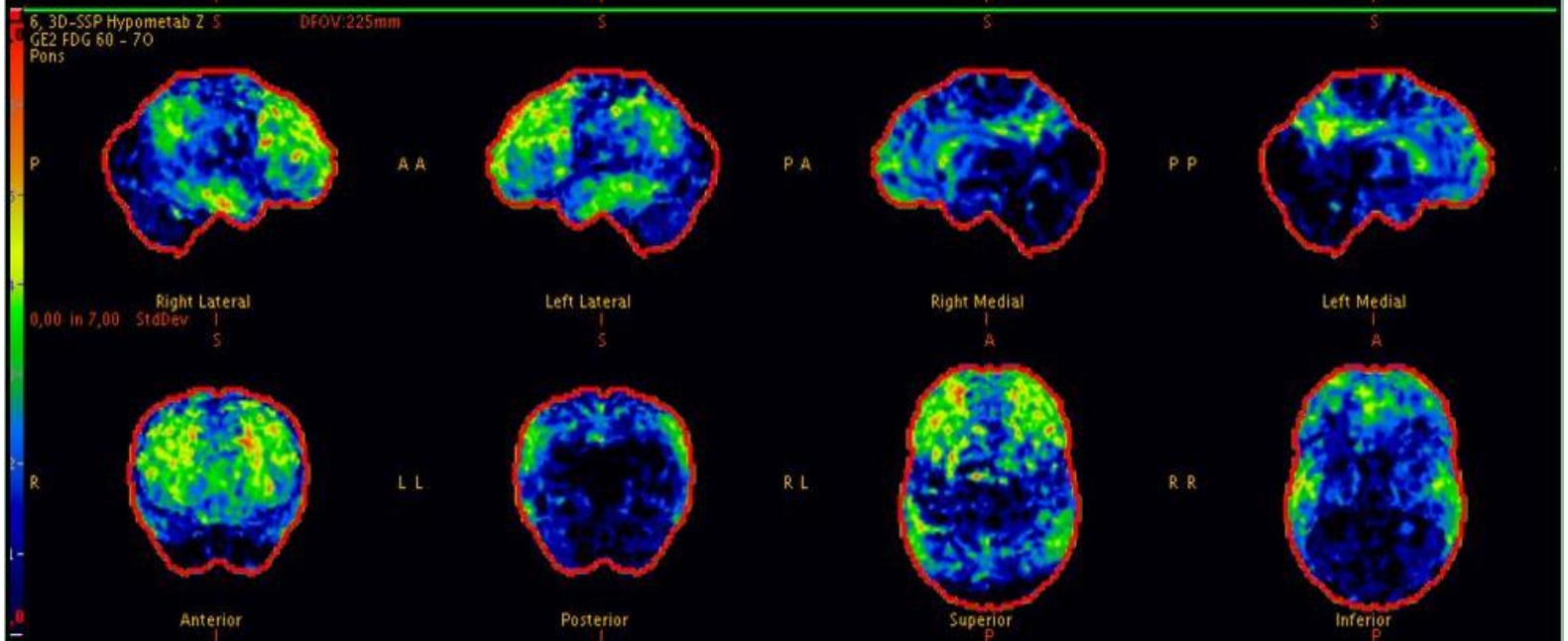
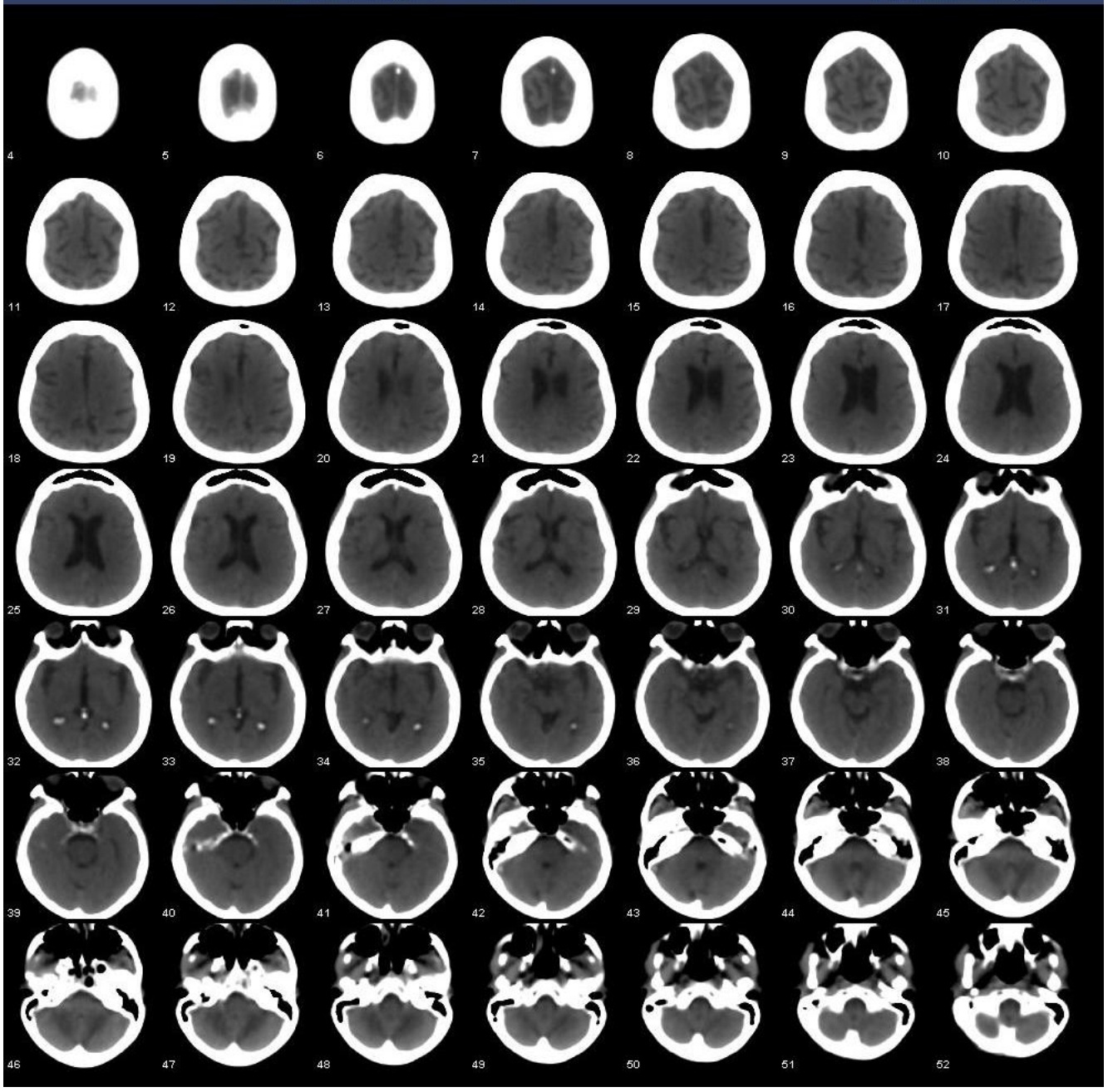
AW92580961.76.1487064911 6/25/2015 U.O. Medicina Nucleare




6, 3D-SSP Uptake
DFOV:225mm
×1.44
0,00 in 100,0 %
Right Lateral
Left Lateral
Right Medial
Left Medial
Anterior
Posterior
Superior
Inferior


6, 3D-SSP Hypometab Z
GE2 FDG 60 - 70
Pons
DFOV:225mm
0,00 in 7,00 StdDev
Right Lateral
Left Lateral
Right Medial
Left Medial
Anterior
Posterior
Superior
Inferior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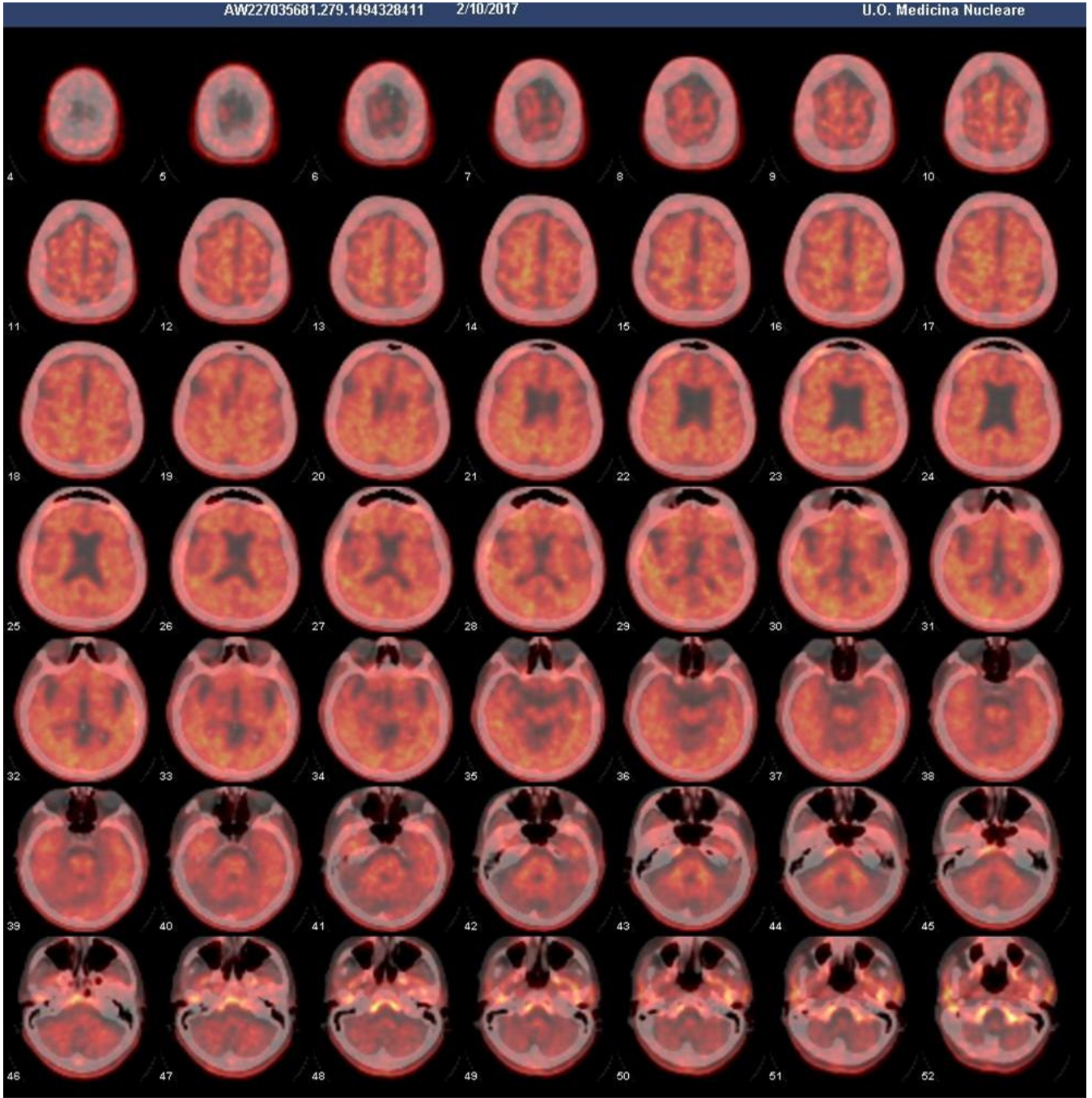
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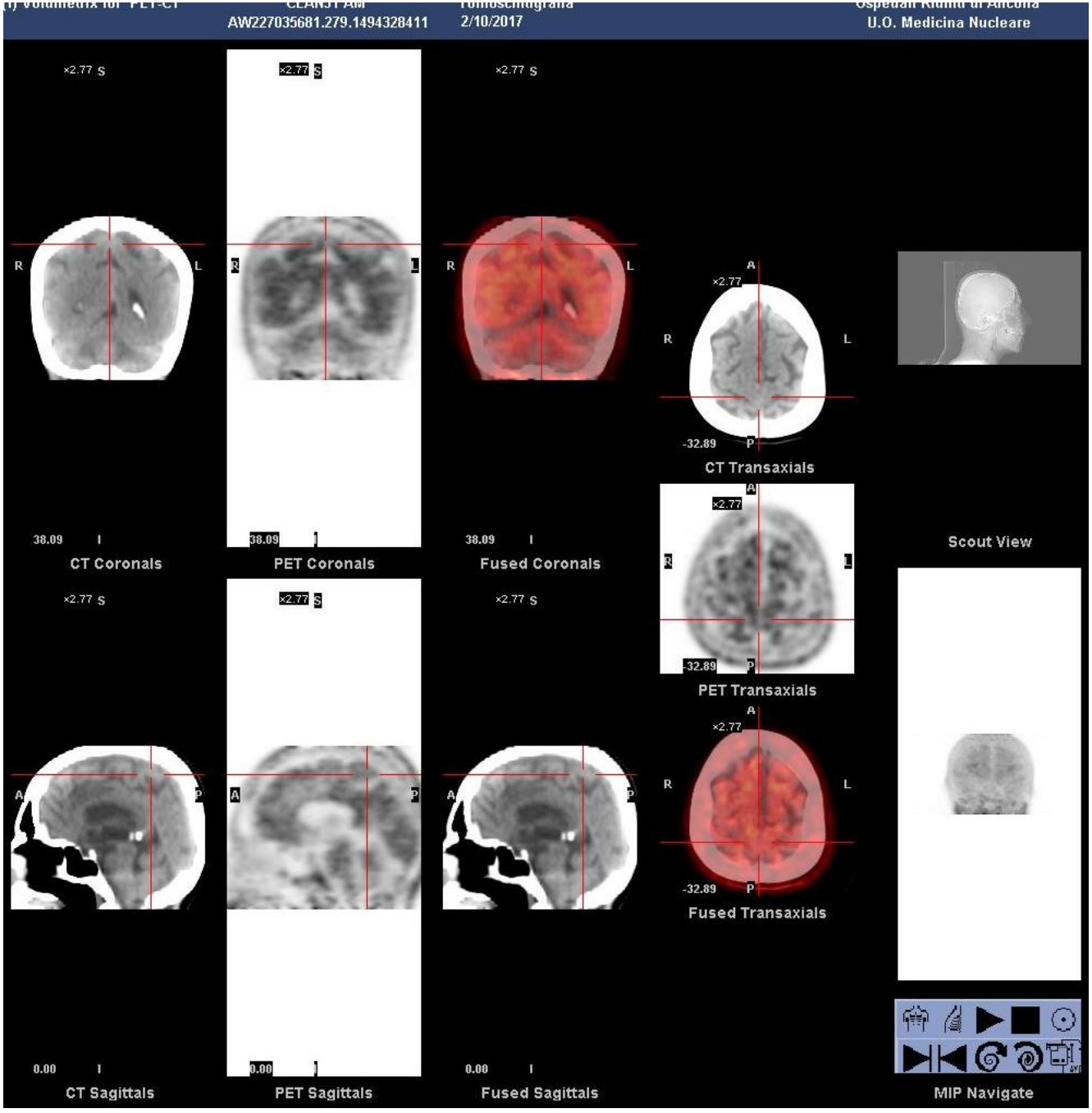
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2/10/2017
U.O. Medicina Nucleare
CT Coronals
PET Coronals
Fused Coronals
CT Transaxials
Scout View
PET Transaxials
CT Sagittals
PET Sagittals
Fused Sagittals
Fused Transaxials
MIP Navigate

SNMMI Procedure Standard/EANM Practice Guideline for Amyloid PET Imaging of the Brain 1.0

Satoshi Minoshima[1], Alexander E. Drzezga[2] (Cochairs), Henryk Barthel[3], Nicolaas Bohnen[4], Mehdi Djekidel[5], David H. Lewis[6], Chester A. Mathis[7], Jonathan McConathy[8], Agneta Nordberg[9], Osama Sabri[10], John P. Seibyl[11], Margaret K. Stokes[12], and Koen Van Laere[13]

[1]University of Utah, Salt Lake City, Utah; [2]University of Cologne, Cologne, Germany; [3]University Hospital Leipzig, Leipzig, Germany; [4]VA Medical Center, University of Michigan, Ann Arbor, Michigan; [5]Yale University, New Haven, Connecticut; [6]Harborview Medical Center, Seattle, Washington; [7]University of Pittsburgh, Pittsburgh, Pennsylvania; [8]Mallinckrodt, St. Louis, Missouri; [9]Karolinska Institutet, Stockholm, Sweden; [10]University Hospital Leipzig, Leipzig, Germany; [11]Institute for Neurodegenerative Disorders, New Haven, Connecticut; [12]Beth Israel Deaconess Medical Center, Boston, Massachusetts; and [13]University Hospital Leuven, Leuven, Belgium

PREAMBLE

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) is an international scientific and professional organization founded in 1954 to promote the science, technology, and practical application of nuclear medicine. Its 18,000 members are physicians, technologists, and scientists specializing in the research and practice of nuclear medicine. In addition to publishing journals, newsletters, and books, the SNMMI also sponsors international meetings and workshops designed to increase the competencies of nuclear medicine practitioners and to promote new advances in the science of nuclear medicine. The European Association of Nuclear Medicine (EANM) is a professional nonprofit medical association that facilitates communication worldwide between individuals pursuing clinical and research excellence in nuclear medicine. The EANM was founded in 1985.

The SNMMI/EANM will periodically define new standards/guidelines for nuclear medicine practice to help advance the science of nuclear medicine and to improve the quality of service to patients. Existing standards/guidelines will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated. Starting February 2014, the SNMMI guide-

The EANM and SNMMI have written and approved these standards/guidelines to promote the use of nuclear medicine procedures with high quality. These standards/guidelines are intended to assist practitioners in providing appropriate nuclear medicine care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the SNMMI/EANM cautions against the use of these standards/guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by medical professionals taking into account the unique circumstances of each case. Thus, there is no implication that an approach differing from the standards/guidelines, standing alone, is below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the standards/guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations of available resources, or advances in knowledge or technology subsequent to publication of the standards/guidelines.

The practice of medicine involves not only the science but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or

E’ evidente che ci troviamo in un periodo di grandi cambiamenti e la parola ‘fine’ sulle Raccomandazioni da seguire non può essere ancora messa

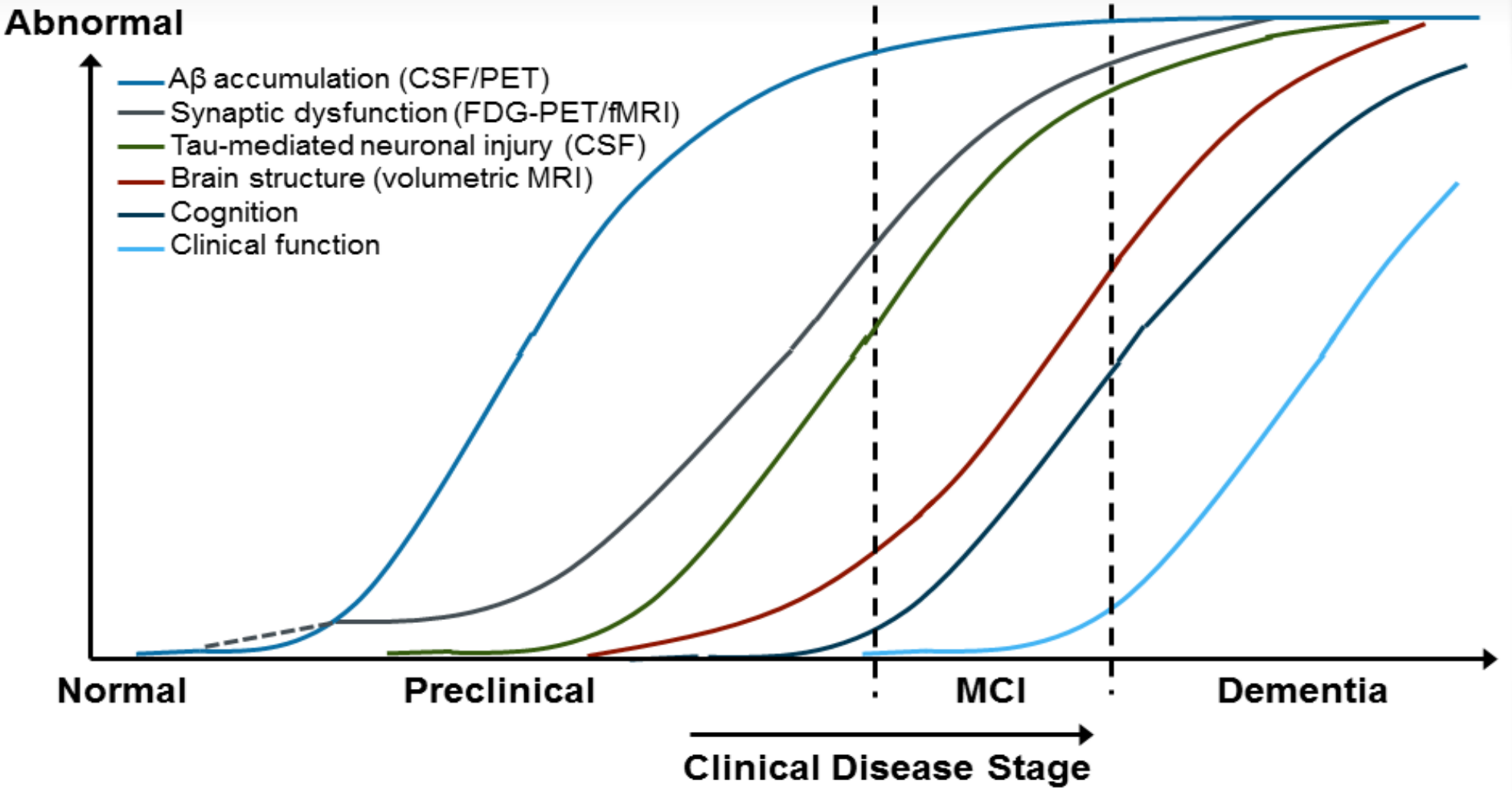
Le indicazioni all’uso dei radiofarmaci per la PET amiloide approvate dalla FDA e dalla EMA dicono con chiarezza che sono indicati per escludere la m. di Alzheimer e non per confermarla

Tuttavia in un paziente con MCI di tipo AD tipico o atipico chiaramente definito sulla base dei criteri clinico-neuropsicologici, la positività della PET amiloide potrebbe essere diagnostica ed essere considerata come una ‘biopsia’ cerebrale. Mancherebbe però a questo punto l’evidenza di inclusi neurofibrillari Tau (i traccianti Tau potrebbero quindi portarci a togliere quel ‘probabile’ che mettiamo da sempre davanti alla diagnosi di Alzheimer, in assenza di biopsia o esame autoptico)

Senza dubbio la PET amiloide sarà obbligatoria qualora avessimo farmaci anti-amiloide (inib secretasi, Ab monoclonali) efficaci

Flavio Nobili -Corso avanzato di medicina nucleare in neurologia – Pesaro 2014

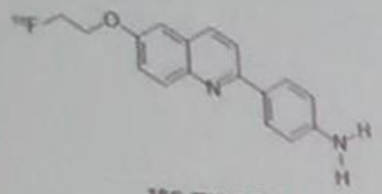
Sequencing of Biomarkers



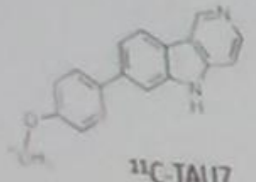
From Sperling RA, et al. *Alzheimers Dement.* 2011;7:280-292.

PET/TC
RADIOFARMACI PER RILEVAZIONE PROTEINA TAU

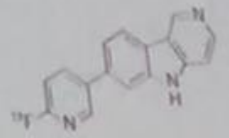
Tau imaging radiotracers



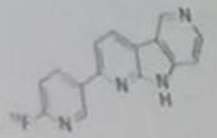
^{18}F-THK-523



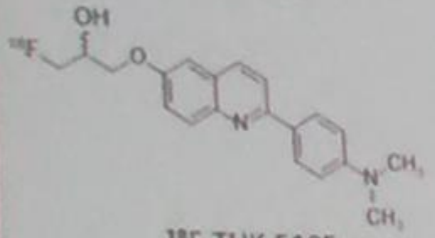
^{11}C-TAU7



^{18}F- AV1451 (a.k.a. T807)



^{18}F-RO69558948



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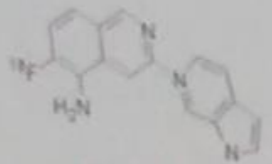
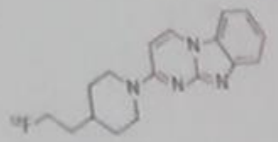
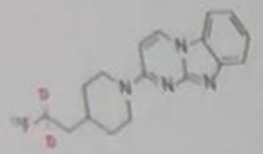


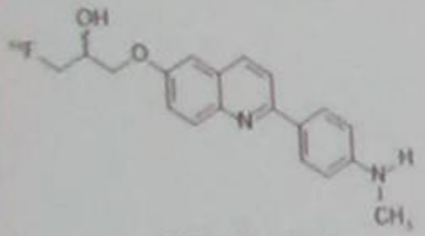
^{18}F-MK-6240



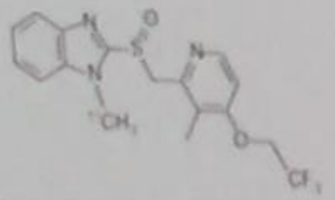
^{18}F-T808



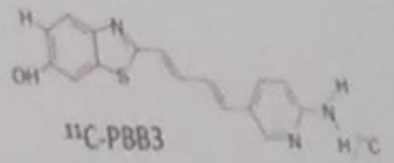
^{18}F-GTP1



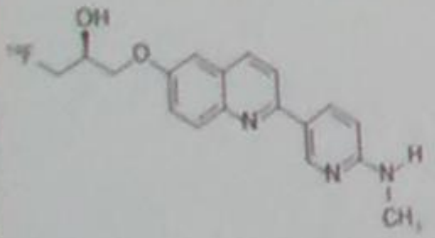
^{18}F-THK-5317



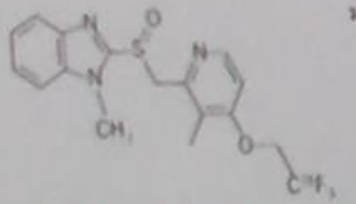
^{11}C-N-Methyl Lansoprazole



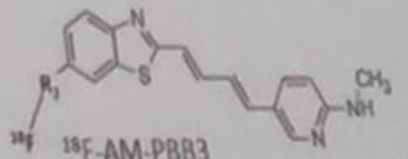
^{11}C-PBB3



^{18}F-THK-5351



^{18}F-N-Methyl Lansoprazole



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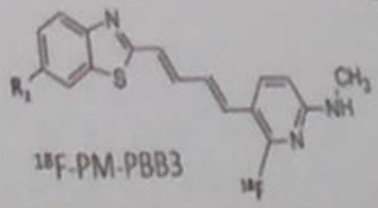
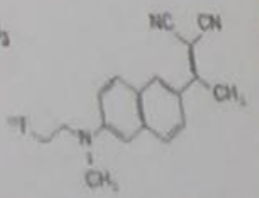
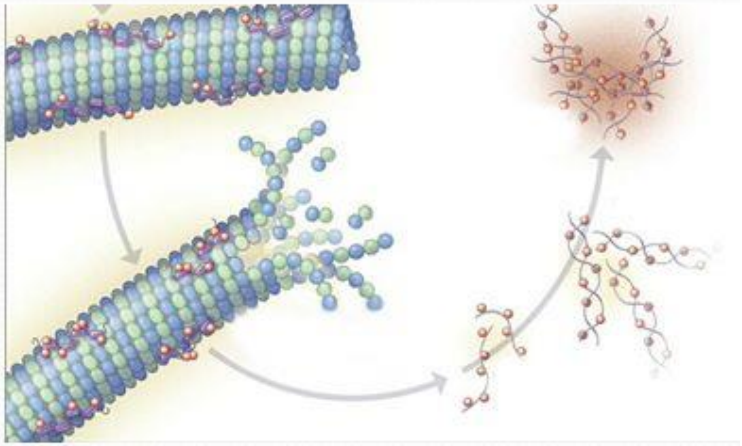


^{18}F-PM-PBB3

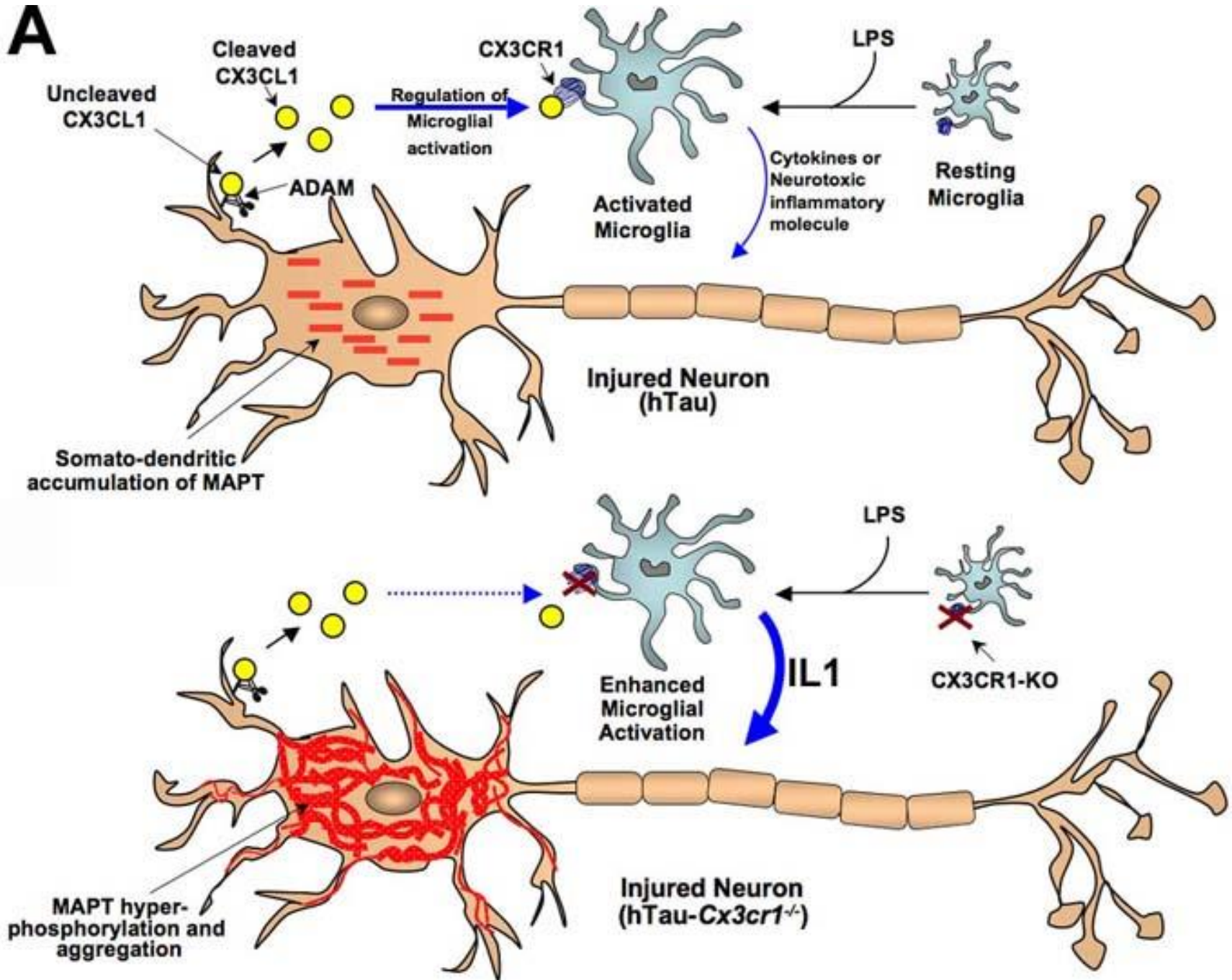


^{18}F-FDDNP

Causes of Alzheimer's-Tau Protein



- Hyper-phosphorylation of tau protein inside neuron cells
- Normal tau proteins stabilizes microtubules
- When hyper-phosphorylated, Tau proteins start clumping together and forming tangles instead of doing their normal job.
- Blocks transportation of essential supplies inside the cell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activation
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Resting
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Cytokines or
Neurotoxic
inflammatory
molecule
Injured Neuron
(hTau)
Somato-dendritic
accumulation of MAPT
LPS
Enhanced
Microglial
Activation
IL1
CX3CR1-KO
MAPT hyper-
phosphorylation and
aggregation
Injured Neuron
(hTau-Cx3cr1-/-)

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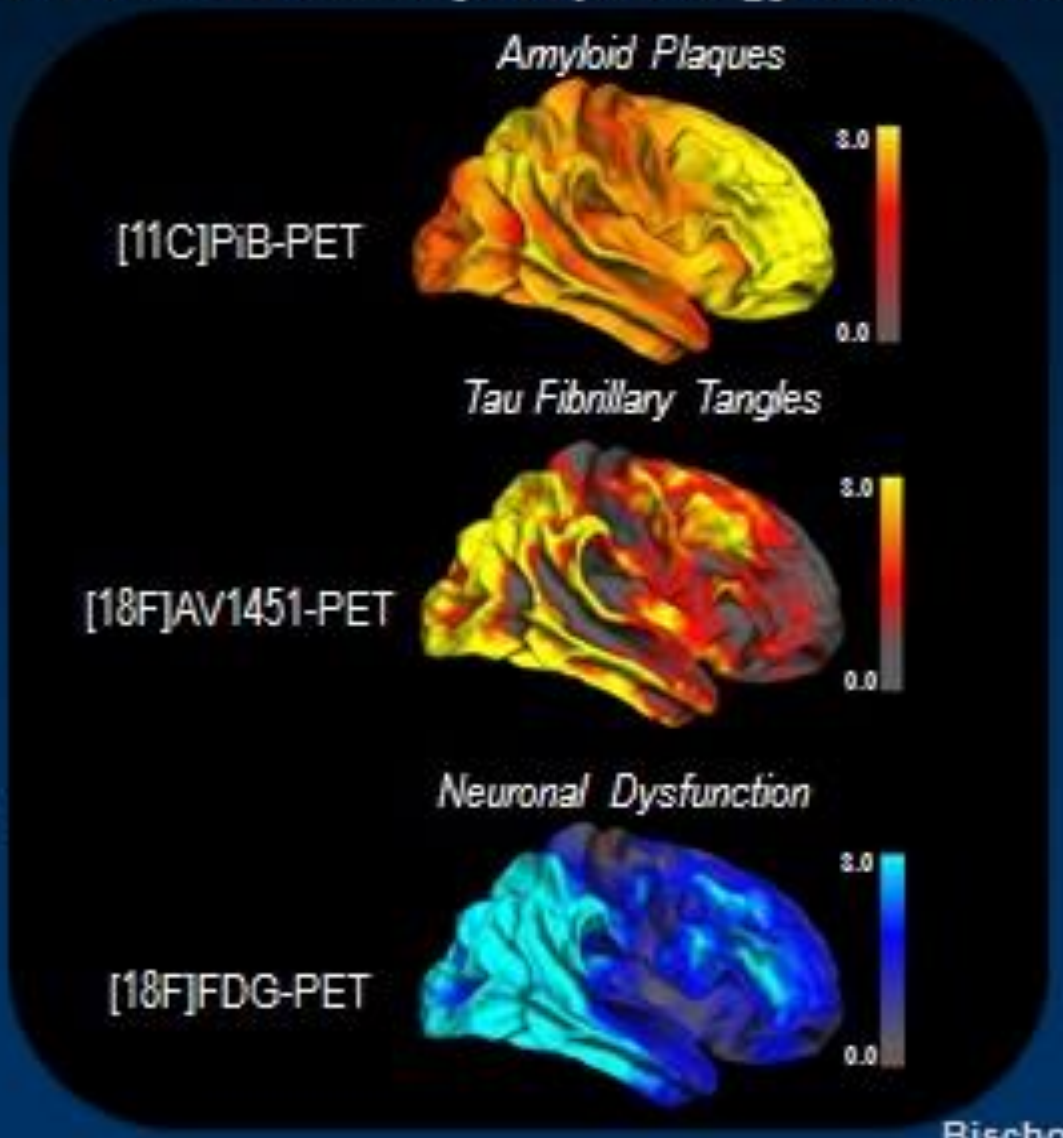
JÜLICH | DZNE

Correspondence of tau- but not amyloid-pathology with neuronal dysfunction



Right lateral surface of projected z-score images, reflecting deviation from healthy controls

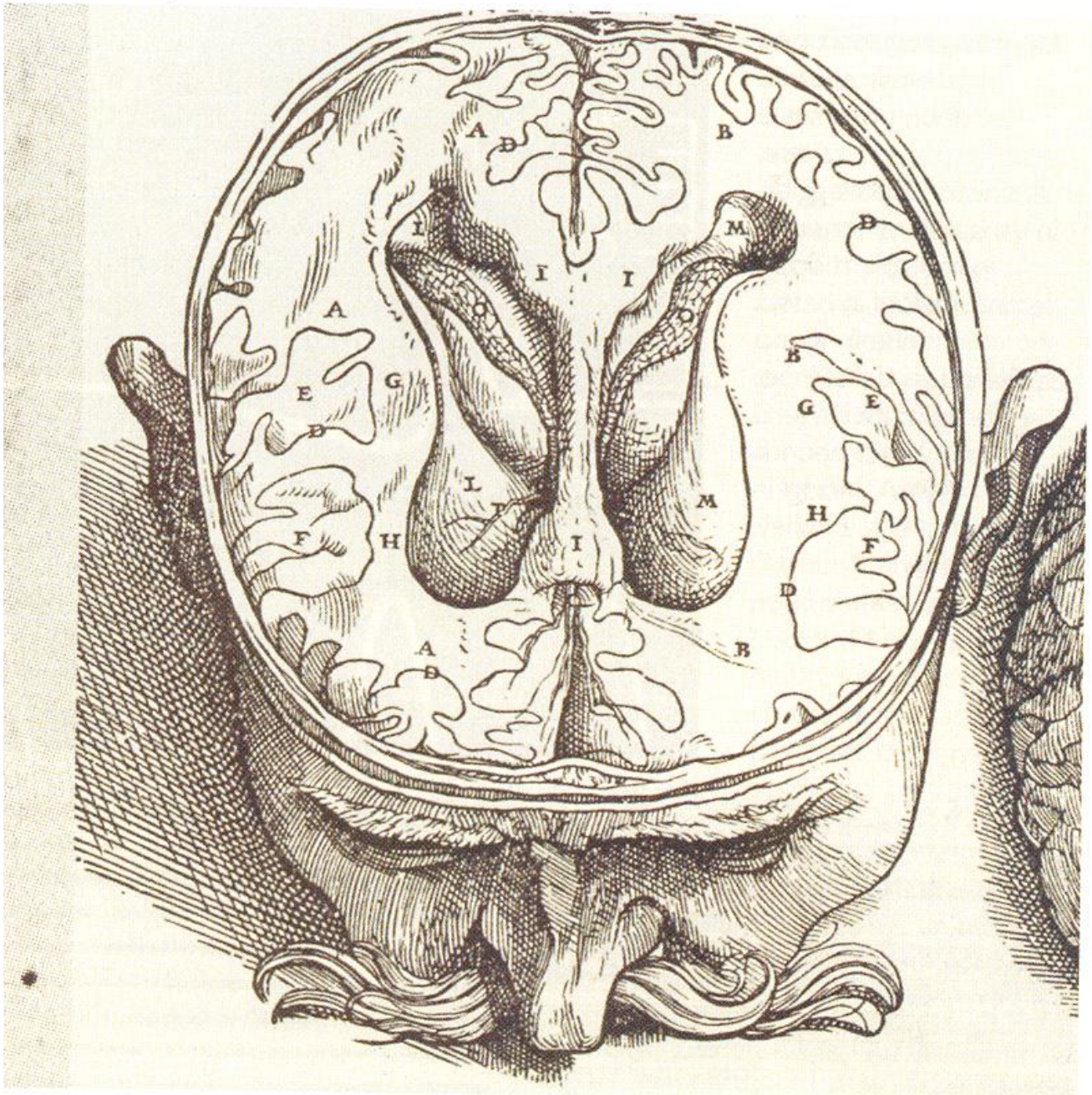
Yellow/red: higher uptake

blue: lower uptake as compared to controls

Bischof et al. Pub. No.: 124.

CONCLUSIONI

In sintesi, nello studio delle patologie degenerative del SNC, l'introduzione di nuovi radiofarmaci (in modo particolare i "marcatori" della sostanza Amiloide) e di altri di prossima introduzione (in modo particolare i "marcatori" della proteina Tau) apre la strada non solo alla diagnosi precoce ma anche offre ai clinici la possibilità di applicazioni terapeutiche mirate.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