Hybrid Imaging PET/MR

Marco Aiello[1], Marco Salvatore[2]

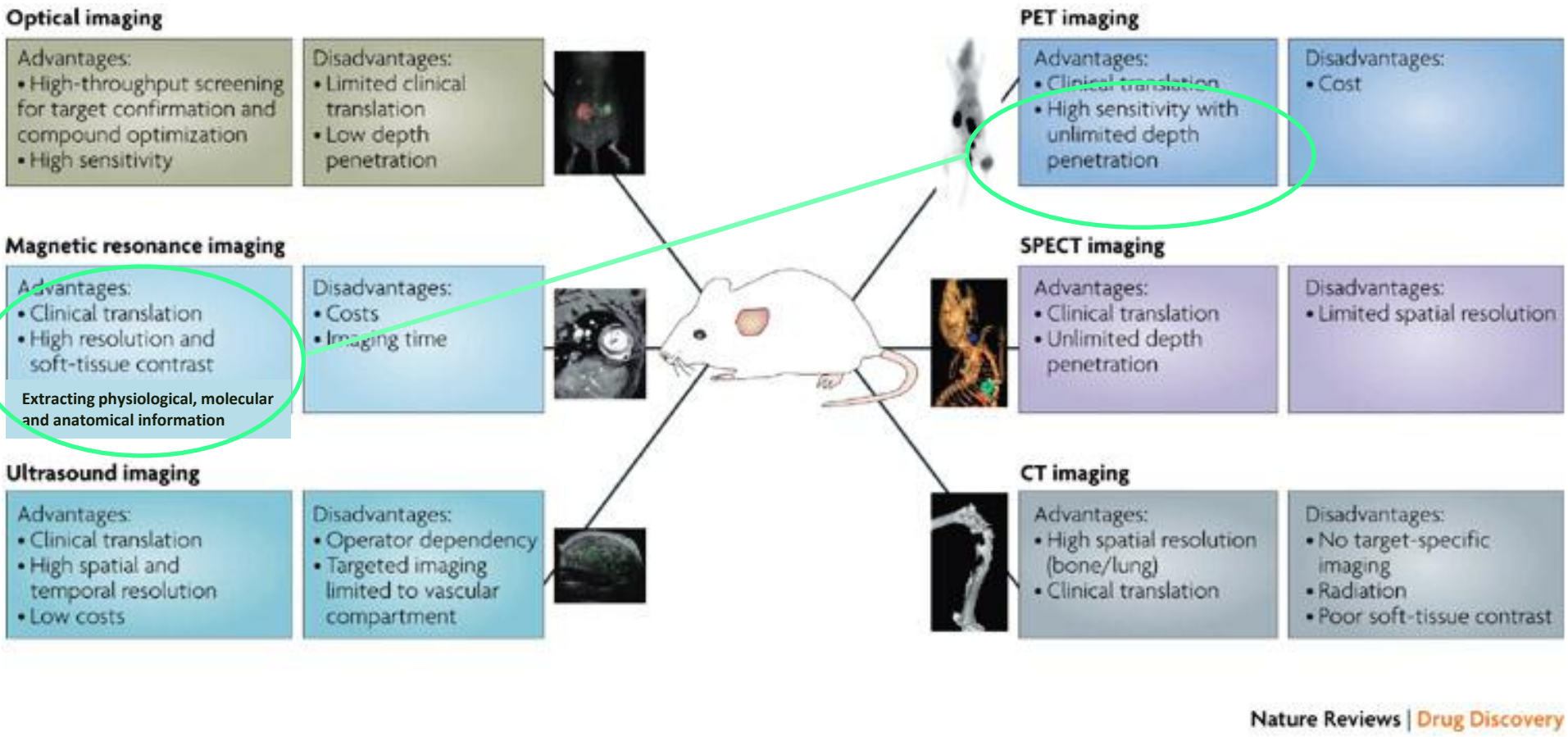
1-IRCCS SDN – Istituto di Ricerca Diagnostica Nucleare, Napoli
2-Istituto di Biostrutture e Bioimmagini, CNR
maiello@sdn-napoli.it

EURO-BIOIMAGING

Outline

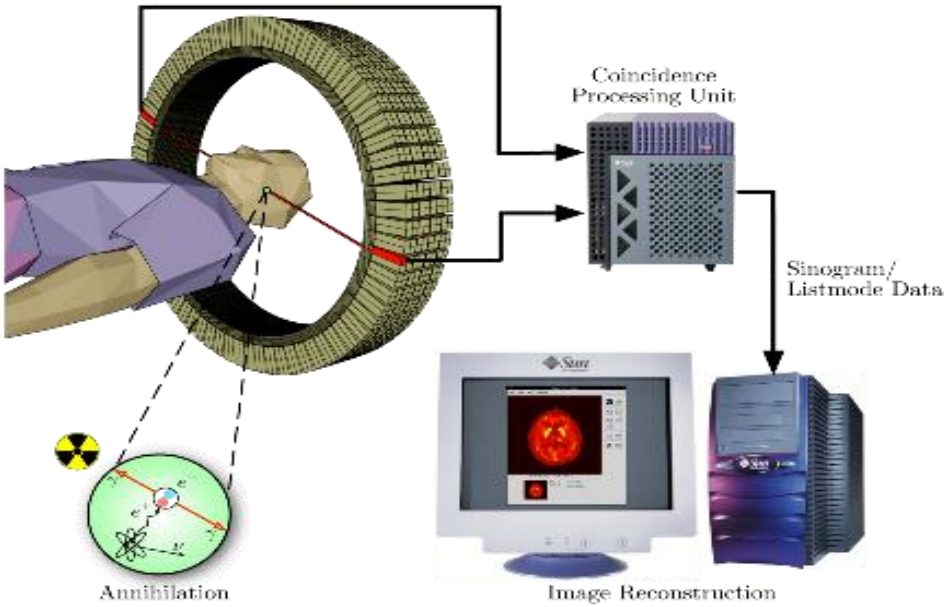
- PET, MR, PET/MR
- Technical Challenges
- Clinical and Preclinical Perspective
- Final Remarks

Molecular Imaging Scenario

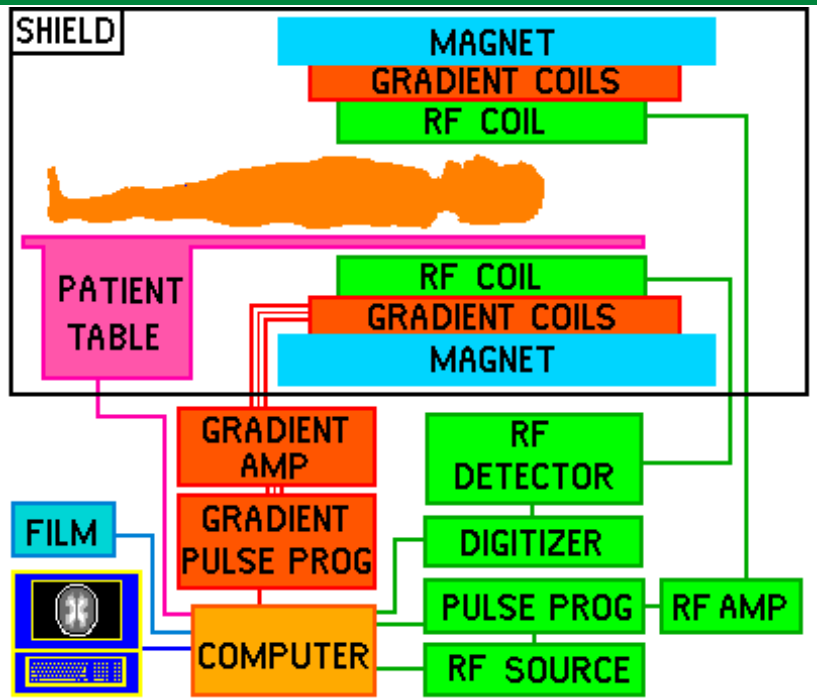


Molecular imaging in drug development
Jürgen K. Willmann et al. Nature Reviews Drug Discovery 7, 591-607 (July 2008)

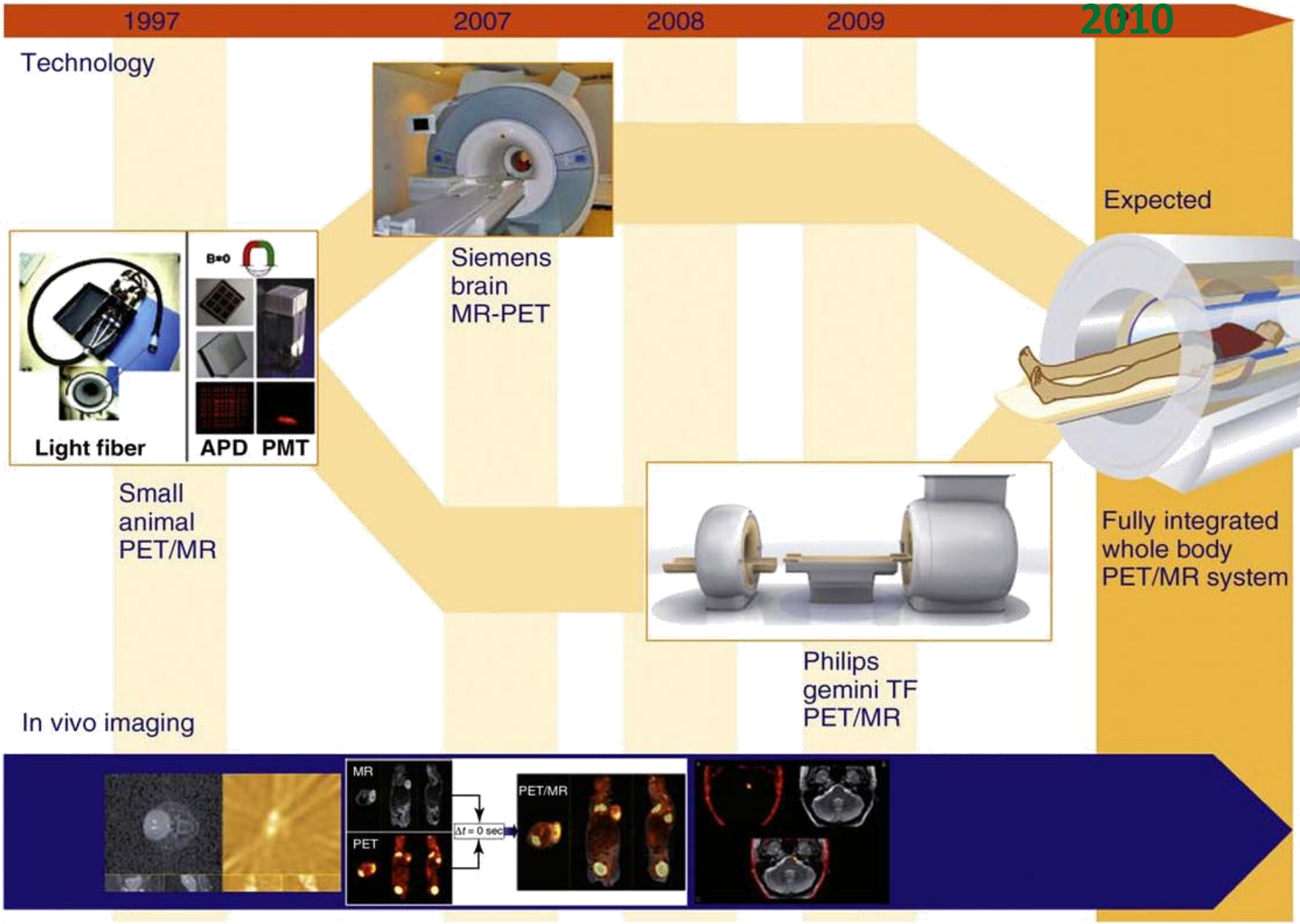
PET



MR



- Limited space of MR gantry
- Ferromagnetic components
- Magnetic Field Inhomogeneity
- Interference between PET electronics and MR coils
- Photomultipliers MR uncompatible
- Cost-effectiveness

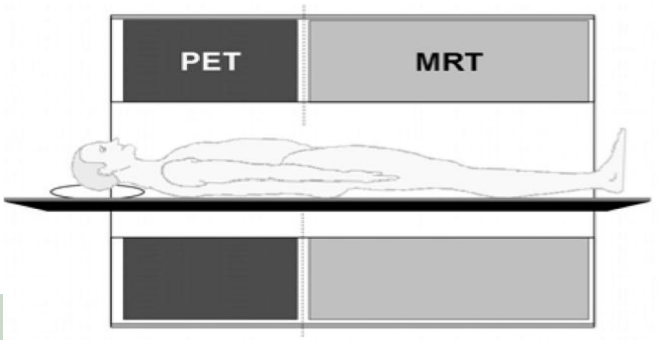


Trends in Molecular Medicine 2010
Vol.16 No.11

TRENDS in Molecular Medicine

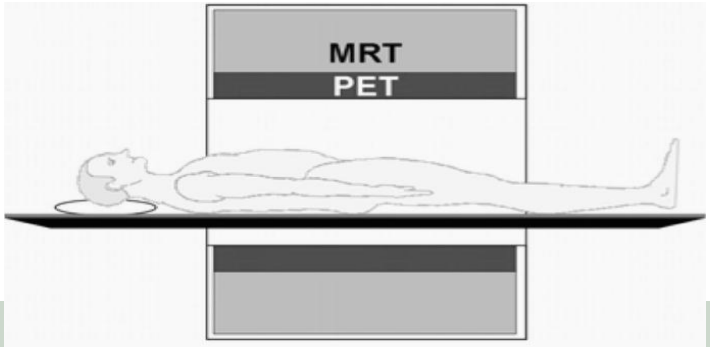
MR- PET Scanner Configurations

Sequential



- Spatial Coregistration
- Fusion software
- Motion Correction with external trigger
- PET TOF

Integrated



- Spatial and Temporal Coregistration
- Automatic Fusion
- MoCo with external trigger and MR-based
- Pharmacokinetic PET-MR
- PET non TOF (...waiting for SiPM)

Clinical PET/MR Scanners

PHILIPS INGENUITY TF

- Coplanar rotating bed
- FDA (11/2011) CE(12/2010)
- Actually working on SiPM integration

GE DISCOVERY PET/CT + MRI

- Shuttle bed PET, RM e TC.

GE SIGNA PET/MR (2015?)

- Simultaneous PET/MR
- SiPM-based (TOF)
- FDA clearance pending)

Integrated PET/MR

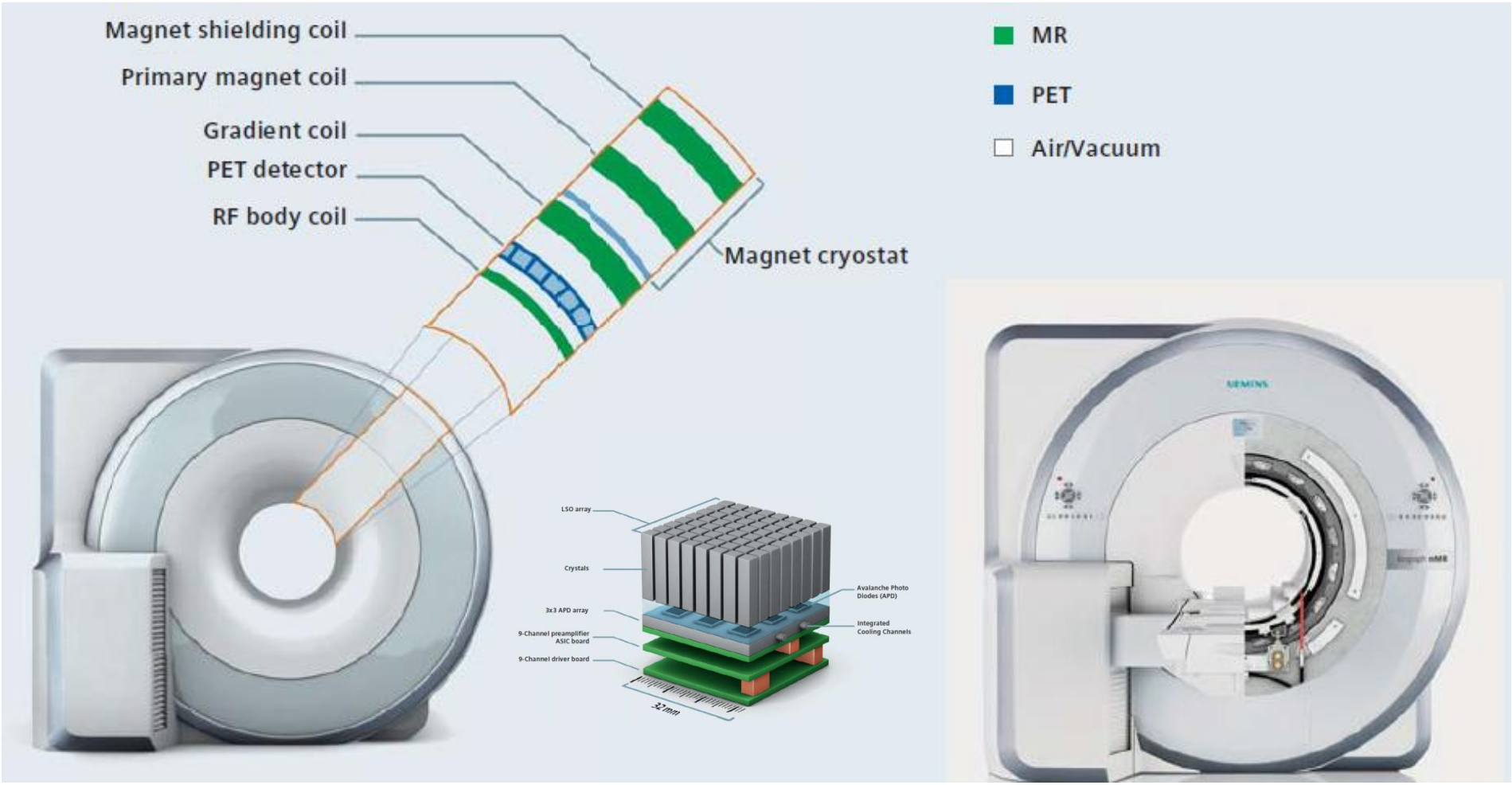
SIEMENS BIOGRAPH mMR

- PET and MR acquired simultaneously
- FDA (06/2011) CE(05/2011)

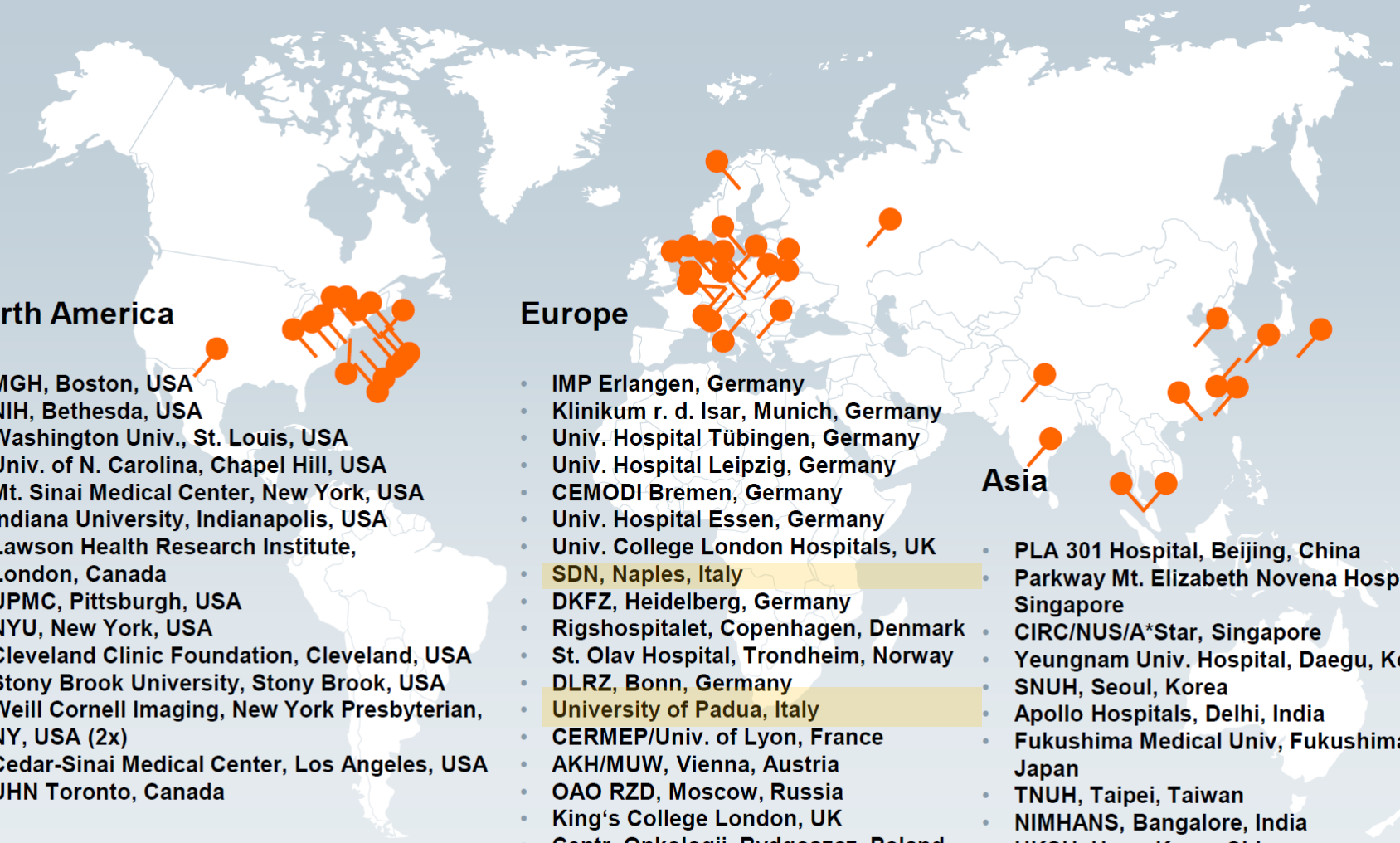
Upgrade B20P (2014)

- Improved AC
- More PET compatible coils
- PSF Pet recon
- Brain PET MOCO (compass)

Inside the scanner



Early Adopters



North America

- MGH, Boston, USA
- NIH, Bethesda, USA
- Washington Univ., St. Louis, USA
- Univ. of N. Carolina, Chapel Hill, USA
- Mt. Sinai Medical Center, New York, USA
- Indiana University, Indianapolis, USA
- Lawson Health Research Institute, London, Canada
- UPMC, Pittsburgh, USA
- NYU, New York, USA
- Cleveland Clinic Foundation, Cleveland, USA
- Stony Brook University, Stony Brook, USA
- Weill Cornell Imaging, New York Presbyterian, NY, USA (2x)
- Cedar-Sinai Medical Center, Los Angeles, USA
- UHN Toronto, Canada

Europe

- IMP Erlangen, Germany
- Klinikum r. d. Isar, Munich, Germany
- Univ. Hospital Tübingen, Germany
- Univ. Hospital Leipzig, Germany
- CEMODI Bremen, Germany
- Univ. Hospital Essen, Germany
- Univ. College London Hospitals, UK
- SDN, Naples, Italy
- DKFZ, Heidelberg, Germany
- Rigshospitalet, Copenhagen, Denmark
- St. Olav Hospital, Trondheim, Norway
- DLRZ, Bonn, Germany
- University of Padua, Italy
- CERMEP/Univ. of Lyon, France
- AKH/MUW, Vienna, Austria
- OAO RZD, Moscow, Russia
- King's College London, UK
- Centr. Onkologii, Bydgoszcz, Poland

Asia

- PLA 301 Hospital, Beijing, China
- Parkway Mt. Elizabeth Novena Hospital, Singapore
- CIRC/NUS/A*Star, Singapore
- Yeungnam Univ. Hospital, Daegu, Korea
- SNUH, Seoul, Korea
- Apollo Hospitals, Delhi, India
- Fukushima Medical Univ, Fukushima, Japan
- TNUH, Taipei, Taiwan
- NIMHANS, Bangalore, India
- HKSH, Hong Kong, China

Università Magna Graecia, Catanzaro (2015?)

Technical Challenges: Open Issues

Before:

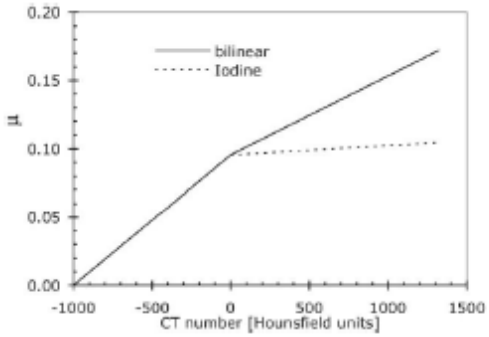
- Limited space of MR gantry
- Ferromagnetic components
- Magnetic Field Inhomogeneity
- Interference between PET electronics and MR coils
- Photomultipliers MR uncompatible
- Cost-effectiveness

Now:

- Higher Performance PhotoMultipliers
- **Attenuation Correction**
- **Motion Correction**
- **Partial Volum Effect Correction**

MR-based AC

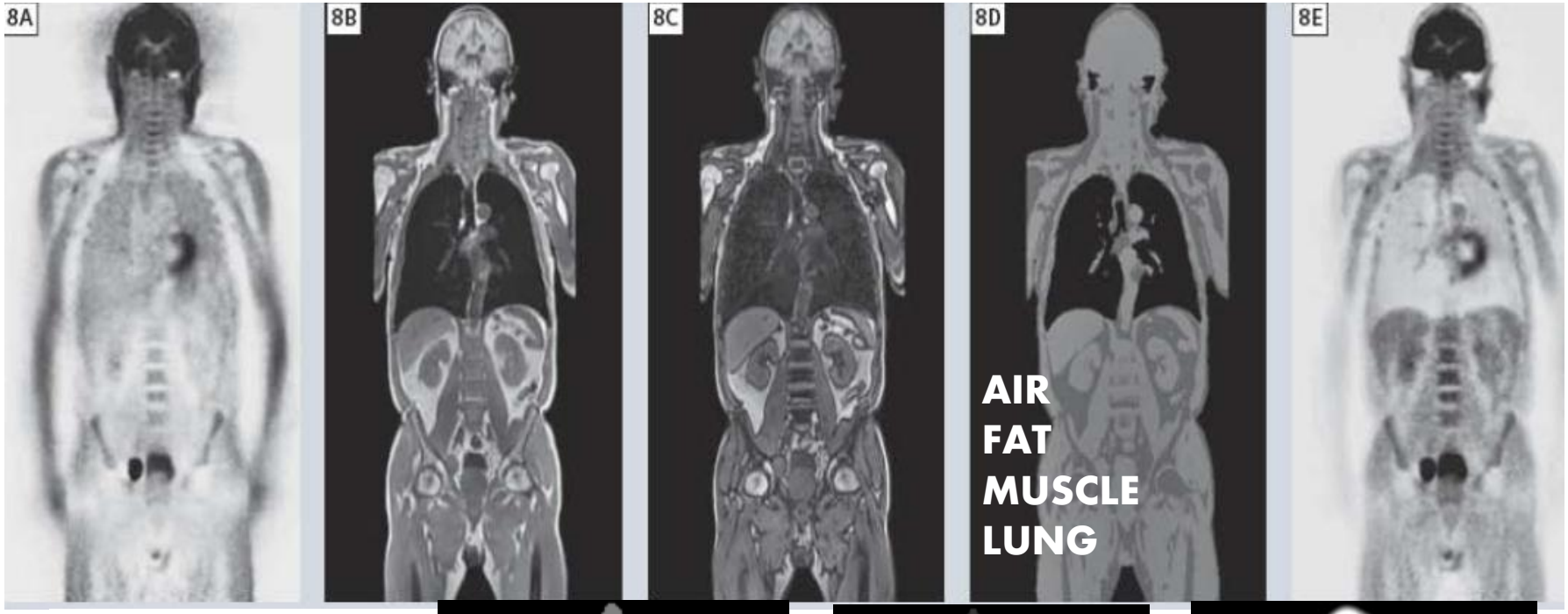
- Attenution: Electrons density of the tissues
- RM signal : Proton density and relaxivity
- There is no direct relationship

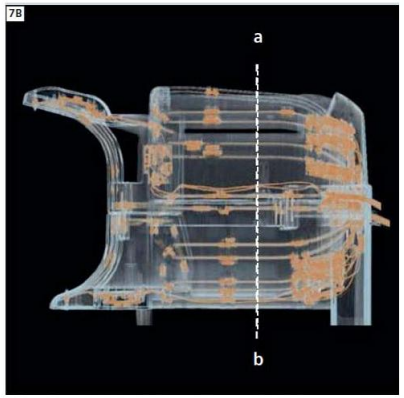


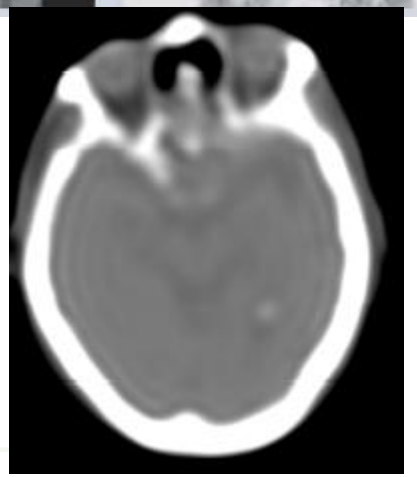
Solutions:

- Segmentation of MR images and tissues recognition
- Bones MR imaging (UTE)
- Template based Approaches

Dixon AC (Soft Tissues segmentation)

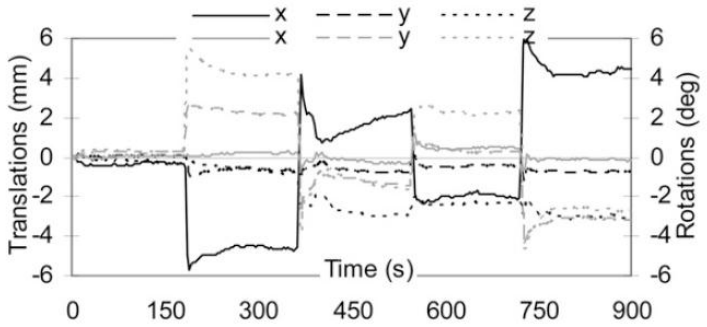




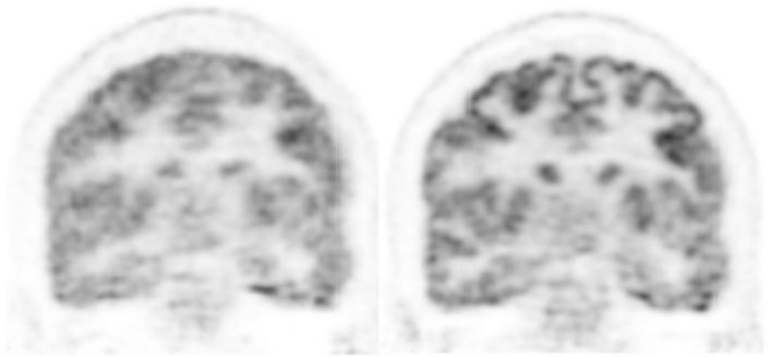


Motion Correction

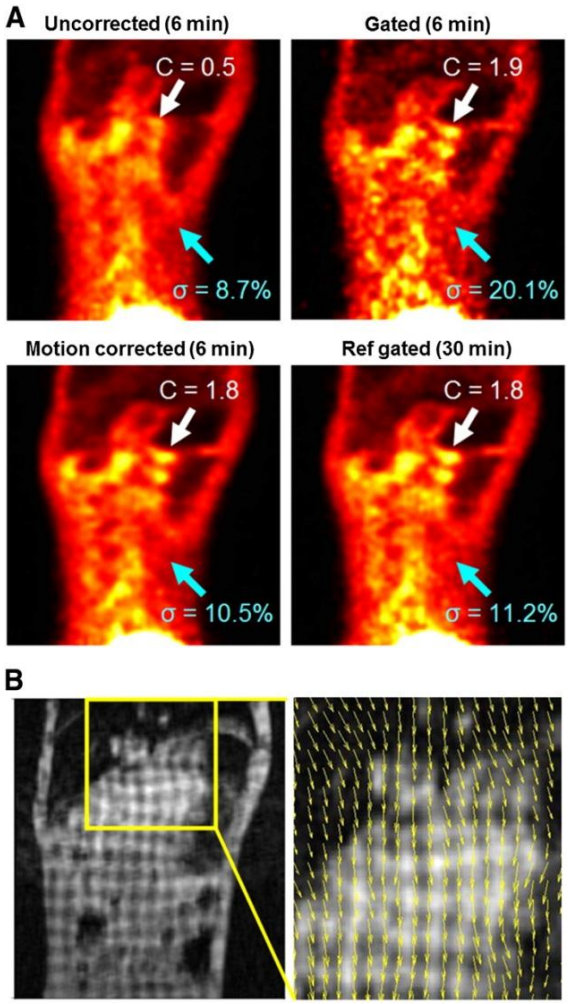
- Registration Based MoCo



MRI-derived motion estimates



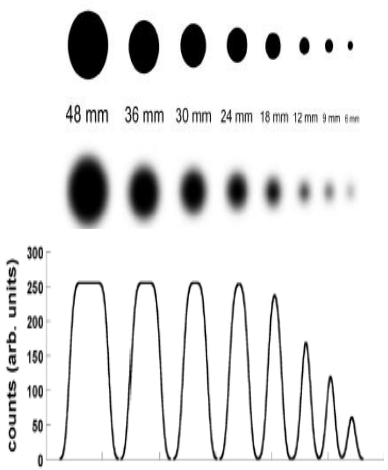
PET before (left) and after (right) MRI-assisted motion correction



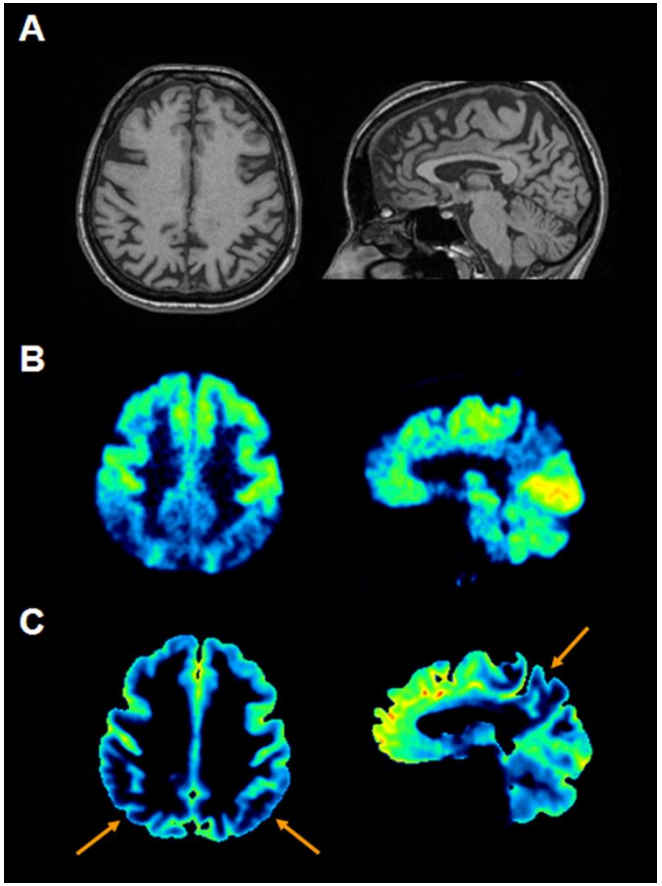
J Nucl Med. 2012 Aug;
Chun. MRI-based nonrigid motion correction in simultaneous PET/MRI.

MRI-guided Partial Volume Correction

Assuming that radioactivity is uniformly distributed in the GM and WM regions and that the mean radioactivity of WM is known



(Cherry SR et al.. Physics in Nuclear Medicine, 3rd ed.)



Original T1-weighted MRI

PET image before partial volume effect correction

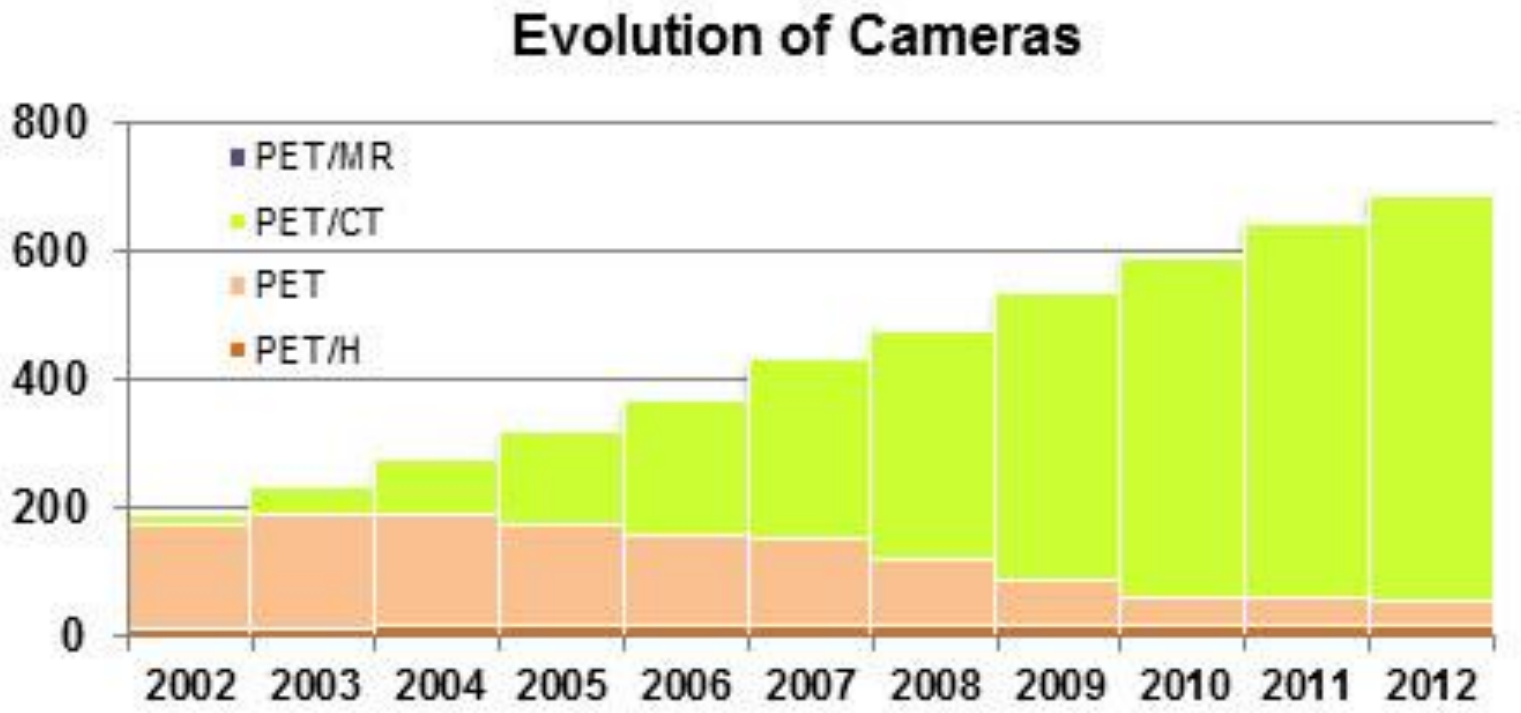
PET image after partial volume effect correction

M Shidahara Neuroimage. (2009).

CLINICAL PERSPECTIVE

PET/MR Vs PET/CT

PET CT Killer Application: Oncological Staging and Follow-up



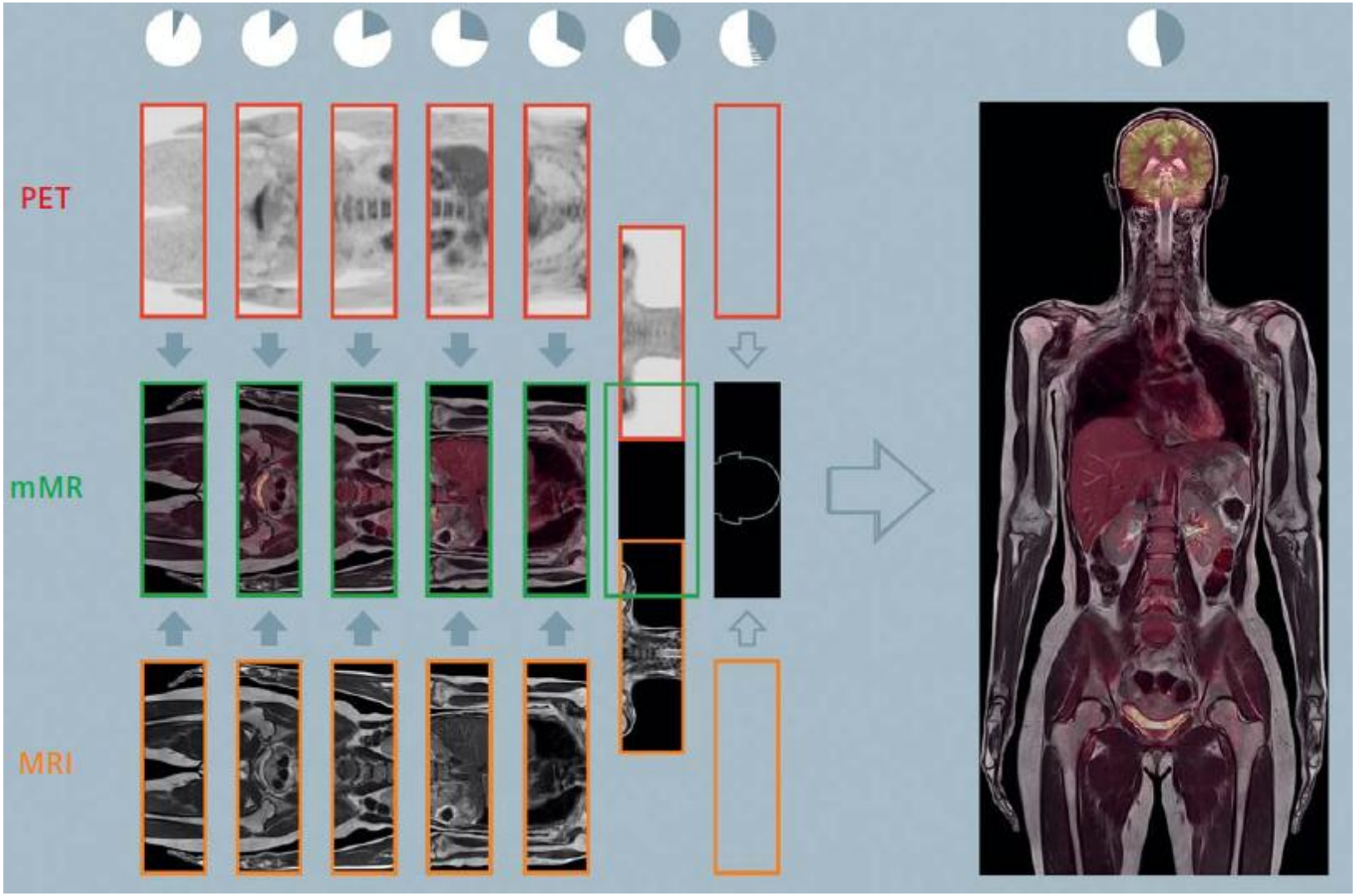
http://www.auntminnieeurope.com/index.aspx?sec=sup&sub=cto&pag=dis&ItemID=608896

PET/MR Vs PET/CT Summary

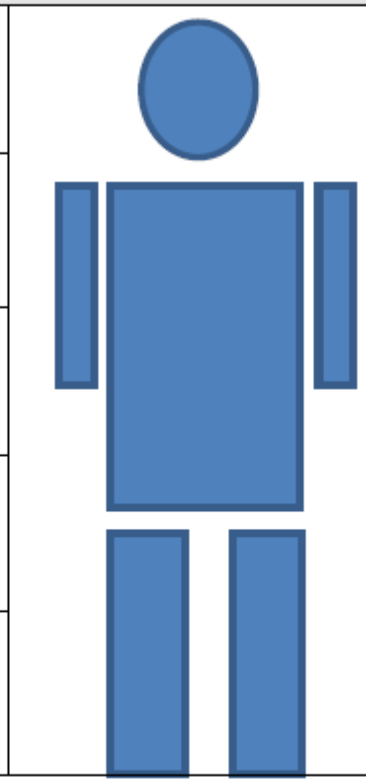
- Over 2000 **single injection dual PET/MR – PET/CT** examinated in 16 articles (IF>3)

- Integrated PET/MR hybrid imaging is **feasible** in a clinical setting with similar detection rates as those of PET/CT.
- Tracer uptake in lesions and background **correlated well** between PET/MR and PET/CT
- Despite differences in attenuation correction PET/MR, including diagnostic T1-weighted TSE sequences, was superior to PET/CT for anatomic delineation and allocation of **bone lesions.**
- PET/MR imaging alone contributed to **clinical management** more often than did PET/CT alone. PET/MR imaging provides information that affects the care of patients with cancer and is unavailable from PET/CT (24/134 patients) [Catalano, Salvatore et al, Radiology 2013]
- **Improved attenuation-correction** algorithms and a PET/MR-specific healthy control database are recommended for reliable and consistent application of PET/MR for clinical **neuroimaging** [Hitz et al., JNM2013].
- **KILLER APPLICATION?** **(pelvis, abdomen, head/neck?)**

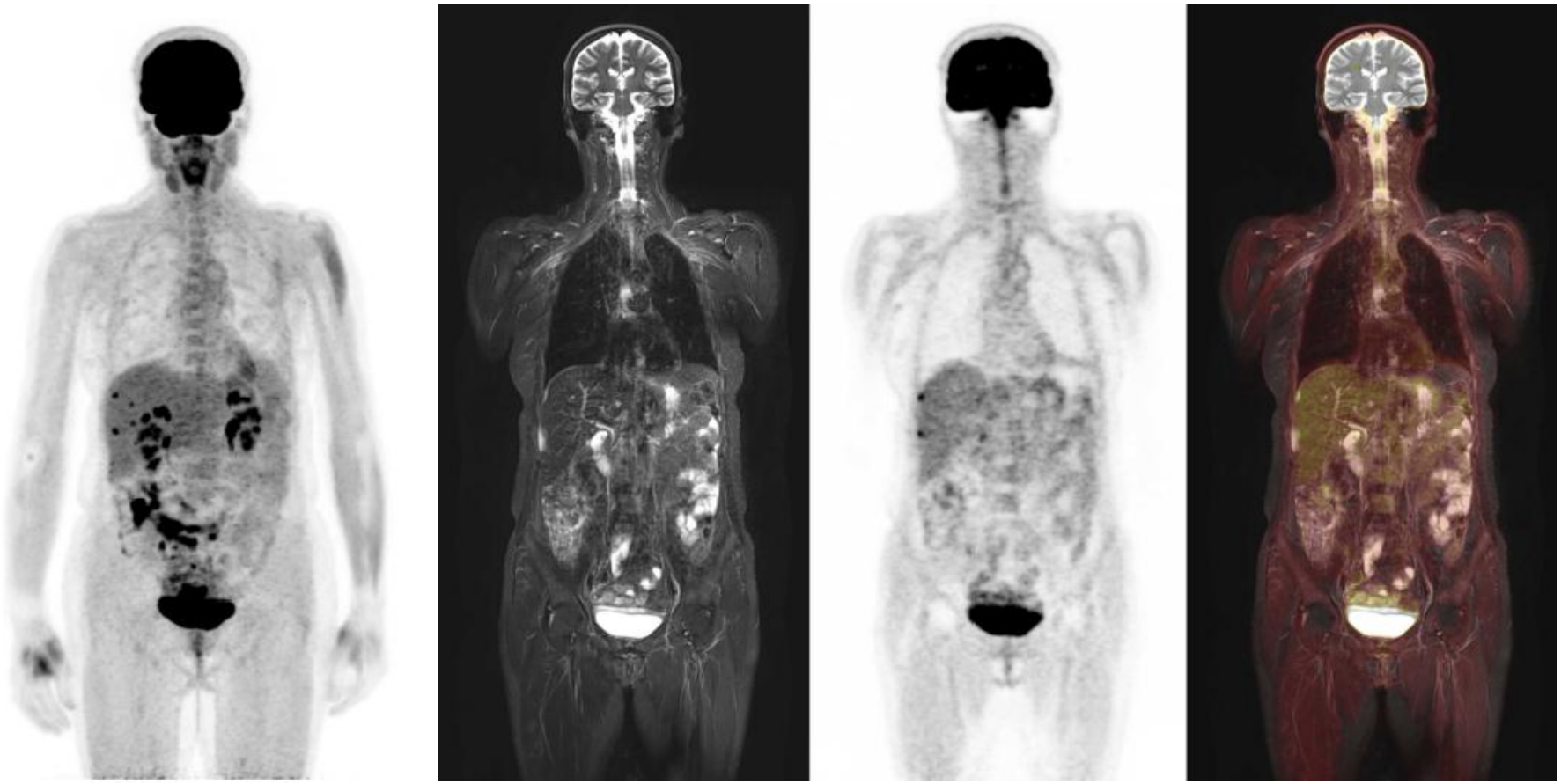
PET/MR acquisition



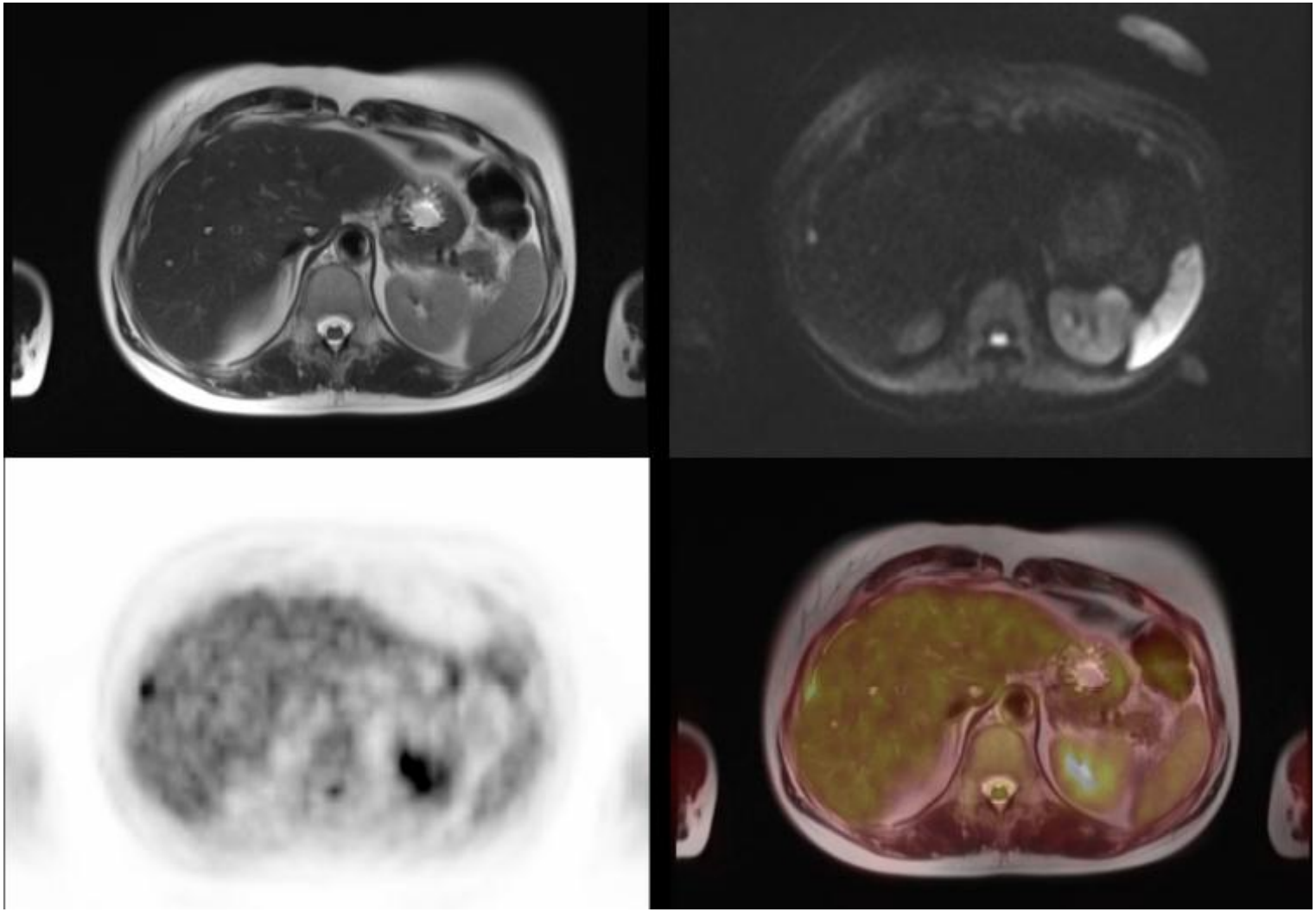
Total Body protocol

SIMULTANEOUS WHOLE BODY MR/PET 3 Tesla					
PROTOCOL NAME : WB_Abdomen_Pelvi_MDC					
PET (AC)		STIR cor DWI ax HASTE ax			
PET (AC)		STIR cor DWI ax HASTE ax	T2 HASTE ax		
PET (AC)		STIR cor DWI ax HASTE ax	T2 HASTE ax T2 HASTE ax T1 DUAL ax	T2 TSE ax fat sat MRCP Vibe pre	VIBE ax dyn VIBE cor tard
PET (AC)		STIR cor DWI ax HASTE ax	T2 TSE sag T2 TSE ax T2 TSE cor	T1 TSE ax T2 TSE ax fat sat T1 TSE ax fat sat Spectroscopy	VIBE ax VIBE sag
PET (AC)		STIR cor DWI ax HASTE ax			
Basic examination			ADVANCED		CONTRAST
Simultaneous acquisition			**MR - ONLY**		
Examination time= 50 min			**Examination time= 60 min**		

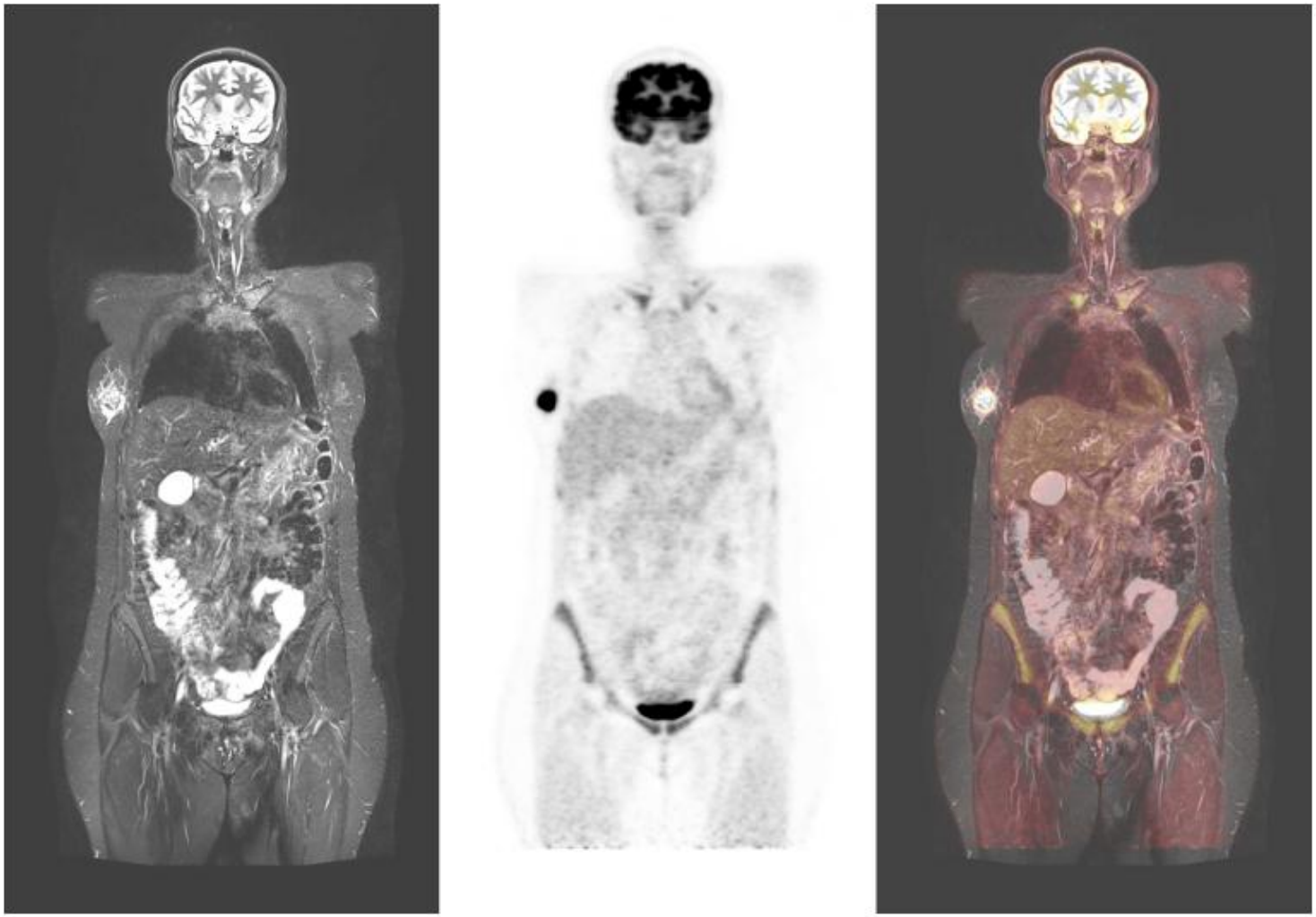
Clinical case



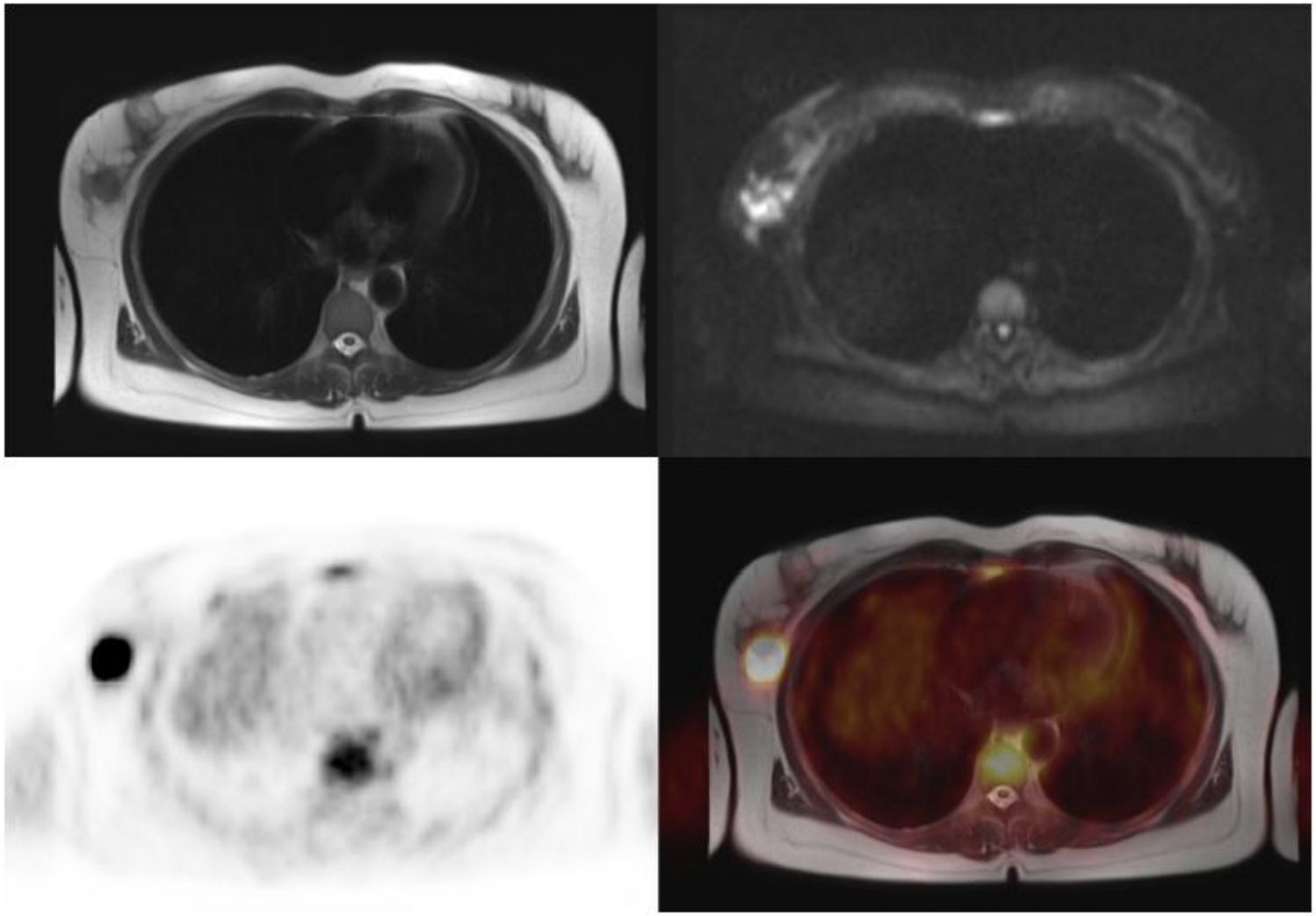
Clinical case



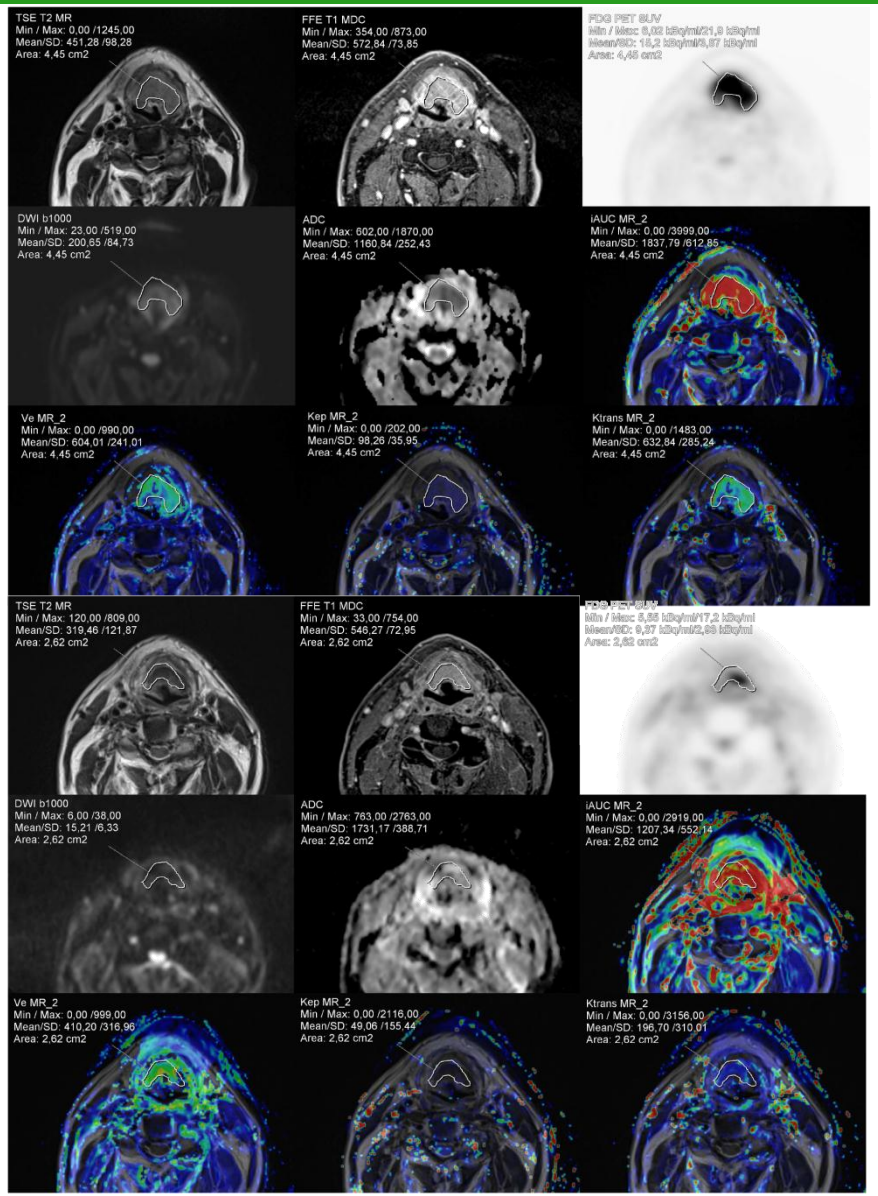
PET/MR Fusion



PET/MR Fusion



PET/MR Multi-Parametric Evaluation



T0

T1

ADC: Apparent Diffusion Coefficient

SUV: Standardised Uptake Value

MTV: Metabolic Tumour Volume

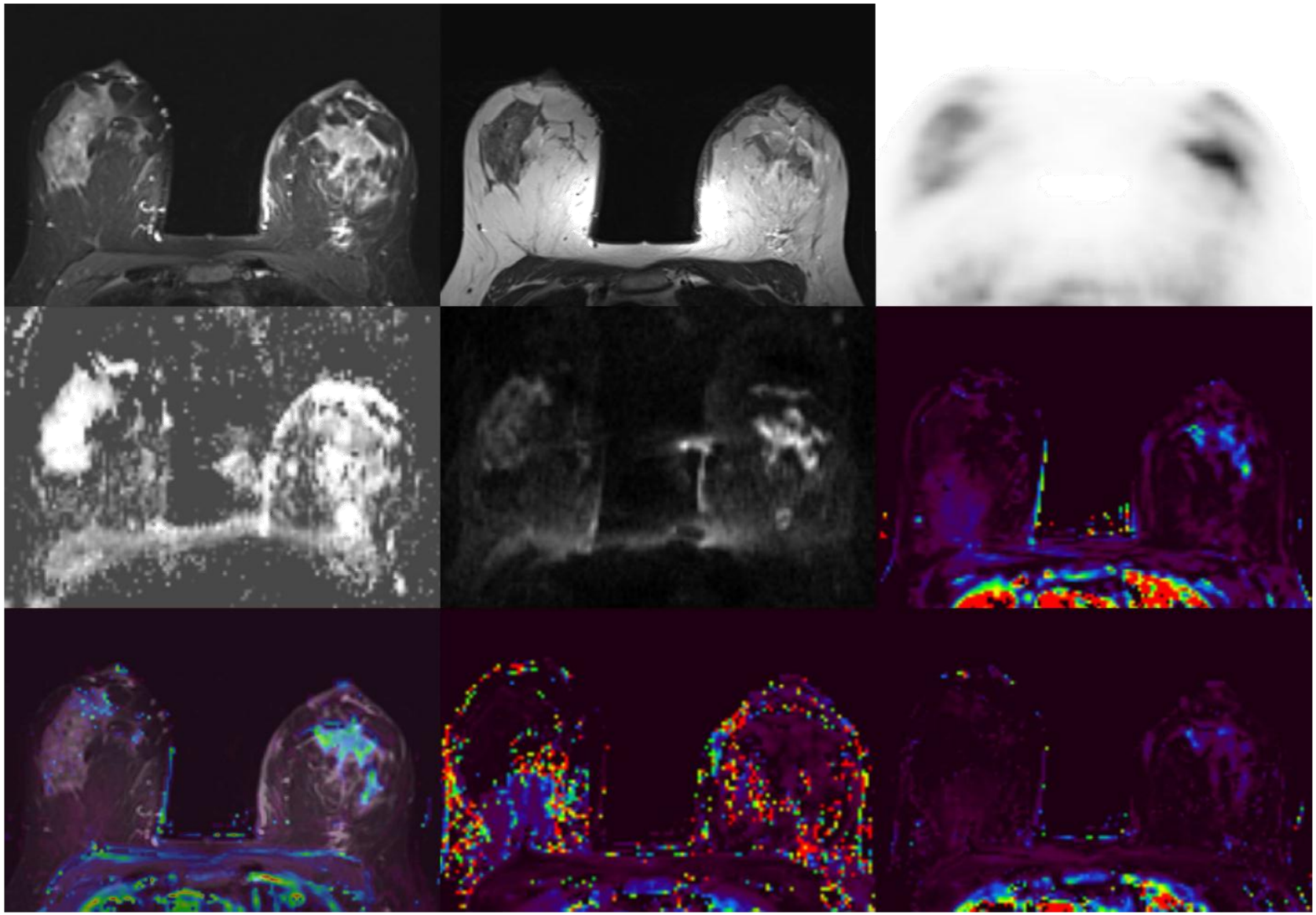
Ktrans: Volume transfer constant between plasma and extracellular extravascular space

Kep: Rate constant between extracellular extravascular space and plasma

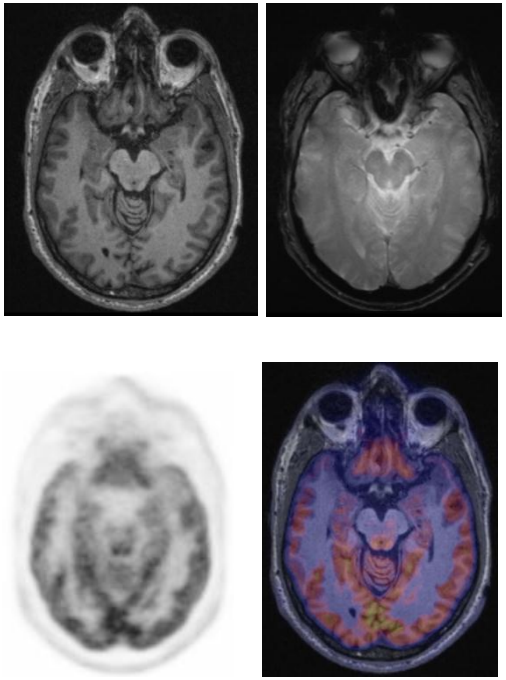
Ve: Volume of extracellular extravascular space per unit volume tissue None

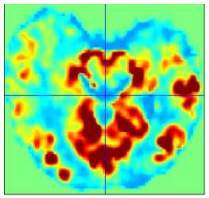
IAUC: Initial area under gadolinium contrast agent concentration–time curve

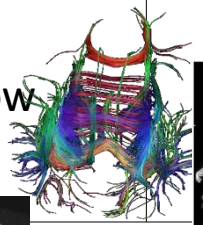
PET/MR Multi-Parametric Evaluation

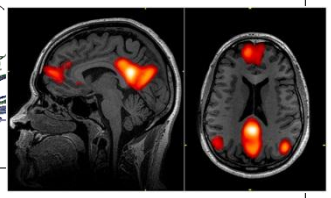


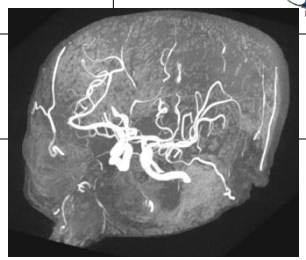
Brain protocol

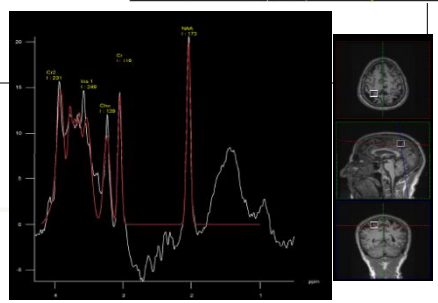
PET		STRUCTURAL	ADVANCED	EV CONTRAST
List Mode 15-20 min 344x344		T2 FLAIR COR T1 MPRAGE T2 AX	ASL SWI DWI DTI spectroCSI spectroSVS TOF3D_art PC_venoso BOLD CSF Flow	T1MPRAGe Perfusion DCE -T1 DCE -T2*
Simultaneous Acquisition 15-20 min				



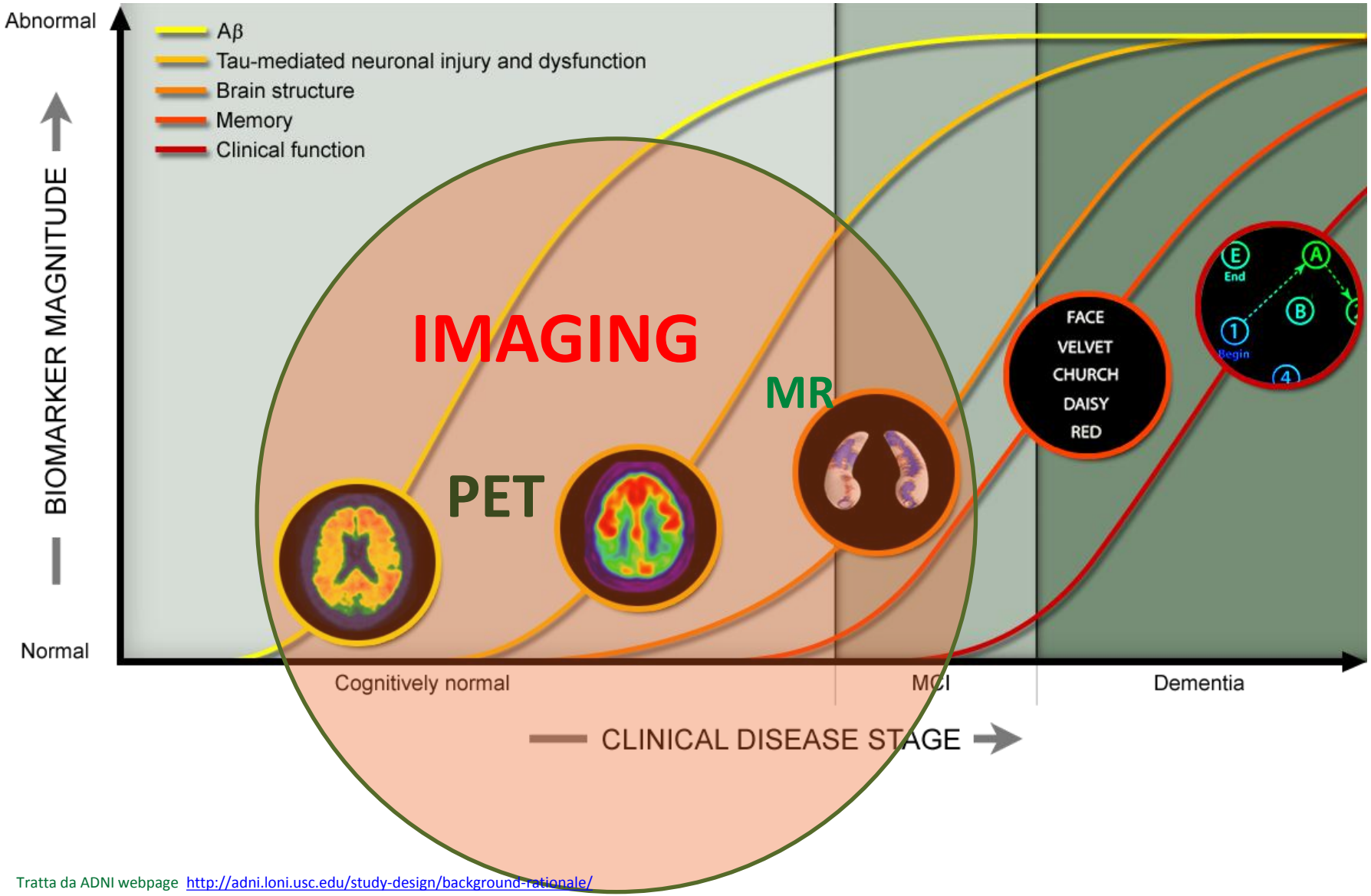






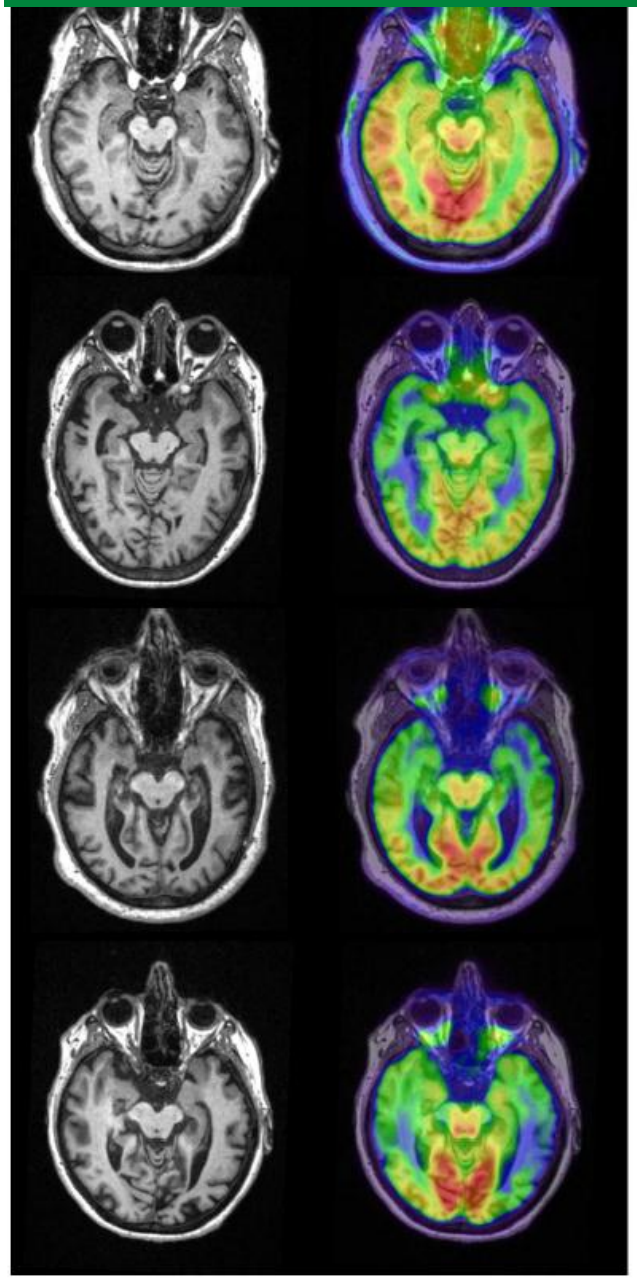


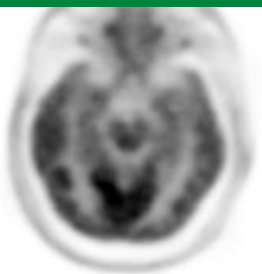
PET/MR in AD



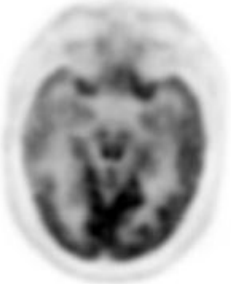
Tratta da ADNI webpage http://adni.loni.usc.edu/study-design/background-rationale/

PET/MR in AD



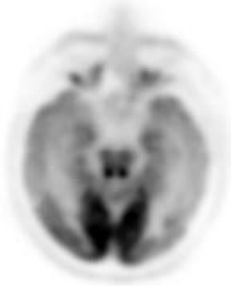


COGNITIVELY NORMAL - M 77 yo, MMSE= 29



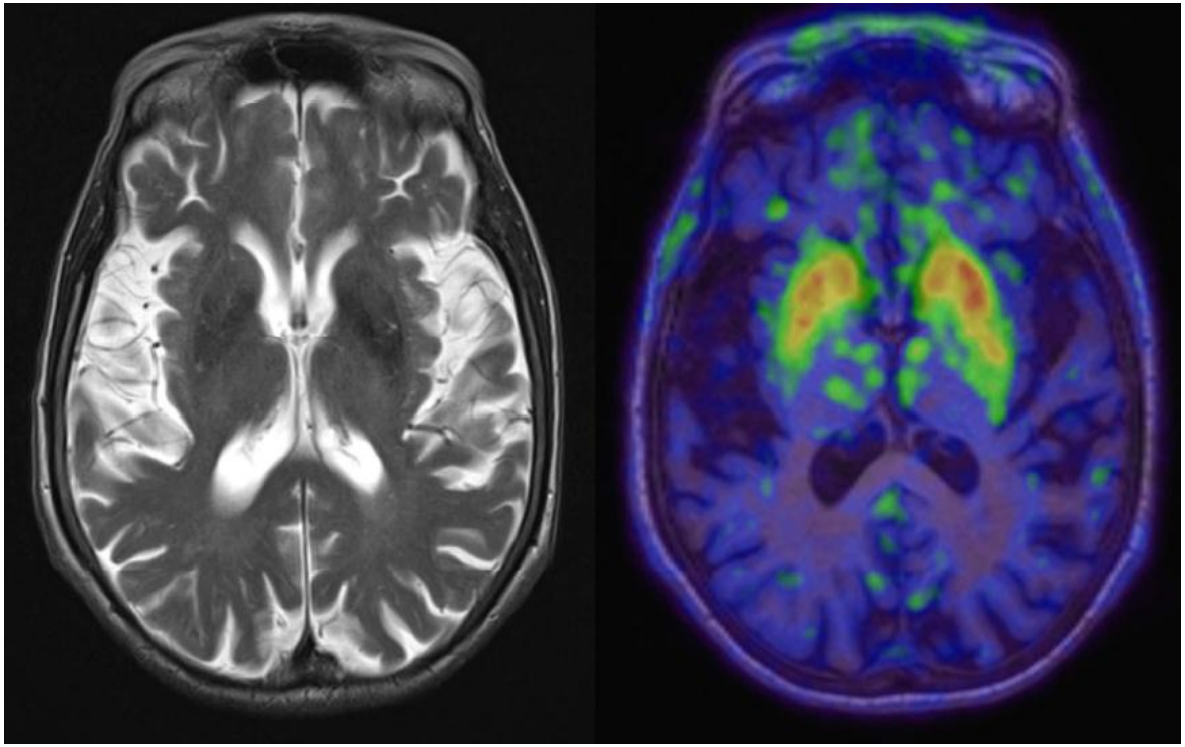
MCI - F 73 yo, MMSE= 24,4

MILD AD - F 66 yo, MMSE=21,7

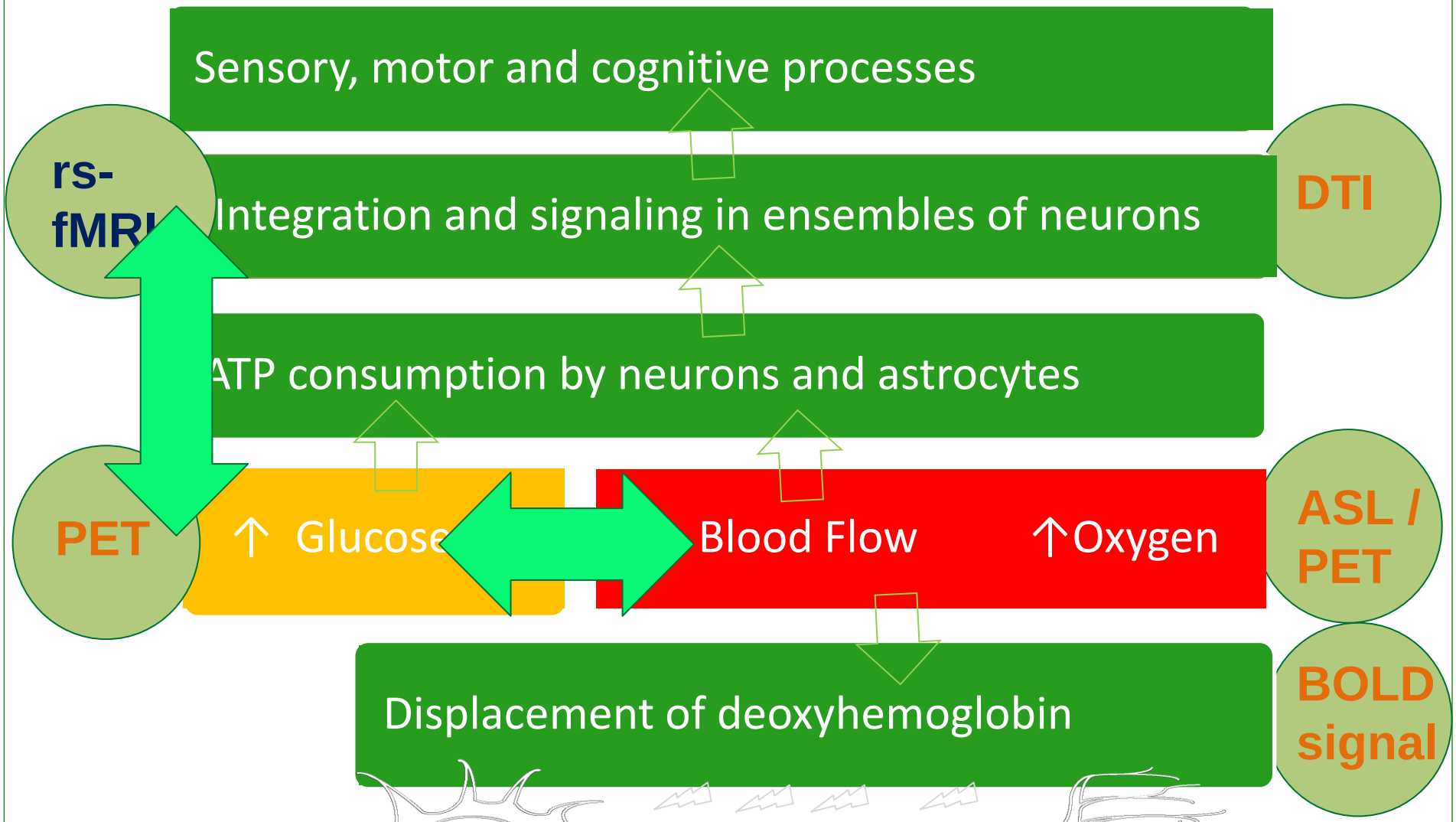


SEVERE AD - F 65 yo, MMSE= 8,5

18F-DOPA-PET/MR



PET/MR Neuroimaging

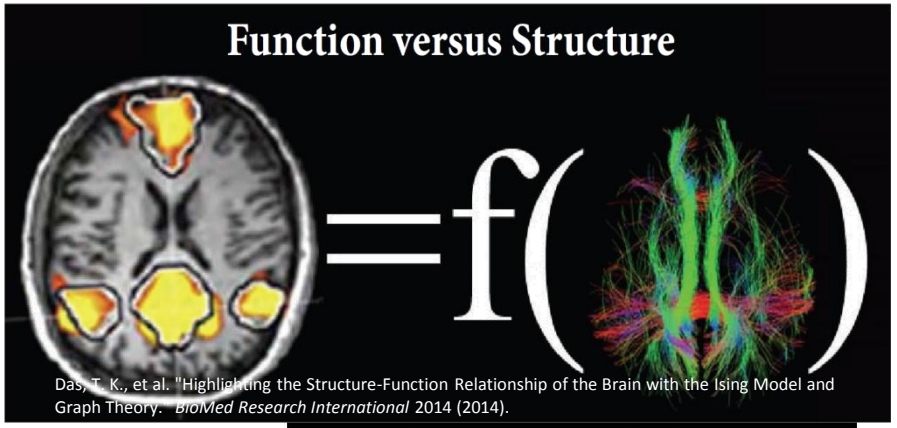


PET/MR and Connectomics

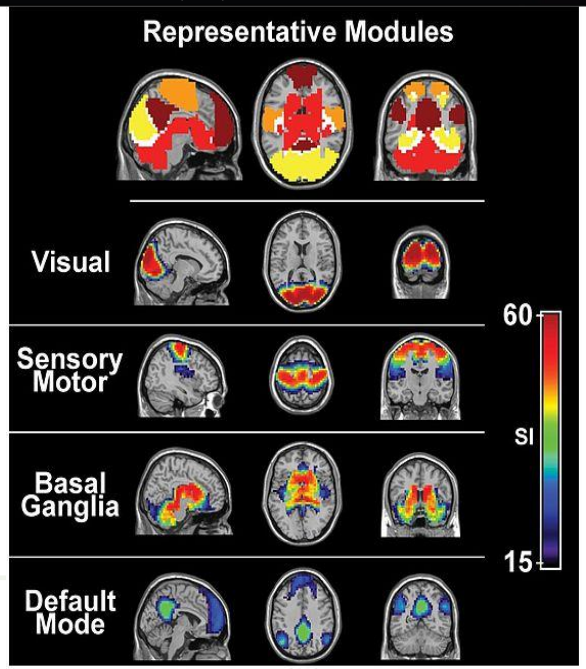
A connectome is a comprehensive map of neural connections in the brain

PET/MR imaging can evaluate:

- Functional Connectivity (MR)
- Structural Connectivity (MR)
- Metabolic Connectivity (PET)



Das, T. K., et al. "Highlighting the Structure-Function Relationship of the Brain with the Ising Model and Graph Theory." *BioMed Research International* 2014 (2014).



Post-processing and analysis methods play a key role!!

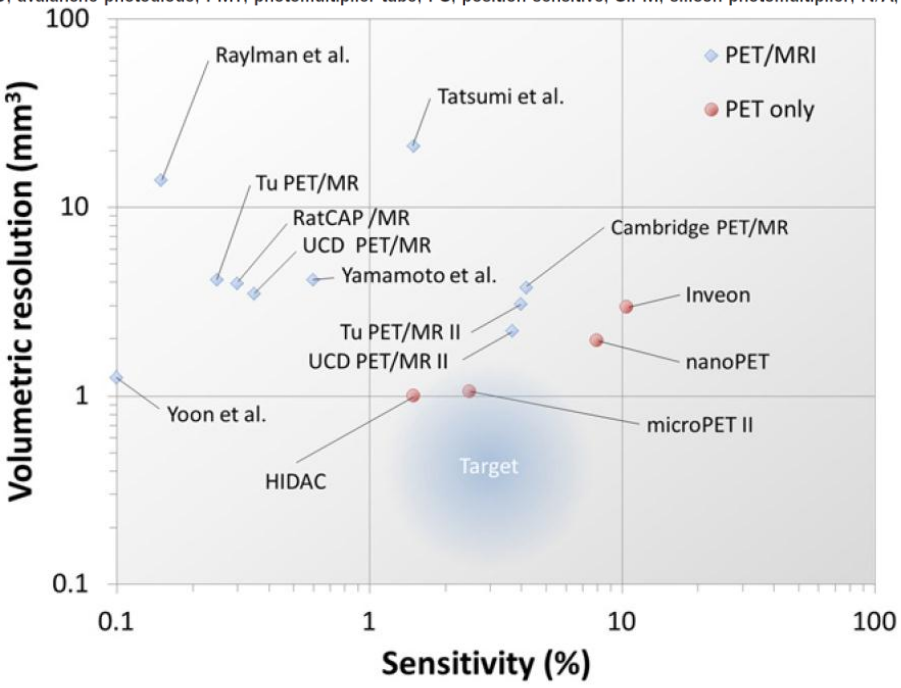
PRE-CLINICAL PERSPECTIVE

Preclinical PET/MR

Table 1 List of current stand-alone PET and PET/MRI systems

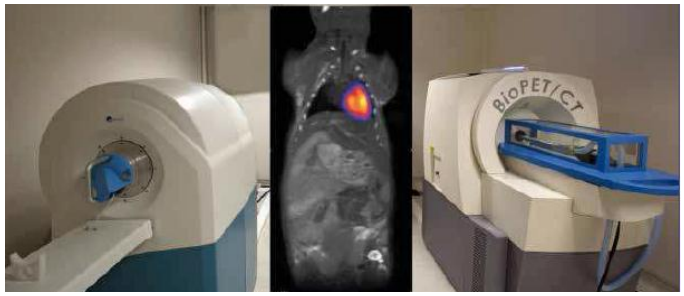
System	MRI Field Strength	Remarks
Raylman et al	3 T	2-detector system/PMT
Tatsumi et al	0.3 T	PS-PMT
Yamamoto et al	0.15 T	SiPM
Tübingen PET/MR	7 T	APD
RatCAP/MR	9.4 T	APD
UC Davis PET/MR	7 T	PS-APD
Cambridge PET/MR	1 T	PS-PMT
Tübingen PET/MR Generation II	7 T	APD—under development
UCD PET/MR Generation II	7 T	PS-APD—under development
Yoon et al	3 T	SiPM
HIDAC	N/A	PET only
microPET II	N/A	PET only
nanoPET	N/A	PET only
Inveon	N/A	PET only

APD, avalanche photodiode; PMT, photomultiplier tube; PS, position-sensitive; SiPM, silicon photomultiplier; N/A, n



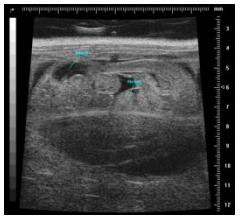
(listing based on publicly available data – July 2012)

Judenhofer, Martin S., and Simon R. Cherry. "Applications for preclinical PET/MRI." *Seminars in nuclear medicine*. Vol. 43. No. 1. WB Saunders, 2013.

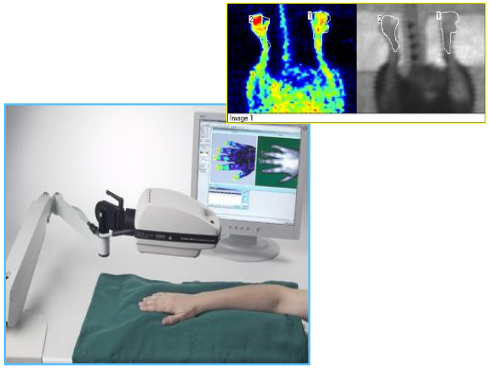


Karolinska Institutet in March 2011

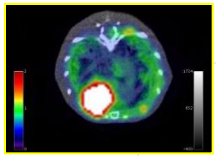
Micro-TC



Ecografia ad altissima risoluzione

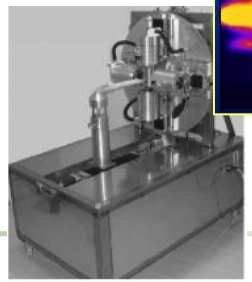


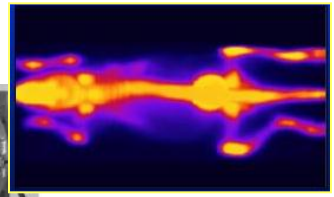
Laser doppler



PET/TC

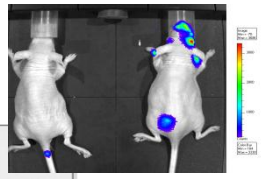
Densitometro osseo



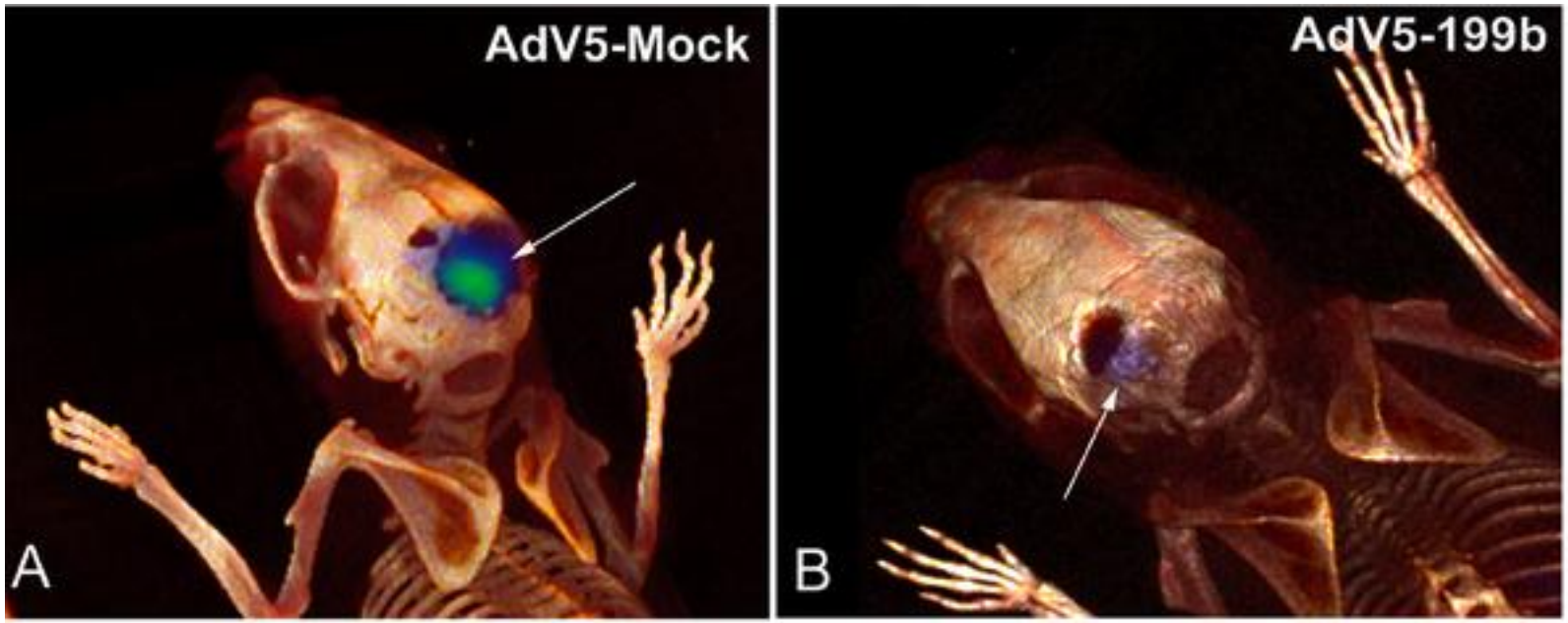


SPECT

Imaging Ottico

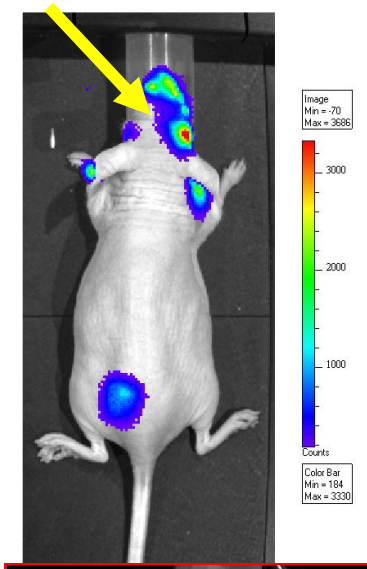


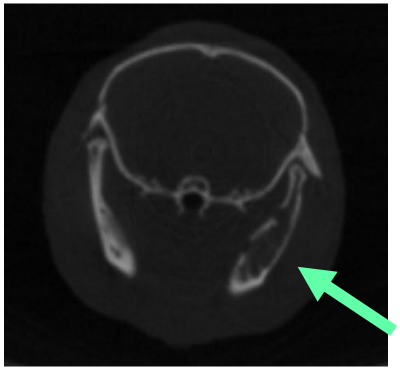
^{18}F-FLT PET/CT:
Mice model of medulloblastoma



Garzia L et al ***MicroRNA-199b-5p impairs cancer stem cells through negative regulation of HES1 in medulloblastoma****. PLoS One 2009*

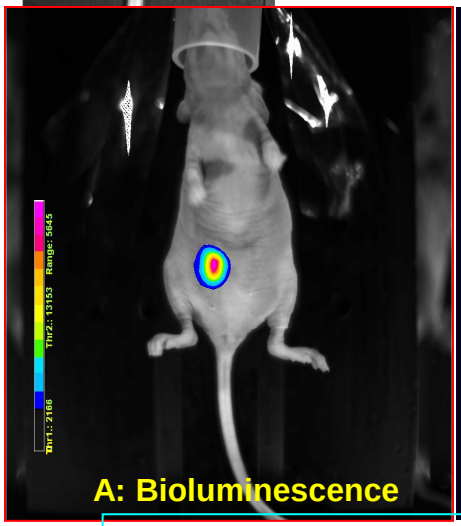
Multimodality Preclinical Imaging

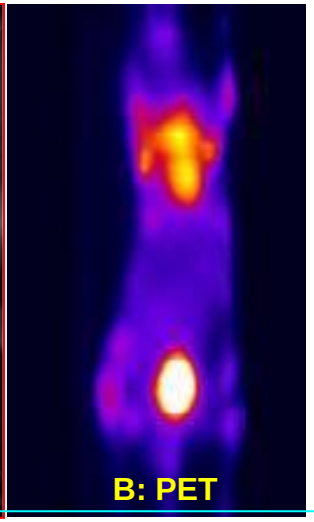


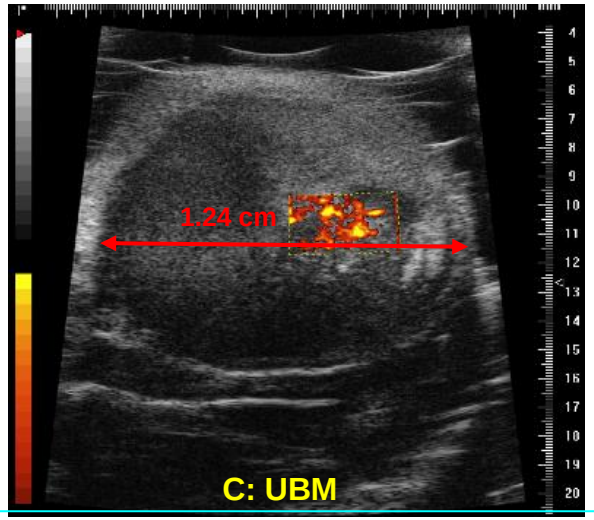


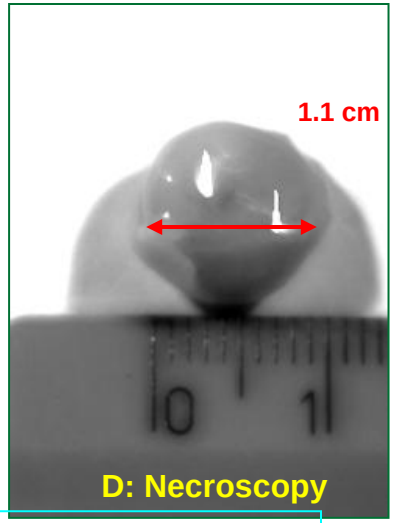
Bioluminescence and CT: mandibular metastasus of mammary carcinoma

Mammary carcinoma





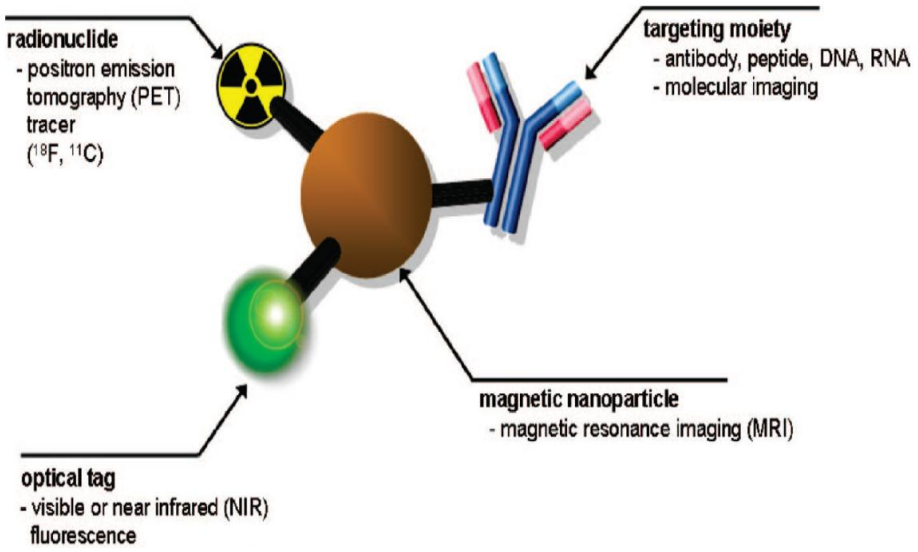




A. Greco, M. Mancini, S. Gargiulo, M. Gramanzini, P.P. Claudio, A. Brunetti and M. Salvatore. Ultrasound Biomicroscopy in small animal research: applications in molecular and pre-clinical imaging. Journal of Biomedicine and Biotechnology 2011

Preclinical PET/MR

- **Simultaneous PET/MR allows access to new fields of physiological investigation**
- **PET as reference for the assessment and validation MR techniques (ASL Vs ^{15}O-labeled water)**
- **Evaluation of concurrent physiological phenomena (brain metabolism / perfusion)**
- **Bimodal Tracers *(Frullano et al (2010) Bimodal MR-PET agent for quantitative pH imaging)***



Cheon and Lee, ACCOUNTS OF CHEMICAL RESEARCH Vol. 41, 2008 1630-1640

Final Remarks

MR to PET

- ROIs for AIF selection or reference for semi-quantitative analysis
- Prior for iterative reconstruction
- Motion Correction
- Partial Volume Effect Correction

PET to MR

- Metabolic detection and characterisation of the lesion
- Early metabolic response (DOPA, FDG, FLT, FET, etc)
- In general, PET can supply ‘’molecular power’’ to MR

Emerging clinical applications

Bimodal Farmacokinetic modelling

Synergistic approach in multiparametric evaluation

PET/MR WorkGroup in Naples

- IRCCS SDN:

Prof. Marco Salvatore, MD
Prof. Andrea Soricelli, MD
Prof. Onofrio A Catalano, MD
Emanuele Nicolai, MD
Mario Covello, MD
Carlo Cavaliere, MD
Marco Aiello, PhD
Serena Monti, PhD Student
Ernesto Forte, PhD Student
Marianna Inglese, PhD Student

- Istituto Biostrutture e Bioimmagini CNR
- Università di Napoli Federico II

- International Collaborations: Massachussets General Hospital, Coma Group Liegi, Western Ontario University, KCL, UCL,

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Thank you!