Brain Perfusion and Glucose Metabolism by Simultaneous FDG-PET/MR-ASL in Patients with Cognitive Disorders: Initial Experience.

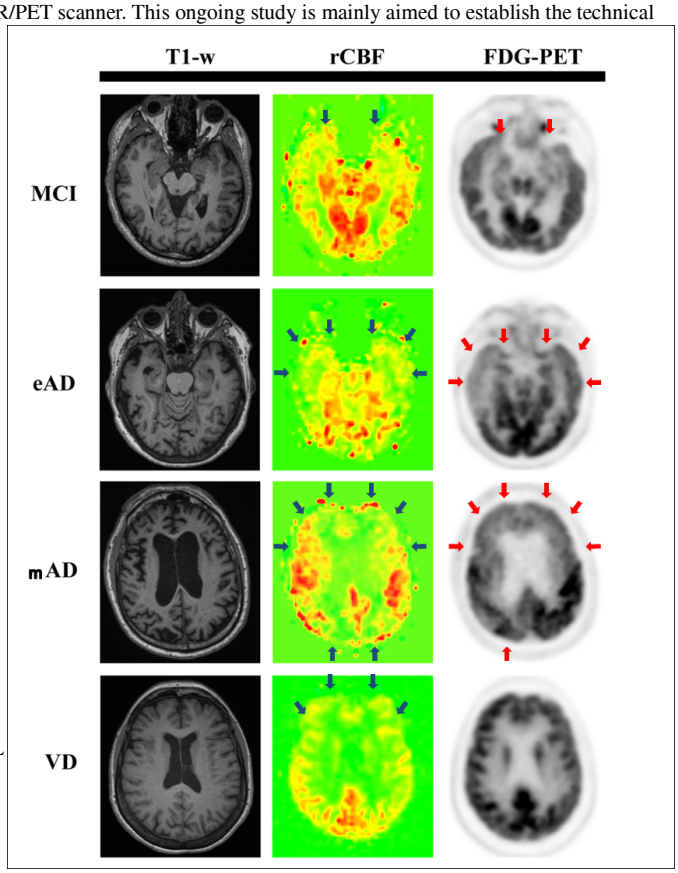
Marco Aiello[1], Carlo Cavaliere[1], Ilaria Boscolo Galeazzo[2], Elena Salvatore[3], Francesca B. Pizzini[4], Alberto Beltramello[4], and Emanuele Nicolai[1]
[1]IRCCS fondazione SDN, Naples, Italy, [2]University of Verona, Italy, [3]Università di Napoli Federico II, Italy, [4]General Hospital, Verona, Italy

• **TARGET AUDIENCE –** Researchers and physicians interested to clinical use of Arterial Spin Labeling and to the investigation of relationship between cerebral blood perfusion and glucose metabolism.

• **PURPOSE –** The recent advent of hybrid Positron Emission Tomography (PET)/Magnetic Resonance (MR) systems with multimodality or even truly simultaneous data acquisition capabilities may provide important insights into brain structure and function and its underlying physio-pathological processes. In the field of dementia, the need of standardized multiple biomarkers for diagnosis and monitoring of the disease, ranging from clinical tests, MR, PET and cerebrospinal fluid studies, is crucial. Combining metabolic studies by fluorodeoxyglucose (FDG)-PET with perfusion studies by Arterial Spin Labeling (ASL) is a challenge[1,2].

Its intrinsic non-invasive nature and cost-effectiveness have lead to an increased interest in ASL. Nonetheless, in order to prove the reliability and trustworthiness of its results, direct comparisons with the information from the more established neuroimaging biomarkers in the dementia field are necessary[3].

A recent study[4] acknowledges the excellent opportunity to perform concurrent ASL/PET acquisition in order to map more precisely the correlations between modalities. To exploit this opportunity, we planned a study on a simultaneous MR/PET scanner. This ongoing study is mainly aimed to establish the technical feasibility of the simultaneous acquisition of both modalities and thus to compare ASL findings with those of PET in cognitive disorders.



• **METHODS –** For a first exploratory evaluation, we selected one patient with Mild Cognitive Impairment (MCI), one with early Alzheimer Disease (eAD), one with moderate AD (mAD) and one with Vascular Dementia (VD) (50-74 age range). Patients were clinically evaluated by Mini Mental State Examination (MMSE), Clinical Dementia Rating (CDR) scale and Hacinski Score (HS).

Patients rested in a quiet dark room 10 minutes before and 30 minutes after the injection of approximately 250 MBq of 18F-FDG. They underwent PET/MR examination on a Siemens 3T Biograph mMR.

For anatomical characterization, mainly for assessing the atrophy level, structural images were acquired using a 3DMPRAGE T1-weighted sequence (TR/TE= 2300/2.96 ms, 176 sagittal slices, voxel size = 1.0 × 1.0 × 1.0 mm3, flip angle = 9°).

ASL data were acquired using a pulsed sequence with the PICORE Q2TIPS labeling scheme. The following parameters were established for the acquisition of 141 2D-EPI volumes (the first was an additional volume for the estimation of the blood equilibrium magnetization M_{0b} and then 70 label-control pairs) : TR/TE =3000/18 ms, TI1/TI2 = 800/1800 ms, FOV = 256x256 mm2, 24 ascending 6 mm thick slices with a 10% gap between each. Relative cerebral blood flow (rCBF) maps were carried out after motion correction and quantification processing as provided by manufacturer.

During MR acquisition, PET data were continuously acquired in sinogram mode for 15 minutes; matrix size was 256 x256 $mm^2$and reconstructed with OSEM algorithm (21 subsets, 4 iterations) taking into account MR-based attenuation correction.

At actual stage of this study, quality of images and clinical overlapping between metabolic and perfusion data have been evaluated by an experienced nuclear medicine specialist and a neuroradiologist.

• **RESULTS –** A good agreement between findings in blood flow measured by ASL (blue arrows) and in glucose metabolism (red arrows) detected by FDG-PET was achieved in MCI and AD patients. In particular, in MCI a focal hypo-perfusion and hypo-metabolism was detected in the medial temporal cortices, bilaterally. In the eAD case, a reduction of perfusion and metabolism was visible in temporal cortices. In mAD, instead, a wider reduction of both ASL and FDG cortical signals were detected, with a relative saving of rolandic areas.

For as vascular dementia patient, a mismatch between perfusion and metabolism raised up, showing a decreased frontal perfusion in absence of evident glucose metabolism in these areas.

Patient	MMSE	CDR	HS	ASL findings	PET findings
MCI, male, 50	28	0,5	1	Focal hypo-perfusion of medial temporal cortex	Focal hypo-metabolism of medial temporal cortex
eAD, female, 74	27	1	2	Diffuse reduction of perfusion in temporal cortices	Diffuse reduction of glucose metabolism in temporal cortices
mAD, male 65	14	2	1	Diffuse cortical hypo-perfusion	Diffuse cortical hypo-metabolism
VD, male, 74	17	2	8	Diffuse reduction of perfusion in frontal cortices	No metabolism alterations were detected

• **DISCUSSION /CONCLUSION:** These preliminary simultaneous FDG-PET/MR-ASL data show good feasibility in terms of image quality and patient endurance. The use of a 2D-EPI sequence for ASL determines the presence of consistent susceptibility artifacts that makes the interpretation of perfusion images difficult in proximity of para-nasal structures. Our case reports show promising preconditions for further developments, confirming the complementarity of findings due to underlying physiological processes measured by each modality, as previously reported[1,4]

The abilities of ASL-MRI and FDG-PET in detecting functional abnormalities associated with cognitive disorders was confirmed.

ASL can easily be inserted in the MRI protocol for the evaluation of cognitive disorders, especially for tracking disease severity in longitudinal studies. More patients are going to be acquired in order to perform a quantitative assessment and a putative discrimination among cognitive disorders. Compared to previous studies based on sequential acquisitions of both modalities, simultaneous MR/PET imaging enables to effectively measure blood perfusion and glucose metabolism concurrently, avoiding a possible variability due to the different acquisition timepoints.

• **REFERENCES**

[1] Chen et al. Neurology. 2011 [2] Wang Z et al. Neuroimage Clin. 2013 [3] Wolk et al. Curr Opin Neurol. 2012 [4] Cha YH et al. J Cereb Blood Flow Metab. 2013

Acknowledgements:
BMBS COST Action BM1103 – Arterial Spin Labelling Initiative in Dementia (AID)
PONa3-00173 "Nuovo Centro Studi di Medicina Molecolare"