DEBBIE

Developing BBB-ASL as non-invasive early biomarker of Alzheimer's disease

Poster number: 12
Poster presenter: Beatriz Padrela

Aims, research questions and working hypothesis
The DEBBIE project was funded by JPND in 2020 with the aim to map blood-brain barrier (BBB) integrity loss using arterial spin labeling (ASL) in preclinical stages of Alzheimer's Disease (AD). The project was organized around four main work packages:

1. Development of a clinically ready ASL sequence to measure BBB water permeability, led by the Fraunhofer MEVIS (FME) group under the direction of Prof. Matthias Günther;
2. Standardization of a processing pipeline for multi-center BBB-ASL data, managed by the Amsterdam University Medical Center (AUMC) group headed by Dr. Henk-Jan Mutsaerts;
3. Validation of BBB-ASL sensitivity through comparison with PET measures of BBB integrity, overseen by Lawson Health Research Institute (LRHI) under the leadership of Dr. Udunna Anazodo; and
4. Assessment of the clinical value of BBB-ASL by incorporating the sequence into ongoing AD studies, conducted by the University of Oslo (UoO) under Prof. Tormod Fladby and by Ghent University Hospital (GUH) under Prof. Eric Achten.

Means/methods implemented by the consortium

1) FME has developed a Walsh-encoded multi-post labeling delay, multi-echo ASL-MRI technique, termed BBB-ASL, optimized for assessment of cerebral blood flow, BBB water permeability and arterial transit time.
2) Development of the ExploreASL software to process BBB-ASL data (DEBBIE sequence). Version 1.11.0, released at the end of 2023, includes basic features for this purpose. Work is underway on Version 1.12.0, which will provide fully integrated BBB-ASL processing and analysis.
3) Data collection for validation using a pig model is ongoing. Progress was delayed by factors such as COVID-19 restrictions, and hardware changes. Ten pigs have been imaged, with scans continuing to complete the preclinical validation phase before moving to human validation.
4) The BBB-ASL sequence is now operational in clinical environments at the UoO, focusing on AD along the continuum with and without a vascular component, and at GUH for cognitively normal participants.

What are the outcomes of the project?
All sites successfully installed and tested the sequences, albeit without patient-specific calibration, as part of this work package. ExploreASL was used to analyze approximately 400 BBB-ASL scans. Efforts have been made to enhance reference atlases, including a dataset of normal BBB integrity maps. As part of the DEBBIE protocol, 219 cognitively normal scans and 83 scans from patients with mild cognitive impairment (MCI) have been acquired from UoO and other ongoing studies. Findings have been widely shared through conference presentations at ISMRM, ESMRMB, OHBM, and ADPD (2022–2024). Publications related to the project by Amnah Mahroo and Beatriz Padrela are available in *JMRI*, *BMJ Open*, and soon in *Neurobiology of Aging.*

Significance and impact of the work on the field
The imaging biomarker developed by the DEBBIE consortium provides a robust, non-invasive method to monitor BBB integrity. It has demonstrated age-related changes and differences between healthy individuals and those with MCI. This approach holds the potential to reduce the burden of Alzheimer's disease by enabling earlier intervention before irreversible damage occurs.

Next steps and future challenges
During the project, many research institutes expressed interest in incorporating BBB-ASL into their clinical protocols. The technique has broader applications in neurological conditions involving BBB dysfunction, including stroke, multiple sclerosis, and brain tumors.