Voxel-Based Morphometry of Retinal OCT (VBM-OCT) in the spectrum of Cerebral Beta-Amyloidosis: Promising Preliminary Findings in Cerebral Amyloid Angiopathy

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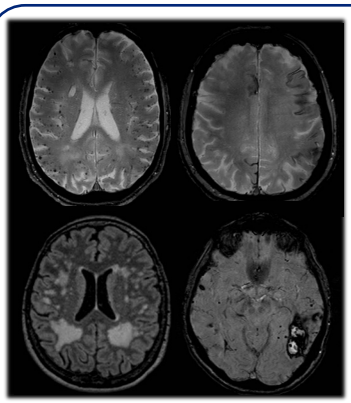

Figure 1: Radiological markers of CAA

Cerebral amyloid angiopathy (CAA) is a beta-related cerebral small vessel disease associated with **cognitive decline** and **spontaneous lobar hemorrhages (Figure 1)**.

Retinal alterations assessed through **optical coherence tomography (OCT)** may represent a non-invasive biomarker; however, this potential remains under-explored.

Voxel-based morphometry applied to OCT (VBM-OCT – Figure 2) is a novel approach that, compared to traditional methods, enhances the sensitivity of detecting retinal changes.

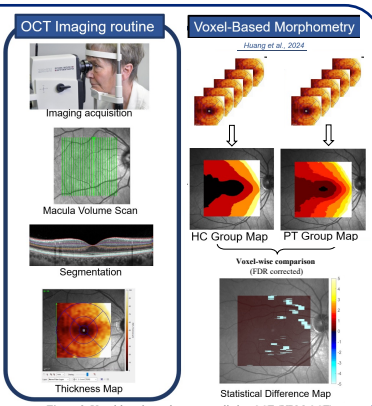

Figure 2: Voxel-based morphometry applied to OCT (VBM-OCT)

Aim of the study: to analyze retinal alterations in the spectrum of cerebral beta-amyloidosis, exploring whether VBM-OCT can serve as a potential diagnostic and/or progression marker.

Methods: We enrolled **probable CAA patients** (Boston criteria v2.0), **MCI/mild dementia due to Alzheimer's disease (AD)** patients, and **cognitively unimpaired subjects (CU)** as a control group. **Macular volumetric OCT** scans were segmented, analyzing different retinal layers. **VBM-OCT performed voxel-wise comparisons of volumetric changes across groups**. Retinal alterations were correlated with clinical-radiological data and CSF biomarkers.

Results

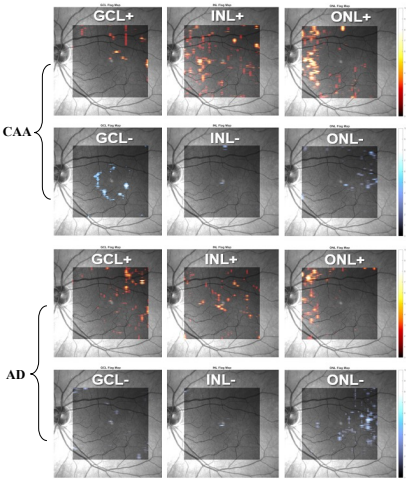

Figure 3: Flag Maps which shows relative thinning (blue) or thickening (orange) compared to CU

Compared to CU (n=28; age: 49.0±11.1), CAA (n=16; age: 76.6±7.2; MMSE: 26.2±3.6) and AD patients (n=19; age=70.6±8.2 years; MMSE: 22.5±4.2) showed **atrophy in the retinal nerve fiber layer (RNFL)** and **ganglion cell layer (GCL - Figure 3), mostly driven by CAA. The GCL atrophy correlated with Aβ40 CSF levels (r = -0.56; p<0.05 - Figure 4) and cortical superficial siderosis (cSS) evaluated with the multifocality score (r = 0.43; p<0.05).**

Conversely, the **inner nuclear layer (INL) and outer nuclear layer (ONL) appeared thickened**, particularly in the macular periphery and in CAA patients, and this was correlated with **Aβ42 levels (r = -0.62; r = -0.77; p<0.05)**

In CAA, several retinal layers (atrophy of RNFL and GCL; thickening of INL and ONL) were **correlated with MMSE scores (p<0.05 – Figure 4)**.
This correlation (MMSE) was not observed in AD subjects.

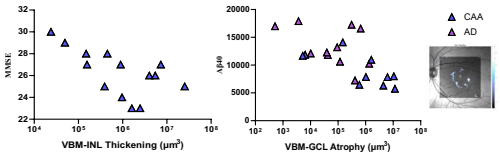

Figure 4: Scatter plot showing the correlation between MMSE/INL thickening (left) and Aβ40/GCL atrophy (right)

Conclusion

Our preliminary observations showed that **VBM-OCT can detect specific retinal patterns in CAA**. The GCL atrophy correlates with **CAA-specific features (Aβ40 levels, cSS)**, so potentially representing a disease surrogate. We also observed **thickening of other layers (INL, ONL),** potentially associated with **local amyloid deposition**.
A greater sample size is required to confirm these findings and define the full potential of VBM-OCT in the spectrum of brain beta-amyloidosis.

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