Imagerie rétinienne par réflectance pour prédire la présence d'amyloïde cérébrale en TEP

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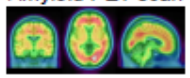
Background

Accessible Aβ biomarkers are needed because:

- **Current methods to identify Aβ *are not adapted for screening purposes.***

Amyloid PET scan



- Injection of radioactive tracer
- Costly
- Availability issues

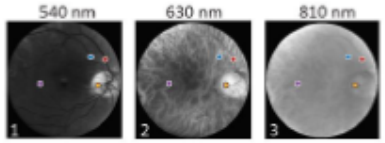
CSF biomarkers

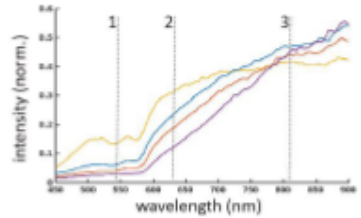
- Invasive lumbar puncture
- Availability issues
- Technical implementation issues

- **Aβ used as a biomarker:** - **Essential** component of AD
  - **Sufficient** to classify on AD continuum
- **Clinical practice could benefit from biomarker-based approaches to improve diagnosis of Alzheimer's disease and other dementias.**

The Retinal Deep Phenotyping platform

Reflectance retinal images are captured in a series of wavelengths with the Metabolic Hyperspectral Retinal Camera (MHRC) yielding spectral information at each pixel.



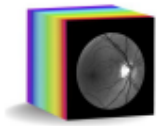


Spatial-spectral features are extracted form the data-rich images and analyzed by a machine learning algorithm relative to a recognized gold standard biomarker (in this case PET amyloid imaging).

Main objective

In this study, a Deep Retinal Phenotyping platform is evaluated for the detection of likely PET amyloid status (negative or positive) in human subjects.

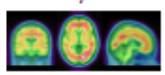
MHRC retina images



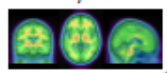
Equivalence ?

Cerebral amyloid PET

Amyloid +



Amyloid -



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Methods

Study cohort & design

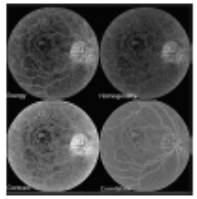
- 134 volunteers from 3 clinical sites (50 years and older)
- 92 subjects with normal and 40 with abnormal cognition
- No retinal disease (retinopathy, glaucoma or macular degeneration)
- No significant media opacity (natural or intra-ocular lens)
- Achievable good pupil dilation (≥ 6mm) and good visual fixation

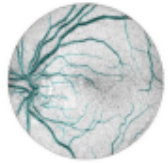
Cognitive evaluation → Pupil dilation & Ophthalmological examination → MHRC acquisition in reflectance (450-900 nm in steps of 5 nm) → Amyloid PET imaging with unanimous read from a panel of 3 reviewers

Hyperspectral image processing

- Spatial/spectral texture maps (4) are built to evaluate subtle features in the datasets invisible to the naked eye in 6 different spectral bands

Texture maps

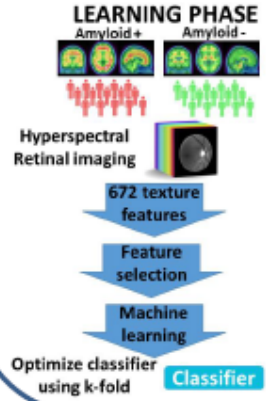


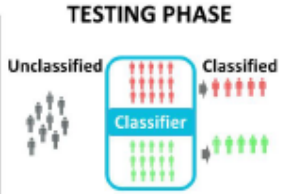


Vessel segmentation

- Image segmentation of 7 specific regions of interest (ROI) in the retina
- Calculation of 4 first order statistics for each ROI (resulting in 672 features)

Machine learning algorithm to detect the amyloid status





- 24 features were select based on F-score ranking.
- A classifier was trained on the datasets from 87 patients (2/3 of the cohort)
- The classification performance was then evaluated with the datasets from the remaining 47 patients.

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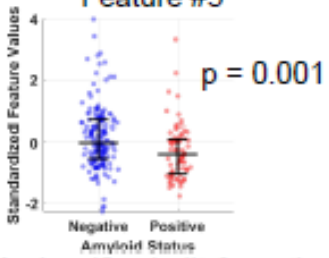
Results

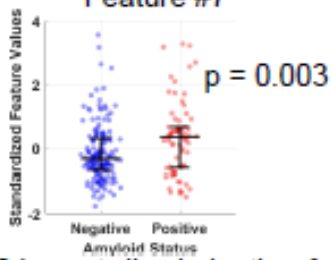
Significant differences exist between amyloid positive and negative subjects for several specific retinal image features (3 examples presented below)

Feature #3



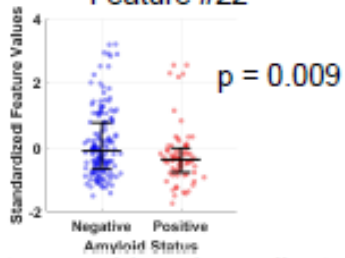
p = 0.001

Feature #7



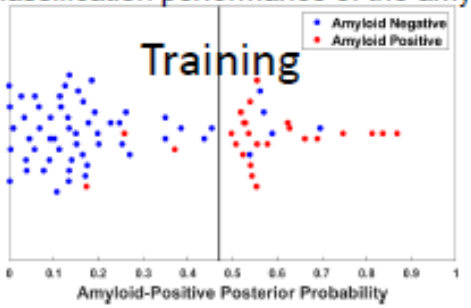
p = 0.003

Feature #22



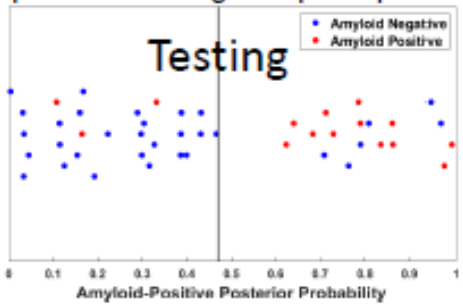
p = 0.009

A classifier built from the 24 most discriminating features achieved excellent classification performance of the amyloid positive and negative participants.



Sensitivity: 88% Specificity: 91%

k-fold loss: 19%, represents the predicted error rate



Sensitivity: 80% Specificity: 81%

Performance in agreement with the expected *k-fold* loss.

Conclusions

The Retinal Deep Phenotyping platform shows promise for detecting the likely cerebral amyloid PET status in human subjects and could serve as a screening tool to identify subjects in the AD continuum, for instance in a clinical or drug development context. The platform could also be used for the detection of other biomarkers involved in cognitive decline.

Acknowledgements

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