

Layer Specific Retinal Thickness as a Marker of Cerebral Amyloid Burden

Isaiah–Lorenzo De Guia¹, Shaun Eslick¹, Swathi Kanduri¹, Purna Poudel², Eugene Hone^{2,3} and Ralph N Martins^{1,2,3,4}

(1) Macquarie University, Macquarie Park, NSW, Australia, (2) Edith Cowen University, Perth, WA, Australia, (3) Alzheimer’s Research Australia, Perth, WA, Australia, (4) Lions Alzheimer’s Foundation, Perth, WA, Australia



MACQUARIE
University
SYDNEY • AUSTRALIA

Macular OCT reveals a depth-dependent retinal signature of cerebral amyloid: inner layers thin while outer layers thicken with increasing amyloid burden

BACKGROUND

- AD pathology begins decades before symptoms, creating demand for early, scalable, non-invasive biomarkers.
- PET/CSF quantify amyloid but are invasive, costly, and unsuitable for broad screening.
- The retina, as a CNS extension, shows amyloid deposition and structural/vascular changes detectable in vivo.^{1, 2, 3}
- OCT provides rapid, reproducible, layer-resolved metrics linked to AD-related neurodegeneration, though findings vary across studies.^{3, 4, 5}
- Few studies have related retinal structure to quantitative cerebral amyloid burden (centiloid) in cognitively unimpaired individuals.⁶

AIM

- To determine whether layer and region-specific retinal thickness is associated with cerebral amyloid burden in cognitively unimpaired adults.

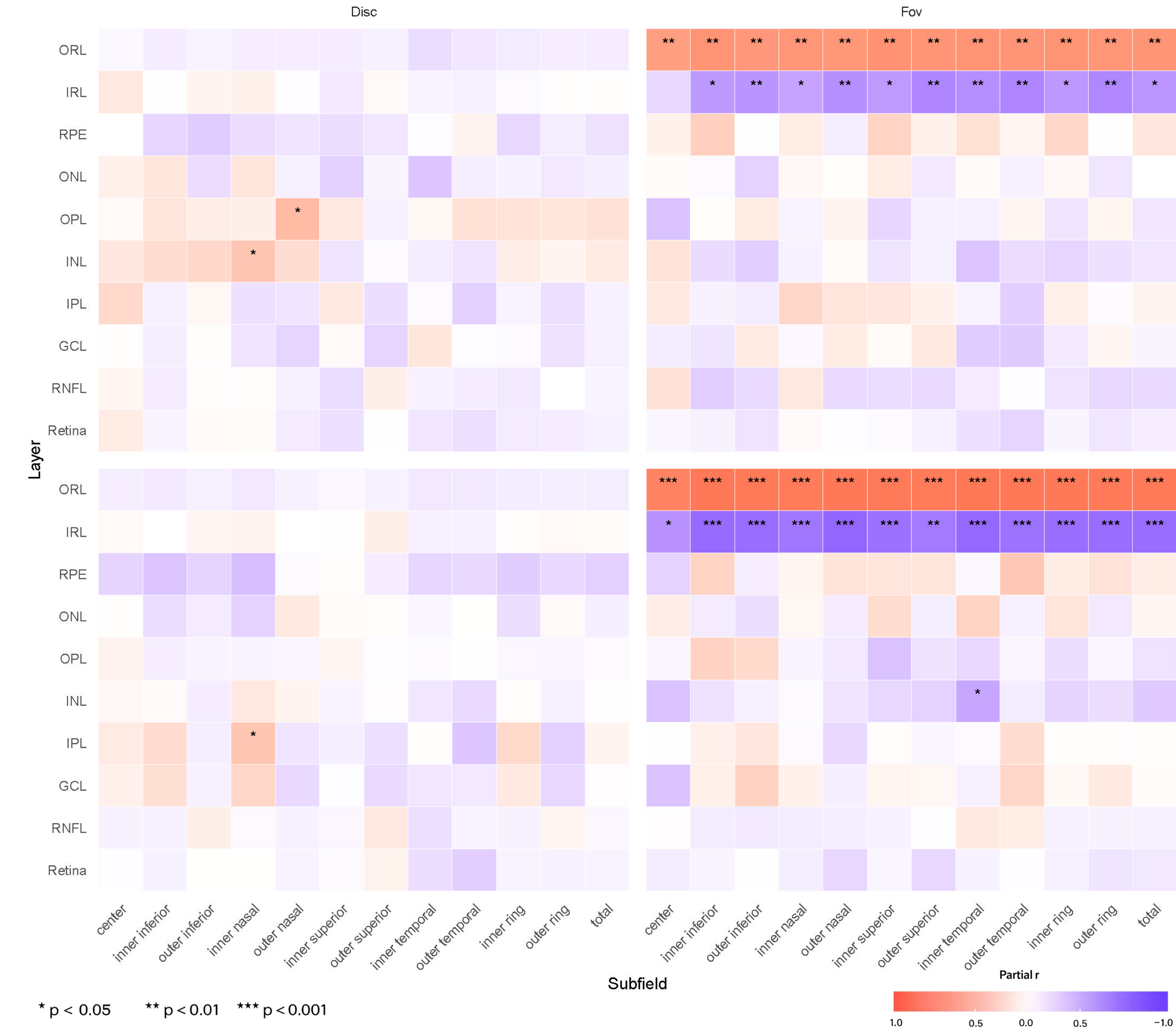
METHODS

- Participants**
- 52 cognitively unimpaired adults
 - Aβ status: 16 Aβ+, 36 Aβ –
- Imaging**
- PET: [18F-Florbetaben]; global amyloid burden (centiloid)
 - OCT: SD-OCT macular & optic-disc scans (OD/OS)
 - Retinal metrics: Layer-resolved thickness (ETDRS subfields)

Table 1. Participant Characteristics

	Age (yrs)	Female (%)	Education (yrs)	MMSE	CDR-Global	APOE ε4 Carrier (%)	Centiloid
Aβ+ (n=16)	70.2 ± 8.0	11 (68.8%)	13.8 ± 3.1	27.9 ± 2.3	0.2 ± 0.2	12 (75.0%)	54.1 ± 28.8
Aβ- (n=36)	67.5 ± 7.1	27 (75.0%)	15.5 ± 3.0	28.4 ± 1.6	0.0 ± 0.1	10 (27.7%)	2.6 ± 7.3
p-value	0.255	0.896	0.085	0.387	0.090	0.004	< 0.001

Figure 1. Layer and subfield specific correlations between macular and optic-disc retinal thickness and cerebral amyloid load



RESULTS

- OD disc:**
- Two nasal subfields showed positive associations with centiloid ($r \approx 0.30$ – 0.36).
- OD macula:**
- Clear depth-dependent pattern, IRL negative ($r \approx -0.40$ to -0.53), ORL positive ($r \approx 0.50$ – 0.56).
- OS disc:**
- One nasal IPL subfield significant ($r \approx 0.30$).
- OS macula:**
- Strong, consistent IRL negative associations ($r \approx -0.47$ to -0.66).
- Overall:**
- Inner thinning and outer thickening with increasing centiloid; spatial extent differed between eyes.

CONCLUSIONS

- Analyses highlighted consistent depth dependent associations with centiloid, where moderate negative IRL correlations and strong positive ORL correlations were observed across macular subfields.
- Divergent IRL thinning and ORL thickening patterns may reflect separate biological processes, aligning with evidence of amyloid-related IRL vulnerability and tau or gliosis related ORL changes.
- These findings highlight a potential dual-signature retinal profile in preclinical AD, warranting validation in larger, prodromal, and symptomatic cohorts.

REFERENCES

- Koronyo-Hamaoui M, Koronyo Y, Ljubimov AV, et al. Neuroimage. 2011;54:S204–17.
- Koronyo Y, Rentsendorj A, Mirzaei N, et al. Acta Neuropathol. 2023;145(4):409–38.
- Yoon SP, Grewal DS, Thompson AC, et al. Ophthalmol Retina. 2019;3(6):489–99.
- Zabel P, Przekoracka-Krawczyk A, Jaworski D, et al. Sci Rep. 2025;15(1):17287.
- Sheriff S, Shen T, Abdal S, et al. Neural Regen Res. 2023;18(11):2504–13.
- Poudel P, Frost SM, Eslick S, et al. J Alzheimers Dis. 2024;100(S1):S131–52.

CONTACT

Isaiah-Lorenzo De Guia
PhD candidate,
Macquarie Medical School,
Macquarie University, Sydney, Australia
E: Isaiah-lorenzo.deguia@mq.edu.au