

A novel imaging method for non-exudative Age-Related Macular Degeneration (AMD) identifies novel features and phenotypes of disease

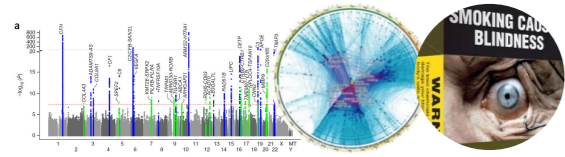
Maria Valeria Pereira da Silva, MD/PhD¹, Nehad Hirmiz, PhD², Markus Rose, PhD², Natalie Pankova, PhD³, Emily Mathieu, PhD³, Hiuyan Liang, BSc³, Matthew Mina Reyad, MSc³, Ali Khan, PhD², Filiberto Altomare, MD¹, Louis Giavedoni, MD¹, Michael Brent, MD⁴, David Wong, MD¹, Rajeev Muni, MD¹, Alan Berger, MD¹, Shelley Boyd, MD^{1,3}

1. Unity Health Toronto (St Michael's Hospital), Department of Ophthalmology & Vision Science (DOVS), University of Toronto (UofT); 2. Robarts Research Institute, Department of Medical Biophysics and Medical Imaging, Western University; 3. Department of Laboratory Medicine & Pathobiology (LMP), UofT; 4. University Health Network, DOVS, UofT

The PROBLEM

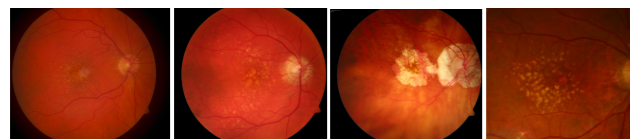
Age Related Macular Degeneration (AMD) is a complex disease

with over 50 genetic variants & significant environmental overlay



But disease classification based on current "Imaging Biomarkers" remains overly simple

with just four major subtypes of disease defined



early intermediate late dry late wet

BACKGROUND

Biomarkers are measures of health, disease, diagnosis, prognosis, response to treatment and safety

In the eye, biomarkers are Image Based, so-called "Imaging Biomarkers". These can be difficult to describe and quantify

AMDi is a novel, dye-based, non-angiographic method

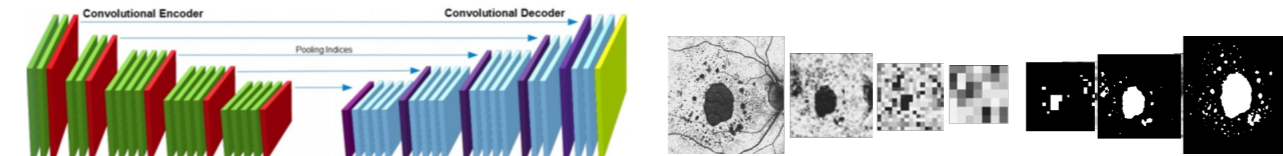
Based on laboratory studies, we suggest that AMDi can identify new features and phenotypes of dry AMD making it a potentially useful tool for improved patient classification & prediction

METHODS

AMDi was translated to the clinical setting in two REB-approved pilot natural history studies

With informed consent, de-identified demographic, health, and ocular data, along with multi-modal images (fundus photography and confocal scanning laser ophthalmoscopy) including AMDi, were reviewed. Non-image-based data were analyzed using classical (non-Bayesian) statistics (GraphPad Prism). REB: protocol 15-052

AMDi images were first analysed manually, then using simple machine learning algorithms. We have now built our own dedicated deep neural networks



HYPOTHESIS: AMDi (AMD imaging) provides new Imaging Biomarkers to describe AMD, and is safe & technically valid

RESULTS

Baseline cohort

CLINICAL CLASSIFICATION	OD	OS	TOTAL
Early AMD eyes	56	58	114
Late Dry AMD eyes	24	28	52
Late wet AMD eyes	14	6	20
Control eyes	14	14	28
Family history	2	2	4
Comparator	9	12	21
Total	119	120	239

Median ETDRS visual acuities at enrollment:

Early AMD: 75 letters (range 18-93, Snellen 20/32)

Late dry AMD: 54 letters (range 4-84, Snellen 20/63)

Definitive GA:

Is defined as >0.5-disc

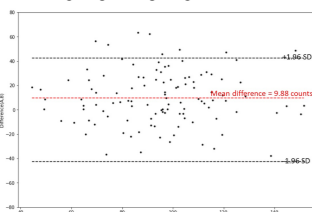
areas of GA, seen using FAF

AMDi is safe With no excess allergic reactions

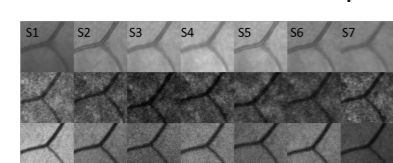
AMDi is technically repeatable at our single site

93% of fixed feature data fall within 1.96 standard deviations

Bland Altman



Fixed measurement comparisons



AMDi identifies & makes quantifiable (ie, segmentable) previously unseen features of early AMD

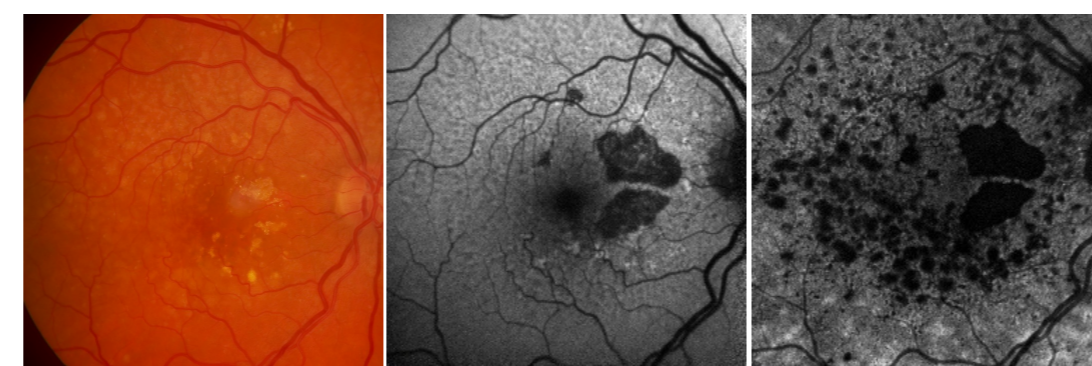


CFP

FAF

AMDi

AMDi identifies more disease, potentially prior to irreversible tissue loss



CFP

FAF

AMDi

CONCLUSION

AMDi was successfully translated from the lab to the clinical setting and found to identify new features and phenotypes of dry AMD. Based on these early translational data, larger, multi-site studies are proposed to evaluate AMDi's clinical utility

FUNDING & DECLARATIONS

Funding Support: Vision Science Research Program (VSRP), Natural Science & Engineering Research Council (NSERC) 20/20 Network, SOSCIP (Southern Ontario Smart Computing & Innovation Platform), SOSCIP/Ontario Centres of Excellence (OCE), MITACS. Dr MVPdS is funded in part by the CNIB, Dr NH is funded in part by Tracery Ophthalmics inc.

Conflict of Interest: St Michael's Hospital and Drs SB, FA, and LG are shareholders of Tracery Ophthalmics inc, an Ontario health technology corporation. SB is founding President & CEO. SB, NP and NH hold intellectual property pertaining to the technology. AK, MR, EM, MB, DW, RM and AB have no relevant declarations.