AI & Oculomics: a new section for *Eye News*

BY NIMA GHADIRI

Inaugurating this new regular section on the exciting landscape of AI and oculomics, we provide an overview which delves into the historical context and the etymology of this field, reviews the current state of play and contemplates possibilities and hopes for the future.

Oculomics refers to the marvellous role of our eye as an intimate portal into our body's health; a transparent window into the otherwise-hidden inner machinery of the body. This new field is flourishing at the intersection of ophthalmology, systemic medicine and big data analytics, and centres on an integrative and information-rich approach.

Etymology

'Omics', whether genome, proteome or even transcriptome, is a neo-suffix which expresses the use of large-scaled data sets to study the totality of a specific biological system. Oculomics blends 'omics' with the prefix 'oculo' – i.e. using information in the eye to provide a biomarker – an object which is empirical, measurable and can evaluate the process of a disease. The objective is to predict, diagnose or prognosticate systemic health conditions often years before they can be spotted.

A view to the past

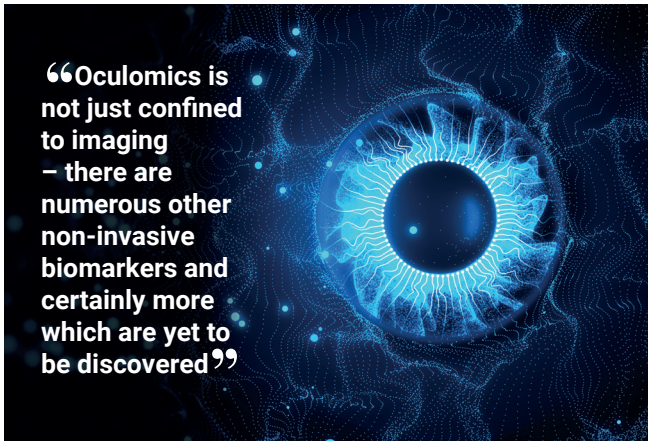
From the era of Earth's ancient empires, the eye has had a symbolic position encompassing healing of the entire body – the Eye of Horus (2686 BC-) represented protection, health and restoration – and this was intimated within early texts from the *Code of Hammurabi* to the *Ebers Papyrus*. All three 'fathers of Western medicine', Avicenna, Hippocrates and Galen, explored this link.

> "The eyes normally sparkle in tuberculosis"
>
> "Squinting eyes in postpartum fever is prognostically bad"
>
> *– Hippocrates (460–375 BC)*

The new dawn of the ophthalmic physician took place in the early 19th century, during which renowned ophthalmologist and internist Sir Arthur Ignacius Conan Doyle epitomised the detective-like approach of this epoch, where the ocular surgeon and physician worked together [1]. Further technological milestones from Herman von Helmholtz' Augenspiegel, Carl Zeiss' fundus camera to Huang, et al's optic coherence tomography (OCT) [2] allowed eye clinicians to observe the impacts of systemic conditions such as diabetes and high blood pressure in the eye – bellwethers for disease severity elsewhere in the body.

Age of oculomics

Coined in the last decade and first published in February 2020 [3], oculomics has been borne out of the desire to identify risk factors and signs of diseases at a preclinical stage, where detection of early clues can lead to earlier intervention and better health outcomes.



The most desirable biomarkers are rapidly quantifiable and cost-effective, and the omnipresence of imaging and large global datasets have meant that ocular imaging has been the keystone for an artificial intelligence (AI) revolution. With colour fundus and OCT imaging (and to a lesser extent external eye imaging) in ophthalmic clinics and community practice, there is bountiful data for training neural networks and progressive advances in multimodal imaging techniques and AI have accelerated these advances.

These last few years have seen a growing body of evidence that routine scans of the retina can reveal early signs of some of the world's most widespread and challenging conditions. For example, quantifiable retinal vascular features can help predict cardiac health and future risk factors. In neurodegenerative diseases, retinal and optic nerve architecture and nerve fibre layer thickness can predict cognitive decline and progression of disease, which yields promise for many conditions from multiple sclerosis to schizophrenia, Parkinson's disease to Alzheimer's disease.

Indeed, the link between Alzheimer's disease and changes on OCT has been accepted for decades [4], however the facility to quantify changes associated with the disease's early stage has emerged from the deep learning revolution and oculomics [5], and earlier screening will mean that the trajectory of disease progression can be diminished or averted. The current age of anticipation relies on collaboration and external validation, and it helps to have open-source, label-efficient models [6] which can be honed to work across demographic groups.

Oculomics is not just confined to imaging – there are numerous other non-invasive biomarkers and certainly more which are yet to be discovered. For example, tears contain over five hundred types of proteins and inflammatory mediators, and minimally invasive

techniques can be used for oculomic analysis. In Parkinson's disease, increased oligomeric α-synuclein in tears [7] can be a surrogate for Lewy body aggregates in the brain (substantia nigra) of patients, and may have value in predicting and prognosticating the disease at different stages. We may well see combined oculomics [8] in disease ranging from multimodal imaging to sampleable biomarkers and examination findings, together with combinations of -omics (e.g. oculomics and genomics to predict future risk of developing arterial aneurysms) [9].

Back to the future – prospects for the eye-systemic axis

Other curiosities have also been uncovered by the deep learning revolution in that certain features in the eye can essentially predict someone's age, blood pressure, body mass index, sex, smoking status, and many other risk factors not previously considered quantifiable or even identifiable in images. Appraising these inferences, discovering new links to systemic health and decoding secret health signatures (to enable earlier prognostication, diagnosis and treatment) needs to be done vigilantly. Medical ophthalmologists, trained in ophthalmology and systemic medicine [10], are essential in rationalising this fast-moving field, navigating future changes and co-ordinating interdisciplinary collaboration.

Not just uncovering new insights into full-body diseases, oculomics is strikingly placed to be the cornerstone of a revolution in Predictive, Preventive and Personalised Medicine (PPPM). This will incorporate digital health integration as devices become capable of extracting and analysing the eye's valuable real-time health data. Affordability and ubiquity of devices will allow for gaps in systemic health to be bridged in isolated or under-resourced areas throughout the world.

Oculomic profiles may become a community stalwart as a simple, quick and less invasive way of predicting systemic disease risk. In the UK, only a fraction of the population attend their regular, free NHS Health Check [11], whereas a much smaller proportion miss their local optician's visit, testament to how importantly patients view their eye health. Whereas blood tests and hospital visits are presently ways of screening for diabetes, stroke, heart disease and other conditions, perhaps oculomic services in primary care or on the high street can provide systemic health risk profiles and deliver referral guidance.

Final thoughts

This all points to an exciting future, however we are still at the clinical validation stage, and need to ensure that implementation of oculomics in screening does not compromise safety, bias and public trust. The target is to improve outcomes, reduce healthcare costs and offer patients a higher quality of life. However, we must promote standardisation, explore generalisability and algorithmic bias, improve transparency to build public trust, and pursue international collaboration towards harmonised approaches.

In the meantime, stay tuned as we continue to provide the latest updates and appraisals of this promising new field.

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Eye News is thrilled to announce the launch of our new AI & Oculomics section. This is set to be an exciting field over the next few decades, as new connections between the eye and the body are unearthed. We call on all experts and enthusiasts within this fascinating interface to share groundbreaking research, insights, innovations and reviews.