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Title	Ophthalmology and the emergence of artificial intelligence

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Ophthalmology and the emergence of artificial intelligence

Rapid advances in AI in ophthalmology are a harbinger of things to come for other fields of medicine

The autonomous detection and triage of eye disease, or even accurate estimations of gender, age, and blood pressure from a simple retinal photo, may sound like the realms of science fiction, but advances in artificial intelligence (AI) have already made this a reality.[1] Ophthalmology is at the vanguard of the development and clinical application of AI. Advances in the field may provide useful insights into the application of this technology in health care more broadly.

Artificial intelligence

Once described as the capacity of intelligent machines to imitate human intelligence and behaviour, AI now describes many theories and practices used to achieve computer intelligence (Box 1).[2] Machine learning is an application of AI that uses algorithms or statistical models to make decisions or predictions. Complex patterns and relationships are learned from data to generate an outcome.[2] Machine learning traditionally relies on the extraction of features from the data by human operators which then serve as input variables to optimise algorithm performance. The performance of these systems is constrained by the features that are recognised as important by humans.

In contrast, artificial neural networks are an advanced method of machine learning able to extract features without explicit programming.[2] Deep learning is the construction of multiple layers of artificial neural networks which can identify features in data that are not recognisable by humans. Although deep learning systems may be powerful, they lack human-crafted inputs, meaning that large quantities of data are typically required to train algorithms.

Artificial intelligence in ophthalmology

As a discipline, ophthalmology is at the forefront of AI system development and translation in clinical practice. Leading uses of the technology include detecting, classifying and triaging a range of diseases, such as diabetic retinopathy, age-related macular degeneration (AMD), glaucoma, retinopathy of prematurity, and retinal vein occlusion, from clinical images.[3] The increasing global burden of eye diseases, coupled with the development of new therapies for previously untreatable conditions, has served as a major driver for AI innovation in ophthalmology. As a case in point, there are presently over 430 million people living with diabetes, most of whom require annual or biennial screening for retinopathy using retinal photography. This vast demand for diabetic eye screening services has stimulated the development of AI algorithms to identify sight-threatening disease. Several algorithms have achieved performance that meets or exceeds that of human experts.[4,5] Accordingly, in 2018, the United States Food and Drug Administration approved an AI system to detect referable diabetic retinopathy from retinal photographs, the first autonomous diagnostic system to be approved in any field of medicine.[6]

Advances in deep learning have extended to other imaging modalities that are commonly used in ophthalmology. Ocular coherence tomography is an imaging technology that produces highly detailed, depth-resolved images of the retina. A recent collaboration between researchers and clinicians at Google DeepMind, Moorfields Eye Hospital and University College London culminated in the development of a deep learning system capable of detecting and triaging more than 50 different retinal conditions at levels equivalent to a panel of experienced ophthalmologists.[7] AI systems with the capacity to detect a wide range of diseases, such as this, are likely to be most useful in clinical practice.

A highly anticipated innovation is the development of AI systems capable of accurate disease prediction. Such tools could assist in managing patient expectations, improve the quality of care and reduce treatment costs.[3] In ophthalmology, prediction models have been trained to personalise re-treatment intervals for patients with neovascular AMD,[8] predict progression from early to late AMD,[9] estimate the extent of future visual field defects in patients with glaucoma,[10] and predict diabetic retinopathy progression.[11] Although these models presently achieve only moderate levels of accuracy, their performance has been shown to be superior to humans in several studies.[3,8] Future advances in the accuracy of prediction models will likely come from the use of large longitudinal datasets drawing on multiple data sources, together with the development of more advanced AI systems.[3]

Despite these significant advances, AI systems are not in widespread clinical use and in some cases real-world performance has been inferior compared with in silico validation.[2,3] Training and validation of deep learning algorithms with large, representative data (eg, data from people of different ethnicities) acquired using multiple devices (eg, different retinal camera models) and data collection protocols (eg, retinal photographs acquired with and without pupil dilation) are key to achieving clinical applicability.[4,5] This approach was used in the development of deep learning systems for retinal photographic screening for diabetic retinopathy, AMD and glaucoma which are now being used in large scale screening programs in Singapore and China.[4,5] In these programs, AI is used to identify images without evidence of disease, so that human graders can focus their efforts on the images of those with disease, enabling improved efficiency and cost savings.[12]

Challenges to the clinical adoption of artificial intelligence

Several obstacles to the adoption of AI in health care remain. The training of deep learning systems requires access to large amounts of medical data which has significant implications relating to privacy and data protection. In the context of ophthalmology, this is particularly pertinent, as the retinal vasculature may be considered biometric data, making it impossible to completely anonymise retinal photographs.[3] Furthermore, characteristics that are not visible to human examiners, such as age and sex, can now be accurately predicted from a single retinal photograph using deep learning.[1] Several recent major breaches of data protection laws relating to AI system development have already come to light.[13] While individual patient data used to train an algorithm do not remain within the system, incorrect handling and sharing of data may lead to patients withdrawing consent to the use of their data under General Data Protection Regulation laws. It is not certain how data withdrawal requests will be dealt with when an individual's data have been used in the process of training a deep learning system. Accordingly, developments in AI need to be accompanied by advanced data protection and security measures.

Another challenge to the acceptance of deep learning algorithms in medicine is the difficulty in determining the basis for clinical decisions made by these systems, informally described as the "black box" problem. Visualisation tools have been developed to assist clinicians by highlighting the salient image features that contribute to the AI system classification (Box 2).[12] This has the potential to create trust in system-generated decisions, particularly if the features correspond with those used by experienced clinicians for clinical decision making.[14]

Interpretability is particularly important when considering legal liability in the event of patient harm arising from the use of AI in medicine. In traditional malpractice cases, a physician may be asked to justify the basis for a particular clinical decision and this is then considered in light of conventional medical practice.[15] In comparison, challenges in identifying the basis for a given decision made by AI might pose problems for clinicians whose actions were based on that decision. The extent to which the clinician, as opposed to the technology manufacturer, should be held accountable for harm arising from AI use is a subject of intense debate.[15] Factors such as the manner in which these AI systems are used and their classification as either products or software are likely to have important bearings on how cases are litigated.[15] Further challenges for existing regulatory frameworks come from algorithms that continue to learn and evolve over time.[15] Understanding how a given system is trained, its accuracy, and its operational limits is of great importance. Oversampling of a particular population or disease severity during training has the potential to introduce bias.[4] Therefore, consideration of performance thresholds will help to inform appropriate use of AI systems.

The Australian Government, through the CSIRO and Data61;[16] the Australian Council of Learned Academies;[17] the Australian Academy of Health and Medical Sciences;[18] and specialty groups, such as the Royal Australian and New Zealand College of Radiologists,[19] have made significant efforts to develop frameworks and policies for the effective and ethical development of AI. These consultative works have highlighted key priorities, including building a specialist AI workforce, ensuring effective data governance and enabling trust in AI through transparency and appropriate safety standards. Through targeted investment in research and development, Australia is aiming to advance its AI competitiveness. These framework documents provide guidance for developers, clinicians and health care consumers to navigate this rapidly evolving field. Broad dissemination of these documents should form part of a wider public engagement and education campaign to ensure that AI is developed and used in a considered and careful manner in health care.

Rapid advances in AI in ophthalmology are a harbinger of things to come for other fields of medicine. While these technologies may eventually lead to more efficient, cost-effective and safer health care, they are not a panacea in isolation. The successful integration of AI into health systems will need to first consider patient needs, ethical challenges and the performance limits of individual systems.

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[Insert boxes]

[Box 1, sch_mja19.01290_gr1]

1 Relationship between artificial intelligence and its subtypes

[Box 2, sch_mja19.01290_gr2]

2 Original retinal photograph of right eye with macular degeneration (A). Heat map of image A showing visualisation of traditional features associated with macular degeneration, such as central scarring (B). Original retinal

photograph of left eye with referable diabetic retinopathy (C). Heat map of image C showing visualisation of traditional features, such as micro-aneurysms and haemorrhages (D)