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Augmented Intelligence in Ophthalmology: The Six Rights

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Globally, at least 2.2 billion people have vision impairment or blindness, of whom at least 1 billion have a vision impairment that could have been prevented or has yet to be addressed.[1] According to the International Council of Ophthalmology,[2,3] the number of ophthalmologists per million population worldwide is approximately 29, ranging from 0 to more than 150 from developing to developed countries.[4] Using the Lewin Model 1, the American Medical Association reported in 2013 that there will be a shortage of 5400 full-time equivalent ophthalmologists and a surplus of 3100 full-time equivalent optometrists in the US by 2026. For the Asia-Pacific region, China and India, the world's most populated countries, only have approximately 28,000 Chinese ophthalmologists and 15,000 Indian ophthalmologists to serve a 1.4 billion population and 1.3 billion population respectively.[2] The manpower shortage would be further burdened by the aging population, made worse by the COVID-19 pandemic crisis started since 2020.[5,6] Where are we now with the declaration of war on diabetes and diabetic retinopathy?[7] What about the growing burden of age-related macular degeneration with the aging population?[8] The abovementioned clinical unmet needs are challenging and require short- and long-term solutions to decrease cost and improve health care efficiency, patient care, and access to care among other issues.

Disruptive technologies such as telemedicine and artificial intelligence are well positioned to help solve some of these issues.[9–11] There are dominant factors driving change and innovations in medicine and ophthalmology, including increase in the population, increase in health care expenditure, physician shortage, and the massive quantity of data needing analytics. There is a large amount of data being generated which can affect physicians decision, including visual testing, visual fields, optical coherent tomography, longitudinal

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data, and, coming soon, remote monitoring data. In this special issue, we discuss a variety of topics ranging from big data, digital transformation of ophthalmic care, data security, augmented intelligence (AI), to the economics and ethics of AI.

In ophthalmology, it has been 5 years since the first paper published by Gulshan et al.[12] Since then, many AI groups reported robust performance in different segmentation, classification, and prediction models for various eye sub-specialties using different imaging modalities including fundus imaging, optical coherence tomography, Humphrey visual fields, etc.[13,14] To develop a robust AI algorithm, it is important to consider the 6 rights to guide the translation of AI technologies from bench to bedside.

IDENTIFY THE RIGHT "INTENDED USE" ENVIRONMENT—FIRST RIGHT

This is primarily driven by the clinicians who are responsible to identify the clinical unmet need. It is important to develop an AI algorithm that can be readily "plugged" into the digital and clinical ecosystem, irrespective of the clinical data or technical methodologies. This can be either data, image, or natural language processing based deep learning algorithms. For the clinical unmet need, it is also crucial to take into account the market size and the potential scalability of the specific AI algorithm in order to achieve the clinical impact, and potentially "return of investment" to sustain the ongoing advancement in information technology, digital integration, and maintenance cost. One could even argue that a financial simulation should be taken into account at the very initial phase to evaluate the cost-effectiveness of an AI algorithm, with its hypothesized diagnostic performance tested under different preset operating threshold (ie, sensitivity or specificity).

IDENTIFY THE RIGHT "TRAINING AND TESTING" DATASET—SECOND RIGHT

Once the intended use environment is defined, it is then important to identify the appropriate training and testing datasets. Ideally, a training dataset should simulate the representation of the population in where the AI algorithm will be implemented. The patients' profile and disease prevalence (or pretest probability) of a screening or diagnostic AI algorithm, the phenotype, data type, size, and distribution between the diseased and control, splitting of training/validation/testing are important considerations, and the power calculation of the testing dataset should be sufficiently powered to detect the difference within the intended use environment. Furthermore, the dataset will need to be appropriately deidentified and anonymized to comply with the data privacy and patients' confidentiality rules.

IDENTIFY THE RIGHT "TECHNIQUES"—THIRD RIGHT

It is crucial to identify the right technical partners to develop an AI algorithm in collaboration with the clinical teams. In the AI domain, the more popular areas are related to data- and image-based projects. Increasingly, natural language processing and speech are gaining more interest from the clinical teams. For data, the common and popular technical methodology is using various machine learning techniques, for example, random forest, XGBoost, support vector machine and others to build AI models; whereas for image,

speech or natural language processing, deep learning (DL) has shown to yield robust and breakthrough performance as compared to the pre-DL based machine learning methods.[15] For image-based DL technical network, many AI systems would have a preprocessing step to enhance the image quality before the AI analysis to boost diagnostic performance, and also identify the nature and site of the images that are uploaded for testing. To increase the AI explainability, many AI developers will also incorporate the visualization maps in an attempt to explain the rationale behind the decisions made by the DL systems. Moving forward, the adoption of novel technical methodologies involving the use of blockchain,[16,17] federated learning,[18] and adversarial attack[19] could facilitate cross-border AI collaboration while preserving data privacy in the respective countries.

IDENTIFY THE RIGHT "REPORTING" GUIDELINES—FOURTH RIGHT

To report the AI diagnostic performance, it is important to follow the international reporting standards as per medical devices. The US Food and Drug Administration (FDA) has published a guideline stating that all software (including AI) will be treated as medical devices for regulatory applications and approvals.[20] The AI performance will need to be tested in the intended use environment. Conventionally, all the diagnostic devices are required to follow the international guidelines such as the Standards for Reporting of Diagnostic Accuracy Studies (STARD),[21] Consolidated Standards of Reporting Trials (CONSORT)[22], and more. In 2020, the CONSORT-AI and Standard Protocol Items: Recommendations for Interventional Trials-AI (SPIRIT-AI) were published to guide the clinical trials related to AI studies,[23] and a few (eg, STARD-AI and Developmental and Exploratory Clinical Investigation of DEcision-support systems driven by Artificial Intelligence)[24,25] are currently underway. Moving forward, all these new AI extension guidelines potentially could help streamline the reporting standards and terminologies.

IDENTIFY THE RIGHT "ENABLER"—FIFTH RIGHT

AI systems could be deployed in the cloud, standalone desktops/laptops, or within the imaging devices. For cloud deployment, it is important for the AI developers to also design a digital telemedicine software to support the deployment, in compliance with the cybersecurity framework in the health care system. Before clinical deployment, it is important for the AI developers to apply for International Organization for Standardization (ISO) 13485:2016 and seek regulatory approval from US FDA, European CE Mark, Chinese FDA or the regulatory body from the individual country. The submission of regulatory applications could be challenging to the clinical or technical teams, and this may sometimes require engagement with the regulatory consultants. Furthermore, the collaboration with the health economists team is equally important to evaluate the cost-effectiveness of an AI algorithm within real-world clinical settings.[26,27]

IDENTIFY THE PATIENT'S RIGHT AND THE ETHICS OF AI—SIXTH RIGHT

As the role of AI in medicine continues to expand, it raises many ethical dilemmas that span the field of medical education, research, practice and impact patient care.

In 2014, President Obama and the White House Office of Science and Technology Policy identified “big data” as both a strategic priority and an area of legal and ethical concern. The administration committed to support big data’s mammoth potential while also ensuring that it does not create unintended ethical and discriminatory consequences.[28–30] Some of the ethical dilemmas or challenges are:[31]

- Data ownership and the ability to share data while protecting patients’ privacy
- Patient-related ethics such as patient’s consent
- Machine learning—accuracy and transparency
- Liability

Before the wide implementation of AI in medicine, there should be an agreed-upon universal standardization for the ethical use of AI in medicine that takes all the stakeholders into consideration.

Apart from the abovementioned 6 rights, there are pressing needs to improve the AI education within the current and next generation of ophthalmologists in both developed and developing countries. The recent call in image standardization by the American Academy of Ophthalmology, endorsed by the Asia-Pacific Academy of Ophthalmology, could also be another big step forward to expedite the use of AI within the ophthalmology space. The challenges of AI adoption consist of “black box” issues, AI trusts and ethics, cost for implementation and deployment, and the “valley of death” between the initial prototype to regulatory application/approval. The COVID-19 pandemic crisis is an unfortunate, disastrous infection that has severely hit the world, although it has also catalyzed the use of digital technologies significantly among the global population, ranging from young children to the elderly.

> “Never let a good crisis go to waste”
>
> Sir Winston Churchill

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