Editorial

Actions are needed to develop artificial intelligence for glaucoma diagnosis and treatment

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Glaucoma is one of the most common ocular diseases that cause irreversible vision loss (1). Because glaucoma has no symptoms until the end stage, with severe visual field defects, patients should be screened for early intervention. To reduce the socioeconomic burden of glaucoma, artificial intelligence (AI) systems are urgently needed to diagnose, monitor, and treat glaucoma. Goldmann *et al.* described the functional requirements for building a patient-centric computerized AI-based system for glaucoma treatment and care ecosystems (2).

There are many obstacles to overcome to develop artificial intelligence for actual clinical practice. This section briefly reviews the efforts required for the development of AI for glaucoma diagnosis and treatment (*Figure 1*). First, the criteria for glaucoma diagnosis should be standardized. As commented by Goldmann *et al.* (2), there is currently a lack of a standardized "ground truth" definition of glaucoma. The spectrum of glaucoma is wide (3), and there is a shortage of glaucoma experts worldwide (4). Therefore, the patterns of dealing with glaucoma are slightly different for each expert, and the treatment criteria differ. This problem poses many obstacles to the development and clinical validation of diagnostic devices for glaucoma. For a more accurate performance, it is important to compare and standardize glaucoma diagnostic data at as many centers as possible and train the AI model based on this verified dataset.

Second, it is important to analyze the time-series and multimodal data of patients with glaucoma. The evaluation of glaucoma commonly involves measuring intraocular pressure, fundus photography, optical coherence tomography, and visual field sensitivity. In addition to the current damage condition, progression of functional or structural damage during follow-up is an important factor in the diagnosis and treatment of glaucoma (5). Each measurement reflects only a few clinical aspects of glaucoma. In addition, errors often occur in one measurement domain; therefore, other domains must be complemented to evaluate glaucoma. Recently, time-series analyses (6) and multimodal deep learning models (7) have been studied for glaucoma diagnosis. In the future, large-scale data analyses based on these approaches will succeed in a more accurate glaucoma evaluation.

Third, detailed data on neurodegenerative and systemic metabolic conditions should be collected along with glaucoma data to predict progression. It is well known that glaucoma is a multifactorial disease associated with metabolic diseases such as diabetes and hypertension (8). In addition, neurodegenerative diseases have been shown to be predictable by fundus photography, and most are closely

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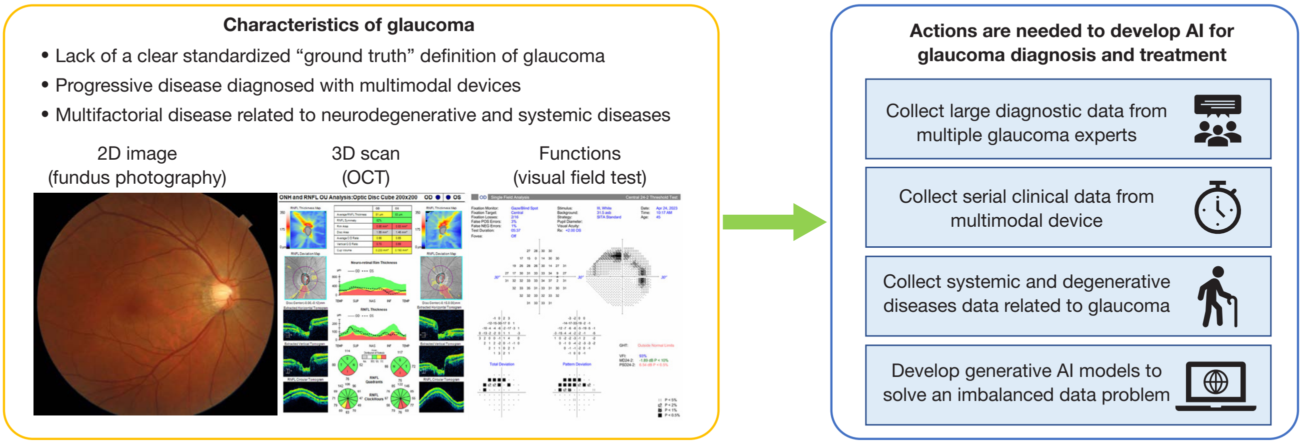

Figure 1 Summary of the proposed actions to develop AI for glaucoma diagnosis. OCT, optical coherence tomography; AI, artificial intelligence.

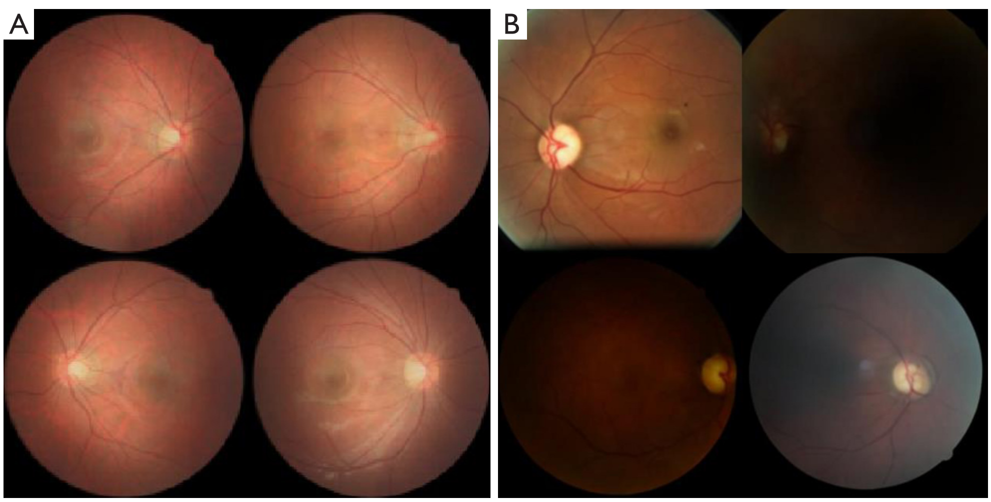

Figure 2 Examples of synthetic fundus photographs using diffusion generative models. (A) Healthy fundus images generated by a basic DDPMs trained with a small dataset (13). (B) Glaucomatous images generated by the Medfusion model trained with a large dataset (14). All images were generated according to publicly available materials (https://github.com/lucidrains/denoising-diffusion-pytorch; and https://huggingface.co/spaces/mueller-franzes/medfusion-app). DDPMs, denoising diffusion probabilistic models.

related to the optic nerve head and the retinal nerve fiber layer in glaucoma (9). AI technology based on multimodal deep learning is increasingly used to analyze high-definition images in every area to reveal the relationship between systemic diseases and retinal images in greater detail (10).

Finally, generative AI techniques should be applied to overcome the lack of pathological data. Data shortages frequently occur because of security or privacy issues. Learning about the imbalanced medical data may result in biased diagnostic model (11). Data augmentation techniques are required for accurate diagnosis in the clinical field, and recently developed generative deep learning models such as generative adversarial networks (GAN) provide solutions to this problem (12). Although still in their infancy (*Figure 2*), diffusion models, which are newly introduced generation technologies after GAN, can generate fundus photographs (13). As data quality is increasingly improved based on a large amount of data, realistic generative fundus images will be synthesized based on a large amount of data in the future (14).

In conclusion, various strategies are required to develop artificial intelligence for glaucoma diagnosis and treatment. As Goldmann *et al.* commented (2), this cannot be solved at once and should be based on the interdisciplinary integration and mutual support of all complementary approaches. I believe that this article summarizes all background factors of computer-aided clinical diagnosis, monitoring, and treatment for glaucoma; therefore, researchers interested in this field must check the issues related to AI for glaucoma.

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