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| **Abstract:** | This submission is in response to the ITU-T Focus Group on Artificial Intelligence for Health (AI4H)’s call for proposal on use cases and data. It presents an initial feasibility analysis of establishing an AI retinal analysis system from both technical and evaluation perspective. The general interpretable architecture and models for detecting diseases, including diabetic retinopathy (DR), glaucoma (GC), and age-related macular degeneration (AMD), will be discussed. Additionally, a retinal image quality assessment module is also proposed to ensure that the eye-disease detection models can be used for various real-world tasks and situations. |

**Overview**

Deep-learning algorithms have shown promise in detecting diabetic retinopathy (DR), glaucoma (GC), and age-related macular degeneration (AMD). Some 285 million people around the world are estimated to live with a form of sight loss, and eye disease is the biggest cause of this condition. If AI algorithms can help triage patients by directing doctors to those most in need of care, it could be incredibly beneficial.

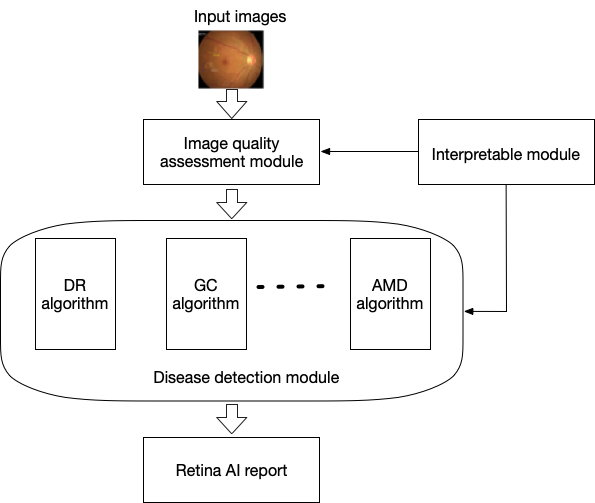
Deep learning-based screening programs offer at least four potential benefits [1].

* Increase efficiency and coverage.
* Reduce barriers to access in areas where an eye-care provider may not be available.
* Provide earlier detection of referable eye disease.
* Decrease overall health-care costs through earlier intervention in treatable disease rather than resorting to more costly interventions in more advanced pathology.

This proposal presents a solution by using AI technology for retinal image analysis. The general algorithm architecture will be discussed first. Detection models are then presented, including diabetic retinopathy (DR), glaucoma (GC), and age-related macular degeneration (AMD). Additionally, a retinal image quality assessment module for ensuring the usability of eye-disease detection models under various situations in real-world tasks is proposed. The AI algorithm integrates valuable clinical knowledge with deep-learning based end-to-end disease detection via interpretable modules. This yield benefits from both data-driven features and clinical experiences for retinal image analysis. We then provide experimental results and real-world efficacy proofing applications of the algorithms. The proposal concludes with an evaluation of AI retinal analysis system.

The general architecture of our AI retinal algorithm (shown in Figure 1) consists of three main modules:

1. *Image quality assessment module.* The fundus images typically come from different types of retinal cameras under various conditions. As a result, the images may contain undesirable artefacts (e.g. background noise), lack focus, exhibit uneven illumination or under-/overexposure, etc. Image quality plays a critical role in retinal image analysis during clinical examination [2]. Baidu utilizes an image quality assessment module to automatically evaluate the quality of a fundus image. The module strives to assess whether input images are suitable for follow-up AI algorithms to detect eye diseases. In the event the input image fails to pass this assessment module, the patient will be requested to retake another picture.
2. *Disease detection module.* This module describes several eye-disease detection algorithms, which assess whether an input image has the target diseases. The disease detection algorithms are developed in parallel. To date, AI algorithms for detecting diabetic retinopathy (DR), glaucoma (GC), and age-related macular degeneration (AMD) have been developed.
3. *Interpretable module*. A medical report relies on reliable interpretation of an AI-based disease conclusion. Therefore, this module is designed to provide evidentiary support for the disease-detection module. As most eye diseases are determined based on the type of lesions at specific areas in the retina, theinterpretable module conducts lesion detection (e.g. differentiating micro-aneurysms, haemorrhage, exudates, etc.) and critical area of interest (AOI) extraction (e.g. optical disk & cup, macular region, blood vessels, etc.) from the retinal images. This module is embedded into both quality assessment and disease detection modules, which aligns clinical experiences with massive data-driven features to make each module more interpretable and more confident.



**Figure 1.** Overview of the AI retinal algorithm architecture. DR, GC and AMD refer to diabetic retinopathy, glaucoma, and age-related macular degeneration, respectively.

# Impact

This section explains the significance of the problem we are going to solve. The general interpretable architecture and models are built for detecting diseases, including diabetic retinopathy (DR), glaucoma (GC), and age-related macular degeneration (AMD). The potential impact of the project can be described as the following three parts.

***Diabetic Retinopathy (DR)***

Diabetes is a growing epidemic both in U.S. and internationally. Current estimates show that more than 30 million Americans have diabetes [3]; this number exceeds 400 million worldwide. Both of these figures continue to rise at staggering rates that surpass most predictive models [1]. Despite well-established guidelines for screening and potential early detection of DR by an eye-care provider, 30 to 50 percent of people with diabetes do not adhere to these recommendations for a multitude of reasons.

***Glaucoma(GC)***

There are nearly 40 million blind people in the world today, according to World Health Organization [9]. Another 285 million have visual impairment. Globally, 8% of all blindness is attributable to glaucoma, is the leading cause of global irreversible blindness [10]. There were 60 million people with glaucoma in the world in 2010 and will be nearly 80 million by 2020. Of these 60 million, 7.4 million were bilaterally blind from glaucoma in 2010 and 11.2 million14%will be bilaterally blind in 2020.

In China, according to a study, it was estimated that 9.4 million (2.6%) people aged 40 years and older have glaucomatous optic neuropathy [11]. Of this number, 5.2 million (55%) are blind in at least one eye and 1.7 million (18.1%) are blind in both eyes.

***Age-related Macular Degeneration (AMD)***

According to Lancet research, the number of people living with macular degeneration is expected to reach 196 million worldwide by 2020 and increase to 288 million by 2040 [16]. And AMD is a leading cause (3rd) of vision loss worldwide, by 2010, it has been responsible for approximately 5% of all blindness globally [17]. Age is a prominent risk factor for AMD. The risk of getting advanced AMD increases from 2% for those ages 50-59, to nearly 30% for those over the age of 75. Studies suggest in China the prevalence of early AMD in Chinese persons aged 50 years or older was 9.5% and that of late AMD was 1.0% [18].

# Existing Work

This project is not starting from scratch. There are lots of experiences that can be used as a basis.

***Diabetic Retinopathy (DR)***

Publicly available datasets include the EyePACS dataset (around 90,000 fundus images, 5 levels of severity), MESSIDOR dataset (1,200 images, 4 levels of severity), the DIARETDB dataset (around 200 images marked with lesions), etc. By now IDx-DR is the first FDA approved device for AI DR screening [7]. Based on a customized CNN architecture and lesion characteristics, this device can achieve a sensitivity of 96.8% and a specificity of 87%. The best reported performance on binary classification of no DR/non-referable DR vs. referable DR is a sensitivity of 94% and specificity of 98% by [4]. This work combined features both from deep ResNet and from meta-data, and classified the features with a gradient boosting decision tree. For five level classification of no DR, mild, moderate, severe non-proliferative DR, and proliferative DR [5, 6, 8], the best accuracy reported is 96% by a combination of GoogleNet and ResNet model [5].

***Glaucoma(GC)***

Existing datasets include Online retinal fundus image dataset for glaucoma Analysis (ORIGA, 650 fundus images), Retinal fundus images for glaucoma analysis (RIGA, 760 images), ACHIKO-K (258 images), DRISHTI-GS (100 images mainly for optic disk and cup segmentation), etc. AI practice on suspected glaucoma classification generally follow two approaches, i.e. an end-to-end whole image classification [12, 13], or a classification based on optic disk and cup information [14, 15]. For the end-to-end approach, [12] reported a resulting AUC of 0.986 by training an inception-v3 network on their private dataset of 48000+ images. [15] set up a multitask deep CNN model based on a U-net sharing features for the glaucoma classification task and the disc and cup segmentation task, achieving an AUC of 0.95 while providing some medical interpretability.

***Age-related Macular Degeneration (AMD)***

Currently, most existing work of detecting AMD in fundus images address the problem as a binary classification between no/early stage AMD and intermediate/advanced stage AMD. The two commonly used datasets are the Age-Related Eye Disease Study (AREDS) dataset, which consists of fundus images from around 4,700 participants, and the Cooperative Health Research in the Region of Augsburg (KORA) dataset, which consists of fundus images from 2,840 patients. Most state-of-the-art methods for AMD binary classification are in one of the three following categories:

1. Using CNNs of existing architectures such as GoogleNet, VGG, etc. [19, 22]. The best reported performance of this type of method is 94.3% accuracy [19], using an ensemble of several CNNs.
2. Using customized deep CNN models [20, 21, 23]. The best reported result is an AUC of 0.96 and an accuracy of 91.6% on AREDS dataset.
3. Using deep image features from pretrained CNN model and then classify with SVM or Random Forest model [24, 25]. The best reported accuracy is 93.4%.

# Feasibility

Currently, Baidu has established automatic detection of DR, AMD and GC through retinal fundus image analysis. Future directions include detection of all diseases that can be detected early by retinal imaging. To achieve this goal, Baidu is expending its collaborations to more hospitals and ophthalmologists. A large-scale fundus image tagging system for more detailed objective clinical annotation is also under development.

In Baidu, the base component guarantees big data storage, processing, and security capacity. The AI technique component will integrate various Baidu AI technologies for reinvigorating retinal imaging, including knowledge graph, voice recognition, face recognition, etc. These extra technologies dramatically enhance the user experience and facilitate the incorporation of the AI retinal image analysis algorithms into an AI retina robot.

Baidu’s DR algorithm is currently being applied in one of its partner companies, which owns 22 eye-disease screening centres in 18 cities of 8 provinces in China. The DR algorithm achieves over 90% on both sensitivity and specificity measures. The sensitivity and specificity results from the real-world screening centres, which apply Baidu’s algorithm, is anticipated to be 92.1% and 90.3%, respectively.

The application of Baidu’s AI algorithm in real-world scenarios creates a positive feedback loop for improving both the algorithm performance and the data collection process. The algorithm can improve when more training data is available. Similarly, the data collection is made easier when the algorithm performs well so that can expand to more application scenarios.

Based on Baidu’s current AI research ability, big data infrastructure, sufficient funds,and close cooperation with top ophthalmic hospitals and fundus camera manufactures, this AI retinal disease detection project is feasible.

# Data Availability

To evaluate the effectiveness of our algorithms, experimental results on several datasets and real-world application performance are provided. The dataset consists of 30,000 images from several hospital partners. Each fundus image is annotated by at least three ophthalmologists, and the final disease label of each fundus image is confirmed by all annotators. Each image is assessed for overall image quality (fully gradable, partially gradable or non-gradable) and gradability (gradable/non-gradable) for DR/AMD/GC. If the overall image quality was graded as low or medium, the grader was asked to further provide label information about brightness/contrast (poor or normal), focus (in or out-of focus), and illumination (even or uneven). The gradability of DR, AMD, and GC are each assessed by a domain expert for the disease.

We, Baidu and one of its major clinical partners, Zhongshan Ophthalmic Centre, Sun Yat-sen University, China, have shared 3 well annotated fundus disease datasets to public, through a serial of online challenges, named iChallenge. iChallenge aims to invite experts and practitioners from research society as well as industrial community to participate in by developing and testing existing and novel AI algorithms. The current on-going challenges are iChallenge-GON, iChallenge-AMD, and iChallenge-PM. They are now available on Baidu Research Open-Access Dataset (BROAD) (<http://ichallenge.baidu.com)>.

For iChallenge-GON, we made available a dataset of 1200 annotated retinal fundus images from both non-glaucoma subjects and glaucoma patients. The dataset is split 1:1:1 into 3 subsets equally for training, offline validation and onsite test, stratified to have equal glaucoma presence percentage. Training set with a total of 400 colour fundus images are provided together with the corresponding glaucoma status and the unified manual pixel-wise annotations (a.k.a. ground truth). Testing consists of 800 colour fundus images and is further split into 400 off-site validation set images and 400 on-site test set images. This challenge consists of three tasks:

*1) Classification of glaucoma.* The reference standard for glaucoma presence obtained from the health records, which is not based on fundus image only, but also take OCT, Visual Field, and other facts into consideration.

*2) Segmentation of optic disc and cup.* Manual pixel-wise annotations of the optic disc and cup were obtained by 7 independent glaucoma specialists from Zhongshan Ophthalmic Centre, Sun Yat-sen University, China. The reference standard for the segmentation task was created from the 7 annotations, which were merged into single annotation by another senior glaucoma specialist.

*3) Localization of fovea (macular center).* Manual pixel-wise annotations of the fovea were obtained by 7 independent glaucoma specialists. The reference standard for localization task was created by using the average of selected annotations from the 7 annotations, for each individual image by another independent glaucoma specialist.

For iChallenge-AMD, we made available a dataset of 1200 annotated retinal fundus images from both non-AMD subjects (~77%) and AMD patients (~23%). Labels of AMD/non-AMD, disc boundaries and fovea locations, as well as boundaries of kinds of lesions are provided to train models for automated AMD assessment. This challenge also gives three tasks for participants:

1) Classification of AMD and non-AMD fundus images. The reference standard for AMD presence obtained from the health records, which is not based on fundus image only, but also take OCT, Visual Field, and other facts into consideration.

2) Localization of disc and fovea. Manual pixel-wise annotations of the optic disc and fovea were obtained by 7 independent ophthalmologists from Zhongshan Ophthalmic Centre, Sun Yat-sen University, China. The reference standard for the segmentation task was created from the seven annotations, which were merged into a single annotation by another senior specialist.

3) Segmentation of lesions related to AMD. Four typical kinds of lesions related to AMD and an individual lesion class of “others” are annotated on each image by the 7 ophthalmologists. Similarly, the reference standard for the segmentation task was created by merging the seven annotations into a single annotation, which is done by an independent senior specialist.

Similarly, we recently released the dataset for pathological myopia (PM). This dataset also consists of 1200 color images and has 3 major tasks, i.e., 1) classification of PM, HM (high myopias) and others/normal; 2) localization of disc boundary and fovea; 3) segmentation of OM related lesions. Currently, only 400 training images of the classification task are released, the annotations for the other two tasks on the training set will be released by Jan 31.

The iChallenge has three major features, comparing to other eye image datasets and challenge platforms, which offers 1) free online computation resources (on Baidu AI Studio); 2) automated performance evaluation, limited to 2 submissions per day per account; 3) onsite challenge with cash awards which also allows participants to present their work in top medical image conferences (e.g. MICCAI and ISBI).We have committed to provide these datasets at no cost for research and personal uses, and at least a new dataset will be provided every 6 months in the next 3 years.

# Benchmarking

The benchmarking process can be described as the following three parts, including the evaluation of data, algorithm and interpretation.

IQA module

We proposed *IQA module* has the following features:

1. Descriptive IQA: Identifies image quality in terms of brightness/contrast, focus, and illumination. This enables the photographer to adjust accordingly to improve image quality. This process involves three key assessment tasks: focus and clarity assessment, brightness and contrast assessment, illumination evenness assessment.
2. Disease-Specific IQA: Determines if an image is gradable for different diseases. The IQA module provides a unique gradability score for each disease classification and lesion detection task.

Detection Algorithm

The benchmarking of the algorithms for detecting DR, GC, AMD would be done on a sufficiently large data set.

The images are assigned into five DR stages (i.e., none, mild, moderate, severe, or proliferative). In the binary DR classification task, moderate, severe, and proliferative DR are considered as referable DR, while none and mild are deemed non-referable. Licensed ophthalmologists are hired to grade the images from the dataset to ensure the grading standards are consistent with accepted literature [26].

To train and test the glaucoma classifier, a large fundus image dataset was collected from several partner hospitals. Each image is labelled as a suspicious glaucoma case or a non-suspicious glaucoma case. This dataset is subdivided into three parts: the training set, the validation set and the testing set.

In Detection Algorithm of Age-related Macular Degeneration use five-fold cross validation.

In all the algorithms, the following key metrics were used for benchmarking: area under the Receiver Operating Characteristics (ROC) curve or AUC, sensitivity, and specificity. The sensitivity is the proportion of positive (disease) results which are classified properly as positive, i.e., True Positive/(True Positive + False Negative). The specificity is the proportion of negative (normal) results which are classified properly as negative, i.e., True Negative/(True Negative + False Positive). The ROC curve is constructed by selecting different operating points of the model to get sensitivity and specificity pairs and plotted on a graph, and the area under the curve can be computed accordingly.

[Interpretable module](#_vx1227)

This module analyses eye diseases in a fine-grain scale and provides convincing evidence for disease detection. Notably, this module is embedded in each aforementioned disease detection algorithm, including DR lesion detection, AMD drusen and neovascularization detection, and GC optic disc/cup segmentation. Additionally, key structure (e.g. optic disc region, macular region, blood vessels, etc.) extraction is also included in the interpretable module, providing valuable information for image quality assessment.

# Organizer Details

The document is proposed by Baidu, which is an international company with leading AI technology and platforms. Our retinal algorithms focus not only on inputting an image and outputting several eye-disease risks, but also building a powerful AI retinal system that integrates all related AI capacity to provide better service and enhance the end-user experience. The AI retinal system aims to build a personal eye-health management and analysis platform for each user. Baidu’s mission is to defend people’s eyes and global health with AI.

Since 2016, Baidu has positioned AI as a strategic driver for the development of its business. Under the strategy of “strengthening the mobile foundation and leading in AI”, Baidu has steadily improved its AI ecosystem, with productization and commercialization continuing to accelerate.

As integral components to its overall AI ecosystem, Baidu has developed two open ecosystems - the Apollo open autonomous driving platform and DuerOS, the company’s conversational AI system, which operates in two important scenarios – intelligent driving and smart homes. So far, with its latest iteration – “Apollo 3.0”, Baidu’s autonomous driving platform has brought together over 130 partners and has been granted the first batches of licenses for autonomous driving public road tests from Beijing, Chongqing and Fujian. In the smart living field, Baidu has co-launched over 160 DuerOS-powered hardware products, covering smart speakers, children’s wearables, televisions, automobiles, hotels and other vertical businesses. In September 2018, the install base of DuerOS reached 141 million devices with over 800 million voice queries. After years of commercial exploration, Baidu has formed a comprehensive AI ecosystem and is now at the forefront of the AI industry in terms of fundamental technological capability, speed of productization and commercialization, and “open” strategy. In the future, Baidu will continue to enhance user experience and accelerate the development of AI applications through the strategy of “strengthening the mobile foundation and leading in AI”.

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