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# Integrating Research, Clinical Practice and Translation: the Singapore Experience

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*Abstract*— **We introduce the experiences of the Singapore ocular imaging team, iMED, in integrating image processing and computer-aided diagnosis research with clinical practice and knowledge, towards the development of ocular image processing technologies for clinical usage with potential impact. In this paper, we outline key areas of research with their corresponding image modalities, as well as providing a systematic introduction of the datasets used for validation.**

## I. INTRODUCTION

Vision health is a key focus in Singapore, a young city-state with an urban multi-ethnic population of 5 million. Singapore has one of the highest prevalence rates of myopia in the world, with 65% of children aged 12 having myopia, in comparison to just 12% of children in Australia and 30% of children in the United Kingdom. This prevalence rises to 70% of youths at age 16, and further to 80% by age 21. The high incidence of myopia at an early age is a cause for concern as this can lead to severe myopia in later life, along with other eye-related complications such as glaucoma, age-related macular degeneration (AMD) and retinal detachment. Further, Singapore faces a rapidly aging population, with the proportion of population over the age of 65 expected to rise from 12% to 23% by 2030, coupled with higher life expectancy. This will have major implications across healthcare, in particular vision health, since many eye diseases, such as glaucoma, AMD and cataracts have been shown to be highly associated with age. To address these needs, policy makers in Singapore have implemented vision screening schemes, as well as identifying the eye and associated areas as a major research direction.

In Singapore, the Intelligent Medical Imaging (iMED) team is focused on the research and development of ocular imaging technologies. Building on years of medical imaging research experience, the iMED team (http://imed.i2r.a-star.edu.sg) works closely with domain experts such as ophthalmologists, pathologists, statisticians, optometrists and opticians to conduct deep, inter-disciplinary research. Through the Ocular Imaging Programme, the iMED team has focused our efforts in four major areas: ocular imaging-based computer-aided diagnosis/screening systems for major eye diseases; ocular imaging-based computer-aided surgical assistance technologies; ocular imaging-based high-performance identification systems and ocular medical

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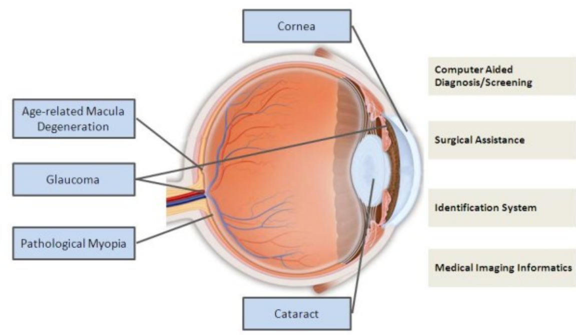


Figure 1: iMED Ocular Imaging Research

image-informatics algorithms. In the following sections of this paper, we describe our experiences, and highlight our recent advances and contributions in the field of ocular imaging research.

## II. RESEARCH AREAS

The iMED team focuses on four specific areas of research related to the eye: Ocular Disease Detection, Ocular Bioinformatics, Ocular Biometrics and Ocular Surgical Assistance, as illustrated in Figure 1. Figure 2 shows examples of some of the typical modalities we focus on.

### A. *Ocular Disease Detection*

1) Glaucoma

Glaucoma is a serious eye disease and a major global health problem; it is the $2^{nd}$ leading cause of blindness worldwide, with approximately 6.7 million blind. As vision loss from glaucoma is irreversible, early detection and timely treatment is critical for the disease management. This has motivated the development of automated detection methods for the detection of glaucoma. In our earliest paper[1], we reported preliminary results on the use of non-stereo fundus imaging for the measurement of cup-to-disc ratio (CDR), as an indicator for glaucoma. Subsequently, we developed various methods on improving the CDR, through the use of level-set based methods[2], key points[3], vessel kinking or bending as indicators of the cup boundary[4], as well as intelligent fusion of some the prior methods for optimal CDR detection[5].

In the detection of glaucoma through retina fundus images, the CDR is one of the key indicators of the disease. However, it is not the only one. Through our research and discussions with the clinical community, we developed the

AGLAIA system[6] which is based on thirteen visual cues often used by ophthalmologists in the detection of glaucoma.

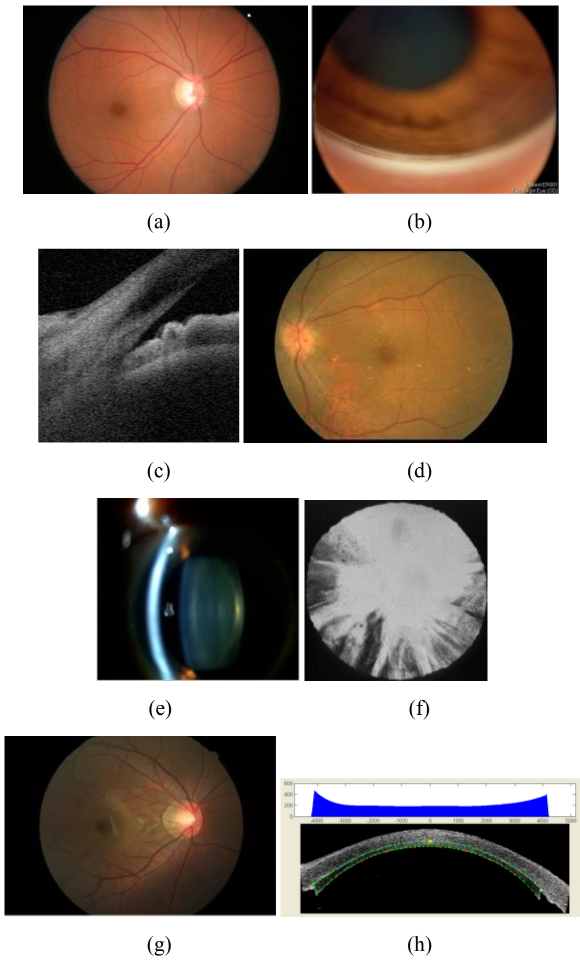


Figure 2: Images used in our research (a) retinal fundus image of a glaucoma patient; (b) RetCam image of an open angle; (c) OCT image of the angle; (d) fundus image of patient with early AMD; (e) slit lamp image of the lens; (f) retroillumination image for cortical cataracts; (g) fundus image with pathological myopia and (h) detection of corneal graft in an anterior segment OCT image.

These cues include the detection of haemorrhages and peripapillary atrophy[7]. As part of the AGLAIA system, we further improved our methods for optic disc detection[8,9] and optic cup detection[9,10], as well as automatic determination of contextual information, such as left/right eye detection[11]. Recently, the technology was non-exclusively licensed to a screening service provider.

Concurrently, beyond retinal fundus imaging, other imaging modalities have been used to classify glaucoma type, in particular from the analysis of the angle in the anterior segment. The RetCam, which was previously used to image the retinas of infants, found a new use for imaging the angle, and we developed a method for open angle or angle closure through RetCam images[12]. Optical Coherence Tomography (OCT) has also been increasingly used to image the angle by providing a cross-sectional view of the trabecular meshwork region. Using these images, a method was also developed to classify glaucoma type in [13].

2) Age-Related Macular Degeneration (AMD)

Age-related macular degeneration is the leading cause of irreversible vision loss as people age. Unlike glaucoma, which affects the peripheral vision first, in AMD, central vision is first affected by a central scotoma, causing difficulty for patients to read, drive or recognize people. AMD comes in two forms: dry, and wet or late-stage AMD. In dry AMD is the presence of drusen in the retina. Due to the lack of visual symptoms, nearly all subjects with drusen are unaware. To address this need, we developed the THALIA system for the automatic detection of drusen images. The THALIA system includes methods for the automatic detection of the macula[14] on fundus images and the automatic classification of drusen images[15]. This technology was also recently licensed to a screening service provider

3) Cataracts

Cataracts remains the leading cause of blindness in the world, accounting for nearly 50% of all blindness worldwide. There are three types of cataracts: nuclear, cortical and poster subcapsular(PSC), which are defined based on their location in the lens. Although blindness in cataracts can be easily reversed through lens replacement, there still remains a need to accurately classify the degree of progression for cataracts. To this end, we have developed automated grading systems to grade cataracts severity for nuclear cataracts[16], which are based on slit-lamp images, as well as cortical and PSC[17], which are based on retro-illumination images.

4) Myopia

Myopia is a condition of the eye in which a visual image is focused in front of the retina instead of on it, leading to shortsightedness. This is often due to the eyeball being too long axially such that the lens is unable to focus at the retina. Pathological myopia, which often occurs in severe myopia, is characterized by visible changes in the fundus image such as posterior staphyloma. If left unchecked, pathological myopia can lead to irreversible blindness. However, an assessment of the retina can often determine the presence of pathological myopia. Using some of the major cues for pathological myopia, we have developed a system[18] to automatically detect the disease, which will aid in differentiating between severe myopia and the pathological variant.

5) Cloud-based Eye Disease Screening

Cloud-based solutions have attracted much interest in lately due to the high availability and scalability offered by such platforms. We have recently begun to develop ALPACIA (Automatic On-Line Medical Image-based Disease Tele-Screening Cloud Platform with PAttern ClassIfication Algorithms), a secure, effective and accurate medical image-based disease tele-screening cloud-based service platform with tele-medicine capability. ALPACIA will be built on the development and deployment of the our ocular disease screening technologies to automate the assessment of ocular images for the tele-screening, tele-diagnosis and prediction of ocular and other diseases. The ubiquitous anywhere access cloud-based nature of ALPACIA will facilitate a more cost-effective and affordable means of disease screening

B. Ocular Medical Imaging Informatics

With the wealth of information available, there is an increasing need to analyze the totality of information available to determine any potential associations with disease. As part of the AGLAIA project, we have developed a framework called Medical Image Informatics (AGLAIA-MII), which aims to combine various sources of information to increase disease prediction. These sources of information include patient personal data, retinal imaging data and genome data. Using a multiple kernel learning approach, we found that the use of all three disparate data sources resulted in better glaucoma prediction than any single source[19].

C. Ocular Surgical Assistance

Surgery in the eye is a very delicate process, due to the small working area and the vulnerability of various parts of the eye to receive permanent irreversible damage during surgery. To assist clinicians, we are developing a framework called AEGIS (Augmented Eye Laser Treatment with Region Guidance for Intelligent Surgery) based on our expertise in ocular landmark detection to identify sensitive areas for avoidance during surgery. This will help to reduce risks and the burden on the surgeon during the surgical process.

We have also developed tools to assist surgeons monitor the outcome of the surgical process post-operatively. Specifically, the DSAEK process involves insertion of a layer of corneal epithelial cells for regeneration of traumatized cells. To track the successful adhesion of the implanted layer, we have developed a system called COLGATE[20] to assist clinicians to closely monitor the thickness of the corneal implant for better post-operative management.

D. Ocular Biometrics

A natural progression from our research into the detection of ocular landmarks is the use of detection results for identification and verification. The use of ocular landmarks is highly attractive since such features can be difficult to spoof or fool. Some of our preliminary work in this area have reported an extremely high accuracy in correctly determining the identify of individuals in a large dataset.

## III. DATASETS

Over the years, through our research, the iMED team has tested its methods using the following datasets. In this section we briefly summarize these datasets.

### *A. ACHIKO-O*

ACHIKO-O, formerly named ORIGA-light [21], is an online retinal fundus image database for glaucoma analysis and research. It is the very first database developed in our group which focuses on optic disc and cup segmentation and Cup-to-Disc Ratio (CDR). ACHIKO-O contains 650 retinal images annotated by expert graders. A wide collection of image signs, critical for glaucoma diagnosis, are annotated.

### *B. ACHIKO-K*

All images in ACHIKO-K are taken from glaucoma patients in a Korean population. The images contain rich information on glaucoma related pathological signs, e.g. hemorrhage, optic nerve drusen and optic cup notching etc. The 258 images are manually annotated with segmentation information and clinical diagnosis data. One special aspect of ACHIKO-K is, the fundus images in ACHIKO-K contains timely information recording retinal changes and can be precious resources for retrospective study. Furthermore, metadata hidden in fundus images are extracted, providing a valuable set of parameters for developing image pre-processing algorithm. For example, an image preprocessing component can make use of the metadata to do adjustment of the intensities of the colors, modification of exposure or contrast correction as well as apply image size alignment etc.

### *C. ACHIKO-I*

ACHIKO-I [22] is a specially designed retinal fundus image database which contains 179 images and is divided into two subsets for different purposes. The database has a few differences from other databases. Firstly, it aims at benchmarking of the optic disc and optic cup segmentation rather than glaucoma diagnosis. Secondly, multiple images are taken for each subject under specified conditions, providing the opportunity of repeatability test. Finally, OCT images are available for some of the images and cross modality analysis could be carried out.

### *D. ACHIKO-NC*

ACHIKO-NC is the slit-lamp lens images dataset selected from SiMES I database [23] to grade nuclear cataracts(NC). In the database of SiMES I slit-lamp lens images, the following types of images is excluded: intraocular lens (IOL) images, bad quality images graded by the clinical grader as ‘not gradable’, lens images on which the lens structure cannot be detected accurately using the automatic software [24], and the images with conflicting clinical records. The distribution of the images is shown in TABLE I.

TABLE I. Statistics of ACHIKO-NC

| Grader’s grades | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| No. of images | 94 | 1874 | 2476 | 897 | 37 |

### *E. ACHIKO-Retro*

ACHIKO-Retro is the retro-illumination lens images selected from SiMES I database [23] to grade cortical cataracts (CC) and posterior sub-capsular cataracts (PSC). Each lens has two images, anterior image and posterior image. Anterior image focuses on the plane centered in anterior cortex of the lens, while posterior image focuses on the posterior capsule of the lens. The dataset is designed to benchmark the computer-aided grading methods. The distribution of the images is as follows. C* is the grader’s grades of CC and P* is the grader’s grades of PSC. TABLE II shows the statistics of ACHIKO-Retro.

TABLE II. Statistics of ACHIKO-Retro

| Grader’s grades | P1 | P2 | P3 |
|---|---|---|---|
| C1 | 755 | 24 | 21 |
| C2 | 35 | 17 | 23 |
| C3 | 34 | 17 | 18 |

## IV. CONCLUSION

The Singapore iMED ocular imaging team has focused on integrating image processing and computer-aided diagnosis research with clinical practice and knowledge, towards the development of ocular image processing technologies for clinical usage with potential impact. The iMED team aims to build a healthy ocular imaging research eco-system enabled by technology advancement. Working with eye care professionals, ophthalmologists, optometrists, opticians, we identify clinical needs, which are used to guide our research direction. Through cutting edge research, we develop ocular imaging platform technologies, which act as the technology enablers for ocular hardware manufactures and screening service providers. Through efforts of the latter, clinicians can be equipped with better systems and the screening service providers can provide a more accurate, economic and objective service for early detection of ocular diseases.

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## WEBSITE

More information can be found at the following website: http://imed.i2r.a-star.edu.sg

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