EyRIS: From the Lab to the Market

Singapore's trailblazer AI algorithm for detecting diabetes-related eye diseases.

by Steven M. Miller, David Gomulya, and Mahima Rao-Kachroo

Can you imagine getting the results of your eye disease screening within minutes rather than days? This capability is what EyRIS, a Singapore-based start-up that uses the AI (Artificial Intelligence)-driven Singapore Eye LEsion Analyzer (SELENA+) algorithm to screen for diabetes-related eye diseases, set out to productise and commercialise.

SELENA+ was designed to screen for diabetic retinopathy[1], glaucoma and age-related macular degeneration (AMD).[2] The AI algorithm had proven that it could detect the early onset or presence of such eye diseases with speed and accuracy. The ready availability of such eye disease screening, and hence disease detection, would reduce the extent of vision degradation or loss related to these three eye diseases across populations in various countries or regions.

Jointly developed by the Singapore National Eye Centre (SNEC), Singapore Eye Research Institute (SERI), and the National University of Singapore (NUS) School of Computing, the SELENA+ algorithm leveraged a deep learning (DL) system. This approach used multiple layers of neural networks to probabilistically learn and identify complex patterns and relationships in data to analyse retinal images and detect eye diseases. Like other DL systems, the more high-quality retinal image data SELENA+ was trained on, the more it learned to improve its ability to accurately detect the eye diseases it was screening for.

In early 2018, the company EyRIS was incorporated in Singapore by a founding team of eight members to transition SELENA+ from a research and development (R&D) project to a commercial product that could be marketed and used in Singapore, as well as internationally. Seven of these co-founders were from the SELENA+ research team, which included ophthalmology researcher and clinician Dr Wong Tien Yin, the lead principal investigator for SELENA+, three other healthcare professionals from SNEC and SERI, and three computer science researchers from the NUS School of Computing. The eighth member was Lai Teik Kin, a health technology entrepreneur who became the founding CEO of EyRIS.

This article details the two-decade journey that led to the development of SELENA+, the establishment of EyRIS, and how the company addressed some of the many challenges it encountered as it launched and strove to develop a base of customers and draw in revenue.

THE GROWING USE OF AI SUPPORT TOOLS IN SINGAPORE HEALTHCARE

In recent years, the Singapore government had decided to leverage DL-based AI systems to improve healthcare delivery across the public healthcare system. Singapore's ageing population already had a high prevalence of chronic diseases, including diabetes. This substantially increased the load on public healthcare facilities. To better manage the increased load, government agencies looked toward the impressive predictive capabilities of DL-based AI systems, which were viewed as a strategic tool that could make certain diagnostic health screenings more accessible and cost-effective. Together with the Integrated Health Information Systems (IHiS)[3], Singapore's national health technology agency, the government initiated the use of DL-based AI systems in multiple healthcare applications.[4] One such initiative under Singapore's Ministry of Health (MOH) involved multiple healthcare research and clinical institutions using image-based algorithms to analyse retinal images to screen for eye diseases often associated with diabetes.

DIABETES-RELATED EYE DISEASES IN SINGAPORE

Diabetes has been a growing health concern for the Singapore government. It was estimated that one in three Singaporeans was at risk of developing the disease.[5] When studies showed that diabetic retinopathy-related vision loss could be prevented with early detection, MOH launched a national-level diabetic retinopathy screening programme as part of its broader nationwide 'War on Diabetes' in the late 1990s. The eye-disease part of this diabetes treatment strategy involved annual screenings for diabetic patients to catch the onset of diabetes-related eye diseases.

Eye screenings were conducted by family physicians who had basic training in diabetic retinopathy grading. Results often took two to four weeks to be returned to the patient, and had a high number (sometimes as high as 38 percent) of false positives, as the physicians tended to err on the side of caution.[6]

Singapore Integrated Diabetic Retinopathy Programme

To address the issues of long turnaround times for diagnostic reports, variability in interpretations across physicians, and false positives, MOH together with several healthcare public sector units started a pilot version of the Singapore Integrated Diabetic Retinopathy Programme (SiDRP) in 2010, expanded it, and officially launched the effort in 2012. Through special infrastructure created to support SiDRP, retinal images were transmitted to a centralised facility via a tele-ophthalmology network. All of these images were reviewed by both a trained Level I human 'grader' (assessor) and an expert Level II human assessor. This ensured a more standardised and controlled process of evaluation by trained human image assessors. This new process eventually led to many advantages. Turnaround time improved significantly from two to four weeks originally to one business day, and often within an hour. The costs of eye screenings also substantially decreased.

SELENA+ AND THE *JAMA* PUBLICATION

In the early 2000s, Dr Wong and two NUS computer science professors, Dr Wynne Hsu and Dr Lee Mong Li, worked together to develop software algorithms to analyse retinal images for common eye diseases. In 2014, ophthalmology researcher and clinician Dr Daniel Ting, who had also been investigating the use of AI-based software algorithms to analyse eye images as part of his ongoing PhD work, joined the effort. The expanded team created a next-generation, deep-learning-based retinal image analysis system called SELENA+.

To train SELENA+, the team utilised the retinal images which had been collected, labelled for the three eye diseases, and then graded during SiDRP's initial years. As the SiDRP effort continued from 2012, multiple healthcare clusters[7] and IHiS worked together to improve the procedures and standardise the workflows associated with the eye screenings. The SELENA+ R&D team used not only high-quality Singapore-based SiDRP data sets, but also several other international data sets that included other ethnicities beyond those in the Singapore sample, to train, test, and evaluate the system. This combination of using the newest generation of DL methods and high-quality data sets led to the success of SELENA+.

The SELENA+ R&D team submitted their findings to the *Journal of the American Medical Association* (*JAMA*), a prominent, high-impact medical research publication. Much to their elation, after a lengthy review process, their results were published in December 2017. The *JAMA* publication was a feather in their cap, as it showcased both the robustness of their results and the rigour of their approach. It validated the software and gave the team a higher standing in the international medical science community, as well as in Singapore's domestic R&D funding community. The team also noticed that applying for R&D grants to refine and more extensively test SELENA+ became easier as the publication helped with securing buy-in from MOH. It also further set the stage for moving ahead to follow on commercialisation and regulatory approval efforts.

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R&D testing of SELENA+ in SiDRP

Given the R&D progress that had been made with SELENA+ as demonstrated by the *JAMA* publication, the natural next step was to use the system within SiDRP. As SELENA+ was still an R&D effort under evaluation, human graders were required to do first- and second-level image evaluations. SELENA+'s results were generated and checked against the human assessors' results.

SELENA+ was tested within SiDRP during 2018 and 2019. This created extra work for the human evaluators and supervisory staff at the centralised image assessment facility. Not only did they have to complete their existing workload of analysing regular evaluations, but they also had to compare their evaluations to those generated by SELENA+ and note if the human-versus-AI algorithm results agreed or disagreed. However, this was the safe and assured way to pilot-test SELENA+'s capabilities in a situation that was very similar to under real-world operating conditions. Towards the end of 2019, this one-year testing effort concluded with an overall positive assessment of SELENA+'s capabilities and performance.

EyRIS

In parallel, while SELENA+ was being tested, the research team felt that the SELENA+ algorithm had real-world applicability. As a commercial product, it could be used by multiple parties, not only a wider audience including private sector healthcare providers in Singapore within SiDRP, but also internationally. SELENA+ seemed like a good solution to meet eye disease screening needs for countries with underserved population segments and overburdened medical staff.

In 2016, Lai Teik Kin, a healthtech and IT entrepreneur with business interests in Singapore and the region, was appointed as a business mentor by SNEC. The SELENA+ research team required commercialisation help and Lai was looking for new business prospects.

Based on discussions with the relevant Singapore authorities, the SELENA+ members became aware that marketing their software had to be done by an independent start-up entity. This was because commercial products could not be marketed by a government healthcare institution, or by a government-sponsored university like NUS. Furthermore, a separate commercial entity was required to apply for regulatory approval. Without such approval, SELENA+ could not be used on an operational basis to support the SiDRP effort, nor could it be commercialised. But first, they needed a CEO for the start-up.

Lai threw his hat into the ring and submitted a business plan for evaluation. He became the founding CEO, and the start-up entity was named EyRIS. In February 2018, the company was officially incorporated as a private limited company in Singapore, partly owned by Lai's healthtech and software technology company novaHEALTH Pte Ltd. EyRIS became the official licence holder for SELENA+ in September 2018 after working out the intellectual property licensing terms with SERI and NUS.

Regulatory approval in Singapore

To commercialise SELENA+, which was previously only used in R&D studies, the EyRIS team had to first apply for regulatory approval. It was a first for both–the Singapore medical regulatory authority receiving a request to approve an autonomous AI software system as a medical device, and EyRIS making a regulatory submission. Dr Gavin Tan, who was Clinical Director of the SNEC Ocular Reading Centre, often accompanied the EyRIS commercial team for their meetings with the Singapore regulatory authorities, and played an important role in answering medical and operational queries regarding screening and image evaluation, during the back-and-forth clarifications between EyRIS and the medical device regulator. EyRIS finally submitted its documents for regulatory approval in July 2019, and in October 2019, it was granted approval to use SELENA+.

This was an important milestone for EyRIS as it could now productise the software for operational usage in Singapore's public healthcare sector via SiDRP and also in the private sector. Regulatory approval had another practical advantage. It eliminated the need for each patient to sign a consent form that granted the research team permission to use SELENA+ to analyse the patient's eye image as part of a research study.

However, regulatory approval came with its own caveats. The team discovered that every time it fine-tuned SELENA+, it had to do so within a well-defined 'limit'. If the changes exceeded this limit, they were considered a major modification, or the newly-revised algorithm was considered a new product altogether. Both scenarios would have required new submissions for regulatory approval. Hence, modifications to improve SELENA+ had to be very carefully targeted.

EyRIS introduces SELENA+ to the market

While Team EyRIS aimed to offer its software as a product to the public and private sectors, it knew that scalability in Singapore would initially come through public sector sales. Hence, after receiving regulatory approval, it commenced parallel discussions on deployment-related technical, regulatory, governance and commercial issues with IHiS, and with the two public healthcare units that would make direct use of SELENA+ as part of SiDRP, the centralised Ocular Reading Centre at SNEC (under SingHealth), and at the National Healthcare Group Eye Institute.

One of the more complex governance issues that had to be worked out was how to arrange for independent evaluation by knowledgeable medical staff at these two public healthcare institutions who had no direct interest with SELENA+ or EyRIS, especially given that four of the EyRIS founding team members were staff members of SNEC, and had been deeply involved in various aspects of SiDRP and SELENA+. It was critical for these evaluations to be above board to avoid any conflict of interest. Another complex issue was working out the proper procurement processes and evaluations for a multi-year exclusive contract. A third complex issue was preliminary planning for how SELENA+ would be integrated and used within the overall SiDRP process, as this would influence technical, regulatory, and commercial issues.

Obviously, these types of investigations and negotiations were complex, and would take a long time to come to fruition and yield revenue. During that time, the use of SELENA+ was put on hold within SiDRP. Then, in November 2019, the Singapore Smart Nation and Digital Government Office (SNDGO) released a national AI strategy document that mentioned the usage of SELENA+ as part of SiDRP as a marquee example of a national AI initiative in the country's healthcare sector.[8] This was an acknowledgement that Singapore's public healthcare sector would likely be embracing the use of SELENA+.

A private-sector expansion strategy that gained traction was inking agreements with international optometry professional associations, large optometry practices, and diabetes prevention associations.

At the same time, the team looked at selling SELENA+'s solutions to Singapore's private sector market to generate near-term revenue. In January 2020, EyRIS signed a contract with the Singapore Optometric Association, which established the company's very first stream of revenue. It had not come easily, as ironically, many private optometry practitioners were worried that the algorithm would eat into their existing revenue streams, while public healthcare sector practitioners were overwhelmed by the sheer number of eye disease screenings that had to be done. By September 2020, 23 private optometry shops had signed up to use SELENA+ to offer eye disease screening as a supplemental service.

While negotiating for licensing and usage within Singapore, the team also actively explored the possibility of entering international markets. After receiving Singapore's regulatory approval, it prepared regulatory submissions to healthcare regulatory authorities in Malaysia, Brazil, Indonesia, and the European Union (EU). Singapore's regulatory 'stamp of approval' was an important enabler in gaining the eventual approvals that followed.

Incorporating SELENA+ into SiDRP as an EyRIS product

Finally, in September 2020, IHiS signed a five-year contract with EyRIS to deploy SELENA+ within the SiDRP national screening programme. This was the world's first implementation of an AI-driven software in a national screening programme. IHiS would pay EyRIS fees for up to 120,000 annual SiDRP screenings.

After finalising the contract with IHiS, another year-long phase of testing started in December 2020. It focused on the detailed operational aspects of how to integrate the SELENA+ system into the overall SiDRP data flows and work processes, and also how to combine the capabilities of both the human assessors and the AI system. SELENA+ was used to provide a 'preliminary assessment' of the retinal image and pre-populate parts of the SiDRP evaluation report template, followed by an accuracy check by both a Level I and Level II assessor.

This hybrid machine-human approach allowed the SiDRP effort to scale to higher levels of daily throughput and yearly output, and at the same time, provided a cautious pathway for assuring quality, managing risks, and gaining more real-world operational experience. It was envisioned that human labour requirements for Level I screening would gradually decrease as SELENA+'s performance within SiDRP was further fine-tuned and incrementally improved. A number of private sector clients chose to use SELENA+ in either a semi-automated mode or a fully automated mode as it had received regulatory approval to be used as a diagnostic screening device in this fashion. This was especially since they did not have the resources and infrastructure of Singapore's public healthcare system to use SELENA+ with Level I and II human assessors.

Despite the successes involved in using SELENA+ within SiDRP, some public healthcare system patients pushed back on the use of AI for their eye screening diagnosis. This concern was managed by informing them that the SiDRP screening process involved two levels of human image evaluation in addition to the first level algorithm assessment.

Strengthening and expanding EyRIS' business development

To drive EyRIS' business expansion, which included obtaining regulatory approval overseas, Lai invited dentist and oral surgeon Dr Steven Ang, who had entrepreneurial interests, to help him with his business development efforts. In April 2020, Dr Ang joined novaHEALTH, EyRIS' parent company, and eventually was transferred to EyRIS to head its business development department.

The EyRIS team also explored leveraging relationships with companies that manufactured the special cameras used to capture retinal images. In November 2020, EyRIS signed a deal with one such manufacturer, Topcon, whereby the latter explored using SELENA+ software in the 18 Asian countries where it had a presence. However, this did not take off and Topcon eventually faded as a potential EyRIS customer and marketing channel. A private-sector expansion strategy that did gain traction though was inking agreements with international optometry professional associations, large optometry practices, and diabetes prevention associations. This approach yielded successful revenue-producing business relationships for EyRIS across multiple countries and in Singapore as well.

Between 2021 and 2023, EyRIS successfully gained traction in its regulatory, marketing, and commercialisation efforts. By early 2024, it had received regulatory approval from seven countries (Singapore, Malaysia, Indonesia, Thailand, Australia, Brazil, South Africa), Dubai, and also from the EU member countries. The team had also developed multiple partnerships and collaborations with medical institutions, health ministries, optometry clinics, and other relevant distribution channels in these and other countries.

Even with this level of progress, EyRIS faced many challenges in expanding its market reach. SELENA+ was by no means the only recognised player in the global market for using an AI-led software medical device to screen for diabetic retinopathy, or other eye diseases such as glaucoma or AMD.

When evaluated by a research study back in 2021, a number of the other algorithms (excluding SELENA+) were found to not be "performing consistently".[9] The inconsistencies were attributed to the lack of testing protocols and insufficient patient diversity. Such studies reiterated the need for a cautious approach when using such systems in the medical community.

Dr Ang had to keep assuring his potential international customers of SELENA+'s validation and ongoing refinement in the Singapore public healthcare setting, and therefore, its quality and reliability. He further highlighted his acknowledgment that *any* means of making a prediction about the presence of a disease (either by a human expert or an AI algorithm) was imperfect and thus had some degree of associated error.

Adoption and business model challenges

As Dr Ang proceeded with EyRIS' business development efforts, he and his team realised that the challenge in scaling up EyRIS' operations was not predominately technological, but rather, it had a lot to do with changing the mindsets of various stakeholders and finding practical ways to realise workable win-win business models with its customers.

A commonly occurring obstacle was the cost involved in adopting the system if the client did not already own the necessary specialised camera–a fundus camera–for taking pictures of the interior of the eye (other key costs were licensing and service fees from EyRIS). A typical table-top fundus camera often costs between US$10,000 and US$30,000. For many smaller businesses, especially those in undeveloped countries, this was a rather prohibitive upfront cost.

To reduce the upfront cost of SELENA+'s adoption, Dr Ang contacted camera manufacturers in India which had created fundus cameras that could be attached to a commercially-available mobile phone such as Apple's iPhone. He worked with one of these manufacturers to customise a lower-cost solution that could be used with SELENA+. Dr Ang also created a subscription model where a client could lease the smartphone-based fundus camera for two years, for an upfront payment of US$1,500. Of this, 30 percent would go to the Indian camera manufacturing partner and EyRIS could keep the rest. The subscriptions could be renewed thereafter. This approach also provided an added benefit: the mobile phone fundus cameras could easily connect to and transmit retinal images over the Internet in any country through the local telco operators or Internet service providers. Once the images were transmitted, EyRIS' cloud system for SELENA+ did the evaluation and sent back the results.

Dr Ang continued to investigate local conditions across a variety of overseas markets, each with their unique set of circumstances. In some places, there was a business opportunity to take a mobile eye imaging camera to the patient. On the other end of the spectrum, some potential customers enquired if they could have a fully automated eye screening station at a fixed location where the patient could undergo screenings. The company also worked on the development of this type of solution with a manufacturing partner.

The team also kept working to further ensure the accuracy of the algorithm. Dr Tan, who was on EyRIS' advisory board, played a key role in the ongoing endeavour to incrementally improve the performance of SELENA+ in ways that remained within the scope of the regulatory approvals. Haslina Binte Hamzah, the Assistant Director at SNEC and one of the co-founders of EyRIS, oversaw the testing of the SELENA+ algorithm with various new types of cameras. Each time the team used a different camera brand, model, and lens, Haslina and her staff made validation adjustments to the disease threshold classification to reduce errors induced by hardware performance issues.

And since he joined the EyRIS effort, Dr Ang and his business development team had to figure out multiple ways to make the eye disease screening capabilities of SELENA+ more accessible and affordable to accommodate the varying needs of a wider range of customers.

LOOKING AHEAD

Team EyRIS recognised that, indeed, achieving success in Singapore's healthcare setting was a tough, multi-faceted affair. From a business perspective, it was essential to convince the government in each country it ventured to about the usefulness of its software, as adopting AI technologies in Asia depended on government-led deployment, given that many countries lacked private sector resources. And all these governments wanted to know the same thing: How has Singapore used this technology? That is why SELENA+'s incorporation into SiDRP was so strategically important for EyRIS.

Dr Wong concluded, "There are always three parties that needed convincing–the patient, the doctor, and the government. The patient had to be told what to do, the doctor could only be convinced of the technology if there was strong evidence to back it, and the government's adoption of the technology depended on the savings it accrued." He further ruminated and added, "...the heavy upfront investments, the paperwork, the quality checks, the algorithm itself, the hardware issues, the market decisions–there were so many mountains to climb."

Nevertheless, the team counted itself lucky for all the national R&D funding and public healthcare institutional support it had received, and Dr Wong acknowledged that "without the strong backbone-like support from the government, this would not have worked".

Looking ahead, the EyRIS team faced a number of questions. From a product perspective, should it focus on marketing diagnostic screening for eye diseases with its existing SELENA+ product, concentrating on creating additional ways to achieve workable business models and offer easier access? Or should it put in more effort into exploring diagnostic screening for other parts of the body such as the brain or kidney via the analysis of eye images though using different AI models (not SELENA+) trained specifically to detect these other types of diseases? It had looked into these types of possibilities, and even licensed another Singapore R&D solution in this space. It also wondered if it should venture into image-based diagnostic screening that was unrelated to eye image evaluation such as screening for melanoma, a type of skin cancer, as this was also an area in which it had done some exploration.

Also from an AI technology perspective, while SELENA+ was built with DL-based methods that were state-of-the-art in 2015, there had been substantial technological developments in this area that had occurred from 2018, including the use of the transformer architecture. Such technological developments coupled with rebuilding and retraining efforts had the possibility of making further performance improvements to SELENA+'s diagnostic accuracy. However, making such major changes to the existing SELENA+ software required new regulatory approvals. The team pondered over the cost of obtaining such approvals vis-à-vis the business benefits to be gained from doing so.

It also wondered if its strategy for international expansion should be concentrated on a focused subset of countries clustered in a few geographic regions, such as Southeast Asia and the Middle East, or if it should take a more expansive, global approach that would expand the addressable market but lead to more head-to-head competition with other international competitors.

Team EyRIS had tasted early signs of success, and at the same time, faced various barriers to expansion. How could it push forward, given the pathways it had already identified? AMI

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Endnotes

1 This condition damaged the tiny blood vessels in the eye's inner nerve lining–the light-sensitive retina–and led to the abnormal growth of new blood vessels. If left unchecked, it would eventually lead to vision loss.

2 CNA, "In a World First, Singapore-Developed Artificial Intelligence System Detects 3 Major Eye Conditions", December 14, 2017.

3 IHiS has been rebranded and relaunched as Synapxe since July 28, 2023.

4 Andy Wee An Ta, Han Leong Goh, Christine Ang, et al., "Two Singapore Public Healthcare AI Applications for National Screening Programs and Other Examples", Health Care Science, August 2022.

5 Ministry of Health Singapore, "Diabetes: The War Continues", August 22, 2017.

6 National Medical Research Council, "The Singapore Integrated Diabetic Retinopathy Program: Achievements and Challenges".

7 Singapore's public healthcare system was organised into three regional clusters designed to bring cohesion to the health and social ecosystem of that region. Each region–Central, Eastern, and Western–was overseen by government healthcare organisations National Healthcare Group, SingHealth, and National University Health System respectively.

8 Smart Nation Singapore, "National Artificial Intelligence Strategy" , November 2019.

9 The University of Washington School of Medicine, "AI Algorithms Detect Diabetic Eye Disease Inconsistently", December 2, 2020.